THE ELECTRON SPIN RESONANCE STUDIES

OF SOME NITROGEN FREE RADICALS

A thesis submitted for the degree of

Doctor of Philosophy

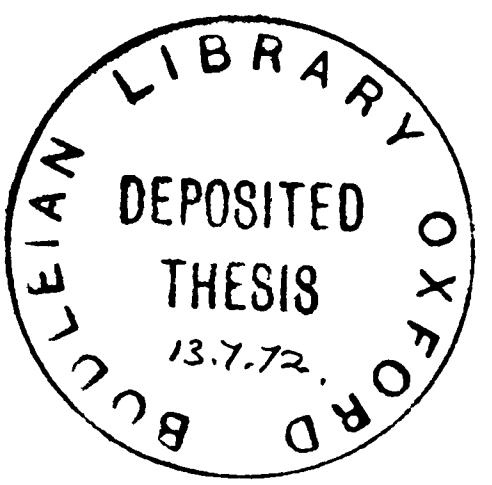
in the University of Oxford

by

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TO

MY FATHER

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Abbreviations

The abbreviations and symbols used throughout this thesis are those recommended in the 'Handbook for Chemical Society Authors' with the following exceptions:

e.s.r.	electron spin resonance spectroscopy
D.M.E.	1,2-dimethoxyethane
D.M.F.	N,N-dimethylformamide
T.H.F.	tetrahydrofuran
EtOH	ethanol
MeNHOH	N-methylhydroxylamine
p-NBA	para-nitrobenzoic acid
p-NBM	para-nitrobenzamide
t.l.c.	thin-layer chromatography.

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CHAPTER 1

The Detection of Free Radicals by electron spin resonance spectroscopy.

1. Introduction

The essential feature of a free radical is the existence of an unpaired electron in a molecular orbital of a molecule. This gives the system two characteristic features; first a high chemical reactivity and, secondly, a magnetic moment, due to the uncompensated spin motion of the odd electron. It is the latter of these properties that enables electron spin resonance spectroscopy (e.s.r.) to be used as a tool for the investigation of free radicals.

This thesis is concerned with organic free radicals, and a number of review articles have appeared on various applications of the use of e.s.r. in the study of these radicals. Carrington[1] has discussed the e.s.r. spectra of stable aromatic radical ions with particular reference to valency theory, and Symons[2] has described the use of e.s.r. for the identification of organic radicals in the liquid and solid phases. The use of e.s.r. in the elucidation of conformations and structures has been reviewed by Geske.[3] A large quantity of data has been published on the applications of e.s.r. to short-lived free radicals, and the subject has been reviewed by Norman and Gilbert.[4] Several recent advances in this field have been discussed in a series of articles introduced by Waters.[5] The reviews by Schneider[6] and co-workers, and by Horsfield[7] cover several aspects of the applications of e.s.r. to organic chemistry. Further

general reviews on diamagnetic scavengers by Perkins,[8] on free radicals in aqueous solutions by Norman,[9] and on free radicals in non-aqueous solutions by Kochi and Krusic[10] have been published. General literature surveys have been carried out by Thompson[11,12] and Gilbert.[13] The essential theoretical background of e.s.r. is covered in works by Ingram,[14] Bersohn and Baird,[15] Ayscough[16] and Atkins and Symons.[17]

2. Principles of e.s.r.

An electron has the following fundamental properties; mass, charge, intrinsic angular momentum or spin, and hence a magnetic moment. The magnetic moment, μ_e, is given by the following expression:

$$\mu_e = - 2\pi \frac{g\beta_e}{h} \cdot S \qquad (1)$$

where g is the Landé g-factor and is a proportionality constant between the magnetic moment and the angular momentum. It is a dimensionless constant with a value of 2.0023 for an unbound electron.

h is Planck's constant.

β_e is the Bohr magneton for the electron and is equal to $\frac{eh}{4\pi m_e c}$.

where e is the charge on an electron

m_e is the mass of an electron

c is the velocity of light.

S is the spin angular momentum, and can take on only the values $\frac{hm_s}{2\pi}$ (where $m_s = \pm \frac{1}{2}$) along the direction of an applied magnetic field. Since the spin angular momentum can take only these values the magnetic moment of the electron is referred to as being aligned parallel or anti-parallel with respect to the applied field. The energy, E, associated with each of these orientations in a magnetic field, H, is given below:

$$E = 2\pi \frac{g\beta_e}{h} \cdot S \cdot H \qquad (2)$$

The difference in energy between these two orientations or spin states is

$$\Delta E = g\beta_e H \qquad (3)$$

because S can take the values $\pm \frac{1}{2} \left(\frac{h}{2\pi}\right)$

The distribution of spins between these two spin states in a sample will normally be given by the Maxwell-Boltzmann expression:

$$\frac{n_1}{n_2} = e^{-\frac{\Delta E}{kT}} \qquad (4)$$

where T is the absolute temperature,

k is the Boltzmann constant, and

n_1 and n_2 are the numbers of spins in the upper and lower spin states respectively.

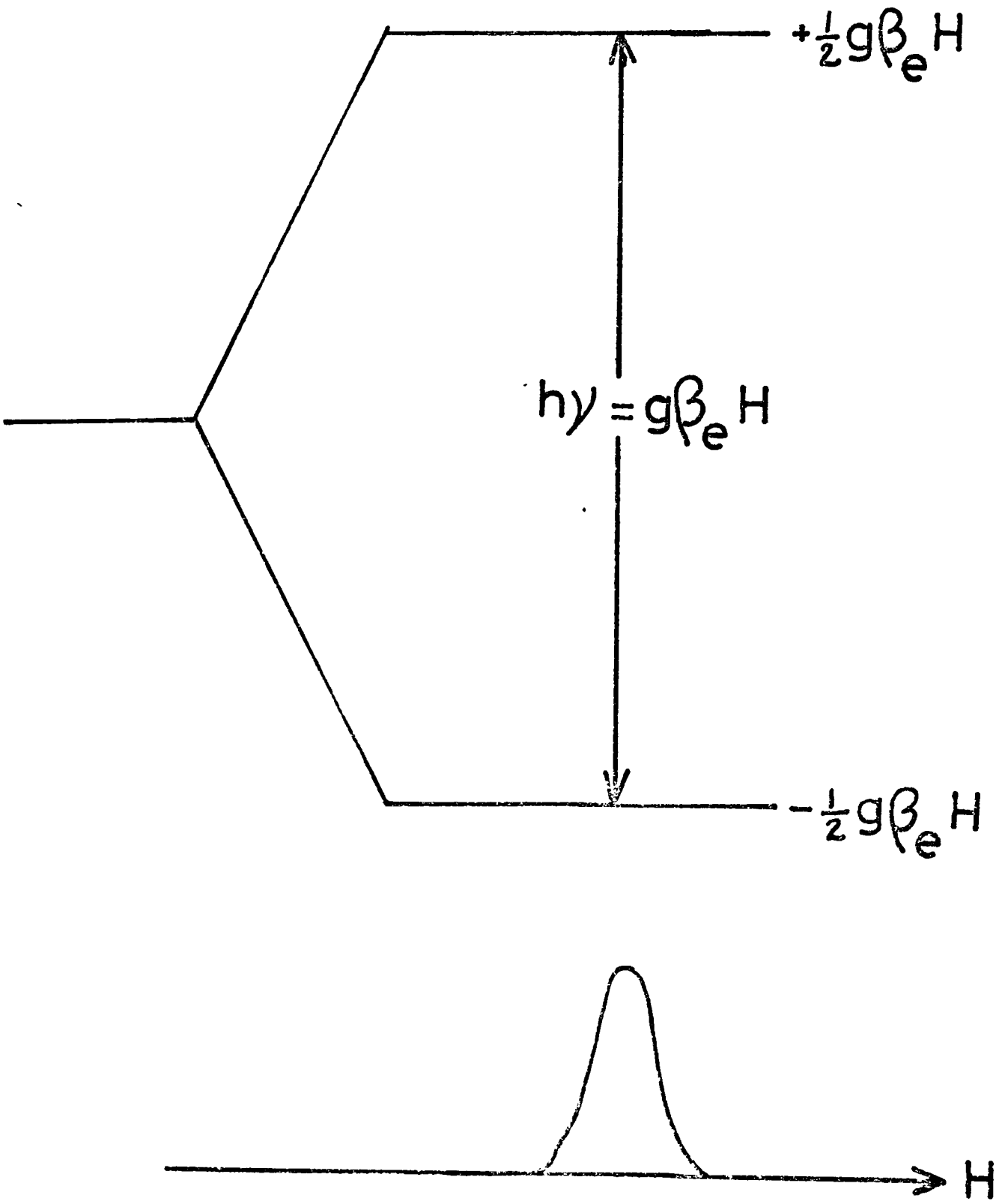
The basic resonance experiment of e.s.r. consists of placing a sample of an element or molecule containing unpaired electrons in a magnetic field, H, and inducing transitions between the two spin states with electromagnetic radiation of frequency, ν, such that

$$h\nu = \Delta E = g\beta_e H \qquad (5)$$

This is the fundamental resonance condition for e.s.r. In practice, it is usual to employ electromagnetic radiation of fixed frequency, and to scan the magnetic field until this resonance condition, (5), is satisfied. This is shown in Fig.1.1. For many purposes it is convenient to operate the magnet with a field strength of about 3,400 gauss and to use microwaves of wavelength of about 3 cm., corresponding to a frequency of approximately 9,000 MHz. i.e., the radar x-band.

Fig.1.1

The basic electron resonance condition.



Resonance condition:- $h\nu = g\beta_e H$

Considering now the distribution of spins between the two energy levels as given by the distribution law, (4), the excess of spins in the lower spin state over those in the upper state at this field value and room temperature is only about 0.07%. The whole phenomenon of e.s.r. depends upon this difference. For continuous absorption to occur, mechanisms must exist by which energy absorbed and stored in the upper spin state can be dissipated in such a manner as to permit return to the lower state. These mechanisms are called "relaxation processes". If however the intensity of the incident radiation is so great as to offset the effects of these relaxation processes, then the Boltzmann distribution is upset, and "saturation" occurs.

Another consequence of the existence of relaxation processes is that they lead directly to an e.s.r. absorption line having a finite width. The resonance condition, (5), seems to imply that absorption of power occurs at a precise value of the magnetic field and at no other value for radiation of a fixed frequency. That lines do have finite widths is a result of the Heisenberg uncertainty principle, according to which, $\Delta\Delta E,\ \Delta t \sim h$, where Δt is a measure of the lifetime of a spin state and $\Delta\Delta E$ is the uncertainty in the measurement of the energy change (i.e., $g\beta\,\Delta H$, is the uncertainty in the line position). Hence, if the relaxation processes are very efficient, Δt will be small and hence $\Delta\Delta E$, the spread in energy levels will be large, leading to a broadened line. In general, Δt must be a finite quantity and so the absorption line will have a finite width. Thus the shape of an e.s.r. absorption line is governed by the relaxation processes.

The most important type of relaxation process in the present context is known as spin-lattice relaxation, in which energy associated with the high-energy spin state is transferred to the surrounding molecules, known as the "lattice". Hence, spin energy is transformed into vibrational and rotational energy with the result that the electron falls to the lower spin state.

3. Characteristics of e.s.r. spectra.

a) g-values.

The g-value of a free radical is a dimensionless quantity known as the spectroscopic splitting factor. In practice it is the factor which determines the position in the spectrum where a radical will absorb radiation according to:

$$h\nu = g\beta_e H \qquad (5)$$

as h and β_e are constants and ν is constant for a given set of experimental conditions e.g., klystron, sample, cavity etc. H is varied as previously explained. In paramagnetic atoms g may vary from 1 to 6 or more[18], and this may be of use for the identification of the species. However in organic free radicals in solution g-values differ from the spin only value of 2.0023 by at most 1% (in the case of sulphur radicals), so its accurate determination is essential. (See Chapter 6.).

The g-value is determined by the degree to which the spin angular momentum of the electron couples with its orbital angular momentum. Thus the greatest deviations occur from the free electron value when the unpaired electron is on an atom for which spin-orbit coupling is strong, i.e., for which there are relatively low lying excited states which can interact with the ground state and thereby introduce some orbital angular momentum. These conclusions are borne out for some aliphatic radicals[19], and for semiquinone radicals containing halogen substituents. The g-value increases in the order I > Br > Cl > F > H, and this order has been correlated with the spin-orbit coupling constants for these atoms.[20]

For radicals which have fixed orientations with respect to applied magnetic fields, e.g., those trapped in solid matrices, the observed g-value varies with the orientation of the radical in the field. This would be expected since the orbital motion of the unpaired electron about the x, y and z axes of the molecular system will be affected differently by an applied magnetic field. Consequently, a crystal requires three g-values, i.e., g_x, g_y, g_z. However, for a radical in solution rapid tumbling occurs and the average of these three values is observed.

b) Hyperfine splitting.

In most radicals the unpaired electron is delocalised over a portion of the radical, and its magnetic moment can interact with the magnetic moments of the neighbouring atomic nuclei. This isotropic interaction, gives rise to hyperfine structure which is independant of the orientation of the radical. Anisotropic interaction, which is important in the solid phase, depends upon the orientation of the molecular axis, with respect to the external field, and can be considered as arising from the classical "dipole-dipole" interaction between two magnetic moments. In liquids these interactions are averaged to zero by the rapid motion, and thus the random orientation of the radicals make the system statistically isotropic and the spectra are symmetrical with respect to their centres.

The magnetic moment of the nucleus, μ_N, is given by the expression:

$$\mu_N = + 2\pi \frac{g_N \beta_N I}{h} \qquad (6)$$

where g_N is the nuclear g-value

β_N is the nuclear magneton, and

I is the spin angular momentum of the nucleus. There are (2I + 1) permissible orientations of the nucleus with respect to an applied field, and the possible values for the spin angular momentum are $\frac{m_I h}{2\pi}$ where m_I is the nuclear spin quantum number and can take the values -I, -(I-1), ...0.... (I-1), I.

At this point it is worth noting that for those nuclei which are most commonly encountered,

I = 0 for ^{12}C, ^{16}O, ^{32}S (i.e., these nuclei have no spin);

I = $\frac{1}{2}$ for ^{1}H, ^{13}C, ^{15}N, ^{19}F, ^{31}P;

I = 1 for ^{2}H, ^{14}N; I = 3/2 for ^{33}S, ^{35}Cl, ^{37}Cl; and I = 5/2 for ^{17}O.

Anisotropic and isotropic interactions will now be considered in more detail.

(i) Anisotropic interaction

Anisotropic splitting arises from the dipole-dipole interaction between the electronic and nuclear magnetic moments. These interactions depend upon the orientation of the radical with respect to the direction of the applied magnetic field, and anisotropic splitting occurs only in radicals held in solid matrices or in powders. In addition an isotropic contribution will also be present and therefore the interpretation of e.s.r. spectra for such radicals is often difficult.

The anisotropic splitting, a is given by

$$a = g g_N \beta_e \beta_N \left\langle \frac{(1 - 3\cos^2\phi)}{r^3} \right\rangle_{av} \qquad (7)$$

where ϕ is the angle between the axis of the dipoles and the line joining them, and r is the distance between the dipoles.

When this equation is applied to the interaction of electron and nuclear moments, the value of the term to be averaged depends on the type of orbital containing the unpaired electron, and on the direction of the applied field with respect to the orientation of this orbital. In particular, for a pure s-orbital, which has spherical symmetry, the average value of $\cos^2\phi$ is 1/3. As a result an s-electron can cause no anisotropic interaction because $\left\langle \frac{(1 - 3\cos^2\phi)}{r^3} \right\rangle_{av} = 0$.

If the radical is tumbling rapidly in solution, then this anisotropic term vanishes and only the isotropic interaction is present. In general, isotropic interactions are easier to interpret than anisotropic ones.

(ii) Isotropic interaction

Whilst the anisotropic interaction is purely classical in concept, arising from dipolar interaction, the isotropic or Fermi contact interaction is a quantum mechanical term. It arises from the fact that an electron in an s-orbital has a finite charge density at the position of the nucleus. The isotropic hyperfine splitting, a, is given by the expression:

$$a = \frac{-8\pi}{3} \cdot g \cdot g_N \beta_e \beta_N \left|\psi^2(0)\right| \qquad (8)$$

where $\left|\psi^2(0)\right|$ is the probability of finding the electron at the nucleus, and is only non-zero if the unpaired electron is in an orbital with s- or σ-character.

The radicals reported in this thesis were all studied in solution, and hence, were able to tumble rapidly and bonds rotate freely. Hyperfine structure, characterised by splitting constants, result from this Fermi contact term, and this will now be discussed.

The case will be considered in which one electron interacts with one proton in a high field. The proton, ^1H, has a value of $I = \frac{1}{2}$, and hence, by the $(2I + 1)$ rule the number of possible orientations in a magnetic field is two. That is, the proton may be aligned parallel or anti-parallel with respect to the field, and so each of the electron energy levels is split into two. This is shown in Fig. 1.2. The transitions which may occur during a resonance experiment are governed by two selection rules:

$$\Delta m_S = 1$$

$$\Delta m_I = 0$$

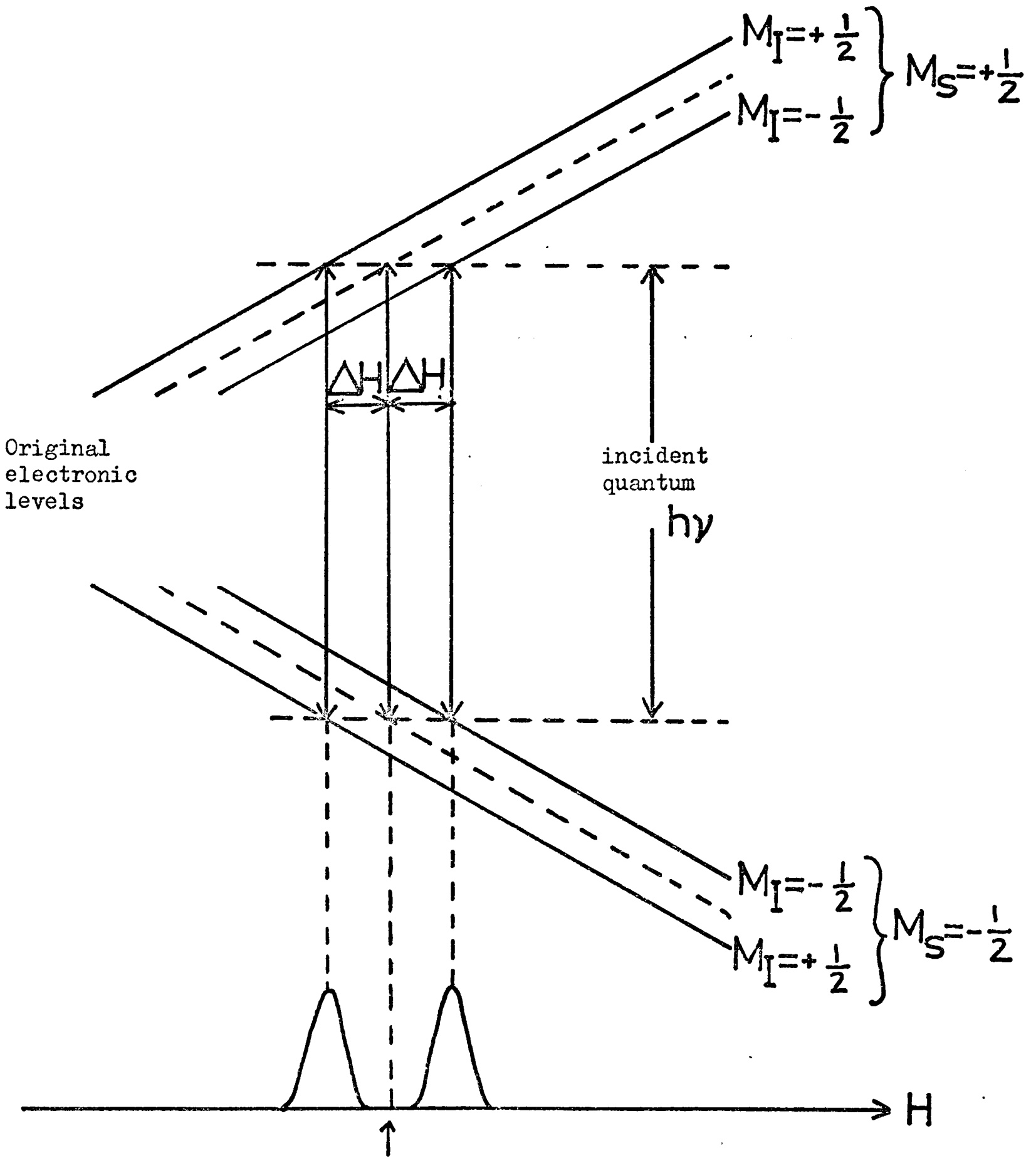
Hence, only the magnetic moment of the electron may change its orientation; the orientations of the nuclear moments remain unchanged. Other transitions are forbidden.

Therefore, when the resonance experiment is performed by scanning the magnetic field, H, using radiation of fixed frequency, ν, resonance absorption occurs at two field positions. Two lines of equal intensity will be observed, because there are equal numbers of nuclei associated with each electronic transition. (This is an extremely good approximation, although in principle a thermal distribution must exist).

Similar remarks apply to a nucleus with $I = 1$, for which there are three possible orientations, according to the $(2I = 1)$ rule. Applying the selection rules it can be seen that three transitions are possible in this case, resulting in three absorption lines of equal intensity.

Fig. 1.2

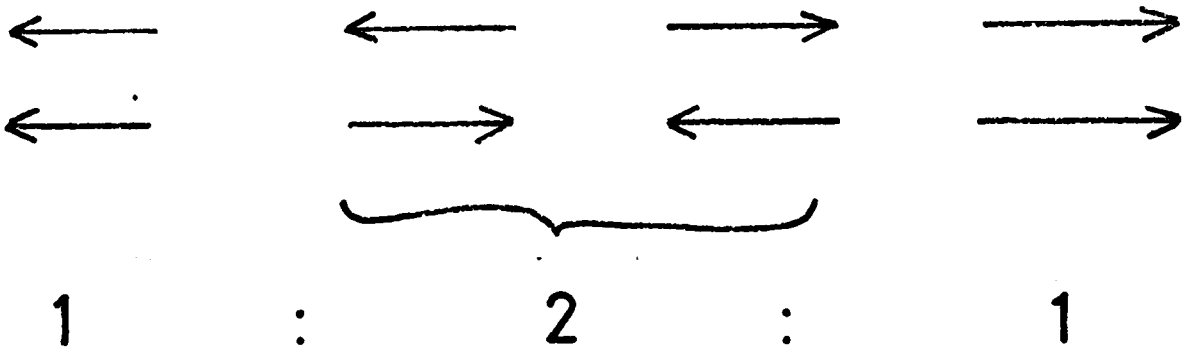
Splitting of electronic energy levels by interaction with one proton.



(Field position of single electronic transition $\frac{h\nu}{g\beta_e H}$.)

^{14}N is an example of this type of nucleus, and the e.s.r. spectrum of potassium peroxylamine disulphonate, (Frémy's salt) is shown in Fig.1.3. The splitting constant is often quoted as 13.0 gauss,[14,16] although the exact value appears to depend on the concentration of other salts in solution.[21]

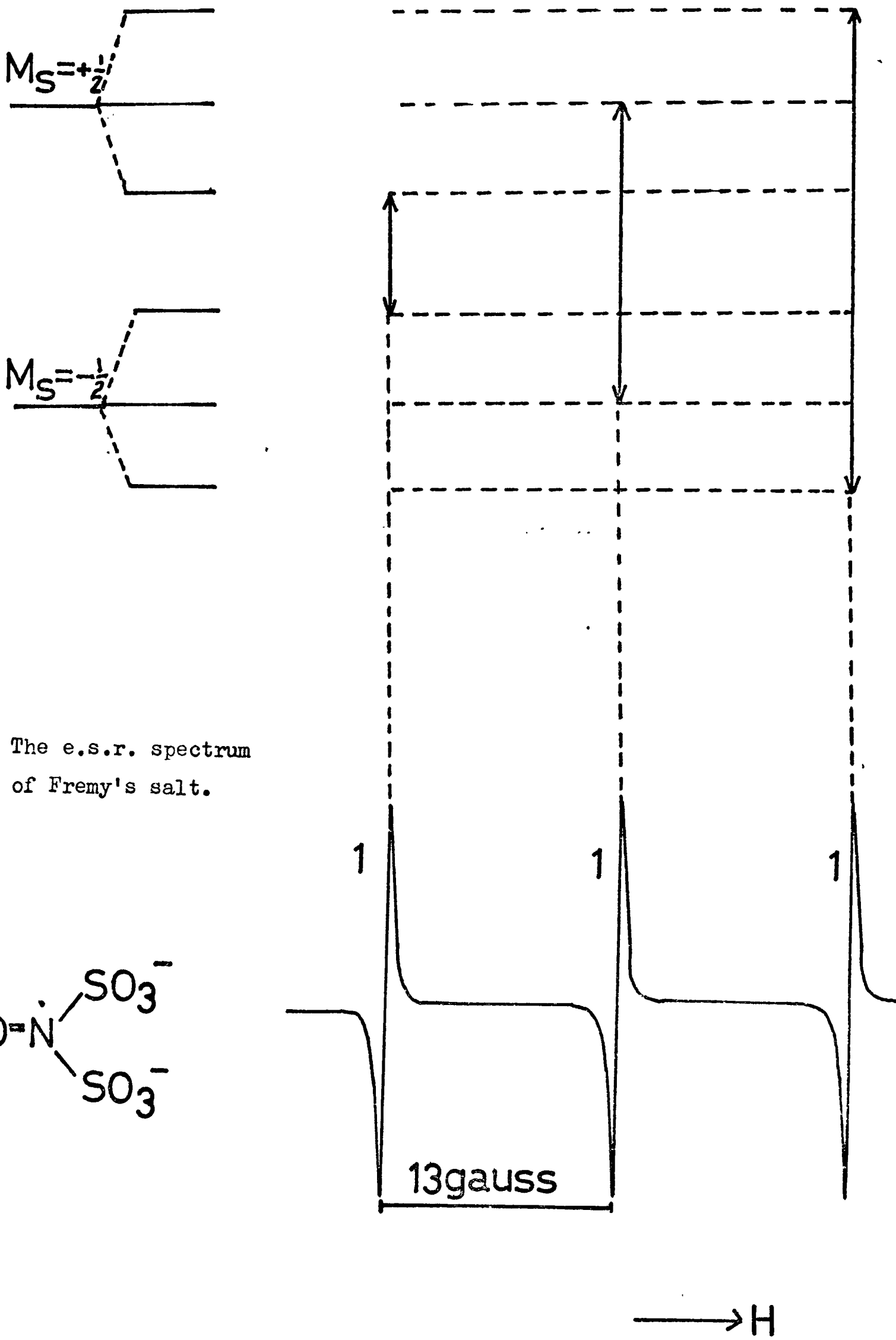
If the electron interacts with two equivalent protons then the result is an e.s.r. spectrum of three equally spaced lines with relative intensities 1 : 2 : 1. The centre line is twice as intense as the outer lines because there are twice as many combinations of opposed nuclear spins as there are combinations which lead to both spins being aligned in the same direction. This is made clear if the direction of nuclear spin is represented by an arrow:



The interaction of an electron with n-equivalent protons leads to an e.s.r. spectrum of n + 1 equally spaced lines and the intensity pattern will be given by the coefficients of x in the binomial expansion of $(1 + x)^n$. Thus, an electron interacting with four equivalent protons (e.g., as in the p-benzosemiquinone ion) will give rise to 5 equally spaced lines with an intensity pattern 1 : 4 : 6 : 4 : 1. This is shown in Figs.1.4 and 1.5. The separation between these

Fig. 1.3

Splitting of electronic energy levels by interaction with one nitrogen atom.



The e.s.r. spectrum of Fremy's salt.

Fig. 1.4

Hyperfine splitting of the energy levels produced by four equally coupled protons.

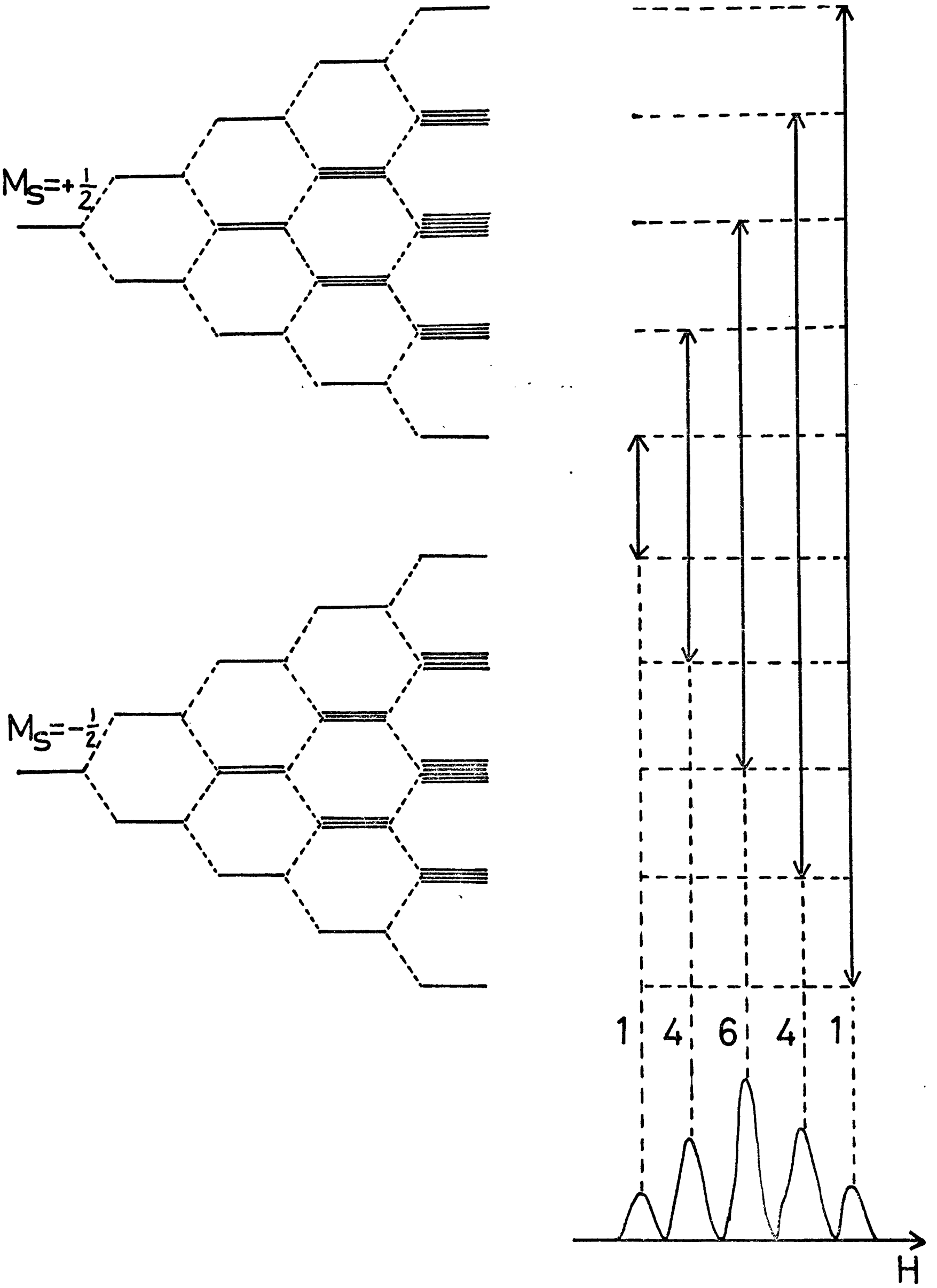
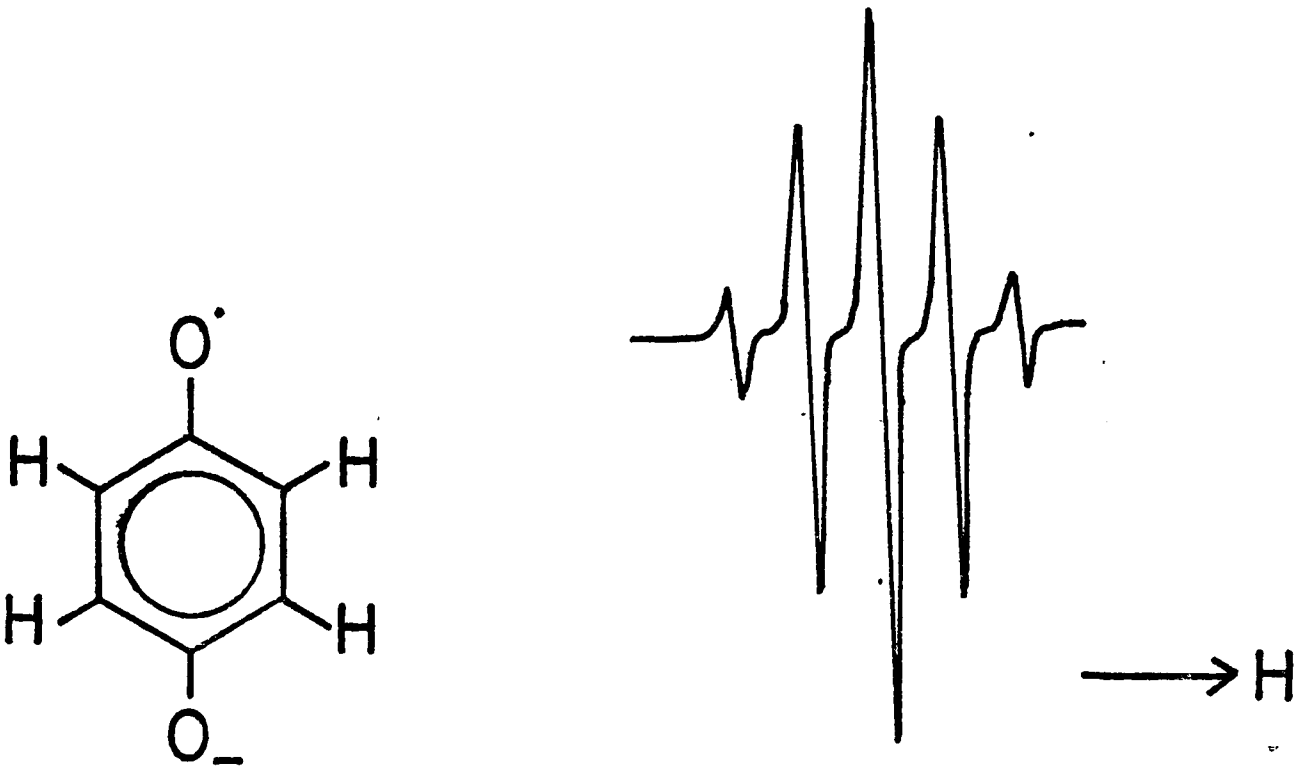
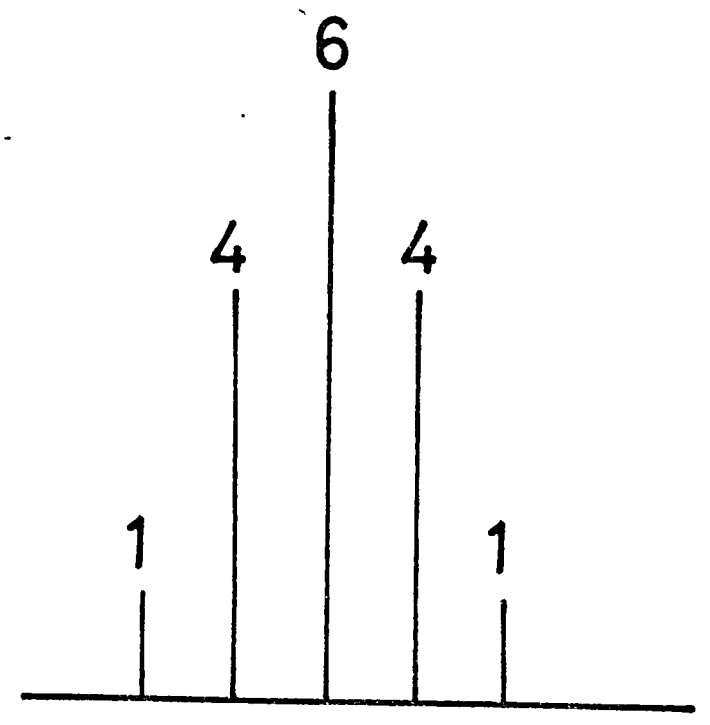


Fig. 1.5

The e.s.r. spectrum of the para-benzosemiquinone radical-anion.

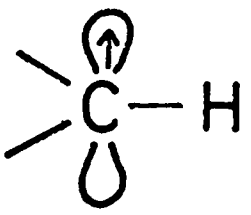




equally spaced lines is called the splitting constant, a, and is measured in gauss.

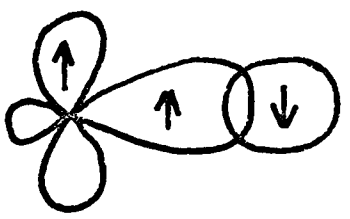
(iii) Mechanisms of isotropic interaction[22]

The mechanisms by which these isotropic splittings arise are relevant here. According to the Fermi contact equation (8), a, the hyperfine splitting constant is directly proportional to the unpaired spin density at the nucleus, $\psi^2(0)$. To observe a hyperfine splitting, spin density must thus be present in an orbital with s- or σ- character. The spectra presented in this thesis are those of aromatic π -radicals in which the unpaired electron is normally considered to be in an orbital with π -character. The ring protons of aromatic π-radicals lie in the nodal plane of the π-orbital, and so, it would be assumed that these protons are not in contact with unpaired spin density. However, hyperfine splittings are observed for this type of proton and also for α-protons in aliphatic radicals which contain the fragment:

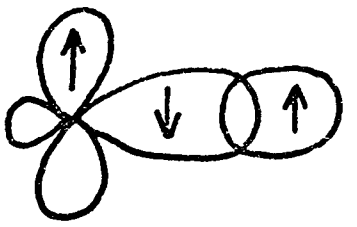


The presence of an unpaired electron in the p- or π -orbital on the carbon atom induces a spin polarisation in the C-H σ -bond. This bond is formed by overlap of the sp^2-orbital of the carbon atom and the 1s-orbital of the hydrogen atom. The way in which this spin polarisation occurs can be visualised in the following way. For the isolated C-H bond there is no 'a priori' preference for a particular spin alignment. However the presence of an unpaired electron in the p-

or π -orbital gives rise to an energetically more favourable situation when the electron in the carbon sp^2 orbital is aligned in the same direction, according to Hund's rules. According to the Pauli principle the electron in the hydrogen 1s-orbital will be aligned in the opposite direction to the electron in the carbon sp^2 orbital, and hence will be aligned in the opposite direction to the unpaired electron in the p- or π -orbital.



(a)



(b)

The overall result is that there is a slightly greater probability of configuration (a) than configuration (b). Thus, an unpaired spin resides in the 1s-orbital of the proton of opposite sign to that in the carbon π - or p- orbital.

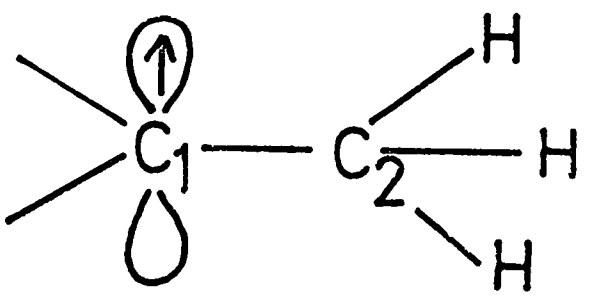
The hyperfine splitting constant, a_α^H for the proton is directly proportional to the unpaired spin density on the carbon atom. This is summarized in the McConnell[23] equation:

$$a_\alpha^H = Q^H \cdot \rho_c \qquad (9)$$

where ρ_c is the fraction of the unpaired spin in the π -orbital on the carbon atom. The value of Q^H varies from molecule to molecule, depending upon the total charge on the carbon atom. However, a

value of -22.5 gauss is generally accepted for simple aromatic systems.

Hyperfine splittings are also observed for the protons of methyl groups attached to such trigonal carbon atoms. In this instance, there exists the possibility that some unpaired spin can find its way into the hydrogen 1s-orbital by a hyperconjugative mechanism. The magnitude of this interaction depends upon the degree of overlap of the carbon, p-orbital which contains the unpaired electron, and the C_2-H bond concerned, which is formed by the overlap of a carbon$_2$ sp^3 orbital and the hydrogen 1s-orbital. This overlap is dependent upon θ, the



angle which the C_2-H bond makes with the axis of the p-orbital. The splitting constant is found to obey the law given below,[24]

$$a_\beta^H = B_1 + B_2 \cos^2\theta \qquad (10)$$

where B_1 = 4 gauss

and B_2 = 50 gauss.

For a freely spinning methyl group, the three protons will be magnetically equivalent and a McConnell relation can be written for the splitting constant, a^{CH_3}:

$$a_{\beta}^{CH_3} = Q^{CH_3}.\rho_c \qquad (11)$$

where ρ_c is the fraction of unpaired spin density on the carbon atom, and Q^{CH_3} has a value of 29.3 gauss.[25,26] Hence the hyperconjugative mechanism depends on a spatial overlap of wave functions with the same symmetry or pseudo symmetry, and not on the mutual interactions of electrons involving excited levels as in the mechanism involving spin-polarisation. It is therefore a more direct and potent effect than the latter and very nearly the same hyperfine splitting is produced by each proton of a methyl group attached to an aromatic ring, as for a proton connected directly to a ring carbon atom.

The nitrogen hyperfine splitting constant in aromatic nitro radical-anions has been shown to be dependent on the spin density on the nitrogen and oxygen atoms. A McConnell-type relationship has been established,[27,28,29] in which the Q-values have the magnitudes shown in the following expression:

$$a_N = 99.0\,\rho_N^{\pi} - 71.6\,\rho_O^{\pi} \qquad (12)$$

A volume of Landolt-Börnstein[30] has appeared which summarises the hyperfine splitting constants published up to 1965.

CHAPTER 2

Background to the work.

1. Introduction

The work described in this thesis is concerned with the electron transfer reaction of hydroxylamine and alkyl hydroxylamines with nitrobenzene and p-substituted nitrobenzenes.

Many redox reactions in inorganic and organic systems, involve the transfer of electrons at one stage or another. However, the most typical electron transfer reaction, in which the very fact of the transfer of just one electron is unquestioned, lead to the formation of radical-ions. In this instance the electron transfer is usually not complicated by side-processes and the radical-ion itself is readily identified by e.s.r. methods. Such reactions are an extremely convenient model for studying electron transfer in organic reactions.

A large number of organic compounds of different classes exhibit the ability to receive one electron with the formation of radical-anions.[31] These include aromatic[32-35] and heterocyclic[36-39] systems and also systems which contain conjugated bonds[40-42] and electron withdrawing groups.[43-44]

Under the action of oxidants, aromatic[45] and heterocyclic[46] compounds and also some amines[47,48] can give up one electron to form radical-cations.

The following section reviews the various types of electron transfer reactions which can result in the formation of radical-ions[49], with particular reference to the production of the nitrobenzene and related radical-anions.

2. The production of nitrobenzene and related radical-anions by electron transfer reactions.

The nitrobenzene radical-anion is produced from nitrobenzene by one-electron reduction:

$$PhNO_2 + e^- \rightarrow PhNO_2^{\cdot -}$$

Six main types of reaction can effect this:

(a) Reduction by metals

The case of formation of radical-anions depends on a series of factors, the most important of which are the affinity of the acceptor for one electron, the solvating capability of the medium and the donor ability of the electron source. Hence the introduction of an electron withdrawing substituent e.g., the nitro group into a benzene ring, will increase the ease of formation of a radical-anion. The ease of transfer of an electron, to the molecule of an acceptor, from a metal is determined by the donor capability of the latter. In most instances alkali or alkaline earth metals or their amalgams are used for reduction.[31]

All the alkali metals have been used as a source of electrons for this reduction, using 1,2-dimethoxyethane (D.M.E.) as solvent.[44,50,51]

$$\text{e.g.,} \quad PhNO_2 + K \rightarrow PhNO_2^{\cdot -} + K^+$$

The e.s.r. spectra of these radical-anions indicate that the main

species present in solution is a strong ion pair of the metal cation and the nitroaromatic anion.[52,53]

Hyperfine splitting constants have been assigned by Ward[44] on the basis of isotopic substitution studies, i.e., various ring positions were selectively deuterated and the effects on the e.s.r. spectra were noted.

Zinc metal has been used as a source of electrons in aqueous alkaline ethanol by Ayscough et al.[54] who reduced a series of monosubstituted nitrobenzenes.

(b) Electrochemical Methods.

These methods have been used extensively for the reduction of nitrobenzenes to their respective radical-anions. Pioneers in the field were Maki and Geske[55] who reduced nitrobenzene dissolved in acetonitrile at a mercury cathode. The hyperfine splitting constants in the e.s.r. spectrum were assigned on the basis of deuterium substitution at the meta-position. This work led to the reduction of a series of meta- and para-substituted nitrobenzenes[56] and alkyl-substituted mono- and dinitrobenzenes.[57] These electrolyses were performed in the cavity of an e.s.r. spectrometer, which enabled unstable radical-anions to be identified. The potential of the mercury cathode was controlled relative to a reference electrode of fixed potential, to give one-electron reduction. For this purpose a saturated calomel electrode was used.

Piette, Ludwig and Adams[58,59,60] have generated the nitrobenzene radical-anion by electrolysis in aqueous solution. They also reduced several aliphatic nitro compounds to their respective radical-anions.

Nekrasov and Podlibner[61] have effected the cathodic reduction of nitrobenzene in aqueous solution on a gold amalgam disc-ring electrode in the presence of potassium hydroxide.

Metcalfe and Waters[62] have produced the nitrobenzene radical-anion in acetonitrile using tetra-n-propyl-ammonium perchlorate as supporting electrolyte, and a mercury pool of relatively large surface area as cathode. The use of electrochemical methods has allowed the effects of various solvents, protic and aprotic, on the distribution of unpaired electron density in various radical-anions to be investigated.[56,63]

A recent development of the electrolytic method of reduction, already described, has been the formation of quaternary ammonium amalgams. These amalgams have been prepared by electrolysis of a solution of a quaternary ammonium salt in dimethylformamide (D.M.F.) by Myatt and Todd.[64] When an amalgam is brought into contact with a solution of nitrobenzene, the radical-anion of the latter is formed:

$$R_4N/Hg + PhNO_2 \rightarrow R_4N^+ + Hg + PhNO_2^{\cdot-}$$

Methods (a) and (b) described above, have involved electron transfer at the interface between a metal or an amalgam and the nitrobenzene in the surrounding solution. The remaining methods to be described involve electron transfer in solution.

(c) Photochemical Methods.

Photolysis of a solution of nitrobenzene in ethanol containing

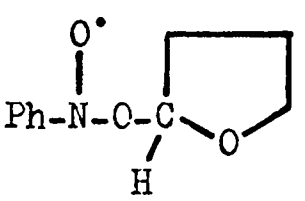
ethoxide results in the formation of the nitrobenzene radical-anion, as reported by Ayscough.[54,65]

$$PhNO_2 \xrightarrow{h\nu} PhNO_2^{*} \xrightarrow{OR^-} PhNO_2^{\cdot -} + OR^{\bullet}$$

This radical-anion was also generated by Asmus et al.[66,67] during their pulse radiolysis experiments with aqueous alkaline or neutral solutions, in which the hydrated electron reacted with nitrobenzene to give the radical-anion. In acid solution, the conjugate acid of this radical-anion, $PhNO_2^{\bullet}H$ was formed and this radical decayed rapidly.[66,68]

It is interesting to note that if a solution of nitrobenzene in tetrahydrofuran (T.H.F.) is photolysed, an e.s.r. signal is observed which was attributed by Ward[69] to the conjugate acid of the radical-anion, $PhNO_2^{\bullet}H$. This radical can be formed by hydrogen atom abstraction from the solvent, and this assignment has been accepted by some subsequent researchers.[70,73]

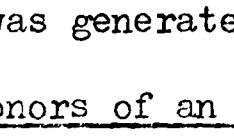
However, this assignment has been questioned by Cowley and Sutcliffe[74] and by Briegleb and Lind.[75] Cowley and Sutcliffe[74] have reinterpreted this spectrum as due to the radical which is formed by addition of a THF radical to nitrobenzene, to give the alkoxy nitroxide radical:



Briegleb and Lind[75] attribute the observed spectrum to the existence of a strong ion pair, consisting of the nitrobenzene radical-anion and the THF radical-cation.

$$PhNO_2 + THF \longrightarrow PhNO_2^{\cdot -} \quad THF^{\cdot +}$$

Chachaty and Forchioni[76] have irradiated nitrobenzene in alcoholic solution, and interpreted the resulting e.s.r. spectrum as that of a nitroxide radical:



when the radical was generated in the alcohol RCH_2OH.

