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THE NITRATION OF SOME REACTIVE AROMATIC COMPOUNDS IN SULPHURIC ACID

by

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A thesis submitted in part fulfilment of the requirements for the degree of Doctor of Philosophy

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ABSTRACT

This thesis is concerned with three aspects of aromatic nitration in aqueous sulphuric acid.

1. The effect of encounter control and *ipso*-substitution for substrates activated by substituents having an oxygen atom adjacent to the nucleus. The rates for anisole, phenol, *p*-methylanisole, *p*-cresol and veratrole (1,2-dimethoxybenzene) and the proportions of the products formed have been determined. These substrates are nitrated at the encounter rate and for anisole and phenol in 56 - 82% sulphuric acid the *o*:*p*-ratios vary from 1.8 to 0.7 and from 2.4 to 0.88 respectively. It is suggested that the rate limiting step is the formation of an encounter pair between a nitronium ion and a hydrogen bonded substrate molecule. The change in the *o*:*p*-ratio may be due to competition between Wheland intermediate formation either directly from the hydrogen-bonded encounter pair or subsequently to loss of the hydronium ion. With *p*-methylanisole 4-methyl-2-nitroanisole and 4-methyl-2-nitrophenol were formed quantitatively in constant ratio in 46 - 80% sulphuric acid. The latter is considered to result from *ipso*-attack by nitronium ion at C-Me and subsequent 1,3- rearrangement of the nitro-group. For *p*-cresol quantitative yields of 4-methyl-2-nitrophenol were obtained in 56 - 78% sulphuric acid. It is suggested that *ipso*-attack again occurs to give

transiently 4-methyl-4-nitrocyclohexa-2,5-dienone. In the case of veratrole quantitative yields of 4-nitroveratrole were obtained in 60 - 74% sulphuric acid and this anomaly is discussed.

2. The investigation of the nitration of some very reactive aromatic compounds at low acidity. The rates for 1,3,5-trimethoxybenzene, 1,3-dimethoxybenzene, and mesitylene at various temperatures have been determined. After correction for C-protonation where necessary, the rate profiles for these reactions were approximately parallel and it is concluded that in as low as 44% sulphuric acid the nitronium ion remains the effective electrophile.

3. The nitration of some molecules having two benzanoid nuclei. For the homogeneous nitration of biphenyl in aqueous sulphuric acid, a high o:p-ratio ($\sim$ 3.6) has been confirmed, and no evidence for ipso-substitution has been found. For the nitration of diphenylmethane good first-order kinetics were obtained and six nitro-compounds were identified. The ratio of mono- to di-substitution is discussed.

Part of the work presented in this thesis has been described in the following publications. R.G. Coombes, J.G. Golding, L.W. Russell, and G.D. Tobin, 'Industrial and Laboratory Nitrations', ed. L.F. Albright and C. Hanson, A.C.S. Symposium series No. 22, American

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J.W. Barnett, R.B. Moodie, K. Schofield, J.B. Weston, R.G. Coombes, J.G. Golding, and G.D. Tobin, J. Chem. Soc., Perkin II, 1977, 248.

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CHAPTER 1

LITERATURE SURVEY

1.1 INTRODUCTION

The first account of nitration was given in 1834 by Mitscherlich[1] who reacted benzene with fuming nitric acid to obtain nitrobenzene.

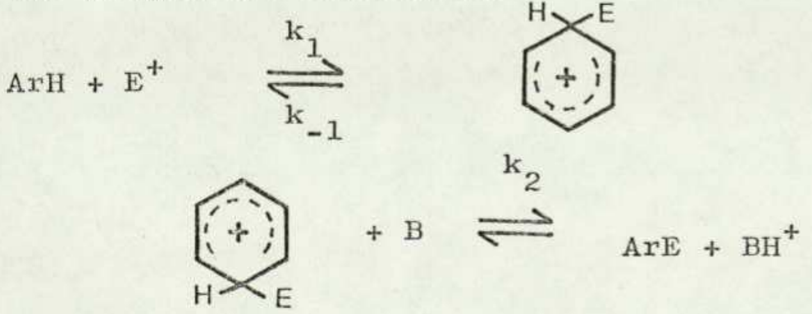
At the turn of the century, Holleman performed many studies of orientation in aromatic substitution[2], and he obtained much valuable data from which the main generalisations could be made regarding orientation of substitution. He recognised the connection between orientation and activation, and observed that *ortho*, *para* directing substituents commonly activate the nucleus, and that *meta* directing substituents deactivate it.

The study of aromatic nitration reactions is important for at least two reasons:-

a) It is the most general process for the preparation of aromatic nitro-compounds.

b) The development of a theoretical basis for organic chemistry has relied heavily on the study of aromatic substitution reactions, and the nitration of aromatic compounds is pre-eminent amongst these reactions.

Two general processes might be applicable to electrophilic substitution. In the first, the S_E2 process, two stages are envisaged.



..... (1.1)

The rate equation applicable to the S_E2 process is, from the steady state approximation, as follows:-

$$\text{rate} = \frac{k_1\ k_2 \left[B\right]\left[ArH\right]\left[E^+\right]}{k_{-1} + k_2\left[B\right]} \quad \ldots\ldots \ (1.2)$$

If $k_2\left[B\right] \ll k_{-1}$ there will be a linear dependence of rate upon the concentration of base, but when $k_2\left[B\right] \gg k_{-1}$ base catalysis will not occur. A range of behaviour between these two extremes is possible.

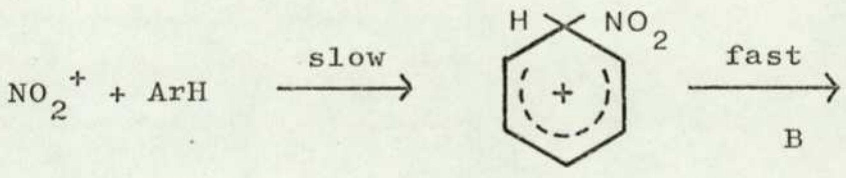
The second process which might be envisaged, the S_E3 process, is a termolecular reaction:-

$$ArH + E^+ + B \xrightarrow{k_3} \left\{(E\ldots.Ar\ldots.H\ldots.B)\right\}^{*}$$
$$\longrightarrow ArE + BH \quad \ldots\ldots\ldots\ldots\ldots \ (1.3)$$

For such a process, the following rate equation would be applicable:-

$$\text{rate} = k_3 \left[ArH\right]\left[E^+\right]\left[B\right] \ldots\ldots \ (1.4)$$

Generally, for electrophilic substitution, the S_E2 mechanism is believed to operate[3,4]. For nitration, the electrophile is believed to be the nitronium ion (NO_2^+) (see Equation 1.5). The rate limiting first step has been confirmed from studies of solvent effects[5] and isotope effects[6], although bulky substituents may force the second stage to become rate limiting.



$$ArNO_2 + \overset{+}{HB} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \ (1.5)$$

Ingold and co-workers[5], in their classic work, appeared to give a complete picture for nitration, but in the last decade, ipso - substitution[63a] (see Section 1.8), diffusion control, and nitration via nitrosation together with the problems associated with these processes, have led to a renewed interest in this area.

1.2 NITRATING SYSTEMS

Nitration can be achieved under a wide variety of conditions. The reagent used controls the character and kinetics of the reaction, but it is found that under most conditions the nitronium ion is the effective species. Most electrophilic reactions do not possess this characteristic of one important effective electrophile, and, therefore, nitration forms a useful model reaction for the study of electrophilic substitution. It is also of importance that the introduction of one nitro-group generally deactivates a molecule to further substitution and clean mono-substitution can be studied.

Reagents often employed for nitration are:- (1) concentrated and aqueous nitric acids, (2) nitric acid in concentrated or aqueous sulphuric or perchloric acids, (3) nitric acid in inert organic solvents (e.g. acetic acid), (4) nitric acid in reactive organic solvents (e.g. acetic anhydride), (5) the oxides of nitrogen (e.g. N_2O_4), (6) nitronium salts, (7) nitrous acid (nitration via nitrosation), (8) with transition-metal nitrato-compounds.

1.3 AQUEOUS AND CONCENTRATED NITRIC ACID

1.31 STATE OF NITRIC ACID IN AQUEOUS AND CONCENTRATED NITRIC ACID SOLUTIONS

In concentrated nitric acid the main species is molecular nitric acid. However, physical measurements have shown the existence of significant concentrations of other species. From studies of the variation of the freezing point of mixtures of dinitrogen pentoxide and water, over a range of concentrations where pure nitric acid is formed, it can be shown[7] that self dehydration occurs.

$$2HNO_3 \rightleftharpoons NO_2^+ + NO_3^- + H_2O \; \ldots\ldots\ldots (1.6)$$

The Raman spectrum of nitric acid[8] shows two weak bands at 1050 and 1400cm^{-1}, and on comparison with the spectra of isolated nitronium salts[9], the band at 1050cm^{-1} was attributed to the nitrate ion and the band at 1400cm^{-1} to the nitronium ion. The infra-red spectrum of nitric acid shows absorption bands due to the nitronium ion[10].

On addition of water, the equilibrium in 1.6 is affected reducing the tendency to form the nitrate and nitronium ions. This is due to the fact that, in nitric acid, water is largely unprotonated[11] and acts as a weak base. This effect is demonstrated by the decrease in the peak due to the nitronium ion in the Raman spectra. On addition of greater than 5% of water the nitronium ion peak disappears completely[8]. The reduction in concentration of ions is also shown by a decrease in the conductivity of the solutions, which reaches a minimum in solutions containing 97% acid. However, on further dilution, the conductivity rises due to the formation of the nitrate and hydronium ions[12].

1.32 NITRATION IN CONCENTRATED NITRIC ACID

Mechanistic information in this medium has been obtained from an investigation of the nitration of nitrobenzene, p-chloronitrobenzene, and 1-nitro-anthraquinone[5]. These compounds were found to undergo reaction according to the following rate law.

$$\text{rate} = k_1 \left[\text{ArH}\right] \quad \dots\dots\dots\dots\dots\dots (1.7)$$

As nitric acid is the solvent, terms involving its concentration cannot enter the rate equation. This form of the rate equation is consistent with reaction via molecular nitric acid, or any species whose concentration throughout the reaction bears a constant ratio to the stoicheiometric concentration of nitric acid.

1.33 NITRATION IN AQUEOUS SOLUTIONS OF NITRIC ACID

Addition of water retards nitration in concentrated nitric acid without disturbing the kinetic order of the reaction[5]. The rate of nitration of nitrobenzene is found to be depressed sixfold by the addition of 5% water but because of the complexity of the equilibria involving water which exist in these media no simple relationship can be found between the concentration of water and its effect on the rate. The operation of the nitronium ion in this medium has been proved conclusively[13a-c]. For some sufficiently reactive aromatic compounds in aqueous nitric acid, the reaction gave zeroth-order kinetics and the identification of the slow reaction with the formation of the nitronium ion followed from the fact that the initial rate under zeroth-order conditions was the same as the rate of ^{18}O-exchange in similar solutions. It was inferred that the exchange of oxygen occurred via heterolysis to the nitronium ion, and it was the rate of this heterolysis which limited the rates of nitration of reactive aromatic compounds. In the process of ^{18}O-exchange the nitronium ion mechanism requires that the rate of nitronium ion formation be that rate at which the label appears in nitric acid; this must also be equal to the zeroth-order rate of nitration. Some results are given in Table 1.1.

1.4 NITRATION IN CONCENTRATED AND AQUEOUS SULPHURIC ACID

1.41 STATE OF NITRIC ACID IN CONCENTRATED AND AQUEOUS SULPHURIC ACID

In concentrated sulphuric acid, nitric acid is completely converted into the nitronium ion, according to the following equilibrium:-

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + NO_3^- + 2HSO_4^- \quad \ldots (1.8)$$

Raman spectroscopy showed that [8a,14a,b] the addition of up to 10% of water does not affect the concentration of the nitronium ion, but that further dilution reduces the concentration of this species, which is not detectable in solutions containing $<$ 85%

Table 1.1

Zeroth-order rates of nitration and ^{18}O-exchange in aqueous nitric acid[a] at 0°

Compound	$10^4 k_o$/mole % s^{-1}	
	nitration	exchange
Mesitylene-α-sulphonate anion	2.12	2.16
Iso-durene-α²-sulphonate anion	1.76	1.93

a) ~ 40 mole %

sulphuric acid. The introduction of water generates bisulphate and hydroxonium ions which tend to repress the formation of nitronium ions but the equilibrium so much favours the nitronium ion that even moderate quantities of water have a negligible effect on its concentration.

The u.v. spectra of solutions of potassium nitrate in various concentrations of sulphuric acid have been studied[15], and absorptions arising from the nitrate ion, molecular nitric acid and the nitronium ion have been identified. The results show that in less than 15% sulphuric acid the nitrate ion is the main species present. In the range 15-70% sulphuric acid, molecular nitric acid and the nitrate ion coexist, with the proportion of molecular nitric acid increasing with acidity. Between 72% and 82% sulphuric acid, molecular nitric acid is the species in major amount and in 89% sulphuric acid the ionisation to the nitronium ion is complete.

1.42 NITRATION IN CONCENTRATED SULPHURIC ACID

A simple kinetic order for the nitration of aromatic compounds was first established by Martinsen[16]. The rate of nitration of nitrobenzene was found to obey a second-order rate law.

$$\text{rate} = k_2(\text{obs}) \left[\text{ArH}\right] \left[\text{HNO}_3\right] \quad \ldots\ldots\ldots\ldots \quad (1.9)$$

Although the proportion of nitric acid present as the nitronium ion does not change between 90% and 100% sulphuric acid, the rate constants for nitration of most compounds decrease over this range. Many aromatic compounds are sufficiently basic to be appreciably protonated in concentrated sulphuric acid. If nitration occurs through attack on the free base, then the reactivity of the conjugate acid will be negligible. Thus by increasing the acidity of the medium, the proportion of free base will be less, reducing the rate of reaction. This explanation is only partially satisfactory because a fall in rate is found with substrates that are not appreciable protonated. For these the decrease in rate is explained in terms of changes in the activity coefficients, which are known to occur in strongly acidic media. From the transition-state theory the rate should be given by:-

$$\text{rate} = k_2\left[NO_2^+\right]\left[ArH\right]\left(f_{NO_2^+}\, f_{ArH}/f^{\ddagger}\right) \quad \ldots(1.10)$$

The nitrations of p-nitrotoluene, p-chloronitrobenzene and o-chloronitrobenzene have been studied over a wide range of concentrations of sulphuric acid[17a,b] and it has been shown that if the rates of nitration are corrected for the decrease of the activity coefficients, which have been determined, the corrected rate coefficients $k_2(obs)/f_{ArH}$ vary only slightly between 90% and 100% sulphuric acid. The rate of nitration of p-dichlorobenzene[136] does not vary over the range of acidity 90-98% sulphuric acid, in contrast to the fall shown by the rates for many other compounds under these conditions.

1.43 NITRATION IN AQUEOUS SULPHURIC ACID

The addition of water to solutions of nitric acid in 90% sulphuric acid reduces the rate of nitration. In the region 90% to 85% sulphuric acid the fall in rate of nitration has been shown to parallel the fall in concentration of nitronium ions[18]. At concentrations of sulphuric acid where the nitronium ion is not detectable, the second-order rate coefficient (k_2(obs)) is found to decrease by a factor of about 10^4 for each 10% decrease in sulphuric acid concentration. Under these conditions the effective electrophile is not molecular nitric acid because the variation in rates is not similar to the corresponding change in concentration of molecular nitric acid, determined by u.v. spectroscopy or measurements of vapour pressures[15,19]. Under such conditions, the continued effectiveness of the nitronium ion has been indicated by comparing the dependence of the rates on the concentration of sulphuric acid, with the acidity-dependence of the ionisation of model compounds. (This is discussed fully in Section 6.1).

1.44 NITRATION AT THE ENCOUNTER RATE IN AQUEOUS MINERAL ACIDS

Consideration of the fall in rate with decreasing sulphuric acid concentration and of the fact that in 90% sulphuric acid nitric acid is completely ionised to the nitronium ion suggests that in 68% sulphuric acid the concentration of nitronium ion is only about 10^{-8} times that of the nitric acid present. It follows that the rate coefficient for the reaction between an aromatic compound and nitronium ion ($k_2 = \text{rate}/\left[\text{ArH}\right]\left[\text{NO}_2{}^+\right]$) at

68% sulphuric acid is about 10^8 times the stoichiometric rate coefficient ($k_2(\text{obs}) = \text{rate}/[\text{ArH}][\text{HNO}_3]$). In the case of benzene[26] $k_2(\text{obs})$ for nitration in 68% sulphuric acid at 25° is 4.2×10^{-2} $\text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$. (This figure of 4.2×10^{-2} $\text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$ is obtained from Table 1 in Ref. 20, on the assumption that the quoted figure is not a second-order rate coefficient but is the first-order rate coefficient) giving $k_2 = 4.2 \times 10^6$ $\text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$. The theoretical rate coefficient for encounter between two species in 68% sulphuric acid is given by $k_2 = 8RT/3\eta$ [21] (where R = Gas constant; T = Temperature; and η = Viscosity of sulphuric acid) and is found to be 6×10^8 $\text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$. Thus the value found for the nitration of benzene in 68% sulphuric acid approaches the theoretically estimated value.

This consideration prompted an investigation in 1968 by Coombes, Moodie and Schofield of the nitration of benzene and some more reactive aromatics in aqueous sulphuric acid and perchloric acid, to establish to what extent the reactions of these compounds were affected by the rate of diffusion together of the active species[22]. For the series of compounds studied, a limiting maximum rate of nitration by nitronium ion was reached in both sulphuric acid, see Table 1.2, and perchloric acid, see Table 1.3.

For reaction in solution, two reacting species remain in proximity for a finite time and the encounter pair (e.p.) can be considered as a transient intermediate.

Table 1.2

Second-order rate coefficients[22] for nitration in 68.3% sulphuric acid at 25.0°

Substrate	k_2(obs)/dm^3 mole^{-1} s^{-1}	Estimated rate[a]
Benzene	5.8×10^{-2}	1
Toluene	1.0	23[b]
Biphenyl	9.2×10^{-1}	35[b]
p-Xylene	2.2	50[c]
o-Xylene	2.2	60[c]
m-Xylene	2.2	400[c]
Mesitylene	2.1	16,000
Naphthalene	1.6	300[d]
2-Methylnaphthalene	1.6	-
1-Methoxynaphthalene	2.0	-
Phenol	1.4	10^4[d]

a) Relative to that of benzene

b) Ref. 23 and 24

Table 1.2 (continued)

c) Calculated from the observed value for toluene and the known isomer ratios by assuming the addivity principle.

d) From data for other substituents assuming a $\underline{\sigma}^+,\rho$ relationship (ref.113)

Table 1.3

Second-order rate coefficients[22] for nitration in 61.05% perchloric acid at 25.0°

Substrate	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}	Estimated rate[a]
Benzene	8.3×10^{-2}	1
Toluene	1.6	23
p-Xylene	7.0	50
Mesitylene	6.5	16,000
Naphthalene	2.2	300
2-Methylnaphthalene	4.7	-
1-Methoxynaphthalene	7.3	-
1-Naphthol	7.0	-
Phenol	2.6	10^4
m-Cresol	4.9	-
Thiophen	4.3	-

a) see Table 1.2

The overall reaction scheme can be written thus:-

$$HNO_3 + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} NO_2^+ + H_2O \quad \ldots. (1.11)$$

$$NO_2^+ + ArH \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} (e.p.) \quad \ldots. (1.12)$$

$$(e.p.) \xrightarrow{k_3} Products \quad \ldots. (1.13)$$

From the fact that in all cases the reaction was found to be first-order in aromatic substrate, the assumption was made that nitric acid and nitronium ion are effectively in equilibrium and reactions (1.11 - 1.13) then lead by the steady state treatment to the following expression,

$$k_2(obs) = \frac{[NO_2^+]}{[HNO_3]st} \quad \frac{k_2k_3}{k_{-2} + k_3} \quad \ldots. (1.14)$$

for the second-order rate coefficient, k_2(obs), in terms of the ratio of the equilibrium concentration of nitronium ion to the stoichiometric concentration of nitric acid. Whether a particular rate of nitration is limited by the encounter rate depends on the relative magnitude of k_{-2} and k_3, k_3 will have little dependence on the medium whereas k_{-2} will depend on the viscosity of the medium, and should decrease with increasing viscosity. From this it follows that the less viscous the medium, the greater must be the reactivity of the substrate to be limited by the encounter rate. The varying viscosity of the medium is presumably the explanation for the fact that mesitylene, a typical encounter rate substrate, has a lower slope than substrates such as benzene, which are not encounter controlled.

The activation energies of some encounter-controlled reactions in 67.1% H_2SO_4 are given in Table 1.4. If the above considerations are correct the activation energy determined must result almost entirely from the high endothermicity of the dissociation of nitric acid to the nitronium ion. This has been investigated[25] and the enthalphy change for the following ionisation in 68.3% H_2SO_4 has been determined. The value found is not

$$HNO_3 \overset{k}{\rightleftharpoons} NO_2^+ + OH^- \quad ....(1.15)$$

in conflict with the theory of encounter control for the nitration of reactive aromatic compounds in aqueous sulphuric acid.

The fact that in 68% sulphuric acid the toluene/benzene rate ratio is close to that observed in perchloric acid and in other less viscous systems[23], and that the rate of nitration of benzene is less than a fortieth of the limit set by the encounter rate, suggests that at this acidity benzene is not affected by encounter control and comparison of reactivity with deactivated compounds and benzene can be made. In this region of acidity a plot of $\log_{10}k_2(\text{obs})$ vs $-(H_R + \log_{10}a_{H_2O})$ is unity for benzene (see Section 6.1).

At higher acidities the slope of $\log_{10} k_2$ vs $-(H_R + \log_{10} a_{H_2O})$ becomes 1.2 and is thus no longer

Table 1.4

Activation parameters for nitration in sulphuric acid[a]

Substrate	H_2SO_4(%)	Temp range ($^\circ$C)	Δ E/kcal mole^{-1}
Benzene	67.1	25 - 44	18.0
Mesitylene	73.2	2 - 25	13.9
Mesitylene	67.1	25 - 53	18.0
Naphthalene	67.1	25 - 44	15.5

a) Ref. 22

parallel to similar plots for a number of deactivated substrates[26]; furthermore, the rate for benzene approaches closely the rate of encounter. Thus in the acidity range 68 - 82% sulphuric acid, comparison must be made with care because the observed relative rates, particularly at the higher acidities, may not be true measures of relative reactivity.

For the two phase nitration of toluene at strengths of sulphuric acid ca 75% lower rates than would have been expected have been observed[27]. These have been accounted for[28] by the observation of a change from first-order to zeroth-order kinetics in the homogeneous nitration of toluene in 74 - 82% sulphuric acid at relatively high substrate concentrations with an excess of nitric acid. It was concluded that the rate of nitration of toluene in $>$ 74% sulphuric acid under the zeroth order conditions is controlled by the rate of formation of the nitronium ion (1.16) and not by the rate of attack on the substrate (1.17).

$$HNO_3 + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} NO_2{}^+ + H_2O \quad \ldots. \ (1.16)$$

$$NO_2{}^+ + ArH \xrightarrow{k_2} \text{products} \quad \ldots. \ (1.17)$$

A plot of the $\log_{10}$ of the zeroth-order rate coefficients (see Table 1.5) determined by Strachan[28] vs $-H_0$ is shown in Fig. 1.1. The straight line of unit slope is consistent with the proposed scheme and indicates that HNO_3 behaves as a Hammett base.

Table 1.5

Rate coefficients for the nitration of toluene in sulphuric acid[28]

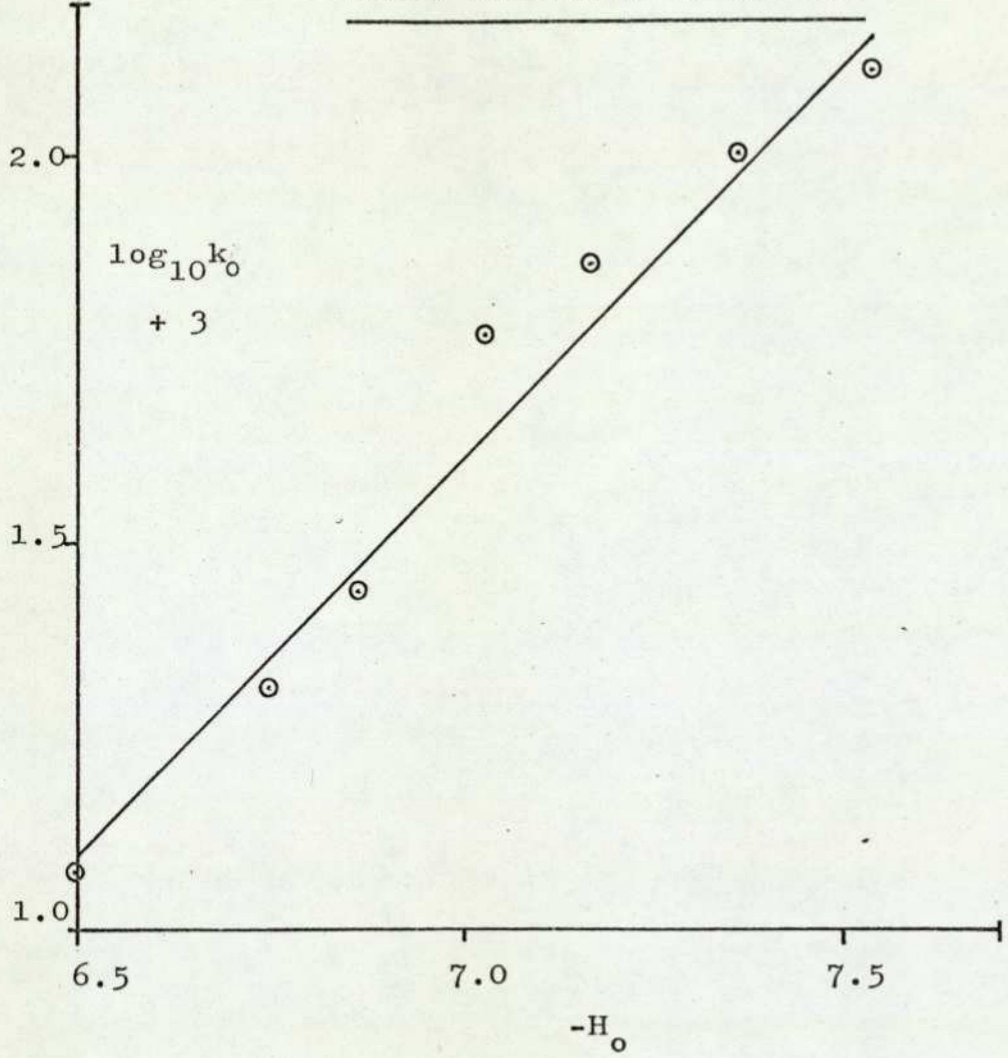
H_2SO_4 (%)	$-H_o^b$	k_o/mole l^{-1} s^{-1}	k_1^a/s^{-1}
74.70	6.50	1.5×10^{-2}	0.8
76.35	6.75	2.1×10^{-2}	1.1
77.00	6.85	3.4×10^{-2}	1.8
78.15	7.03	7.5×10^{-2}	4.0
78.95	7.17	9.4×10^{-2}	5.0
80.10	7.35	1.2×10^{-1}	6.4
81.45	7.53	1.6×10^{-1}	8.3

a) $k_1 = k_o/\left[HNO_3\right]$, $\left[HNO_3\right] = 1.88 \times 10^{-2}$ mole l^{-1}

b) Ref. 87

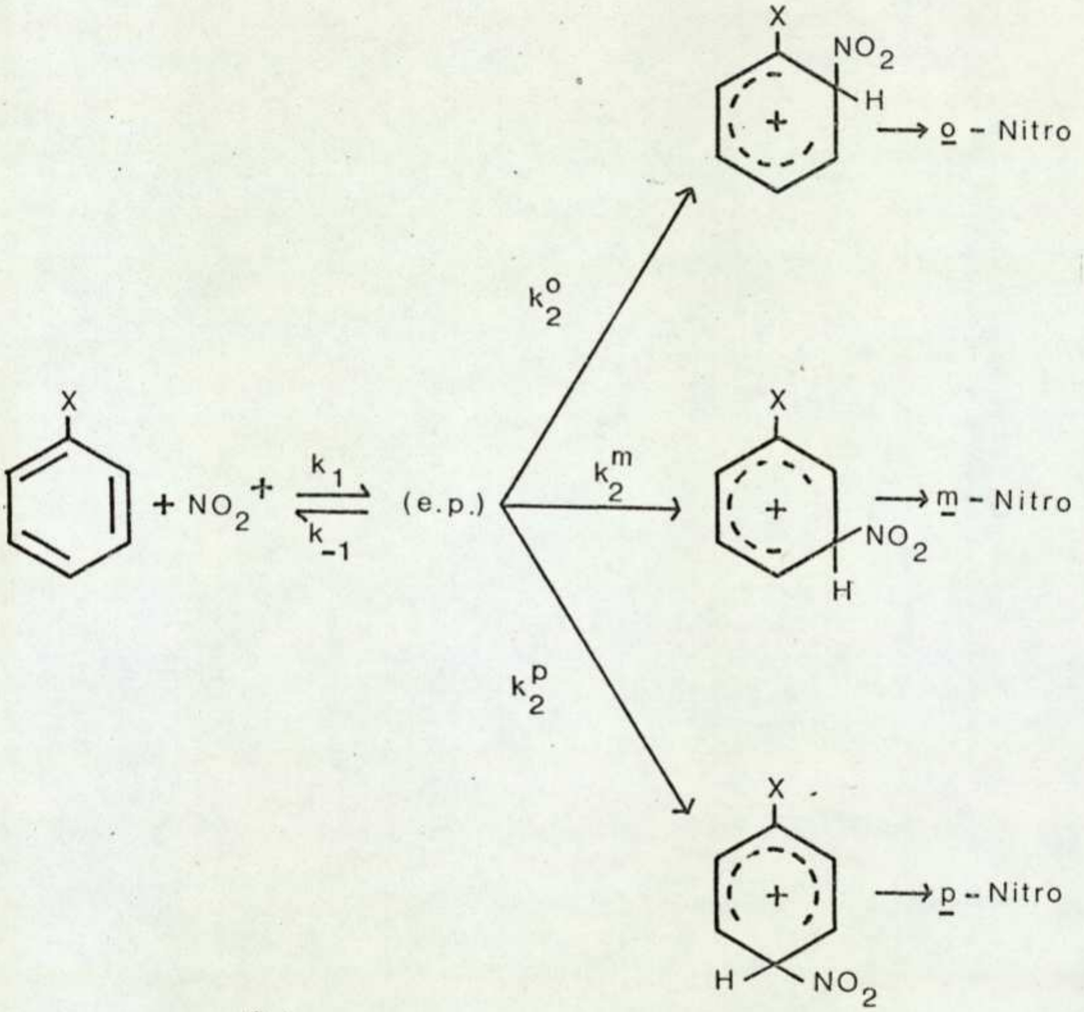
Figure 1.1

Plot of $\log_{10} k_o$ vs $-H_o$ for the zeroth-order nitration of toluene



1.441 SELECTIVITY IN ENCOUNTER CONTROLLED NITRATIONS

For nitration in sulphuric acid it is suggested that at the limit the rate-determining step changes to one in which the encounter pair is formed (see Scheme 1.1).



Scheme. 1.1

By analogy with literature discussions[29] of diffusion-controlled processes it was implied that there was no interaction within the encounter pair. If this were the case, as k_{-1} can be estimated[30] as about 10^9 - 10^{10} s^{-1} and k_2 can in the limit approach 10^{12} - 10^{13} s^{-1}, it would be possible for considerable intramolecular selectivity to remain between positions in a substrate which are sufficiently reactive to be nitrated at the limiting rate[31].

Another suggestion[32,33] has been that the existence of a limiting rate might be explained by what has been called the Hammond effect. As one increases the reactivity along a series of suitable substrates the transition state will become progressively earlier, bonding from the electrophile to the carbon atom increasingly less developed and the activation energy lower until differences might have effectively disappeared. It has been envisaged that these transition states might be positionally oriented[33] and in this circumstance selectivity between sufficiently reactive positions should disappear at the limiting rate. This would also be the situation if there existed separate encounter pairs for different positions of substitution in a molecule[34]. If these early transition states are not positionally oriented the existence of a common discrete intermediate, prior to formation of Wheland intermediates, seems obligatory and therefore the suggestion would be of a change in rate-determining step to that of formation of this intermediate.

Recent expressions[33a] of these ideas suggest that the intermediate has in fact an orientated Π-complex type of structure. For it to be necessary to postulate a change of rate-determining stage to one in which a common intermediate which involves attractive interaction is formed, an intramolecular selectivity greater than that possible for a non-interacting encounter pair would have to be observed[31].

On other occasions[33b] the oriented π-complex type of structure has been drawn as a representation of early transition stages of the positionally orientated type to which the previous arguments would apply.

Present evidence on these points comes from the work of Schofield and co-workers[31]. They have studied the nitration of pseudocumene (1,2,4-trimethylbenzene) and have shown that there is about a 9:1 selectivity of attack on positions 5 and 6 provided that one makes the reasonable assumption that any *ipso*-attack is not followed by rearrangement under the chosen conditions. Both positions are reactive enough to achieve the limiting rate and have similar steric requirements. This deduction rules out the explanation in terms of early transition states of the positionally orientated type and also precludes the possibility of positionally orientated intermediates prior to the Wheland intermediates. It means that there must be a common intermediate prior to Wheland intermediate formation, but the extent of intramolecular selectivity is certainly not sufficient to make it necessary to postulate any attractive interaction in this intermediate.

1.5 NITRATIONS IN INERT ORGANIC SOLVENTS

The identification of the nitronium ion in organic solvents is not possible by physical methods[35,36,37], and the evidence for its existence and effectiveness has been obtained largely from detailed kinetic studies. Ingold and co-workers[38] were the first to correctly interpret the features of nitration in organic solvents. This arose from studies of nitric acid in nitromethane and acetic acid. A large excess of nitric acid was used when the reactions were carried out. For sufficiently reactive substrates, the nitration rates were found to show zeroth-order kinetics[39]. Under such conditions, the rate is independent of the nature and concentration of the substrate.

The following reaction scheme can be envisaged:-

$$HNO_3 \underset{(2)}{\overset{(1)}{\rightleftharpoons}} NO_2^{+} + ArH \xrightarrow{(3)} ArNO_2 \quad .... \quad (1.18)$$

The kinetic order of nitration depends on the fate of the nitronium ion. If process (3) is very fast then zeroth-order kinetics will be observed, but if process (2) is important, a first-order dependence on substrate concentration will be observed. Process (2) becomes important with decreased reactivity of the substrate or decreased concentration of the substrate. Deviation from zeroth to first-order kinetic has been observed in several compounds[40] and is often a consequence of the decrease in the concentration of the aromatic towards the end of the reaction.

Evidence for the production and effectiveness of the nitronium ion was obtained from a consideration of the effects that certain species had on the rate of nitration. The addition of nitrate ion[38] produced anti-catalysis without changing the kinetic form of the reactions.

Addition of small quantities of water depressed the zeroth-order rate without changing the kinetic form. The addition of larger quantities of water caused a change to first-order kinetics. The addition of nitrate ion showed that it was not consuming a proportion of the effective species, but it must be reacting with the precursor to the effective species. The effect of water showed that appreciable concentrations of the electrophile were reacting with water. Both these facts are consistent with the following scheme, and the existence of the nitronium ion as the effective species.

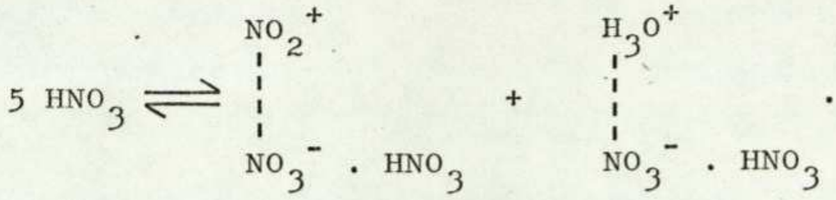
$$2HNO_3 \overset{\text{fast}}{\rightleftharpoons} H_2NO_3^+ + NO_3^- \quad .... \ (1.19)$$

$$H_2NO_3^+ \overset{\text{slow}}{\rightleftharpoons} NO_2^+ + H_2O \quad .... \ (1.20)$$

$$NO_2^+ + ArH \longrightarrow \text{products} \quad .... \ (1.21)$$

The fact that nitrations in acetic acid[7], sulpholan[41] and carbon tetrachloride[42,43] were kinetically similar to that in nitromethane, is important because it removes any possibility of chemical involvement of the solvent in the slow step of the reaction.

In 1969, Coombes[42] found that for the nitration of reactive aromatic compounds in carbon tetrachloride, the zeroth-order rate constant depended approximately on the nitric acid concentration to the fifth power. The high order in nitric acid concentration in dilute solution indicates that a total of five nitric acid molecules are associated with the pre-equilibrium step or are present in the transition state. Nitronium ion formation was represented by:-



$$5\ \mathrm{HNO_3} \rightleftharpoons \begin{array}{c} \mathrm{NO_2}^{+} \\ \vdots \\ \mathrm{NO_3}^{-} \cdot \mathrm{HNO_3} \end{array} + \begin{array}{c} \mathrm{H_3O}^{+} \\ \vdots \\ \mathrm{NO_3}^{-} \cdot \mathrm{HNO_3} \end{array} \quad \ldots. \ (1.22)$$

This scheme was used to explain temperature effects on the rate of nitration. At lower temperatures, enhanced rates of nitration were correlated with increased production of molecular aggregates.

1.51 NITRATION AT THE ENCOUNTER RATE IN INERT ORGANIC SOLVENTS

As previously described, see Section 1.44, for nitration reactions in greater than 68% sulphuric acid, the observed rates of nitration for a series of substituted benzenes could not be raised above about 40 times the observed rate of benzene, despite the introduction of activating species. This limiting rate, or the rate of encounter between the substrate molecules and nitronium ions, has also been detected in several organic solvents[41]. In both nitromethane and sulpholan, as well as some aqueous solutions of these solvents, a limit was detected. Also in carbon tetrachloride[42], nitration at the encounter rate has been observed but not yet fully examined. In organic media, the limiting rate appears less sharply defined than that observed in aqueous mineral acids.

1.6 NITRATION IN REACTIVE ORGANIC SOLVENTS

1.61 ACETIC ANHYDRIDE

Of all the media used for nitration, acetic anhydride has caused the most controversy, and is the least well understood. Acetic anhydride differs from most organic solvents in that nitric acid reacts with it:-

$$(CH_3CO)_2O + HNO_3 \rightleftharpoons CH_3CO_2NO_2 + CH_3COOH \quad .... \quad (1.23)$$

Further, much slower reaction finally produces tetranitromethane.

The kinetics of nitration in this medium are complex[32,40], and acetoxylation, which occurs at the same time as nitration, adds to the complications. The early work in this medium failed to demonstrate clearly the effective electrophile. The involvement of acetyl nitrate and the nitronium ion have been suggested[23,44,45,46].

Some work carried out with reactive aromatic substrates[47a] in acetic anhydride has shown that the kinetics of the reaction decrease from first-order to zeroth-order when substrate concentration is increased. This was explained in terms of nitronium ion attack giving zeroth-order kinetics when the substrate concentration is high and attack by solvated nitronium ion ($NO_2^+(HNO_3)$) at low aromatic concentrations giving first-order kinetics. Ridd and co-workers[47b], have confirmed that for the nitration of reactive aromatic compounds in acetic anhydride, the order of the reaction, with respect to the aromatic compound, decreases from first-order to zeroth-order, as the concentration of the aromatic compound is increased. However, this change in order was shown to arise mainly from a medium effect, and not from the rate determining formation of the electrophile. Similar medium effects were reported for the addition of inert aromatic compounds to the reaction mixture. These workers were able to reach no definite conclusions as to the identity of the electrophile, although certain restrictions on this were established.

Nitrations in acetic anhydride have long been associated with the formation from some aromatics of higher proportions of o-nitro compounds than are formed under other conditions. Several explanations have been suggested to account for this:-

a) The change has been attributed to an electrostatic effect arising from the dipole of the substituent[86a]. In the case of anisole (see 2.1) and acetanilide the positive end of the dipole is directed away from the ring, resulting in the o-positions being negatively polarised with respect to the p-position and therefore more susceptable to electrophilic attack. This electrostatic effect was considered to be stronger in acetic anhydride, a solvent of lower dielectric constant, than in mixed acids. However, high o:p-ratios are not obtained in acetic acid, a solvent of lower dielectric constant than acetic anhydride.

b) A general change in the nitrating species might occur. This explanation has been regarded as unlikely[48], for the change in orientation of substitution is not always very significant as, for example, in the cases of such compounds as toluene[49], tert-butylbenzene and halogenobenzenes.

c) The existence of a special mechanism of o-nitration has been suggested. This has been used to explain the high ortho-substitution obtained for the nitration of anisole (see Section 2.1), biphenyl (see Section 5.1), acetanilide[86b,c], benzylmethyl ether[86d,e], and methyl-2-phenethyl ether[86e] in acetic anhydride.

Schofield and co-workers[86f] have reinvestigated the nitration of some anilides and aromatic ethers in sulphuric acid and in acetic anhydride. It was not found necessary from this work to postulate a different electrophile in acetic anhydride, but the evidence did support the presence of a special mechanism of ortho-substitution in some cases.

The o:p-ratios for the nitration of anisole and phenol are discussed in Sections 2.1 and for biphenyl in Section 4.1.

As previously described a limiting rate of nitration has been established for nitration reactions in aqueous sulphuric acid, (see Section 1.44) and in several organic solvents (see Section 1.51). This limiting rate, or the rate of encounter between the substrate molecules and the electrophile, has also been detected in acetic anhydride[49]. Table 1.6 gives the calculated and observed relative rates of nitration of benzene, toluene, m-xylene and mesitylene in acetic

Table 1.6

Calculated and observed relative rates of nitration in acetic anhydride

Compound	k rel(obs)	krel (calc)*
Benzene	1	(1)
Toluene	50	(50)
m-Xylene	870	4700
Mesitylene	5000	454,000

* Calculated from the partial rate factors for toluene for nitration in acetic anhydride, the Additivity Principle being assumed to apply.

anhydride.

1.7 NITRATION VIA NITROSATION

Nitrous acid has been found to catalyse the nitration of some very reactive aromatic compounds, and in particular amines and phenols. Oxidation was found to occur of some of these compounds under the reaction conditions, and the formation of more nitrous acid led to autocatalysis. The following mechanism for nitration involving NOX has been suggested, where NOX represents

$$ArH + NOX \xrightarrow{slow} ArNO + HX \; .... \; (1.24)$$

$$ArNO + HNO_3 \xrightarrow{fast} ArNO_2 + HNO_2 \; ... \; (1.25)$$

the nitrosating species. This scheme accounts for the constant concentration of nitrous acid throughout the reaction. Nitric acid was thought to be responsible for the oxidation of the nitroso-compound but Bonner[43] and his co-workers have obtained evidence that dinitrogen tetroxide may function as both a nitrosating and an oxidising agent in carbon tetrachloride.

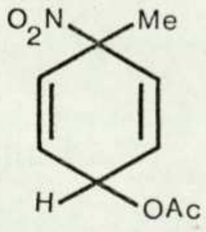
The data obtained by many workers who have ignored the possibility of nitrosation have given a misleading picture of the relative reactivity of certain reactive substrates to nitration[40]. The importance of this effect has been demonstrated by work carried out on the rates of nitration of some naphthalene derivatives [32,49] relative to that of benzene. The relative rate for naphthalene was found to be 62, where as that for 1-methylnaphthalene was found to be 20,600, which suggested an unreasonable activating effect of the methyl group. The concentration of nitrous acid was low in both cases (ca 5 x 10^{-4} mole dm^{-3}) but the result was wholly ascribed to the effect of nitrosation.

Nitrosation is also an important factor affecting positional selectivity for certain reactive aromatic compounds. The nitrations in sulphuric acid of anisole, phenol (see Section 2.1), and biphenyl (see Section 5.1) illustrate this point. The autocatalytic effect of nitrosation can be removed by the addition to the reaction mixture of an excess of compounds which react with nitrous acid. Examples of such compounds are urea, sulphanilic acid, and sulphamic acid.

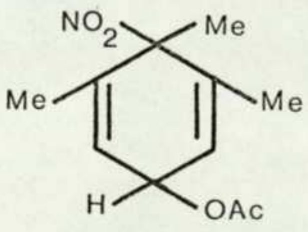
1.8 IPSO NITRATION

1.81 ADDUCTS

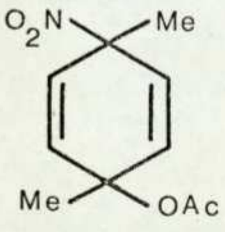
In 1970, whilst a study was being carried out on the side reactions involved in the nitration of polymethyl benzenes in acetic anhydride, the following intermediates were isolated[50a,b]. Two intermediates were isolated in



(1·I)



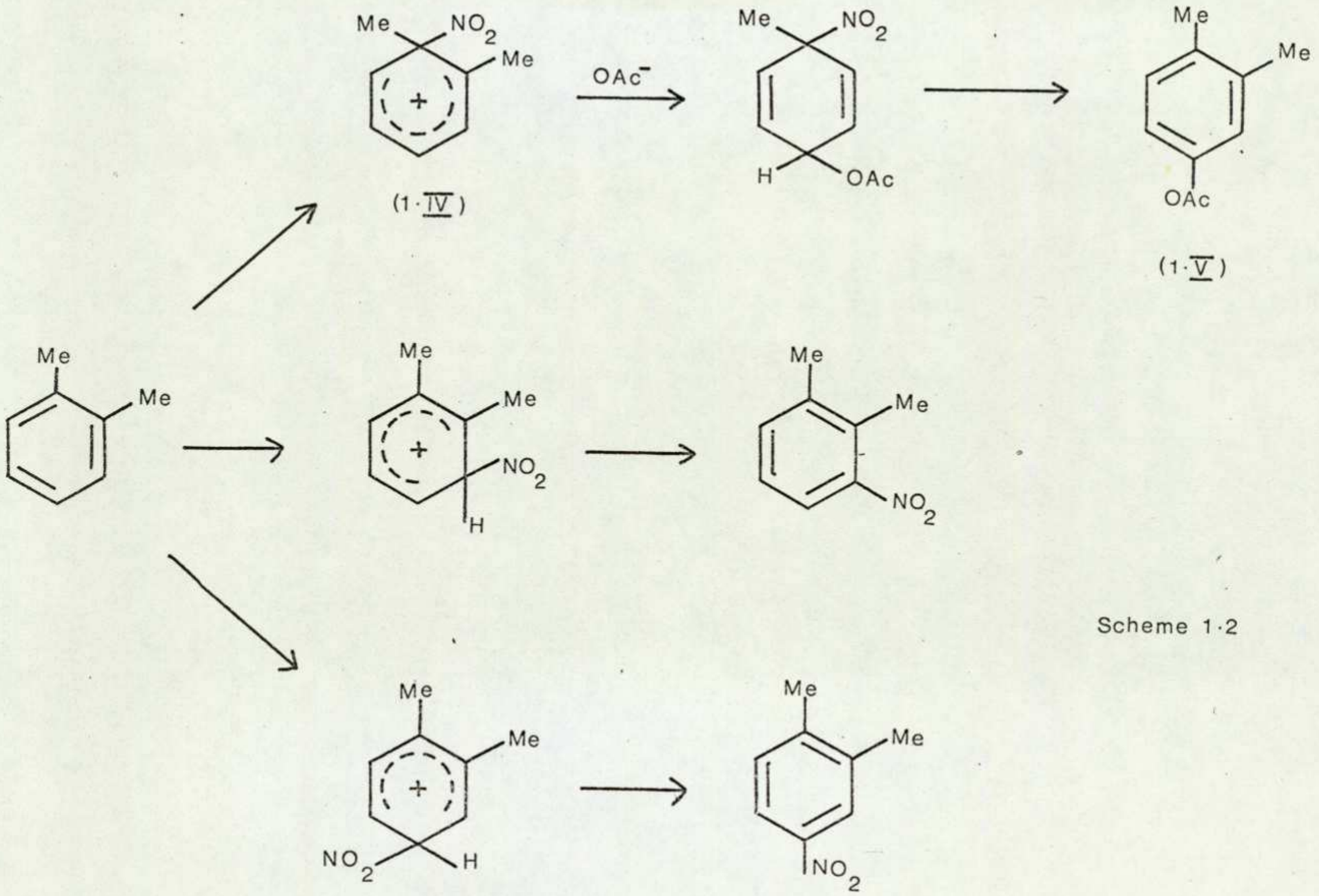
(1·II)



(1·III)

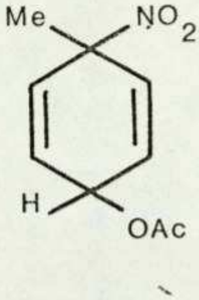
each case, and shown by spectrophotometric methods to be cis - trans isomers. Fisher and his co-workers concluded that a suggestion by Ridd[23] was essentially correct, and that these addition products were intermediates in the acetoxylation reactions which often accompanied nitration. Acetoxylation occurred then, by an addition-elimination process (Scheme 1.2) and not by the direct electrophilic substitution mechanism which was previously proposed by Fischer[51]. The 1,4-diene adducts give aryl acetates on decomposition. Thus, the intermediates give rise to polymethyl phenyl acetates; the adduct obtained from (1.III) gave 2,5-dimethylphenyl acetate, indicating an intramolecular 1,2-shift of the acetate.

Attack by the electrophile at a ring position bearing a hydrogen atom leads to normal nitration (via a Wheland intermediate), but initial attack at an ipso position (an aromatic position bearing a substituent other than hydrogen) leads to the formation of a Wheland intermediate of the type (1.IV) followed by nucleophilic attack by $\bar{O}Ac$. A number of 1,4-adducts have now been isolated from nitrations and a summary of these is shown in Table 1.7. The extent of acetoxylation accompanying nitration depends upon the structure of the substrate[60]. Appreciable adduct formation occurs with substrates such as o-xylene, p-xylene and hemimellitene where the ipso-position is activated by another alkyl substituent, but not with those such as toluene and m-xylene where this is not the case. If nucleophilic trapping is complete the amount of non-conventional product will depend on the formation of the ipso-Wheland intermediate, (1.IV) see



Scheme 1·2

Table 1.7. Some 1,4-Adducts isolated from nitrations in acetic anhydride



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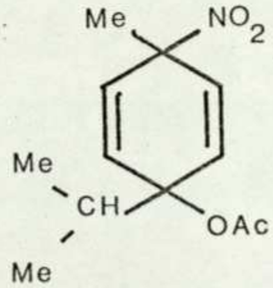

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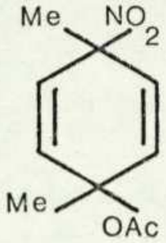

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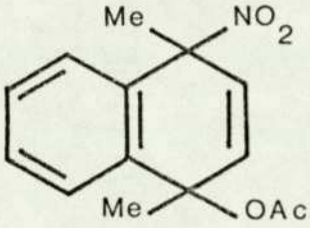

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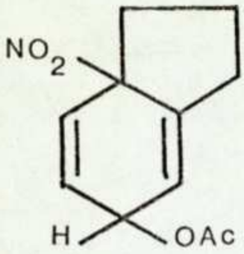

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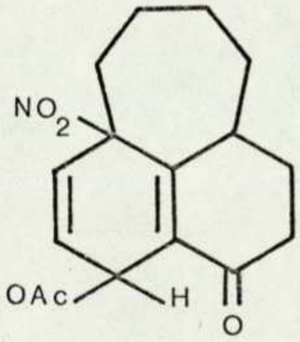

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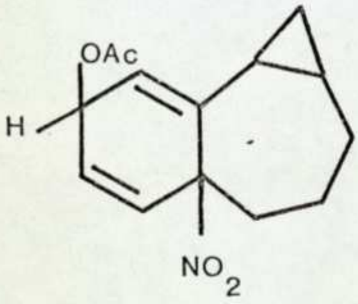

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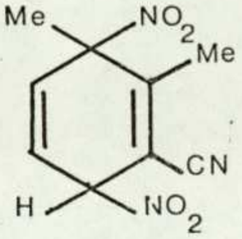

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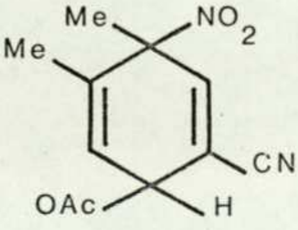


Ref. 59

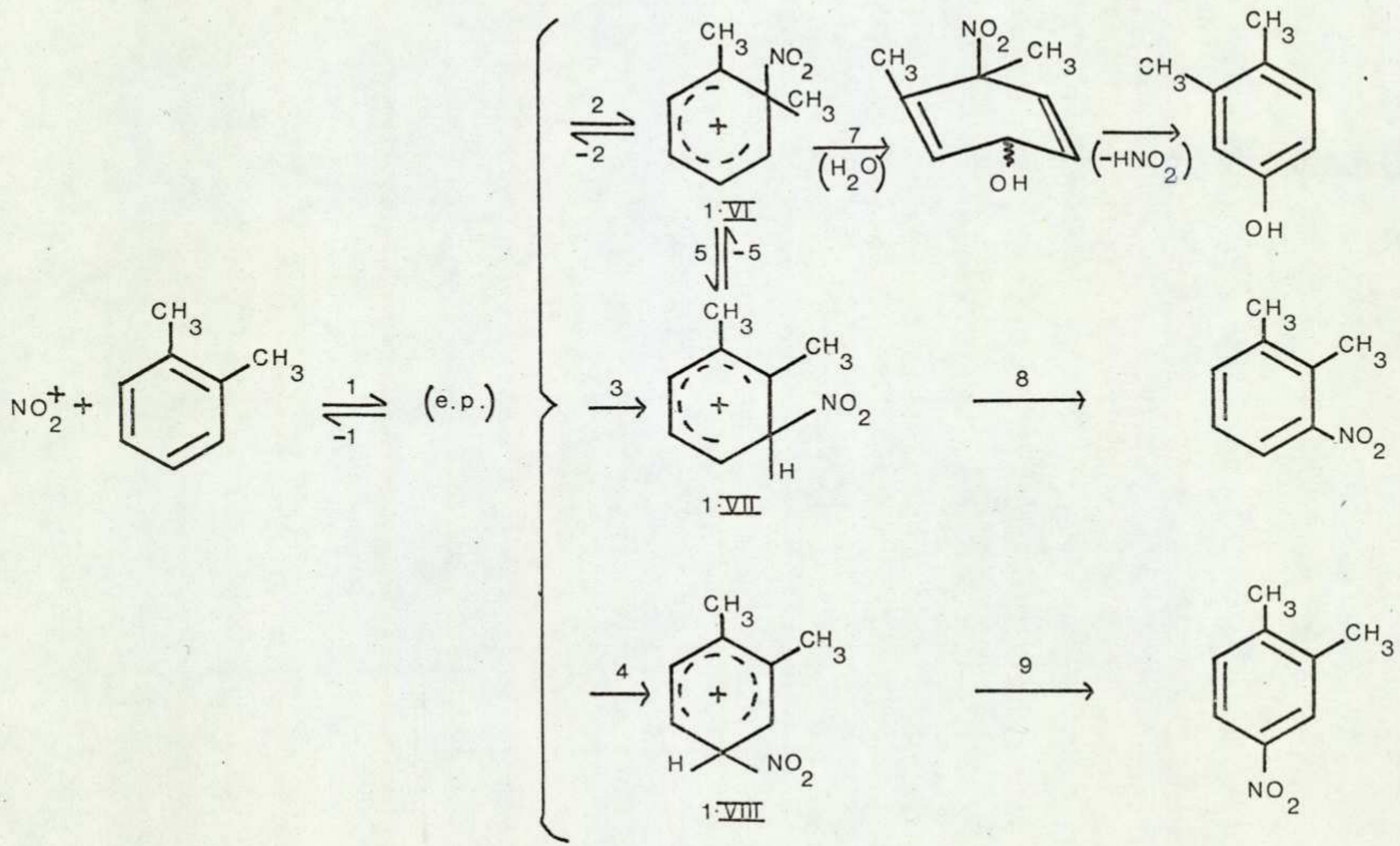
Scheme 1.2.

1.82 IPSO-NITRATION IN SULPHURIC ACID

Extensive investigation into *ipso*-nitration has been carried out since 1970, the majority of the work being carried out in acetic anhydride. However, *ipso*-substitution occurs in other media, and the use of the concept of *ipso*-substitution has led to the reinterpretation of some results which were difficult to explain.

In 1971, Coombes and Russell[34] studied the nitration of *o*-xylene in various concentrations of aqueous sulphuric acid. The isomer ratio of 1,2-dimethyl-3-nitrobenzene to 1,2-dimethyl-4-nitrobenzene was found to vary from 0.44 at 49% H_2SO_4 to 1.5 at 72% H_2SO_4. Above 72% H_2SO_4 the ratio was constant within experimental error. Myhre[61] accounted for this change in ratio by the formation of the 1,2-dimethyl-1-nitrocyclohexadienyl cation (1.VI) which is competitive with the formation of the isomeric cyclohexadienyl cations (see Scheme 1.3). It was suggested that (1.VI) could undergo a 1,2 shift of the nitro group thus enhancing the 3-nitro product. The isomer ratio change with acidity can be associated with a change in the dominant reaction pathway of (1.VI). At low acidities, nucleophilic capture leading to the formation of a phenol is more likely owing to the larger amount of water present. Above 70% H_2SO_4 rearrangement is preferred. Myhre tested this theory by studying the solvolysis of 3,4-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate in 50 to 85% aqueous sulphuric acid. 1,2-Di-

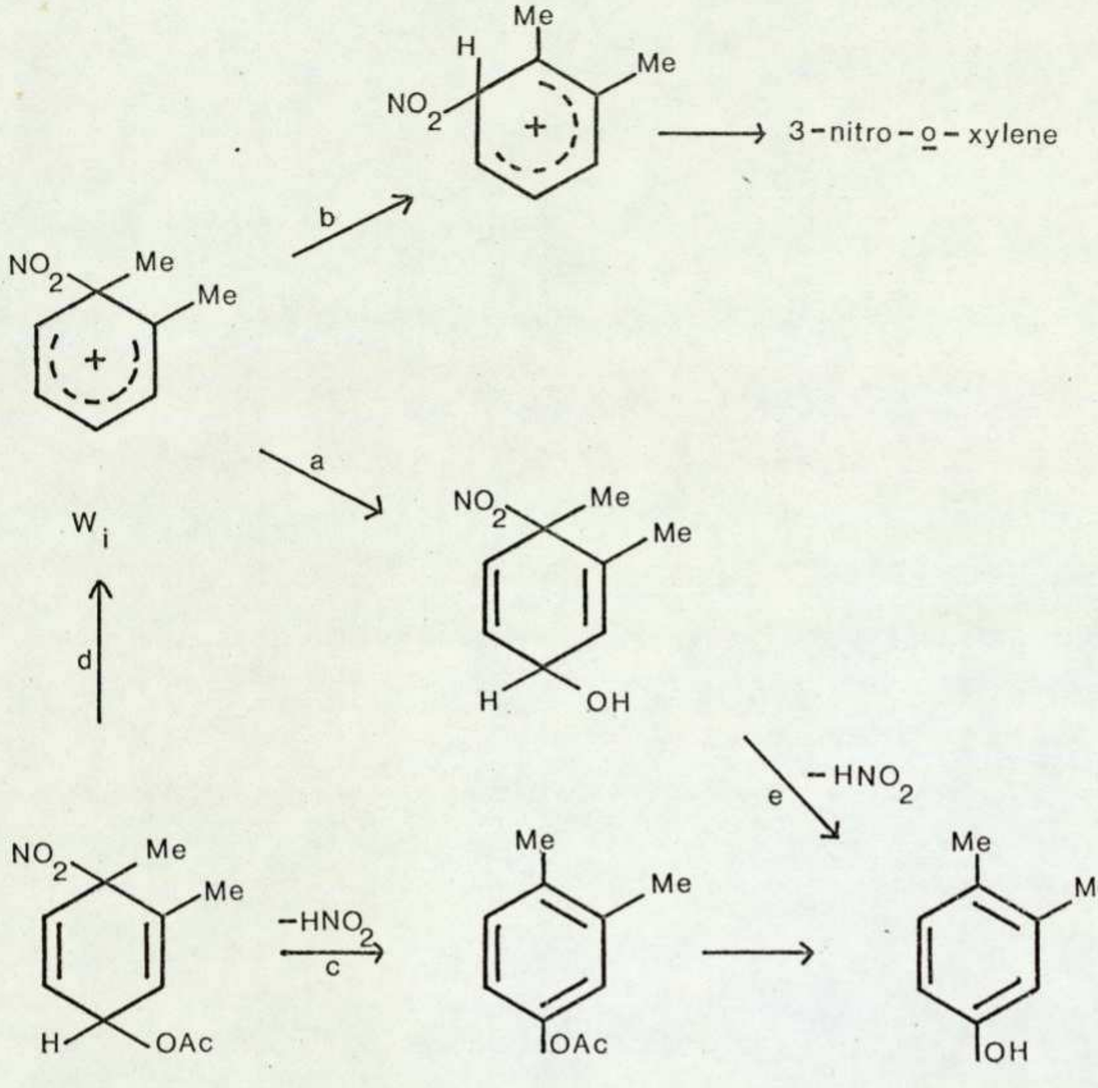
Scheme 1·3



methyl-3-nitrobenzene was isolated in yields of 2 to 93% respectively. No 1,2-dimethyl-4-nitrobenzene ($\not> 0.5\%$) was found.

Moodie and co-workers[65b] have shown that the decomposition of 3,4-dimethyl-4-nitrocyclohexa-2,5-dienyl acetate (1.IX Scheme 1.4) at all acidities is too rapid to follow, and occurs by two competing pathways:- elimination of HNO_2 (Scheme 1.4 step c) to give 1.X which is then hydrolysed to 1.XI, and hydrolysis (step d) to give a mixture of 1.XI and 3-nitro-o-xylene. Step d (Scheme 1.4) becomes increasingly important with increasing acidity, and is the important pathway above about 55% sulphuric acid. Above that acidity, data from the acidolysis of the acetate reflects the competition between paths a and b and is relevant to studies of the nitration of o-xylene.

Studies[62] of the adducts from hemimellitene also support Scheme 1.3 although in this case detailed studies of the solvolysis have yet to be made. The yield of 4-nitrohemimellitene derived from solvolysis of cis - 4-nitro-3,4,5-trimethylcyclohexa-2,5-dienyl acetate is nearly quantitative in sulphuric acid solutions in the 85 to 75% range, but the yield falls off rapidly through the 65 to 55% region and becomes zero below 50% sulphuric acid. No 5-nitrohemimellitene was detected under any of the solvolytic conditions.

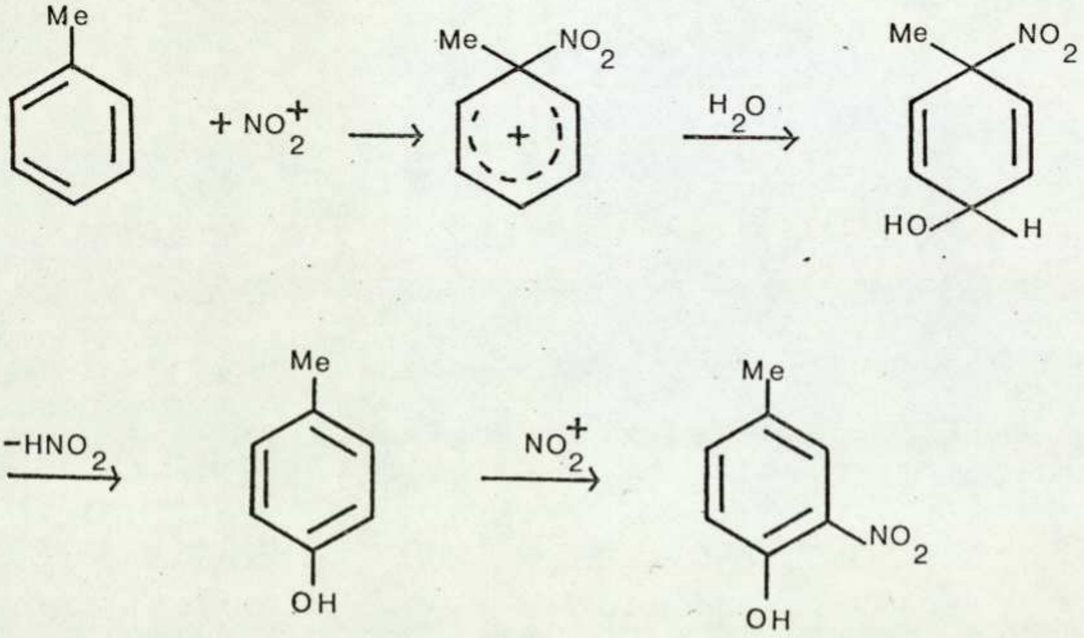


(1·IX) (1·X) (1·XI)

Scheme 1·4

A study by Moodie et al^{65a} has been carried out to determine the yields of the mono-nitro products of toluene, o-, m-,and p-xylenes, pseudocumene and hemimellitene. Earlier studies on products in this field relied upon the ratio of mono-nitro products formed and this did not take into account the side products through ipso - substitution. The results of this study showed that: (a) the yield of nitrotoluenes and nitro-m-xylenes varied little with acidity and accounted for virtually 100% of the products, (b) the products for o- and p-xylene, pseudocumene and hemimellitene increased in yield with increasing acidity.

