FORMATION AND REACTIONS OF ADDUCTS FROM *IPSO* NITRATION OF NITROARENES

by

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ABSTRACT

Nitration of 1,2-dimethyl-4-nitrobenzene with nitric acid in a mixture of acetic anhydride and trifluoroacetic anhydride gives the adduct 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate as a pair of diastereomers. 1,2-Dimethyl-3-nitrobenzene under similar conditions affords a mixture of *cis*- and *trans*-3,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetates. Nitration of 1,4-dimethyl-2-nitrobenzene in acetic anhydride results in the formation of 1,4-dimethyl-3,4-dinitrocyclohexa-2,5-dienyl acetate and 1,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate, each as a pair of diastereomers. In addition, one isomer of 3,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate is also obtained. In all three cases, the expected nitro substituted products are also formed. Nitration of 4-methyl-2-nitrophenol in acetic anhydride gives a mixture of 4-methyl-2,6-dinitrophenol and 4-methyl-2,4-dinitrocyclohexa-2,5-dien-1-one. Crystallization of the nitrodienone from the reaction product with methanol results in its conversion to 5-methoxy-4-methyl-4,6-dinitrocyclohexa-2-en-1-one.

The formation of the various diene adducts can be explained in terms of *ipso* attack by an incipient or free nitronium ion at an alkylated position *ortho* or *meta* to the nitro group in the substrate followed by attack of the acetate nucleophile at the *para* or *ortho* position resulting in 1,4- or 1,2-diene adducts. In the case of 4-methyl-2-nitrophenol, deprotonation of the hydroxyl group from the

ipso-Wheland intermediate results in the formation of the nitrodienone.

The stereochemistry of the acetoxynitro adducts has been studied using the lanthanide shift reagent; tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-d_6-4,6-octanedionato-d_3)europium(III). In acidified methanol, the adducts undergo transesterification at the acetate function, each adduct giving that diastereomer of the dienol with the corresponding stereochemistry. These dienols can be methylated with methyl iodide and moist silver oxide to the corresponding methyl ethers.

Under mildly acidic conditions, the acetoxynitro adducts obtained from 1,2-dimethyl-4-nitrobenzene give primarily the product arising from loss of acetyl nitrate. Under strongly acidic conditions, significant amounts of the three dinitro-1,2-dimethylbenzenes are also obtained. On treatment with amine bases, the adducts undergo a formal 1,4 shift of the nitro group to give 1,2-dimethyl-4,5-dinitrobenzene as the major product. Under suitable conditions, the adducts undergo S_N2' exchange of the acetate with various nucleophiles to give dienyl or rearomatized products after work-up.

The adducts obtained from 1,4-dimethyl-2-nitrobenzene also exhibit a similar behavior, though in this case, benzylic products are also obtained under suitable conditions. That the rearomatization under acidic conditions involves the formation of an intermediate cyclohexadienyl cation is shown by the isolation of biphenyl derivatives when the secondary adducts of 1,2-dimethyl-4-nitrobenzene and the secondary and tertiary adducts of 1,4-dimethyl-2-nitrobenzene are

rearomatized in the presence of mesitylene.

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A. Watton

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CHAPTER I

INTRODUCTION

1.1

Electrophilic nitration of aromatic compounds is one of the most widely-studied reactions in organic chemistry. Studies on nitration have played an important role in the development of the mechanistic theory of organic chemistry. The reaction has served as a model for electrophilic substitution. Aromatic nitro-compounds are also extremely versatile intermediates in the industrial synthesis of various compounds. Because of its importance to theoretical and industrial chemistry, it is not surprising that nitration has been the subject of extensive reviews (1-14).

Various nitrating agents have been employed for nitrating aromatic compounds. For reactive substrates like phenols, dilute nitric acid is used. Solutions of nitric acid in varying concentrations of sulfuric acid provide nitrating reagents of varying strength. Acetic acid is perhaps the most frequently used solvent for preparative nitration. Nitrating agents involving aqueous nitric acid, alkyl nitrates and sodium ethoxide, nitric acid in acetic anhydride and other organic solvents as well as nitronium salts in solvents such as tetramethylene sulfone or acetonitrile have also been employed (15). The choice of the reagent is usually determined by the nature of the substrate and the products desired. Compounds which are sensitive to mineral acids can be conveniently nitrated by using solutions of nitric acid in organic solvents. Such solutions have the advantage of

increased substrate solubility and relatively mild nitrating power, compared to solutions of sulfuric acid in nitric acid or aqueous nitric acid. Similarly, substrates such as aryl nitriles, which often undergo hydrolysis under nitration conditions, can be conveniently mono or dinitrated (without hydrolysis of the cyano group) by using nitronium salts (15).

1.2 *The Mechanism of Nitration*

Kinetic and mechanistic studies on nitration require a homogeneous system, a process free of side-reactions, a reaction rate amenable to measurement and a clear identification of the nitrating species. The effective electrophile over a wide range of conditions has been shown to be the nitronium ion. The reactivity pattern for nitration in organic solvents is similar to the behaviour in highly acidic solvents, suggesting that a common intermediate, presumably the nitronium ion, is also involved (16). The only solvent for which there has been significant controversy concerning the nature of the nitrating species is acetic anhydride. Recent work identifies the active nitrating electrophile in acetic anhydride as the nitronium ion, although it may be solvated by other species (17). The complex kinetic data, which render acetic anhydride a less than ideal solvent for kinetic studies, can be related, at least in part, to the solvent effect on variations in the concentrations of the aromatic (18). The marked anticatalytic effect of small amounts of impurities, which also act as bases, also complicates the kinetics considerably.

The competition method developed by Ingold (5) has been used

to determine the reactivities of many aromatic compounds relative to benzene. Isomer distributions and relative rates are normally essentially independent of nitrating conditions. However, Olah (19) and co-workers reported that in the nitration with nitronium salts, neither *m*-xylene nor mesitylene was significantly more reactive than benzene. Such anomalous results derived from competition experiments were suggested to be due to the occurrence of significant reaction before the reagents were adequately mixed; the rate of mixing plays an important role in these reactions (20). This was demonstrated by studies on the nitration of bibenzyl in which nitration in one benzene ring does not deactivate the second ring towards further nitration (21, 22). Incomplete mixing should give a high dinitro to mononitrobibenzyl product ratio. This was indeed observed in the nitration with nitronium salts but was not observed in the case of nitration with nitric acid in acetic anhydride. Thus the anomalous relative reactivity results, found by Olah, may be attributed to incomplete mixing of the reagent and substrate (macroscopic diffusion control).

For nitration in sulfuric acid of compounds thirty-eight or more times as reactive as benzene, reactions occur at the encounter rate between nitronium ion and substrate and the differentiation between highly reactive substrates disappears (23). In organic solvents, the limiting rate of nitration is 300-400 times the rate of nitration in benzene (24). Consequently, an adequate comparison cannot be made between compounds, whose reaction rates lie above and those which lie below the encounter rate since the rate-limiting step is different in the two cases. For arenes which are more reactive than toluene, the

second-order rate constants reach a limiting value, the encounter rate. The results for the nitration of some arenes in 68.3% sulfuric acid are summarised in Table 1.1 (6b).

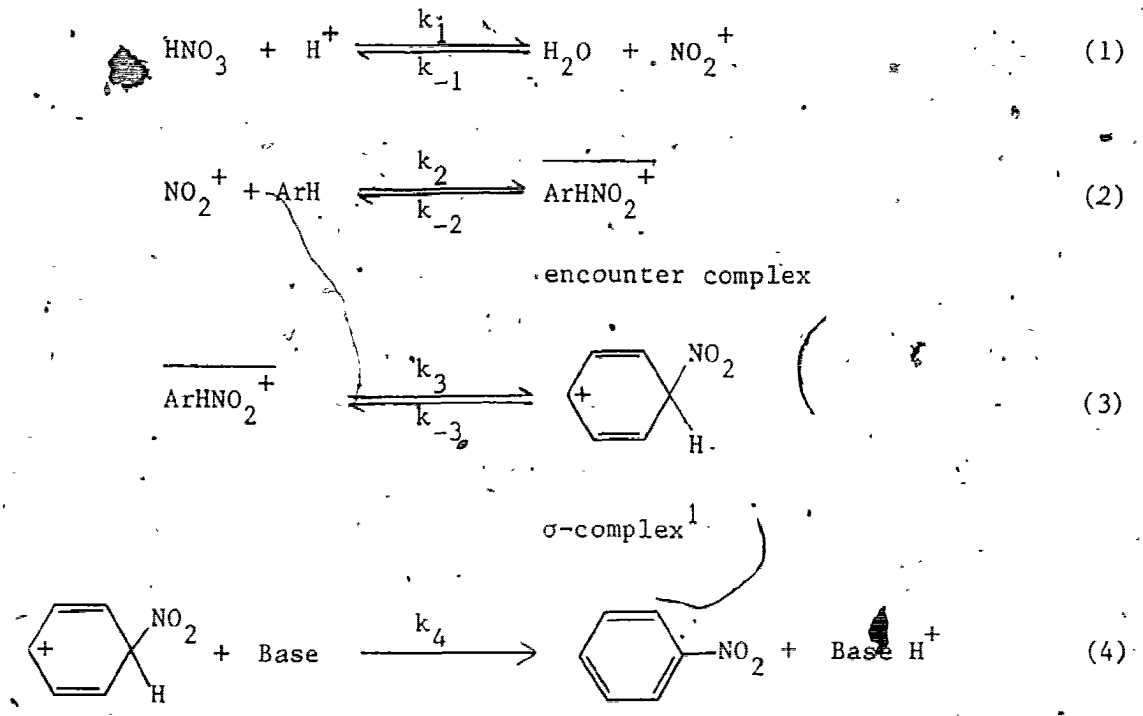
TABLE 1.1

RELATIVE RATE CONSTANTS FOR THE NITRATION OF AROMATIC COMPOUNDS IN 68.3% SULFURIC ACID AT 25°

COMPOUND	RELATIVE RATE
Benzene	1.00
Toluene	17
o-Xylene	38
m-Xylene	38
p-Xylene	38
Mesitylene	36

Nitration of toluene in aqueous sulfuric acid has been shown to proceed by both first and second-order paths (25). The reaction is zeroth-order in toluene in more concentrated acid but first-order in toluene in less acidic solvents.

The simplest explanation which accounts for all such observations is shown in the following mechanism (11):



encounter complex

σ-complex[1]

Here, the encounter complex is specifically considered as an intermediate. Except in a few cases (26), the last step of the reaction (*i.e.* deprotonation) is not rate-determining and hence the rate of formation of the benzenonium ion, or one of the earlier steps must be rate-determining. Based on the steady state approximations for the encounter complex and the nitronium ion, the following rate law has been obtained (7):

$$\text{Rate} = \frac{k_1 k_2 k_3 [\text{ArH}] [\text{HNO}_3] a_{\text{H}^+}}{k_{-1} a_{\text{H}_2\text{O}}(k_3 + k_{-2}) + k_2 k_3 [\text{ArH}]}$$

---

[1] Also called a Wheland intermediate, a benzenonium ion or a cyclohexadienyl cation.

TABLE 1.2

KINETIC RATE LAWS FOR NITRATION IN AQUEOUS ACID (11)

	A	B	C
Conditions	$k_{-1}a_{H_2O}(k_3 + k_{-2}) \ll k_2k_3[ArH]$	$k_{-1}a_{H_2O} \gg k_2k_3[ArH]/(k_3 + k_{-2})$	
		$k_3 \gg k_{-2}$	$k_3 \ll k_{-2}$
Rate	$k_{obsd.}[HNO_3]a_{H^+}$	$k_{obsd.}[ArH][HNO_3]a_{H^+}$	$k_{obsd.}[ArH][HNO_3]a_{H^+}$
Rate-determining step	Formation of NO_2^+ (step 1)	Formation of encounter complex (step 2)	Formation of σ-complex (step 3)

The conditions required to make the various steps in the mechanism rate-determining and the corresponding kinetic expressions are summarised in Table 1.2.

Thus, under conditions in which the nitration of toluene is zeroth-order in the aromatic compound, the rate-determining step corresponds to the formation of the nitronium ion. When the reaction occurs at the diffusion-limit, as observed for reactive substrates, the formation of the encounter complex becomes rate-determining, with the observed rate being the diffusion-limited maximum. The rate-determining step for the nitration of toluene, benzene and other less reactive substrates is the formation of the σ-complex and the reaction is first-order in the substrate. Thus the nature of the rate-determining step depends on the rate-coefficients of the various steps and on the concentration of the substrate. The concept of encounter pair is, in some ways, similar to the concept of π-complex suggested by Olah (27). For aromatic compounds more reactive than toluene, the reaction with nitronium ion is encounter-limited, so that the reaction rate for all such aromatics is the same. Though intermolecular selectivity is lost, intramolecular selectivity is retained, *i.e.* the formation of the σ-complex followed by deprotonation gives the expected product distribution of the various isomers. This behaviour has been explained in terms of oriented encounter pairs (6c) or π-complexes (28). Such oriented encounter pairs or π-complexes can then exhibit selectivity.

An alternate mechanism, in which the electrophilic attack on reactive aromatics occurs by electron transfer followed by radical pair collapse, has also been proposed (29). The mechanism can be

represented schematically as follows:

$$NO_2^+ + ArH \xrightarrow[\text{controlled}]{\text{encounter}} \overline{NO_2^{\cdot} + ArH^{+\cdot}} \longrightarrow \underset{\sigma\text{-complex}}{HArNO_2^+} \xrightarrow{\text{fast}} ArNO_2$$

Intermolecular selectivity is not observed because all the aromatics more reactive than toluene are capable of transferring an electron to the nitronium ion at every encounter. Intramolecular selectivity is then related to the observation that the attacking species in the radical pair is nitrogen dioxide and not the nitronium ion, which exhibits no intermolecular selectivity. Because of the non-uniform spin density in the aromatic radical cation, radical pair collapse can exhibit selectivity. Evidence in favour of the proposed mechanism was shown by the observation that the ratio of 1-nitro to 2-nitronaphthalene obtained by electrolysis of a mixture of naphthalene and nitrogen dioxide is similar to the ratio obtained in the nitration of naphthalene under normal conditions. However, such an agreement of the product composition obtained from nitration under normal and radical conditions is not always observed.

Nitration of mesitylene with nitric acid gives nitromesitylene in nearly quantitative yield. However, when the cation radical of mesitylene is generated by adding ceric ammonium nitrate to the nitrating medium, a substantial amount of 3,5-dimethylbenzyl nitrate is also obtained (30). Absence of this product in the direct nitration of mesitylene with nitric acid indicates either that the cation radical is not involved in the nitration, or that the normal reactions of this

species are not exhibited because the life-time of the cation radical, when formed by electron transfer to the nitronium ion, is too short. In any case, the products of nitration are not always the same as those obtained from the cation radical of a reactive substrate, generated independently in the same solution.

The kinetics and mechanism for the nitration of aromatic compounds in acetic anhydride can be discussed in a manner similar to that developed for nitration in aqueous acid (31,32). Nitric acid reacts with acetic anhydride to form acetyl nitrate and equation (1) is therefore replaced by the following equilibria:

$$Ac_2O + HONO_2 \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} AcONO_2 + AcOH \qquad (5)$$

$$AcONO_2 + H^+ \underset{k_{-6}}{\overset{k_6}{\rightleftharpoons}} AcONO_2H^+ \qquad (6)$$

$$AcONO_2H^+ \underset{k_{-7}}{\overset{k_7}{\rightleftharpoons}} AcOH + NO_2^+ \qquad (7)$$

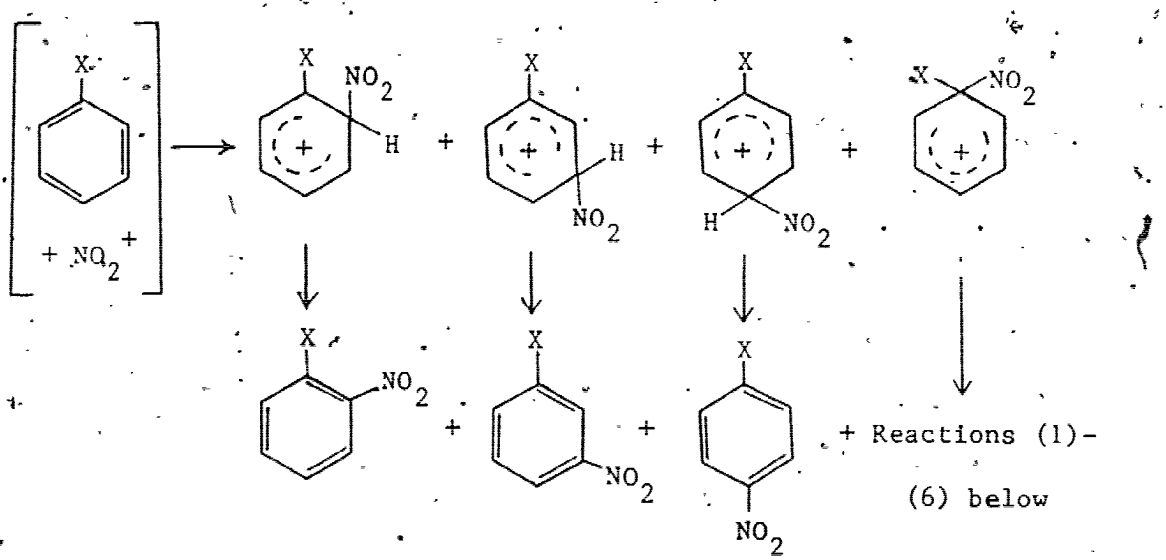
Nitration of reactive substrates such as mesitylene, anisole, *o*- and *m*-xylene in acetic anhydride also exhibit the behaviour characteristic of encounter-controlled reactions.

1.3 *Ipso Attack: Formation of Diene Adducts*

In the nitration mechanism, reaction step (3), involving the transformation of the encounter complex to the benzenonium ion or, more generally, substituted benzenonium ions (Wheland intermediates), and the subsequent product-forming steps is of particular interest in the

present work.

Encounter of the nitronium ion with a mono-substituted benzene derivative C_6H_5X can result in Wheland intermediates in which the nitronium ion is (i) geminal to a hydrogen (three isomers); *i.e.* W_i or (ii) geminal to the substituent X; *i.e.* W_i^X



In the (Wheland) intermediates formed by addition of the nitronium ion at a nuclear carbon bearing a hydrogen, rapid deprotonation occurs to form the expected *ortho*, *meta* and *para* nitro derivatives. Addition at the nuclear carbon bearing the substituent is described as *ipso* addition. The term *ipso* was introduced by Perrin and Skinner (33). The intermediate formed from such an attack is referred to as an *ipso*-Wheland intermediate, W_i^X. It can undergo the following reactions (10):

(1) Return to the encounter pair or starting materials. This behaviour is encountered in the nitration of *o*- and *p*-methoxytoluene (34).

(2) loss of X, resulting in *ipso*-substitution; *e.g.* nitration of *p*-cymene under various conditions gives *p*-nitrotoluene (*ca.* 10%) by nitrodealkylation (35).

(3) 1,2 migration of the nitro group, followed by deprotonation, to give products also obtained by direct nitration (discussed later).

(4) similar migration of X, followed by deprotonation, to give a rearranged product. This behaviour is quite rare.

(5) loss of a proton or other leaving group from a substituent remote from the *ipso* position, as observed in the nitration of phenols and anisoles.

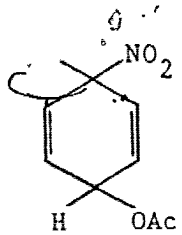
(6) capture by a nucleophile.

Of the above listed reactions of W_i^X, the last is of special significance since it results in the formation of adducts. The reaction is encountered in the nitration of various substrates in acetic anhydride. A large number of addition products resulting from nucleophilic capture of the *ipso*-Wheland intermediate have been obtained, largely due to the efforts of Fischer and co-workers, and are listed in Table 1.3.

All except two of the acetoxynitro adducts listed in Table 1.3 are 1,4 adducts. The 1,4 adducts are almost always formed as a mixture of diastereomers, corresponding to the fact that the acetate nucleophile can add to either face of the cyclohexadienyl cation. However, only one diastereomer of 1,2 adducts were obtained from 4-*tert*-butyltoluene and from 4-*tert*-butyl-*o*-xylene. In the latter case, the 1,2 adduct was unstable.

TABLE 1.3

ADDITION COMPOUNDS OBTAINED BY *IPSO* NITRATION



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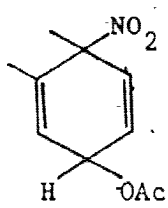

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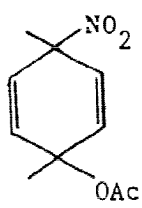

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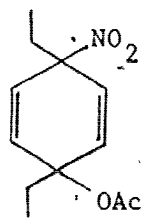

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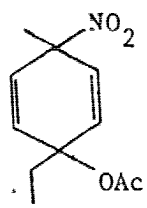

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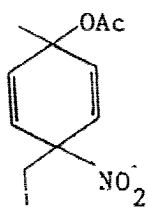

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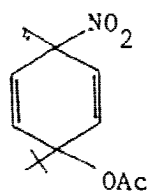

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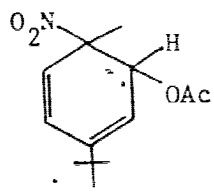

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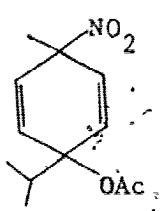

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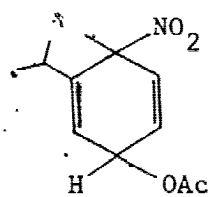

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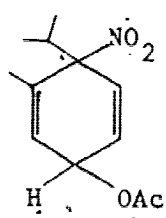

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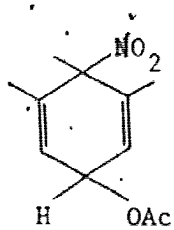

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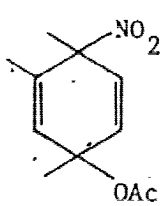

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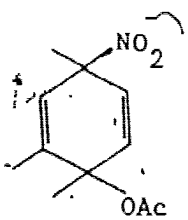

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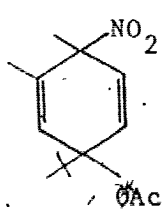

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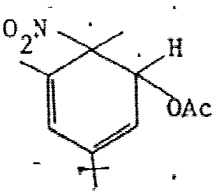

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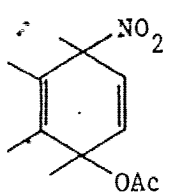

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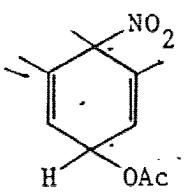

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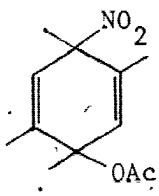

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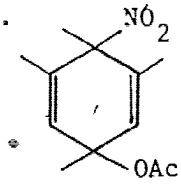

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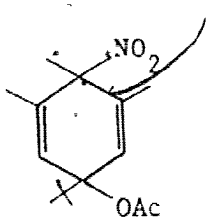

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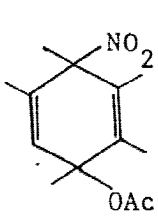

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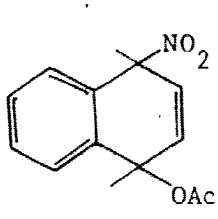

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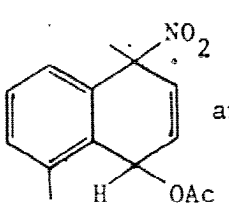

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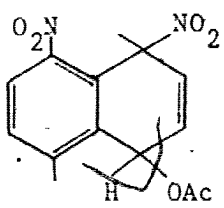

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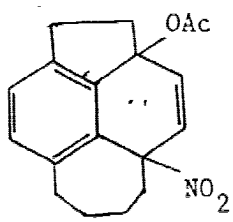

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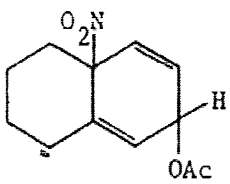

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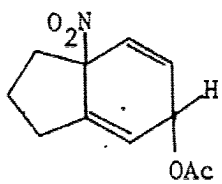

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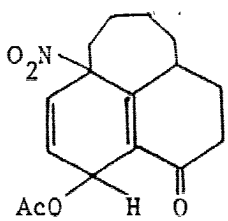

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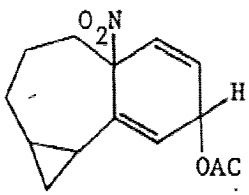

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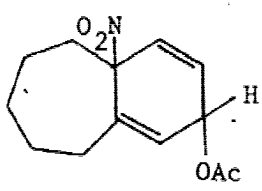

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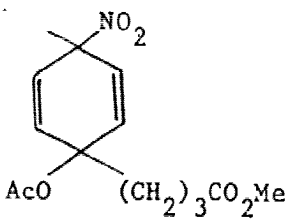

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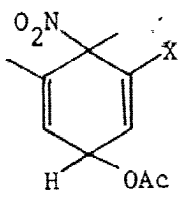
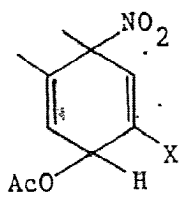
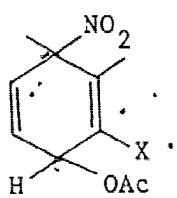


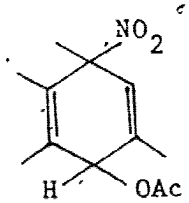
X = Cl, 29% (54)
X = Br, (55)
X = F, (56)



X = CN, 29% (57)
X = COMe, 70% (58)
X = COPh, 70% (58)



X = CN, 22% (57)
X = NO_2, 37% (59)



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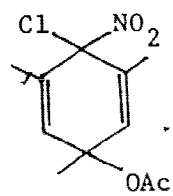
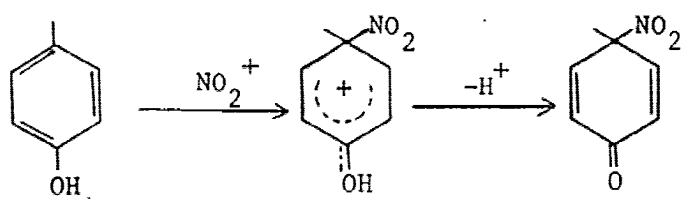


30% (60)

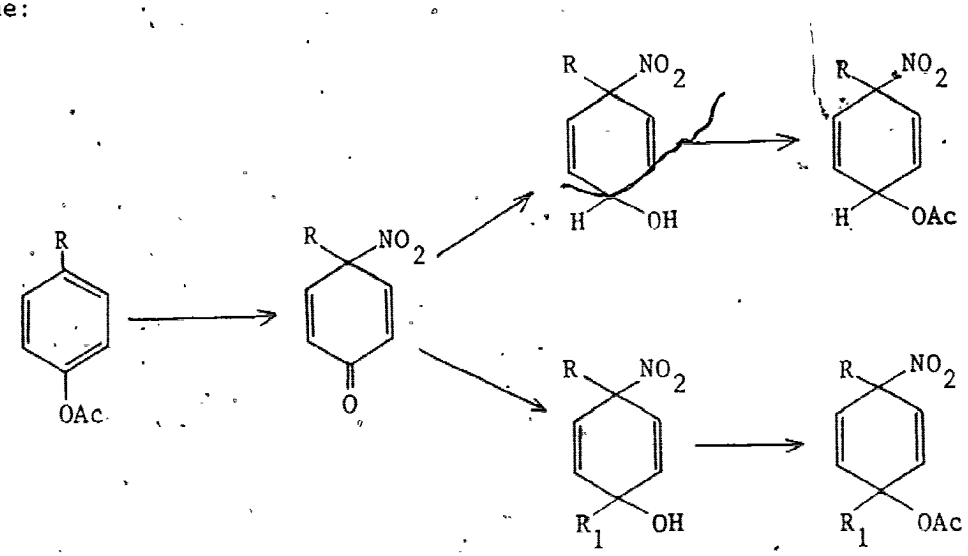
Acetic anhydride is a particularly good solvent for the formation of adducts. This is in part because the acetic anhydride or the acetic acid also present is sufficiently nucleophilic to capture the *ipso* cation before it can undergo one of the other reactions listed above. Also important is the fact that because of the formation of acetyl nitrate (p. 9, equation 5), a solution of nitric acid in acetic anhydride is not strongly acidic; the stronger acid, nitric acid, is replaced by a weaker acid, acetic acid. Strong acid would lead to the acid-catalyzed loss of acetate from the adduct and the reformation of the *ipso* cation, resulting in further opportunity for it to react.

When the substrate is a phenol or a phenyl acetate, dienones rather than diene adducts are obtained (61,62). This is an example of reaction 5 (p.11) of the *ipso*-Wheland intermediate.



The reaction has been exploited by Myhre and co-workers (63) to develop an efficient synthesis of adducts, which is particularly useful in those cases where direct nitration of an arene (*e.g.* toluene) gives a low yield. The 4-alkyl-4-nitrocyclohexadienones undergo 1,2 addition at the carbonyl group by metal hydrides or alkyllithium reagents to give secondary and tertiary dienols respectively. Acetylation of these dienols gives the desired acetates. Overall yields of the acetoxynitro adducts are generally high (60%), which makes the process

quite attractive. The procedure can be represented by the following scheme:



σ-complexes, arising from *ipso* attack have been observed by n.m.r. in the case of fully substituted aromatic compounds, such as hexamethylbenzene (64) and, more recently, in the nitration of N,N-dimethyl-*p*-toluidine (65). The observance of these σ-complexes

and formation of diene adducts, as shown above, indicate that electrophilic attack need not be restricted to the aromatic carbon bearing hydrogen. Therefore, in a discussion of the mechanism for nitration, the formation of an *ipso*-Wheland intermediate (W_i^{XY}), should be considered. Products corresponding to nitrodealkylation (reaction 2, p. 11) have been observed in the nitration of isopropyl- and tert-butylalkylbenzenes with nitronium tetrafluoroborate in tetramethylene sulfone,

a non-nucleophilic medium (42). The extent of formation of such nitrodealkylated products defines the degree of attack *ipso* to the isopropyl or tert-butyl functions.

Nitration of *p*-cymene with nitric acid in acetic anhydride resulted in the formation of a 1,4 adduct, which arises from attack by the electrophile *ipso* to the methyl group (40). No adduct corresponding to attack at the isopropyl position was obtained. Nitration of *o*-cymene (42), however, resulted in the formation of positional isomers arising from attack *ipso* to either the methyl or isopropyl functions. Thus, the isopropyl function is not necessarily expelled on attachment of a geminal nitro group, in marked contrast to the behaviour observed in the case of *p*-cymene. The results obtained in the nitration of *o*-cymene have been attributed to the strain introduced in making the vicinal methyl and nitro groups coplanar during deisopropylation. In such a case, the formation of adducts, along with products from deisopropylation, may be considered as a measure of attack *ipso* to the isopropyl group.

The effects of substituents in electrophilic substitution have been extensively studied and these substituents have been classified as *ortho-para* or *meta* directing, depending on whether *ortho-para* or *meta* isomers, are obtained. Substituent effects on the reactivity towards electrophilic substitution can be defined in terms of the partial rate factors o_f^X, m_f^X and p_f^X, which give the reactivity of a ring position *ortho*, *meta* and *para* to the substituent X, relative to a single position in benzene (4). For di- and polysubstituted benzenes, the reactivity at a given position can be considered in terms of the partial rate factors and the additivity principle; which assumes that the influence of

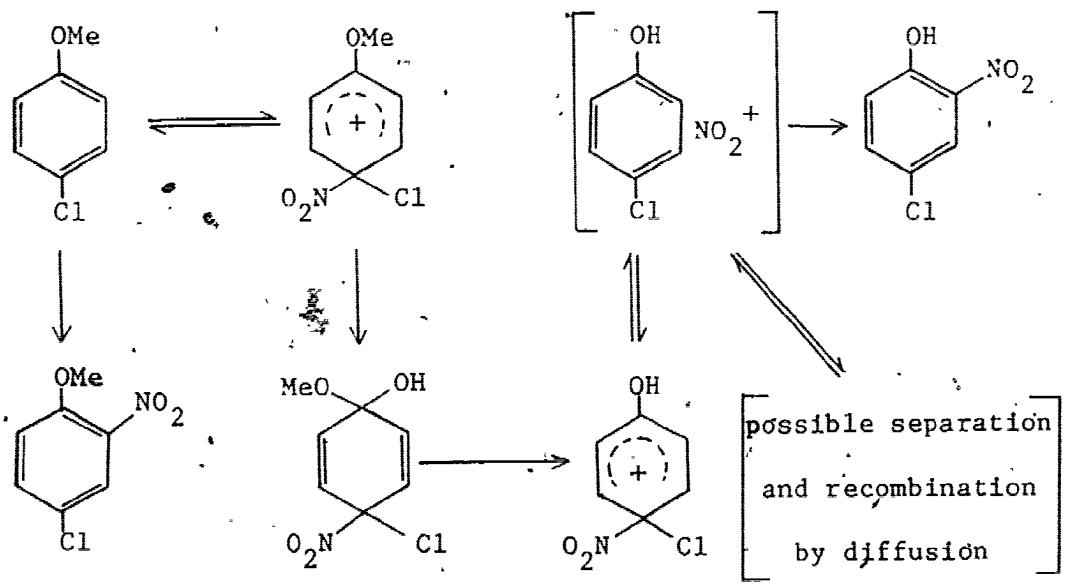
substituents is independent and additive in terms of the free energy of activation. The measure of the reactivity of a ring position to which a substituent is attached will therefore be determined, not only by the partial rate factors of other substituents in the ring corresponding to that position, but also by the *ipso* partial rate factor (33), defined as

$$i_f^X = \frac{k_{ArX}^{total} \times \%\ \text{attack at X}}{k_{ArH}^{total} \times \%\ \text{attack at H}}$$

The choice of substrates for studies on *ipso* nitration is partly governed by the partial rate factors for electrophilic attack at various positions. Thus, the degree of attack at a substituted position, compared to attack at an unsubstituted position, will be determined by the overall activating or deactivating substituents at various positions. Even if the substrate is weakly activated or deactivated relative to benzene, adducts should be formed when the reactivity of a substituted position, relative to an unsubstituted position, is high. Thus, *ipso* attack may be expected in the case of suitably substituted *o*- and *p*-dialkylbenzenes, but not in *m*-dialkylbenzenes. Acetoxynitro adducts have also been isolated wherein the non-alkyl substituents are cyano (57), acetyl (58), benzoyl (58) and chlorine (54). In the first three cases, in accordance with the *meta* directing nature of these substituents, attack takes place *meta* to these substituents.

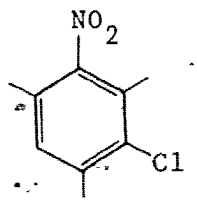
The behavior of chlorine and methoxy has been studied in the nitration of *p*-chloroanisole (33,66), in which 4-chloro-2-nitroanisole

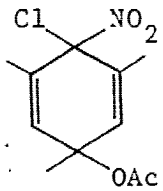
was obtained as the main product. When the nitration was carried out in acetic acid, which is a poorer nitrating medium than acetic anhydride, 4-chloro-2-nitrophenol was also obtained, the yield of which reached a maximum (40%) in more aqueous mixtures. The maximum yield of the nitrophenol was therefore used to measure the extent of *ipso* attack, since both *p*-chloroanisole and 4-chloro-2-nitroanisole are stable to demethylation under the conditions employed. The nitration of *p*-chloroanisole in aqueous sulfuric acid has also been studied (66) and the following mechanism suggested for the formation of 4-chloro-2-nitrophenol.



The ratio of partial rate factors $m_f^{Cl}:i_f^{Cl}$ has been obtained as 1.1:1 from the nitration of *p*-chloroanisole (33); *i.e.* a chlorine atom deactivates the *meta* and *ipso* positions to a similar extent. This ratio is in close agreement with the results obtained in the nitration of chloromesitylene (60). The relative amounts of nitromesitylene and diene adduct (arising from attack *ipso* to chlorine), after correcting for the

statistical factor of 2 favouring substitution, show the ratio of $m_f^{Cl}:i_f^{Cl}$ to be 1.2:1.





The concept of partial rate factors could therefore be employed for predicting the extent of *ipso* attack and the *ipso* Wheland intermediates formed by such an attack could be captured, in acetic anhydride, to give diene adducts.

1.4 *Reactions of Adducts*

The adducts obtained by such a nucleophilic capture readily rearomatize in solution. The mechanisms of rearomatization have been extensively investigated, and two principal modes, both involving the intermediacy of a cyclohexadienyl cation, have been established. Solvolytic displacement can occur either by loss of acetate or by loss of nitro group as nitrite. Under strongly acidic conditions, the former process is preferred. Protonation of the more basic ester function provides a low energy path for the loss of acetate as acetic acid (67). The *ipso*-nitrocyclohexadienyl cation thus formed, can rearomatize by a variety of pathways, depending on the conditions. Under strongly ionising conditions, such as those obtained using hydroxylic solvents, unimolecular ionisation of the nitro group as nitrite (68) produces an acetoxycyclohexadienyl cation which can give rise to a wide

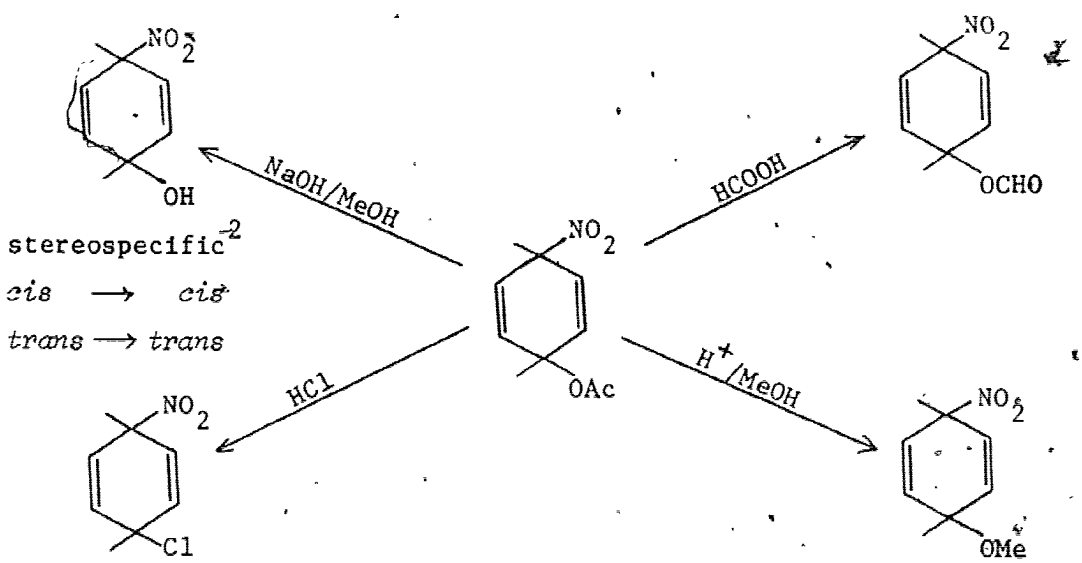
range of reactions. The reactions of diene adducts can therefore be broadly classified under two categories:

(A) reactions proceeding through replacement of the acetate group; and

(B) reactions proceeding through replacement of the nitro group.

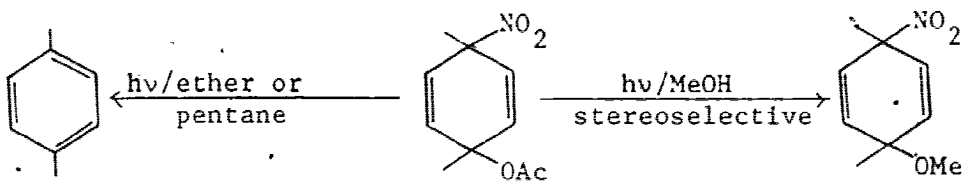
(A) Reactions proceeding through replacement of the acetate group

The acetate function in the diene adducts can be replaced with other nucleophiles under suitable conditions. The adducts from *p*-xylene serve as an excellent model for such studies. On treatment with methanolic alkali, acidified methanol, formic acid or hydrochloric acid, the acetoxy dienes are converted to hydroxy, methoxy, formoxy and chloro dienes respectively (36,39b).

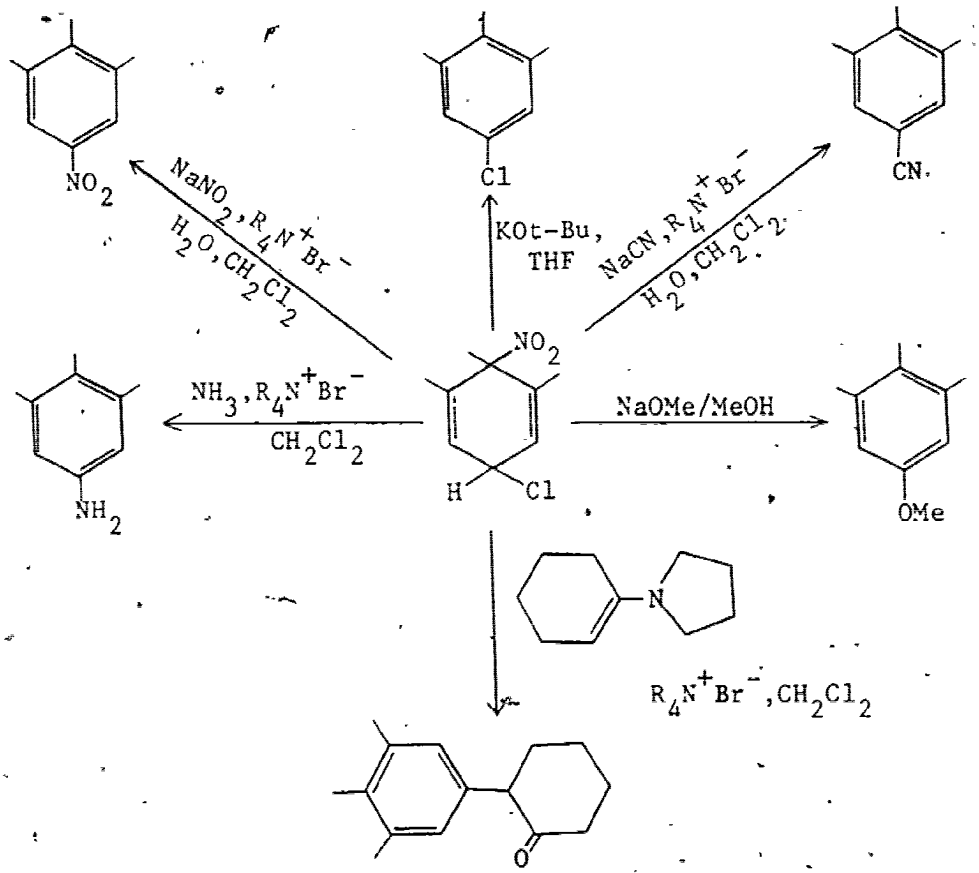


[2]Hydrolysis occurs through acyl-oxygen bond fission.

Recently, the exchange of acetoxy for methoxy function has been carried out photochemically (69). Photosolvolysis of the acetoxynitro adducts of *p*-xylene in methanol proceeded in a stereoselective manner to give methoxynitro adducts. Substitution of methanol with ethanol, propanol and allyl alcohol gave the corresponding ethyl, propyl and allyl ethers stereoselectively. Irradiations in ether or pentane yielded *p*-xylene, through the intermediacy of a cyclohexadienyl radical.

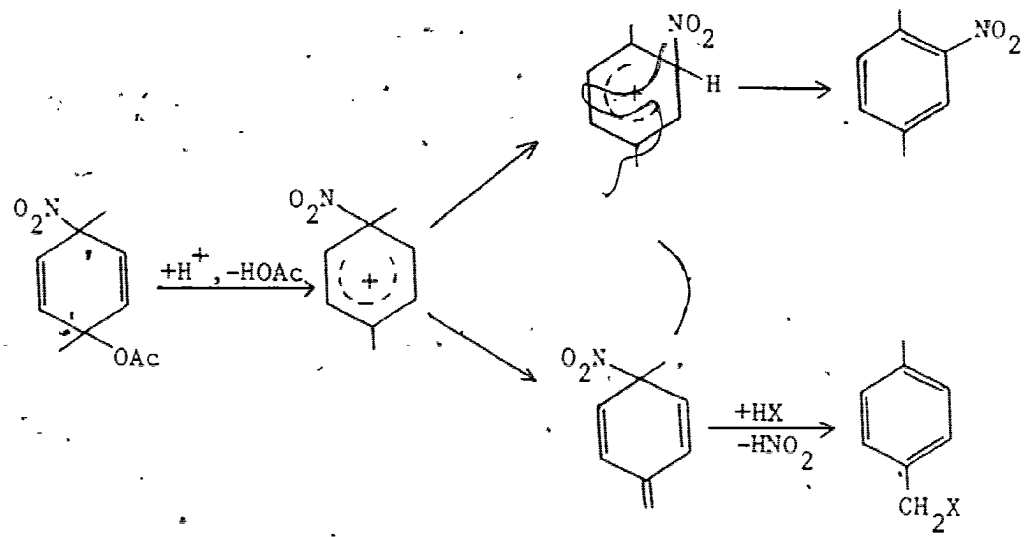


The chloro dienes, obtained by the reaction of the acetoxy dienes with hydrochloric acid, can also undergo a variety of transformations. Nucleophilic exchange of the halogen and subsequent rearomatization can give a series of useful products in consistently high yields (70). Since the acetoxynitro adducts can be obtained in high yields, either by *ipso* nitration of the aromatic hydrocarbons or through the nitrodienones, the ease of these transformations shows that, besides providing useful mechanistic information, these adducts have considerable synthetic potential.