(d) Anions as donors of an electron.

The transfer of an electron from a diamagnetic anion to an organic molecule was apparently first recognised by Schlenk[77,78], who found that triphenylmethyl sodium reacted with benzophenone and other diaryl ketones to produce products, which upon hydrolysis and atmospheric oxidation, yielded triphenylmethyl peroxide and the pinacol.

$$(Ph)_3C^- + Ar_2CO \rightleftharpoons Ph_3C^{\cdot} + Ar_2\dot{C}O^-$$

Aromatic nitro radical-anions have been produced using a large number of anionic reagents.

Using an aqueous flow system of the type first described by Stone and Waters[79], and Dixon and Norman[80], in which the two reactant solutions mix immediately before entering the cavity of the e.s.r. spectrometer, Kolker and Waters[81,82] effected the reduction of a series of para-substituted mononitro-benzenes, using alkaline sodium dithionite solution:

$$RC_6H_4NO_2 + S_2O_4^{2-} \rightarrow RC_6H_4NO_2^{\bullet-} + SO_2^{\bullet-} + SO_2$$

Gutch and Waters[83] used this method in their examination of the effect of variations in the solvent on the e.s.r. spectra of anions of dinitro compounds.

Ayscough et al[54] used an aqueous solution of glucose in sodium ethoxide as the reducing agent in their studies of a series of para-substituted nitro radical-anions.

Russell and Geels[84] noted that the action of hydroxyl ion on a nitroso compound in the presence of nitrobenzene led to the formation of the nitro radical-anion.

$$PhNO + OH^- \rightarrow Ph\text{-}\underset{\underset{OH}{|}}{N}\text{-}O^-$$

$$Ph\text{-}\underset{\underset{OH}{|}}{N}\text{-}O^- + PhNO_2 \rightarrow 2PhNO_2^{\bullet-} + H^+$$

The reaction between a base and phenyl hydroxylamine with nitro-

benzene present also leads to the formation of the nitrobenzene radical-anion.[84]

$$PhNHOH + 2B \rightleftharpoons (PhNO)^{=} + 2BH^{+}$$

$$(PhNO)^{=} + PhNO_2 \rightarrow PhNO^{\bullet -} + PhNO_2^{\bullet -}$$

$$2PhNO^{\bullet -} \rightarrow (PhNO - ONPh)^{=}$$

$$(PhN(O)\text{-}(O)NPh)^{=} + H^{+} \rightarrow PhN(O){=}N.Ph. + OH^{-}$$

Russell and Janzen[85,86] discovered that ortho- and para-nitrotoluenes spontaneously disproportionate in basic solution, forming as the reduced species the radical-anion derived from the parent nitroaromatic:

$$4CH_3.C_6H_4.NO_2 + 2t\text{-}BuO^{-} \rightarrow 2t\text{-}BuOH + 2CH_3.C_6H_4.NO_2^{\bullet -}$$
$$+ O_2N.C_6H_4.CH_2.CH_2.C_6H_4NO_2.$$

Gutch, Waters and Symons[87] have reported that persisting e.s.r. spectra of radical-anions $Ar.NO_2^{\bullet -}$, not obscured by spectra of other radicals, could be obtained by the reduction of aromatic nitro-compounds by alkaline solutions of hydroxylamine:

$$NH_2O^{-} + ArNO_2 \rightarrow ArNO_2^{\bullet -} + NH_2O^{\bullet}$$

One of the aims of the present work has been to extend this method of production of nitro-radical-anions using a range of N-aryl and N-alkyl substituted hydroxylamines.

Russell[88] has listed a number of anionic electron donors which, in solution, donate an electron to nitrobenzene with the formation of the nitrobenzene radical-anion; for example, the anions formed by loss of a proton from acetone and benzoin in basic solution. Further examples are given of this type of electron donor in Table 2.1.

(e) Radicals as donors of an electron.

Free radicals, which exhibit high electron affinity, usually emerge as vigorous oxidants. However, the available experimental data suggest that free radicals in the accepted sense, are capable of both capture of an electron and supply of an unpaired electron to a sufficiently strong acceptor with the formation of the corresponding cation.

The best known example of the donor ability of free radicals is the reduction of heavy metal salts by the triphenyl methyl radical.[91]

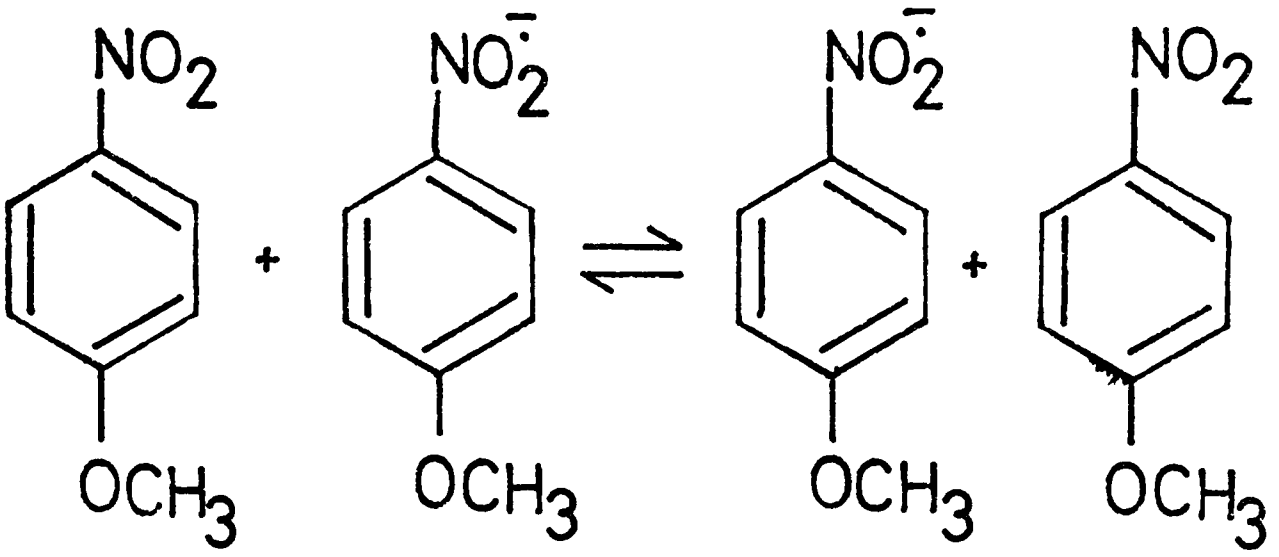
$$Ph_3C^{\bullet} + AgClO_4 \rightarrow Ph_3C^{+}\ ClO_4^{-} + Ag^{\bullet}$$

Katkova and co-workers[91] have studied the exchange reaction which takes place during the nucleophilic substitution reaction of para-nitroanisole with piperidine. E.s.r. and n.m.r. techniques have established that the nitro-radical-anion transfers an electron to the parent nitro compound:

Table 2.1.

Compounds which donate an electron to nitrobenzene

Anions of;	Reference
trans-stilbene 1,5-naphthalene disulphonate pyrazine anthracene para-nitroaniline 9-fluorenone para-nitrotoluene	89
terephthalonitrile	90
benzoin acetone	88
hydroxylamine and related compounds	84,87
sodium dithionite	81,82,83



Metcalfe and Waters[62] have investigated the range of compounds that will receive an electron from the nitrobenzene radical-anion. These include two well known electron acceptors, tetracyanoethylene and tetracyanoquinodimethane, as well as quinones, 1,2-dibenzoyl ethylene, some cyclohexadienones, benzil, biacetyl and a range of substituted aromatic nitro compounds. The results were in accord with expectations based on a knowledge of polarographic half-wave reduction potentials.

The neutral radical derived from an alcohol,[80] an ether[92] or an aldehyde[92] by hydrogen atom abstraction is able to donate an electron to an aliphatic[93] or aromatic[88,92] nitro compound to form the nitro radical-anion. This type of radical is formed from the parent compound by the action of the hydroxyl radical, which in turn is produced in a flow-system by mixing solutions of a titanous salt and hydrogen peroxide.[80]

$$Ti^{3+} + H_2O_2 \rightarrow Ti^{4+} + OH^- + OH^{\bullet}$$

and $$OH^{\bullet} + RCH_2OH \rightarrow \dot{R}CHOH + H_2O$$

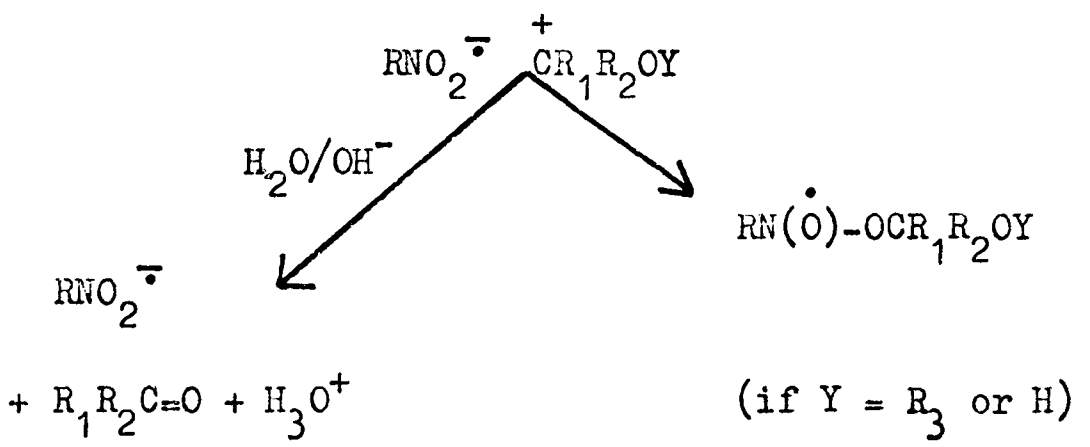
or $\dot{OH} + RCH_2OR \rightarrow \dot{R}CHOR + H_2O$

or $\dot{OH} + RCH(OH)_2 \rightarrow \dot{R}C(OH)_2 + H_2O.$

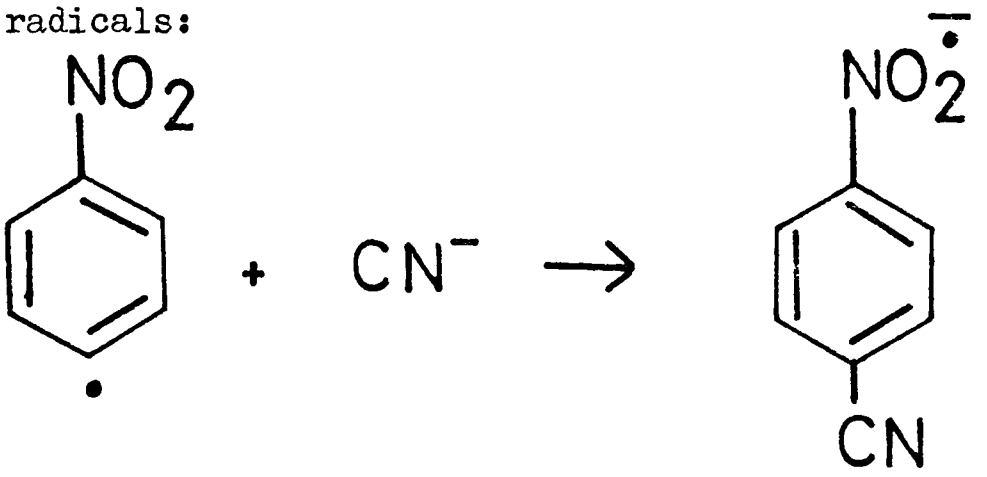
Griffiths et al.[94,95] have also studied the transfer of an electron from these neutral radicals to aliphatic and aromatic nitro-compounds. They have concluded that ion pairs were responsible for the e.s.r. spectra obtained:

$$RNO_2 + \dot{R}CHOH \rightarrow RNO_2^{-\cdot}\overset{+}{C}RHOH$$

However McMillan and Norman[93] reject this conclusion and have shown that the products of the reaction between neutral alcohol radicals or ether radicals and aliphatic nitro compounds depend upon the pH and on the alcohol or ether used. Their general conclusion is that for ethers and alcohols in acid solution, an alkoxy nitroxide radical is formed, whilst for alcohols in alkaline solution the nitro radical-anion is obtained. The ion pair which is formed initially reacts in one of two ways to give these products:



Bartak, Danen and Hawley[96] have shown that aromatic nitro radical-anions can be formed by the coupling of anions with nitrophenyl radicals:



The nitrophenyl radicals were generated from para-iodobenzene electrochemically.

(f). Neutral molecules as donors of electrons.

A large number of aromatic and heterocyclic compounds, and also compounds which contain a hetero atom, have an unshared pair of electrons capable of acting as a donor of an electron in relation to a strongoxidant with the formation of a radical-cation. For example, electron transfer has been observed for the reaction between pyridine and trinitrobenzene.[97]

Dihydroflavins have been shown to reduce aromatic nitro compounds in DMF.[98] The corresponding nitro radical-anions were not observed but are presumed to be intermediates, the first stage of reaction being proposed as an electron transfer from the dihydroflavins to the aromatic nitro compounds.

3. The e.s.r. spectrum of the nitrobenzene radical-anion. (Fig. 2.1.).

The nitrobenzene radical-anion contains six atoms which possess nuclear spin, and which thus contribute to the observed hyperfine splitting pattern in the e.s.r. spectrum. These are the five nuclear protons of $I = \frac{1}{2}$, and the ^{14}N atom of the nitro group of $I = 1$. The ^{14}N atom will give rise to a triplet in which the three lines are of equal intensity. Of the five protons, the two in the ortho- positions should be magnetically equivalent as should the two in the meta- positions. Each magnetically equivalent pair of protons will give rise to a set of triplets, each of intensity ratio 1: 2 : 1 as explained in Chapter 1, and the para- proton will give rise to a doublet.

From the spectrum of the nitrobenzene radical-anion, therefore, it is not possible to assign the splitting constants of the two sets of proton triplets unambiguously. However this problem has been solved by Ward[44] and by Maki and Geske[55], by deuterium substitution. Maki and Geske[55] replaced one meta- proton by a deuteron, and thereby removed one of the triplets from the spectrum. It was found that $^{a}para > {}^{a}ortho > {}^{a}meta$.

In addition to deuteration studies, the e.s.r. spectrum has been recorded for the nitrobenzene radical anion enriched with the oxygen isotope ^{17}O. An oxygen hyperfine splitting was observed.[99]

The magnitudes of the hyperfine splitting constants in the e.s.r. spectra of nitroaromatic radical-anions vary according to the solvent conditions and as to which cations are present in solution.

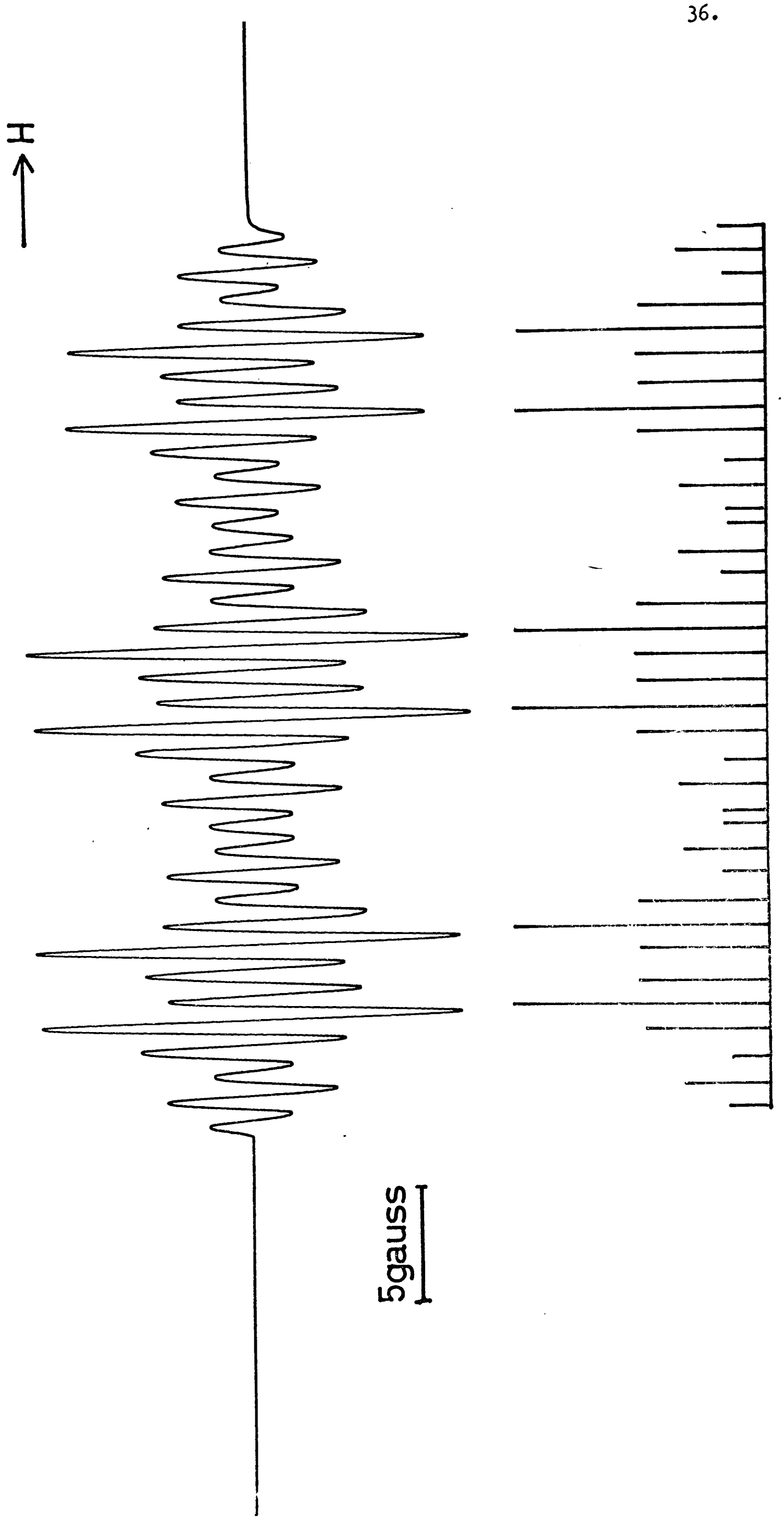


Fig. 2. 1 The e.s.r. spectrum of the nitrobenzene radical-anion.

In all solvents the ^{14}N triplet splitting dominates the e.s.r. spectrum of the nitrobenzene radical-anion, however its magnitude can change significantly with a change in solvent. Adams and co-workers[63] have determined the splitting constants for the nitrobenzene radical-anion in a full range of DMF/water mixtures. They noted that whilst the ortho- and meta- values remain fairly constant over the whole range of mixtures, there is a unique value for a_{para} for a given value of a_N. This study was extended to other solvent mixtures and to ortho- and para- substituted nitrobenzenes.[27]

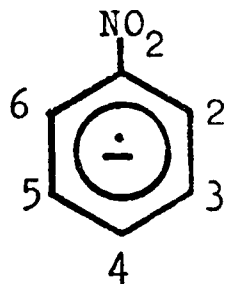
These features are shown in Table 2.2. Protic solvents tend to exhibit the highest values of a_N, e.g., the value of the nitrogen splitting constant is almost 45% greater in water than in DMF.

The greatest changes in a_N occur in the region of small concentrations of water or ethanol. This corresponds to an increase of unpaired spin density in the nitrogen 2s orbital.[54] On the basis of e.s.r. spectra, Symons[72] has calculated that for the nitrobenzene radical-anion 30% of the unpaired spin density is on the aromatic ring, 30% is on the oxygen atoms and 40% is on the nitrogen atom.

The generation of nitroaromatic radical-anions by alkali metal reduction results in the formation of a strong ion-pair between the radical-anion and the metal cation.[52,53] The close approach of the small metal cation to the π-electron system of the nitroaromatic anion radical, results in an increase in the nitrogen splitting constant. For metals whose nuclei possess

Table 2.2.

Splitting constants for the nitrobenzene radical-anion in various solvents and solvent mixtures.



where $a_2 = a_6$

$a_3 = a_5$

Solvent	a_N	a_2	a_3	a_4	Reference
DMF	9.83	3.32	1.09	3.97	27
80% DMF/20% water	12.06	3.30	1.10	3.63	27
50% DMF/50% water	13.15	3.33	1.11	3.59	27
Water	13.87	3.30	1.12	3.52	60
70% DMF/30% EtOH	11.40	3.31	1.08	3.71	27
40% DMF/60% EtOH	12.07	3.33	1.09	3.65	27
EtOH	13.5	3.3	1.1	3.6	54
50% aqueous EtOH	13.50	3.50	1.17	3.50	this thesis

N.B. a) All the nitro radical-ions were generated electrochemically except for those in ethanol and aqueous ethanol. These were generated by chemical reduction.

b) All the splitting constants refer to room-temperature.

c) Absolute values are given for the splitting constants and these are measured in gauss.

spin, unpaired spin density may interact with the metal ion leading to hyperfine splittings characteristic of the metal nucleus.[100] Hence the e.s.r. spectra of nitroaromatic radical-anions generated in this way differ from those generated by electrolytic reduction. Here the larger cations that are usually employed, e.g., tetralkyl ammonium cations, cannot approach the π system of the nitroaromatic radical-anion so closely and thus do not affect the electron distribution of the radical to such a great extent.[101]

Two other factors that may influence the e.s.r. spectrum of a nitro aromatic radical-anion, but which do not affect the radicals produced in this thesis, will be mentioned only briefly.

Firstly, steric repulsion between a nitro group and an ortho- substituent can cause the nitro group to be twisted out of the plane of the aromatic ring. This results in some decoupling of the π systems of the nitro group and the aromatic ring and thus causes an increase of spin density on the nitro group and hence an increase of the nitrogen splitting constant and a decrease in the ring proton hyperfine splittings.[57] This effect is particularly marked if one tertiary-butyl group is placed ortho- to the nitro group, when the value of a_N increases by almost 50% over that for the unsubstituted radical.

Secondly, an alternating line width effect can be observed for polynitroaromatic radical-anions. This effect does not occur with mono-nitro radical-anions. If an aromatic compound contains two nitro groups, one may be twisted out-of-plane with the aromatic ring as a result of steric hinderance, when the other is in-plane.

In this case, the two nitro groups will rotate in- and out-of-plane but each nitro group is in a plane perpendicular to the other at any point in time. In this process, the spin density environment of each nitro group is changing, but the nuclear spin states of these nitrogen atoms are quite unaffected. Hence the two nitrogen atoms exchange hyperfine splitting constants during the rotation process.

Freed and Fraenkel[102] have made an analysis of this "two-jump" model and studied the effects on the e.s.r. spectrum. Instead of the nine lines of equal intensity, which would be expected from two non-equivalent nitrogen atoms, a single sharp triplet appears. The apparent splitting constant for this triplet is equal to the sum of the individual splitting constants for the two nitrogen atoms. In addition, midway between these sharp lines two much broader lines are seen. Such features can be observed in the e.s.r. spectrum of the radical anion of dinitrodurene.[102]

Hence the alternating line width effect is caused by hindered rotation. It may also arise from solvation effects[28,84], as with the meta-dinitrobenzene radical-anion, or from the effect of cations.

4. Chemical Reactivity of the nitrobenzene radical-anion.

In the literature the nitrobenzene radical-anion is described as reacting in one of two ways. It can react with a proton, leading to disproportionation, or alternatively it can transfer its unpaired electron to another compound, with consequent oxidation.

(a) Reaction with protons.

When the nitrobenzene radical-anion is generated in an aprotic solvent such as DMF, THF, DME or acetonitrile, it does not decay quickly. However Piette, Ludwig and Adams[58] discovered that when generated in aqueous solution this radical decayed fairly quickly, with a half life of about two seconds.

This decay in aqueous solvents has been studied both kinetically and with respect to the products.

In the product studies by Kastening[103] and by Farnia and his co-workers[104], the only products of decay that were observed were nitrobenzene and phenylhydroxylamine. This was established by polarographic techniques. The equation for the reaction was found to be:

$$4PhNO_2^{\cdot-} + 3H_2O \rightarrow 3PhNO_2 + PhNHOH + 4OH^-$$

Thus, the decay process may be described as a disproportionation, with nitrobenzene as the oxidation product and phenylhydroxylamine as the reduction product.

The kinetics of the decay of the nitrobenzene and related radical-anions have been studied by a number of workers,[103-111] in aqueous

buffers, using polarography and e.s.r. techniques to measure the decay rates of the radical.

Farnia and co-workers[104] found that at low pH's (e.g., 5) the nitrobenzene radical-anion decays according to a rate law which is first-order with respect to both the radical-anion and the protons:

$$-\frac{d\,[PhNO_2^{\bullet -}]}{dt} = k_1\,[PhNO_2^{\bullet -}]\,[H^+]$$

This strong pH dependence was expressed as:

$$k_1 = 10^8\,[H^+] \text{ litres.}^2 \text{ moles.}^{-2} \text{ sec.}^{-1} \quad \text{at } 25^\circ C.$$

At high pH values (e.g. > 12) the rate becomes second order with respect to the radical-anion:

$$-\frac{d\,[PhNO_2^{\bullet -}]}{dt} = k_2\,[PhNO_2^{\bullet -}]^2$$

This second order rate constant includes both a proton dependent, and a proton independent term and may be expressed as:

$$k_2 = a + b\,[H^+]$$

where $a = 3.8$ litres. moles.$^{-1}$ sec.$^{-1}$

$b = 3.2 \times 10^{12}$ litres.^{2} moles.$^{-2}$ sec.$^{-1}$

Thus the nitrobenzene radical-anion is more stable at high pH values. This data supports the previous report in the literature that two simultaneous, independent paths exist for the decay of the nitrobenzene radical-anion.[103]
An equilibrium exists between the anion radical and its conjugate acid, the pK for which has been measured to be 3.2[66] and 3.4.[104]

$$PhNO_2^{\bullet -} + H^+ \rightleftharpoons PhNO_2^{\bullet}H$$

It is this protonation step which Koopman and Gerischer postulate as being the rate-determining step in their experiments since the rate was first order with respect to both protons and nitrobenzene radical-anions.[108] The following sequence of reactions is then proposed to follow:

$$PhNO_2^{\bullet}H + PhNO_2^{\bullet -} \longrightarrow PhNO + PhNO_2 + OH^-$$
$$PhNO + PhNO_2^{\bullet -} \longrightarrow PhNO^{\bullet -} + PhNO_2$$
$$PhNO^{\bullet -} + H^+ \rightleftharpoons PhN^{\bullet}OH$$
$$PhN^{\bullet}OH + PhNO_2^{\bullet -} \longrightarrow PhNO_2 + PhNOH^-$$
$$PhNOH^- + H^+ \longrightarrow PhNHOH$$

This gives the overall equation:

$$4PhNO_2^{\bullet -} + 4H^+ \longrightarrow PhNHOH + 3PhNO_2 + H_2O$$

The proton-independent second order process probably arises from the direct disproportionation of two radical-anions.[103-105].

$$2PhNO_2^{\cdot-} \rightleftharpoons (PhNO_2)_2^{=}$$

followed by a fast reaction of the very basic dianion with water to give nitrosobenzene:

$$(PhNO_2)_2^{=} + H_2O \longrightarrow PhNO + PhNO_2 + 2OH^-$$

The nitrosobenzene found is reduced further to phenylhydroxylamine as shown in the reaction scheme above. This scheme agrees with the experimental observations that the only products are nitrobenzene and phenyl hydroxylamine.[103,104,108] The nitroso compound proposed in this sequence cannot be isolated since it is itself reduced more easily than the nitro compound. Therefore it can pick up an electron either from the nitro radical-anion in solution, or if the reduction is carried out polarographically an electron can be supplied by the cathode:

$$PhNO_2^{\cdot-} + PhNO \longrightarrow PhNO_2 + PhNO^{\cdot-}$$

The nitroso radical-anion then forms the corresponding hydroxylamine with the uptake of a further electron and two protons.

Further work on the decay of the para-nitrobenzoate radical-dianion and the nitrobenzene radical-anion has shown that it is dependent on the presence of cations,[109] alcohols[110] and oxygen.[111]

An electron transfer between two negatively charged species may be catalysed by a cation.[112] At pH's 9-13, when the direct disproportionation reaction of two nitro aromatic radical-anions predominates, the second order rate constant is linearly dependent on cation concentration.

$$k_2 = k_o + k_1 c$$

where c = cation concentration.
Thus for sodium ions in solution, the expression for the decay becomes:

$$k_2 = 42 + 56[Na^+] \text{ litres. moles.}^{-1} \text{ sec.}^{-1}$$

for the nitrobenzene radical-anion.[109] Both k_1 and k_o are pH dependent. In this work k_o is a factor of ten greater than in previous work, which was carried out in solutions of various alcohols, which have been shown to retard the decay due to solvation effects.[110]

Kolb and Koopman[111] have shown that oxygen has a positive catalytic effect on this disproportionation reaction. The second order rate constant shows a linear dependence on oxygen concentration according to the expression:

$$k_2 = k_o^1 + k_3 c^1$$

where c^1 = oxygen concentration.

For the nitrobenzene radical anion $k_3 = 7.5 \times 10^7$ litres.^{2} moles.$^{-2}$ sec.$^{-1}$. Hence traces of oxygen can affect drastically the rates of decay of nitro aromatic radical-anions.

Polynitro aromatic compounds have been reduced electrolytically to the corresponding amines in DMF containing traces of acid. The same mechanism is proposed[113] as for the mono nitro compounds, the hydroxylamine formed reacting further as shown:

$$ArNHOH \xrightarrow[H^+]{e} (Ar\dot{N}H_2)^+ + OH^-$$

$$(Ar\dot{N}H_2)^+ \xrightarrow[e]{H^+} (ArNH_3)^+.$$

(b) Electron transfer reactions.

One-electron reduction of nitrobenzene yields the radical-anion and this reaction is reversible:

$$PhNO_2 + e^- \rightleftharpoons PhNO_2^{\dot{-}}$$

In the absence of a proton donor this radical-anion will not disproportionate [114], but will donate its unpaired electron to other electron acceptors in solution, with consequent oxidation to nitrobenzene and the formation of the radical-anion of the acceptor. A range of compounds that will receive an electron from the nitrobenzene radical-anion has been investigated by Metcalfe and Waters.[62] In addition, oxygen may also accept an electron.[115]

$$PhNO_2^{\dot{-}} + O_2 \rightarrow PhNO_2 + O_2^{\dot{-}}$$

5. The present work.

The aim of the work described in this thesis has been to effect a complete study of the reaction between hydroxylamine and related compounds and mononitro aromatic compounds. Having investigated the range of aromatic nitro compounds to which hydroxylamine and N-alkyl substituted hydroxylamines may transfer an electron (this is reported in Chapter 3), the work was developed to look quantitatively at the rates of electron transfer to various aromatic nitro compounds and the subsequent rates of decay of the radical-anions formed. By using a stopped flow technique, e.s.r. spectrometry was used to follow the build-up and decay of the nitro aromatic radical-anions. The results are reported in Chapter 4. From these kinetic studies a reaction scheme could be proposed and this was then verified and completed by a study of the products of the reaction. These studies are described in Chapter 5. Experimental procedures are recorded in the final chapter.

CHAPTER 3.

Hydroxylamine and related compounds as reducing agents.

1. Introduction.

Nitrogen blown 50% aqueous ethanolic solutions of the hydroxylamine compound and of the nitro compound in alkali were mixed within the cavity of an e.s.r. cell, using the aqueous flow system described in Chapter 6. On stopping the flow, the e.s.r. spectrum of the radical-anion of the nitro compound under investigation would build up if electron transfer from the hydroxylamine compound had taken place. The rate of appearance of an e.s.r. signal varied considerably with the reagents used; these quantitative aspects of the reactions are discussed in the following chapter.

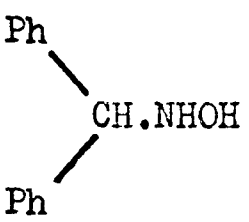
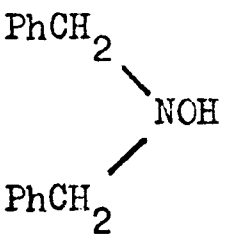
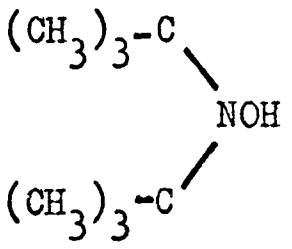
In this chapter the e.s.r. spectra, hyperfine splitting constants and g values are recorded for those mono nitro aromatic compounds to which hydroxylamine and substituted hydroxylamines will electron transfer. If the expected e.s.r. spectrum had not appeared within five minutes of mixing .01M solutions of reagents in 0.25M sodium hydroxide, it was considered that no electron transfer had taken place. Hence it was possible to obtain an idea of the reducing power of the hydroxylamine compounds under-investigation.

2. Results.

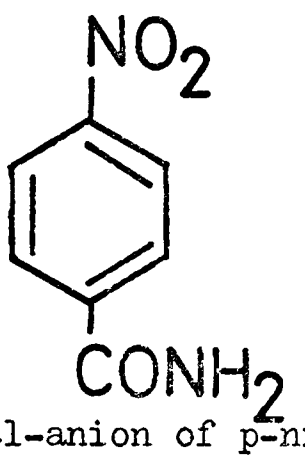
The seven hydroxylamines used in reactions with mono nitro-aromatic compounds are shown in Table 3:1. N,N-dibenzylhydroxylamine (6) and N,N-di-t-butylhydroxylamine (7) did not react with any of the nitro compounds investigated, in the absence of oxygen.

Qualitatively, no difference in reducing power was noted between hydroxylamine (1), N-methylhydroxylamine (2), N-phenylhydroxylamine (3), N-benzylhydroxylamine (4) and N-benzhydrylhydroxylamine (5), although, as will be seen in the following chapter, the rates of electron transfer vary. Hence if electron transfer was observed to occur to a given nitro compound, any of the hydroxylamines (1) - (5) could effect this.

Table 3:1.

1.	NH_2OH	hydroxylamine
2.	CH_3NHOH	N-methylhydroxylamine
3.	PhNHOH	N-phenylhydroxylamine
4.	$PhCH_2.NHOH$	N-benzyl hydroxylamine
5.		N-benzhydrylhydroxylamine
6.		N,N-dibenzylhydroxylamine
7.		N,N-di-t-butylhydroxylamine

(a) <u>p-Nitrobenzamide.</u>



The e.s.r. spectrum of the radical-anion of p-nitrobenzamide was observed to be produced rapidly, showing that electron transfer had taken place. This is shown in Fig.3.1. It consists of a large nitrogen triplet, and two smaller triplets with intensity ratios of 1 : 2 : 1. Whilst it is not possible to assign these two sets of triplets unambiguously on the basis of this spectrum alone, it is reasonable to attribute the set with the larger splitting constants to the ortho protons, and the set with the smaller to the meta protons.

The splitting constants were found to be:

a_N = 11.92 gauss (11.95)

a_{Ho} = 3.25 gauss (3.30)

a_{Hm} = 1.08 gauss (1.10)

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

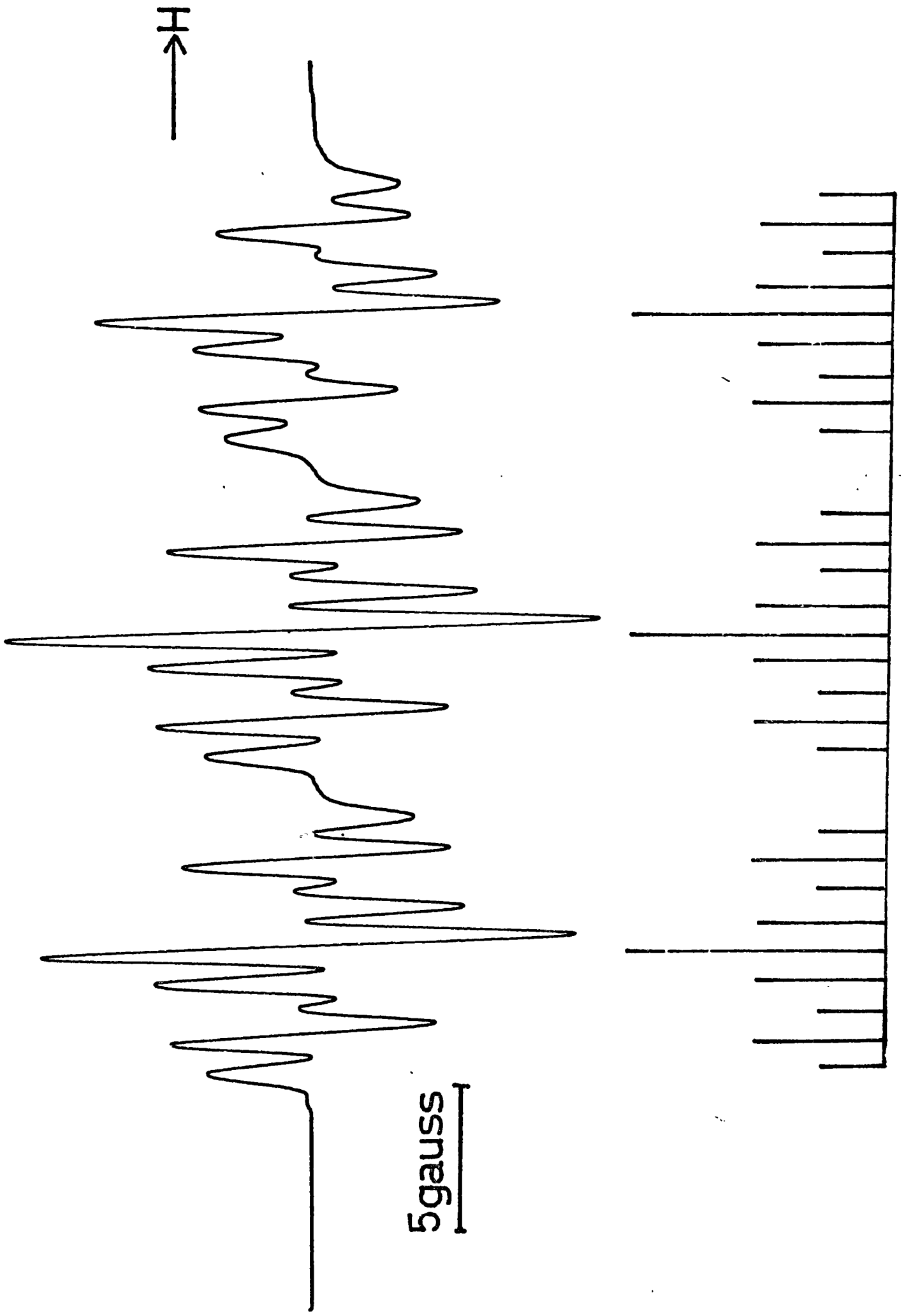
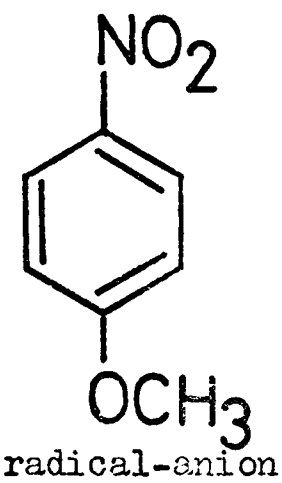


Fig. 3.1 The e.s.r. spectrum of the para-nitrobenzamide radical-anion.

(b) <u>p-Nitroanisole</u>.



A weak e.s.r. spectrum of the radical-anion from p-nitroanisole was observed. This is shown in Fig. 3.2.

This spectrum shows a large nitrogen triplet and two smaller triplets of intensity ratios of 1 : 2 : 1. The larger of these triplets is assigned to the magnetically equivalent pair of ortho protons.

The splitting constants were found to be:

a_N = 14.45 gauss (14.25)

a_{Ho} = 3.50 gauss (3.45)

a_{Hm} = 1.08 gauss (1.15)

On expansion of the spectrum, a further splitting due to the para substituent ($-OCH_3$) was observed. The three magnetically equivalent protons of the substituent group give rise to a quartet of intensity ratio 1 : 3 : 3 : 1.

a_{OCH_3} = 0.36 gauss (0.40)

The expansion of one of the lines of the major nitrogen triplet is shown in Fig. 3.3.

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

Fig.3. 2 The e.s.r. spectrum of the para-nitroanisole radical-anion

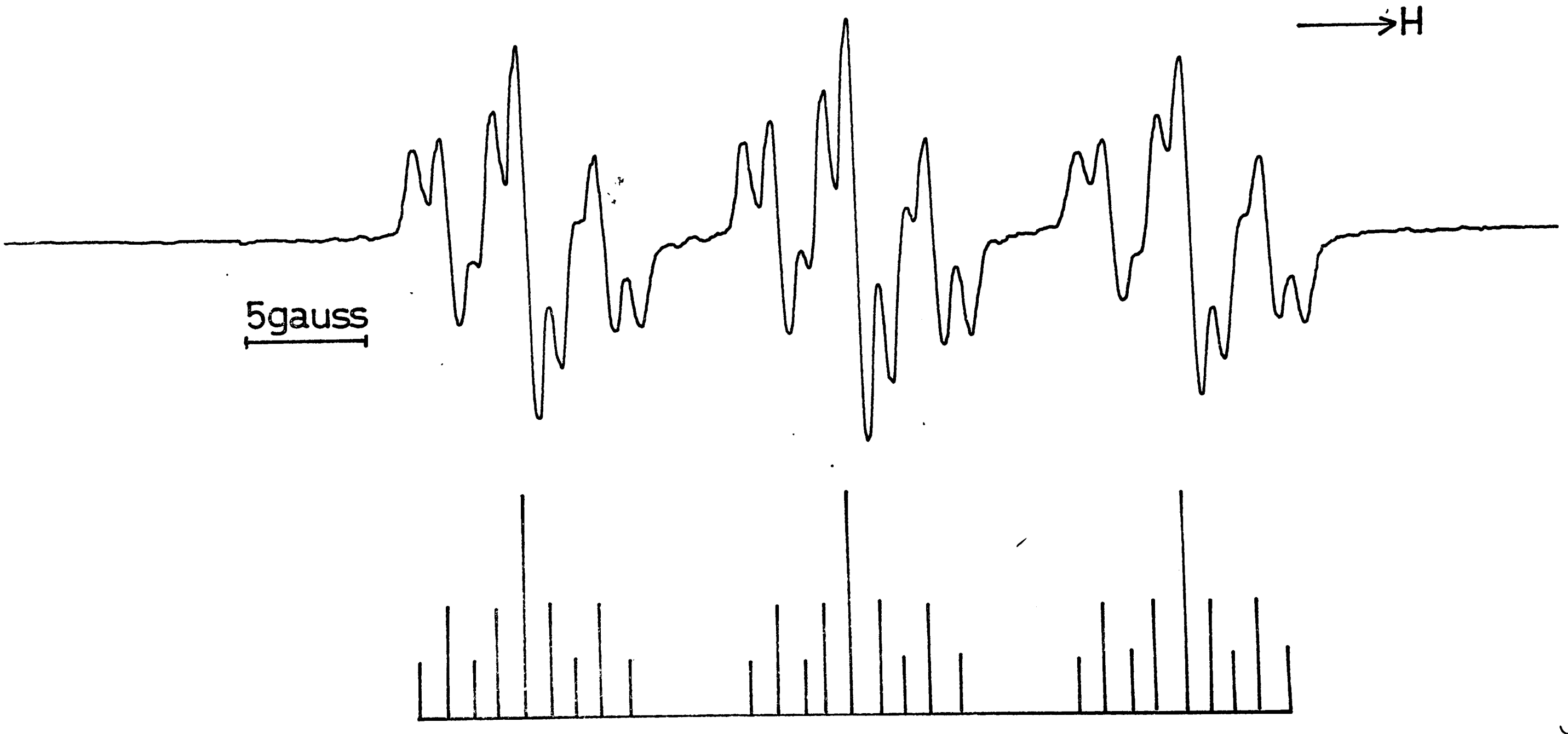
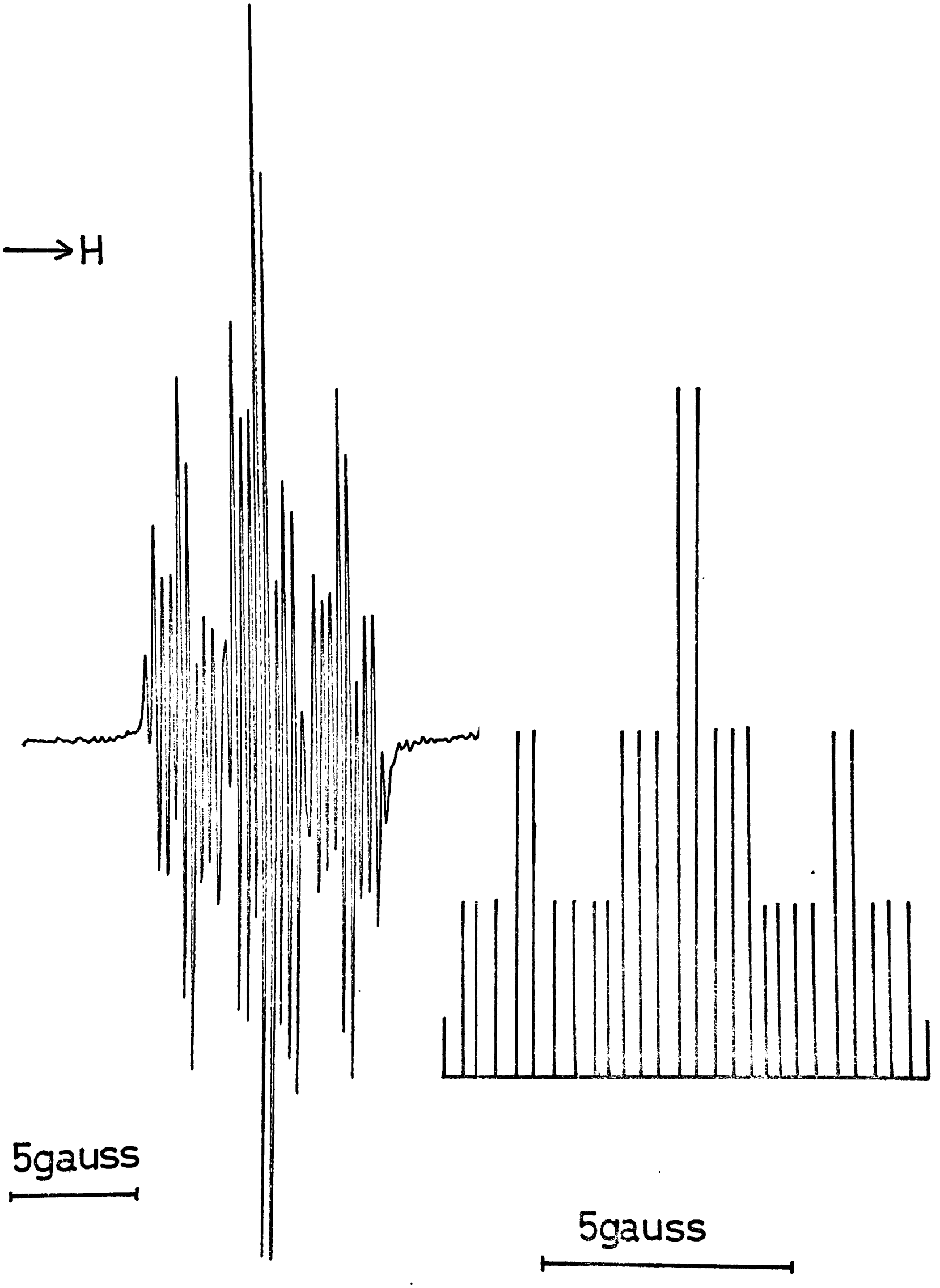
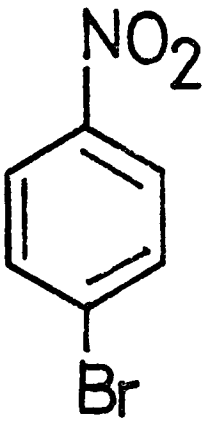


Fig. 3.3

The e.s.r. spectrum of the para-nitroanisole radical-anion: expansion of one of the lines of the major nitrogen triplet.