These results agree well with the previous observations and indicate considerable ipso-substitution in o-and p- xylenes, pseudocumene and hemimellitene. The ipso-positions in toluene and m-xylene are not activated to electrophilic attack. Small amounts of a side product were detected in the nitration of toluene carried out in less than 55% H_2SO_4. This was identified as 4-methyl-2-nitrophenol and the suggested mode of formation was as follows(Scheme 1.5). It was concluded that the isomer yield can vary with acidity of the medium in two distinct ways; the variation with acidity of the

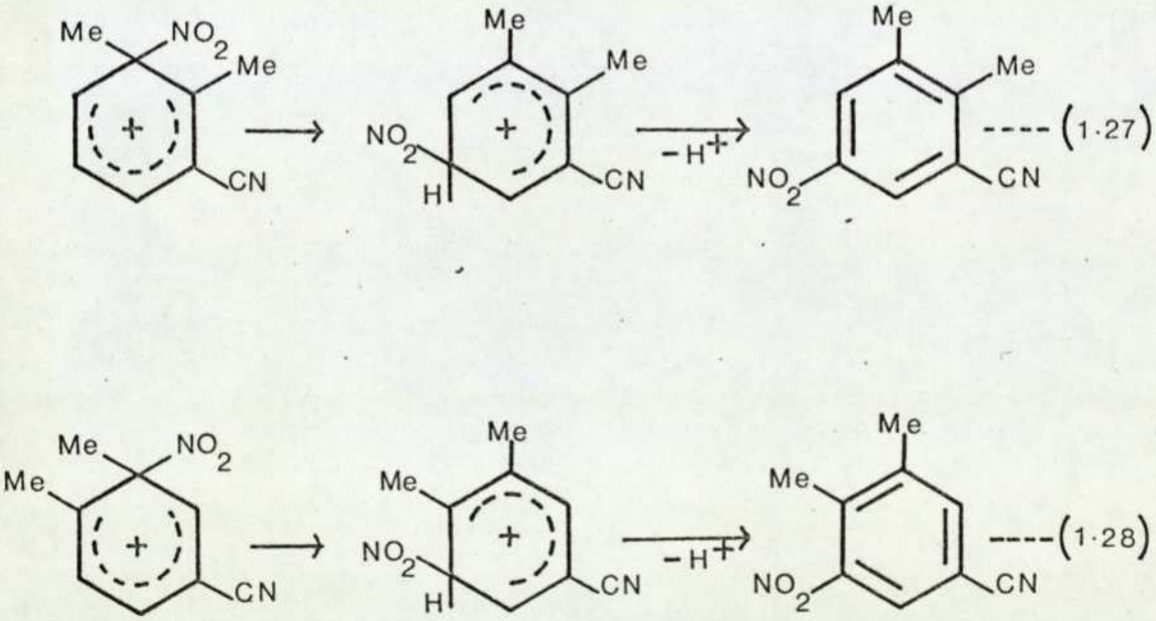


Scheme 1·5

relative reactivities of all nuclear positions, and the medium-dependent partitioning of the ipso Wheland intermediate between rearrangement and nucleophilic capture. The presumed capture of ipso-substituted Wheland intermediates, at low acidities in sulphuric acid, seems to correlate with the extent of $\bar{O}$Ac capture in acetic anhydride, suggesting capture is essentially complete in both cases.

1.83 1,3-SHIFTS

Migration of a nitro group across an unsubstituted position has also been shown to occur. A 1,3-nitro shift has been shown by Fischer and Grieg[59] in the nitrations of 2,3- and 3,4-dimethylbenzonitriles (Scheme 1.6) where the following rearrangements took place.



Scheme 1·6

It was suggested that 1,2-shifts in these cases would result in Wheland intermediates with the sp^3 carbon ortho- or para- to the cyano group and, therefore, would be energetically unfavourable.

Perrin and Skinner[63a] also postulated a 1,3-shift to explain the formation of 4-chloro-2-nitrophenol in the nitration of p-chloroanisole in acetic acid, and also suggest that ipso-substitution and 1,3-migration is responsible for some of the 4-chloro-2-nitroanisole, which is by far the major product of nitration in acetic anhydride. For 2,3- and 3,4-dimethylbenzonitriles, 1,3-nitro-shifts were concluded to be intramolecular processes since, firstly, there was not evidence for the formation of other nitro substitution products, and secondly, the product obtained from the 1,3-nitroshift was not suppressed in the presence of reactive arenes.

Other studies have shown that nitro migrations are not limited to a simple 1,2-shift. Hahn and Groen[58] have reported a 1,3-nitro-shift involving two consecutive 1,2-nitro-shifts. Olah and co-workers[64] have reported obtaining a compound (the nitrohexamethylbenzenium ion) in which the position of the nitro group is not fixed, and it is claimed that the nitro-group migrates around the ring by a series of 1,2-shifts.

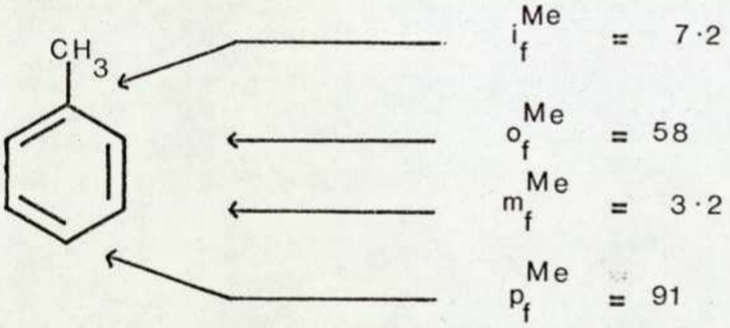
1.84 PARTIAL RATE FACTORS FOR IPSO-SUBSTITUTION

Perrin[63a] suggested the following expression to determine the partial rate factor for an ipso-substitution

$$i_f^R = \frac{k_{ArR}^{total} . \text{ \% attack at R}}{k_{ArH}^{total} . \text{ \% attack at H}} \quad .... (1.29)$$

As with other partial rate factors the ipso-partial rate factor i_f^R is characteristic not only of the substituent R but also of the aromatic substrate, the attacking electrophile, and the reaction conditions.

Fischer and Wright[66] determined i_f^R for nitration ipso to a methyl group. This factor is difficult to measure directly, since the methyl group is rarely displaced in aromatic substitution. The yields of aryl acetates were used to provide a measure of the extent of ipso nitration. They concluded that i_f^R for nitration ipso to a methyl group is three times the partial rate factor at the m-position. Myhre[62] estimated the partial rate factor for the nitration of toluene in acetic anhydride from data given by Hartshorn[63b], as follows:-



However, such conclusions rely on nucleophilic capture being complete.

1.9 OBJECTIVES OF THE PRESENT STUDY

From the preceding sections it can be seen that the nitration reaction has been the subject of study for many years, and indeed quantitative studies of the rates of nitration and isomer proportions produced under a variety of conditions, have contributed largely to the development of theories of electrophilic substitution.

Developments over the past ten years have led to the recognition of three important new factors, which in some cases have been shown to control the rates of nitration and the proportion and nature of products. These factors are encounter control of reaction rates, _ipso_-substitution and nitration _via_ nitrosation.

The work described in this thesis is concerned with three main aspects of nitration of reactive aromatic compounds by nitric acid in aqueous sulphuric acid.

(a) The effects of encounter control and _ipso_-substitution on the nitration of reactive aromatic compounds activated by substituents which provide an oxygen atom adjacent to the aromatic nucleus have been studied. (Chapters 2,3 and 4).

(b) The investigation of the nitration of very reactive aromatic compounds in aqueous sulphuric acid of low acidity has been investigated in an attempt to establish whether the nitronium ion remains the effective electrophile. (Chapter 6).

(c) The study of some molecules with two benzenoid nuclei has been undertaken. In the case of biphenyl the objective was:- (i) to check the high _o_:_p_-ratio previously obtained for nitration, (ii) to check that under the conditions used nitration is occuring in homogenous solution, and (iii) to obtain evidence pertaining to the possibility of _ipso_-substitution for this substrate. (Chapter 5).

The remaining substrate diphenylmethane is a simple two-ring system where the rings are separated and isolated by a methylene group. Study of this molecule (Chapter 5) is preliminary to a planned study of selectivity between two aromatic rings in a molecule, each sufficiently activated to react at the encounter rate, but separated to different extents, and designed to give information concerning the detailed structure of encounter pairs.

In the case of (b) and biphenyl, studies have relevance to 'special mechanisms' of ortho-substitution.

CHAPTER 2

THE NITRATION OF ANISOLE AND OF PHENOL

2.1 INTRODUCTION

Many reports concerned with the nitration of anisole have concentrated on the o:p- ratio of the mono-nitroanisoles produced. Information from these reports is summarised in Table 2.1. Thus, depending on the reaction conditions, the o:p- ratio of mono-nitroanisoles from the nitration of anisole varies from 0.06 to 3.0.

Halvarson and Melander[68] offered two explanations for the high o:p- ratios for the nitration of anisole by benzoyl nitrate and acetyl nitrate. Either the predominant initial attack of the nitrating species took place at the oxygen, followed by intra-molecular rearrangement to give o- nitroanisole, a special mechanism of o-substitution, or the orientation observed was the normal mode of orientation and lower o:p- ratios obtained in more strongly acidic media were due to interference by nitrosation. Ridd[23] has discussed the fact that this type of orientation change was associated with the existence of a lone electron pair on the substituent, either adjacent to, or near to, the ring. This lone pair could provide a site suitable for attachment of the nitronium ion to the substrate prior to migration into the ring. If this occurs, then the reason that high o:p- ratios are obtained with benzoyl nitrate and acetyl nitrate could be that the effective electrophile discriminates in favour of attack at these extra-cyclic lone pairs. It is not, however, necessary to assume

Table 2.1

Variation in the *o*:*p* ratios for the nitration of anisole

Conditions	*o*:*p* Ratio	Temp. (^{o}C)	Ref.
HNO_3, H_2SO_4 (1:1)	0.46	45	67
HNO_3 (d 1.42)	0.69	45	67
25% HNO_3 (d 1.5) in acetic acid	0.82	65	67
HNO_3 in Ac_2O ($AcONO_2$, Ac_2O)	2.53	10	68
Benzoyl chloride/$AgNO_3$ MeCN ($BzONO_2$, MeCN)	3.0	0	68
HNO_3 (3×10^{-2} mole dm^{-3}) 68.9% H_2SO_4 $[\text{urea}] =$ 2×10^{-2} mole dm^{-3}	1.5	25	69
HNO_3 (3×10^{-2} mole dm^{-3}) 65.9% H_2SO_4 $[\text{urea}] =$ 2×10^{-2} mole dm^{-3}	1.56	25	69
HNO_3 (3×10^{-2} mole dm^{-3}) 65.9% H_2SO_4 $[NaNO_2]$ *ca* 4×10^{-2} mole dm^{-3}	0.06	25	69

Table 2.1 (continued)

	o:p Ratio	Temp. (^{o}C)	Ref.
0.8×10^{-2} mole dm^{-3} anisole 4.1×10^{-2} mole dm^{-3} $Ti(NO_3)_4$ in CCL_4	1.78	20	70
2.7×10^{-2} mole dm^{-3} anisole 2.7×10^{-2} mole dm^{-3} $Ti(NO_3)_4$ in CCL_4	0.7	20	70
3.6×10^{-1} mole dm^{-3} anisole 3.6×10^{-1} mole dm^{-3} $Ti(NO_3)_4$ in CCL_4	0.43	20	70
HNO_3 in acetic acid	0.8	-	144
NO_2^+ BF^-in sulpholan	2.70	-	144
$CH_3ONO_2{\cdot}BF_3$ in nitromethane	0.39	-	144

different effective agents in different media. It is possible that the lone electron pairs are hydrogen bonded in the more strongly acidic media involving molecular nitric acid, and this would give rise to the change in orientation. Another suggestion due to Paul[46] is that the change in orientation could be correlated with the differences between the dielectric constants of acetic anhydride and the other media.

In 1969 Hoggett[71] found that anisole was nitrated in solutions of acetyl nitrate in acetic anhydride at the limiting rate. An o:p- ratio of 2.4 was obtained. When anisole was nitrated at the encounter rate in 65% sulphuric acid in the presence of urea (ca 2×10^{-2} mol dm^{-3}), under conditions in which the nitronium ion was the effective electrophile, the orientation was found to be similar to that using acetyl nitrate in acetic anhydride. However, when anisole was nitrated in 65% sulphuric acid in the absence of urea and in the presence of sodium nitrite (ca 4×10^{-2} mol dm^{-3}), an o:p- ratio of 0.06 was obtained. It is a reasonable interpretation of these data that a high o:p- ratio (ca 60 - 70% o-nitroanisole) is due to nitration by the nitronium ion, and that low values observed under various conditions are the results of nitration catalysed by the presence of fortuitous nitrous acid[72]. This was the second of Halvarson and Melander's alternatives.

A rate profile for the nitration of anisole by nitric acid in 41 - 63% sulphuric acid, when nitrosation was precluded, was reported by Deno and Stein[20]. This indicated that in 57.3% sulphuric acid, anisole reacted 70 times faster than benzene. From the more accurate work involving lower substrate concentrations[22], a limiting rate of nitration corresponding to the rate of encounter of sufficiently reactive molecules with the nitronium ions in this medium has been established. Deno and Stein's data suggest that anisole reacts surprisingly, at a rate a little less than the limiting one.

Phenol exhibits a similar change in orientation to that of anisole. In aqueous sulphuric acid a change from an o:p- ratio of 2.7 under nitrating conditions to an o:p- ratio of 0.1 under nitrosating conditions has been recorded[73]. In 61.05% perchloric acid, under conditions where the nitronium ion is the effective species, an o:p- ratio of 1.86 has been reported[22]. Challis and Lawson[74] have shown experimentally that the nitrosation of phenol takes place predominantly at the p- position. In solutions of acetyl nitrate in acetic anhydride the situation seems to be complex[40], and differences that occur may be due to a change in nitrosating agent. Phenol was found to be nitrated at a rate again surprisingly a little less than the limiting encounter rate in sulphuric and perchloric acid, when nitrosation was precluded[22].

2.2 EXPERIMENTAL

2.21 MATERIALS

These were as described in Section 7.2 with the addition of the following. Anisole (bp. 155°, lit.[75] bp. 153.6°), phenol (bp. 182°, lit.[76] bp. 182°), *o*- nitroanisole (bp. 268°, lit.[77] bp. 265°), and *p*- nitroethylbenzene (bp. 156°/40mm, lit.[78] bp. 154°/37mm) were commercial grade reagents purified by distillation. *m*-Nitroanisole (mp. 37 - 38°, lit.[79] mp. 38 - 39°), *p*-nitroanisole (mp. 54 - 55°, lit.[77] mp. 54°), *o*-nitrophenol (mp. 44.0°, lit.[80] mp. 44.3°), *m*-nitrophenol (mp.95°, lit.[81] mp. 95 - 96°), *p*-nitrophenol (mp. 114°, lit.[82] mp. 114°), 2,4-dinitroanisole (mp. 85 - 86°, lit.[83] mp. 88°) and 4-nitroveratrole (mp. 95 - 96°, lit.[84] mp. 96°) were commercial grade reagents purified by recrystallisation.

2.211 2,6-DINITROANISOLE

A solution of 1.0g (0.043 moles) of sodium in 50 cm^3 of dried methanol (molecular sieve type 4A) was cooled, and 5g (0.025 moles) of 1-chloro-2,6-dinitrobenzene was added. The mixture was refluxed for two hours and the resultant liquid was diluted with methanol and filtered hot. After concentration by rotary evaporation, crystallisation was allowed to occur. The product was twice recrystallised from methanol to give a straw coloured crystalline solid (mp. 118°, lit.[83] 118°), ^{1}Hn.m.r. spectrum:- $\left[\tau\right.$ ($CDCL_3$) 1.92 - 20 (2H,d, aromatic C-H), 2.5 - 2.8 (1H,q,aromatic C-H), 5.9 (3-H,s,OCH_3)]. The mass spectrum (molecular ion 198.0272 calculated 198.0277) is shown Fig. 2.1.

2.212 4-METHYL-2-NITROPHENOL

As Section 3.212

2.22 KINETIC MEASUREMENTS

For both anisole and phenol as described in Section 7.3.

2.23 PRODUCT ANALYSIS

2.231 ANISOLE

The conventional g.l.c. method as described in Sections 7.41 and 7.42 was used. Tables 2.2(i), (ii) and (iii) give the details of the g.l.c. procedure.

2.232 PHENOL

An attempt was made to use the g.l.c. method described in Sections 7.41 and 7.42. It was found that m- and p-nitrophenol were retained on all the columns available, presumably due to their highly-polar nature. The formation of the silyl derivatives by direct reaction at ambient temperature between the nitro-compounds and Tri-Sil/B.S.A. (Pierce Chemical Co.), which was found to be quantitative, was then attempted. Separation of the silyl derivatives was found to be possible under the g.l.c. conditions detailed in Table 2.3. A simulated reaction mixture was then prepared by addition of the nitrophenols (4.4×10^{-5} mole dm^{-3}) to 67.7% sulphuric acid (250 cm^3). After dilution with distilled water,

Figure 2.1 Mass spectrum of 2,6-dinitroanisole

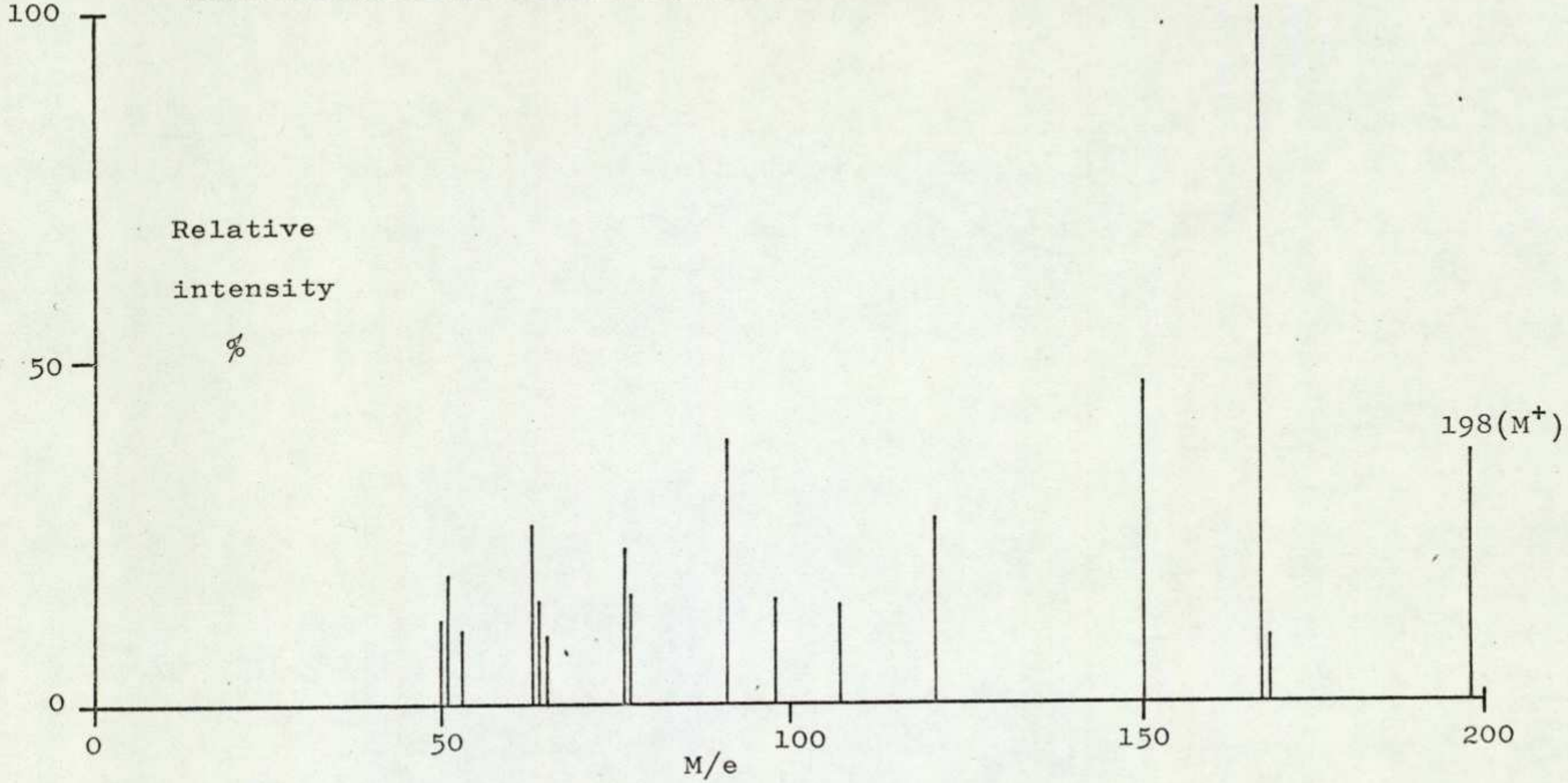


Table 2.2(i)

G.l.c. conditions for the separation of o, m and p-nitroanisoles

Column: 1m x $\frac{1}{4}$" S.S. 5% PEG A on 1% H_3PO_4 washed Chromosorb W 60 - 85 mesh

Oven Temperature: 140 ± 0.5°

Carrier Gas: Nitrogen

Flow Rate: $60 cm^3 min^{-1}$

Compound	Retention times /s
o-Nitroanisole	586
m-Nitroanisole	354
p-Nitroanisole	657
Anisole	38
p-Nitroethylbenzene (Reference standard)	227

Table 2.2(ii)

G.l.c. conditions for the estimation of 2,4-dinitroanisole

Column:	1.5m x $\frac{1}{4}$" S.S. $1\frac{1}{2}$% OV225 on 68 - 85 mesh universal support
Oven temperature:	208 ± 0.5°
Carrier gas:	Nitrogen
Flow rate:	60cm^3 min^{-1}

Compound	Retention times /s
2,4-Dinitroanisole	324
4-Nitroveratrole (Reference standard)	147

Table 2.2(iii)

G.l.c. conditions for the separation of o-nitroanisole, p-nitroanisole and 2,6-dinitroanisole

Column:	1.5m x $\frac{1}{4}$" S.S. $1\frac{1}{2}$% OV225 on 60 - 85 mesh universal support
Oven temperature:	145 ± 0.5°
Carrier gas:	Nitrogen
Flow rate:	$60cm^3\ min^{-1}$

Compound	Retention times /s
2,6-Dinitroanisole	658
o-Nitroanisole	223
p-Nitroanisole	265
4-Nitroveratrole (Reference standard)	852

Table 2.3

G.l.c. conditions for the separation of the silyl derivatives of o, m and p-nitrophenol

Column:	1.5m x ¼" S.S. 1½% OV1 on 60 - 85 mesh universal support
Oven temperature:	131 ± 0.5°
Carrier gas:	Nitrogen
Flow rate:	60cm^3 min^{-1}

Compound	Retention times /s
Silyl derivative of o-Nitrophenol	317
Silyl derivative of m-Nitrophenol	406
Silyl derivative of p-Nitrophenol	570
p-Nitroethylbenzene (Reference standard)	214

extraction with chloroform and dichloromethane was attempted and it was found that although o-nitrophenol could be extracted quantitatively (100.9%) only partial extraction of m- and p-nitrophenols was possible in ca 40% and 28% yields respectively. This low extraction is thought to be due to the high degree of solvation of the m- and p-nitrophenols, the o-nitrophenol being capable of intramolecular hydrogen bonding.

Three methods were then used to ascertain the isomer distribution from the nitration of phenol.

A. A u.v. spectrophotometric method

B. A high pressure liquid chromatography (h.p.l.c.) method

C. A g.l.c. estimation of o-nitrophenol

2.2321 Method A. (U.v. spectrophotometric method)

The method as described by Dewar and Urch[85] was used. Consider a solution containing substances 1,2, ...i at known concentrations x_1, x_2, ...x_i mole dm^{-3}. Standard solutions of 1,2, ...i have known concentrations of c_1, c_2, ...c_i mole dm^{-3} and give rise to absorptions (measured as log I_o/I) of A_1, A_2, ...A_i at wavelength λ. If R is the observed value of $\log_{10} I_o/I$ for the unknown solution and if Beer's Law is obeyed, then:-

$$R = \frac{x_1}{c_1} A_1 + \frac{x_2}{c_2} A_2 \ldots\ldots + \frac{x_i}{c_i} A_i \qquad 1$$

where all measurements refer to the same value for λ.

Dividing throughout by A_1 gives:-

$$\frac{R}{A_1} = \frac{x_1}{c_1} + \frac{x_2}{c_2} \cdot \frac{A_2}{A_1} + \ldots\ldots\ \frac{x_i}{c_i}\ \frac{A_i}{A_1} \qquad \text{———} \qquad 2$$

For a two component system, R, A_1, A_2, c and c_2 are known experimentally. If the values of R/A, for various wavelengths are plotted against the corresponding values of A_2/A_1 the points should lie on a straight line of slope x_2/c_2 and the intercept on the R/A_1 axis gives x_1/c_1. Any deviation from a straight line indicates the presence of other absorbing components.

Solutions were prepared in the same manner as for the kinetic studies, i.e. 25.0 cm^3 aqueous sulphuric acid containing 2×10^{-2} mole dm^{-3} sulphamic acid, 1.66×10^{-4} mole dm^{-3} phenol and the appropriate concentration of nitric acid at 25°. The reaction was allowed to proceed for ten half lives (determined from kinetic measurements) and the absorption curve was then determined in the range 270 - 380mm. Absorption curves were also determined for a known concentration of o-nitrophenol (8.65×10^{-5} mole dm^{-3}), of p-nitrophenol (8.76×10^{-5} mole dm^{-3}) and of the appropriate concentration of nitric acid in the same concentration of aqueous sulphuric acid. The method of calculation described above was applied to obtain values for the yields of o- and p-nitrophenols.

2.2322 Method B. (High pressure liquid chromatography method)

(i) From reactions in less than 71% sulphuric acid.

A solution of phenol in acetic acid was prepared (1.05 mole dm^{-3}) and an aliquot (0.10cm^{-3}) was added to the appropriate concentration of aqueous sulphuric acid (25cm^{3}) containing 0.05g sulphamic acid. This solution was kept at 25° for 30 minutes. Nitric acid of the appropriate concentration was prepared by dilution of 70% nitric acid. 1.0cm^{3} of this solution was added to the substrate solution, the solution was mixed and the reaction was allowed to proceed for 10 half lives (calculated from the concentration of nitric acid and the previously determined second-order rate coefficients). The reaction was quenched by dilution with 10cm^{3} of ice water, and 0.5cm^{3} of a solution of 0.1240 mole dm^{-3} 4-methyl-2-nitrophenol in acetic acid was added as a reference standard. The solution was neutralised with ammonia solution (S.G. 0.88).

10μl samples were injected onto an h.p.l.c. chromatograph under the conditions given in Table 2.4. The nitro-products were identified by comparison of their retention times on high pressure liquid chromatography analysis with those of independently identified authentic samples. The yields of nitrophenols were calculated by a method based on relative response factors as given in Section (7.5).

(ii) From reactions in greater than 71% sulphuric acid.

Reactions were on the scale described above but

Table 2.4

H.p.l.c. conditions for the separation of o- and p-nitrophenol

Column: 1m x $\frac{1}{8}$" S.S. Permaphase E.T.H.

Solvent: Deionised water

Flow rate: 1.0cm^3 min^{-1}

Wavelength: 286nm

Detector: Cecil 272

Pump: Waters Associates model 6000A

Temperature: Ambient

Compound	Retention times /s
o-nitrophenol	414
p-nitrophenol	588
4-methyl-2-nitrophenol (Reference standard)	870

the nitric acid and the substrate were in equimolar proportions to avoid complications due to dinitration. Phenol in acetic acid (0.092cm^{-3}, 1.05 mole dm^{-3}) was added to the appropriate concentration of aqueous sulphuric acid (25cm^{3}) containing 0.05g sulphamic acid and nitric acid (3.77×10^{-3} mole dm^{-3}) and the mixture was stirred vigorously. The nitric acid was added first, to overcome any problems due to sulphonation. Termination, neutralization and h.p.l.c. analysis were as previously described.

2.2323 Method C. (G.l.c. method for the determination of o-nitrophenol)

The conventional method as described in Sections 7.41 and 7.42 was used. o-Nitrophenol alone could be estimated in this way. The g.l.c. procedure is given in Table 2.5.

2.3 RESULTS

2.31 KINETICS

2.311 ANISOLE

The results and subsequent calculation required for a typical determination of a rate coefficient for the nitration of anisole are given below

Sulphuric acid	60.8%
$[HNO_3]$	5.5×10^{-2} mole dm^{-3}
[Anisole]	1.0×10^{-4} mole dm^{-3}
[Urea]	3×10^{-2} mole dm^{-3}
Temperature	25± 0.2°
Wavelength of measurement	330nm.

Table 2.5

G.l.c. conditions for the estimation of o-nitrophenol

Column:	1m x $\frac{1}{4}$" S.S. 5% PEG. A on 60 - 85 mesh, 1% H_3PO_4 washed Chromosorb W.
Oven temperature:	118 ± 0.5°
Carrier gas:	Nitrogen
Flow rate:	60cm^3 min^{-1}

Compound	Retention times /s
o-Nitrophenol	252.0
4-Methyl-2-nitrophenol (Reference standard)	341.0

Table 2.6 shows the data obtained from the above nitration. Fig. 2.2 shows a plot of $\log_{10}(A_{\infty} - A_t)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[\text{HNO}_3]} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$= \frac{2.303 \times 1.66 \times 10^{-4}}{5.5 \times 10^{-2}} \text{ dm}^3 \text{ mole}^{-1} \text{s}^{-1}$$

$$\therefore \; k_2(\text{obs}) = 6.96 \times 10^{-3} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients for the nitration of anisole, o-nitroanisole and p-nitroanisole at various percentages of sulphuric acid are given in Table 2.7. A rate profile ($\log_{10}(A_{\infty} - A_t)$ vs % H_2SO_4) is shown in Fig. 2.3 in which data for mesitylene and benzene are also shown.

2.312 PHENOL

The results and subsequent calculations required for a typical determination of a rate coefficient for the nitration of phenol are given below.

Sulphuric acid	66.1%
$[\text{HNO}_3]$	3.88×10^{-3} mole dm^{-3}
[Phenol]	1.36×10^{-4} mole dm^{-3}
Temperature	$25.0 \pm 0.2^{\circ}$
Wavelength of measurement	295 nm.

Fig. 2.4 shows the absorption curve obtained, Table 2.8 shows the data obtained from the above nitration, and Fig. 2.5 shows a plot of $\log_{10}(A_{\infty} - A_t)$ vs t.

Table 2.6

Data from a typical determination of the rate of nitration of anisole in 60.8% sulphuric acid at 25.0 ± 0.2^{o}

Time (t) /s	Absorbance (A_t)	($A_\infty - A_t$)	Log_{10} ($A_\infty - A_t$)
240	0.040	0.547	-0.2620
360	0.067	0.52	-0.2840
480	0.090	0.497	-0.3036
600	0.110	0.477	-0.3215
720	0.130	0.457	-0.3401
840	0.152	0.436	-0.3615
960	0.172	0.416	-0.3819
1080	0.191	0.396	-0.4023
1200	0.210	0.377	-0.4236
1440	0.240	0.347	-0.4597
1680	0.271	0.316	-0.5003
1920	0.300	0.287	-0.5421
2160	0.325	0.262	-0.5817
2400	0.348	0.239	-0.6216
2760	0.378	0.209	-0.6799
3120	0.406	0.181	-0.7423

Table 2.6 (continued)

Time (t) /s	Absorbance (A_t)	$(A_\infty - A_t)$	$\log_{10} (A_\infty - A_t)$
3600	0.436	0.151	-0.8210
4200	0.468	0.119	-0.9245
4800	0.490	0.097	-1.0132
6000	0.527	0.060	-1.2218
7200	0.549	0.038	-1.4202
	0.587 (A_∞)		

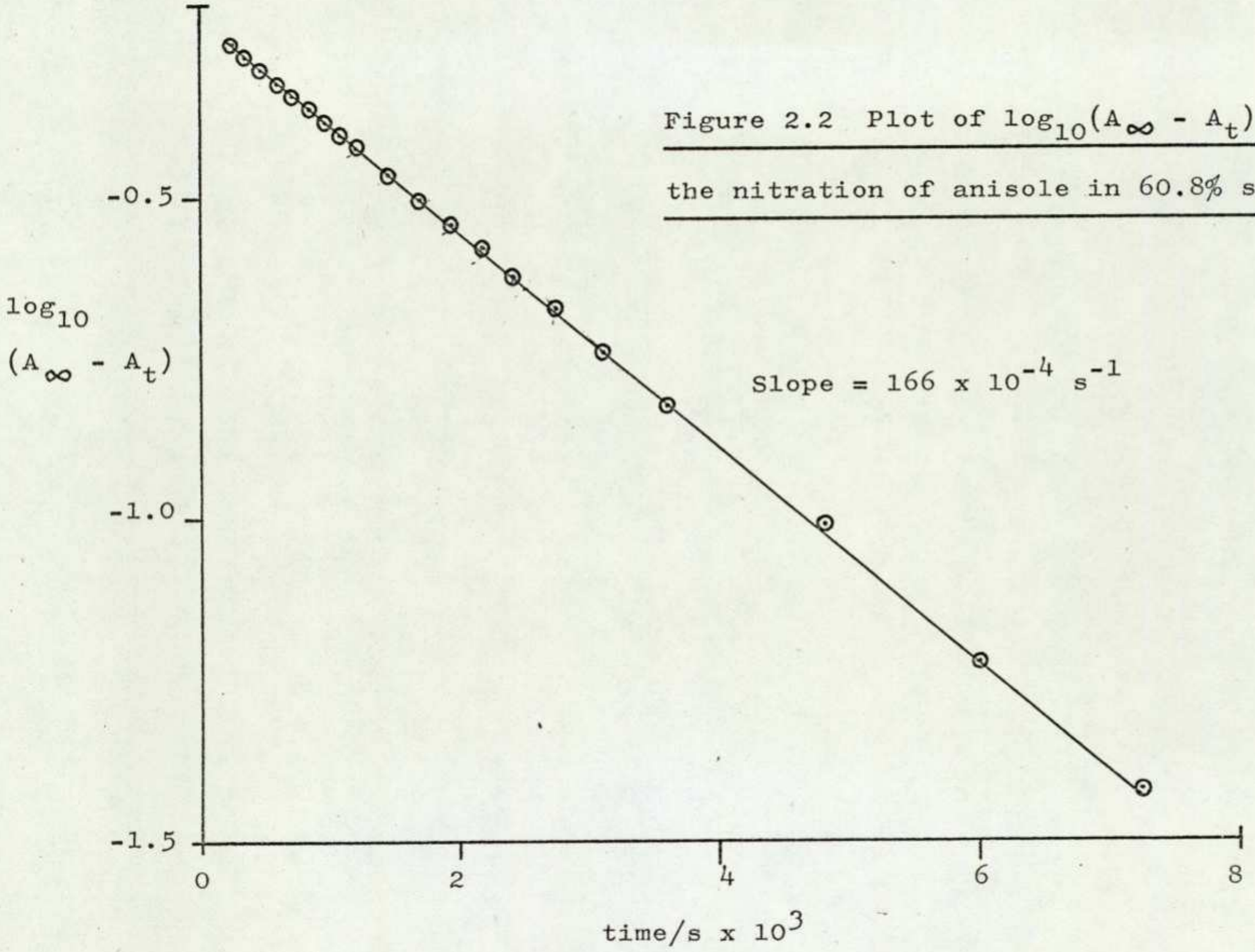


Figure 2.2 Plot of $\log_{10}(A_{\infty} - A_t)$ vs time from the nitration of anisole in 60.8% sulphuric acid

Table 2.7

Second-order rate coefficients for nitration in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[c]	$[HNO_3]/10^{-2}$ mole dm^{-3}	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}
Anisole[a,b]		
54.2[d]	5.5	2.48×10^{-4}
54.2[e]	5.5	2.28×10^{-4}
54.2[f]	5.5	2.49×10^{-4}
56.1[d]	5.5	5.20×10^{-4}
56.1[e]	5.5	5.58×10^{-4}
56.1[f]	5.5	$5:48 \times 10^{-4}$
58.1[d]	5.5	1.38×10^{-3}
58.1[e]	5.5	1.40×10^{-3}
58.1[f]	5.5	1.39×10^{-3}
60.8[d]	5.5	6.96×10^{-3}
60.8[e]	5.5	7.39×10^{-3}
60.8[f]	5.5	7.60×10^{-3}
63.2[d]	0.39	2.89×10^{-2}
63.2[e]	0.39	3.07×10^{-2}
63.2[f]	0.39	3.18×10^{-2}

Table 2.7 (continued)

H_2SO_4 (%)[c]	$[HNO_3]/10^{-2}$ mole dm^{-3}	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}
Anisole[a,b]		
66.1[d]	0.17	0.19
66.1[e]	0.17	0.21
66.1[f]	0.17	0.22
68.3[d]	0.089	0.80
68.3[e]	0.089	0.75
68.3[f]	0.089	0.79
70.41[d]	0.089	4.03
70.41[e]	0.089	4.08
70.41[f]	0.089	4.06
72.57[d]	0.046	16.58
72.57[e]	0.046	16.25
72.57[f]	0.046	16.36
o-Nitroanisole[e,g,h]		
72.5	5.5	8.3×10^{-3}
p-Nitroanisole[e,h,i]		
72.5	5.5	7.7×10^{-3}

Table 2.7 (continued)

a) [ArH] *ca* 1 x 10^{-4} mole dm^{-3}

b) Measurement at 330 nm.

c) ± 0.1%

d) [Urea] *ca* 3 x 10^{-2} mole dm^{-3}

e) [Sulphanilic acid] *ca* 1 x 10^{-2} mole dm^{-3}

f) [Sulphamic acid] *ca* 2 x 10^{-2} mole dm^{-3}

g) Measurement at 320 nm.

h) [ArH] *ca* 6 x 10^{-5} mole dm^{-3}

i) Measurement at 350 nm.

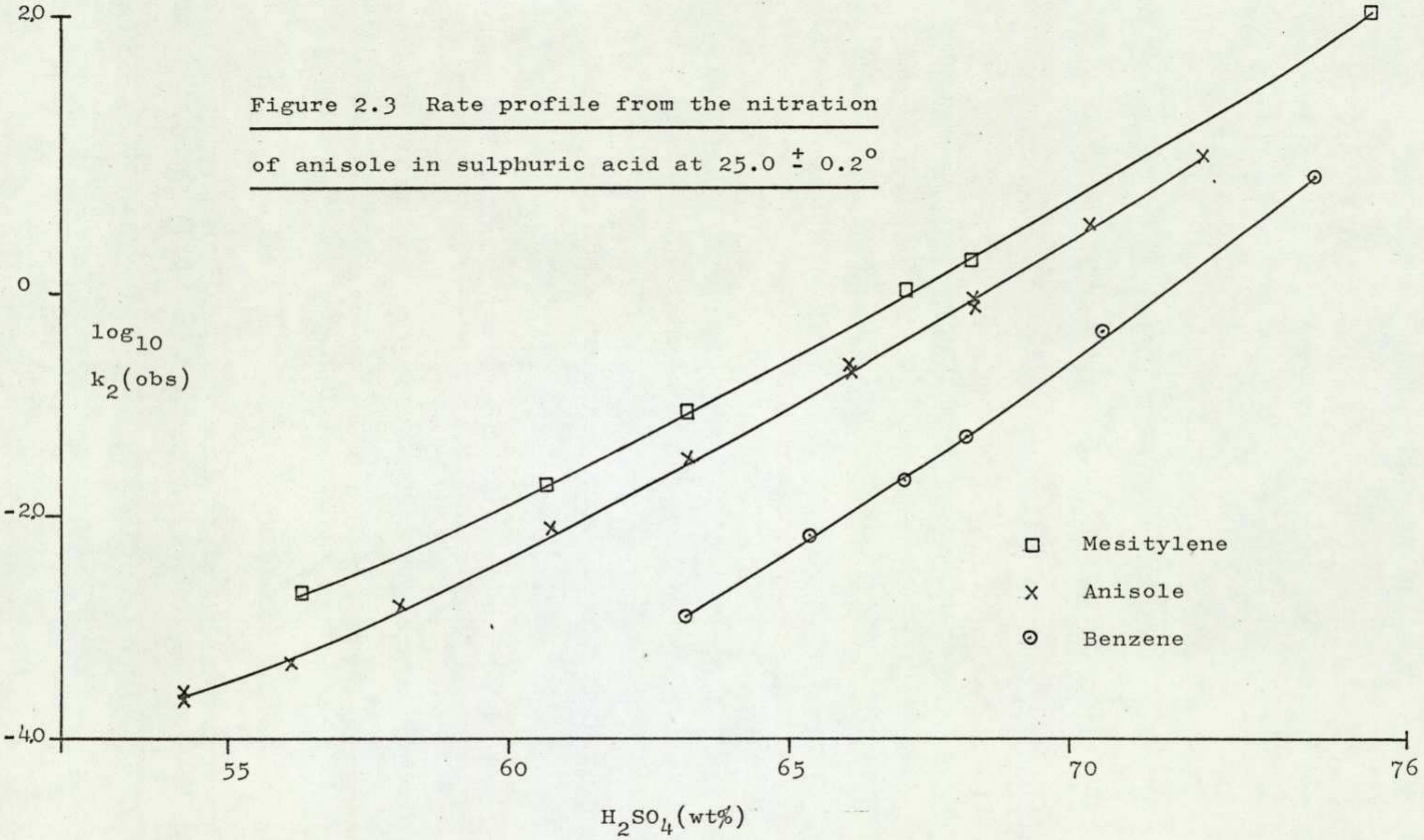


Figure 2.3 Rate profile from the nitration of anisole in sulphuric acid at 25.0 ± 0.2°

Figure 2.4 Absorption curve from the nitration of phenol in 66.1% sulphuric acid

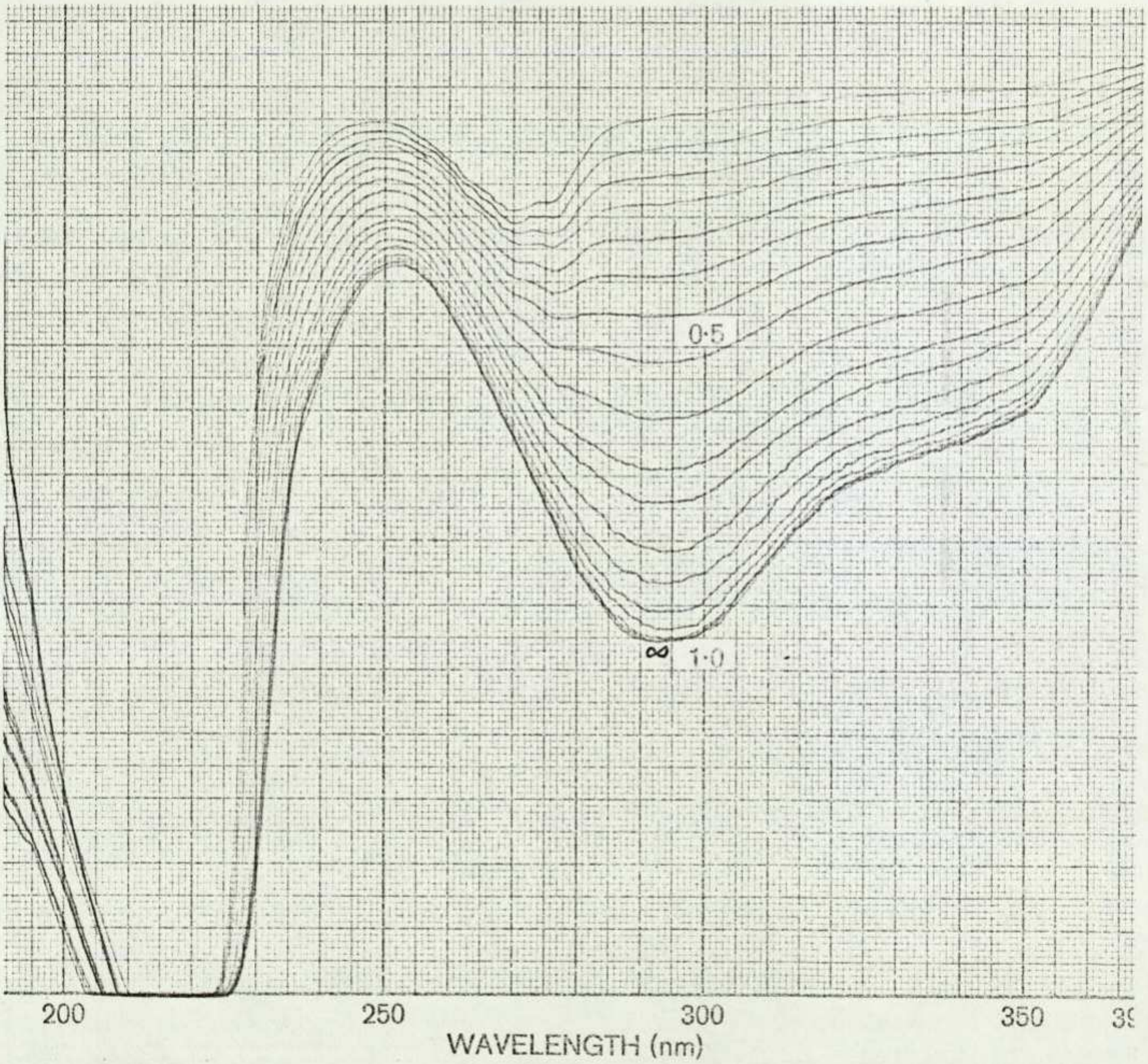


Table 2.8

Data from a typical determination of the rate of nitration of phenol in 66.1% sulphuric acid at 25.0 ± 0.1°

Time (t) /s	Absorbance (A_t)	($A_\infty - A_t$)	$\log_{10}$ ($A_\infty - A_t$)
17	0.140	0.815	-0.0888
90	0.190	0.765	-0.1163
145	0.235	0.720	-0.1427
210	0.280	0.675	-0.1707
300	0.330	0.625	-0.2041
405	0.390	0.565	-0.2479
532	0.450	0.505	-0.2967
705	0.520	0.435	-0.3615
950	0.610	0.345	-0.4622
1265	0.690	0.265	-0.5768
1504	0.740	0.215	-0.6676
1928	0.815	0.140	-0.8539
2400	0.860	0.095	-1.0223
3070	0.910	0.045	-1.3468
	0.955 (A_∞)		

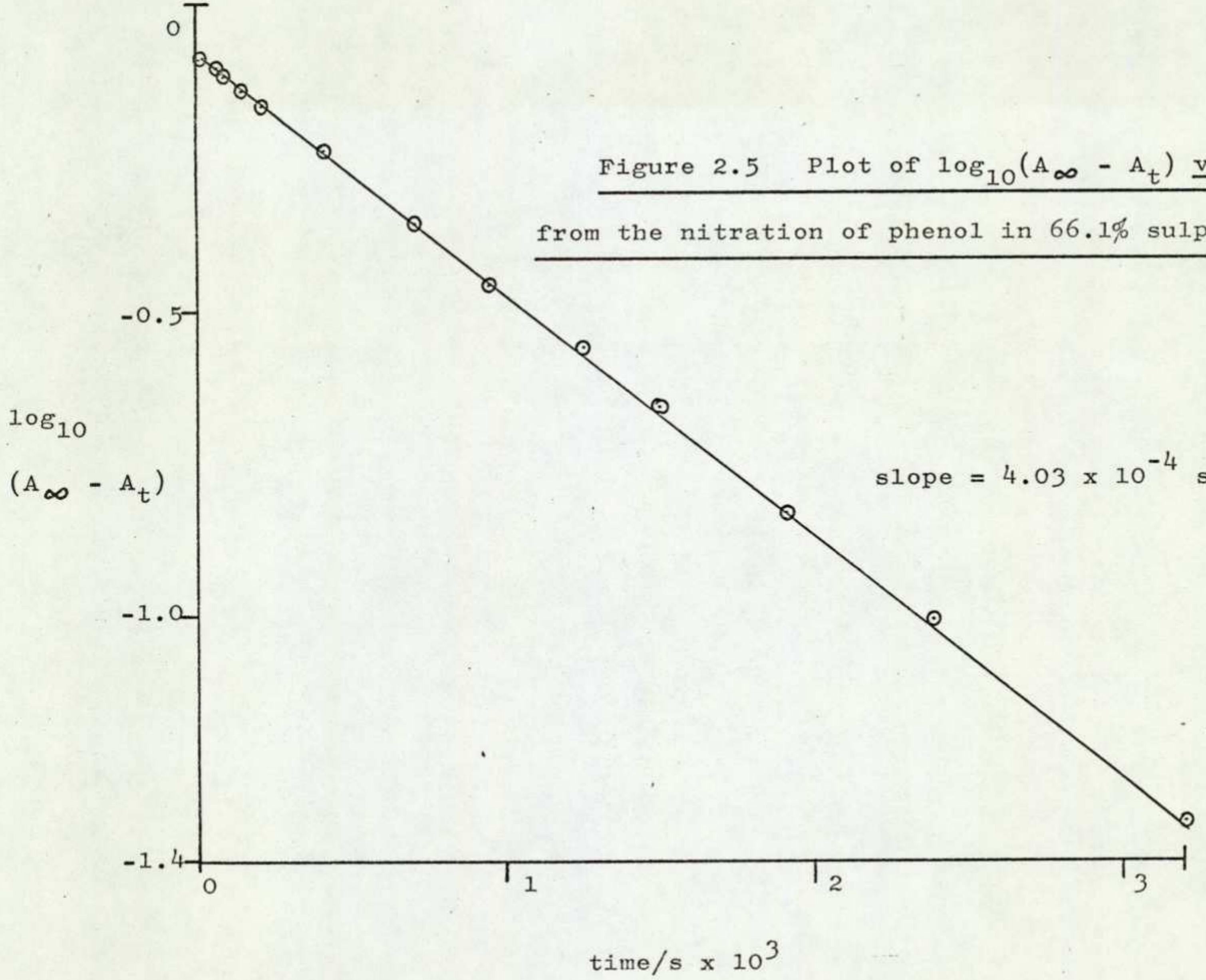


Figure 2.5 Plot of $\log_{10}(A_\infty - A_t)$ vs time from the nitration of phenol in 66.1% sulphuric acid

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[\text{HNO}_3]} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$= \frac{2.303 \times 4.03 \times 10^{-4}}{3.88 \times 10^{-3}} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$\therefore \; k_2(\text{obs}) = 0.24 \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients for the nitration of phenol, o-nitrophenol and p-nitrophenol for a range of percentages of sulphuric acid are given in Table 2.9. A rate profile is shown in Fig. 2.6 in which data for mesitylene and benzene are also shown.

2.32 YIELDS OF NITRO-COMPOUNDS

2.321 ANISOLE

An example of the method for calculating the yield of nitro-compounds from the nitration of anisole is given below.

Sulphuric acid	79.5%
Amount of anisole	5.79×10^{-5} moles
Amount of HNO_3	5.79×10^{-5} moles
Amount of reference standard p-nitroethylbenzene	6.52×10^{-6} moles

The reaction was carried out in 260cm^3 of sulphuric acid. Fig. 2.7 shows the chromatogram obtained (g.l.c. conditions as Table 2.2(i)).

Peak Areas from Fig. 2.7	Area/mm^2
o-Nitroanisole	1285
p-Nitroanisole	1322
p-Nitroethylbenzene	440

Table 2.9

Second-order rate coefficients for nitration in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[a]	$[HNO_3]/10^{-2}$ mole dm^{-3}	$k_2(obs)/dm^3$ $mole^{-1}$ s^{-1}
Phenol[d,e]		
56.1[c]	5.5	8.56×10^{-4}
56.1[c]	5.5	8.56×10^{-4}
58.1[c]	5.5	2.46×10^{-3}
58.1[c]	5.5	2.51×10^{-3}
60.8[c]	5.5	1.01×10^{-2}
60.8[b,f]	5.5	9.98×10^{-3}
63.2[c]	5.5	2.51×10^{-2}
63.2[c]	5.5	2.69×10^{-2}
66.1[c]	0.38	2.43×10^{-1}
66.1[c]	0.38	2.52×10^{-1}
68.0[c]	0.089	7.59×10^{-1}
68.0[c]	0.17	7.90×10^{-1}
70.4[c]	0.089	3.92
70.4[c]	0.089	4.12
72.6[g]	0.046	20.49

Table 2.9 (continued)

H_2SO_4 (%)[a]	$[HNO_3]/10^{-2}$ mole dm^{-3}	$k_2(obs)/dm^3$ $mole^{-1}$ s^{-1}
Phenol[d,e]		
72.6[g]	0.046	18.81
74.4[g]	0.046	57.2
74.4[g]	0.046	58.6
_o_-Nitrophenol[d,h,i]		
75.5	5.5	8.02×10^{-3}
75.5	5.5	8.00×10^{-3}
_p_-Nitrophenol[d,j,k]		
75.5	5.5	2.0×10^{-2}
75.5	5.5	1.9×10^{-2}

a) ± 0.1%

b) 1mm cell

c) $[ArH] = 1.37 \times 10^{-4}$ mole dm^{-3}

d) [Sulphamic acid] _ca_ 2×10^{-2} mole dm^{-3}

e) Measurement taken at 295 or 300nm.

f) $[ArH] = 1.39 \times 10^{-4}$ mole dm^{-3}

g) $[ArH] = 7.0 \times 10^{-5}$ mole dm^{-3}

Table 2.9 (continued)

h) Measurement taken at 266nm.

i) $\left[\mathrm{ArH}\right] = 8.4 \times 10^{-5} - 4.78 \times 10^{-5}$ mole dm^{-3}

j) Measurement taken at 270 nm.

k) $\left[\mathrm{ArH}\right] = 6.2 \times 10^{-5} - 3.7 \times 10^{-5}$ mole dm^{-3}

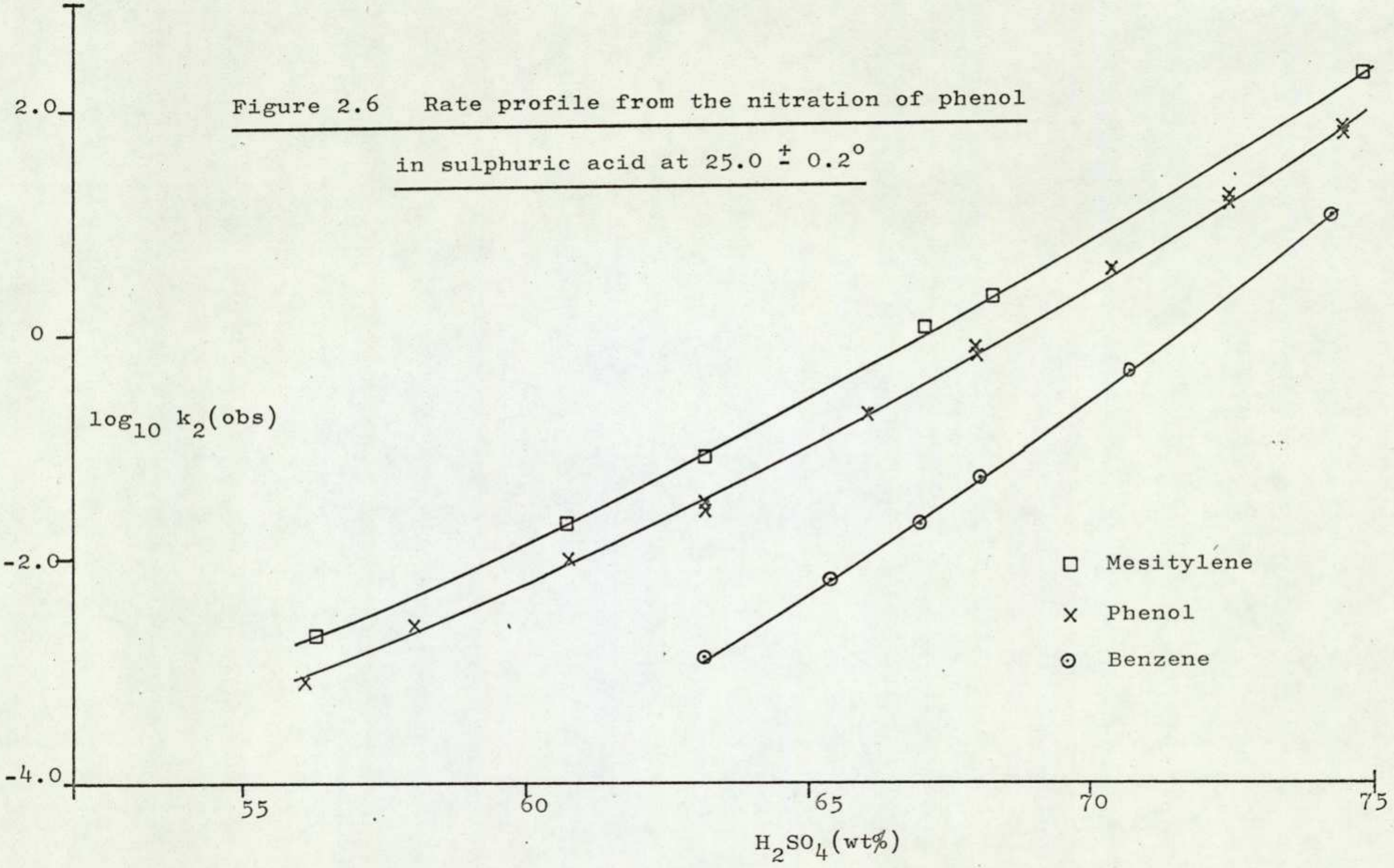
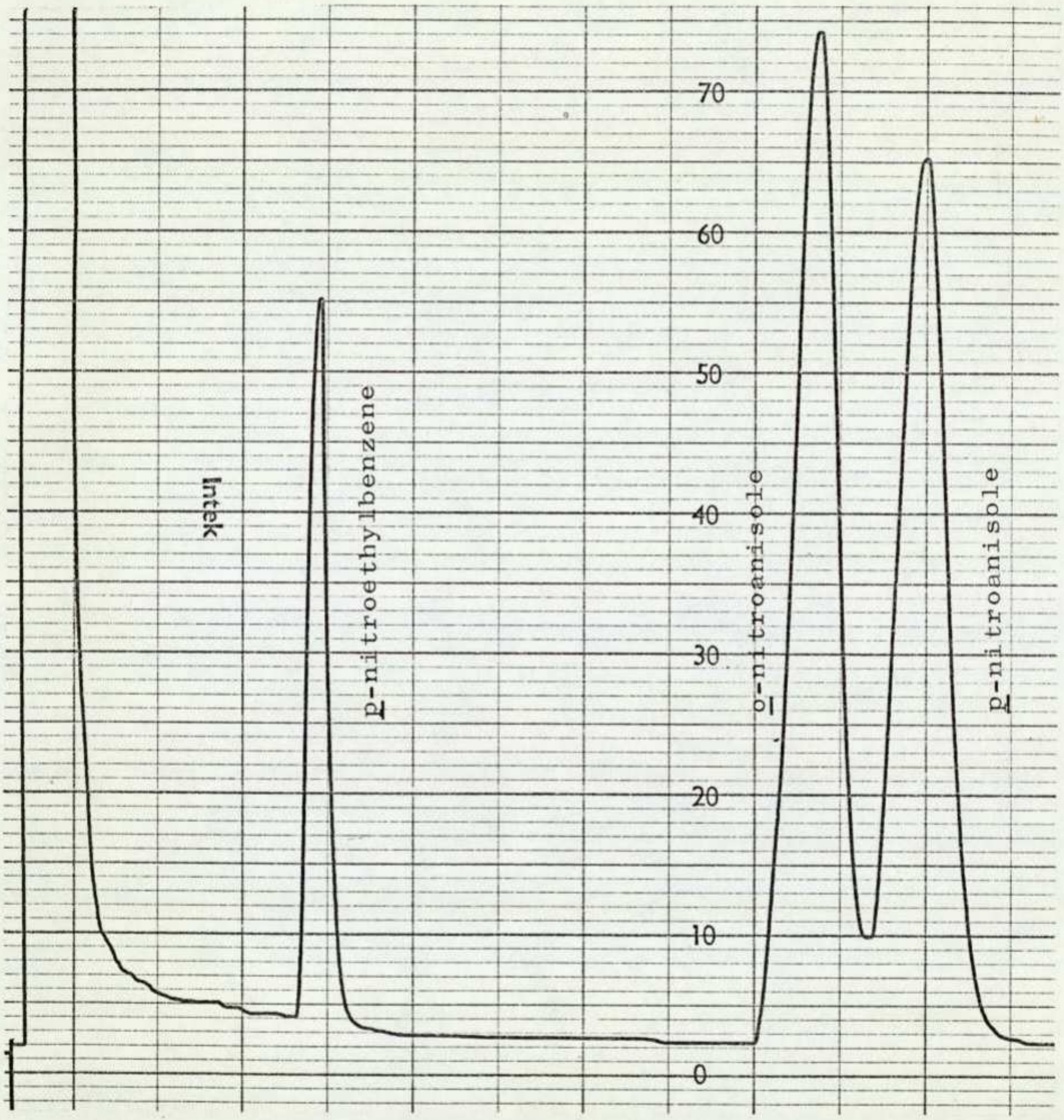


Figure 2.6 Rate profile from the nitration of phenol in sulphuric acid at 25.0 ± 0.2°

Figure 2.7. Chromatogram of the products from the nitration of anisole in 72.5% sulphuric acid



From Section 7.5 $\frac{c_x}{c_s} = \frac{(A_x)}{(A_s)} \times f$

Response factor f for o-nitroanisole = 1.50

Response factor f for p-nitroanisole = 1.60

Amount of o-nitroanisole = $\frac{1285}{440} \times 6.26 \times 10^{-6} \times 1.5$ moles

$= 2.74 \times 10^{-5}$ moles

Amount of p-nitroanisole = $\frac{1322}{440} \times 6.26 \times 10^{-6} \times 1.6$ moles

$= 3.00 \times 10^{-5}$ moles

$\therefore$ Yield of o-nitroanisole = 51.9%

and yield of p-nitroanisole = 47.4%

Table 2.10 and Fig. 2.8 give the yields of mono-nitro-compounds from the nitration of anisole in various concentration of aqueous sulphuric acid. m-Nitroanisole would have been detected in yields greater than 10^{-3}%. The yields of mono-nitroanisoles were not quantitative above 82% H_2SO_4.

o- and p- Nitroanisoles (6×10^{-5} mole dm^{-3}) were recovered quantitatively (99.2% and 100.8% respectively) by the normal extraction method, described in Section 7.41, from their solution in 89% sulphuric acid, which had been kept at 25.0° for 1 hour.

The possibility that dinitration was affecting the yield of mono-nitro-compounds in $>$ 82% sulphuric acid was investigated and the results are shown in Table 2.11. Significant amounts of dinitration were found to occur in $>$ 86% sulphuric acid. In calculating

Table 2.10

Yields of mono-nitro-compounds from the nitration of anisole[b,c] in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[a]	Yield of Products[d] (%)		Mass Balance (%)
	o-nitroanisole	*p*-nitroanisole	
54.2[e]	64.1	34.8	99
56.1[e]	63.1	36.0	99
58.1[e]	63.0	37.0	100
60.8[e]	61.7	38.7	99
63.2[e]	59.8	40.2	100
66.1[e]	58.8	41.2	100
68.3[e]	57.0	42.0	99
70.4[e]	56.0	43.0	99
72.5[e]	52.5	45.3	98
76.3[f]	48.9	50.5	99
79.5[f]	47.4	51.5	99
82.1[f]	40.5	58.3	99
84.7[f]	35.6	51.0	87
89.0[f]	29.0	49.0	78

a) ± 0.1%

b) [Sulphamic acid] *ca* 2 x 10^{-2} mole dm^{-3}

Table 2.10 (continued)

c) $[HNO_3] = 2 \times 10^{-4} - 5.5 \times 10^{-2}$ mole dm^{-3}

d) No m-nitroanisole was detected

e) $[ArH] = 1.45 \times 10^{-4}$ mole dm^{-3}

f) $[ArH] = [HNO_3] = 2.2 \times 10^{-4}$ mole dm^{-3}

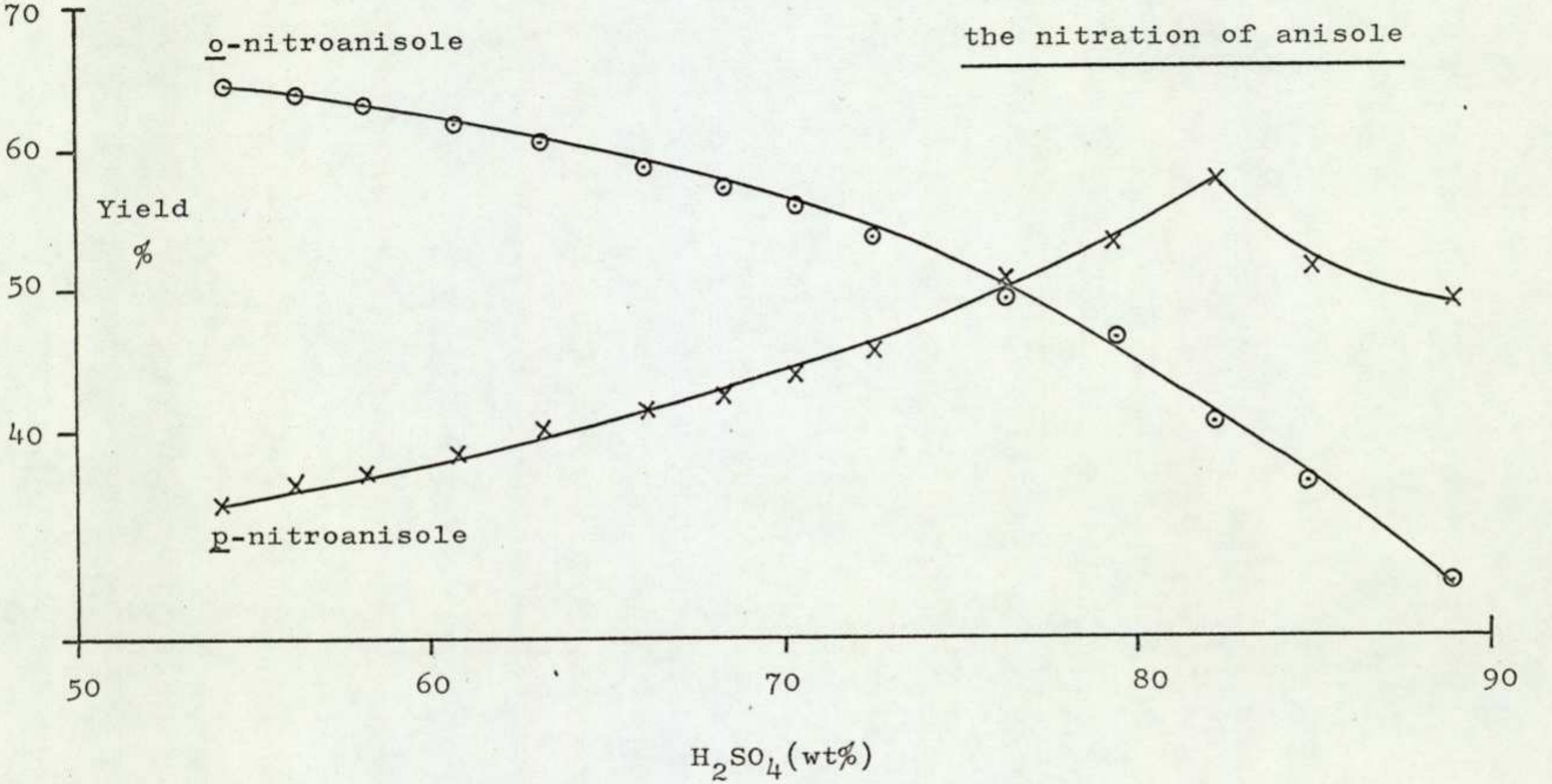


Figure 2.8 Yield of nitro compounds from the nitration of anisole

Table 2.11

Yields of nitro-compounds from the nitration of anisole[a,b] in 82% sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[c]	Yield of Products (%)				Mass Balance (%)
	o-nitro -anisole	p-nitro -anisole	2,4-Dinitro -anisole	2,6-Dinitro -anisole	
83.2	36.4	51.9	0.1	c	88
86.2	31.8	49.8	5.0	c	87
90.3	26.2	39.6	6.7	c	73
91.8	20.5	40.6	8.5	0.2	70
94.3	20.5	39.8	21.9	2.2	84

Table 2.11 (continued)

a) $[\text{ArH}] = [\text{HNO}_3] = 2.2 \times 10^{-4}$ mole dm^{-3}

b) $[\text{Sulphamic acid}]$ ca 2 x 10^{-2} mole dm^{-3}

c) 10^{-2}%

d) ± 0.1%

these yields allowance was made for the anisole which must be unchanged when dinitration occurs in equimolar reactions. 2,4- and 2,6-dinitroanisole were found to be extracted quantitatively from sulphuric acid solutions. Table 2.12 shows the recovery of 2,4- and 2,6-dinitroanisole from various concentrations of sulphuric acid.