The rearomatization pathways available to the intermediate nitrocyclohexadienyl cation, generated by loss of the acetate group, could result in the formation of benzylic products, or products resulting from migration of the nitro group. Internal competition, between deprotonation to give benzylic products and nitro group migration, will be determined by the basicity of the solvent, with increasing basicity favouring the former process. Consequently, under strongly acidic conditions, the formation of nitroarenes is favoured. The formation of nitroarenes occurs by an intramolecular 1,2 nitro shift

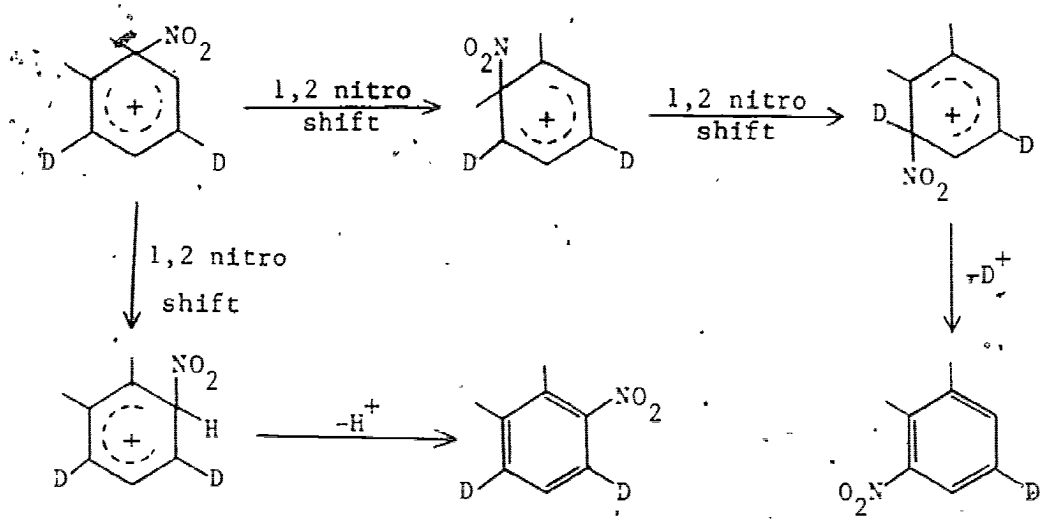
in the nitrocyclohexadienyl cation in acidic, weakly nucleophilic media (71,72). The following scheme has been used to explain the important transformations observed in the case of tertiary adducts (45,58).



The acid-catalyzed reaction, leading to benzylic products, is dependent on the presence of a *para*-methyl group and the availability of suitable nucleophiles. Under suitable conditions, benzylic nitrites, nitrates, acetates and methyl ethers have been obtained (43). A number of other mechanisms have also been proposed (9), to account for the formation of benzylic nitro compounds in other systems.

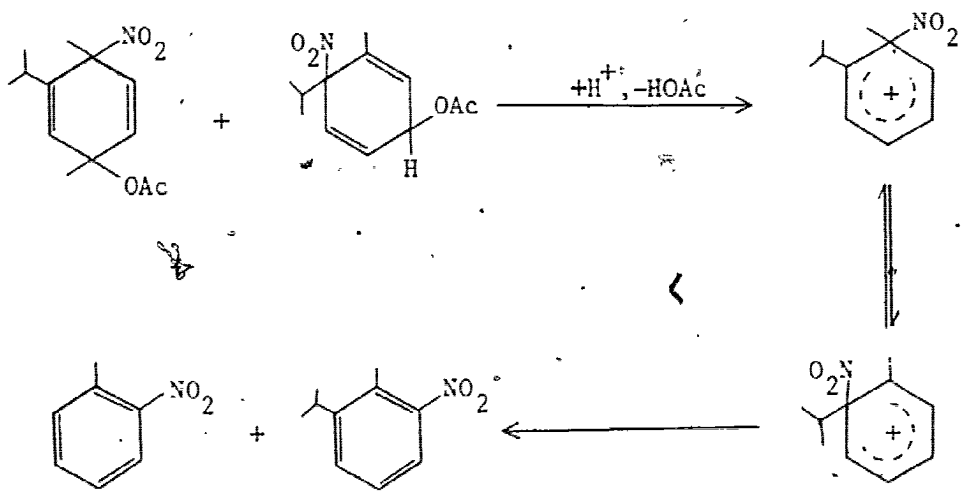
The migratory aptitude of the nitro group in 1,2-dimethyl-1-nitrocyclohexadienyl cation has been studied and it has been recently demonstrated (73), that a 1,2 nitro shift to an adjacent substituted position is faster then to an open position. The absence of 1,2-dimethyl-4-nitrobenzene as a product (71) shows that migration across an unsubstituted position does not occur. The 1,3 migration

across a substituted position can be considered as sequential 1,2 shifts.



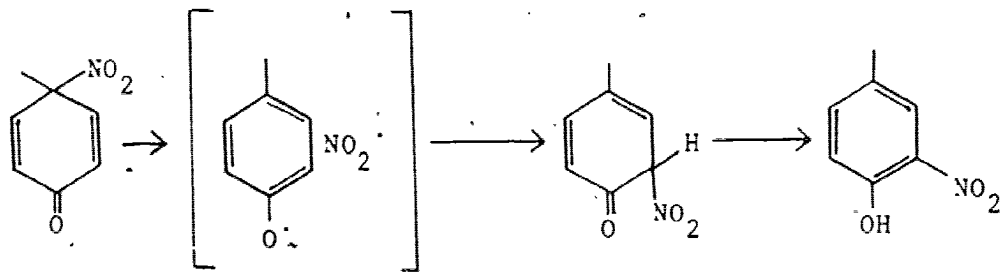
In the absence of a 1,2 shift to a substituted position, the di-deuterated product should be formed exclusively. However, since the rate of migration between two adjacent *ipso* positions is faster than the rate from an *ipso* to an open position, the ratio of mono-:di-deuterated 1,2-dimethyl-3-nitrobenzene approaches 1:1.

Interestingly enough, when the substituted *ortho* position has an isopropyl (rather than a methyl) substituent, deisopropylation occurs from the rearranged nitrocyclohexadienyl cation. Acid-catalyzed rearomatization of the adducts from *o*-cymene gave *o*-nitrotoluene as the main product (42). Again, *ipso-ipso* migration (and subsequent deisopropylation) is favoured over migration to an open position (and subsqunent deprotonation). Absence of any 3-nitro-*o*-cymene shows that nitrodeisopropylation is greatly favoured over migration to C-3.

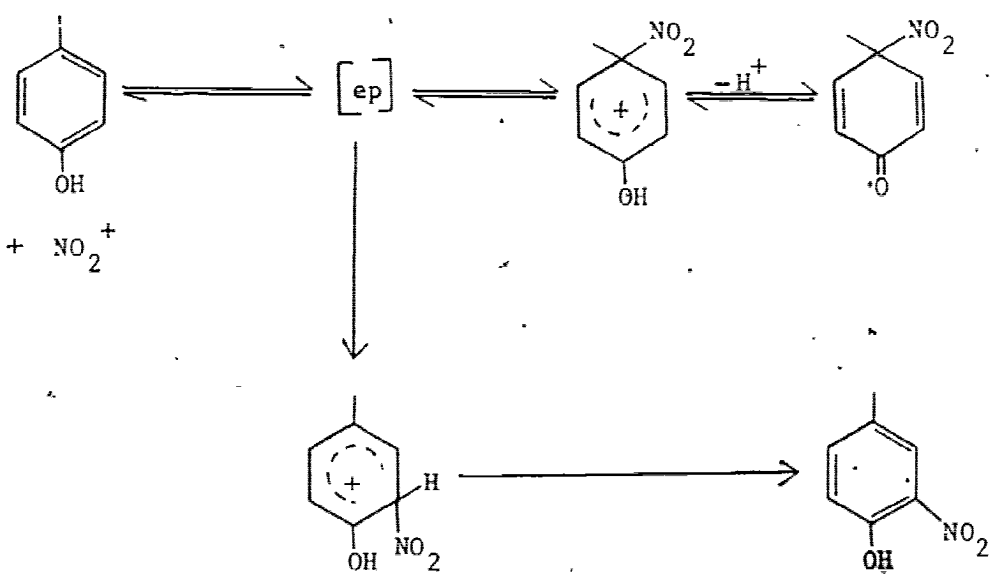


The symmetry of 1,4-disubstituted compounds such as *p*-xylene and *p*-diethylbenzene makes it difficult to distinguish 1,2 from 1,3 nitro shifts. Studies on polymethylbenzenes such as pseudocumene, prehnitene and isodurene (45) have also enabled the sequence of these rearrangements to be deduced. Such a differentiation is especially important since 1,3 nitro shifts, across an open position, have been observed in the reactions of the adduct from 2,3-dimethylbenzonitrile (57), and in the decomposition of nitrodienones (33,61,62,74).

Studies on the 1,3 nitro shift in the decomposition of nitrodienones show that, in non-acidic media, a radical dissociation-recombination mechanism is involved (75). In strongly acidic media, reversion of the conjugate acid of the nitrodienone to the encounter pair, followed by recombination at the *ortho* position, is likely (75,76). The mechanisms for the decomposition, under various conditions, are shown in the following schemes:

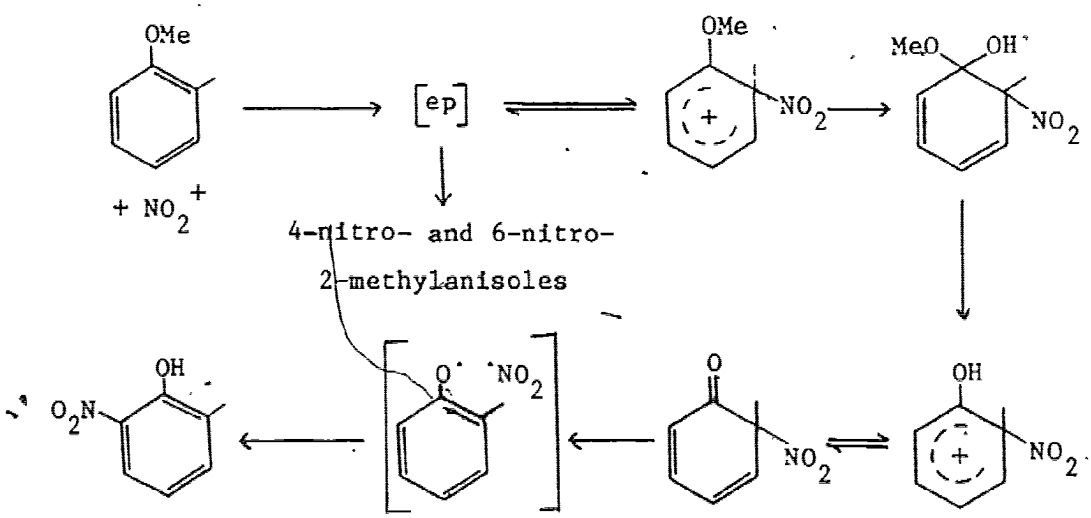


Scheme 1.1 Decomposition of nitrodienones in non-acidic media

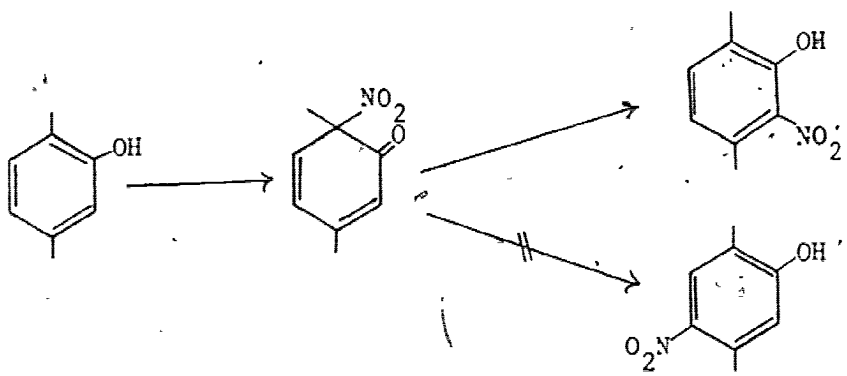


Scheme 1.2 Decomposition of nitrodienones in strongly-acidic media

Under suitable conditions, the 1,3 migration of the nitro group may be selective; *i.e.*, out of two possible products, only one may be formed. This can occur when only one of the two migration termini is unsubstituted, or when a suitable group, capable of selectively directing the nitro group to a given position, is present. The former situation is encountered in this study, whereas, the latter phenomenon has been observed in the nitration of *o*-methylanisole. Nitration of *o*-methylanisole (34), in aqueous sulfuric acid, gave 2-methyl-6-nitrophenol, but not the 4-nitro isomer, as a product of the reaction. Demethylation prior to nitration is unlikely, as shown by the absence of the 4-nitro isomer, which is obtained in the nitration of *o*-cresol. Hence, the reaction is believed to proceed through the intermediacy of a nitrocyclohexadienone; the specific 1,3 rearrangement of the nitro group to the C-6 position being associated with the presence of the adjacent oxygen substituent facilitating the process, presumably through the intermediacy of a phenyl nitrate (77).

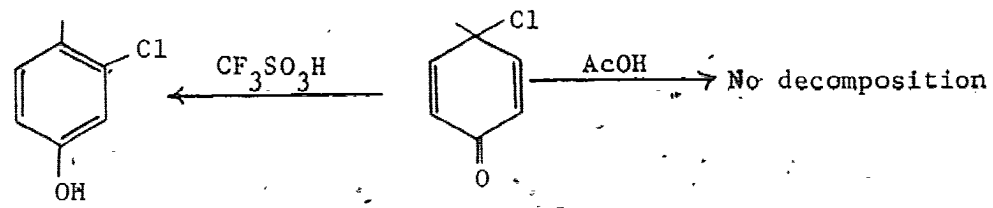


A similar phenomenon is observed in the nitration of 2,5-dimethylphenol in acetic anhydride (78). ^{1}H n.m.r. studies showed the formation of a nitrodienone (~90%), which decomposed on work-up to give, exclusively, 2,5-dimethyl-6-nitrophenol, without any of the 4-nitro isomer. Again, oxo-participation may be involved.



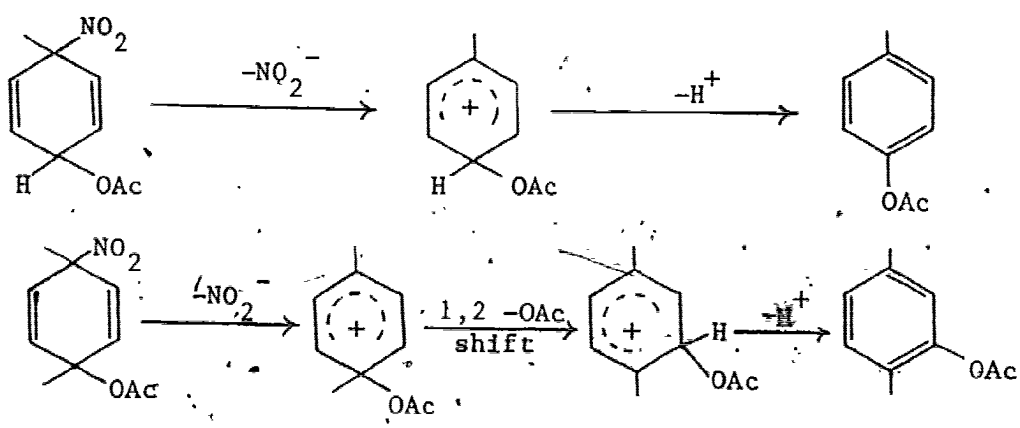
Thus, a 1,3 migration of the nitro group has been observed in the decomposition of nitrodienones and, under suitable conditions, the process maybe specific.

Dienone-phenol rearrangements have also been studied in the case of 4-chloro-4-methylcyclohexadienones (79), which decompose rapidly in trifluoromethanesulfonic acid, to give products arising from a 1,2 shift of the chlorine. Energy requirements render a radical pathway less likely, whereas, loss of chlorine from the conjugate acid of the chlorodienone would require a good nucleophile. Hence, a 1,3 shift is not observed in these rearrangements.

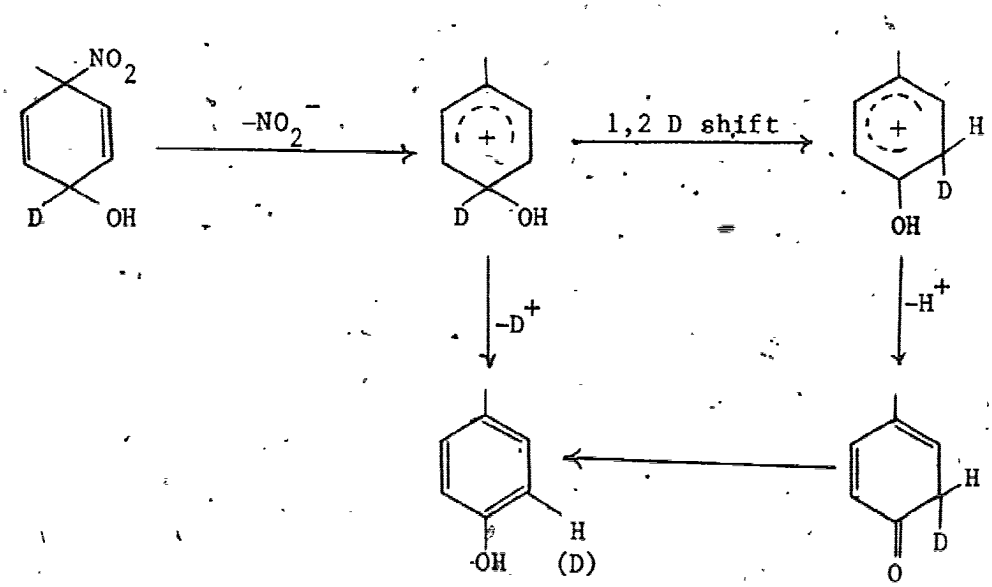


(B) Reactions proceeding through loss of the nitro group.

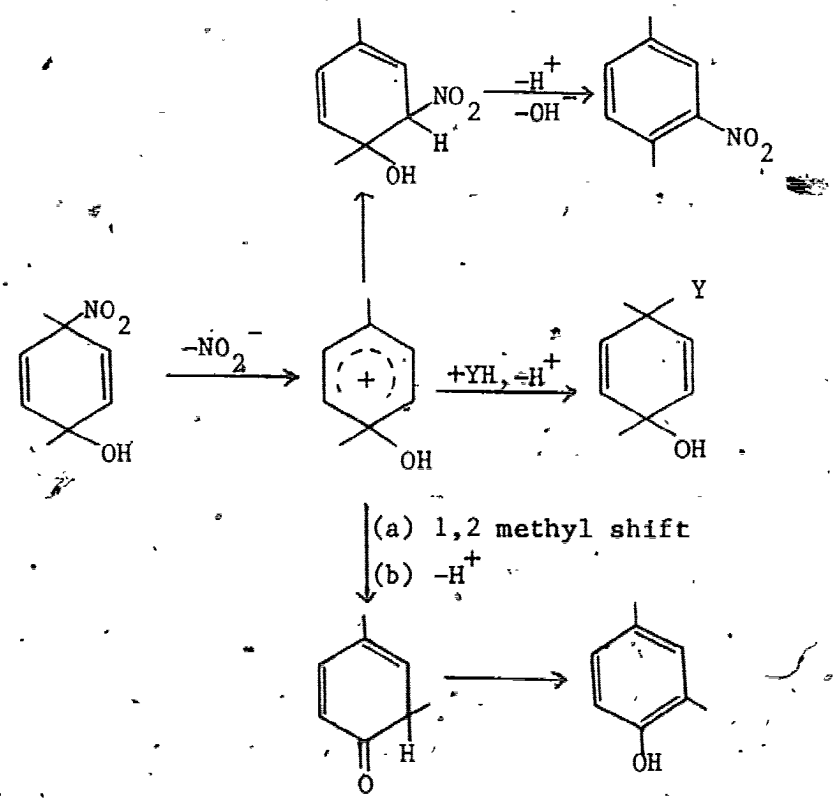
In strongly ionising media, the adducts undergo loss of the elements of nitrous acid, to give aryl acetates. The behaviour of the secondary adducts is usually different from that of tertiary adducts (38). The dominant reaction, of adducts not having an alkyl group at the site the acetate, is 1,4 elimination of nitrous acid (36,45,49,54). Myhre (68) has shown that the reaction occurs by an El type mechanism. The formation of rearranged acetates in the case of tertiary adducts occurs by a similar mechanism. The acetate group can migrate without exchange with the solvent (*e.g.* acetic acid-d_4) and hence, the process is intramolecular.



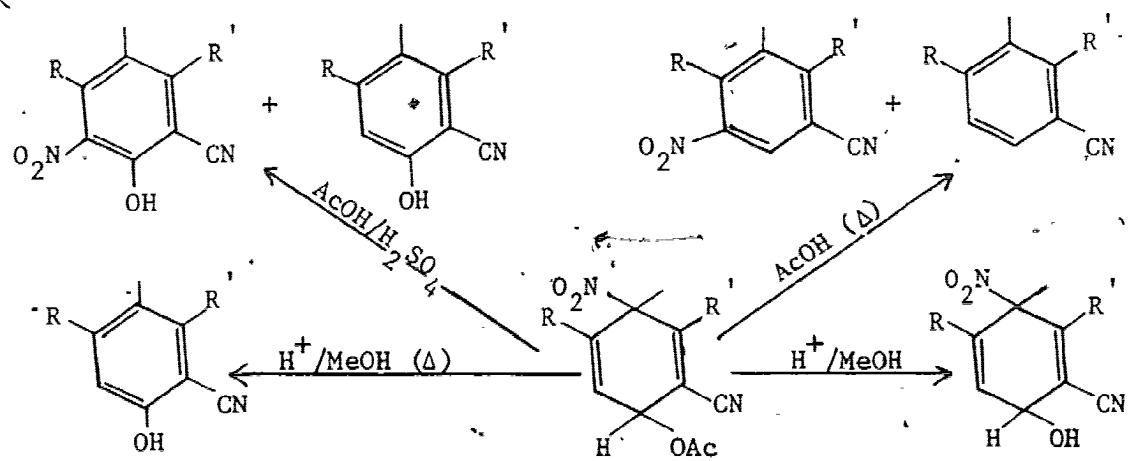
Solvolytic eliminations of nitrodienols have also been studied and the behaviour shown to be different from that of the corresponding secondary, nitrodienyl acetates (80). Intramolecular hydrogen migration (NIH shift) has been observed in the solvolysis of the nitrodienols, the extent of migration being measured by retention of a deuterium label. This was shown to be *ca.* 25-30% in the case of the nitrodienols, but 0.3% in the corresponding acetates. Thus, changeover from an acetate to a hydroxyl results in rearrangement (and subsequent deprotonation) being favoured over direct deprotonation from the intermediate cyclohexadienyl cation. The difference in behaviour has been attributed to the greater stabilizing effect of the hydroxyl substituent, as compared to the acetoxyl substituent, in the rearranged cation.



Under suitable conditions, the hydroxycyclohexadienyl cation, generated by loss of the nitro group, could be trapped by various nucleophiles (81). Solvolysis of 1,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-ol, in aqueous methanol, resulted in the formation of 1,4-dimethyl-cyclohexa-2,5-diene-1,4-diol and its methyl ether. The intermediate cation could also be trapped by added nitrite to give 1,4-dimethyl-2-nitrobenzene. Unlike the hydroxycyclohexadienyl cation, the corresponding acetoxycyclohexadienyl cation could not be trapped by added nucleophiles, but rearranged to form 2,5-dimethylphenyl acetate. The cation from the nitrodienol also rearranged to 2,4-dimethylphenol as the main phenolic product. The migratory aptitude is, therefore, of the order acetoxyl > methyl > hydroxyl in these rearrangements.

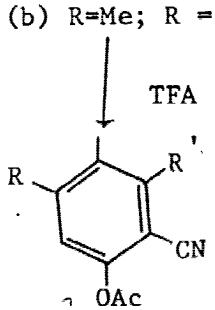


The exchange and rearomatization reactions discussed in this section have been observed in the adducts obtained from di- and poly-methylbenzenes, which have been extensively investigated. The behaviour of adducts obtained from dimethylbenzenes carrying cyano (57), oxo (58) and chloro (54) substituents have also been studied and are summarised in the following schemes:

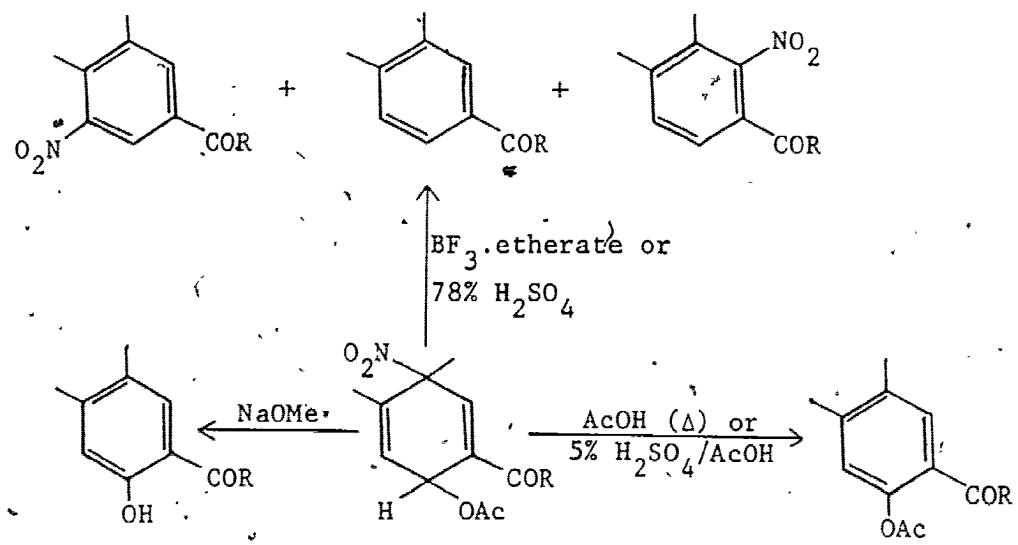


(a) R=H; R' = Me

(b) R=Me; R' = H



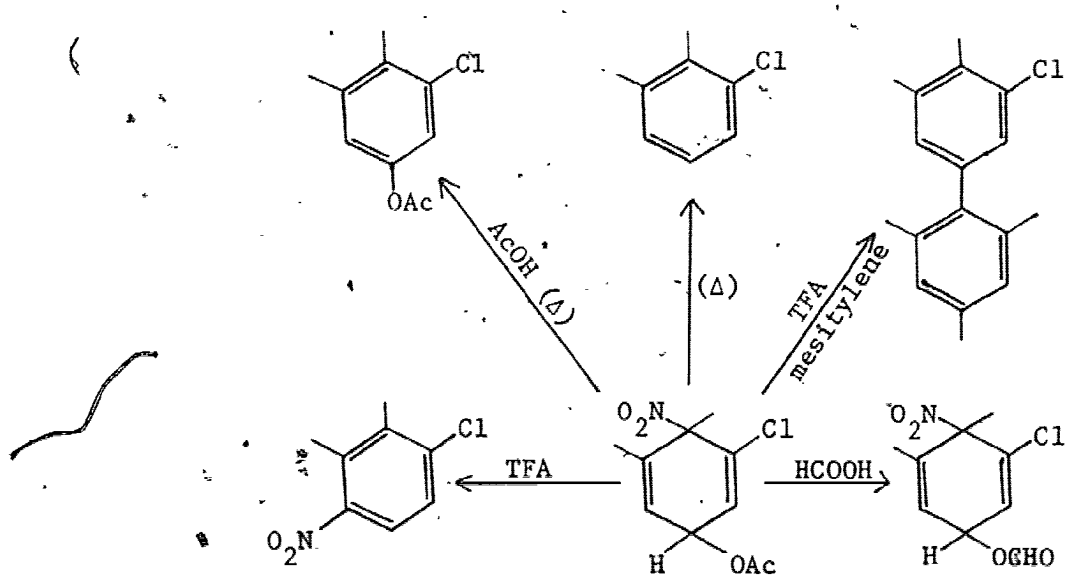
Scheme 1.3 Reactions of the adducts from (a) 2,3-dimethylbenzonitrile; and (b) 3,4-dimethylbenzonitrile.



(a) R = Me;

(b) R = Ph.

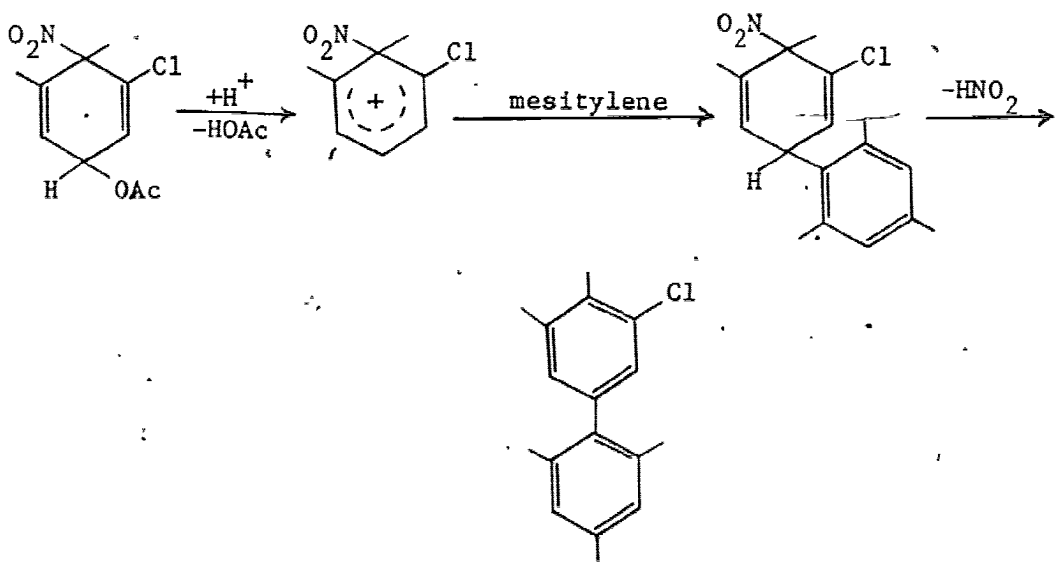
Scheme 1.4 Reactions of the adducts from (a) 3,4-dimethylacetophenone; and (b) 3,4-dimethylbenzophenone.



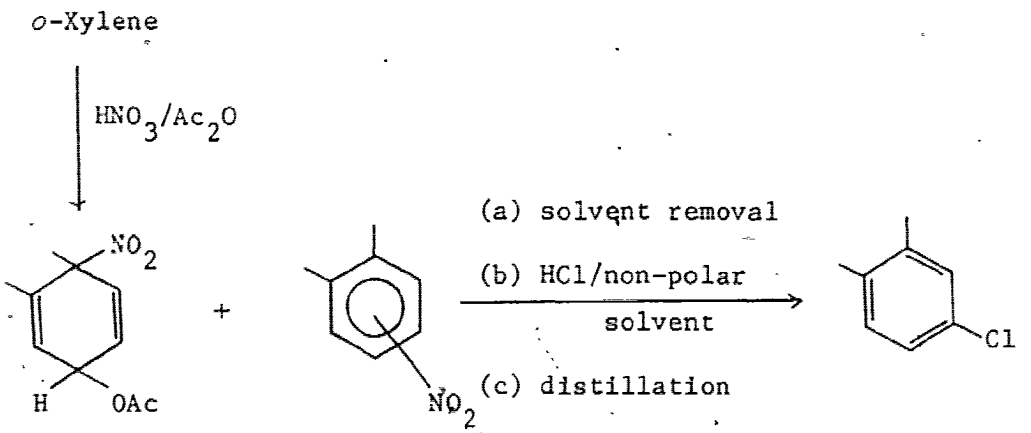
Scheme 1.5 Reactions of the adducts from 1-chloro-2,3-dimethylbenzene.

The rearomatization reactions in these systems (schemes 1.3-1.5) generally involve the formation of products arising from loss of nitrous acid or migration of the nitro group.. The formation of a biphenyl, when the adduct from 1-chloro-2,3-dimethylbenzene is rearomatized in the presence of mesitylene, is of special interest and is discussed below.

Nitration of alkylbenzenes often results in the formation of biphenyls when nitric acid is added to the hydrocarbon. The reaction is sensitive to the structure of the hydrocarbon (14) and is usually obtained from compounds which give secondary adducts on *ipso* nitration. This reaction, which has synthetic potential, proceeds through an *ipso* cyclohexadienyl cation, as shown below. Attack by mesitylene, followed by loss of nitrous acid, gives the biphenyl, usually in high yields (54, 82).



The synthetic utility of the products of *ipso* nitration of aromatic compounds has been discussed. A further application of these adducts is in the synthesis of 1-chloro-3,4-dimethylbenzene, an intermediate in the synthesis of riboflavin (42). A one-pot synthesis of this potentially useful intermediate would involve *ipso* nitration of *o*-xylene, followed by rearomatization of the adducts with hydrochloric acid. 1-Chloro-3,4-dimethylbenzene can then be obtained, free of the nitro compounds formed in the nitration, by fractional distillation.



Thus the sequence *ipso* attack, acetate capture, acetate replacement and rearomatization has furnished excellent routes for the synthesis of compounds which are difficult to obtain by conventional methods.

1.5 *Objectives of the Present Work*

The formation of adducts in the nitration of dimethylbenzenes carrying moderately electron-withdrawing groups such as -CN, $-COCH_3$ and $-COC_6H_5$ has been studied previously and the rearomatization reactions of the adducts, under various conditions, have been described (57,58). The effect of a strongly electron-withdrawing group like the nitro on the formation and reactions of adducts has not yet been actively studied. This may be attributed to the extreme difficulty in forming the adducts under the vigorous conditions necessitated by the deactivation of the substrate by the nitro group. The nitro substituent, by virtue of its steric and electronic properties, when placed on an aromatic substrate, is expected to produce a substantial effect on the mode of reactivity of, not only the substrate, but also the diene adducts obtained by *ipso* nitration.

The object of this work then is to study the formation, characteristics, rearomatization and rearrangements of the diene adducts obtained from the *ipso* nitration of various nitroarenes.

CHAPTER II

EXPERIMENTAL PROCEDURES

2.1 *Instrumentation*

I.r. spectra, calibrated with polystyrene, were recorded on a Pye-Unicam SP1000 or a Perkin-Elmer 283, in nujol or potassium bromide discs for solids and as thin films between sodium chloride plates for oils. ^{1}H n.m.r. spectra were recorded on a Perkin-Elmer R-32 (90 MHz) and, for column fractions, on a Perkin-Elmer R-12-A (60 MHz). Spectra were routinely recorded in chloroform-d_1, with tetramethylsilane as an internal standard. ^{13}C n.m.r. were obtained in chloroform-d_1, with tetramethylsilane as an internal reference, on a Nicolet TT-14 (15.1 MHz) spectrometer. U.v. spectra were recorded on a Cary-17 spectrometer, with methanol as the solvent. Mass spectra were recorded on a Perkin-Elmer-Hitachi RMU-7 spectrometer at 70 eV. G.l.c. analyses were performed on a Varian Aerograph 2400, using a 1.3 m X 3 mm column of 3% SE-30 on Chromosorb P at 180°C. A Finnegan 3300 g.l.c.-m.s.-c.i. system was used for the mass spectral analysis of mixtures. A Waters-Associates Prep LC/System 500 was routinely employed for the separation of adducts in the later stages of this work.

2.2 *Reagents*

Acetic anhydride was certified ACS, Fisher; trifluoroacetic anhydride was Aldrich Gold Label (99+%). Nitric acid (fuming, Fisher) was purified by distilling (300 cm^3) at 1 mm from urea (10 g, reagent, Fisher) and sulfuric acid (500 cm^3) and stored at -25°C. Solvents used

for chromatography including pentane (reagent, Fisher), anhydrous ether (reagent, Amachem) and benzene (reagent, Amachem) were further purified by drying over sodium followed by distillation and storage in glass bottles containing molecular sieves. Non-deuterated solvents employed for spectroscopy were certified ACS, spectranalyzed (Fisher) and deuterated solvents including chloroform-d_1, methylene chloride-d_2, deuterium oxide-d_2, acetonitrile-d_3, methanol-d_4, pyridine-d_5 and acetone-d_6 were obtained from Merck, Sharp and Dohme. Silica gel (60–200 mesh) was Davison commercial grade H and neutral alumina (Camag, Activity I), deactivated with 3% of distilled water, was used.

1,2-Dimethyl-4-nitrobenzene (Aldrich), 1,2-dimethyl-3-nitro benzene (technical, Baker), 4-methyl-2-nitrophenol (Aldrich) and 4-methyl-3-nitrophenol (Aldrich) were deemed pure and used without further purification. 1,4-Dimethyl-2-nitrobenzene was prepared as follows:

Sulfuric acid (40 g, 0.42 mol) was added dropwise, over 1 h, to a well-stirred mixture of *p*-xylene (100 g, 0.96 mol) and nitric acid (120 g, 1.90 mol) in methylene chloride (800 cm^3) at 0°C. The mixture was allowed to warm to 20°C and stirred for 18 h. Evaporation of the solvent, after treatment of the reaction product with water (2 X 250 cm^3) and saturated sodium bicarbonate (2 X 150 cm^3) followed by drying over anhydrous magnesium sulfate, gave a crude product containing mainly 1,4-dimethyl-2-nitrobenzene (98% by ^1H n.m.r.). The product was distilled at 75°C and 0.5 mm to give 1,4-dimethyl-2-nitrobenzene, pure by g.l.c. and having i.r. (Neat) 1530 and 1350 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.30 (s,3,4-$C\underline{H}_3$), 2.43 (s,3,1-$C\underline{H}_3$), 7.10 (d,1,6-$\underline{H}$)

7.22 (dd,1,5-H), 7.67 (d,1,3-H), J_{35} = 1.66 Hz, J_{56} = 8.0 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) 19.8 (4-CH_3), 20.5 (1-CH_3), 124.8 (C-3), 130.4 (C-1), 132.6 (C-6), 133.9 (C-5), 137.2 (C-4), 149.0 (C-2).

2.3 *Optimization of Reaction Conditions*

A series of reactions was carried out on a small-scale (1 mmol substrate) to optimize the conditions for maximum diene formation. The procedure involved adding nitric acid at -20°C to a mixture of trifluoroacetic anhydride and half of the required amount of acetic anhydride at -78°C. The mixture was allowed to warm to 0°C, maintained at this temperature for 5 min, and recooled to -78°C. This was then added to the substrate, in the remaining half of the acetic anhydride, at -78°C. The reaction temperature was raised to 0°C and aliquots withdrawn at regular intervals. The ^1H n.m.r. spectra of these aliquots were recorded at -20°C, the instrument being locked on acetic anhydride (δ 2.15 ppm). The aliquots were then subjected to an aqueous bicarbonate work-up, after dissolution in ether, and the ^1H n.m.r. spectra recorded. A few reactions were also carried out in the absence of trifluoroacetic anhydride to study medium-effects. Best results were obtained with trifluoroacetic anhydride in the nitration of 1,2-dimethyl-3- and 4-nitrobenzenes whereas, in the nitration of 1,4-dimethyl-2-nitrobenzene, 4-methyl-2- and 3-nitrophenols, better yields were obtained in the absence of trifluoroacetic anhydride.

2.4. *Preparative Reactions*

A cold solution (-20°C) of nitric acid was added dropwise with stirring to a mixture of trifluoroacetic anhydride and acetic anhydride (or acetic anhydride alone) at -78°C. On completion of the addition, the mixture was warmed to 0°C to complete the formation of acetyl nitrate and cooled to -78°C. This was then added to the substrate in acetic anhydride at -78°C with stirring and the temperature raised to 0°C, the temperature at which the best results were obtained in the small-scale experiments. The reaction mixture was stirred until ^{1}H n.m.r. of an aliquot showed that the reaction was complete; *i.e.* no signals corresponding to the substrate were present.

2.5 *Work-up Procedures*

The crude reaction mixture was originally worked-up by adding ether to the mixture at -78°C and treating the resulting solution with liquid ammonia, condensed from the gas by passage through a condenser, at -78°C. The rate of addition was adjusted so the temperature of the reaction mixture did not rise above -40°C. The neutralization procedure was stopped when further addition of ammonia did not result in a rise in the temperature and the reaction mixture was alkaline (pH *ca.* 8). The excess ammonia was removed by an aspirator and the reaction mixture treated with ice-water. The ether extract was washed, dried and evaporated at 15°C. ^{1}H n.m.r. of the product indicated partial decomposition of the diene adducts and hence the following work-up procedure was adopted:

On completion of the reaction, the reaction mixture was treated

with ice-water and sodium bicarbonate was added in portions till the mixture was alkaline (pH *ca.* 8). The product was extracted with ether and the ether extract washed with water and dried. ^{1}H n.m.r. of the product, after removal of the solvent ether, showed that very little decomposition of the diene adducts had occurred in the work-up.

2.6 *Chromatography*

Chromatographic separation of the crude reaction product was performed at low-temperature ($-30^{\circ}C$ to $-40^{\circ}C$). Cold methanol was circulated through the the jacket of a chromatography column by means of a self-priming pump (Jabsco) and through a coil which pre-cooled the solvent. This insulated coil was connected in series with the jacket and supported on top of the column. The refrigerated methanol was further cooled in a Dewar flask containing carbon dioxide-acetone and then circulated through the jacket of the column. Initial experiments with various adsorbents such as (a) basic alumina, deactivated with 3% of 10% acetic acid; (b) neutral alumina, deactivated with 3% water and (c) silica gel indicated that the product recovery was highest (75% to 85%) with silica gel. A ratio of 100:1 of silica to the reaction product was found to give a satisfactory separation.

The columns were packed in the usual manner and topped up with an inch of sea-sand. The reaction product was dissolved in minimum ether and loaded onto the column. The elution process was initiated immediately by forcing the solvent (pentane and then pentane-ether mixtures) under pressure of nitrogen (5 p.s.i.) through the column. This offset the increased viscosity of the solvent at low temperatures

and shortened the time that the adducts spent on the column, an important factor which proved crucial in determining the net recovery of the diene adducts from the process.

The separation could be improved by using benzene (instead of pentane-ether mixtures) as the solvent. The efficacy of the operation was greatly enhanced by employing a Prep LC/System 500, using pre-cooled benzene (*ca.* 5°C) as the solvent and employing a flow-rate of 0.1 dm^3/min.

2.7 *Shift Reagent Studies*

The shift reagent tris-(1,1,1,2,2,2,3,3-heptafluoro-7,7-dimethyl-d_6-4,6-octanedionato-d_3)europium(III) was used in several cases during n.m.r. analysis of the diene adducts to (a) induce separation of diene protons in order to calculate coupling constants, as illustrated in the case of adducts from 1,2-dimethyl-3-nitrobenzene and (b) distinguish *trans* from *cis* adducts by observing the rate of shift of the proton signals and plotting the shift of various protons *vs.* the shift of the acetate protons.

The shift reagent was added in small increments (5-10 mg) to a solution of the pure diene (35-50 mg) in chloroform-d_1 at 0°C. The weight of the reagent added and the n.m.r. spectrum (tetramethylsilane as standard) were recorded after each addition. The volume increase resulting on addition of the reagent was ignored. The observed variation in the lanthanide-induced shifts could be related to the different proton-europium distances.

2.8 *Kinetics*

Due to the wide variety of reagents employed to effect exchange and rearomatization, reaction conditions had to be suitably tailored to meet the reagent requirements of solubility and reactivity. In principle, the reactions with various acids and amines were carried out by adding the reagent to the diene adducts in a suitable solvent at -78°C and then bringing the reaction mixture to a temperature convenient to monitor the reaction. Exchange reactions with various nucleophiles were usually carried out by adding the diene to a solution of the reagent in a suitable solvent at an optimum temperature.

The reactions were worked-up by transferring the contents of the n.m.r. tube to a small flask (25 cm^3 capacity), rinsing with ether and neutralising (wherever necessary) at low temperatures. The ether extract was dried over anhydrous magnesium sulfate and filtered. Evaporation of the solvent at 15°C, on a rotary evaporator, yielded products which were analyzed by u.v., i.r., ^1H n.m.r. and g.l.c.-m.s.-c.i..

Diene adducts obtained by exchange reactions were isolated, for positive identification and further exchange reactions, by repeating the exchange on the crude nitration product and isolating the desired diene on a Waters Associates Prep LC/ system 500, using benzene as the solvent. The adducts thus obtained were recrystallised from ether at -20°C.

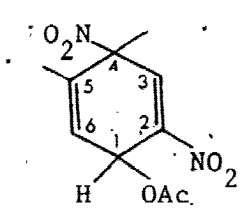
2.9 *G.L.C. Analysis*

The aromatic compounds obtained by rearomatization of diene adducts were analyzed on a Varian Aerograph 2400 using a 1.3 m long 3% SE-30 stainless steel column. The instrument was equipped with a hydrogen flame ionization detector, with helium as the carrier gas at a flow-rate of 20 cm^3/min at 50 p.s.i.

The column packing was prepared by suspending the support in a solution of the liquid phase in chloroform and removing the solvent on a rotary evaporator after ensuring thorough mixing. The column temperature during the analysis was 180°C and the injector and detector temperatures were *ca.* 50°C above that of the column temperature, all runs being isothermal. The identity of the compounds were confirmed by comparison of their retention times with those of authentic samples and also by g.l.c.-m.s.-c.i. analysis.

