The Mechanism of Nitrosation of 4-Nitrophenol with Aqueous Nitrous Acid

By **Alan P. Gosney** and **Michael I. Page,*** Department of Chemical Sciences, The Polytechnic, Huddersfield HD1 3DH

The nitrous acid catalysed nitration of 4-nitrophenol to give 2,4-dinitrophenol in aqueous solution has been studied under a variety of conditions. At low concentrations of nitrous acid the rate of reaction is dependent upon the concentration of nitrous acid but the rate becomes independent of nitrous acid at high concentrations of nitrous acid when the latter is in excess of 4-nitrophenol concentration. This saturation phenomenon is attributed to the conversion of 4-nitrophenol to its corresponding nitrite ester which then undergoes an acid-catalysed rearrangement to give the accepted normal nitroso σ-complex. Other kinetic parameters, such as salt effects, acidity dependence, and kinetic isotope effects are very similar under the conditions of 'high' and 'low' concentrations of nitrous acid.

THE nitration of aromatic compounds is usually retarded by the addition of nitrous acid because of the removal of the nitronium ion. However, in the presence of activating substituents such as OH, OR, and NR_2 nitration occurs by the intermediate formation of a nitroso-compound which is then oxidised to the corresponding nitro-compound.[1] The overall transformation in nitric acid has been studied as the 'special nitrous acid-catalysed' mechanism of nitration.[2] Because the nitroso-compound is easily oxidised [3] and nitrous acid is unstable in moderately acidic solutions at high temperatures [4] aromatic nitrosation has not been easily examined. However, Challis and his co-workers have carried out extensive kinetic investigations of aromatic nitrosation and shown that proton loss from the σ-complex is usually rate limiting [5] but the formation of this complex is rate limiting for some reactive aromatic substrates in weakly acidic media.[6]

In addition to *C*-nitrosation reactions nitrogen, oxygen, and sulphur centres are known to react with aqueous nitrous acid.[7] Despite the complexities associated with the identification of the exact nature of the nitrosating species kinetic studies have shown that the nitrosation of basic electronegative atoms can occur very rapidly.[8] For example, the rate constants for the *N*-nitrosation of primary aromatic amines, leading to diazotisation, by nitrosyl halides, approach that expected for a diffusion controlled process.[8-10]

We therefore felt that there is a possibility that the *C*-nitrosation of phenols occurs by preliminary *O*-nitrosation to give the nitrite ester. Previous kinetic studies of the nitrosation of phenols have been carried out with an excess of phenol over nitrous acid. Herein is reported a kinetic study of the nitrous acid catalysed nitration of 4-nitrophenol with excess nitrous acid which suggests the initial formation of a nitrite ester.

EXPERIMENTAL

General.—4-Nitrophenol was recrystallised four times from water. Nitric acid (70% w/w) of AnalaR grade was monitored periodically for nitrous acid. Inorganic salts were of AnalaR grade and were dried by vacuum desiccation.

Attempts to prepare 4-nitro-2-nitrosophenol by the Baudisch reaction or modification [11] were unsuccessful.

[2,6-$^2H_2$]-4-*Nitrophenol.*—4-Nitrophenol (3.0 g) was refluxed with 20% DCl–D_2O (50 cm^3) for 90 h, the solution cooled, ether extracted, washed with D_2O, dried, and the solvent evaporated. Dideuteriated ($\geqslant 98\%$) 4-nitrophenol (2.1 g) was recrystallised from D_2O.

DNO_3.—Nitrogen dioxide, dried over phosphorus pentaoxide, was passed into D_2O until the solution was saturated and a deep blue colouration prevailed (*ca.* 1 h). Oxygen was then passed through the solution for *ca.* 3 h. The solution was analysed for nitrous acid (none detected) and titrated to determine its concentration. N.m.r. indicated $\geqslant 98\%$ deuteriation.