(c) p-Bromonitrobenzene



A strong e.s.r. spectrum of the radical-anion of p-bromonitrobenzene was observed to be produced rapidly, showing that electron transfer had taken place. This is shown in Fig.3.4. It consists of a large nitrogen triplet, and two smaller triplets with intensity ratious of 1 : 2 : 1.

As with the other nitro radical-anions under investigation, the larger of these two sets of triplets is assigned to the two magnetically equivalent ortho protons.

The splitting constants were found to be:

a_N = 12.88 gauss (12.80)

a_{Ho} = 3.50 gauss (3.40)

a_{Hm} = 1.20 gauss (1.00)

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

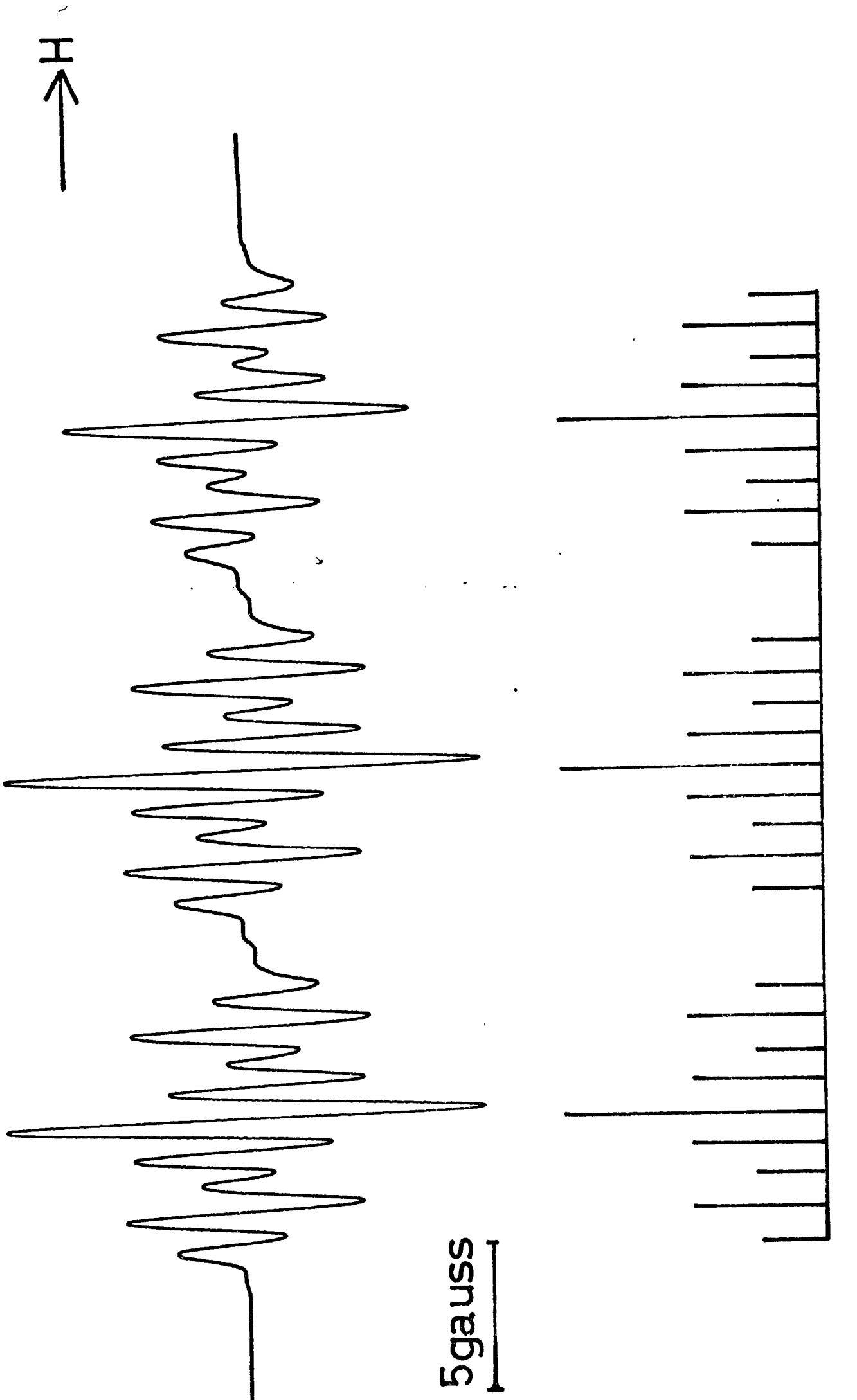
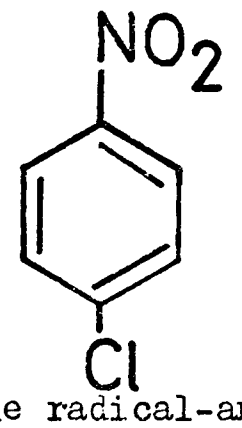


Fig. 3.4 The e.s.r. spectrum of the para-bromonitrobenzene radical-anion

(d) <u>p-Chloronitrobenzene</u>



A strong e.s.r. spectrum of the radical-anion of p-chloronitrobenzene was observed to be produced rapidly, and is shown in Fig.3.5. It consists of a large nitrogen triplet, and two smaller triplets with intensity ratios of 1 : 2 : 1. As with the p-bromonitrobenzene radical-anion the larger of these two sets of triplets is assigned to the two magnetically equivalent ortho protons.

The splitting constants were found to be:

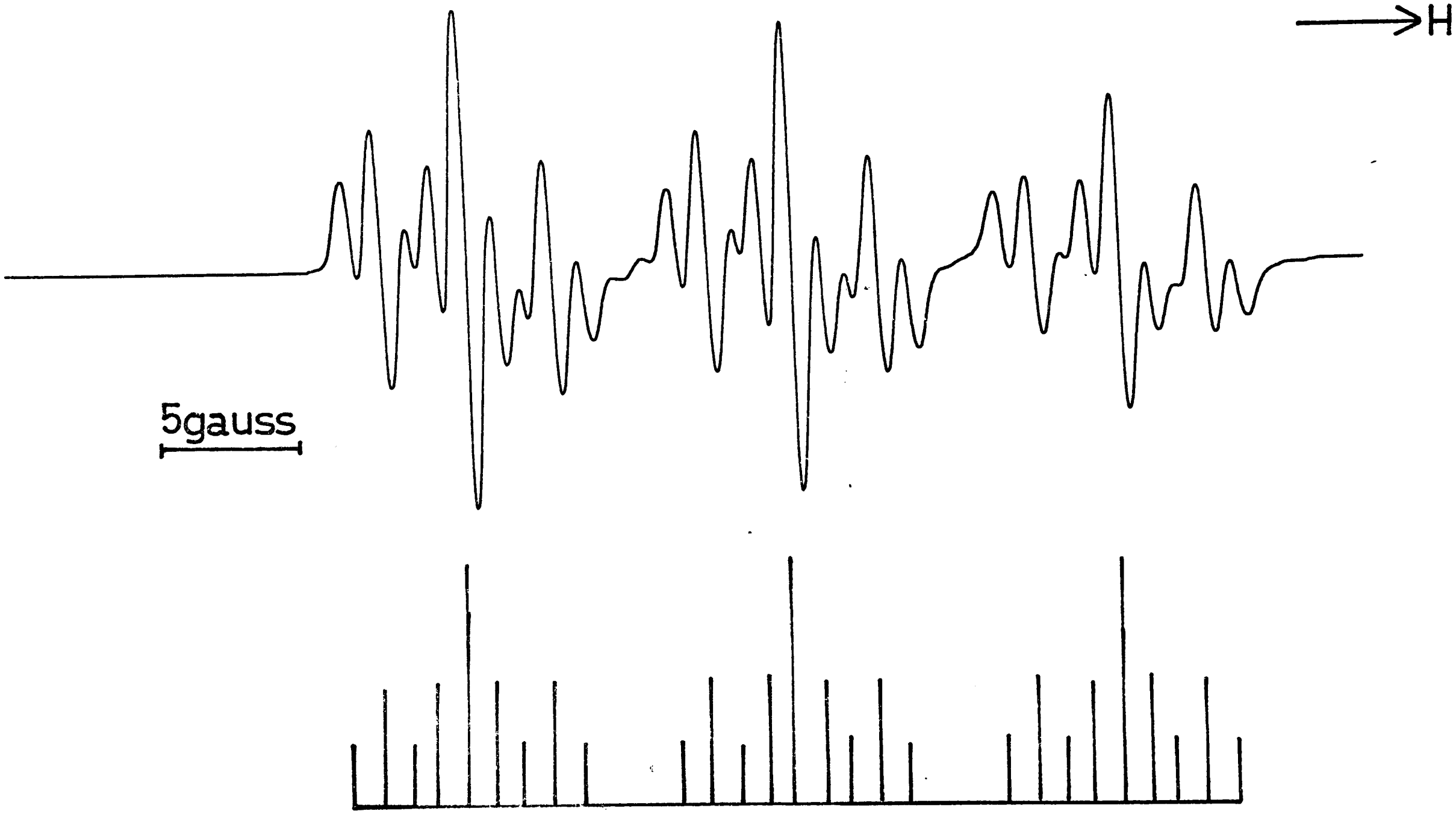
a_N = 12.88 gauss (12.90)

a_{Ho} = 3.50 gauss (3.30)

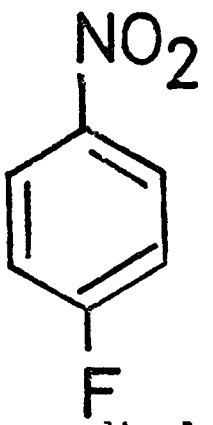
a_{Hm} = 1.20 gauss (0.90)

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

Fig. 3.5 The e.s.r. spectrum of the para-chloronitrobenzene radical-anion



(e) <u>p-Fluoronitrobenzene</u>



A strong e.s.r. spectrum of the radical-anion of p-fluoronitrobenzene was observed, showing that electron transfer had taken place. The spectrum is shown in Fig. 3.6. A relatively complicated e.s.r. absorption pattern is observed. This differs significantly from the corresponding chloro- and bromo- isomers because the fluorine atom gives rise to hyperfine splitting (^{19}F has a nuclear spin $I = \frac{1}{2}$). Hence in addition to the large nitrogen triplet and the two smaller triplets of intensity ratios of 1 : 2 : 1, due to the magnetically equivalent pairs of ortho and meta protons, a doublet due to the fluorine atom is observed.

The splitting constants were found to be:

a_N = 13.84 gauss (13.20)

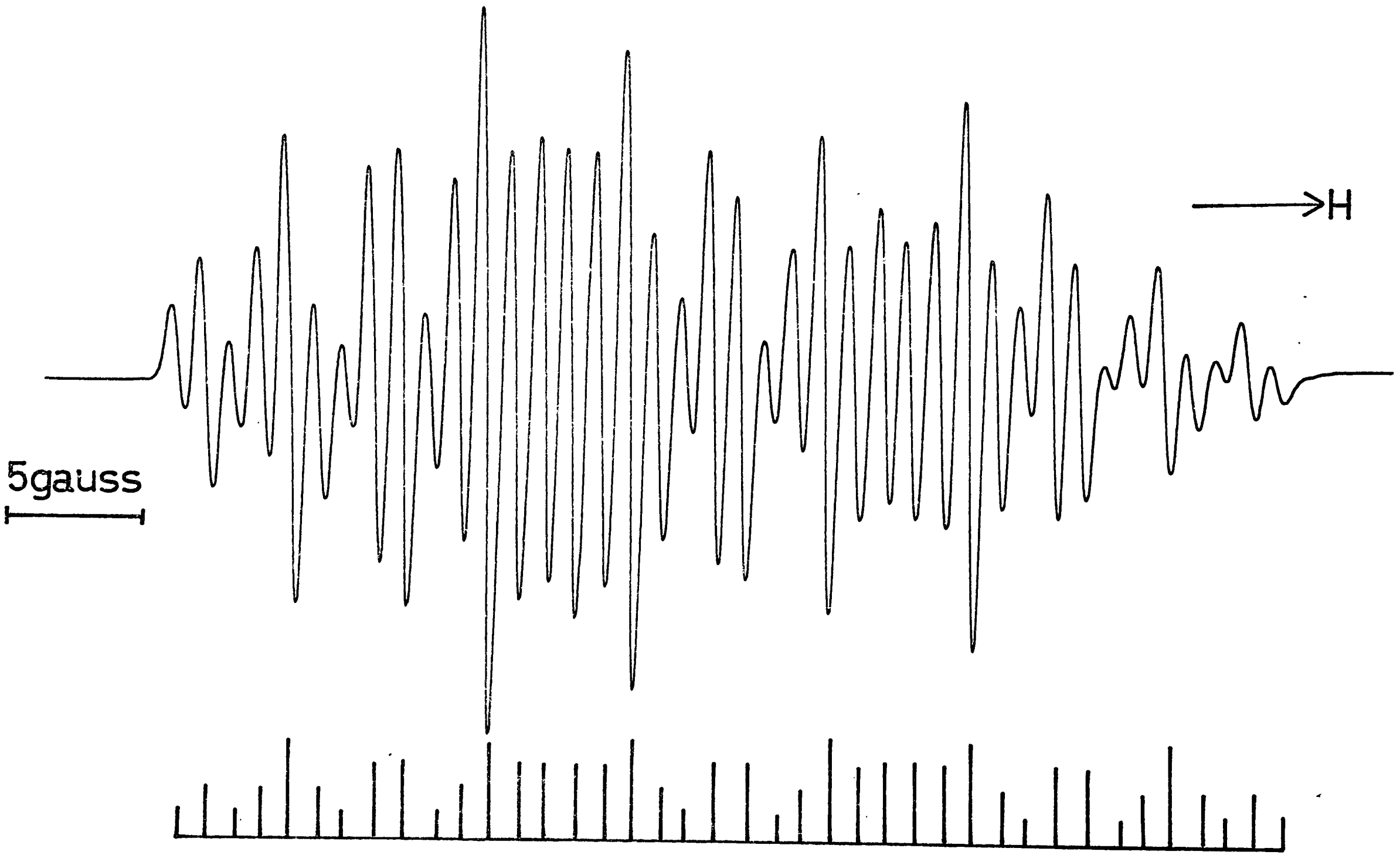
a_F = 7.95 gauss (7.95)

a_{Ho} = 3.37 gauss (3.40)

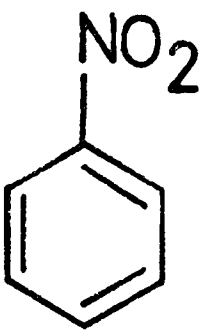
a_{Hm} = 1.08 gauss (1.15)

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

Fig. 3.6 The e.s.r. spectrum of the para-fluoronitrobenzene radical-anion



(f) Nitrobenzene



The appearance of the e.s.r. spectrum of the nitrobenzene radical-anion showed that electron transfer had taken place. The spectrum is shown in Fig. 3.7.

The analysis of the spectrum was described in detail in Chapter 2. In the spectrum shown, the resolution was not great enough to distinguish between ortho and para proton hyperfine splittings. Hence a quartet with intensity ratio of 1 : 3 : 3 : 1 can be seen due to three protons of identical splitting constants. Under conditions of greater resolution $a_{Hp} > a_{Ho}$. The other features of the absorption pattern that are observed are due to a large nitrogen triplet and a small triplet of intensity ratio 1 : 2 : 1, due to the magnetically equivalent meta protons. The splitting constants were found to be:

$$a_N = 13.72 \text{ gauss} \qquad (13.30)$$

$$a_{Ho} = a_{Hp} = 3.37 \text{ gauss} \qquad (3.40)$$

$$a_{Hm} = 1.08 \text{ gauss} \qquad (0.90)$$

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

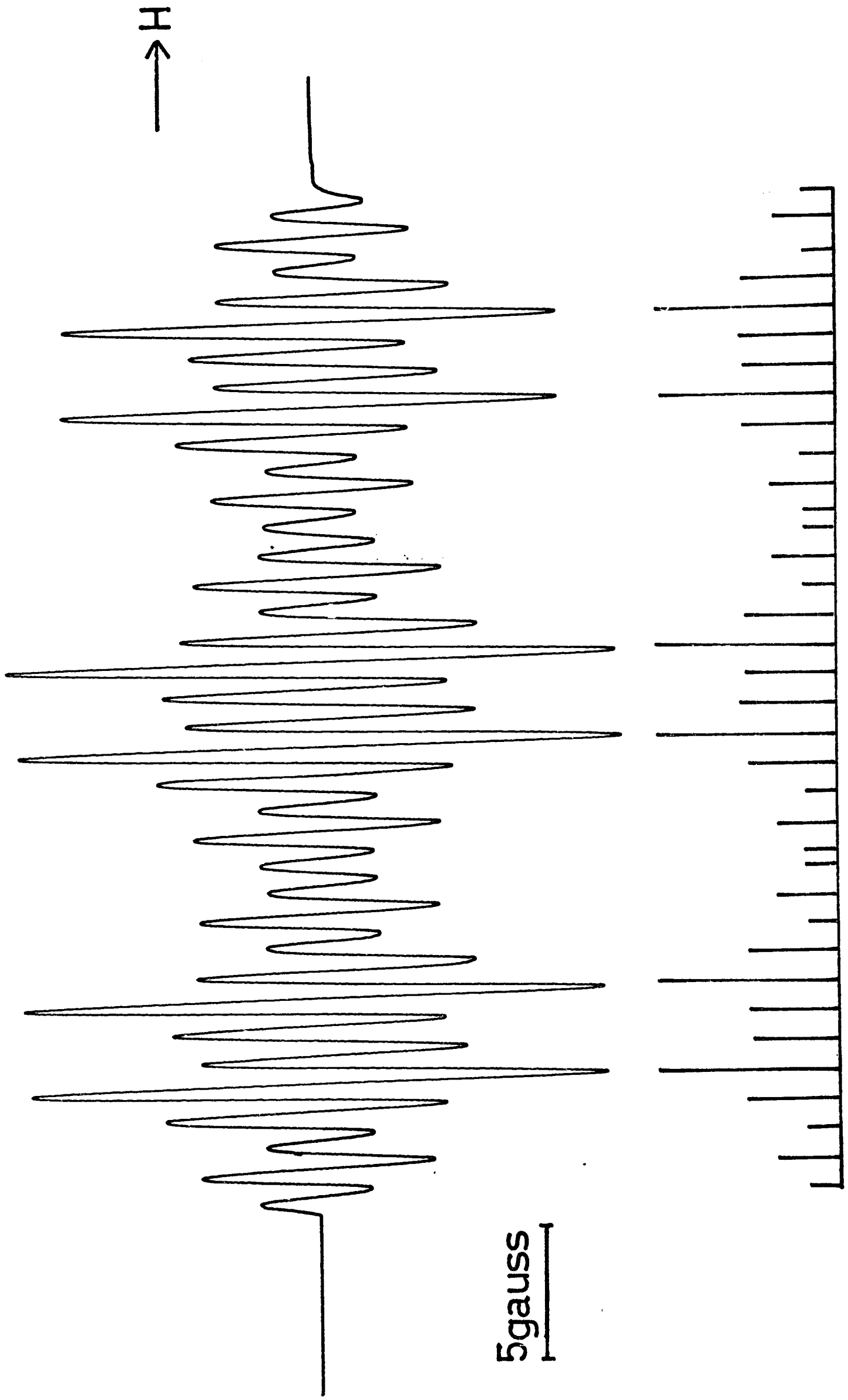
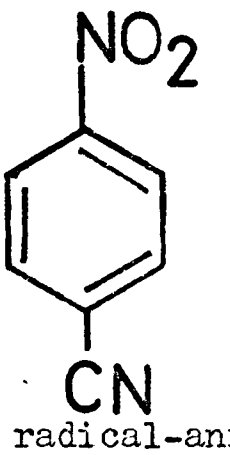


Fig. 3.7 The e.s.r. spectrum of the nitrobenzene radical-anion

(g) <u>p-Nitrobenzonitrile</u>



A strong e.s.r. spectrum of the radical-anion of p-nitrobenzonitrile was obtained, showing that electron transfer had taken place. The spectrum is shown in Fig. 3.8. It consists of a large nitrogen triplet, and two smaller triplets with intensity ratios of 1 : 2 : 1. The larger of these two sets of triplets is assigned to the pair of magnetically equivalent ortho protons. No splitting from the nitrogen atom of the substituent cyano group is observed.

The splitting constants were found to be:

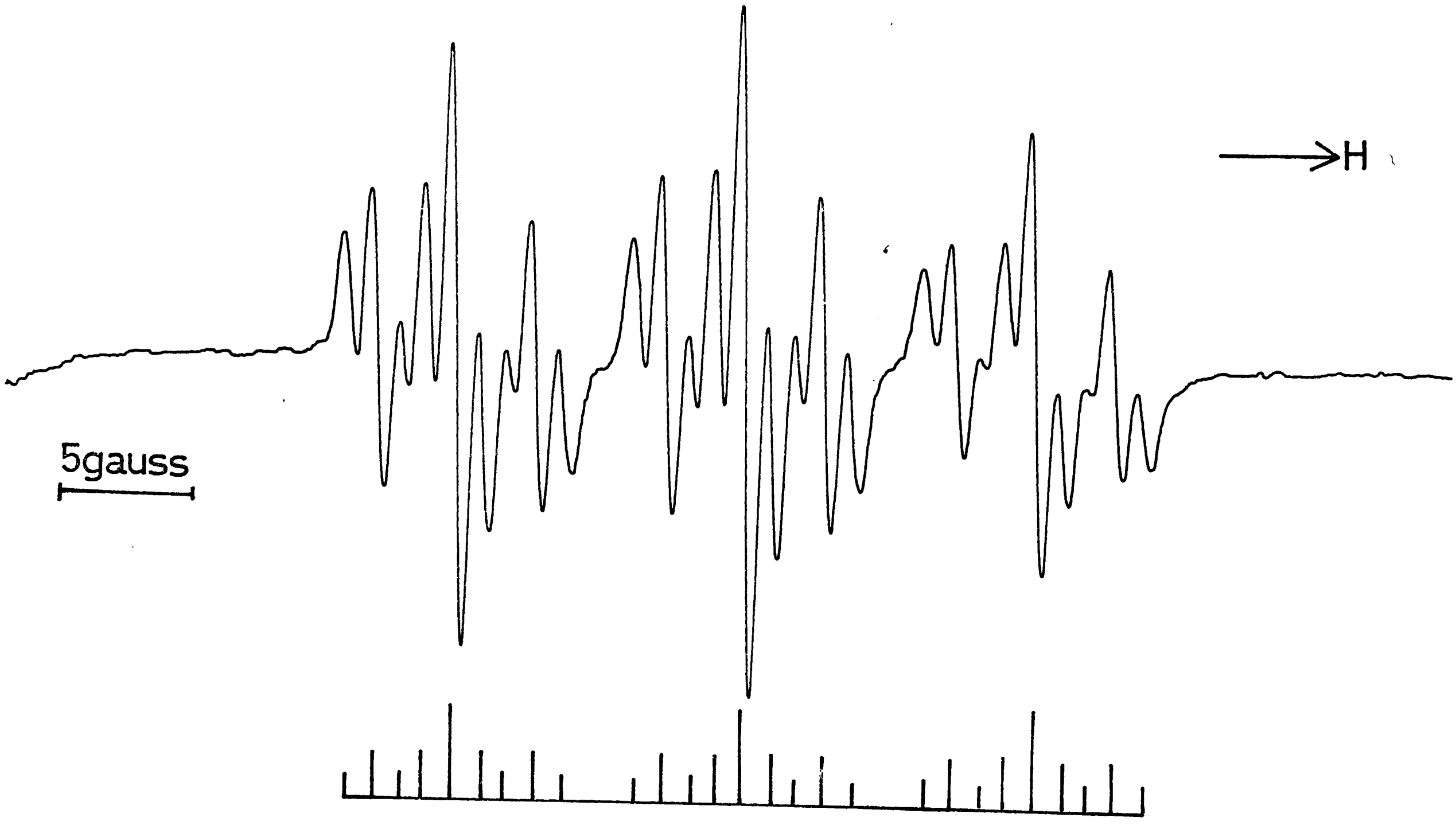
a_N = 12.16 gauss (11.10)

a_{Ho} = 3.37 gauss (3.25)

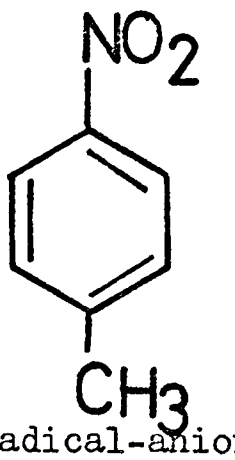
a_{Hm} = 1.08 gauss (1. 05)

The values of Kolker and Waters[82] are quoted in parenthesis for comparison.

Fig. 3.8 The e.s.r. spectrum of the para-nitrobenzonitrile radical-anion.



(h) p-Nitrotoluene.



An e.s.r. spectrum of the radical-anion of p-nitrotoluene was observed. This is shown in Fig. 3. 9. The spectrum shows a large nitrogen triplet and hyperfine splittings from seven protons. The two meta protons give rise to a small triplet of intensity ratio 1 : 2 : 1. The remaining ortho protons and the protons from the substituent methyl group appear to have the same splittings constants at this resolution. Those five equivalent protons give rise to a sextet with intensity ratio of 1 : 5 : 10 : 10 : 5 : 1. The splitting constants were found to be:

a_N = 13.84 gauss (14.10)

a_{H_o} = 3.50 gauss (3.50)

a_{H_m} = 1.08 gauss (1.10)

a_{CH_3} = 3.50 gauss (3.80)

The values of Kolker and Waters[82] are given in parenthesis for comparison.

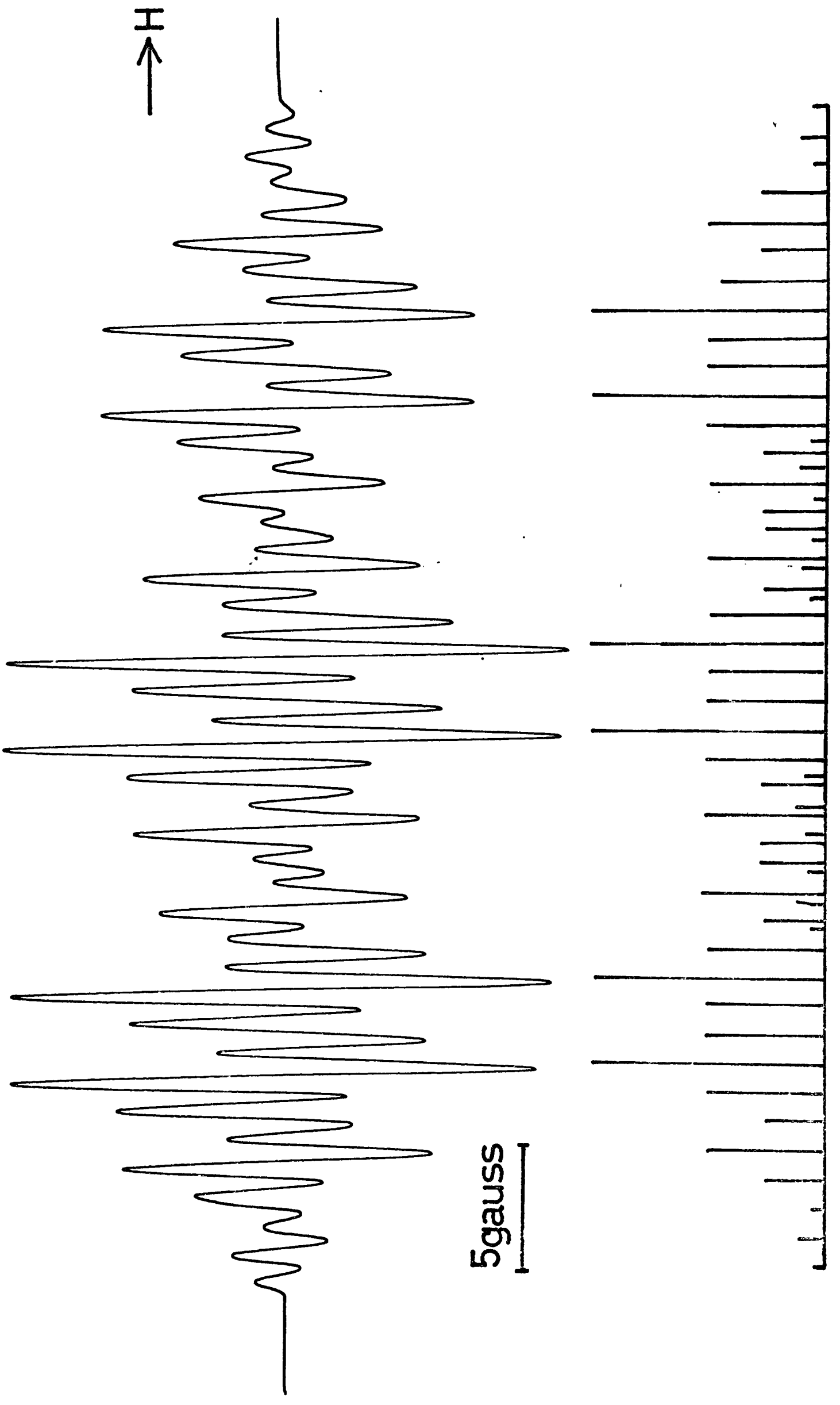
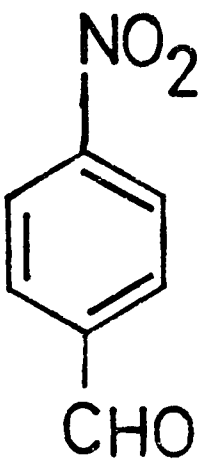


Fig.3.9 The e.s.r. spectrum of the para-nitrotoluene radical-anion

(i) p-Nitrobenzaldehyde.



The e.s.r. spectrum of the radical-anion from p-nitrobenzaldehyde was obtained showing that electron transfer had taken place. The spectrum is shown in Fig. 3.10. It consists of a large nitrogen triplet, and two smaller triplets with intensity ratios of 1 : 2 : 1. The larger of these two sets of triplets is assigned to the pair of magnetically equivalent ortho protons. In addition traces of a secondary radical, displaced to lower field appear to be present.

The splitting constants were found to be:

a_N = 12.52 gauss (12.85)

a_{Ho} = 3.37 gauss (3.30)

a_{Hm} = 1.08 gauss (1.15)

The values of Kolker and Waters[82] are given in parenthesis for comparison.

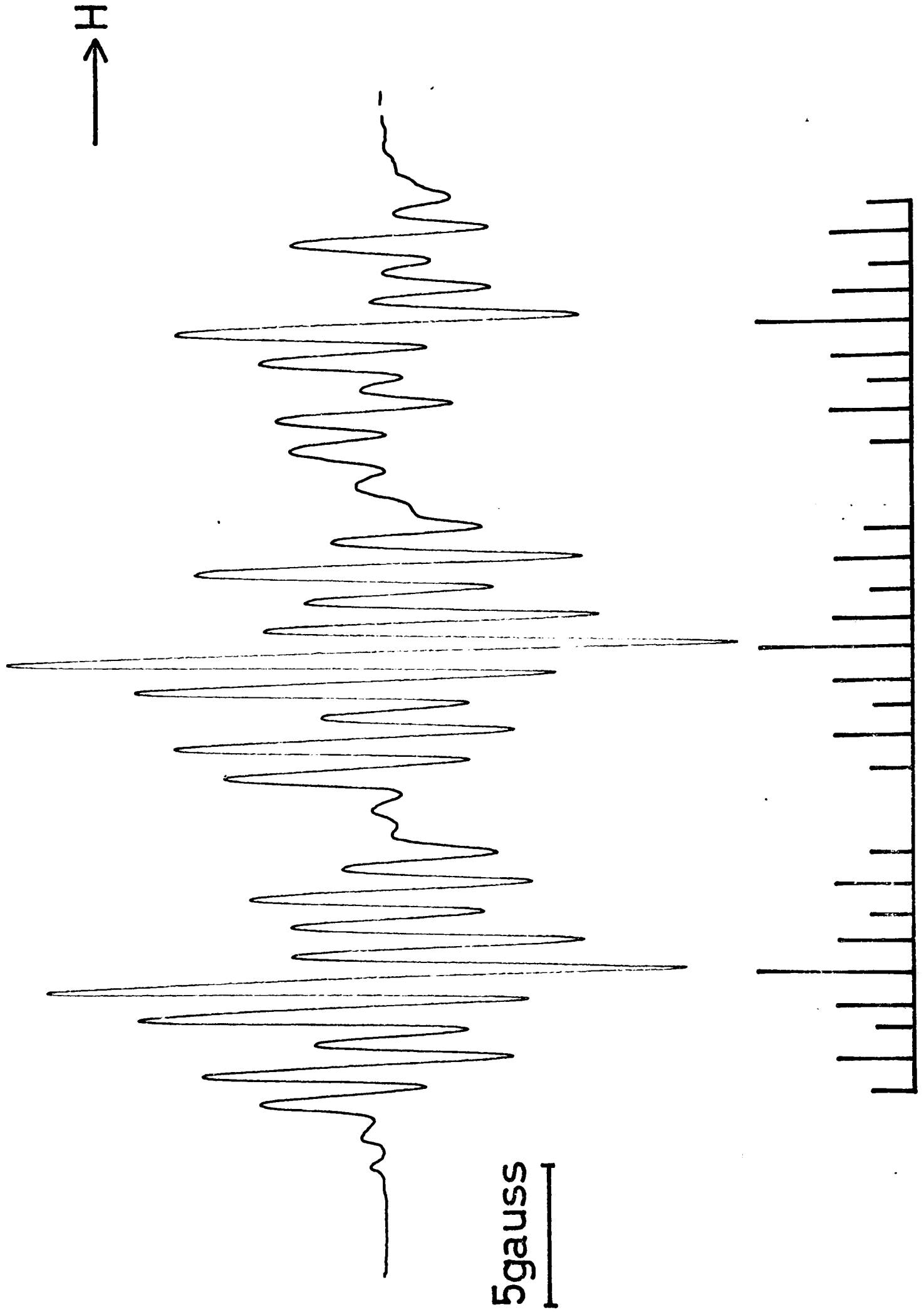
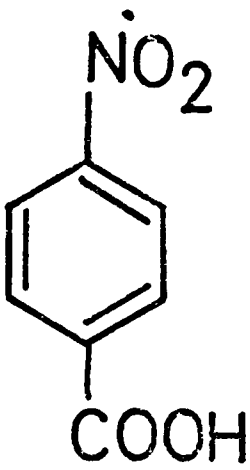


Fig.3.10 The e.s.r. spectrum of the para-nitrobenzaldehyde radical-anion.

(j) <u>p-Nitrobenzoic acid</u>



A strong e.s.r. spectrum of the radical-dianion of p-nitrobenzoic acid was observed, owing to the basic conditions employed. This is shown in Fig. 3.11. It consists of a large nitrogen triplet, and two well defined smaller triplets with intensity ratios of 1 : 2 : 1. The larger of these two sets of triplets is assigned to the pair of magnetically equivalent ortho protons.

The splitting constants were found to be:

a_N = 12.64 gauss (12.60)

a_{H_o} = 3.37 gauss (3. 40)

a_{H_m} = 1.20 gauss (1.15)

The values of Kolker and Waters[82] are given in parenthesis for comparison.

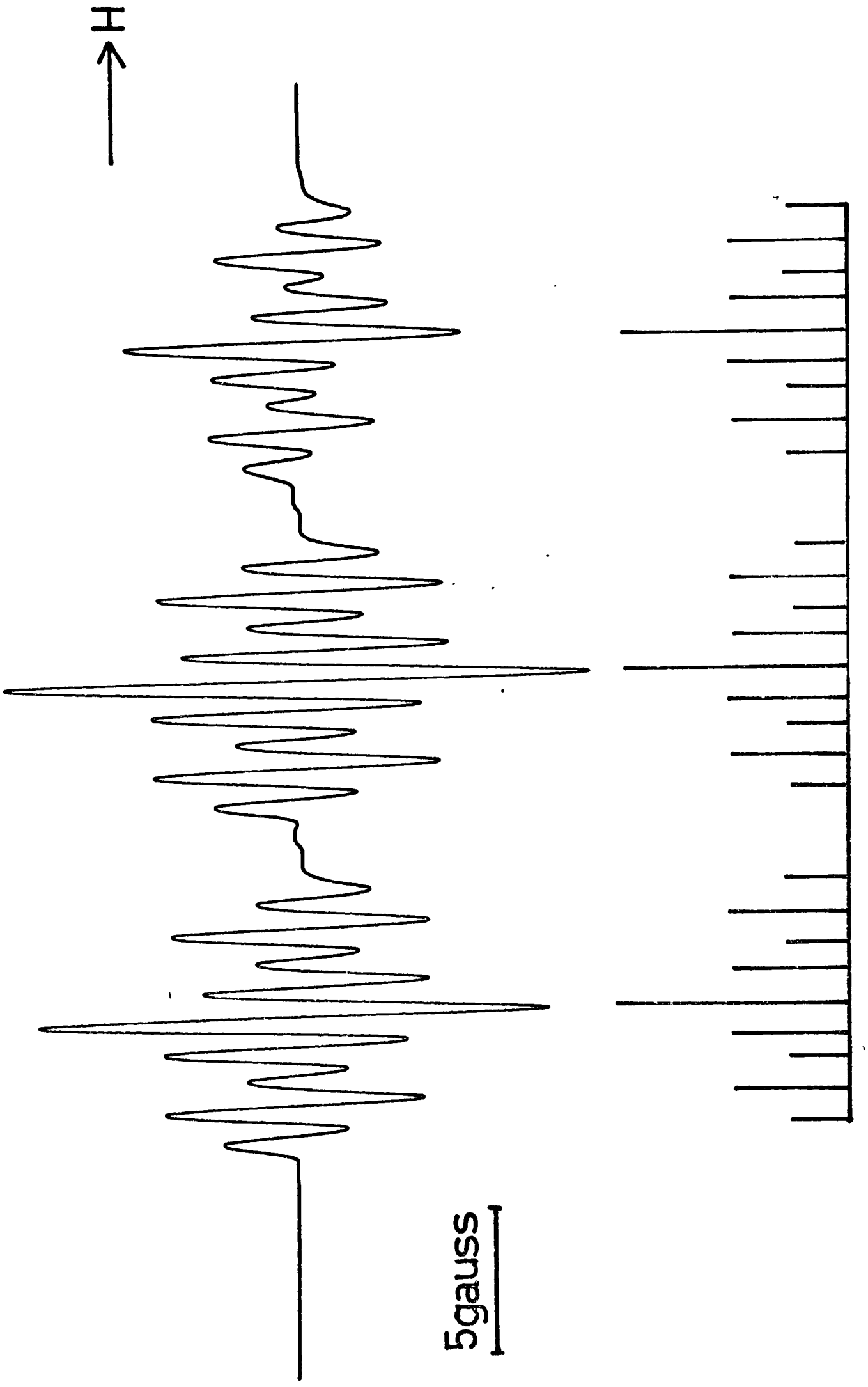
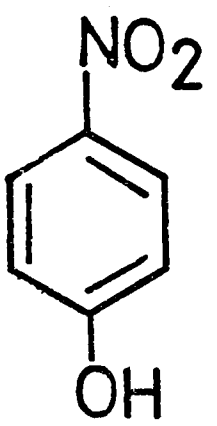


Fig.3.11 The e.s.r. spectrum of the para-nitrobenzoate radical-anion.

(k) p-Nitrophenol.



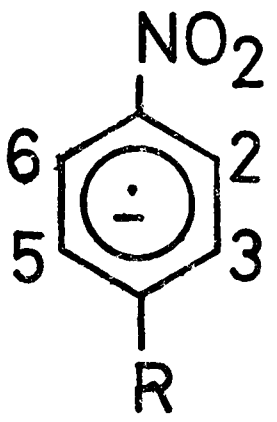
The expected radical-dianion of p-nitrophenol was not observed during experiments with any of the hydroxylamines under investigation.

The hyperfine splitting constants for the ten mononitro-aromatic radical-anions which were obtained are summarized in Table 3.2. This table also includes the g-values for these radicals, which were obtained by the method described in Chapter 6.

The values of Kolker and Waters[82] that have been quoted for comparison are for nitro radical-anions obtained during reduction with alkaline sodium dithionite in 10-15% aqueous acetone.

TABLE 3.2

Splitting constants and g-values for mononitroaromatic radical-anions.



R	a_N	$a_2 = a_6$	$a_3 = a_5$	a_R	g.
$CONH_2$	11.92	3.25	1.08	-	2.0047
OCH_3	14.45	3.50	1.08	0.36(a)	2.0046
Br	12.88	3.50	1.20	-	2.0057
Cl	12.88	3.50	1.20	-	2.0049
F	13.84	3.37	1.08	7.95(b)	2.0047
H	13.72	3.37	1.08	3.37(c)	2.0045
CN	12.16	3.37	1.08	-	2.0047
CH_3	13.84	3.50	1.08	3.50(d)	2.0045
CHO	12.52	3.37	1.08		2.0048
COO^-	12.64	3.37	1.20	-	2.0047

Notes: (i) Splitting constants are measured in gauss.

(ii) (a) a_{OCH_3} (d) a_{CH_3}

(b) a_F

(c) a_H

(iii) Data refers to room temperature ($22^\circ \pm 1^\circ$).

3. Discussion

(a) Of the seven hydroxylamines investigated (see Table 3.1.), five were shown to be able to effect electron transfer to a range of mononitroaromatic compounds. These were:

1. Hydroxylamine
2. N-methylhydroxylamine
3. N-phenylhydroxylamine
4. N-benzylhydroxylamine
5. N-benzylhyrylhydroxylamine

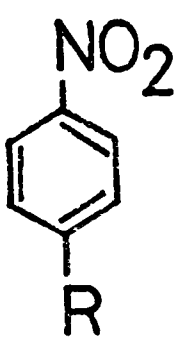
(b) No qualitative difference was noted in the reducing power of these hydroxylamines. The limit of their reducing power was reached with p-nitrophenol.

Table 3.3. shows $E_{\frac{1}{4}}$ values for the range of nitro compounds investigated, relative to the saturated calomel electrode. These values were obtained by Seely[116] for compounds in pyridine: ethanol : water, 63 : 27 : 10. This system is considered to be the closest to that under investigation, for which such data is available. $E_{\frac{1}{4}}$ values rather than $E_{\frac{1}{2}}$ values are quoted for the following reason:

For easily reduced nitrobenzenes e.g., p-nitrobenzaldehyde, the polarographic wave in pyridine: ethanol : water approaches a shape corresponding to a reversible one electron reaction. However for others there is a change to a more gradual slope or even to an inflexion near the middle of the wave. This gives it the appearance of two coalesced electron waves, the first of which is more nearly reversible than the second.

TABLE 3.3.

Polargraphic data of Seely[116] for parasubstituted nitro compounds

Nitro compounds 	$E_{1/4}$ in volts (measured relative to the saturated calomel electrode).
R = -CHO	-0.626v
R = -CN	-0.640v
R = $-COOCH_3$	-0.694v
R = $-COO^-$	-0.790v
R = -F	-0.810v
R = -Cl	-0.822v
R = -H	-0.881v
R = $-NH.CO.CH_3$	-0.924v
R = $-CH_3$	-0.930v
R = $-OCH_3$	-0.957v
RNHO$^\bullet$	
R = $-O^-$	

Note: Supporting electrolyte is lithium perchlorate + 0.01% polyvinyl pyrrolidine.

Now $E_{\frac{1}{2}}$ has theoretical significance for reversible waves only and not for irreversible waves. Only the first stage of the four electron reduction of nitrobenzene or a substituted nitrobenzene is reversible. Hence $E_{\frac{1}{2}}$ of a four electron wave is not an appropriate value to consider when estimating the potential of the reversible first step. Thus $E_{\frac{1}{4}}$ is chosen as the potential reference for the wave.

This is only necessary when working in protic solvents. In aprotic solvents the polarographic wave corresponding to the first step is well separated from the succeeding waves.

The value of $E_{\frac{1}{4}}$ for the p-nitrophenolate ion in the pyridine: ethanol : water system has not been ascertained. With p-nitrophenol neither the addition of base nor acid affected the polargographic waves. Hence it was impossible to say whether the ionized or unionized form was reactive. From the present work it would be predicted that the $E_{\frac{1}{4}}$ of the ionized form would be lower than -0.957v, i.e., the value for p-nitroanisole which was successfully reduced by this range of hydroxylamines.

The $E_{\frac{1}{4}}$ value for the radical $RNHO^{\bullet}$, the product of one electron oxidation of hydroxylamine or a substituted hydroxylamine in basic solution, would lie between that for p-nitroanisole and that for the p-nitrophenolate ion.

Hence electron transfer from a range of hydroxylamines to mononitroaromatic compounds in nitrogen-blown, aqueous alkaline ethanol would appear to be a useful method for the generation of nitro radical-anions, providing that $E_{\frac{1}{4}}$ of the nitro compound lies

at or above 0.957v. Thus it would be prodicted that many other mononitro radical-anions e.g., methyl p-nitrobenzoate, $E_{\frac{1}{4}}$ = -0.694v and p-nitroacetanilide, $E_{\frac{1}{4}}$ = -0.924v, could be generated by this technique.

(c) The g-values of all the radical-anions investigated were in the range 2.0045 - 2.0049, except for that of the p-bromonitrobenzene radical-anion, which was 2.0057. These values agree closely with that of Metcalfe and Waters[62], who found the g-value of the nitrobenzene radical-anion and the p-chloronitrobenzene radical-anion to be 2.0048. It can be seen that for the radical-anions containing halogen substituents, the g-value increases:

$$Br > Cl > F > H$$

This has also been observed for semiquinone radicals containing halogen substituents[20]. The order is correlated with the spin orbit coupling constant for these atoms.

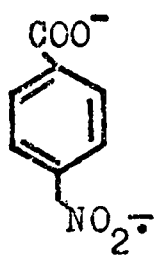
CHAPTER 4

Kinetic Studies

1. Introduction

In the previous chapter it has been shown that the e.s.r. spectra for a range of aromatic mono nitro radical-anions can be obtained by reduction of the nitro compound using alkaline solutions of hydroxylamine and some related compounds. The e.s.r. spectra obtained are not obscured by spectra of other radicals as a rule. By using a stopped flow technique, e.s.r. spectroscopy can be used to study the kinetics of many reactions involving the formation and decay of free radicals.[117,118] This procedure has been adopted for the study of the initial stages of the reaction between hydroxylamine and related compounds and aromatic mono nitro compounds.