TABLE 2.1

LIST OF ADDUCTS OBTAINED IN THE PRESENT STUDY



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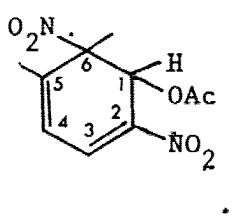

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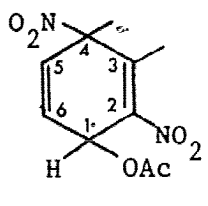

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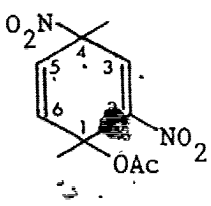

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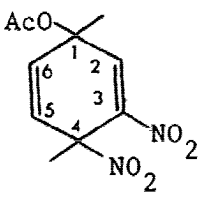

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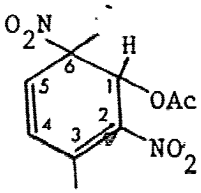

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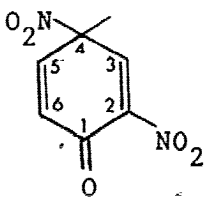

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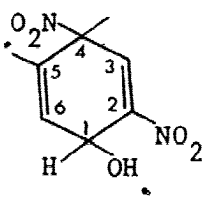

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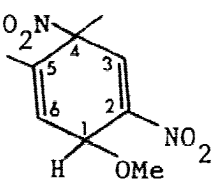

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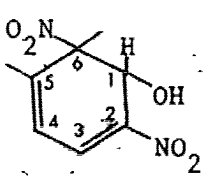

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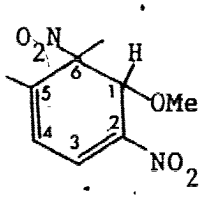

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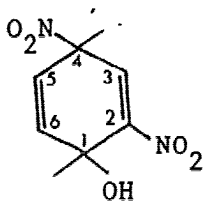

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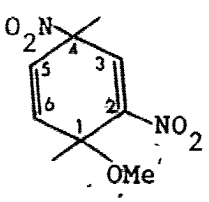

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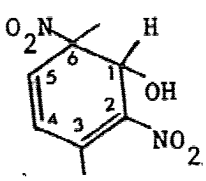

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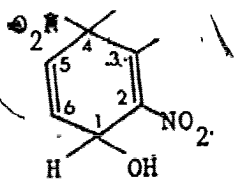

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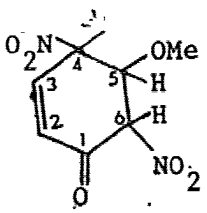

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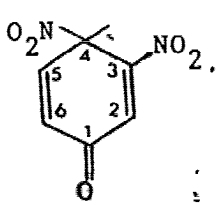

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2.10 *Isolation of the Diene Adducts*

The diastereomer of a pair of isomeric dienes eluted first from the column will be designated as isomer A and the isomer eluted later will be designated as isomer B. In the case where more than one pair of diastereomers is present, the second pair, in order of elution, is designated as isomer D and isomer E respectively. Between the positional isomers A and D, the isomer A is eluted prior to isomer D.

The structures of the various adducts and the system of numbering employed are given in Table 2.1.

(a) 1,2-Dimethyl-4-nitrobenzene

Nitric acid (32 g, 0.51 mol) at -20°C was added in small portions with stirring to a mixture of acetic anhydride (80 g, 74 cm^3) and trifluoroacetic anhydride (100 g, 67 cm^3) at -78°C. The temperature of the mixture was raised to 5°C, maintained for 5 min to ensure complete reaction and then lowered to -78°C. This nitrating mixture was added dropwise, over 10 min, to a solution of 1,2-dimethyl-4-nitrobenzene (15 g, 0.1 mol) in acetic anhydride (20 g, 18 cm^3) at -78°C. The reaction temperature was then raised to 0°C and maintained for 2 h with stirring. At the end of this period, the reaction mixture was poured into a beaker containing ice (800 g) and ether (800 cm^3). The aqueous medium was neutralised using sodium bicarbonate till it was mildly alkaline (pH *ca.* 8). The ether extract was washed with distilled water (2 X 600 cm^3), dried over anhydrous magnesium sulfate and evaporated at 15°C. Integration of the ^1H n.m.r. spectrum of the crude reaction product showed that the diene adducts constituted *ca.* 50% of the total mixture.

The product was chromatographed on silica gel at -40°C using pentane-ether mixtures. Elution upto 40% ether in pentane gave 1,2-dimethyl-3,5-dinitrobenzene (16) as the principal product m.p. 75°C (lit (83) 77°C); i.r. (KBr) 1520 and 1348 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.46 (s,3,1-$C\underline{H}_3$), 2.51 (s,3,2-$C\underline{H}_3$), 8.18 (d,1,6-$\underline{H}$), 8.35 (d,1, 4-$\underline{H}$), J_{46} = 2 Hz; mass spectrum (70 eV) m/e (relative intensity) 196 (40, M), 180 (15,M-O), 179 (100,M-OH), 133 (27), 132 (13), 104 (26), 103 (36), 91 (24), 78 (19), 77 (34), metastable peak at 163.5 corresponding to 196 → 179.

The 45% and 50% ether-pentane fractions gave a mixture containing 1,2-dimethyl-4,5-dinitrobenzene (*ca.* 20%) and diene adducts (*ca.* 80%), which on recrystallization from ether at -20°C gave one diastereomer of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate (7A) m.p. 95°C; u.v. (CH_3OH) 225 nm (775 m^2mol^{-1}), 194 nm (1540 m^2mol^{-1}); i.r. (Nujol) 1238 and 1742 cm^{-1} ($OCOCH_3$), 1560 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.88 (d,3,5-$C\underline{H}_3$), 1.95 (s,3,4-$C\underline{H}_3$), 2.06 (s,3,$OCOC\underline{H}_3$), 5.98 (m,1,6-$\underline{H}$), 6.46 (d,1,1-$\underline{H}$), 7.44 (s,1,3-$\underline{H}$), J_{16} = 4 Hz, $J_{6,5\text{-}CH_3}$ = 1.5 Hz, $J_{1,5\text{-}CH_3}$ = 1.3 Hz. On a 300 Hz expanded spectrum, the peak due to 5-CH_3 appeared as a triplet (overlapping doublets) and the peak due to 1-H appeared as a multiplet. Irradiation of the methyl resonance at δ 1.88 collapsed the peaks at δ 5.98 and δ 6.46 to two doublets; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 17.4 (5-$\underline{C}H_3$), 20.6 ($OCO\underline{C}H_3$), 23.4 (4-$\underline{C}H_3$), 61.4 (C-1), 88.9 (C-4), 124.3 (C-6), 133.6 (C-3), 134.8 (C-5), 148.3 (C-2), 169.5 ($O\underline{C}OCH_3$).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,47.02; H,4.70; N,10.82

The mother liquor from these fractions was subjected to another recrystallization to give 1,2-dimethyl-4,5-dinitrobenzene (17) which was recrystallized from ethanol m.p. 118°C (lit (83) 118°C); i.r. (KBr) 1528, 1548, 1378 and 1338 cm^{-1}; ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.37 (s,6, 1-CH_3 and 2-CH_3), 7.63 (s,2,3-H and 6-H); mass spectrum (70 eV) m/e (relative intensity) 197 (12), 196 (100,M), 180 (20,M-O), 150 (14,M-NO_2), 108 (48), 103 (24), 92 (14), 91 (79), 80 (24), 79(26), 78 (21), 77 (45).

The 55% ether-pentane column fraction gave a mixture of 1,2-dimethyl-4,5-dinitrobenzene, 1,2-dimethyl-3,4-dinitrobenzene and the diene adducts in the ratio 1:4:5. This fraction was recrystallized from ether at -20°C to give the other isomer of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate (18) m.p. 115°C (d); u.v. (CH_3OH) 227 nm (830 m^2mol^{-1}), 195 nm (1620 m^2mol^{-1}); i.r. (Nujol) 1240 and 1750 cm^{-1} ($OCOCH_3$), 1560 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.86 (s,6,4-CH_3 and 5-CH_3), 2.04 (s,3,$OCOCH_3$), 5.96 (m,1,6-H), 6.34 (d,1,1-H), 7.34 (s, 1,3-H), J_{16} = 4 Hz, $J_{6,5\text{-}CH_3}$ = 1.5 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 17.4 (5-CH_3), 20.6 ($OCOCH_3$), 24.1 (4-CH_3), 60.9 (C-1), 87.7 (C-4), 124.3 (C-6), 132.8 (C-3), 133.9 (C-5), 148.4 (C-2), 169.8 ($OCOCH_3$)

Anal. Calcd.for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,46.70; H,4.72; N,10.65

Further elution with 60% ether-pentane followed by recrystallization from carbon tetrachloride gave 1,2-dimethyl-3,4-dinitrobenzene (15) which was recrystallized from ethanol m.p 82°C (lit (83) 82°C); i.r. (KBr) 1352 and 1540 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.22 (s,3,1-CH_3), 2.41 (s,3,2-CH_3), 7.41 (d,1,5-H), 7.92 (d,1,6-H), J_{56} = 8.5 Hz; mass spectrum (70 eV) m/e (relative intensity) 196 (57,M),

180 (16,M-O), 179 (100,M-OH), 148 (13), 150 (96,M-NO_2), 105 (11), 104 (14), 103 (23), 92 (13), 91 (63), 79 (12), 78 (27), metastable peak at 163.5 corresponding to 196 → 179.

Attempts to improve the degree of separation of the diene adducts from each other and from the aromatic compounds by changing the eluent to benzene, keeping the proportion of silica constant, proved highly successful. At temperatures ranging from 5°C to 10°C, a vastly improved separation and recovery resulted. The efficacy of this operation was enhanced by employing a Prep LC/ System 500. Under optimum conditions, the diene adducts were easily separable from each other and were separated and used for characterization. The Prep LC/ System 500 was also suitably employed for purification of the diene adducts emanating from exchange reactions on the adduct 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate (7).

(b) 1,2-Dimethyl-3-nitrobenzene

Nitric acid (32 g, 0.51 mol) at -20°C was added in small portions with stirring to a mixture of acetic anhydride (80 g, 74 cm^3) and trifluoroacetic anhydride (100 g, 67 cm^3) at -78°C. The temperature of the mixture was raised to 5°C, maintained for 5 min to ensure complete reaction and then lowered to -78°C. This nitrating mixture was added dropwise, over 10 min, to a solution of 1,2-dimethyl-3-nitrobenzene (15 g, 0.1 mol) in acetic anhydride (20 g, 18 cm^3) at -78°C. The reaction temperature was then raised to 0°C and maintained for 2 h with stirring. At the end of this period, the reaction mixture was poured into a beaker containing ice (800 g) and ether (800 cm^3). The

aqueous medium was neutralized using sodium bicarbonate till it was alkaline (pH *ca.* 8). The ether extract was washed with water (2 X 600 cm^3), dried over anhydrous magnesium sulfate and evaporated at 15°C. Integration of the ^1H n.m.r. spectrum of the crude product showed that the diene adducts constituted *ca.* 40% of the total mixture.

The product was chromatographed on silica gel at -10°C using pentane-ether mixtures. Elution upto 20% ether in pentane gave a 1:1 mixture of 1,2-dimethyl-3,5-dinitrobenzene (16, also obtained in the nitration of 1,2-dimethyl-4-nitrobenzene) and 1,2-dimethyl-3,6-dinitrobenzene (18). The latter compound was not isolated but its presence was clearly evident from the ^1H n.m.r. spectra and it had (90 MHz, $CDCl_3$) δ 2.41 (s,6,1-$C\underline{H}_3$ and 2-$C\underline{H}_3$), 7.61 (s,2,4-$\underline{H}$ and 5-$\underline{H}$). The 30% ether-pentane fraction gave mainly 16. The 35% ether-pentane fraction, after recrystallization from ether at -20°C, gave one diastereomer of 3,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate (9A) m.p. 58°C; u.v. (CH_3OH) 242 nm (490 m^2mol^{-1}), 195 nm (1650 m^2mol^{-1}); i.r. (KBr) 1225 and 1745 cm^{-1} ($OCOCH_3$), 1555 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.92 (s,3,4-$C\underline{H}_3$), 2.03 (d,3,3-$C\underline{H}_3$), 2.05 (s,3,$OCOC\underline{H}_3$), 6.05 (d,1,5-$\underline{H}$), 6.26 (dd,1,6-$\underline{H}$), 6.52 (m,1,1-$\underline{H}$) J_{56} = 10 Hz, J_{16} = 3.4 Hz, J_{15} = 1.5 Hz, $J_{1,3\text{-}CH_3}$ = 1.3 Hz. Shift reagent was added to the solution and the decoupler frequency set at the 1-H resonance when the following changes occurred: the 6-H (dd) resonance collapsed to a doublet, the 5-H (dd) resonance collapsed to a doublet and the 3-$C\underline{H}_3$ (d) resonance collapsed to a singlet; ^{13}C n.m.r. ($CDCl_3$,ppm) δc 15.6 (3-$\underline{C}H_3$), 20.5 ($OCO\underline{C}H_3$), 23.5 (4-$\underline{C}H_3$), 63.3 (C-1), 90.2 (C-4), 127.1 (C-6), 129.0 (C-5), 136.3 (C-3), 146.9 (C-2) and 169.6 ($O\underline{C}OCH_3$).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,46.48; H,4.76; N,10.97

Further elution with 40% ether-pentane gave a 1:2 mixture of 1,2-dimethyl-3,4-dinitrobenzene (15, also obtained in the nitration of 1,2-dimethyl-4-nitrobenzene) and the adduct 9A, which on recrystallization from carbon tetrachloride at -20°C gave pure 15 (^{1}H n.m.r. and g.l.c.). The diene 9A was recrystallized from the mother liquor using ether at -20°C.

The 45% ether-pentane fraction gave mainly a mixture of diene adducts which on recrystallization from ether at -20°C gave the other diastereomer of 3,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate. (9B) m.p.108°C; u.v. (CH_3OH) 240 nm (410 m^2 mol^{-1}), 195 nm (1340 m^2 mol^{-1}); i.r. (KBr) 1230 and 1745 cm^{-1} ($OCOCH_3$), 1540 cm^{-1} (NO_2), ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 1.85 (s,3,4-$C\underline{H}_3$), 2.07 (m,6,3-$C\underline{H}_3$ and $OCOC\underline{H}_3$), 6.04 (d,1,5-$\underline{H}$), 6.19 (dd,1,6-$\underline{H}$), 6.33 (m,1,1-$\underline{H}$), J_{56} = 9.5 Hz, J_{16} = 3.4 Hz, J_{15} = 1.5 Hz, $J_{1,3\text{-}CH_3}$ = 1.3 Hz. Shift reagent was added to the solution and a 300 Hz spectrum recorded. This resulted in the resolution of the resonances of the ring protons and the overlapping resonances due to 3-$C\underline{H}_3$ and $OCOC\underline{H}_3$; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 14.2 (3-$\underline{C}H_3$), 20.5 ($OCO\underline{C}H_3$), 24.3 (4-$\underline{C}H_3$), 62.7 (C-1), 88.8 (C-4), 126.1 (C-6), 128.8 (C-5), 134.8 (C-3), 146.5 (C-2), 169.6 ($O\underline{C}OCH_3$).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,46.64; H,4.64; N,10.69

(c) 1,4-Dimethyl-2-nitrobenzene

Small-scale experiments revealed that in the presence of trifluoroacetic anhydride, only one pair of diastereomeric 1,4 adducts was obtained whereas in the absence of trifluoroacetic anhydride, two pairs of diastereomeric 1,4 adduct along with a 1,2 adduct were obtained.

Nitric acid (32 g, 0.51 mol) at -20°C was added in small portions with stirring to acetic anhydride (51 g, 47 cm^3) at -78°C. The temperature of the mixture was raised to 5°C, maintained for 5 min, to ensure complete reaction and then lowered to -78°C. This nitrating mixture was added dropwise, over 10 min, to the substrate (15 g, 0.1 mol) at -78°C. The reaction temperature was raised to 0°C and maintained for 18 h with stirring. At the end of this period, the reaction mixture was poured into a beaker containing ice (800 g) and ether (800 cm^3). The aqueous medium was neutralized using sodium bicarbonate till it was alkaline (pH *ca.* 8). The ether extract was washed with water (2 X 600 cm^3), dried over anhydrous magnesium sulfate and evaporated at 15°C. Integration of the ^1H n.m.r. spectrum of the crude product showed that the diene adducts constituted *ca.* 60% of the total mixture.

Preliminary attempts to chromatograph the reaction product over silica or alumina at low temperatures (-20°C to -40°C), using ether-pentane mixtures, showed that the product recovery and degree of separation were quite poor, presumably because of the number of adducts involved. The diene adducts could be isolated with less difficulty on a Prep LC, using pre-cooled benzene or ether as the solvent.

Crystallization of the reaction product from ether at -20°C gave a 1:2 mixture of the three dinitroxylenes and the adduct 12. The cubic crystals of the adduct 12 were manually separated from the needle-like crystals of the dinitroxylenes. Recrystallization of the cubic crystals from ether at -20°C gave the adduct 3,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (12) m.p. 109°C; u.v. (CH_3OH) 295 nm (655 m^2 mol^{-1}), 207 nm (995 m^2 mol^{-1}); i.r. (KBr) 1760 and 1200 cm^{-1} ($OCOCH_3$), 1550 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.81 (s,3,6-CH_3), 1.96 (s,3,$OCOCH_3$), 2.26 (s,3,3-CH_3), 6.14 (d,1,4-H), 6.25 (d,1,1-H), 6.80 (dd,1,5-H), J_{45} = 10 Hz, J_{15} = 1.46 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 19.7 (6-CH_3), 20.3 ($OCOCH_3$), 22.6 (3-CH_3), 68.6 (C-1), 89.6 (C-6), 127.6 (C-4), 132.5 (C-5), 139.7 (C-3), 140.6 (C-2), 168.8 ($OCOCH_3$)

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,46.62; H,4.72; N,10.50

The mother liquor (after recrystallization of the main reaction product) was injected, in 0.500 g portions, into the inlet of a Prep LC system using pre-cooled benzene (*ca.* 5°C) as solvent and a flow rate of 0.1 dm^3 min^{-1}.

The first fraction eluted from the column contained mainly a mixture of dinitroxylenes. This fraction was mixed with the needle-like crystals (obtained from crystallization of the reaction product) and chromatographed over alumina (discussed later).

The second fraction, after recrystallization from ether at -20°C, gave one diastereomer of 1,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate (10A) m.p. 83°C; u.v. (CH_3OH) 245 nm (970 m^2 mol^{-1}),

195 nm (2120 $m^2 mol^{-1}$); i.r. (KBr) 1740 and 1230 cm^{-1} ($OCOCH_3$), 1545 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.72 (s,3,1-$C\underline{H}_3$), 1.92 (s,3,4-$C\underline{H}_3$), 2.02 (s,3,$OCOC\underline{H}_3$), 5.94 (d,1,6-$\underline{H}$), 6.15 (dd,1,5-$\underline{H}$), 7.43 (d,1,3-$\underline{H}$), J_{56} = 10 Hz, J_{35} = 1.76 Hz. Irradiation of the 3-H doublet resulted in the collapse of the 5-H (dd) resonance to a doublet; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 21.2 ($OCO\underline{C}H_3$), 24.7 (4-$\underline{C}H_3$), 26.0 (1-$\underline{C}H_3$), 71.2 (C-1), 86.6 (C-4), 124.2 (C-5), 129.6 (C-6), 133.8 (C-3), 151.2 (C-2), 169.8 ($O\underline{C}OCH_3$).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,46.35; H,4.77; N,10.51

The third and fourth fractions contained a small amount of a mixture of mainly two diene adducts in nearly equal proportions. Attempts to separate the adducts by crystallization were unsuccessful. Hence the following procedure was adopted:

The mixture was injected into the inlet of a Prep LC system using pre-cooled ether (5°C) as the solvent and a flow rate of 0.15 $dm^3 min^{-1}$. The first fraction contained mainly aromatic compounds, presumably formed by decomposition of the adducts. The second fraction gave one diastereomer of 1,4-dimethyl-3,4-dinitrocyclohexa-2,5-dienyl acetate (11 D) i.r. (neat) 1740 and 1235 cm^{-1} ($OCOCH_3$), 1535 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.62 (s,3,1-$C\underline{H}_3$), 2.04 (s,6, 4-$C\underline{H}_3$ and $OCOC\underline{H}_3$), 5.89 (d,1,5-$\underline{H}$), 6.01 (dd,1,6-$\underline{H}$), 7.60 (d, 1,2-$\underline{H}$), J_{56} = 10 Hz, J_{26} = 1.5 Hz. Irradiation of the 2-$\underline{H}$ (d) resonance resulted in the collapse of the 6-$\underline{H}$ (dd) resonance

to a doublet; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 21.3 ($OCO\underline{C}H_3$), 21.8 (1-$\underline{C}H_3$), 26.7 (4-$\underline{C}H_3$), 74.3 (C-4), 84.7 (C-1), 127.3 (C-5), 131.7 (C-6), 139.6 (C-2), 145.3 (C-3), 169.9 ($O\underline{C}OCH_3$). The third fraction gave a mixture of (11 D) and another diene adduct, also obtained from the fifth fraction using benzene as solvent.

The fifth fraction contained a 1:1 mixture of (12) and another adduct. The adduct (12) was recrystallized from this mixture using ether at -20°C. The mother liquor was subjected to another recrystallization to give the other diastereomer of 1,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate (10 B) m.p. 82°C; u.v. (CH_3OH) 245 nm (715 m^2 mol^{-1}), 197 nm (1408 $m^2 mol^{-1}$); i.r. (KBr) 1740 and 1230 cm^{-1} ($OCOCH_3$), 1542 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.67 (s,3,1-$\underline{C}H_3$), 1.86 (s,3,4-$\underline{C}H_3$), 2.00 (s,3,$OCOC\underline{H}_3$), 5.98 (d,1,6-$\underline{H}$), 6.30 (dd,1,5-$\underline{H}$), 7.57 (d,1,3-$\underline{H}$), J_{56} = 10 Hz, J_{35} = 1.75 Hz. Irradiation of the 3- $\underline{H}$ (d) resonance resulted in the collapse of the 5-H (dd) resonance to a doublet; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 21.2 ($OCO\underline{C}H_3$), 25.9 (4-$\underline{C}H_3$), 27.6 (1-$\underline{C}H_3$), 70.7 (C-1), 83.7 (C-4), 124.4 (C-5), 130.1 (C-6), 132.9 (C-3), 150.6 (C-2), 169.6 ($O\underline{C}OCH_3$).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,47.02; H,4.72; N,11.05

The sixth fraction gave a small amount of the adduct (10 B) and another adduct, presumably the other diastereomer of 1,4-dimethyl-3,4-dinitrocyclohexa-2,5-dienyl acetate (11 E). The latter compound, being a minor component, could not be isolated but its presence was evident in the ^1H n.m.r. spectra and it had (60 MHz, $CDCl_3$) δ 1.70

(s,3,1-$C\underline{H}_3$), 1.89 (s,3,4-$C\underline{H}_3$), 2.00 (s,3,$OCOC\underline{H}_3$), 5.85 (d,1,5-H), 6.05 (dd,1,6-$\underline{H}$) and 7.70 (d,1,2-$\underline{H}$).

As described earlier, the first fraction from the Prep LC system contained a mixture of dinitroxylenes. This was chromatographed over alumina at 20°C using ether-pentane mixtures. Fractions upto 12.5% ether gave a mixture of 1,4-dimethyl-2,5-dinitrobenzene (20) and 1,4-dimethyl-2,6-dinitrobenzene (21) in the ratio 1:5. Recrystallization from ethanol gave pale yellow crystals containing a 1:1 mixture of (20) and (21). The product (20) was not purified but its identity was confirmed from the ^{1}H n.m.r. spectra (84) and it had (90 MHz, $CDCl_3$) δ 2.58 (s,6,1-$C\underline{H}_3$ and 4-$C\underline{H}_3$), 7.88 (s,2,3-$\underline{H}$ and 6-$\underline{H}$).

The 15% ether fraction, after recrystallization from ethanol, gave 1,4-dimethyl-2,6-dinitrobenzene (21) m.p. 124°C (lit (84) 124°C); i.r. (KBr) 1530 and 1345 cm^{-1} (NO_2); ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 2.47 (s,6,1-$C\underline{H}_3$ and 4-$C\underline{H}_3$), 7.78 (s,2,3-$\underline{H}$ and 5-$\underline{H}$); ^{13}C n.m.r. ($CDCl_3$, ppm) δc 14.4 (4-$\underline{C}H_3$), 20.6 (1-$\underline{C}H_3$), 124.0 (C-1), 127.9 (C-3 and C-5), 138.6 (C-4), 151.4 (C-2 and C-6); mass spectrum (70 eV) m/e (relative intensity) 196 (12,M), 180 (11,M-O), 179 (100,M-OH), 162 (20), 149 (15), 135 (18), 105 (22), 104 (64),103 (33).

The 20% ether fraction, after recrystallization from ethanol, gave 1,4-dimethyl-2,3-dinitrobenzene (19) m.p. 94°C (lit (84) 94°C); i.r. (KBr) 1525 and 1355 cm^{-1} (NO_2); ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 2.35 (s,6,1-$C\underline{H}_3$ and 4-$C\underline{H}_3$), 7.35 (s,2,5-$\underline{H}$ and 6-$\underline{H}$); ^{13}C n.m.r. ($CDCl_3$, ppm) δc 17.7 (1-$\underline{C}H_3$ and 4-$\underline{C}H_3$), 130.7 (C-1 and C-4), 134.2 (C-5 and C-6), 143.6 (C-2 and C-3); mass spectrum (70 eV) m/e (relative intensity) 196 (76,M), 180 (14,M-O), 179 (100,M-OH), 148 (95), 104 (20), 103 (29), metastable

peak at 163.5 corresponding to 196 → 179.

After characterizing the various diene adducts, re-examination of the ^{1}H n.m.r. of the small-scale reactions using trifluoroacetic anhydride revealed that the diastereomeric pair of 1,4 adducts not obtained under these conditions were the adducts 10A and 10B.

(d) 4-Methyl-2-nitrophenol

Small-scale reactions showed that 4-methyl-2-nitrophenyl acetate, prepared by acetylation of the phenol with acetic anhydride (86a), did not react with the nitrating mixture under various conditions; *e.g.* ^{1}H n.m.r. of a reaction mixture using nitric acid (1.5 mol) and acetic anhydride (5 mol) per mole of the substrate showed that no reaction had occurred after 48 h at 0°C. Hence the nitration was performed on the phenol, rather than the phenyl acetate.

Nitric acid (6.2 g, 0.1 mol) at -20°C was added to acetic anhydride (24 g, 22 cm^3) at -78°C. The temperature of the mixture was brought to 5°C, maintained for 5 min to ensure complete reaction and then lowered to -78°C. This nitrating mixture was added dropwise, over 5 min, to the substrate (10 g, 0.066 mol) in acetic anhydride (9.3 g, 8.6 cm^3) at -78°C. The reaction temperature was raised to 0°C and maintained for 30 min with stirring. Integration of the ^{1}H n.m.r. spectrum (lock: acetic anhydride δ 2.15 ppm) of an aliquot showed that the mixture contained *ca.* 55% of 4-methyl-2,4-dinitrocyclohexa-2,5-dien-1-one (13) ^{1}H n.m.r. (90 MHz; Ac_2O) δ 6.45 (d,1,6-H), 7.36 (dd,1,5-H) 7.87 (d,1,3-H), J_{56} = 10 Hz, J_{35} = 2 Hz.

The nitrodienone was quite unstable and usually decomposed on

work-up to give 4-methyl-2,6-dinitrophenol (14) m.p. 83°C (lit (85) 85°C); i.r. ($CDCl_3$) 3150 cm^{-1} (OH), 1535 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.40 (s,3,4-$\underline{CH}_3$), 8.09 (s,2,3-$\underline{H}$ and 5-$\underline{H}$); ^{13}C n.m.r. ($CDCl_3$, ppm) δc 20.2 (4-$\underline{C}H_3$), 129.9 (C-1), 131.8 (C-3 and C-5), 137.2 (C-4), 147.3 (C-2 and C-6).

The reaction was repeated under similar conditions and the methods employed in an attempt to isolate the dienone are briefly described below:

(i) Cold pentane (550 cm^3) at -78°C was added to the product mixture at -78°C. The colorless pentane extract was withdrawn (after 1 h at -78°C) and the solvent evaporated at 0°C when very little product was obtained.

(ii) The oily mixture left after removal of the pentane extract was dissolved in a 50% ether-pentane mixture (50 cm^3) at -78°C and the solution allowed to stand for 1 h at -78°C. The pale-yellow crystals obtained contained mainly 4-methyl-2,6-dinitrophenol. The mother liquor, after removal of the solvent at 0°C, also gave 4-methyl-2,6-dinitrophenol, presumably by decomposition of the nitrodienone.

(iii) The reaction was repeated under similar conditions and the product mixture divided into two halves: Cold ether (250 cm^3) at -78°C was added to one portion and liquid ammonia was passed into the solution (below -40°C) till the mixture was alkaline. Excess ammonia was removed and the temperature raised to 0°C. The mixture was filtered and the residue washed with ether (50 cm^3) at 0°C. The ether extract was washed with saturated sodium chloride (0°C), dried over anhydrous magnesium sulfate. The product, by ^1H n.m.r., was 4-methyl-2,6-dinitrophenol.

(iv) The other half of the reaction product was also cooled to -78°C and sodium acetate (5 g) added when the reaction attained a bright-red colour. The temperature of the mixture was raised to 0°C and then lowered to -40°C after 5 min. Cold ether (250 cm^3) at -78°C was then added and the mixture filtered. The filtrate, after removal of the solvent at 0°C, gave 4-methyl-2,6-dinitrophenol as the main product.

(v) The reaction was repeated under similar conditions and, after completion, loaded on a column of alumina (deactivated with 3% water) at -40°C. Four fractions of eluent ether (800 cm^3 each) at -40°C were collected and the solvent removed at 0°C. ^1H n.m.r. of each fraction showed 4-methyl-2,6-dinitrophenol to be the main product.

(vi) The reaction was repeated under similar conditions and the product cooled to -78°C. Cold methanol (250 cm^3) at -78°C was added and the solution set aside for 1 h. The pale-yellow crystals obtained on filtration contained 4-methyl-2,6-dinitrophenol as the main product (by ^1H n.m.r.).

The solvent was removed from the filtrate at 0°C. The white, crystalline product after washing with methylene chloride (25 cm^3) at 0°C, was identified as 5-methoxy-4-methyl-4,6-dinitrocyclohexa-2-en-1-one (42). m.p. 125°C (d); i.r. (KBr) 1710 cm^{-1} ($OCOCH_3$), 1550 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, GD_3COCD_3) δ 2.09 (s,3,4-$\underline{CH}_3$), 3.60 (s,3,$O\underline{CH}_3$), 4.89 (d,1,5-$\underline{H}$), 5.93 (d,1,6-$\underline{H}$), 6.53 (d,1,2-$\underline{H}$), 7.14 (d,1,3-$\underline{H}$), J_{56} = 11.33 Hz, J_{23} = 10 Hz; ^{13}C n.m.r. (CD_3COCD_3, ppm) δc 22.6 (4-$\underline{C}H_3$), 63.3 ($O\underline{C}H_3$), 81.7 (C-5), 82.9 (C-4), 92.7 (C-6), 131.6 (C-2), 145.6 (C-3).

Anal. Calcd. for $C_8H_{10}N_2O_6$: C,41.75; H,4.38; N,12.17

Found : C,41.81; H,4.25; N,11.85

(e) 4-Methyl-3-nitrophenol

Nitric acid (0.835 g, 13 mmol) at -20°C was added with stirring to acetic anhydride (3.4 g, 3 cm^3) at -78°C. The temperature was raised to 5°C, maintained for 5 min and then lowered to -78°C. This nitrating mixture was added to a solution of 4-methyl-3-nitrophenol (1 g, 6.6 mmol) in acetic anhydride (3.4 g, 3 cm^3) at -78°C. After 30 min, integration of the ^1H n.m.r. spectrum (lock: acetic anhydride δ 2.15 ppm) showed that the mixture contained *ca.* 30% of 4-methyl-3,4-dinitrocyclohexa-2,5-dien-1-one (71) ^1H n.m.r. (90 MHz, Ac_2O) δ 6.58 (dd,1,6-H), 7.15 (d,1,5-H), 7.47 (d,1,2-H), J_{56} = 10 Hz, J_{26} = 2 Hz.

The nitrodienone could not be crystallized from methanol at -78°C. Hence, after completion of the reaction, methylene chloride (100 cm^3) was added and liquid ammonia passed into the solution (below -40°C) till the mixture was alkaline. Excess ammonia was removed and the solution filtered at -20°C. Cold methylene chloride (100 cm^3) was added to the residue and the methylene chloride extract, after washing with saturated sodium chloride (2 X 25 cm^3) at -5°C, dried over anhydrous magnesium sulfate and filtered. The solvent was removed at 0°C to give, by ^1H n.m.r., 4-methyl-3,6-dinitrophenol (72) ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.47 (s,3,4-CH_3), 7.64 (s,1,2-H), 8.09 (s,1,5-H).

The filtrate (after removal of ammonia) was worked-up in a similar manner to give a 1:1 mixture of 4-methyl-3,5-dinitrophenol (73) ^1H n.m.r. (90 MHz, CD_3COCD_3) δ 2.30 (s,3,4-CH_3), 7.14 (s,2,2-H and 6-H) and 4-methyl-2,3-dinitrophenol (74) ^1H n.m.r. (90 MHz, CD_3COCD_3) δ 2.21 (s,3,4-CH_3), 6.44 (d,1,6-H), 6.62 (d,1,5-H), J_{56} = 10 Hz.

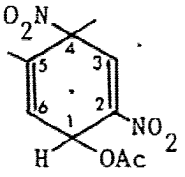
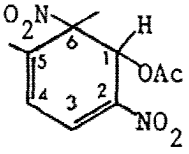
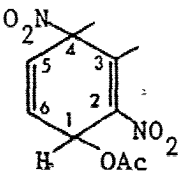
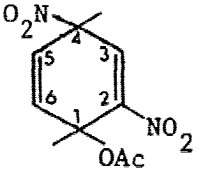
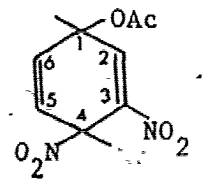
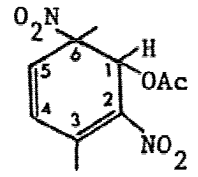
2.11 *Stereochemistry of the Adducts*

As previously described, the stereochemical assignments of *cis* and *trans* to the configuration of a diastereomeric pair of diene adducts were made on the basis of shift reagent studies. These assignments were made by comparing the lanthanide-induced shift of the 4-CH_3 protons in a given pair of 1,4 adducts. The gradients of linear plots of shift of various protons *vs.* shift of $-OCOCH_3$ protons are given in Table 2.2

The shift reagent studies were also used as an aid in the assignment of ^{13}C chemical shifts, especially to distinguish between proton-carrying carbons. The procedure involved adding the shift reagent in small portions (40-60 mg) to a solution of the adduct (350-400 mg) in chloroform-d_1 (1-2 cm^3) at 0°C and recording the ^{13}C n.m.r. after each addition. This technique was also used to verify (a) the ^{13}C n.m.r. assignment and (b) the stereochemical assignment in the case of the adducts obtained from *p*-xylene (39b).

TABLE 2.2

RELATIVE GRADIENTS OF PROTON CHEMICAL SHIFTS FOR DIENE ADDUCTS RESULTING FROM THE ADDITION OF $Eu(fod)_3$-d_{27} (GRADIENT 1-$OCOCH_3$ = 1.00)

Diene Adduct		Relative Gradient C-1	C-2	C-3	C-4	C-5	C-6
	7A	1.62	-	0.24	0.16	0.03	0.70
	7B	1.57	-	0.28	0.09	0.06	0.69
	8	1.73	-	0.34	0.22	0.16	0.50
	9A	1.48	-	0.18	0.14	0.11	0.74
	9B	1.51	-	0.19	0.06	0.14	0.72
	10A	0.69	-	0.70	0.30	0.29	0.94
	10B	0.63	-	0.52	0.24	0.43	1.02
	11D	0.59	1.09	-	0.38	0.37	0.80
	12	1.50	-	0.22	0.22	0.30	0.22

2.12 *Synthesis of Authentic Compounds*

The following section describes the synthesis of compounds required for comparison with the products obtained in the reactions of diene adducts. The purity of these products was determined by ^1H n.m.r. and i.r. (data given in Table 2.3)

(i) 1,4-Dimethyl-2-nitrobenzene was brominated in carbon tetrachloride with N-bromosuccinimide (86b) to form a mixture of benzylic bromides. The mixture, after work-up, was converted to the corresponding acetates with sodium acetate in glacial acetic acid (86c). The mixture of benzylic acetates was chromatographed over silica using pentane-ether mixtures. The 10%, 15% and 20% ether fractions were combined and, after recrystallization from ether at -20°C, gave 4-methyl-2-nitrobenzyl acetate (44a). 4-Methyl-3-nitrobenzyl acetate (45a) was prepared by acetylation of the corresponding alcohol (Aldrich, commercial grade) with acetic anhydride and pyridine (86d).

(ii) 4-Methyl-2-nitrobenzyl alcohol (44b) was prepared from the corresponding acetate by alkaline hydrolysis with sodium hydroxide in methanol (86e). An alternative procedure involving transesterification with acidified methanol also gave a good yield of 44b.

(iii) 4-Methyl-2-nitrobenzyl bromide (44c) was prepared from the corresponding acetate by reaction with excess of a saturated HBr in ether solution at 20°C for 36 h. 4-Methyl-3-nitrobenzyl bromide (45c) was prepared from the corresponding acetate using a similar procedure.

(iv) 4-Methyl-2-nitrobenzyl nitrate (44d) was prepared from the corresponding bromide by reaction with silver nitrate in acetonitrile

(86f). 4-Methyl-3-nitrobenzyl nitrate (45d) was also obtained in a similar manner from the corresponding bromide.

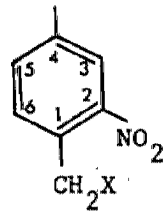
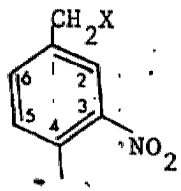
(v) (4-Methyl-2-nitrophenyl)nitromethane (44e) was prepared from the corresponding bromide by reaction with silver nitrite in ether (86g). (4-Methyl-3-nitrophenyl)nitromethane (45e) was prepared in a similar manner from the corresponding bromide.

(vi) 4-Methyl-3-nitrobenzyl nitrite (45f) was prepared from the corresponding alcohol by reaction with sodium nitrite in aqueous sulfuric acid (86h). A similar reaction with 4-methyl-2-nitrobenzyl alcohol gave back the alcohol.

(vii) 3,6-Dimethyl-2-nitrophenyl acetate (47) was prepared by acetylation of the corresponding phenol with acetic anhydride (86a). The phenol was obtained by the decomposition of the nitrodienone from the *ipso* nitration of 2,5-dimethylphenol (78).

TABLE 2.3

^{1}H n.m.r. AND i.r. SPECTRAL DATA OF AUTHENTIC COMPOUNDS SYNTHESIZED FOR COMPARISON PURPOSES

COMPOUND		^{1}H n.m.r. (δ)						i.r. (cm^{-1})
	X =	CH_3	CH_2	C-2	C-3	C-5	C-6	
 44	(a) OAc	2.38	5.39	2.08 (OAc)	7.82	7.41	7.41	1730, 1520, 1335 and 1230
	(b) OH	2.39	4.88	–	7.89	7.43	7.60	3320, 1555, 1365 and 1045
	(c) Br	2.40	4.76	–	7.82	7.40	7.40	1515 and 1345
	(d) ONO_2	2.43	5.80	–	7.97	7.48	7.48	1640, 1535, 1350 and 1280
	(e) NO_2	2.47	5.73	–	8.04	7.36	7.53	1555, 1525, 1370 and 1360
 45	(a) OAc	2.50	5.08	7.90	2.07 (OAc)	7.29	7.46	1740, 1530, 1345 and 1235
	(b) OH	2.49	4.61	7.85	–	7.21	7.42	3400, 1530, 1345 and 1040
	(c) Br	2.50	4.44	7.97	–	7.28	7.51	1520 and 1345
	(d) ONO_2	2.55	5.45	7.98	–	7.36	7.98	1620, 1525, 1340 and 1270
	(e) NO_2	2.58	5.44	8.04	–	7.38	7.57	1550, 1525, 1376 and 1340
	(f) ONO	2.56	5.68	7.85	–	7.21	7.42	1680, 1610, 1510 and 1335

COMPOUND	C-1	C-2	C-3	C-4	C-5	C-6	
3,6-Dimethyl-2-nitrophenyl acetate (47)	2.16	-	2.30	7.05	7.25	2.24	1770, 1530, 1360 and 1215
Compounds obtained from the nitration of nitroarenes							
1,2-Dimethyl-3,4-dinitrobenzene (15)	2.22	2.41	-	-	7.41	7.92	1540 and 1352
1,2-Dimethyl-3,5-dinitrobenzene (16)	2.46	2.51	-	8.35	-	8.18	1520 and 1348
1,2-Dimethyl-4,5-dinitrobenzene (17)	2.37	2.37	7.63	-	-	7.63	1548, 1528, 1378 and 1338
1,2-Dimethyl-3,6-dinitrobenzene (18)	2.41	2.41	-	7.61	7.61	-	(not isolated)
1,4-Dimethyl-2,3-dinitrobenzene (19)	2.35	-	-	2.35	7.35	7.35	1525 and 1355
1,4-Dimethyl-2,5-dinitrobenzene (20)	2.58	-	7.88	2.58	-	7.88	(not isolated)
1,4-Dimethyl-2,6-dinitrobenzene (21)	2.47	-	7.78	2.47	7.78	-	1530 and 1345

2.13 *Reactions of the Adducts*

(a) 1,2-Dimethyl-4-nitrobenzene

The exchange and rearomatization reactions on the adducts from 1,2-dimethyl-4-nitrobenzene were carried out on a 2:1 mixture of the adducts 7(A) and 7(B). The reactions were generally followed by ^{1}H n.m.r. spectroscopy and when isomerisation or exchange was observed, the reaction was repeated on the pure isomers 7(A) and 7(B). The reactions can be classified under two sections

(i) Reactions under acidic conditions; and

(ii) Reactions with nucleophiles.

(i) Reactions under acidic conditions: Reactions of the diene 7 with

(1) Borontrifluoride Etherate

Cold BF_3-etherate solution (300 mm^3) was added to the diene 7 (100 mg, 0.39 mmol) in an n.m.r. tube also at -78°C. The temperature was raised to 0°C when the diene went into solution and decomposed within 5 min. After work-up and examination by ^{1}H n.m.r. and g.l.c.-m.s., the products were identified as 1,2-dimethyl-4-nitrobenzene (78%, m/e 151), 1,2-dimethyl-3,5-dinitrobenzene (8%, m/e 196) and 1,2-dimethyl-3,4-dinitrobenzene (14%, m/e 196).

(2) Borontrifluoride Etherate and Mesitylene

Cold BF_3-etherate solution (250 mm^3) was added to a solution of the diene 7 (100 mg, 0.39 mmol) and mesitylene (250 mg, 2.1 mmol) in methylene chloride (250 mm^3) at -78°C. The solution was allowed to warm to 20°C and left to stand for 1 h. After work-up, the composition of the the product by ^{1}H n.m.r. and g.l.c.-m.s. was found to be 1,2-dimethyl-4-

nitrobenzene (1%, m/e 151) and 2-nitro-2',4,4',5,6'-pentamethyl biphenyl (99%, m/e 269). ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 1.88 (s,6,2'-CH_3 and 6'-CH_3), 2.25 (s,6,4-CH_3 and 4'-CH_3), 2.28 (s,3,5-CH_3), 6.81 (s,2,3'-H and 5'-H), 6.90 (s,1,6-H), 7.73 (s,1,3-H).

Mass calculated for $C_{17}H_{19}NO_2$: 269.142

Found : 269.143

(3) Trifluoroacetic Acid

Cold trifluoroacetic acid (450 mm^3) was added to the diene 7 (64 mg, 0.25 mmol) in an n.m.r. tube at -78°C. The temperature was raised to 0°C and ^{1}H n.m.r. after 1 h indicated no decomposition. The temperature was raised to 20°C and ^{1}H n.m.r. after 4 h indicated partial rearomatization. Hence, the reaction mixture was left at 20°C for 18 h and then worked-up to give, by ^{1}H n.m.r. and g.l.c.-m.s., 1,2-dimethyl-4-nitrobenzene (72%, m/e 151), 1,2-dimethyl-3,5-dinitrobenzene (13%, m/e 196) and 1,2-dimethyl-3,4-dinitrobenzene (15%, m/e 196).