2.322 PHENOL

2.3221 Method A (U.v. spectrophotometric method)

An example of the method of calculating the yield of nitro-products by the method of Dewar and Urch[13], from the nitration of phenol is given below.

Sulphuric acid 72.5%

$[\text{phenol}] = 1.71 \times 10^{-4}$ mole dm^{-3}

$[HNO_3] = 4.6 \times 10^{-4}$ mole dm^{-3}

$[\underline{\text{o}}\text{-nitrophenol}]\ (c_o) = 8.65 \times 10^{-5}$ mole dm^{-3}

$[\underline{\text{p}}\text{-nitrophenol}]\ (c_p) = 8.77 \times 10^{-5}$ mole dm^{-3}

Fig. 2.9 shows the absorption curve obtained from the nitration of phenol. Figs. 2.10, 2.11 and 2.12 show the absorption curves obtained for o-, p-nitroanisole and nitric acid solutions respectively. Table 2.13 shows the data obtained from the absorption curves, and Fig. 2.13 shows the plot of R/A_1 vs A_2/A_1.

Where (see Section 2.3221)

R = observed value of $\log_{10} I_o/I$ for the unknown mixture

A_1 = observed value of $\log_{10} I_o/I$ for o-nitrophenol

A_2 = observed value of $\log_{10} I_o/I$ for p-nitrophenol

The intercept = x_o/c_o and the slope = x_p/c_p

Table 2.12

Recovery of 2,4[a]- and 2,6[b]-dinitroanisole from sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[c]	Recovery of Compounds (%)	
	2,4-Dinitroanisole	2,6-Dinitroanisole
82.8	97	99
85.0[d]	99	-
85.0	97	-
87.8	99	100
91.3	90	98

a) $[ArH] = 1.51 \times 10^{-4}$ mole dm^{-3}

b) $[ArH] = 8.4 \times 10^{-5}$ mole dm^{-3}

c) ± 0.1%

d) Kept for 1 hour before extraction

Figure 2.9. Absorption curve from the nitration of phenol in 72.5% sulphuric acid

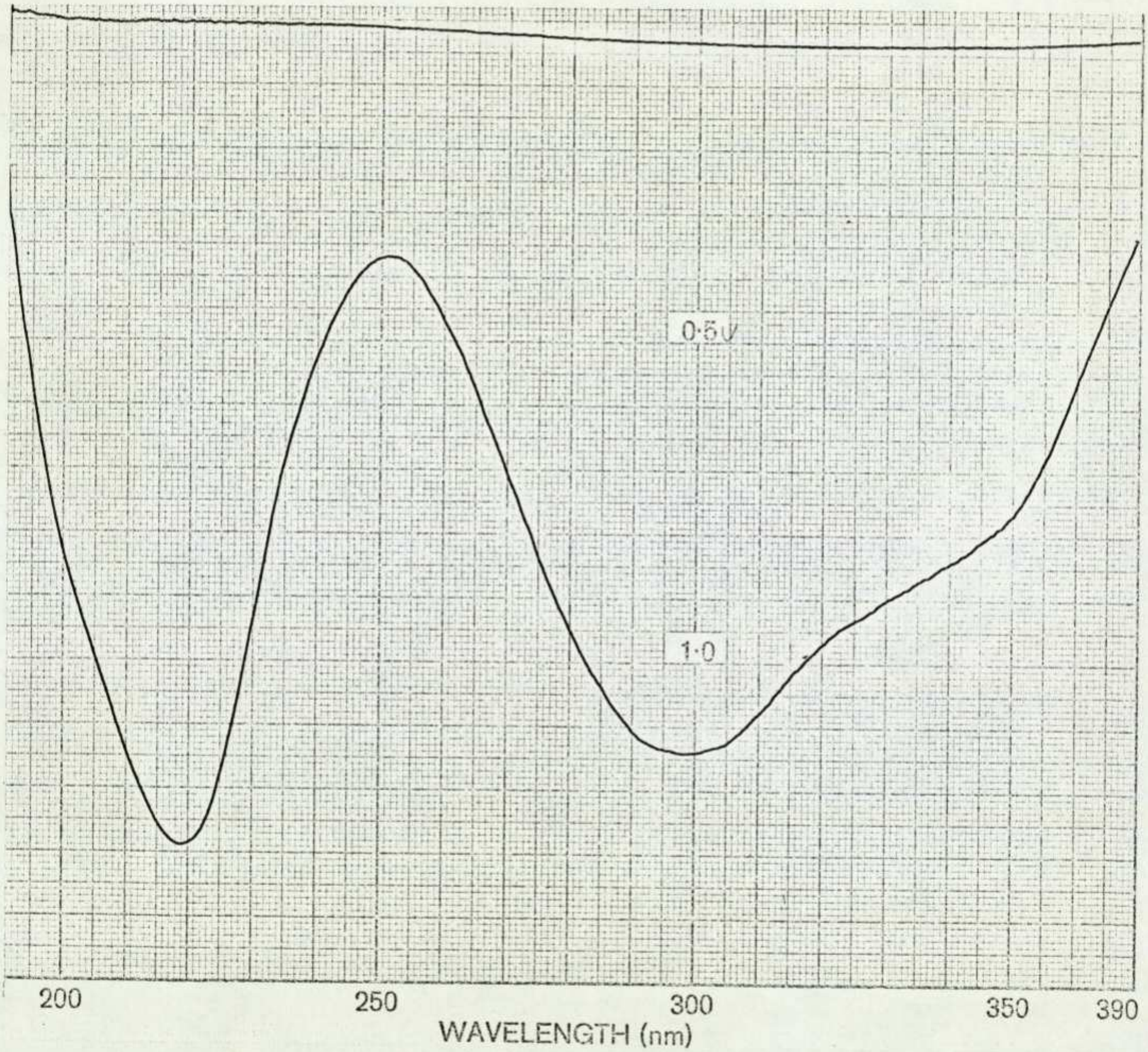


Figure 2.10. Absorption curve for

o-nitrophenol in 72.5% sulphuric acid

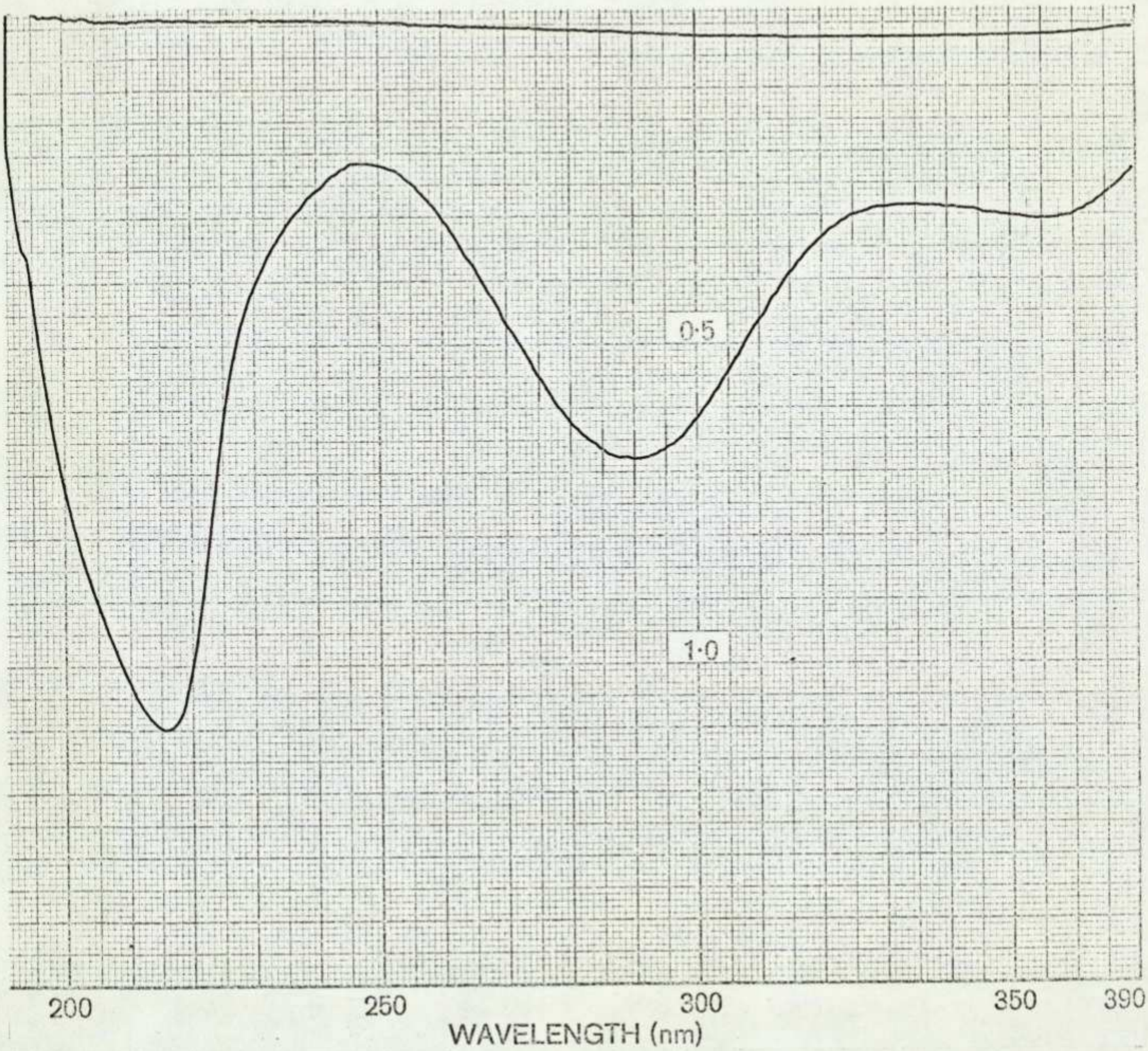


Figure 2.11. Absorption curve for p-nitrophenol in 72.5% sulphuric acid

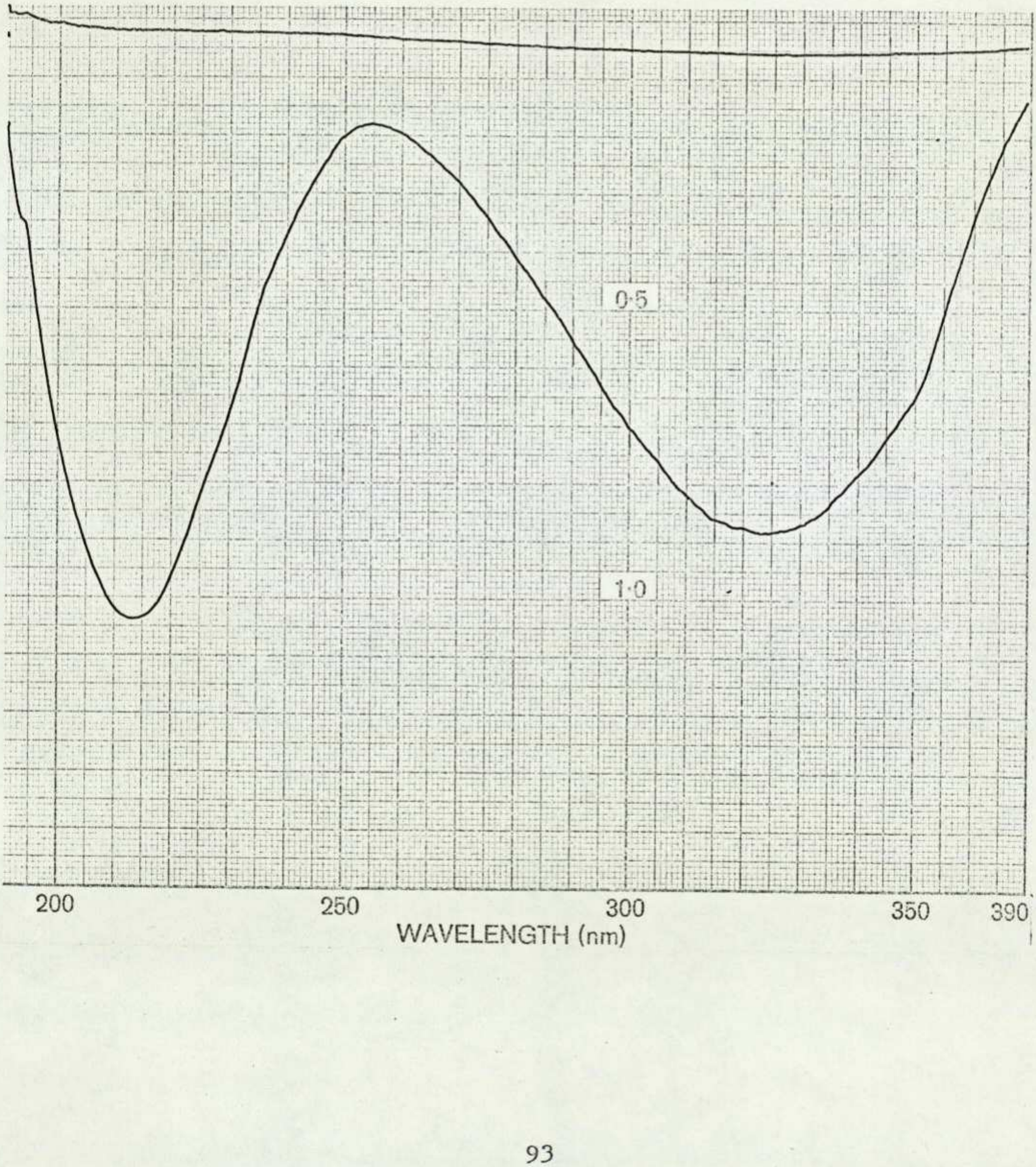


Figure 2.12. Absorption curve for nitric acid in 72.5% sulphuric acid

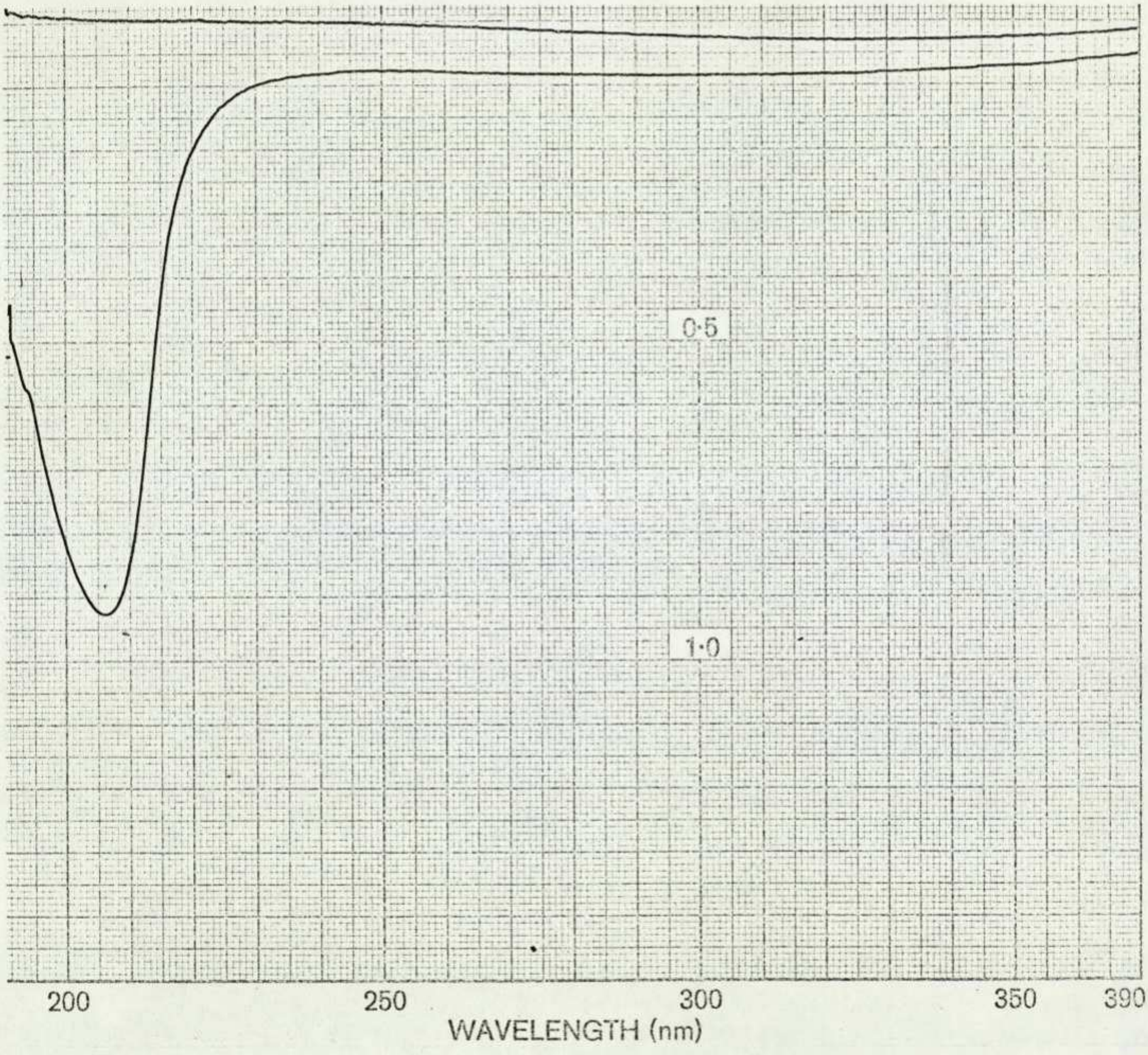


Table 2.13

Data from a typical Dewar and Urch calculation for the nitration of phenol in 72.5% sulphuric acid.

Wavelength (nm)	R	A_1	A_2	R/A_1	A_2/A_1
270	0.608	0.407	0.186	1.671	0.457
275	0.742	0.485	0.244	1.676	0.503
280	0.860	0.558	0.316	1.658	0.566
285	0.947	0.602	0.386	1.678	0.641
290	1.017	0.614	0.456	1.759	0.743
295	1.043	0.598	0.531	1.846	0.888
300	1.050	0.548	0.604	2.024	1.102
305	1.033	0.474	0.663	2.302	1.398
310	0.990	0.395	0.721	2.646	1.825
315	0.932	0.322	0.765	3.060	2.376
320	0.880	0.270	0.776	3.452	2.874
325	0.843	0.235	0.783	3.800	3.332
330	0.786	0.226	0.772	3.700	3.416
335	0.784	0.224	0.740	3.723	3.304
340	0.756	0.226	0.690	3.562	3.053
345	0.734	0.235	0.629	3.306	2.677
350	0.690	0.245	0.562	2.996	2.294
355	0.648	0.253	0.502	2.739	1.984

Table 2.13 (continued)

Wavelength (nm)	R	A_1	A_2	R/A_1	A_2/A_1
360	0.605	0.254	0.414	2.559	1.650
365	0.546	0.251	0.340	2.351	1.355
370	0.520	0.247	0.257	2.267	1.040
375	0.439	0.241	0.189	1.855	0.784
380	0.373	0.225	0.136	1.822	0.604

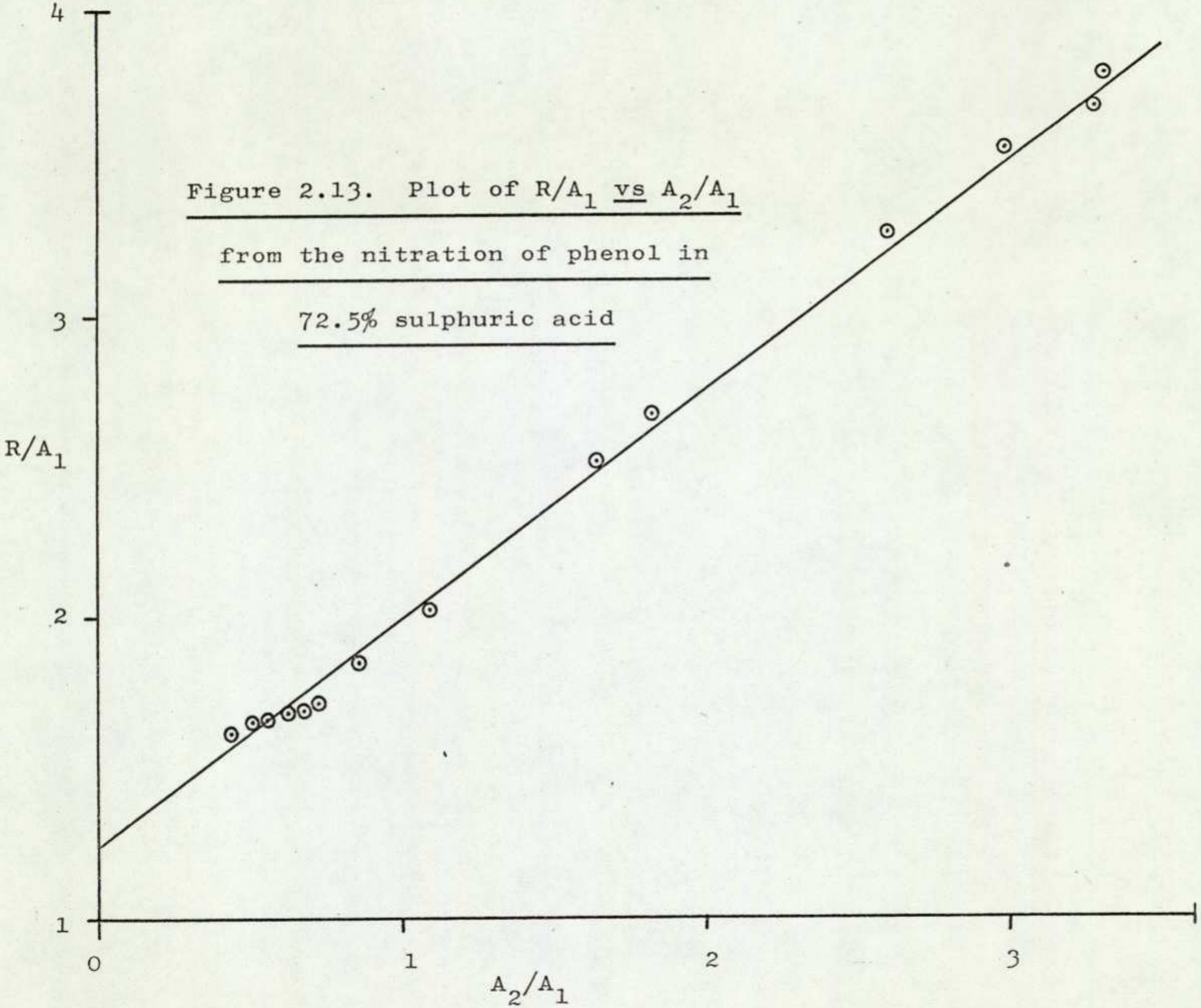


Figure 2.13. Plot of R/A_1 vs A_2/A_1 from the nitration of phenol in 72.5% sulphuric acid

$$
\begin{aligned}
\text{Where } x_o &= \left[\underline{o}\text{-nitrophenol}\right] \text{ in the unknown} \\
x_p &= \left[\underline{p}\text{-nitrophenol}\right] \text{ in the unknown} \\
c_o &= \left[\underline{o}\text{-nitrophenol}\right] \text{ in the standard} \\
c_p &= \left[\underline{p}\text{-nitrophenol}\right] \text{ in the standard}
\end{aligned}
$$

Intercept = 1.25

$\therefore \quad 1.25 \times 8.65 \times 10^{-5} = x_o$

$\therefore \quad \left[\underline{o}\text{-nitrophenol}\right] = 1.05 \times 10^{-4} \text{ mole dm}^{-3}$

Slope = 0.775

$\therefore \quad 0.775 \times 8.76 \times 10^{-5} = x_p$

$\therefore \quad \left[\underline{p}\text{-nitrophenol}\right] = 6.65 \times 10^{-5} \text{ mole dm}^{-3}$

$\therefore \quad$ total yield = 1.70×10^{-4} mole dm^{-3}

% o-nitrophenol = 61.2%

% p-nitrophenol = 58.8%

(Normalised to 100%)

Table 2.14 and Fig. 2.14 give the yield of nitro-compounds from the nitration of phenol in various concentrations of aqueous sulphuric acid.

2.3222 Method B. (High pressure liquid chromatography method).

An example of the calculation of the yields of nitro-compounds by this method from the nitration of phenol in sulphuric acid is given below.

Sulphuric acid	75.2%
Amount of phenol	9.66×10^{-5} moles
Amount of nitric acid	9.70×10^{-5} moles

Table 2.14

Yield of nitro-compounds from the nitration of phenol[f] in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[b]	Yield of Products (%)		Mass balance (%)
	o-nitrophenol	*p*-nitrophenol	
	(Method A)[a]		
56.1[c,e]	70.6	29.4	107.0
60.8[c,e]	66.2	33.8	95.6
62.5[c,e]	66.8	33.2	97.7
65.9[c,e]	65.0	35.0	94.2
68.0[c,e]	64.0	36.0	94.2
70.3[c,e]	64.2	35.8	98.3
72.5[c,e]	61.3	38.6	102.0
74.6[c,e]	59.7	40.3	98.5
76.6[d]	54.8	45.2	95.7
78.2[d]	52.0	48.0	98.7
79.8[d]	50.6	49.4	94.9
81.7[d]	48.9	51.2	102.1
83.3[d]	46.7	53.3	99.6
86.3[d]	39.0	61.0	89.9

Table 2.14 (continued)

H_2SO_4 (%)[b]	Yield of Products (%)		Mass balance (%)
	o-nitrophenol	p-nitrophenol	
	(Method B)		
66.6[e,g]	64.2	33.8	98.0
69.1[e,g]	61.7	36.3	98.0
71.2[h]	58.4	41.9	100.3
72.5[h]	59.7	38.6	98.3
75.2[h]	52.4	48.0	100.4
78.2[h]	52.7	46.8	99.5
80.8[h]	47.3	52.7	100.0
	(Method C)		
67.9[e,i]	63.2	-	-
75.2[j]	57.0	-	-
80.8[j]	49.1	-	-
82.8[j]	45.8	-	-

a) normalised to 100%

b) ± 0.1%

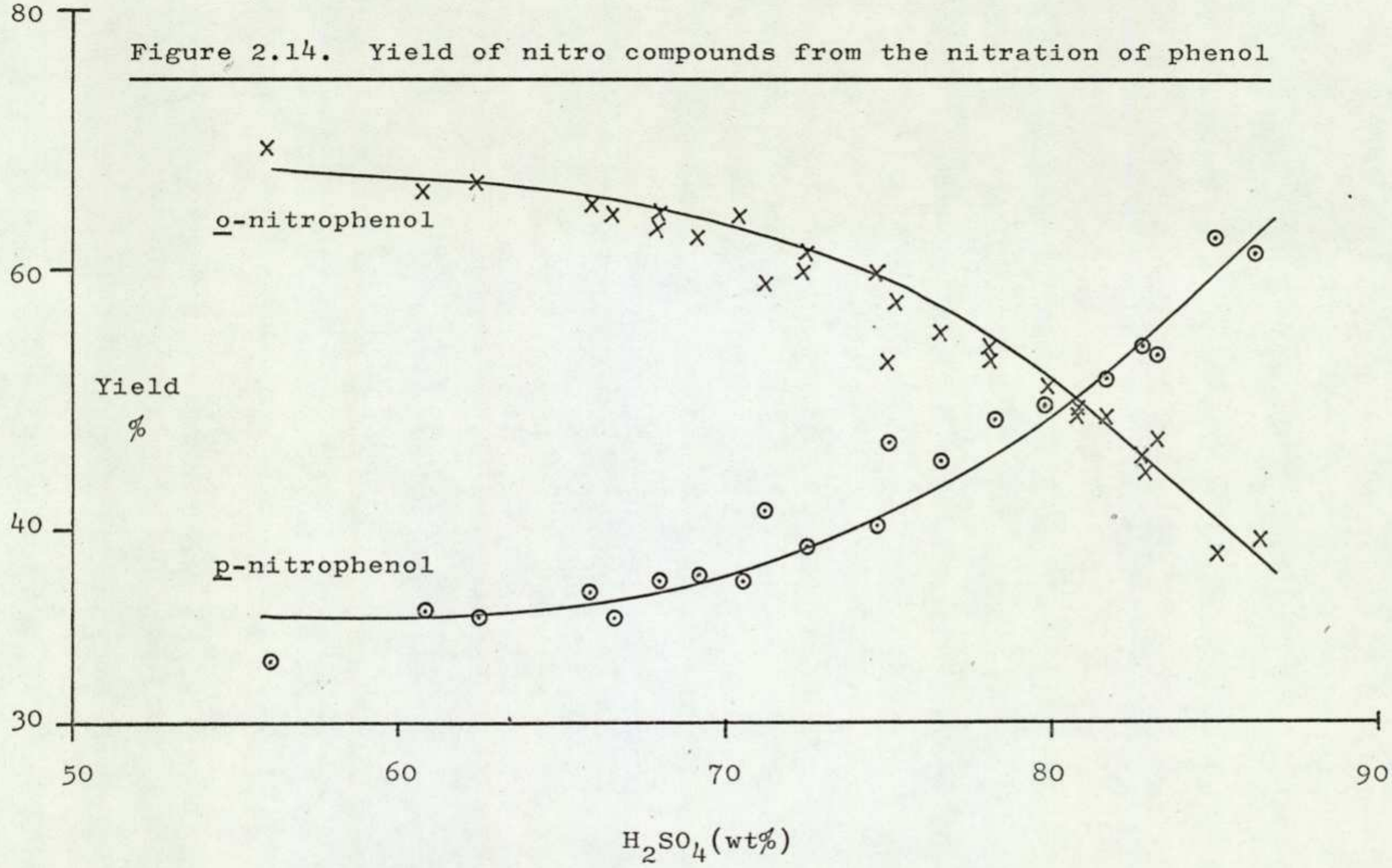
c) $[\mathrm{ArH}] = 1.67 \times 10^{-4}$ mole dm^{-3}

d) $[\mathrm{ArH}] = [\mathrm{HNO_3}] = 1.8 \times 10^{-4}$ mole dm^{-3}

Table 2.14 (continued)

e) $[HNO_3] = 2.0 \times 10^{-4} - 5.5 \times 10^{-2}$ mole dm^{-3}
f) Sulphamic acid 2×10^{-2} mole dm^{-3}
g) $[ArH] = 4.02 \times 10^{-3}$ mole dm^{-3}
h) $[ArH] = [HNO_3] = 3.70 \times 10^{-3}$ mole dm^{-3}
i) $[ArH] = 1.50 \times 10^{-4}$ mole dm^{-3}
j) $[ArH] = [HNO_3] = 2.2 \times 10^{-4}$ mole dm^{-3}

Figure 2.14. Yield of nitro compounds from the nitration of phenol



Amount of reference
standard 4-methyl-2-
nitrophenol 6.2×10^{-5} moles

Reaction carried out in 26.0cm^3 of sulphuric acid.

Fig. 2.15 shows the chromatogram obtained (H.p.l.c. condition as Section 2.3222).

Peak Areas from the chromatogram (Fig. 2.15)

Compound	Area/mm^2
o-nitrophenol	999
p-nitrophenol	816
4-methyl-2-nitrophenol	1170

The method of relative response factors as described in Section 7.5 for g.l.c. was used.

$$\frac{c_x}{c_s} = \left(\frac{A_x}{A_s}\right) \times f$$

Factor f for *o*-nitrophenol = 0.96

Factor f for *p*-nitrophenol = 1.07

∴ Amount of *o*-nitrophenol

$$= \frac{999}{1170} \times 6.20 \times 10^{-5} \times 0.96$$

$$= 5.08 \times 10^{-5} \text{ moles}$$

$$= \frac{5.08 \times 10^{-5}}{9.66 \times 10^{-5}} \times 100$$

= 52.4% *o*-nitrophenol

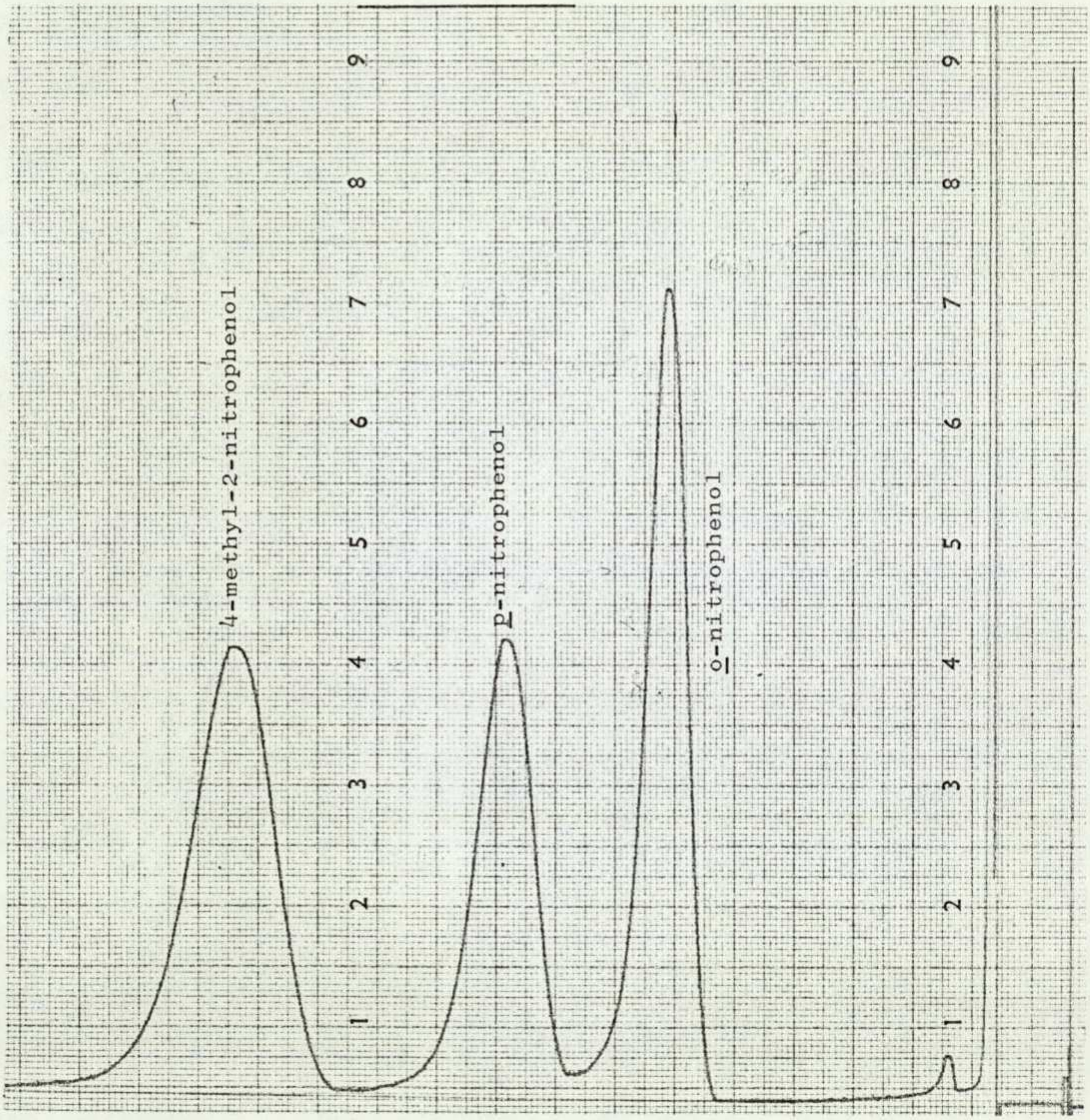
Amount of *p*-nitrophenol

$$= \frac{8.6}{1170} \times 6.20 \times 10^{-5} \times 1.07$$

$$= 4.62 \times 10^{-5} \text{ moles}$$

$$= \frac{4.62 \times 10^{-5}}{9.66 \times 10^{-5}} \times 100$$

Figure 2.15. Chromatogram of the products from the nitration of phenol in 75.2% sulphuric acid



= 47.9% p-nitrophenol

Table 2.14 and Fig. 2.14 give the yield of nitro-compounds from the nitration of phenol in various concentrations of sulphuric acid.

2.3223 Method C. (G.l.c. method for the estimation of o-nitrophenol).

An example of the calculation of the yield of o-nitrophenol from this method is given below.

Sulphuric acid	75.2%
Amount of phenol	5.68×10^{-5} moles
Amount of HNO_3	5.70×10^{-5} moles
Amount of reference standard 4-methyl-2-nitrophenol	3.38×10^{-5} moles

The reaction was carried out in 260cm^3 of sulphuric acid. Fig. 2.16 shows the chromatogram from which the peak areas were obtained:- o-nitrophenol, 806mm^2 and 4-methyl-2-nitrophenol, 929mm^2.

From Section 7.5

$$\frac{c_x}{c_s} = \left(\frac{A_x}{A_s}\right) \times f$$

Factor f for o-nitrophenol = 1.10

$$\therefore \text{Amount of o-nitrophenol} = \frac{806.}{929} \times 3.38 \times 10^{-5} \times 1.10$$

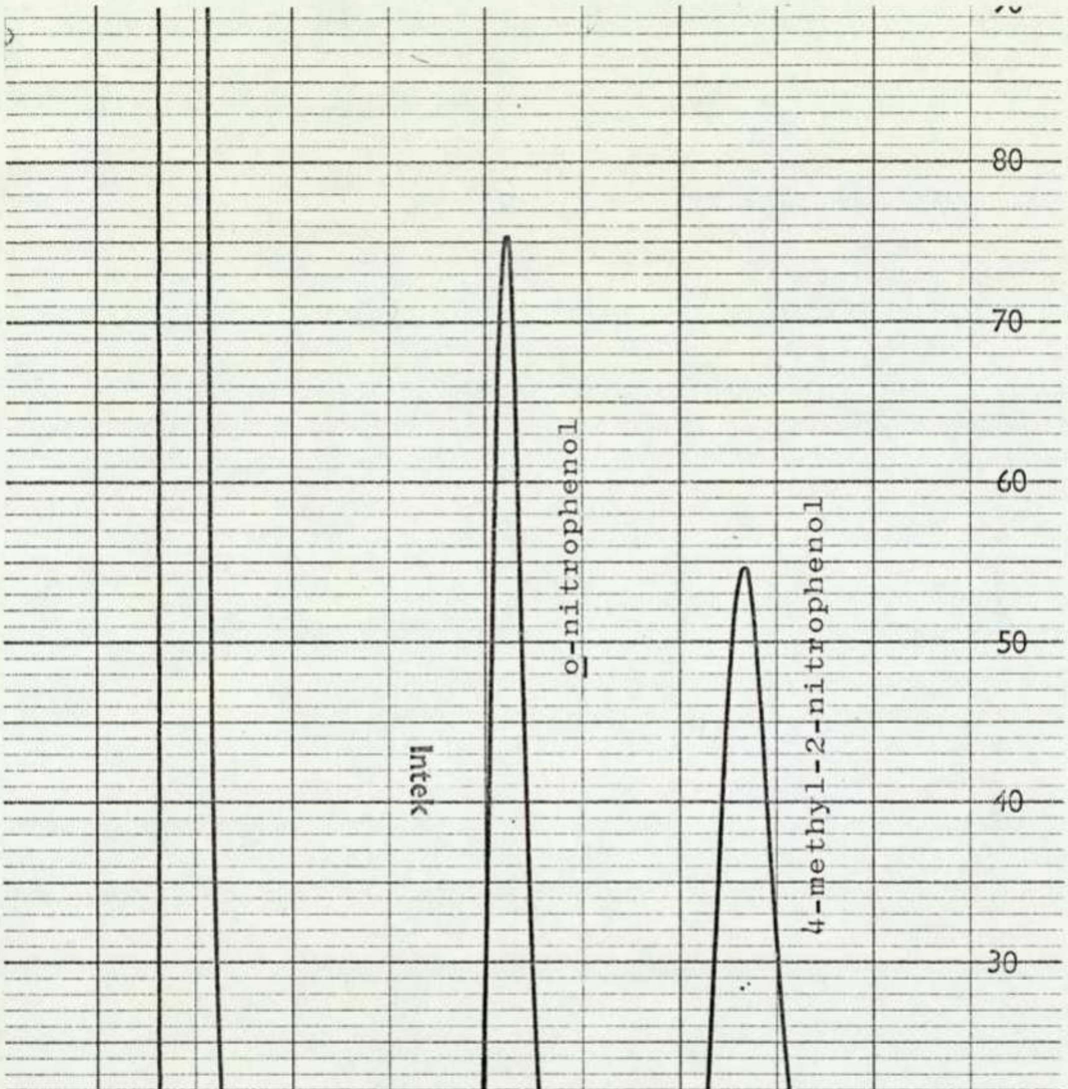
$$= 3.25 \times 10^{-5} \text{ moles}$$

$$= \frac{3.25 \times 10^{-5}}{5.68 \times 10^{-5}} \times 100$$

= 56.8% o-nitrophenol

Table 2.14 and Fig. 2.14 give the yield of nitro-

Figure 2.16. Chromatogram of the product from the nitration of phenol in 75.2% sulphuric acid



compounds from the nitration of phenol in various concentrations of sulphuric acid.

2.4 DISCUSSION

2.41 RATE PROFILES

Mesitylene is representative of a number of compounds more reactive than toluene, which give almost exactly the same rate profile,[22,95] which has been identified as the limiting rate of encounter of aromatic compound with the nitronium ion. The rate profiles for anisole and phenol, are almost identical, see Figs. 2.3 and 2.6. Both are parallel to, but slightly below, that for mesitylene. The observation of a rate profile which is parallel and close to that given by mesitylene may well be a better indication that the compound undergoes reaction at the limiting rate of encounter, than the observation of a certain specific rate. Substituent constants[87] suggest that anisole should be reactive enough to be nitrated at the encounter rate, phenol would be expected to be of similar reactivity. If anisole and phenol are hydrogen bonded in strongly acidic solution, presumably to the hydronium ion, this could reduce the rate of encounter (for electrostatic reasons[88]) and the intrinsic reactivity. Either or both of these effects could explain the apparent departure from maximum value of the limiting encounter rate.

2.42 ISOMER PROPORTIONS

In 54 - 82% sulphuric acid anisole is quantitatively mono-nitrated, but the <u>o</u>:<u>p</u>- ratio varies steadily from

1.84 to 0.71, being 1.0 at 76% sulphuric acid, see Table 2.10 and Fig. 2.8. In 56 - 83% sulphuric acid, phenol is quantitatively mono-nitrated, but the *o*:*p*-ratio varies steadily from 2.40 to 0.83, being 1.0 at 81% sulphuric acid, see Table 2.14 and Fig. 2.14.

From the results obtained it is clear that anisole and phenol behave in a qualitatively similar manner and it is reasonable to assume that these results have a common explanation. If, as it seems likely, the initial encounter involves a hydrogen bonded species ($A\ldots H_3O^+$, A = anisole or phenol, in Scheme 2.1) it is possible that the encounter pair[65a] (e.p.) so formed ($NO_2^+ . A\ldots H_3O^+$) can form the *ortho*-(W_o) or *para*-(W_p) Wheland intermediates, either directly or after loss of the hydronium ion. Since the latter process is likely to compete less effectively as the acidity increases, the marked change in isomer proportions may be from those characteristic of $NO_2^+ . A$ to those characteristic of $NO_2^+ . A\ldots H_3O^+$. In the latter case, *ortho*-substitution needing close approach of two positive charges, would be relatively disfavoured. It may be of importance that in solvents where hydrogen bonding is expected to be insignificant, a high (2.3) *o*:*p*- ratio is obtained.

$$\begin{tikzcd}
NO_2^+ + A\ldots H_3O^+ \arrow[r, shift left] & (NO_2^+ . A\ldots H_3O^+) \arrow[l, shift left] \arrow[r] \arrow[dr] \arrow[d, shift left] & W_o \arrow[r] & \textit{o}\text{-nitroanisole} \\
 & (NO_2^+ . A) \arrow[u, shift left] \arrow[r] \arrow[ur] & W_p \arrow[r] & \textit{p}\text{-nitroanisole} \\
 & + H_3O^+ & &
\end{tikzcd}$$

Scheme 2.1

Regarding the drop in yield observed for the nitration of anisole in $>$ 82% sulphuric acid under equimolar conditions, at these acidities the rate of nitration should obey a first-order law (zeroth-order in $[\text{ArH}]$)[28]. Thus the rate of nitration will be dependent on the rate of formation of the nitronium ion. Table 1.5 and Fig. 1.1 show the data obtained by Chapman and Strachan for the nitration of toluene in sulphuric acid. From these data (by extrapolation), the estimated rate of nitration in 89% sulphuric acid is:-

$$k_1 = 1.3 \times 10^2 \text{ s}^{-1}$$

$$\therefore \quad t_{\frac{1}{2}} = \frac{0.69}{1.3 \times 10^2} = 5.3 \times 10^{-3} \text{ s}$$

The measured first-order rate constant for the sulphonation of anisole[89] in 89% sulphuric acid is:-

$$k_1 = 1 \times 10^{-2} \text{ s}^{-1}$$

$$\therefore \quad t_{\frac{1}{2}} = \frac{0.69}{1 \times 10^{-2}} = 69 \text{ s}$$

From these data it can be seen that the estimated half-life for nitration is about 10^4 times smaller than the measured half-life of sulphonation in 89% sulphuric acid. Sulphonation does, however, prevent study of the rates of possible demethylation of anisole at the highest acidities, but it is unlikely that demethylation which is not seen in 82.0% sulphuric acid could become faster than the estimated rate of nitration ($t_{\frac{1}{2}} \sim 5 \times 10^{-3}$ s in 89% sulphuric acid). This deduction is supported by the fact that no nitrophenols were detected from the nitration of anisole in 92% sulphuric acid. Demethylation of the mononitro-compounds also does not occur, as quantitative extraction of o- and p-nitroanisoles was found to be possible from 89% sulphuric acid.

Product studies at high acidities, i.e. $>$ 72.5% sulphuric acid, were performed with equimolar proportions of reactants, to prevent problems due to dinitration. However, approximate calculations would indicate that at the highest acidities the rate of dinitration is so large that significant dinitration could occur during the mixing process. In 89% sulphuric acid the approximate rate constant for the nitrations of both ortho- and para-nitroanisoles is $k_2(\text{obs}) = 3 \times 10^4\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$.

$$\text{as } k_2(\text{obs}) = \frac{2.3 \times 0.3}{[\text{HNO}_3] \times t_{\frac{1}{2}}}$$

$$\therefore\ t_{\frac{1}{2}} = \frac{0.69}{3 \times 10^4 \times 2.4 \times 10^{-4}} \simeq 0.1\ \text{s}$$

As the data of Table 2.11 show, 2,4-dinitroanisole was formed when reactions were carried out in $>$ 83.2% sulphuric acid and also 2,6-dinitroanisole was formed in reactions carried out in $>$ 90.3% sulphuric acid. For anisole, however, dinitration is not the complete explanation for the drop in yield which occurs above 82.0% sulphuric acid, and 12 - 30% of the anisole remains unaccounted for.

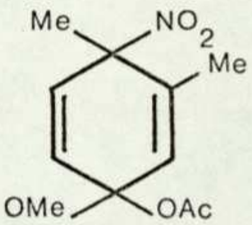
It is now clear that in addition to the problems caused by fortuitous nitrosation, the nitration of anisole and phenol by the nitronium ion is influenced greatly by medium effects which have been attributed in this thesis to the combined effects of hydrogen bonding and a diffusion controlled reaction. Such effects further complicate comparisons of nitration reactions in different media for these and perhaps other related substrates.

CHAPTER 3

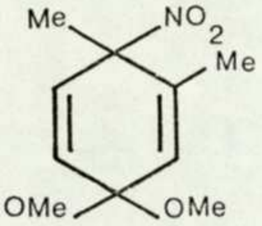
THE NITRATION OF p-METHYLANISOLE AND OF p-CRESOL

3.1 INTRODUCTION

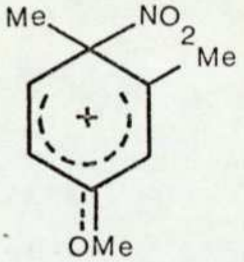
Shabarov and Mochalov[90] demonstrated that p-methylanisole undergoes demethylation during nitration by 55% HNO_3 in acetic anhydride at -10°, and 45% 4-methyl-2-nitrophenol was obtained. The authors concluded that the demethylation takes place simultaneously with attack on the aromatic nucleus. Fischer and Leonard[54] found that on nitration of 3,4-dimethylanisole with nitric acid in acetic anhydride at -78° the adducts (3.I) and (3.II) were obtained. It was suggested that (3.II) was formed when the phenonium ion (3.III) obtained on ionisation of (3.I) scavenges methanol. These compounds decomposed to give 3,4-dimethyl-4-nitrocyclohexa-2,5-dienone.



(3·I)

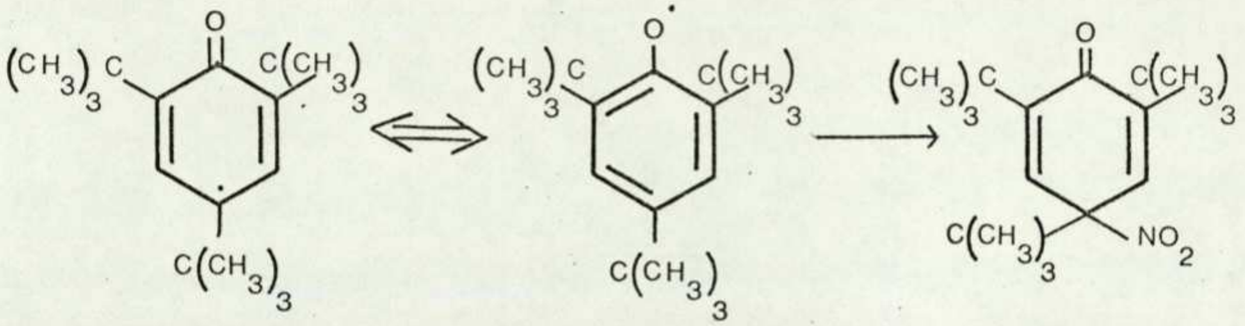


(3·II)



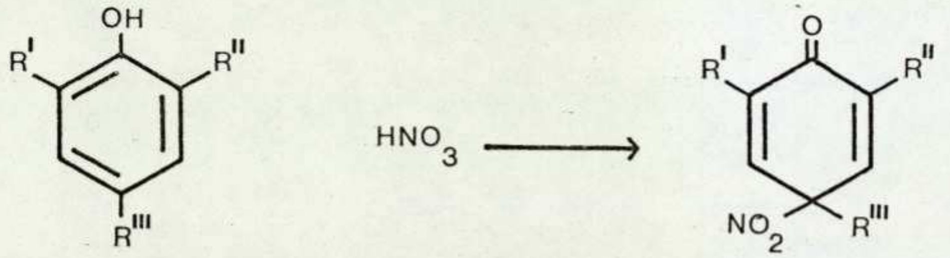
(3·III)

Cyclohexadienones are known as products of nitration of phenols where reactive positions are blocked by alkyl substituents. Cook and Woodworth[91] have shown that the reaction of 2,4,6-tri-t-butylphenoxyradical (3.V) with nitrogen dioxide leads to the formation of 2,4,6-tri-t-butyl-4-nitro-2,5-cyclohexadienone (3.VI).



(3·IV) (3·V) (3·VI)

Compound (3.VI) was found to have a u.v. absorption at 241nm (solvent cyclohexane). Ershov and Zlobina[92a] found that the nitration of 2,4,6-trialkylphenols in organic media gave the 'quinonitroles' (4-nitro-2,4,6-trialkylcyclohexa-2,5-dienones) (3.VIII). These compounds had u.v. absorptions in the range 233 - 240nm. The data of these workers are summarised in Table 3.1. A further claim[92b] to have observed cyclohexadienones in the nitration of 2,6-dialkylphenols is clearly erroneous. In many reactions dienones, although not actually isolated, are thought to be reaction intermediates[93,94]. Scheme 3.1 shows possible modes of decomposition of such intermediates.



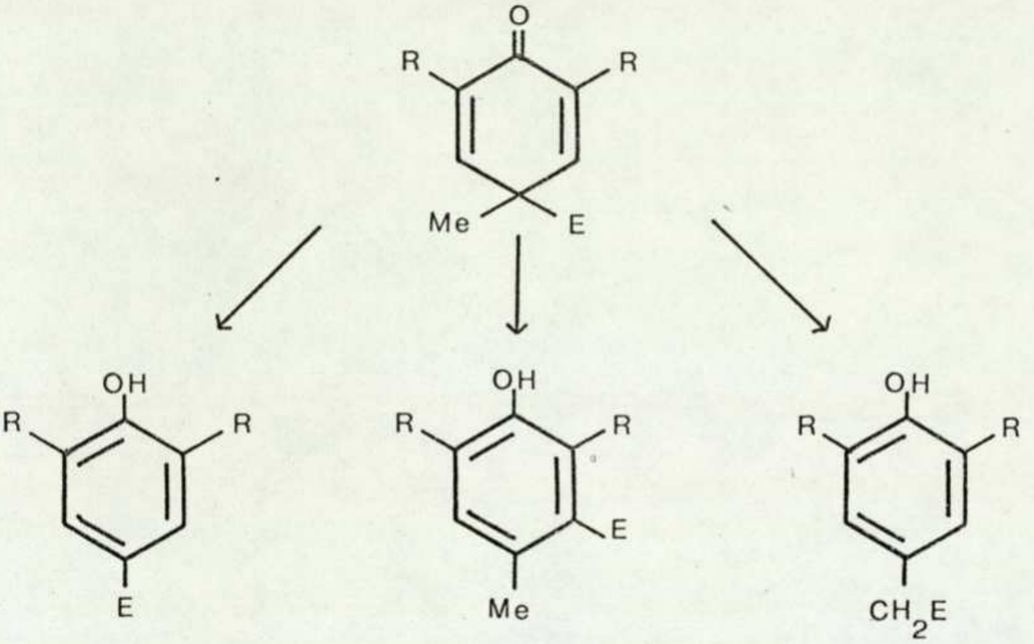
(3·VII) (3·VIII)

Table 3.1

The u.v. absorptions[92a] for a series of tri-substituted dienones [a]

R^1	R^{11}	R^{111}	λ_{max}/nm
$C(CH_3)_3$	$C(CH_3)_3$	$C(CH_3)_3$	239
$C(CH_3)_3$	$C(CH_3)_3$	CH_3	233
C_6H_{11}	C_6H_{11}	CH_3	240
CH_3	CH_3	CH_3	230
CH_3	$C(CH_3)_3$	CH_3	233
CH_3	$C(CH_3)_3$	$C(CH_3)_3$	238

a) n-Hexane was used as the solvent in all cases.



Scheme 3·1

Ipso-substitution at methoxy bearing carbon atoms is also known[95]. Dienone products were reported from the reaction of substituted trimethoxybenzenes with nitric acid/acetic anhydride mixtures. Reaction of 5-acetoxy-1,2,3-trimethoxybenzene with nitric acid in acetic anhydride at -70° yielded a mixture of 4-nitro-3,4,5-trimethoxycyclohexa-2,5-dienone and 2,6-dimethoxy--*p*-benzoquinone.

For both of the substrates dealt with in this chapter *ipso*-substitution at C - Me should be of importance.

3.2 EXPERIMENTAL

3.21 MATERIALS

These were as described in Section (7.2) with the addition of the following:- *p*-methylanisole (bp. 175-176°, lit[75] bp. 176-7°), *p*-cresol (bp. 200-202°, lit[96] bp. 202°), and 4-methyl-3-nitroanisole (bp. 152/20mm, lit[97] bp. 150/20mm) were commercial grade reagents purified by distillation. 4-Methyl-3-nitrophenol (mp. 78-79°, lit[98] mp. 77-77.4°) and 2-nitrophenol (mp. 44-45°, lit[80] mp. 44.27°) were commercial grade reagents purified by recrystallisation.

3.211 4-METHYL-2-NITROANISOLE

This was prepared by oxidising the corresponding amino-compound[99]. Trifluoroacetic anhydride ($8.5cm^3$) was added to 89% hydrogen peroxide ($1.4cm^3$) in dichloromethane ($25cm^3$) at 0°. After stirring for 5 min., 4-methyl-2-aminoanisole (1.7g. 0.012 moles) in dichloromethane ($15cm^3$) was added over 30 min. The mixture was boiled for 1h. The crude product was washed successively with 5M hydrochloric acid (three times), water and 10% sodium carbonate solution. After drying ($MgSO_4$) and solvent removal a brown solid resulted. This was extracted with diethyl ether and, after drying and solvent removal, 4-methyl-2-nitroanisole was obtained as a dark yellow oil.

^1H n.m.r. spectrum:-$\left[\tau \right.$ (CCL_4) 1.35 - 2.06 (3H,m, aromatic C - H), 5.03 (3H,s,OMe), 6.6 (3H,s,CH_3)$\left.\right]$. Calc. for $C_8H_9NO_3$: C,57.5; H, 5.4; N, 8.3%, Found C, 58.4; H, 5.5; N, 7.8%. The sample gave one peak on g.l.c. analysis, using the conditions given in Table 3.2(i).

3.212 4-METHYL-2-NITROPHENOL

70% Nitric acid ($10cm^3$) was added to a solution of p-methylanisole ($10cm^3$ 0.08 moles) in chloroform ($100cm^3$) and the mixture was shaken vigorously. After a few minutes the solution was washed with water, and after drying ($MgSO_4$) the chloroform was removed. The resultant oil exhibited three peaks on g.l.c. analysis (Table 3.2(i), corresponding to *p*-methylanisole, 4-methyl-2-nitroanisole (A) and a third component (B). The ratio of A to B was *ca* 0.7. *p*-Methylanisole was removed by vacuum distillation and the residue was dissolved in chloroform and passed down a 12in. column of alkaline alumina (Brockmann activity 2). An initial fraction was discarded. Chloroform was removed from the yellow middle fraction to yield a yellow crystalline solid (mp. 32.5 - 33.0°, lit[100] mp. 32.5°).

The ^1H n.m.r. spectrum :- [τ (CCL_4) - 0.5 (s, 1H, -OH), 2.0 - 3.0 (3H, m, aromatic C-H) and 7.7 (3H, s, $-CH_3$)]. Calc. for $C_7H_7NO_3$: C, 54.9; H, 4.6; N, 9.2%. Found: C, 54.8; H, 4.6: N, 9.1%.

A commercially available sample of 4-methyl-2-nitrophenol had similar physical properties.

3.213 2,4,6-TRIMETHYL-4-NITROCYCLOHEXA-2,5-DIENONE

This was prepared by the nitration of mesitol (2,4,6-trimethylphenol) in n-hexane[92]. 5cm^3 of nitric acid (s.g.1.5) was added with continuous stirring to a solution of 5g (0.037 moles) of mesitol in 50cm^3 of n-hexane. The excess of nitric acid was removed by washing with water. The hexane fraction was dried ($MgSO_4$) and the mixture was allowed to stand at -70°. The crystals which deposited were removed by filtration, (mp. 40 - 41°, lit[92] mp. 43 - 45°); λ_{max} (n-hexane)

236nm, lit[92] 230nm.

3.214 2,4,6-TRI-t-BUTYL-4-NITROCYCLOHEXA-2,5-DIENONE

This was prepared by the nitration of 2,4,6-tri-t-butylphenol in n-hexane[92]. 5cm^3 of nitric acid (s.g. 1.5) was added with continuous stirring to a solution of 5g (0.024 moles) 2,4,6-tri-t-butylphenol in 50cm^3 of n-hexane. The excess of nitric acid was removed by washing with water. The resultant hexane mixture was dried ($MgSO_4$) and the mixture was allowed to stand at -70°. The crystals which deposited were removed by filtration, (mp. 82 - 83°, lit[92] mp. 84.5°); λ_{max} (n-hexane) 244nm, lit[8] 239 - 241nm.

3.22 KINETIC MEASUREMENTS

For both p-methylanisole and p-cresol these were as described in Section 7.3.

3.23 PRODUCT ANALYSIS

3.231 p-METHYLANISOLE

The conventional g.l.c. method as described in Sections 7.41 and 7.42 was used. Tables 3.2(i) and (ii) give the g.l.c. procedures. The conditions given in Table 3.2(ii) were found to give the better separation of 4-methyl-2-nitrophenol and 4-methyl-2-nitroanisole.

3.232 p-CRESOL

The conventional g.l.c. method described in Sections 7.41 and 7.42 was used. Table 3.3 gives the details of the g.l.c. procedure, 4-methyl-3-nitrophenol was not eluted using these conditions. An h.p.l.c. method was used to separate 4-methyl-2-nitrophenol and

Table 3.2(i)

G.l.c. conditions for the separation of 4-methyl-2-nitrophenol, 4-methyl-3-nitroanisole and 4-methyl-2-nitroanisole

Column: 1.5m x $\frac{1}{4}$" S.S. $1\frac{1}{2}$% OV225 on universal support

Oven Temperature: 168 ± 0.5°

Carrier gas: Nitrogen

Flow rate: $90 cm^3 min^{-1}$

Compounds	Retention times /s
4-Methylanisole	24
4-Methyl-2-nitrophenol	58
4-Methyl-3-nitroanisole	68
4-Methyl-2-nitroanisole	138
4-Nitroveratrole (Reference standard)	480

Table 3.2(ii)

G.l.c. conditions for the separation of 4-methyl-2-nitrophenol, 4-methyl-3-nitroanisole and 4-methyl-2-nitroanisole

Column:	1m x ¼" S.S. 5% PEG.A on 1% H_3PO_4 washed Chromosorb W. 60 - 85 mesh
Oven Temperature:	154 ± 0.5°
Carrier gas:	Nitrogen
Flow rate:	40cm^3 min^{-1}

Compounds	Retention times /s
4-Methyl-2-nitrophenol	51
4-Methyl-2-nitroanisole	105
4-Methyl-3-nitroanisole	169
4-Nitroveratrole (Reference standard)	470

Table 3.3

G.l.c. conditions for the separation of 4-methyl-2-nitrophenol and 4-methyl-3-nitrophenol

Column:	1m x ¼" 5% PEG.A on 1% H_3PO_4 washed Chromosorb W
Oven Temperature:	115 ± 0.5°
Carrier Gas:	Nitrogen
Flow rate:	$60 cm^3 min^{-1}$

Compounds	Retention times /s
4-Methyl-2-nitrophenol	340
4-Methyl-3-nitrophenol[a]	-
2-Nitrophenol (Reference standard)	252

a) Retained on column

4-methyl-3-nitrophenol. The conditions are given in Table 3.4.

3.3 RESULTS

3.31 KINETICS

3.311 p-METHYLANISOLE

The results and subsequent calculations for a typical determination of a rate coefficient for the nitration of p-methylanisole are given below. Table 3.5

Sulphuric acid	68.3%
$[HNO_3]$	8.94×10^{-4} mole dm^{-3}
[p-Methylanisole]	9.35×10^{-5} mole dm^{-3}
[Sulphanilic acid]	1×10^{-2} mole dm^{-3}
Temperature	25.0 ± 0.2°
Measurement taken at	295 nm

shows the data obtained from the above nitration and Fig. 3.1 shows a plot of $\log_{10}(A_\infty - A_t)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[HNO_3]} \ \text{dm}^3 \ \text{mole}^{-1} \ \text{s}^{-1}$$

$$= \frac{2.303 \times 4.72 \times 10^{-4}}{8.94 \times 10^{-4}} \ \text{dm}^3 \ \text{mole}^{-1} \ \text{s}^{-1}$$

$$\therefore k_2(\text{obs}) = 1.22 \ \text{dm}^3 \ \text{mole}^{-1} \ \text{s}^{-1}$$

Second-order rate coefficients for the nitration of p-methylanisole, 4-methyl-2-nitroanisole and 4-methyl-3-nitroanisole in aqueous sulphuric acid are given in Table 3.6. A rate profile is shown in Fig. 3.2. Data for mesitylene and benzene are presented for comparison.