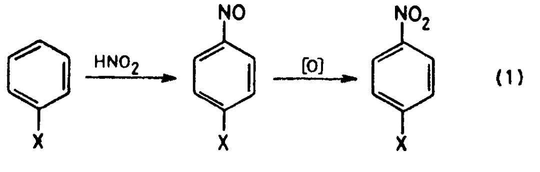
Nitrous Acid Determination.—The concentration of the azo-dye produced from the diazonium salt of 4-aminobenzenesulphonic acid and 1-naphthol was measured spectrophotometrically and hence the nitrous acid concentration was estimated.[12] A suitable portion (neutralised if from concentrated acid) containing up to 4×10^{-6} mol of nitrous acid was added to 2 cm^3 of 4×10^{-2}M-4-aminobenzenesulphonic acid in 2M-hydrochloric acid. After 5 min 2M-sodium acetate solution (2 cm^3) was added followed by 4×10^{-3}M-1-naphthol (2 cm^3) in 0.5M-sodium hydroxide and made up to 100 cm^3 with water. After 20 min the absorbance was measured in 10 mm silica cells at 474 nm where absorbance $\times 3.3 \times 10^{-7}$ = mols of nitrous acid.

Kinetics.—4-Nitrophenol was nitrated to give 2,4-dinitrophenol. The concentration of these were estimated spectrophotometrically by measuring the absorbance of portions at pH 4.0 at 260 and 317 nm, where the extinction coefficients of 4-nitrophenol are 1,350 and 9 800 l mol^{-1} cm^{-1}, respectively, and those for 2,4-dinitrophenol are 9 600 and 6 200 l mol^{-1} cm^{-1}, respectively. However, because of problems associated with nitrous acid decomposition, the majority of the kinetic data were obtained by the method of initial rates at 50 °C, which covered up to the first 10% of reaction and gave a reproducibility of $\pm 7\%$.

An aqueous solution (100 cm^3) of 4-nitrophenol, sodium nitrite, and any other salts were equilibrated to the required temperature ($50.0 \pm 0.1°$). The reaction was initiated by adding nitric acid solution (100 cm^3) of known concentration at the same temperature. Portions were removed periodically and analysed for reaction products or nitrous acid. For example, 10 cm^3 of the reaction mixture was quenched in 50 cm^3 of water and sufficient 1M-sodium hydroxide to ensure neutralisation, and then made up to 100 cm^3 with water. 25 cm^3 of this solution was then added to 25 cm^3 of acetate buffer pH 4.0 and made up to 100 cm^3 with water and the pH checked. The absorbance of this solution was measured at 260 nm. A standard was obtained by repeating the experiment of the absence of 4-nitrophenol.

RESULTS AND DISCUSSION

The nitrous acid catalysed nitration of aromatic substrates in aqueous solutions of nitric acid proceeds by the intermediate formation of the nitroso-compound which is then oxidised to the corresponding nitro-derivative [equation (1)].[13] Phenol, for example, is smoothly nitrated under aqueous conditions with 1M-nitric acid in the presence of nitrous acid.[14] When nitrous acid is initially absent an induction period is observed during which small concentrations of nitrous acid are formed by an oxidative side reaction.[15] However, detailed kinetic studies of the nitrous acid catalysed nitration of phenol are hindered by autocatalysis and the exothermic nature of the reaction. The corresponding reaction of less activated compounds removes the problem of oxidative side-products.[16]



(1)

Although C-nitrosation of phenols takes place O-nitrosation of acetate ion, hydrogen peroxide,[7] and alcohols [17] also occurs and therefore there is the possibility of the intermediate formation of a nitrite ester. To overcome the problem of the reduction of nitric to nitrous acid the nitration of 4-nitrophenol to 2,4-dinitrophenol in aqueous solution was studied. To overcome the problem of the known decomposition of nitrous acid [18] initial rates were measured. 2,4-Dinitrophenol is not very soluble in aqueous solution and so concentrations of <0.02M-4-nitrophenol were used. Previous investigations of nitrosation have used excess phenol over nitrous acid concentration and therefore it was decided to study the reaction over a wide range of nitrous acid concentration.

