^{15}N Nuclear Polarisation in Nitration and Related Reactions. Part 3.[1] Reactions Initiated by *ipso*-Attack in the Nitration of Amines

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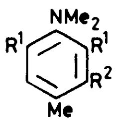
The reactions of *N,N*,4-trimethylaniline (**1a**), *N,N*,2,4,6-pentamethylaniline (**1b**), and *N,N*,3,4,-tetramethylaniline (**1c**) with nitric acid in aqueous sulphuric acid have been followed by ^{15}N n.m.r. spectroscopy using ^{15}N-labelled compounds. When the amines react with $H^{15}NO_3$ by the nitrous acid-catalysed pathway of *ipso*-attack, a strong emission signal is seen at the start of reaction for the $^{15}NO_2$ group in the *ipso*-intermediates formed. When the same reaction is carried out using the ^{15}N-labelled amines (**1a, b**) the signal for the amino group in the ^{15}N n.m.r. spectrum of the *ipso*-intermediates shows enhanced absorption. The *ipso*-intermediates from the amines (**1a, b**) undergo a nitro-group exchange reaction with nitric acid in the solvent and this can lead to either emission or enhanced absorption signals for the $^{15}NO_2$ group in the *ipso*-intermediate, depending on the direction of the exchange. The 1,3-rearrangement of the nitro group in the *ipso*-intermediate from the amine (**1a**) can also lead to either an emission or an enhanced absorption signal for the $^{15}NO_2$ group in the *N,N*,4-trimethyl-2-nitroaniline formed, depending on the conditions of reaction. The phase of the nuclear polarisation in the amino and nitro groups from *ipso*-attack, exchange, and rearrangement reactions is shown to be consistent with the partition of the radical pair $[Ar\overset{+}{N}Me_2{}^{\cdot}\ NO_2{}^{\cdot}]$ between dissociation and combination. The e.s.r. spectrum of the radical cation of the amine (**1b**) has been observed in solutions of the corresponding *ipso*-intermediate in aqueous sulphuric acid in the presence of hydrazine.

Recent work has shown that a number of methyl-substituted aromatic amines, including those of structures (**1a**—**c**), react with nitric acid in aqueous sulphuric acid by *ipso*-attack to yield intermediates of the type shown in structures (**2a**—**c**).[2,3] High concentrations of such intermediates can be formed and, in some examples, salts can be isolated.[4] There appear to be two mechanisms of *ipso*-attack in these systems: one involves the direct reaction of the protonated amine with the nitronium ion;[3] the other requires the presence of nitrous acid and appears to involve the intermediate formation of the cation radical of the amine.[2] The *ipso*-intermediates can undergo reaction by rearrangement [*e.g.* (**2a**) ⟶ (**3**)],[2,5] addition of water,[4] or displacement of a substituent by a nucleophile.[4] Many of these reactions are similar to those seen following *ipso*-attack in the nitration of substituted phenols.[6]

Other studies have shown that the nitrous acid-catalysed nitration of *N,N*-dimethylaniline,[7] mesitylene,[8] and *p*-nitrophenol[1] by $H^{15}NO_3$ gives rise to nuclear polarisation of the ^{15}N atoms in the introduced nitro groups. This provides further evidence for radical intermediates in these reactions. There is also evidence for ^{15}N nuclear polarisation in the rearrangement of nitro-amines[9] and in a nitro group rearrangement during the nitration of nitrophenol.[1]

The present work brings these two lines of investigation together, for it is concerned with the ^{15}N nuclear polarisation in three types of reaction related to *ipso*-attack in the nitration of aromatic amines. The reactions are (*a*) the formation of *ipso*-intermediates, (*b*) nitro-group exchange in *ipso*-intermediates, and (*c*) the 1,3-rearrangement of nitro groups following *ipso*-attack. The experimental results on these topics are presented separately but the mechanistic implications are considered together.

Formation of ipso-*Intermediates.*—The present work involves three of the amines studied previously (**1a**—**c**) and the corresponding *ipso*-intermediates (**2a**—**c**), together with the related



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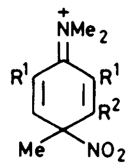

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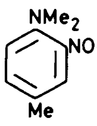


(3)

a ; $R^1 = R^2 = H$
b ; $R^1 = Me$, $R^2 = H$
c ; $R^1 = H$, $R^2 = Me$

compounds labelled with ^{15}N in the nitro group and/or the amino group.

The reaction of the amine (**1b**) with nitric acid in aqueous sulphuric acid is known to give the *ipso*-intermediate (**2b**), and the ^{1}H and ^{13}C spectra for this intermediate have been reported.[2] In the present work, this *ipso*-intermediate has been generated by the reaction of the amine with phenyltrimethylammonium nitrate in aqueous sulphuric acid because, in some of the runs, it was desirable to have the (^{15}N)phenyltrimethylammonium ion present as a standard.

The reaction was studied first using ^{1}H n.m.r. spectroscopy under conditions giving the nitrous acid-catalysed mechanism of *ipso*-attack. In sulphuric acid (70.7%; *d* 1.621) at 5 °C, the amine (**1b**) (0.21 mol kg^{-1}) reacts with phenyltrimethylammonium nitrate (0.25 mol kg^{-1}) in the presence of sodium nitrite (0.01 mol kg^{-1}) to give 50% conversion into the *ipso*-intermediate (**2b**) in *ca.* 12 min and almost complete conversion into the *ipso*-intermediate in 30 min. Details of one of the kinetic runs are given in the Experimental section. These were chosen as the standard conditions for the runs using ^{15}N n.m.r. spectroscopy. The ^{1}H n.m.r. spectra of the solutions indicated that there was no significant decomposition of the *ipso*-intermediate over the 60 min following the end of reaction.

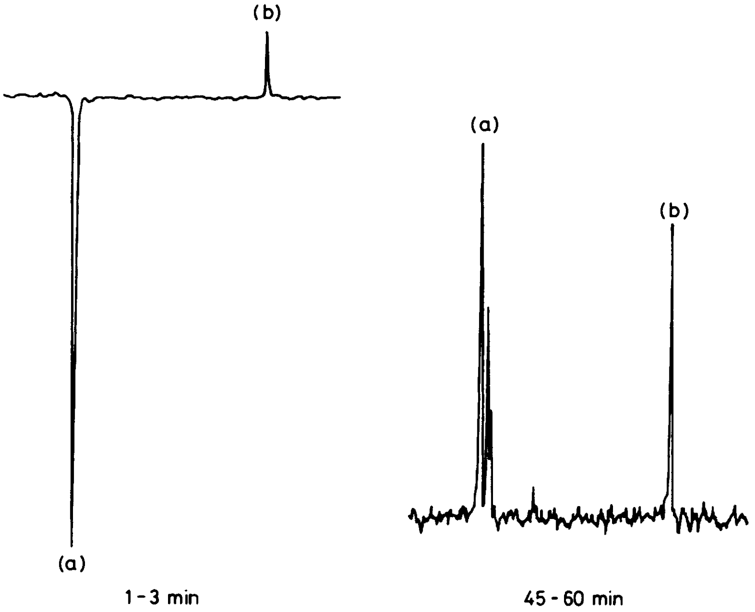


Figure 1. ^{15}N N.m.r. spectra during the reaction of the amine (**1b**) with $PhNMe_3{}^{15}NO_3$ in sulphuric acid (70.7%) at 5 °C: peak (a), $^{15}NO_2$-labelled *ipso*-intermediate (**2b**); peak (b), $H^{15}NO_3$. Number of pulses 256 (1—3 min), 2 222 (45—60 min); pulse repetition time 0.4 s; pulse angle 25°