Table 3.4

H.p.l.c. conditions for the separation of 4-methyl-2-nitrophenol and 4-methyl-3-nitrophenol

Column:	1m x $\frac{1}{8}$" corosil II
Solvent:	10% ethylacetate, 90% cyclohexane
Flow Rate:	1.3cm^3 min^{-1}
Wavelength	280nm
Temperature:	ambient
Detector:	Cecil CE272 linear readout U.V. Spectrophotometer

Compound	Retention times /s
4-Methyl-2-nitrophenol	93
4-Methyl-3-nitrophenol	180

Table 3.5

Data from a typical determination of the rate of nitration of p-methylanisole in 68.3% sulphuric acid at 25.0 ± 0.2°

Time (t)/s	Absorbance at time t (A_t)	$(A_\infty - A_t)$	$\mathrm{Log}_{10}(A_\infty - A_t)$
20	0.100	0.470	-0.327
65	0.115	0.455	-0.342
110	0.130	0.440	-0.356
157	0.148	0.422	-0.374
235	0.173	0.397	-0.401
366	0.220	0.350	-0.455
480	0.260	0.310	-0.508
620	0.305	0.265	-0.576
785	0.350	0.220	-0.657
960	0.400	0.170	-0.469
1295	0.450	0.120	-0.920
1590	0.480	0.090	-1.045
1920	0.510	0.060	-1.221
	0.570(A_∞)		

Figure 3.1. Plot of $\log_{10}(A_{\infty} - A_t)$ vs time from the nitration of p-methylanisole in 68.3% sulphuric acid

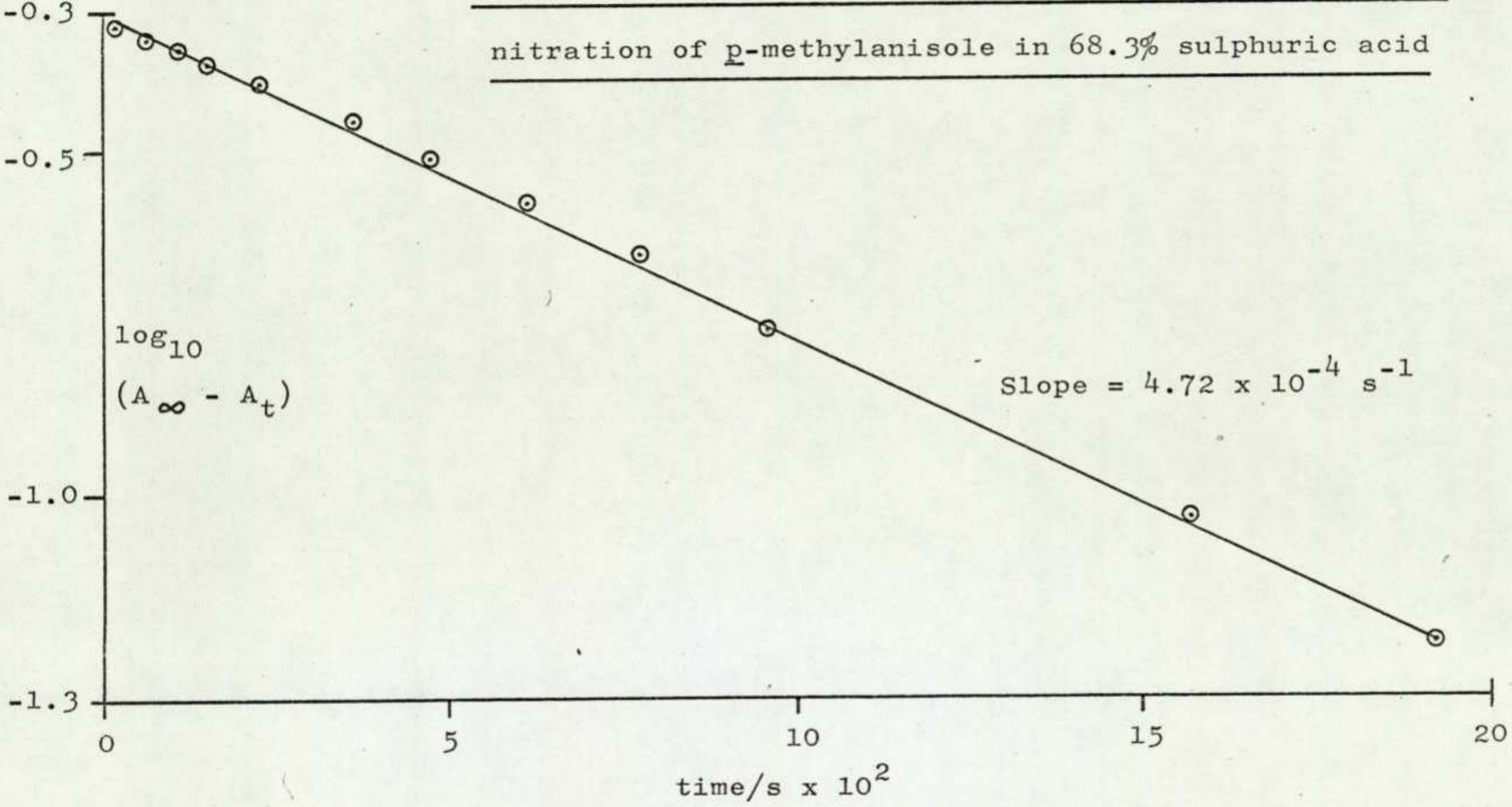


Table 3.6

Second-order rate coefficients for nitration in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[a]	$[HNO_3]/10^{-2}$ mole dm^{-3}	$k_2(obs)/dm^3$ $mole^{-1}$ s^{-1}
	p-Methylanisole[b,c]	
60.8[d]	5.5	6.7×10^{-3}
60.8[d]	5.5	6.8×10^{-3}
64.6[d]	0.33	9.8×10^{-2}
64.6[d]	0.33	9.9×10^{-2}
67.6[d]	0.089	8.9×10^{-1}
67.6[d]	0.089	9.1×10^{-1}
67.6[d]	0.089	9.0×10^{-1}
68.3[d]	0.089	1.22
68.3[d]	0.089	1.18
70.4[e]	0.089	4.81
70.4[e]	0.089	4.84
72.6[e]	0.047	20.91
72.6[e]	0.047	20.84
72.6[e]	0.047	21.13
	4-Methyl-2-nitroanisole[b,d,f]	
74.4	0.089	1.00
75.3	0.089	1.77

Table 3.6 (continued)

H_2SO_4 (%)[a]	$[HNO_3]/10^{-2}$ mole dm^{-3}	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}
	4-Methyl-3-nitroanisole[b,d]	
74.4	5.5	4.2×10^{-3}

a) ± 0.1%

b) [Sulphanilic acid] ca 1×10^{-2} mole dm^{-3}

c) Measurement at 295 or 300nm

d) [Substrate] = 1×10^{-4} mole dm^{-3}

e) [Substrate] = 3×10^{-5} mole dm^{-3}

f) Measurement at 260 nm

g) Measurement at 285 nm

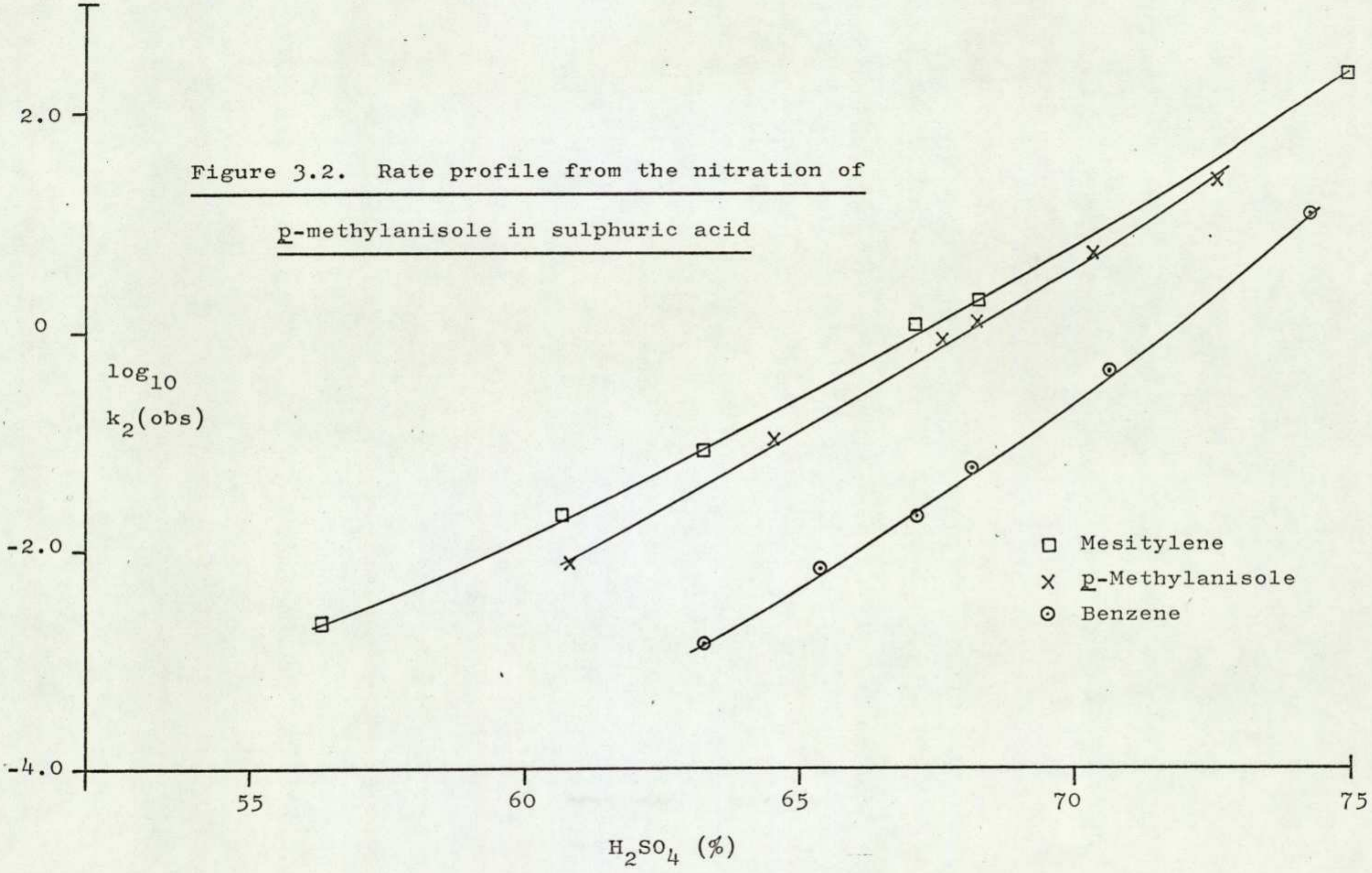


Figure 3.2. Rate profile from the nitration of p-methylanisole in sulphuric acid

3.312 p-CRESOL

The results and subsequent calculations for a typical determination of a rate coefficient for the nitration of p-cresol are given below. Fig. 3.3 shows the absorption curve, Table 3.7 the data obtained therefrom and Fig. 3.4 the plot of $\log_{10}(A_{\infty} - A_t)$ vs t.

Sulphuric acid	70.4%
$[HNO_3]$	8.94×10^{-4} mole dm^{-3}
[p-Cresol]	1.0×10^{-4} mole dm^{-3}
[Sulphamic acid]	2×10^{-2} mole dm^{-3}
Temperature	$25.0 \pm 0.2^{\circ}$

Measurement taken at 288 nm

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[HNO_3]} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$= \frac{2.303 \times 1.69 \times 10^{-3}}{8.94 \times 10^{-4}} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$\therefore k_2(\text{obs}) = 4.36 \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients for the nitration of p-cresol determined over a range of percentages of sulphuric acid are given in Table 3.8 together with similar data for 4-methyl-2-nitrophenol. A rate profile is shown in Fig. 3.5; data for mesitylene and benzene are also shown for comparison.

3.313 RATE OF DECOMPOSITION OF THE INTERMEDIATE FORMED DURING THE NITRATION OF p-CRESOL

When carrying out the studies of the reaction kinetics for the nitration of p-cresol, it was observed that between 230 - 255nm an absorption occurred initially and then disappeared slowly, (see Fig. 3.3). By increasing

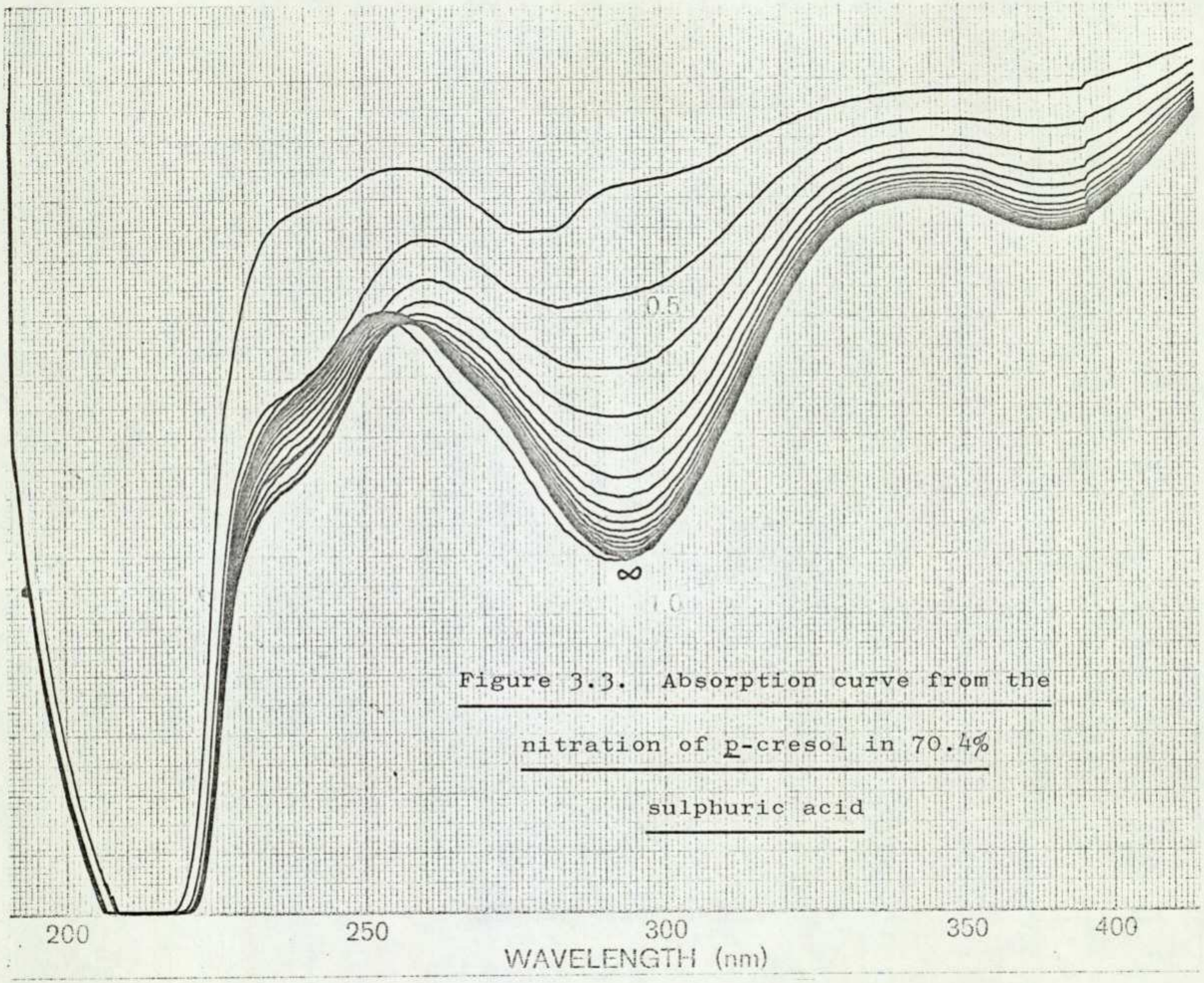


Figure 3.3. Absorption curve from the nitration of p-cresol in 70.4% sulphuric acid

Table 3.7

Data from a typical determination of the rate of nitration of p-cresol in 70.4% sulphuric acid

Time /s	Absorbance at time t (A_t)	($A_\infty - A_t$)	$\log_{10}(A_\infty - A_t)$
12	0.290	0.620	-0.207
86	0.470	0.440	-0.356
159	0.585	0.325	-0.488
232	0.665	0.245	-0.610
304	0.720	0.190	-0.721
377	0.765	0.145	-0.838
450	0.800	0.110	-0.958
523	0.820	0.090	-1.045
599	0.840	0.070	-1.154
669	0.855	0.055	-1.259
742	0.865	0.0455	-1.346
	0.91 (A_∞)		

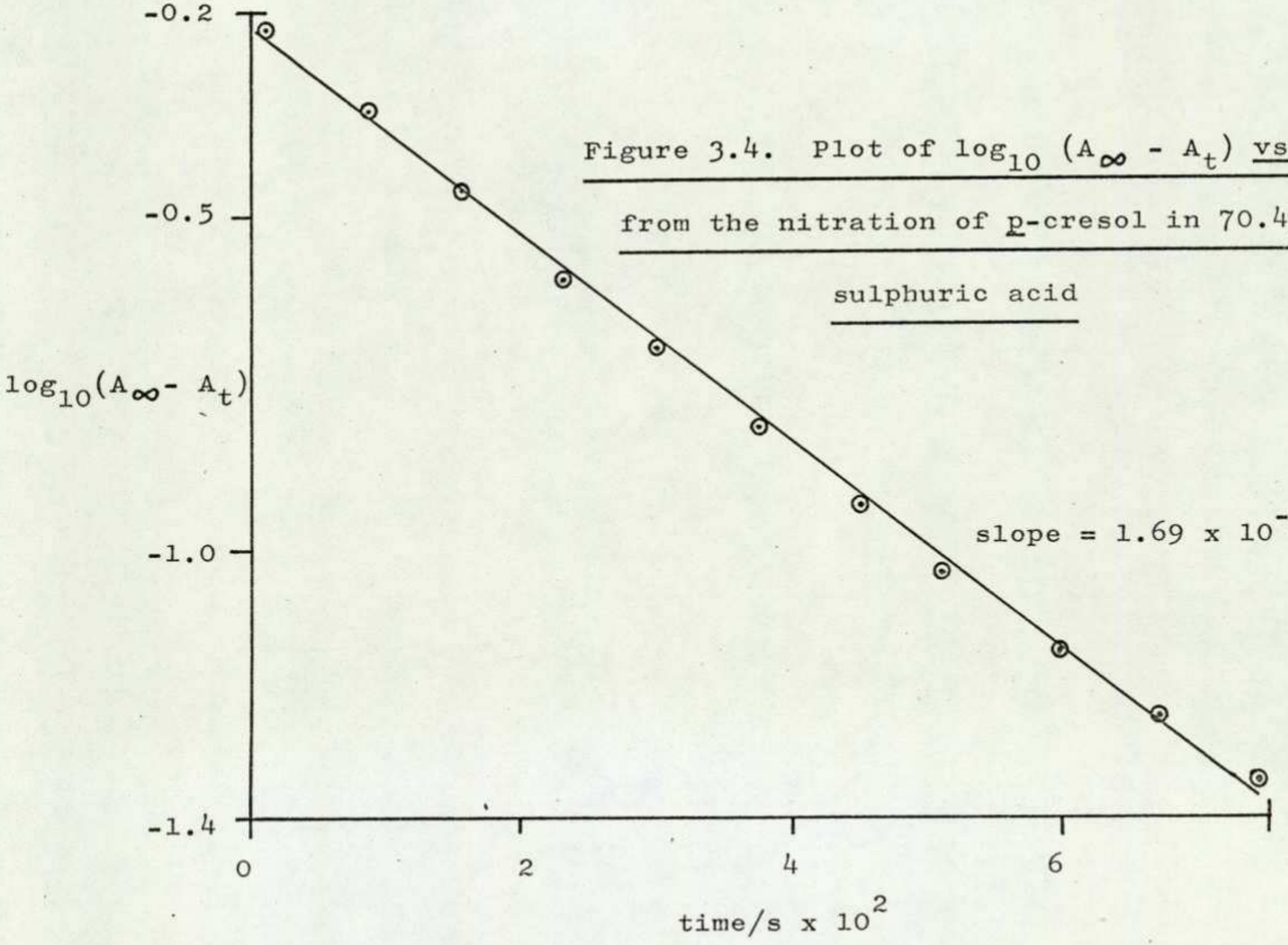


Figure 3.4. Plot of $\log_{10}(A_{\infty} - A_t)$ vs time from the nitration of p-cresol in 70.4% sulphuric acid

Table 3.8

Second-order rate coefficients for nitration in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[d]	$[HNO_3]/10^{-2}$ mole dm^{-3}	$k_2(obs)/dm^3$ $mole^{-1}$ s^{-1}
	p-Cresol[a,b,c,g]	
56.1	5.5	2.14×10^{-3}
56.1	5.5	2.14×10^{-3}
58.1	5.5	3.65×10^{-3}
58.1	5.5	3.62×10^{-3}
60.8	5.5	1.25×10^{-2}
60.8	5.5	1.30×10^{-2}
63.2	2.33	5.26×10^{-2}
63.2	1.19	5.71×10^{-2}
66.1	0.38	2.94×10^{-1}
66.1	0.38	3.09×10^{-1}
68.0	0.172	9.10×10^{-1}
68.0	0.172	8.69×10^{-1}
70.4	0.089	4.40
70.4	0.089	4.36
70.4	0.089	4.08
72.6	0.089	18.9

Table 3.8 (continued)

H_2SO_4 (%)[d]	$[HNO_3]/10^{-2}$ mole dm^{-3}	k_2(obs)/dm^3 mole^{-1} s^{-1}
	p-Cresol[a,b,c,g]	
72.6	0.089	20.0
	4-Methyl-2-nitrophenol[a,e,f]	
71.2	2.8	2.2×10^{-2}

a) [Sulphamic acid] *ca* 2×10^{-2} mole dm^{-3}

b) Measurement at 286nm

c) [ArH] = $1 \times 11 \times 10^{-4}$ mole dm^{-3}

d) ± 0.1%

e) [ArH] = 9.0×10^{-5} mole dm^{-3}

f) Measurement at 286nm

g) Isosbestic point at 258nm

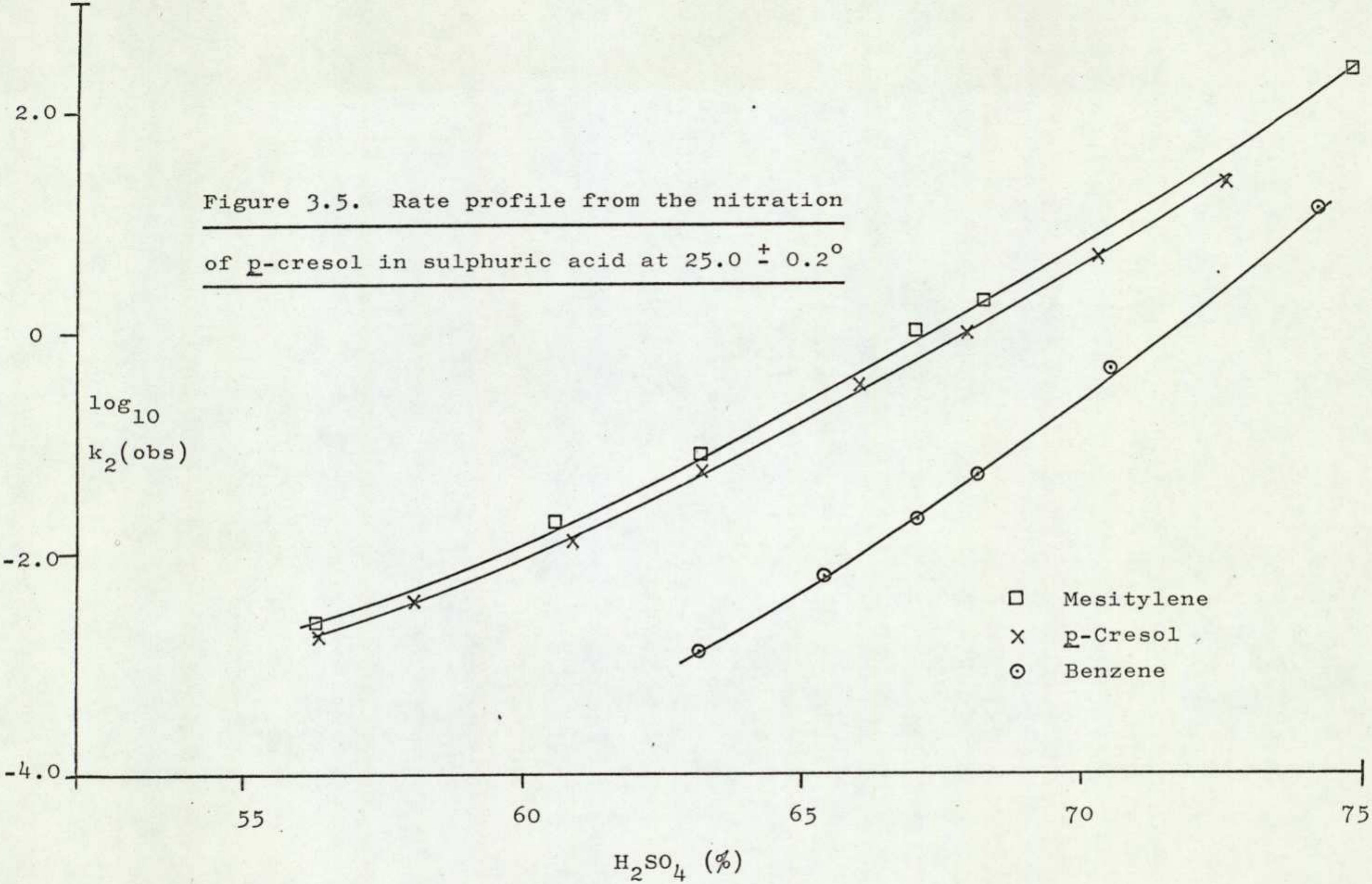


Figure 3.5. Rate profile from the nitration of p-cresol in sulphuric acid at 25.0 ± 0.2°

the concentration of nitric acid in the reaction mixture at a particular acidity it was possible to obtain the maximum absorbance after approximately 120s. This corresponds to about 7 half-lives for the reaction of which the rate was measured in Section 3.312.

The results and subsequent calculations for a typical determination of the rate of disappearance of the intermediate formed under these conditions are given below. Table 3.9 shows the data obtained from the above nitration, Fig. 3.6 shows the absorption curve and Fig. 3.7 shows the plot of $\log_{10}(A_{\infty} - A_t)$ vs t. It was necessary to calculate the infinity value for these reactions, because it was not possible to obtain a stable infinity reading due to problems caused by dinitration.

Sulphuric acid	71.2%
[p-Cresol]	1.233×10^{-3} mole dm^{-3}
[Sulphamic acid]	2×10^{-2} mole dm^{-3}
Temperature	$25.0 \pm 0.2^{\circ}$
Measurement taken at	380nm
1mm cell used	
[HNO_3]	1.18×10^{-2} mole dm^{-3}

Calculation of A_{∞}^{380} :- At 330nm (isosbestic point for dinitration see Fig. 3.6) $A_{\infty}^{330} = 0.265$. For a solution of 4-methyl-2-nitrophenol of quite similar concentration (3.21×10^{-5} mole dm^{-3}) (see Fig. 3.8), $A_{\max}^{380} = 0.35$ and $A^{330} = 0.27$. $\therefore A_{\infty}^{380} = \dfrac{0.265}{0.27} \times 0.35$ $= 0.34$ for the kinetic experiment, on the assumption that

Table 3.9

Data from a typical determination of the decomposition of the intermediate formed in the nitration of p-cresol in 71.2% sulphuric acid at 25.0 ± 0.2°

Time (t) /s	Absorbance at time t(A_t^{380})	($A_\infty - A_t$)	$\log_{10}(A_\infty - A_t)$
80	0.240	0.100	-1.00
175	0.270	0.070	-1.15
261	0.290	0.050	-1.30
348	0.302	0.038	-1.42
440	0.314	0.026	-1.58
∞ (calc)	0.340		

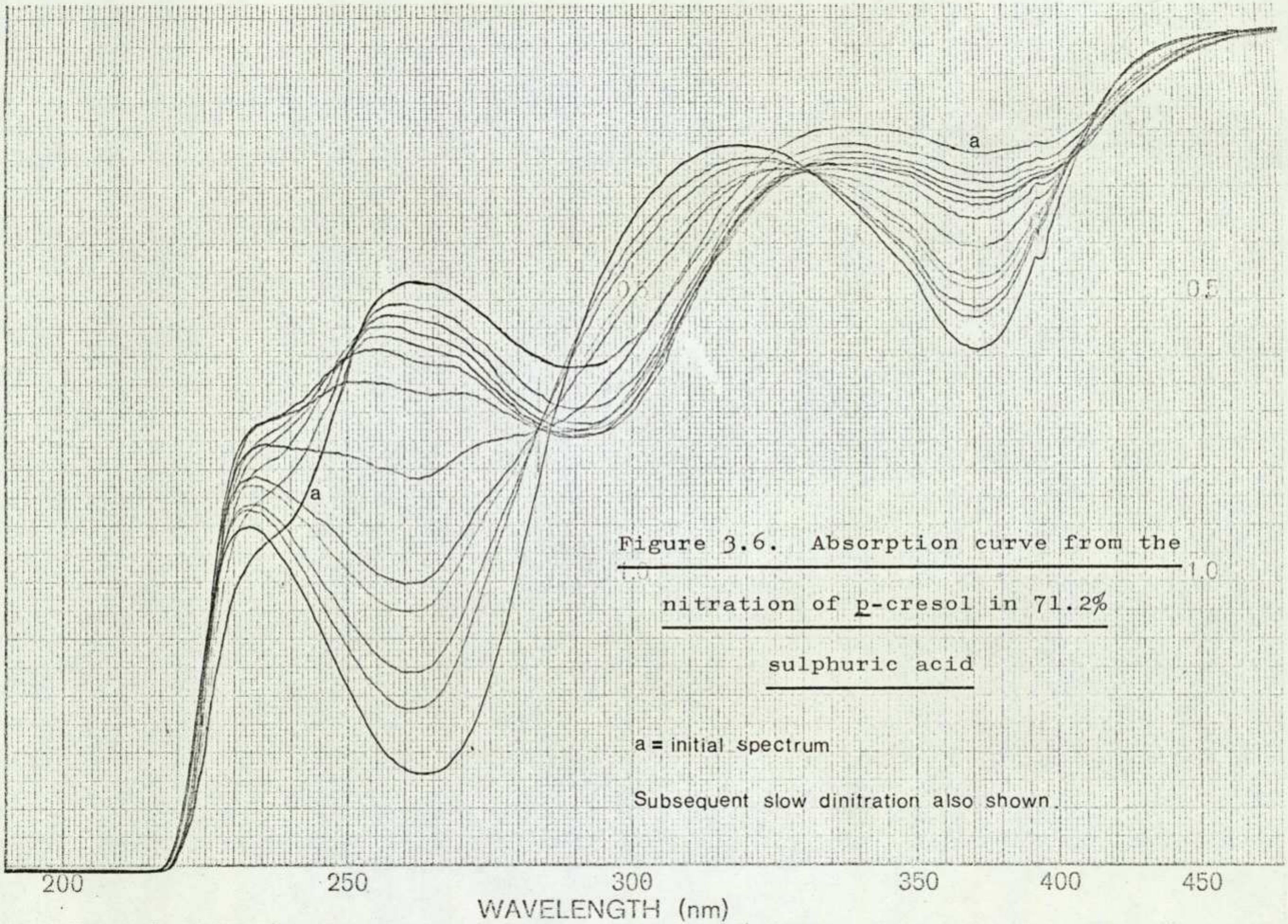


Figure 3.6. Absorption curve from the nitration of p-cresol in 71.2% sulphuric acid

a = initial spectrum

Subsequent slow dinitration also shown.

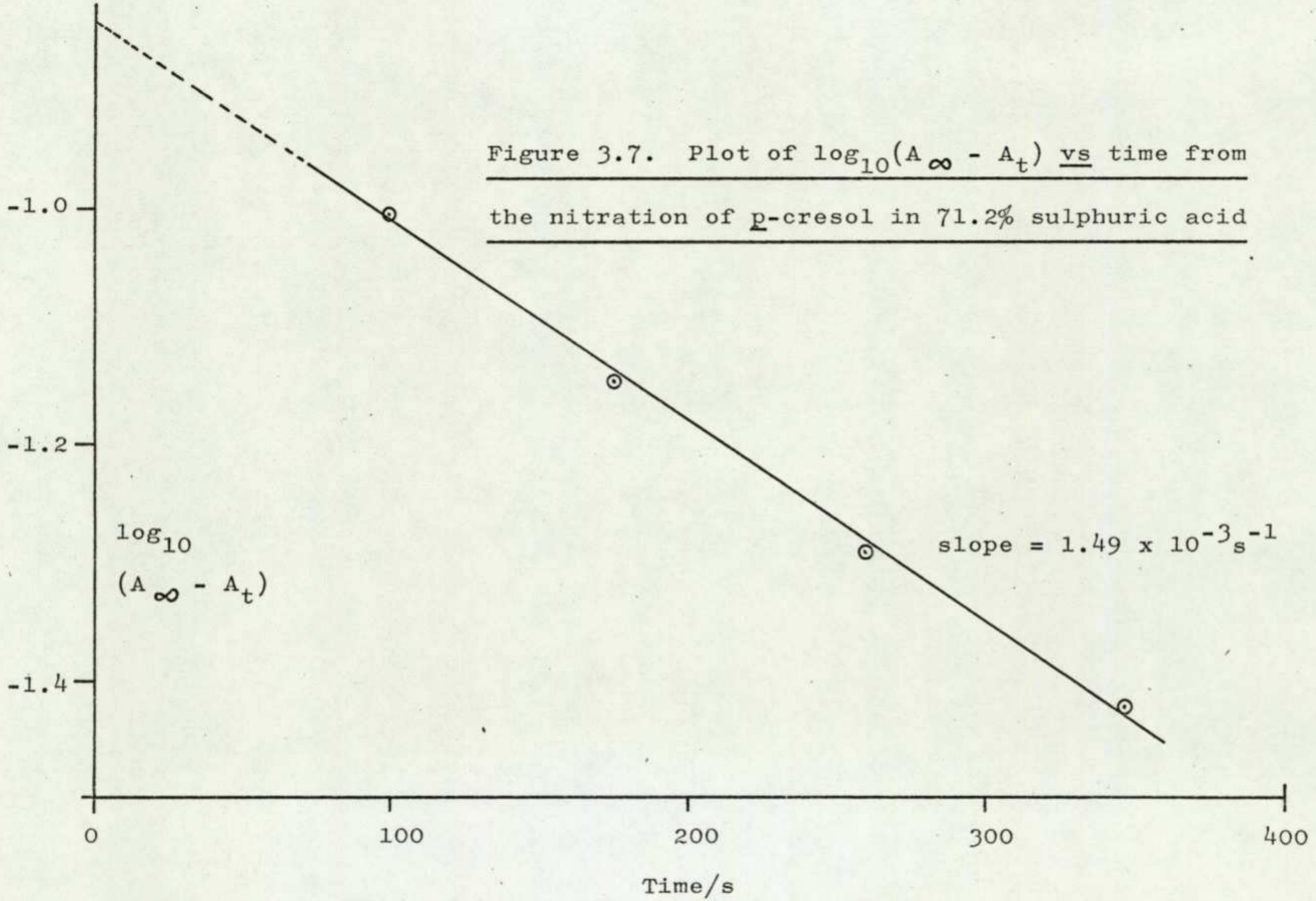


Figure 3.7. Plot of $\log_{10}(A_\infty - A_t)$ vs time from the nitration of p-cresol in 71.2% sulphuric acid

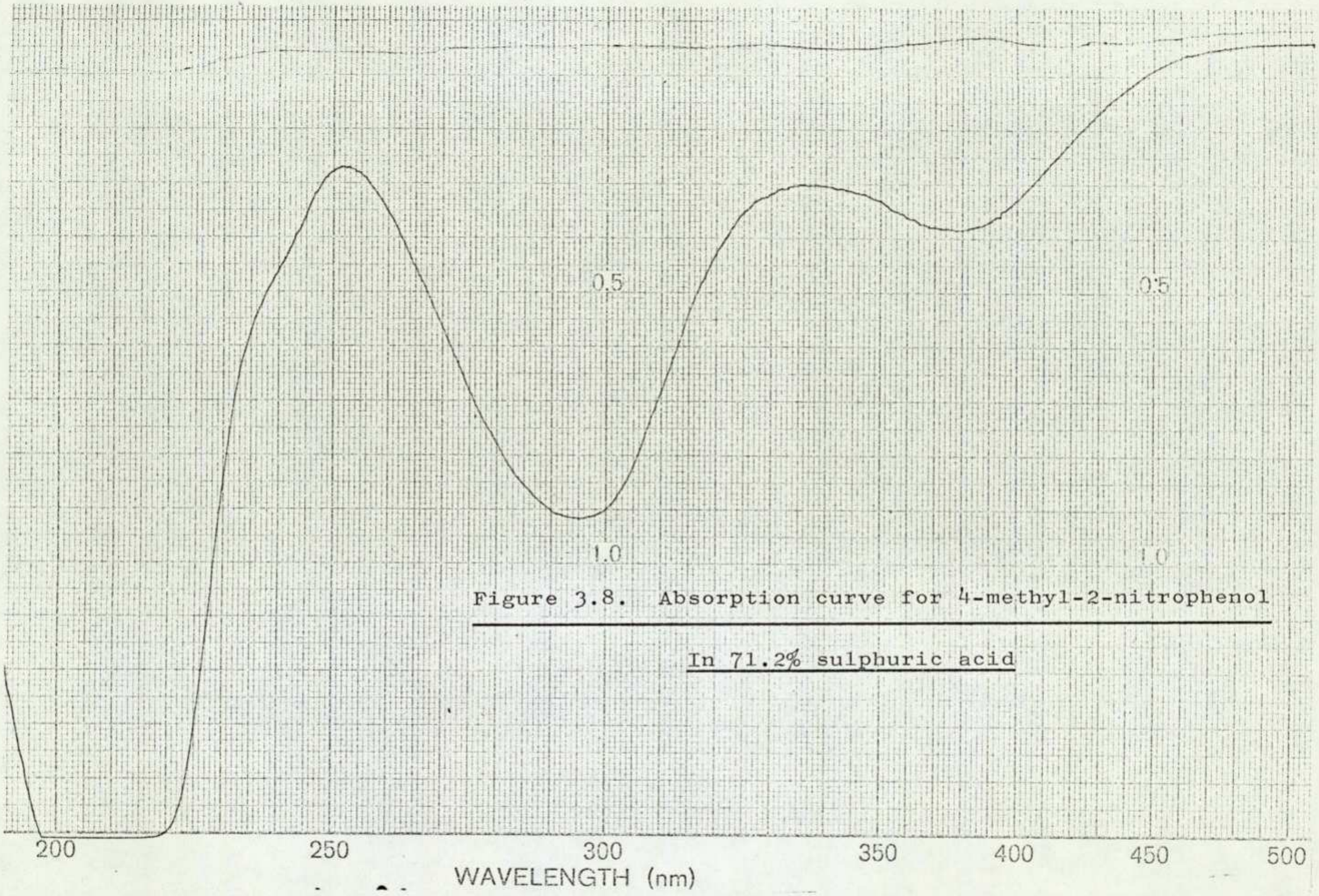


Figure 3.8. Absorption curve for 4-methyl-2-nitrophenol

In 71.2% sulphuric acid

4-methyl-2-nitrophenol is the sole product of this reaction (see Table 3.14).

$$k_1 = 2.303 \times \text{slope} \qquad s^{-1}$$
$$= 2.303 \times 1.49 \times 10^{-3}\ s^{-1}$$
$$\therefore k_1 = 3.43 \times 10^{-3} \qquad s^{-1}$$

First-order rate coefficients for the decomposition of the presumed intermediate over a range of percentages of sulphuric acid are given in Table 3.10. A rate profile ($\log_{10}k_1$ vs - H_o) is shown on Fig. 3.9.

3.32 YIELDS OF NITRO-COMPOUNDS

3.321 p-METHYLANISOLE

An example of the method for calculating the yield of nitro-compound for the nitration of p-methylanisole is given below, (g.l.c. conditions as Table 3.2(i), Section 3.231).

Sulphuric acid	73.5% (wt/wt)
Amount of p-methylanisole	5.76×10^{-5} moles
Amount of HNO_3	5.78×10^{-5} moles
Amount of reference standard 4-nitroveratrole	4.14×10^{-5} moles

Reaction carried out in 260cm^3 of sulphuric acid

Compound	Area/mm^2(of chromatographic peak)
4-Methyl-2-nitrophenol	753
4-Methyl-2-nitroanisole	1251
4-Nitroveratrole	1524

From Section 7.5 $\frac{c_x}{c_s} = \left(\frac{A_x}{A_s}\right) \times f$

Response factor f for 4-methyl-2-nitrophenol = 1.10

Table 3.10

First-order rate coefficients for the decomposition of the intermediate formed in the nitration of p-cresol[c,d]

H_2SO_4(%)	$-H_o$[g]	$[HNO_3]$ /mole dm^{-3}	k_1/s^{-1}
67.9[a,e]	5.50	5.5×10^{-2}	9.80×10^{-4}
69.1[b,f]	5.69	5.5×10^{-2}	1.68×10^{-3}
71.2[a,e]	6.00	1.18×10^{-2}	3.43×10^{-3}
72.5[b,f]	6.20	2.50×10^{-3}	3.90×10^{-3}
72.5[b,f]	6.20	2.50×10^{-3}	3.90×10^{-3}

a) [p-Cresol] = 1.23×10^{-3} mole dm^{-3}

b) [p-Cresol] = 1.23×10^{-4} mole dm^{-3}

c) [Sulphamic acid] = 2×10^{-2} mole dm^{-3}

d) Measurement at 380nm.

e) 1mm cell used

f) 10mm cell used

g) Ref. 101

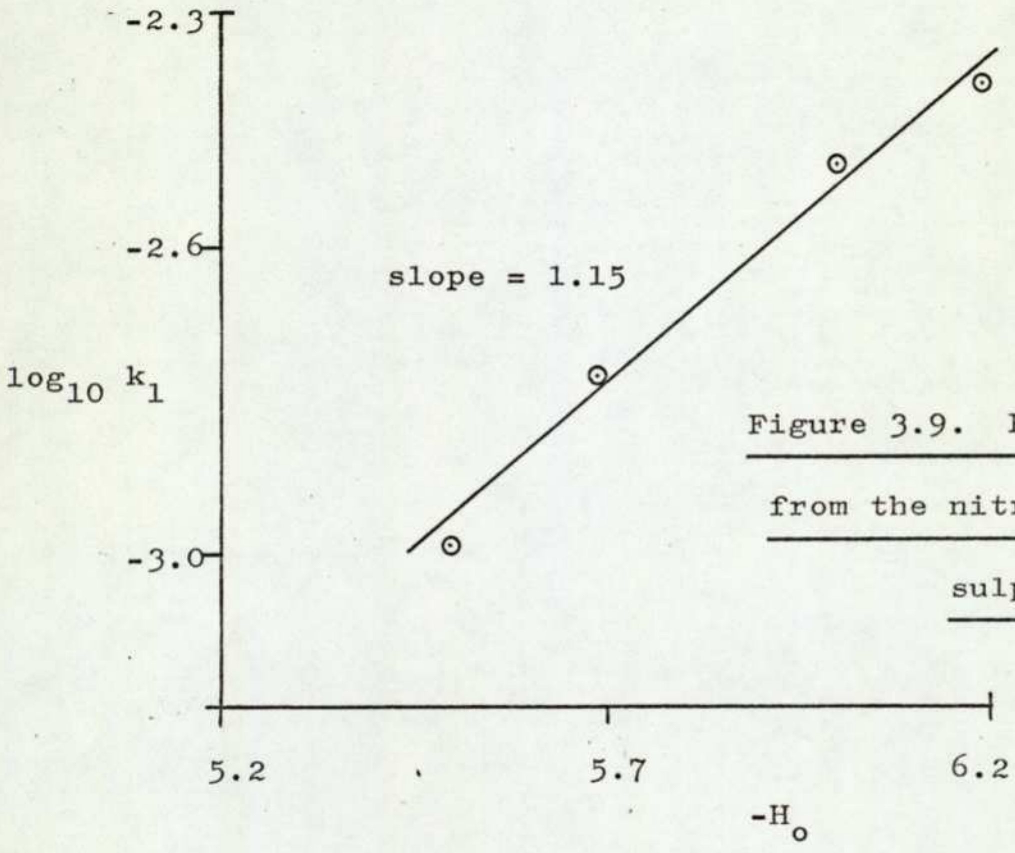


Figure 3.9. Plot of $\log_{10} k_1$ vs $-H_o$ from the nitration of p-cresol in sulphuric acid

$\therefore$ amount of 4-methyl-2-nitrophenol

$$= \frac{7.53}{15.24} \times 4.14 \times 10^{-5} \times 1.10 \text{ moles}$$

$$= 2.26 \times 10^{-5} \text{ moles}$$

% yield of 4-methyl-2-nitrophenol

$$= \frac{2.26 \times 10^{-5}}{5.76 \times 10^{-5}} \times 100$$

$$= 39.2\%$$

Response factor f for 4-methyl-2-nitroanisole = 1.04

$\therefore$ amount of 4-methyl-2-nitroanisole

$$= \frac{12.51}{15.24} \times 4.14 \times 10^{-5} \times 1.04 \text{ moles}$$

$$= 3.52 \times 10^{-5} \text{ moles}$$

% yield of 4-methyl-2-nitroanisole

$$= \frac{3.52 \times 10^{-5}}{5.76 \times 10^{-5}} \times 100$$

$$= 60.8\%$$

Table 3.11 and Fig. 3.10 show the yield of mononitro-compounds from the nitration of p-methylanisole in various concentrations of sulphuric acid, Table 3.12 gives the ratio of 4-methyl-2-nitrophenol to 4-methyl-2-nitroanisole formed during the course of a single nitration reaction.

4-Methyl-2-nitrophenol, 4-methyl-2-nitroanisole, and 4-methyl-3-nitroanisole (4×10^{-5} mole dm^{-3}) were recovered quantitatively (99%, 100% and 99% respectively) by the normal extraction method, described in Section 7.41, from 68% sulphuric acid containing 9×10^{-4} mole dm^{-3} of nitric acid and 2×10^{-2} mole dm^{-3} of sulphamic

Table 3.11

Yields of mono nitro-compounds from the nitration of *p*-methylanisole[b,c] in aqueous sulphuric acid at 25.0 ± 0.2°

H_2SO_4[a] (%)	Yield of Product (%)		Mass Balance (%)
	4-methyl-2-nitrophenol	4-methyl-2-nitroanisole	
46.0[d,e,f]	40.0	61.1	101.1
54.2[e]	40.0	63.6	103.6
58.1[e]	38.2	63.4	101.6
60.8[e]	36.2	63.1	99.3
63.2[e]	36.1	60.7	96.8
66.1[e]	33.9	65.7	99.6
67.6[e]	39.0	62.4	101.4
70.3[e,g]	40.8	59.8	99.6
73.5[e,g]	39.2	60.8	100.0
78.8[e,g]	38.2	64.3	102.5
79.8[g,h]	34.2	65.7	99.9
82.5[e,g]	18.7	79.9	98.6
83.0[g,h]	7.0	82.3	89.3
86.3[g,h]	4.0	68.1	72.1
90.8[g,h]	5.0	46.2	51.2

Table 3.11 (continued)

a) ± 0.1%

b) $[HNO_3] = 2 \times 10^{-4}$ mole dm^{-3} - 5×10^{-2} mole dm^{-3}

c) $[ArH]$ ca 2×10^{-4} mole dm^{-3}

d) Light excluded

e) [Sulphanilic acid] ca 1×10^{-2} mole dm^{-3}

f) at 60 ± 0.5°

g) $[ArH] = [HNO_3] = 2.2 \times 10^{-4}$ mole dm^{-3}

h) [Sulphamic acid] ca 2×10^{-2} mole dm^{-3}

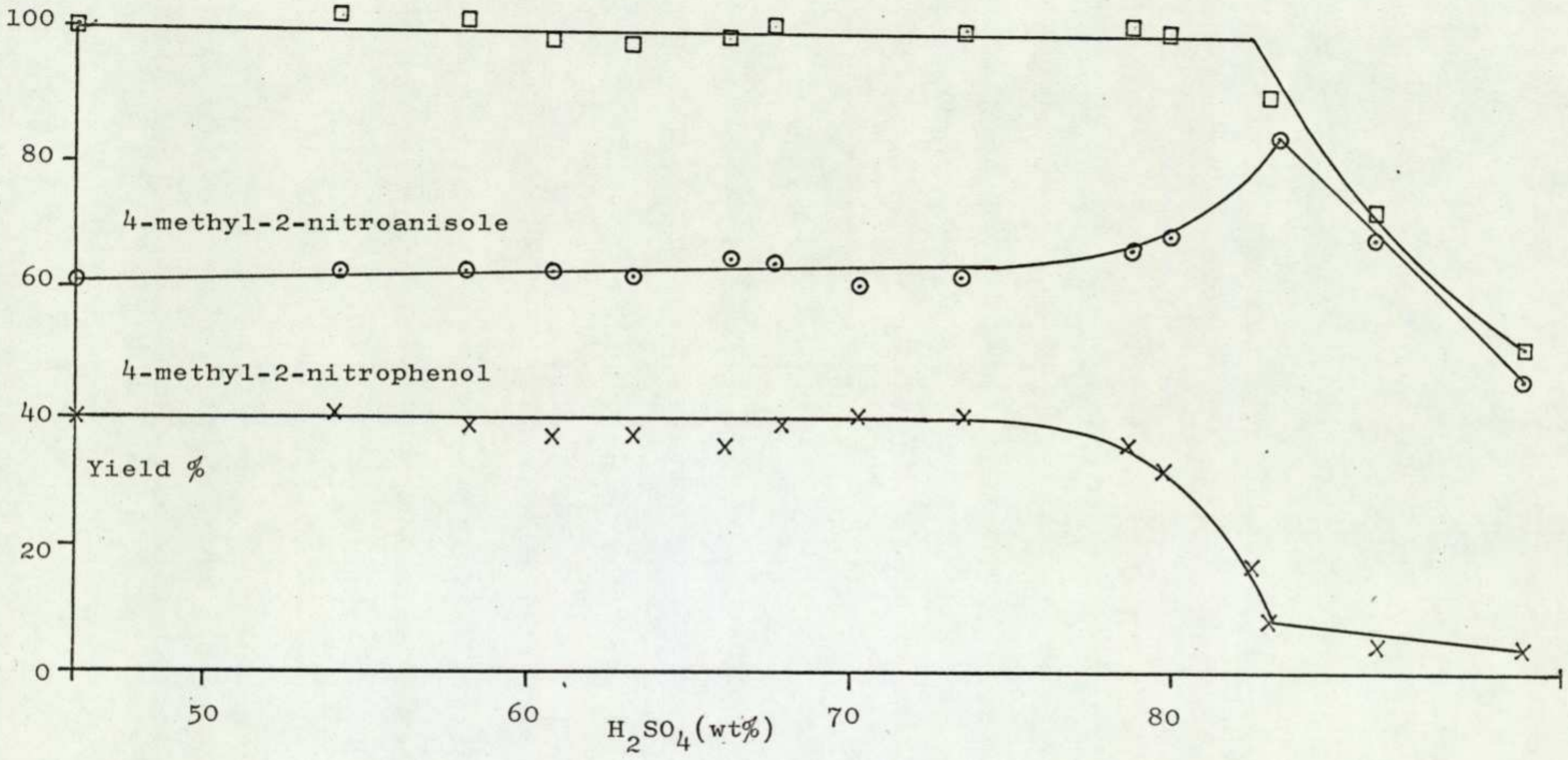


Figure 3.10. Yield of nitro compounds from the nitration of p-methylanisole

Table 3.12

Ratio of amounts of products formed in the nitration[a] of p-methylanisole in 68.5% sulphuric acid at 25.0 ± 0.2°

Extent of Reaction (%)	4-Methyl-2-nitrophenol/ 4-Methyl-2-nitroanisole
30	0.67
45	0.72
70	0.73
90	0.72

a) $\left[ArH\right] = 9.5 \times 10^{-5}$ mole dm^{-3},
$\left[HNO_3\right] = 8.2 \times 10^{-4}$ mole dm^{-3} and,
$\left[\text{sulphamic acid}\right] = 1 \times 10^{-2}$ mole dm^{-3}

acid after 100 mins at 25.0° (*ca* 10 half-lives for the nitration of *p*-methylanisole). 4-Methyl-2-nitroanisole and 4-methyl-2-nitrophenol (4×10^{-5} mole dm^{-3}) were found to be quantitatively extractable (98.5% and 100.3% respectively) by the normal methods, see Section 7.41, from their solution in 86.3% sulphuric acid, which had been kept at 25.0° for 40 mins.

p-Cresol was not detected ($>$ 1% would have been detected) in the extract from a solution of *p*-methylanisole (1×10^{-4} mole dm^{-3}) in 82.5% sulphuric acid, which had been kept at 25.0° for 3hr. *p*-Cresol was found to be extractable from its solution in 82.5% H_2SO_4 in 94% yield (initial $[p\text{-cresol}] = 1 \times 10^{-4}$ mole dm^{-3}).

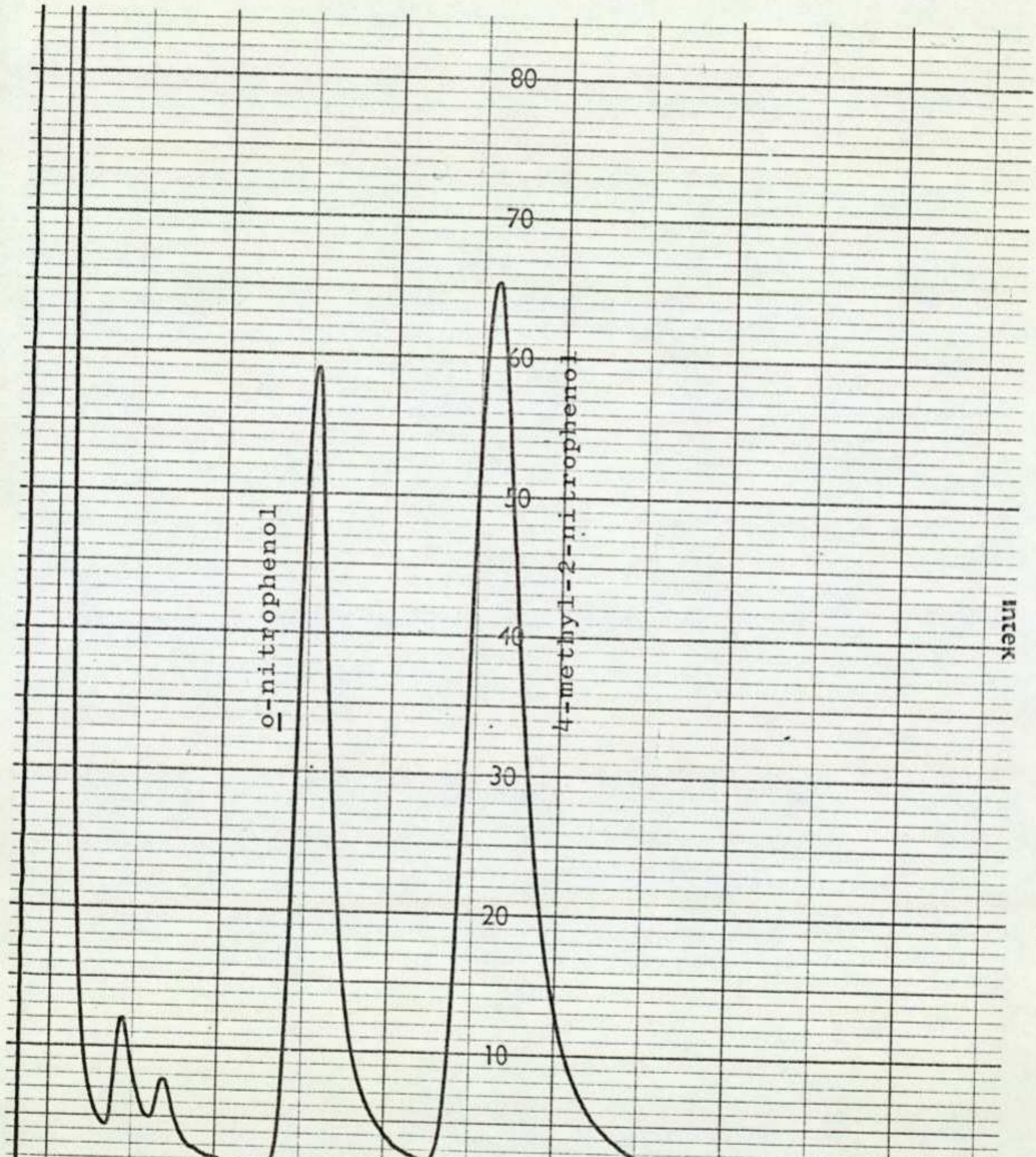
3.322 *p*-CRESOL

An example of the method for calculating the yield of nitro-compound for the nitration of *p*-cresol is given below. Fig. 3.11 shows the chromatogram obtained (g.l.c. conditions as Table 3.3, Section 2.232).

Sulphuric acid	62.5%
Amount of *p*-cresol	3.12×10^{-5} moles
Amount of HNO_3	3.09×10^{-3} moles
Amount of reference standard *o*-nitrophenol	1.87×10^{-5} moles

Reaction carried out in 260cm^3 of sulphuric acid.

Figure 3.11. Chromatogram of the product from the nitration of *p*-cresol in 62.5% sulphuric acid



Peak Areas from Fig. 3.11

Compound	Area/mm^2
4-Methyl-2-nitrophenol	11.44
o-Nitrophenol	6.54

From Section 7.5 $\frac{c_x}{c_s} = \frac{A_x}{A_s} \times f$

Response factor f for 4-methyl-2-nitrophenol = 0.96

$\therefore$ amount of 4-methyl-2-nitrophenol

$$= \frac{11.44}{6.60} \times 1.87 \times 10^{-5} \times 0.96 \text{ moles}$$

$$= 3.10 \times 10^{-5} \text{ moles}$$

% yield of 4-methyl-2-nitrophenol

$$= \frac{3.10 \times 10^{-5}}{3.12 \times 10^{-5}} \times 100 \quad = 99\%$$

Table 3.13 gives the yield of nitro-compound from the nitration of p-cresol, when it is presumed nitrosation was not completely suppressed by sulphamic acid. Table 3.14 gives the yield of nitro-compound from the nitration of p-cresol in various concentrations of sulphuric acid when nitrosation was precluded by the addition of sulphanilic acid to both the substrate solution and the nitric acid solution.

3.323 AMOUNT OF INTERMEDIATE PRODUCT FORMED IN THE NITRATION OF p-CRESOL

An example of the method for calculating the amount of intermediate formed in the nitration of p-cresol is given below. Fig. 3.6 shows the absorbance curve obtained.

Table 3.13

Yield of mono nitro-compounds from the nitration of p-cresol[b] in aqueous sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[a]	Amount of p-cresol used/ moles x 10^{-5}	Amount of 4-methyl-2-nitrophenol/ moles x 10^{-5}	Mass Balance (%)
60.8	4.29	2.29	53.6
60.8	4.29	2.30	53.9
60.8[d]	5.7	2.62	51.9
62.5	5.7	3.74	65.6
65.9[d]	5.7	3.17	74.0
67.7[d]	5.7	2.72	71.9
67.9	4.29	3.21	74.8
70.3[d]	4.29	3.38	78.9
72.2[d]	5.7	4.86	85.2
75.6[c]	5.7	5.28	92.7
78.2[c,d]	5.7	5.65	99.1
80.0[c]	5.7	5.70	100.0
83.3[c]	5.7	2.41	41.8
85.4[c]	5.7	1.92	33.7
87.8[c]	5.7	1.52	26.3
90.8[c,d]	5.7	0.67	11.5

Table 3.13 (continued)

a) ± 0.1%

b) $\left[\text{Sulphamic acid}\right]$ ca 2×10^{-2} mole dm^{-3}

c) $ArH = HNO_3 = 5.7 \times 10^{-5}$ moles

d) No 4-methyl-3-nitrophenol was found by h.p.l.c. analysis, using the conditions given in Table 3.3, 0.2% would have been detected.

Table 3.14

Yield of mono nitro-compounds from the nitration of p-cresol[a,b] in aqueous sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[c]	Amount of p-cresol used/ moles x 10^{-5}	Amount of 4-methyl-2-nitrophenol/ moles x 10^{-5}	Mass Balance (%)
56.1	3.12	3.12	100
58.1	3.12	3.11	99.7
60.8	3.12	3.16	101.2
62.5	3.12	3.12	100
64.3	3.12	3.09	99.0
66.6	3.12	3.09	99.0
67.9	3.12	3.14	100.6
71.2	3.12	3.08	98.7
72.5	3.12	3.08	98.7
75.2	3.12	3.08	98.7
76.6[d]	5.78	5.77	99.7
78.2[d]	5.78	5.72	98.6
80.8[d]	5.78	4.94	85.6
81.7[d]	5.78	4.75	80.6
84.6[d]	5.78	3.33	57.5
87.8[d]	5.78	2.97	51.2
91.3[d]	5.78	1.87	32.4

Table 3.14 (continued)

a) Sulphanilic acid present in both the nitric acid and substrate solutions $\left[\text{sulphanilic acid}\right] = 1 \times 10^{-2}$ mole dm^{-3}

b) $\left[HNO_3\right] = 2 \times 10^{-4}$ moles dm^{-3} - 5.5×10^{-2} mole dm^{-3}

c) ± 0.1%

d) $ArH = HNO_3 = 5.78 \times 10^{-5}$ moles

Sulphuric acid	71.2%
$[\underline{p}\text{-Cresol}]$	1.233×10^{-3} mole dm^{-3}
$[HNO_3]$	1.18×10^{-2} mole dm^{-3}
Temperature	25.0 ± 0.2^{o}

At 330 nm (isosbestic point for dinitration) A = 0.265. In the spectrum of 4-methyl-2-nitrophenol (3.21×10^{-5} mole dm^{-3} in 71.2% H_2SO_4) (see Fig. 3.8) $A^{330} = 0.27$ and $A^{380}_{max} = 0.35$

$$\therefore \quad A^{380}_{\infty} = \frac{0.265}{0.27} \times 0.35$$

$$= 0.34$$

By extrapolation of Fig. 3.7 $\log_{10}(A^{380}_{\infty} - A^{380}_{o})$ = 0.855

$$\therefore \quad A^{380}_{\infty} - A^{380}_{o} = 0.138$$

$\therefore$ % of total of 4-methyl-2-nitrophenol measured at 380nm which was formed via the intermediate =

$$\frac{0.138}{0.34} \times 100 = 41\%.$$

Table 3.15 gives the percentages of intermediate product formed in the nitration of p-cresol. The u.v. maximum for the intermediate appears to change with acidity, figs. 3.6 and 3.12 show the absorption curves obtained from the nitration of p-cresol in 71.2% and 67.9% sulphuric acid, respectively. A possible reason for this was investigated by determining the u.v. absorptions of 2,4,6-trimethyl-4-nitrocyclohexa-2,5-dienone and 2,4,6-tri-t-butyl-4-nitrocyclohexa-2,5-dienone in several percentages of sulphuric acid (67.9 - 72.5%).

Table 3.15

Percentage of intermediate product formed in the nitration of p-cresol[b] in aqueous sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[a]	Amount of Intermediate (%)
67.9	45
69.1	43
71.2	43
72.5	39
72.5	39

a) ± 0.1%

b) $[\mathrm{ArH}] = 3.21 \times 10^{-5}$ mole dm^{-3}

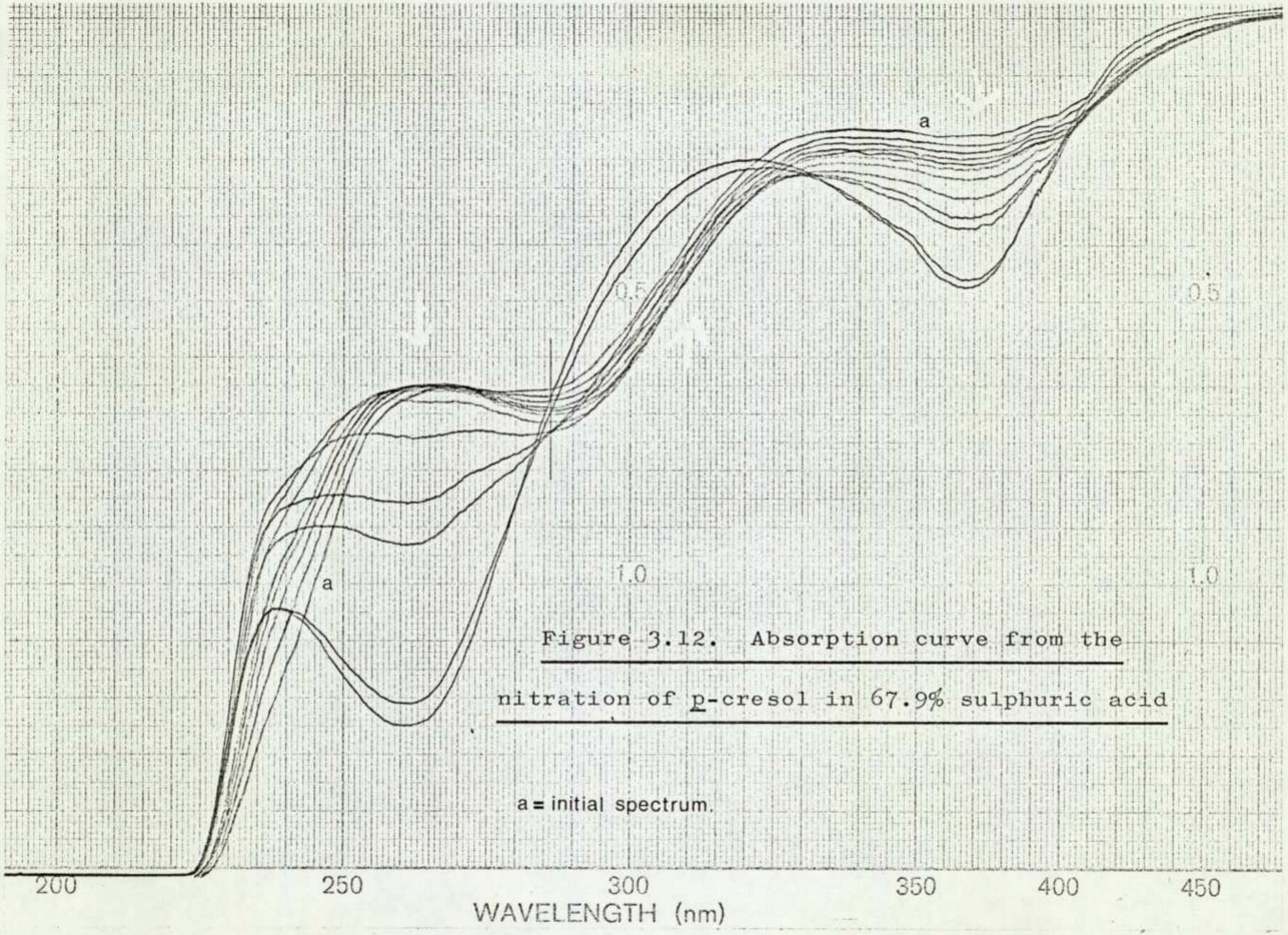


Figure 3.12. Absorption curve from the nitration of p-cresol in 67.9% sulphuric acid

a = initial spectrum.