When nitrogen flushed aqueous solutions of hydroxylamine hydrochloride and of p-nitrobenzoic acid in an excess of alkali are mixed within the cavity of an e.s.r. cell the spectrum of the radical dianion (I),



I.

immediately appears, soon reaches a maximum intensity corresponding to radical formation of the order of 10^{-2} of the initial concentration of p-nitrobenzoic acid, and then very slowly decays. However after several minutes the strength of the e.s.r. signal varies irregularly,

and inspection of the reaction mixture shows that this is due to the formation of gas bubbles in the e.s.r. cell. The reactions of alkaline hydroxylamine with other aromatic mono nitro compounds are similar in character.

The interpretation of kinetic data obtained under such circumstances must be treated with caution, as fluctuations in the e.s.r. signal due to gas evolution in the cell may completely mask the reaction under investigation.

However the reactions in aqueous ethanolic alkali, under nitrogen, of p-nitrobenzoic acid with N-methyl, N-benzyl and N-benzhydrylhydroxylamines also give the spectrum of radical (I) only. These mixtures eventually become deep red or brown in colour, but there is no evolution of gas and so it is possible to monitor changes in radical concentration for several hours and to analyse the data kinetically.

During the reaction of p-nitrobenzoic acid with N-phenylhydroxylamine, the e.s.r. spectrum of the phenylnitroxide anion $(Ph\text{-}NO)^{\bullet -}$, as well as that of (I), is observable for 2-3 seconds after the flow is stopped, but thereafter only the spectrum of (I) persists.

N,N-dibenzylhydroxylamine and N,N-di-t.butylhydroxylamine do not react with aromatic mono nitro compounds in the absence of oxygen, as noted in the previous chapter. Hence data obtained during the reactions of N-alkyl and N-aryl hydroxylamines with aromatic mono nitro compounds would appear to be more reliable for

kinetic analysis than that obtained with hydroxylamine itself, and it has been possible to establish the mechanisms of the initial reactions in these cases.

This chapter is subsequently divided into three sections. The first of these reports results pertaining to the mechanism of the initial reactions, and is followed by their discussion.

The second reports results concerning the relative rates of electron transfer from various hydroxylamines to a range of aromatic mono nitro compounds, and discusses these variations.

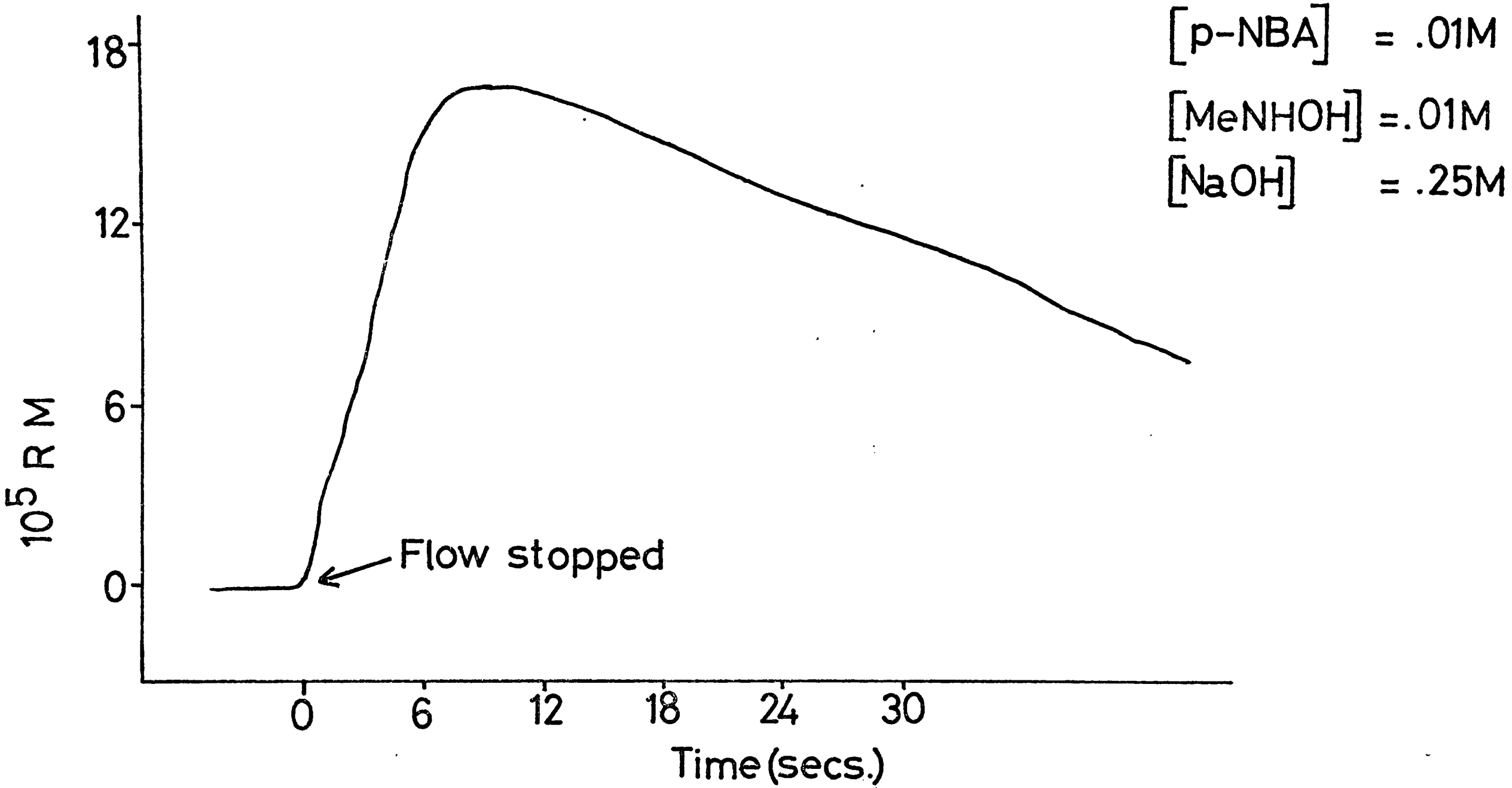
Finally data obtained for reactions in which hydroxylamine itself is involved, will be shown to be consistent with these proposals.

A - The Mechanism of the initial reactions

1. Results

Kinetically the reactions between RNHOH (R = Me, $PhCH_2$, Ph_2CH or Ph) and p-nitrobenzoic acid or p-nitrobenzamide (the two aromatic mono nitro compounds for which extensive kinetic measurements have been made) resemble very closely those leading to the formation and destruction of dibenzylnitroxide during the autoxidation of N,N-dibenzylhydroxylamine.[117] In these reactions the e.s.r. spectrum of the nitro radical-anion reaches its maximum intensity within a minute of the time of mixing of the reactants in a stopped flow apparatus, but decays very slowly indeed (Fig.4.1). Experimental details of this procedure and the method used for the measurement of radical concentrations are given in Chapter 6. This general pattern of build up and decay of the radical under investigation, is typical of consecutive reactions in which a stationary state intermediate is being destroyed much more rapidly than it is being produced. A pseudo equilibrium is reached as soon as the radical concentration has reached a maximum. This is in accordance with the observation that the maximum radical concentration is never more than 10% of the initial concentrations of the reactants.

Fig. 4.1 Build up and decay of the e.s.r. spectrum of the para-nitrobenzoate radical-dianion.



Figs. 4.2 and 4.3 show that the maximum concentration of the nitro radical-anion, $[R^{\bullet}]_{max}$, is approximately proportional to the square root of the concentration of the nitro compound, $[ArNO_2]$.

Figs. 4.4 and 4.5 show that $[R^{\bullet}]_{max}$ is approximately proportional to the square root of the concentration of the hydroxylamine derivative, [RNHOH].

Figs. 4.6 and 4.7 show that $[R^{\bullet}]_{max}$ is approximately proportional to the square root of the free alkali concentration until this reaches about 1M, and thereabove appears to have reached a maximum.

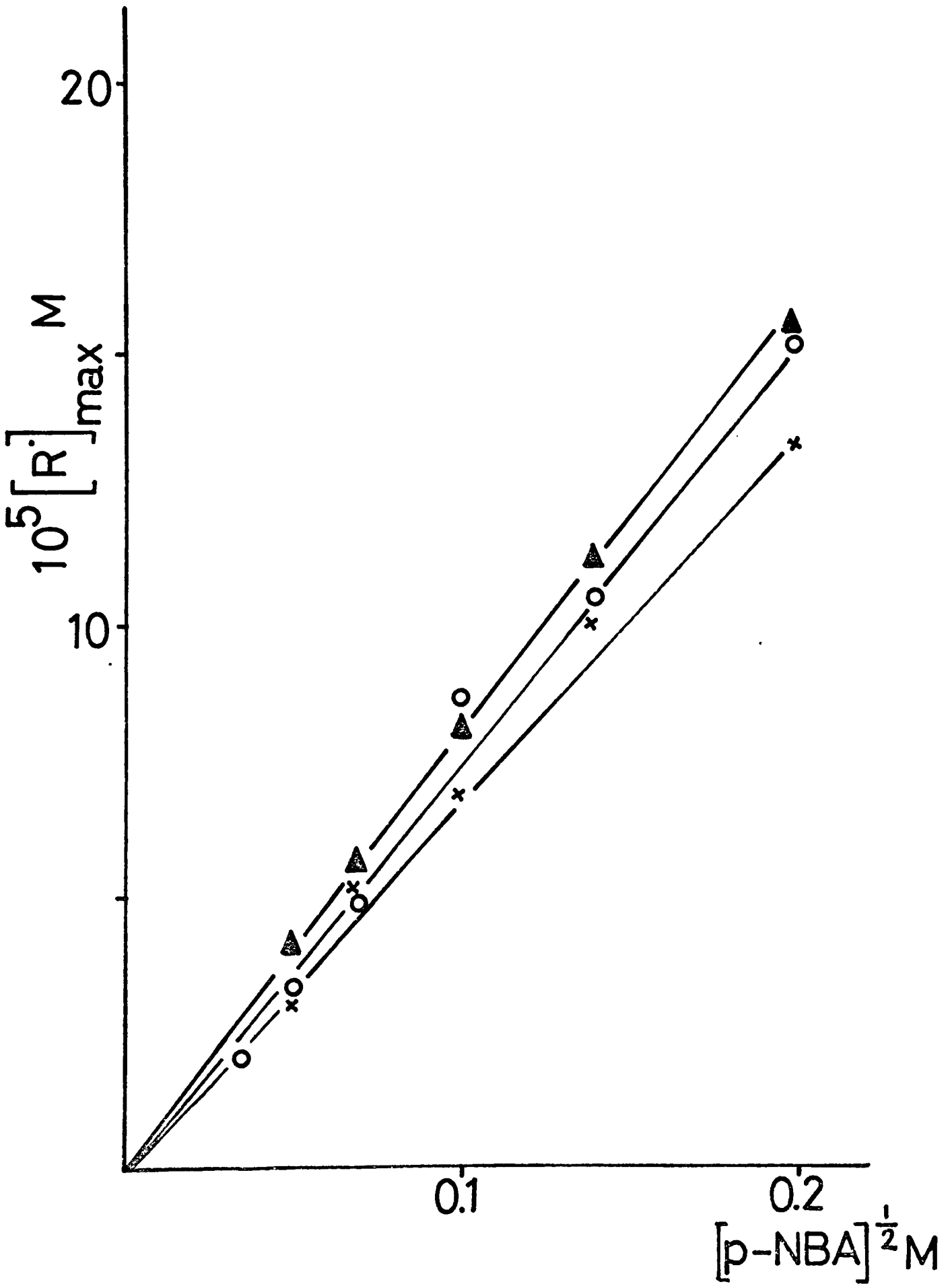
From these measurements at room temperature ($22^{\circ} \pm 1$) it can be seen that:

$$[R^{\bullet}]_{max} \propto [ArNO_2]^{\frac{1}{2}} . [RNHOH]^{\frac{1}{2}} . [OH^-]^{\frac{1}{2}}$$

In addition Tables 4.1, 4.2 and 4.3 show that the initial rate of the reaction, determined graphically, varies as the first power of the free alkali concentration over the range 1.25×10^{-2} M to 1.5M, the first power of the hydroxylamine derivative over the range 0.25×10^{-2}M to 4×10^{-2}M, and the first power of the aromatic nitro compound

Fig. 4.2

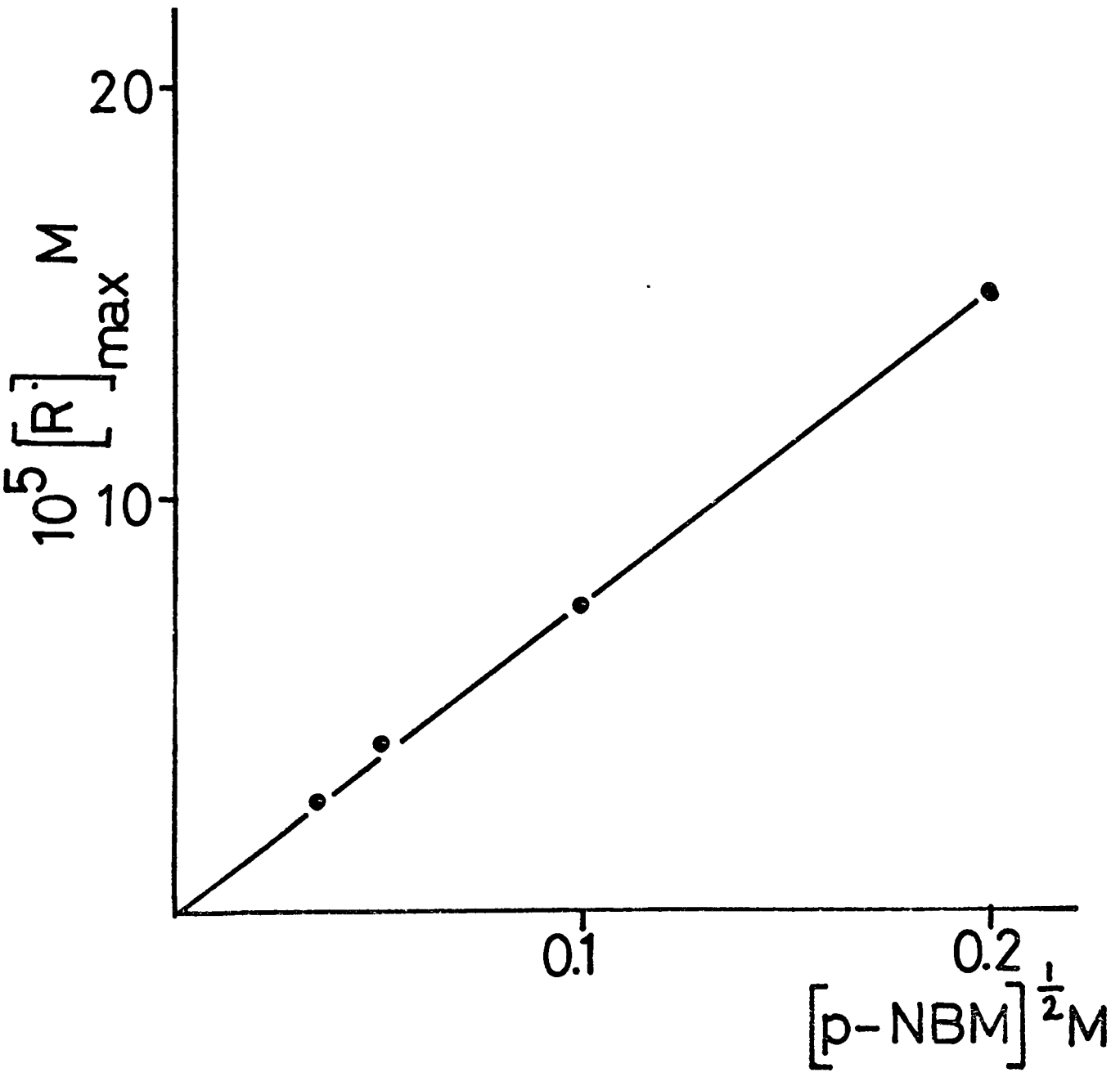
Relation between the maximum concentration of the para-nitrobenzoate radical-dianion and the square root of the initial concentration of para-nitrobenzoic acid.



▲ [PhNHOH] = .01M: [NaOH] = .50M
o [MeNHOH] = .01M: [NaOH] = .25M
× [$PhCH_2NHOH$] = .01M: [NaOH] = .50M

Fig.4.3

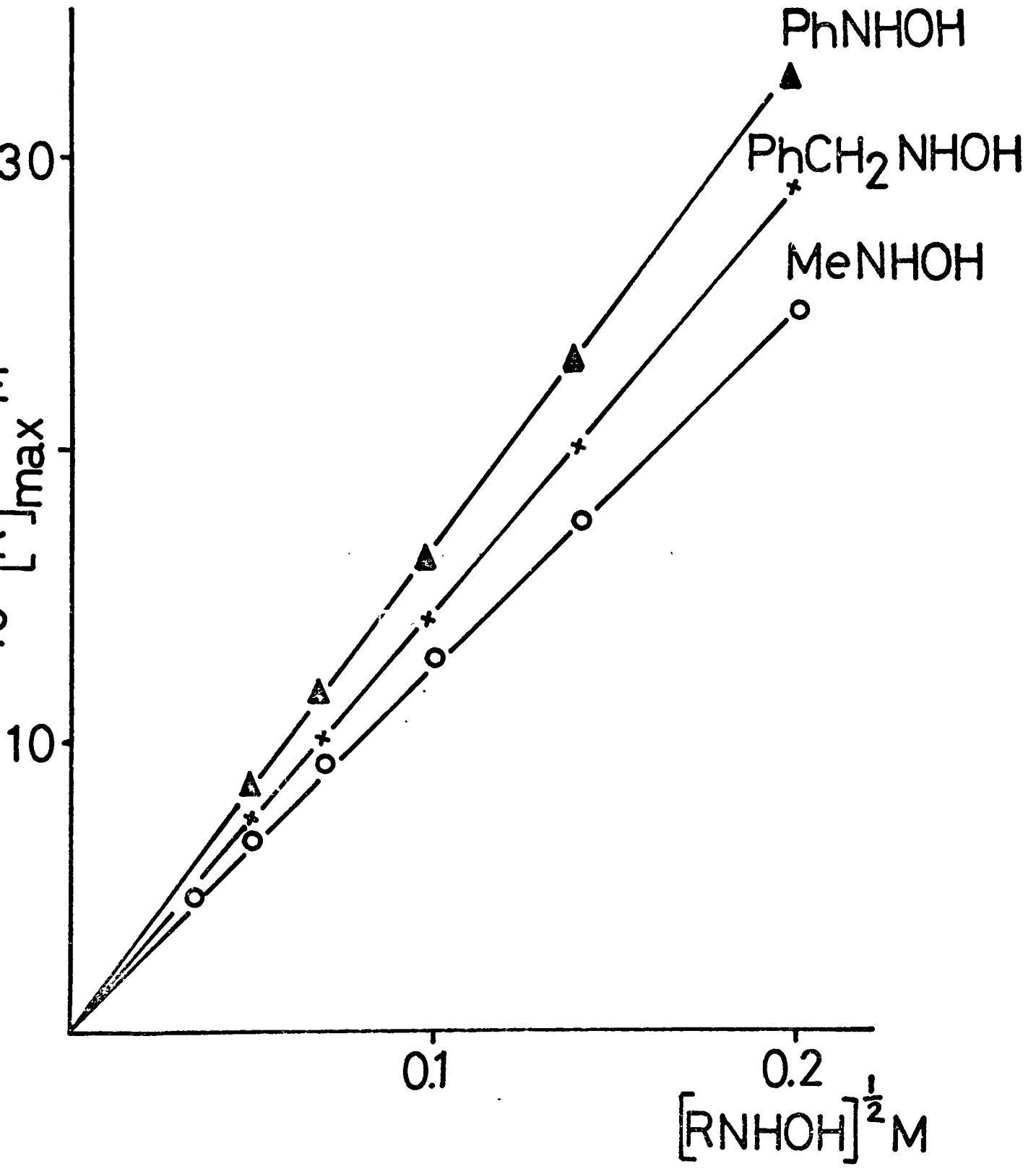
Relation between the maximum concentration of the para-nitrobenzamide radical-anion and the square root of the initial concentration of para-nitrobenzamide.



• [MeNHOH]= .01M : [NaOH]= .25M

Fig. 4.4

Relation between the maximum concentration of the para-nitrobenzoate radical-dianion and the square root of the initial concentration of hydroxylamine derivative.



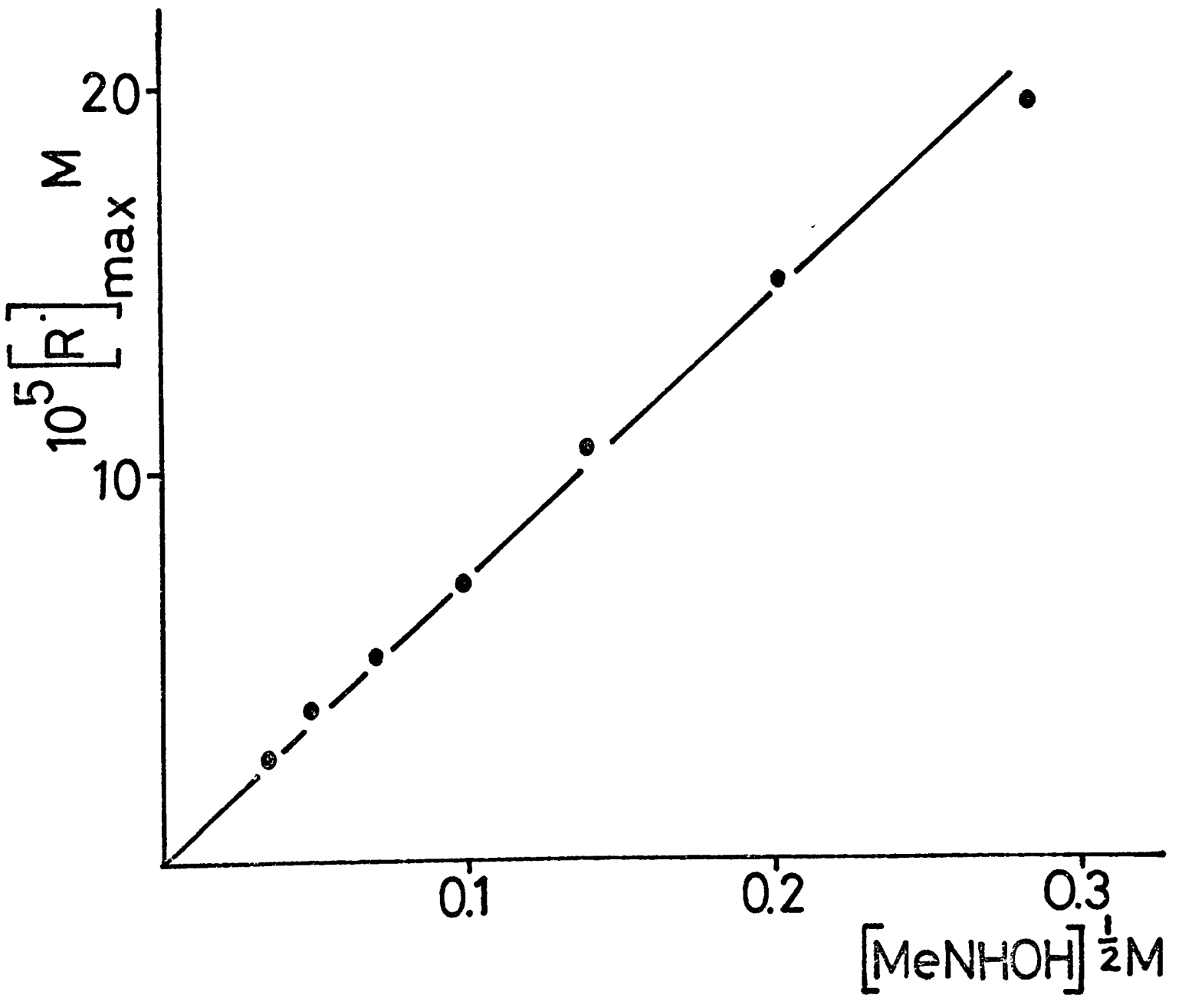
▲ [p-NBA]=.01M : [NaOH] =.50M

○ [p-NBA]=.01M : [NaOH]=.25M

× [p-NBA]=.01M: [NaOH]=.50M

Fig. 4.5

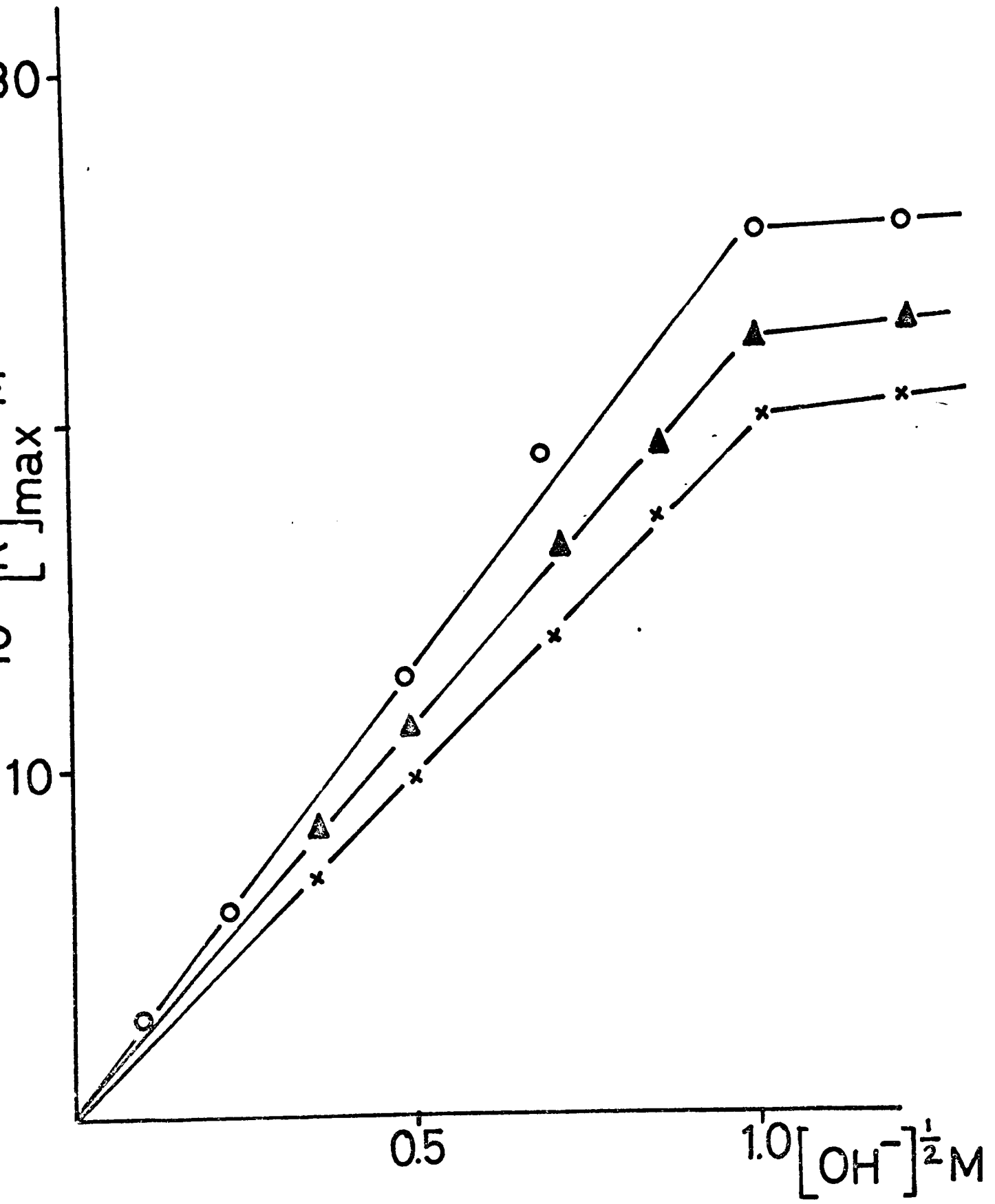
Relation between the maximum concentration of the para-nitrobenzamide radical-anion and the square root of the initial concentration of N-methylhydroxylamine.



•[p-NBM]=.01M : [NaOH]=.25M

Fig. 4.6

Relation between the maximum concentration of the para-nitrobenzoate radical-dianion and the square root of the free hydroxyl ion concentration.



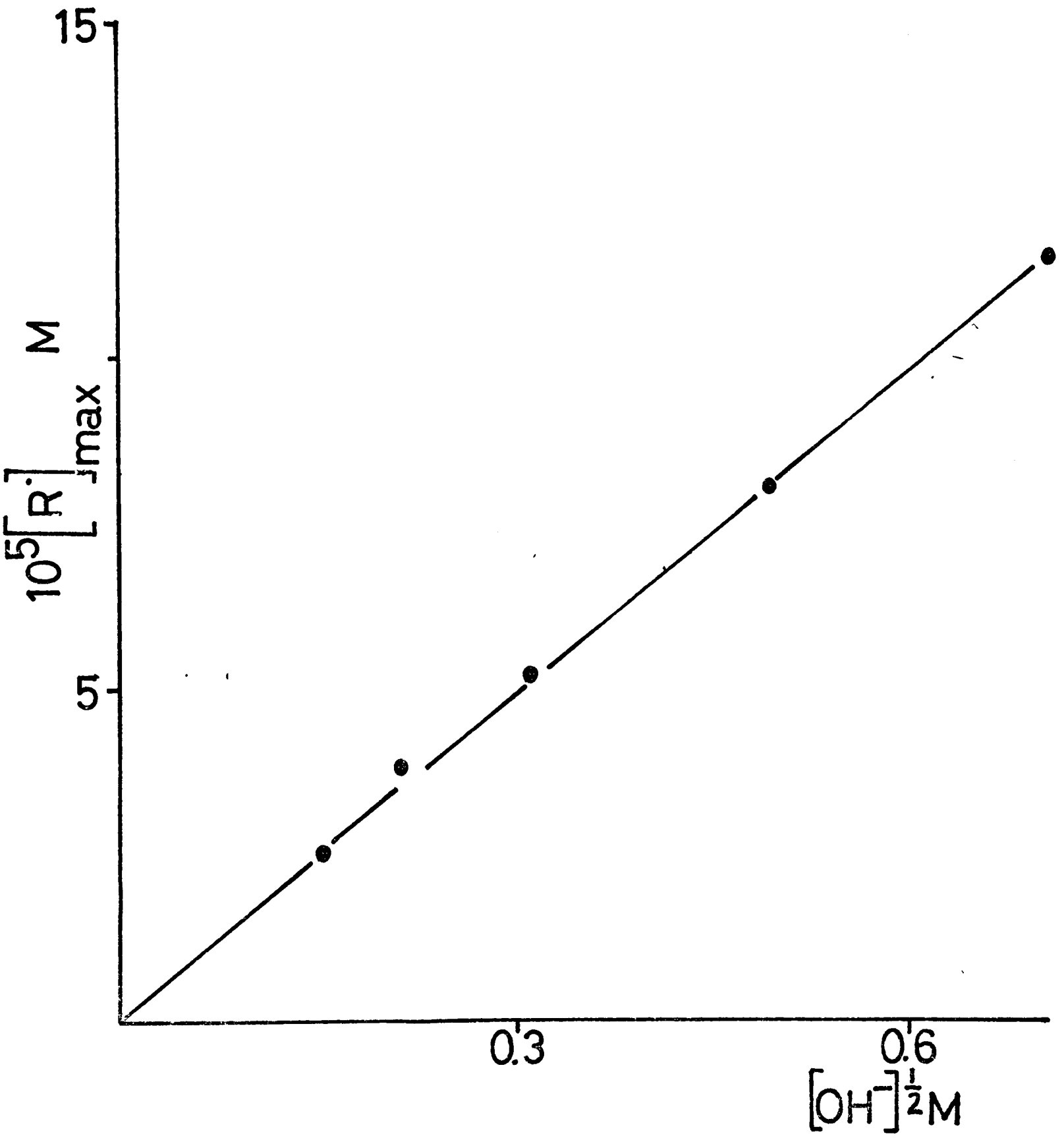
▲ [p-NBA] = .01M : [PhNHOH] = .01M

o [p-NBA] = .01M : [MeNHOH] = .01M

× [p-NBA] = .01M : [$PhCH_2NHOH$] = .01M

Fig. 4.7

Relation between the maximum concentration of the para-nitrobenzamide radical-anion and the square root of the free hydroxyl ion concentration.



• [p-NBM] = .01M : [MeNHOH] = .01M

Table 4.1.

Initial rates of formation of the p-nitrobenzoate radical-dianion in the reaction of p-nitrobenzoic acid with N-methylhydroxylamine.

a) [MeNHOH] = 10^{-2}M

10^2[NaOH]M	$10^5 \times dR^\cdot/dt \,/\, [NaOH]$ sec^{-1}.
5.0	6.4
10.0	6.5
25.0	6.0
50.0	5.8
100.0	6.0
150.0	6.2

b) [MeNHOH] = 10^{-2}M

[NaOH] = 0.25M

10^3 [p-NBA]M	$10^3 \times dR^\cdot/dt \,/\, [p\text{-NBA}]$ sec.$^{-1}$
2.5	2.0
5.0	1.9
10.0	1.5
20.0	1.8
40.0	2.0

c) [p-NBA] = 10^{-2}M

[NaOH] = 0.25M

10^3 [MeNHOH]M	$10^3 \times dR^\cdot/dt \,/\, [MeNHOH]$ sec.$^{-1}$
2.5	1.9
5.0	1.9
10.0	1.5
20.0	1.8
40.0	2.0

Table 4.2

Initial rates of formation of the p-nitrobenzoate radical-dianion in the reaction of p-nitrobenzoic acid with N-benzylhydroxylamine.

a) $[PhCH_2NHOH] = 10^{-2}M$

$10^2[NaOH]M$	$10^6 \times dR^\bullet/dt \,/\, [NaOH]^{sec.^{-1}}$
12.5	9.6
25.0	8.9
50.0	9.7
75.0	9.7
100.0	10.2
150.0	9.7

b) $[PhCH_2NHOH] = 10^{-2}M$ $[NaOH] = 0.5M$

$10^3[p\text{-}NBA]M$	$10^4 \times dR^\bullet/dt \,/\, [p\text{-}NBA]^{sec.^{-1}}$
2.5	4.8
5.0	5.2
10.0	4.9
20.0	3.8
40.0	4.5

c) $[p\text{-}NBA] = 10^{-2}M$ $[NaOH] = 0.5M$

$10^3[PhCH_2NHOH]M$	$10^4 \times dR^\bullet/dt \,/\, [PhCH_2NHOH]^{sec.^{-1}}$
2.5	4.9
5.0	5.3
10.0	4.9
20.0	4.6
40.0	4.5

Table 4.3

Initial rates of formation of the p-nitrobenzamide radical-anion in the reaction of p-nitrobenzamide with N-methylhydroxylamine.

a) $[MeNHOH] = 10^{-2}M$

$10^2\ [NaOH]M$	$10^5 \times dR^{\cdot}/dt \,/\, [NaOH]\ sec.^{-1}$
2.5	4.2
5.0	4.2
10.0	4.3
25.0	4.1
50.0	4.2

b) $[MeNHOH] = 10^{-2}M$ $[NaOH] = 0.25M$

$10^3\ [p\text{-}NBM]M$	$10^3 \times dR^{\cdot}/dt \,/\, [p\text{-}NBM]\ sec^{-1}$
1.25	0.9
2.5	1.1
5.0	1.2
10.0	1.0
20.0	1.0

c) $[p\text{-}NBM] = 10^{-2}M$ $[NaOH] = 0.25M$

$10^3[MeNHOH]M$	$10^3 \times dR^{\cdot}/dt \,/\, [MeNHOH]\ sec.^{-1}$
1.25	1.0
2.5	1.3
5.0	1.1
10.0	1.0
50.0	1.2

over the range 0.25×10^{-2}M to 4×10^{-2}M

Hence the following expression arises:

Initial rate of reaction $\propto [ArNO_2].[RNHOH].[OH^-]$.

From these results it would follow that the nitro radical-anion is formed by a slow bimolecular reaction between the aromatic nitro compound and the anion of the hydroxylamine derivative (2), but decays by a much faster reaction (3).

$$RNHOH + OH^- \overset{K}{\rightleftharpoons} RNHO^- + H_2O \qquad (1)$$

$$RNHO^- + ArNO_2 \xrightarrow{k_1} RNHO^{\bullet} + ArNO_2^{\bullet -} \qquad (2)$$

$$2ArNO_2^{\bullet -} \xrightarrow{k_2} \text{products} \qquad (3)$$

$$2RNHO^{\bullet} \xrightarrow{\text{fast}} \text{products} \qquad (4)$$

Using this scheme, an expression may be derived for the maximum radical concentration, $[R^{\bullet}]_{max}$.

$k_2 >> Kk_1$ and K is small, then:

$$K = \frac{[RNHO^-]}{[RNHOH]\,[OH^-]} \qquad (5)$$

$$\frac{d[ArNO_2^{\bullet -}]}{dt} = k_1 [ArNO_2]_t [RNHO^-]_t - k_2 [ArNO_2^{\bullet -}]_t^2 \qquad (6)$$

- the subscript t denotes concentrations after time t.

Substituting (5) into (6):

$$\frac{d[ArNO_2^{\bullet -}]}{dt} = Kk_1 [ArNO_2]_t [RNHOH]_t [OH^-]_t - k_2 [ArNO_2^{\bullet -}]_t^2 \qquad (7)$$

For the stationary state reached at the radical maximum:

$$\frac{d[ArNO_2^{\bullet -}]}{dt} = 0$$

and $$[ArNO_2^{\bullet -}]_t = [R^\bullet]_{max.}$$

Therefore

$$Kk_1 [ArNO_2]_t [OH^-]_t [RNHOH]_t = k_2 [R^\bullet]^2_{max.}$$

and $$[R^\bullet]_{max} = \left(\frac{Kk_1}{k_2} [ArNO_2]_t [OH^-]_t [RNHOH]_t \right)^{\frac{1}{2}}$$

In the stationary state the concentrations of reactants are nearly equal to their initial concentrations, hence:

$$[R^\bullet]_{max} = \left(\frac{Kk_1}{k_2} [ArNO_2]_o [OH^-]_o [RNHOH]_o \right)^{\frac{1}{2}} \qquad (8)$$

-where the subscript o denotes initial concentrations of reactants. The observed dependences of the maximum radical concentrations that have already been described are thus in accordance with the proposed scheme and the kinetics that can be deduced from it.

During the radical build up, if concentrations of reactants are regarded as being constant at their initial values, then the following expression may be derived, from which the value of k_2 may be evaluated.

$$\frac{d[ArNO_2^{\bullet -}]}{dt} = Kk_1[ArNO_2]_o[RNHOH]_o[OH^-]_o - k_2[ArNO_2^{\bullet -}]^2 \qquad (7)$$

Let $[ArNO_2]_o = A$

$[RNHOH]_o = B$

$[OH^-]_o = C$

$[ArNO_2^{\bullet -}] = R$

$[ArNO_2^{\bullet -}]_t = R_t$

Then $$\frac{dR}{dt} = Kk_1ABC - k_2R^2$$

$$\frac{dR}{Kk_1ABC - k_2R^2} = dt.$$

$$\frac{dR}{Kk_1ABC - k_2R^2} = \frac{dR}{2(Kk_1ABC)^{\frac{1}{2}}} \left(\frac{1}{(Kk_1ABC)^{\frac{1}{2}} + k_2^{\frac{1}{2}}R} + \frac{1}{(Kk_1ABC)^{\frac{1}{2}} k_2^{\frac{1}{2}}R} \right)$$

On integration between the limits t = 0 and t = t:

$$\frac{1}{2(Kk_1ABC)^{\frac{1}{2}}} \left(\frac{1}{k_2^{\frac{1}{2}}} \ln\left\{(Kk_1ABC)^{\frac{1}{2}} + K_2^{\frac{1}{2}}R_t\right\} - \frac{1}{K_2^{\frac{1}{2}}} \ln \left\{(Kk_1ABC)^{\frac{1}{2}} - k_2^{\frac{1}{2}}R_t\right\} \right)$$

$$= t$$

But $$[R^\bullet]_{max} = \left(\frac{Kk_1}{k_2} \cdot ABC \right)^{\frac{1}{2}} \qquad (8)$$

Therefore:

$$\frac{1}{2k_2[R^\bullet]_{max}} \ln \left(\frac{[R^\bullet]_{max} + R_t}{[R^\bullet]_{max} - R_t} \right) = t$$

$$\ln\left(\frac{[R^\bullet]_{max} + R_t}{[R^\bullet]_{max} - R_t}\right) = 2k_2t[R^\bullet]_{max} \qquad (9)$$

-where R_t is the radical concentration at time t.

Hence from a plot of t against $\ln \left(\frac{[R^\bullet]_{max} + R_t}{[R^\bullet]_{max} - R_t} \right) \Big/ [R^\bullet]_{max}$

k_2 may be evaluated.

Fig.4.8 shows a plot of equation (9) for the reaction between N-methylhydroxylamine and p-nitrobenzoic acid over a wide range of concentrations of both alkali and of the organic reactants. It confirms that the nitro radical-anion disappears bimolecularly (equation (3)) and gives:

$$k_2 = 6.5 \times 10^2 \quad \text{l.mol.}^{-1} \text{ sec.}^{-1}$$

A similar plot for the reaction between p-nitrobenzoic acid and N-benzylhydroxylamine is shown in Fig. 4.9. The concentration range of alkali and of organic reactants is not as great as in Fig.4.8.

$$k_2 = 8 \pm 2 \times 10^2 \quad \text{l.mol.}^{-1}\text{. sec.}^{-1}$$

The much slower reaction between p-nitrobenzoic acid and N-benzhydrylhydroxylamine gives:

$$k_2 = 7 \pm 2 \times 10^2 \text{ l.mol.}^{-1} \text{ sec.}^{-1}$$

This is shown in Fig.4.10 over the same concentration range of alkali and organic reactants as in Fig.4.9.

The constancy of k_2 in these reactions confirmsthat k_2 in each case is a measure of the rate of the same reaction, i.e., reaction (3),

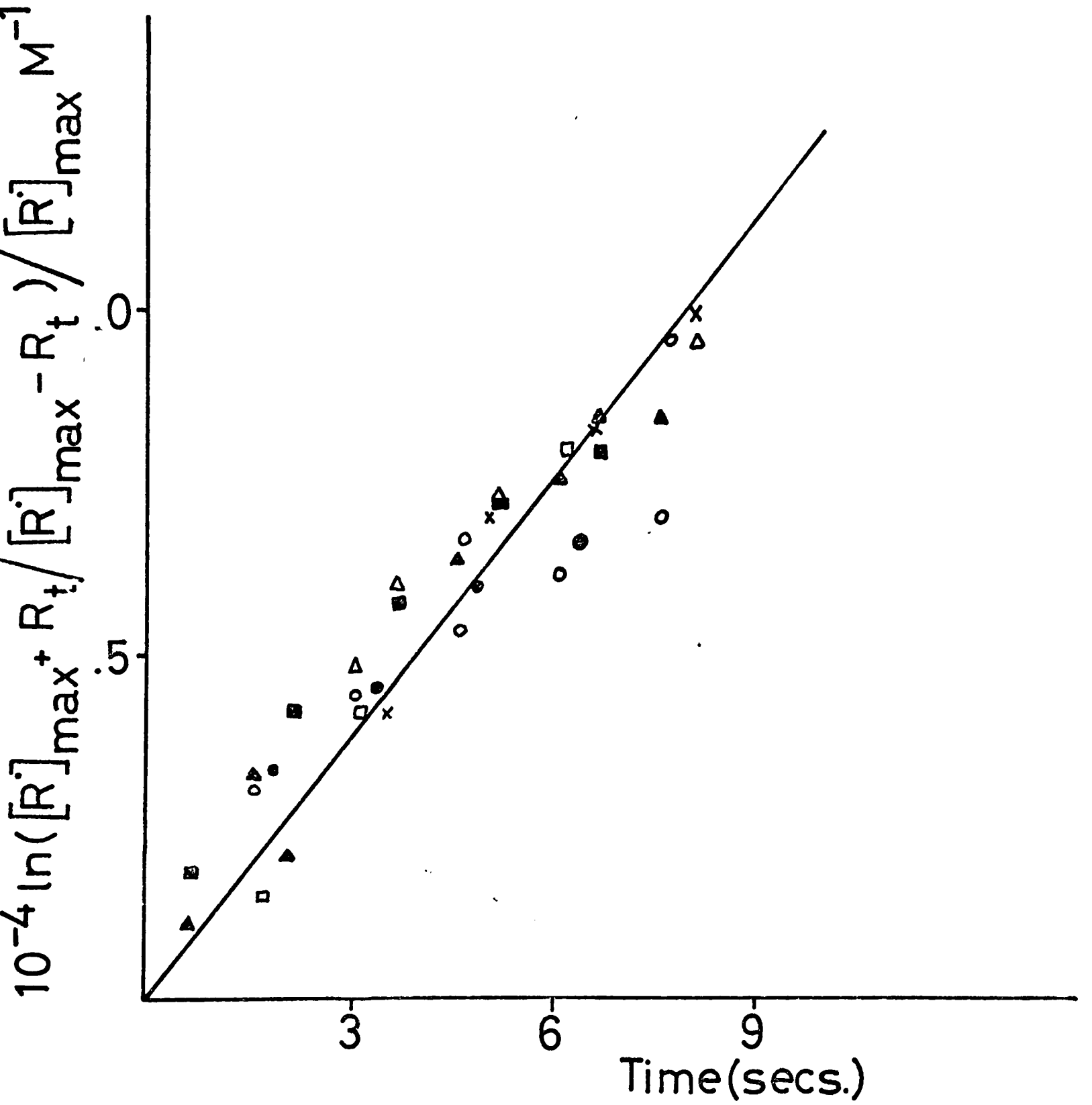
$$2ArNO_2^{\bullet -} \longrightarrow \text{products} \qquad (3)$$

and depends only upon the nitro compound under investigation and not upon the hydroxylamine.