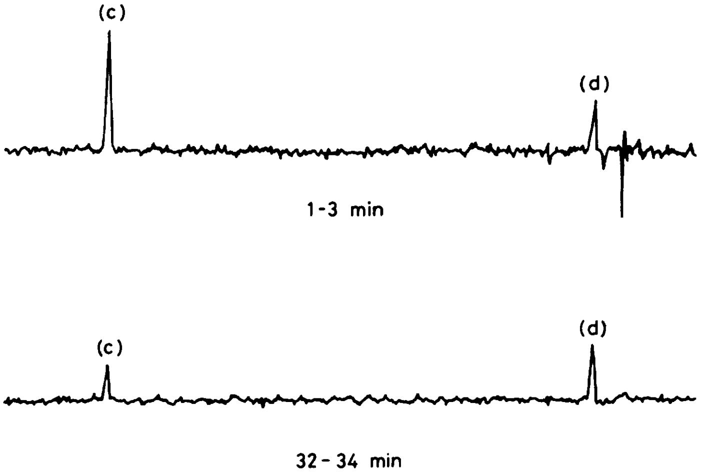


Figure 2. ^{15}N N.m.r. spectra during the reaction of the $^{15}NMe_2$-labelled amine (**1b**) with $Ph^{15}NMe_3NO_3$ in sulphuric acid (70.7%) at 5 °C: peak (c), $^{15}NMe_2$-labelled *ipso*-intermediate (**2b**); peak (d), $Ph^{15}NMe_3{}^+$. Number of pulses 40; pulse repetition time 3.4 s; pulse angle 25°

When the same reaction is carried out using $PhNMe_3{}^{15}NO_3$ and followed by ^{15}N n.m.r. spectroscopy, the signal for the ($^{15}NO_2$)-intermediate (**2b**) appears 49.5 p.p.m. downfield from that for $H^{15}NO_3$ and 333.9 p.p.m. downfield from that of the standard ($Ph^{15}NMe_3{}^+$). The signal for the *ipso*-intermediate appears first in emission (Figure 1), as might be expected from the emission signals observed in the nitrous acid-catalysed nitrations of mesitylene[8] and *p*-nitrophenol.[1] The intensity of the signal over the period 1—3 min is greater than the final intensity by a factor of 18 (the vertical scales of the two spectra in Figure 1 differ by a factor of 15). Since the ^{1}H n.m.r. spectra indicate that only about 11% reaction has occurred at the mean time (2 min) for the first spectrum, the enhancement is by a factor of *ca.* 160. After about 40 min, the conventional absorption signal is seen. The line about 1.8 p.p.m. to high field of the signal for the *ipso*-intermediate comes from the nitrosonium ion, the concentration of which may be increased through oxidative side-reactions. The weak line 0.7 p.p.m. to high field of that comes from an unidentified side-product.

This experiment was repeated using the labelled amine (2,4,6-$Me_3C_6H_2{}^{15}NMe_2$) and $Ph^{15}NMe_3NO_3$. In aqueous sulphuric acid, this amine gives a doublet in the ^{15}N n.m.r. spectrum[10] (9.5 p.p.m. upfield of the signal for $Ph^{15}NMe_3{}^+$, J 75.0 Hz), but during some of the kinetic runs this signal was ill defined, perhaps because of electron exchange between the cation radical and the amine. During reaction, the peak for the ($^{15}NMe_2$)-*ipso*-intermediate (**2b**) appears 125.3 p.p.m. to low field of the standard (Figure 2). The initial absorption is clearly enhanced, for the results in Figure 2 show that the absorption relative to the standard decreases during the kinetic run. When the extent of reaction is taken into account, the initial enhancement is seen to be a factor of *ca.* 29 but this factor decreases rapidly with time (Table 1).

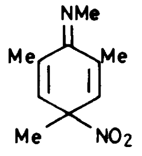
During 1 h at room temperature, or 1 week at −25 °C, the

Table 1. Relative intensities (I/I_s) of the ^{15}N n.m.r. signals for the $^{15}NMe_2$-labelled *ipso*-intermediate (**2b**) and the standard ($Ph^{15}NMe_3^+$) during the *ipso*-nitration of the ^{15}N-labelled amine (**1b**) in sulphuric acid (70.7%) at 5 °C

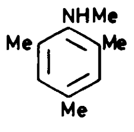
Time (min)	I/I_s	% Reaction[a]	Enhancement factor
1—3	2.09	11	29
4—6	1.36	24	8.6
8—10	1.07	39	4.1
15—17	0.93	64	2.2
23—25	0.79	82	1.5
66—68	0.66	100	1.0

[a] Interpolated from the results of a run based on the ^{1}H n.m.r. spectrum of the reaction mixture (see Experimental section).

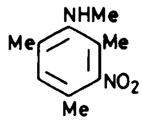
solution of the *ipso*-intermediate (**2b**) in 70.7% sulphuric acid decomposes almost completely to yield what, from the ^{1}H, ^{13}C, and ^{15}N n.m.r. spectra, appears to be the imine (**4**). Attempts to isolate this by pouring into water and extracting with methylene dichloride yielded a large number of products which, after separation by h.p.l.c., appeared from the ^{1}H n.m.r. and mass spectra to include the amines (**5**)—(**7**). The rearrangement



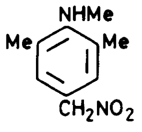
(**4**)



(**5**)



(**6**)



(**7**)