The λ_{max} in both cases were found to be constant at 245 and 250nm respectively.

3.4 DISCUSSION

3.41 RATE PROFILES

The rate profiles for p-methylanisole and p-cresol are very similar and clearly the rate is limited by encounter (see Figs. 3.2 and 3.5). Both profiles are parallel to but slightly below that of mesitylene, (mesitylene is representative of a compound being nitrated at the limiting encounter rate). The value of k_2(obs) mesitylene/k_2(obs) ArH for both compounds is ca 2.0. The observation of this type of rate profile seems to be characteristic of an aromatic compound containing a substituent with a lone pair of electrons capable of hydrogen bonding to the hydronium ion. This is discussed in Section 2.41.

3.42 PRODUCTS FROM THE NITRATION OF p-METHYLANISOLE

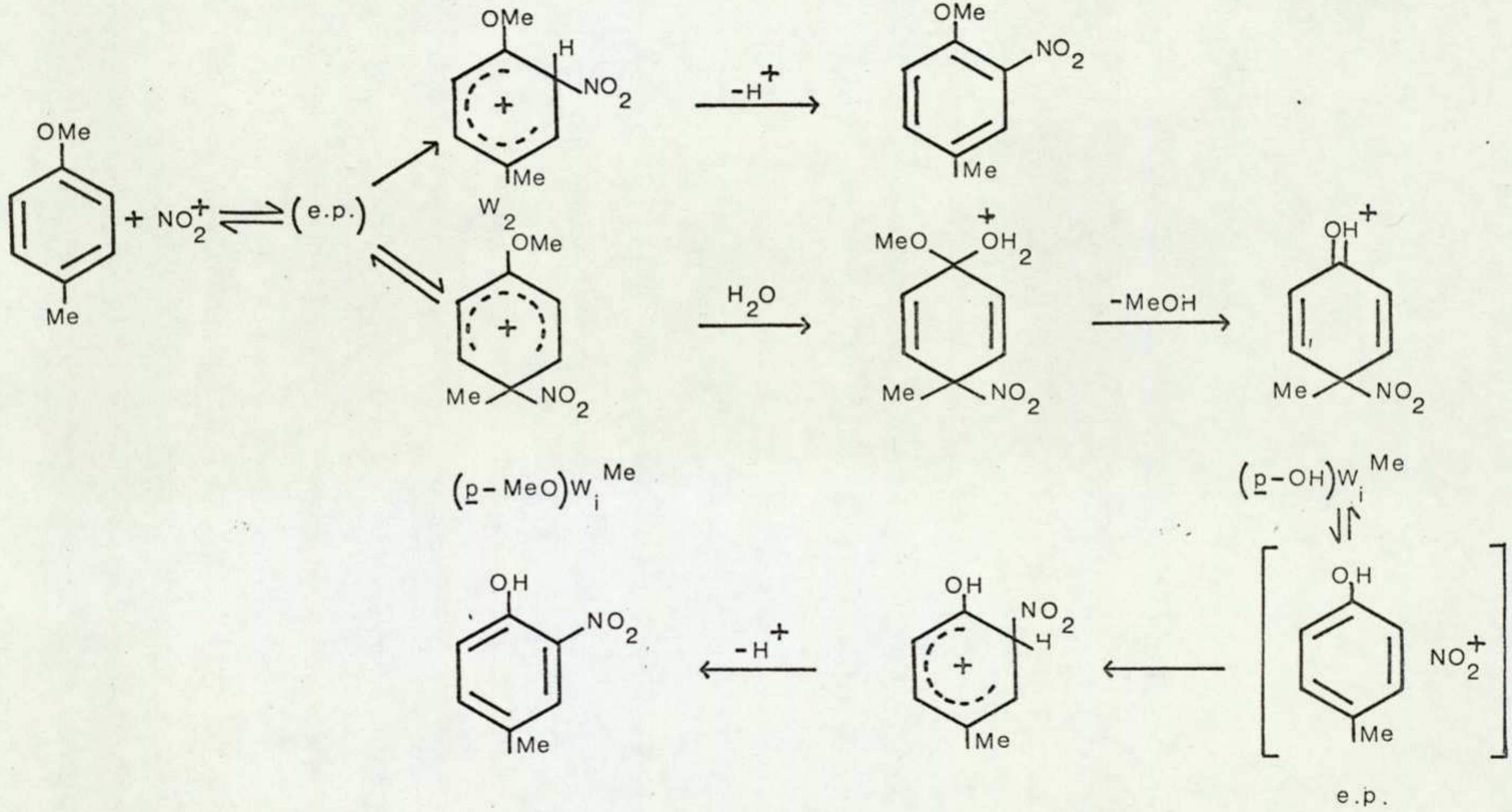
For p-methylanisole quantitative yields of mono nitro-compounds are observed in the range 46 - 82.5% sulphuric acid, see Fig. 3.10. The ratio of 4-methyl-2-nitroanisole to 4-methyl-2-nitrophenol is constant at 1.6, up to ca 80% H_2SO_4, but above this acidity the proportion of demethylated product diminishes rapidly. The behaviour of 4-methyl-2- and 3-nitroanisoles and of p-methylanisole in simulated reaction media demonstrates that demethylation does not occur prior or subsequent to nitration. This conclusion is supported by the constant product ratio over a wide range of acidity.

<u>Ipso</u> - substitution at C-Me is to be expected in this molecule and the proposed reaction mechanism is shown in Scheme 3.2. Demethylation of W_2 cannot be occuring as the route to 4-methyl-2-nitrophenol, as it would have to compete with proton loss from W_2 and the ratio of products should vary with acidity.

It is, therefore, suggested that the demethylated product is formed <u>via</u> W_i^{Me} with a <u>p</u>-methoxyl group. Demethylation leads to W_i^{Me} with a <u>p</u>-hydroxyl group. Loss of nitronium ion from this species would yield an encounter pair (e.p.) and in view of the known reactivity of <u>p</u>-cresol the formation of 4-methyl-2-nitrophenol would be expected to be faster than the dissociation of the e.p. In accord with this conclusion that free <u>p</u>-cresol would not be present, the ratio of products remains constant during the course of an individual reaction, see Table 3.12.

The analogy with the mechanism of acid hydrolysis of anisoles[102] suggests that demethylation may involve aryl oxygen fission by attack of water at the carbon atom bearing the methoxyl group to give an adduct, and subsequent loss of methanol. In 80 - 82.5% H_2SO_4 as the water concentration falls the rate of this process fails to compete with the return to the e.p. The yield of demethylated product falls, and is replaced by 4-methyl-2-nitroanisole. The absence of 4-methyl-3-nitroanisole under any conditions suggests not only that direct formation of W_3 does not occur, but also that rearrangement of W_i^{Me} to W_3 does not occur.

Scheme 3·2


OMe
Me
+ NO$_2^+$
(e.p.)
OMe
H
NO$_2$
Me
W$_2$
-H$^+$
OMe
NO$_2$
Me
OMe
Me
NO$_2$
(p-MeO)W$_i^{Me}$
H$_2$O
MeO
OH$_2$
+
Me
NO$_2$
-MeOH
OH$^+$
Me
NO$_2$
(p-OH)W$_i^{Me}$
OH
NO$_2^+$
Me
e.p.
OH
NO$_2$
H
Me
-H$^+$
OH
NO$_2$
Me

This mechanism involves a 1,3-shift within the encounter pair. Ipso-substitution followed by a 1,3-shift has been reported (Section 1.83) for the nitration of 4-chloro-2-nitroanisole[63a], (in which demethylation also occured), 1,1a,2,3,4,8b-hexahydrobenzo[a]cyclopropa[c]cycloheptene[58], and 2,3-, and 3,4-dimethylbenzonitriles[59]. For the two activated compounds 4-chloro-2-nitroanisole and 1,1a,2,3,4,8b-hexahydrobenzo[a]cyclopropa[c]cycloheptene, it is possible that the 1,3-shift could be occuring within the encounter pair. However, this argument cannot be applied to 1,3-shifts occuring in the nitration of deactivated compounds such as 2,3- and 3,5-dimethylbenzonitriles.

3.43 PRODUCTS FROM THE NITRATION OF p-CRESOL

p-Cresol seems to be extremely sensitive to nitrosation and the yield of products obtained from the nitration of p-cresol in the presence of sulphamic acid as the nitrous acid inhibitor were not quantitative (see Table 3.13). Quantitative yields of 4-methyl-2-nitrophenol were, however, observed in the range 56 - 78% H_2SO_4, when nitrosation was precluded by the addition of sulphanilic acid to both the nitric acid and substrate solutions (see Table 3.14). No 4-methyl-3-nitrophenol was ever detected.

3.44 FORMATION OF 4-METHYL-4-NITROCYCLOHEXA-2,5-DIENONE

Further studies from the nitration of p-cresol showed that a transient intermediate was formed in these reactions, with a u.v. absorption at ~ 240nm, (see Figs. 3.3 and 3.6). In view of the similarity in u.v. maxima to previously reported compounds (see Section 3.1) it is suggested that this intermediate is 4-methyl-4-nitrocyclohexa-2,5-dienone formed by the expected ipso attack at C-Me (Scheme 3.3). Data have been obtained for the first-order rate coefficients (k_1) of decomposition of the intermediate to 4-methyl-2-nitrophenol which should be independent of the concentration of nitric acid.

A plot of $\log_{10} k_1$ vs $-H_o$ was found to be a straight line of unit slope (Fig. 3.9). This would be so if the cyclohexadienone acts as a Hammett base and if the mechanism involves a fast pre-equilibrium protonation followed by slow unimolecular reaction of the protonated cyclohexadienone.

$$A + H^+ \overset{\text{fast}}{\rightleftharpoons} AH^+ \xrightarrow{\text{slow}} \text{product}$$

Scanning of the u.v. spectra of the reactions, however, reveals the anomaly that the shapes of the extinction curves appear to vary with acidity (see Figs. 3.6 and 3.12). The initial absorption maxima of the synthesized 2,4,6-trimethyl-4-nitrocyclohexa-2,5-dienone and 2,4,6-tri-t-butyl-4-nitrocyclohexa-2,5-dienone, however, did not vary with acidity. Construction of the spectra of the proposed intermediate from the initial spectra of Figs. 3.6 and 3.12 by removal of the spectrum of 4-methyl-2-nitrophenol gave a λ max for the intermediate of 240 ± 2nm (Fig. 3.13) in both cases. It is, therefore, suggested that the spectral difference evident between Figs. 3.6 and 3.12 is due to a broad absorption

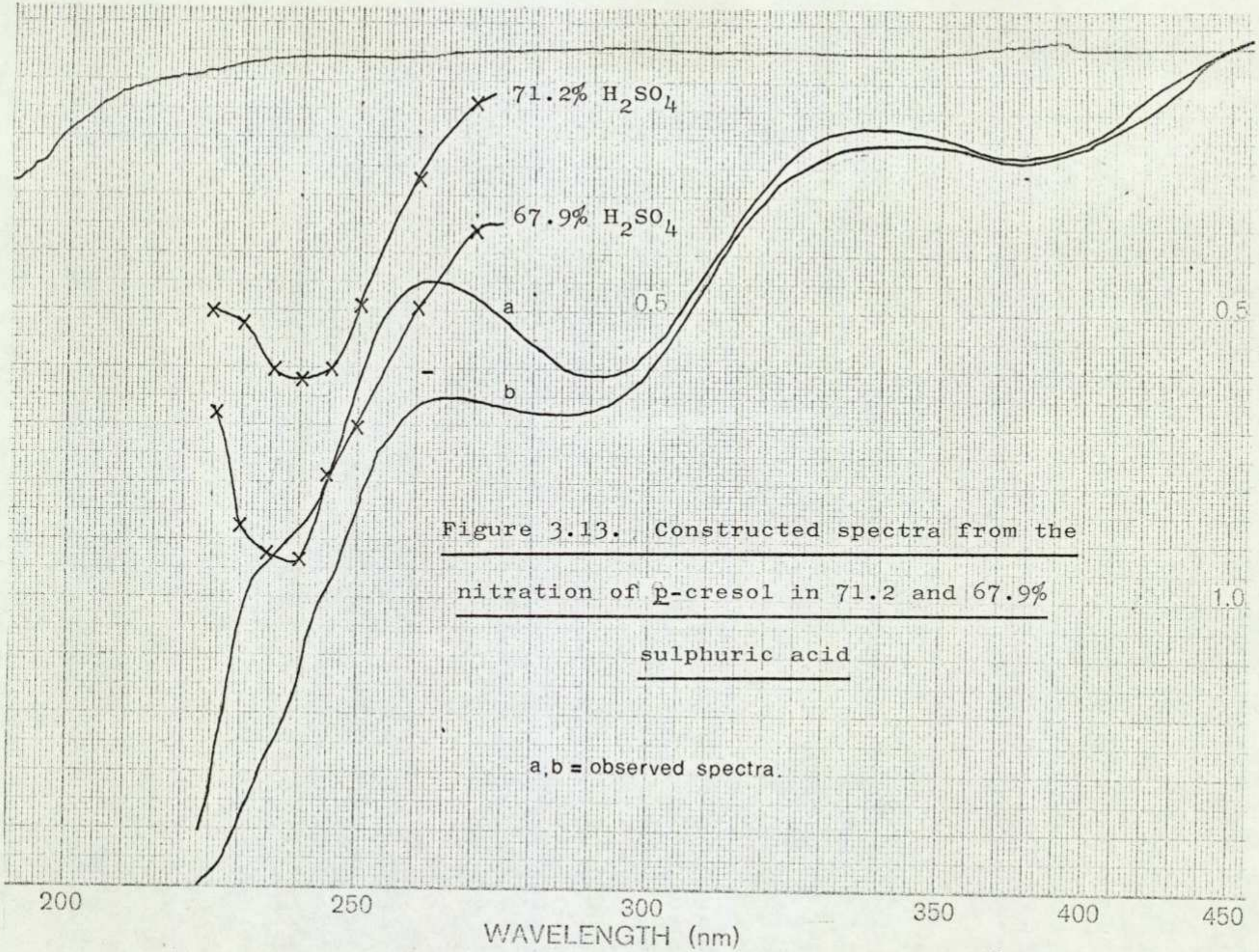
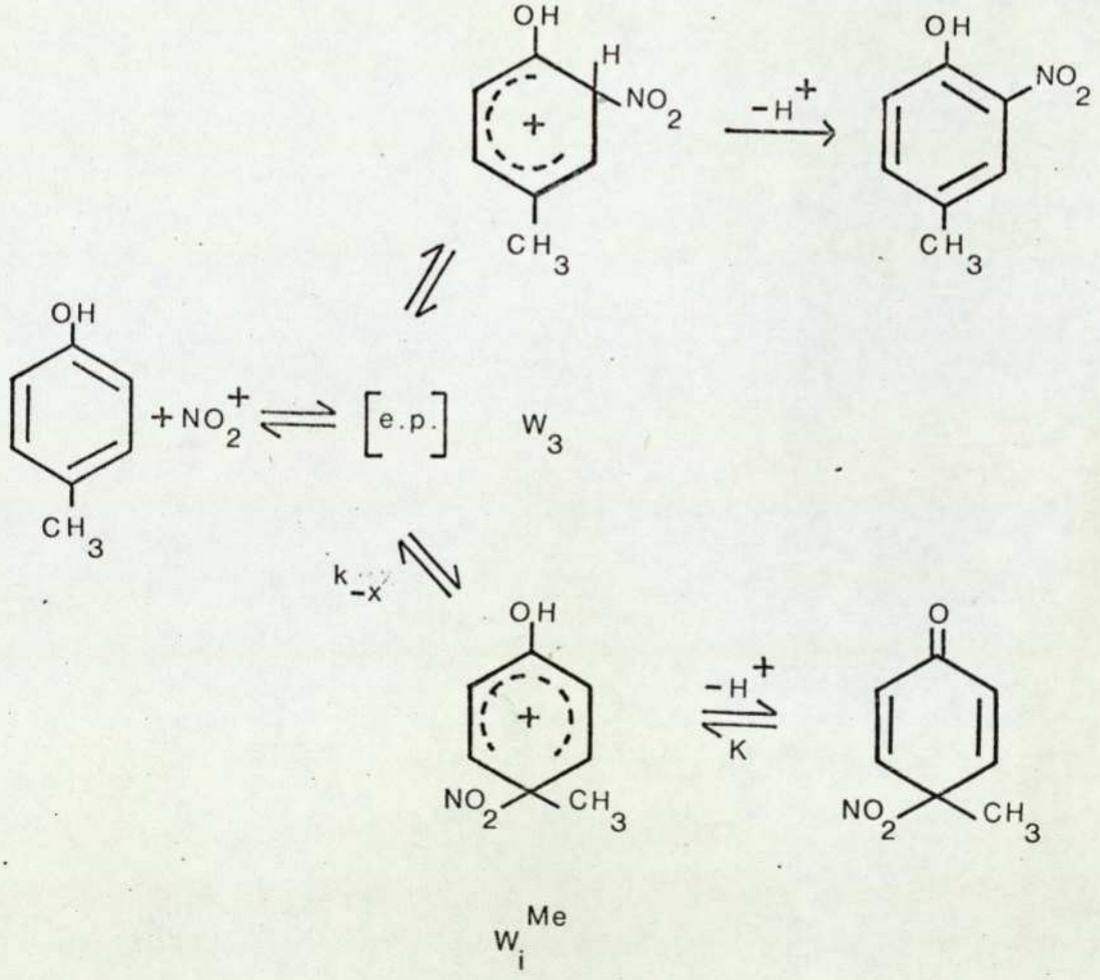


Figure 3.13. Constructed spectra from the nitration of p-cresol in 71.2 and 67.9% sulphuric acid

a,b = observed spectra.

in this region, and that is probably associated with the fortuitous nitrosation which it has been found impossible to remove in the product studies using sulphamic acid. The high nitric acid concentration would favour such a reaction and because of its u.v. absorption it is not possible to use sulphanilic acid in these spectral studies.

The reaction Scheme 3.3 is, therefore, suggested for the nitration of p-cresol in sulphuric acid.



Scheme 3·3

Initial attack by the nitronium ion on *p*-cresol can occur at either C_3 or C_i^{Me} to give the Wheland intermediates W_3 and W_i^{Me} respectively. Attack to give W_3 will lead directly to the formation of 4-methyl-2-nitrophenol. Attack at the *ipso* position will lead to the formation of 4-methyl-4-nitrocyclohexa-2,5-dienone, the observed intermediate, and this appears to occur to the extent of about 40%. This then decomposes to the encounter pair, and the rate of its disappearance, which has been measured as a function of acidity, is then that of the formation of e.p., by the reverse of the route which led to intermediate formation (i.e. $k_1 = K k_{-x}$). The absence of 4-methyl-3-nitrophenol under any conditions suggests not only that direct formation of W_2 does not occur, but also a 1,2-migration of the nitro group in W_i^{Me} fails to occur, as has been noted previously for *p*-methylanisole presumably because it would be from a position *para* to the hydroxyl group to a position *meta* to it and, therefore, be energetically unfavourable.

3.45 YIELDS OF NITRO-COMPOUNDS IN $>$ 78% (p-CRESOL) AND $>$ 82.5% (p-METHYLANISOLE) SULPHURIC ACID

Regarding the drop in yield observed for both *p*-methylanisole and *p*-cresol in $>$ 82.5 and 78.0% H_2SO_4 respectively, an estimated half-life in 89% sulphuric acid ($t_{\frac{1}{2}} = 5 \times 10^{-3}$s) (see Section 2.4, Fig. 1.1 and Table 1.5) for nitration, the rate of which should obey a first-order law at these acidities[28] is about 2×10^4 times smaller than the measured half-lives of sulphonation ($t_{\frac{1}{2}} = 90$s) in 89% sulphuric acid[89]. Sulphonation does, however, prevent the study of decomposition reactions of these compounds at the highest acidities. It is most unlikely, however, that decomposition of either of the substrates which is insignificant at 82.5% H_2SO_4 could become faster than the estimated rate of nitration ($t_{\frac{1}{2}} = 5 \times 10^{-3}$ s in 89% H_2SO_4). Decomposition of the mono-nitro compounds also does not occur, and it is clear that demethylation of p-methylanisole is not involved.

Product studies at high acidities were performed with equimolar proportions of reactants, to avoid complications due to dinitration. However, (by extrapolation from Tables 3.6 and 3.8) approximate calculations for the nitration of 4-methyl-2-nitroanisole, 4-methyl-3-nitroanisole, and 4-methyl-2-nitrophenol in 89% sulphuric acid (see Table 3.16), suggest that for both p-methylanisole and p-cresol, the rate of dinitration may be large enough for reaction to occur during the mixing process. This has been found to be so for anisole *via* the less reactive nitro-anisoles (see Section 2.42). No data on the amount of dinitration during nitration of p-methylanisole or p-cresol are available and it is possible, in these cases, that dinitration may be the complete explanation for the low yields.

Table 3.16

Extrapolated rates of nitration in 89% sulphuric acid

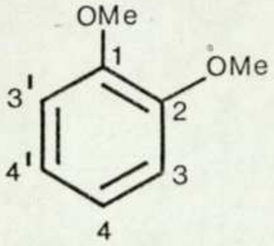
Compound	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}	$t_{\frac{1}{2}}$/s
4-methyl-2-nitroanisole	5.6×10^5	6×10^{-3}
4-methyl-3-nitroanisole	1×10^3	3
4-methyl-2-nitrophenol	2×10^5	2×10^{-2}

CHAPTER 4

THE NITRATION OF VERATROLE

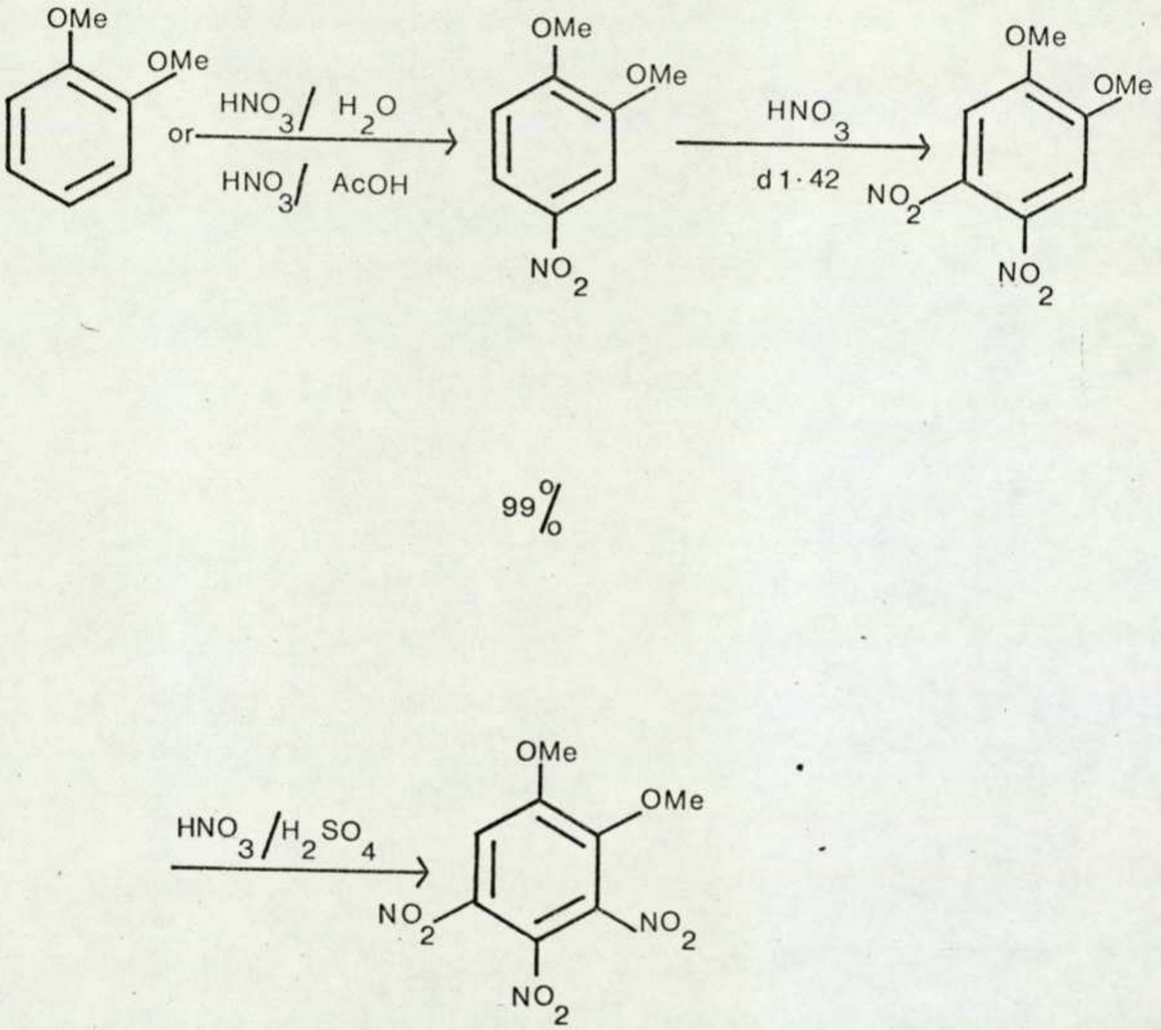
4.1 INTRODUCTION

Veratrole (1,2-dimethoxybenzene) would be expected to undergo electrophilic substitution in the 3- and 4-positions. The two 3-positions are each *ortho* to one methoxyl group and *meta* to the other. The two



4-positions are *para* to one methoxyl and *meta* to the other. For the nitration of anisole (Chapter 2) in sulphuric acid the ratio of partial rate factors (f_o/f_p) varies from 0.9 to 0.35 over the range 60 - 80% H_2SO_4. Thus it would be expected that, if substituent effects were additive, the nitration of veratrole under similar conditions would lead to considerable 3-substitution (26 - 47%).

Robinson[103] has stated that the successive mono-, di- and tri-nitration of veratrole occurs with the results shown in Scheme 4.1, and that each stage is easily separated by altering the conditions. The apparent production of only 4-nitroveratrole in stage 1 of the reaction could be due to nitration *via* nitrosation, and the present work was undertaken to see whether this was in fact the case.



Scheme 4·1

4.2 EXPERIMENTAL

4.21 MATERIALS

These were as described in Section 7.2, with the addition of the following. Veratrole (bp. 205°, lit.[104] bp. 205°) was purified by distillation. p-Chloronitrobenzene (mp. 83°, lit.[105] m.p. 82.2°) and 4-nitroveratrole (mp. 95°, lit.[84] m.p. 96°) were purified by recrystallisation.

4.211 3-NITROVERATROLE

4.2111 Introduction

The preparation of 3-nitroveratrole was attempted using the method reported by Oxford[106], involving the nitration of 2-methoxyphenyl acetate with silver nitrate to give 2-methoxy-3-nitrophenyl acetate, which then gives 3-nitroveratrole on methylation. Several attempts to isolate 2-methoxy-3-nitrophenyl acetate by the prescribed procedure failed.

Nitration of guiaicol (2-methoxyphenol) was then attempted in various solvents (sulphuric acid, acetic acid, carbon tetrachloride and chloroform). The best medium for nitration was found to be chloroform. The 3- and 4-nitroguiaicols could be separated by dissolving the former isomer in 40 - 60 petroleum ether. This isomer was then reacted with iodomethane.

4.2112 Method

25g (0.20 moles) of guiaicol was dissolved in 500cm^3 of chloroform. The solution was heated and stirred and a solution of 12.5cm^3 HNO_3 (s.g. 1.5) in 125cm^3 of chloroform was slowly added. The mixture was then stirred for a further ½h. The chloroform was removed by distillation and the 3-nitroguiaicol was extracted into 40 - 60 petroleum ether. After removal of the petroleum ether by distillation, 1.5g of 3-nitroguiaicol was dissolved in the minimum amount of alcoholic sodium hydroxide. The solvent was evaporated off and the sodium salt was recrystallised from dry methanol.

The salt was then dissolved in 50cm^3 of dry methanol to which was added 25g (0.019 moles) of iodomethane, and the mixture was refluxed for 2h. The solvent was removed and the 3-nitroveratrole was recrystallised from a methanol/water mixture (50:50) to give light yellow crystals (mp. 63-64°, lit.[2] mp. 64-64°). (Found: C, 52.4; H, 5.05; N, 8.0% Calc. for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65%)

^{1}H n.m.r. spectrum:- $\Big[\tau$ (CCl_4) 2.7 - 3.05 (6H, m, aromatic C - H), 6.12 - 6.17 (6H, s, $-OCH_3$)$\Big]$.
The mass spectrum (molecular ion 183.0537, calculated mass 183.0532), is shown Fig. 4.1.

4.22 KINETIC MEASUREMENTS

These were as described in Section 7.3.

4.23 PRODUCT ANALYSIS

The conventional g.l.c. technique as described in Sections 7.41 and 7.42 was used. Table 4.1 gives the g.l.c. conditions.

4.3 RESULTS

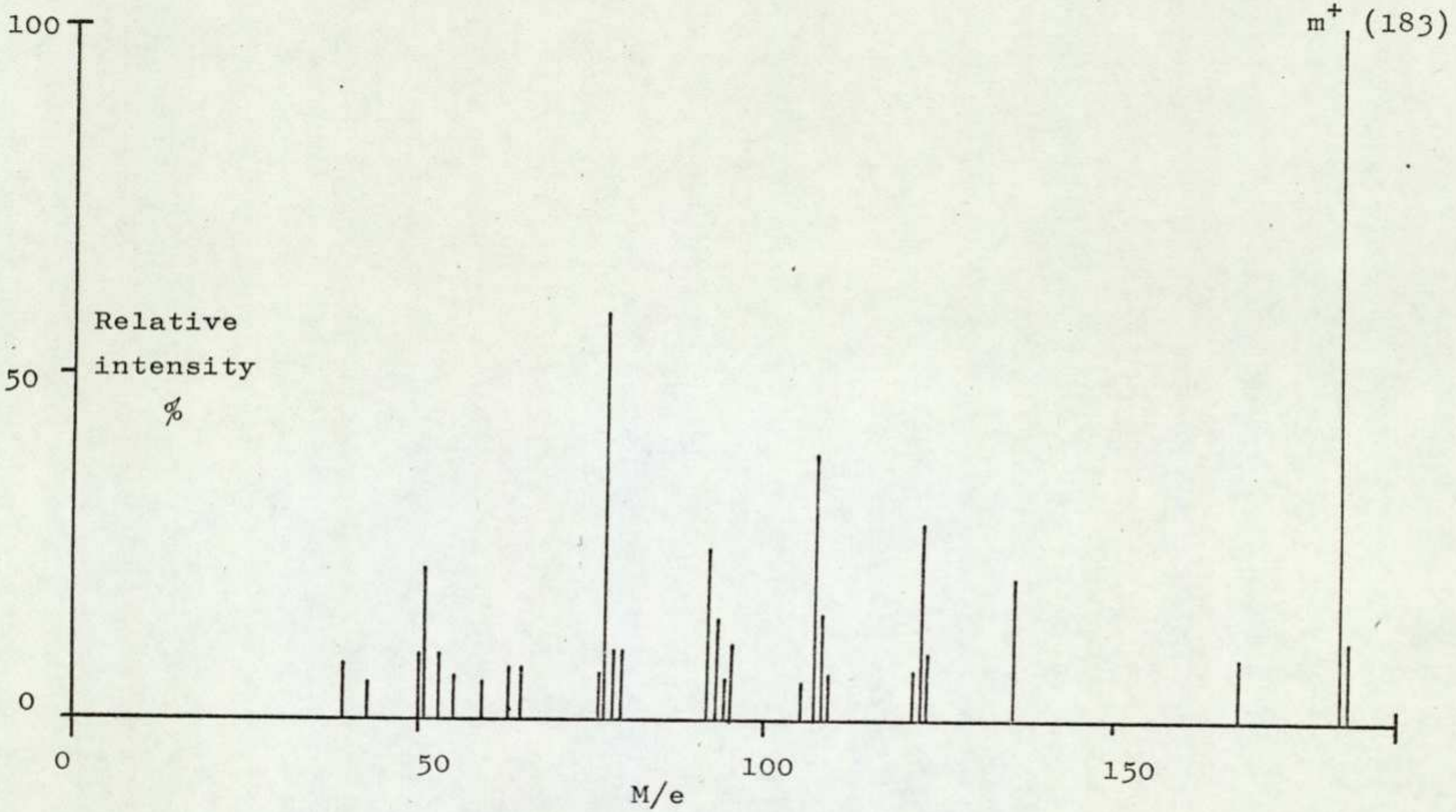


Figure 4.1. Mass spectrum of 1,2-dimethoxy-3-nitrobenzene

Table 4.1

G.l.c. conditions for the separation of 3- and 4-nitroveratrole

Column: 1.5m x $\frac{1}{4}$" S.S. $1\frac{1}{2}$% O.V. 225 on 60 - 85 mesh universal support

Oven temperature: 165 ± 0.5°

Carrier gas: Nitrogen $40 cm^3 min^{-1}$

Compound	Retention times /s
Veratrole	115
3-Nitroveratrole	600
4-Nitroveratrole	1100
p-Chloronitrobenzene (Reference standard)	190

4.31 KINETICS

The results and subsequent calculations for a typical determination of a rate coefficient for the nitration of veratrole are given below:

Sulphuric acid	68.1%
$[HNO_3]$	8.94×10^{-4} mole dm^{-3}
[Veratrole]	6.1×10^{-5} mole dm^{-3}
[Urea]	3×10^{-2} mole dm^{-3}
Temperature	25.0 ± 0.2°
Wavelength of measurement	350nm

Fig. 4.2 shows the absorption curve, Table 4.2 shows the data obtained from the above nitration and Fig. 4.3 the plot of $\log_{10}(A_\infty - A_t)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[HNO_3]} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$= \frac{2.303 \times 6.14 \times 10^{-4}}{8.94 \times 10^{-4}} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$\therefore k_2(\text{obs}) = 1.55 \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients determined over a range of percentages of sulphuric acid are given in Table 4.3 together with similar data for 3-nitroveratrole and 4-nitroveratrole. A rate profile is shown in Fig. 4.4 and data for mesitylene and benzene are also shown.

4.32 YIELDS OF NITRO COMPOUNDS

An example of the method for calculating the yield of nitro compounds from the nitration of veratrole in 78.8% sulphuric acid is given below:

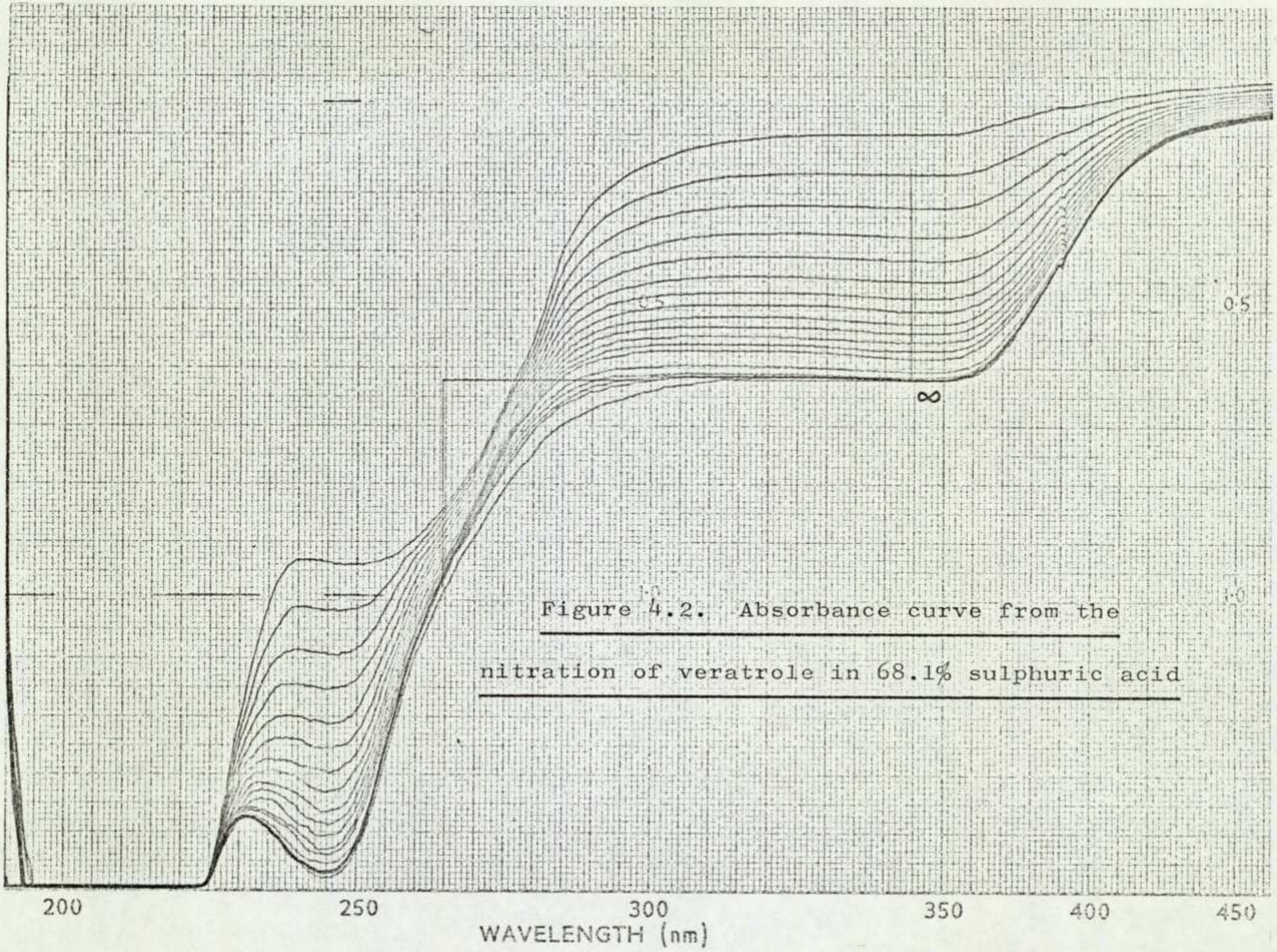


Figure 4.2. Absorbance curve from the nitration of veratrole in 68.1% sulphuric acid

Table 4.2

Data from a typical determination of the rate of nitration of veratrole in 68.1% sulphuric acid at 25.0 ± 0.2°

Time (t) /s	Absorbance (A_t)	($A_\infty - A_t$)	$\log_{10}(A_\infty - A_t)$
30	0.20	0.42	-0.3767
165	0.27	0.35	-0.4559
296	0.325	0.295	-0.5302
428	0.375	0.245	-0.6108
559	0.415	0.205	-0.6882
690	0.45	0.17	-0.7696
819	0.48	0.14	-0.8539
946	0.50	0.12	-0.9208
1034	0.52	0.10	-1.0000
1204	0.54	0.08	-1.0969
1359	0.555	0.065	-1.1871
1515	0.57	0.05	-1.3010
1670	0.58	0.04	-1.3979
	0.62 (A_∞)		

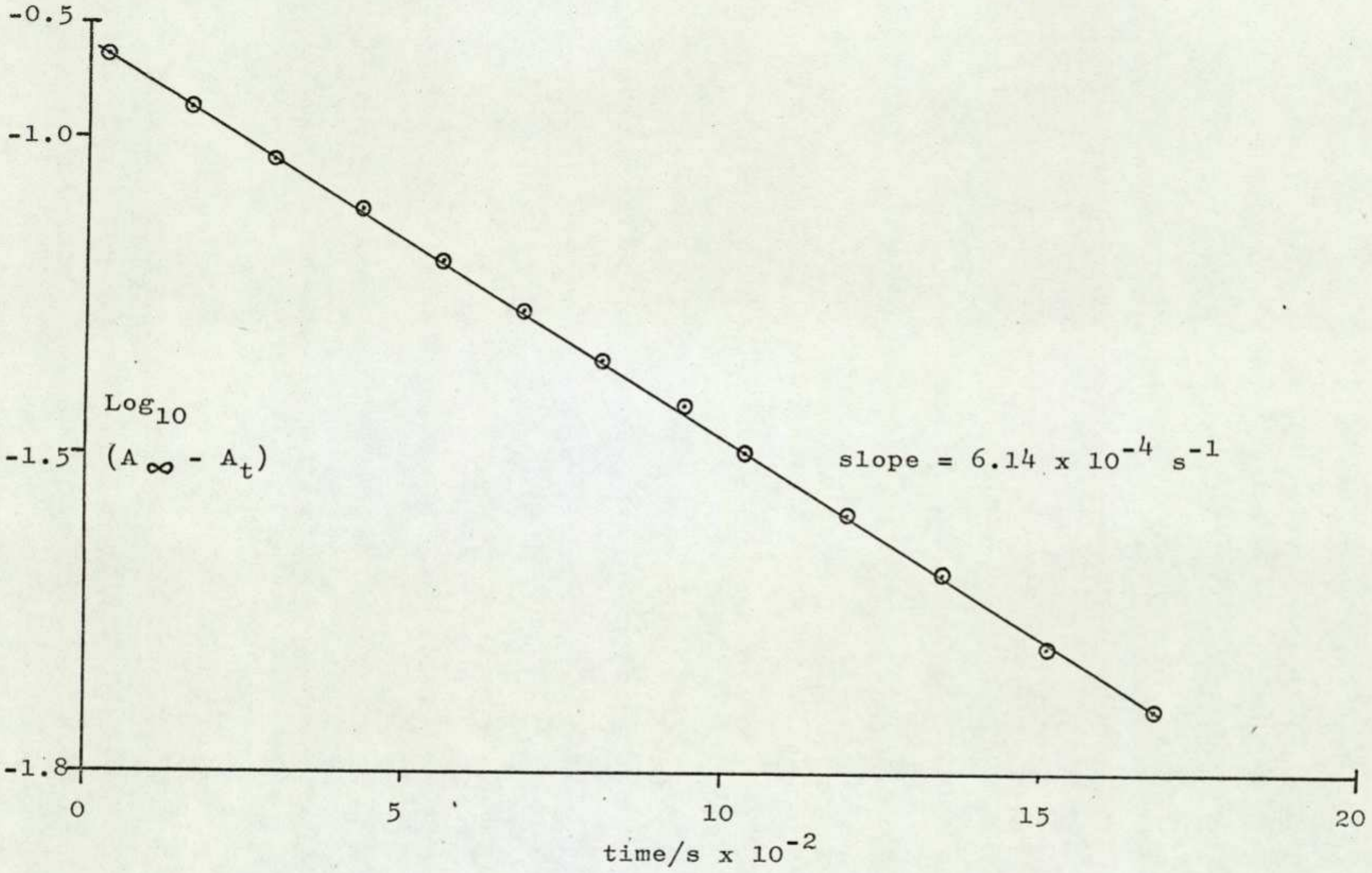


Figure 4.3. Plot of $\log_{10}(A_\infty - A_t)$ vs time from the nitration of veratrole in 68.1% sulphuric acid

Table 4.3

Second-order rate coefficients for nitration in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[c]	$[HNO_3]/10^{-2}$ mole dm^{-3}	$k_2(obs)/dm^{-3}$ $mole^{-1}$ s^{-1}
	Veratrole[a,b]	
60.2[d]	1.28	8.84×10^{-3}
60.2[d]	5.5	9.31×10^{-3}
60.2[d]	5.5	1.00×10^{-2}
60.0[d]	5.5	8.21×10^{-3}
60.0[d]	5.5	7.83×10^{-3}
60.0[d]	5.5	9.81×10^{-3}
63.7[e]	0.089	9.01×10^{-2}
63.7[d]	0.39	7.65×10^{-2}
63.8[d]	5.5	7.51×10^{-2}
63.8[d]	5.5	7.34×10^{-2}
63.8[d]	5.5	7.20×10^{-2}
65.9[e]	0.089	3.61×10^{-1}
66.1[d]	0.089	2.99×10^{-1}
66.1[d]	0.39	3.36×10^{-1}
66.5[d]	0.39	4.02×10^{-1}
68.0[e]	0.089	1.52

Table 4.3 (continued)

H_2SO_4 (%)[c]	$[HNO_3]/10^{-2}$ mole dm^{-3}	k_2(obs)/dm^{-3} mole^{-1} s^{-1}
	Veratrole[a,b]	
68.0[e]	0.089	1.55
68.0[e]	0.089	1.34
68.0[e]	0.089	1.40
68.1[d]	0.089	1.70
68.4[d]	0.66	1.57
68.4[d]	0.66	1.64
68.4[d]	0.66	1.53
68.4[d]	0.66	1.75
70.4[e]	0.046	5.81
70.4[e]	0.046	5.83
70.4[d]	0.046	6.48
70.6[e]	0.089	5.6
72.0[e]	0.030	17.7
72.0[e]	0.030	18.9
72.0[e]	0.030	17.6
72.0[d]	0.030	20.0
72.5[e]	0.030	27.2
74.1	0.030	75.3
74.1	0.030	78.8
74.1	0.030	74.0

Table 4.3 (continued)

H_2SO_4 (%)[c]	$[HNO_3]/10^{-2}$ mole dm^{-3}	k_2(obs)/dm^{-3} $mole^{-1}$ s^{-1}
	3-Nitroveratrole[f,g]	
79.5[e]	5.5	5.2×10^{-3}
	4-Nitroveratrole[f,g]	
79.5[e]	5.5	7.7×10^{-3}

a) [ArH] <u>ca</u> 3 - 6 x 10^{-5} mole dm^{-3}

b) Measurement at 350 nm.

c) ± 0.1%

d) [Sulphanilic acid] <u>ca</u> 1 x 10^{-2} mole dm^{-3}

e) [Urea] <u>ca</u> 3 x 10^{-2} mole dm^{-3}

f) [ArH] = 3.1 x 10^{-5} mole dm^{-3}

g) Measurement at 270 nm.

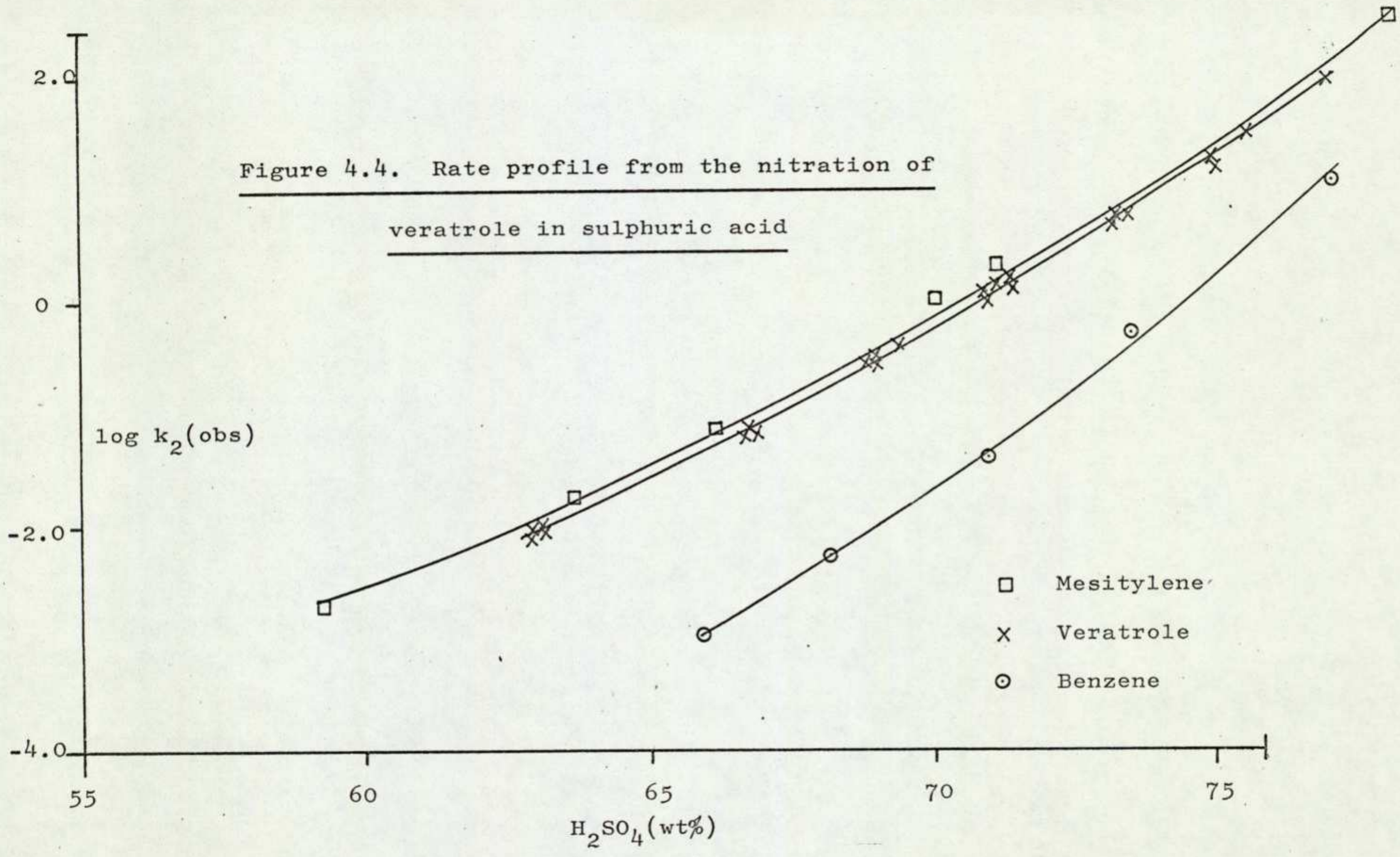


Figure 4.4. Rate profile from the nitration of veratrole in sulphuric acid

Sulphuric acid	78.8%
Amount of veratrole	5.72×10^{-5} moles
Amount of HNO_3	5.72×10^{-5} moles
Amount of reference standard p-chloronitrobenzene	1.12×10^{-5} moles

The reaction was carried out in 260cm^3 of sulphuric acid. Fig. 4.5 shows the chromatogram obtained (g.l.c. conditions as Table 4.1 Section 4.23).

Peak areas from Fig. 4.5

	Area/mm^2
Veratrole	51
4-Nitroveratrole	262
p-Chloronitrobenzene	1166

From Section 7.5 $\frac{c_x}{c_s} = \frac{A_x}{A_s} \times f$

Factor f for veratrole = 0.98

Factor f for 4-nitroveratrole = 1.14

$$\text{Amount of veratrole} = \frac{51}{262} \times 1.12 \times 10^{-5} \times 0.98 \text{ moles}$$

$$= 2.12 \times 10^{-6} \text{ moles}$$

$$= \frac{2.12 \times 10^{-6} \times 100}{5.8 \times 10^{-5}} \ \%$$

Amount of veratrole = 3.6%

$$\text{Amount of 4-nitroveratrole} = \frac{1166}{262} \times 1.12 \times 10^{-5} \times 1.14 \text{ moles}$$

$$= 5.64 \times 10^{-5} \text{ moles}$$

$$= \frac{5.64 \times 10^{-5}}{5.8 \times 10^{-5}} \times 100\%$$

Yield of 4-nitroveratrole = 97.2%

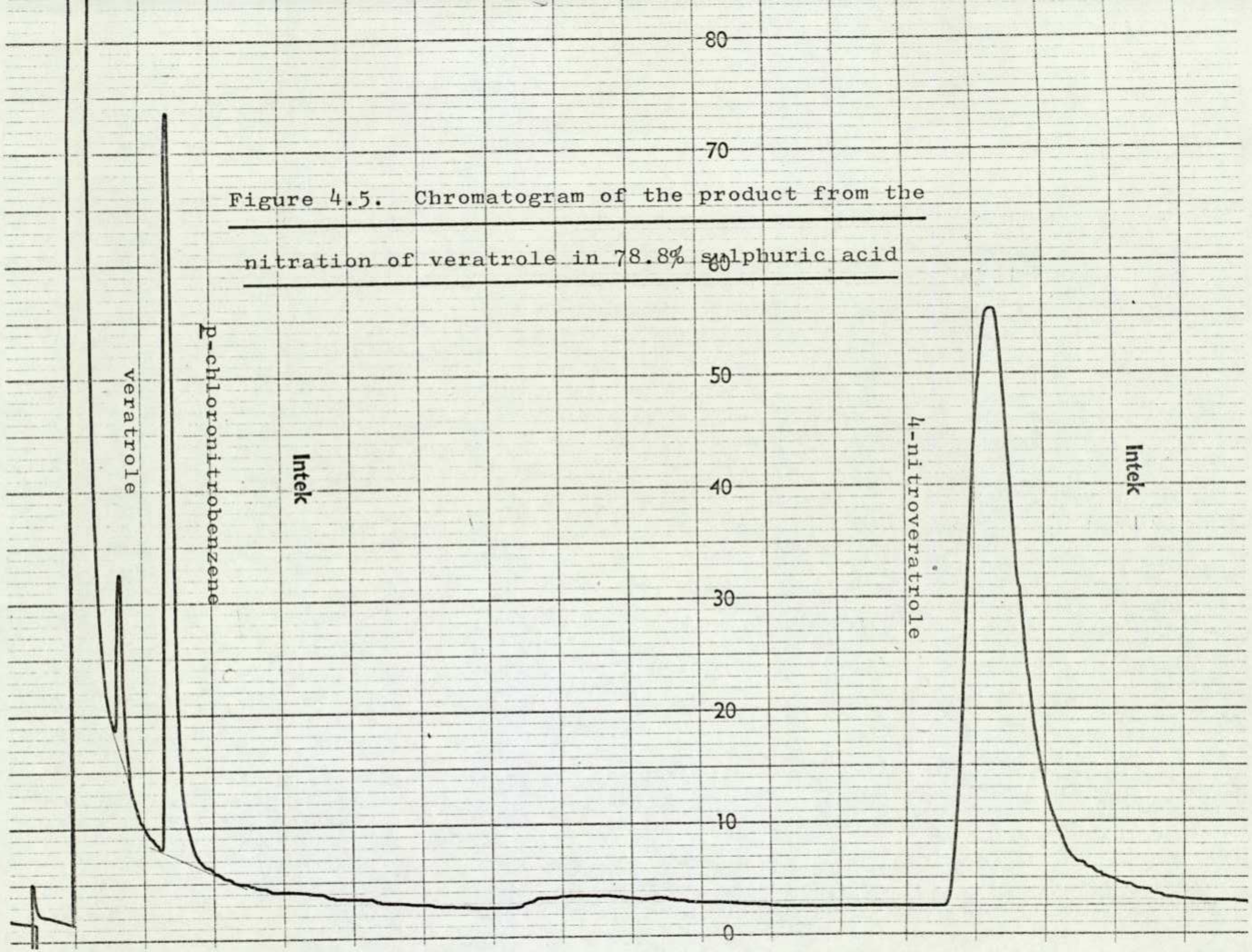


Figure 4.5. Chromatogram of the product from the nitration of veratrole in 78.8% sulphuric acid

Table 4.4

Yield of 4-nitroveratrole from the nitration of veratrole[a,b] in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[h]	Amount of veratrole recovered moles x 10^{-5}	Amount of 4-nitroveratrole found/ moles x 10^{-5}	Mass Balance
60.1[c,d]	-	1.56	99
60.1[c,d]	-	1.57	100
60.1[c,e]	0.07	1.41	99
63.8[c,d]	-	1.56	99
63.8[c,d]	0.04	1.53	99
63.8[c,e]	0.07	1.41	99
66.5[c,d]	0.10	1.43	97
66.5[c,d]	0.05	1.50	98
66.5[c,e]	0.07	1.33	95
68.4[c,d]	0.05	1.47	96
68.4[c,d]	0.08	1.47	98
70.6[f,d]	0.03	1.47	95
70.6[f,d]	-	1.50	95
70.6[f,d]	0.06	1.49	98
72.5[f,d]	-	1.49	95

Table 4.4 (continued)

H_2SO_4 (%)[h]	Amount of veratrole recovered moles x 10^{-5}	Amount of 4-nitroveratrole found/ moles x 10^{-5}	Mass Balance
72.5[f,d]	-	1.55	98
72.5[f,d]	-	1.56	99
73.9[c,d]	0.05	1.43	93
73.9[c,d]	-	1.47	93
73.9[c,d]	0.10	1.44	97
73.9[c,d]	0.03	1.47	95
78.8[c,g]	0.20	5.64	102
82.5[c,g]	0.06	5.66	100
83.3[c,g]	-	5.74	100
85.3[c,g]	0.11	4.30	77
86.3[c,g]	0.21	3.85	71
87.8[c,g]	0.12	3.02	55
90.8[c,g]	0.20	2.73	51

a) Reactions carried out in $260 cm^3$ of sulphuric acid

b) $HNO_3 = 5.2 \times 10^{-5} - 1.43 \times 10^{-2}$ moles

c) $\left[\text{Sulphanilic acid}\right]$ ca 1×10^{-2} mole dm^{-3}

d) $ArH = 1.58 \times 10^{-5}$ moles

e) $ArH = 1.48 \times 10^{-5}$ moles

f) $\left[\text{Urea}\right]$ ca 3×10^{-2} mole dm^{-3}

g) $ArH = HNO_3 = 5.72 \times 10^{-5}$ moles

h) ± 0.1%

Table 4.4 gives the yield of 4-nitroveratrole and the amount of unreacted veratrole from the nitration of veratrole in various concentrations of sulphuric acid.

3-Nitroveratrole was not found, but had there been greater than 0.2% it would have been detected. Above 83.0% sulphuric acid the yield was not quantitative. 3- and 4-Nitroveratrole were, however, recovered quantitatively (99.3% and 99.6% respectively) by the normal extraction method, described in Section 7.41, from their solution in 87.8% sulphuric acid which had been kept at 25.0° for 40 mins.

4.4 DISCUSSION

4.41 RATE PROFILE

The rate profile for veratrole falls slightly below and parallel to that for mesitylene, see Fig. 4.4, which is similar to that noticed for anisole, phenol, (see Section 2.4) p-methylanisole, and p-cresol (see Section 3.4). It is believed that a common explanation holds for this type of rate profile (see Section 2.4).

4.42 ISOMER PROPORTIONS

In the acidity range 60 - 90% sulphuric acid, under conditions where nitrosation was precluded, only 4-nitroveratrole was obtained and the yield was quantitative in the acidity range 60 - 84% sulphuric acid. This situation, where only 4-substitution was found, was unexpected and might be due to either of the following or their combined effect:-

a) steric hindrance of the 3-position due to some interaction between the two methoxyl groups

b) the effects of hydrogen bonding

If, as is believed to occur with anisole and phenol, the initial encounter involves a hydrogen bonded species ($H_3O^+ \ldots V$), but unlike anisole and phenol, Wheland intermediate formation occurs directly from the hydrogen bonded encounter pair ($H_3O^+ \ldots V.NO_2^+$) at all acidities (due to possibly the greater hydrogen bonding capability of veratrole), it is not unreasonable that predominantly 4-substitution would occur (see Scheme 4.2) for electrostatic reasons. If this is the correct explanation for the lack of 3-substitution in veratrole, it follows either that in anisole and phenol reaction via ($H_3O^+ \ldots A.NO_2^+$) is incomplete, even at the highest acidities studied, or that with veratrole there is a special hindrance of the 3-position due to the mutually adjacent methoxyl groups.

$$\begin{tikzcd}
NO_2^+ + V.....xH_3O^+ \arrow[r, rightleftharpoons] & (NO_2^+.V.....xH_3O^+) \arrow[r, "\times" description] \arrow[d, leftrightarrows, "\times" description] \arrow[dr] & W_3 \\
 & (NO_2^+.\ V) + xH_3O^+ & W_4 \arrow[r] & \text{4-nitroveratrole}
\end{tikzcd}$$

Scheme 4.2

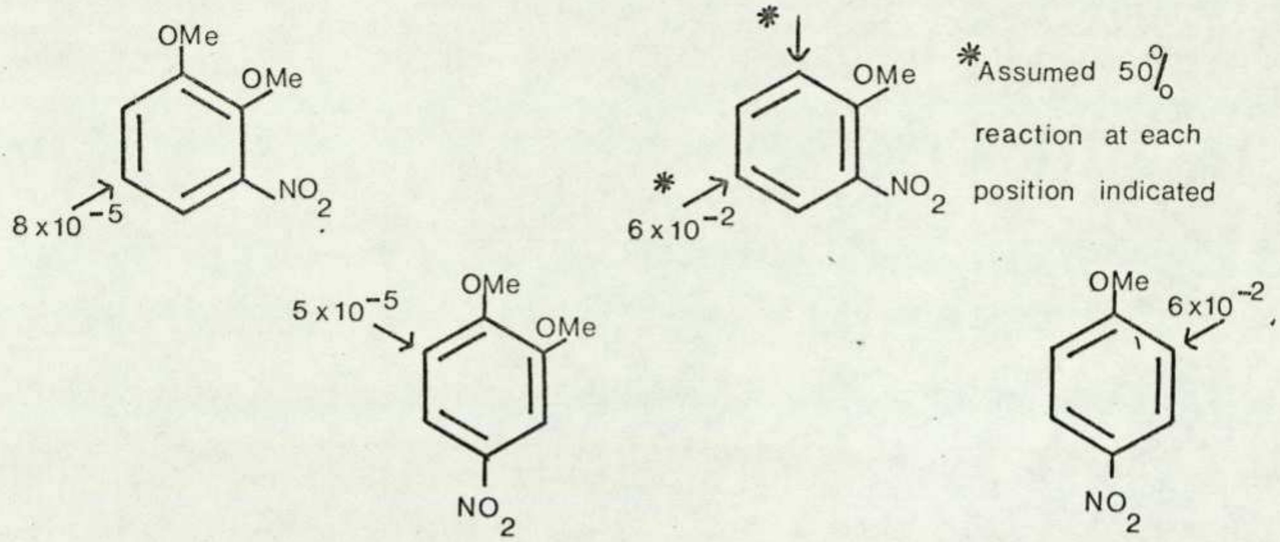
Regarding the drop in yield observed for nitration carried out in $>$ 84% sulphuric acid, as for the anisoles and phenols (Sections 2.4 and 3.3) the estimated half-life for nitration, the rate of which should obey a first-order law at these acidities[28] (see Section 2.4), is about 10^4 times smaller than the measured half-life for the sulphonation[89] of veratrole in 89% sulphuric acid ($t_{\frac{1}{2}} \simeq 69$s). Sulphonation does, however, prevent the study of the rates of possible demethylation at the highest acidities, but since demethylation is insignificant at 83% sulphuric acid (see Table 4.4) it is unlikely that it could become faster than the estimated rate of nitration ($t_{\frac{1}{2}} \simeq 4 \times 10^{-3}$ s) in 89% H_2SO_4. Demethylation of the mono-nitro compounds also does not occur, as quantitative recovery of 3- and 4-nitroveratrole was found to be possible from 88% sulphuric acid. Product studies at high acidities, i.e.

74% sulphuric acid, were performed with equimolar proportions of reactants to prevent problems due to dinitration. Extrapolation from the rates of nitration of 3- and 4-nitroveratrole in Table 4.3, suggest that k_2(obs) $\simeq 14$ dm^3 mole^{-1} s^{-1} in 89% sulphuric acid, and hence the half-life of reaction will be about 4 minutes. This indicates that the rate of dinitration is too slow to interfere in the mononitration of veratrole. The observed rates of nitration of the nitro-veratroles are surprizingly low compared with rates of nitration of the nitroanisoles (see Table 4.5). The anomaly can be illustrated by the comparison of partial rate factors (Scheme 4.3) on the assumption that reaction occurs at the positions indicated for the nitroveratroles, as might be conventionally expected.

Table 4.5

Extrapolated rates of nitration in 89% sulphuric acid

Compound	k_2(obs)/dm^3 mole^{-1} s^{-1}
3-Nitroveratrole	20
4-Nitroveratrole	14
2-Nitroanisole	3×10^4
4-Nitroanisole	3×10^4
4-Methyl-2-nitroanisole	5.6×10^5
4-Methyl-3-nitroanisole	1×10^3
Benzene	1.6×10^6



Scheme 4·3

The σ^{+}_{m} value[87] for a *m*-methoxyl is +0.05, and it should therefore have only a small deactivating effect. In the case of 4-nitroveratrole the substitution is again at a position *ortho* to two methoxyl groups and it is perhaps relevant that Robinson gives the products of this reaction as the unexpected 4,5-dinitroveratrole. The anomaly however persists with 3-nitroveratrole.

CHAPTER 5

THE NITRATION OF BIPHENYL AND OF DIPHENYLMETHANE

5.1 INTRODUCTION

In the study of nitration reactions some of the most controversial and puzzling results have been obtained from the nitration of biphenyl. The o:p- ratio has been found to vary considerably with the conditions of nitration, and no satisfactory explanation has been offered despite the large amount of work carried out. A summary of the results previously obtained is given in Table 5.1.

In 1966 Taylor[107] investigated the nitration of biphenyl in several solvent systems:-

a) Sulphuric acid - nitric acid mixtures:- The o:p-ratio was found to be 1.4 at 0°C but dropped to 0.6 at 30°C and then remained constant up to 70°C.

b) Sulphuric acid - nitric acid mixtures with nitrobenzene:- The o:p-ratio was found to be constant at 0.7 over the range 0 - 70°C.

c) Nitric acid in acetic anhydride:- An o:p-ratio of 2.0 - 2.7 was found, in the range -40 - 25°C.

d) Dinitrogen pentoxide in acetonitrile:- An o:p-ratio of 2.6 - 2.8 was obtained, in the range -20 - 25°C.

e) Nitric acid in Analar acetic acid:- The o:p-ratio was found to be 0.7 - 1.40.