(4) 5% Sulfuric Acid in Methanol

Cold 5% sulfuric acid in methanol (25 cm^3) was added to the diene 7A (600 mg, 2.34 mmol) at 0°C. The mixture was allowed to warm to 20°C and the solution stirred for 18 h. The product was transferred with ether (25 cm^3) to a two-necked flask and neutralized with liquid ammonia at -78°C. The solution was filtered and the solvent removed from the filtrate at 0°C. The product was dissolved in ether (50 cm^3) and washed with water (2 X 25 cm^3). The ether extract was dried over anhydrous magnesium sulfate, filtered and the solvent removed at 0°C. The product was identified as one diastereomer of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dien-1-ol (33A) i.r. (Neat) 3400 and 1050 cm^{-1}(OH), 1555 cm^{-1}(NO_2);

^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 1.84 (d,3,5-C$\underline{H}_3$), 1.89 (s,3,4-C$\underline{H}_3$), 3.42 (s, 1,-O$\underline{H}$), 5.25 (d,1,1-$\underline{H}$), 5.94 (m,1,6-$\underline{H}$), 7.19(s,1,3-$\underline{H}$), J_{16} = 4 Hz, $J_{6,5\text{-}CH_3}$ = 1.40 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 17.5 (5-$\underline{C}H_3$), 23.5 (4-$\underline{C}H_3$), 60.3 (C-1), 89.1 (C-4), 127.5 (C-6), 131.2 (C-3) 132.8 (C-5) 151.6 (C-2).

Under similar conditions, the diene 7B gave the other diastereomer of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dien-1-ol (33B) i.r. (Neat) 3420 and 1053 cm^{-1} (OH), 1550 cm^{-1} (NO_2); ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 1.82 (s,6,4-C$\underline{H}_3$ and 5-C$\underline{H}_3$), 3.42 (s,1,-O$\underline{H}$), 5.18 (d,1,1-$\underline{H}$), 6.00 (m,1, 6-$\underline{H}$), 7.17 (s,1,3-$\underline{H}$), J_{16} = 4 Hz, $J_{6,5\text{-}CH_3}$ = 1.40 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 17.4 (5-$\underline{C}H_3$), 23.9 (4-$\underline{C}H_3$), 60.2 (C-1), 88.3 (C-4), 127.6 (C-6), 130.4 (C-3), 132.5 (C-5), 151.6 (C-2).

(5) Trifluoromethanesulfonic Acid

Cold trifluoromethanesulfonic acid (300 mm^3) was added to the diene 7 (90 mg, 0.35 mmol) in an n.m.r. tube at -78°C. The temperature was raised to -20°C and the diene decomposed completely in 5 min (^{1}H n.m.r.). After work-up, the product composition by ^{1}H n.m.r. and g.l.c.-m.s. was found to be 1,2-dimethyl-4-nitrobenzene (31%, m/e 151), 1,2-dimethyl-3,5-dinitrobenzene (31%, m/e 196), 1,2-dimethyl-3,4-dinitrobenzene (25%, m/e 196) and 1,2-dimethyl-4,5-dinitrobenzene (13%, m/e 196).

(6) Hydrogen Bromide in Ether

Cold ethereal solution (500 mm^3) of saturated hydrogen bromide was added to the diene 7 (64 mg, 0.25 mmol) at -78°C. The temperature was raised to 0°C and the ^{1}H n.m.r. after 90 min indicated partial decomposition. The reaction mixture was left for 18 h at 0°C and after work-up, the product composition by ^{1}H n.m.r. was 1,2-dimethyl-4-nitro-

benzene (95%) and 1,2-dimethyl-4,5-dinitrobenzene (5%).

(7) Acetic Acid

Acetic acid (450 mm^3) was added to the diene 7 (70 mg, 0.27 mmol) at 20°C. ^1H n.m.r. of the reaction mixture, after 30 days at 20°C, showed the absence of any reaction. The solution was heated for 15 min at 100°C when brown fumes were evolved from the reaction mixture. ^1H n.m.r. of the product indicated that the rearomatization was complete. After work-up, the product composition, as determined by ^1H n.m.r. and g.l.c.-m.s. was 1,2-dimethyl-4-nitrobenzene (49%, m/e 151) and 1,2-dimethyl-3,5-dinitrobenzene (51%, m/e 196).

10% Acetic anhydride (v/v) in acetic acid (320 mm^3) was heated to 100°C for 10 min, cooled to 20°C and the diene 7 (50 mg, 0.20 mmol) added. The solution was heated to 100°C for 10 min after which ^1H n.m.r. indicated complete decomposition. After work-up, the product composition by ^1H n.m.r. and g.l.c.-m.s. was 1,2-dimethyl-4-nitrobenzene (44%, m/e 151) and 1,2-dimethyl-3,5-dinitrobenzene (56%, m/e 196).

A solution of the diene 7 (64 mg, 0.25 mmol) and hydroquinone (28 mg, 0.25 mmol) in acetic acid (400 mm^3) was heated for 20 min at 100°C. After work-up, the product composition, by ^1H n.m.r. and g.l.c.-m.s. was 1,2-dimethyl-4-nitrobenzene (68%, m/e 151) and 1,2-dimethyl-3,5-dinitrobenzene (32%, m/e 196).

(ii) Reactions with nucleophiles: Reactions of the diene 7 with

(8) Pyridine-d_5

Cold pyridine-d_5 (315 mm^3) was added to the diene 7 (70 mg, 0.27 mmol) in an n.m.r. tube at -78°C. The solution immediately attained an orange-red colour. The temperature of the mixture was raised to 0°C and ^1H n.m.r., after 2 [illegible]m, indicated complete decomposition. After work-up, the product composition by ^1H n.m.r. and g.l.c.-m.s. was shown to be 1,2-dimethyl-4-nitrobenzene (3%, m/e 151), 1,2-dimethyl-3,4-dinitrobenzene (5%, m/e 196) and 1,2-dimethyl-4,5-dinitrobenzene (92%, (92%, m/e 196).

The reaction was repeated by adding pyridine-d_5 (21 mm^3) to a solution of the diene 7 (64 mg, 0.25 mmol) in chloroform-d_1 (290 mm^3) at -60°C. The temperature was raised to 0°C (in 10° intervals) and the progress of the reaction monitored by ^1H n.m.r. for 2 h. The conversion of the diene to 1,2-dimethyl-4,5-dinitrobenzene proceeded smoothly as seen from the following table:

Time	Product Composition	
	Diene	Arenes
30 min	63%	37%
60 min	43%	57%
120 min	36%	63%

The reaction mixture was worked-up after 18 h at 0°C and the product composition, by ^1H n.m.r. and g.l.c.-m.s. was shown to be 1,2-dimethyl-4-nitrobenzene (2%, m/e 151), 1,2-dimethyl-3,4-dinitrobenzene (3%, m/e 196) and 1,2-dimethyl-4,5-dinitrobenzene (95%, m/e 196).

(9) 2,6-Dimethylpyridine

Cold 2,6-dimethylpyridine (15 mm^3) was added to the diene 7A (64 mg, 0.25 mmol) in an n.m.r. tube at -78°C. The mixture was allowed to warm to 0°C and ^1H n.m.r. after 5 min indicated that the diene was still present. The decomposition was complete after 15 min and the product composition, by ^1H n.m.r. and g.l.c.-m.s., was shown to be 1,2-dimethyl-4-nitrobenzene (2%, m/e 151), 1,2-dimethyl-3,4-dinitrobenzene (4%, m/e 196) and 1,2-dimethyl-4,5-dinitrobenzene (94%, m/e 196).

The reaction was repeated by adding cold 2,6-dimethylpyridine (58 mm^3) to a solution of the diene (64 mg, 0.25 mmol) in chloroform-d_1 (290 mm^3) at -60°C. The temperature of the mixture was raised to 0°C and maintained for 2 h at this temperature. After work-up, the product composition by ^1H n.m.r. was shown to be 1,2-dimethyl-4,5-dinitrobenzene (15%), diene 7A (67%) and another diene, later identified as 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (17%).

(10) *tert*-Butylamine

Cold *tert*-butylamine (26 mm^3) was added to a solution of the diene 7 (64 mg, 0.25 mmol) in chloroform-d_1 (290 mm^3) at 0°C. There was no perceptible decomposition (by ^1H n.m.r.) after 30 min at 0°C. The reaction mixture was worked-up after 18 h at 0°C and ^1H n.m.r. of the product in chloroform-d_1 showed the presence of a compound with a *tert*-butyl group (δ 1.48 ppm). The product composition, by ^1H n.m.r. and g.l.c.-m.s. was shown to be 1,2-dimethyl-4-nitrobenzene (4%, m/e 151), 1,2-dimethyl-3,5-dinitrobenzene (7%, m/e 196), 1,2-dimethyl-3,4-dinitrobenzene (10%, m/e 196), 1,2-dimethyl-4,5-dinitrobenzene (60%, m/e 196) and a compound of mass 222, which was tentatively identified as

N-*tert*-butyl-4,5-dimethyl-2-nitroaniline (19%).

(11) Sodium Methoxide in Methanol

Sodium methoxide (42 mg, 0.78 mmol) was added to a solution of the diene 7A (100 mg, 0.39 mmol) in methanol (350 mm^3) at -78°C. The mixture attained an immediate orange-red colour. The temperature of the mixture was raised to 0°C and maintained for 2 h to ensure complete reaction. After work-up, the product was identified by ^1H n.m.r. as one diastereomer of 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl methyl ether. The reaction was repeated under similar conditions on the diene 7B when the same diastereomer of 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl methyl ether was obtained.

The reaction was repeated on the crude nitration product of 1,2-dimethyl-4-nitrobenzene (containing *ca.* 50% diene adducts) under similar conditions. The product, after work-up, was injected into the inlet of a Prep LC system using benzene as the solvent at a flow-rate of 0.1 $dm^3 min^{-1}$. The first fraction contained mainly a mixture of aromatic compounds, present in the nitration product. The second fraction, after recrystallization from ether at -20°C gave 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl methyl ether (36) m.p. 69°C; u.v. (CH_3OH) 328 nm (395 $m^2 mol^{-1}$), 203 nm (950 $m^2 mol^{-1}$); i.r. (Nujol) 1555 cm^{-1} (NO_2), 1090 cm^{-1} (C-O-C); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.88 (s,3,6-CH_3), 2.19 (d,3,5-CH_3), 3.55 (s,3,OCH_3), 5.12 (s,1,1-H), 6.25 (dd,1,4-H), 7.38 (d,1,3-H); J_{34} = 6 Hz, $J_{4,5\text{-}CH_3}$ = 1.5 Hz. Irradiation of the 5-CH_3 (d) resonance resulted in the collapse of the 4-H (dd) resonance to a doublet whereas, irradiation of the 3-H (d) resonance resulted in the collapse of the 4-H (dd) resonance to a different doublet; ^{13}C n.m.r. ($CDCl_3$, ppm) δc

19.6 (6-$\underline{C}H_3$), 20.0 (5-$\underline{C}H_3$), 60.5 ($O\underline{C}H_3$), 75.1 (C-1), 91.6 (C-6), 123.4 (C-4), 129.6 (C-3), 142.8 (C-5), 146.0 (C-2).

Anal. Calcd. for $C_9H_{12}N_2O_5$: C,47.37%; H,5.30%; N,12.27%

Found : C,47.55%; H,5.24%, N,12.14%

(12) Potassium Hydroxide in Acetonitrile-d_3

Acetonitrile-d_3 (315 mm^3) was added to a mixture of potassium hydroxide (28 mg, 0.5 mmol) and 18-crown-6 (132 mg, 0.5 mmol). The mixture was warmed to 40°C, cooled to -78°C and the diene 7 (64 mg, 0.25 mmol) added. The temperature was raised to 0°C and the dark-green solution worked up after 30 min to give, by ^1H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene as the sole product.

(13) Potassium *tert*-Butoxide in Acetonitrile-d_3

Potassium *tert*-butoxide (42 mg, 0.375 mol) was added to the diene 7 (64 mg, 0.25 mmol) in acetonitrile-d_3 (315 mm^3) at -35°C. The temperature was raised to 0°C and maintained for 30 min. The dark-green solution was worked-up and the product composition, by ^1H n.m.r. and g.l.c.-m.s. was 1,2-dimethyl-4-nitrobenzene (24%, m/e 151), 1,2-dimethyl-3,5-dinitrobenzene (12%, m/e 196), 1,2-dimethyl-3,4-dinitrobenzene (4%, m/e 196) and 1,2-dimethyl-4,5-dinitrobenzene (60%, m/e 196).

(14) Sodium Phenoxide

Sodium phenoxide was prepared in the following manner:

A solution of 0.5N sodium hydroxide (100 cm^3) was added to a solution of phenol (5 g) in ether (60 cm^3) in a separatory funnel and thoroughly mixed. The aqueous layer was withdrawn and washed with ether (10 X 100 cm^3). The solvent was distilled under reduced pressure and the product vacuum-dried.

Sodium phenoxide (78 mg, 0.5 mmol) was added to a solution of the diene 7 (64 mg, 0.25 mmol) in acetonitrile (64 mg, 0.25 mmol) at -40°C. The mixture immediately attained an orange-red colour. The temperature of the mixture was raised to 0°C and maintained for 30 min. The dark-brown solution was then worked-up and the product, as analyzed by ^{1}H n.m.r. and g.l.c.-m.s. was found to be 1,2-dimethyl-4-nitrobenzene (17%, m/e 151), 1,2-dimethyl-3,5-dinitrobenzene (3%, m/e 196), 1,2-dimethyl-3,4-dinitrobenzene (3%, m/e 196) and 1,2-dimethyl-4,5-dinitrobenzene (77%, m/e 196).

(15) Sodium Thiophenoxide

Sodium thiophenoxide was prepared as follows:

A solution of thiophenol (6 g, 0.06 mol) in toluene (30 cm^3) was added to molten sodium (1.15 g, 0.05 mol) in toluene (20 cm^3). The mixture was heated under reflux for 30 min and the solvent then removed under reduced pressure. The product was powdered and vacuum-dried.

Sodium thiophenoxide (50 mg, 0.38 mmol) was added to a solution of the diene 7 (64 mg, 0.25 mmol) in acetonitrile (400 mm^3) at -40°C. The temperature was increased to 0°C and ^{1}H n.m.r. after 5 min indicated complete decomposition of the diene. After work-up, the product composition by ^{1}H n.m.r. and g.l.c.-m.s. was 1,2-dimethyl-4-nitrobenzene (1%, m/e 151) and a compound of mass 259 (99%). The product, on recrystallization from ether gave pale-yellow, cubic crystals of 4,5-dimethyl-2-nitrophenyl phenyl sulfide (32) m.p. 79°C; ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 2.07 (s,3,4-CH_3), 2.21 (s,3,5-CH_3), 6.60 (s,1,6-H), 7.45 (m,5,C_6H_5), 7.96 (s,1,3-H); mass spectrum (70 eV) m/e (relative intensity) 259.057 (36, Mass calculated for $C_{14}H_{13}NO_2S$: 259.067), 199 (16), 198 (55), 196 (45),

195 (100), 182 (20), 181 (95), 166 (15).

(16) Potassium Nitrite

Methanol-d_4 (315 mm^3) was added to a mixture of the diene 7 (70 mg, 0.27 mmol), potassium nitrite (35 mg, 0.42 mmol) and 18-crown-6 (35 mg, 0.41 mmol) at -78°C in an n.m.r. tube. The ^1H n.m.r. of the solution after 5 min at 0°C indicated complete decomposition. The product, after work-up was shown by ^1H n.m.r. and g.l.c.-m.s. to be 1,2-dimethyl-4,5-dinitrobenzene (100%, m/e 196).

(17) Potassium Acetate

A mixture of potassium acetate (37 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) in acetonitrile-d_3 (400 mm^3) was warmed to 50°C, cooled to 0°C and the diene 7 (64 mg, 0.25 mmol) added. The decomposition was complete in 5 min and the product, by ^1H n.m.r. was found to be 1,2-dimethyl-4,5-dinitrobenzene.

(18) Potassium Cyanide

Cold methanol-d_4 (315 mm^3) was added to a mixture of the diene 7 (64 mg, 0.25 mmol), potassium cyanide (25 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) at -78°C. The mixture was allowed to warm to 0°C and maintained for 30 min. After work-up, the major product, by ^1H n.m.r. and g.l.c.-m.s. was 2,3-dimethyl-6-nitrobenzonitrile (94%, m/e 176) (25) (90 MHz, $CDCl_3$) δ 2.45 (s,3,2-CH_3), 2.60 (s,3,3-CH_3), 7.54 (d,1,4-H), 8.04 (d,1,5-H) J_{45} = 8.6 Hz. The minor product obtained was 1,2-dimethyl-4,5-dinitrobenzene (6%, m/e 196).

The reaction was repeated under similar conditions using acetonitrile-d_3 (315 mm^3) as the solvent and the product composition by ^1H n.m.r. was found to be 2,3-dimethyl-6-nitrobenzonitrile (70%) and

1,2-dimethyl-4,5-dinitrobenzene (30%).

When the reaction was carried out in 50% pyridine-methanol (v/v; 700 mm^3), the product composition by ^1H n.m.r. and g.l.c.-m.s. was found to be 2,3-dimethyl-6-nitrobenzonitrile (58%; m/e 176) and 1,2-dimethyl-4,5-dinitrobenzene (42%, m/e 196).

(19) Potassium Halide in Methanol-d_4

Cold methanol (400 mm^3) was added to a mixture of the diene 7 (64 mg, 0.25 mmol), 18-crown-6 (99 mg, 0.38 mmol) and potassium iodide (62 mg, 0.38 mmol) at -78°C. The temperature was raised to 0°C and ^1H n.m.r. after 1 h showed that no reaction had occurred. The mixture was allowed to warm to 20°C and maintained for 48 h. After work-up, ^1H n.m.r. showed the products to be 1,2-dimethyl-4,5-dinitrobenzene (58%) and 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl (d_3) ether (34, 42%), identified later by comparison of its spectrum with that of the authentic sample.

The reaction was repeated under similar conditions with potassium bromide and the mixture worked-up after 78 h at 20°C to give, by ^1H n.m.r., 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl (d_3) ether (34, 45%), 1,2-dimethyl-4,5-dinitrobenzene (22%) and 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (8, 33%). The last compound was identified by comparison of its spectrum with that of an authentic sample.

The reaction was repeated with potassium chloride under similar conditions and the mixture worked-up after 7 days at 20°C to give, by ^1H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene as the only product.

With potassium fluoride under similar conditions, the product composition by ^{1}H n.m.r. after 20 h at 0°C was 1,2-dimethyl-4,5-dinitrobenzene (28%), 4,5-dimethyl-2,6-dinitrocyclohexa-2,5-dienyl methyl (d_3) ether (57%) and 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (15%).

(20) Potassium Halide in Acetonitrile-d_3

Acetonitrile-d_3 (400 mm^3) was added to a mixture of potassium fluoride (22 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol). The mixture was warmed to 50°C and the solution cooled to 0°C. The diene 7 (64 mg, 0.25 mmol) was added and the reaction worked-up after 20 min at 0°C to give, by ^{1}H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene (*ca.* 100%).

The reaction was repeated with potassium bromide under similar conditions (18 h, 0°C) to give, by ^{1}H n.m.r. and g.l.c.-m.s., 1,2-dimethyl-4,5-dinitrobenzene (95%, m/e 196), 1,2-dimethyl-3,4-dinitrobenzene (3%, m/e 196) and 1,2-dimethyl-3,5-dinitrobenzene (2%, m/e 196). The reaction was repeated under similar conditions and the mixture worked-up after 5 h at 0°C to give, by ^{1}H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene (32%) and 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (68%). The product mixture from this reaction on treatment with potassium iodide (62 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) in acetonitrile (400 mm^3) for 18 h at 0°C gave, by ^{1}H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene as the main product.

The reaction was repeated with potassium iodide under similar conditions and the reaction mixture worked-up after 1 h at 0°C to give, by ^{1}H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene (77%) and 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (23%). The product mixture from

this reaction on treatment with potassium iodide (62 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) in methanol (400 mm^3) for 18 h at 0°C gave, by ^1H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene as the main product.

(21) Potassium Bromide in Acetic Anhydride

Cold 50% acetic anhydride in acetonitrile (v/v, 700 mm^3) was added to a mixture of potassium bromide (45 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) in an n.m.r. tube. The mixture was warmed to 50°C, cooled to 0°C and the diene 7 (64 mg, 0.25 mmol) added. The reaction mixture was worked-up after 18 h at 0°C to give, by ^1H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene (3%), diene 7 (22%) and 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (8, 75%).

The reaction was repeated under similar conditions using acetic anhydride (400 mm^3) to give, by ^1H n.m.r., diene 7 (22%) and, as in other cases where this compound was formed, one diastereomer of 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (8, 75%).

The reaction was repeated on the crude nitration product of 1,2-dimethyl-4-nitrobenzene (containing *ca.* 50% dienes) using a proportional amount of potassium bromide and acetic anhydride. The reaction product was worked-up after 48 h at 0°C and injected into the inlet of a Prep LC system using benzene as the solvent at a flowrate of 0.11 dm^3 min^{-1}. The first fraction contained mainly aromatic compounds, present in in the nitration product. The second fraction, after recrystallization from ether at -20°C, gave one diastereomer of 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (8) m.p. 99°C; u.v. (CH_3OH) 325 nm (1145 m^2 mol^{-1}), 195 nm (1380 m^2 mol^{-1}); i.r. (Nujol) 1753 and 1210 cm^{-1} ($OCOCH_3$), 1555 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.78 (s,3,6-CH_3),

2.08 (s,3,OCOC$\underline{H}_3$), 2.12 (d,3,5-C$\underline{H}_3$), 6.35 (dd,1,4-$\underline{H}$), 6.93 (s,1,1-$\underline{H}$), 7.48 (d,1,3-$\underline{H}$), J_{34} = 7 Hz, $J_{4,5\text{-}CH_3}$ = 1.5 Hz. Irradiation of the 4-H (dd) resonance resulted in the collapse of the 5-CH_3(d) resonance to a singlet and also, the 3-H (d) resonance to a singlet; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 19.3 (6-C$\underline{H}_3$), 19.8 (5-C$\underline{H}_3$), 20.4 (OCOC$\underline{H}_3$), 65.5 (C-1), 90.9 (C-6), 123.4 (C-4), 130.6 (C-3), 130.9 (C-5), 142.2 (C-2), 169.0 (O$\underline{C}$OCH$_3$).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C,46.88; H,4.72; N,10.93

Found : C,46.80; H,4.79; N,10.82

(22) Potassium Thiocyanate

Acetonitrile-d_3 (400 mm^3) was added to a mixture of potassium thiocyanate (36 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol). The mixture was warmed to 50°C, cooled to 0°C and the diene 7 (64 mg, 0.25 mmol) added. The reaction mixture was worked-up after 18 h at 0°C to give, by ^{1}H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene (86%) and the diene 8 (14%).

The reaction was repeated using methanol (400 mm^3) as the solvent and the reaction mixture worked-up after 18 h at 0°C to give, by ^{1}H n.m.r. and g.l.c.-m.s., 1,2-dimethyl-4,5-dinitrobenzene (100%, m/e 196).

(23) Thermal Decomposition

A solution of diene 7 (64 mg, 0.25 mmol) in toluene (10 cm^3) was heated under reflux for 1 h. The solvent was then removed from the yellow solution under reduced pressure and the product composition, by ^{1}H n.m.r. and g.l.c.-m.s., was 1,2-dimethyl-4-nitrobenzene (78%, m/e 151) and 1,2-dimethyl-3,5-dinitrobenzene (22%, m/e 196). A similar result was obtained when a 1% solution of the diene 7 in acetone was injected

into the inlet (270°C) of a gas chromatograph.

(24) 80% Methanol in Water

A cold solution of 80% methanol in water (v/v, 350 mm^3) was added to the diene *7* (64 mg, 0.25 mmol) and the resulting mixture was left in an ultrasonic bath at ambient temperature until the solution was complete (72 h). The ^1H n.m.r. of the product indicated complete decomposition of the diene and the composition by g.l.c.-m.s. was found to be 1,2-dimethyl-4-nitrobenzene (82%, m/e 151) and 1,2-dimethyl-4,5-dinitrobenzene (18%, m/e 196).

(B) Reactions of 4,5-Dimethyl-2,4-dinitrocyclohexa-2,5-dien-1-ol (33)

The reactions were carried out on a 2:1 mixture of the adducts 33A and 33B. The reactions were followed by ^{1}H n.m.r. spectroscopy and wherever stereochemical integrity was maintained, the reactions were repeated on the pure isomers.

(25) Sulfuric Acid in Acetic Anhydride

Cold 2% sulfuric acid in acetic anhydride (v/v, 250 mm^3) was added to a solution of the diene 33 (90 mg, 0.42 mmol) in acetic anhydride (250 mm^3) at 0°C. The temperature was raised to 35°C and ^{1}H n.m.r., after 30 min, indicated that no reaction had occurred. The mixture was left at 35°C for 18 h, after which ^{1}H n.m.r. indicated slight rearomatization (*ca.* 5%).

To the above solution at 0°C was added conc. sulfuric acid (10 mm^3) and the temperature raised to 35°C. The decomposition was complete in 2 min and the product composition after work-up was (by ^{1}H n.m.r.) 1,2-dimethyl-4-nitrobenzene (82%), 1,2-dimethyl-3,5-dinitrobenzene (11%) and 1,2-dimethyl-3,4-dinitrobenzene (7%),

(26) Pyridine-d_5 and Acetic Anhydride

Cold pyridine-d_5 (300 mm^3) was added to the diene 33 (90 mg, 0.42 mmol) at -78°C. The solution was allowed to warm to 0°C and ^{1}H n.m.r., after 18 h, showed that no reaction had occurred. Cold acetic anhydride (450 mm^3) was added to the solution at 0°C. The mixture immediately attained a dark-brown colour and ^{1}H n.m.r. showed that the decomposition was complete. After work-up, the product composition by ^{1}H n.m.r. was 1,2-dimethyl-4,5-dinitrobenzene (*ca.* 100%).

The reaction was repeated by adding cold pyridine-d_5 (40 mm^3) to a solution of the diene 33 (70 mg, 0.33 mmol) in acetic anhydride (300 mm^3) at -40°C. The temperature was raised to 0°C and the ^1H n.m.r. (lock: acetic anhydride δ2.15 ppm) recorded. The acetylation of the diene 33 to the diene 7 was complete within 6 min, although partial isomerisation to 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (8, *ca.* 5%) was also observed. The reaction mixture was left for 18 h at 0°C and the product, after work-up, was 1,2-dimethyl-4,5-dinitrobenzene (^1H n.m.r.).

(27) 2,6-Dimethylpyridine and Acetic Anhydride

Cold 2,6-dimethylpyridine (58 mm^3) was added to a solution of the diene 33 (70 mg, 0.33 mmol) in acetic anhydride (300 mm^3) at -60°C. The temperature was raised to 0°C and ^1H n.m.r. after 150 min showed that acetylation had occurred, although the diene 33 was still present (*ca.* 50%). The reaction mixture was left for 18 h at 0°C and then worked-up. The product composition by ^1H n.m.r. was 1,2-dimethyl-4,5-dinitrobenzene (3%), diene 7 (40%) and 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate (8, 57%).

(28) Methyl Iodide and Moist Silver Oxide

Moist silver oxide was prepared in the following manner:

5N Sodium hydroxide (10 cm^3) was added to a solution of silver nitrate (3.38 g) in distilled water (5 cm^3). The precipitate of silver oxide was filtered under suction and washed with distilled water (5 X 20 cm^3) to remove excess alkali. Freshly prepared moist silver oxide was then used for the reaction.

A mixture of moist silver oxide (1.90 g), methyl iodide (7 cm^3), potassium hydroxide (0.01 g) and the diene 33A (0.52 g) was stirred for 5 h at 20°C. The mixture was then filtered and the residue washed with ether (5 X 60 cm^3). The ether extract was dried over anhydrous magnesium sulfate and the solvent (ether and excess methyl iodide) removed at 15°C. The product, after vacuum drying, was found to be one diastereomer of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl ether (34A) ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.86 (d,3,5-CH_3), 1.89 (s,3, 4-CH_3), 3.35 (s,3,OCH_3), 4.99 (d,1,1-H), 6.04 (m,1,6-H), 7.18 (s,1,3-H), J_{16} = 4 Hz, $J_{6,5\text{-}CH_3}$ = 1.35 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 17.6 (5-CH_3), 23.3 (4-CH_3), 56.8 (OCH_3), 68.0 (C-1), 88.9 (C-4), 125.5 (C-6), 131.6 (C-3), 133.6 (C-5), 150.4 (C-2).

The reaction was repeated on the diene 33B to give the other diastereomer of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl ether (34B) ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.86 (s,6,4-CH_3 and 5-CH_3), 3.30 (s,3,OCH_3), 4.99 (d,1,1-H), 5.96 (m,1,6-H), 7.15 (s,1,3-H), J_{16} = 4 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 18.7 (5-CH_3), 23.9 (4-CH_3), 54.9 (OCH_3), 67.1 (C-1), 88.1 (C-4), 125.9 (C-6), 131.4 (C-3), 133.7 (C-5), 150.3 (C-2).

(C) Reactions of 5,6-Dimethyl-2,6-dinitrocyclohexa-2,4-dienyl Methyl Ether (36) with

(29) Borontrifluoride Etherate

Cold borontrifluoride etherate (250 mm^3) was added to diene 36 (70 mg, 0.30 mmol) in an n.m.r. tube at -78°C. The temperature was raised to 0°C and ^1H n.m.r. after 30 min showed no decomposition. The mixture was warmed to 20°C and ^1H n.m.r. after 7 days indicated partial decomposition of the diene. The reaction mixture was worked-up after 20 days at 20°C to give, by ^1H n.m.r. and g.l.c.-m.s., 1,2-dimethyl-4-nitrobenzene (58%, m/e 151) and 2,3-dimethyl-6-nitroanisole (42%, m/e 181). The latter compound was identified from the ^1H n.m.r. spectrum and it had (90 MHz, $CDCl_3$) δ 2.22 (s,3,2-CH_3), 2.29 (s,3,3-CH_3), 3.82 (s,3,OCH_3), 6.95 (d,1,4-H), 7.54 (d,1,5-H), J_{45} = 9 Hz.

(30) Pyridine-d_5

Cold pyridine-d_5 (150 mm^3) was added to a solution of the diene 36 (56 mg, 0.25 mmol) in chloroform-d_1 (300 mm^3) at -78°C. The temperature was raised to 0°C and ^1H n.m.r. after 30 min gave no evidence of docomposition of the diene. The mixture was left at 20°C for 48 h and then worked-up to give, by ^1H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene.

(31) Potassium Iodide in Acetonitrile-d_3

Acetonitrile-d_3 (415 mm^3) was added to potassium iodide (62 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) and the mixture cooled to 0°C after warming to 50°C. The diene 36 (60 mg, 0.26 mmol) was then added and the mixture warmed to 20°C. After 18 h, the mixture was worked-up to give, by ^1H n.m.r., 1,2-dimethyl-4,5-dinitrobenzene.

(32) Potassium Nitrite in Methanol-d_4

Cold methanol-d_4 (315 mm^3) was added to a mixture of the diene 36 (60 mg, 0.26 mmol), potassium nitrite (35 mg, 0.41 mmol) and 18-crown-6 (108 mg, 0.41 mmol) at -78°C. The temperature was raised to 20°C and ^1H n.m.r., after 8 h, showed that no reaction had occurred. The reaction mixture was left for 15 days at ambient temperature and worked-up to give, by ^1H n.m.r. and g.l.c.-m.s., 1,2-dimethyl-4-nitrobenzene (44%, m/e 151) and 1,2-dimethyl-4,5-dinitrobenzene (56%, m/e 196).

(33) Potassium Cyanide in Acetonitrile-d_3

Acetonitrile-d_3 (415 mm^3) was added to a mixture of potassium cyanide (25 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol). The mixture was warmed to 50°C and then cooled to 0°C. The diene 36 (60 mg, 0.38 mmol) was added and ^1H n.m.r., after 5 min, showed that the rearomatization was complete. After work-up, the product composition by ^1H n.m.r. and g.l.c.-m.s. was 4,5-dimethyl-2-nitrobenzonitrile (70%, m/e 176) i.r. (Nujol) 2235 cm^{-1} (CN), 1525 and 1350 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.40 (s,3,CH_3), 2.43 (s,3,CH_3), 7.59 (s,1,2-H), 8.05 (s,1,5-H) and 4,5-dimethyl-1,2-benzene dicarbonitrile (30%, m/e 156.068, Mass required for $C_{10}H_8N_2$: 156.064) ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.37 (s, 2,4-CH_3 and 5-CH_3), 7.51 (s,2,3-H and 6-H).

(34) Thermal Decomposition

A 1% solution of the diene 36 in acetone was injected into the inlet of a gas chromatograph (260°C). The products, by g.l.c.-m.s., were 1,2-dimethyl-4-nitrobenzene (98%, m/e 151) and 2,3-dimethyl-6-nitroanisole (2%, m/e 181).

(D) Reactions of 5,6-Dimethyl-2,6-dinitrocyclohexa-2,4-dienyl Acetate (8) with

(35) 5% Sulfuric Acid in Methanol

A cold solution of 5% sulfuric acid in methanol (v/v, 15 cm^3) was added to the diene 8 (300 mg, 1.14 mmol) at 0°C. The temperature was raised to 20°C and the mixture stirred for 18 h. After work-up, the product was determined by ^1H n.m.r. to be 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dien-1-ol (35) (90 MHz, $CDCl_3$) δ 1.85 (s,3,6-CH_3), 2.06 (d,1, 5-CH_3), 3.80 (s,1,OH), 5.43 (s,1,1-H), 6.26 (dd,1,3-H), 7.30 (d,1,4-H). A small amount (*ca.* 10%) of decomposition products was also evident. The dienol 35 was not very stable and on vacuum-drying decomposed extensively, presumably to nitrophenols (brown fumes were evolved during this process). Attempts to methylate the dienol 35 using methyl iodide and moist silver oxide were also accompanied by extensive decomposition.

(36) Potassium Cyanide in Methanol-d_4

Methanol-d_4 (315 mm^3) was added to a mixture of potassium cyanide (25 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol). The mixture was warmed to 50°C and cooled to -78°C. The diene 8 (64 mg, 0.25 mmol) was then added and the temperature raised to 0°C. After 2 h, the mixture was worked-up and the product composition by ^1H n.m.r. and g.l.c.-m.s. was 4,5-dimethyl-2-nitrobenzonitrile (87%, m/e 176) and 1,2-dimethyl-4,5-dinitrobenzene (13%, m/e 196).

(37) Sodium Methoxide in Methanol

To a solution of the diene 8 (100 mg, 0.39 mmol) in methanol (1 cm^3) in an n.m.r. tube at -78°C was added sodium methoxide (42 mg, 0.78 mmol) and the mixture allowed to warm to 0°C. After stirring for

2 h, the mixture was worked-up to give, by ^{1}H n.m.r., one diastereomer of 5,6-dimethyl-2,6-dinitrocyclocyclohexa-2,4-dienyl methyl ether (36, 23%) and both the diastereomers of 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl ether (34, 77%). The ratio of the diastereomers 34A and 34B (by integration of the methoxy peaks) was 9:1.

(b) 1,4-Dimethyl-2-nitrobenzene

The reactions of the adducts can be discussed under the two main sections:

(i) Reactions under acidic conditions

(ii) Reactions with nucleophiles

(i) Reactions under acidic conditions: Reactions of the dienes 10A and 12 with

(1) Borontrifluoride Etherate

Cold BF_3-etherate solution (250 mm^3) was added to a solution of the diene 10A (64 mg, 0.25 mmol) in chloroform-d_1 (150 mm^3) at -78°C. The temperature was raised to 0°C and ^{1}H n.m.r. after 25 min indicated partial decomposition (*ca.* 60%) of the diene, although isomerization to the diene 12 (*ca.* 15%) was also evident. The reaction mixture was worked-up after 4 h, to give, by ^{1}H n.m.r. and g.l.c.-m.s., 1,4-dimethyl-2-nitrobenzene (62%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (29%, m/e 196), 1,4-dimethyl-2,6-dinitrobenzene (7%, m/e 196) and 3,6-dimethyl-2-nitrophenyl acetate (2%, m/e 209).

Under similar conditions, (0°C, 18 h), the diene 12 rearomatized to give the following products: 1,4-dimethyl-2-nitrobenzene (21%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (49%, m/e 196), 1,4-dimethyl-2,5-

dinitrobenzene (6%, m/e 196), 1,4-dimethyl-2,6-dinitrobenzene (13%, m/e 196) and 3,6-dimethyl-2-nitrophenyl acetate (11%, m/e 209)

(2) Borontrifluoride Etherate and Mesitylene

Cold BF_3-etherate solution (250 mm^3) was added to a solution of the diene 10A (100 mg, 0.39 mmol) and mesitylene (250 mg, 2.1 mmol) in methylene chloride (250 mm^3) at -78°C. The solution was allowed to warm to 20°C and maintained for 1 h. After work-up, the composition of the product by ^1H n.m.r. and g.l.c.-m.s. was found to be 1,4-dimethyl-2-nitrobenzene (27%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (26%, m/e 196), 1,4-dimethyl-2,6-dinitrobenzene (7%, m/e 196), 3,6-dimethyl-2-nitrophenyl acetate (2%, m/e 209), 2-nitro-2',3,4',6,6'-pentamethyl biphenyl (24, 7%, m/e 269) and 4-nitro-2,2',4',5,6'-pentamethyl biphenyl (23, 31%, m/e 269).

Under similar conditions, the diene 12 gave 1,4-dimethyl-2-nitrobenzene (9%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (26%, m/e 196), 1,4-dimethyl-2,5-dinitrobenzene (5%, m/e 196), 1,4-dimethyl-2,6-dinitrobenzene (8%, m/e 196), 3,6-dimethyl-2-nitrophenyl acetate (15%, m/e 209), the biphenyl 24 (8%, m/e 269) and the biphenyl 23 (28%, m/e 269).

For positive identification of the two biphenyls and the phenyl acetate, the reaction was repeated on the diene 12 (0.400 g, 1.6 mmol) under similar conditions and the products separated by Prep GC.

The first fraction contained mainly mesitylene and 1,4-dimethyl-2-nitrobenzene. The second fraction, after recrystallization from ether at -20°C, gave pale-yellow crystals of 3,6-dimethyl-2-nitrophenyl acetate (47). The ^1H n.m.r. and retention time of this sample (on g.l.c.)

was identical with the authentic sample m.p. 52°C; i.r. (KBr) 1770 and 1215 cm^{-1} ($OCOCH_3$), 1530 and 1360 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 2.16 (s,3,$OCOCH_3$), 2.24 (s,3,6-CH_3), 2.30 (s,3,3-CH_3), 7.05 (d,1,4-H), 7.25 (d,1,5-H); J_{45} = 7.5 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 15.8 (6-CH_3), 17.1 (3-CH_3), 20.0 ($OCOCH_3$), 128.5 (C-4), 129.3 (C-6), 130.8 (C-3), 132.8 (C-5), 141.1 (C-1), 144.6 (C-2), 167.7 ($OCOCH_3$); mass spectrum (70 eV) m/e (relative intensity) 209.075 (18,M,Mass calculated for $C_{10}H_{11}NO_4$: 209.069), 167 (100,M-$OCOCH_2$), 150 (52), 120 (44).

The third fraction contained a mixture of the nitroxylenes and was discarded. The fourth fraction gave 2-nitro-2',3,4',6,6'-pentamethyl biphenyl (24) i.r. ($CDCl_3$) 1525 and 1365 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.92 (s,9,2'-CH_3,6-CH_3 and 6'-CH_3), 2.27 (s,6,4'-CH_3 and 3-CH_3), 6.87 (s,2,3'-H and 5'-H), 7.24 (d,1,5-H), 7.28 (d,1,4-H); mass spectrum (70 eV) m/e (relative intensity) 269.142 (52,M,Mass calculated for $C_{17}H_{19}NO_2$: 269.142), 239 (25), 238 (25), 224 (20), 223 (24), 222 (100,M-HNO_2), 221 (15), 209 (20), 208 (15), 207 (16).

The fifth fraction gave 4-nitro-2,2',4',5,6'-pentamethyl biphenyl (23) i.r. ($CDCl_3$) 1525 and 1350 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.89 (s,6,2'-CH_3 and 6'-CH_3), 2.08 (s,3,4'-CH_3), 2.31 (s,3,2-CH_3), 2.37 (s,3,5-CH_3), 6.95 (s,2,3'-H and 5'-H), 7.10 (s,1,6-H), 7.65 (s,1,3-H); mass spectrum (90 eV) m/e 270 (21), 269.141 (100,M,Mass calculated for $C_{17}H_{19}NO_2$: 269.142), 253 (15), 252 (62), 237 (31), 234 (14), 224 (23), 223 (26), 222 (21,M-HNO_2), 210 (14), 209 (54), 208 (50), 207 (46).

(3) Trifluoroacetic Acid

Cold trifluoroacetic acid (450 mm^3) was added to the diene 10A (64 mg, 0.25 mmol) in an n.m.r. tube at -78°C. The temperature was raised to 20°C and ^1H n.m.r. after 2 h showed that no reaction had occurred. The decomposition of the diene was complete in 72 h and the reaction mixture was worked-up to give, by ^1H n.m.r. and g.l.c.-m.s., 1,4-dimethyl-2-nitrobenzene (56%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (35%, m/e 196) and 1,4-dimethyl-2,6-dinitrobenzene (8%, m/e 196).

Under similar conditions, the diene 12 rearomatized to give, by ^1H n.m.r. and g.l.c.-m.s., 1,4-dimethyl-2-nitrobenzene (33%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (27%, m/e 196), 1,4-dimethyl-2,5-dinitrobenzene (5%, m/e 196), 1,4-dimethyl-2,6-dinitrobenzene (11%, m/e 196) and 3,6-dimethyl-2-nitrophenyl acetate (22%, m/e 209).

(4) 5% Sulfuric Acid in Methanol

Cold 5% sulfuric acid in methanol (w/v, 2 cm^3) was added to the diene 10A (200 mg, 0.78 mmol) at 0°C. The temperature was raised to 20°C and the solution stirred for 18 h. The product was then dissolved in ether (75 cm^3), washed with saturated sodium bicarbonate (2 X 10 cm^3) and water (2 X 20 cm^3). The ether extract was dried over anhydrous magnesium sulfate, filtered and the solvent removed at 15°C to give one diastereomer of 1,4-dimethyl-2,4-dinitrocyclohexa-2,5-dien-1-ol (37A) i.r. ($CDCl_3$) 3550 cm^{-1} (OH), 1548 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.68 (s,3,1-C$\underline{H}_3$), 1.88 (s,3,4-C$\underline{H}_3$), 3.55 (s,1,O$\underline{H}$), 6.00 (dd,1,5-$\underline{H}$), 6.12 (d,1,6-$\underline{H}$), 7.32 (d,1,3-$\underline{H}$), J_{56} = 10Hz, J_{35} = 1.5 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 26.2 (1-$\underline{C}H_3$), 27.8 (4-$\underline{C}H_3$), 66.2 (C-1), 85.8 (C-4), 122.9 (C-6), 129.1 (C-5), 137.0 (C-3), 153.9 (C-2).

Under similar conditions, the diene 12 gave one diastereomer of 3,6-dimethyl-2,6-dinitrocyclohexa-2,4-dien-1-ol (39) which, after recrystallization from ether at -20°C, had m.p. 92°C; i.r. (KBr) 3490 and 1040 cm^{-1} (OH), 1545 cm^{-1} (NO_2); ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.67 (s, 3,6-CH_3), 2.28 (s,3,3-CH_3), 3.25 (s,1,OH), 5.16 (d,1,1-H), 6.10 (d,1,4-H), 6.78 (dd,1,5-H), J_{45} = 10 Hz; J_{15} = 1.5 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 20.8 (6-CH_3), 23.0 (3-CH_3), 69.3 (C-1), 90.9 (C-6), 128.1 (C-4), 133.4 (C-5), 140.8 (C-3), 142.7 (C-2).

(5) Trifluoromethanesulfonic Acid.

Cold trifluoromethanesulfonic acid (450 mm^3) was added to the diene 10A (64 mg, 0.25 mmol) in an n.m.r. tube at -78°C. The temperature was raised to 0°C and the mixture worked-up after 10 min to give, by ^1H n.m.r. and g.l.c.-m.s., 1,4-dimethyl-2-nitrobenzene (21%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (45%, m/e 196), 1,4-dimethyl-2,6-dinitrobenzene (30%, m/e 196) and a compound of mass 209, corresponding to a dimethyl-nitrophenyl acetate (4%).

Under similar conditions, the diene 12 rearomatized to give, by ^1H n.m.r. and g.l.c.-m.s., 1,4-dimethyl-2-nitrobenzene (15%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (58%, m/e 196) and 1,4-dimethyl-2,6-dinitrobenzene (27%, m/e 196).

(6) Acetic Acid

Acetic acid (450 mm^3) was added to the diene 10A (64 mg, 0.25 mmol) at 20°C. ^1H n.m.r. of the reaction mixture, after 30 days at 20°C, showed the absence of any reaction. The solution was heated for 60 min at 100°C when brown fumes were evolved from the reaction mixture. ^1H n.m.r. of the product indicated that the rearomatization was complete.

After work-up, the product composition by ^{1}H n.m.r. and g.l.c.-m.s. was found to be 1,4-dimethyl-2-nitrobenzene (80%, m/e 151) and 1,4-dimethyl-2,6-dinitrobenzene (20%, m/e 196).

The reaction was carried out on the diene 12 under similar conditions. As before, ^{1}H n.m.r. of the reaction mixture after 30 days at 20°C showed the absence of any reaction. When the reaction mixture was heated to 100°C, brown fumes were evolved from the reaction mixture. The solution had to be heated for 90 min before the decomposition was complete (by ^{1}H n.m.r.). After work-up, the composition of the product, as determined by ^{1}H n.m.r. and g.l.c.-m.s. was 1,4-dimethyl-2-nitrobenzene (37%, m/e 151), 1,4-dimethyl-2,6-dinitrobenzene (47%, m/e 196) and 3,6-dimethyl-2-hitrophenyl acetate (16%, m/e 209).