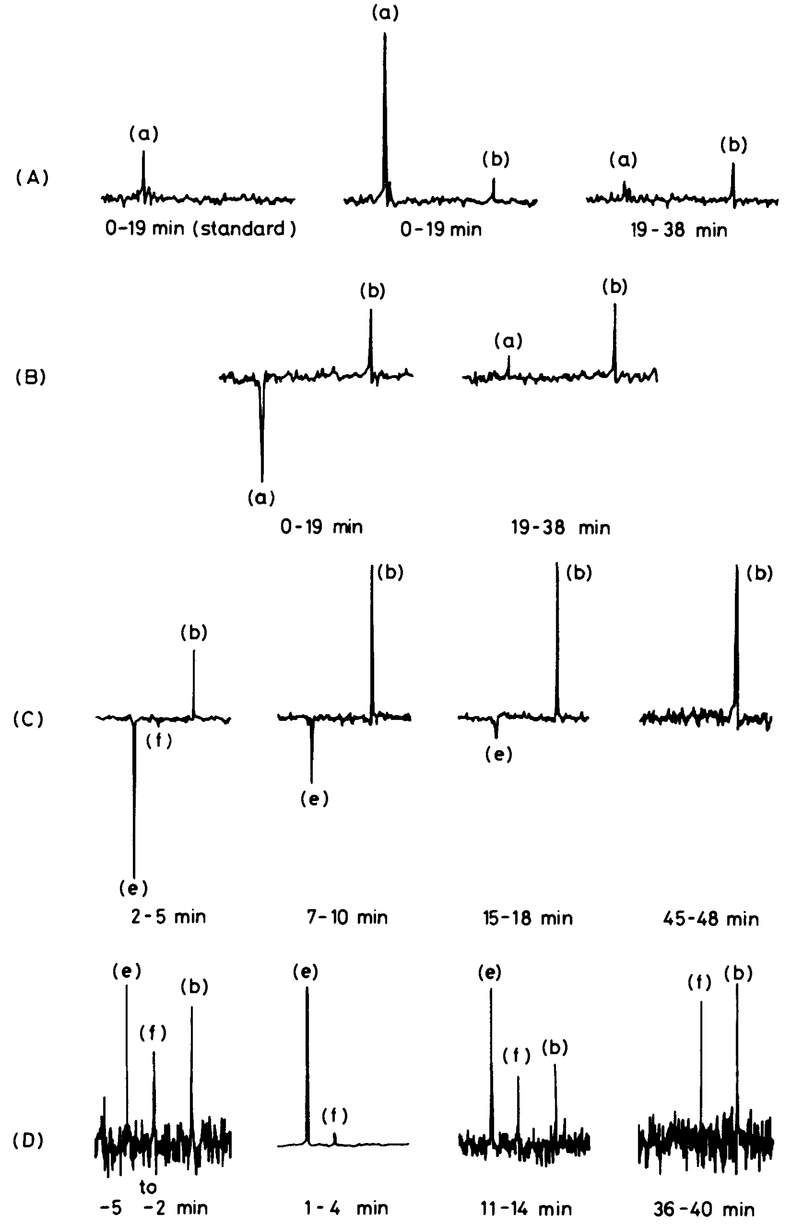


Figure 3. ^{15}N N.m.r. spectra during the exchange of nitro groups between *ipso*-intermediates and nitric acid in aqueous sulphuric acid [series (A), (B), 72.1%; series (C), (D), 73.6%] at 0 °C: (A) $^{15}NO_2$-labelled *ipso*-intermediate (**2b**) and HNO_3; (B) unlabelled *ipso*-intermediate (**2b**) and $H^{15}NO_3$; (C) unlabelled *ipso*-intermediate (**2a**) and $H^{15}NO_3$; (D) $^{15}NO_2$-labelled *ipso*-intermediate (**2a**) and HNO_3; peak (a), $^{15}NO_2$-labelled *ipso*-intermediate (**2b**); peak (b), $H^{15}NO_3$; peak (e), $^{15}NO_2$-labelled *ipso*-intermediate (**2a**); peak (f), $^{15}NO_2$-labelled nitro product (**3**). Number of pulses 256 [series (A), (B)], 192 [series (C), (D)]; pulse repetition time 4.4 s [(A), (B)], 1.0 s [(C), (D)]; pulse angle 23°

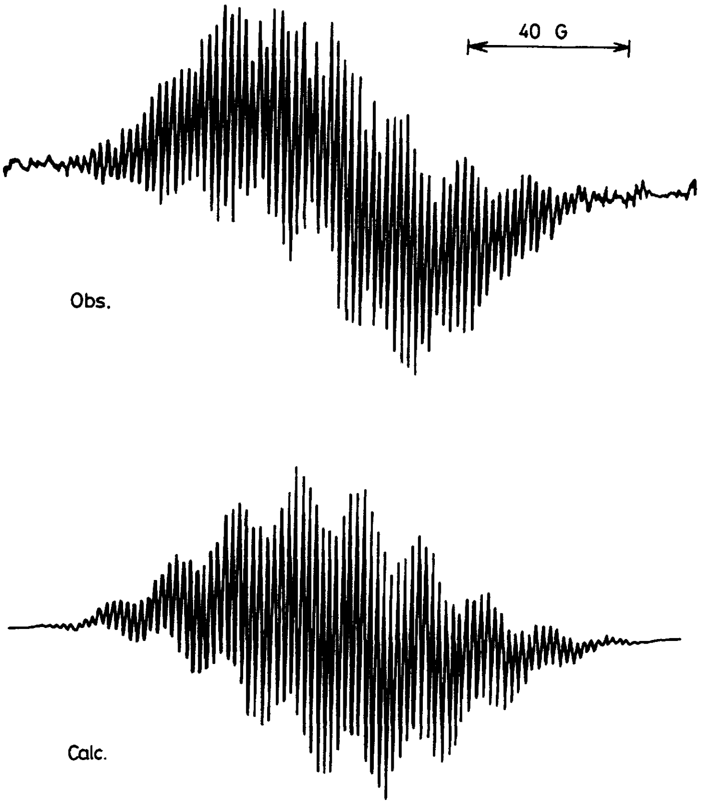


Figure 4. E.s.r. spectrum obtained from a solution of the *ipso*-intermediate (**2b**) in sulphuric acid (72.2%) at 0 °C compared with that calculated for the cation radical of the amine (**1b**) using the following hyperfine coupling constants: a_{N} 14 G; a_{MeN} 17.5 G; $a_{MeC(2)C(6)}$ 3.5 G; $a_{m\text{-}H}$ 1.75 G; $a_{MeC(4)}$ 12.25 G

(**4**) ⟶ (**7**) is similar to that observed with the related nitrocyclohexadienones.[4,11]

Corresponding studies of *ipso*-attack by ^{1}H and ^{15}N n.m.r. spectroscopy have been carried out on the amine (**1a**) and with very similar results: the signal for the $^{15}NO_2$ groups in the *ipso*-intermediate appears first in emission and that for the $^{15}NMe_2$ group initially shows enhanced absorption. However since this work is complicated by the subsequent rearrangement of the nitro group the experimental results are included in the section on rearrangements.

In some related work at higher acidities,[12] the reactions of the amine (**1c**) with $H^{15}NO_3$ in sulphuric acid (83%) at 7 °C were followed by ^{15}N n.m.r. spectroscopy but there was then no evidence for nuclear polarisation in the *ipso*-intermediate. Under these conditions the *ipso*-intermediate is considered to be formed by a fast reaction between the protonated amine and the nitronium ion.[3] When the concentration of sulphuric acid is reduced to 73.6%, the rate of reaction with the nitronium ion is greatly decreased and the signal for the $^{15}NO_2$ group in the *ipso*-intermediate is then initially in emission,[12] as expected for the nitrous acid-catalysed mechanism of *ipso*-attack.