From these data Taylor concluded that an o:p-ratio of ~ 0.6 for nitration in sulphuric acid arose from an essentially homogeneous reaction and that the higher o:p-ratio at lower temperatures were due to an increasing amount of heterogeneous reaction. Thus the low o:p-

Table 5.1

Variation in the o:p-ratio for the nitration of biphenyl

Reagent	Temp/^{o}C	o:p-ratio	Ref.
HNO_3 - Ac_2O	85 - 90	0.6	108
HNO_3 - Ac_2O	0	3.35	109
HNO_3 - Ac_2O	0	2.25	110
HNO_3 - AcOH	0	1.81	110
1:5 HNO_3 - H_2SO_4 in $PhNO_2$	0	0.73	110
HNO_3 - H_2SO_4 (heterogeneous)	35	0.76	110
HNO_3 - Ac_2O	0 - 18	2.3	111
HNO_3 - AcOH	85 - 90	0.6	111
HNO_3 - AcOH	25	0.7 - 1.4	107
HNO_3 - Ac_2O	-40	2.7	107
	0	2.2	107
	25	2.0	107
N_2O_5 - MeCN	-20	2.8	107
	0	2.7	107
	25	2.6	107

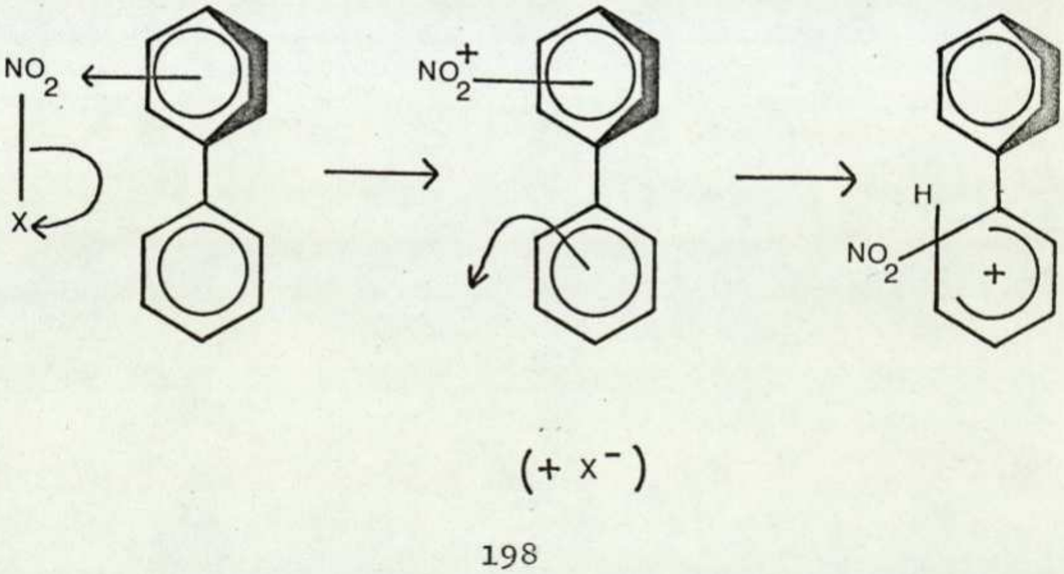
Table 5.1 (continued)

Reagent	Temp/^oC	o:p-ratio	Ref.
$NO_2^+ BF_4^-$ in sulpholane	10	2.0	107
	20	1.8	107
	60	1.2	107
$HNO_3 - H_2SO_4$ in $PhNO_2$	0	0.7	107
	25	0.7	107
	40	0.7	107
	70	0.7	107
$HNO_3 - H_2SO_4$	0	1.4	107
	18	1.2	107
	25	0.8	107
	30	0.6	107
	40	0.6	107
	50	0.6	107
	70	0.6	107
57.1% H_2SO_4 - 5×10^{-2} mole dm^{-3} HNO_3 (urea present)	25	3.7 ± 0.6	34
68.3% H_2SO_4 - 2×10^{-3} mole dm^{-3} HNO_3 (urea present)	25	3.3 ± 0.6	34

Table 5.1 (continued)

Reagent	Temp/°C	*o*:*p*-ratio	Ref.
dil. HNO_3 - H_2SO_4 (HNO_3 prepared from HNO_3 d.1.42)		1.4	113
dil. HNO_3 - H_2SO_4 (HNO_3 prepared from fuming HNO_3)		0.7 - 0.8 *ca*	112

ratio obtained in sulphuric acid seemed to be the normal mode of orientation, derived from attack by the nitronium ion. The outstanding problem was to deduce the nature of the nitrating entity in nitric acid - acetic anhydride which results in a high *o*:*p*-ratio. From the similarity of the results obtained using solutions prepared from nitric acid and acetic anhydride and solution of dinitrogen pentoxide in acetonitrile, and in the light of evidence for protonated acetyl nitrate being the electrophile in other systems, Taylor argued that nitration with the nitronium ion gave low *o*:*p*-ratios, whilst reagents of the type NO_2X (e.g. protonated acetyl nitrate or dinitrogen pentoxide) gave a high *o*;*p*-ratio. A special mechanism was proposed, in which the π electrons of the (subsequently) unsubstituted ring carry out nucleophilic displacement of X from NO_2X to give a π - complex involving NO_2^+. The most accessible ring position for subsequent σ -complex formation is then the *ortho*-position of the uncomplexed ring in view of the non-coplanarity of the phenyl rings.



In this way both reagents would give rise to enhanced ortho-substitution and the observed o:p- ratio would depend upon the relative proportion of nitration by this mechanism and by the nitronium ion mechanism.

Certain objections can be raised to this approach. Firstly, for nitration by nitric acid in acetic acid it has not been necessary in any other case, to postulate the efficacy of a nitrating electrophile other than the nitronium ion.

Secondly, the idea was consistent with the theory that rate determining π -complex formation occurred for nitrations of substrates of this reactivity in these systems[33b]. It is less consistent with the interpretation [33c] that partial diffusion control of reaction rates is responsible for results which were, at first sight, anomalous. Why should such a mechanism not also apply to the more electrophilic nitronium ion and why do other substrates of comparable aromatic reactivity show no signs of reacting with the electrophile $\dot{NO_2}$-X?

In 1971 Coombes and Russell[34] investigated the nitration of biphenyl in solutions of sulphuric acid, and observed an o:p-ratio of ∼3.5 under 'homogeneous' conditions where the effective species is known to be the nitronium ion. It was suggested that the previously reported low o:p-ratios found in this medium could be due to nitration via nitrosation, where enhancement of the para-isomer would be expected to occur. The implications of this work are that a high o:p-ratio for the nitration of biphenyl is normal, and, therefore, the special mechanism previously given is not necessary to account for the results obtained in acetic anhydride and other media.

In 1972 Taylor[112] attempted to repeat the work of Coombes and Russell. The high o:p-ratio was confirmed, but he was unable to prepare solutions of the required concentration of biphenyl, even after stirring for 24 hours at 25°C, and, therefore, suggested that nitration under the conditions described by Coombes and Russell was a heterogeneous reaction. Taylor also confirmed that the low o:p-ratio he had previously observed (with added $PhNO_2$) was due to nitration via nitrosation, but was unable to raise the o:p-ratio above 1.4. He concluded that the results of Coombes and Russell did not reflect normal nitration of biphenyl by the nitronium ion, being most probably 'vitiated by problems of encounter control' and that a special mechanism for ortho-substitution in acetonitrile and acetic anhydride was still necessary.

The $f_o : f_p$ ratios for the hydrogen-exchange reactions of biphenyl decrease with increasing f_p, the values varying from 1.0 (when $f_p = 52$) to 0.19 (when $f_p = 2800$)[114]. The trend has been interpreted in that the more selective the reagent, the more important is the difference in the stabilities of the Wheland intermediates for ortho- and para-substitution, the latter being the more stable. It has been suggested that even with the most unselective electrophiles the ratio will not rise above the statistical value of 1[114]. *Ipso*-substitution has been recently suggested as a possible explanation of the anomalies[119].

Nitration of diphenylmethane in acetic anhydride[115] has been found to yield the 2- and 4-nitro-isomers and the partial rate factors have been determined as $f_o = 13$ and $f_p = 32$. The rate of nitration relative to benzene has been found to be 19.5[40]. The benzyl group appears to be marginally less activating than the methyl group. Gehring and Reddy[116] studied the nitration of diphenylmethane with nitric acid, and were able to identify six products using ^{1}H n.m.r. Their results are summarised in Table 5.2.

This chapter is concerned with a reinvestigation and considerable extension of the earlier work[34] on biphenyl, and a preliminary study of the nitration of diphenylmethane.

5.2 EXPERIMENTAL

5.21 MATERIALS

These were as described in Section 7.2 with the addition of the following:- Biphenyl (bp. 254°, lit.[117] 252 - 253°) and diphenylmethane (bp. 265°, lit.[118] 264.7°) were commercial grade reagents purified by distillation. 2-Nitrobiphenyl (mp. 35°, lit.[108] 35 - 37°), 3-nitrobiphenyl (mp. 58.5°, lit.[120] 58 - 59°) and 4-nitrobiphenyl (mp. 112°, lit.[108] 114°) were commercial grade reagents purified by recrystallisation.

Table 5.2

Nitro-products from the nitration of diphenylmethane by nitric acid[116]

Compound	Mole % found
Diphenylmethane	1 - 2
4-Nitrodiphenylmethane	1 - 2
4,4′-Dinitrophenylmethane	20
2,4′-Dinitrophenylmethane	25
2,2′,4-Trinitrodiphenylmethane	22
2,2′,4,4′-Tetranitrodiphenylmethane	4
2,4,4′-Trinitrodiphenylmethane	27

No 2-nitrodiphenylmethane or 2,2′-dinitrodiphenylmethane was detected

5.22 KINETIC MEASUREMENTS

For both biphenyl and diphenylmethane these were as described in Section 7.3.

5.23 PRODUCT ANALYSIS

5.231 BIPHENYL

The conventional g.l.c. method as described in Sections 7.41 and 7.42 was used, with the exception that one litre of sulphuric acid was used, and the reaction was terminated after 3 half-lives (87.5% reaction) as calculated from the kinetic data. Table 5.3 gives the g.l.c. conditions.

5.232 DIPHENYLMETHANE

Nitration reaction was carried out in the normal manner, as given in Sections 7.41 and 7.42, but one litre of sulphuric acid was used. Identification and estimation of the nitration products was achieved using an n.m.r. method as given by Gehring and Reddy. All spectra were recorded using a Jeol MH100 spectrometer. Product mixtures were prepared in 0.5cm^3 d_6-acetone containing 1% tetramethylsilane (T.M.S.).

5.24 SOLUBILITY OF BIPHENYL

A solution of biphenyl in acetic acid was prepared and aliquots of this were added to the appropriate concentration of sulphuric acid (25cm^3). This solution was thermostatted at 25° for 30 minutes and then its u.v. absorbance was measured over the range 190 - 390nm.

5.3 RESULTS

5.31 KINETICS

Table 5.3

G.l.c. conditions for the separation of biphenyl and 2-,3- and 4-nitrobiphenyls

Column:	1.5m x $\frac{1}{4}$" s.s. $1\frac{1}{2}$% OV225 on 60-85 mesh universal support
Oven temperature:	200 ± 0.5^{o}
Carrier gas:	Nitrogen
Flow rate:	$40cm^{3}\ min^{-1}$

Compound	Retention times /s
Biphenyl	150
2-Nitrobiphenyl	480
3-Nitrobiphenyl	732
4-Nitrobiphenyl	828
p-Dinitrobenzene (Reference standard)	282

5.311 BIPHENYL

The results and subsequent calculation required for a typical determination of a rate coefficient for the nitration of biphenyl are given below:

Sulphuric acid	70.8% (W/W)
$[HNO_3]$	8.95×10^{-4} mole dm^{-3}
[Biphenyl]	1.91×10^{-5} mole dm^{-3}
[Urea]	3×10^{-2} mole dm^{-3}
Temperature	$25.0 \pm 0.2^{\circ}$
Wavelength of measurement	250nm

Fig. 5.1 shows the absorption curve obtained, Table 5.3(i) shows the data obtained from the above nitration, and Fig. 5.2 shows a plot of $\log_{10}(A_t - A_{\infty})$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[HNO_3]} \ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

$$= \frac{2.303 \times 2.10 \times 10^{-3}}{8.95 \times 10^{-4}} \ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

$$\therefore k_2(\text{obs}) = 5.4\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

Second-order rate coefficients for the nitration of biphenyl in sulphuric acid and perchloric acid are given in Table 5.4. A rate profile is shown in Fig. 5.3 together with those for mesitylene and benzene.

5.312 DIPHENYLMETHANE

The results and subsequent calculation required for a typical determination of a rate coefficient for the nitration of diphenylmethane are given below:-

Sulphuric acid	68.3% (W/W)

$[HNO_3]$	8.95×10^{-4} mole dm^{-3}
$[\text{Diphenylmethane}]$	4.93×10^{-5} mole dm^{-3}
$[\text{Urea}]$	3×10^{-2} mole dm^{-3}
Temperature	$25.0 \pm 0.2^\circ$
Wavelength of measurement	273nm.

Table 5.5 shows the data obtained from the above nitration. Fig. 5.4 shows a plot of $\log_{10}(A_\infty - A_t)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{HNO_3}\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

$$= \frac{2.303 \times 5.16 \times 10^{-5}}{8.95 \times 10^{-4}}\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

$$\therefore k_2(\text{obs}) = 0.13\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

Second-order rate coefficients for the nitration of diphenylmethane at various percentages of sulphuric acid are given in Table 5.6. A rate profile is shown in Fig. 5.5 together with those for mesitylene and benzene.

5.32 SOLUBILITY OF BIPHENYL

Solutions of different concentrations of biphenyl in sulphuric acid (25cm^3) were prepared by addition of different amounts of substrate solution in acetic acid. The u.v. absorbances at 250 and 350nm. were measured. Tables 5.7(i), (ii) and (iii) give these and Fig. 5.6 shows the Beer's Law plot obtained from the mean value of the three sets of data. This plot was linear to 4.0×10^{-5} mole dm^{-3} and in the region $4 - 5 \times 10^{-5}$ mole dm^{-3} the substrate began to fail to dissolve. In the region 7.5×10^{-5} mole dm^{-3} the solution became misty as observed

Figure 5.1. Absorbance curve from the nitration of biphenyl in 70.8% sulphuric acid

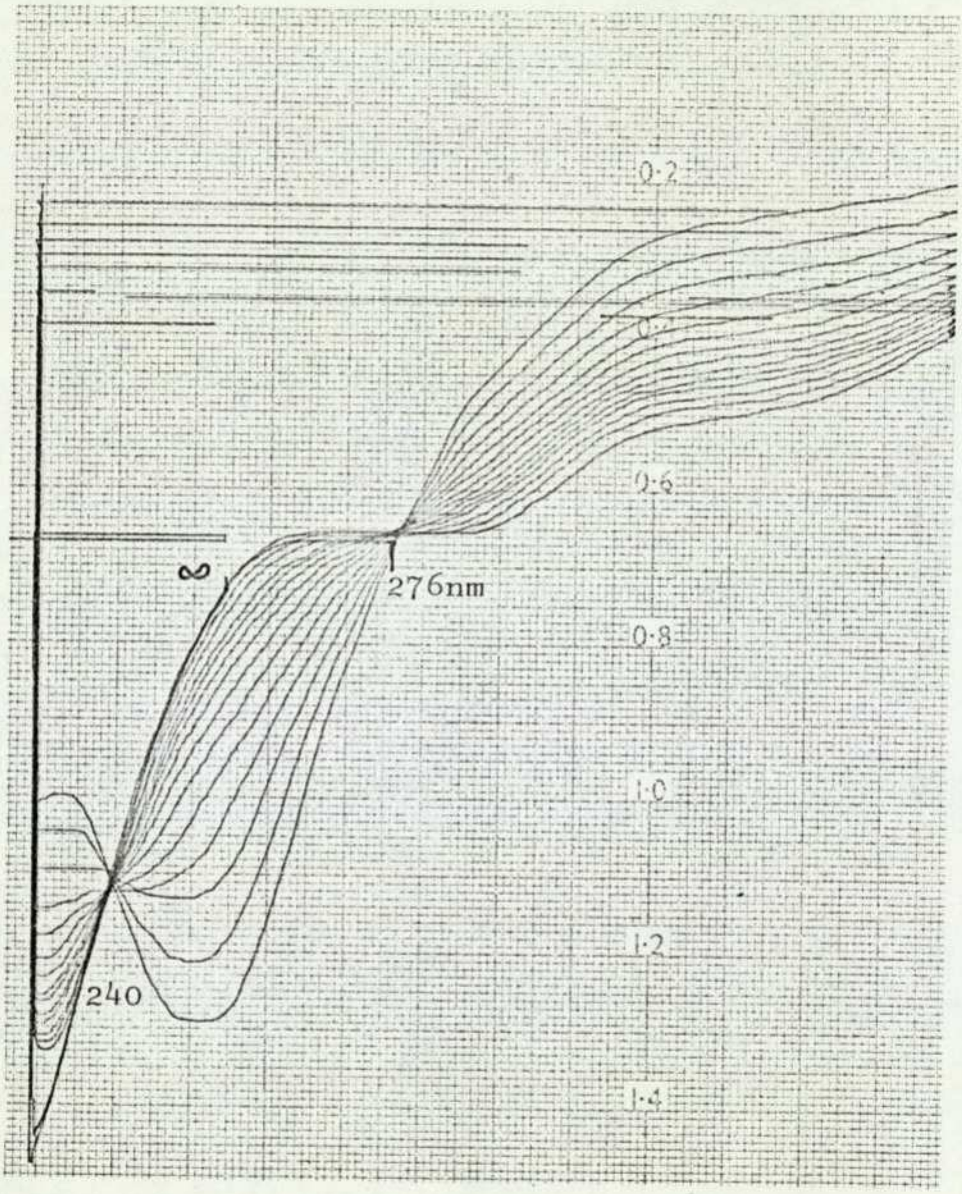


Table 5.3(i)

Data from a typical determination of the rate of nitration of biphenyl in 70.8% sulphuric acid at $25.0 \pm 0.2^\circ$

Time (t) /s	Absorbance (A_t)	(A_t-A_∞)	Log_{10}(A_t-A_∞)
30	1.29	0.49	-0.309
75	1.21	0.41	-0.387
118	1.13	0.33	-0.482
163	1.09	0.29	-0.538
206	1.03	0.23	-0.638
250	0.98	0.18	-0.745
295	0.94	0.14	-0.854
338	0.91	0.11	-0.959
382	0.89	0.09	-1.046
427	0.87	0.07	-1.260
471	0.855	0.055	-1.260
	0.80(A_∞)		

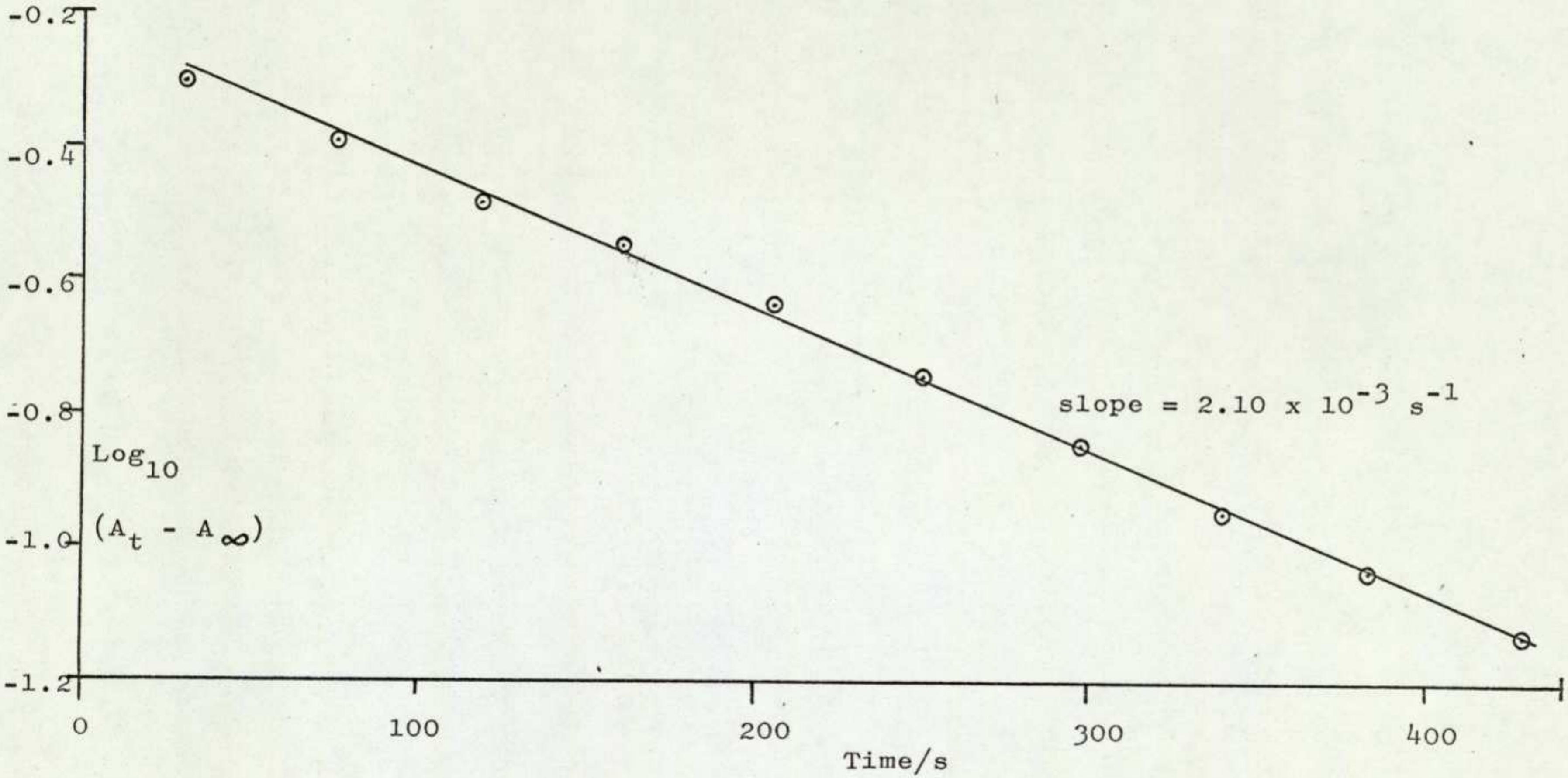


Figure 5.2. Plot of $\log_{10}$ (A_t - A_∞) vs time from the nitration of biphenyl in 70.8% sulphuric acid

Table 5.4

Second-order rate coefficients for the nitration of biphenyl at 25.0 ± 0.2°

H_2SO_4 (%)	$[HNO_3]$/ 10^{-2} mole dm^{-3}	$k_2(obs)$ /dm^3 $mole^{-1}$ s^{-1}
$56.0^{d,e}$	5.5	3.1×10^{-3}
60.3^{b}	5.5	2.2×10^{-3}
61.0^{e}	5.5	4.1×10^{-3}
61.0^{e}	5.5	3.9×10^{-3}
61.0^{e}	5.5	4.2×10^{-3}
62.5^{f}	5.5	7.4×10^{-3}
63.1^{b}	5.5	1.4×10^{-2}
63.7^{e}	5.5	1.9×10^{-2}
63.7^{e}	5.5	1.9×10^{-2}
63.7^{e}	5.5	2.1×10^{-2}
65.7^{e}	0.32	0.1
65.7^{e}	2.3	9.5×10^{-2}
65.7^{e}	2.3	8.9×10^{-2}
65.9^{f}	5.5	0.12
68.3^{c}	0.2	0.93

Table 5.4 (continued)

	H_2SO_4 (%)	$[HNO_3]$/ 10^{-2} mole dm^{-3}	k_2(obs) /dm^3 $mole^{-1}$ s^{-1}
	68.3^b	0.09	0.92
	68.7^e	0.17	1.20
	68.7^e	0.17	1.18
	68.7^e	0.17	1.17
	70.6^f	0.09	5.7
	70.8^e	0.09	5.6
	70.8^e	0.09	5.9
	70.8^e	0.09	5.5
	72.6^e	0.05	23.1
	72.6^e	0.05	22.8
	72.6^e	0.05	25.4
$HClO_4$	60.0^e	0.09	0.45
	62.2^e	0.09	3.9

a) [Urea] *ca* 3 x 10^{-2} mole dm^{-3}. Measurement at 250nm an isosbestic point for dinitration[34].

b) Ref. 34

c) Ref. 22

d) At 60.0 ± 0.2°

e) [Biphenyl] = 1.9 x 10^{-5} mole dm^{-3}

f) [Biphenyl] = 3.3 x 10^{-5} mole dm^{-3}

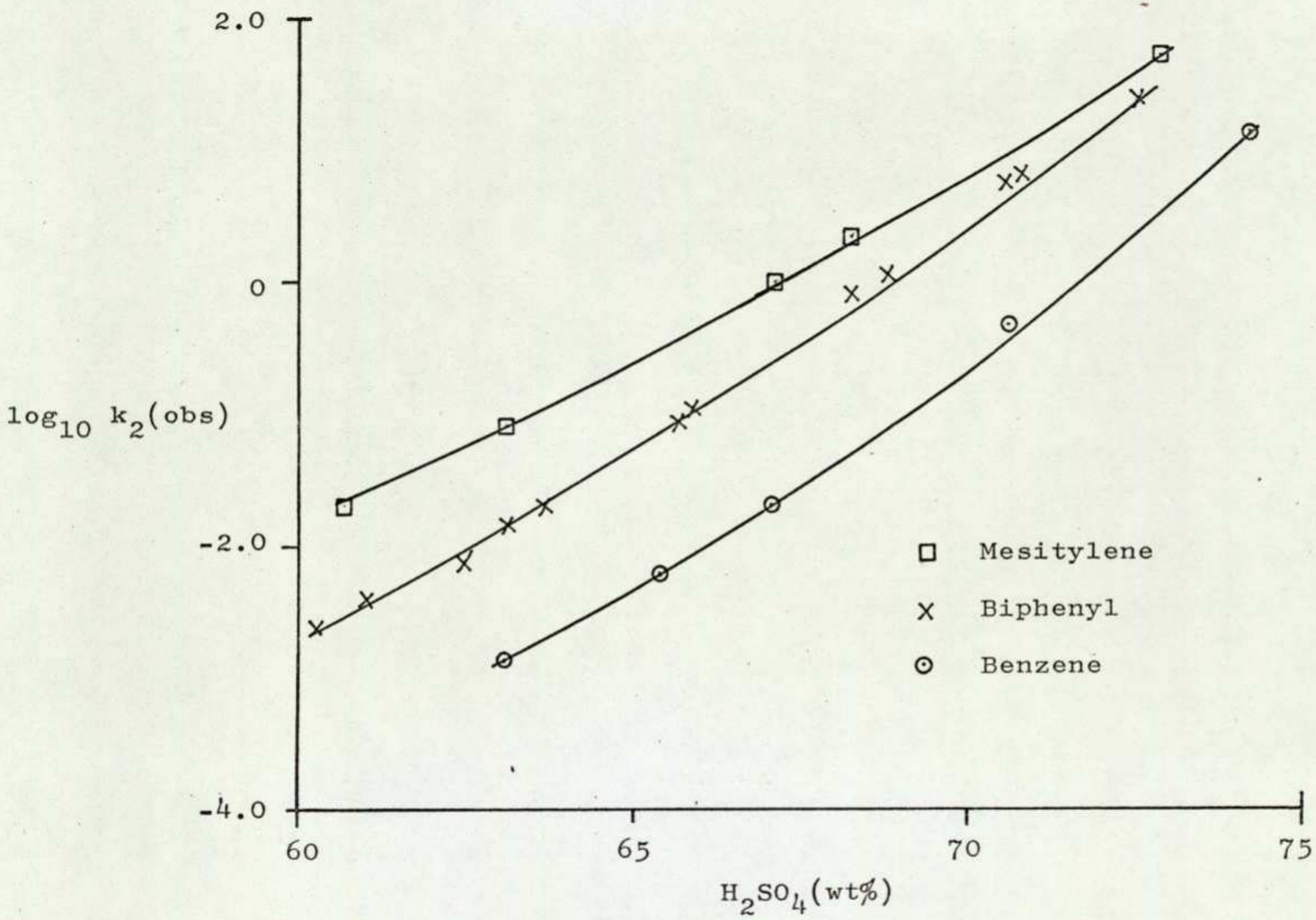


Figure 5.3. Rate profile from the nitration of biphenyl in sulphuric acid at 25°

Table 5.5

Data from a typical determination of the rate of nitration of diphenylmethane in 68.3% sulphuric acid at 25.0 ± 0.2°

Time (t) /s	Absorbance (A_t)	(A_{∞} -A_t)	$\text{Log}_{10}(A_{\infty}-A_t)$
150	0.020	0.596	-0.225
210	0.022	0.593	-0.227
270	0.029	0.586	-0.232
450	0.035	0.580	-0.237
570	0.045	0.570	-0.244
690	0.051	0.564	-0.249
990	0.070	0.545	-0.264
1290	0.093	0.522	-0.282
1590	0.103	0.512	-0.291
1890	0.123	0.492	-0.308
2490	0.163	0.452	-0.345
3090	0.205	0.410	-0.387
3690	0.237	0.378	-0.423
4860	0.280	0.335	-0.475
6090	0.330	0.285	-0.545
9090	0.405	0.210	-0.678

Table 5.5 (continued)

Time (t) /s	Absorbance (A_t)	$(A_\infty - A_t)$	$\mathrm{Log}_{10}(A_\infty - A_t)$
12090	0.468	0.147	-0.833
15210	0.510	0.105	-0.979
	0.615 (A_∞)		

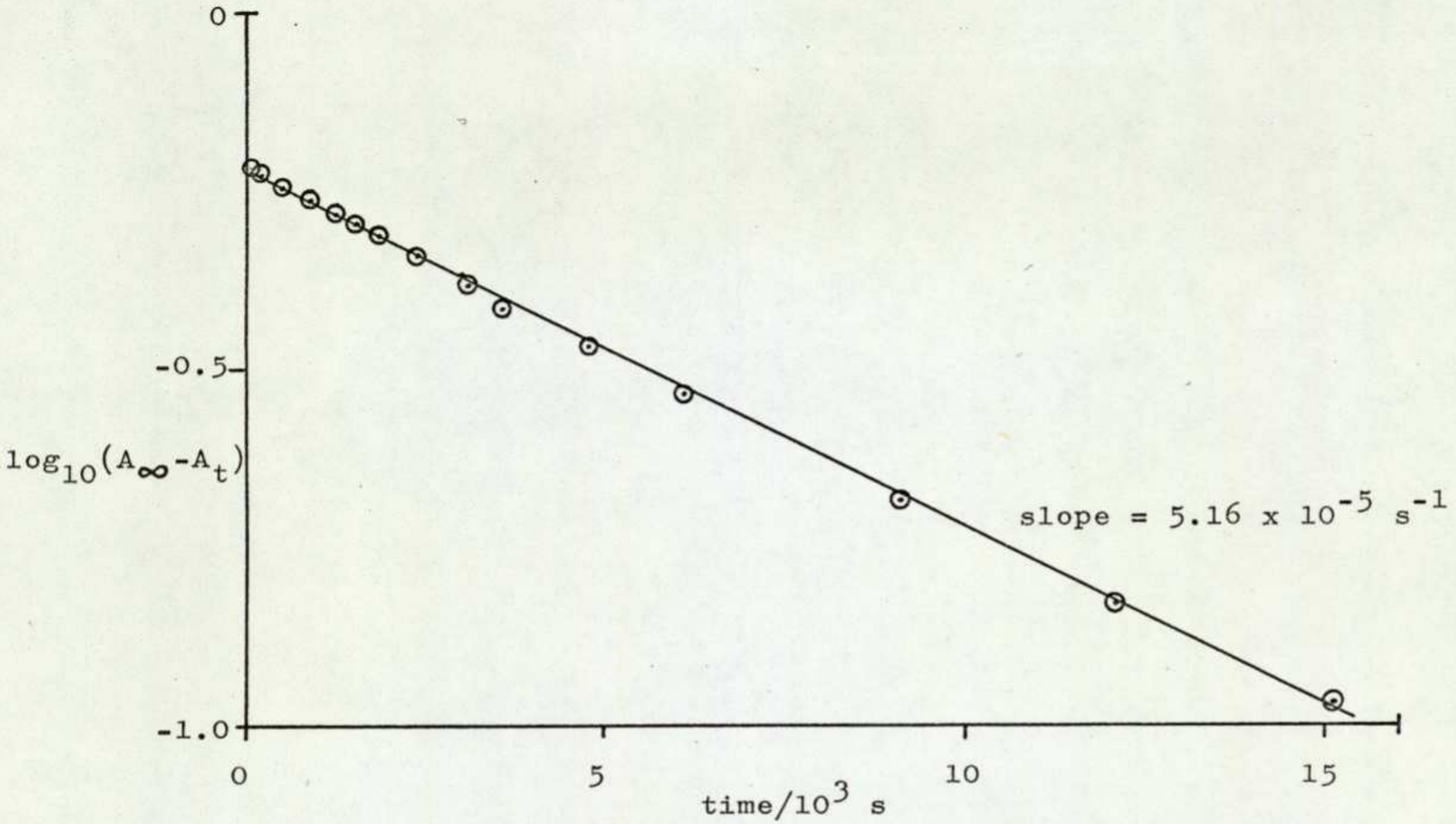


Figure 5.4. Plot of $\log_{10}$ $(A_\infty - A_t)$ vs time from the nitration of diphenylmethane in 68.3% sulphuric acid

Table 5.6

Second-order rate coefficients for the nitration of diphenylmethane[b] in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)[a]	$[HNO_3]$/ 10^{-2} mole dm^{-3}	k_2(obs) /dm^3 $mole^{-1}$ s^{-1}
60.8	5.5	5.9×10^{-4}
60.8	5.5	6.2×10^{-4}
63.2	0.77	2.5×10^{-6}
63.2	0.77	2.4×10^{-3}
66.1	0.17	0.17
66.1	0.17	0.17
68.3	0.09	0.13
68.3	0.09	0.12
70.4	0.09	0.53
70.4	0.09	0.53
72.5	0.09	2.3
72.5	0.09	2.6
74.4	0.05	13.9
74.4	0.05	13.1

a) ± 0.1%. [Urea] _ca_ 3×10^{-2} mole dm^{-3},
Measurement at 273nm.

b) [Diphenylmethane] = 4.9×10^{-5} mole dm^{-3}

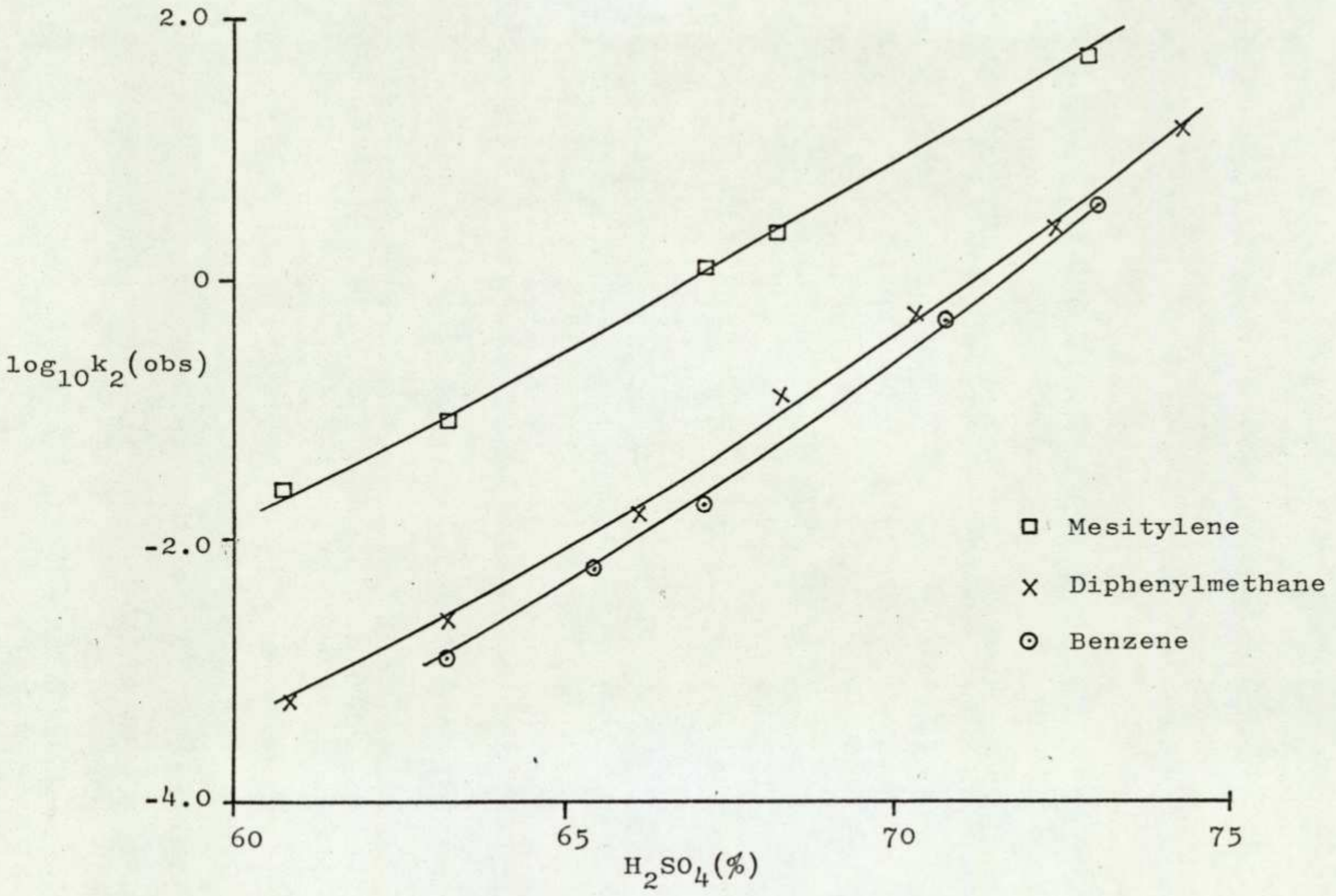


Figure 5.5. Rate profile from the nitration of diphenylmethane in sulphuric acid at 25°

Table 5.7

U.v. absorbance for various concentrations of biphenyl[a] in sulphuric acid

(i)

67.8% H_2SO_4

Biphenyl /mole dm^{-3}	Absorbance 250nm	Absorbance 350nm
1.33×10^{-6}	0.022	0.0
3.32×10^{-6}	0.035	0.0
6.63×10^{-6}	0.075	0.0
9.95×10^{-6}	0.110	0.0
1.33×10^{-5}	0.160	0.0
1.99×10^{-5}	0.235	0.0
2.65×10^{-5}	0.280	0.02
3.32×10^{-5}	0.365	0.03
4.64×10^{-5}	0.390	0.04
6.63×10^{-5}	0.425	0.05
1.33×10^{-4}	0.460	0.08
1.99×10^{-4}	0.570	0.14

Table 5.7 (continued)

(ii)

68.8% H_2SO_4

Biphenyl /mole dm^{-3}	Absorbance 250nm	Absorbance 350nm
3.32×10^{-6}	0.036	0.0
6.63×10^{-6}	0.080	0.0
9.95×10^{-6}	0.120	0.0
1.32×10^{-5}	0.165	0.0
1.99×10^{-5}	0.241	0.0
3.32×10^{-5}	0.370	0.0
6.63×10^{-5}	0.425	0.02
9.95×10^{-5}	0.440	0.04
1.32×10^{-4}	0.480	0.07
1.64×10^{-4}	0.530	0.11
	(iii)	
	70.8% H_2SO_4	
3.32×10^{-6}	0.04	0.0
6.63×10^{-6}	0.08	0.0
9.95×10^{-6}	0.115	0.0
1.32×10^{-6}	0.160	0.0
1.99×10^{-5}	0.235	0.0
3.32×10^{-5}	0.373	0.0
6.63×10^{-5}	0.420	0.02

Table 5.7 continued

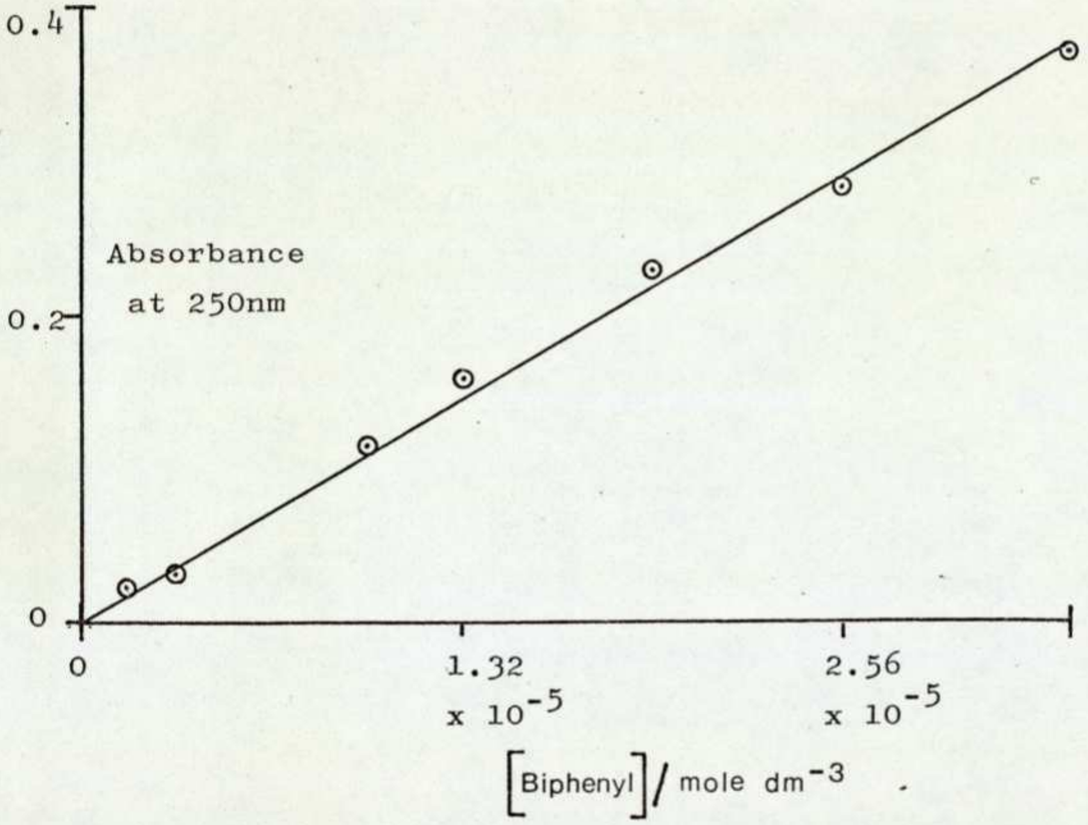
(iii)

70.8% H_2SO_4

Biphenyl /mole dm^{-3}	Absorbance 250nm	 350nm
9.95×10^{-5}	0.445	0.03
1.32×10^{-4}	0.490	0.08
1.64×10^{-4}	0.54	0.10

a) 10mm cells used

Figure 5.6. Beer Law plot for biphenyl in sulphuric acid at 25°



by absorbance readings at 350nm.

From the combined Beer Lambert Law, the molar extinction absorptivity is given by:-

$$A = \mathcal{E}.c.l.$$

Where A = Absorbance

c = Concentration of sample

l = Path length

$\mathcal{E}$ = Molar absorptivity

From Fig. 5.6 the slope is equal to A/c $dm^3\ mole^{-1}$

$$\therefore \mathcal{E} = \text{slope} \times 1\ dm^3\ mole^{-1}\ cm^{-1}$$

$$= \frac{0.145}{1.32 \times 10^{-5}} \times 1.0\ dm^3\ mole^{-1}\ cm^{-1}$$

$$= 1.1 \times 10^3\ dm^3\ mole^{-1}\ cm^{-1}$$

5.33 YIELDS OF NITRO COMPOUNDS

5.331 BIPHENYL

An example of the method for calculating the yields of nitro compounds from the nitration of biphenyl is given below.

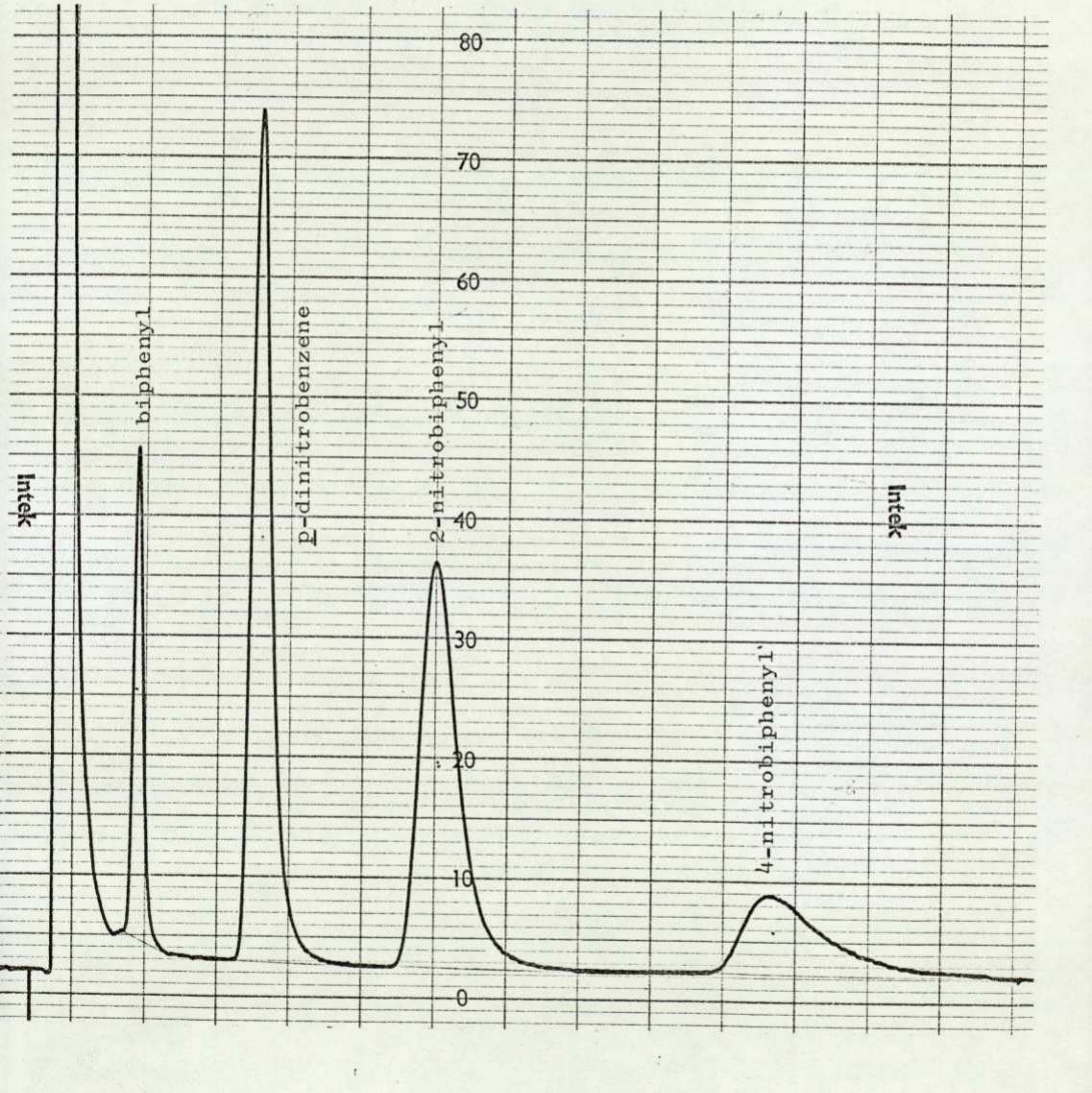
Sulphuric acid	74.7% (W/W)
Amount of biphenyl	3.31×10^{-5} moles
Amount of HNO_3	5.93×10^{-5} moles
Amount of reference p-dinitrobenzene	3.54×10^{-5} moles

The reaction was carried out in one litre of sulphuric acid.

Fig. 5.7 shows the chromatogram obtained (g.l.c. conditions as Table 5.3).

Peak areas from Fig. 5.7

Figure 5.7. Chromatogram of the products from the nitration of biphenyl in 74.7% sulphuric acid



	Area/mm^2
Biphenyl	176
2-Nitrobiphenyl	568
4-Nitrobiphenyl	210
p-Dinitrobenzene	621

From Section 7.5 $$\frac{c_x}{c_s} = \frac{(A_x)}{(A_s)} \times f$$

Response factor f for 2-nitrobiphenyl = 0.61

Response factor f for 4-nitrobiphenyl = 0.45

Response factor f for biphenyl = 0.40

$$\text{Amount of biphenyl} = \frac{176}{621} \times 3.54 \times 10^{-5} \times 0.4 \text{ moles}$$

$$= 4.0 \times 10^{-6} \text{ moles}$$

$$\text{Amount of 2-nitrobiphenyl} = \frac{568}{621} \times 3.54 \times 10^{-5} \times 0.61$$

$$= 1.95 \times 10^{-5} \text{ moles}$$

$$\text{Amount of 4-nitrobiphenyl} = \frac{210}{621} \times 3.54 \times 10^{-5} \times 0.45$$

$$= 5.38 \times 10^{-6} \text{ moles}$$

∴ o:p-ratio = 3.6

Table 5.8 gives the yield of mono-nitro compounds from the nitration of biphenyl in sulphuric acid.

Biphenyl (1.66×10^{-6} mole dm^{-3}), 2-nitrobiphenyl (1.99×10^{-5} mole dm^{-3}), and 4-nitrobiphenyl (8.4×10^{-6} mole dm^{-3}) were recovered quantitatively (95%, 96% and 94% respectively) by the normal extraction method, described in Section 7.41 from their solution in 58.0% sulphuric acid which had been kept at 25.0° for 2 hours.

Table 5.8

Yields of mono-nitro compounds from the nitration of biphenyl[a,b,c] in sulphuric acid at 25.0 ± 0.2°

H_2SO_4 (%)	2-nitrobiphenyl (%)	4-nitrobiphenyl (%)	Mass[d] Balance	o:p-ratio
44.6[e]	22	7	87[f]	3.2
56.1[e]	70	21	91	3.2
61.0	57	16	76	3.5
61.0	67	19	81	3.5
63.7	67	19	92	3.5
63.7	65	20	90	3.3
65.7	63	21	84	3.0
65.7	65	21	90	3.1
68.7	64	17	83	3.8
68.7	68	19	89	3.6
70.8	63	17	83	3.7
70.8	71	19	93	3.7
72.6	68	21	95	3.3
72.6	66	20	93	3.3
74.7	69	19	88	3.6
74.7	65	99	85	3.4

a) $\left[\text{Biphenyl}\right] = 3.3 \times 10^{-5}$ mole dm^{-3}

b) $\left[\text{Urea}\right]$ ca 3×10^{-2} mole dm^{-3}

(Table 5.8 (continued)

c) $\left[HNO_3\right]$ ca $6 \times 10^{-5} - 6 \times 10^{-2}$ mole dm^{-3}

d) Except for that in 44.6% H_2SO_4 reactions were allowed to proceed for 3 half lives and mass balances are calculated from a possible total yield of 87%

e) At 60 ± 0.2°

f) 59% biphenyl recovered

2.332 DIPHENYLMETHANE

Gehring and Reddy[116] determined the chemical shifts of the methylene protons for diphenylmethane and its nitro-derivatives, these are given in Table 5.9.

An example of the method for calculating the yields of nitro compounds from the nitration of diphenylmethane is given below:-

Sulphuric acid	72.2% (W/W)
[Diphenylmethane]	5.8 mole dm^{-3}
$[HNO_3]$	5.9 mole dm^{-3}
[Sulphamic acid]	2×10^{-2} mole dm^{-3}
Solvent (for n.m.r. after extraction)	d_6-acetone

Figs. 5.8(i) and (ii) show the ^1H n.m.r. spectra obtained, (i) was carried out at 1080 Hz sweep width and (ii) at 270 Hz sweep width. Table 5.10 shows the results obtained from these spectra. From the integral a normalised percentage of each of the components can be calculated and these are given in Table 5.11. Table 5.12 gives the yields of nitro compounds from the nitration of diphenylmethane in various concentrations of aqueous sulphuric acid.

Rate measurements for the nitration of diphenylmethane under equimolar conditions were carried out in 69.1%, 72.2% and 75.2% sulphuric acid. The spectra obtained are shown in Figs. 5.9, 5.10 and 5.11. For nitration in 75.2% sulphuric acid, 50% of the reaction was over before the scan was started (see Fig. 5.11). However,

Table 5.9

Observed chemical shifts[a] for diphenylmethane and its nitro-derivatives[116]

Compound	Chemical Shifts τ
Diphenylmethane	6.07
4-Nitrodiphenylmethane	5.90
$4,4'$-Dinitrodiphenylmethane	5.73
$2,4'$-Dinitrodiphenylmethane	5.58
$2,2',4$-Trinitrodiphenylmethane	5.28
$2,2',4,4'$-Tetranitrodiphenylmethane	5.10
$2,4,4'$-Trinitrodiphenylmethane	5.43
2-Nitrodiphenylmethane	5.75
$2,2'$-Dinitrodiphenylmethane	5.43

a) For methylene protons

Figure 5.8(i). H^1 n.m.r. spectrum of the products from the nitration of diphenylmethane in 72.2% sulphuric acid

(Sweep width 10800 Hz)

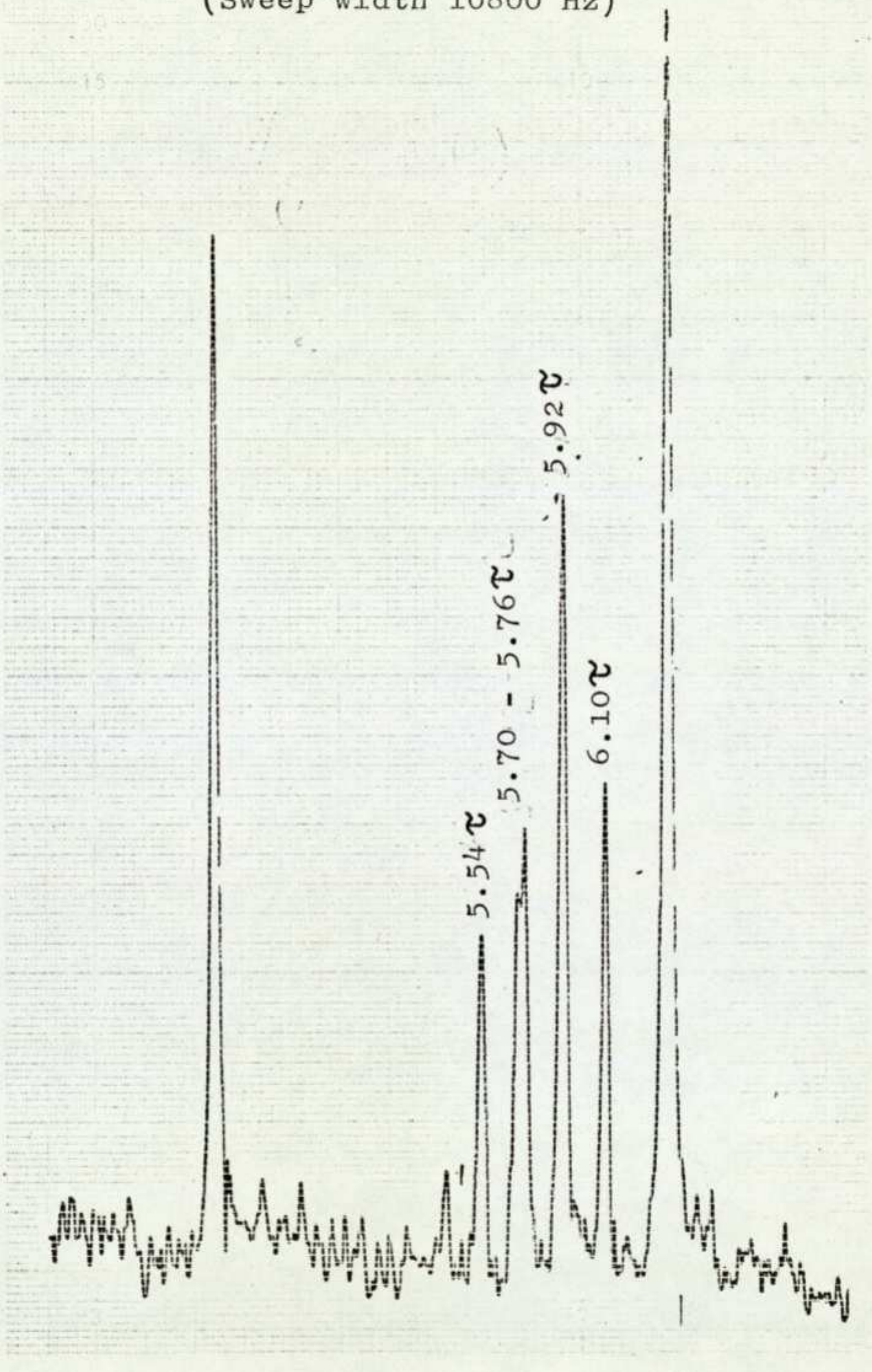


Figure 5.8(ii). H^1 n.m.r. spectrum of the products from the nitration of diphenylmethane in 72.2% sulphuric acid

Sweep width 270 Hz

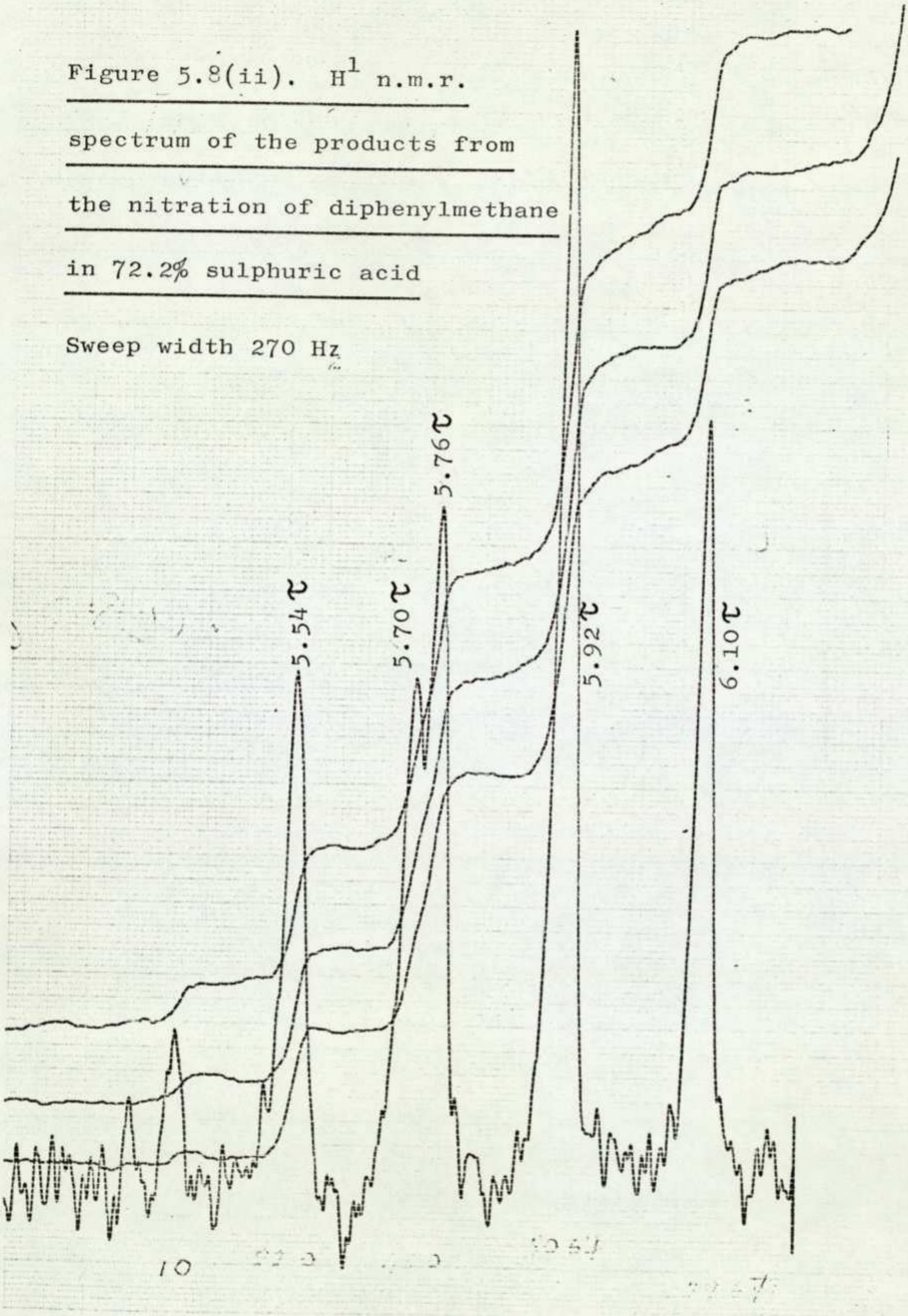


Table 5.10

Chemical shifts obtained from the ^{1}H n.m.r. spectrum of the products of the nitration of diphenylmethane in 72.2% sulphuric acid

Compound	Observed Chemical Shifts τ		Integral
Diphenylmethane	6.10		29
4-Nitrodiphenylmethane	5.92		50
2-Nitrodiphenylmethane	5.76	a	42
4,4'-Dinitrodiphenylmethane	5.70		
2,4'-Dinitrodiphenylmethane	5.59		22
2,2'-Dinitrodiphenylmethane or 2,4,4'-Trinitrodiphenylmethane	5.54		10

a) In ~ equal proportions ± 10%

Table 5.11

Relative yields of nitro compounds from the nitration of diphenylmethane in 72.2% sulphuric acid

		% total	% nitro-compounds
Diphenylmethane		19	-
4-Nitrodiphenylmethane		33	40
2-Nitrodiphenylmethane and 4,4′-Dinitrodiphenylmethane	a	27	34
2,4′-Dinitrodiphenylmethane		14	18
2,2′-Dinitrodiphenylmethane or 2,4,4′-Trinitrodiphenylmethane		7	8

a) In ~ equal proportions ± 10%

Table 5.12

Yields of nitro compounds from the nitration of diphenylmethane[a,b] in sulphuric acid

H_2SO_4 (%)	Compound (%)[g]				
	Diphenylmethane	~~2~~4-Nitrodiphenylmethane	~~4~~2-Nitrodiphenylmethane[f] and 4,4′-Dinitrodiphenylmethane	2,4′-Dinitrodiphenylmethane	2,2 -Dinitrodiphenylmethane or 2,4,4′-Trinitro
66.6[c]	11	3	35	33	17
69.1[d,e]	33	17	25	18	8
72.2[d,e]	19	33	27	14	7
75.2[d,e]	29	24	27	15	6
77.1[d]	13	11	35	29	12
84.1[d]	19	11	30	31	9
84.1[d]	18	12	34	30	6

Table 5.12 (continued)

a) $[\text{Diphenylmethane}] = 5.8 \times 10^{-5}$ mole dm^{-3}

b) $[\text{Sulphamic acid}] = 2 \times 10^{-2}$ mole dm^{-3}

c) $[HNO_3] = 4.46 \times 10^{-2}$ mole dm^{-3}

d) $[HNO_3] = 5.9 \times 10^{-5}$ mole dm^{-3}

e) Kinetic runs carried out on these solutions

f) In equal proportions ± 10%

g) Normalised to 100%

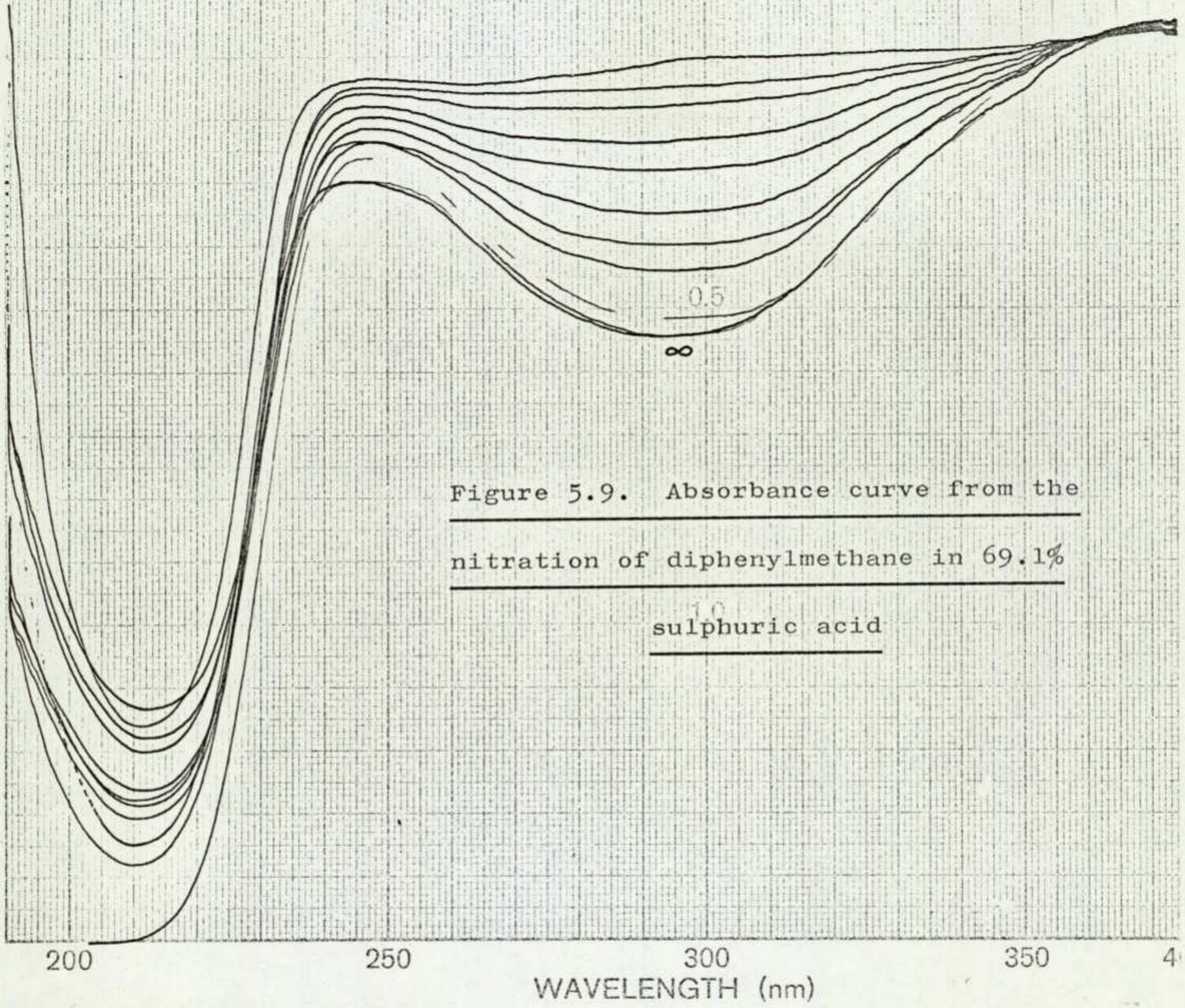


Figure 5.9. Absorbance curve from the nitration of diphenylmethane in 69.1% sulphuric acid

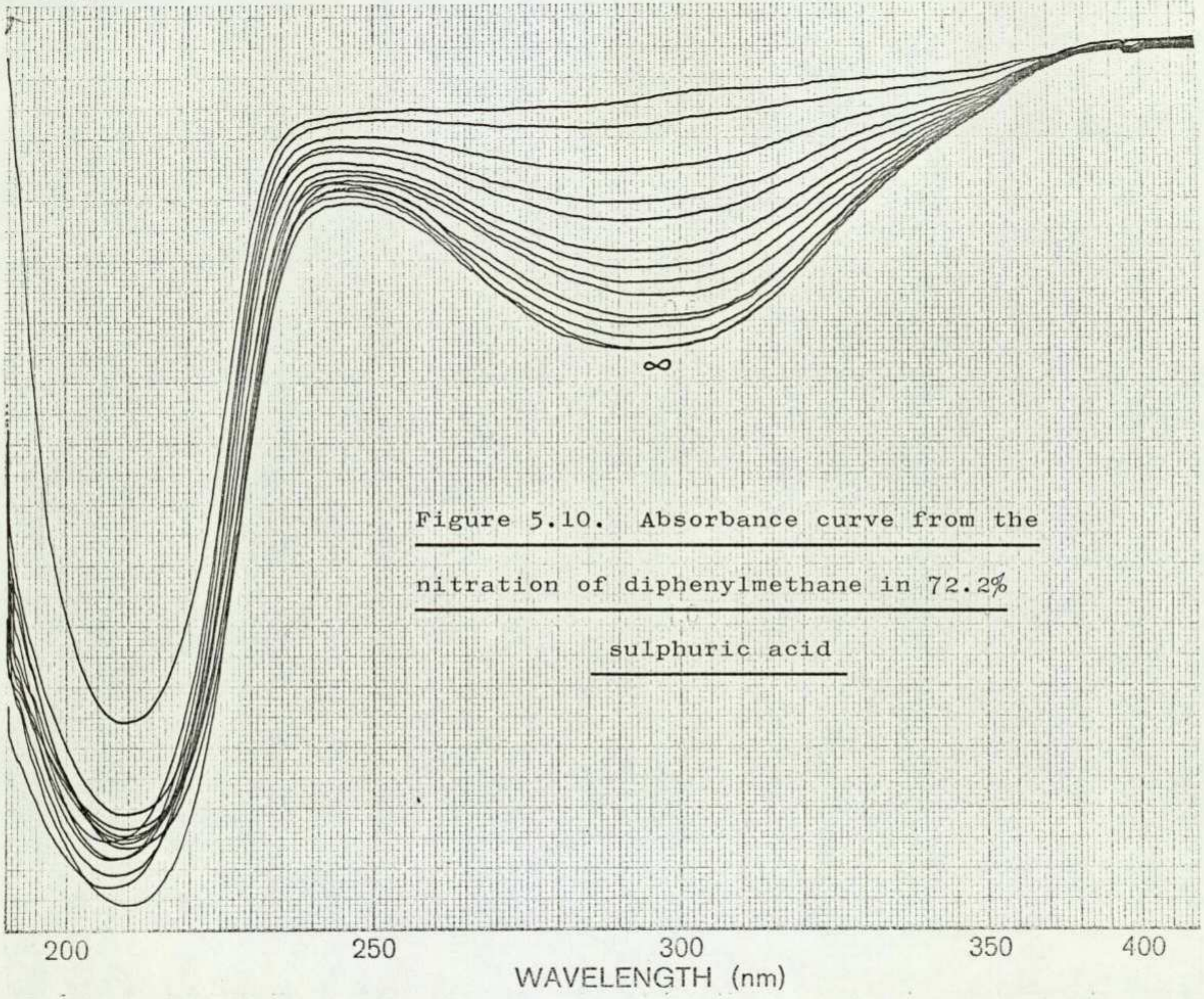


Figure 5.10. Absorbance curve from the nitration of diphenylmethane in 72.2% sulphuric acid

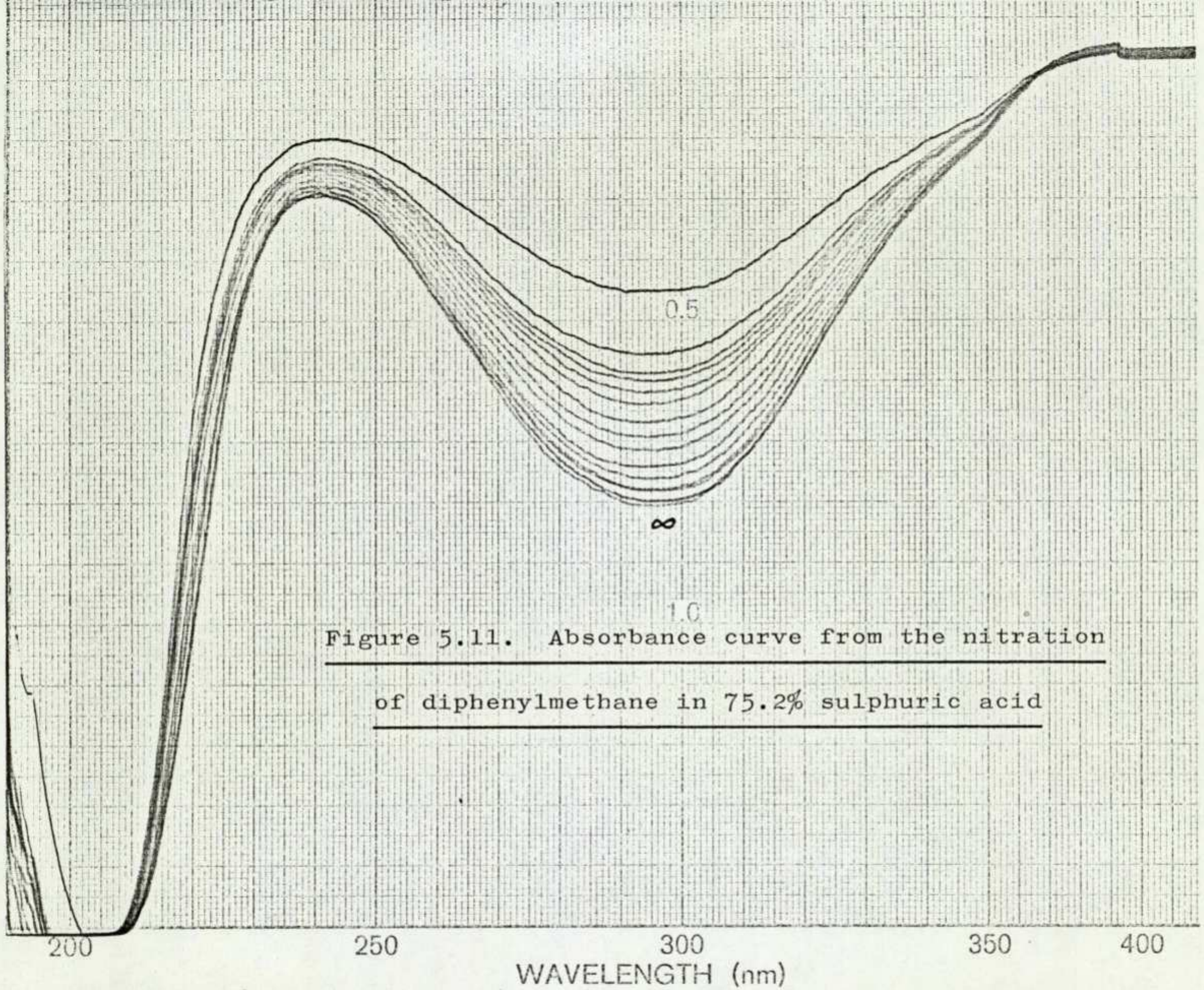


Figure 5.11. Absorbance curve from the nitration of diphenylmethane in 75.2% sulphuric acid

normal scans were obtained for nitration in 69.1% and 72.2% sulphuric acid (see Fig. 5.9 and 5.10).