(ii) Reactions with nucleophiles: Reactions of the dienes 10A and 12 with

(7) Pyridine-d_5

Cold pyridine-d_5 (21 mm^3) was added to a solution of the diene 10A (64 mg, 0.25 mmol) in chloroform-d_1 (315 mm^3) at -60°C. The temperature of the mixture was raised to 0°C and ^{1}H n.m.r. of the mixture, after 24 h, showed no evidence of reaction. The mixture was warmed to 20°C and ^{1}H n.m.r., after 24 h, showed that *ca.* 80% of the diene was still present. The reaction mixture was worked-up after one week at 20°C and ^{1}H n.m.r. showed that the rearomatization was complete and a mixture of compounds was present, among which were identified 4-methyl-2-nitrobenzyl alcohol (44b) and (4-methyl-2-nitrophenyl)nitromethane (44e) in the ratio 4:3. These two compounds were almost always obtained in the reactions of the dienes with various nucleophiles.

The reaction was carried out on the diene 12 under similar conditions. As before, the decomposition was quite slow (one week, 0°C) and a mixture of products was obtained, in which the compounds 44b and 44e were present in the ratio 5:1 (by ^{1}H n.m.r.).

(8) Sodium Methoxide in Methanol

Sodium methoxide (42 mg, 0.78 mmol) was added to a solution of the diene 10A (100 mg, 0.39 mmol) in methanol at 0°C. The mixture mixture was stirred for 24 h and then worked-up to give, by ^{1}H n.m.r., a mixture of aromatic compounds (*ca.* 60%) and the diene 10A (*ca.* 40%). The reaction was repeated under similar conditions and the mixture worked-up after one week at 0°C to give, by ^{1}H n.m.r., 1,4-dimethyl-2-nitrobenzene (19%), 1,4-dimethyl-2,3-dinitrobenzene (33%), 1,4-dimethyl-2,5-dinitrobenzene (8%), 4-methyl-2-nitrobenzyl alcohol (44b, 27%) and (4-methyl-2-nitrophenyl)nitromethane (44e, 12%).

The reaction was carried out under similar conditions on the diene 12, and, after 24 h at 0°C, a significant amount of the diene was still present (*ca.* 50%). After one week, the decomposition was complete and the product composition by ^{1}H n.m.r. was 1,4-dimethyl-2-nitrobenzene (27%), 1,4-dimethyl-2,3-dinitrobenzene (23%), 1,4-dimethyl-2,5-dinitrobenzene (11%) and 4-methyl-2-nitrobenzyl alcohol (39%).

(9) Potassium Acetate

A mixture of potassium acetate (37 mg, 0.38 mmol), and 18-crown-6 (99 mg, 0.38 mmol) in acetonitrile-d_3 (400 mm^3) was warmed to 50°C, cooled to 0°C and the diene 10A (64 mg, 0.25 mmol) added. The decomposition was complete in 18 h and the product composition, by ^{1}H n.m.r., was

1,4-dimethyl-2-nitrobenzene (36%), 1,4-dimethyl-2,3-dinitrobenzene (41%) 4-methyl-2-nitrobenzyl alcohol (23%).

Under similar conditions, diene 12 rearomatized to give 1,4-dimethyl-2-nitrobenzene (33%), 1,4-dimethyl-2,3-dinitrobenzene (53%) and 4-methyl-2-nitrobenzyl alcohol (14%).

(10) Potassium Nitrite

Methanol-d_4 (315 mm^3) was added to a mixture of the diene 10A (64 mg, 0.25 mmol), potassium nitrite (32 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol) at -78°C. The temperature was raised to 0°C and ^{1}H n.m.r. after 30 min indicated incomplete reaction (*ca.* 50% diene present). The reaction mixture was worked-up after 18 h to give, by ^{1}H n.m.r., 1,4-dimethyl-2,3-dinitrobenzene (100%).

Under similar conditions, the diene 12 also gave 1,4-dimethyl-2,3-dinitrobenzene as the only product (by ^{1}H n.m.r.).

(11) Potassium Cyanide

Acetonitrile-d_3 (350 mm^3) was added to a mixture of potassium cyanide (25 mg, 0.38 mmol) and 18-crown-6 (99 mg, 0.38 mmol). The mixture was warmed to 50°C, cooled to 0°C and the diene 10A (64 mg, 0.25 mmol) added. After 30 min, the reaction mixture was worked-up to give the following products (by ^{1}H n.m.r. and g.l.c.-m.s.): 1,4-dimethyl-2-nitrobenzene (2%, m/e 151), 1,4-dimethyl-2,3-dinitrobenzene (33%, m/e 196) and 3,6-dimethyl-2-nitrobenzonitrile (65%, m/e 176). The reaction was repeated under similar conditions and the mixture worked-up after 2 min at 0°C when a similar product composition was obtained. However, when the reaction was carried out in a diluted medium (acetonitrile, 5 cm^3)

under similar conditions (0°C, 30 min), the only product by ^{1}H n.m.r. was 3,6-dimethyl-2-nitrobenzonitrile i.r. (CCl_4) 2225 cm^{-1} (CN), 1545 and 1360 cm^{-1} (NO_2); ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 2.34 (s,3,6-CH_3), 2.55 (s,3,3-CH_3); 7.42 (s,2,4-H and 5-H).

The reaction was carried out under similar conditions (acetonitrile-d_3, 315 mm^3) on the diene 12 and the mixture worked up after 30 min at 0°C to give 1,4-dimethyl-2-nitrobenzene (3%), 1,4-dimethyl-2,3-dinitrobenzene (49%), 3,6-dimethyl-2-nitrobenzonitrile (35%), 4-methyl-2-nitrobenzyl alcohol (4%) and (4-methyl-2-nitrophenyl)nitromethane (9%).

(B) Reactions of Dienols 37A and 39 with

(12) Methyl Iodide and Moist Silver Oxide

A mixture of moist silver oxide (1.90 g, see p.84), methyl iodide (7 cm^3), potassium hydroxide (0.01 g) and the diene 37A (0.52 g) was stirred for 5 h at 0°C. After work-up, the product was found to be one diastereomer of 1,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl ether (38A) which was recrystallized from ether at -20°C and had m.p. 77°C, i.r. (KBr) 1550 cm^{-1} (NO_2), 1100 cm^{-1} (C-O-C); ^{1}H n.m.r. δ 1.68 (s,3,1-CH_3), 1.90 (s,3,4-CH_3), 3.07 (s,3,OCH_3), 5.90 (d,1,6-H), 6.22 (dd,1,5-H), 7.22 (d,1,3-H), J_{56} = 10 Hz, J_{35} = 2 Hz; ^{13}C n.m.r. ($CDCl_3$, ppm) δc 26.2 (1-CH_3), 26.5 (4-CH_3), 52.8 (OCH_3), 71.8 (C-1), 85.2 (C-4), 126.0 (C-6), 131.1 (C-5), 136.2 (C-3), 152.6 (C-2).

Anal. Calcd. for $C_9H_{12}N_2O_5$: C,47.37; H,5.30; N,12.28

Found : C,46.85; H,5.33; N,11.95

Attempts to convert the diene 39 to the corresponding methyl ether by a similar method resulted in rearomatization. Reaction of the diene 37A (or 39) with thionyl chloride (30 mm^3) and pyridine (70 mm^3)

for 5 min at -20°C (using 0.25 mmol diene) resulted in rearomatization.

(13) Pyridine-d_5 and Acetic Anhydride

Cold pyridine-d_5 (40 mm^3) was added to a solution of the diene 39 (70 mg, 0.33 mmol) in acetic anhydride (300 mm^3) and the temperature raised to 0°C. The progress of the reaction was monitored by ^{1}H n.m.r. at 0°C. The acetylation was complete in 11 min and the product, after work-up, was identified as diene 12. ^{1}H n.m.r. showed that partial rearomatization to benzylic products 44b and 44e had also occurred (15%).

Under similar conditions, the diene 37A did not react. When a longer reaction time was employed, products resulting from rearomatization were obtained (-40°C, 1 h).

(c) 1,2-dimethyl-3-nitrobenzene

(1) 5% Sulfuric Acid in Methanol

Cold 5% sulfuric acid in methanol (w/v, 1 cm^3) was added to the the diene 9A (50 mg, 0.19 mmol) at 0°C. The temperature was raised to 20°C and the solution stirred for 18 h. After work-up, the product was identified as one diastereomer of 3,4-dimethyl-2,4-dinitrocyclohexa-2,5-dien-1-ol (40A) by ^{1}H n.m.r. (90 MHz, $CDCl_3$) δ 1.80 (s,3,4-C<u>H</u>$_3$), 1.94 (d,3,3-C<u>H</u>$_3$), 3.50 (s,1,O<u>H</u>), 5.15 (broad,1,1-<u>H</u>), 5.96 (dd,1,5-<u>H</u>), 6.25 (dd,1,6-<u>H</u>), J_{56} = 10 Hz, J_{16} = 3.5 Hz, $J_{5,3\text{-}CH_3}$ = 1.3 Hz.

(2) Pyridine-d_5

Cold pyridine-d_5 (21 mm^3) was added to a solution of the diene 9A (64 mg, 0.25 mmol) in chloroform-d_1 (330 mm^3) at -78°C. The temperature was raised to 0°C and ^{1}H n.m.r. after 24 h showed that no reaction had occurred. The reaction was repeated using pyridine (350 mm^3) when

the diene slowly rearomatized (48 h, 0°C) to give mainly benzylic products.

(d) 4-Methyl-2-nitrophenol

The following reaction was carried out on the adduct 4-methyl-5-methoxy-4,6-dinitrocyclohexa-2-en-1-one (42) in an attempt to convert it to the nitrodienone (13) or the nitrodienol (37).

A solution of the adduct 42 (0.23 g, 1 mmol) in ether (50 cm^3) was cooled to -78°C. A solution of methyllithium in ether (2.2 mmol) was added at -78°C and the mixture stirred for 1 h in an atmosphere of argon. A 1% solution of acetic acid in ether (v/v, 10 cm^3) was then added and the solution stirred for 10 min at -40°C. The mixture was then transferred to a prechilled separatory funnel and treated with methylene chloride (250 cm^3) at -5°C. The methylene chloride extract was washed with saturated sodium chloride (2 X 40 cm^3) and water (2 X 25 cm^3) at 0°C. After drying over anhydrous magnesium sulfate, the solvent was removed at 0°C. The product obtained was partially soluble in chloroform-d_1 (0°C) but more soluble in acetone-d_6. ^1H n.m.r. of the product showed that a major amount of the adduct was recovered, although a minor amount of the nitrodienone 13 (*ca.*5%) was observed. A significant amount of rearomatized products (including 4-methyl-2,6-dinitrophenol) was also formed.

(e) Reactions of adducts obtained from other systems with

(1) Thionyl Chloride

A solution of *trans*-1,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-ol (39b, 84 mg, 0.5 mmol) in chloroform-d_1 (350 mm^3) and pyridine-d_5 (100 mm^3) was cooled to -40°C. Cold, freshly-distilled thionyl chloride (50 mm^3) was added to the above solution and ^1H n.m.r. of the mixture after 1 min showed that the reaction was complete. After work-up, the product was identified by comparison of the ^1H n.m.r. spectrum with an authentic sample (39b) as *trans*-1-chloro-1,4-dimethyl-4-nitrocylohexa-2,5-diene (43b) ^1H n.m.r. (90 MHz, $CDCl_3$) δ 1.75 (s,6,1-CH_3 and 4-CH_3), 6.05 (d,2,2-H and 6-H), 6.17 (d,2,3-H and 5-H).

(2) Pyridine-d_5.

A solution of 2-cyano-4,5-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate (57, 70 mg, 0.30 mmol) in chloroform-d_1 (315 mm^3) was cooled to 0°C. Cold pyridine-d_5 (400 mm^3) was added to the above solution and the temperature raised to 20°C. The reaction mixture was worked-up after one week at 20°C and ^1H n.m.r. of the residue showed that the starting diene had been recovered (*i.e.* no reaction had occurred).

(3) Potassium Cyanide

Acetonitrile (5 cm^3) was added to a mixture of potassium cyanide (40 mg, 0.62 mmol) and 18-crown-6 (160 mg, 0.62 mmol). The mixture was warmed to 50°C, cooled to 0°C and the adduct 2-cyano-4,5-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate (57, 100 mg, 0.42 mmol) added. The reaction mixture was stirred for 10 min and then worked-up to give, by ^1H n.m.r. and g.l.c.-m.s., 2-cyano-4,5-dimethylphenol (68%, m/e 147) and 2-cyano-4,5-dimethylphenyl acetate (32%, m/e 189). The ^1H n.m.r.

of the two compounds (in CD_3OD) was compared with the spectra for the authentic samples (57) and the phenyl acetate had (90 MHz, CD_3OD) δ 2.25 (s,3,4-$C\underline{H}_3$), 2.28 (s,3,5-$C\underline{H}_3$), 2.30 (s,3,$OCOC\underline{H}_3$), 7.06 (s,1, 6-$\underline{H}$), 7.40 (s,1,3-$\underline{H}$). The phenol had (90 MHz, $CDCl_3$) δ 2.12 (s,3,4-$C\underline{H}_3$), 2.20 (s,3,5-$C\underline{H}_3$), 4.80 (broad,1,$O\underline{H}$), 6.71 (s,1,6-$\underline{H}$), 7.14 (s,1,3-$\underline{H}$).

(4) Potassium Nitrite

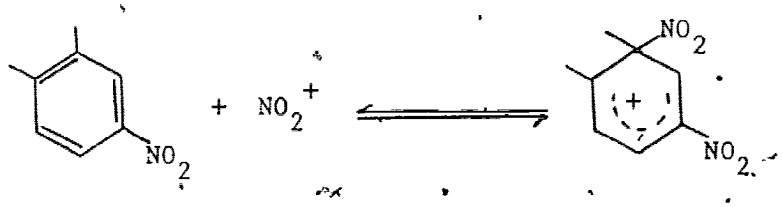
Methanol-d_4 (315 mm^3) was added to a mixture of the adduct 2-cyano-4,5-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate (57, 59 mg, 0.25 mmol), potassium nitrite (32 mg, 0.38 mmol) and 18-crown-6 (99 mg; 0.38 mmol) at -78°C. The temperature was raised to 20°C and the mixture stirred for 72 h. After work-up, ^1H n.m.r. revealed that the major component of the product mixture was the unreacted diene. The reaction was repeated under similar conditions and the mixture worked-up after two weeks at 20°C to give, by ^1H n.m.r., 2-cyano-4,5-dimethylphenyl acetate (100%).

CHAPTER III

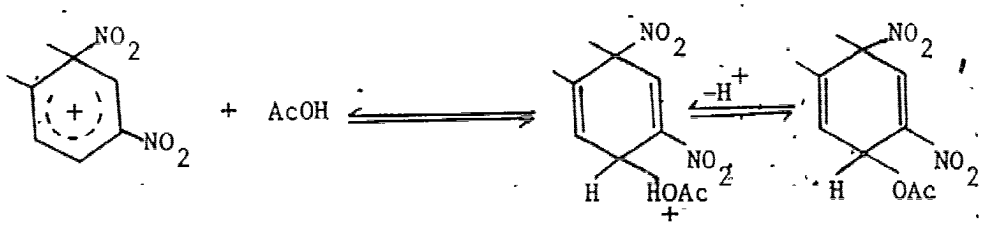
DISCUSSION

3.1 *Formation of Diene Adducts*

The studies on the *ipso* nitration of various nitroarenes showed that both *cis* and *trans* diastereomeric 1,4 acetoxynitro adducts were formed. The adduct formation is associated with an initial bonding of the nitronium ion to a suitably-substituted carbon. The resulting *ipso* Wheland intermediate (W_i^X, 48) is attacked by nucleophilic acetate from either side of the newly-introduced nitro group leading to *cis* and *trans* adducts respectively. The mechanistic details have been discussed in Chapter I and (for the nitration of 1,2-dimethyl-4-nitrobenzene) the reaction can be represented by the following scheme:



4 W_i^X, 48



48 7A (B)

An unusual feature of the reaction conditions used for

nitration in this study is the employment of trifluoroacetic anhydride, in addition to acetic anhydride, as a solvent for the *ipso* nitration of 1,2-dimethyl-3- and 4-nitrobenzenes. These substrates are apparently too deactivated to react with nitric acid in acetic anhydride alone; *e.g.* 1,2-dimethyl-4-nitrobenzene did not react at all when treated with nitric acid (5 mol) and acetic anhydride (10 mol) for 48 h at 0°C (under similar conditions, the reaction with 1,2-dimethylbenzene would be effectively instantaneous). However, when trifluoroacetic anhydride (5 mol), acetic anhydride (15 mol) and nitric acid (5 mol) per mole of the substrate was used, the nitration proceeded smoothly to completion (0°C, 30 min) to give diene adducts (*ca.* 50%) and nitro derivatives (*ca.* 50%).

3,4-Dimethylbenzonitrile, which is less deactivated than the nitro-*o*-xylenes, on nitration with nitric acid-acetic anhydride at 15°C for 24 h gave a diene adduct (*ca.* 30%) and various nitrobenzonitriles (*ca.* 30%), with *ca.* 40% of the substrate remaining unreacted (57). By using trifluoroacetic anhydride (1 mol), acetic anhydride (2.5 mol) and nitric acid (1.3 mol) per mole of the substrate, the yield of the diene adducts, after 1 h at 0°C, was enhanced to 45%, with only 15% of the substrate remaining unaffected (87). Thus employment of trifluoroacetic anhydride results in a significant improvement, both in the rate of the reaction and in the yield of the adducts obtained (59).

The activation of the aromatic nucleus by the two methyl groups is reduced significantly by the cyano group and to a greater extent, by the more strongly electron-withdrawing nitro group. This necessitates the carrying out of the reactions under conditions which would normally be considered drastic for the *ipso* nitration of alkylbenzenes and which

would likely lead to rearomatization of adducts formed from these substrates. In the nitration of 1,4-dimethyl-2-nitrobenzene, trifluoroacetic anhydride was not used as a co-solvent. This substrate is apparently more reactive than 1,2-dimethyl-3- and 4-nitrobenzenes since it reacted completely with nitric acid in acetic anhydride over 24 h at 0°C. Furthermore, when trifluoroacetic anhydride was used, only one pair of diastereomeric 1,4 acetoxynitro adducts was obtained. Using acetic anhydride alone, two pairs of diastereomeric 1;4 acetoxynitro adducts, together with a 1,2 adduct, were formed.

Nitration by nitric acid in acetic anhydride is different from that in acetic acid or nitromethane in that the nitric acid is converted to acetyl nitrate (equation 5). The addition of trifluoroacetic anhydride results in a significant shift of the equilibrium (equation 8) to the right which increases the nitronium ion concentration because of the effective replacement of the acetate ion by the more weakly nucleophilic trifluoroacetate ion (equation 9).

$$Ac_2O + HONO_2 \rightleftharpoons AcONO_2 + AcOH \qquad (5)$$

$$AcONO_2 \rightleftharpoons AcO^- + NO_2^+ \qquad (8)$$

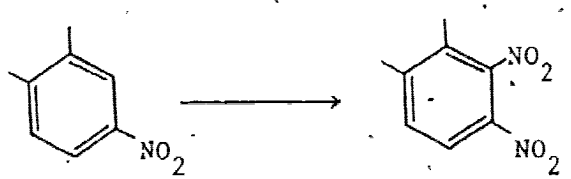
$$AcO^- + (CF_3CO_2)O \rightleftharpoons CF_3COOAc + CF_3COO^- \qquad (9)$$

The recombination of nitronium ion with trifluoroacetate anion is less favoured than is the recombination with acetate ion because of the poorer nucleophilicity of the trifluoroacetate.

As discussed in Chapter I, studies on the nitration of reactive substrates such as mesitylene show that the reaction occurs at an encounter rate. In the case of deactivated substrates like the nitroarenes, this is obviously not likely. Although detailed kinetic studies have not been made, it would seem that the conversion of the encounter pair to the cyclohexadienyl cation is the rate-determining step of the reaction. Thus, the increase in the equilibrium concentration of the nitronium ion brought about by addition of trifluoroacetic anhydride leads to an increase in the rate of the reaction.

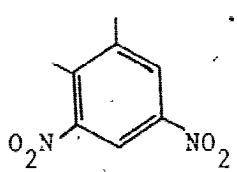
(a) Products from addition of nitronium ion to nitroxylenes

Nitration of 1,2-dimethyl-4-nitrobenzene gives the following products:

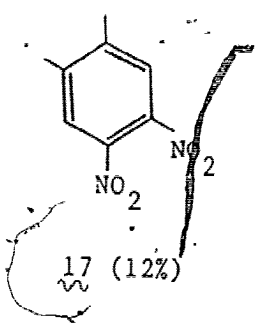


4

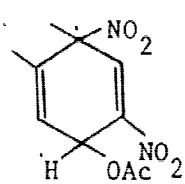
15 (16%)



16 (22%)



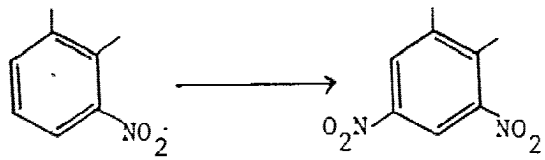
17 (12%)



7A (40%)

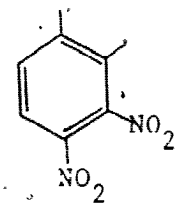
7B (10%)

Nitration of 1,2-dimethyl-3-nitrobenzene gives the following products:

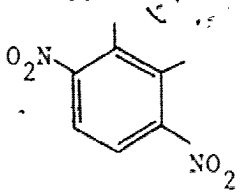


3

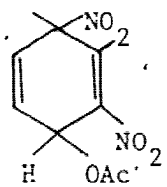
16 (28%)



15 (14%)



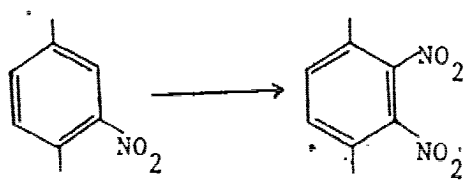
18 (18%)



9A (28%)

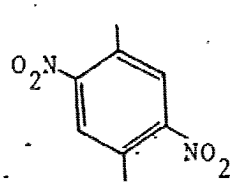
9B (12%)

Nitration of 1,4-dimethyl-2-nitrobenzene gives the following products:

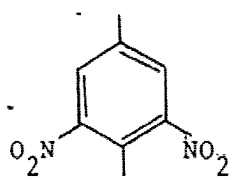


2

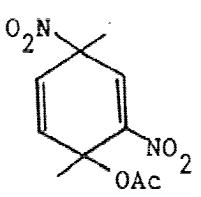
19 (23%)



20 (5%)

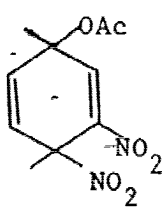


21 (13%)



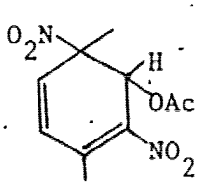
10A (17%)

10B (7%)



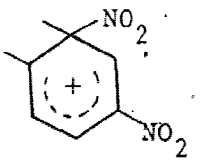
11D (9%)

11E (5%)

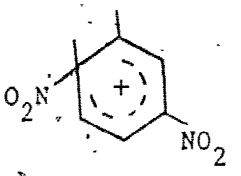


12 (21%)

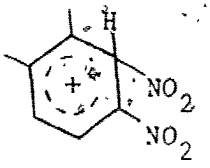
Addition of the nitronium ion to any of the nitroxylenes can lead to six distinct cyclohexadienyl cations. In the case of 1,2-dimethyl-4-nitrobenzene, these are shown below:



48



54



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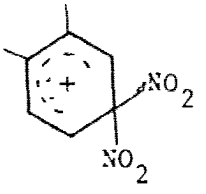
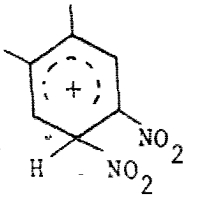
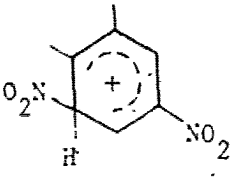


56



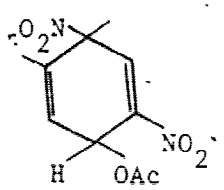
57



58

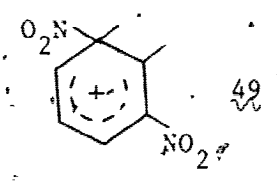
Ions 55, 57 and 58 formed by addition of the nitronium ion to an unsubstituted position are apparently extremely rapidly deprotonated to form the corresponding dinitro-*o*-xylenes, which were present in the product mixture. The remaining ions are those formed by *ipso* attack. Ion 56 is a cation with two, powerful electron-withdrawing substituents attached to the same carbon atom. It may not be formed to any significant extent since in the transition state, the nitronium ion would be repelled by the positive centre of the substituent nitro group. Hence no products are obtained which can only be attributed to the intermediate formation of 56. Ions 48 and 54 are formed by addition of the nitronium

ion *ipso* to a methyl substituent. Ion 54, (resulting from attack *para* to the nitro group) should be formed much less readily than the ion 48 (attack *meta* to the nitro group). The partial rate factor for attack *para* to the nitro group (discussed later) is only 4% of the attack *meta* to the nitro group. Therefore, it is not unexpected that the only adduct obtained is 7.

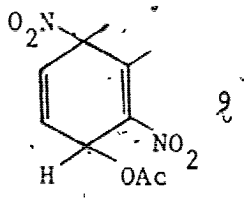


7

Similar analysis of the 1,2-dimethyl-3-nitrobenzene system explains the formation of the adduct 9 in addition to dinitro-*o*-xylenes.

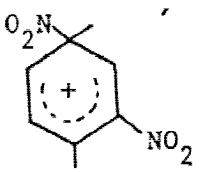


49



9

However, 1,4-dimethyl-2-nitrobenzene gives the *ipso* adducts 10 and 11 indicative of the intermediate formation of the two cyclohexadienyl cations 50 and 51. The occurrence of *ipso* attack at a position *ortho* (but not *para*) to the nitro group is in agreement with the high *o*:*p* ratios observed in the nitration of nitrobenzene (29).



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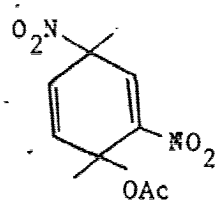

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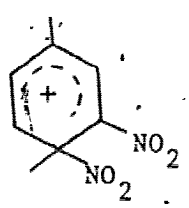
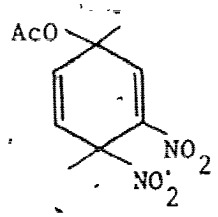


51

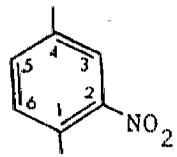


11

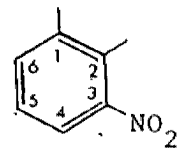
It is useful to examine the results of nitration of the nitroxylenes in terms of the partial rate factors and the additivity principle. The partial rate factors for substitution in these compounds can be calculated by considering the partial rate factors for substitution in toluene and nitrobenzene. Isomer distribution can thus be predicted for further substitution. The ratio of partial rate factors for nitration of toluene in acetic anhydride have been determined (88) and found to be in agreement with the values obtained in other solvents (89). These ratios ($o_f : m_f : p_f : i_f$ 20.8 : 1 : 25.6 : 2.2) were then used to calculate the product distribution expected on nitration of various polymethylbenzenes. The partial rate factors for the nitration of nitrobenzene were estimated (2) but these values were revised (90) on the basis of more accurate values for the rate of nitration (relative to benzene). The revised values for the nitration of nitrobenzene in nitric acid-sulfuric acid are $o_f^Y = .1.08 \times 10^{-8}$, $m_f^Y = 16.2 \times 10^{-8}$ and $p_f^Y = 0.726 \times 10^{-8}$ (where Y = NO_2). By using the ratio of partial rate factors and assuming that (a) the effect of substituents is additive and (b) the above values for nitration of nitrobenzene do not change significantly in acetic anhydride, the product composition can be calculated. It is expected that the nitro group would strongly deactivate the position *ipso* to it. Table 3.1 shows the calculated and observed product distributions for the nitration of the the various nitroxylenes.

TABLE 3.1 -

CALCULATED (A) AND OBSERVED (B) PRODUCT DISTRIBUTION IN THE NITRATION OF NITROARENES



2



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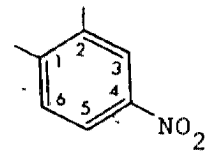


4

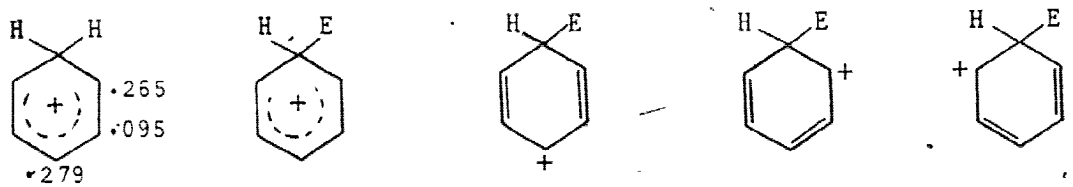
POSITION	A	B	A	B	A	B
C-1	5%	14%	59%	40%	3%	-
C-2	-	-	4%	-	63%	50%
C-3	2%	23%	-	-	2%	16%
C-4	67%	45%	2%	14%	-	-
C-5	1%	5%	33%	28%	3%	12%
C-6	25%	13%	1%	18%	29%	22%
OVERALL *IPSO* ATTACK	72%	59%	63%	40%	66%	50%

The extent of overall *ipso* attack observed in all three cases is less than expected. The results obtained also seem to indicate a higher degree of attack at positions *ortho* to the nitro group in the substrate, especially when these positions are non-substituted. Hence, though the additivity principle can be employed to advantage to predict isomer distributions, the observed values indicate that these predictions should be attached qualitative, and not quantitative, importance.

Marked deviations from the additivity principle have been observed in bromination and (to a greater extent) in nitration of aromatic substrates carrying a methyl substituent and a deactivating substituent (91). Product compositions obtained from the nitration of methoxy- or dimethyl-substituted anilinium ions also show a deviation from the additivity principle (92). The results of the work on nitroarenes and the above results can be understood if the presence of an activating substituent influences the directing effect of the deactivating substituent through mutual interaction. In this event, the effects of the substituents are not independent, vitiating a necessary condition for the additivity principle to apply.

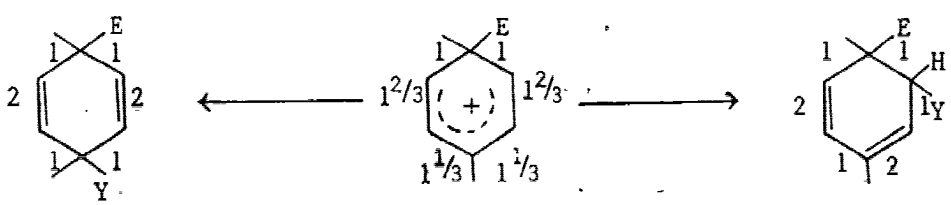
Once the *ipso*-cyclohexadienyl cation (48 to 51) is formed, nucleophilic attack can take place either at *para* or *ortho* to give a 1,4 or a 1,2 diene adduct respectively. The formation of the 1,4 rather than the 1,2 diene adduct in various systems may be attributed to the uneven distribution of the positive charge in the cyclohexadienyl cation (4). Nuclear magnetic resonance studies on pentamethylcyclohexadienyl cation indicate a greater concentration of the positive charge at the

para than in the *ortho* position. The higher degree of positive charge at the *para* position indicates a greater contribution to 63 from 64 than from 65 or 66. Hence, nucleophilic attack at a *para* position is generally preferred.



62 63 64 65 66

Even if the three forms were to contribute equally, the preferential formation of 1,4 diene adducts may be rationalised in terms of the Hines principle of least motion (93), according to which "those elementary reactions will be favored that involve the least change in atomic position and electronic configuration". This principle can be applied in a simplified manner to the present case. The valence bond orders for the six carbon-carbon bonds are (going around the ring) 1, $1^{2}/_{3}$, $1^{1}/_{3}$, $1^{1}/_{3}$, $1^{2}/_{3}$, 1. On conversion of the cyclohexadienyl cation to a diene, the bond orders change as follows:



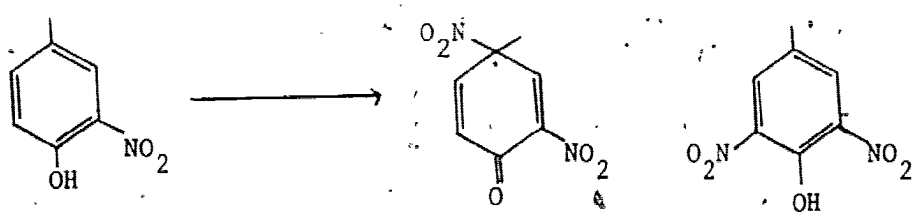
59 61 60

The two bonds whose bond order is 1 are unchanged in the two products 59 and 60. When the 1,2 adduct 60 is formed the change in bond order is $0 + {}^{2}/_{3} + {}^{2}/_{3} + {}^{1}/_{3} + {}^{1}/_{3} + 0$ whereas for the 1,4 adduct 59, the change is $0 + {}^{1}/_{3} + {}^{1}/_{3} + {}^{1}/_{3} + {}^{1}/_{3} + 0$. Since a greater change is required to form the 1,2 adduct, the principle of least motion predicts formation of the 1,4 adduct. Thus, in the absence of steric or other factors, the formation of the 1,4 adduct is preferred and this is indeed the case for cations 48 and 49 and seems to be generally true for almost all substrates (see Chapter I). Steric factors would also inhibit nucleophilic attack at C-2 in 49 whereas in 48, the buttressing effect of the methyl at C-6 on the substituents at C-1 reduces the prospects of nucleophilic attack at C-2, which is flanked on the other side by the nitro-substituted C-3. These effects are absent in 50 in which addition at C-4 would experience a certain degree of steric hindrance by the adjacent nitro group. Hence, nitration of 1,4-dimethyl-2-nitrobenzene results in a significant amount (*ca.* 21%) of a 1,2 diene adduct arising from 50, along with the expected 1,4 diene adduct (*ca.*24%) as a pair of diastereomers resulting from the same cation. From the cyclohexadienyl cation 51 leading to another pair of 1,4 diene adducts, no 1,2 diene adducts were obtained. In this case, addition of the nucleophile to the *para* position is not hindered. These arguments regarding steric influence are in accord with previous observations regarding the absence of such 1,2 diene adducts in the *ipso* nitration of *p*-xylene (38) and the formation of such an adduct in the cases of 4-*tert*-butyltoluene (41) and (to a lesser extent) 5-*tert*-butyl-1,2,3-trimethyl benzene (44). In the case of *tert*-butyltoluenes, 1,2 adducts have been obtained but not positional isomers and in the

nitration of *p*-ethyltoluene (39), diastereomeric 1,4 positional isomers (corresponding to *ipso* attack at -Me at -Et) have been obtained, but not 1,2 adducts. The nitration of 1,4-dimethyl-2-nitrobenzene represents the first case wherein both a 1,2 diene adduct and structurally isomeric 1,4 diene adducts, each of the latter as a pair of diastereomers, are obtained.

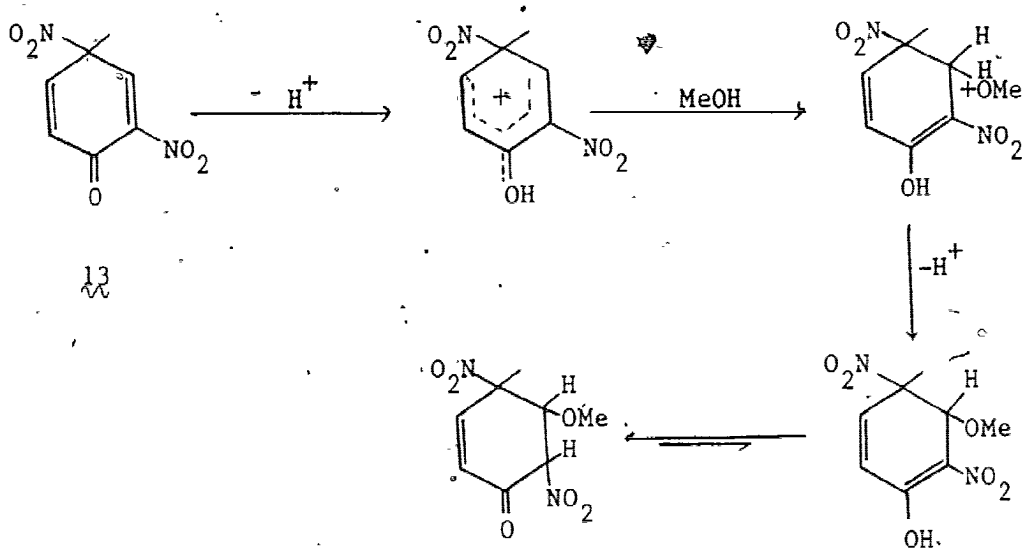
(b) Products from the addition of nitronium ion to nitrocresols.

Nitration of 4-methyl-2-nitrophenol at 0°C gave the expected nitrodienone (*ca.* 55%) and 4-methyl-2,6-dinitrophenol (*ca.* 45%). The nitrodienone was stable in acetic anhydride solution (0°C) but decomposed on work-up to 4-methyl-2,6-dinitrophenol.



5 13 14

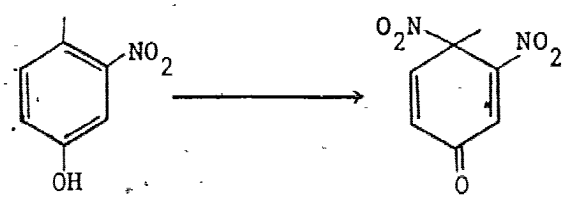
Nitrodienones have been isolated by low-temperature crystallization of the reaction product from methanol (63). Attempts to crystallize the nitrodienone obtained from 4-methyl-2-nitrodienone resulted in its conversion to highly insoluble 42. This transformation is attributed to formal, acid-catalyzed 1,4 addition of solvent methanol to the nitrodienone as shown in the following scheme:



13

42

Nitration of 4-methyl-3-nitrophenol gave the expected nitrodienone (*ca.* 30%) which decomposed on work-up with ammonia. The nitrodienone, being in such low yield, could not be crystallized from methanol at -78°C.



6

71

3.2 *Structural Assignment of Diene Adducts*

The diene adducts obtained by the *ipso* nitration of the various nitroarenes were quite labile under both acidic and basic conditions. Since they also undergo thermal decomposition to aromatic compounds, mass spectral data were of little use in structural assignments. As a result, ultraviolet, infrared, ^{1}H and ^{13}C nuclear magnetic resonance spectra, together with elemental analysis were used in the characterization of the diene adducts. The exchange reactions with different nucleophiles were studied by ^{1}H n.m.r. Mixtures of the rearomatized products were usually analyzed by ^{1}H n.m.r. and gas-liquid chromatography in conjunction with mass spectrometry.

The ^{1}H n.m.r. spectral assignments are given in Table 3.2 and shift reagent data in Table 2.2 and Figures 3.1 to 3.9.

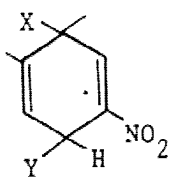
3.2.1 Diastereomers 7A and 7B: 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate.

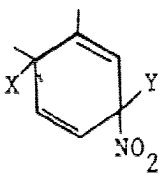
The presence of nitro and acetoxy groups in the diene 7A was established by the absorptions at 1560 cm^{-1} (NO_2) and at 1238 and 1742 cm^{-1} ($OCOCH_3$). Similar absorptions at 1560 cm^{-1} and at 1240 and 1750 cm^{-1} were recorded for the isomer 7B.

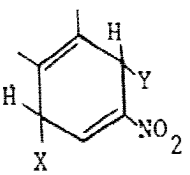
U.v spectroscopy (7A, 225 nm; 7B, 227 nm) showed that the isomers were 1,4 adducts.

The ^{1}H and ^{13}C n.m.r. spectra both indicated that in the formation of 7A (and 7B), the aromatic ring had been converted into a diene system *i.e.* 7A was an adduct as was 7B.

The ^{1}H n.m.r. spectrum of both the adducts could be suitably interpreted. For such 1,4 diene adducts, six pairs of diastereomers can be envisaged. The six structural isomers can be sub-classified into three pairs of "positional" isomers. In members of each pair of positional isomers, the location of the double donds with respect to the original substituents is the same. The location of the double bonds is different in members of different pairs.







7: X = NO_2, Y = OAc 76: X = NO_2, Y = OAc 78: X = NO_2, Y = OAc

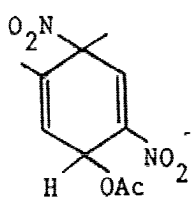
75: X = OAc, Y = NO_2 77: X = OAc, Y = NO_2 79: X = OAc, Y = NO_2

In the case of structures 76 and 77, a 10 Hz coupling between the two adjacent vinylic ring protons would be observed. For structures 78 and 79, the proton resonance at the lowest field (5-H) should be coupled to an adjacent ring proton. In the ^{1}H n.m.r. spectrum of the adducts 7A and 7B, the maximum coupling observed is 4 Hz and the absorption at the lowest field is a sharp singlet. These observations rule out structures 76, 77, 78 and 79 and show that the 1,4 diene adducts can be adequately represented by the structures 7 or 75. Structure 75, representing a secondary nitro compound is chemically unlikely since it would eliminate acetic acid readily on exposure to base to form 1,2-dimethyl-4,5-dinitrobenzene.

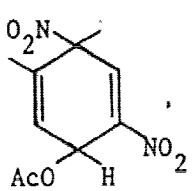
Ring protons in the diene adducts obtained by previous workers

(38, 39) typically absorb in the region δ 5.5- 6.5 ppm. The very low field singlet absorption in the spectrum of 7A at δ 7.44 ppm is assigned to 3-H. The corresponding absorption in diastereomeric 7B is at δ 7.34 (s,1,3-H). The nitro group attached to the other end of the double bond moves this proton to a low field.

Absorptions at δ 6.46 and 5.98 in the ^{1}H n.m.r. spectrum of 7A are assigned to the other two ring protons. The acetate absorption occurs at δ 2.06 whereas the doublet at δ 1.88 and the singlet at δ 1.95 are assigned to 5-CH_3 and 4-CH_3 respectively. Similarly, for the adduct 7B, absorptions at δ 6.34, 5.96 and 2.04 are assigned to 1-H, 6-H and acetate respectively. The ring methyls 4-CH_3 and 5-CH_3 show an identical absorption at δ 1.86. Irradiation techniques enabled the spectrum to be assigned without ambiguity. In the ^{1}H n.m.r. spectrum of the diene 7A, irradiation at δ 1.88 collapsed the peaks at δ 5.98 and at δ 6.46 to two doublets (J_{16} = 4 Hz). On a 300 Hz expanded spectrum, both 1-H and 6-H appeared as multiplets and 5-CH_3 appeared as a triplet (overlapping doublets). Irradiation at either δ 5.98 or δ 6.46 resulted in the collapse of 5-CH_3 to a doublet ($J_{6,5\text{-}CH_3}$ = 1.5 Hz, $J_{1,5\text{-}CH_3}$ = 1.3 Hz). Thus, by simultaneous expansion and double resonance studies, the assignment and coupling constants were verified (Table 3.2).



7A



7B

A similar approach was adopted for interpreting the ^1H n.m.r. spectrum of 7B, though in this case, the absorptions due to 4-CH_3 and 5-CH_3 overlapped.

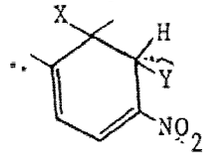
Shift reagent studies were employed to determine the stereochemistry of the diene adducts 7A and 7B. Induced shifts can be attributed to a pseudo-contact or dipolar interaction between the shift reagent and the nucleophile (94) and the magnitude of the paramagnetic shift is inversely proportional to the cube of the distance between the proton in question and the lanthanide ion. In both the diastereomers, the induced shift for the acetate methyl protons is higher than that for the ring methyl groups (Table 2.2) since the europium ion is complexed at the acetate functionality. The magnitude of downfield shift is much higher for 1-H than for the other ring protons since it is closer to the complexing site. The induced downfield shift of 6-H is higher than that for 3-H. This observation may be attributed to the fact that 6-H is closer to the site of complexation than 3-H. Addition of the shift reagent, which complexes with the acetate function, should shift the 4-CH_3 protons in the *trans* isomer (in which OAc is *cis* to 4-CH_3) more rapidly downfield than in the *cis* isomer. On the basis of this observation, the diene 7A (m.p. 95°C), which is eluted prior to the diene 7B from the column, is assigned the *trans* configuration and diene 7B is assigned the *cis* configuration. A comparison of the relative induced shifts of the various protons in both isomers can be made by plotting the observed shifts against the shift of the acetate protons (Figures 3.1 and 3.2 and Table 2.2). In both the adducts, the absorptions move downfield in the order 1-H > 6-H > 3-H > 4-CH_3 > 5-CH_3 consistent with 7.

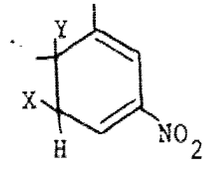
3.2.2 Diene 8: 5,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate

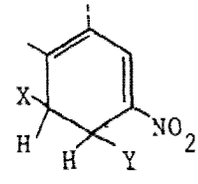
I.r. bands at 1555 cm^{-1} and at 1753 and 1210 cm^{-1} showed the presence of nitro and acetoxy groups in the diene.