Nitro-group Exchange in ipso-*Intermediates*.—The *ipso*-intermediate (**2b**) is stable for several hours in 70% sulphuric acid at 0 °C. During this time exchange occurs between the nitro groups on the intermediate and nitric acid in the solution. The exchange has been followed using ^{15}N labelling and ^{15}N n.m.r. spectroscopy. The exchange reactions lead to nuclear polarisation in the $^{15}NO_2$ group and the phase of this polarisation depends on the direction of the exchange. Polarisation is not seen during exchange when the *ipso*-intermediate is labelled with ^{15}N in the amino group.

The first line of spectra in Figure 3 comes from the exchange reaction of the ($^{15}NO_2$)-*ipso*-intermediate (**2b**) (0.27 mol dm^{-3}) with $H^{14}NO_3$ (0.4 mol dm^{-3}) in 72.1% sulphuric acid at 0 °C. The first spectrum provides a standard and refers to the *ipso*-intermediate after dilution to the same volume as the sample undergoing exchange but in the absence of added nitric acid. The next spectrum shows that, while exchange is occurring, an enhanced absorption signal is observed. The final spectrum refers to the state when isotopic equilibrium has been reached.

The experiment has been repeated using an *ipso*-intermediate labelled with ^{15}N in both nitro and amino groups.[10] Since, in the formation of *ipso*-intermediates, the polarisation at these nitrogen atoms is of opposite phase, it might seem that when the polarisation at the nitro group leads to enhanced absorption, that at the amino group should give an emission signal. However, there was no evidence for polarisation at the amino nitrogen (see Discussion section).

The spectra in the second line of Figure 3 refer to exchange between the unlabelled *ipso*-intermediate (**2b**) and labelled nitric acid under the same conditions as before. There is then no signal for the *ipso*-intermediate until exchange starts, when an emission signal is observed. The final spectrum is as before.

The above experiments were repeated with a small amount of hydrazine added to the solutions; a trace of a solid, presumably hydrazine bisulphate, was then present. No exchange was then found over a period of 4 h. In the presence of hydrazine, the colour of the reaction mixture changes from pale green to pink and the solution gives an e.s.r. spectrum which corresponds to the cation radical of the amine (**1b**) (Figure 4). The *g*-value (measured by Dr. J. C. Brand) was 2.0032. The spectrum of the ^{15}N-labelled cation radical has also been observed,[10] and that of the cation radical of the amine (**1a**) has been detected in the

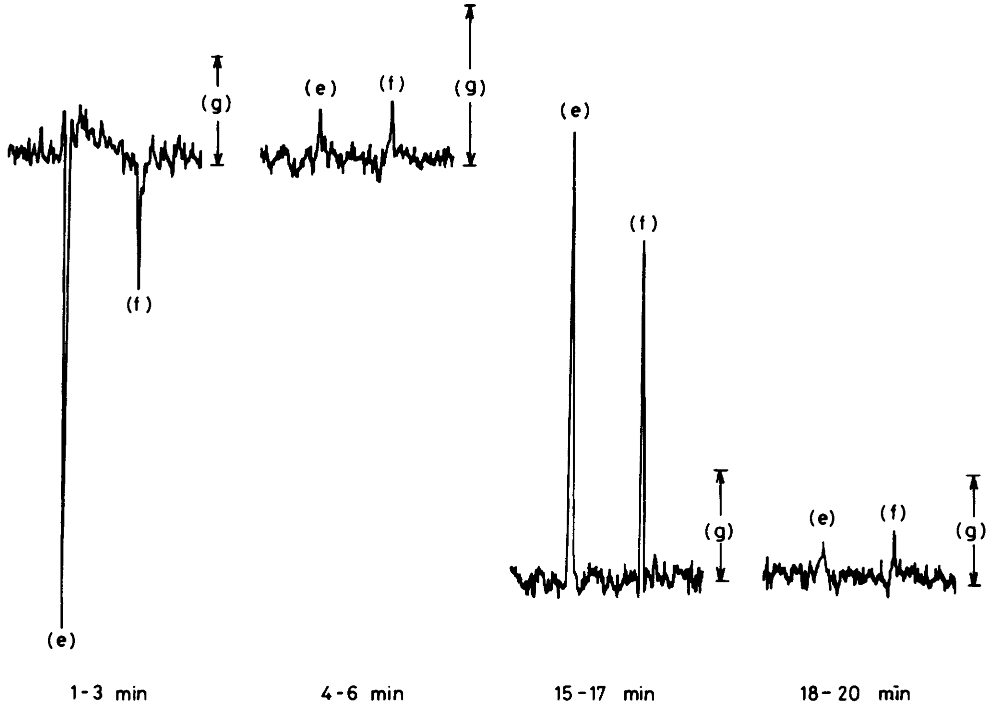


Figure 5. ^{15}N N.m.r. spectra during the reaction of the amine (**1a**) with $Ph^{15}NMe_3{}^{15}NO_3$ in sulphuric acid (70.7%) at -10 °C: peak (e), $^{15}NO_2$-labelled *ipso*-intermediate (**2a**); peak (f), $^{15}NO_2$-labelled nitro product (**3**); distance (g), height of peak for the $Ph^{15}NMe_3{}^{+}$ ion. Number of pulses 40; pulse repetition time 0.4 s; pulse angle 25°

course of *ipso*-attack.[2] No e.s.r. signals from the *ipso*-intermediate (**2b**) were detected in the absence of the hydrazine.

Exchange reactions were also observed with the *ipso*-intermediate (**2a**), but since these are complicated by the rearrangement of the *ipso*-intermediate they are considered in the following section.

The 1,3-*Rearrangement of Nitro Groups following* ipso-*Attack*.—The formation of *ipso*-intermediates of the type shown in structures (**2a**—**c**) is followed by a 1,3 rearrangement of the nitro group if a suitable vacant site appears on the ring and if the rearrangement is not hindered sterically by adjacent substituents.[3] In the present work the rearrangement (**2a**) $\longrightarrow$ (**3**) has been chosen for studies of nuclear polarisation. When the formation and rearrangement of this intermediate are carried out using an excess of $H^{15}NO_3$ in 73.6% sulphuric acid at 0 °C, the initial signals for both the *ipso*-intermediate and the rearranged product are in emission but, as the reaction proceeds, first the product signal and then that for the *ipso*-intermediate appear in absorption without any obvious polarisation.