Pseudo-first-order rate constants for the nitration of 4-nitrophenol (4NP) in aqueous solution at 50°

	10^5k_{obs} [a]/s^{-1}		
[HNO_2]/mol l^{-1}	3.0M-HNO_3 0.01M-4NP	3.0M-HNO_3 0.02M-4NP	2.0M-HNO_3 0.01M-4NP
0.001	0.81	0.713	
0.002	1.06		
0.005	1.72	1.62	0.770
0.0075	2.21		
0.01	2.78	2.60	
0.015	3.35	3.11	
0.025	3.62	3.43	
0.05	3.30		
0.10	3.53	3.94	1.95
0.20	4.54	4.47	1.97
0.35	4.69		
0.50	5.00		

[a] Initial reaction rate/concentration of 4NP.

At low concentrations of nitrous acid the rate law is as shown in equation (2) [see Figures 1 and 2 and Supplementary Publication No. SUP 22882 (6 pp.)*] where 4NP is the concentration of 4-nitrophenol, in agreement

$$\text{Rate} = k[\text{4NP}][HNO_2][H^+] \qquad (2)$$

with previous studies.[5,6] In the absence of nitrous acid there is no detectable reaction. However, with increasing concentration of nitrous acid there is a change in the kinetic dependence upon nitrous acid concentration (Table, Figure 1). At high concentrations of nitrous acid ([HNO_2] > [4NP]) the rate of reaction is independent of nitrous acid concentration. This was shown to occur under a variety of reaction conditions. We considered three possibilities to explain this phenomenon: (1) a change in rate-limiting step with increasing nitrous acid concentration; (2) nitrous acid is converted into a non-nitrosating species; (3) 4-nitrophenol is completely converted into a reactive intermediate which then gives 2-nitroso-4-nitrophenol.

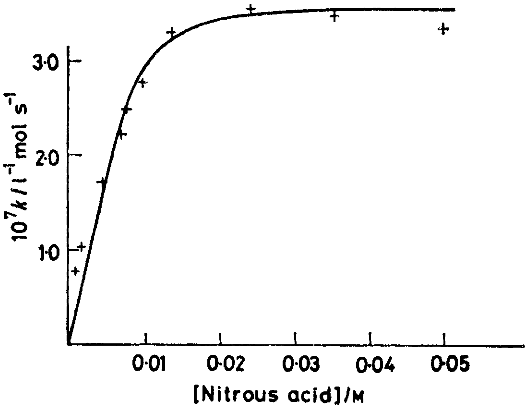


FIGURE 1 Plot of the initial reaction rate of nitration of 4-nitrophenol (0.01M) in aqueous 3.0M-nitric acid against the nitrous acid concentration at 50 °C. The solid line is calculated from the parameters given in the text

A general pathway for the nitrous acid catalysed nitration of 4-nitrophenol is outlined in the Scheme. A change in the rate-limiting step of the reaction with increasing nitrous acid concentration may also be reflected in the dependency of the reaction rate on other parameters at 'high' and 'low' concentrations of nitrous acid. Nitrous acid exists as different species, *e.g.* HNO_2, $H_2NO_2^+$, NO^+, NOX, with changing acid solutions.[18,19] However, there is no meaningful difference in the kinetic dependence upon acid type and concentration at 'high' and 'low' concentrations of nitrous acid. For example the linear plots of log k against H_R for nitric acid (Figure 2) give slopes of 0.625 and 0.563 for 'high' and 'low' concentrations of nitrous acid, respectively. The corresponding slopes against H_0 are 1.29 and 1.21, respectively. (Detailed kinetic data are given in SUP 22882.) Increasing nitric acid concentration increases both H^+ and NO_3^- con-

---

* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1979, Index issue.

centrations. However, maintaining the anion concentrations constant (3M-chloride and 1M-nitrate) but increasing the hydronium concentration still revealed no significant difference in the rate dependency at ' high ' and ' low ' concentrations of nitrous acid. The effect of added salts also revealed little difference in the kinetic behaviour at ' high ' and ' low ' nitrous acid concentrations. For example, Figure 3 shows the increase in rate with increasing concentration of added salts with ' high ' nitrous acid concentration that has been observed in other systems using ' low ' concentrations of nitrous acid.[20] With ' high ' and ' low ' concentrations of nitrous acid the increase in rate is in the order $ClO_4^- > NO_3^- > Cl^-$. Anions can affect the nature of the nitrosating species by forming NOX where X is the anion.[18,20] In summary, neither the acidity or salt dependence of the reaction is indicative of different rate-limiting steps at ' high ' and ' low ' nitrous acid concentrations.