Fig. 4.8

Determination of k_2 for the reaction between N-methylhydroxylamine and para-nitrobenzoic acid in .25M NaOH.

$$k_2 = 6.5 \times 10^2 \text{ l.mol.}^{-1}\text{. sec.}^{-1}$$



[MeNHOH] = .01M

[p-NBA] = •.005M, °.01M, ▲.02M, △.04M

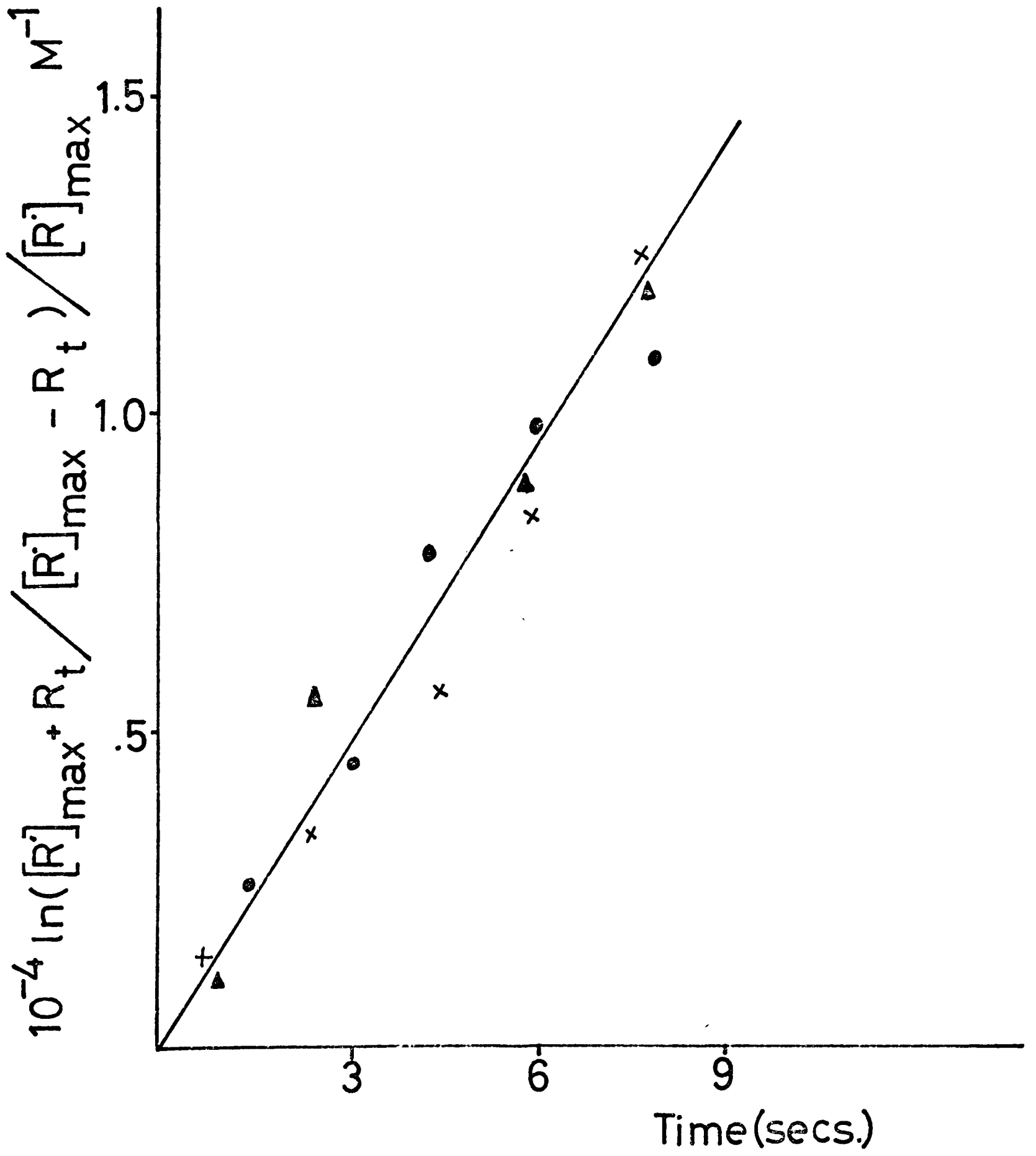
[p-NBA] = .01M

MeNHOH = ▣.005M, °.01M, □.02M, ×.04M

Fig. 4.9

Determination of k_2 for the reaction between N-benzylhydroxylamine and para-nitrobenzoic acid in .25M NaOH.

$$k_2 = 8 \pm 2 \times 10^2 \text{ l. mol.}^{-1}\text{. sec.}^{-1}$$



× $[PhCH_2NHOH] = .01M : [p\text{-}NBA] = .01M$

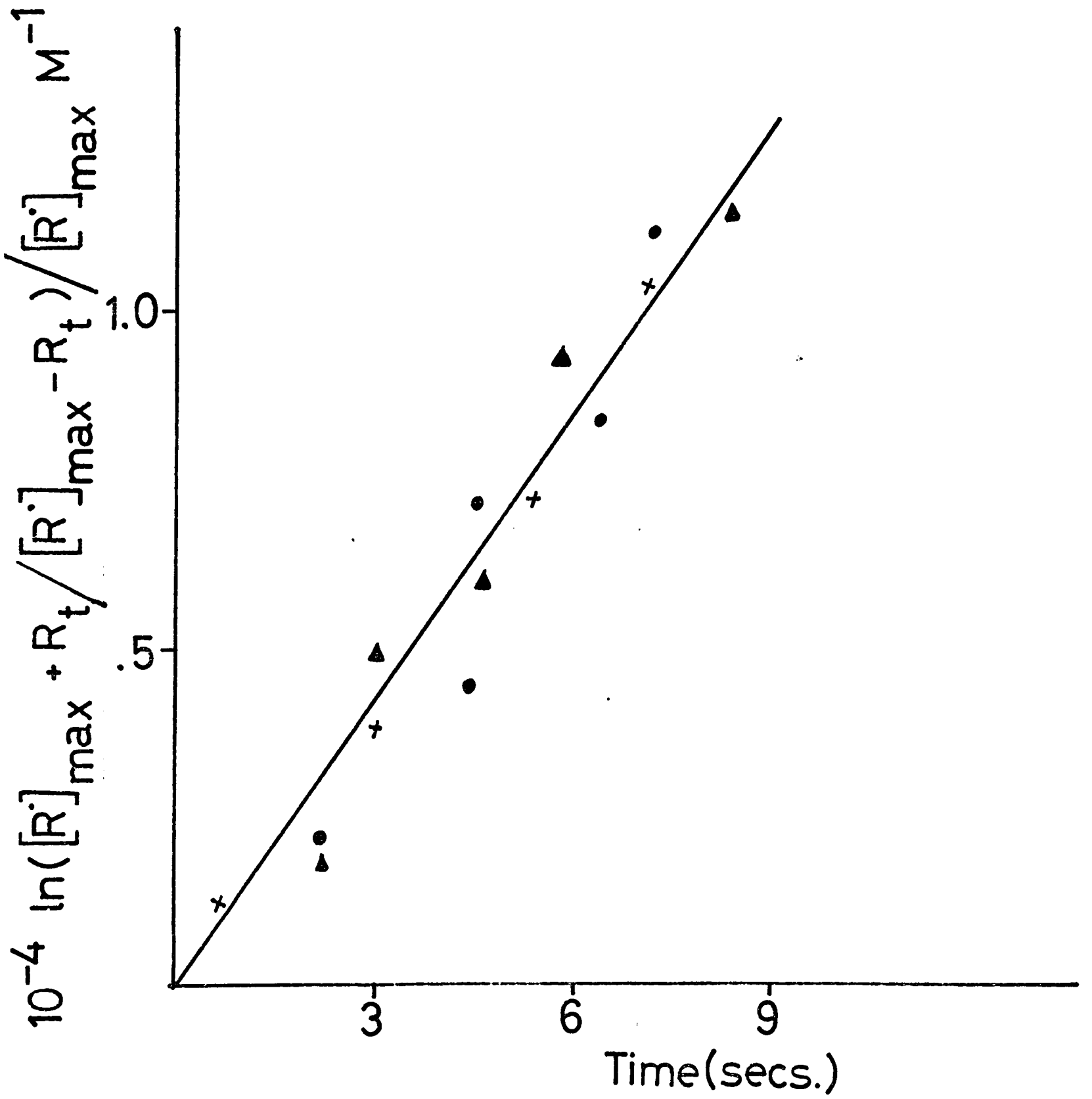
• $[PhCH_2NHOH] = .01M : [p\text{-}NBA] = .02M$

▲ $[PhCH_2NHOH] = .02M : [p\text{-}NBA] = .01M$

Fig. 4.10

Determination of k_2 for the reaction between N-benzhydrylhydroxylamine and para-nitrobenzoic acid in .25M NaOH.

$$k_2 = 7 \pm 2 \times 10^2 \text{ l.mol.}^{-1}\text{. sec.}^{-1}$$



x $[Ph_2CHNHOH] = .01M : [p-NBA] = .01M$

• $[Ph_2CHNHOH] = .01M : [p-NBA] = .02M$

▲ $[Ph_2CHNHOH] = .01M : [p-NBA] = .04M$

Table 4.4 summarizes data evaluated for the rate constants in the reactions under investigation. It can be seen that rates calculated from $[R^{\bullet}]_{max}$ and k_2 using equation (8), according reasonably with the very approximate graphical measurements of initial rates.
It should be noted that these kinetic equations would also hold for a more complicated reaction sequence involving additional (radical) + (molecule) reactions provided:

(a) that the final radical destruction occurs by (radical) + (radical) interaction,

and

(b) that the radical producing reactions are all of first order with respect to the initial reactants.

Table 4.4.

Rate constants -

Reaction	$10^5 Kk_1/k_2$ l.mol.$^{-1}$	$10^2 Kk_1$ l.^{2} mol.$^{-2}$ sec.$^{-1}$ From $[R^\cdot]_{max}$ (a)	$10^2 Kk_1$ l.^{2} mol.$^{-2}$ sec.$^{-1}$ from initial rates
p-nitrobenzoic acid + MeNHOH	3.9 ± 0.2	2.6 ± 0.1	3.7 ± 0.5
p-nitrobenzoic acid + $PhCH_2NHOH$	2.0 ± 0.1	1.3 ± 0.1	0.7 ± 0.2
p-nitrobenzoic acid + $Ph_2CHNHOH$	0.3	0.2	-
p-nitrobenzoic acid + PhNHOH	3.25	2.1	-

a) $k_2 = 6.5 \times 10^2$ l.mol.$^{-1}$ sec.$^{-1}$ (see text)

2) Discussion

Two further points arise from the results described in the previous section.

Firstly, the constancy of k_2 shows that the disappearance of the radical-anion, $(ArNO_2^{\bullet})^-$, is not due to any reaction between it and radicals $RNHO^{\bullet}$ or $(RNO^{\bullet})^-$.

Secondly, because radicals $RNHO^{\bullet}$ or $(RNO^{\bullet})^-$ are not observable, except with phenylhydroxylamine, reaction (4) must be much faster than reaction (3). Russell and Geels[118] quote 1.4×10^2 $l.mol.^{-1}.sec^{-1}$ for the bimolecular rate of destruction of the phenylnitroxide radical-anion, $(PhNO^{\bullet})^-$. This is of the same order as the calculated rate of destruction of the p-nitrobenzoate radical di-anion, and both radicals can be observed simultaneously in the reaction between p-nitrobenzoic acid and N-phenyl hydroxylamine. The other hydroxylamine derivatives employed ($MeNHOH$, $PhCH_2NHOH$, $Ph_2CHNHOH$) give rise to radical-anions or nitroxide radicals that are much less stable than $(PhNO^{\bullet})^-$ and these have not been observed during the current work.

The value of k_2, for the bimolecular disappearance of the p-nitrobenzoate radical di-anion, that has been obtained by the method described in the previous section, is much higher than the values of the rate constants for the disproportionation of the nitrobenzene radical-anion obtained by Kastening[103,105-7], Farnia[104], Koopman[108] and Kolb[109-111].

Two explanations are put forward in an attempt to explain this discrepancy.

Kolb and Koopman[111] have shown that oxygen has a positive catalytic effect on the disproportionation of aromatic nitro radical-anions. They describe this effect by the following expression:

$$k_2 = k_o^1 + k_3 c^1$$

c^1 = oxygen concentration

For the nitrobenzene radical-anion $k_3 = 7.5 \times 10^7$ l.^{2} mol.$^{-2}$ sec.$^{-1}$. Thus the presence of oxygen in a system would increase the rate of decay of the aromatic nitro radical-anion drastically.

It has been shown that vigorous freeze-pump-thaw techniques of deoxygenating solutions still result in residual oxygen of a concentration in the order of 10^{-7} -10^{-8}M. In the current work removal of oxygen was effected by nitrogen blowing solutions only. Although this was undertaken for a considerable time and solutions were transferred to the e.s.r. cell without further contact with the atmosphere, the concentration of oxygen in the solutions may have been as high as 10^{-5}M. According to the equation of Kolb and Koopman this could account for the observed discrepancy.

Other factors e.g. alkali concentration, described by Farnia[104] or the presence of ethanol, described by Kolb[110], may serve to retard the disproportionation reaction. Hence a balance of a number of factors may account for the current result.

The second explanation that is offered, in an attempt to reconcile the values of k_2 obtained in this thesis with those quoted in literature,

involves a closer inspection of the reactions for which the rate constant, k_2, is being measured.

It may be that the rate constant:

$$k_2 = 6.5 \times 10^2 \text{ l.mol.}^{-1} \text{ sec.}^{-1}$$

is not measuring the rate of the disproportionation reaction:

$$2ArNO_2^{\cdot -} \longrightarrow ArNO_2 + (ArNO_2)^{2-}$$

However it has been shown that k_2 is certainly measuring a bimolecular disappearance of the aromatic nitro radical-anion in the system. This alone is sufficient to justify the kinetic arguments put forward in the previous section.

But consider a system:

$$R + R \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} X + Y \qquad (10)$$

$$Y + Z \xrightarrow{k_3} \text{products} \qquad (11)$$

Then:

$$\frac{d[R]}{dt} = -k_2[R]^2 + k_{-2}[X][Y]$$

$$\frac{d[Y]}{dt} = k_2[R]^2 - k_{-2}[X][Y] - k_3[Y][Z]$$

If $\frac{d[Y]}{dt} = 0$

$$[Y] = \frac{k_2[R]^2}{k_{-2}[X] + k_3[Z]}$$

Considering two limits:

(a) If $k_3[Z] >> k_{-2}[X]$

$$\frac{d[R]}{dt} = -k_2[R]^2$$

and

(b) $k_3[Z] << k_{-2}[X]$

$$\frac{d[R]}{dt} = -k_2[R]^2 \cdot \frac{k_3[Z]}{k_{-2}[X]}$$

Thus situation (b) represents a much slower apparent decay of R.

Now if $R = ArNO_2^{\bullet-}$

$X = ArNO_2$

$Y = (ArNO_2)^{2-}$

In the systems investigated in the literature[103-111]

$$Z = H_2O$$

whereas in the system described in this thesis

$$Z = \text{hydroxylamine derivative or } H_2O.$$

Thus reaction (11) may be:-

$$2(ArNO_2)^{2-} + H_2O \xrightarrow{k_3} ArNO_2 + ArNO + 2OH^- \qquad (11a)$$

or

$$2(ArNO_2)^{2-} + \begin{pmatrix} RNHOH \\ Ar'NHOH \end{pmatrix} \xrightarrow{k_3} ArNO_2 + ArNO + \begin{pmatrix} RNHO^- \\ Ar'NHO^- \end{pmatrix} + OH^- \qquad (11b)$$

If reaction (11b) is more rapid than (11a) then $k_3[Z]$ may be large and $k_3[Z] >> k_{-2}[X]$ i.e. limit (a) could arise. Hence the measured rate of decay of the radical-anion would be higher than in the system in which the hydroxylamine derivative is not present.

This reasoning may imply that in the system which contains a hydroxylamine derivative, the true value of k_2 is measured, as the removal of $(ArNO_2)^{2-}$ could be so rapid as to make the back reaction (k_{-2}) in equation (10) negligible. This equilibrium has been shown to exist by several workers[88,119]. But if the removal of $(ArNO_2)^{2-}$ is not rapid, the back reaction becomes important, and the rate constant for the disproportionation of the radical-anion that is measured, approximates to:

$$k_2 \cdot \frac{k_3[Z]}{k_{-2}[X] + k_3[Z]}$$

and this is smaller than k_2 as $k_3[Z] << k_{-2}[X]$.

This may be the case when $Z = H_2O$ only.

Now in the above derivations, the setting of two limiting cases, (a) and (b), will impinge upon the validity of the steady state approximation $\frac{d[Y]}{dt} = 0$, although the general balance in the system can be described in this way. Hence the discrepancy between values of k_2 in this thesis and those in the literature[103-111] may be due to the measurement of rate constants that do not strictly refer to identical reactions.

However the value of obtaining measurements of k_2 in this work has lain chiefly in the justification of the proposed reaction scheme, equations (1) - (4). Further evidence arises from the nature of the reaction products, which is described and discussed in the following chapter.

B. Variations in initial rates of electron transfer

There is a considerable variation in the rate at which hydroxylamine and its related compounds will transfer an electron to a range of aromatic mono nitro compounds, under the conditions described in this thesis. This rate depends upon the nature of both the organic reactants, and these will be considered separately.

1) Variations depending upon hydroxylamine derivative

With reference to Table 4.4, it can be seen that the initial rates of the electron transfer reaction to p-nitrobenzoic acid are in the sequence:

$$MeNHOH > PhNHOH > PhCH_2NHOH > Ph_2CHNHOH.$$

As the reaction depends upon the availability of an electron for transfer, the more strongly electron attracting the substituent on the nitrogen atom is, the slower the reaction will be. Of the various substituents under consideration, the methyl group attracts electrons least strongly and hence the rate of initial electron transfer is greatest in reactions involving N-methylhydroxylamine. As will be seen in the following section hydroxylamine, itself, gives rise to a much slower reaction than any of the above mentioned related compounds. Taft polar substituent constants, σ^*, would be expected to correlate, at least qualitatively, with this experimentally obtained sequence

The Taft, σ^*, constants vary:[120]

$$CH_3- < PhCH_2- < Ph_2CH- < H- ,$$

representing an increase in electron attracting power across the sequence. This does correspond with the sequence obtained from initial rate measurements.

The phenyl, Ph– , group is not included in the sequence referring to Taft, σ^* , constants, as in N-phenylhydroxylamine the nitrogen atom of the functional group is attached directly to the aromatic ring. It is thus an aromatic hydroxylamine, and a direct comparison with the other hydroxylamines under investigation, which may be regarded as aliphatic in this context, would not be valid.

2) Variation depending upon the aromatic nitro compound.

When different aromatic nitro compounds are investigated the rates of formation and presumably of disproportionation of their radical-anions vary widely.

By inspection of the curves for the build-up and decay of e.s.r. spectra obtained with N-methylhydroxylamine in 50% aqueous ethanol, containing 0.25M sodium hydroxide, a reactivity sequence for $pX.C_6H_4.NO_2$ has been drawn up. This was found to be:

$$CN > Br > Cl > CHO > CO_2^- > CONH_2 > F > H > CH_3 > OCH_3$$

The Kk_1 values at this alkalinity ranged from 10^{-1} $l^2.mol.^{-2}$ $sec.^{-1}$, for p-nitrobenzonitrile to 10^{-4} $l^2.mol.^{-2}$ $sec.^{-1}$ for p-nitroanisole. As previously stated, with p-nitrophenol no electron transfer occurred. This sequence is that of the Hammett, σ , constants for the para substituents in the aromatic ring.

Evidently resonance stabilization of the radical-anion by electron withdrawal towards the benzene ring and the electrophilic group X facilitates reaction (2), in which an electron is transferred from an anion of a hydroxylamine to the nitro compound. The correlation between initial rates and Hammett, σ , constants has been qualitative rather than quantitative owing to difficulties in measuring some of the slower reactions with any great accuracy, by the stopped-flow technique. However applying the Hammett equation over the range of compounds studied gives:

$$\log \frac{k_1}{k_2} = \rho (\sigma_1 - \sigma_2)$$

The initial rates vary from 10^{-1} to 10^{-4} l^2. mol.$^{-2}$ sec.$^{-1}$ approximately, and the σ values[121] from + 0.63 for p-nitrobenzonitrile to . - 0.27 for p-nitroanisole.

Hence:

$$\log 10^3 = \rho (+ 0.63 \quad + 0.27)$$

$$\underline{\rho = + 3.3}$$

This value agrees well with ρ values for similar electron transfer reactions. Gibian and Baumstark[98] obtained a value of + 3.6 for the electron transfer reaction of dihydroflavins to p-substituted nitrobenzenes. Russell et al[122] studied the substituent effects on the one electron transfer from fluorenide anion and from acetophenone enolate to substituted aromatics, and obtained ρ values of + 2.0 and + 2.7 respectively.

C. Reactions involving hydroxylamine.

Because it was possible that the effects of the evolution of gas in the e.s.r. cell would mask kinetic features of the reaction, the mechanism of the initial stages of the reaction was established avoiding the use of hydroxylamine itself. However having justified the proposed mechanism - equations (1) - (4) - it has been possible to show that data obtained using hydroxylamine ~~is~~ are consistent with these proposals.

1) Results

Para-nitrobenzoic acid reacts much more slowly with hydroxylamine than with the mono substituted hydroxylamines already mentioned. Even using 0.1M hydroxylamine in 1.0M sodium hydroxide, the build-up of the p-nitrobenzoate radical-dianion (I) can be followed for several minutes, and $[R^{\bullet}]_{max}$ values are again in the order of 10^{-4} M. Figs. 4.11 and 4.12 show that $[R^{\bullet}]_{max}$ again varies proportionally to the square roots of the concentrations of the nitro compound, of hydroxylamine and of free hydroxyl ions. Consequently reactions (1) and (2) of the scheme proposed in section A of this chapter are also valid for the hydroxylamine reaction.

From data concerning $[R^{\bullet}]_{max}$, the approximate value of $\frac{Kk_1}{k_2}$ in 0.25M sodium hydroxide is calculated as 2.4×10^{-6}. l.mol.$^{-1}$. By using $k_2 = 6.5 \times 10^{2}$ l.mol.$^{-1}$ sec.$^{-1}$, it can be seen that Kk_1 is of the order of 1.6×10^{-3} l^{2}. mol.$^{-2}$. sec.$^{-1}$. This represents a slower initial electron transfer step than with any of the other hydroxylamines investigated.

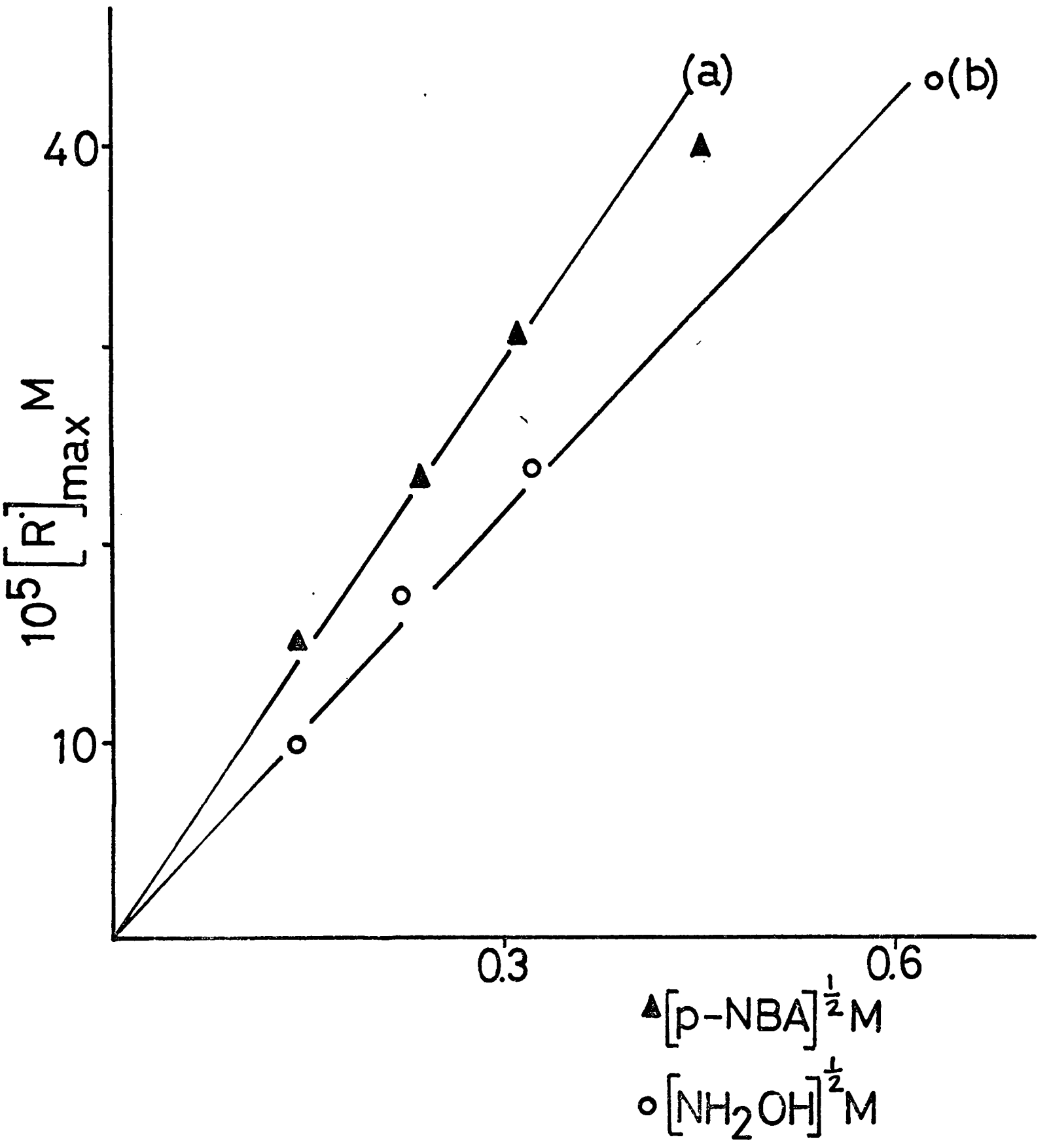
Fig. 4.11

Relation between the maximum concentration of the para-nitrobenzoate radical-dianion and the square root of the initial concentration of

a) para-nitrobenzoic acid

and

b) hydroxylamine.

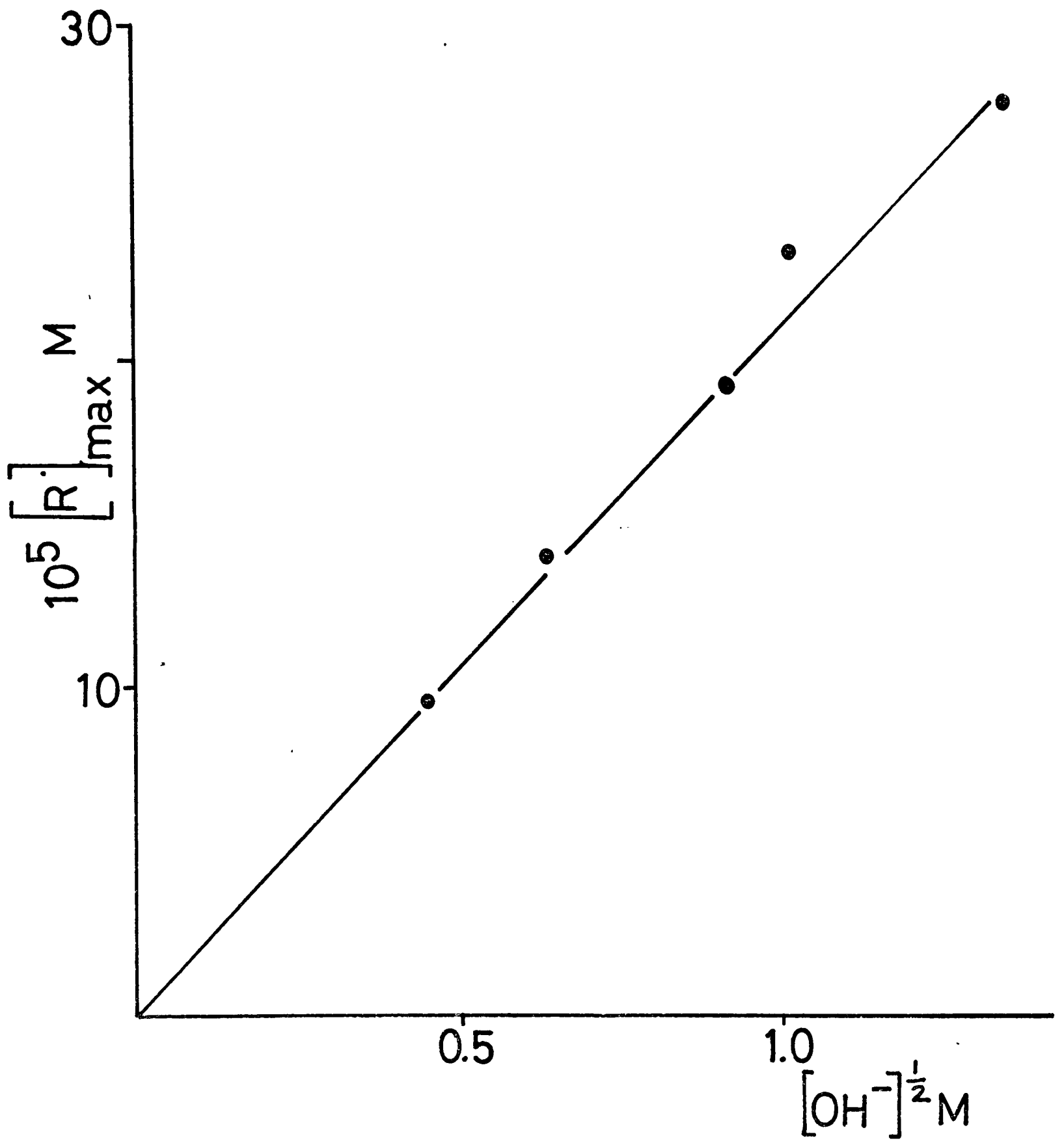


▲ [NH_2OH] = .10M : [NaOH] = 1.2M

o [p-NBA] = .05M : [NaOH] = 1.2M

Fig. 4.12

Relation between the maximum concentration of the para-nitrobenzoate radical-dianion and the square root of the free hydroxyl ion concentration.



• $[p\text{-NBA}] = .05M$: $[NH_2OH] = .10M$

2) Discussion.

Having established, by e.s.r. stopped-flow techniques, that reactions involving hydroxylamine were similar to those involving mono substituted hydroxylamines, no further quantitative experiments were carried out. However it is reported in the literature[123] that gasometric measurements have been carried out on this reaction. These measurements have established that in any one reaction the rate of gas evolution approximates to the first order decay of an intermediate:

$$V_t = V_\infty \quad (1 - e^{-kt}) \qquad (11)$$

When hydroxylamine is not in a large excess over the p-nitrobenzoice acid the reactions have the overall stoichiometry approximating to equation (12):

$$ArNO_2 + 4NH_2OH \longrightarrow ArN_3 + N_2 + 6H_2O \qquad (12)$$

A detailed discussion of the products of the reactions is given in the following chapter.

For example, a reaction of 2.73×10^{-4} moles of p-nitrobenzoic acid (an excess) with 5×10^{-4} moles of hydroxylamine eventually gives 2.8 ml. of gas. Using this value for V_∞ in equation (11) a plot of log $(V_\infty - V_t)$ against t enables first order reaction velocity constants to be evaluated. These are in the range $1.5 - 8.8 \times 10^{-4}$ sec.$^{-1}$. The plot also shows that with p-nitro-

benzoic acid in excess, the rate of gas evolution is approximately of the first order with respect to p-nitrobenzoic acid, and that with constant p-nitrobenzoic acid and hydroxylamine in excess, it does not begin to rise until:

$$[NH_2OH] > 3\ [p\text{-}NBA]$$

This accords with an overall reaction corresponding to equation (12), provided that one concludes that the gas evolved is nitrogen.
After the disproportionation of the nitro radical-anion, (13),

$$2(ArNO_2^{\cdot-}) + H_2O \longrightarrow ArNO_2 + ArNO + 2OH^- \qquad (13)$$

the resulting nitrosobenzene reacts first to give a diazotate[125,126] and then an azide[127,128].
The reaction sequence, equations (14) - (15), will account for the large consumption of hydroxylamine found:

$$ArNO + NH_2OH \longrightarrow ArN_2OH + H_2O \qquad (14)$$

$$ArN_2OH + NH_2OH \longrightarrow ArN_3 + 2H_2O \qquad (15)$$

The initial reactions, (1) and (2), and the disproportionation reaction (13) combine to give equation (16):

$$2ArNO_2 + 2NH_2OH \rightarrow ArNO + ArNO_2 + 2NH_2O^{\cdot} + H_2O \qquad (16).$$

From this it is rational to assume that the $NH_2O^{\bullet}$ radicals formed by reaction (2) dimerize to $(NH_2O)_2$, which then decomposes to nitrogen and water.

With regards to the rates of these reactions, it can be said that when hydroxylamine is available in excess both (14) and (15) are faster than (2). However since (14) has to complete with dimerisation and other reactions which aromatic nitroso compounds undergo in alkali, the overall reaction (12) is not quantitatively accurate.

CHAPTER 5

Product Studies

1. Introduction

In the preceeding chapter it was established that the initial reaction, in the absence of oxygen, between aromatic nitro compounds and hydroxylamine or N-alkyl and N-aryl substituted hydroxylamines, in alkaline solution is a one electron transfer followed more rapidly by disproportionation of the two radicals formed thereby.
This may be represented:

$$RNHOH + OH^- \rightleftharpoons RNHO^- + H_2O \qquad (1)$$

$$RNHO^- + ArNO_2 \rightarrow RNHO^{\bullet} + ArNO_2^{\bullet -} \qquad (2)$$

then

$$2RNHO^{\bullet} \rightarrow RNO + RNHOH \qquad (3)$$

and

$$2\ ArNO_2^{\bullet -} \rightleftharpoons ArNO_2 + (ArNO_2)^{2-} \qquad (4)$$

$$(ArNO_2)^{2-} + H^+ \rightarrow ArN(O^-)OH \qquad (5)$$

$$ArN(O^-)OH \rightarrow ArNO + OH^- \qquad (6)$$

Under the experimental conditions chosen reaction (3) is too rapid for the detection by e.s.r. of radicals $RNHO^{\bullet}$ or radical-anions $R\text{-}\dot{N}\text{-}O^{-}$, but reaction (4) has been followed kinetically, since alkali retards the breakdown (5) of the dianion $(ArNO_2)^{2-}$.

Hence the overall chemical change resulting from these reactions can be written as:

$$RNHOH + ArNO_2 \longrightarrow R.NO + Ar.NO + H_2O \qquad (7)$$

However neither aliphatic nor aromatic nitroso compounds have been detected as ultimate reaction products, as would be predicted from this equation.

This chapter describes the reaction products that have been detected and isolated, and attempts to explain their formation as a consequence of the reaction scheme outlined above.

2. Results

From previous chapters it would appear that neither N,N-dibenzyl hydroxylamine nor N-di-tert-butyl hydroxylamine reacts with nitrobenzene or para substituted mononitrobenzenes, in aqueous alkaline ethanol in the absence of oxygen.

This has been confirmed by attempted product studies on the reaction between N,N-dibenzyl hydroxylamine and nitrobenzene, when after one day 94% of the nitrobenzene and 96% of the N,-N-dibenzyl-hydroxylamine were recovered unchanged. The results of the other product studies are given in Tables 5.1 - 5.5. These results are discussed in the following section.

TABLE 5.1

The reaction of hydroxylamine with aromatic nitro compounds in aqueous alkaline ethanol in the absence of oxygen.

Nitro compound	Products isolated	
p-Nitrobenzoic acid	Unchanged p-nitrobenzoic acid	10%
	p-Nitrosobenzoic acid	30%
	p-Azido benzoic acid	56%
	Nitrogen	93%

TABLE 5.2.

The reaction of N-methyl hydroxylamine with aromatic nitrocompounds in aqueous alkaline ethanol in the absence of oxygen.

Nitro compound	Products isolated	
Nitrobenzene	Azoxybenzene	26%
	N-Methyl-N'-phenyl diazine N'-oxide	7%
	1,2 Diphenyl formazan	21%
p-Nitrobenzoic acid	pp'-Azoxydibenzoic acid	21%
	Traces of N-methyl-N'-p-carboxy-phenyl diazine N'-oxide detected by mass spectrometry $m/_e$ = 180	
	1,2 Di (p-carboxyphenyl) formazan detected by mass spectrometry $m/_e$ = 312 (impure)	

TABLE 5.3.

The reaction of N-phenylhydroxylamine with aromatic nitro compounds in aqueous alkaline ethanol in the absence of oxygen.

Nitro compound	Products isolated	
Nitrobenzene	Azoxybenzene	76%

TABLE 5.4.

The reaction of N-benzylhydroxylamine with aromatic nitro compounds in aqueous alkaline ethanol in the absence of oxygen.

Nitro compound	Products isolated	
Nitrobenzene	Unchanged N-benzylhydroxylamine	13%
	Azoxybenzene	33%
	Benzaldoxime	33%
	1,3,5 Triphenyl formazan	33%
p-Nitrotoluene	pp'-Azoxytoluene	33%
	Benzaldoxime	34%
	3-Phenyl, 1,4 di-p-tolyl-formazan	40%
p-Nitrobenzoic acid	A dark red solution containing a formazan.	
p-Nitrobenzamide	A dark red solution containing a formazan.	

TABLE 5.5.

The reaction of N-benzhydrylhydroxylamine with aromatic nitro compounds in aqueous alkaline ethanol in the absence of oxygen.

Nitro compound	Products isolated	
Nitrobenzene	Azoxybenzene	76%
	Benzophenone oxime	81%

3. Discussion of results

Since nitroso compounds in general are unstable in alkali it is not surprising that those predicted in equation (7) are not detected as ultimate reaction products.

As the type of ultimate reaction product varies according to the reagents employed, each hydroxylamine compound investigated will be considered separately.

In most cases the reaction with nitrobenzene itself has been studied in detail.

(a) Hydroxylamine

From hydroxylamine the predicted nitroso compound would be H.NO. However this is unknown. It immediately dimerizes to hyponitrous acid, which rapidly decomposes to nitrous oxide and water:

$$2HNO \longrightarrow (HNO)_2 \longrightarrow N_2O + H_2O \qquad (8)$$

Alternatively the radical $H_2NO^{\bullet}$ produced in reaction (2) could dimerize and then decompose to nitrogen and water:

$$2H_2NO^{\bullet} \longrightarrow (H_2NO)_2 \longrightarrow 2H_2O + N_2 \qquad (9)$$

This alternative route resulting in the production of nitrogen was discussed in the previous chapter. Hence dimerisation of the radical, produced from hydroxylamine after electron transfer, according to equation (9), rather than disproportion as proposed in equation (3), occurs.

When hydroxylamine reacts with an aromatic nitro compound the nitroso compound, corresponding to the latter is not detected either.

Feigl, Anger and Frenden[124] describe how the formation of coloured complexes during the reaction of pentacyanoamino ferroates with aromatic nitroso compounds has been adapted to the qualitative detection of nitroso compounds -

$$Na_3[Fe(CN)_5.NH_3] + R.NO \longrightarrow Na_3[Fe(CN)_5.R.NO] + NH_3.$$

This distinctive colour reaction failed to detect an aromatic nitroso compound in reaction mixtures. It follows therefore, that reactions (4), (5) and (6) must be followed by other more rapid reactions. Bamberger[125] and later Hantsch[126] have found that the reaction of hydroxylamine with nitrosobenzene yields a diazotate:

$$PhNO + H_2NOH \longrightarrow PhN{=}NOH + H_2O \qquad (10)$$

Fischer[127] and Mai[128] have both shown that diazonium salts react with hydroxylamine in alkali to give azides:

$$ArN{=}N{-}OH + H_2NOH \longrightarrow ArN_3 + 2H_2O \qquad (11)$$

This gives the overall reaction:

$$ArNO_2 + 4NH_2OH \longrightarrow ArN_3 + N_2 + 6H_2O \qquad (12)$$

Hence the isolation of p-azidobenzoic acid in 56% yield from the reduction of p-nitrobenzoic acid with a five-fold excess of hydroxylamine in alkali, is in accordance with these observations.

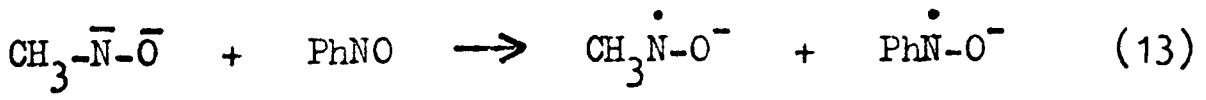
In this reaction 30% of p-nitrosobenzoic acid was isolated. Due to its sparing solubility this was not detected in the preliminary colour test with potassium pentacyanoamino ferroate. This lack of solubility in the reaction medium may also account for the incomplete reaction of the nitroso intermediate to give the diazotate (10), and hence its isolation.

The pattern of the reaction of hydroxylamine with an aromatic nitro compound has thus been demonstrated using p-nitrobenzoic acid. Nitrobenzene itself was not used in this investigation due to possible dangers involved in attempting to isolate the expected reaction product i.e., phenylazide, PhN_3.

(b) N-Methylhydroxylamine

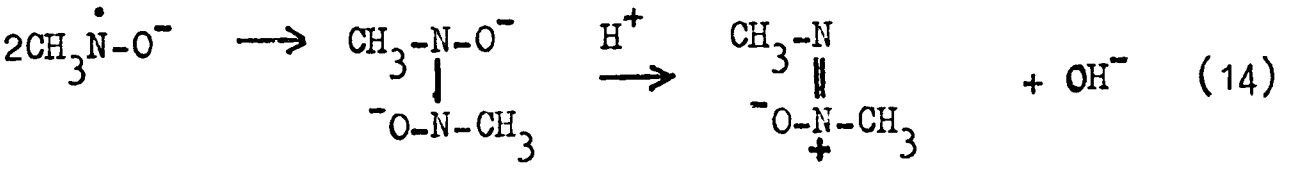
The reaction between N-methylhydroxylamine and nitrobenzene in nitrogen flushed solutions of aqueous alkaline ethanol was found, by t.l.c., to yield identical products with a similar reaction in which nitrosobenzene was substituted for nitrobenzene. Thus nitrosobenzene was established as an intermediate in the reaction, although it could not be detected by the colour reaction with potassium pentacyanoamino ferroate. This confirms that reactions (4), (5) and (6) are involved in the decay of the nitrobenzene radical-anion formed in the initial stages of the reaction.

It is well known that aromatic nitroso compounds are reduced more easily than aromatic nitro compounds. Consequently reaction (13) occurs, in which two different nitroso radical-anions are produced. These radicals may dimerize to form symmetrical azoxy compounds or combine with each other to form a mixed azoxy compound.[118,129] Hence in the reaction under investigation products may arise via the following routes:-



(13)

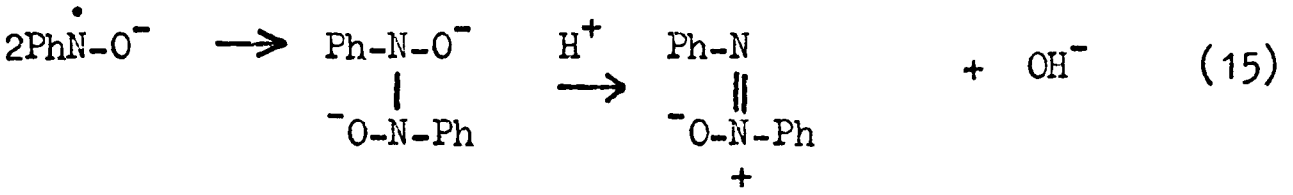
then



(14)

I

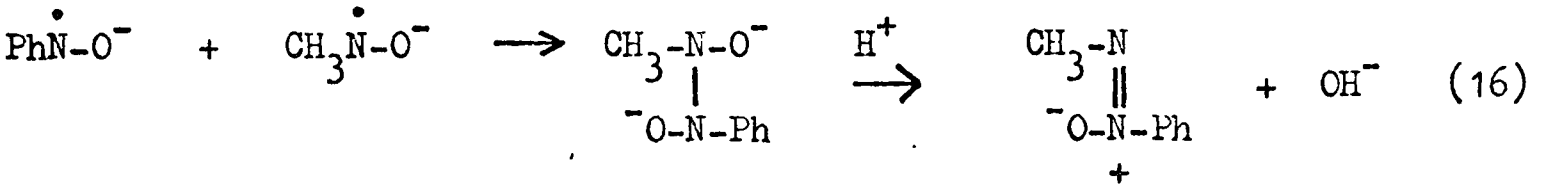
and



(15)

II

or



(16)

III

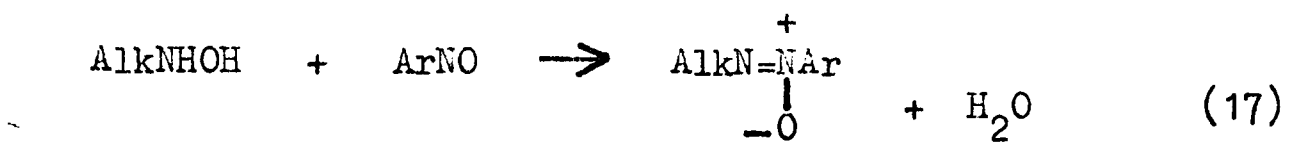
The formation of azoxymethane (I) has not been detected. Azoxybenzene (II) has been isolated in 26% yield from the reaction between nitrobenzene and N-methylhydroxylamine.

Similarly in the reaction between p-nitrobenzoic acid and N-methyl hydroxylamine 21% of pp'-azoxydibenzoic acid was isolated. Azobenzene and related compounds were never detected as reaction products, so further reduction does not occur.

N-methyl-N' phenyldiazine N'-oxide (III) was detected by t.l.c. and later isolated in 7% yield.

Aliphatic hydroxylamines and aromatic nitroso compounds are known to condense together to give mixed azoxy compounds (IV), in

which the oxygen atom is attached to the nitrogen atom adjacent to the aromatic group:[130]



(17)

IV

Hence the occurrence of reactions (13), (15) and (16) has been established experimentally. Thus reaction (16) is an alternative to reaction (3) for the destruction of the radical-anion produced during the oxidation of N-methylhydroxylamine. Reaction (3) would result in nitrosomethane, which would tautomerize to formaldoxime:

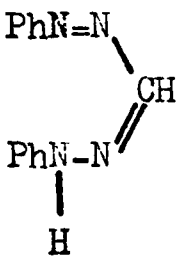


(18)

Formaldoxime is only known in solution and would thus not have been isolated by the techniques employed.

An authentic sample of III was prepared by the method of Freeman[130,131] for comparison during the preliminary experiments using t.l.c. techniques. This authentic sample was isolated in a much greater yield (44%) from the reaction between nitrosobenzene and N-methylhydroxylamine in neutral solution, than from the same reaction in alkaline solution. Hence it would seem that the alkaline conditions employed in the reactions under investigation effect a further reaction in which the mixed azoxy compounds formed, according to equation (16), are destroyed. The alkaline alcoholic mixture of

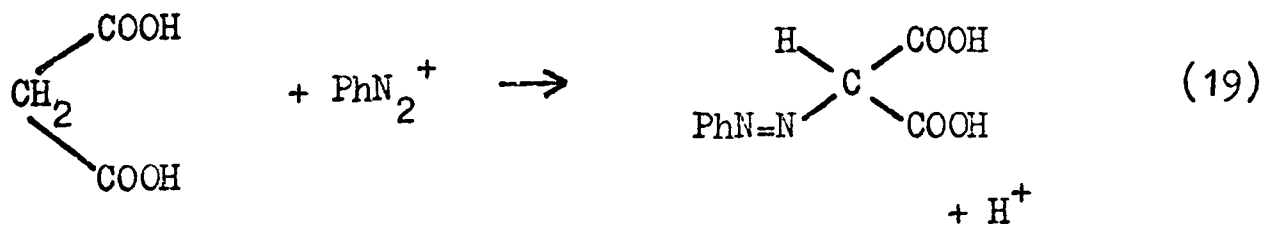
nitrobenzene with N-methylhydroxylamine quickly gave a deep red solution from which glistening crystals with a deep purple sheen later separated. After purification, analysis, supported by mass spectrometry showed that this product was 1,2 diphenylformazan (V).[132]



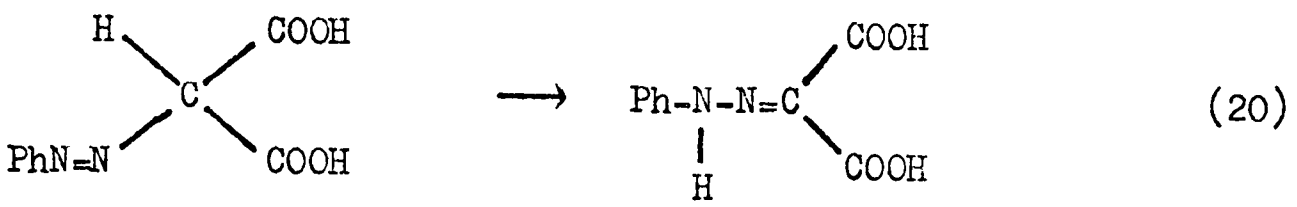
V

Both i.r. and n.m.r. spectroscopies proved to be unhelpful for identification and so direct comparison with an authentic sample was used for final proof of the structure.