For reasons outlined later (see Discussion section), this experiment was also performed in two stages by carrying out the initial *ipso*-attack in 70% sulphuric acid at -10 °C with added sodium nitrite as a catalyst (conditions where the formation of the *ipso*-intermediate is fast but the rearrangement is relatively slow) and then waiting until the polarisation has disappeared before diluting the solution to 60% sulphuric acid (conditions where the rearrangement is relatively fast and the isotope effect near unity.

A solution in 70.7% sulphuric acid of the amine (**1a**) (0.21 mol kg^{-1}), the standard salt $Ph^{15}NMe_3{}^{15}NO_3$ (0.5 mol kg^{-1}), and sodium nitrite (0.02 mol kg^{-1}) was prepared and the ^{15}N n.m.r. spectrum taken at -10 °C. For 1—3 min, strong emission signals were observed for both the *ipso*-intermediate and the 2-nitro product (Figure 5). These were to low field of the standard by 329.1 and 310.5 p.p.m., respectively. Only about one third of the signal for the *ipso*-intermediate is shown in the Figure. The next spectrum (4—6 min) shows these signals in absorption and little further change was observed over the next 9 min. At 15 min after starting, the solution was diluted with 40% sulphuric acid. The spectrum for the period 15—17 min shows enhanced absorption for both the *ipso*-intermediate and the 2-nitro product (Figure 5), but this enhancement rapidly decays and the final part of the rearrangement does not seem to give rise to marked nuclear polarisation.

A similar experiment was carried out with the addition of hydrazine at the same time as the dilution of the acid. The enhanced absorption signals for the *ipso*-intermediate and the 2-nitro product were then replaced by signals of normal intensity.

Other experiments showed that enhanced absorption signals for the *ipso*-intermediate and the 2-nitro product could be observed without the foregoing dilution procedure if an excess of amine were present. One particularly informative experiment was carried out using the (^{15}N)-amine (**1a**) and $H^{15}NO_3$. The reaction of the amine (0.18 mol dm^{-3}) and $H^{15}NO_3$ (0.12 mol dm^{-3}) in 72.2% sulphuric acid at 5 °C in the presence of sodium nitrite (0.02 mol dm^{-3}) was followed by ^{15}N n.m.r. spectroscopy and the results are in Figure 6. The initial spectrum (6—7.4 min) shows the signal for the $^{15}NO_2$ group of the *ipso*-intermediate in emission and that for the $^{15}NMe_2$ group of the *ipso*-intermediate in enhanced absorption. The next spectrum (10—11.4) shows the opposite phase for each of these signals. The reduced signal-to-noise ratio in the final spectrum shows that nuclear polarisation is then much reduced.

Some studies have been made on concurrent exchange and rearrangement reactions, and the results of one are shown in Figure 3, series (C). In these experiment, the *ipso*-intermediate (**2a**) was formed rapidly from the unlabelled amine (**1a**) (0.3 mol dm^{-3}) and unlabelled nitric acid (0.5 mol dm^{-3}) in the presence of sodium nitrite (0.08 mol dm^{-3}) in 73.6% sulphuric acid at 0 °C. After 15 min, when formation of the *ipso*-intermediate was

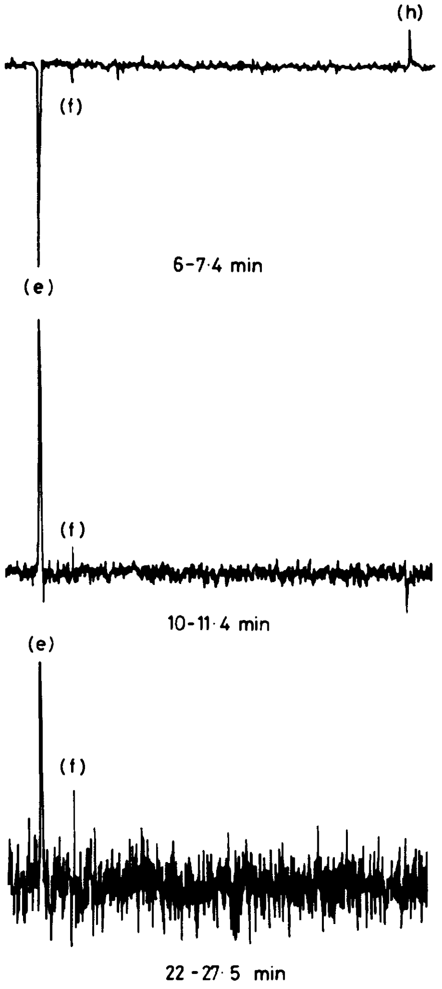
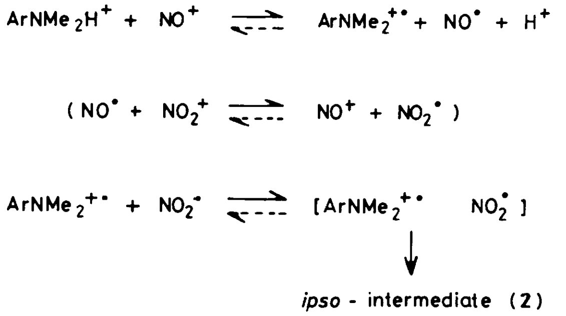


Figure 6. ^{15}N N.m.r. spectra during the nitration of the ^{15}N-labelled amine (**1a**) with insufficient $H^{15}NO_3$ in sulphuric acid (72.2%) at 5 °C: peak (e), $^{15}NO_2$ signal for *ipso*-intermediate (**2a**); peak (f), $^{15}NO_2$ signal for nitro product (**3**); peak (h), $^{15}NMe_2$ signal for *ipso*-intermediate (**2a**). Number of pulses 50 (last spectrum, 200); pulse repetition time 1.6 s; pulse angle 45°

expected to be complete, and about 25% rearrangement should have occurred, the reacting solution (2 cm^3) was mixed with a solution of $H^{15}NO_3$ (0.8 mol dm^3) in 73.6% sulphuric acid (1 cm^3). At 2—5 min after addition of the labelled nitric acid, the ^{15}N n.m.r. spectrum showed a strong emission signal for the *ipso*-intermediate and a weak emission signal for the 2-nitro product, indicating that some exchange has occurred. However, these signals disappeared in the course of reaction indicating that the exchange must be considerably slower than the rearrangement. An experiment was also carried out using the $^{15}NO_2$-labelled *ipso*-intermediate and unlabelled nitric acid under the same conditions [Figure 3, series (D)]; the addition of the unlabelled nitric acid then leads to a marked enhancement of the signal for the *ipso*-intermediate and some enhancement of the signal for the 2-nitro product. The enhancement is shown by the change in the signal-to-noise ratio.