U.v. spectroscopy (325 nm) showed that a cyclohexa-1,3-dienyl system (with a nitro group in conjugation) was present.

For a 1,2 adduct, twelve pairs of diastereomers are envisaged. There are six pairs of positional isomers which differ in the location of the double bonds with respect to the original nitro and methyl substituents. They can be represented as shown below:

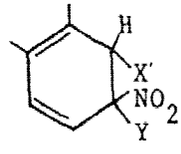


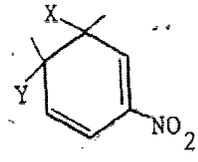


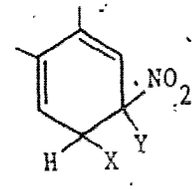


8: X = NO_2, Y = OAc 81: X = NO_2, Y = OAc 83: X = NO_2, Y = OAc

80: X = OAc, Y = NO_2 82: X = OAc, Y = NO_2 84: X = OAc, Y = NO_2







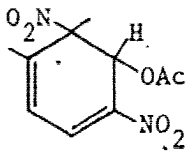
85: X = NO_2, Y = OAc 87: X = NO_2, Y = OAc 89: X = NO_2, Y = OAc

86: X = OAc, Y = NO_2 88: X = OAc, Y = NO_2 90: X = OAc, Y = NO_2

Only structure 8 (or 80) can accommodate the requirements of a fully conjugated nitrodiene system and the ^1H n.m.r. spectrum (Table 3.2). Structure 80, being a secondary nitro compound, is chemically

unlikely since it would readily lose acetic acid to give 1,2-dimethyl-3,4-dinitrobenzene.

In the ^{1}H n.m.r. spectrum, the low-field proton (δ 7.48 ppm) is assigned to 3-H, which is attached to the same double bond as the nitro group. This proton has an adjacent (coupled) proton which itself has an adjacent (coupled) methyl group. The remaining ring methyl group and the proton are not coupled. Structure 8 uniquely meets the requirements imposed by the ^{1}H n.m.r. spectrum.



8

The absorptions at δ 6.93 and 6.35 are assigned to 1-H and 4-H respectively. The acetate methyl occurs at δ 2.08. The 5-CH_3 is observed as a lower-field doublet (δ 2.12) whereas the singlet at δ 1.78 is due to 6-CH_3.

Decoupling techniques were used to verify the assignment. When the decoupler frequency was set at δ 2.12, the absorption at δ 6.35 collapsed to a doublet (J_{34} = 7 Hz). Irradiation at δ 7.48 also collapsed the peak at δ 6.35 to a different doublet ($J_{4,5\text{-}CH_3}$ = 1.5 Hz). Thus, the ^{1}H n.m.r. spectrum is compatible only with 8.

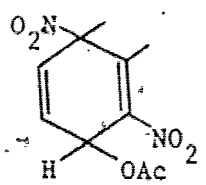
Shift reagent studies lent further support to the assigned structure. Addition of shift reagent and observations of the methyl absorptions showed that the downfield shift is of the order OAc > 6-CH_3 > 5-CH_3. (Figure 3.3). As in other secondary adducts (7), the shift of 1-H is the greatest since it is closest to the site of complexation.

That the shift of 3-H is greater than that for 4-H may be attributed to weak complexation of the lanthanide ion with the C-2 nitro group resulting in its being located closer to 3-H than to 4-H. Thus, the observed order of induced shifts *i.e.* 1-H > 6-CH_3 > 3-H > 4-H > 5-CH_3 is satisfactorily explained.

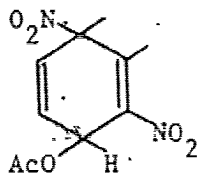
Since only one of the two diastereomers corresponding to 8 was obtained, its stereochemistry could not be ascertained. However, the substantial difference in the induced chemical shifts between 6-CH_3 and 5-CH_3 (Table 2.2) indicates that 6-CH_3 is much closer to 1-OAc than 5-CH_3. Hence, it is not unlikely that the 6-CH_3 and 1-OAc are *cis* to each other indicating that this diastereomer is probably the *trans* adduct.

3.2.3 Diastereomers 9A and 9B: 3,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate

The structures of these diene adducts (obtained from 1,2-dimethyl-3-nitrobenzene) were determined from the u.v., i.r. and ^{1}H n.m.r. spectra and following arguments (which will not be repeated in detail) similar to that employed for dienes 7A and 7B. The adducts have structures 9A and 9B.



9A



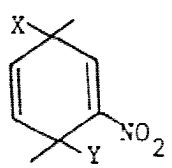
9B

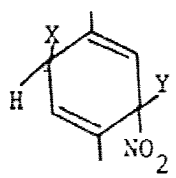
In both the adducts, the ring proton *ipso* to the acetate group (1-H) absorbs at the lowest field (Table 3.2). A 10 Hz coupling is observed between the two vinylic protons in 9A. The ring proton 1-H is also coupled to 3-CH_3 (d) which itself occurs at a lower field than the 4-CH_3 (s) in both adducts. The ring protons appear in the region δ 6.0-6.6 ppm which rendered irradiation studies difficult. Frequently, coupling constants which are initially difficult to measure because of peak overlap can be estimated from a shifted spectrum (94). The values obtained maybe valid for unaltered spectra, though some caution must be exercised (94c). The multiplets in the region δ 6.0-6.6 ppm were separated by the addition of shift reagent and an expanded 300 Hz spectrum provided the relevant coupling information. When the deccupler frequency was set at the 1-H absorption in a shifted spectrum, the absorptions due to 5-H (dd), 6-H (dd) and 3-CH_3 collapsed to a doublet, a doublet and a singlet respectively. This shows that 1-H is coupled to 3-CH_3 and to the two vinylic protons as expected and consistent with the structures 9A and 9B.

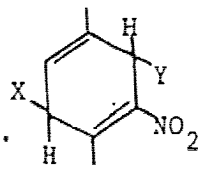
On addition of shift reagent, the magnitude of induced shifts for the ring protons was found to be of the order 1-H > 6-H > 5-H. The shifts for the methyl groups decreased in the order OAc > 3-CH_3 > 4-CH_3 (Figures 3.4 and 3.5). The gradient for the 4-CH_3 in the isomer 9A (eluted prior to 9B in column chromatography) is higher than in 9B (Table 2.2). Hence 9A is the *trans* adduct and 9B is the *cis* adduct.

3.2.4 Diastereomers 10A and 10B: 1,4-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl acetate; diastereomers 11D and 11E: 1,4-dimethyl-3,4-dinitrocyclohexa-2,5-dienyl acetate

Four 1,4 adducts were obtained from the nitration of 1,4-dimethyl-2-nitrobenzene and were generally recognised as such by (i) the appropriate microanalysis for carbon, hydrogen and nitrogen; (ii) characteristic peaks for NO_2 and $OCOCH_3$ in the i.r. spectrum ; (iii) u.v. λ_{max} < 254 nm and (iv) presence of three vinylic protons in the ^1H n.m.r. spectrum. All of the possible 1,4 adducts from 1,4-dimethyl-2-nitrobenzene are encompassed by the structures shown below:







10: X = NO_2, Y = OAc 91: X = NO_2, Y = OAc 93: X = NO_2, Y = OAc

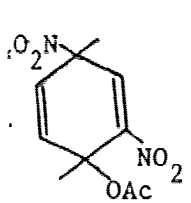
11: X = OAc, Y = NO_2 92: X = OAc, Y = NO_2 94: X = OAc, X = NO_2

Each of the six structural isomers of the 1,4 adducts can occur as a pair of diastereomers. Of these, two pairs were observed in the nitration under study. The ^1H n.m.r. spectrum of all the adducts isolated showed a 10 Hz coupling showing the presence of adjacent,vinylic protons and both the ring methyl groups (in all adducts) appeared as sharp singlets (Table 3.2). These observations indicate that the adducts obtained correspond to the structures 10 and 11.

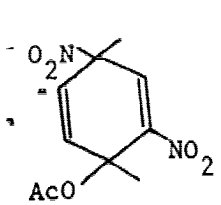
In all the adducts, the absorption at the lowest field is a doublet and is assigned to the ring proton "conjugated" with the vinylic

nitro group. The other two ring protons can be easily differentiated since one appears as a doublet (6-H in 10, 5-H in 11) and the other proton appears as a doublet of a doublet (5-H in 10, 6-H in 11). The methyl absorptions of the adducts were assigned by comparison with other 1,4 adducts and analyzing the data from shift reagent studies (Table 3.2).

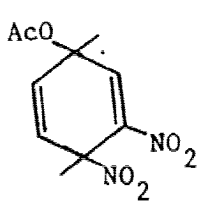
On addition of the shift reagent, the magnitude of shift for the acetate methyl was the highest. The shift of the ring methyl *ipso* to the acetate (1-CH_3) was larger than the shift for the 4-CH_3 (Figures 3.6, 3.7, 3.8 and Table 2.2). In the diastereomers 10A (eluted prior to 10B) and 10B, the induced downfield shift follow the order 6-H > 3-H > 5-H. In the adduct 11D, the induced downfield shift follow the order 2-H > 6-H > 5-H. The magnitude of induced shift for the 2-H in 11D is much greater than for the corresponding proton (3-H) in 10A or 10B lending further support to the assigned structures. The greater downfield shift of the 3-H in 10 (2-H in 11) relative to 5-H (6-H in 11) can be attributed to weak complexing with the C-2 (C-3) nitro group which results in 3-H (2-H) being closer to the complexing site than 5-H (6-H). In view of the higher gradient of the 4-CH_3 in 10A relative to 10B, 10A is assigned the *trans* configuration and 10B is assigned the *cis* configuration. Because of the small difference in the gradient and a greater difference in gradients for the other protons, the assignment is, at best, speculative.



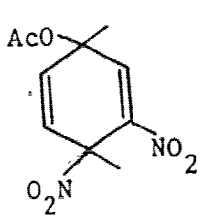
10A



10B



11D



11E

Irradiation techniques were successfully employed to obtain the information about coupling between the ring protons. When the decoupler frequency was set at the doublet at the lowest field (3-H in 10, 2-H in 11), the doublet due to 6-H in 10A and 10B (5-H in 11D) was unaffected whereas the doublet of a doublet due to 5-H (6-H in 11D) collapsed to a doublet. Thus, the ^{1}H n.m.r. spectra in all the adducts can be unambiguously assigned.

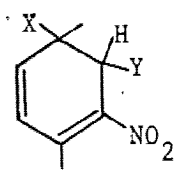
Since the diene 11E, formed in minor amounts (5%), could not be isolated, the stereochemistry of the diastereomers 11D and 11E cannot be ascertained. However, 11D is most likely to be the *trans* isomer since it is formed to a greater extent than, and eluted prior to, 11E. These observations are in agreement with the results obtained with the diastereomers in other systems in the present study.

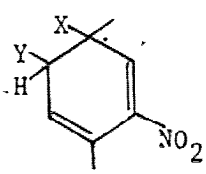
3.2.5 Diene 12: 3,6-dimethyl-2,6-dinitrocyclohexa-2,4-dienyl acetate

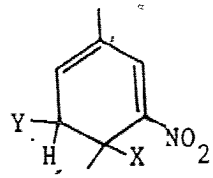
U.v. spectroscopy (295 nm) and ^{1}H n.m.r. (Table 3.2) showed that the major isomer from the nitration of 1,4-dimethyl-2-nitrobenzene is a 1,2 adduct.

The i.r. spectrum shows peaks at 1550 cm^{-1} and at 1760 and 1200 cm^{-1} indicating the presence of nitro and acetoxy groups.

For a 1,2 adduct, there are twelve possible structures consisting of six pairs of positional isomers, as represented in the following diagram:

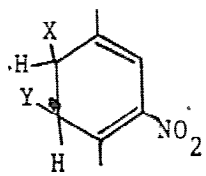


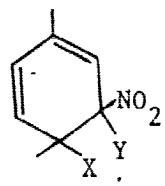


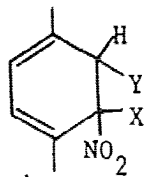


12: X = NO_2, Y = OAc 95: X = NO_2, Y = OAc 97: X = NO_2, Y = OAc

105: X = OAc, Y = NO_2 96: X = OAc, Y = NO_2 98: X = OAc, Y = NO_2







99: X = NO_2, Y = OAc 101: X = NO_2, Y = OAc 103: X = NO_2, Y = OAc

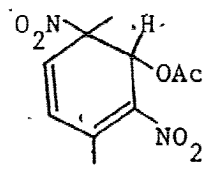
100: X = OAc, Y = NO_2 102: X = OAc, Y = NO_2 104: X = OAc, Y = NO_2

In compounds 95 to 104, an allylic coupling between a ring proton and a ring methyl would be expected, in analogy with the diene adducts 7A and 7B. In the adducts 95 to 98, one of the ring protons ("conjugated" with the nitro group) should absorb in the region δ 7-8 ppm. In the ^{1}H n.m.r. spectrum of the adduct obtained, the three methyl resonances appear as sharp singlets and there is no absorption in the region δ 7-8 ppm. Hence, structures 95 to 104 can be rejected. Structure 105, corresponding to a secondary nitro compound, can also be rejected for reasons discussed earlier (see 3.2.1)

The ^{1}H n.m.r. spectrum of the diene has an absorption at δ 6080 (dd) corresponding to 5-H. The other ring proton absorptions occur at δ

6.25 (d) and 6.14 (d) and are assigned to 1-H and 4-H respectively (J_{45} = 10 Hz, J_{15} = 1.46 Hz). The absorptions at δ 1.81 and 1.96 are assigned to 6-CH_3 and the acetate methyl respectively. The low-field absorption at δ 2.26 is assigned to the 3-CH_3 (which is "conjugated" with the C-2 nitro group).

On addition of the shift reagent, the acetate methyl moves downfield more rapidly than the ring methyl groups, whose relative shifts are the same (Figure 3.9 and Table 2.2). The shift of 5-H is higher than that for 4-H. Thus, all these observations are in accord with the structure 12 for the 1,2 adduct.



12

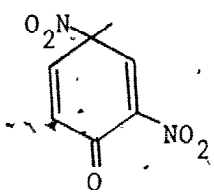
3.2.6 Dienone 13 : 4-methyl-2,4-dinitrocyclohexa-2,5-dien-1-one;

Adduct 42: 5-methoxy-4-methyl-4,6-dinitrocyclohexa-2-en-1-one.

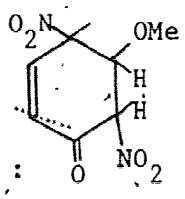
The nitrodienone obtained by the *ipso* nitration of 4-methyl-2-nitrophenol was quite unstable and usually decomposed on work-up to 4-methyl-2,6-dinitrophenol.

The ^1H n.m.r. spectrum of the dienone in acetic anhydride (in the reaction mixture) is easily interpreted. The low-field absorption at δ 7.87 (d) is assigned to 3-H and the absorption at δ 6.45 (d) is assigned to 6-H. The doublet of a doublet at δ 7.36 is assigned to 5-H. The coupling information (J_{56} = 10 Hz; J_{35} = 2 Hz) supports these

observations. On crystallization from methanol, a white, crystalline compound was obtained which was assigned the structure 42 on the basis of the following observations:



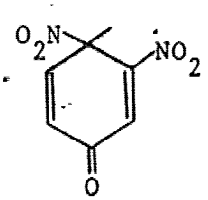
13



42

The i.r. spectrum of the adduct showed the presence of nitro and carbonyl groups as evidenced by absorptions at 1550 cm^{-1} and at 1710 cm^{-1} respectively. The compound is insoluble in chloroform and methanol. ^1H n.m.r. spectrum of the adduct in acetone-d_6 shows a 10 Hz coupling for the adjacent, vinylic protons and a 11.33 Hz coupling for the other two protons. Among the ring protons, the absorptions at δ 7.14, 6.53, 5.93 and 4.89 ppm are assigned to 3-H, 2-H, 6-H and 5-H respectively. The singlet at δ 3.60 shows the presence of the methoxy group and the singlet at δ 2.10 is assigned to the 4-CH_3. The adduct decomposed during ^{13}C n.m.r. studies (0°C, 4 h) to 4-methyl-2,6-dinitrophenol. The phenol was also obtained when the adduct was reacted with methyllithium at -78°C.

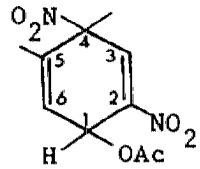
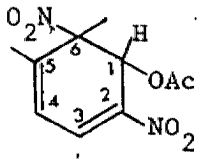
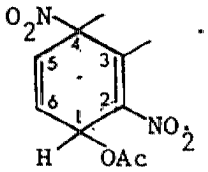
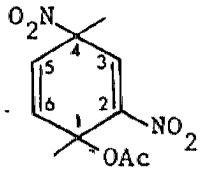
Arguments similar to those used for 13 could be extended to interpret the spectrum of 4-methyl-3,4-dinitrocyclohexa-2,5-dien-1-one (71), obtained from the nitration of 4-methyl-3-nitrophenol.

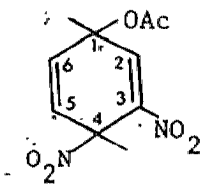
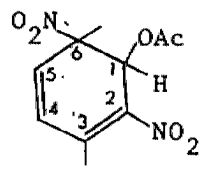
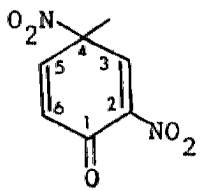
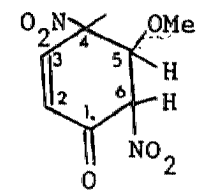
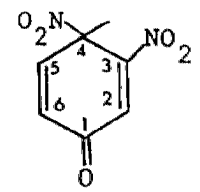


71

TABLE 3.2

δ VALUES OF ACETATE AND OTHER SUBSTITUENTS IN THE ADDUCTS OBTAINED

ADDUCT		OAc	C-1	C-2	C-3	C-4	C-5	C-6	COUPLING CONSTANTS (Hz)	ASSIGNMENT
	7A	2.06	6.46	-	7.44	1.95	1.88	5.98	$J_{16} = 4$, $J_{56} = 1.5$, $J_{15} = 1.3$	*trans*
	7B	2.04	6.34	-	7.34	1.86	1.86	5.96	$J_{16} = 4$, $J_{56} = 1.5$	*cis*
	8	2.08	6.93	-	7.48	6.35	2.12	1.78	$J_{34} = 7$, $J_{45} = 1.5$	
	9A	2.05	6.52	-	2.03	1.92	6.05	6.26	$J_{56} = 10$, $J_{16} = 3.4$, $J_{15} = 1.5$, $J_{13} = 1.3$	*trans*
	9B	2.07	6.33	-	2.07	1.85	6.04	6.19	$J_{56} = 9.5$, $J_{16} = 3.4$, $J_{15} = 1.5$, $J_{13} = 1.3$	*cis*
	10A	2.02	1.72	-	7.43	1.92	6.15	5.94	$J_{56} = 10$, $J_{35} = 1.76$	*trans*
	10B	2.00	1.67	-	7.57	1.86	6.30	5.98	$J_{56} = 10$, $J_{35} = 1.75$	*cis*

	11D	2.04	1.62	7.60	–	2.04	5.89	6.01	$J_{56} = 10$, $J_{26} = 1.5$
	11E	2.00	1.70	7.70	–	1.89	5.85	6.05	(not isolated)
	12	1.96	6.25	–	2.26	6.14	6.80	1.81	$J_{45} = 10$, $J_{15} = 1.46$
	13	–	–	–	7.87	–	7.36	6.45	$J_{56} = 10$, $J_{35} = 2$
	42	3.60 (OMe)	–	6.53	7.14	2.09	4.89	5.93	$J_{56} = 11.33$, $J_{23} = 10$
	71	–	–	7.47	–	–	7.15	6.58	$J_{56} = 10$, $J_{26} = 2$

(i) The spectra of the dienones 13 and 71 were obtained from the reaction mixtures (lock: acetic anhydride δ 2.15 ppm).

(ii) The spectrum of 42 was recorded in CD_3COCD_3; all other spectra were recorded in $CDCl_3$.

Figure 3.1: Plot Showing the Chemical Shifts of Protons in Diene 7A v/s the Chemical Shift of the Acetate-Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

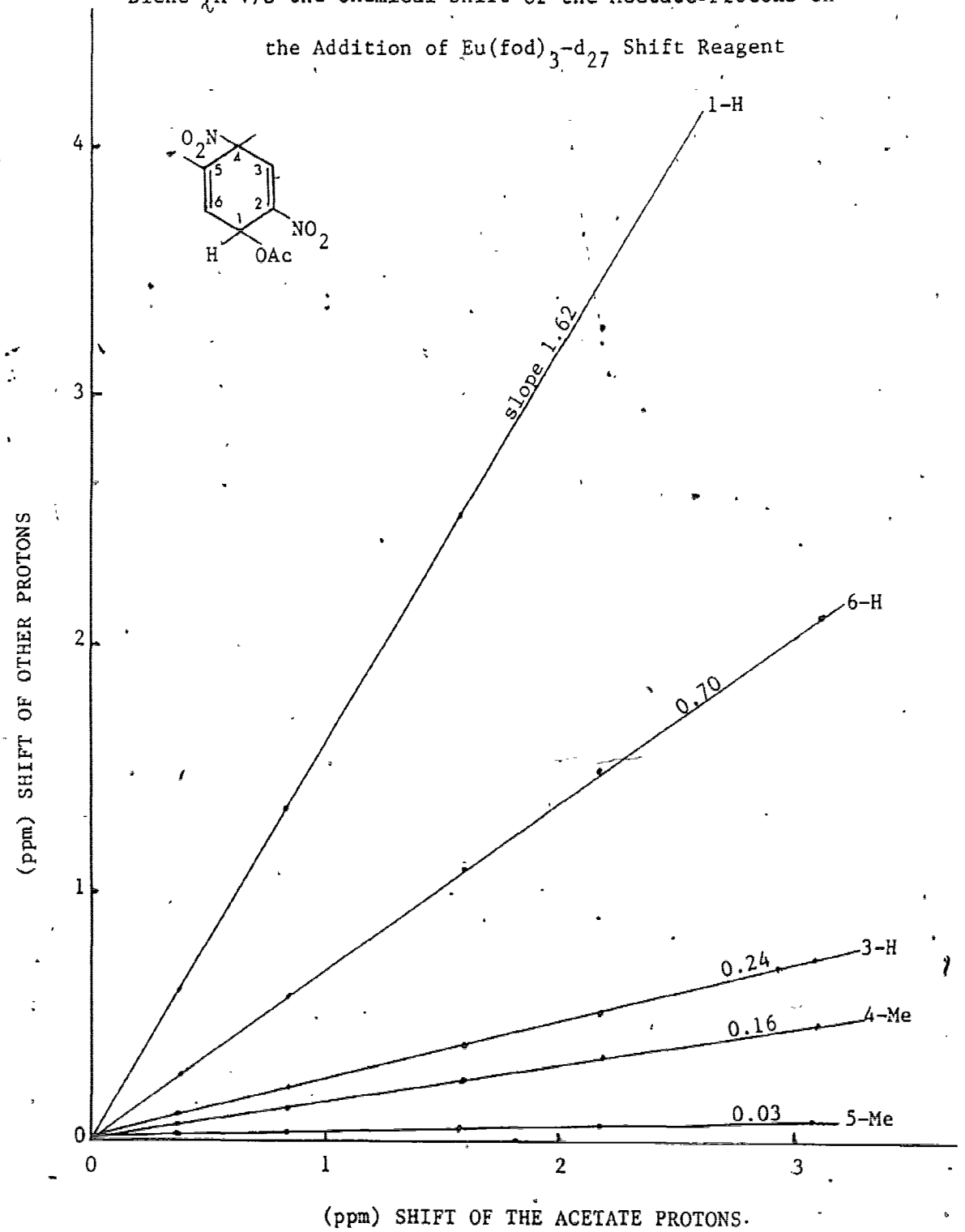


Figure 3.2: Plot Showing the Chemical Shifts of Protons in Diene 7B v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

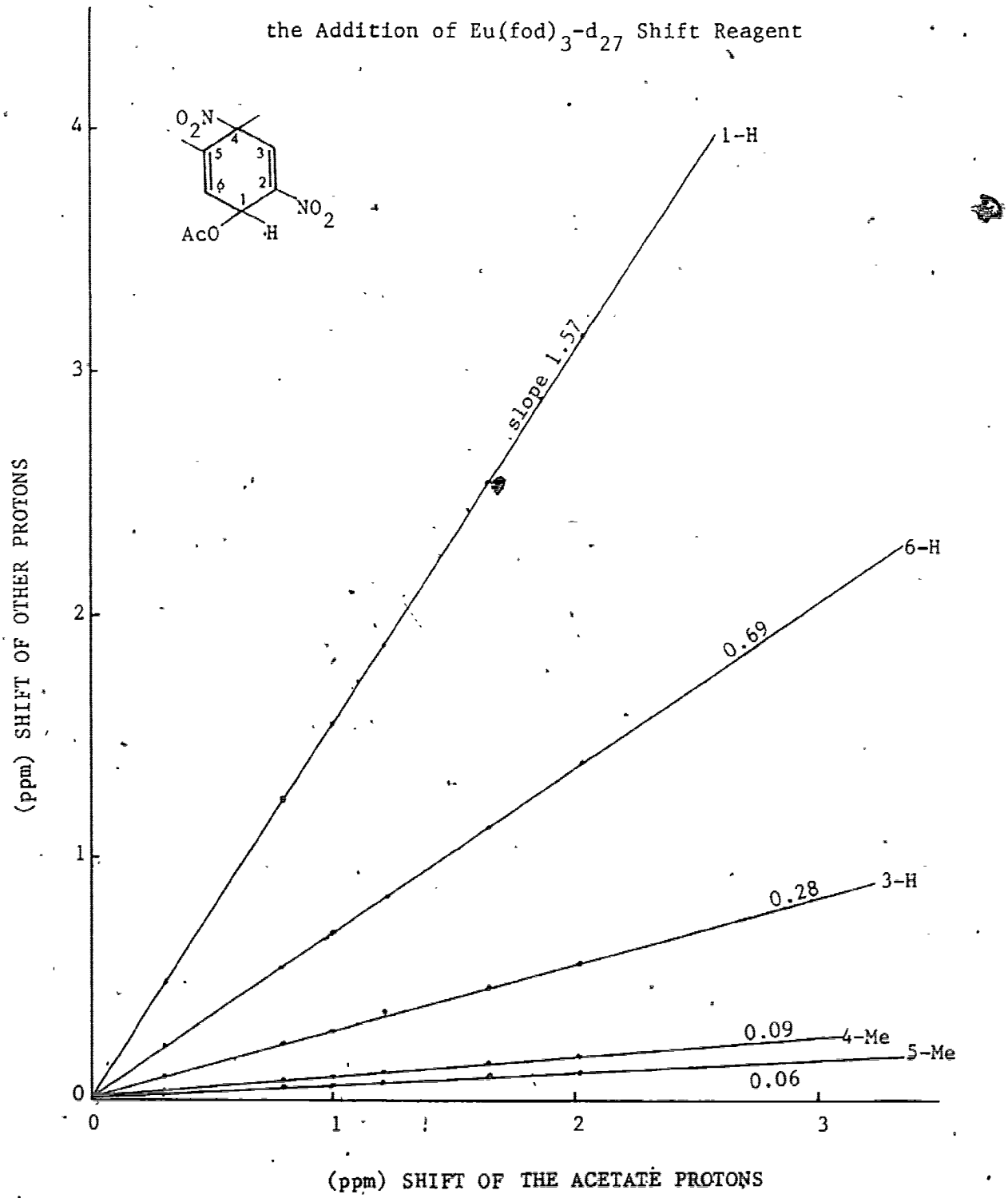


Figure 3.3: Plot Showing the Chemical Shifts of Protons in Diene δ v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

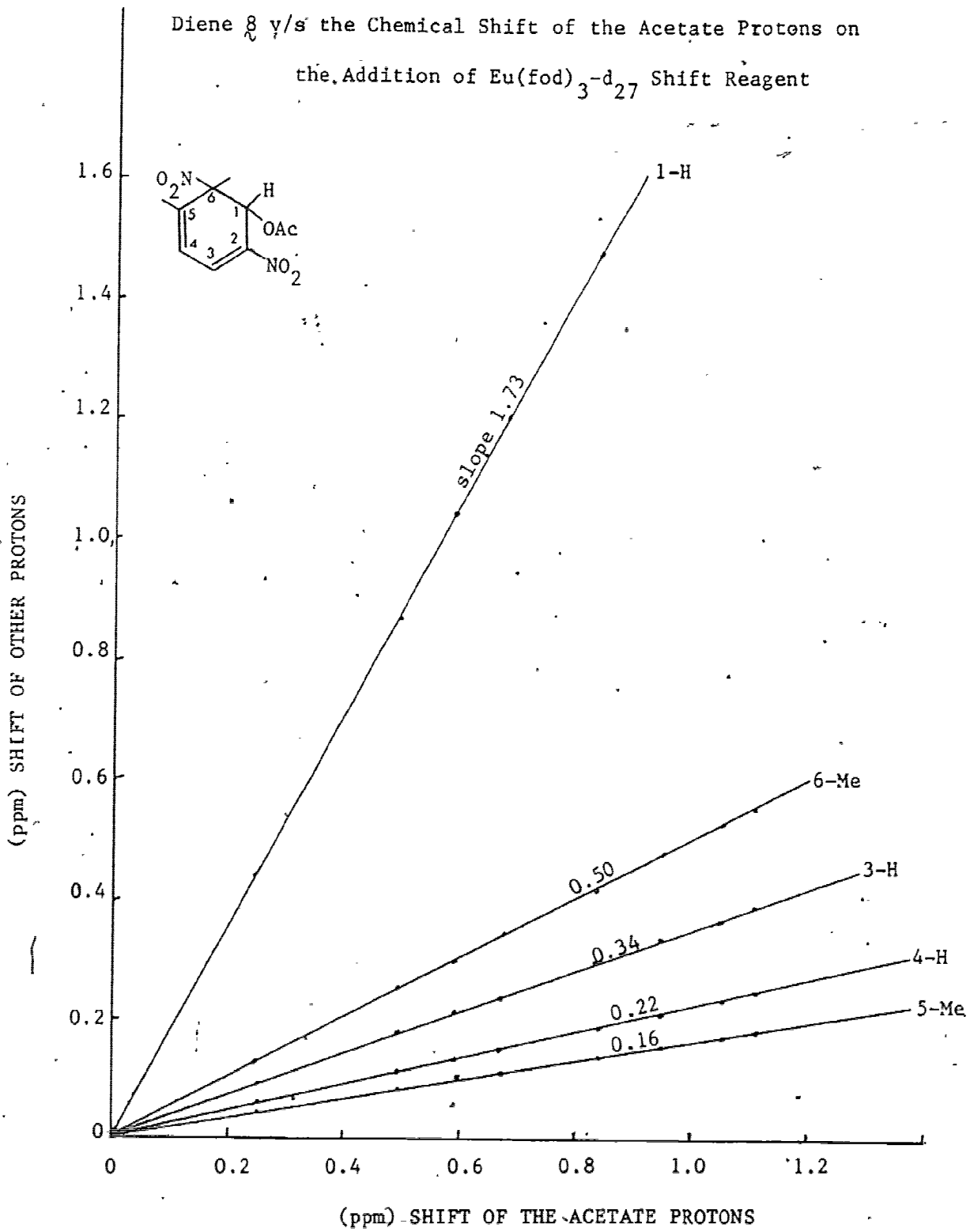


Figure 3.4: Plot Showing the Chemical Shifts of Protons in Diene 9A v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

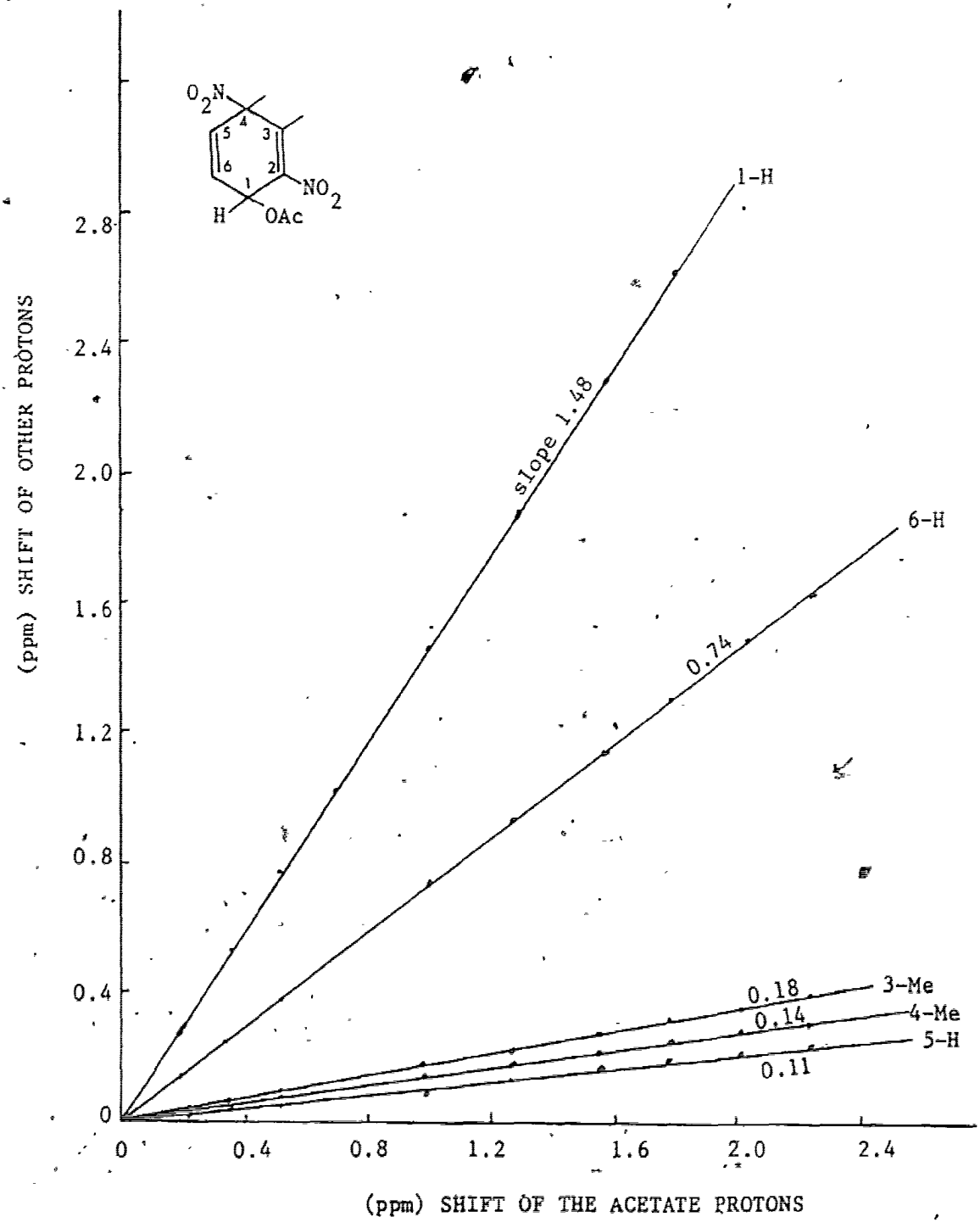


Figure 3.5: Plot Showing the Chemical Shifts of Protons in Diene 8B v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

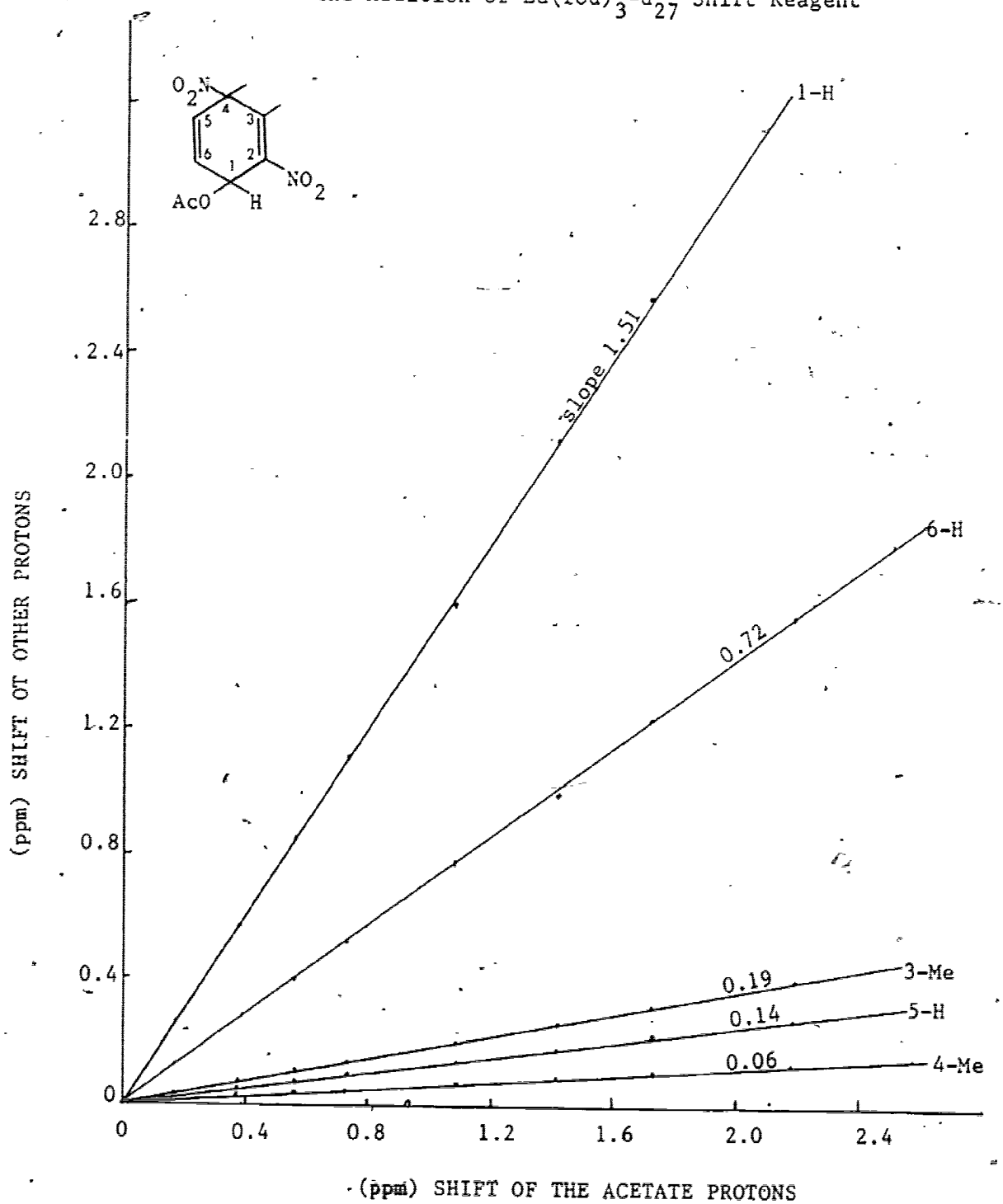


Figure 3.6: Plot Showing the Chemical Shifts of Protons in Diene 10A v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

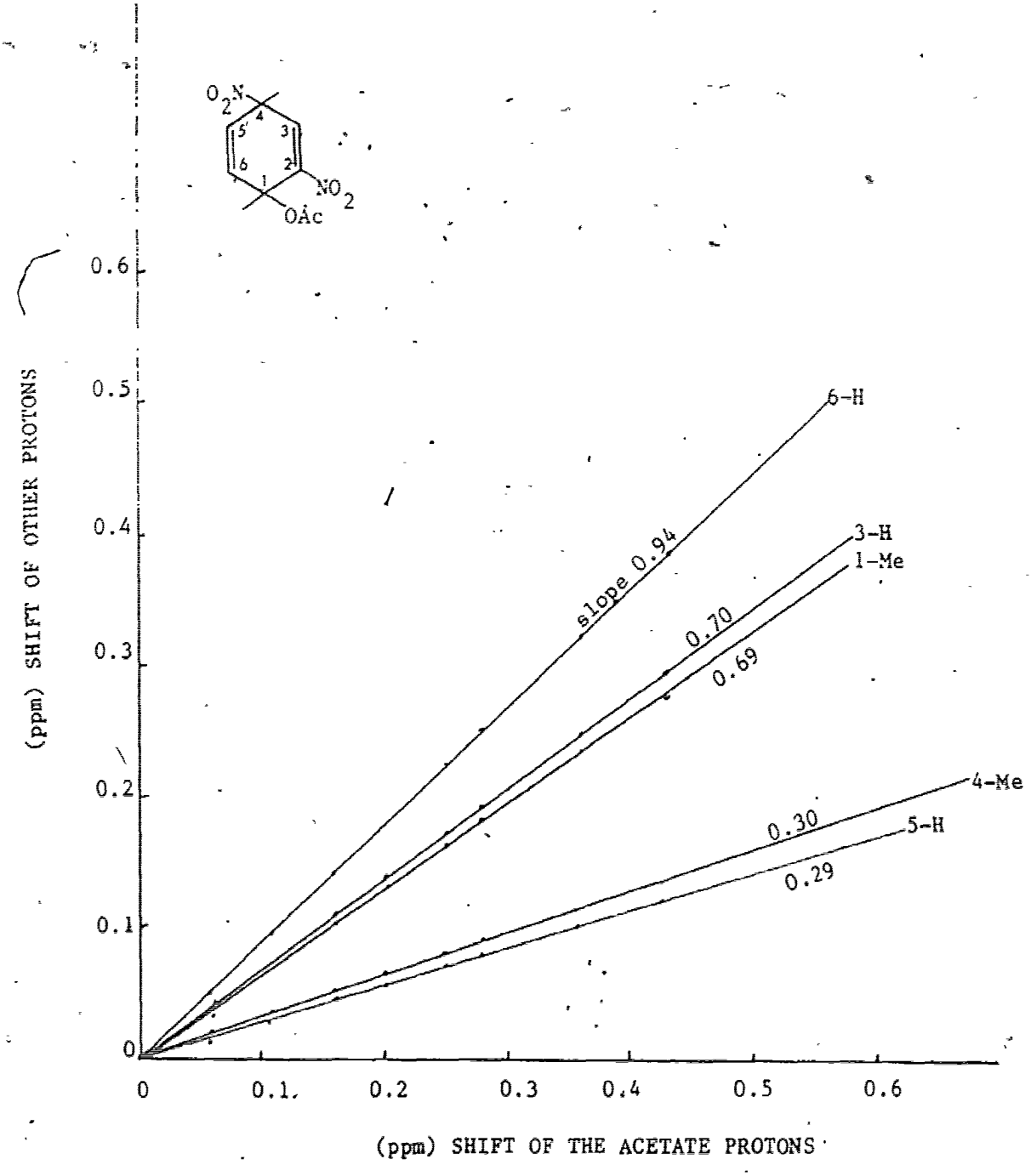


Figure 3.7: Plot Showing the Chemical Shifts of Protons in Diene 10B v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

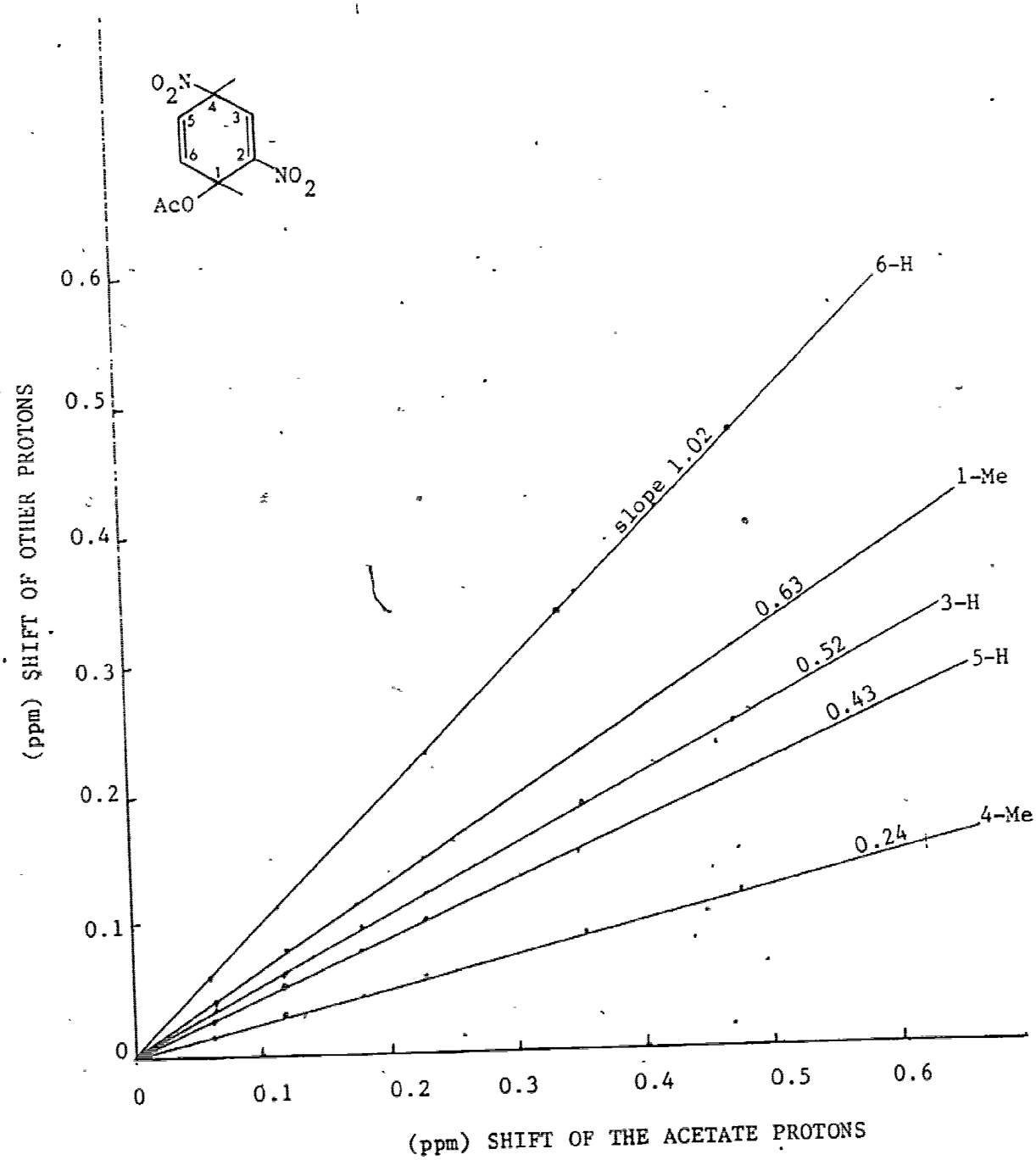


Figure 3.8: Plot Showing the Chemical Shifts of Protons in Diene 11D v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent

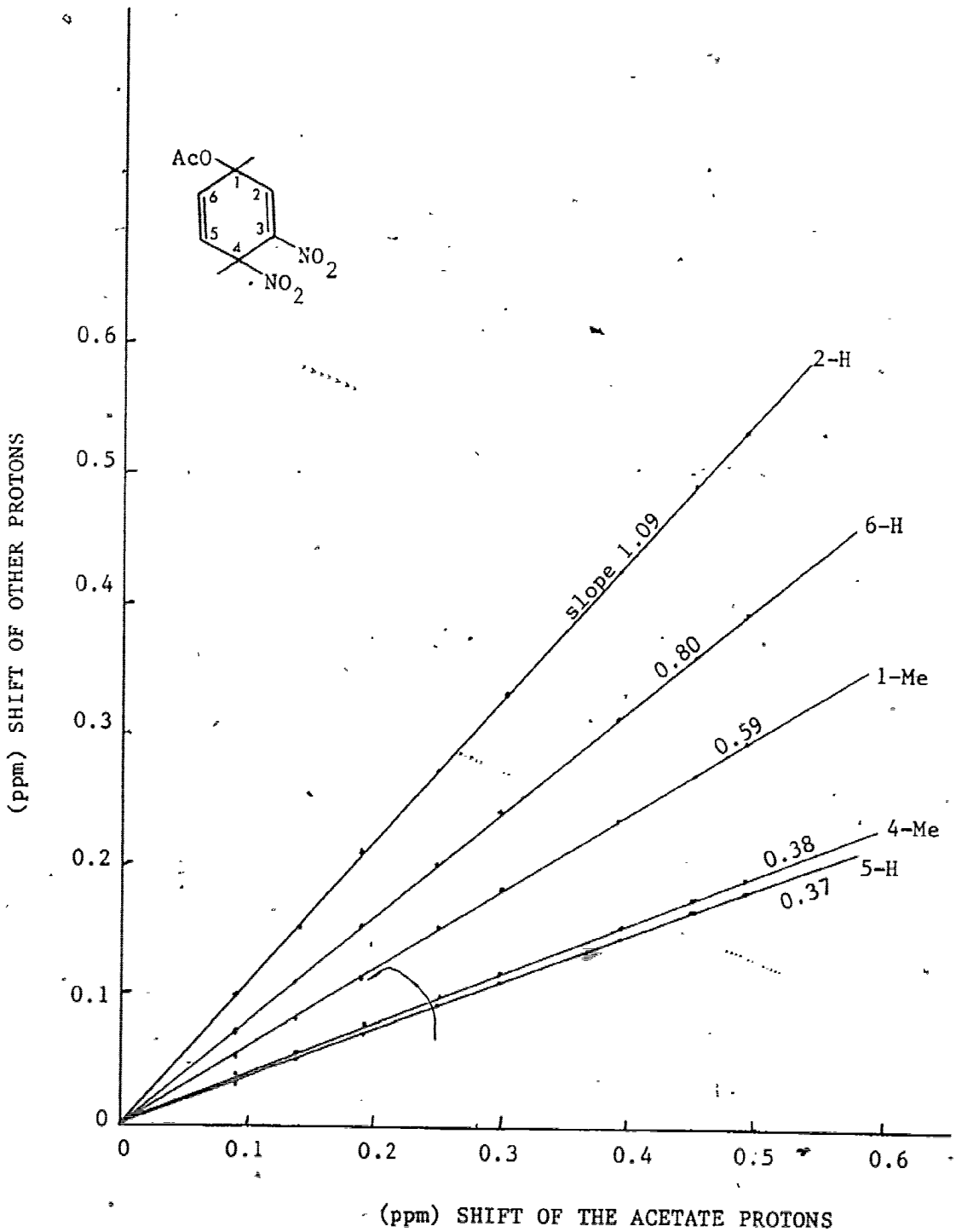
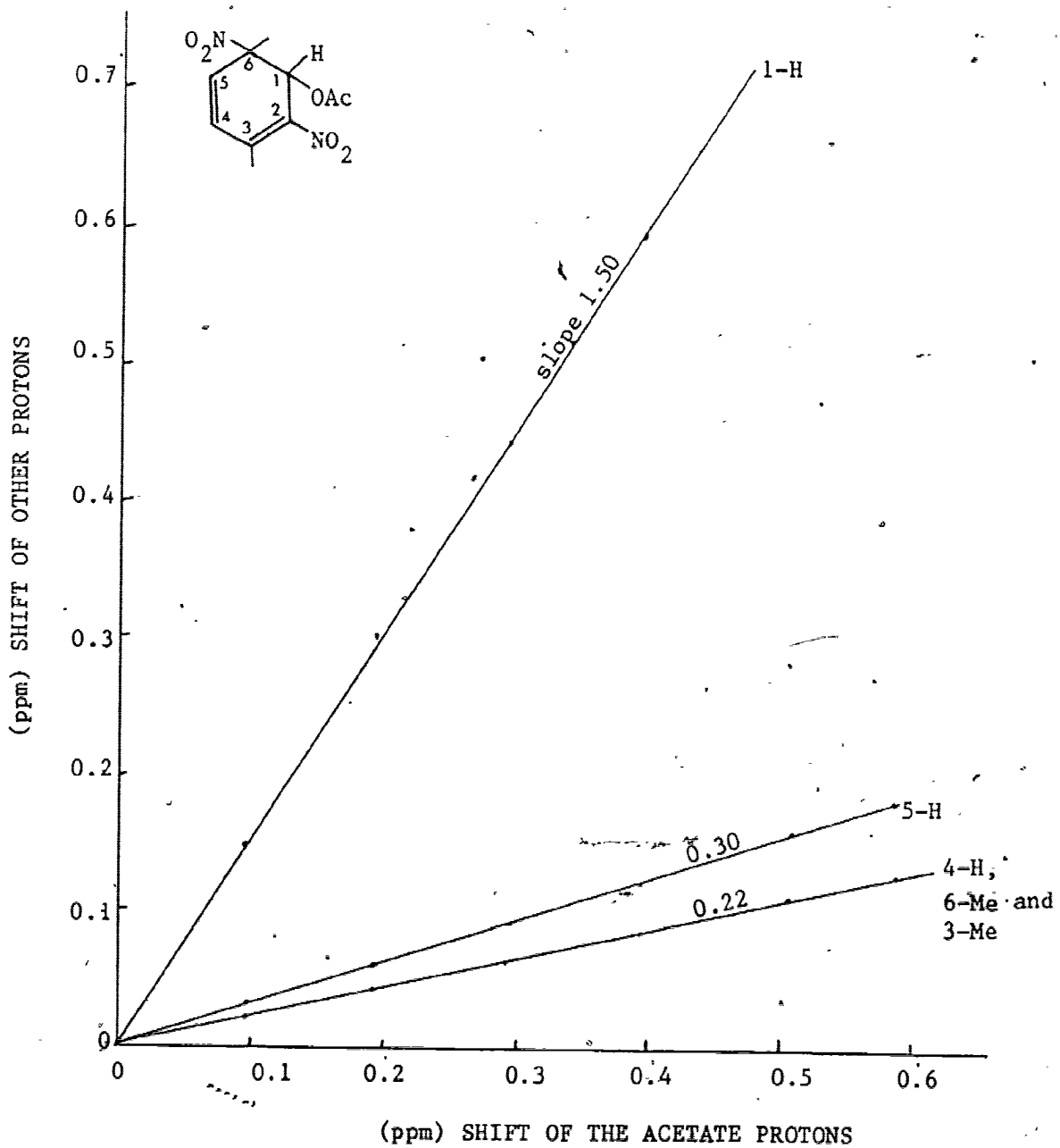


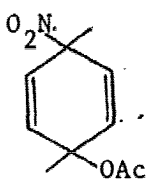
Figure 3.9: Plot Showing the Chemical Shifts of Protons in Diene 12 v/s the Chemical Shift of the Acetate Protons on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent



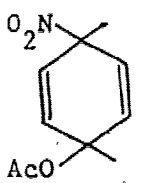
3.2.7 Diastereomers 1A and 1B: 1,4-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate

Shift reagent studies were also employed as a useful aid in assigning the ^{13}C n.m.r. spectra of the various diene adducts in this study. The studies were especially useful in distinguishing the proton-carrying vinylic carbons from each other.

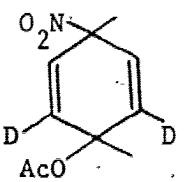
A model compound, 1,4-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate (39) was chosen for the study. ^{13}C n.m.r. of this compound, 1B (m.p. 57-58°C) showed absorptions at δc 126.3 and 132.7 ppm due to the vinylic carbons. On addition of the shift reagent, the magnitude is expected to be higher for the carbons closer to the site of complexation *i.e.* absorptions due to C-2 and C-6 should move downfield more rapidly than those due to C-3 and C-5. On this basis (Figure 3.11), the high-field absorption at δc 126.3 in 1B was assigned to C-3 and C-5 and the signal at 132.7 was assigned to C-2 and C-6. These assignments are in agreement with the results obtained on the di-deutero analogue of 1B (81), but in conflict with the assignments made previously (39b). The gradient of the 4-CH_3 carbon in 1A (m.p. 46-47°C) is higher than in 1B (Figures 3.10 and 3.11) support the observation that 1A is *trans* and 1B is the *cis* isomer. However, the plot corresponding to 1-$\underline{C}H_3$ in 1A did not pass through the origin (contrary to expectations), but a linear relationship with the shift of the acetate $\underline{C}H_3$ was exhibited.



1A



1B



1B-d_2

Figure 3.10: Plot Showing the Chemical Shifts of Carbons in Diene 1A v/s the Chemical Shift of the Acetate Carbon ($\underline{CH}_3$) on the Addition of Eu(fod)$_3$-d$_{27}$ Shift Reagent

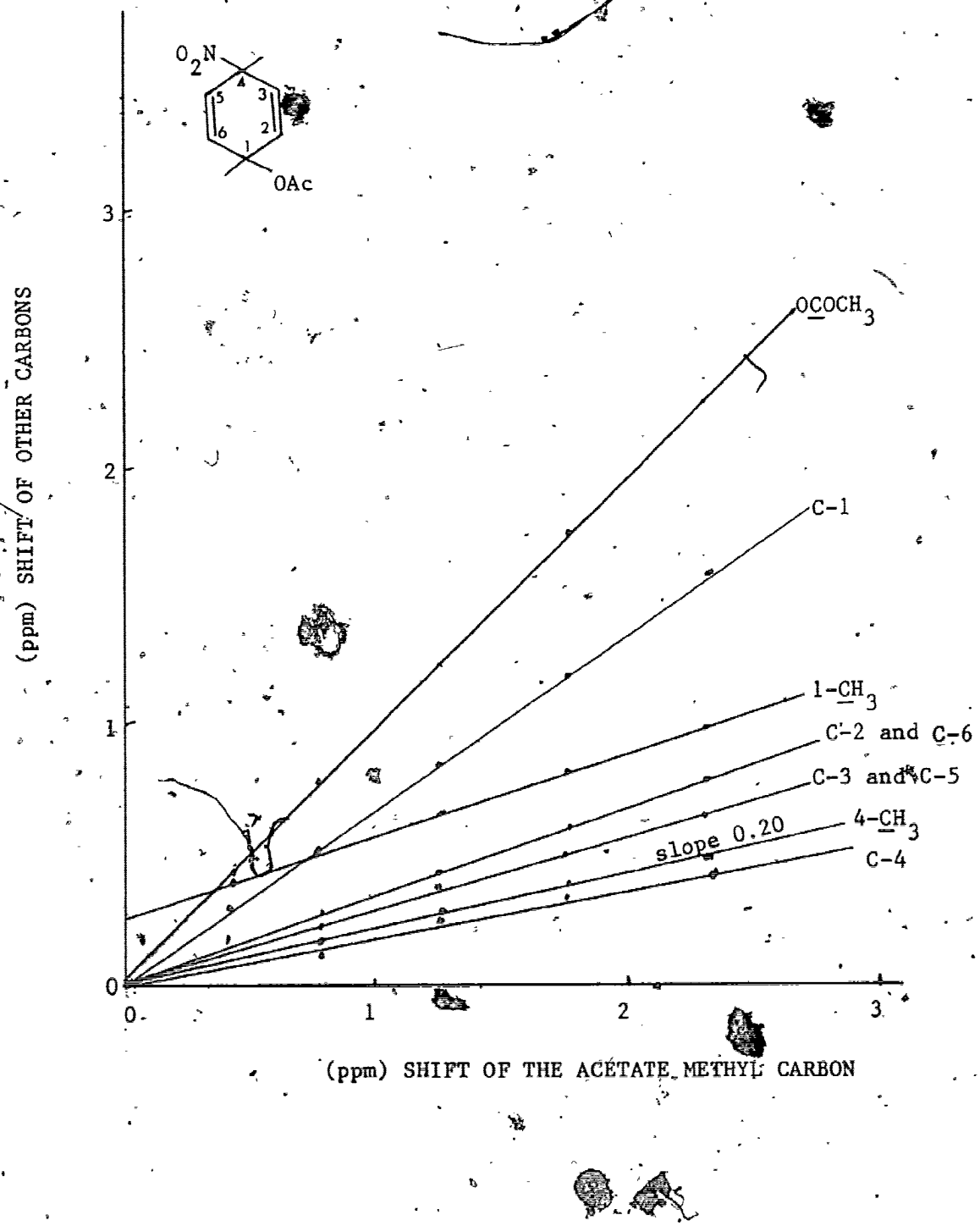
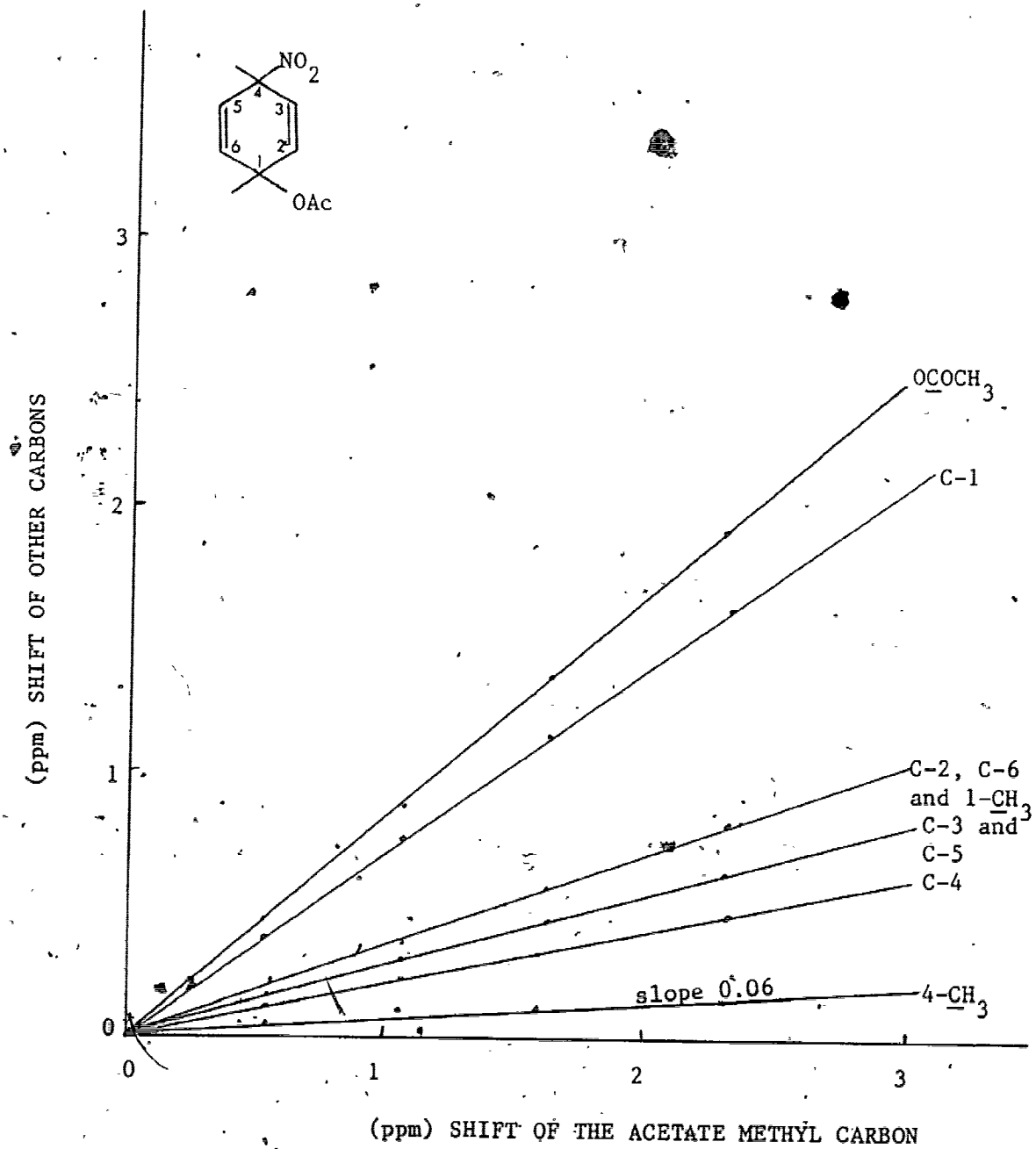


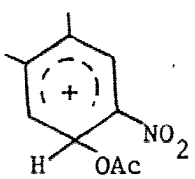
Figure 3.11: Plot Showing the Chemical Shifts of Carbons in Diene 1B v/s the Chemical Shift of the Acetate Carbon ($\underline{CH}_3$) on the Addition of $Eu(fod)_3$-d_{27} Shift Reagent



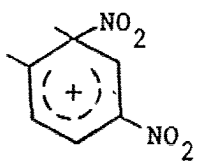
3.3 *Reactions of the Adducts*

The dienes obtained by the *ipso* nitration of various nitroarenes undergo a variety of exchange (diene interconversion) and rearomatization reactions. The nitroxylene adducts are more stable and resistant to rearomatization than the adducts of alkylbenzenes (38,39). The acetate functionality could be formally replaced by other nucleophiles under suitable conditions. The reactions of the secondary acetates obtained from 1,2-dimethyl-4-nitrobenzene were remarkably different from those of the secondary and tertiary acetates obtained from 1,4-dimethyl-2-nitrobenzene.

The products obtained by the rearomatization of the adducts were dependent on the conditions employed. Consideration of the rearomatization pathways invoking the acetoxy- and nitrocyclohexadienyl cations indicates that introduction of the nitro substituent should favour formation of the latter.



67



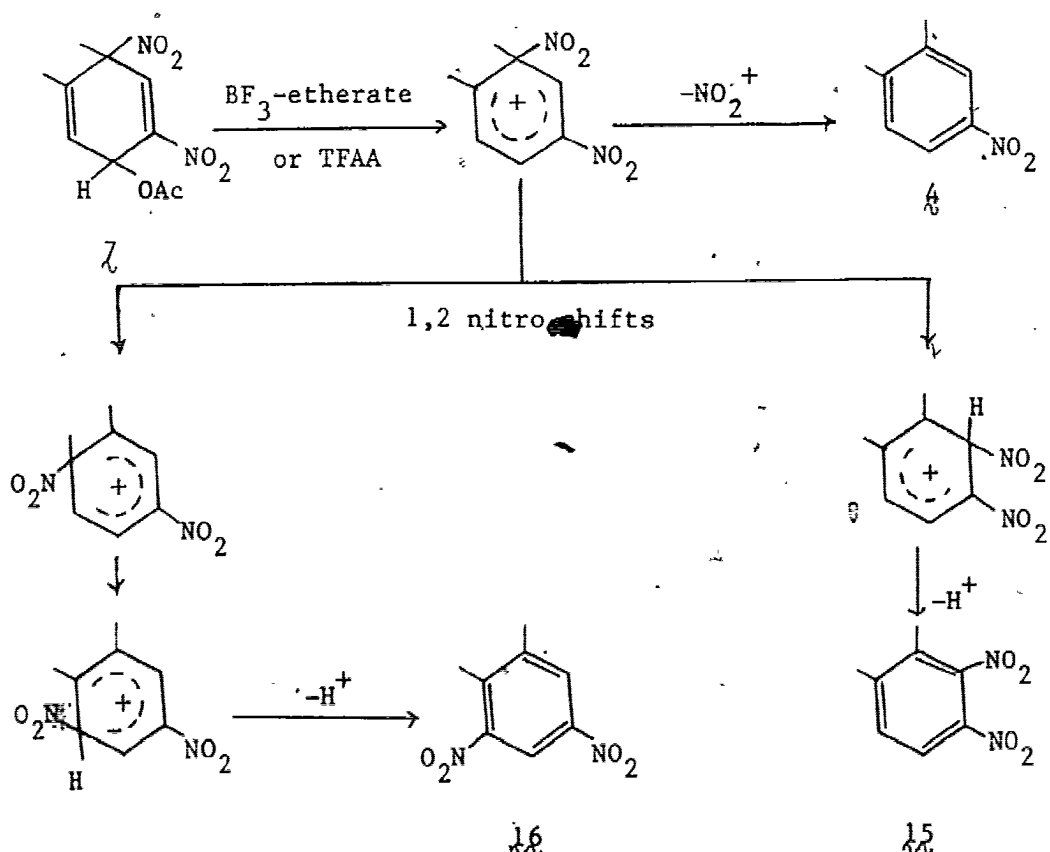
48

Formation of 67 would involve the placement of a formal positive charge at a nitro-substituted carbon. Formation of 48 involves the generation of a formal positive charge at a carbon adjacent to that carrying the nitro group and is energetically favoured. Hence, 48 is the preferred intermediate and its formation constitutes the principal route to the formation of rearomatized products.

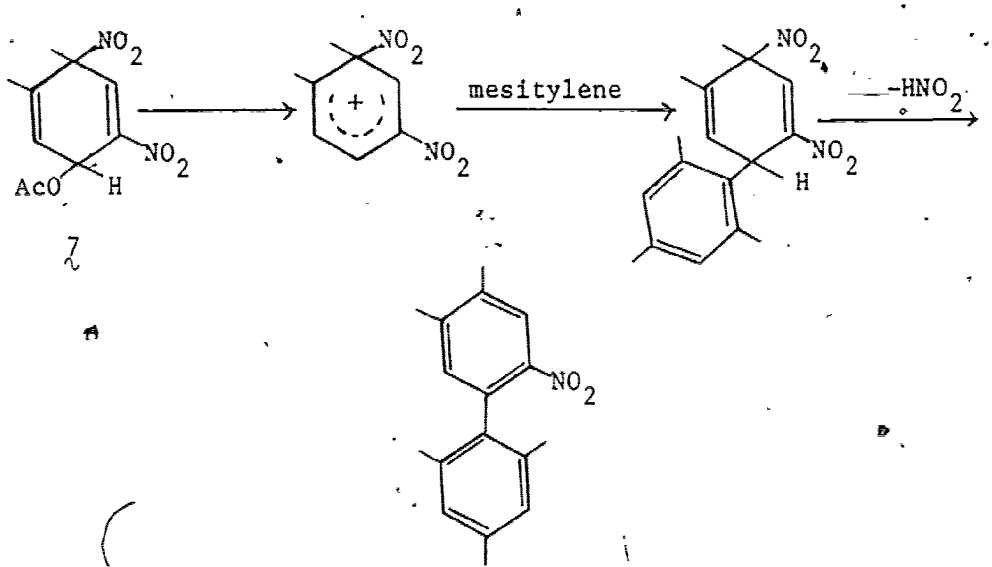
The main reaction pathways are represented schematically at the end of this Chapter and the product distribution obtained in the reactions of the adducts are shown in Appendix II.

3.3.1 *Reactions under Acidic Conditions*

The diene adducts 7A (B) on treatment with borontrifluoride-etherate or with trifluoroacetic acid gave 1,2-dimethyl-4-nitrobenzene as the main product (70-80%). Products which could arise from 1,2 nitro shifts in an intermediate nitrocyclohexadienyl cation (48) were also obtained in nearly equal amounts.



That an intermediate nitrocyclohexadienyl cation was involved was shown by rearomatizing the diene in the presence of mesitylene when the biphenyl 22 was obtained as the major product[3] (99%).



7

22 (99%)

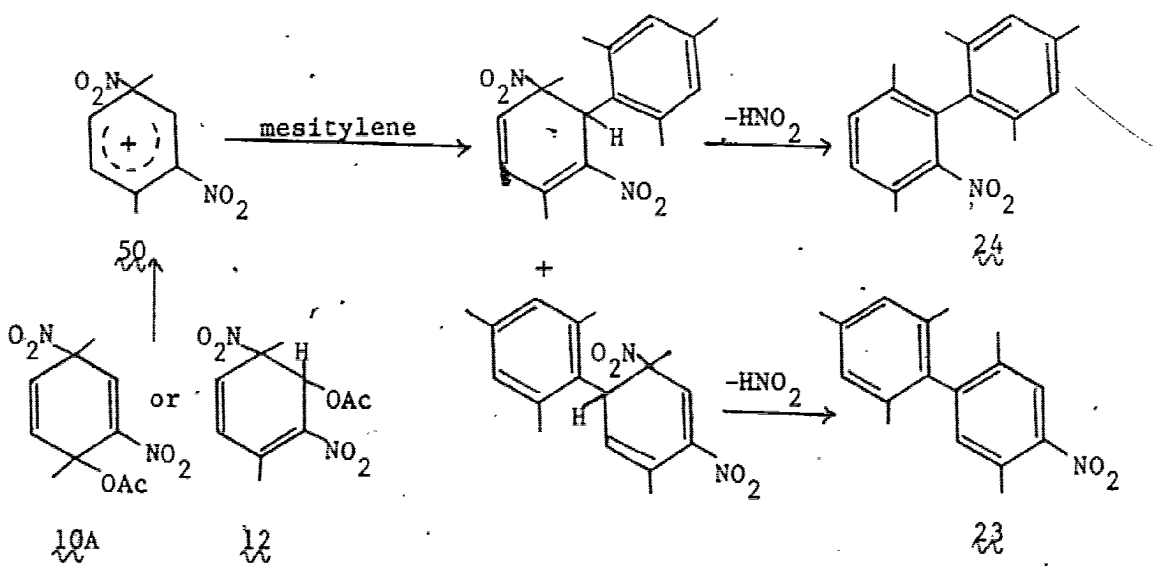
The rearomatization of the adducts 10A and 12 from 1,4-dimethyl-2-nitrobenzene was similar. ^{1}H n.m.r. studies showed that in the case of the adduct 10A, partial isomerization (*ca.* 15%) to the diene 12 occurred prior to rearomatization. In the case of the secondary adduct

---

[3]Since *ipso* nitration of 1,2-dimethyl-4-nitrobenzene gives *ca.* 50% diene adducts and the conversion of the adducts to the biphenyl is quantitative, this is an excellent method for the formation of such compounds. The diene route is much superior to obtaining 22 by nitrating the suitable pentamethylbiphenyl, in which substitution would be preferred in the trialkyl- rather than the dialkylbenzene ring.

12, an aryl acetate resulting from loss of nitrous acid was also obtained. With both adducts, a minor product (1,4-dimethyl-2,6-dinitrobenzene) arising from renitration was also obtained. The absence of such renitration products under similar conditions in the case of the adducts 7A (B) could be related to the lower reactivity of 1,2-dimethyl-4-nitrobenzene, nitration of which required more drastic conditions than 1,4-dimethyl-2-nitrobenzene.

Rearomatization of the adducts 10A and 12 with BF_3-etherate in mesitylene gave, along with the expected dinitroxylenes, the biphenyls 23 and 24 in the ratio 4:1. Formation of the biphenyls from 10A is unusual since similar products have been generally obtained from secondary adducts (54,82) and only one biphenyl is formed. The electronic effect of the (original) nitro group should make the adjacent unsubstituted position in the cyclohexadienyl cation more positive and favour the formation of 24. However, attack at this position should be more hindered and, on this ground, 23 should be favoured. Evidently, the steric effect is more important.



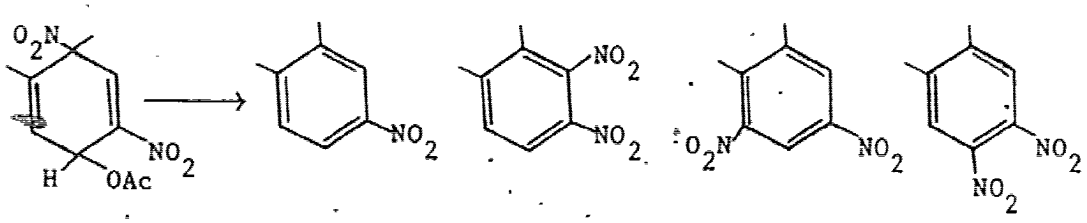
The adducts 7A (B) were stable to acetic acid at room temperature but rearomatized on heating to give 1,2-dimethyl-4-nitrobenzene and 1,2-dimethyl-3,5-dinitrobenzene in nearly equal amounts. The latter product is obtained by a formal 1,3 shift of the nitro group. Such 1,3 shifts have also been observed in the rearomatization of other diene adducts (57) but the mechanism is not established. The 1,3 shift cannot arise from consecutive 1,2 shifts since an initial 1,2 shift to an unsubstituted position would give the cyclohexadienyl cation precursor of 1,2-dimethyl-3,4-dinitrobenzene. As discussed earlier, the reaction with BF_3-etherate gave products arising from 1,2 nitro shifts in nearly equal amounts. The absence of any 1,2-dimethyl-3,4-dinitrobenzene in the rearomatization in acetic acid indicates that the observed dinitro product does not arise either by consecutive 1,2 nitro shift or by a process of renitration. In the presence of a radical scavenger, the amount of 1,2-dimethyl-3,5-dinitrobenzene is reduced (32%) and a greater amount of 1,2-dimethyl-4-nitrobenzene (68%) is obtained. These results suggest that a radical dissociation-recombination mechanism, similar to that observed in the decomposition of nitrodienones (see Chapter I), is likely.

A 1,3 nitro shift was also observed in the thermal decomposition of the adducts 10A and 12 in acetic acid. By analogy with the results obtained from 7A (B) and nitrodienones, the formal 1,3 shift across an unsubstituted position can occur through a free radical mechanism.

Since 1,2-dimethyl-4-nitrobenzene was obtained as the major product when the adducts 7A (B) were rearomatized under weakly acidic

conditions (BF_3-etherate or trifluoroacetic acid), the rearomatizations under strongly acidic conditions were studied and the product composition determined. The decomposition in trifluoromethanesulfonic acid was complete in 5 min at -20°C. Product analysis by ^1H n.m.r. and g.l.c. showed a depletion in the amount of 1,2-dimethyl-4-nitrobenzene and the formation of all the three dinitro-*o*-xylenes in significant amounts.

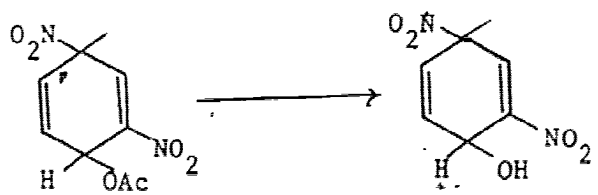
Comparison of these results with those obtained in the reaction with BF_3-etherate indicated that renitration had occurred. The calculated values for the product distribution, taking into consideration that renitration would result in the formation of 15, 16 and 17 in the ratio 1.33:1.80:1 (from this work) are 29%, 29% and 11% respectively. These values are in agreement with the product distribution actually obtained in the reaction with trifluoromethanesulfonic acid. The formation of 1,2-dimethyl-4,5-dinitrobenzene and the close correspondence of the observed product distribution with the calculated values showed that renitration had accompanied the process of 1,2 nitro shifts in the rearomatization of the adducts 7A (B) in trifluoromethanesulfonic acid.



7	4	15	16	17
BF_3-Etherate	78%	14%	8%	–
CF_3SO_3H				
(a) Observed	31%	25%	31%	13%
(b) Calculated	--	29%	29%	11%

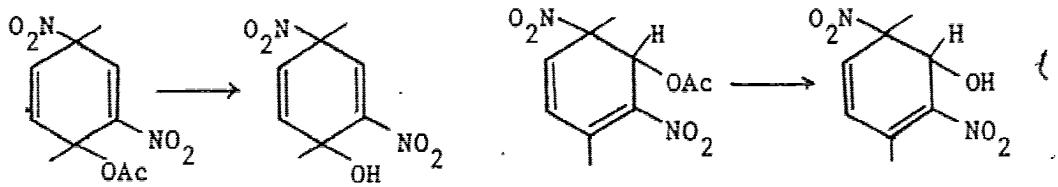
A similar drop (50-70%) in the amount of 1,4-dimethyl-2-nitrobenzene was observed when the rearomatization of the adducts 10A or 12 in BF_3-etherate was compared with the result obtained in trifluoromethanesulfonic acid. The product distribution showed an enhancement of the dinitro-*p*-xylenes. The absence of significant amount of 1,4-dimethyl-2,5-dinitrobenzene (detectable limit, 3%) may be attributed to the low degree of substitution *para* to the nitro group in the nitration of 1,4-dimethyl-2-nitrobenzene.

On treatment of the adducts 7A (B) with acidified methanol, an $A_{AC}2$ transesterification to form 33A (B) is preferred to an $A_{AL}1$ exchange of OAc for OMe which would otherwise be expected through the intermediate nitro-substituted phenonium ion (38). The adducts 10A and 12 were also converted to the corresponding nitrodienols in nearly quantitative yields.



7A 33A

7B 33B



10A 37A 12 39

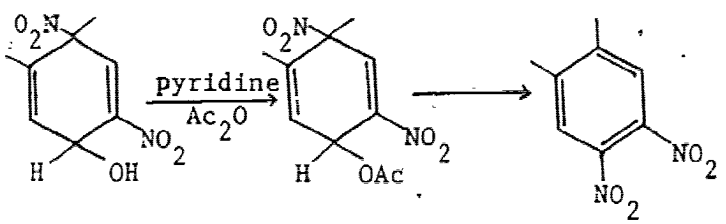
An interesting feature of the rearomatization reactions was the absence of any benzylic products under various conditions of acidity. Benzylic products are usually obtained when the deprotonation of an alkyl substituent of the cyclohexadienyl cation is an effective competing process with rearrangement and nuclear deprotonation (see Chapter I). These products are obtained from tertiary acetoxynitro adducts of 1,4 disubstituted arenes, such as *p*-xylene, whose adducts rearomatize in acetic acid or nitric acid to give substantial amounts of benzylic products (38).

In the reactions of the diene adducts obtained from the nitroarenes, the absence of benzylic products under various conditions of acidity indicates that migration of the nitro group and deprotonation, or alternatively, loss of nitro group (to regenerate the nitroarene) is preferred to deprotonation. Consequently, it is expected that with the increase in basicity of the reaction medium and the availability of suitable nucleophiles, nucleophilic exchange or formation of benzylic products would be an effective competing pathway. Therefore, the reactions of the diene adducts with various nucleophiles was investigated.

3.3.2 *Reactions with Nucleophiles*

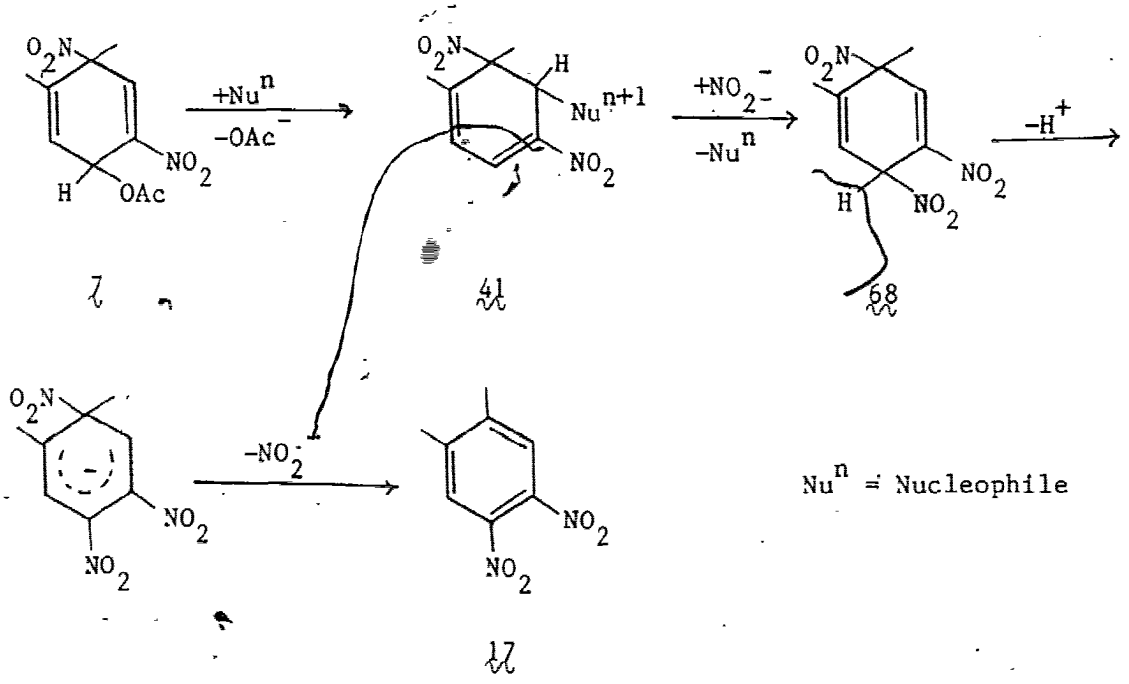
An unusual feature of the diene adducts obtained from the nitroarenes is their ability to undergo exchange and rearomatization reactions with nucleophiles. This was first observed in the attempted acetylation of the dienols 33A (B) with the acetic anhydride-pyridine reagent, conventionally employed for acetylation of hydroxy groups (86d).

Addition of acetic anhydride to a solution of the diastereomeric dienols in pyridine resulted in the rapid formation of 1,2-dimethyl-4,5-dinitrobenzene (17) as the only product. The dienols themselves were stable to pyridine, indicating that acetylation preceded rearomatization. This was confirmed by reacting the acetoxynitro adducts 7A (B) with acetic anhydride and pyridine, when 17 was obtained in nearly quantitative yield. Since *ipso* nitration of 1,2-dimethyl-4-nitrobenzene gives *ca.* 50% diene adducts (and 12% of 17) and the reaction of the adducts with pyridine gives a high yield of 17, this route is of synthetic importance in the preparation of 1,2-dimethyl-4,5-dinitrobenzene (17).



33 7 17

The mechanism shown in scheme 3.1 is proposed for the formal 1,4 migration of the nitro group (95). The mechanism involves consecutive S_N2' processes as shown in the scheme. For each substitution, the normally unreactive vinyl carbon is activated by conjugation of the double bond with the non-migrating nitro group. The proton α to the nitro group in 68 is acidic and is readily removed in the basic medium to form an anion. The anion in turn should rapidly lose the nitro group as a nitrite anion (which is thus regenerated) to give 17. The small amount of nitrite ion initially required in the second step can arise from the loss of elements of nitrous acid from 7 in the basic medium.



Scheme 3.1 Reaction of the adduct 7 with a nucleophile

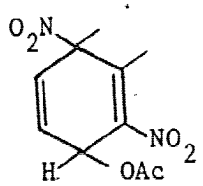
The acetate ion released in the first step of the reaction can compete with pyridine as the effective nucleophile so that the conjugated dienyl intermediate 41 can have Nu^{n+1} = OAc or $Nu^{n+1} = C_5H_5\overset{+}{N}$. If 41 and 68 are indeed intermediates in the above transformation, then

(i) It should be possible to isolate and characterize analogues of 41 using suitable nucleophiles;

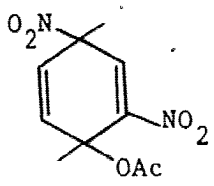
(ii) These analogues could, under suitable conditions, undergo S_N2' attack with various nucleophiles to give compounds analogous to diene 68 or the rearomatized product 17;

(iii) Use of a sterically-hindered nucleophile should retard the rate of the transformation; and

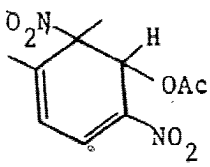
(iv) In the adducts 9A (B) and 10A (B), the methyl groups would hinder nucleophilic substitution in the first and second steps respectively.



9A (B)



10A (B)



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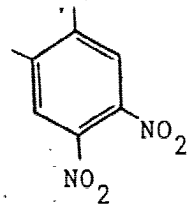
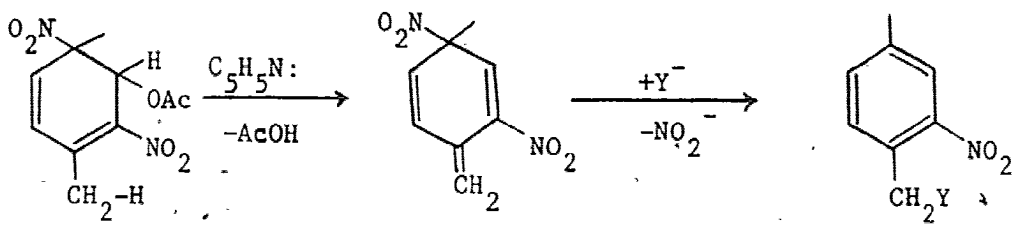


17

A detailed investigation of the exchange and rearomatization reactions lent support to the above observations. Rearomatization of the adducts 7A (B) in pyridine is *ca.* five times as rapid as in 2,6-dimethylpyridine. In the latter case, the reaction mixture was worked-up before completion to give a significant amount (15%) of the diene 8, along with 7A (B) (70%) and 17 (15%). This is attributed to attack by the acetate (Scheme 3.1, nucleofuge from the first step) on the diene 7 to give the isomerized, conjugated diene 8 (41, Nu^{n+1} = OAc). That the product 17 also arose from 8 was shown by allowing the reaction to proceed to completion, when 1,2-dimethyl-4,5-dinitrobenzene (17) was obtained in quantitative yield.

Reaction of the adducts 10A, 12 and 9A (B) with pyridine under similar conditions were quite slow and resulted in the formation of benzylic products. Clearly, unlike the adducts 7A (B) which reacted rapidly and cleanly to give a single product, the adducts 10A, 12 and 9A gave a mixture of benzylic products. Deprotonation of the alkyl function, with formal loss of the elements of acetic acid, occurs in conjunction with S_N2' attack. The intermediate triene undergoes

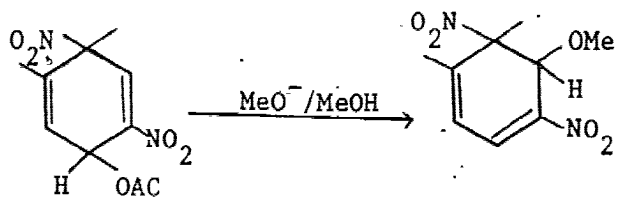
rearomatization to give benzylic products.



12

Y = NO_2 or OH

Further evidence that the reactions of 7A (B) proceed by S_N2' attack was adduced by reacting the diene 7A (B) with sodium methoxide in methanol when a conjugated, dienyl methyl ether (36) was obtained as the sole product.