Formazans may be synthesized by the action of diazonium salts on compounds containing active methylene groups. An authentic sample of 1,2 diphenylformazan (V) was thus prepared from malonic acid and benzene diazonium chloride, according to von Pechmann,[133] (19-22). In the reaction one diazonium ion is substituted into the methylene group to give the azo compound, which then rearranges to give a phenyl hydrazone.

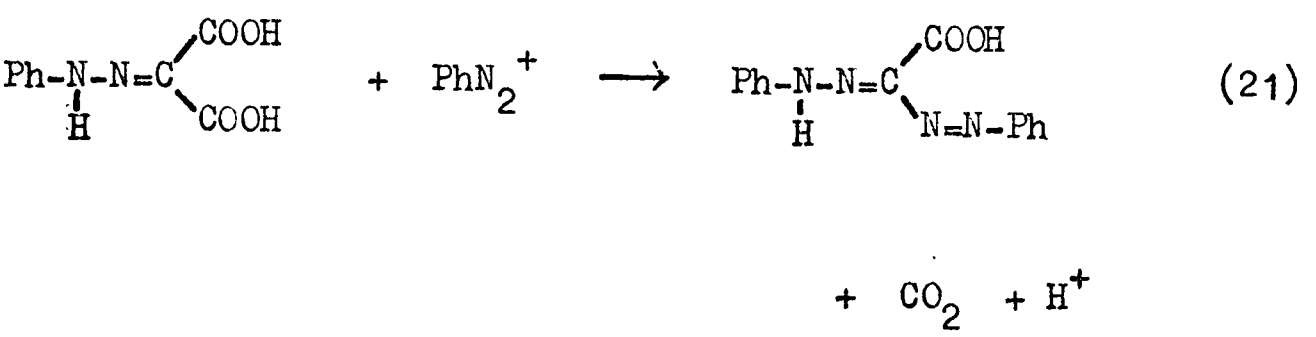


(19)



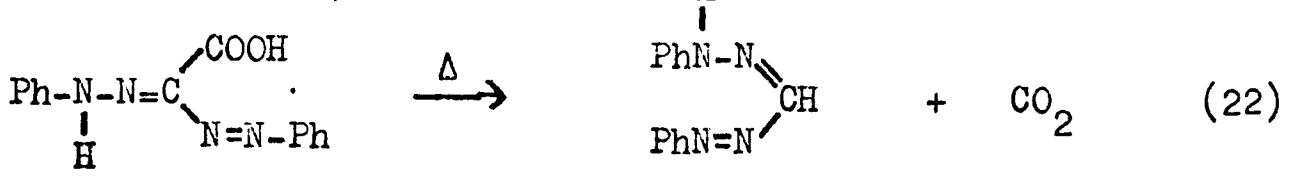
(20)

A second diazonium ion may then couple to the phenyl hydrazone molecule first formed.



(21)

Decarboxylation yields 1,2 diphenyl formazan:



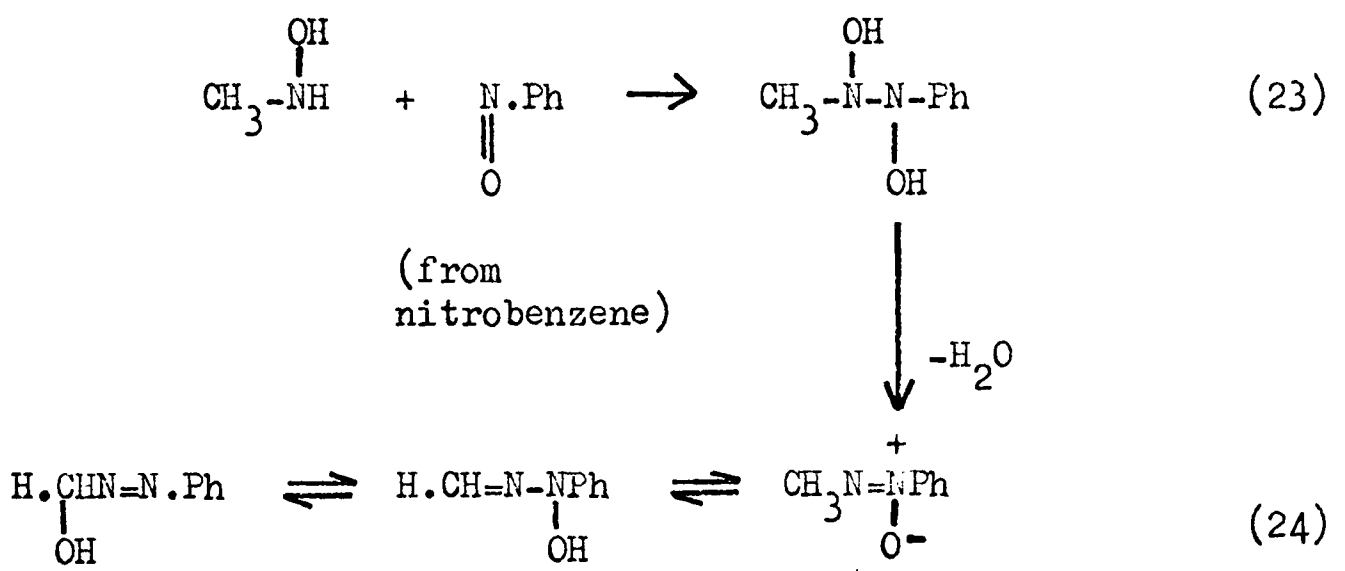
(22)

V

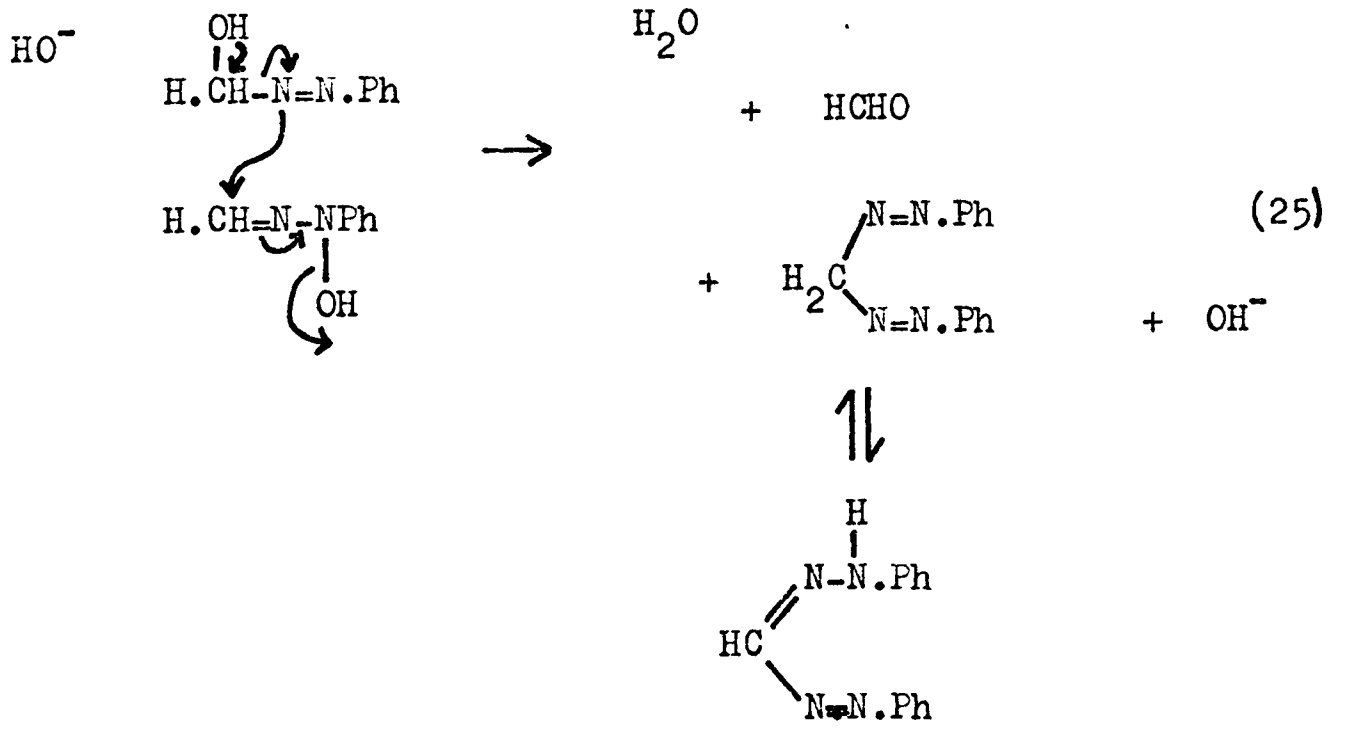
A suggested mechanism for the formation of 1,2 diphenylformazan in the reaction between nitrobenzene and N-methylhydroxylamine is given in Fig. 5.1.

FIG. 5.1

The formation of 1,5 diphenylformazan from nitrobenzene and N-methylhydroxylamine



III



V

This scheme suggests that reactive tautomers of N-methyl-N'phenyl diazine N'-oxide (III) are converted into the 1,2 diphenylformazan (V) by the action of base. In accordance with this view it was noted that N-methyl-N'-phenyldiazine N'-oxide could be isolated in a greater yield from a neutral solution than from an alkaline solution.

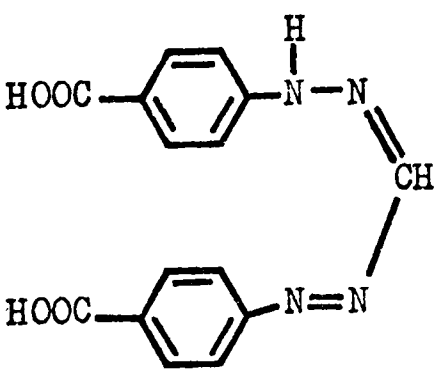
Further evidence for a scheme of this type is presented in section (d) of this discussion relating to N-benzylhydroxylamine. Formaldehyde would be predicted as an additional product, according to this scheme. However under the basic conditions employed it would easily be destroyed.

A smilar pattern emerged in the products detected in the reaction of p-nitrobenzoic acid and N-methylhydroxylamine. The isolation of 26% of pp'azoxydibenzoic acid has been mentioned previously.

However, as during the reaction of hydroxylamine with p-nitro-benzoic acid, difficulties were encountered during isolation of products due to the limited solubility of the various compounds.

1,2 Di-(p-carboxyphenyl) formazan (VI) was isolated as an insoluble red powder, and attempts at further purification were unsuccessful. However mass spectrometry showed that the major component of this powder was the formazan VI.

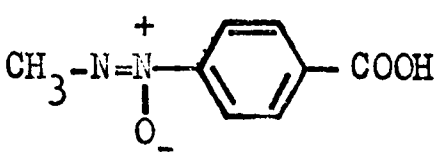
VI



m/e = 312

The structure of this formazan (VI) is that which would be predicted by the mechanism for formazan formation outlined above.

Traces of the mixed azoxy compound N-methyl-N'-p-carboxy-phenyl diazine N'-oxide (VII) may have been present in the impure red powder that was isolated, as a weak ion was observed at $^{m}/_{e}$ = 180 in its mass spectrum.



VII

However this evidence could not be regarded as conclusive of the presence of this compound.

(c) N-Phenylhydroxylamine

Both nitrobenzene and nitrosobenzene on reaction with N-phenylhydroxylamine, in aqueous alkaline ethanol in the absence of oxygen, yield a single product - a high yield (76%) of azoxybenzene.

Azoxybenzene may be produced directly from the nitrobenzene in the reaction via reactions corresponding to reactions (13) and (15) which have already been described. In these reactions the nitrobenzene radical-anion produced by a second electron transfer from N-phenylhydroxylamine, dimerizes to azoxybenzene.

$$PhNO + Ph\text{-}\bar{N}\text{-}\bar{O} \longrightarrow 2Ph\dot{N}\text{-}O^{-} \qquad (26)$$

cf (13).

followed by reaction (15).

The same radical-anion results from the oxidation of N-phenylhydroxylamine in reaction (26), which will also dimerize to azoxybenzene. The radical-anion produced from other hydroxylamines at this stage has differed from the radical-anion derived from the aromatic nitro compound and this has led to the possibility of the two different nitroso radical-anions combining to form mixed azoxy compounds, cf reaction (16). However in this case cross combination of nitroso radical-anions will again result in the production of azoxybenzene. Hence the isolation of a single reaction product. This reaction has been studied in detail by Russell and Geels.[118,129]

(d) N-Benzylhydroxylamine.

The reaction between N-benzylhydroxylamine and nitrobenzene or a para substituted nitrobenzene in nitrogen flushed solutions of aqueous alkaline ethanol was found, by t.l.c., to yield identical products with a similar reaction in which the corresponding nitrosobenzene substituted for the nitrobenzene. Thus the nitroso derivative of the nitro compound was established as an intermediate in the reaction, although it could not be detected by the colour reaction with potassium pentacyanoamino ferroate. Further reduction of the nitroso derivative resulting from the initial stages of the reaction leads to the formation of the nitroso radical-anion which dimerizes (27).

$$PhNO + PhCH_2\dot{N}\text{-}O^- \longrightarrow Ph\dot{N}O^- + PhCH_2\dot{N}\text{-}O^- \qquad (27)$$

In the reaction with nitrobenzene, the nitrosobenzene radical-anion formed, dimerizes to azoxybenzene (reaction 15), which was isolated in 33% yield.

Dimerization of the nitroso radical-anion derived from N-benzyl hydroxylamine would result in the formation of α-azoxy toluene (28):

$$2PhCH_2\dot{N}\text{-}O^- \longrightarrow PhCH_2N(-O)\text{-}N\text{-}CH_2Ph \xrightarrow{H^+} PhCH_2N^+(-O^-)\text{-}N\text{-}CH_2Ph + OH^- \qquad (28)$$

However this product has not been detected. The product of disproportionation of this radical-anion would be α-nitrosotoluene (29);

$$2PhCH_2\dot{N}\text{-}O^- \longrightarrow PhCH_2NO + PhCH_2\bar{N}\text{-}\bar{O} \qquad (29)$$

which would tautomerize to benzaldoxime (30).

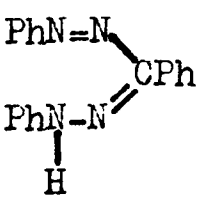
$$PhCH_2NO \rightleftharpoons PhCH{=}NOH \qquad (30)$$

Benzaldoxime was isolated in a 33% yield.

No cross combination of the two different nitroso radical-anions resulting in a mixed azoxy compound is detected. This would indicate that the nitroso radical-anion derived from N-benzylhydroxylamine is destroyed exclusively by disproportionation and subsequent tautomerism. This is in contrast with the reaction involving N-methylhydroxylamine and nitrobenzene in which the product of cross combination of the appropriate radicals is detected and isolated, 13% of unchanged N-benzyl hydroxylamine was recovered after this reaction.

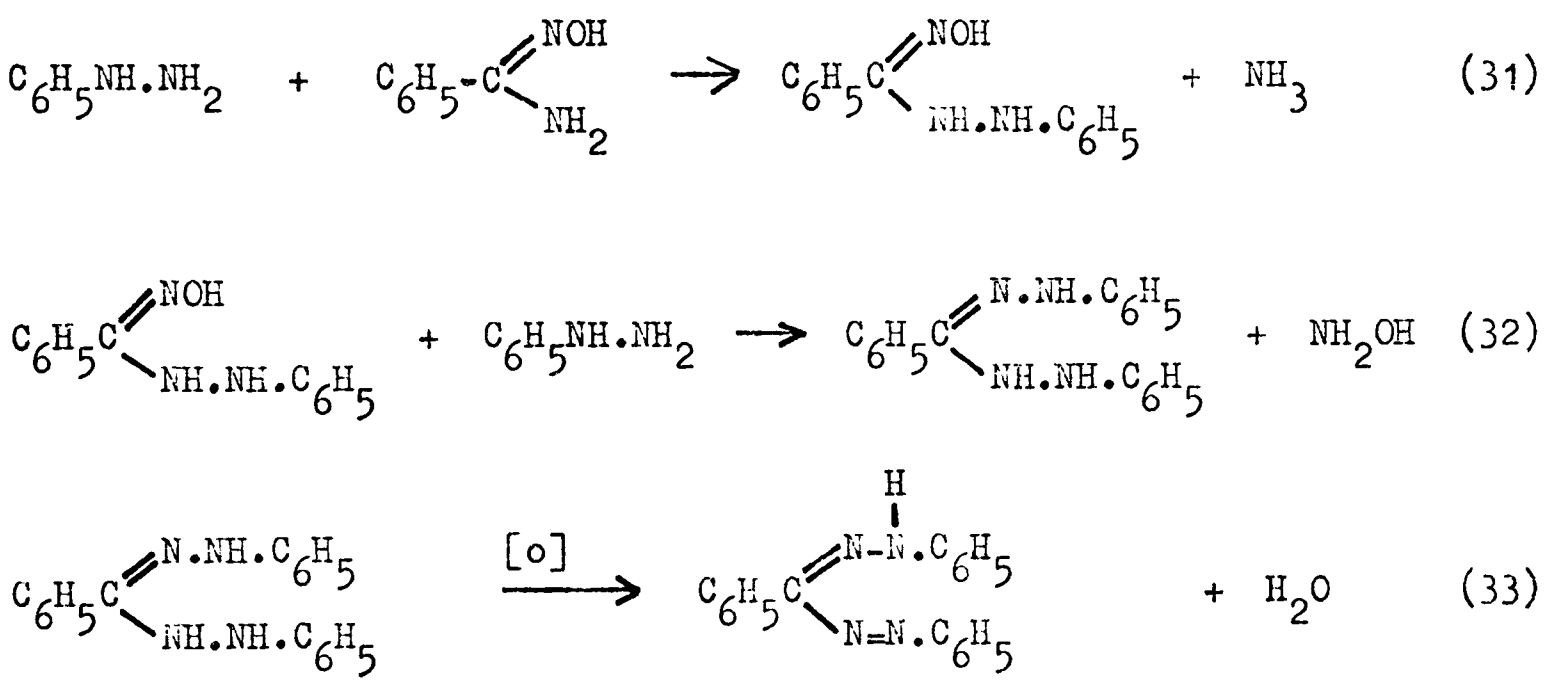
In the reaction of N-benzylhydroxylamine with p-nitro toluene corresponding products were isolated i.e. pp'-azoxytoluene was obtained in a 33% yield and benzaldoxime in 34% yield, but no unchanged N-benzyl-hydroxylamine was recovered.

A major product of the reaction between N-benzylhydroxylamine and nitrobenzene was isolated from the deep red reaction mixture, as glistening crystals with a green sheen. After purification, analysis, supported by mass spectrometry showed that the product was 1,3,5 triphenyl formazan (VIII).



VIII

Direct comparison with an authentic sample of VIII was used for final structure proof, as both i.r. and n.m.r. spectroscopies proved to be unhelpful for identification. An authentic sample of 1,3,5 triphenylformazan (VIII) was prepared from benzamidoxime and phenylhydrazine, according to Bamberger.[134]



(31)

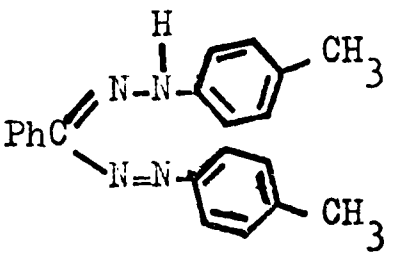
(32)



(33)

VIII

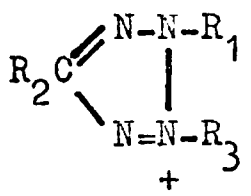
The major product of the reaction between N-benzyl hydroxylamine and p-nitrotoluene was also isolated as glistening crystals with a green sheen. After purification, analysis, supported by mass spectrometry, showed that the product was 3-phenyl 1,5 dip-tolylformazan (IX).



IX

The identity of IX was confirmed by comparison of physical properties with those cited in the literature[10], for this compound (see Chapter 6).

It was also attempted to isolate the products from the reactions of p-nitrobenzoic acid and p-nitrobenzamide with N-benzylhydroxylamine. However this did not prove to be successful. Both reactions resulted in deep red solutions from which product isolation was not practicable. By reaction with lead tetracetate in chloroform it was shown qualitatively that both these red solutions contained formazans. On treatment with this reagent formazans oxidise to colourless tetrazolium salts X:

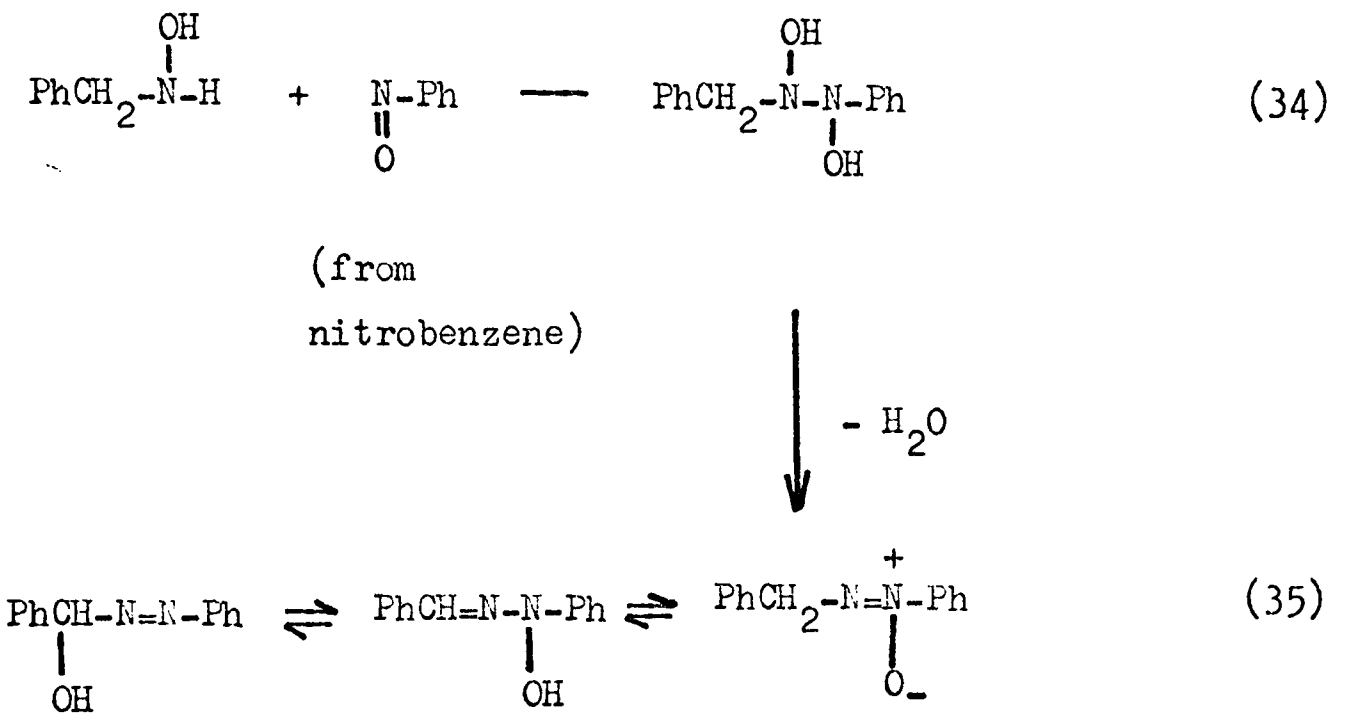


X

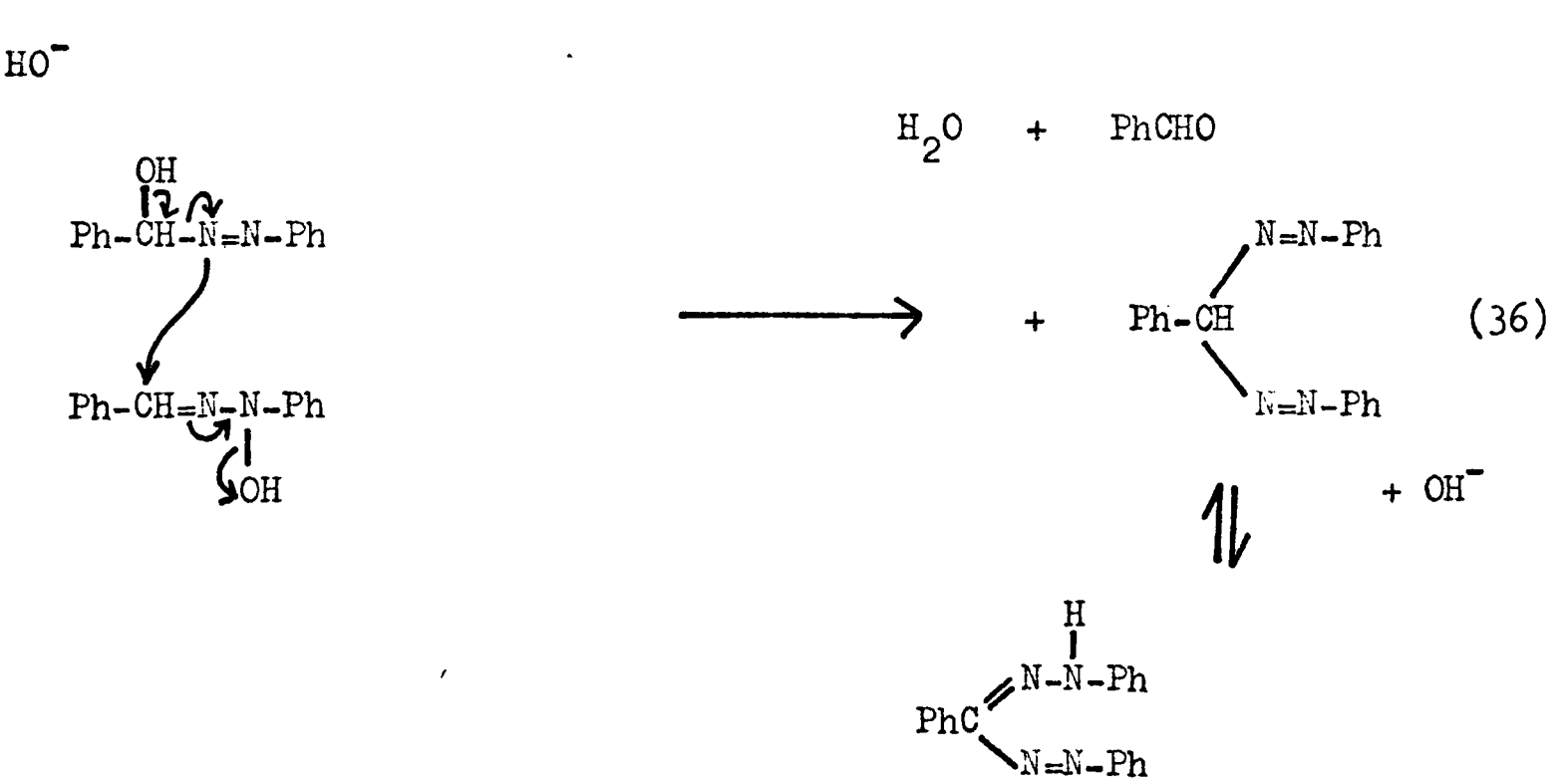
The rapid discharge of the deep red colour of the formazan is a useful qualitative test of its presence in this reaction. Hence N-benzylhydroxylamine will react with several nitro compounds to give rise to formazans. A mechanism for their formation was suggested in section (b) of this discussion. Further evidence for this scheme will be considered at this stage. The formation of 1,3,5 triphenyl-formazan from nitrobenzene and N-benzylhydroxylamine may be represented by the following series of reactions given in Fig.5.2.

Fig.5.2

The formation of 1,3,5 triphenylformazan from nitrobenzene and N-benzylhydroxylamine.



XI



VIII

The following evidence can be cited to support this mechanism:

i) When p-nitrotoluene is substituted for nitrobenzene in the reaction with N-benzylhydroxylamine, 3-phenyl 1,5 dip-tolylformazan (IX) is formed.

ii) When N-methyl hydroxylamine is substituted for N-benzyl hydroxylamine in the reaction with nitrobenzene 1,5 diphenylformazan (V) is formed.

iii) An active methylene group adjacent to the nitrogen atom in the hydroxylamine compound would appear to be essential for formazan formation. In hydroxylamine, N-phenylhydroxylamine and N-benzhydryl hydroxylamine (section ($_e$) of this discussion) an active methylene group is not present. No formazans are formed in the reactions of these hydroxylamines with aromatic nitro compounds in aqueous alkaline ethanol in the absence of oxygen .

iv) In neutral solution N-benzylhydroxylamine and nitrosobenzene condense to form N-benzyl-N'-phenyldiazine N'-oxide[135] (XI). In alkaline solution this compound is not detected as an intermediate. Hence the presence of alkali must affect its stability. Similarly, in the reaction of N-methylhydroxylamine with nitrosobenzene in alkaline solution, N-methyl-N'-phenyldiazine N'-oxide (III) is formed, but in a much lower yield than in the same reaction in neutral solution.

v) In the above scheme N-benzyl-N'-phenyldiazineN'oxide (XI) is proposed as an intermediate. A confirmatory experiment showed that a synthesised sample of this colourless compound, XI, is converted by alkali into 1,3,5 triphenyl formazan (VIII). The reaction appears to be slow but this may be accounted for by the

sparing solubility of this mixed azoxy compound. The formazan formation may possibly, as shown, involve more reactive tautomers of XI, and thus the 'in situ' reaction could proceed at a much greater rate.

vi) This mechanistic scheme would predict the formation of benzaldehyde. No benzaldehyde was detected in reaction mixtures. However, under the alkaline conditions employed, benzaldehyde would be quickly destroyed e.g. by the Cannizzaro reaction (37):

$$2PhCHO \xrightarrow{OH^-} PhCOO^- + PhCH_2OH \qquad (37)$$

Both these products would be very difficult to detect and isolate in the system under investigation.

(e) N-Benzhydrylhydroxylamine.

The reaction of N-benzhydrylhydroxylamine with both nitrobenzene and nitrosobenzene in aqueous alkaline ethanol in the absence of oxygen results in the same products. This confirms that nitrosobenzene is a reaction intermediate, despite the fact that it cannot be detected in reaction mixtures. The products isolated are azoxybenzene (76%) and benzophenone oxime (81%).

Azoxybenzene is formed from the nitrobenzene according to the scheme proposed in reactions (38) and (15), in which a second electron transfer reaction from N-benzhydrylhydroxylamine to the intermediate nitrosobenzene results in the nitrosobenzene radical-anion which dimerizes to azoxybenzene.

$$Ph_2CHN\text{-}O + PhNO \longrightarrow Ph_2CHN\text{-}O^- + PhN\text{-}O^- \qquad (38)$$

Disproportionation of the nitroso radical-anion derived from N-benzhydrylhydroxylamine (39), followed by tautomerism of the nitroso compound thus formed, gives rise to benzophenone oxime (40).

$$2Ph_2\dot{C}H\bar{N}\text{-}O^- \longrightarrow Ph_2CHNO + Ph_2CH\bar{\bar{N}}\text{-}O \qquad (39)$$

$$Ph_2CHNO \longrightarrow Ph_2C{=}NOH \qquad (40)$$

The high yield of benzophenone oxime and the lack of formation of a mixed azoxy compound indicates that disproportionation of the nitroso radical-anion from N-benzhydryl hydroxylamine and subsequent tautomerism,

(39) and (40), occurs to the exclusion of any cross combination of this radical-anion with the nitrosobenzene radical-anion, derived from nitrobenzene, which would result in a mixed azoxy compound. Thus reaction (39) would appear to be the only reaction in which the nitroso radical-anion from N-benzhydrylhydroxylamine is destroyed.

The absence of a formazan amongst the products of this reaction would be in accordance with predictions of the previous section of this discussion, where an active methylene group adjacent to the nitrogen atom of a substituted hydroxylamine was essential in the mechanism proposed for the formation of formazans. N-Benzhydryl-hydroxylamine does not fulfil this requirement and hence no formazan is produced.

CHAPTER 6

EXPERIMENTAL WORK

A. Preparation and purification of materials

1. Introduction

The methods employed for the preparation and purification of the compounds which were used are described in the following section. The relevant physical constants for these compounds are recorded, and values to be found in the literature are quoted for comparison. These literature values are preceeded by the abbreviation "lit", and the appropriate reference number.

Solids were characterized by the melting point and liquids by their boiling points and refractive indices. Melting points were determined on an electrically heated Kofler block and are uncorrected. Temperatures refer to the centigrade scale.

2. Hydroxylamines

1.) Hydroxylamine hydrochloride.

Recrystallised from water; m. p. = 149-50°
(lit:[136] m.p. = 151°)

2.) N-Methyl hydroxylamine hydrochloride.

N-Methyl hydroxylamine hydrochloride was prepared according to the method of Meisenheimer and Chou.[137]

Nitromethane (100 g., 1.64 mol.), ammonium chloride (60 g., 1.12 mol.) and water (800 ml.) were cooled in an ice/salt mixture and stirred mechanically. Zinc dust (275 g., 4.2 mol.) was added in portions so as to maintain a temperature below 8°. The grey white precipitate of zinc hydroxide was filtered off, and washed with water. The filtrate was acidified with concentrated hydrochloric acid, and evaporated at 40° under reduced pressure, until no more water distilled over. On cooling in ice, a yellowish solid was formed. This crude product was ground up with ethanol (100 ml.) and the solid filtered off. This procedure was repeated with small quantities of ethanol (25 ml.), until the extracts were no longer yellow, and white ammonium chloride remained in the filter paper. The combined extracts (175 ml.) were cooled overnight in the refrigerator. White needles of N-methyl-hydroxylamine hydrochloride were formed, which were filtered off, washed with a little ethanol, and dried in a desiccator. The filtrate was concentrated and returned to the refrigerator. A further crop of crystals was obtained, and treated as before.

Total Yields: i) 41.0 g., (30%); m.p. = 85-86°

ii) 42.8 g., (32%); m.p. = 85-86°

iii) 50.0 g., (37%); m.p. = 82-85°

iv) 34.0 g., (25%); m.p. = 86.87°

(Lit[138] : m.p. = 88-90°)

3.) N,N-Dibenzyl hydroxylamine

N,N-Dibenzyl hydroxylamine was prepared by the method of Jones and Sneed.[139] Hydroxylamine hydrochloride (28 g., 0.4 mol.), benzyl chloride (100 g., 0.8 mol.) and sodium carbonate (120 g., 1.2 mol.) were refluxed for three hours in 70% aqueous ethanol (280 ml. ethanol, 120 ml. water). The hot mixture was filtered, and the filtrate on cooling yielded colourless needles of N,N-dibenzylhydroxylamine. The solid residue was extracted with boiling 70% aqueous ethanol (3 x 200 ml.). On cooling this extract a further crop of crystals was obtained; it was filtered off and dried.

All the solid obtained was washed with ether then recrystallised from ethanol to give pure N,N-dibenzyl hydroxylamine.

Yields: i) 54.2 g., (64%); m.p. = 122-124°

ii) 51.2 g., (60%); m.p. = 121-123°

iii) 37.0 g., (44%); m.p. = 122-123°

iv) 57.0 g., (67%); m.p. = 122-124°

v) 55.0 g., (65%); m.p. - 121-122°

(Lit[138]: m.p. = 123°)

4.) N-Benzylhydroxylamine.

N-Benzylhydroxylamine was prepared from N,N-dibenzylhydroxylamine by its oxidation to N-benzyl-isobenzaldoxime and hydrolysis of the latter.

N,N-Dibenzylhydroxylamine (42.6 g., 0.2 mol.), potassium hydroxide (28 g., 0.5 mol.) and potassium ferricyanide (165 g., 0.5 mol.) in concentrated aqueous solution, were shaken together with ether (200 ml.) for two hours. The ether layer was then removed and the aqueous phase was extracted with ether (3 x 150 ml.). The combined ethereal extracts were dried over magnesium sulphate. On evaporation to dryness, a pale yellow solid remained. Recrystallisation from 60-80° petroleum ether gave N-benzyl-isobenzaldoxime, $PhCH_2\overset{+}{N}(\overset{-}{O}) = CH.Ph$ which was pure to t.l.c..

Yields: i) 27.0 g., (64%); m.p. = 79-80°
ii) 32.8 g., (78%); m.p. = 77-79°
iii) 28.6 g., (68%); m.p. = 79-80°
iv) 30.2 g., (72%); m.p. = 80-81°

(Lit[138]: m.p. = 81°)

N-Benzyl-isobenzaldoxime (42.2 g., 0.2 mol.), water (500 ml.), concentrated hydrochloric acid (100 ml.) and ether (500 ml.) were shaken together mechanically for three hours. The layers were separated and the ether layer was extracted with concentrated hydrochloric acid (50 ml.) in water (250 ml.). The combined aqueous extracts

were made alkaline with solid sodium carbonate, and then extracted with ether (4 x 500 ml.). The ethereal extract was dried over magnesium sulphate, and then evaporated to dryness to yield the crude product.

Recrystallisation from 40-60° petroleum ether gave colourless needles of N-benzylhydroxylamine.

Yields: i) 15.2 g., (62%); m.p. = 54-57°
ii) 12.0 g., (49%); m.p. = 56-57°
iii) 13.6 g., (56%); m.p. = 55-56°

(Lit[138]: m.p. = 57°)

The product was stored in a desiccator at 0°C to prevent decomposition to benzylamine.

5.) N-Phenylhydroxylamine

N-Phenylhydroxylamine was prepared as described in Organic Syntheses.[140]

Ammonium chloride (25 g., 0.5 mol.), nitrobenzene (50 g., 0.4 mol.) and water (800 ml.) were stirred together mechanically, and zinc dust (62 g., (85%) 0.8 mol.) was added in small portions so that the temperature was held constant at 50°. The mixture was stirred until the temperature began to fall. The warm mixture was filtered and the residue washed with hot water. The filtrate was saturated with salt (ca.300 g.) and left to stand in an ice/salt bath for two hours. The yellow crystals were

filtered off at the pump. The solid was dissolved in ether and insoluble inorganic matter filtered off. After drying over magnesium sulphate and evaporating to dryness, crude N-phenylhydroxylamine was obtained.

Pale yellow crystals of the pure product were obtained on recrystallisation from benzene/40-60° petroleum ether.

Yield: 18 g., (81%); m.p. = 80°

(Lit[138]: m.p. = 81°)

6.) N-Benzhydryl hydroxylamine, $Ph_2CHNHOH$.

N-Benzhydryl hydroxylamine was prepared by the reaction of acetoxime with benzhydryl bromide[141]; the latter was obtained by the reaction of a calculated amount of bromine on diphenyl methane.[142]

Diphenylmethane (40 g., 0.24 mol.) was heated to 150-160° and bromine (44 g., 0.24 mol.) was slowly added at this temperature, with constant stirring. Distillation under reduced pressure (146-148°/1.7 mm.) gave an almost colourless liquid which readily solidified.

Yield: 32 g., (55%); m.p. = 46-47°

(Lit[138]: m.p. = 45°)

Benzhydryl bromide (30 g., 0.12 mol.), acetoxime[143] (12.5 g., 0.17 mol.), glacial acetic acid (30 ml.) and water (10 ml.) were heated on a boiling water bath for half an hour. After evaporation to dryness, the solid

residue was distributed between water (50 ml.) and ether (50 ml.). The extraction of the hydroxylamine as described in the literature[141] proved unsuccessful so the following procedure was adopted.

The aqueous layer was made alkaline with solid sodium carbonate and the free hydroxylamine was extracted into ether, dried over magnesium sulphate and evaporated to dryness. An oil was obtained which on dissolving in methanol and cooling in dry ice/methanol, gave colourless crystals of N-benzhydrylhydroxylamine.

Yield; 6.1 g., (25%); m.p. = 76°

(Lit[141]: m.p. = 75-76°)

A low resolution mass spectrum showed a molecular ion at m/e = 199 and the expected breakdown pattern.

Analysis: Found: N = 7.16%

Calculated for $C_{13}H_{13}NO_2$: N = 7.04%

7.) Di-tert.-butyl hydroxylamine.

Di-tert.-butyl hydroxylamine was prepared by converting tertiary nitrobutane into di-tert.-butyl nitroxide followed by reduction of this radical.[144]

Tert.-nitrobutane was prepared by the oxidation of tert.-butylamine.[145] Tert.-butylamine (25 g., 0.34 mol.) was added to a stirred mixture of potassium permanganate (163 g., 0.97 mol.) in water (750 ml.), during the course of fifteen minutes. After gentle warming initially, the temperature rose to 45°, and after stirring for eight

hours without further external heating, the mixture was left to stand for three days. It was then held at 55-60° for a further four hours and the product was isolated by steam distillation. The steam distillation was repeated and the product washed with dilute hydrochloric acid (2 x 25 ml.) and water (2 x 25 ml.) then dried over sodium sulphate. The clear colourless liquid obtained freezes to a semicrystalline colourless solid.

Yield: 22.0 g., (60%); m.p. = 24-26°

(Lit[138]: m.p. = 26.23°)

1.2.Dimethoxyethane (300 ml.), previously dried over calcium hydride and distilled from lithium aluminium hydride under nitrogen, directly into the reaction flask, tert-nitrobutane (22 g., 0.2 mol.) and small pieces of sodium (6 g., 0.25 mol.) were stirred rapidly under dry nitrogen for thirty hours at 25-30°. Initially the sodium pieces became golden in colour and then the solution became lavender. The final colour of the reaction mixture was greenish grey. The remaining solvent was removed under reduced pressure, at room temperature. Water (70 ml.) was added to the residue, when a violent reaction set in. From this stage onwards it was no longer necessary to work in the absence of air. The red-brown organic layer was removed and the alkaline aqueous layer extracted with 30-40° petroleum ether (3 x 10 ml.), until the organic layer was substantially colourless. The combined organic extracts were cooled overnight in the refrigerator, then washed with ice cold .25N hydrochloric acid (2 x 20 ml.) to remove any hydroxylamines.

The organic nitroxide layer was immediately washed with cold water (20 ml.) followed by cold .2N aqueous sodium hydroxide (20 ml.). After drying the organic layer over magnesium sulphate, the nitroxide was distilled under reduced pressure and the dark red product collected.

Yield: 9.3 g., (30%); b.p. = 38-42°/1 mm.
(Lit[144]: b.p. = 60°/11 mm.)

Di-tert.-Butyl nitroxide was converted into di-tert.-butyl hydroxylamine by reduction with sodium. Dry, freshly distilled 1.2 dimethoxyethane (100 ml.) di-tert.-butyl nitroxide (8 g., 0.6 mol.) and sodium (1.3 g., 0.06 mol.) were stirred magnetically for two days, at room temperature, under a blanket of dry nitrogen. The solution was filtered and dry hydrogen chloride passed through the filtrate. Di-tert.-butyl hydroxylamine hydrochloride was precipitated as a white powder and dried in vacuo.

Yield: 2 g., (20%); m.p. = 184°
(Lit[144]: m.p. = 184°)

3. Substituted Nitrobenzenes

1) Nitrobenzene

Redistilled under reduced pressure: b.p. = 84-86°/10 mm.

(Lit[138]: b.p. = 85.4°/10.)

Refractive index = 1.552 at 22°

(Lit[138]: refractive index = 1.552 at 20°).

2) p-Nitrobenzoic acid

Recrystallised from water: m.p. = 240-241°

(Lit[138]: m.p. = 241.50°)

3) p-Nitrobenzaldehyde.

Recrystallised from water: m.p. = 105-106°

(Lit[138]: m.p. = 106°)

4) p-Fluoronitrobenzene

Recrystallised from ethanol: m.p. = 21.5°

(Lit[138]: m.p. = 21.5° - labile form)

5) p-Chloronitrobenzene

Recrystallised from ethanol: m.p. = 82-83°

(Lit[138]: m.p. = 83°)

6) p-Bromonitrobenzene

Recrystallised from ethanol: m.p. = 125-126°

(Lit[138]: m.p. = 127°)

7) p-Nitrophenol

Recrystallised from toluene below 63°: m.p. = 110-112°

(Lit[138]: m.p. = 114°)

8) p-Nitroanisole

Recrystallised from ethanol: m.p. = 52-53°

(Lit[138]: m.p. = 54°)

9) Ethyl p-nitrobenzoate.

Recrystallised from ethanol: m.p. = 56-57°

(Lit[138]: m.p. = 57°)

10) p-Nitrotoluene.

Recrystallised from ethanol: m.p. = 53°

(Lit[138]: m.p. = 54.5°)

11) p-Nitrobenzonitrile[146]

p-Nitrobenzoic acid (25 g., 0.15 mol.), p-toluenesulphonamide (27.5 g., 0.16 mol.) and phosphorus pentachloride (65.5 g., 0.32 mol., 5% excess) were stirred together mechanically in a round bottomed flask. The apparatus was adjusted for distillation and very slowly heated. After

the inital reaction had subsided, the contents of the flask were liquid and the temperature was gradually raised to 205°. This temperature was maintained until no more phosphorus halides distilled over. The cooled reaction mixture was dissolved, with slight warming, in pyridine (60 ml.). Water (250 ml.) was slowly added to this solution, with stirring, and on cooling the suspended material was filtered off. The solid was washed with water and suspended in 5% sodium hydroxide solution (100 ml.). After stirring for half an hour, the light tan solid was filtered off, washed with water and dried. Recrystallisation from acetic acid, and then from ethanol gave pure p-nitrobenzonitrile.

Yield: 18 g., (80%); m.p. = 148-149°
(Lit[138]: m.p. = 149°)

12) p-Nitrobenzamide.

p-Nitrobenzamide was prepared from p-nitrobenzoic acid via p-nitrobenzoyl chloride.[147]

p-Nitrobenzoic acid (50 g., 0.3 mol.) and phosphorus pentachloride (53 g., 0.25 mol.) were gently heated together in a flask fitted with a drying tube. Once the initial reaction had begun, heating was continued for half an hour.

Phosphorus oxychloride was removed by distillation at normal pressures. The oil bath was maintained at 210° until no more material distilled over. The water condenser was replaced by an air condenser, and the remaining reaction mixture was distilled under reduced pressure. Yellow p-nitrobenzoyl chloride distilled over (130°/5 mm.) and solidified readily.

Yield: 25 g., (53%); m.p. = 71°
(Lit[138]: m.p. = 73°)

Solid p-nitrobenzoylchloride (25 g., 0.13 mol.) was ground up under .880 ammonia (250 ml.) and the mixture shaken for an hour. The solid formed was filtered off and recrystallised from water.

Yield: 18 g., (80%) ; m.p. = 198°
(Lit[138]: m.p. = 200°)

4. Substituted Nitrosobenzenes.

1) Nitrosobenzene

Recrystallised from aqueous ethanol; m.p. = 66-68°

(Lit[138]: m.p. = 67.5-68°)

2) p-Nitrosobenzoic acid[148]

p-Nitrobenzoic acid (10 g., 0.06 mol.) was dissolved in a small amount of warm ethanol, and glacial acetic acid (20 ml., 0.36 mol.) was added, shaking constantly. Zinc dust (10 g., 0.25 mol.) was added to this solution in small portions, with stirring. The resultant yellow solution contained crude p-hydroxylaminobenzoic acid, which was poured into a cold 10% ferric chloride solution (200 ml.). After warming to 45° the yellow precipitate formed was filtered and and washed well with water, to remove traces of ferric salts, and ether, to remove traces of starting material. After extraction with boiling ethanol (2 x 200 ml.) a green solution was obtained which on evaporation to half volume, and standing precipitated a pale yellow powder as the product, p-Nitrosobenzoic acid did not melt, but decomposed above 250°.

Yield: 4.8 g., (50%)

Analysis: Calculated for $C_7H_5O_3N$: N = 9.30%

Found N = 9.48%

A low resolution mass spectrum showed a molecular ion at $^m/_e$ = 151, and the expected breakdown pattern.