Discussion

This section is mainly concerned with the extent to which the observed nuclear polarisation is consistent with the mechanisms that have been proposed for these reactions.



$$ArNMe_2H^+ + NO^+ \rightleftharpoons ArNMe_2^{+\bullet} + NO^\bullet + H^+$$

$$(NO^\bullet + NO_2^+ \rightleftharpoons NO^+ + NO_2^\bullet)$$

$$ArNMe_2^{+\bullet} + NO_2^\bullet \rightleftharpoons [ArNMe_2^{+\bullet} \quad NO_2^\bullet] \rightarrow \textit{ipso}\text{-intermediate } (\mathbf{2})$$

Scheme 1.

The mechanism that has been proposed for the nitrous acid-catalysed mechanism of *ipso*-attack [2] is shown in Scheme 1 with addition of dotted arrows for the possible back reactions. The mechanism of oxidation of nitric oxide may be more complex than is shown in the middle line of the Scheme,[2] and must be more complex in less acidic media;[8] this line of the Scheme should therefore be taken as showing merely the stoicheiometry involved.

The application of Kaptein's rules [13] (as modified to apply to the ^{15}N nucleus) [14] with the g-values of $NO_2^\bullet$ (g 2.0000) [15] and aromatic cation radicals ($g > 2.002\,49$) [16] indicates that, if nuclear polarisation is derived from the radical pair $[Ar\overset{+}{N}Me_2^\bullet\ NO_2^\bullet]$, the reaction path in Scheme 1 should give rise to an initial emission signal for the $^{15}NO_2$ group in the ^{15}N n.m.r. spectrum of the *ipso*-intermediate (**2**). This accords with the experimental results [Figures 1, 3(C), and 6] and with related results on the nitration of mesitylene [8] and p-nitrophenol. On this interpretation, the nuclear polarisation comes from the partition of the radical pair $[Ar\overset{+}{N}Me_2^\bullet\ NO_2^\bullet]$ between dissociation and combination.

The enhanced absorption found for the signal of the $^{15}NMe_2$ group in the *ipso*-intermediate formed from the ^{15}N-labelled amine (**1b**) (Table 1 and Figure 2) is the first example of nuclear polarisation in the aromatic component of the radical pair giving rise to CIDNP effects in nitration. The phase of the polarisation is consistent with the application of Kaptein's rules to the mechanism in Scheme 1, provided the sign of the hyperfine coupling constant of the ^{15}N atom in the radical cation $ArNMe_2^{+\bullet}$ is negative. An INDO calculation of the sign of the coupling constant at the nitrogen atom in the radical cation* $Ph^{14}NMe_2^{+\bullet}$ showed it to be positive and to remain positive when the NMe_2 group was twisted by 20° and 40° out of the plane of the ring.[10] The corresponding ^{15}N coupling constant should therefore be negative because of the negative magnetogyric ratio of the ^{15}N nucleus. This result therefore accords with the proposed mechanism, and provides additional evidence on the radical pair involved. The relaxation time T_1 of the ^{15}N nucleus in the *ipso*-intermediate (**2b**) was shown to be 31 s (see Experimental section); this is considerably less than that found for the $^{15}NO_2$ groups in nitrobenzene (170 s) [17] and (2-^{15}N)-2,4-dinitrophenol (182 s).[1]

The mechanism that has been suggested [18] for the nitro-group exchange reaction is shown in Scheme 2; it starts with the reverse of the final stage of Scheme 1 and also involves the partition of the radical pair $[ArMe^{+\bullet}\ NO_2^\bullet]$ between dissociation and recombination. When the *ipso*-intermediate is

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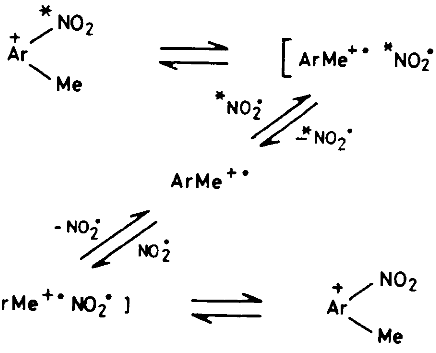
* A limitation on molecular size in the INDO programme prevented us from carrying out the calculation on the radical cation from the amine (**1b**); the radical cation $PhNMe_2^{+\bullet}$ was therefore used as a model.



Scheme 2.

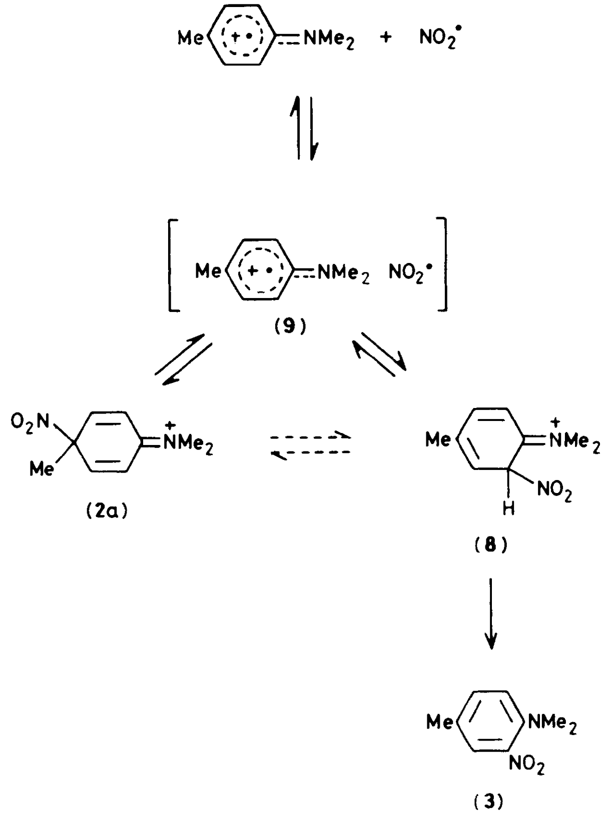
initially labelled with $^{15}NO_2$, the first radical pair [ArH$^{+\cdot}$ $^{15}NO_2^{\cdot}$] is formed from a singlet precursor and the recombination product is being studied: under these conditions the application of Kaptein's rules predicts that, if nuclear polarisation is present, the $^{15}NO_2$ signal of the *ipso*-intermediate should show enhanced absorption, and this is observed [Figure 3, series (A)].

When the initial *ipso*-intermediate is unlabelled, the reaction followed is the diffusion together of the radicals ArH$^{+\cdot}$ and $^{15}NO_2^{\cdot}$ to form the corresponding radical pair, followed by combination: this is identical with the initial formation of the *ipso*-intermediate and should have given an emission signal for the $^{15}NO_2$ group as observed [Figure 3, series (B)].

The reason why nuclear polarisation is not seen at the $^{15}NMe_2$ group during these exchange reactions presumably comes from the constancy of the chemical shift of this nitrogen in the exchange reaction. The analogy with the formation of the *ipso*-intermediate suggests that the polarisation at the $^{15}NMe_2$ group following exchange should be opposite to that at the $^{15}NO_2$ group, but the absence of a chemical shift at the amino nitrogen during exchange implies that the observed signal is the resultant of those from molecules before and after exchange. In such a combined group, the Boltzmann distribution of nuclear energies should be maintained.