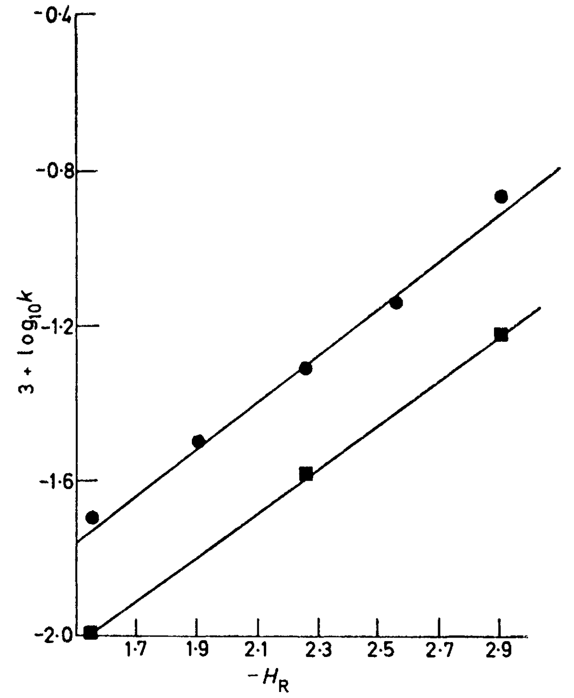


FIGURE 2 Plot of the logarithm of the initial reaction rate of nitration of 4-nitrophenol (0.01M) at 50° catalysed by 0.01M-nitrous acid and 0.20M-nitrous acid against the H_R value of nitric acid

There is a significant kinetic isotope effect for the nitrosation of many aromatic compounds indicative of rate-limiting carbon–hydrogen bond fission in the σ-complex (Scheme).[5] However some reactive aromatic substrates such as indoles do not show an isotope effect for the formation of the σ-complex and an earlier step is thought to be rate limiting.[6] There is the possibility of isotope exchange occurring at a faster rate than nitrosation but the rate of reaction of [2,6-$^2H_2$]-4-nitrophenol was the same in D_2O and H_2O : $k^D{}_{H_2O}/k^D{}_{D_2O} = 1.00 \pm 0.05$. At ' low ' concentrations of nitrous acid $k_H{}^{H_2O}/k_D{}^{H_2O} = 1.00 \pm 0.07$ and at ' high ' concentrations $k_H{}^{H_2O}/k_D{}^{H_2O} = 1.45 \pm 0.03$. There is thus a significant difference in isotope effects with increasing concentration of nitrous acid. However, the value of 1.45 is too low to be taken as indicative of rate-limiting carbon–hydrogen bond fission.[6]