5. Potassium Peroxylamine Disulphonate

Potassium peroxylamine disulphonate (Frémy's Salt)

$$\begin{matrix} ON - (SO_3K)_2 \\ | \\ ON - (SO_3K)_2 \end{matrix}$$

was prepared according to Palmer.[149]

Crushed ice (100 g.) was stirred into a solution of sodium nitrite (17.5 g., 0.25 mol.) in water (50 ml.). A solution of sodium bisulphite (25 g., 0.25 mol.) in water (50 ml.) was then stirred into this solution, followed by glacial acetic acid (10 ml.). One drop of this solution was diluted and tested with iodine and starch, to ensure that all the bisulphite had been brought into reaction. The mixture was then made alkaline by the addition of .880 ammonia (7 ml.). A solution of potassium permanganate (6.3 g., 0.04 mol.) in water (200 ml.) was stirred into the mixture, and the precipitate of manganese dioxide which was formed was filtered off immediately, without suction. A saturated solution of potassium chloride (250 ml., 0.1 mol.) was added to the violet coloured filtrate, and the orange yellow crystalline precipitate formed was filtered off. The precipitate was washed several times with a 5% potassium hydroxide solution, and then successively with ethanol and acetone. After drying in warm air, the product was stored in a closed bottle in a refrigerator.

Yield: 15 g., (50%).

The purity of the product was estimated by iodometric titrations[150] before use.

B. E.S.R. measurements.

The Spectrometer.

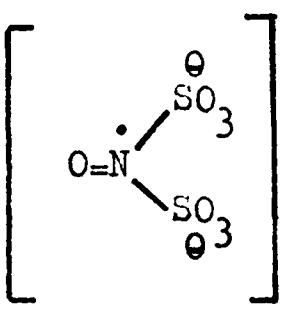
The E.S.R. spectrometer used in all the experiments was the Varian V.4500. This operates at a frequency of 9,000 MHz (λ = 3 cm.) with a field strength of 3,000 gauss, supplied by a six inch magnet of inhomogeneity less than 1 in 100,000. The field is modulated at 100 KHz., and calibration or direct measurement of the spectra can be effected by the "Fieldial" control unit. The instrument records the first derivative of the absorption spectrum.

Determination og g-values

g-Values were determined by recording the spectrum of the radical concerned simultaneously with that of Frémy's salt and measuring the relative displacement of the two spectra (in gauss) by means of the "Fieldial" unit (Fig. 6.1). Since the instrument has only a single cavity, a very dilute aqueous solution of Frémy's salt was placed in a glass capillary tube, which was then sealed and fixed to the outside of the flattened portion of the cell, with a smear of grease. The cell was then placed in the cavity of the spectrometer in the usual manner.

Frémy's salt is a diamagnetic yellow solid which dissociates to a purple, paramagnetic species when it is dissolved in water.

$$K_4(NO)_2(SO_3)_4 \rightleftharpoons 2K_2^+$$



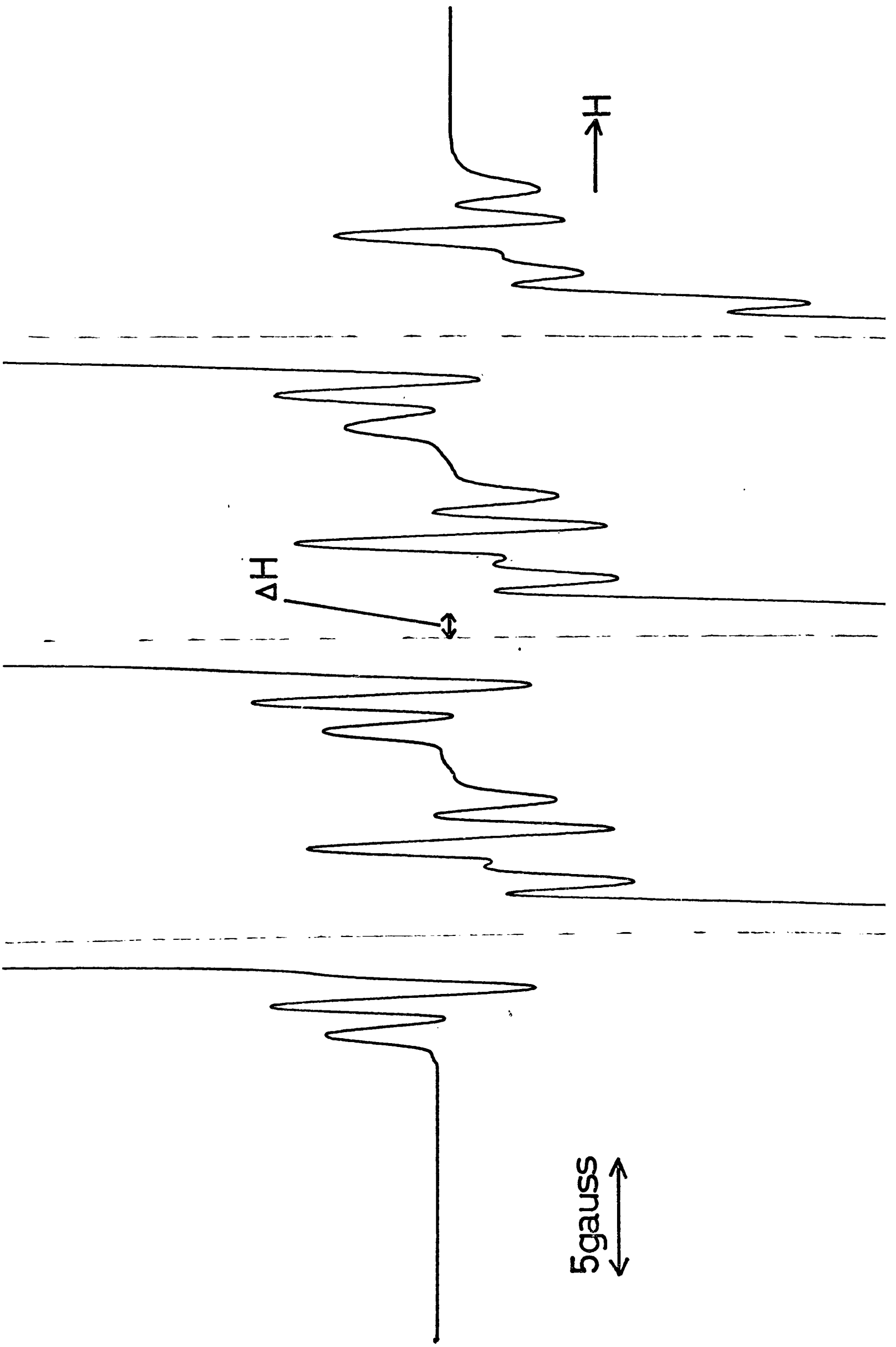


Fig. 6. 1 Determination of the g-value of para-chloronitrobenzene.

This radical exhibits a spectrum consisting of three lines of equal intensity (Fig. 6.2), and splitting 13.0 gauss, due to the nitrogen nucleus.[14,16] It has the g-value, $g = 2.0055 \pm 0.00005$.

If the two radicals have g-values, g and g' respectively, and the spectra when irradiated with the same microwave frequency, are centred at H and H', then as:

$$h\nu = g\,\beta_e H \quad \text{for the radical from Frémy's salt}$$

and

$$h\nu = g'\beta_e H' \quad \text{for the radical under investigation}$$

$$\frac{g}{g'} = \frac{H'}{H}$$

$$g' = \frac{H}{H'} \cdot g$$

Now $H' = H \pm \Delta H$, where ΔH is the displacement of the centre of the spectrum of the radical under investigation, from the centre of that of the radical from Frémy's salt.

The centre of the spectrum of the radical from Frémy's salt (H) can be measured with an accuracy of $\pm$ 1 gauss in 300. The displacement (ΔH) can be measured to within $\pm$ 0.1 gauss. Hence the g-value of the radical under investigation (g') can be determined to within $\pm$ .0001, by comparison with Frémy's salt.[19]

The stopped-flow system used for kinetic measurements.

All the work carried out in this thesis involved the use of a stop-flow system, the reagents being degassed prior to mixing.

The mixing chamber used was as shown in Fig. 6.3. It consists of a T joint, which has one arm tapered in order to fit into the

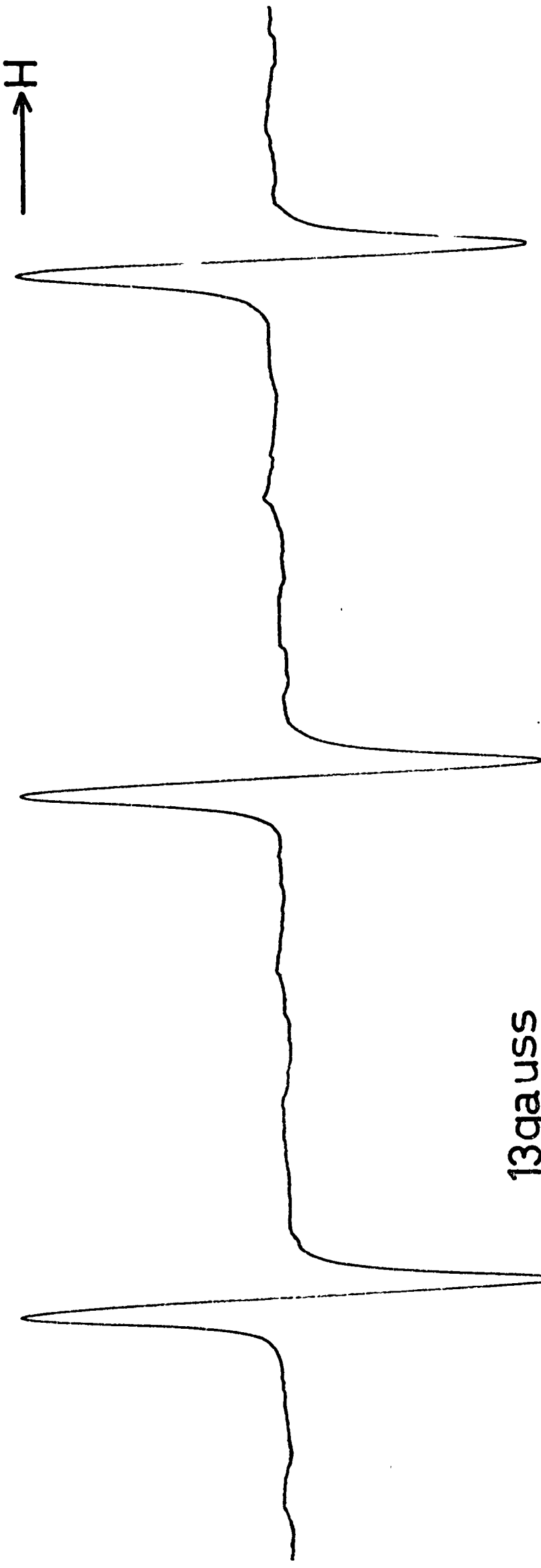
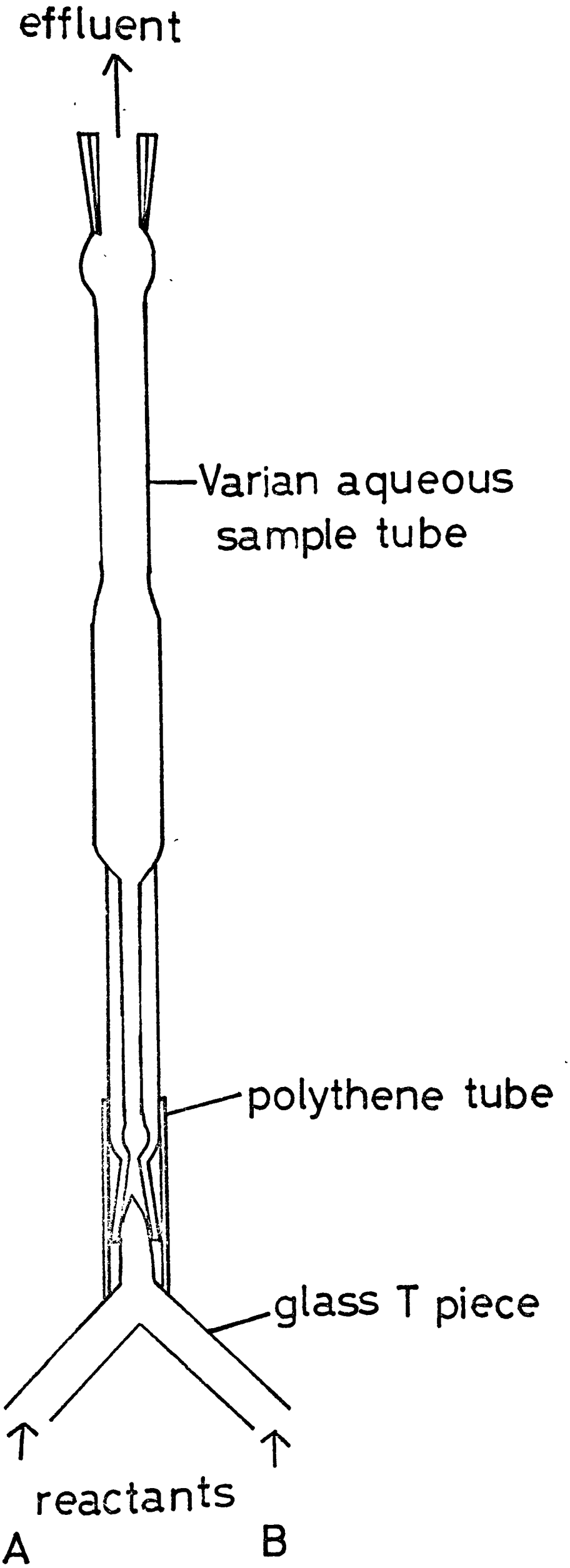


Fig. 6.2 The e.s.r. spectrum of Fremy's salt.

Fig.6.3. The e.s.r. cell and mixing chamber



capillary end of a standard Varian aqueous sample cell. The reactants are forced together at right angles thus producing efficient mixing.

Degassing prior to mixing was effected by means of the apparatus shown in Fig.6.4.

The rubber tubing connecting the two 2-litre reservoirs to the mixing chamber was filled with 50% aqueous ethanol and then clipped at the top and fitted to the reservoirs. By turning the two 3-way taps so that points A and B were connected and the 2-way taps so that C and D were connected, the reservoirs could be evacuated while nitrogen leaks purged the solutions. The reservoirs could be restored to atmospheric pressure by cautiously turning the 3-way taps to connect points C and B. By repeating this cycle of operations large volumes of solutions could effectively be degassed in a short period of time. By opening the two clips the solutions could then be forced out of the reservoirs under a positive nitrogen pressure. It was regularly checked, during the experiments with this system, that the flow rate through each arm of the mixing chamber was identical to within 2%. The total flow rate was ca. 200 ml./min., and the dead volume between mixing and observation points was < 0.5 ml.. Thus radicals could be observed approximately .1 sec. after mixing.

The flow could be arrested by either rapid closure of a tap on the exit tube from the e.s.r. cell or by rapid closure of a double tap (Fig. 6.5) inserted into the flow system prior to mixing of the reagents. The latter method resulted in more consistently reproduceable kinetic curves and was thus used in all the experiments.

Fig. 6.4 Apparatus for degassing reactants prior to mixing in e.s.r. cell.

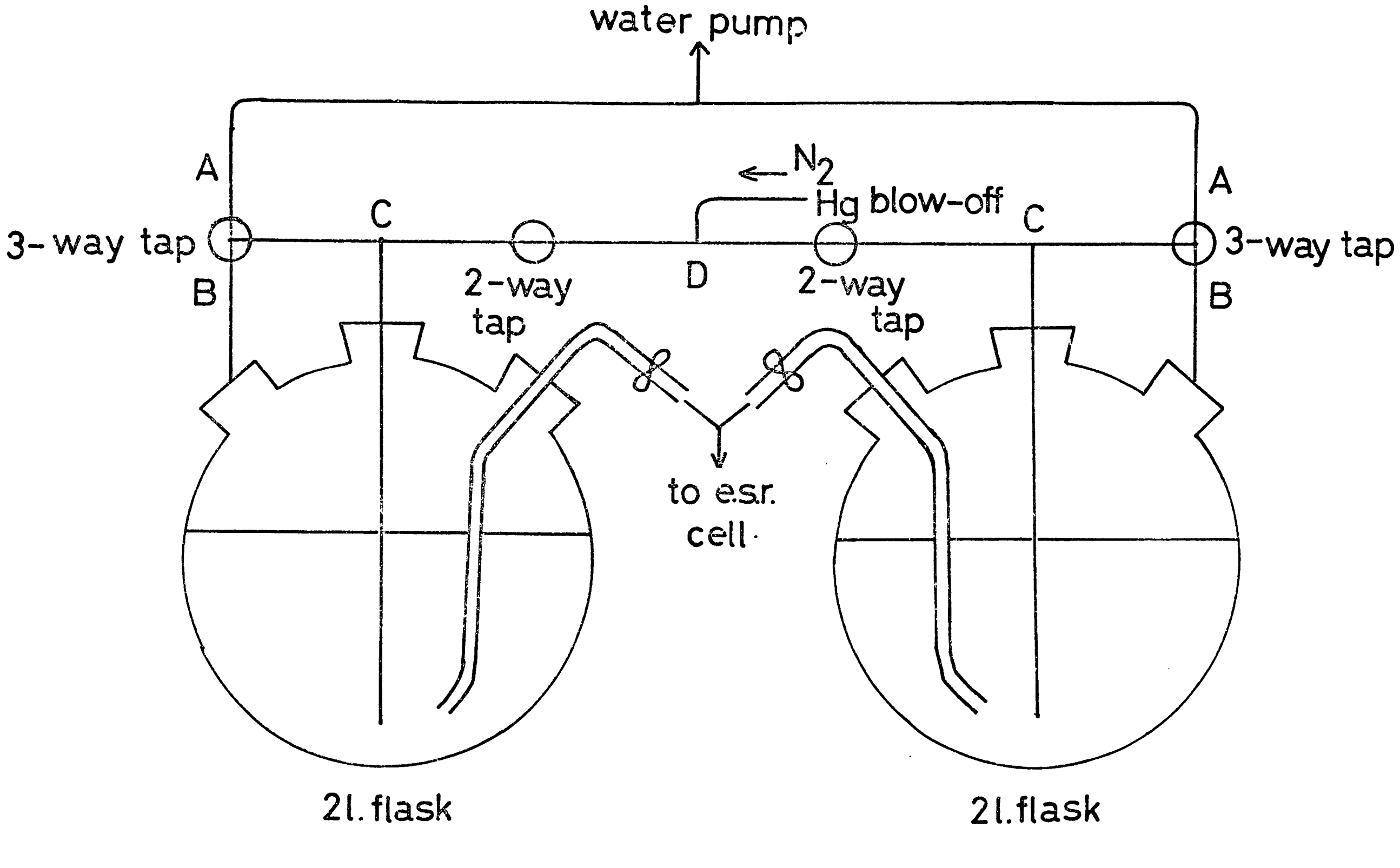
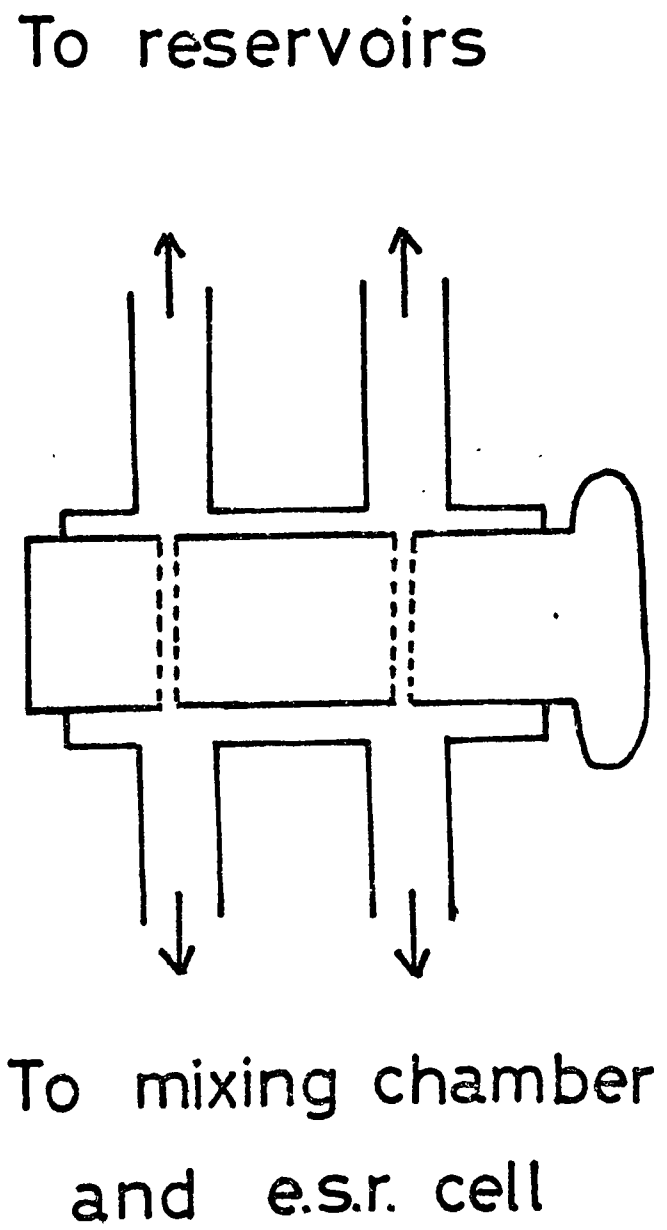


Fig.6.5.

The double tap used to arrest the flow of reactants during kinetic experiments.



During a typical 'flow', one reservoir would contain a hydroxylamine (.005M - .16M) in 50% aqueous ethanol and the other a nitro compound (.005M - .16M) in 50% aqueous ethanol containing sodium hydroxide (.125M - 2.0M).

Concentration measurements

The radical concentration was monitored by adjusting the Fieldial control so that the change with time of the height of a chosen peak X (Fig.6.6) could be recorded instrumentally. Whilst the solutions were flowing a base line was obtained; on stopping the flow, as described above, the radical concentration, and hence the height of peak X , increased to a maximum and then began to decay. (Fig.6.7).

Relative concentrations of the radical were obtained from the peak to peak height of line X, under standard conditions of cavity turning, microwave power, modulation and field sweep.

Absolute concentrations were estimated by comparison of the peak to peak height of line X with that of a line in the spectrum of Frémy's salt, under identical instrument settings. Allowance was made for the relative concentration weightings of the two lines. e.g. line X in the spectrum of the p-nitrobenzoic acid radical-dianion is $^1/_{12}$ of the total, compared with a line in the spectrum of Frémy's salt which is $^1/_3$ of the total. A modulation amplitude of ca. 0.6 gauss was used, the e.s.r. spectral widths of both lines being 0.7 gauss. The normalised line shape functions of each line was obtained in the following manner.

The centre line in the Frémy's salt spectrum and line X in the p-nitrobenzoic acid radical-dianion spectrum were both recorded at the same very slow scan speed (50 gauss/50 min.), and the same instrument

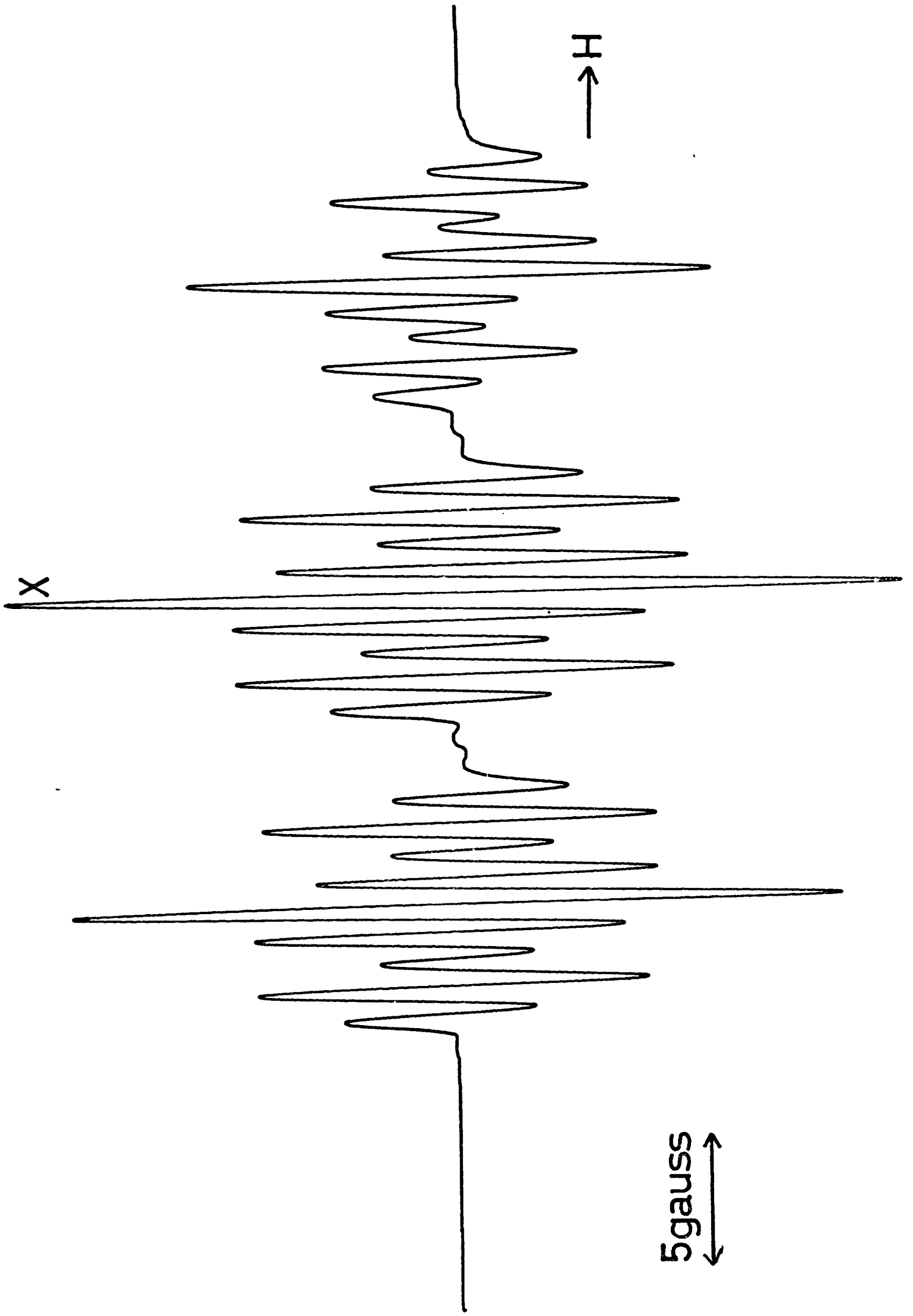
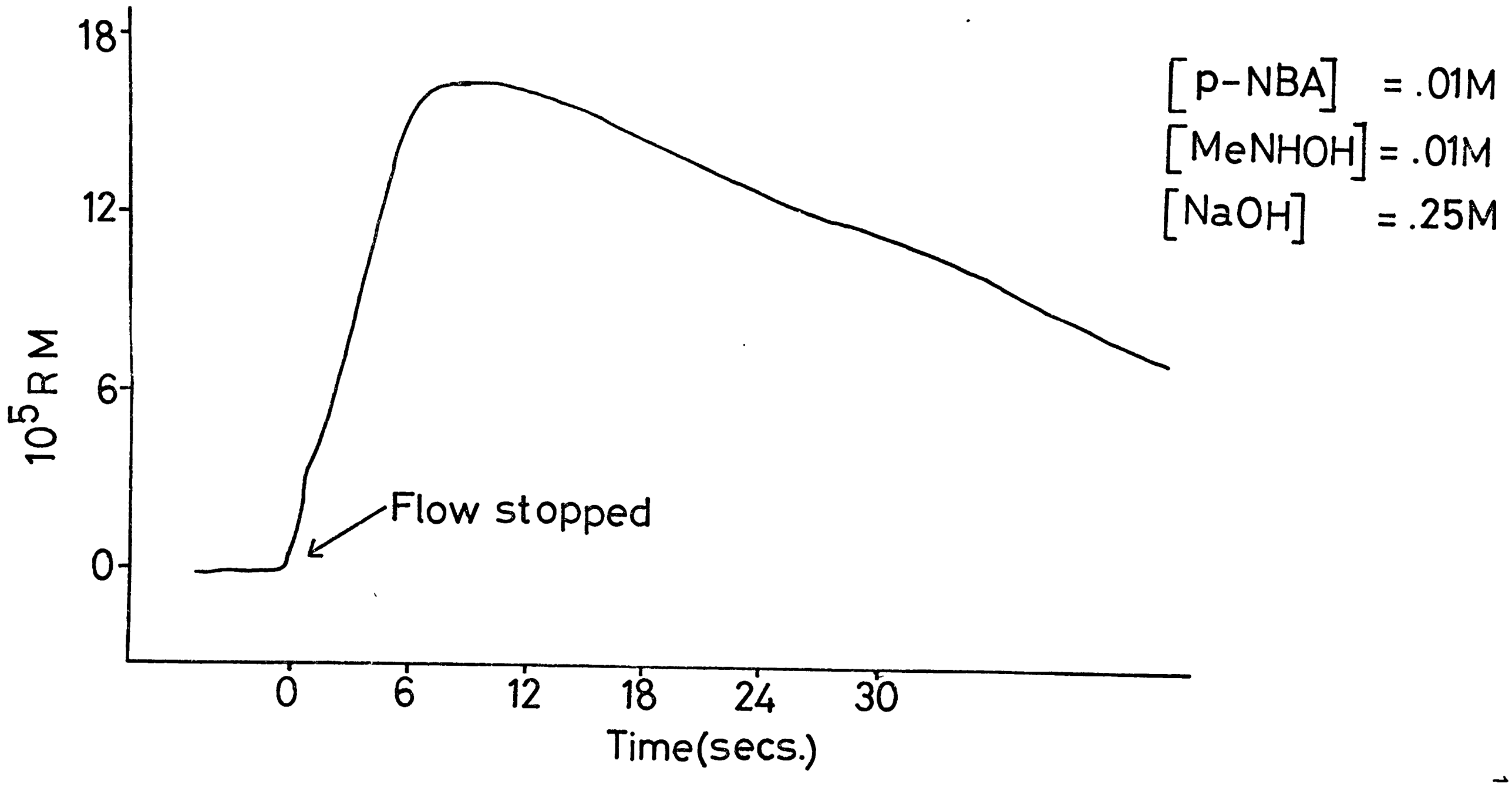


Fig. 6. 6 E.s.r. spectrum of the para-nitrobenzoate radical-dianion- X marks the spectral line used for concentration measurements.

Fig. 6. 7 Build up and decay of the e.s.r. spectrum of the para-nitrobenzoate radical-dianion.



settings. For each line, the average height as a percentage of the maximum height was calculated at varying distances from its centre. The results for the two lines are shown in Table 6.1. and graphically in (Fig. 6.8). This shows that they are identical to within 5% and hence comparison of concentrations by comparison of peak heights of the two species is valid. The normalised line shape functions for the other nitro compounds investigated also showed this agreement. Solutions of the standard were made by dissolving Frémy's salt (approx. 95% purity) in deionized water and their concentrations were estimated by iodometric titrations[14] at intervals during the calibration. The calibration that was established during the course of the experiments was that:

a) <u>For Fremy's salt</u>

Gain: 100
Modulation: 80
} pk to pk height of 100 mms obtained in a solution $1.82 \pm .01 \times 10^{-5}$ molar.

b) <u>For p-nitrobenzoic acid radical dianion</u>.

Gain: 100
Modulation: 80
} pk to pk height of 100 mms was obtained in a solution $7.28 \pm .04 \times 10^{-5}$ molar.

The modulation setting was kept constant throughout all experiments and the gain setting varied linearly with concentration.

The same Varian aqueous sample cell was used throughout and all measurements were made at room temperature ($23 \pm 1^{\circ}$).

TABLE 6.1

Frémy's salt

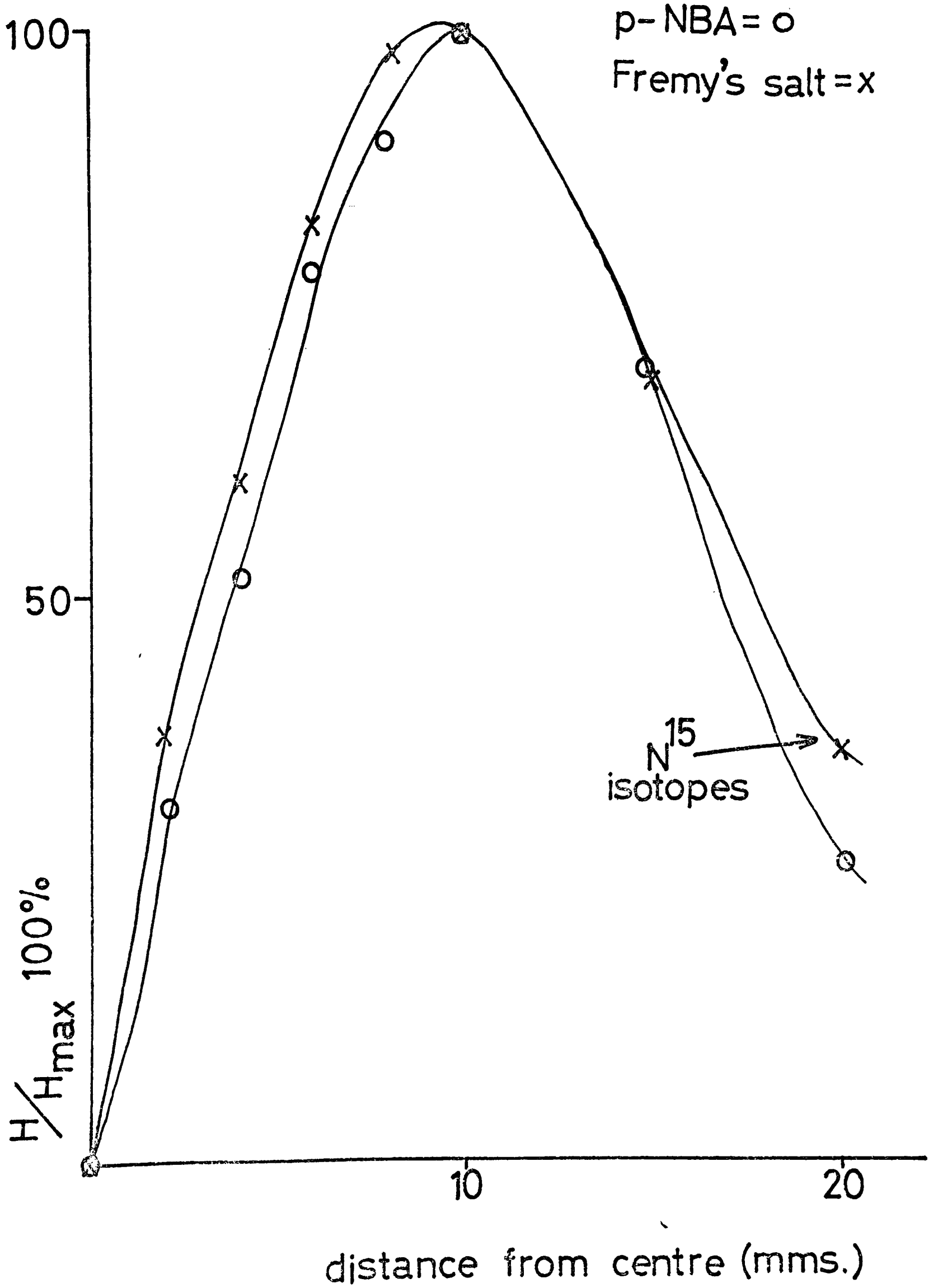
mms from centre	Height (mms)	mean H.	$^{H}/_{H\ max}$ X 100%
0	0;0	0	0
± 2	16;20	18	37.7
± 4	29.5;34.5	32	60.3
± 6	40.5;47.5	44	83
± 8	47;56	51.5	97.3
± 10	51;55	53	100
± 15	39;33	36	68
± 20	22;16	19	36

p-Nitrobenzoic acid radical-dianion

0	0;0	0	0
± 2	10;12	11	30.6
± 4	15;22	18.5	51.2
± 6	28;29	28.5	79
± 8	32;33	32.5	90
±10	33;39	36	100
±15	24;26	25	70
±20	9.3;9.5	9.4	26

Fig.6.8

The normalized line shape functions for lines from the radical from Fremy's salt and the para-nitrobenzoate radical-dianion.



C. Product studies

1. Nitroso compounds as intermediates.

In the reaction between a nitro compound and a hydroxylamine the corresponding nitroso compound is predicted as an intermediate (Chapter 5). In order to detect this nitroso intermediate and confirm the prediction, the following work was carried out. Potassium ferricyanide reacts with nitrosobenzene with displacement of a cyanide ion:[151]

$$K_4Fe(CN)_6 + PhNO \longrightarrow K_3Fe(CN)_5ONPh + KCN$$

The formation of similar complexes from penta-cyanoamino ferroates is particularly easy, and since the products are intensly coloured, their formation has been adapted to the qualitative detection of nitroso compounds.[124] Finely powdered sodium nitroprusside was covered with four times its weight of .880 ammonia and allowed to stand in ice for twenty-four hours. The solution was then diluted with ethanol and the yellow solid filtered off, washed with ethanol and dried.

A 1% solution of this reagent (sodium pentacyanoamino ferroate.) was made up in 2N sodium hydroxide and added to:

1) Nitrobenzene + methylhydroxylamine in 50% aqueous ethanol containing .25M sodium hydroxide.

2) p-Nitrobenzoic acid + methylhydroxylamine in 50% aqueous ethanol containing .25M sodium hydroxide.

According to the literature[124] nitrosobenzene if produced in (1) should give an intense purple colour after several minutes. The p-nitrosobenzoic acid predicted in reaction (2) should give a dark green complex.

Neither reaction gave a positive result so it was only possible to conclude that -

a) the nitroso derivative was not formed as an intermediate

or

b) that if formed it did not remain in solution long enough to form an intensely colured complex with the pentacyanoamino ferroate reagent.

An alternative way of investigating the possibility of the nitroso intermediate was to compare the products obtained when the reaction with a given hydroxylamine was carried out, substituting the corresponding nitroso compound for the nitro compound under investigation. In fact it was found that the reaction between nitrosobenzene and N-benzyl hydroxylamine in 50% aqueous ethanolic alkali under nitrogen, yielded exactly the same products, according to t.l.c. analysis as did the reaction between nitrobenzene and N-benzyl hydroxylamine under the same conditions. These experiments will be described in more detail at a later stage. Assuming the formation of a nitroso compound as a short-lived intermediate in the reaction azoxy compounds, mixed azoxy compounds, azo compounds and mixed azo compounds seemed to be likely reaction products.[118] Consequently the syntheses of a number of these were carried out for comparison with reaction products obtained.

1.) Azoxybenzene

Recrystallised from aqueous methanol: m.p. = 36°

(Lit[138]: m.p. = 36°)

2.) Azobenzene

Recrystallised from aqueous methanol: m.p. = 66.7°

(Lit[138]: m.p. = 67-8°)

3.) p,p'Azoxydibenzoic acid[152]

p-Nitrobenzoic acid (6.4 g., 0.04 mol.), potassium hydroxide (30 g. of 85%, 0.45 mol.) and methanol (300 ml.) were refluxed in a thermostat at 80° for twenty four hours. Methanol was removed under reduced pressure, and the remaining yellow residue was stirred with water (300 ml.). The residue was filtered off and discarded. The filtrate was adjusted to pH 7 by the addition of 10% hydrochloric acid. The suspension was centrifuged and the solid redissolved in dilute ammonium hydroxide. After reprecipitation with 10% hydrochloric acid and centrifugation the solid was washed with hot ethanol and dried in air.

The yellow powder, insoluble in all except basic organic solvents, decomposed slowly c 400°.

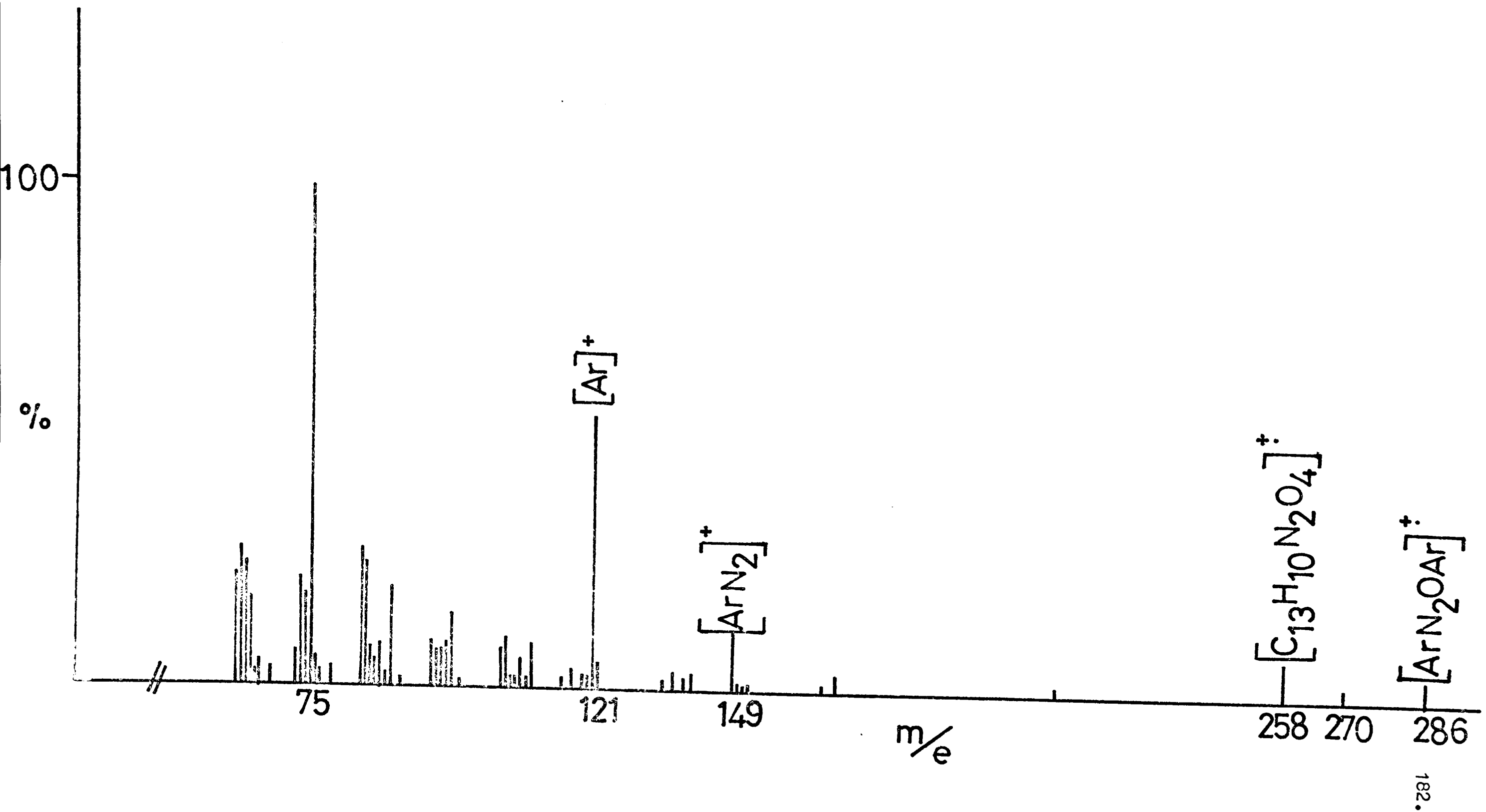
Yield:	1.8 g., ; (33%)
Analysis:	Calculated for $C_{14}H_{10}N_2O_5$:
	C = 58.74% H = 3.52% N = 9.79%
Found:	C = 58.23% H = 3.86% N = 9.41%
Ultra violet	λ_{max} = 268 mμ (ϵ = 11,600)
in 1N NaOH.	λ_{max} = 334 mμ (ϵ = 18,500)
(Lit[152]:	λ_{max} = 268 mμ (ϵ = 11,700)
	λ_{max} = 334 mμ (ϵ = 18,400))

A low resolution mass spectrum (Fig. 6.9) gave a molecular ion at $^{m}/e$ = 286 and the breakdown pattern associated with an azoxy compound.[153]

4) p,p'-Azodibenzoic acid.[152]

p-Nitrobenzoic acid (3.4 g., 0.02 mol.) in 30% aqueous sodium hydroxide (100 ml.) was reduced at 80-85° with a 10% excess of zinc dust, over that required to form the azoxy derivative (2.2 g., (90%), 0.03 mol.). When the zinc was nearly consumed the mixture was diluted with water (400 ml.) and refluxed with a 25% excess of zinc dust over that necessary to convert the azoxy compound to the hydrazo derivative (1.84 g., (90%), 0.025 mol.). When the solution became almost colourless it was allowed to cool slowly while air was bubbled through it. The resulting azo salt precipitated slowly during three days, and was collected and dissolved in water (600 ml.). Acidification of the salt solution with acetic acid precipitated the crude azo acid, which was collected and washed

Fig. 6.9 The mass spectrum of p,p'-azoxydibenzoic acid



with water and alcohol. The azo acid was then dissolved in dilute ammonia, filtered and reprecipitated with acetic acid. The mixture was made 10% in hydrochloric acid and heated with stirring for thirty minutes on a steam bath.

The product was then collected, washed with water, alcohol and ether and finally air dried.

The pinkish orange powder, insoluble in all except basic organic solvents, decomposed slowly c 400° but did not melt.

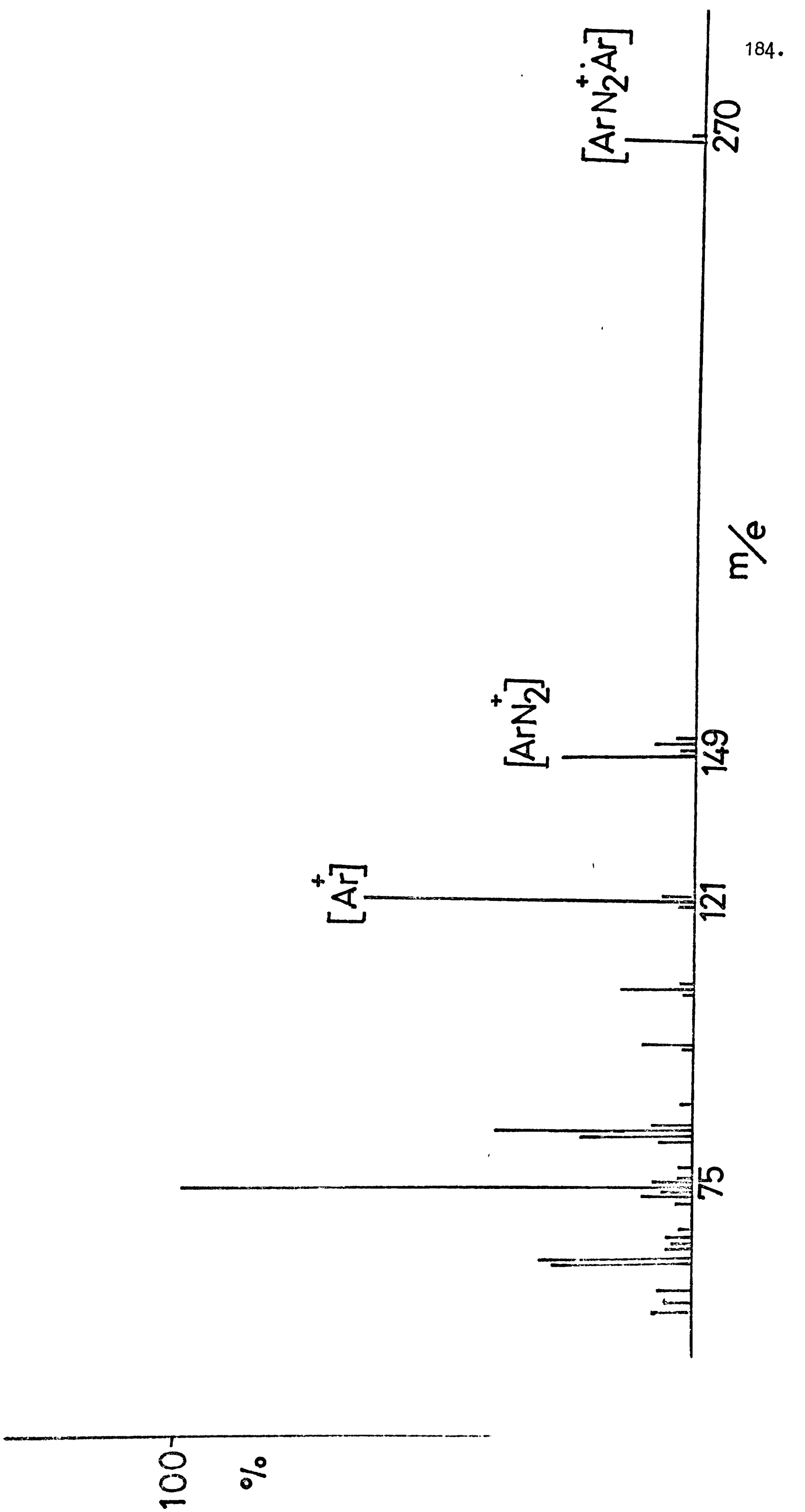
Yield:	1.16 g., (42%)
Analysis:	Calculated for $C_{14}H_{10}N_2O_4$:
	C = 62.22% N = 10.37%
Found:	C = 62.13% N = 10.11%
Ultra violet	λ_{max} 230 mμ (ε = 12,000)
in 0.1% NaOH	λ_{max} 333 mμ (ε = 25,400)
	λ_{max} = 440 mμ (ε 1,300)
(Lit[152]	λ_{max} = 225 mμ (ε 11,900)
	λ_{max} = 331 mμ (ε 25,600)
	λ_{max} = ca.430 mμ (ε 1,300))

A low resolution mass spectrum (Fig.6.10) gave a molecular ion $^{m}/_{e}$ = 270 and the expected breakdown pattern.