The effect of hydrazine in stopping the exchange reaction presumably derives from its action as a nitrous acid scavenger.[19] In the presence of hydrazine, the concentration of dinitrogen tetraoxide in the solution (and hence also that of nitrogen dioxide) should be much reduced, while that of the aromatic radical cation should be correspondingly increased as a result of the equilibrium resulting from the dissociation of the *ipso*-intermediate. This change increases the probability that a $^{*}NO_2$ radical derived from an *ipso*-intermediate will encounter an aromatic radical cation before it meets another NO_2 radical, and will hence return whence it came. The detection of the e.s.r. spectra of cation radicals in the presence of hydrazine (Figure 4; see also ref. 10) provides support for this interpretation.

It is interesting to consider the extent to which the reactions in Schemes 1 and 2 can provide an understanding of the 1,3-rearrangement which follows *ipso*-attack on some amines. One set of reaction paths for the rearrangement of the *ipso*-intermediate (**2a**) is shown is Scheme 3: this scheme includes the radical pair* [ArH$^{+\cdot}$ $NO_2^{\cdot}$] and accords with the reactions in the earlier Schemes. The involvement of radicals in this 1,3-rearrangement receives support from the work of Barnes and Myhre[21] on the analogous 1,3-rearrangement in cyclohexadienones.



Scheme 3.

If nuclear polarisation is present in the product (3) of this 1,3-rearrangement, then Kaptein's rules suggest that the signal for the $^{15}NO_2$ group in the product should show enhanced absorption. This arises from the partition of the radical pairs [ArH$^{+\cdot}$ $NO_2^{\cdot}$] between dissociation and recombination. However, since from the foregoing arguments concerning the formation of *ipso*-intermediates, the collapse of the radical pair gives mainly attack at the 4-position, it follows that the $^{15}NO_2$ signal in the *ipso*-intermediate should also show enhanced absorption.

The ^{15}N n.m.r. spectra taken during the reaction of the amine (**1a**) with an excess of $H^{15}NO_3$ in *ca.* 70% sulphuric acid do not accord with this prediction, for the initial signal of the $^{15}NO_2$ group in the product (3) normally appears in emission. In the interpretation of this result there are two complications to be considered. One comes from the extensive nuclear polarisation introduced during the formation of *ipso*-intermediates, which can, in principle, be carried over into the rearranged product. The other comes from the fact that proton loss from the Wheland intermediate (8) becomes increasingly rate-determining[5] when the concentration of sulphuric acid is raised above 60%.

These complications were overcome as far as possible by carrying out the experiment in two stages and the results are shown in Figure 5. The first two spectra show the formation of the *ipso*-intermediate in 70.7% sulphuric acid at −10 °C, conditions where the rearrangement is relatively slow.‡ The initial

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* Following the work of White and his co-workers,[20] we should probably consider several types of radical pair depending on the relative positions of the radicals involved. For simplicity, this complication has been omitted from the present argument.

† From the rate profile and activation energy for this reaction,[5] the rate coefficient for the rearrangement should be 2.0×10^{-4} s^{-1} at −10 °C, giving a half-life of 58 min. However the extent of formation of the nitro product (3) would be greater than this would suggest since, in the presence of added nitrous acid, some of the nitro product (3) is formed at the same time as the *ipso*-intermediate (**2a**).[2]

emission signal for the 2-nitro product is very clear. After 6 min, the normal absorption signals were seen and the solution was then diluted with 40% sulphuric acid to give a final concentration of 60% sulphuric acid [conditions where the rate of rearrangement is much faster and proton loss from the Wheland intermediate (**8**) is no longer rate-determining]. The results in Figure 5 show enhanced absorption signals for both the *ipso*-intermediate and the 2-nitro product as expected for reaction through the radical pairs in Scheme 3.

Unfortunately, this enhancement is short-lived (Figure 5), whereas calculations from earlier kinetic studies[5] suggest that the half-life of the rearrangement under these conditions should be about 13 min. It appears therefore that the enhanced absorption signals came more from the disturbance in diluting the solutions than from the rearrangement reaction. Also, when hydrazine is present in the rearrangement stage, no enhanced absorption signals are seen but the rate of rearrangement is unaffected.

It appears therefore that the signal for the 2-$^{15}NO_2$ group in the product (**3**) can show either no polarisation or emission or enhanced absorption, and that where polarisation is present it reflects the polarisation of the *ipso*-intermediate. There is no evidence in the foregoing work that the rearrangement reaction itself generates a marked CIDNP effect.

One interpretation of the foregoing results is that the rearrangement reaction does not involve radical pairs. There is a great deal of evidence against a rearrangement *via* heterolysis to form a nitronium ion,[2,5] but some form of concerted reaction, represented by the dotted arrows in Scheme 3, is possible. Such a reaction would have to involve inversion at the nitrogen atom in order to agree with the Woodward–Hoffmann rules. Related reactions involving a 1,5 migration of the nitro group have been suggested,[22] but these would not require inversion at the nitrogen.

Another possibility is that some of or all the rearrangement reaction occurs by the radical pathway in Scheme 3, but that this fails to lead to nuclear polarisation because, in the presence of an excess of nitric acid, there is an absence of effective side-reactions for those radical pairs that dissociate. In the absence of such side-reactions, the radical pairs that dissociate would later go on to form the normal product and this would tend to re-establish the Boltzmann distribution of nuclear spins in the product.* On this interpretation, the polarisation that arises during the formation of the *ipso*-intermediates occurs because the radical pairs that dissociate take part in side-reactions involving the amine molecules. This interpretation has been tested by carrying out the rearrangement reaction in the presence of an excess of amine (Figure 6), and the results show that the initial emission signals for the *ipso*-intermediate and the product change to enhanced absorption signals during the rearrangement stage. This experiment was carried out using the ^{15}N-labelled amine (**1a**) and $H^{15}NO_3$: it shows clearly that the ^{15}N-polarisations of the NMe_2 and NO_2 groups of the *ipso*-intermediates are in opposite senses, for where the signal for the nitro group shows enhanced absorption, that of the amino group is in emission.

Other relevant experiments concern concurrent rearrangement and exchange reactions. Figure 3, series (C), shows the ^{15}N n.m.r. signals during the rearrangement of an unlabelled *ipso*-intermediate (**2a**) in the presence of $H^{15}NO_3$. Under these conditions, the exchange reaction should lead to an emission signal for the *ipso*-intermediate, but the 1,3-rearrangement following exchange should in itself lead to an enhanced absorption signal for the 2-nitro product (**3**). Only the polarisation corresponding to the exchange reaction is seen, and the absence of any final signal for the 2-nitro product indicates that the emission signal must be greatly enhanced and that rearrangement must be considerably faster than exchange under these conditions. The results in Figure 3, series (D), show the corresponding exchange reaction carried out in the reverse direction using the $^{15}NO_2$-labelled *ipso*-intermediate (**2a**) and unlabelled nitric acid. The marked enhancement in the signal for the *ipso*-intermediate at the start of exchange is obvious from the change in the signal-to-noise ratio and agrees with the other results already described. These experiments show therefore that nitro-group exchange in the *ipso*-intermediate *via* the formation of $NO_2^{\bullet}$ accompanies the rearrangement reaction.