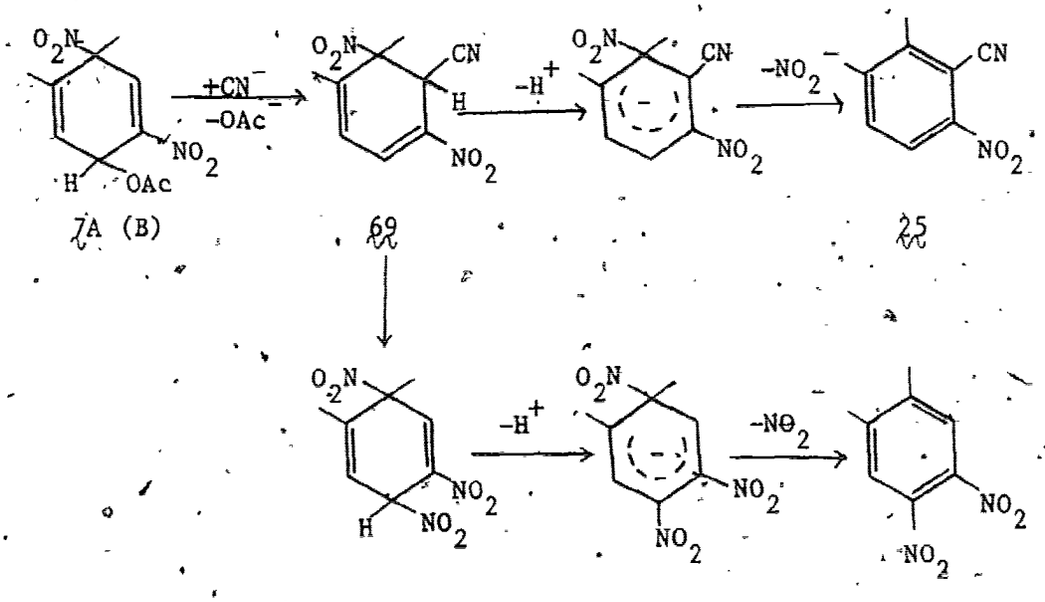


7A (B) 36

The reaction was complete in 5 min at 0°C. Reactions of the adducts 10A, 12 and 9A (B) with sodium methoxide were quite slow (0°C, one week) and, as in the reaction with pyridine, a mixture of benzylic products was obtained.

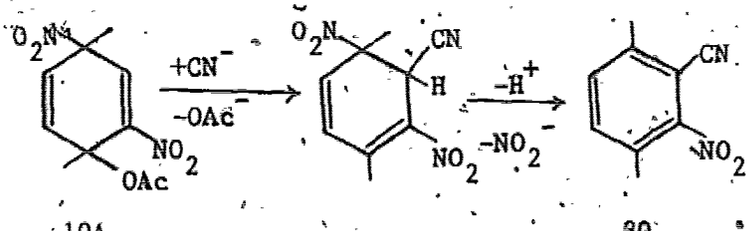
The reactions of the adducts with other nucleophiles were also investigated. When the adducts 7A (B) were treated with potassium cyanide, the major product obtained was 2,3-dimethyl-6-nitrobenzonitrile (25), along with a small amount of 17. S_N2' attack by the cyanide nucleophile on the diene 7A (B) would give 69, in which the proton α to the nitrile group is acidic and is therefore readily lost to form an anion

which in turn loses the nitro group as nitrite to form 25. Furthermore, cyanide is a poorer leaving group and this is another factor which makes the process 69 → 25 more favourable than the normal 69 → 17 pathway.



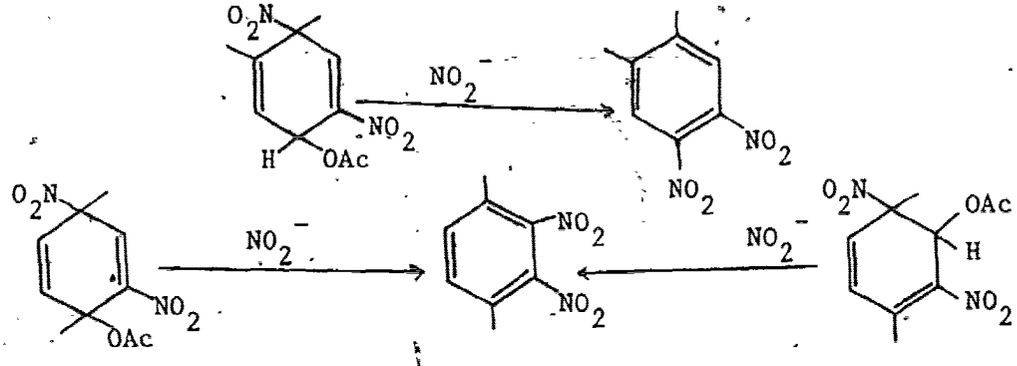
7A (B) 69 25 17

Reactions of the adducts 10A and 12 with cyanide anion in acetonitrile gave 1,4-dimethyl-2,3-dinitrobenzene (19) and 2,5-dimethyl-6-nitrobenzonitrile (30) as the major products. However, when the reaction of 10A was carried out in a dilute medium (in which the solubility of potassium cyanide would be promoted), 30 was obtained as the only product.

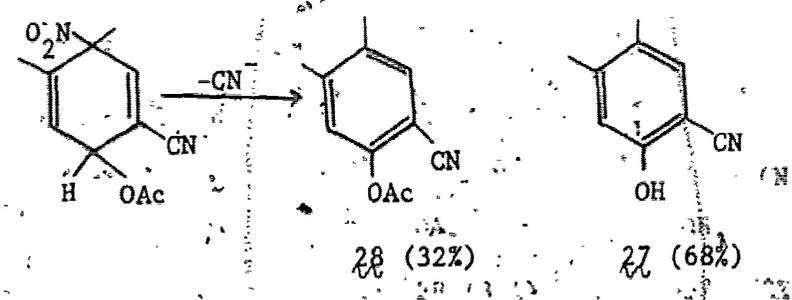


10A 30

In all the above reactions leading to 17 and 19, it is expected that added nitrite should facilitate the reaction. Reaction of the adducts 7A (B) with potassium nitrite resulted in the rapid formation of 1,2-dimethyl-4,5-dinitrobenzene (17) in a quantitative yield. The nitrite ion is subject to greater steric hindrance than the linear cyanide and this is the most likely reason for its apparent failure to attack at the severely hindered vinylic position of 7A (B). Similarly, reaction of 10A or 12 with potassium nitrite gave 19 as the sole product. There is obviously a fine balance between steric and electronic factors in these rearomatization reactions.



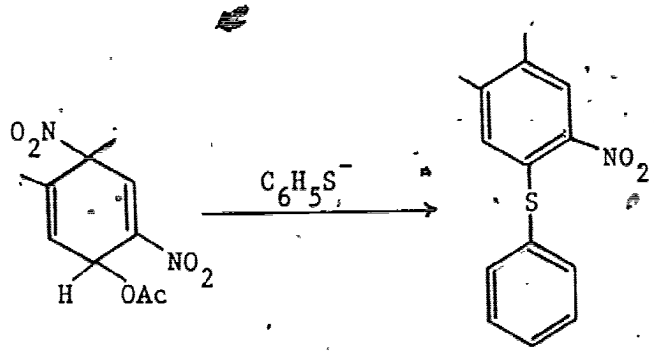
That a strongly electron-withdrawing group (like the nitro) facilitates the reaction was shown by reaction of the cyano-analogue of 7 with potassium cyanide, when a mixture of 2-cyano-4,5-dimethylphenyl acetate (28) and the corresponding phenol (27) was obtained.



28 (32%) 27 (68%)

With potassium nitrite, 28 was obtained as the only product. Elimination of the elements of nitrous acid supersedes S_N2' processes. In the reaction with cyanide, the phenol was probably formed by hydrolysis of the acetate precursor because of the basicity of the medium.

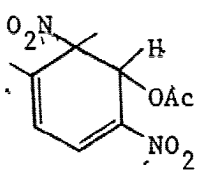
Thus, in the reactions of the adducts from the nitroarenes, the acetate functionality could be replaced formally by other nucleophiles to give dienyl or rearomatized products. The reaction was extended to sulfur nucleophiles. Reaction of the adduct 7A (B) with sodium thiophenoxide resulted in the formation of 4,5-dimethyl-2-nitrophenyl phenyl sulfide (32) as the sole product. S_N2' attack by the thiophenoxide releases the acetate (Scheme 3.1, $Nu^n = C_6H_5S^-$) which competes effectively with the bulky thiophenoxide to give a conjugated cyclohexadienyl intermediate (41, Nu^{n+1} = OAc or SC_6H_5). S_N2' attack by thiophenoxide on the conjugated diene is followed by loss of the elements of nitrous acid to give 32.



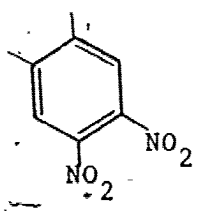
7 32 (99%)

Since, in the reaction of the dienes 7A (B) with pyridine, an intermediate 41 ($Nu^{n+1} = C_5H_5\overset{+}{N}$) was believed to be an intermediate, the reaction was repeated with *tert*-butylamine. If the analogue of 41 (Nu^{n+1} = *tert*-$Bu\overset{+}{N}H_2$) is formed in a significant amount, deprotonation

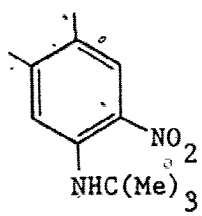
should be faster than attack by nitrite and an amino analogue of the diene 41 (Nu^{n+1} = *tert*-BuNH) may be expected. However, if the released acetate competes effectively with the bulky *tert*-Butylamine as a nucleophile in the first step (Scheme 3.1), then the diene 8 will be preferentially formed . The diene 8 can then undergo S_N2' attack by nitrite anion or *tert*-butylamine to form, after rearomatization, 17 or the corresponding amino analogue (31). Reaction of the dienes 7A (B) with *tert*-butylamine resulted in the formation of 17 as the major product (60%). A minor product (20%) of mass 222 was also obtained and this is assigned the structure 31 in accord with the observation that the rearomatized products obtained with bulky nucleophiles (*e.g.* NO_2, C_6H_5S) are 1,2-dimethyl-4,5-disubstituted benzenes.



8



17



31

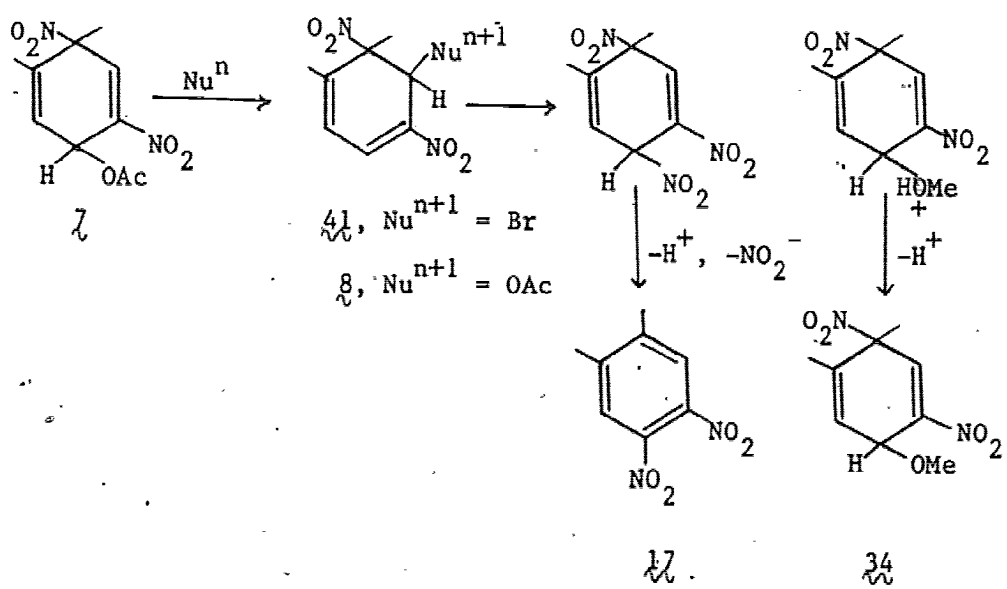
Reaction of the adducts 7A (B) with various oxygen nucleophiles like hydroxide, phenoxide and *tert*-butoxide resulted in the formation of 17 as the main product (60-100%).

Reaction of the adducts 7A (B) with iodide, bromide, chloride or fluoride resulted in the formation of 17 as the main product (>90%).

In the above reactions, a conjugated cyclohexa-1,3-diene was postulated as an intermediate and in the reaction of the adduct 7A (B), with methoxide, a conjugated diene (36) was isolated and characterized. Since in the reaction with 2,6-dimethylpyridine, a conjugated diene (8) was observed as an intermediate, it was hoped that the isomerization

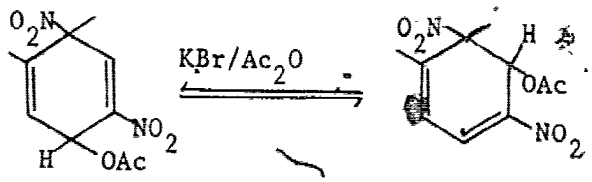
of the diene 7A (B) could be enhanced to provide a method of preparation of diene 8. Reaction with added acetate did result in the formation of 8 though extensive rearomatization also occurred.

When the adducts 7A (B) were allowed to react with bromide or fluoride in methanol and the reaction mixture worked-up before complete rearomatization had occurred, a mixture of 8, 17, and 4,5-dimethyl-2,4-dinitrocyclohexa-2,5-dienyl methyl ether (34) was obtained. Apparently, acetate anion released by nucleophilic attack on the diene 7A (B) brought about isomerization to diene 8. Solvent methanol competes effectively as a nucleophile with the nitrite anion for S_N2' attack on the conjugated diene (41, Nu^{n+1} = Br), resulting in the formation of 34 and 17 respectively. Reaction with iodide gave 34 and 17 as the only products.



7 17 34

In methanol or acetonitrile as the solvent, abstraction of a proton α to the acetate function in 7A (B) is followed by loss of the nitro group as nitrite anion, which is involved in S_N2' attack on the conjugated diene 8. Acetic anhydride proved to be a solvent of choice for optimum formation of the diene 8. Treatment of the dienes 7A (B) with bromide in acetic anhydride resulted in the formation of 8 (75%), the product 17 was not formed under these conditions. Presumably, bromide in acetic anhydride is not sufficiently basic to deprotonate the diene 7 which, in turn, would release nitrite anions. Thus, isomerization is preferred to rearomatization when the reaction is carried out in acetic anhydride.



7 (25%) 8 (75%)

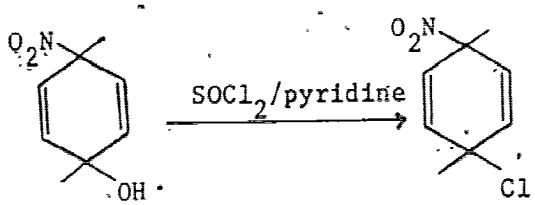
3.3.3 *Reactions of Other Adducts*

Having isolated and characterized the diene adducts obtained by formal exchange of the acetate function with other nucleophiles, the reactions of these adducts were studied.

Acetylation of the dienols 33A (B) with acetic anhydride and 2,6-dimethylpyridine gave the dienes 7A (B) and 8, along with 17. The dienols could be converted to the corresponding methyl ethers on treatment with methyl iodide and moist silver oxide. The dienol obtained from 10A was also converted to the corresponding methyl ether in a

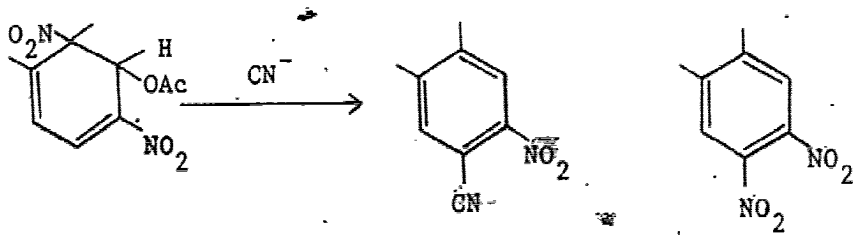
similar manner. Attempted acetylation of the dienols from 10A and 12 resulted in extensive rearomatization.

Dienol 43a (obtained from *p*-xylene adduct) was converted to the corresponding chloro-diene (43b) on treatment with thionyl chloride and pyridine. A similar reaction with the dienol 37A resulted in the formation of rearomatized products.

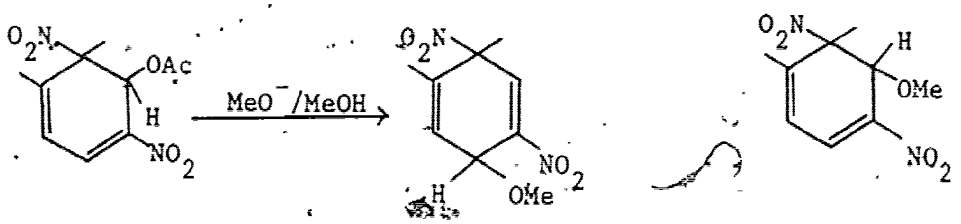


43a 43b

Reactions of the conjugated diene 8 with various nucleophiles resulted in products which arose from S_N2' attack. With cyanide ion, the the major product was 4,5-dimethyl-2-nitrobenzonitrile (26). With methoxide, the products were 36 (23%) and 34 (77%). The latter product was obtained as a mixture of *trans* and *cis* isomers in the ratio 9:1. The stereochemistry of these 1,4 adducts could be related to the corresponding acetoxynitro adducts from which they could be obtained with retention of stereochemistry.



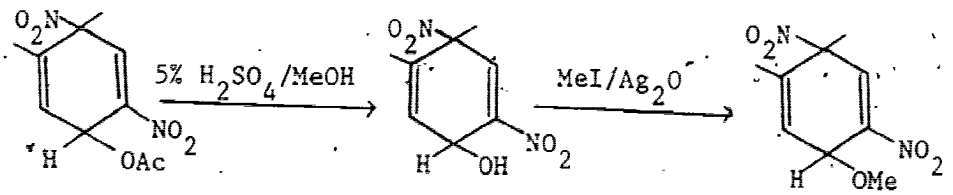
8 26 (87%) 17 (13%)



8 34 (77%) 36 (23%)

A:B

9:1

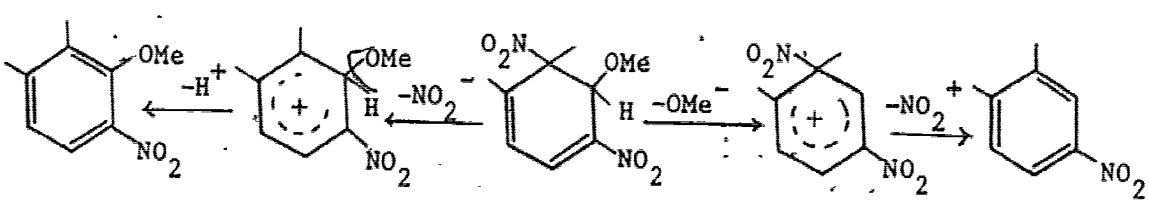


7A 33A 34A

7B 33B 34B

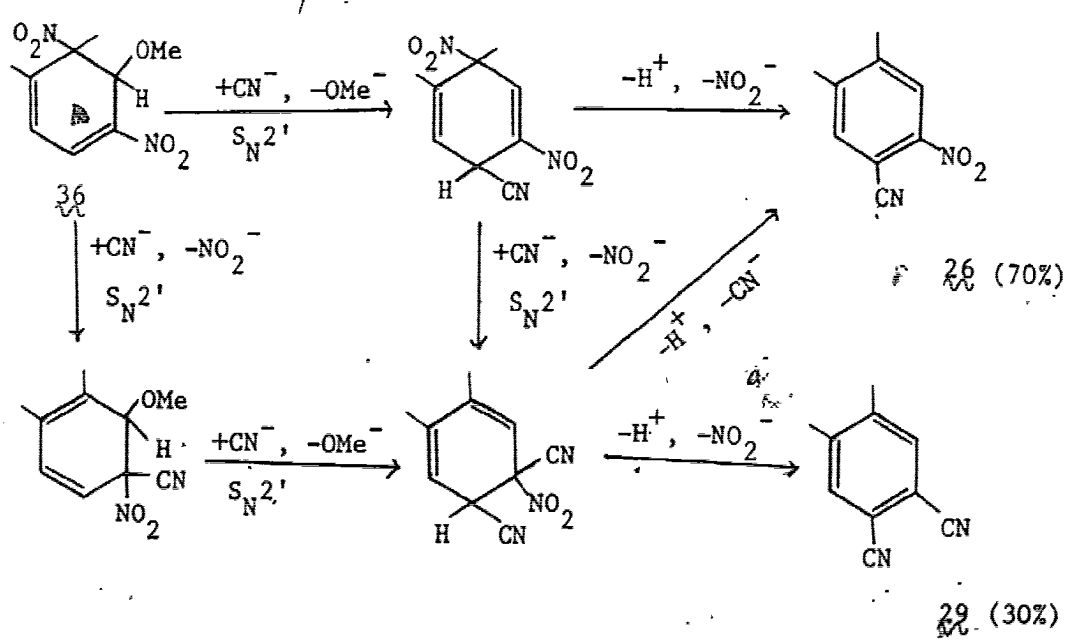
The minor product (36) could result from S_N2' attack by the methoxide on 7, which can be obtained by the isomerization of 8.

Reaction of the methoxy diene (36) with BF_3-etherate proved quite interesting. In this case, complexation apparently occurred at both the methoxy and nitro functions to give 4 and 2,3-dimethyl-6-nitroanisole in the ratio 3:2. Formation of the two products is due to loss of nitro and methoxy groups to generate methoxy- and nitrocyclohexadienyl cations respectively. Deprotonation of the former and loss of nitro group from the latter gives the products 46 and 4.



46 36 4

The methoxy diene 36 on treatment with nitrite anion gave 17 and 4, the former arising from the now-established S_N2' attack. Reaction with cyanide with the diene 36 gave the expected product 26 (70%), along with another compound of mass 156. ^1H n.m.r. spectrum of the latter product showed that the compound was symmetric. These observations led to the assignment of structure 29 for the minor product. This product was not obtained in the reaction of the diene 8 with cyanide. Since it was obtained in the methoxy analogue of 8 (*i.e.* 36), the differences in behaviour are perhaps related to differences in nucleofugic abilities. Since OMe is a poorer leaving group (than OAc), competition between OMe and NO_2 could allow for the following competing pathways:



Conclusion

This dissertation describes the formation, isolation, characterization and reactions of products arising from *ipso* attack in the nitration of 1,2-dimethyl-4-nitrobenzene, 1,2-dimethyl-3-nitrobenzene, 1,4-dimethyl-2-nitrobenzene, 4-methyl-2-nitrophenol and 4-methyl-3-nitrophenol.

These products are formed by *ipso* attack of the nitronium ion at an activated position followed either by addition of nucleophilic acetate at a *para* (or *ortho*) position or by deprotonation at a remote position. In the case of 1,4-dimethyl-2-nitrobenzene, two pairs of diastereomeric 1,4 adducts, along with a 1,2 adduct, are obtained. In the nitration of 4-methyl-2-nitrophenol, crystallization of the reaction mixture results in a 1,4 addition of the solvent methanol to the nitrodienone. This represents the first example of such an adduct from the nitrodienones.

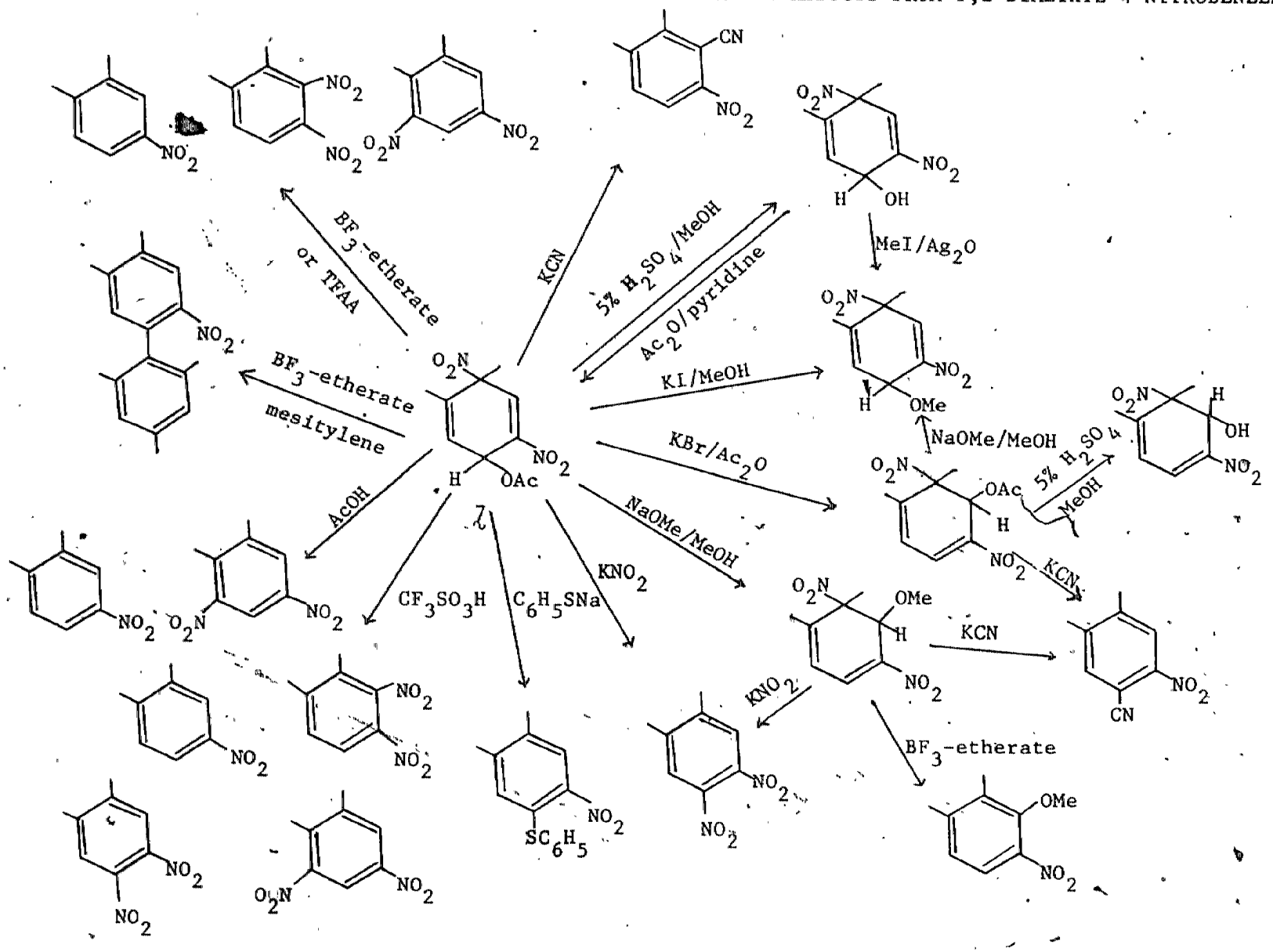
The acid-catalyzed rearomatization of the adducts provide an interesting contrast. Depending on the conditions, products arising from either a 1,2 migration of the nitro group or loss of the elements of acetyl nitrate are obtained. Under strongly acidic conditions, products arising from renitration are also observed. Acid-catalyzed nitrative coupling of the secondary adducts of 1,2-dimethyl-4-nitrobenzene and the secondary and tertiary adducts of 1,4-dimethyl-2-nitrobenzene gives pentamethylnitrobiphenyls.

The acetate function can be formally replaced by other nucleophiles in single or sequential S_N2' reaction (s). The dienes or rearomatized products formed from such an exchange could be obtained in

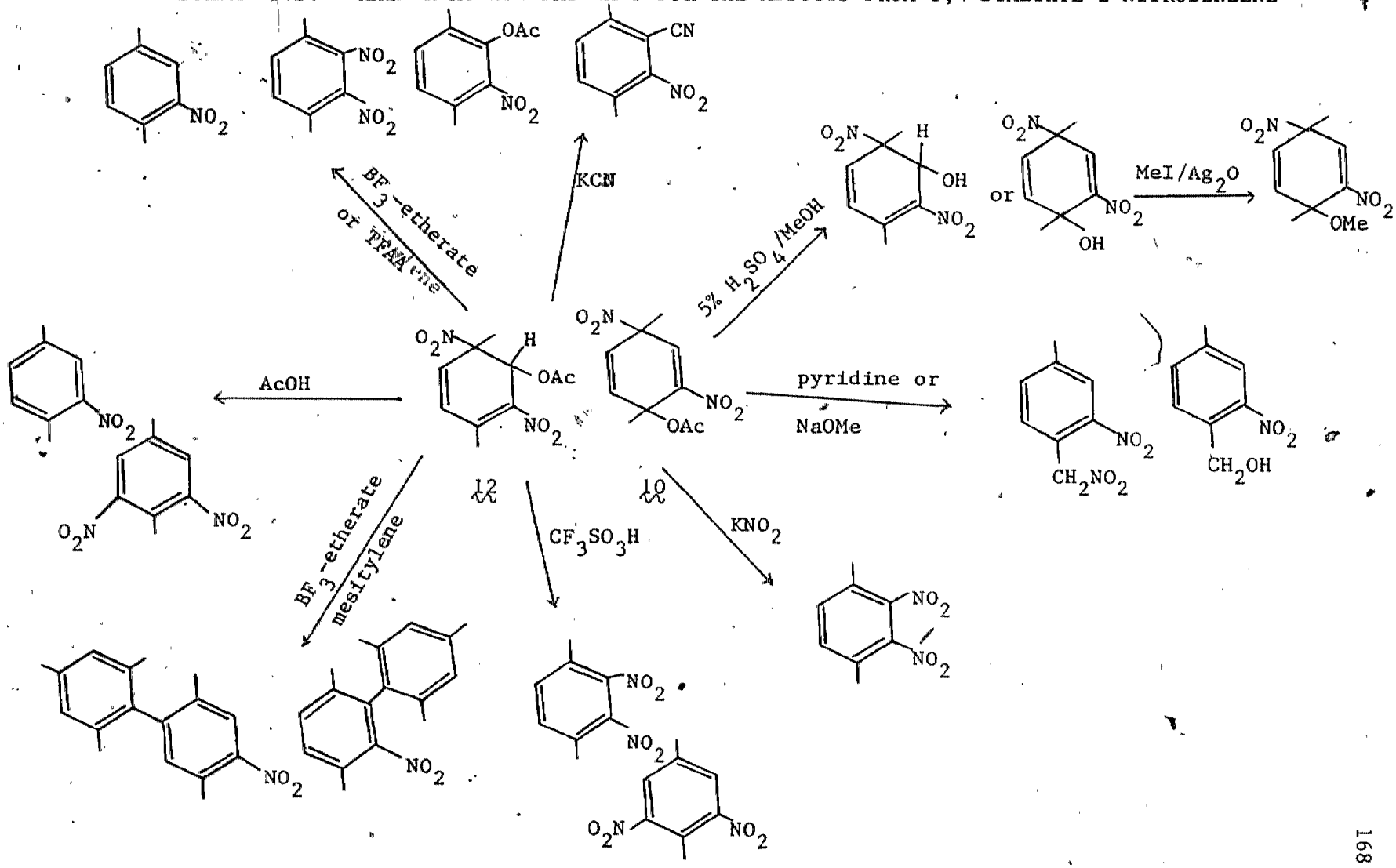
quantitative yields under suitable conditions. The dienes obtained from a single S_N2' exchange can also be further isomerized or rearomatized under suitable acidic or nucleophilic conditions.

One of the more prominent features of the reactions in this study is the observation that the nitro group migrates 1,2 under acidic conditions, 1,3 under free radical conditions and 1,4 under nucleophilic conditions. These results, combined with the fact that the acetate group can be conveniently replaced with other nucleophiles, exemplify the utility of these adducts as versatile intermediates in organic synthesis.

SCHEME 3.2: MAIN REACTION PATHWAYS FOR THE ADDUCTS FROM 1,2-DIMETHYL-4-NITROBENZENE



SCHEME 3.3: MAIN REACTION PATHWAYS FOR THE ADDUCTS FROM 1,4-DIMETHYL-2-NITROBENZENE



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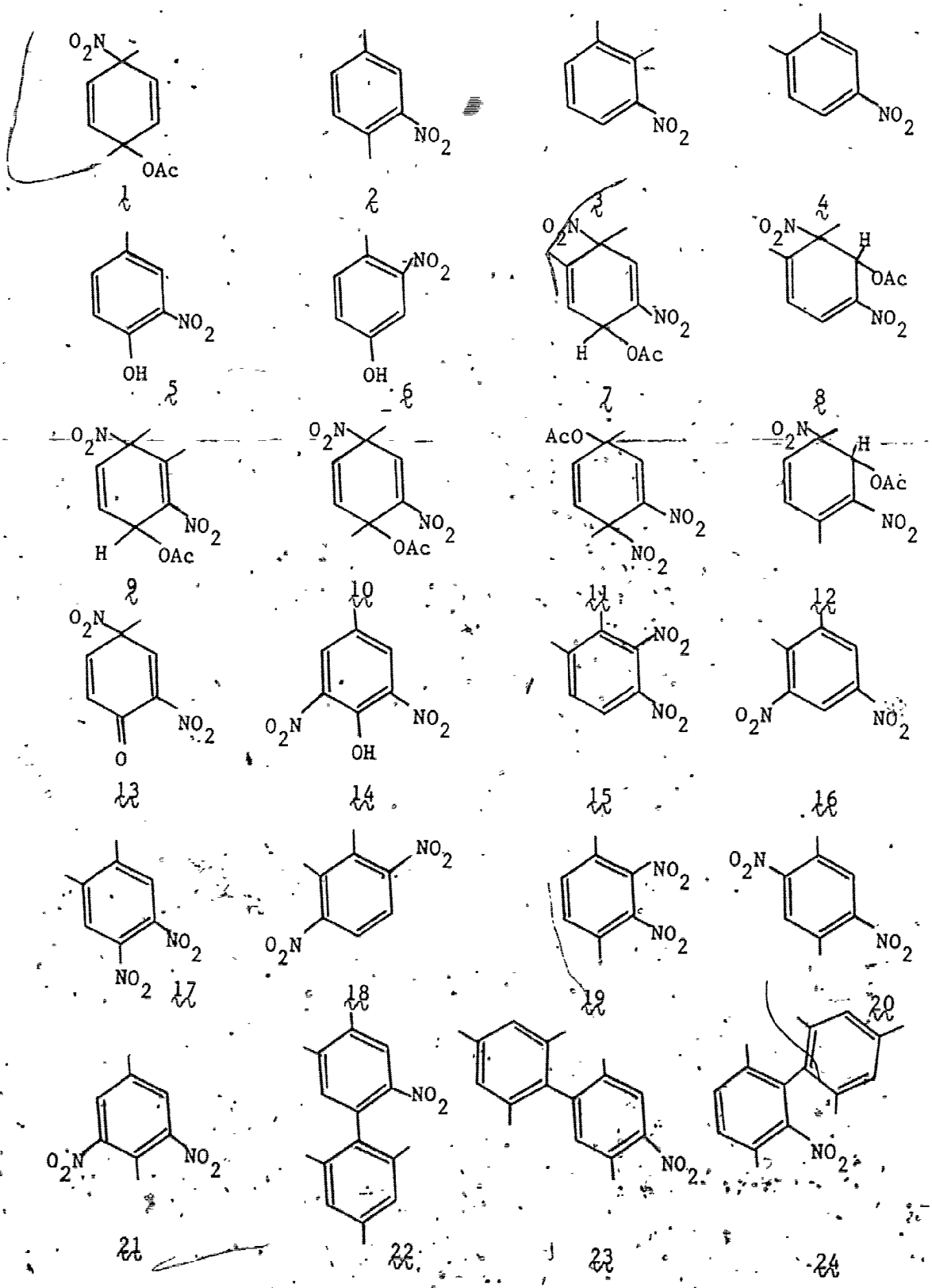
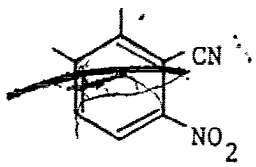
APPENDIX I: KEY TO NUMBERED STRUCTURES





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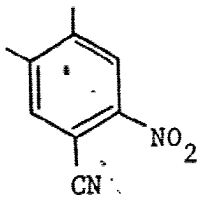

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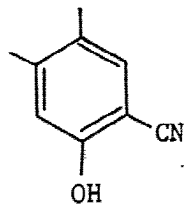

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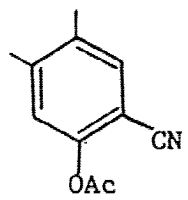

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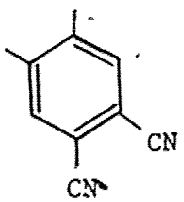

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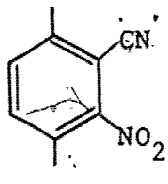

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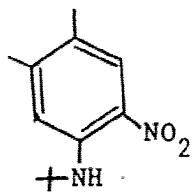

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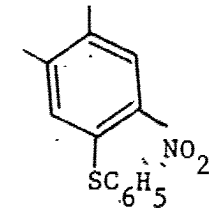

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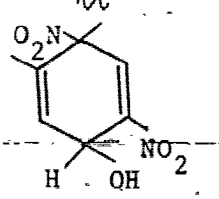

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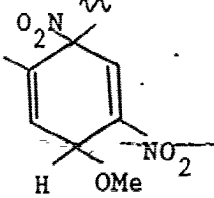

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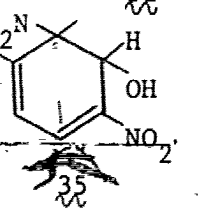

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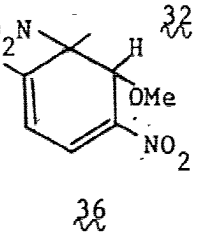

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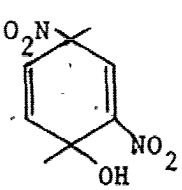

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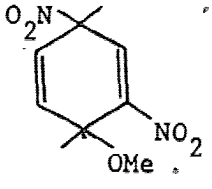

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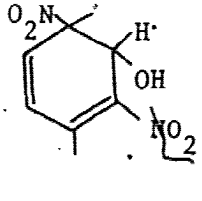

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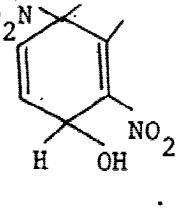

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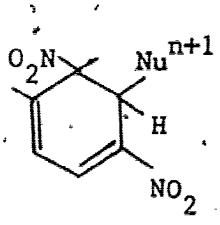

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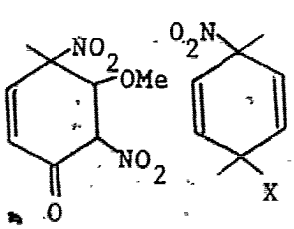

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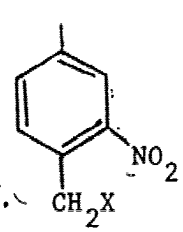
43: X =

(a) OH

(b) Cl



44: X =

(a) OAc

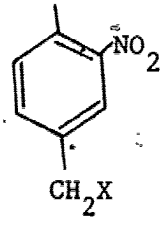
(b) OH

(c) Br

(d) ONO_2

(e) NO_2

(f) ONO



45: X =

(a) OAc

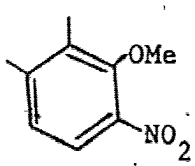
(b) OH

(c) Br

(d) ONO_2

(e) NO_2

(f) ONO



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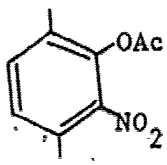

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APPENDIX II: REACTIONS OF DIENES

Reactions of diene 7

Experiment No.	Reagent	Product Composition (%)				
		4	15	16	17	Others
a.1	BF_3-Etherate	78	14	8	-	-
a.2	BF_3-Etherate/ mesitylene	1	-	-	-	22 (99)
a.3	TFAA	72	15	13	-	-
a.4	5% H_2SO_4/MeOH	-	-	-	-	33 (100)
a.5	CF_3SO_3H	31	25	31	13	-
a.6	HBr/ether	95	-	-	5	-
a.7 (i)	AcOH (20°C)	No Reaction				
(ii)	AcOH (100°C)	49	-	51	-	-
(iii)	AcOH/Hydroquinone (100°C)	68	-	32	-	-
a.8	Pyridine-d_5	2	3	-	95	-
a.9 (i)	2,6-Dimethyl-pyridine	2	4	-	94	-
(ii)	2,6-Dimethyl-pyridine/$CDCl_3$	-	-	-	15	8 (17) 7 (67)
a.10	*tert*-Butylamine	4	10	7	60	31 (19)
a.11	NaOMe/MeOH	-	-	-	-	36 (100)
a.12	KOH/CD_3CN	-	-	-	100	-
a.13	*t*-BuOK/CD_3CN	24	4	12	60	-
a.14	C_6H_5ONa/CD_3CN	17	3	3	77	
a.15	C_6H_5SNa/CD_3CN	1	-	-	-	32 (99)

Experiment No.	Reagent	Product Composition (%)				
		14	15	16	17	Others
a.16	KNO_2	-	-	-	100	-
a.17	KOAc	-	-	-	100	-
a.18 (i)	KCN/CD_3OD	-	-	-	6	25 (94)
(ii)	KCN/CD_3CN	-	-	-	30	25 (70)
(iii)	KCN/pyridine-d_5/ CD_3OD	-	-	-	42	25 (58)
a.19 (i)	KI/CD_3OD	-	-	-	58	34 (42)
(ii)	KBr/CD_3OD	-	-	-	22	34 (45) 8 (33)
(iii)	KCl/CD_3OD	-	-	-	100	
(iv)	KF/CD_3OD	-	-	-	28	34 (57) 8 (15)
a.20 (i)	KF/CD_3CN	-	-	-	100	-
(ii)	KBr/CD_3CN (18 h)	-	3	2	95	-
(iii)	KBr/CD_3CN (5 h)	-	-	-	32	8 (68)
(iv)	KI/CD_3CN	-	-	-	77	8 (23)
a.21 (i)	KBr/50% Ac_2O-CD_3CN	-	-	-	3	8 (75) 7 (22)
(ii)	KBr/Ac_2O	-	-	-	-	8 (75) 7 (25)
a.22 (i)	$KSCN/CD_3CN$	-	-	-	86	8 (14)
(ii)	$KSCN/CD_3OD$	-	-	-	100	
a.23	Pyrolysis (g.l.c.)	78	-	22	-	-
a.24	$MeOH/H_2O$	82	-	-	18	

Reactions of diene 33

Experiment No.	Reagent	Product Composition (%)				
		4	15	16	17	Others
a.25	4% H_2SO_4/Ac_2O	82	7	11	-	-
a.26	Pyridine-d_5/Ac_2O	-	-	-	100	-
a.27	2,6-Dimethyl-pyridine/Ac_2O	-	-	-	3	7 (40) 8 (57)
a.28	MeI/moist Ag_2O	-	-	-	-	34 (100)

Reactions of diene 36

a.29	BF_3-Etherate	58	-	-	-	46 (42)
a.30	Pyridine-$d_5/CDCl_3$	-	-	-	100	-
a.31	KI/CD_3CN	-	-	-	100	-
a.32	KNO_2	44	-	-	56	-
a.33	KCN	-	-	-	-	26 (70) 29 (30)
a.34	Pyrolysis (g.l.c.)	98	-	-	-	46 (2)

Reactions of diene 8

a.35	5% H_2SO_4/MeOH					35 (90)
a.36	KCN	-	-	-	13	26 (87)
a.37	NaOMe/MeOH	-	-	-	-	34 (77) 56 (23)

Reactions of Diene 10A

Experiment No.	Reagent	Product Composition (%)					
		2	19	20	21	47	Others
b.1	BF_3-Etherate	62	29	–	7	2	–
b.2	BF_3-Etherate/ mesitylene	27	26	–	7	2	23 (31) 24 (7)
b.3	TFAA	56	35	–	8		
b.4	5% H_2SO_4/ MeOH	–	–	–	–	–	37 (100)
b.5	CF_3SO_3H	21	45	–	30	–	–
b.6 (i)	AcOH (20°C)	No Reaction					
(ii)	AcOH (100°C)	80	–	–	20	–	–
b.7	Pyridine-d_5 (1 week)						44b:44e 4:3
b.8	NaOMe/MeOH (1 week)	19	33	8	–	–	44b (27) 44e (12)
b.9	KOAc	36	41	–	–	–	44b (23)
b.10	KNO_2	–	100	–	–	–	–
b.11 (i)	KCN/CD_3CN (350 mm^3)	2	33	–	–	–	30 (65)
(ii)	KCN/CH_3CN (5 cm^3)	–	–	–	–	–	30 (100)
b.12	Diene 37 + MeI/moist Ag_2O	–	–	–	–	–	38 (100)

Reactions of diene 12

b.1	BF_3-Etherate	21	49	6	13	11	
b.2	BF_3-Etherate/ mesitylene	9	26	5	8	15	23 (28) 24 (8)
b.3	TFAA	33	27	5	11	22	

Experiment No.	Reagent	Product Composition (%)					
		2	19	20	21	47	Others
b.4	5% H_2SO_4/MeOH	-	-	-	-	-	39 (100)
b.5	CF_3SO_3H	15	58	-	27	-	-
b.6 (i)	AcOH (20°C)	No Reaction					
(ii)	AcOH (100°C)	37	-	-	47	16	
b.7	Pyridine-d_5 (1 week)						44b:44e 5:1
b.8	NaOMe/MeOH (1 week)	27	23	11	-	-	44b (39)
b.9	KOAc	33	53	-	-	-	44b (14)
b.10	KNO_2	-	100	-	-	-	-
b.11	KCN	3	49	-	-	-	30 (35) 44b (4) 44e (9)
b.12	Diene 39 + MeI/moist Ag_2O	Decomposition					

VITA

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UNIVERSITY OF VICTORIA, VICTORIA, CANADA	1977 to 1980
	____ to ____

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Publications:

1,4-Migration of a Nitro-group in the Rearomatization of 4,5-Dimethyl-2,4-dinitrocyclohexa-2,5-dienyl Acetate. Alfred Fischer and Lokanathan M. Iyer, J. Chem. Soc., Chem. Commun., 1096 (1979).

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FORMATION AND REACTIONS OF ADDUCTS

FROM *IPSO* NITRATION OF NITROARENES

Author _____
Signature

LOKANATHAN M. IYER
Name

April 24, 1980
Date