5) N-Methyl-N'-phenyldiazine N'-oxide[130] $CH_3N{=}\overset{+}{N}(\overset{-}{O})Ph$

To a solution of nitrosobenzene (9.5 g., 0.09 mol.) in ethanol (50 ml.), N-methylhydroxylamine (2.8 g., 0.06 mol.) was slowly added. After standing overnight ethanol was removed under reduced pressure. The mixture was then distilled under reduced pressure to give a yellow oil.

Fig. 6.10 The mass spectrum of p,p'-azodibenzoic acid.



Yield: 3.6 g., (44%); b.p. = 78°/3.5 mm.
(Lit[130]: b.p. = 78°/3.5 mm.)

The infra-red spectrum of this material corresponded to that reported in ref.131 and its ultra-violet spectrum (λ_{max} = 245 mμ, ϵ_{max} = 10,300) with that reported in ref.130 for N-methyl-N'-phenyldiazine N'-oxide. The methyl proton resonance, in carbon tetrachloride was at 6.60 τ[130].

A low resolution mass spectrum showed a molecular ion at $^{m}/e$ = 136, and the expected breakdown pattern. On standing for several days the yellow N-methyl-N'-phenyldiazine N'-oxide darkened and was shown by t.l.c., to be decomposing to give azoxybenzene and aniline, probably due to the presence of traces of moisture.

6) N-Benzyl-N'-phenyldiazine N'-oxide[130] $PhCH_2N=\overset{+}{N}(\overset{-}{O})Ph$

To a cooled solution of nitrosobenzene (9.5 g., 0.09 mol.) in ethanol (50 ml.), N-benzylhydroxylamine (7.3 g., 0.06 mol.) was added, all at once, keeping the temperature below 5°. After the initial exothermic reaction, the mixture was stirred at room temperature overnight.

On cooling the mixture, a white solid separated out, and was recrystallised from o-xylene.

Yield: 7.8 g., (41%); m.p. = 187° when put onto block at 170°.
(Lit[135]; m.p. = 187° when put onto block at 170°).

The ultra-violet spectrum of the product (λ_{max} = 255 mμ ε = 11,400) corresponded to that reported in the literature[130] for N-benzyl-N'-phenyldiazine N'-oxide.

Analysis: Calculated for $C_{13}H_{12}N_2O$:

C = 73.50% N = 13.20% H = 7.55%

Found: C = 74.03% N = 13.20% H = 7.55%

A low resolution mass spectrum showed a molecular ion at $^{m}/e = 212$ and the expected breakdown pattern.

7) N-Benzhydryl-N'-phenyldiazine N'-oxide $Ph_2CH\text{-}N{=}\overset{+}{N}(O)Ph$

To a solution of nitrosobenzene (3.2 g., 0.03 mol.) in ethanol (50 ml.), N-benzhydryl hydroxylamine (4.0 g., 0.02 mol.) was added, and the mixture stirred overnight. A small amount of a white solid was filtered off and washed with ether.

Yield: 1.0 g., (17%) m.p. = 102-3°

Analysis: Calculated for $C_{19}H_{16}N_2O$:

C = 79.17% H = 5.56% N = 9.72%

Found: C = 79.32% H = 5.51% N = 9.65%

A low resolution mass spectrum showed a weak molecular ion at $^{m}/e = 288$, and the expected breakdown pattern for N-benzhydryl-N'-phenyldiazine N'-oxide, with a very strong fragment at $^{m}/e = 166$ (Ph_2C^+).

The major reaction products were obtained by removal of the ethanol from the original filtrate. A brownish solid was obtained which was dissolved in hot cyclohexane. A whitish powder was filtered off and recrystallised from methanol. White crystals were obtained which were identified as benzophenone oxime by comparison of its infra-red spectrum with an authentic sample.

Yield: 2.1 g., (52%) m.p. = 141-2°
(Lit[138]: m. p. = 144°)

Cyclohexane was removed from the filtrate which resulted in a brownish-yellow solid. This was recrystallised from aqueous methanol to give pale yellow crystals, identified as azoxybenzene by comparison of their infra-red spectrum with that of an authentic sample.

Yield: 1.4 g., (47%) m.p. = 35-36°
(Lit[138]: m.p. = 36°)

2. Investigation of final reaction products.

The reaction under investigation was that between an aromatic nitro compound and hydroxylamine or an N-substituted hydroxylamine in 50% aqueous ethanolic alkali (pH 14, NaOH) in an atmosphere of nitrogen. The products of the reaction of each hydroxylamine with nitrobenzene and nitrosobenzene were studied in detail. In some cases substituted nitrobenzenes were studied in addition.

Product studies showed that an identical reaction occurred when a nitroso benzene was substituted for its nitro analogue and therefore only the studies involving aromatic nitro compounds will be described in detail.

a) Hydroxylamine

p-Nitrobenzoic acid (3.3 g., 0.02 mol.) and sodium hydroxide (12.8 g., 2.0 mol. free sodium hydroxide) were dissolved in 50% aqueous ethanol (100 ml.) and the resulting solution was nitrogen blown for three quarters of an hour. A solution of hydroxylamine hydrochloride (6.95 g., 0.1 mol.) in 50% aqueous ethanol (100 ml.) was nitrogen blown for three quarters of an hour. The two solutions were then mixed and stirred under an atmosphere of nitrogen for half an hour. An exothermic reaction took place initially, with some effervescence, and the solution gradually darkened.

The reaction was quenched by acidification with 10% hydrochloric acid. The ethanol was removed under reduced pressure and the resulting aqueous solution extracted with ether (2 x 100 ml.). The ethereal extract was dried over sodium sulphate and the ether removed.

The resulting orange-brown solid showed a major product, a minor product and traces of starting material, when examined by t.l.c. - Kieselgel H.F. 254 eluted with benzene : chloroform : methanol, 1 : 1 : 2 mixture.

The solid was recrystallised from aqueous ethanol (3 : 1) to give a creamy-white powder - the major product.

m.p. = 178°

N.M.R. on this solid in dioxan showed the presence of an AB quartet 1.79, 1.93, 2.70, 2.84 τ of an azide.

The infra-red spectrum showed a strong band at 2060 cm.$^{-1}$, characteristic of azides.

The solid was identified as p-azidobenzoic acid.

(Lit[154] : m.p. = 179°)

Yield: 1.78 g., (56%)

It was attempted to isolate the minor product of the reaction by an investigation of the pK_a values of the various components of the reaction mixture.

The reaction was repeated and a potentiometric titration was carried out on a small sample of the aqueous, slightly alkaline solution of reaction products. The pK_a of the major component p-azidobenzoic acid - was ca. 5.0., and that of the minor component ca. 2.0. Traces of the original p-nitrobenzoic acid (pK_a = 3.44)[155] did not show up during the titration. On the basis of these results, fractional precipitation was attempted to isolate the minor reaction product. The aqueous reaction mixture was adjusted to pH 4.5 by the addition of 10% hydrochloric acid. The pale yellow precipitate was extracted with ether (2 x 100 ml.), dried over sodium sulphate, and the solvent removed.

Recrystallisation from aqueous ethanol (3:1) gave a creamy-white powder

Yield: 1.70 g., m.p. = 179° (53%)

(p-azidobenzoic acid - (Lit[154]: m.p. = 179°))

The pH of the aqueous solution was then adjusted to 3.0 and the slight precipitate formed extracted with ether, dried over sodium sulphate and the solvent (2 x 50 ml.) removed.

Recrystallisation from water gave a small amount of pale yellow crystals.

Yield: 35 g., (10%); m.p. = 240-2°

(p-nitrobenzoic acid - (Lit[138]: m.p. = 241.5°))

The remainder of the aqueous layer was acidified to a final pH of < 1.5. The yellow precipitate formed was difficult to dissolve in ether, but was extracted (5 x 100 ml.), dried over sodium sulphate and the solvent removed.

The yellow powder was insoluble in all except basic organic solvents and did not melt, but began to decompose ca.240°.

A low resolution mass spectrum showed a strong ion at $^{m}/e$=151, attributed to the molecular ion of p-nitrosobenzoic acid. A weak ion at $^{m}/e$ = 167 was attributed to traces of p-nitrobenzoic acid.

Yield: .9 g. (30%)

(p-nitrosobenzoic acid - Lit[148]: decomposes above 250°)

The reaction of hydroxylamine with nitrobenzene was not carried out because:

i) the reaction pattern of hydroxylamine with an aromatic nitro compound had been shown clearly using p-nitrobenzoic acid and

ii) possible dangers in attempts to isolate the expected reaction product - phenyl azide.

b) N-Methylhydroxylamine

i) Nitrobenzene

Nitrobenzene (6.15 g., 0.05 mol.), sodium hydroxide (6 g., 0.10 mol. free sodium hydroxide) and 50% aqueous ethanol (100 ml.) were mixed together and the resulting solution nitrogen blown for three quarters of an hour. N-methylhydroxylamine hydrochloride (4.2 g., 0.05 mol.) in 50% aqueous ethanol (100 ml.) was nitrogen blown for three quarters of an hour. The two solutions were mixed and stirred overnight at room temperature in an atmosphere of nitrogen.

A dark red colour developed very quickly and glistening crystals gradually formed on the surface of the reaction mixture. The ethanol was removed and the remaining oily aqueous mixture extracted with ether (2 x 100 ml.). The red ethereal extract was shown by t.l.c. - Kieselgel H.F. 254 eluted with benzene, to contain a major red product, the mixed azoxy compound (N-methyl-N'-phenyldiazine N'-oxide), azoxy benzene and traces of aniline - the latter probably formed by the decomposition of the mixed azoxy compound. After drying over magnesium sulphate and evaporation of the ethereal extract the residue was taken up in benzene and chromatographed on a column of silica gel M60, eluting with benzene. The central red band was isolated (200 ml.)

and shown by t.l.c. to contain only the major red product. After drying over magnesium sulphate and removal of solvent moist red crystals were obtained. These were taken up in a small amount of benzene:petrol, 1:1, and the chromatographic procedure repeated using this solvent mixture as eluent.

Small traces of impurities remained on the column after the major red band had been eluted. This was dried over magnesium sulphate and the solvent removed to give red needles with a violet reflex.

Yield: 1.2 g., m.p. = 119-120°

Analysis: Found: C = 69.32% H = 5.34% N = 25.10%

Calculated for $C_{13}H_{12}N_4$:

C = 69.64% H = 5.36% N = 25.00%.

A low resolution mass spectrum showed a molecular ion at $^{m}/e$ = 224, confirming the molecular formula derived from the results of analysis. The ultra violet spectrum in ethanol showed:

λ_{max} = 260 mμ (ϵ = 13,000)

λ_{max} = 285 mμ (ϵ = 7,400)

λ_{max} = 420 mμ (ϵ = 31,000)

(ϵ values are calculated assuming a molecular weight of 224 as determined by analysis and mass spectrometry). After a literature search[132] the above properties were found to be consistent with 1,2-diphenyl formazan which was then synthesized by an independant route. The same physical constants were observed for the synthesized sample and a mixed melting point confirmed the identification.

The formation of 1.2 g., of 1,2-diphenylformazan represents a yield of 21%.

(Lit[132]: m.p. = 119-120°)

All the fractions not containing the major product from the reaction, obtained in the first chromatographic separation were combined together. T.l.c. showed this combined fraction to contain azoxybenzene, N-methyl-N'-phenyldiazine N'-oxide and traces of aniline.

Chromatography of this fraction on a column of silica gel M60, eluting with a chloroform/benzene, 1:3, mixture, gave two main fractions.

The first (200 ml.) was dried over magnesium sulphate and the solvent removed. A yellow crystalline solid was obtained.

Yield: 1.2 g., : m.p. = 34-36°

This was identified as azoxybenzene by comparison of its infra-red spectrum with that of an authentic sample.

(Lit[138]: m.p. = 36°)

1.2 g., of azoxybenzene represents a yield of 26%. The second main fraction (100 ml.) was dried over magnesium sulphate and the solvent removed. A dark yellow oil was obtained.

Yield: 0.5 g.,

This was identified as N-methyl-N'-phenyldiazine N'-oxide by a low resolution mass spectrum which showed a molecular ion at $^{m}/e$ = 136. As with the synthesized sample of this compound decomposition to aniline and azoxybenzene could be detected in the mass spectrum.

A yield of 7% is represented by the isolation of 0.5 g., of N-methyl-N'-phenyldiazine N'-oxide.

ii)p-Nitrobenzoic acid

p-Nitrobenzoic acid (3.34 g., 0.02 mol.), sodium hydroxide (9.6 g., 0.2 mol. free sodium hydroxide) and 50% aqueous ethanol were mixed together and the resulting solution nitrogen blown for three quarters of an hour.

N-methyl hydroxylamine hydrochloride (1.67 g., 0.02 mol.) in 50% aqueous ethanol (100 ml.) was nitrogen blown for three quarters of an hour. The two solutions were then mixed and stirred overnight at room temperature in an atmosphere of nitrogen.

A dark red colour developed. The reaction was quenched by acidification with 10% hydrochloric acid when a dark red precipitate was formed. After removal of ethanol the aqueous solution was extracted with ether (3 x 100 ml.). Not all of the precipitated material extracted into the ethereal layer. That which did gave a red solution. This was dried over magnesium sulphate and the solvent removed. A red solid was obtained which was sparingly soluble in ether and insoluble in all but basic organic solvents. Attempts were made to purify this solid by investigating possibilities for chromatography, but the major red component remained inert to t.l.c. with all combinations of support materials and eluents. Qualitatively the red material appeared to be a formazan. On oxidation, by shaking with lead tetra-acetate in chloroform, the red solution of the suspected formazan was completely decolourised. This could be interpreted as the formation of a colourless tetrazolium salt. A low resolution mass spectrum on the red solid produced a very complex spectrum, which

included a peak at $^{m}/e$ = 312, which could be attributed to the molecular ion of the predicted formazan.

No further investigations were carried out on this material.

The insoluble material that had remained in aqueous solution after ether extraction of the red solid, was filtered off. It was dissolved in dilute ammonia and any insoluble matter filtered off. The filtrate was acidified with 10% hydrochloric acid. The yellow powder precipitated was filtered off and dried. It was insoluble in all except basic organic solvents and decomposed slowly ca.400°.

A low resolution mass spectrum showed a molecular ion at $^{m}/e$ = 286, and the breakdown pattern associated with pp'-azoxydibenzoic acid. Comparison of the infra red spectrum of this yellow powder with that of an authentic sample of pp'-azoxydibenzoic acid confirmed this identification.

Yield: 0.6 g., : (21%)

No other compound could be isolated and positively identified from the reaction mixture.

c) N-Benzylhydroxylamine

i) Nitrobenzene

Nitrobenzene (3.0 g., 0.024 mol.), sodium hydroxide (4 g., 0.1 mol.) and 50% aqueous ethanol (100 ml.) were mixed together and the resulting solution nitrogen blown for three quarters of an hour. N-Benzylhydroxylamine (3.0 g., 0.024 mol.) in 50% aqueous ethanol (100 ml.) was nitrogen blown for three quarters of an hour. The two solutions were then mixed and stirred at room temperature in

an atmosphere of nitrogen for forty eight hours. Initially a yellow colour developed which darkened and became deep red after several hours, when a dark glistening solid was filtered off. T.l.c. (Kieselgel H.F. 254 - eluted with petrol:benzene, 1:1 mixture) showed the presence of traces of N-benzylhydroxylamine, benzaldoxime, and azoxybenzene in addition to a major red component. The solid was taken up in 60-80° petrol and chromatographed on a column of silica gel M60, eluting initially with 60-80° petrol, changing gradually to a 1:1 mixture of petrol:benzene. The first four fractions (200 ml.) were shown by t.l.c. to contain the major red product only. On drying over magnesium sulphate and removal of solvent, recrystallisation from 30-40° petrol gave red leaflets with a green reflex.

Yield: 1.2 g., : m.p. = 173°

Analysis: Found: C = 75.76% H = 5.34% N = 18.77%

Calculated for $C_{19}H_{16}N_4$ (M = 300) :

C = 76.00% H = 5.33% N = 18.67%

A low resolution mass spectrum showed a molecular ion at $^m/e$ = 300, confirming the molecular formula derived from the results of analysis. The infra red spectrum of the compound was recorded (Fig.6.11).

The ultra violet spectrum in benzene showed:

λ_{max} = 290 mμ (ε = 10,000)

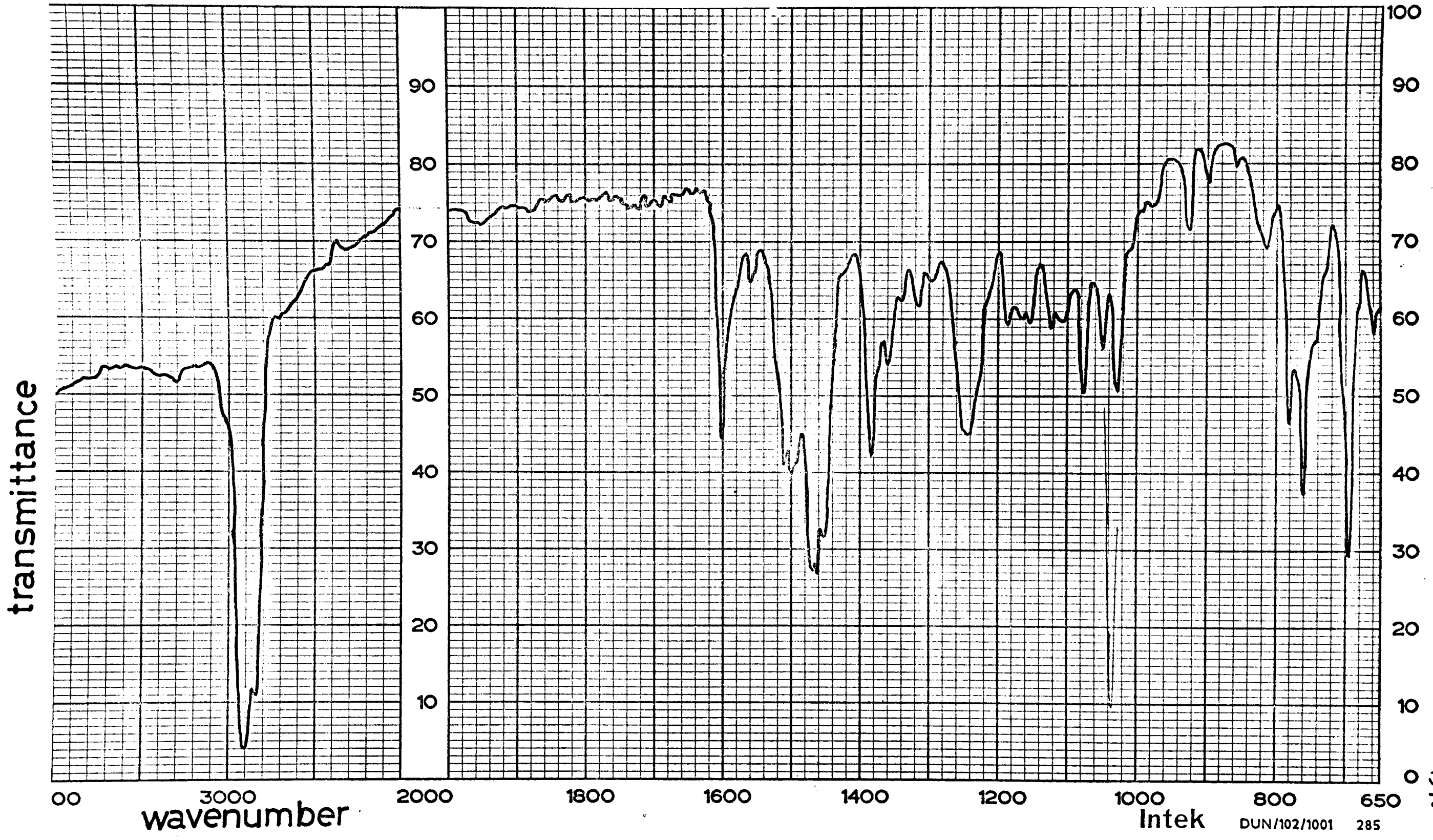
λ_{max} = 405 mμ (ε = 30,800)

On standing in the benzene solution the red colour faded leaving a yellow solution which had:

λ_{max} = 300 mμ (ε = 21,800)

λ_{max} = 500 mμ (ε = 16,100)

Fig. 6.11 The infra-red spectrum of 1,3,5-triphenyl formazan (nujol).



(ε values are calculated assuming a molecular weight of 300 as determined by analysis and mass spectrometry).

From the literature[132] the product appeared to resemble 1,3,5-triphenylformazan, which was later synthesized by an independant route. The same physical constants were observed for the synthesized sample and a mixed melting point confirmed this identification. The formation of 1.2 g., of 1,3,5-triphenylformazan represents a yield of 33%.

(Lit[132]: m.p. = 173.5°)

The remaining fractions from the chromatographic separation were combined with the original filtrate and solvents were removed leaving an aqueous solution. Acidification with 10% hydrochloric acid and extraction with ether (3 x 100 ml.) removed all organic matter from the aqueous layer except the unchanged N-benzyl hydroxylamine which was retained as its hydrochloride. Evaporation of the ethereal extract, after drying over magnesium sulphate, resulted in a dark red-brown oil. T.l.c. (Kieselgel HF 254 eluted with benzene) showed traces of the formazan still to be present, together with azoxybenzene and benzaldoxime. The red-brown oil was taken up into ether and chromatographed on an alumina (H) column, eluting with ether.
The first fraction (20 ml.) contained further traces of the formazan. The second fraction (150 ml.) was collected and dried over magnesium sulphate and the solvent removed. Yellow crystals were obtained

Yield: 0.8 g., m.p. = 34-36°

This was identified as azoxybenzene by comparison of the infra-red

spectrum with that of an authentic sample. 0.8 g., of azoxybenzene represents a yield of 33%.

(Lit[138]: m.p. = 36°)

The final band (200 ml.) contained a single component. After drying over magnesium sulphate and removal of solvent, pale yellow crystals were obtained.

Yield: 1.0 g., : m.p. = 34-5°

This was identified as benzaldoxime by comparison of the infra red spectrum with that of an authentic sample.

(Lit[138]: m.p. = 35°)

A yield of 1.0 g., of benzaldoxime represents 33%. The unchanged N-benzylhydroxylamine was recovered from the aqueous acidic extract by addition of solid sodium carbonate until the solution was alkaline. The free hydroxylamine was extracted with ether (2 x 100 ml.), dried over magnesium sulphate and the solvent removed.

The whitish solid obtained was confirmed to be unchanged N-benzylhydroxylamine by comparison of its infra red spectrum with that of an authentic sample.

Yield: 0.4 g., (13%) - unchanged N-benzylhydroxylamine
m.p. = 74-76° (Lit[6]: m.p. = 75-6°)

ii) p-Nitrotoluene

p-Nitrotoluene (4.11 g., 0.03 mol.), sodium hydroxide (8 g., 0.2 mol.) and 50% aqueous ethanol (100 ml.) were mixed together and the resulting solution was nitrogen blown for three quarters of an hour. N-Benzylhydroxylamine (3.7 g., 0.03 mol.) in 50% aqueous ethanol was nitrogen blown for three quarters of an hour.

The two solutions were then mixed and stirred at room temperature for six days. Initially a yellow colour developed, which darkened gradually and after several days a dark red oil began to separate out. The ethanol was removed and the aqueous layer was extracted with ether (2 x 200 ml.). T.l.c. (Kieselgel H.F.254- eluted with benzene) showed the presence of benzaldoxime, pp!azoxyltoluene and a major dark red product. The mixture was worked up exactly as for the reaction of nitrobenzene with N-benzylhydroxylamine, with the following results. The major red product on recrystallisation from 30-40° petrol gave black needles with a green reflex.

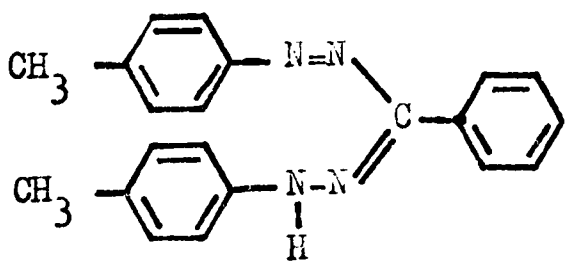
Yield: 2.0 g., m.p. = 166° (dec).

Analysis: Found C = 76.96% H = 6.17% N = 16.8%

Calculated for $C_{21}H_{20}N_4$ (M = 328):

C = 76.80% H = 6.09% N = 17.00%.

A low resolution mass spectrum showed a molecular ion at $^{m}/e$ = 328, confirming the molecular formula derived from the results of analysis. The breakdown pattern was that expected for a formazan. (See Fig.6.12). The compound was thus identified as 1,5-ditolyl 3-phenyl formazan

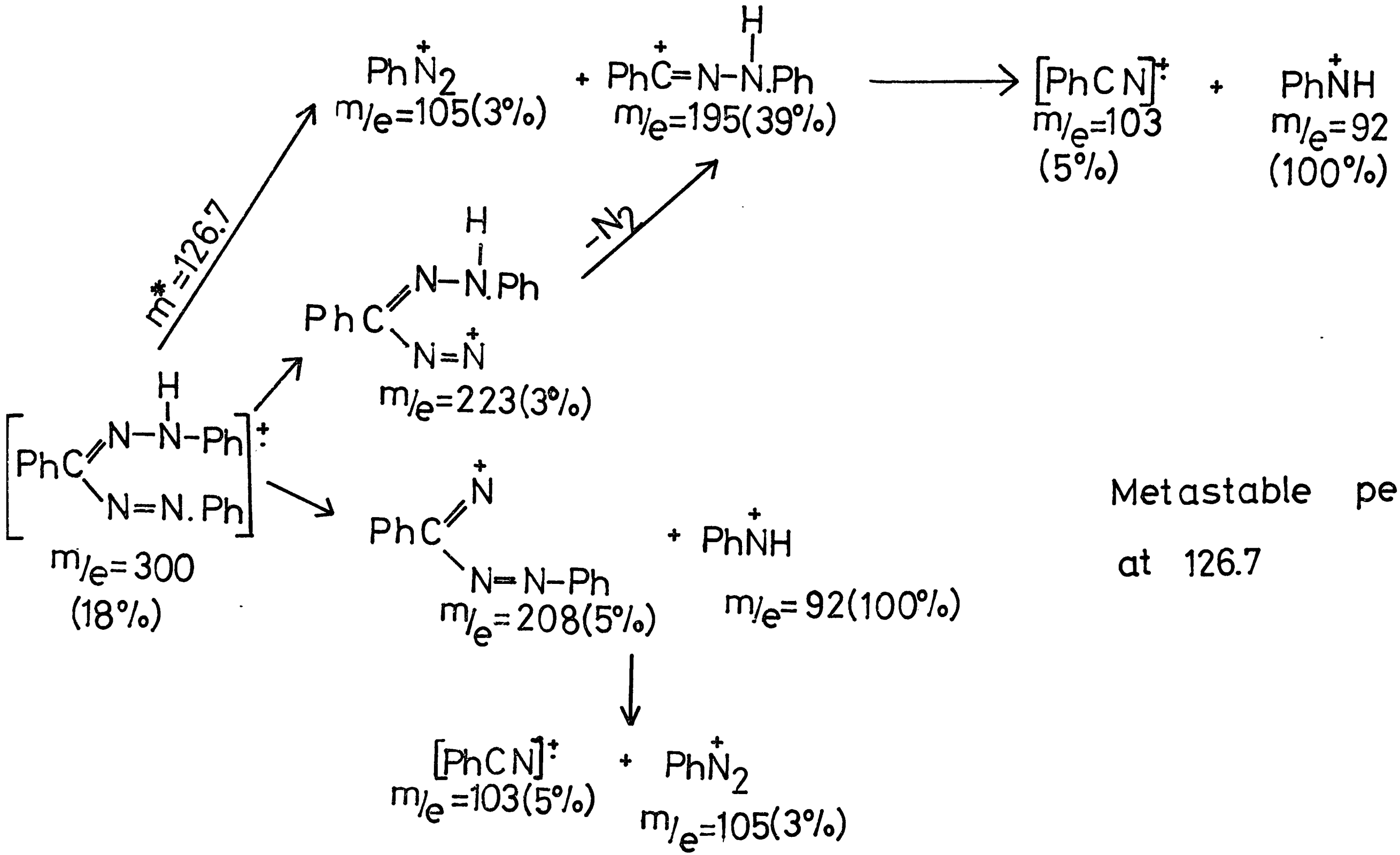


by comparison of the physical constants obtained with those reported in the literature for this compound[156].

(Lit[156]: m.p. = 166° (dec.))

2.0 g., of 1,5-ditolyl,3-phenyl formazan represents a yield of 41%.

Fig. 6.12 The fragmentation of 1,3,5-triphenylformazan on electron impact.



Metastable peak at 126.7

Benzaldoxime

Yield: 1.2 g., (34%): m.p. = 33-35°
(Lit[138]: m.p. = 35°)

p,p'-Azoxytoluene

Yield: 1.1 g., (33%): m.p. = 69-70°
(Lit[138]: m.p. = 70°)

No unchanged N-benzyl hydroxylamine was recovered after acidification of the alkaline aqueous layer as in the previous experiment.

iii) Other nitro compounds.

Product studies were attempted on the reactions of p-nitrobenzoic acid and p-nitrobenzamide with N-benzylhydroxylamine, using the procedures devised for the isolation of 1,3,5-triphenyl-formazan from the reaction involving nitrobenzene and 1,5-ditolyl, 3-phenylformazan from the reaction involving nitrotoluene. However it did not prove possible to isolate the predicted formazans from the deep red reaction mixtures. In both cases the presence of a formazan was indicated qualitatively by the decolourisation of the solutions on oxidation to the tetrazolium salts, using lead tetra-acetate in chloroform as oxidant.

d) N-Benzhydrylhydroxylamine

Nitrobenzene (2.46 g., 0.02 mol.), sodium hydroxide (8 g., 0.2mol.) and 50% aqueous ethanol (100 ml.) were mixed together and nitrogen blown for three quarters of an hour. N-Benzhydryl hydroxylamine (3.98 g., 0.02 mol.) in 50% aqueous ethanol was nitrogen blown for three quarters of an hour. The two solutions were mixed and

stirred overnight at room temperature in an atmosphere of nitrogen. A deep yellow-brown colour developed.

The ethanol was removed and the aqueous solution extracted with ether (4 x 100 ml.). The ethereal extract was dried over magnesium sulphate and the solvent removed leaving a yellow solid.

Hot cyclohexane was added to the solid when the yellow component dissolved leaving a white residue which was filtered off.

Recrystallisation of the white powder from methanol gave white crystals which were identified as benzophenone oxime by comparison of the infra-red spectrum with that of an authentic sample.

Yield: 3.2 g., (81%) : m.p. = 143-4°
(Lit[138]: m.p. = 144°)

Removal of the cyclohexane from the filtrate left a yellow solid which was recrystallised from aqueous methanol to give yellow crystals. These were identified as azoxybenzene by comparison of the infra-red spectrum with that of an authentic sample.

Yield: 1.5 g., (76%) : m.p. = 35-6°
(Lit[138]: m.p. = 36°)

No other products were detected in this reaction.

e) N-Phenylhydroxylamine

Nitrobenzene (3.7 g., 0.03 mol.), sodium hydroxide (8 g., 0.2 mol.) and 50% aqueous ethanol (100 ml.) were mixed together and the resulting solution nitrogen blown for three quarters of an hour. N-Phenylhydroxylamine (3.3 g., 0.03 mol.) in 50% aqueous ethanol (100 ml.) was nitrogen blown for 3/4 of an hour. The two solutions were mixed and stirred overnight, at room temperature, in an atmosphere of nitrogen. Oily yellow droplets formed on the surface of the solution.

Ethanol was removed and the aqueous residue was steam distilled until no more oily drops distilled over.

The aqueous distillate was extracted with ether (2 x 100 ml.) and the extract dried over magnesium sulphate, and the solvent removed to give a colourless liquid. The unchanged nitrobenzene recovered was identified by comparison of the infra-red spectrum with that of an authentic sample.

Yield: 0.7 g., (19%).

The residue after the steam distillation was extracted with ether (4 x 100 ml.), dried over magnesium sulphate and the solvent removed.

A yellow solid obtained which was recrystallised from aqueous methanol to give pale yellow crystals. These were identified as azoxybenzene by comparison of their infra-red spectrum with that of an authentic sample.

Yield: 4.5 g., (76%) : m.p. = 34.5°
(Lit[138]: m.p. = 36°)

No other products were detected in this reaction.

f) N,N-Dibenzylhydroxylamine.

Nitrobenzene (6.15 g., 0.05 mol.), sodium hydroxide (8 g., 0.2 mol.) and 50% aqueous ethanol (10 ml.) were mixed together and the resulting solution was nitrogen blown for three quarters of an hour. N,N-Dibenzylhydroxylamine (10.65 g., 0.05 mol.) in 50% aqueous ethanol (100 ml.) was nitrogen blown for three quarters of an hour. The two solutions were mixed, and the heterogeneous reaction mixture was stirred, overnight at room temperature,

in an atmosphere of nitrogen. No colour change was observed. Ethanol was removed and the aqueous solution acidified with 10% hydrochloric acid. The acidic solution was extracted with ether (3 x 100 ml.). The extract was dried over magnesium sulphate and the solvent removed.

The colourless liquid obtained was shown to be unchanged nitrobenzene by comparison of its infra-red spectrum with that of an authentic sample.

Yield: 5.8 g., (94%)

The acidic aqueous extract was made alkaline with solid sodium carbonate and extracted with ether (4 x 200 ml.). The ethereal extract was dried over magnesium sulphate and solvent removed. The white crystals obtained were identified as unchanged N,N-dibenzylhydroxylamine by comparison of the infra-red spectrum with that of an authentic sample.

Yield: 10.2 g., (96%). m.p. = 121-3°
(Lit[138]: m.p. = 123°)

These results infer that no reaction has occurred. The oxidation of NN-dibenzylhydroxylamine would result in the formation of benzaldehyde and N-benzyl isobenzaldoxime. The former could not be detected by a dinitrophenylhydrazine test on the original reaction mixture, and the latter was not observed during the t.l.c. (Kieselgel HF 254 - eluted with ether) of either the acidic or basic ethereal extracts.

Azoxybenzene would be expected by the reduction of nitrobenzene and this was not detected.

3. Effect of base on N-Benzyl-N'-phenyldiazine N'-oxide.

N-Benzyl N'-phenyldiazine N'-oxide was predicted as intermediate in the reaction of nitrobenzene with N-benzylhydroxylamine to form 1,3,5-triphenylformazan. (3.0 g., 0.014 mol.) N-Benzyl-N'-phenyldiazine N'-oxide, sodium hydroxide (4 g., 0.1 mol.) and 50% aqueous ethanol (100 ml.) were heated on a water bath to give a homogeneous mixture, which was then nitrogen blown for three quarters of an hour. The mixture was left to stir, in an atmosphere of nitrogen and at room temperature, overnight. A pink colour developed which was shown by t.l.c. to be 1,3,5-triphenylformazan. However overnight the majority of the starting material (2.6 g., 87%) had come out of solution. Thus if this mixed azoxy compound is an intermediate in the proposed reaction, it is not allowed to accumulate but removed by a fast further reaction. Otherwise on accumulation it would precipitate out of solution and only very slowly be attacked by base, as in the above experiment. This may account for the fact that no N-benzyl-N'-phenyldiazine N'-oxide was isolated in the reaction between nitrobenzene and N-benzylhydroxylamine.

4. Synthesis of formazans.

a) 1,5-Diphenylformazan.

1,5-Diphenyl formazan was synthesised according to Pechmann.[133]

Several attempts were made at this preparation before it was successful,as if care was not taken tarry residues were obtained. A solution of benzene diazonium acetate (0.05 mol.) was prepared from the following: aniline (4.6 g., 0.05 mol.), hydrochloric acid (11.4 g., S.G. = 1.18), sodium acetate (10 g.) and sodium nitrite (3.6 g.,) in the necessary amount of water. This solution was cooled in ice and added quickly to a cooled aqueous solution of malonic acid (5.2 g., 0.05 mol.) and sodium acetate (10 g., 0.12 mol.).

The liquid became red and turbid. Gradually red crystals began to form on the surface. The reaction mixture was left overnight in the refrigerator. The following day the red crystals were filtered off and dried in a desiccator. They were then dissolved in a small amount of methanol with gentle warming, and as the solution cooled to room temperature water was added dropwise, with shaking, causing turbidity. After cooling in ice, the precipitate that had collected was filtered off and dried in a desiccator. It was then dissolved in benzene, reprecipitated with 60-80° petrol, and finally recrystallised twice from a small amount of methanol, and dried under vacuum at 50°. Red needles with a violet reflex were obtained.

Yield: 1.4 g., (25%) m.p. = 119-120°
(Lit[133]: m.p. = 119-120°)

Analysis: Calculated for $C_{13}H_{12}N_4$

C = 69.64% H = 5.36% N = 25.00%

Found: C = 69.65% H - 5.17% N = 24.81%

A low resolution mass spectrum showed a molecular ion at $^{m}/e = 224$ and the expected breakdown pattern.

The ultra-violet spectrum in ethanol showed[157]:

λ_{max} = 260 mμ (ε =13,000)

λ_{max} = 285 mμ (ε = 7,400)

λ_{max} = 420 mμ (ε = 31,000)

b) 1,3,5-Triphenylformazan.

It was attempted to synthesize 1,3,5-triphenylformazan according to Pinner[158], by the reaction of benzaldehyde phenylhydrazone with benzene diazonium chloride. However this proved unsuccessful.

The method of Bamberger[134] by the reaction of benzamidoxime with phenylhydrazine in acetic acid proved to be successful. Benzamidoxime was prepared according to the method of Fuller and King[159].

Benzonitrile (10.3 g., 0. 1 mol.), sodium carbonate (10.6 g., 0.1 mol.) and hydroxylamine hydrochloride (8.35 g., 0.1 mol.) were refluxed for 18 hours in aqueous ethanol, enough ethanol being added to maintain a clear solution. After cooling the ethanol was removed and the aqueous residue was extracted with ether (2 x 100 ml.).

The ethereal extract was shaken with excess of 24% hydrobromic acid. After removal of ether and concentration of the aqueous solution, benzamidoxime hydrobromide crystallised out as pale brown prisms. The product was recrystallised from ethanol/ether to give white prisms.

Yield: 14.1 g., (65%) : m.p. = 180°
(Lit[159]: m.p. = 183°)

After purification via the hydrobromide, as described above, the free benzamidoxime was prepared by making an aqueous solution of the hydrobromide alkaline with solid sodium carbonate and extraction with ether. The ethereal extract was dried over magnesium sulphate and the solvent removed to give the free benzamidoxime.

Benzamidoxime (6 g., 0.045 mol.), phenylhydrazine (6 g., 0.05 mol.) and 10% acetic acid (40 ml.) were heated together under reflux on a boiling water bath for one hour. The boiling liquid was filtered and the residue washed with hot water.

The red precipitate was dried in a desiccator and then recrystallised from 30-40° petrol, finally being dried under vacuum at 70°, to give red leaflets with a green reflux.

Yield: 2.3 g., (28%) : m.p. = 173°
(Lit[134]: m.p. = 173°)

Analysis: Calculated for $C_{19}H_{16}N_4$
C = 76.00% H = 5.33% N = 18.67%

Found : C = 75.80% H = 5.34% N = 18.39%

A low resolution mass spectrum showed a molecular ion at $^{m}/e = 300$.

The breakdown pattern is shown in (Fig. 6.12).

The ultra-violet[157] spectrum in benzene showed:

$$\lambda_{max} = 290\ m\mu \quad (\ \epsilon\ = 10,000)$$

$$\lambda_{max} = 405\ m\mu \quad (\ \epsilon\ = 30,900)$$

On standing in the benzene solution the red colour faded leaving a yellow solution which had:

$$\lambda_{max} = 300\ m\mu \quad (\ \epsilon\ = 21,700)$$

$$\lambda_{max} = 500\ m\mu \quad (\ \epsilon\ = 16,100)$$

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Thesis submitted for the D.Phil. degree of Oxford University

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"Electron Spin Resonance studies of some Nitrogen Free Radicals"

SUMMARY

A survey of the literature showed that nitrobenzene and related radical-anions could be obtained from a variety of electron transfer reactions. The possibility of using hydroxylamine and N-substituted hydroxylamines as electron donors to aromatic mono nitro compounds, in oxygen free, aqueous, alkaline ethanol, was investigated. Five of the seven hydroxylamine compounds investigated, hydroxylamine, N-methylhydroxylamine, N-phenylhydroxylamine, N-benzylhydroxylamine and N-benzhydrylhydroxylamine, were effective in transferring an electron to a wide range of nitro compounds, the radical-anions produced being detected by electron spin resonance spectroscopy.

The spectra of these radicals were recorded, and hyperfine splitting constants measured and compared with values in the literature. g-Values of the radicals were also measured and it was found for the nitro radical-anions containing halogen substituents that this increased - Br > Cl > F > H.

The limit of the reducing power of the hydroxylamine compounds was reached with para-nitroanisole, $E_{1/4}$ = 0.957v, para-nitrophenol not being reduced by this method.

An investigation into the mechanism of this reaction and its products then followed.

The build-up and decay of the nitro radical-anions were followed using stopped flow techniques. The general pattern which emerged was

that of a very rapid build-up of the radical, reaching the maximum intensity within a minute of mixing the reactants, followed by a very slow decay. This is characteristic of consecutive reactions in which a stationary state intermediate is being destroyed much more rapidly than it is being produced. It was found that:

$$\text{Initial rate} \propto [OH^-]\,[ArNO_2]\,[RNHOH]$$

and that

$$[\text{Radical}]_{max} \propto [OH^-]^{\frac{1}{2}}\,[ArNO_2]^{\frac{1}{2}}\,[RNHOH]^{\frac{1}{2}},$$

and the following scheme was proposed:

$$RNHOH + OH^- \overset{K}{\rightleftharpoons} RNHO^- + H_2O$$

$$RNHO^- + ArNO_2 \xrightarrow{k_1} RNHO^{\bullet} + ArNO_2^{\bullet -}$$

$$2ArNO_2^{\bullet -} \xrightarrow{k_2} \text{products.}$$

$$2RNHO^{\bullet} \xrightarrow{\text{fast}} \text{products.}$$

This was verified by the evaluation of k_2 as a rate constant for the bimolecular disappearance of the nitro radical-anion, in a series of experiments with para-nitrobenzoic acid and a range of hydroxylamine compounds.

$$k_2 = 6.5 \times 10^2 \text{ l.mol.}^{-1} \text{ sec.}^{-1}$$

This value for k_2 is higher than literature values of rate constants for the disproportionation of nitro radical-anions. This may be due

to traces of oxygen, present in the current work, or to the fact that k_2 may not be the rate constant for a direct disproportionation reaction.

The relative rates at which the various hydroxylamines will transfer an electron was found to be:

$$MeNHOH > PhCH_2NHOH > Ph_2CHNHOH > NH_2OH$$

the sequence that would be expected from the electron releasing powers of the substituents on the nitrogen atom of the hydroxylamine group.

Using a single hydroxylamine in reaction with a range of nitro compounds an approximate value of ρ = + 3.3 was obtained for the electron transfer reaction. This indicated that a low electron density at the site of reaction in the nitro compound would be favourable i.e. the rates with the following substituents would vary:

$$p\text{-}CN > p\text{-}COO^- > p\text{-}OCH_3$$

With hydroxylamine itself, kinetic measurements were much less accurate, owing to a pseudo unimolecular gas evolution which appeared to come from the reactions:

$$2NH_2O^{\bullet} \longrightarrow (H_2NO)_2 \longrightarrow N_2 + 2H_2O$$

From the mechanism that has been proposed for the general reaction, it would be expected that nitroso compounds would be among the products. However these compounds were not isolated.

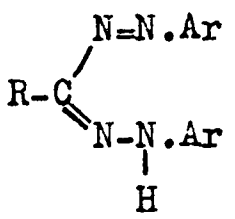
With hydroxylamine, itself, the reaction proceeded further via a diazotate and a diazonium salt to yield an azide.

From N-alkylhydroxylamines, $R_2CH.NHOH$, the intermediate aliphatic nitroso compounds in part tautomerized to the oximes, $R_2C{=}NOH$, which have been isolated.

The subsequent reactions of the aromatic nitroso compounds fall into two categories.

In the reactions involving N-benzhydryl and N-phenylhydroxylamines, the intermediate nitroso compounds derived from the original nitro compound underwent a further one electron reduction, followed by dimerisation to give an azoxy compound. In the case of N-phenylhydroxylamine this was also the fate of the $PhNO^{\bullet}$ radicals, derived from the hydroxylamine.

In the reactions involving N-alkylhydroxylamines, $R\text{-}CH_2\text{-}NHOH$, deep red products were isolated and, with difficulty, purified. These were ultimately identified as formazans (I), by comparison of a range of their physical properties with those of synthesized materials.



(I)

The mechanism proposed to account for their formation from the intermediate nitroso compounds had to satisfy the following:

1. In the reaction, variations in the nitro compound alters the Ar-group in I,

2. In the reaction, variation in the hydroxylamine compound alters the R- group in I,

3. The lack of formation of formazans with other hydroxylamines indicates that an active methylene group adjacent to the nitrogen atom in the hydroxylamine is essential.

The mechanism proposed depended upon the cross combination of nitroso radical-anions derived from both reactants to give an unsymmetrical azoxy compound, $R.CH_2N{=}N(O)Ar$. Attack by base at the active methylene group resulted in the formation of formazan (I). Evidence to support this mechanism has been gained by synthesizing the intermediate unsymmetrical azoxy compound and allowing it to react with base, with the result that traces of the predicted formazan were detected.

The work that has been described in this thesis has been published in the Journal of the Chemical Society - Section B, 1971, 2393, 2398. The titles of the papers are:
'Reactions between Aromatic Nitro-compounds and Hydroxylamines in Alkaline Solution': Part I Kinetic Studies.
Part II Product Studies.