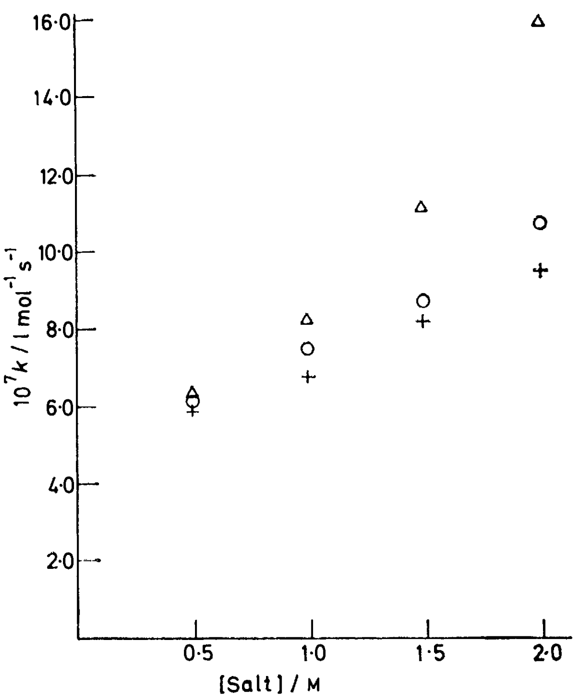
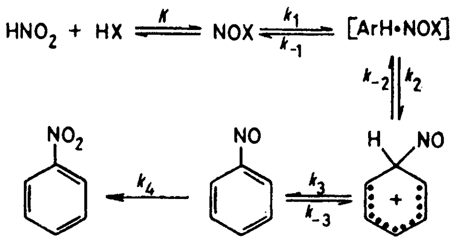
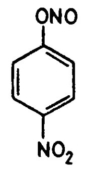


FIGURE 3 The initial reaction rate of nitration of 4-nitrophenol (0.01M) at 50° in aqueous 3.0M-nitric acid with 0.2M-nitrous acid as a function of salt concentration: △, $NaClO_4$; ○, $NaNO_3$, +, NaCl

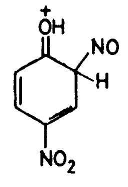


SCHEME

It appears that the simplest interpretation of the results is the complete conversion of 4-nitrophenol to a reactive intermediate at high concentrations of nitrous acid. Nitrite esters are rapidly formed.[17,21] It is therefore proposed that there is a pre-equilibrium formation of the corresponding nitrite ester (I) which undergoes an acid-catalysed rearrangement to give the



(I)



(II)

normal σ-complex (II). The formation of the nitroso-derivative is analogous to the Fischer–Hepp rearrangement of *N*-nitrosoalkylanilines to give 2- and 4-nitroso-alkyl anilines.[22,23] The formation of *N*-nitrosoanilines is reversible and denitrosation is catalysed by bases X to form NOX.[24] The formation of the nitrite ester is given in equation (3) and the rate law for this in equation (4). At ' low ' nitrous acid concentration $1 > K[\mathrm{HNO_2}]$

$$\mathrm{ArOH} + \mathrm{HNO_2} \overset{K}{\rightleftharpoons} \mathrm{ArONO} \xrightarrow{k[\mathrm{H^+}]} \text{nitrosophenol} \qquad (3)$$

$$\text{Rate} = \frac{kK[\mathrm{ArOH}][\mathrm{HNO_2}][\mathrm{H^+}]}{1 + K[\mathrm{HNO_2}]} \qquad (4)$$

and the rate is dependent upon nitrous acid concentration, but at ' high ' concentrations $K[\mathrm{HNO_2}] > 1$ and the rate is independent of nitrous acid concentration. The solid line in Figure 1 is calculated using K 2 000 $\mathrm{l\ mol^{-1}}$ and k $3.60 \times 10^{-5}\ \mathrm{s^{-1}}$, obtained from the rate at saturating concentrations of nitrous acid. The acid-catalysed rearrangement of the nitrite ester to the nitrosophenol could occur by either a concerted or stepwise process.

Other possible explanations for the kinetic independence upon nitrous acid concentration can be dismissed. Formation of the nitrosating species cannot be rate limiting as the rate of reaction is dependent upon the concentration of 4-nitrophenol at ' high ' and ' low ' concentrations of nitrous acid. It is conceivable that nitrite ion could act as a general base catalyst facilitating carbon–hydrogen bond fission [equation (5)]. There could thus be a change in rate-limiting step with increasing nitrous acid concentration *i.e.*, as $k_2[\mathrm{B}] > k_{-1}$. However, if this were the case the observed rate would be second order with respect to nitrous acid at low concentrations of nitrous acid and first order at high concentrations.

$$\mathrm{ArH} + \mathrm{E^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ArHE^+} \xrightarrow{k_2[\mathrm{B}]} \mathrm{ArE} + \mathrm{BH} \qquad (5)$$