5.4 DISCUSSION

5.41 BIPHENYL

In the present work the solubility of biphenyl was determined, and it was found to be soluble up to 4.0×10^{-5} mole dm^{-3} in 67.8 - 70.8% sulphuric acid (see Section 5.32). Therefore, to ensure homogeneity of solutions, kinetic measurements were carried out at substrate concentrations of 1.9 and 3.3×10^{-5} mole dm^{-3} with product determination at 3.3×10^{-5} mole dm^{-3}.

In the earlier work by Coombes and Russell[34], the estimated concentration of biphenyl was _ca_ 4×10^{-5} mole dm^{-3}. By using the value of ε found in the present study it is now realised that the original estimate for the concentration of biphenyl was high, and the true concentration of biphenyl used by Coombes and Russell was _ca_ 2×10^{-5} mole dm^{-3}.

In attempting to dissolve 4×10^{-5} mole dm^{-3} of biphenyl, Taylor[112] was clearly working at the limit of solubility and his inability to obtain complete solution is explicable.

The rate profile for biphenyl is above and parallel to that for benzene (see Fig. 5.3). The ratio k_2(obs) biphenyl/k_2(obs) benzene = 12, where as the ratio k_2(obs) mesitylene/k_2(obs) biphenyl varies from 8 to 2 over the range 60 - 73% H_2SO_4 (see Table 5.13). This parallelism, the fact that the relative rate of nitration of biphenyl

Table 5.13

Comparison of Rate Profile for biphenyl with those of benzene and mesitylene

H_2SO_4 (%)	$\log_{10}k_2$(obs) - $\log_{10}$ k_2(obs) (benzene)	$\log_{10}k_2$(obs)(mesitylene) - $\log_{10}k_2$(obs)
62.5	0.97	0.88
63.7	1.04	0.76
65.7	1.10	0.64
68.7	1.18	0.41
70.6	1.16	0.29
72.6	1.01	0.28

benzene by nitric acid in aqueous perchloric acid is 14, and that the ratio for nitration by nitric acid in sulpholan[109] is 16, suggests that the rate of reaction is not much affected by encounter control in this region of acidity. The behaviour is that expected for nitration by the nitronium ion[22]. Isosbestic points were observed, as in previous work[34], at 240 and 276nm. The linearity of the Beer's Law plot in this region, the isosbestic points and the excellent kinetic behaviour offer incontravertible evidence that these data refer to homogeneous solutions of biphenyl.

Product studies were carried out in the usual way (see Sections 7.41 and 7.42) and the results are given in Table 5.8. Reactions were only allowed to proceed for 3 half lives (87% reaction) to avoid complications due to dinitration[34]. Over the whole range of acidities (44 - 75% sulphuric acid), the o:p-ratio is high (3.1 - 3.7), and in all cases the total yield is good. In this region of acidity it is known that the effective species is the nitronium ion, therefore, it is apparent that normal nitration of biphenyl by the nitronium ion gives a high o:p-ratio, and that a special mechanism[107] proposed to account for the high o:p-ratio obtained in acetic anhydride is unnecessary.

The fact that the o:p-ratio is nearly constant, and that the total yields are good over the whole range of acidity, means that, if *ipso*-substitution is important, rearrangement must compete favourably with nucleophilic capture of the ipso-substituted Wheland intermediate even in 45% H_2SO_4. It is felt that this fact together with the fact that the ipso-position is not expected to be activated to electrophilic attack, makes this route most unlikely.

In most of Taylor's original work[107] and his more recent study[112] of the nitration of biphenyl in sulphuric acid, which he suggests gives the difinitive nitronium ion value of 1.4, one should note that the reaction medium was heterogeneous. It consisted of two phases, one containing mainly nitric acid in about 68% aqueous sulphuric and the other containing mainly biphenyl in nitrobenzene. The difference then lies between values from this system and the values obtained in homogeneous solution in the present work. Two explanations may be put forward. Firstly, it is possible that under Taylor's conditions nitrous acid catalysis has not been completely suppressed, and secondly, the low o:p-ratio may be a direct consequence of the heterogeneity of the reaction mixture.

It is, therefore, suggested that the o:p-ratio for the nitronium ion nitration of biphenyl is greater than the statistical value of 2[114].

5.42 DIPHENYLMETHANE

Good first-order kinetic plots were obtained for the nitration of diphenylmethane over a range of acidity. This is at first sight at variance with the observation of considerable amounts of dinitration. Dr. R.B. Moodie[121] has provided an analysis of the $X \xrightarrow{k_1} Y \xrightarrow{k_2} Z$ situation and shown that good first-order kinetics will be observed, when a wavelength is used at which Y and Z (but not X) absorb, if either $\varepsilon_Y = \varepsilon_Z$ (any $^{k}2/k_1$) or $\frac{\varepsilon_Y}{\varepsilon_Z} = \frac{k_2}{k_1}$ (ε is the molar absorptivity)

a = initial concentration of X

The arguments are as follows:-

$$\left[X\right] = ae^{-kt} \qquad \ldots.1$$

$$\left[Y\right] = \frac{ak_1}{k_2-k_1}\left(e^{-k_1t}-e^{-k_2t}\right) \qquad \ldots.2$$

$$\left[Z\right] = a\left[1-e^{-k_1t}-\frac{k_1}{k_2-k_1}e^{-k_1t}+\frac{k_1}{k_2-k_1}e^{-k_2t}\right] \ldots.3$$

If only Y and Z absorb at a particular wavelength, the absorbance A is given in terms of the molar absorptivities (ε_y and ε_z) of Y and Z by $A = \varepsilon_y\left[Y\right] + \varepsilon_z\left[Z\right]$

dividing by $\varepsilon_y a$ and putting $\varepsilon_z/\varepsilon_y = r$

$$\frac{1}{\varepsilon_y a} A = \frac{[Y]}{a} + \frac{r[Z]}{a} \qquad \ldots.4$$

at $t = \infty$, $A = A_\infty = \varepsilon_z a$, so that $1/\varepsilon_y a\ A_\infty = r$ 5

From 4 and 5

$$\frac{A - A_\infty}{\varepsilon_y a} = \frac{[Y]}{a} + r\left(\frac{[Z]}{a} - 1\right)$$

Using 2 and 3

$$\frac{A - A_\infty}{\varepsilon_y a} = \frac{k_1}{k_2-k_1}\left(e^{-k_1t} - e^{-k_2t}\right) + r\left(-e^{-k_1t} - \frac{k_1e^{-k_1t}}{k_2-k_1}\right.$$

$$+ \quad \frac{k_1 e^{-k_2 t}}{k_2-k_1} \quad)$$

$$= \frac{(k_1-r(k_2-k_1)-k_1 r)}{(\quad k_2-k_1 \quad)} e^{-k_1 t} + \frac{(k_1 r-k_1)}{(k_2-k_1)} e^{-k_2 t}$$

$$= \frac{(k_1-rk_2)}{(k_2-k_1)} e^{-k_1 t} + \frac{(k_1(r-1))}{(k_2-k_1)} e^{-k_2 t}$$

Multiplying by k_2-k_1

$$\frac{(k_2-k_1)}{(\mathcal{E}_y a)} (A - A_\infty) = (k_1-rk_2)e^{-k_1 t} + k_1(r-1)e^{-k_2 t} \quad \ldots 6$$

A normal first order plot is $-\ln(A_\infty-A)$ vs t and to examine the straightness of such a plot we look at the variation with time of slope $S = -d \ln (A_\infty-A)/dt$

$$-d \frac{\ln(A_\infty-A)}{dt} = \frac{-1}{A_\infty-A} \frac{d(A_\infty-A)}{dt} = S$$

From 6

$$-\left(\frac{k_2-k_1}{\mathcal{E}_y a}\right) d \left(\frac{A_\infty-A}{dt}\right) = k_1(k_1-rk_2)e^{-k_1 t} + k_2 k_1 (r-1)e^{-k_2 t} \quad \ldots 7$$

$S = 7/6$

$$S = k_1 \left[\frac{(k_1-rk_2)e^{-k_1 t} + k_2(r-1)e^{-k_2 t}}{(k_1-rk_2)e^{-k_1 t} + k_1(r-1)e^{-k_2 t}}\right]$$

Introducing $p = k_2/k_1$

$$S = k_1 \left[\frac{1-rp + p(r-1)e^{(1-p)k_1 t}}{1-rp + (r-1)e^{(1-p)k_1 t}}\right] \ldots . \; 8$$

This is independent of time if:-

a) $r = 1$ ($S = k_1$) This is the familiar case using an isosbestic point between Y and Z

b) $rp = 1$ ($S = k_2$) i.e. $\varepsilon_z/\varepsilon_y = k_1/k_2$

It follows that an explanation of the good first-order behaviour observed would be that $\varepsilon_z/\varepsilon_y = k_1/k_2$. Now it is quite likely that $\varepsilon_z/\varepsilon_y$ will be 2 and it follows that a value of $k_1/k_2 \sim 2$ allows an explanation of the results and such a value is not unreasonable.

The rate profile obtained is slightly above and almost parallel to that for benzene (see Fig. 5.5). This suggests that the observed rate is not much affected by encounter control in this region of acidity. The relative rate k_2(obs) diphenylmethane/k_2(obs) benzene is 2, this is at variance with that observed[40], for the nitration of diphenylmethane in acetic anhydride where a relative rate of 19.5 was obtained.

Product studies were carried out using an ^{1}H n.m.r. method and the results are given in Table 5.12. It was not possible to separate the peaks due to 2-nitrodiphenylmethane and 4,4′-dinitrodiphenylmethane, it is estimated that these compounds are formed in approximately equal amounts. The sum of the rings (in %) containing nitro-groups is given in Table 5.14. This should equal 100 for equimolar conditions. For nitration in 66.6% H_2SO_4 with an excess of nitric acid, no diphenylmethane should have been left and, therefore, it appears that

Table 5.14

Sum of the rings containing nitro-groups from the nitration of diphenylmethane[a]

H_2SO_4 (%)	Σ of rings containing nitro-groups (%)
66.6	154
69.1	106
72.2	114
75.2	105
77.1	145
84.1	134
84.1	133

a) The amount of 2-nitrodiphenylmethane and 4,4^1-dinitrodiphenylmethane are assumed to be equal.

the reaction must have been stopped before it had gone to completion. In the region 77 - 84% H_2SO_4 the reaction was carried out using equimolar conditions, but under these conditions the reaction is fast ($t\frac{1}{2}$ 77% H_2SO_4 = 36s, $t\frac{1}{2}$ 84% H_2SO_4, = 0.02s) and some dinitration might occur during mixing in the latter case. In 75.2% sulphuric acid equimolar conditions were used but 50% of the reaction was over before the scan was started (~80s), see Fig. 5.11. It is possible that some rapid initial reaction, perhaps nitrosation, is affecting the products in this case and at higher acidities. In 69% and 72% sulphuric acid the sum of the rings containing nitro-groups equals 106 and 114 respectively. The reactions were carried out using equimolar conditions and the rates of reaction were slow, see Figs. 5.9 and 5.10. The data here, then appears relevant to the uncomplicated homogeneous nitronium ion nitration of diphenylmethane.

On the assumption of independent substitution in the two aromatic rings of diphenylmethane and complete mixing of the reactant solutions, the fraction of unsubstituted (x), mono-substituted (y) and disubstituted (z) products should accord with random pairing of substituted and unsubstituted rings[122]. The relationships between these fractions and the ratio R of the number of aromatic rings to nitronium ions are shown below.

$x = (1-1/R)^2$

$y = (2/R)(1-1/R)$

$z = 1/R^2$

$\therefore$ for equimolar nitration of diphenylmethane $(R = 2)$

$x = \frac{1}{4}$

$y = \frac{1}{2}$

$z = \frac{1}{4}$

This applies if the rate ratio $k_1/k_2 = 1$, but if as is proposed for the nitration of diphenylmethane the rate ratio $k_1/k_2 = 2$, then

$x = \frac{1}{8}$

$y = \frac{3}{4}$

$z = \frac{1}{8}$

For the nitration of diphenylmethane in 69.1 and 72.2% H_2SO_4 the % of products is given below. In calculating these data it was assumed that 2-nitrodiphenylmethane and 4,4′-dinitrodiphenylmethane were formed in equal amounts, and also that there was no tri-substitution.

% H_2SO_4	%		
	unsubstituted	monosubstituted	disubstituted
69.1	33	30	38
72.2	19	46	34

The amount of disubstitution seems anomalously high in both cases, especially as the kinetic studies indicate that the second stage is half as fast as the first stage. However, in view of the spread of results and the inconsistencies in them (e.g. Σ of rings $>$ 100), the unknown recovery of any of the compounds, and the inability to separate completely the peaks for 2-nitrodiphenylmethane and 4,4 -dinitrodiphenylmethane, the conclusion that this substrate is reacting anomalously must remain an extremely tentative one.

CHAPTER 6

THE NITRATIONS OF 1,3,5-TRIMETHOXYBENZENE, 1,3-DIMETHOXYBENZENE, AND MESITYLENE OVER A RANGE OF TEMPERATURES IN AQUEOUS SULPHURIC ACID

6.1 INTRODUCTION

Rates of nitration by nitric acid are reduced by the addition of water to a medium of 90% sulphuric acid. Between 90% and 85% sulphuric acid the decrease in rate, parallels the independently established fall in the concentration of the nitronium ion[123]. This fact is good evidence for the operation of the nitronium ion, both in solutions more acidic than 90% and in weakly diluted solutions in which the nitronium ion is still spectroscopically detectable. Further reduction of the concentration of sulphuric acid renders the nitronium ion undetectable, and the second-order rate coefficient is found to decrease by a factor of about 10^4 for each decrease of 10% in the concentration of sulphuric acid. Bayliss and Watts[15] have shown, from u.v. spectra of potassium nitrate in aqueous sulphuric acid, that in the range 0 - 15% H_2SO_4 the dissolved nitrate exists as the nitrate ion and that from 15 - 70% H_2SO_4 the nitrate ion and molecular nitric acid are present in comparable amounts. In sulphuric acid of the range 72 - 82% molecular nitric acid accounts for all the dissolved nitrate, and in the region 82 - 90% H_2SO_4 nitric acid was converted into the nitronium ion.

The active electrophile is not molecular nitric acid, because the variation in the rate is not similar to the corresponding change in the concentration of nitric acid. The continued effectiveness of the nitronium ion in relatively dilute solutions has been indicated by comparing the dependence of the rates on the concentration of sulphuric acid with the acidity-dependence of the ionization of model compounds. The H_R acidity scale[124,125,126] was determined from the ionisation of a series of tri-arylcarbinols, which undergo ionization as follows:

$$Ar_3COH + H^+ \rightleftharpoons Ar_3C^+ + H_2O \quad ..... \; 6.1$$

The acidity function H_o[101], however, is based on the behaviour of indicators ionising according to the scheme below.

$$ArNH_2 + H^+ \rightleftharpoons ArNH_3^+ \quad ..... \; 6.2$$

If the assumption is made that the ionisation characteristics of nitric acid are similar to those of the organic bases used to define the acidity functions then a correspondence between the acidity dependence of rates of nitration and H_R would suggest the involvement of the nitronium ion. A correspondence with H_o would support the idea that nitric acidium ion ($H_2NO_3^+$) was the effective electrophile. The formal similarities are clear from the following equations.

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^- \quad ... \; 6.3$$

$$Ar_3COH + 2H_2SO_4 \rightleftharpoons Ar_3C^+ + H_3O^+ + 2HSO_4^- \; .. \; 6.4$$

$$HNO_3 + H_2SO_4 \rightleftharpoons H_2NO_3^+ + HSO_4^- \quad .... \; 6.6$$

$$ArNH_2 + H_2SO_4 \rightleftharpoons ArNH_3^+ + HSO_4^- \quad .... \; 6.7$$

Specific structural differences of organic indicators are now thought to lead to a diminishing of the generality of the derived acidity scales[127], and the assumption that nitric acid behaves in quantitatively similar manner to an organic indicator must be in doubt. However, in view of the large differences in the H_R and H_o scales and the correspondence of the acidity dependence of nitration so much more closely with H_R than with H_o, the effectiveness of the nitronium ion is firmly established[123]. Although the difference between H_o and H_R is great enough to allow gross mechanistic distinction to be made, the acidity dependence of nitration deviates from an exact correspondence with H_R[20].

A better correlation has been found by comparing $\log_{10} k_2(\text{obs})$ with $-(H_R + \log_{10} \underline{a}_{H_2O})$[26,128,129]. In these comparisons a straight line of slope approximating to 1 for a number of compounds has been found, where the bulk species present is being nitrated. Some typical data are summarised in Table 6.1. A possible explanation for this behaviour is that in these acidities[26], the nitric acid molecule is present predominantly as the monohydrate (see Equation 6.8).

$$HNO_3.H_2O + H^+(H_2O)_n \rightleftharpoons NO_2^+ + (n + 2)\ H_2O \quad \ldots\ 6.8$$

Recently the values and temperature dependence of H_R have been redetermined by Katritzky and his co-workers[131], a table of comparison is shown in Table 6.2. Previous studies[22,26] have used the values of H_R that were determined by Deno[125]. In the present study the values obtained

Table 6.1

Acidity dependence of nitration

Substrate	Range of acidity (%) H_2SO_4	$\frac{-d \log_{10} k(\text{obs})}{d(H_R + \log_{10} \underline{a}_{H_2O})}$	Ref.
Benzene	58 - 68	1.05	22
Benzene	68 - 80	1.20	22
Fluorobenzene	60 - 70	1.05	26,136
Chlorobenzene	60 - 72	1.06	26,136
Bromobenzene	60 - 72	1.06	26,136
Isoquinolinium ion	71 - 84	1.01	26
Quinolinium ion	80 - 84	0.95	26
N-Methylquinolinium ion	80 - 84	1.00	26
Mesitylene	56 - 80	1.00	22
Naphthalene	60 - 70	1.00	22
Toluene	63 - 80	1.00	22

Table 6.2

Comparison of H_R values

$\%H_2SO_4$	Katritzky[131] 25°	Deno[125] 25°	Arnett[132] 30°	Katritzky[131] 40°
30	-3.15	-3.22	-2.78	-3.10
40	-5.00	-4.80	-4.50	-4.65
50	-7.05	-6.60	-6.40	-6.50
60	-9.05	-8.92	-8.61	-8.85
70	-12.05	-11.52	-11.67	-11.25
80	-14.34	-14.12	-15.28	-13.50

by Katritzky[131] have been used throughout. Arnett's[132] data for H_R at 30° and 45° indicated that the unit slopes obtained for plots of $\log_{10}k_2(\text{obs})$ vs $-(H_R + \log_{10} \underline{a}_{H_2O})$ at 25° were fortuitous because the slope of the acidity function behaved in an opposite manner to that of typical nitration rate profiles. However, Katritzky's[131] new data removes this anomaly. Recalculation of the data for the nitration of benzene[22] using the values of H_R determined by Katritzky[131], shows the same variation as previously found[22], see Fig. 6.1.

The aim of the work described in this chapter was to try and obtain evidence for any other electrophile operating at low acidities with sufficiently activated compounds. The compounds chosen for this study were mesitylene, 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene. These compounds would be expected to have intrinsic reactivities of about 10^4, 10^8 and 10^{12} times that of benzene, respectively, although this reactivity might be modified by steric effects. If another electrophile was operating such as $H_2NO_3^+$ the slope of a plot of $\log_{10} k_2(\text{obs})$ vs acidity would change. The expected situation is shown in Fig. 6.2.

The nitration of mesitylene[22,34] and 1,3-dimethoxybenzene[135] in $>$ 55% sulphuric acid, have been previously studied.

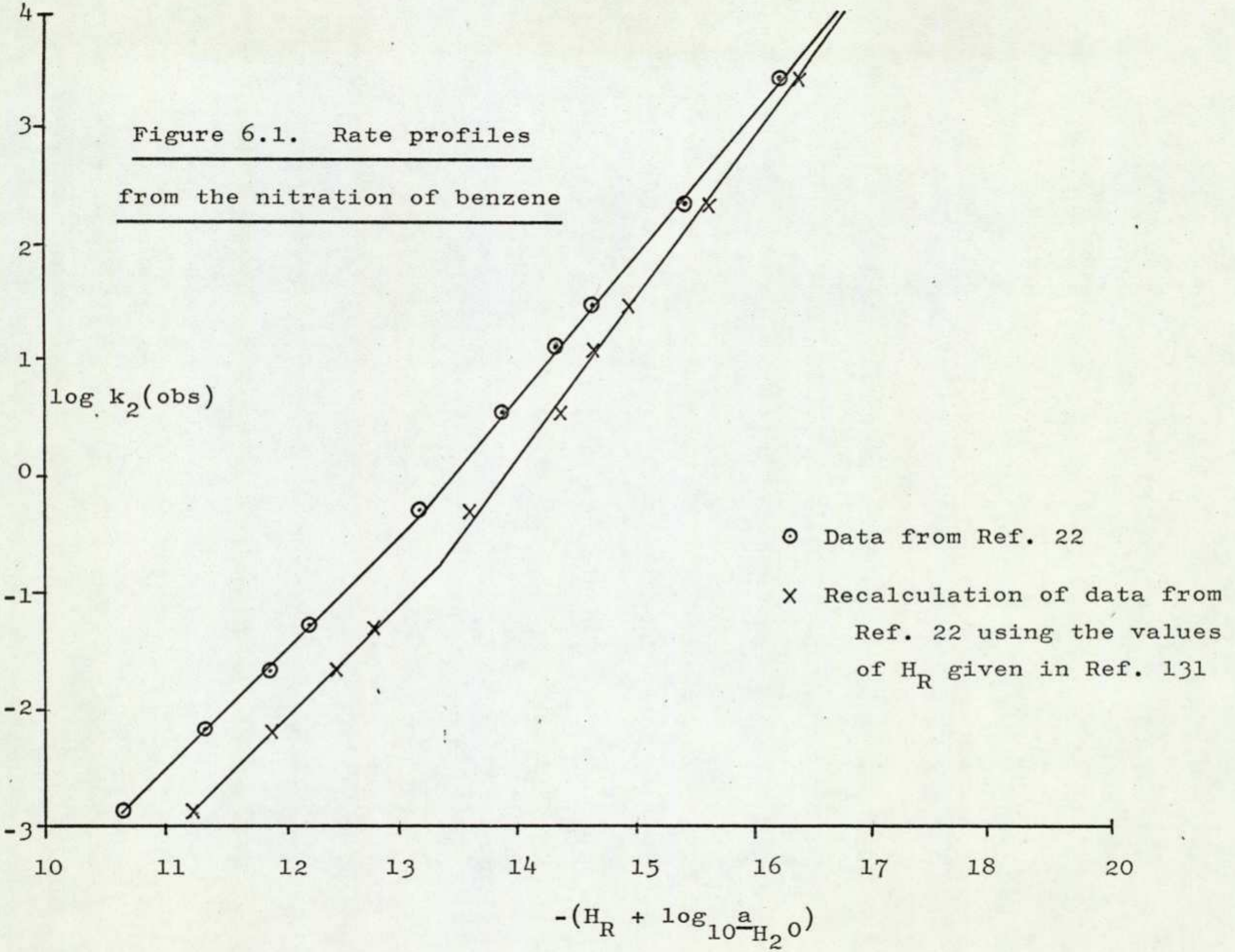


Figure 6.1. Rate profiles from the nitration of benzene

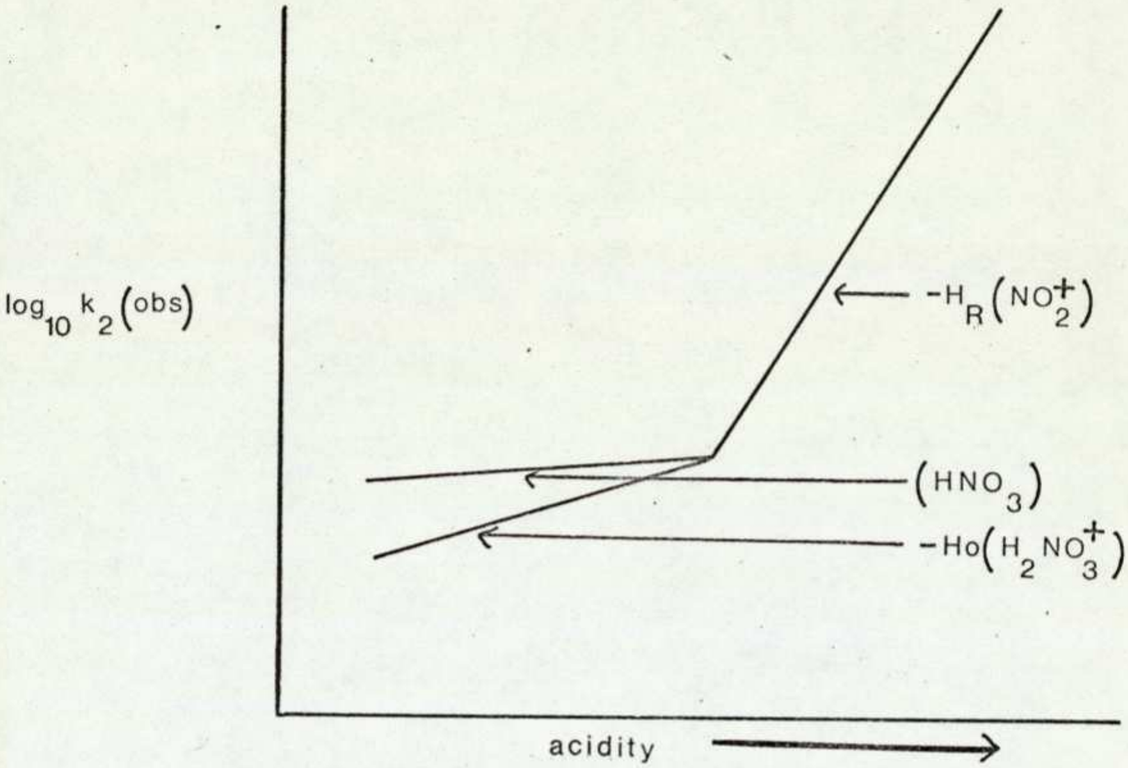


Figure 6·2

6.2 EXPERIMENTAL

6.21 MATERIALS

These were as described in Section 7.2 with the addition of the following. 1,3,5-Trimethoxybenzene was purified by recrystallisation (mp. 51 - 52°, lit[133] mp. 52°). Mesitylene (bp. 165°, lit[134] bp. 164.1°) and 1,3-dimethoxybenzene (bp. 217.0°, lit[96] 216.5 - 217.7°) were purified by distillation. 4-Nitroveratrole was purified as in Section 4.21.

6.211 1,3,5-TRIMETHOXY-2-NITROBENZENE

A method of preparation as given by Hodgson and Batty[134] involving the reaction of sodium methoxide with 2,4,6-trichloronitrobenzene in a sealed tube was attempted but was unsuccessful due to fracturing of the tubes. The method was then modified as follows. Anhydrous sodium methoxide was prepared by dissolving 1.5g (0.065 moles) of sodium in 40cm^3 of anhydrous methanol (dried with molecular sieve type 4A) and removing the excess of methanol by vacuum distillation. 4.5g (0.02 moles) of 1,3,5-trichloro-2-nitrobenzene and 60cm^3 dimethyl sulphoxide were then added and the mixture was refluxed with stirring for five hours. The resulting solution was poured into 500cm^3 of distilled water and the product was removed by filtration. After recrystallisation (twice) from methanol it had mp. 152 - 153°, (Lit[134] mp. 153°).

(Found: C, 50.94; H, 5.36; N, 6.60. Calc. for $C_9H_{11}NO_5$; C, 50.71; H, 5.20; N, 6.60%). ^{1}H n.m.r. spectrum [τ (d^6 acetone) 3.66 - 3.68 (2H, s, aromatic C - H), 6.12 - 6.2 (9H, s, -OCH_3)]. The mass spectrum was found to have a molecular ion of 213.0639 (calculated 213.0637).

6.212 1,3,5-TRIMETHOXY-2,4-DINITROBENZENE

The method used was that described by Hodgson and Batty[134]. 1g (0.005 mole) of 1,3,5-trimethoxy-2-nitrobenzene in 2cm^3 of Analar acetic anhydride was cooled to 0° and treated with a cooled solution of acetic anhydride (1.5cm^3) containing 0.3cm^3 fuming nitric acid (sg. 1.5).

The reaction mixture was allowed to reach room temperature and then poured onto ice water. The insoluble product was removed by filtration and after recrystallisation (twice) from methanol it had mp. 167°, (lit.[134] mp. 166°). (Found: C, 42.11; H, 3.88; N, 10.89. Calc. for $C_9H_{10}N_2O_7$; C, 41.87; H, 3.9; N, 10.85%). ^1H n.m.r. spectrum $\left[\tau\right.$ (d^6-acetone) 3.08 (1H, s, aromatic C - H), 5.95 (6H, s, $-OCH_3$), 6.10 (3H, s, $\left.-OCH_3\right)\right]$ The mass spectrum was found to have a molecular ion of 258.0488 (calculated 258.0486).

6.23 KINETIC MEASUREMENTS

For mesitylene and 1,3-dimethoxybenzene these were as Section 7.3. For 1,3,5-trimethoxybenzene an absorbance value at infinity was calculated from the molar extinction coefficient of 1,3,5-trimethoxy-2-nitrobenzene, in the appropriate concentration of sulphuric acid. This was done to overcome problems due to dinitration, the rate of which was insufficiently separated from that of mononitration. For reactions carried out above 25° the nitric acid concentration has been corrected to allow for the dilution caused by the expansion of the sulphuric acid.

6.24 PRODUCT ANALYSIS FOR THE NITRATION OF 1,3,5-TRIMETHOXYBENZENE

This was as described in Section(7.41 and 7.42). Table 6.3 gives the g.l.c. procedure.

6.3 RESULTS

Table 6.3

G.l.c. conditions for the separation of 1,3,5-trimethoxybenzene, 1,3,5-trimethoxy-2-nitrobenzene and 1,3,5-trimethoxy-2,4-dinitrobenzene

Column:	1.5m x $\frac{1}{4}$" S.S. $1\frac{1}{2}$% OV225 on 60 - 85 mesh universal support
Oven Temperature:	$226 \pm 0.5^{\circ}$
Detector " :	300°
Carried Gas:	Nitrogen
Flow rate:	$40 cm^{3} min^{-1}$

Compound	Retention times /s
1,3,5-trimethoxybenzene	60
1,3,5-trimethoxy-2-nitrobenzene	310
1,3,5-trimethoxy-2,4-dinitrobenzene	420
4-nitroveratrole (Internal standard)	130

6.31 KINETICS

6.311 1,3,5-TRIMETHOXYBENZENE

The results and subsequent calculations for a typical determination of a rate coefficient for the nitration of 1,3,5-trimethoxybenzene are given below.

Sulphuric acid	62.3%
$[HNO_3]$	0.055
[1,3,5-trimethoxybenzene]	7.32×10^{-5} mole dm^{-3}
[Sulphamic acid]	2×10^{-2} mole dm^{-3}
Temperature	25.0 ± 0.2°
Measurement taken at	350nm

Due to the interference of dinitration a calculated absorbance at infinity had to be determined from the molar absorbtivity of 1,3,5-trimethoxy-2-nitrobenzene. Table 6.4 gives the molar extinction coefficients (average of 3 determinations) for 1,3,5-trimethoxy-2-nitrobenzene in various concentrations of sulphuric acid. Fig. 6.3 shows the absorption curve obtained, Table 6.5 the u.v. data obtained from the above nitration and Fig. 6.4 the plot of $\log_{10}(A_t - A_\infty)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{[HNO_3]} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$= \frac{2.303 \times 1.71 \times 10^{-5}}{0.055} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$\therefore k_2(\text{obs}) = 7.16 \times 10^{-4} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients determined at various percentages of sulphuric acid at 25 and 40° are

Table 6.4

Molar absorbtivities for 1,3,5-trimethoxy-2-nitrobenzene[b,c] in various concentrations of sulphuric acid

H_2SO_4(%)[a]	/dm^3 $mole^{-1}$ cm^{-1}
67.8	3675
66.6	3370
64.3	3310
62.3	3041
60.8	2992
58.1	2951
56.1	2801

a) ± 0.1%

b) $\left[\text{1,3,5-trimethoxy-2-nitrobenzene}\right]$ = 7.5×10^{-5} mole dm^{-3}

c) Measurement at 350nm.

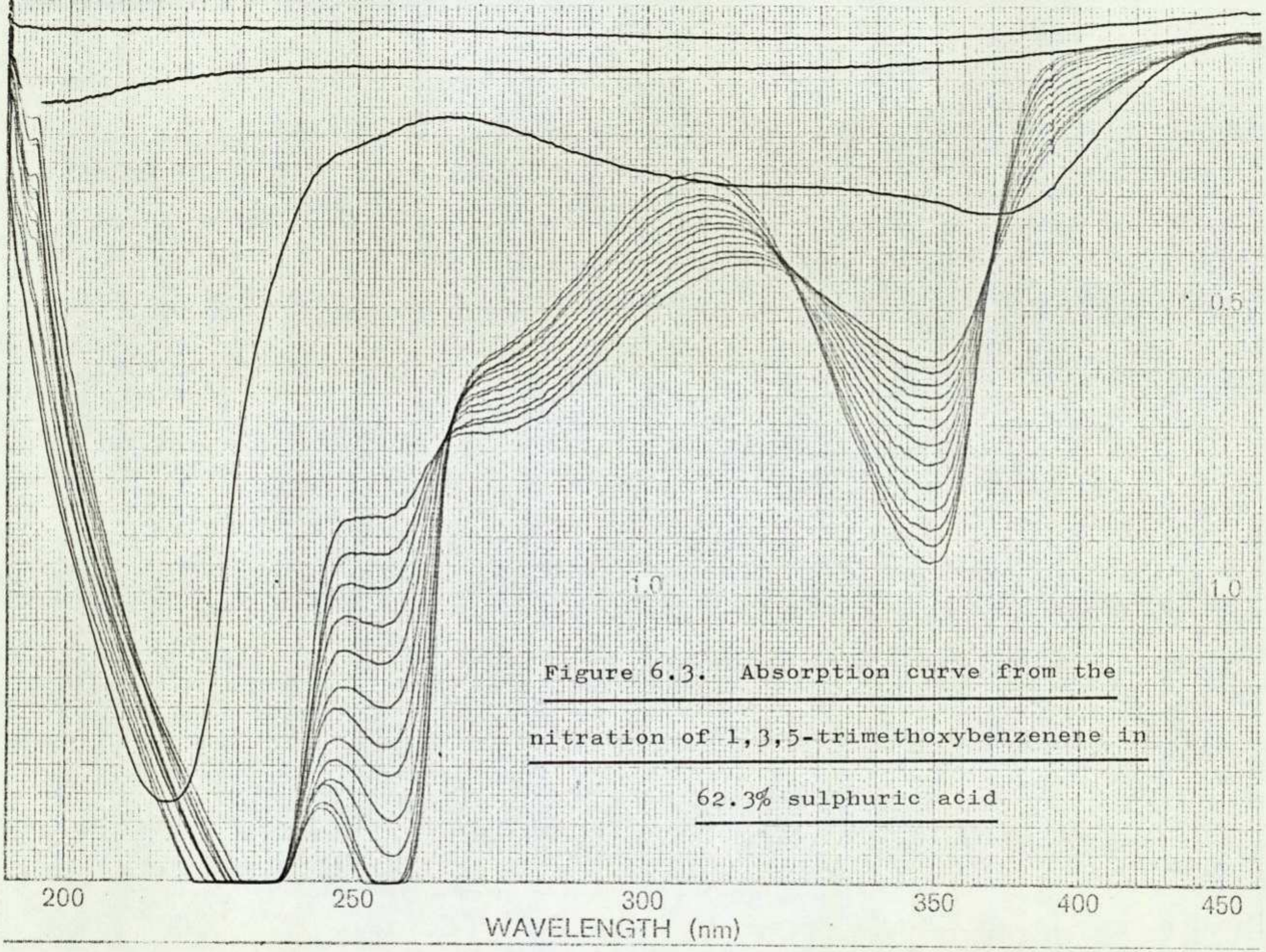


Figure 6.3. Absorption curve from the nitration of 1,3,5-trimethoxybenzenene in 62.3% sulphuric acid

Table 6.5

Data from a typical determination of the rate of nitration of 1,3,5-trimethoxybenzene in 62.3% sulphuric acid at 25.0 ± 0.2°

Time (t) /s	Absorbance at time t (At)[a]	(At - A_∞)	Log_{10}(At - A_∞)
195	0.870	0.635	-0.197
840	0.840	0.605	-0.218
1760	0.810	0.575	-0.240
2900	0.780	0.545	-0.263
4265	0.740	0.505	-0.296
6155	0.695	0.400	-0.337
8300	0.665	0.430	-0.366
10770	0.635	0.400	-0.397
13686	0.605	0.370	-0.431
b	0.235 (A_∞)		

a) Blank reading of 0.07 removed

b) Calculated from the molar absorptivity of 1,3,5-trimethoxy-2-nitrobenzene in 62.3% H_2SO_4

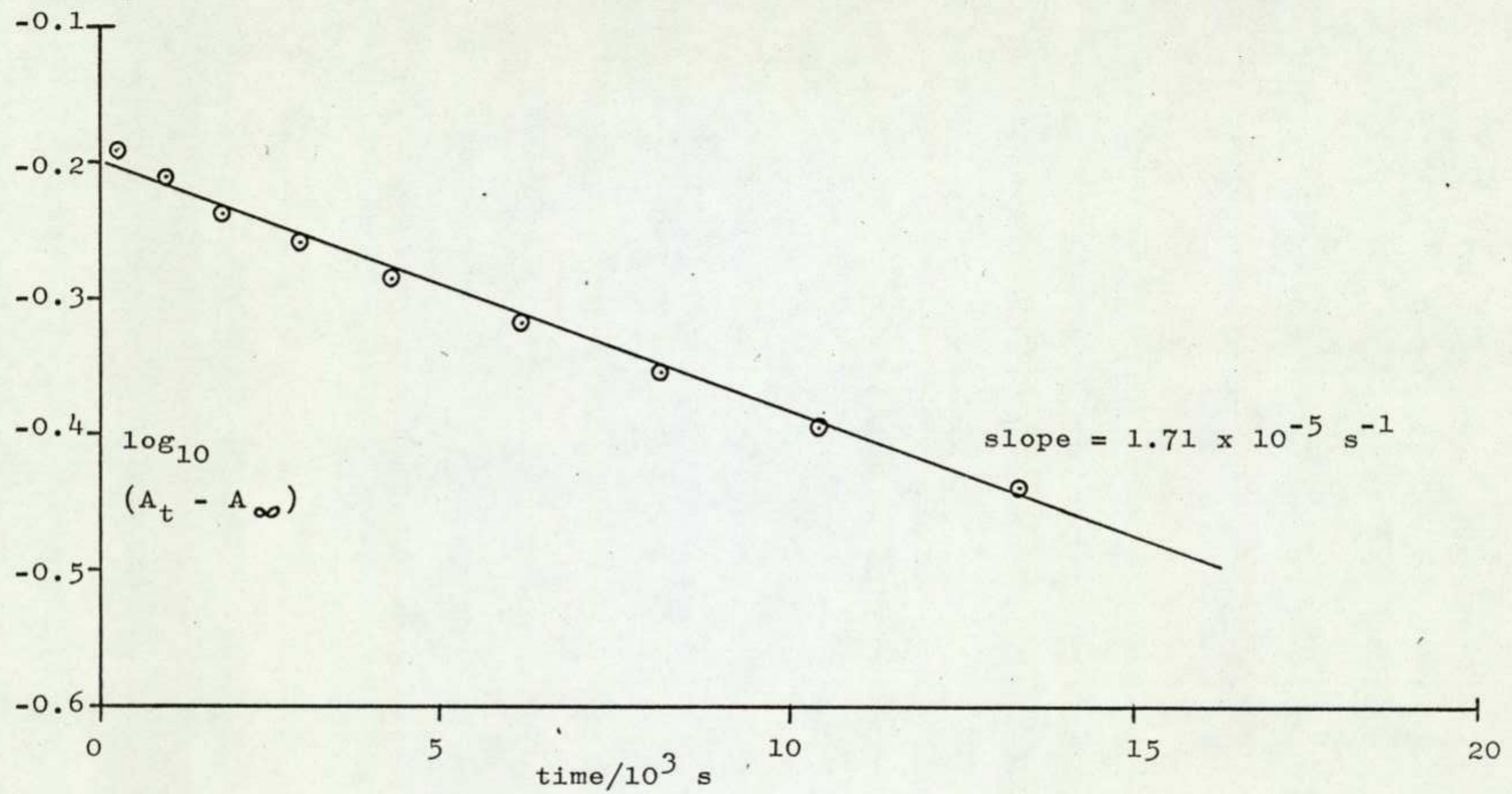


Figure 6.4. Plot of $\log_{10}$ $(A_t - A_\infty)$ vs time from the nitration of 1,3,5-trimethoxybenzene in 62.3% sulphuric acid

given in Table 6.6, $\log_{10} k_2(\text{obs})$ is plotted against H_2SO_4 in Fig. 6.5. It was not possible to measure the rate of nitration for 1,3,5-trimethoxybenzene above 40° due to the interference of a secondary reaction, which may well have been nitrosation.

Table 6.7 gives the Arrhenius activation parameters for the nitration of 1,3,5-trimethoxybenzene, calculated from the following expression.

$$\log\left(\frac{k_2^{\,2}(\text{obs})}{k_2^{\,1}(\text{obs})}\right) = \frac{E}{2.303R}\;\frac{(T_2 - T_1)}{(T_1 \times T_2)}$$

where $k_2^{\,1}(\text{obs})$ = the rate constant at Temperature T_1

$k_2^{\,2}(\text{obs})$ = the rate constant at Temperature T_2

R = Gas constant

E = Activation energy

6.312 1,3-DIMETHOXYBENZENE

The results and subsequent calculation for a typical determination of a rate coefficient for the nitration of 1,3-dimethoxybenzene are given below.

Sulphuric acid	62.3% (wt/wt)
$[HNO_3]$	2.33×10^{-2} mole dm^{-3}
[1,3-Dimethoxybenzene]	9.8×10^{-5} mole dm^{-3}
[Sulphamic acid]	2×10^{-2} mole dm^{-3}
Temperature	25.0 ± 0.2°
Measurement taken at	360nm

Fig. 6.6 shows the absorption curve, Table 6.8 the data

Table 6.6

Second-order rate coefficients for the nitration of 1,3,5-trimethoxybenzene[a,b,c,d] in sulphuric acid

H_2SO_4(%)[e]	$-(H_R + \log_{10}a_{H_2O})$[f,g]	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}
	At 25.0 ± 0.2°	
67.8	12.758	3.31×10^{-3}
67.8	12.758	2.90×10^{-3}
67.8	12.758	2.92×10^{-3}
66.6	12.304	2.58×10^{-3}
66.6	12.304	2.35×10^{-3}
64.3	11.566	1.13×10^{-3}
64.3	11.566	1.13×10^{-3}
62.4	10.994	6.91×10^{-4}
62.4	10.994	7.16×10^{-4}
60.8	10.521	5.0×10^{-4}
	At 40.0 ± 0.2°	
60.8	9.871	7.54×10^{-3}
60.8	9.871	7.73×10^{-3}
58.1	9.03	2.01×10^{-3}
58.1	9.03	2.12×10^{-3}
56.1	8.52	1.35×10^{-3}
56.1	8.52	1.28×10^{-3}

Table 6.6. (continued)

a) $\left[\text{Sulphamic acid}\right]$ ca 2×10^{-2} mole dm^{-3}

b) Measurement at 350nm

c) $\left[\text{Substrate}\right] = 7.35 \times 10^{-5}$ mole dm^{-3}

d) $\left[HNO_3\right] = 5.5 \times 10^{-2}$ mole dm^{-3}

f) Refs. 125 and 142

g) $\underline{a}_{H_2O}$ assumed to be constant at various temperatures

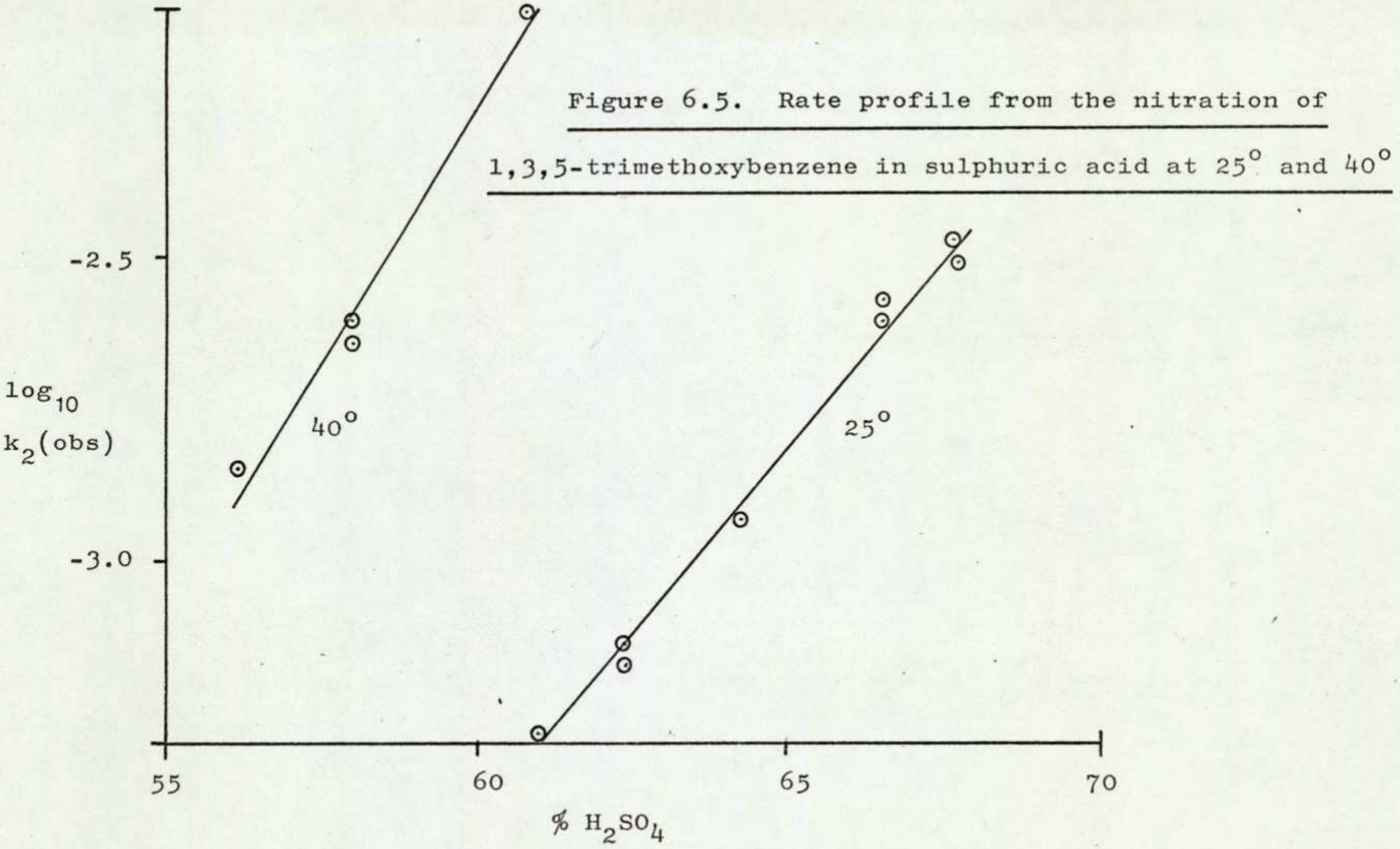


Figure 6.5. Rate profile from the nitration of 1,3,5-trimethoxybenzene in sulphuric acid at 25° and 40°

Table 6.7

Activation parameters for the nitration of 1,3,5-trimethoxybenzene

H_2SO_4(%)	Temp range (°C)	/k cal mole^{-1}	$\log_{10}A$
60.8	25 - 40	33.5	21.3

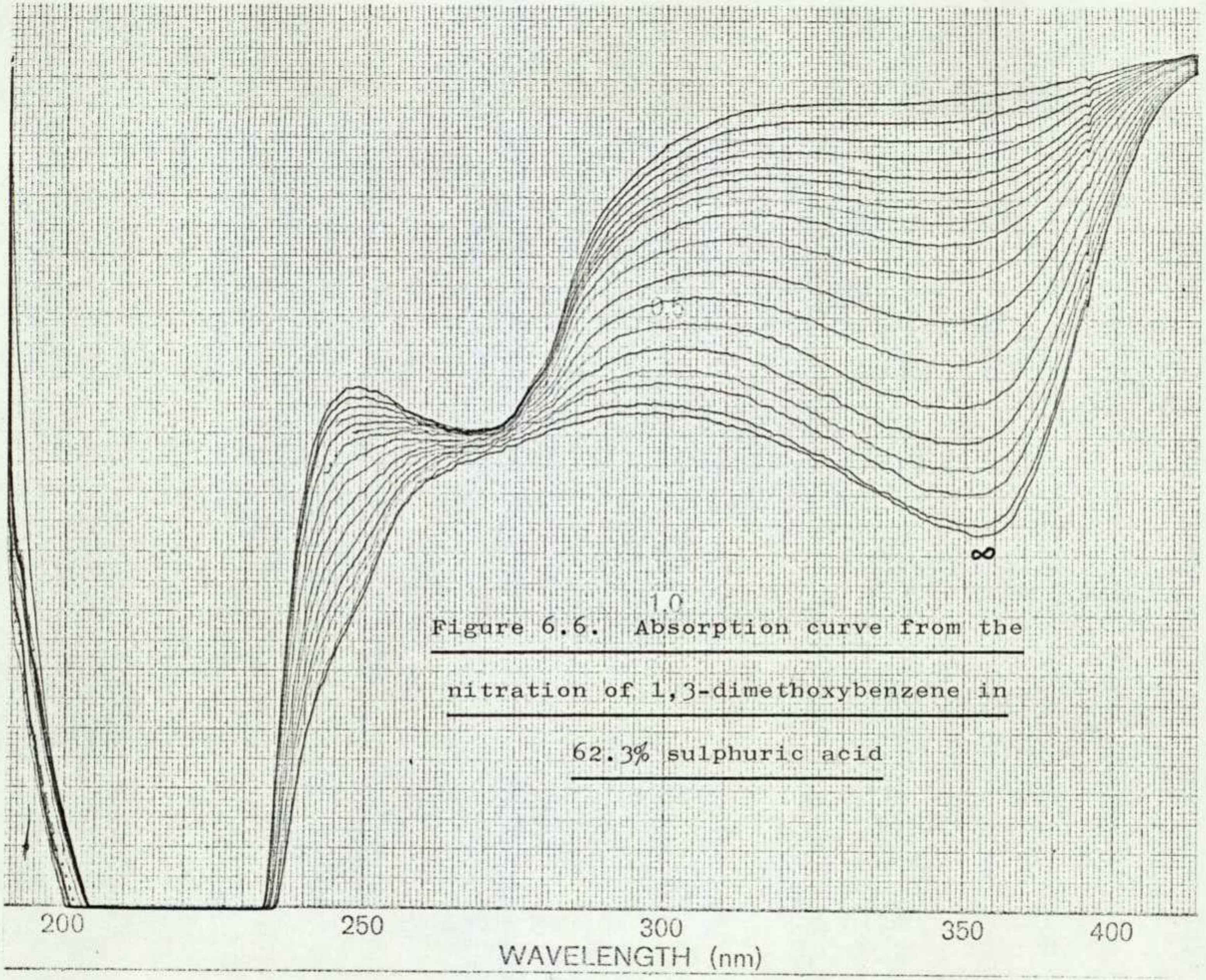


Figure 6.6. Absorption curve from the nitration of 1,3-dimethoxybenzene in 62.3% sulphuric acid

Table 6.8

Data from a typical determination of the rate of nitration of 1,3-dimethoxybenzene in 62.3% sulphuric acid at 25.0 $\pm$ 0.2°

Time	Absorbance at time t (At)	$(A_\infty - A_t)$	$\log_{10}(A_\infty - A_t)$
12	0.120	0.740	-0.130
85	0.150	0.710	-0.148
159	0.185	0.675	-0.170
232	0.216	0.644	-0.191
305	0.250	0.610	-0.214
378	0.270	0.590	-0.229
451	0.300	0.560	-0.251
525	0.320	0.540	-0.267
630	0.356	0.504	-0.297
825	0.412	0.448	-0.348
1115	0.480	0.380	-0.420
1445	0.558	0.302	-0.519
1880	0.631	0.229	-0.640
2440	0.691	0.169	-0.772
3012	0.740	0.120	-0.920
3650	0.780	0.080	-1.096
	0.860 (A_∞)		

obtained therefrom and Fig. 6.7 the plot of $\log_{10}(A_\infty - A_t)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{\text{HNO}_3} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$= \frac{2.303 \times 2.64 \times 10^{-4}}{2.33 \times 10^{-2}} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$\therefore \ k_2(\text{obs}) = 2.6 \times 10^{-2} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients determined over a range of percentages of sulphuric acid at various temperatures are given in Table 6.9. A graph of $\log_{10} k_2(\text{obs})$ vs % H_2SO_4 at 25° (and 22.7°) is shown in Fig. 6.8 and at various temperatures in Fig. 6.9. Table 6.10 gives the Arrhenius activation parameters for the nitration of 1,3-dimethoxybenzene.

6.32 YIELD OF NITRO COMPOUNDS

6.321 1,3,5-TRIMETHOXYBENZENE

Product from the nitration of 1,3,5-trimethoxybenzene in 56.1% sulphuric acid at 60° for 90 min. 3.9×10^{-5} moles 1,3,5-trimethoxybenzene used. 1.57×10^{-2} moles nitric acid used. Found: (35%) 1.4×10^{-5} moles 1,3,5-trimethoxybenzene, (40%) 1.59×10^{-5} moles 1,3,5-trimethoxy-2-nitrobenzene. No 1,3,5-trimethoxy-2,4-dinitrobenzene was found.

1,3,5-trimethoxybenzene and 1,3,5-trimethoxy-2-nitrobenzene were recovered quantitatively (98.7% and 96.3% respectively) by the extraction methods described in Section (7.41) from a solution in 56.1% sulphuric acid at 60.0 ± 0.2°, after allowing the solution to stand for

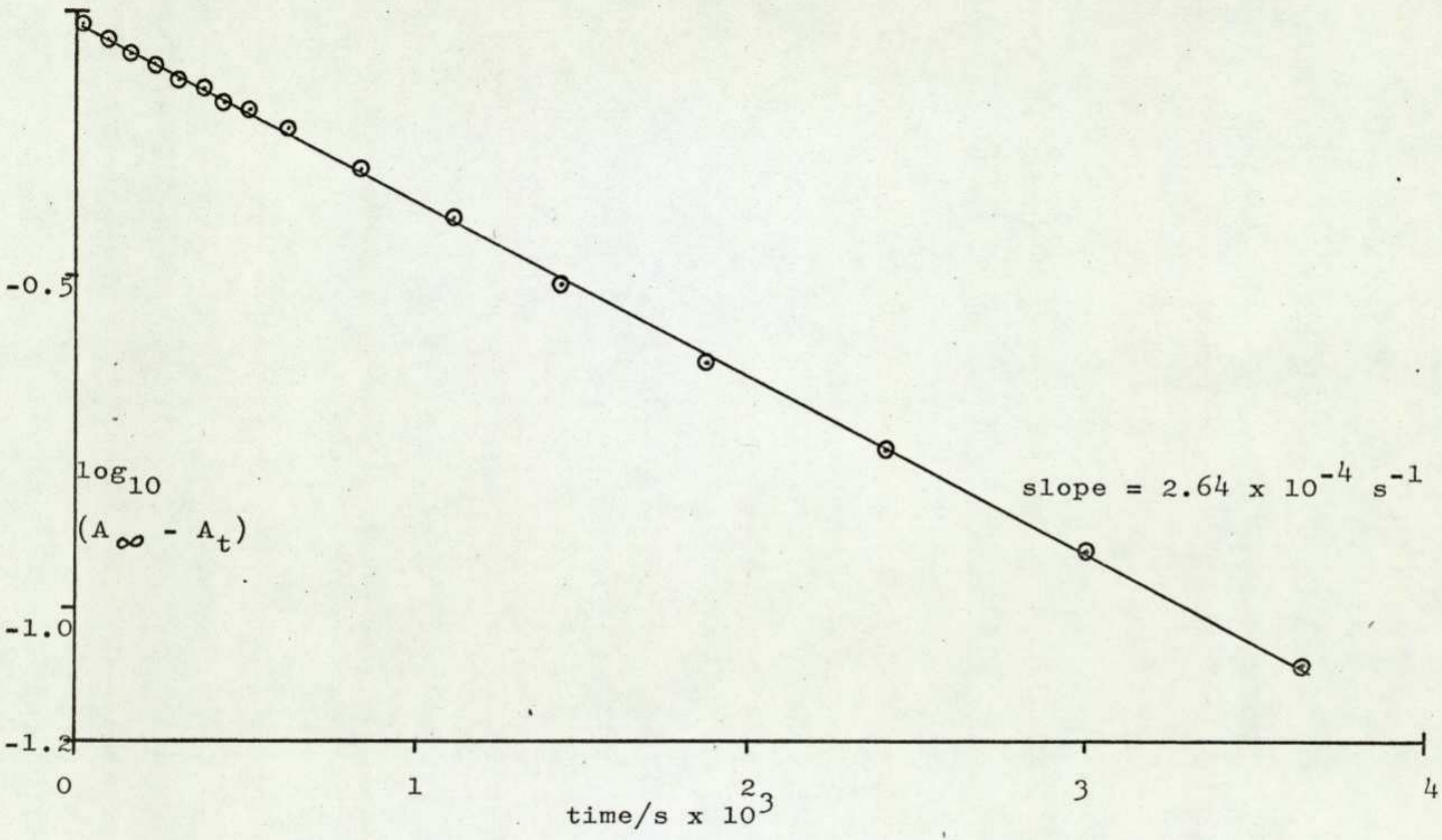


Figure 6.7. Plot of $\log_{10} (A_\infty - A_t)$ *vs* time from the nitration of 1,3-dimethoxybenzene in 62.3% sulphuric acid

Table 6.9

Second-order rate coefficients for the nitration of 1,3-dimethoxybenzene[c,d,e] in sulphuric acid

H_2SO_4 (%)[b]	$[HNO_3]$/ 10^{-2} mole dm^{-3}	$-(H_R + \log_{10} a_{H_2O})^{f,g}$	$k_2(obs)/dm^3$ $mole^{-1}$ s^{-1}
	At[a] 22.7°		
64.24		11.627	0.069
63.08		11.282	0.035
61.83		10.918	0.019
58.27		9.888	0.0019
57.67		9.777	0.0014
	At 25.0 ± 0.2°		
69.1	0.089	13.137	1.65
66.1	0.17	12.118	2.6×10^{-1}
62.4	2.30	10.994	2.6×10^{-2}
58.1	5.50	9.74	2.4×10^{-3}
56.1	5.50	9.06	8.6×10^{-4}
	At 40.0 ± 0.2°		
56.1	5.44	8.52	3.8×10^{-3}
54.0	5.44	8.00	1.3×10^{-3}
52.0	5.44	7.40	4.8×10^{-4}

Table 6.9 (continued)

H_2SO_4 (%)[b]	$[HNO_3]$/ 10^{-2} mole dm^{-3}	$-(H_R + \log_{10} a_{H_2O})$[f,g]	$k_2(obs)/dm^3$ $mole^{-1}$ s^{-1}
		At 60.0 ± 0.2°	
52.0	5.40	6.55	5.0×10^{-3}
49.8	5.40	6.164	1.9×10^{-3}
48.2	5.40	5.785	9.8×10^{-4}
		At 85.0 ± 0.5°	
48.2	5.32	4.606	6.4×10^{-3}
46.0	5.32	4.286	2.8×10^{-3}
44.4	5.32	4.051	1.2×10^{-3}

a) Ref. 135

b) ± 0.1%

c) [Substrate] 9.8×10^{-5} mole dm^{-3}

d) [Sulphamic acid] ca 2×10^{-2} mole dm^{-3}

e) Measurement at 350 or 360nm

f) Refs. 125 and 142

g) a_{H_2O} assumed to be constant over the temperature range in this study.