In conclusion, the presence and phase of the nuclear polarisation described agrees fully with the mechanisms proposed for the formation of these *ipso*-intermediates and for the nitro-group exchange reactions (Schemes 1 and 2).

For the nitro-group rearrangement (Scheme 3), the nuclear polarisation is still consistent with the proposed mechanism but the evidence for the radical reaction is less compelling, partly because the nuclear polarisation is not always obvious and partly because, where enhanced absorption signals are found for the 2-nitro product (**3**), they are found also for the *ipso*-intermediate (**2a**); the polarisation could hence be carried over by a concerted process. At present, it is perhaps best to conclude that the rearrangement is accompanied by the formation of radical pairs, *e.g.* (**9**), but that the rearrangement may not require the formation of such pairs.

Experimental

Materials.—The amines (**1a**—**c**)[2,3] and (^{15}N)-2,4,6-trimethylaniline[8] were prepared as described previously. The last-named amine was methylated with trimethyl phosphate[23] to give (^{15}N)-*N*,*N*,2,4,6-pentamethylaniline (yield 83%) and this was distilled twice before use. (^{15}N)-*N*,*N*,4-Trimethylaniline was prepared in the same way starting with the nitration of toluene by $H^{15}NO_3$ and including also column chromatography to separate the *p*-nitro isomer. (^{15}N)-*N*,*N*,*N*-Trimethylanilinium nitrate was prepared from benzene using the same techniques for nitration and reduction to (^{15}N)aniline. In our hands the reported direct methylation to the phenyltrimethylammonium ion[24] did not always work well and so the methylation was carried out in two stages using trimethyl phosphate to form (^{15}N)-*N*,*N*-dimethylaniline[25] followed by the reaction of this amine with methyl iodide in dry acetone to give (^{15}N)-*N*,*N*,*N*-trimethylanilinium iodide. This iodide was dissolved in water and treated with a slight excess of silver nitrate followed by hydrogen sulphide (to remove the excess of the silver salt). Filtration of the solution followed by evaporation and recrystallisation (ethanol–acetone) of the resulting solid gave (^{15}N)-*N*,*N*,*N*-trimethylanilinium nitrate, m.p. 119 °C (lit.,[26] 119.5 °C) in an overall yield (from benzene) of 31%. The doubly labelled salt (^{15}N)-*N*,*N*,*N*-trimethylanilinium (^{15}N)nitrate was prepared by a similar procedure using $Ag^{15}NO_3$ [prepared by treating an aqueous suspension of Ag_2CO_3 with aq. $H^{15}NO_3$ (40%)]. The unlabelled salt was made by analogous procedures starting with $PhNMe_3I$. The purity of the labelled compounds was checked by ^1H and ^{15}N n.m.r. spectroscopy; the only impurity detected was some of the corresponding *ortho*-isomer in the ^1H n.m.r. spectrum of (^{15}N)-*N*,*N*,4-trimethylaniline, but this was not detectable in the ^{15}N n.m.r. spectrum of the sample and should not affect the foregoing conclusions. The other reagents used were as described previously.[8]

Products.—The major products from the reactions reported have already been identified,[2,3] and so this section is limited to

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* This argument assumes that the lifetime of the free $NO_2^{\bullet}$ radicals is short in comparison with the relaxation time T_1 for the ^{15}N nucleus in this species.

Table 2. Kinetic results

[amine (**1a**)] 0.21 mol kg^{-1}; [$PhNMe_3NO_3$] 0.25 mol kg^{-1}; [$NaNO_2$] 0.01 mol kg^{-1}

Time (min)	3	5	7.7	9.8	12	14.5	16.8	19.1	21.3
Reaction (%)	18	26	34	46	50	57	69	71	76
Time (min)	23.5		25.9						
Reaction (%)	83		86						

the products formed from the decomposition of the *ipso*-intermediate (**2b**). The evidence that the first product is the imine (**4**) comes from the following spectra: δ_H (71% H_2SO_4) 7.0 (2 H, s), 3.9 (3 H, s), 2.2 (9 H, s); δ_C (71% H_2SO_4)[*] 16.4 (*o*-Me), 20.6 (*p*-Me), 50.5 (d, NMe), 78.9 (C-4), 139.0 (d, C-1), 142.0 and 146.6 (C-2, C-3, C-5, C-6); δ_N (71% H_2SO_4) 172.3 to low field of $Ph\overset{+}{N}Me_3$. The products from the unlabelled *ipso*-intermediate (**2b**) were isolated by pouring into water, extracting with methylene dichloride, and separating by h.p.l.c. (10 cm × 4.5 mm and 2 × 25 cm × 5 mm Partisil 5 silica gel columns with elution by 20% ethanol–light petroleum). The ^1H n.m.r. spectra of three of the products accorded with structures (**5**)—(**7**) but what appeared to be the parent peak in the corresponding high-resolution mass spectra consistently indicated compositions with one hydrogen atom less. Experiments with *N*-methylaniline also gave a $P - 1$ peak of greater abundance than the parent peak.

Spectroscopic Studies.—The kinetic runs, followed by ^1H n.m.r. spectroscopy, were carried out with a JEOL FX 90 Q spectrometer. The majority of the ^{15}N n.m.r. studies were carried out with a Varian XL-200 FT spectrometer, but the results in Figure 6 were obtained from the JEOL FX 90 Q instrument. Measurements of the relaxation times T_1 were carried out in sulphuric acid (70.1%) by the fast inversion recovery method,[26] with wait time *ca.* 1.5 T_1, and yielded values of 31 s for ($^{15}NMe_2$)-*ipso*-intermediate (**2b**) and 15 s for $Ph^{15}NMe_3^+$. The e.s.r. spectra were recorded with a Varian E4 instrument.

Kinetic Studies.—The kinetic forms and rate coefficients for a number of the reactions discussed have been reported,[2,3,5] but in the present work it was necessary to determine the rate of reaction of the amine (**1b**) to give the intermediate (**2b**) in the presence of $PhNMe_3NO_3$. The results in Table 2 were obtained for reactions in 70.7% sulphuric acid at 5 °C by using the change in the heights of the Ar*H* peaks during reaction together with the change in the height of the peak for the $=\overset{+}{N}Me_2$ group in the product.

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[*] Obtaining by using the *ipso*-intermediate from the ^{15}N-labelled amine and unlabelled nitric acid.

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