Increasing the concentration of nitrous acid could cause the oxidation of the nitroso-derivative to become kinetically significant. For example, at low concentrations of nitrous acid the formation of the nitroso-derivative could be rate limiting but at high concentrations of nitrous acid the oxidation step could become rate limiting. If the oxidation step was independent of nitrous acid this could explain the observed kinetic behaviour. However, nitrous acid is essential for the oxidation of 4-nitrosophenol by nitric acid.[25] Furthermore, attempts to prepare 2-nitroso-4-nitrophenol were unsuccessful, even in the absence of oxygen, and the only product isolated was 2,4-dinitrophenol. Also, kinetic runs in the absence of added nitrate ions and oxygen still resulted in an observed rate of formation of 2,4-dinitrophenol (Figure 4). The oxidising agent presumably arises from the decomposition of nitrous acid.[18]

Finally, nitrous acid could be converted into an inactive nitrosating species at high concentrations of nitrous acid. For example, if $\mathrm{N_2O_3}$ were an ineffective nitrosating agent compared with, say, $\mathrm{NO^+}$, the rate of reaction would decrease with increasing concentration of nitrous acid. However, it is difficult to justify this explanation on a quantitative basis. The equilibrium constant for the dimerisation of $\mathrm{HNO_2}$ to $\mathrm{N_2O_3}$ is 18 $\mathrm{l\ mol^{-1}}$ [18] so the equilibrium concentration of nitrous acid does not reach a limiting value with the concentration of nitrous acid used.

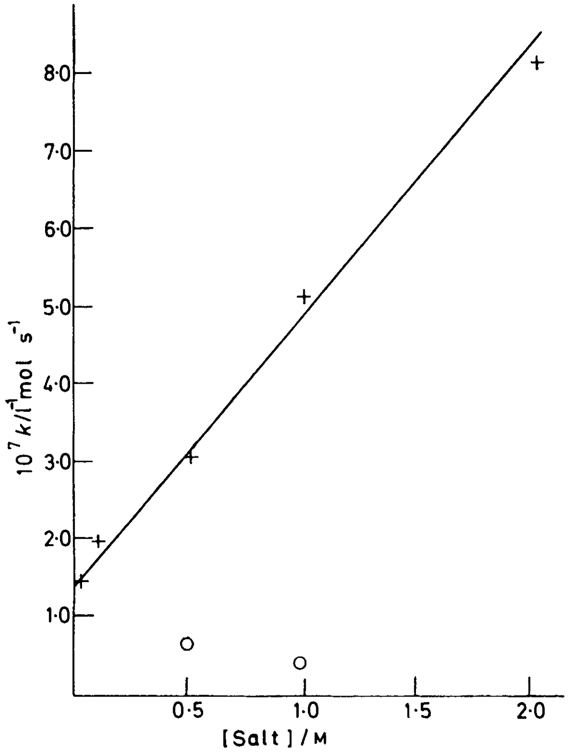


FIGURE 4 The initial reaction rate of nitration of 4-nitrophenol (0.01M) at 50° in aqueous 3.0M-hydrochloric acid with 0.2M-nitrous acid as a function of salt concentration: +, $\mathrm{NaNO_3}$; ○, NaCl

We thank Kirklees Metropolitan Council for supporting A. P. G.

[0/616 *Received*, 28*th April*, 1980]

REFERENCES

[1] E. L. Blackhall, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1952, 28; R. M. Schramm and F. H. Westheimer, *J. Amer. Chem. Soc.*, 1948, **70**, 1782.

[2] C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed, *J. Chem. Soc.*, 1950, 2628; J. Glazer, E. D. Hughes, C. K. Ingold, A. T. James, G. T. Jones, and E. Roberts, *ibid.*, p. 2657.

[3] J. H. Boyer, ' Chemistry of the Nitro- and Nitroso-groups, Part I,' ed. H. Feuer, Wiley, London, 1969, p. 215.

[4] N. S. Bayliss and D. W. Watts, *Austral. J. Chem.*, 1963, **16**, 927.