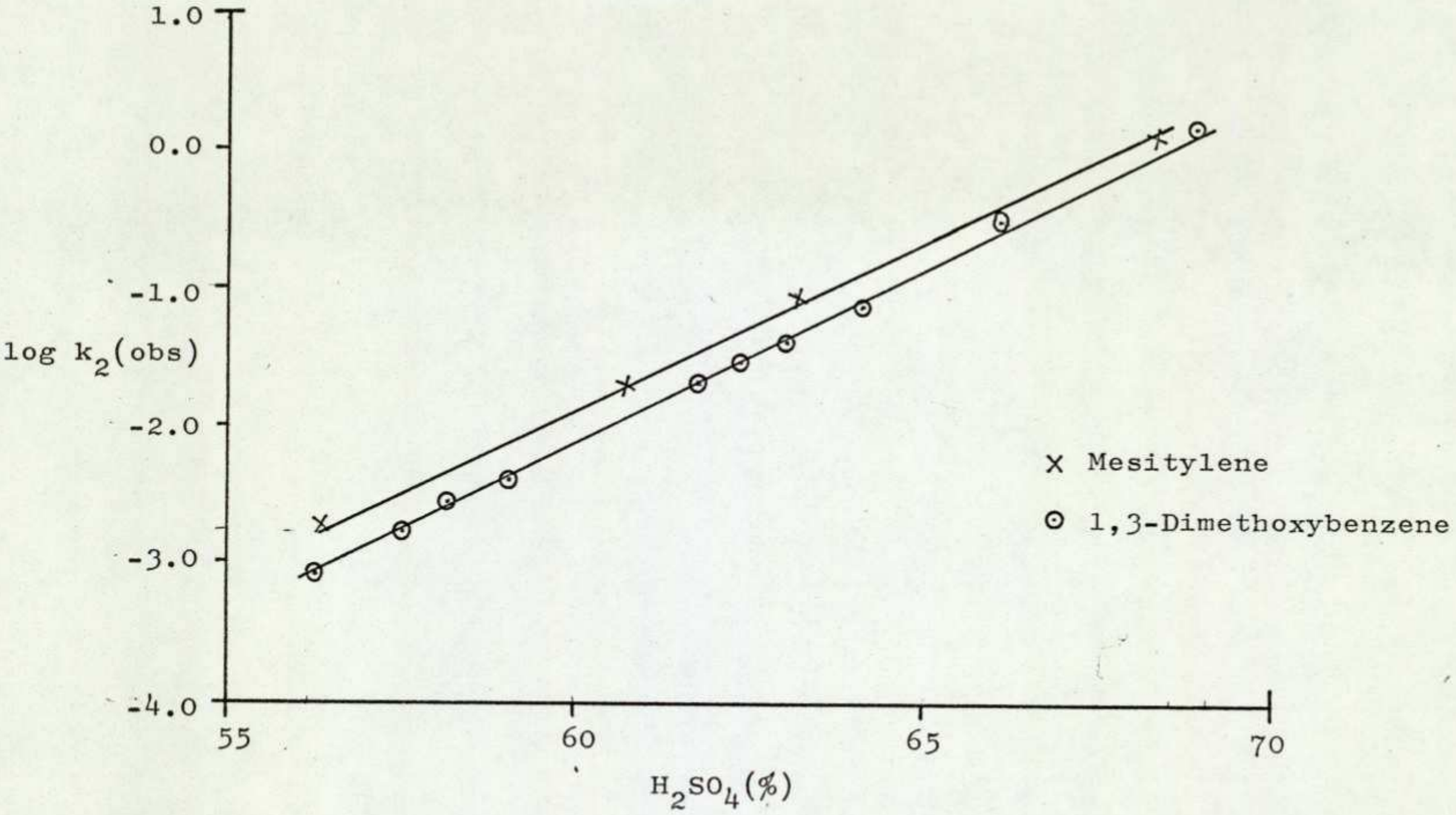


Figure 6.8. Rate profile from the nitration of 1,3-dimethoxybenzene in sulphuric acid

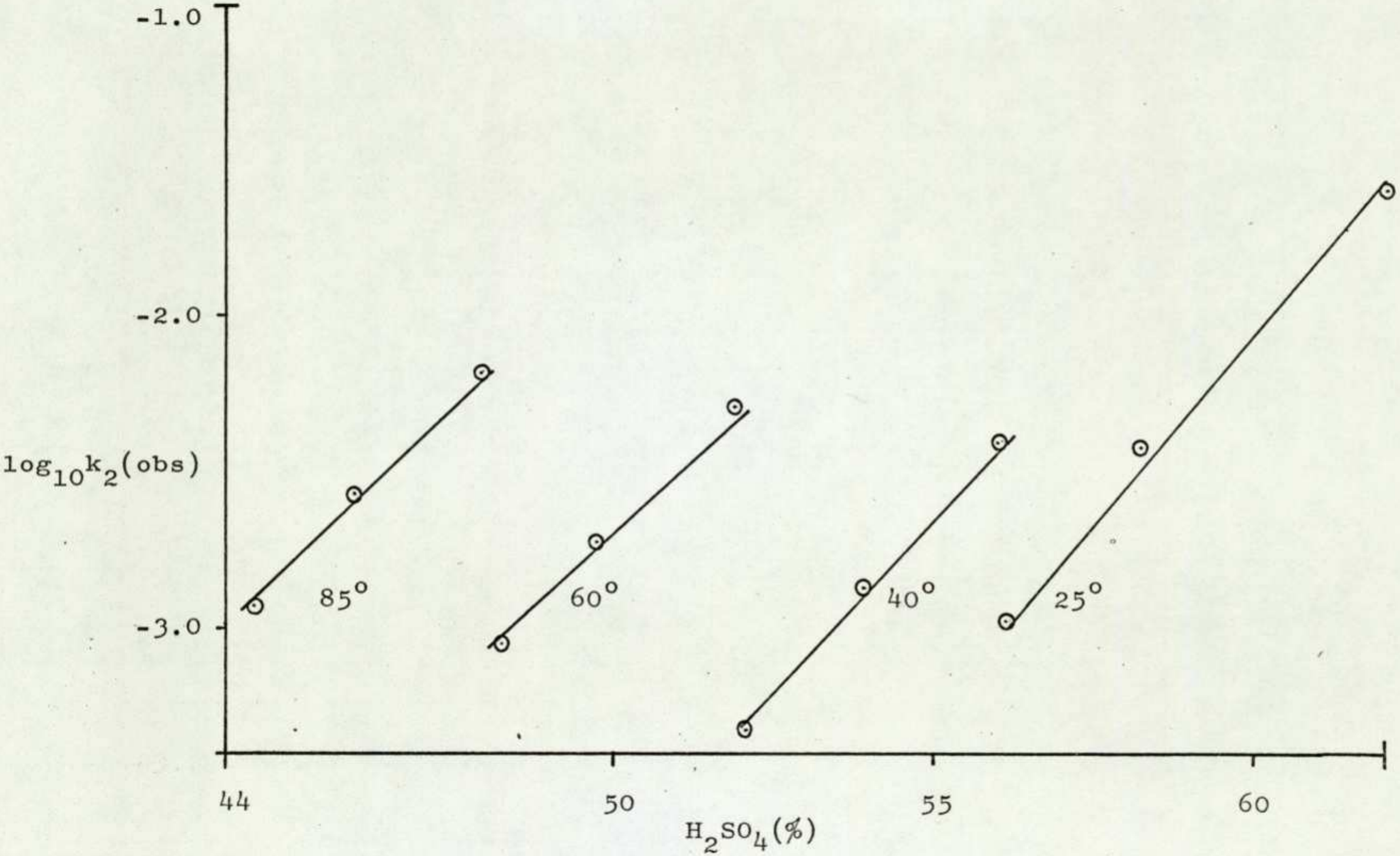


Figure 6.9. Rate profile from the nitration of 1,3-dimethoxybenzene in sulphuric acid at various temperatures

Table 6.10

Activation parameters for the nitration of 1,3-dimethoxybenzene[a] in sulphuric acid

H_2SO_4 (%)[b]	Temp range (^oC)	E_A /k cal $mole^{-1}$	$log_{10}A$
56.1	25 - 40	18	10
52.0	40 - 60	24	14
48.2	60 - 85	18	9

a) $\left[\text{Substrate}\right] = 9.8 \times 10^{-5}$ mole dm^{-3}
b) ± 0.1%

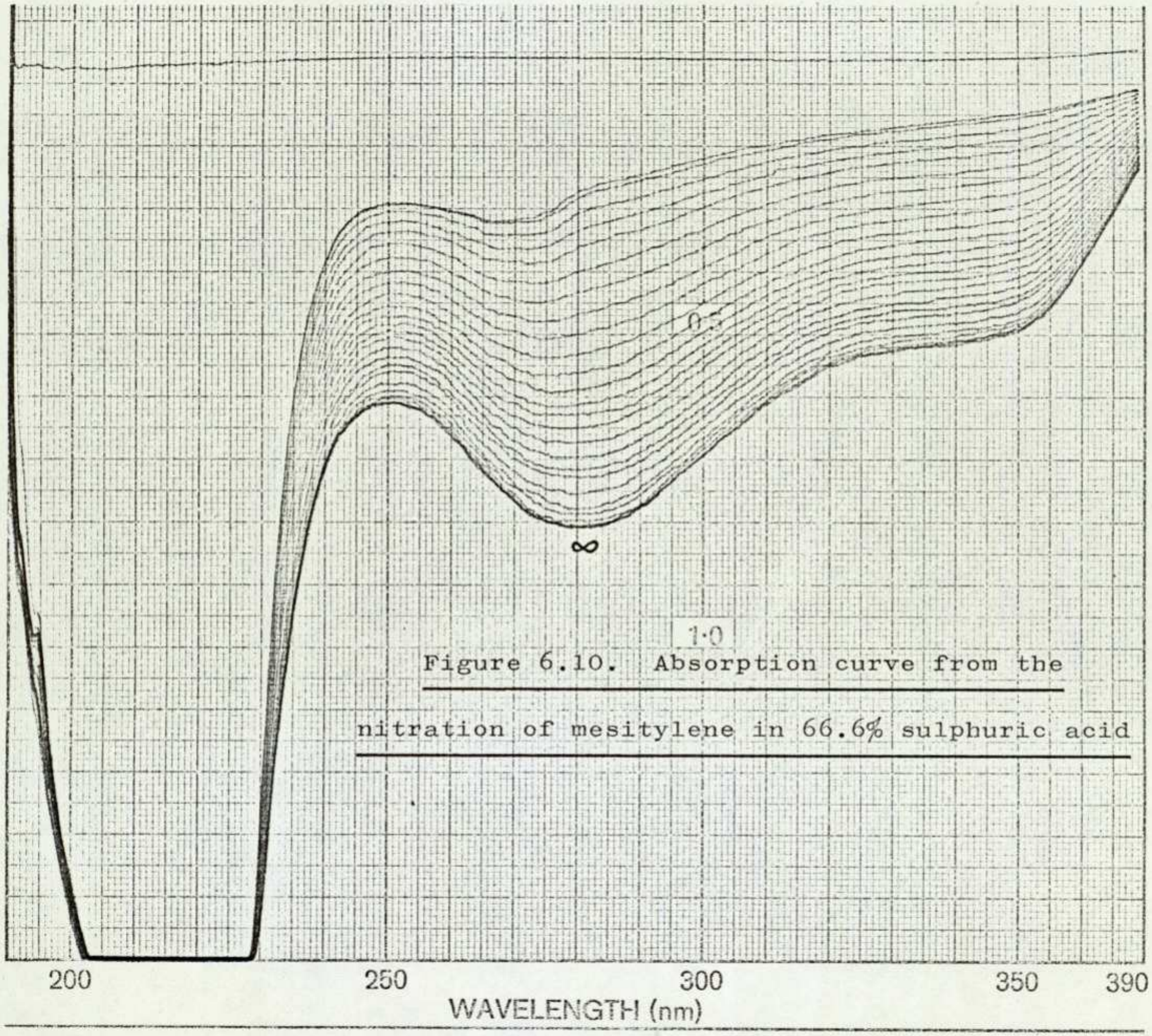


Figure 6.10. Absorption curve from the nitration of mesitylene in 66.6% sulphuric acid

Table 6.11

Data from a typical determination of the rate of nitration of mesitylene in 66.6% sulphuric acid at 25.0 ± 0.2°

Time (t)/s	Absorbance at time t (A_t)	(A_∞ - A_t)	$\log_{10}$(A_∞ - A_t)
20	0.271	0.539	-0.268
85	0.283	0.527	-0.278
195	0.308	0.502	-0.299
295	0.335	0.475	-0.323
403	0.360	0.450	-0.346
557	0.400	0.410	-0.387
717	0.431	0.379	-0.421
892	0.468	0.342	-0.465
1004	0.500	0.310	-0.508
1265	0.532	0.278	-0.555
1525	0.562	0.248	-0.605
1665	0.578	0.232	-0.634
1858	0.612	0.198	-0.703
2076	0.630	0.180	-0.744
2275	0.650	0.160	-0.795
2592	0.672	0.138	-0.860
2962	0.697	0.113	-0.946

Table 6.11 (continued)

Time $(t)/s$	Absorbance at time t (A_t)	$(A_\infty - A_t)$	$\log_{10}(A_\infty - A_t)$
3328	0.715	0.095	-1.022
3685	0.725	0.085	-1.070
4380	0.755	0.055	-1.259
5360	0.778	0.032	-1.494
	0.810 (A_∞)		

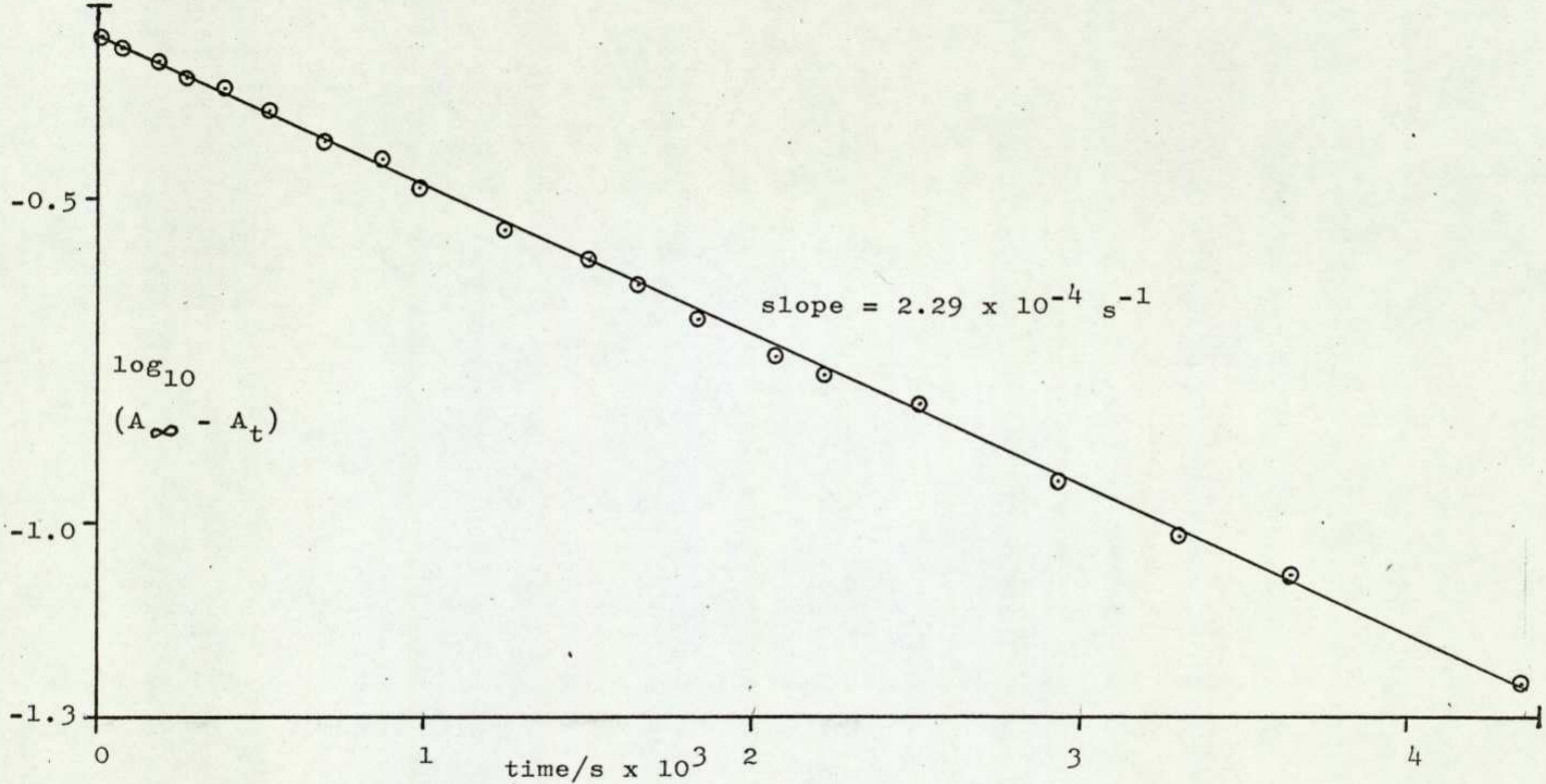


Figure 6.11. Plot of $\log_{10}$ $(A_\infty - A_t)$ vs time for the nitration of mesitylene in 66.6% sulphuric acid

Table 6.12

Second-order rate coefficients for the nitration of mesitylene[a,b,c] in sulphuric acid

H_2SO_4 (%)[d]	$[HNO_3]$/ 10^{-2}mole dm^{-3}	$-(H_R + \log_{10}a_{H_2O})$	k_2(obs)/dm^3 mole^{-1} s^{-1}
	At 25.0 ± 0.2°		
68.3[e]	0.087	12.925	2.1
66.6[f]	0.089	12.304	6.1×10^{-1}
63.2[e]	2.30	11.222	8.6×10^{-2}
62.2[g]	2.30	10.994	4.7×10^{-2}
60.7[e]	5.30	10.495	2.0×10^{-2}
60.3[j]	5.50	10.377	1.6×10^{-2}
58.1[g]	5.50	9.440	5.0×10^{-3}
57.2[j]	5.50	9.439	2.7×10^{-3}
56.3[e]	5.30	9.130	1.8×10^{-3}
	At 40.0 ± 0.2°		
58.1[h]	5.44	9.03	2.3×10^{-2}
58.1[h]	5.44	9.03	2.3×10^{-2}
56.1[h]	5.44	8.52	9.8×10^{-3}
56.1[h]	5.44	8.52	9.4×10^{-3}
53.9[h]	5.44	7.917	2.9×10^{-3}

Table 6.12 (continued)

H_2SO_4 (%)[d]	$[HNO_3]$/ 10^{-2}mole dm^{-3}	$-(H_R + \log_{10}a_{H_2O})$	k_2(obs)/dm^3 $mole^{-1}$ s^{-1}
	At 60.0 ± 0.2°		
53.9[i]	5.39	6.977	3.0×10^{-2}
52.0[i]	5.39	6.55	1.1×10^{-2}
49.8[i]	5.39	6.164	2.8×10^{-2}
	At 85.0 ± 0.5°		
49.8[i]	5.32	4.927	5.0×10^{-2}
48.2[i]	5.32	4.606	2.6×10^{-2}
46.2[i]	5.32	4.281	8.9×10^{-3}
44.0[i]	5.32	3.993	4.1×10^{-3}

a) [Sulphamic acid] <u>ca</u> 2×10^{-2} mole dm^{-3}

b) [Substrate] 1.10×10^{-4} mole dm^{-3}

c) 40mm cells used

d) ± 0.1%

e) Ref. 22

f) Measurement at 280nm

g) Measurement at 340nm

h) Measurement at 345nm

i) Measurement at 350nm

j) Ref. 136

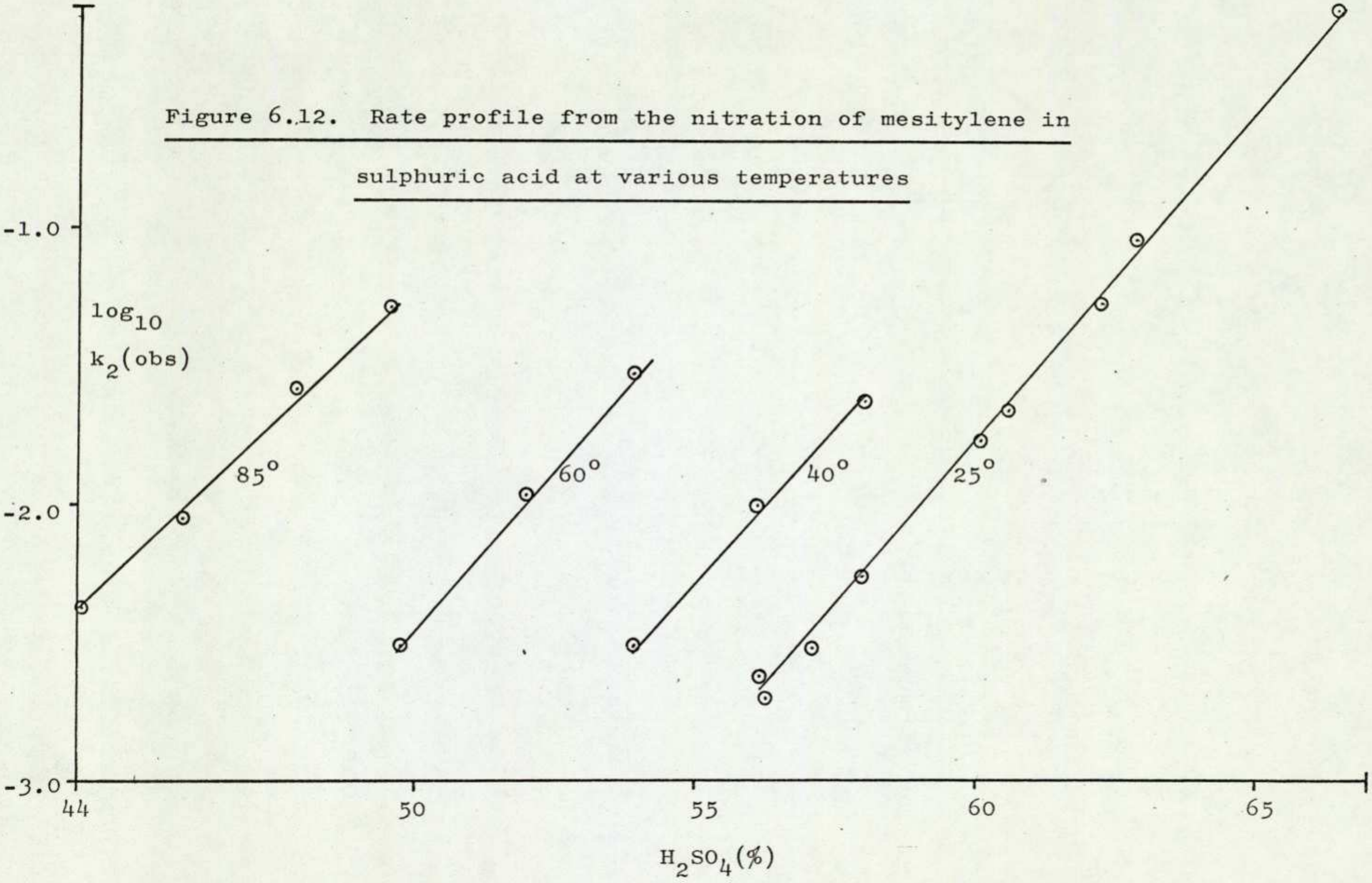


Figure 6.12. Rate profile from the nitration of mesitylene in sulphuric acid at various temperatures

Table 6.13

Activation parameters for the nitration of mesitylene[a] in sulphuric acid

H_2SO_4 (%)[b]	Temp range (^{o}C)	E_A /k cal mole^{-1}	$\log_{10}A$
58.1	25 - 40	19	12
56.1	25 - 40	21	13
53.9	40 - 60	24	14
49.8	68 - 85	27	15

a) $\left[\text{Substrate}\right] = 1.10 \times 10^{-4}$ mole dm^{-3}

b) ± 0.1%

90 mins.

6.33 MESITYLENE

The results and subsequent calculation for a typical determination of a rate coefficient for the nitration of mesitylene are given below.

Sulphuric acid	66.6% (wt/wt)
$[HNO_3]$	8.94×10^{-4} mole dm^{-3}
[Mesitylene]	1.10×10^{-4} mole dm^{-3}
[Sulphamic acid]	2×10^{-2} mole dm^{-3}
Temperature	25.0 ± 0.2^{o}
Measurement taken at	280nm

Fig. 6.10 shows the absorption curve, Table 6.11 the data obtained therefrom, and Fig. 6.11 the plot of $\log_{10}(A_t - A_\infty)$ vs t.

$$k_2(\text{obs}) = \frac{2.303 \times \text{slope}}{HNO_3} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

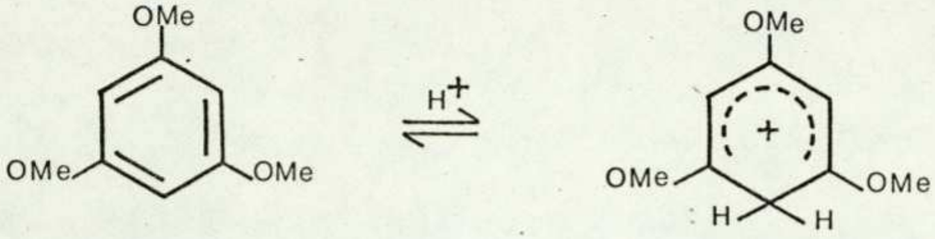
$$= \frac{2.303 \times 2.29 \times 10^{-4}}{8.94 \times 10^{-4}} \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

$$\therefore k_2(\text{obs}) = 0.59 \text{ dm}^3 \text{ mole}^{-1} \text{ s}^{-1}$$

Second-order rate coefficients determined over a range of percentages of sulphuric acid at various temperatures are given in Table 6.12 and a graph of $\log_{10} k_2(\text{obs})$ vs % H_2SO_4 is shown in Fig. 6.12. Table 6.13 gives the Arrhenius activation parameters for the nitration of mesitylene.

6.4 DISCUSSION

1,3,5-Trimethoxybenzene has been shown to undergo reversible protonation[137] in aqueous acids, to give the protonated species (6.I).



(6·I)

1,3,5,-Trimethoxybenzenonium ion

Table 6.14 gives the values of $\log_{10}$ I (indicator ratio) of 1,3,5-trimethoxybenzene in sulphuric acid. Fig. 6.13 shows a plot of $\log_{10}$ I (indicator ratio of 1,3,5-trimethoxybenzene in sulphuric acid) vs the acidity function $-H_c$ (where H_c is based on the protonation of certain aromatic carbon bases such as azulene). From this plot which has a linear unit slope the indicator ratio can be determined for a given concentration of sulphuric acid. The indicator ratio (I) can be used to find the amount of unprotonated species by the following equation.

$$I = \frac{BH^+}{B}$$

Where I = Indicator ratio

BH^+ = Concentration of protonated species

B = Concentration of aromatic base

Thus for 66.6% sulphuric acid

$$I = 133.5$$

$$\therefore \% \text{ unprotonated } B = \frac{100}{I + 1}$$

$$B = \frac{100}{134.5} \qquad B = 0.75\%$$

Table 6.14

Indicator ratios for 1,3,5-trimethoxybenzene in sulphuric acid

H_2SO_4(%)	$-H_c$[138]	$\log_{10}I$[137]
44.22	4.47	-1.521
46.84	5.03	-1.136
48.23	5.32	-0.887
49.26	5.42	-0.721
50.76	5.66	-0.468
51.87	5.84	-0.302
52.97	6.02	-0.130
54.79	6.33	0.181
55.34	6.43	0.259
56.62	6.66	0.450
58.41	7.00	0.791
60.29	7.31	1.068
61.71	7.58	1.404

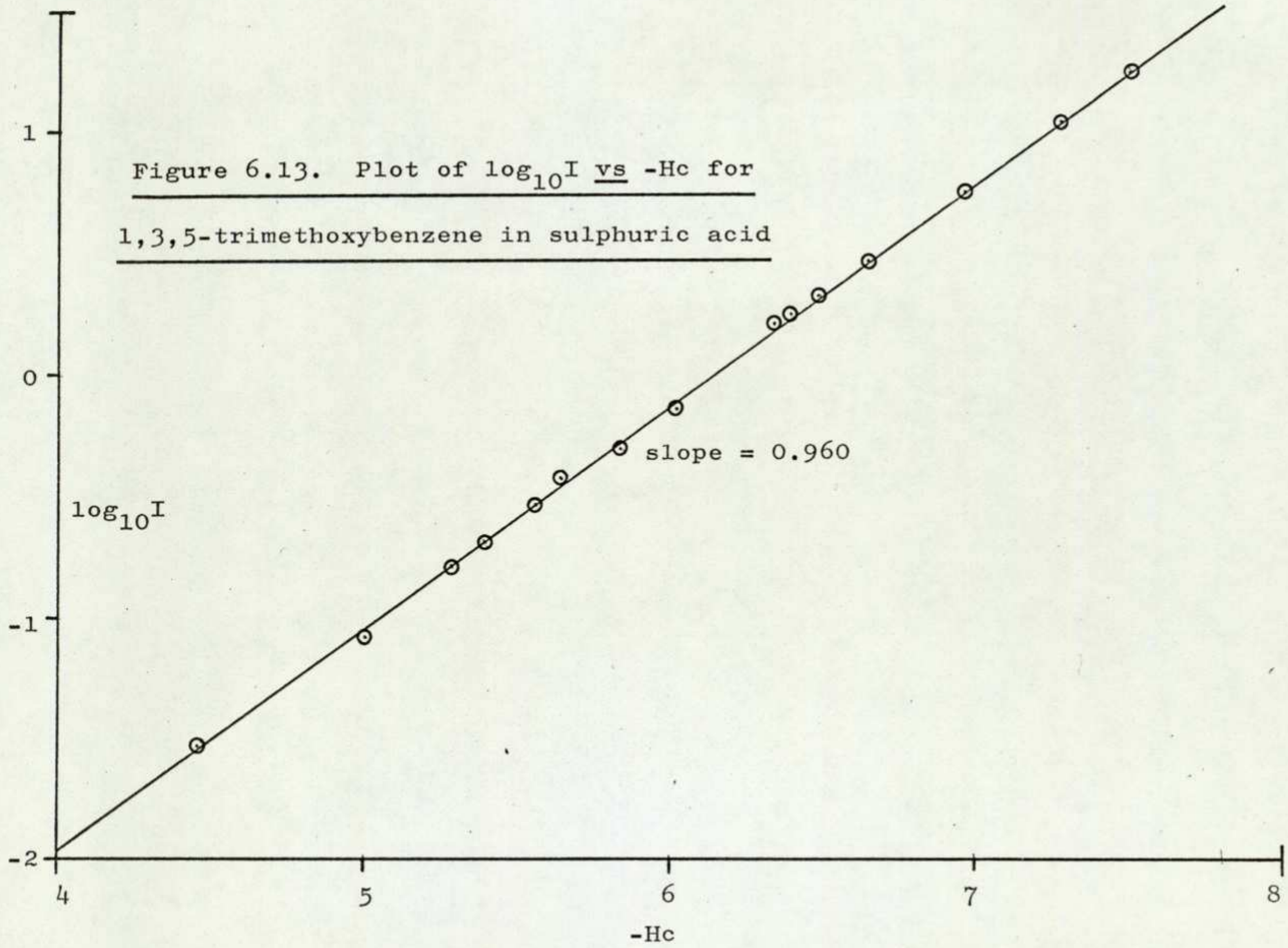


Figure 6.13. Plot of $\log_{10}I$ *vs* -Hc for 1,3,5-trimethoxybenzene in sulphuric acid

Protonation of 1,3,5-trimethoxybenzene caused the observed rate of nitration to be lower than might have been expected, and the increase in rate with increasing acidity is less than that found for unprotonated compounds. The observed rate of nitration for 1,3,5-trimethoxybenzene and the degree of protonation can be used to calculate the rate of nitration for the unprotonated species.

$$k_2\ (B) = \frac{100}{\%\ B} \times k_2(\text{obs})\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

Thus for nitration in 66.6% sulphuric acid

$$k_2\ (B) = \frac{100}{0.75} \times 2.45 \times 10^{-3}\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

$$k_2\ (B) = 3.3 \times 10^{-1}\ \text{dm}^3\ \text{mole}^{-1}\ \text{s}^{-1}$$

Table 6.15 gives the calculated rates of reaction for the unprotonated species B, together with the observed second-order rate coefficients for mesitylene, and Fig. 6.14 shows a plot of log k_2 (B) vs acidity with a plot for mesitylene as a comparison. From Table 6.15 it can be seen that the calculated second-order rate coefficient for the unprotonated species, is approximately half that of mesitylene and from Fig. 6.14 it can be seen that the rate profile is parallel to that of mesitylene. This type of rate profile is characteristic of some compounds that are nitrated at the encounter rate (see Section 2.41). Above 40° a fast secondary reaction occurs. This may be fortuitous nitrosation, and might have been stopped by the addition of sulphanilic acid to both the

Table 6.15

Second-order rate coefficients for the nitration of 1,3,5-trimethoxybenzene and mesitylene at 25.0 and 40.0°

		1,3,5-Trimethoxybenzene		Mesitylene
H_2SO_4 (%)	%B	k_2(obs)/ dm^3 $mole^{-1}$ s^{-1}	k_2(B)/ dm^3 $mole^{-1}$ s^{-1}	k_2(obs)/ dm^3 $mole^{-1}$ s^{-1}
67.8[a]	0.63	3.0×10^{-3}	4.8×10^{-1}	1.4
66.6[a]	0.75	2.5×10^{-3}	3.3×10^{-1}	7.0×10^{-1}
64.3[a]	1.75	1.1×10^{-3}	6.5×10^{-2}	1.6×10^{-1}
62.4[a]	3.20	7.0×10^{-4}	2.1×10^{-2}	5.0×10^{-2}
60.8[a]	7.00	5.0×10^{-4}	7.2×10^{-3}	1.9×10^{-2}
60.8[b]	7.00	7.6×10^{-3}	1.1×10^{-1}	1.8×10^{-1}
58.1[b]	14.8	2.1×10^{-3}	1.4×10^{-2}	2.3×10^{-2}
56.1[b]	31.0	1.3×10^{-3}	4.2×10^{-3}	9.4×10^{-3}

a) 25.0 ± 0.2°

b) 40.0 ± 0.2°

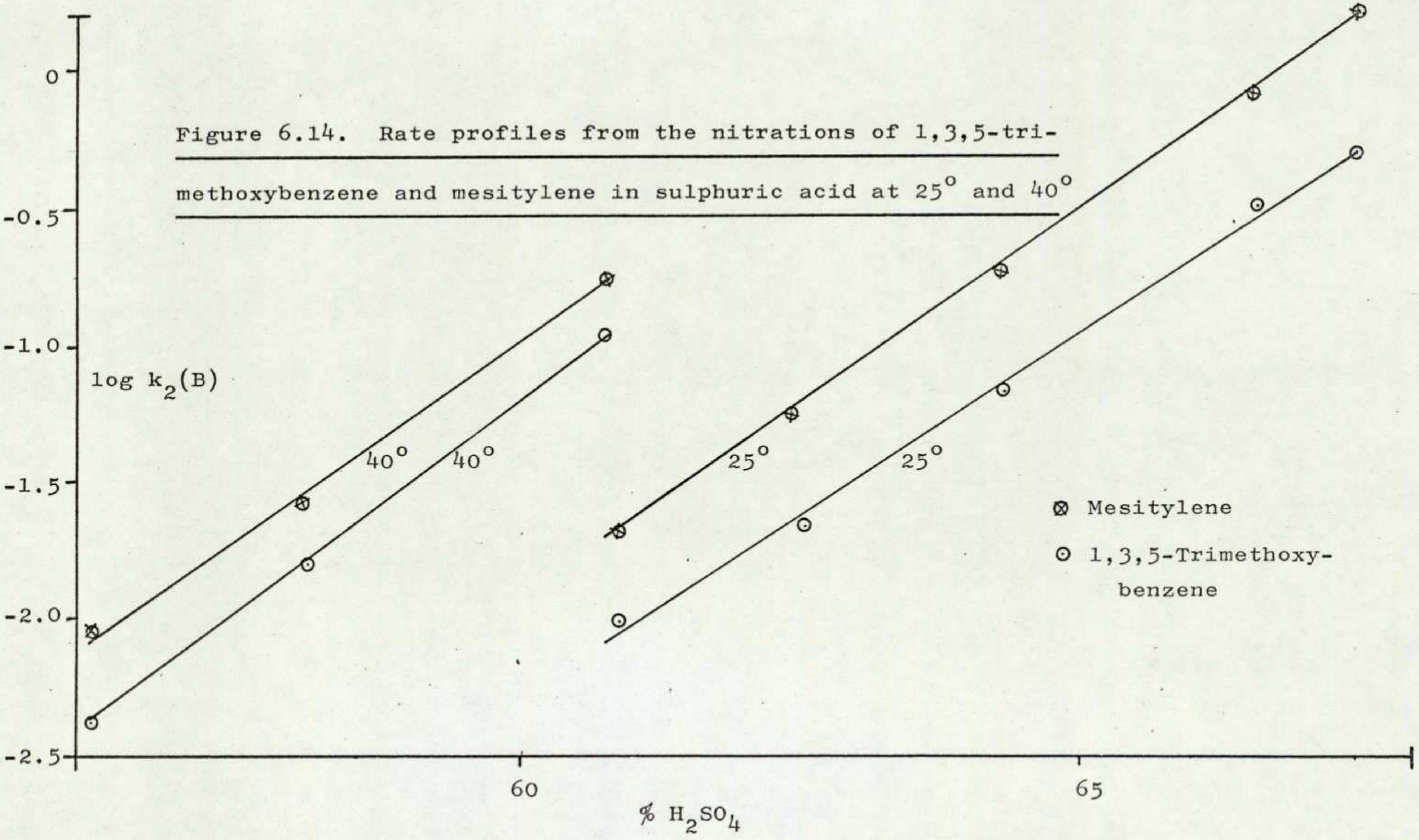


Figure 6.14. Rate profiles from the nitrations of 1,3,5-trimethoxybenzene and mesitylene in sulphuric acid at 25° and 40°

nitric acid solution and the substrate solution. This procedure was found to be effective in stopping the fortuitous nitrosation of p-cresol (see Section 3.32). The final u.v. spectrum was indicative of other than the expected nitro compounds. When the reaction products were determined for the nitration of 1,3,5-trimethoxybenzene in 56.1% sulphuric acid at 60°, only a 75% recovery of products and starting material was found indicating the formation of an undetected product.

1,3-Dimethoxybenzene is only protonated[137] to a small extent in 70% sulphuric acid. Table 6.16 shows the calculated amount of unprotonated species in various concentrations of sulphuric acid. The rate profile for the nitration of 1,3-dimethoxybenzene at 25.0° falls below and parallel to that of mesitylene (see Fig. 6.8). This is again characteristic of a compound reacting at the encounter rate, (see Section 2.41). The rates of nitration of 1,3,5-trimethoxybenzene (at 25° and 40°), and 1,3-dimethoxybenzene are approximately half that of mesitylene at 25.0°, 40.0° and 60.0°. For 1,3-dimethoxybenzene at 85.0° the rate is a third that of mesitylene. This situation is summarised in Tables 6.17 and 6.18.

This chapter is concerned with the search for electrophiles other than the nitronium ion, for the nitration of reactive aromatic compounds in low acidities. The operation of other electrophiles would be expected to change the slope of a plot of $\log_{10} k_2(\text{obs})$ vs $-(H_R + \log_{10} a_{H_2O})$, see Fig. 6.2. A plot of $\log_{10} k_2$ (B) vs

Table 6.16

Amount of unprotonated 1,3-dimethoxybenzene in various concentrations of sulphuric acid

H_2SO_4 (%)	Unprotonated Species (%)
70	86.2
65	98.4
60	99.7
55	99.95

Table 6.17

Comparison of the rate of nitration of 1,3-dimethoxybenzene and mesitylene

H_2SO_4 (%)	Temp (^oC)	$\frac{k_2\text{(obs) mesitylene}}{k_2\text{(obs) 1,3-dimethoxybenzene}}$
65	25.0	1.99
56	25.0	2.00
54	40.0	2.23
52	60.0	2.20
46	85.0	3.18

Table 6.18

Comparison of the rate of nitration of 1,3,5-trimethoxybenzene and mesitylene

H_2SO_4 (%)	Temp (^oC)	$\frac{k_2(\text{obs})\ \text{mesitylene}}{k_2(\text{B})\ \text{1,3,5-trimethoxybenzene}}$
68	25	2.92
65	25	2.46
61	25	2.60
61	40	1.64
56	40	2.24

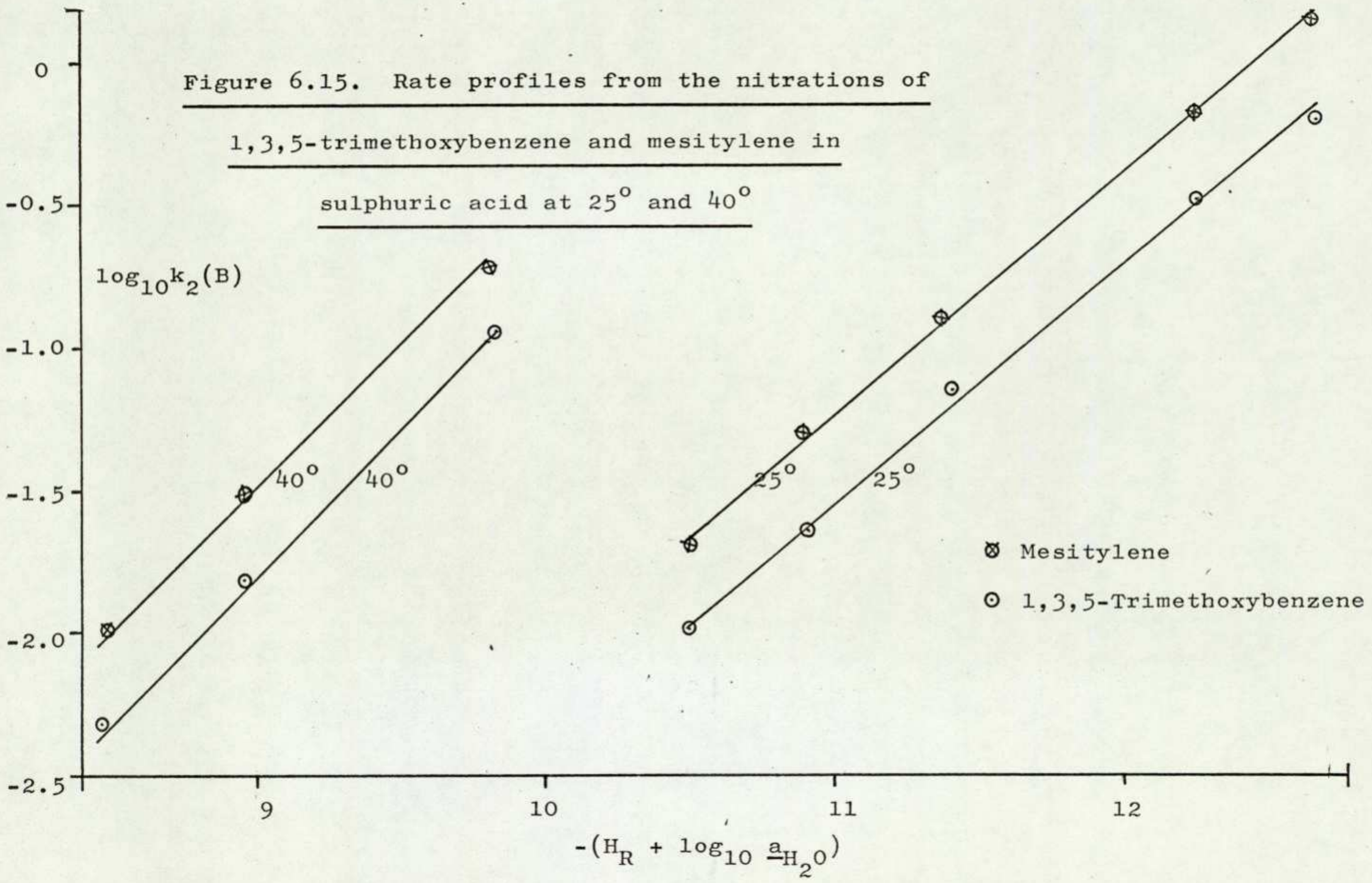


Figure 6.15. Rate profiles from the nitrations of 1,3,5-trimethoxybenzene and mesitylene in sulphuric acid at 25° and 40°

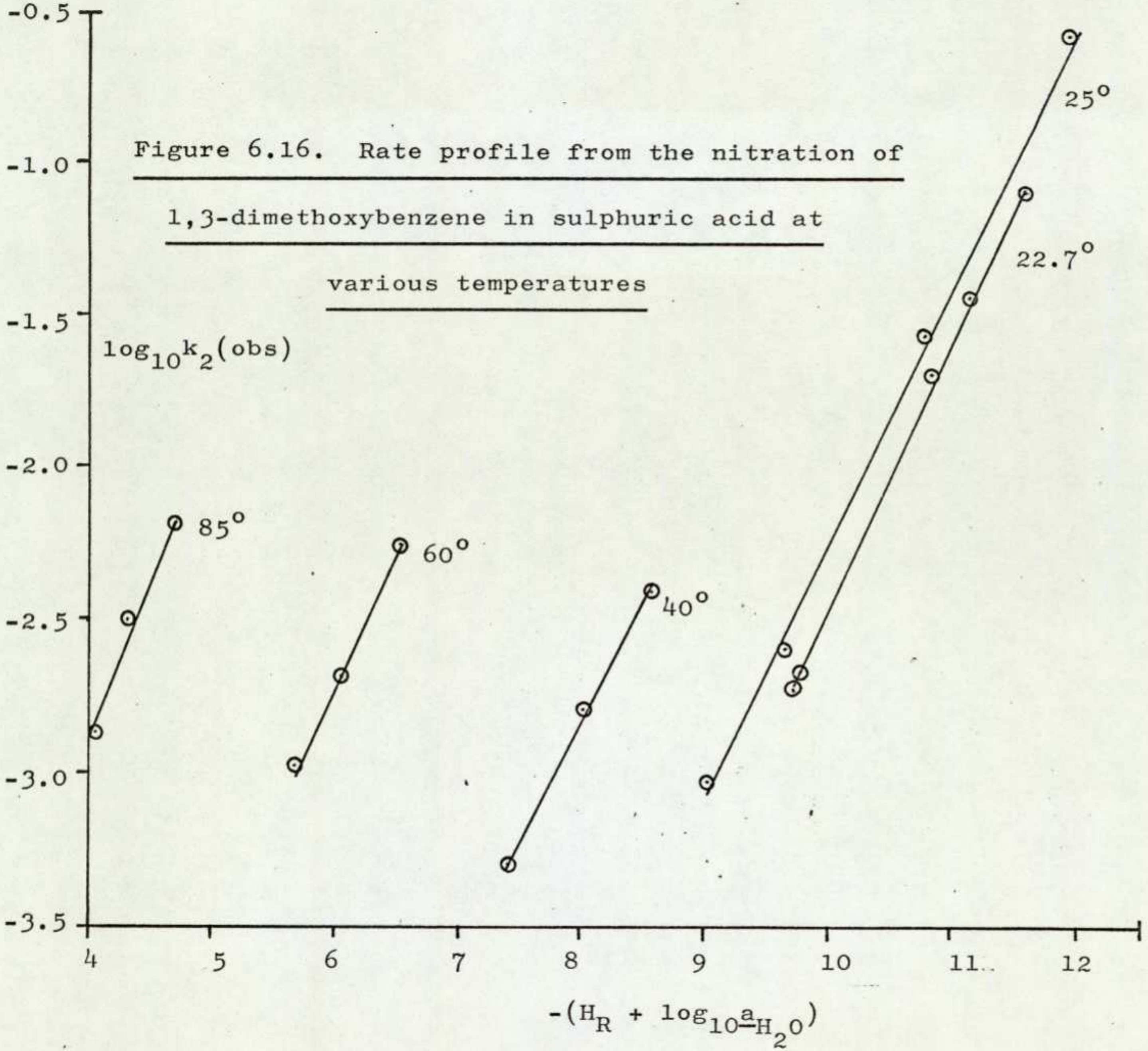


Figure 6.16. Rate profile from the nitration of 1,3-dimethoxybenzene in sulphuric acid at various temperatures

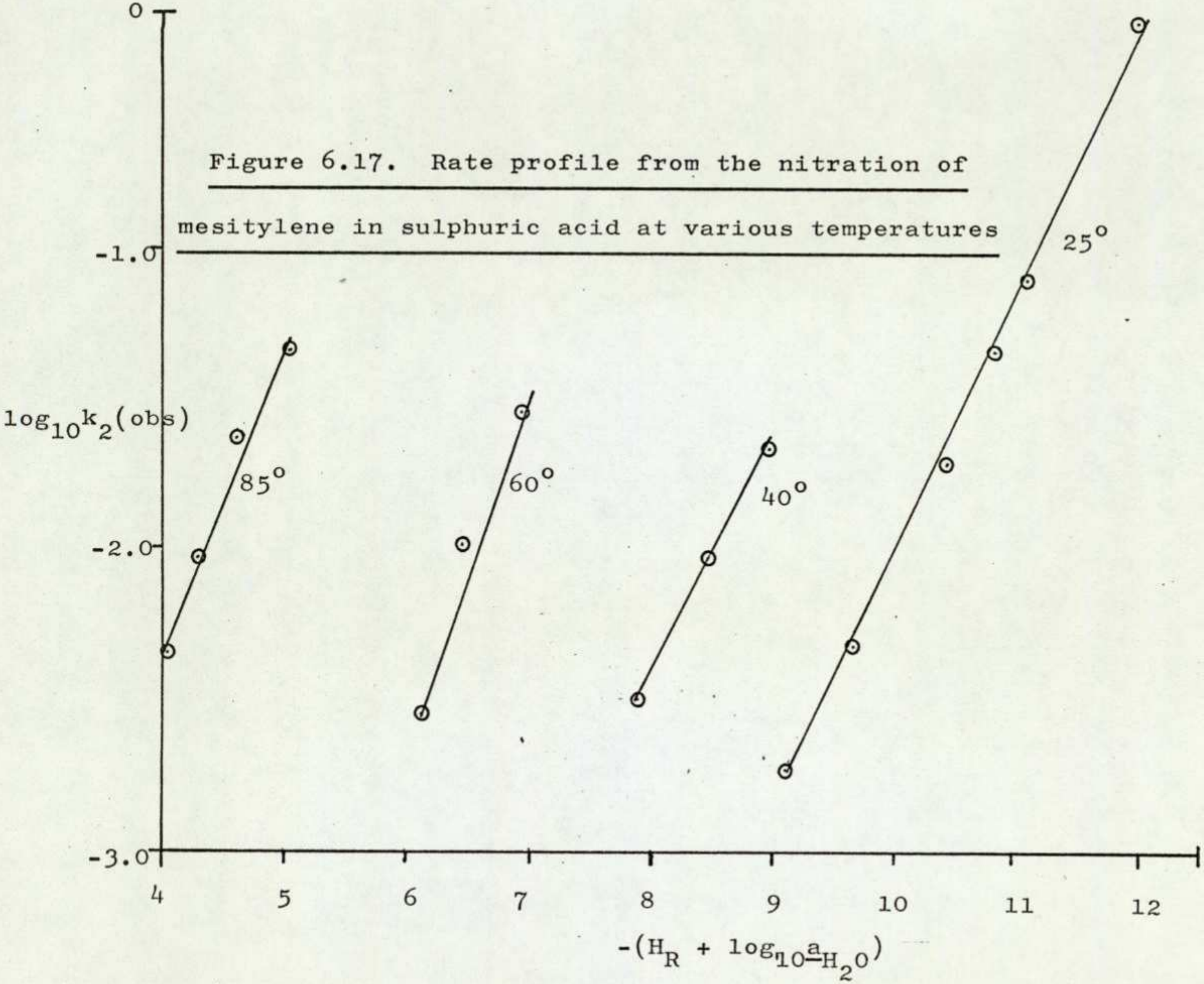


Figure 6.17. Rate profile from the nitration of mesitylene in sulphuric acid at various temperatures

$-(H_R + \log_{10} \underline{a}_{H_2O})$ is shown in Fig. 6.15 for 1,3,5-trimethoxybenzene. Plots of $\log_{10} k_2$ (obs) vs $-(H_R + \log_{10} \underline{a}_{H_2O})$ are shown in Fig. 6.16 for 1,3-dimethoxybenzene and Fig. 6.17 for mesitylene. For all three substrates the profiles form nearly parallel straight lines. For 1,3-dimethoxybenzene, mesitylene and 1,3,5-trimethoxybenzene the slopes were approximately 1 and the variation in slope with temperature is given in Table 6.19. The small variations are perhaps due to the change in $\underline{a}_{H_2O}$ with temperature and the inadequacy of the acidity function, but it is clear that there is no significant change in the slope of these profiles at lower acidities.

In this study $\underline{a}_{H_2O}$ has been assumed to be constant with increasing temperature. The variation of $\underline{a}_{H_2O}$ with temperature is known for sulphuric acid below 40 wt % from e.m.f. measurements[140]. At acidities up to 40% H_2SO_4, $\log_{10} \underline{a}_{H_2O}$ increases in a linear fashion with temperature according to the following equation[141].

$$\log_{10} \underline{a}_{H_2O} (T^{o}) = \log_{10} \underline{a}_{H_2O} (25^{o}) + (T - 298.15) B$$

B is a constant at a given percentage of sulphuric acid. A plot of B against wt % H_2SO_4 is a smooth curve, and in the region 0 - 40% H_2SO_4 $\log_{10}B$ can be fitted to a polynomial of third degree. However, this implies that B reaches a maximum at 44.5% H_2SO_4 and thereafter decreases with increasing acidity. Thus it is implied that $\underline{a}_{H_2O}$ decreases with temperature at high acidities, in contrast to its behaviour at low acidities. Such a conclusion is thought to be unlikely[145]. Therefore, $\underline{a}_{H_2O}$ has assumed

Table 6.19

Variation in the slope of $\log_{10} k_2(\text{obs})$ vs $-(H_R + \log_{10}a_{H_2O})$ for the nitration of 1,3-dimethoxybenzene and mesitylene in sulphuric acid at various temperatures

H_2SO_4 (%)	Temperature ($^\circ C$)	$\frac{-d \log_{10}k_2(\text{obs})}{d\,(H_R + \log_{10}a_{H_2O})}$ 1,3-dimethoxybenzene	mesitylene
64-58	22.7	0.90	-
69-56	25.0	0.83	0.90
58-52	40.0	0.80	0.86
52-48	60.0	0.82	0.93
48-44	85.0	1.05	1.05

to be constant.

From this study there is no evidence for a change of electrophile from the nitronium ion for substrates as reactive as mesitylene or more importantly, 1,3-dimethoxybenzene (expected to be 10^8 times as reactive as benzene towards the nitronium ion in the absence of encounter control) in as low as 44% sulphuric acid, or for 1,3,5-trimethoxybenzene in as low as 56% sulphuric acid.

The activation energies for the nitration of 1,3-dimethoxybenzene and mesitylene tend to increase with decreasing acidity (see Tables 6.10 and 6.13). The value obtained at 60.0 - 85.0° for 1,3-dimethoxybenzene is anomalous but this could be due to complications caused by a secondary reaction such as demethylation at the high temperatures.

The enthalpy of dissociation of nitric acid to the nitronium ion and hydroxide ion has been shown to decrease with increasing acidity[25], i.e. 10.8k cal mole^{-1} in 68.3% H_2SO_4, and 5.3 k cal mole^{-1} in 79.2% H_2SO_4. The mechanism of nitration is thought to be

$$HNO_3 \overset{K}{\rightleftharpoons} NO_2^+ + OH^- \quad .... \quad 6.8$$

$$NO_2^+ + Ar \xrightarrow{k_1} \text{Products} \quad .... \quad 6.9$$

If the second step is an encounter-controlled process, its apparent activation energy arising largely from the temperature coefficient of the viscosity of the medium should be 6 - 7 k cal mole^{-1}. The enthalpy change for the first step is 10.8 k cal at 68.5% H_2SO_4, thus the expected activation energy for encounter controlled nitration at 68.3% H_2SO_4 would be 18 k cal mole^{-1}, and this value would be expected to increase with decreasing acidity due to the larger contribution of the first process. The activation energies obtained for mesitylene agree with this theory, as do the first two values obtained for 1,3-dimethoxybenzene.

The activation energy for the nitration of 1,3,5-trimethoxybenzene in 60.8% sulphuric acid is higher than expected (i.e. 33.5 k cal mole^{-1}). This high value is probably due to the temperature variation of the protonation equilibrium. This should lead to an activation energy[139] contribution of 8 k cal mole^{-1}. Therefore, the activation energy obtained for the nitration of 1,3,5-trimethoxybenzene in 60.8% H_2SO_4 is of the expected order.

CHAPTER 7

GENERAL EXPERIMENTAL DETAILS

7.0 EXPERIMENTAL

7.1 INTRODUCTION

In this section a general description will be given of the materials used and the experimental methods employed in this study. Where changes were made or where the syntheses of standard compounds were carried out, reference has been made in the appropriate sections in each chapter.

7.2 MATERIALS

98% Sulphuric acid (Fison's A.R.), 70% nitric acid (Fison's A.R.), glacial acetic acid (Fison's A.R.), perchloric acid, sulphanilic acid and urea were Analar grade reagents. Concentrations of diluted H_2SO_4 solutions were determined from density measurements carried out using a Stanton specific gravity balance (Westphall type). The determined density at known temperature, was compared with values given in International Critical Tables of Numerical Data, Physics, Chemistry and Technology. A similar method was used to determine the concentration of perchloric acid and the concentration of the stock Analar nitric acid solution (nominally 70%) which was found to be 70.6%. Chloroform, dichloromethane, diethyl ether and sulphamic acid were of G.P.R. grade.

7.3 KINETIC MEASUREMENTS

A solution of the substrate in acetic acid was prepared and an aliquot (typically 0.10cm^3 of solution containing <u>ca</u> 4 x 10^{-4}g of substrate) was added to the appropriate concentration of aqueous sulphuric acid ($25cm^3$) containing 5×10^{-2}g of nitrous acid inhibitor (urea, sulphanilic acid or sulphamic acid). This solution was thermostatted at the appropriate temperature for 30 minutes. The thermometer used was calibrated against a thermometer standardised by the B.S.I. A solution of nitric acid, of the appropriate concentration, was prepared by dilution of the stock (70%) nitric acid sometimes with water, and then with the appropriate concentration of sulphuric acid. $1.0cm^3$ of this nitric acid solution was then added to the substrate solution (to give a concentration of nitric acid of 5.5×10^{-2} - 4.5×10^{-4} mole dm^{-3}).

The addition of the substrate in acetic acid and the nitric acid solution dilute the sulphuric acid. Calculations show that a correction of -0.05% should be applied for the latter. When pipetting viscous solutions the correct volume was found to be delivered by blowing out the final drop of liquid from the pipette. After mixing, the solution was rapidly transferred to a silica cell in the thermostatted cell compartment ($\pm$ 0.2° at 25.0, 40.0 and 60.0° and $\pm$ 0.5° at 85.0°) of a Perkin Elmer PE402, or a Pye Unicam S.P. 1800 or 8000 spectrophotometer. The change in absorbance with time was measured (t = 0 at time of mixing) either over a range of wavelengths, or at one predetermined wavelength. The course of the reaction was followed until the absorbance reached a constant value recorded as the 'infinity' reading (A_{∞}), usually taken after 7 - 10 half-lives.

From these measurements plots of $\log_{10}(A_\infty - A_t)$ vs t were constructed. From these, values of k_2(obs) were obtained using the following expression.

$$k_2(\text{obs}) = \frac{2.303 \log \dfrac{(A_\infty - A_t)}{t}}{[HNO_3]}$$

7.4 PRODUCT ANALYSIS

(i) From reactions in less than 75% sulphuric acid

A solution of the substrate in acetic acid was prepared and an aliquot (typically $1.0cm^3$ of solution containing ca 4×10^{-3}g of substrate) was added to sulphuric acid ($250cm^3$) of the required concentration, containing 2×10^{-1}g of nitrous acid inhibitor (urea, sulphanilic acid or sulphamic acid). This solution was equilibrated at 25.0 ± 0.2° in a thermostatically controlled water bath.

A nitric acid solution of the appropriate concentration was prepared by the dilution of 70% nitric acid. $10cm^3$ of this solution was then added to the substrate solution to give a concentration of nitric acid of $5.5 \times 10^{-2} - 8.94 \times 10^{-4}$ mole dm^{-3}.

The solutions were initially shaken to ensure mixing (the dead space in the reaction was negligible). The reactions were allowed to proceed for ten half-lives and then quenched in distilled water ($750cm^3$). The mixture was extracted 10 times with either chloroform or dichloromethane. After drying ($MgSO_4$), a known amount of reference standard was added, the solvent was removed on a water bath by fractional distillation through a 12" glass column. The column was then washed down with 1 - 2cm^3 of dichloromethane (diethyl ether if chloroform was the extracting solvent) to yield a solution of the nitration products suitable for g.l.c. analysis.

(ii) <u>From reactions in greater than 75% sulphuric acid</u>

Reactions were of the scale described above 7.4 (i). The substrate in acetic acid was added to a vigorously stirred solution of nitric acid (<u>ca</u> 2.3 x 10^{-4} mole dm^{-3}) and nitrous acid inhibitor (2 x 10^{-1}g of urea, sulphanilic acid or sulphamic acid) in the appropriate concentration of sulphuric acid.

The nitric acid and the substrate were in equimolar amounts in an attempt to avoid complications due to dinitration. The substrate was added to the nitric acid solution to avoid any problems due to sulphonation. Termination of the reaction and the extraction of the reaction products were as described in Section 7.42(i).

All nitro-products (except where specific references are made) were identified by comparison of their retention times on g.l.c. analysis with those of independently identified authentic samples of the compounds.

7.5 GAS CHROMATOGRAPHY

G.l.c. was performed on a Pye-Unicam series 104 chromotograph, fitted with a flame ionisation detector (F.I.D.) which used hydrogen (15 p.s.i. inlet pressure) in an atmosphere of compressed air (10 p.s.i. inlet pressure). Nitrogen was used as the carrier gas and the flow rates are given in the individual sections. The columns, retention times and reference standards used for analysis, are given in the section dealing with particular substrates.

The yields of nitro-products were calculated by a method based on relative response factors. The relative response factors of the nitro-products were measured with respect to a given reference standard which was added to the sample prior to analysis. The area (A_p) of a given peak is proportional to the amount of (c_p) of the respective solute, i.e.

$$A_p = f_p . c_p$$

where f_p is a constant, and depends on the chemical characteristics of component p. Therefore, using this relationship it is possible to obtain expression for two peaks, of components s and x, where s is a standard and the amount of x is to be determined.

$$A_s = f_s . c_s$$

$$\text{and} \quad A_x = f_x . c_x$$

$$\therefore \frac{c_x}{c_s} = \frac{A_x}{A_s} \times \frac{f_x}{f_s}$$

The constant ratio $\frac{f_s}{f_x} = f$ can be obtained from standard solution of both reference standard and the unknown.

$$\therefore c_x = c_s \times \frac{A_x}{A_s} \times f$$

Relative peak areas were determined either by comparison of height x width at half height or by cutting out peaks from the traces and weighing them.

7.6 MASS SPECTROMETRY

Accurate mass measurements and fragmentation spectra were obtained from the Physio-Chemical Measurement Unit, Harwell, using an A.E.I. MS.902 spectrometer. The electron energy was 70 ev.

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