[5] B. C. Challis and A. J. Lawson, *Chem. Comm.*, 1968, 818; *J. Chem. Soc.* (*B*), 1971, 770; B. C. Challis and R. J. Higgins, *J.C.S. Perkin II*, 1972, 2365.

[6] B. C. Challis and A. J. Lawson, *J.C.S. Perkin II*, 1973, 918; B. C. Challis and R. J. Higgins, *ibid.*, 1975, 1498.

[7] G. Stedman, *J. Chem. Soc.*, 1960, 1702; D. J. Benton and

P. Moore, *J. Chem. Soc.* (*A*), 1970, 3179; P. Collings, K. Al-Mallah, and G. Stedman, *J.C.S. Perkin II*, 1975, 1734; G. Stedman, *J. Chem. Soc.*, 1959, 2943, 29, 49; J. R. Perrott, G. Stedman, and N. Uysal, *J.C.S. Dalton*, 1976, 2058.

[8] J. H. Ridd, *Adv. Phys. Org. Chem.*, 1978, **16**, 1.

[9] H. Schmid and C. Essler, *Monatsh.*, 1957, **88**, 631.

[10] M. R. Crampton, J. T. Thompson, and D. L. H. Williams, *J.C.S. Perkin II*, 1979, 18.

[11] O. Baudisch, *Science*, 1940, **92**, 336; G. Cronheim, *J. Org. Chem.*, 1947, **12**, 1; J. O. Konecny, *J. Amer. Chem. Soc.*, 1955, **77**, 5748; K. Maruyama, I. Tanimoto, and R. Goto, *J. Org. Chem.*, 1967, **32**, 2516.

[12] G. A. Benford and C. K. Ingold, *J. Chem. Soc.*, 1938, **177**, 929; E. D. Hughes, C. K. Ingold, and R. I. Reed, *J. Chem. Soc.*, 1950, 2400.

[13] F. Arnall, *J. Chem. Soc.*, 1923, **123**, 311; C. A. Bunton, E. D. Hughes, G. J. Minkoff, and R. I. Reed, *Nature*, 1946, **158**, 514; C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Nones, G. J. Minkoff, and R. I. Reed, *J. Chem. Soc.*, 1950, 2642.

[14] S. Veibel, *Ber.*, 1930, **63**, 1577.

[15] C. A. Bunton, E. D. Hughes, G. J. Minkoff, and R. I. Reed, *J. Chem. Soc.*, 1950, 2628.

[16] L. Blackwall, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1952, 28.

[17] S. E. Aldred and D. L. H. Williams, *J.C.S. Chem. Comm.*, 1980, 73.

[18] K. Singer and P. A. Vamplew, *J. Chem. Soc.*, 1956, 3971; T. A. Turney and G. A. Wright, *Chem. Rev.*, 1959, **59**, 497; T. Taylor, E. Wignall, and J. Cowley, *J. Chem. Soc.*, 1927, 1923; E. Abel and H. Schmid, *Z. Phys. Chem.*, 1928, **136**, 430; T. Suzawa, M. Honda, O. Monabe, and H. Hiyama, *J. Chem. Soc.*, 1955, 744.

[19] N. S. Bayliss and D. W. Watts, *Austral. J. Chem.*, 1956, **9**, 319.

[20] D. R. Goddard, E. H. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1950, 2559; E. D. Hughes, C. K. Ingold, and J. H. Ridd, *J. Chem. Soc.*, 1958, 58.

[21] N. V. Sidgewick, 'The Organic Chemistry of Nitrogen,' Clarendon Press, Oxford, 1966, 3rd edn., p. 84.

[22] O. Fischer and E. Hepp, *Ber.*, 1886, **19**, 2991.

[23] D. L. H. Williams, *J.C.S. Perkin II*, 1975, 655.

[24] I. D. Biggs and D. L. H. Williams, *J.C.S. Perkin II*, 1976, 601.

[25] A. Granzow and A. Wilson, *J. Org. Chem.*, 1972, **37**, 1189.