Indirect Measurement of the Rate Constants for the Diazotisation of Substituted Anilines by Nitrosyl Chloride and Nitrosyl Thiocyanate

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By using an indirect method described earlier, the relative rate constants for the diazotisation of a series of *para*-substituted anilines in 4.75M hydrochloric acid and also in 3.45M-sulphuric acid containing potassium thiocyanate (4×10^{-3}M) have been determined. The results are consistent with a mechanism involving rate-determining electrophilic nitrosation at the amino-nitrogen atom of the free base. *para*-Methoxy-substitution increases the reactivity by a factor of *ca.* 9, whereas a *para*-nitro-group deactivates by *ca.* 180 in the chloride-catalysed reaction; similar results were obtained for the thiocyanate-catalysed reaction. A good correlation was found between log (relative rate constant) and σ_p in both cases with a slope of *ca.* −3. These results argue against the suggestion that these reaction rates are diffusion-controlled, as is predicted by the early work of Schmid and his co-workers for diazotisation in 0.4M-hydrochloric acid. The kinetic substituent effects are similar to those obtained by Ridd and his co-workers for the diazotisation of *para*-substituted anilines under conditions where reaction occurs *via* the protonated form of the base. This suggests that the same factor (π-electron donation) operates in both systems.

DIAZOTISATION [1] of primary aromatic amines occurs by *N*-nitrosation, followed by a number of rapid steps involving proton transfers and loss of a water molecule. However if the amine is secondary, the reaction stops at the *N*-nitroso-amine stage. A number of nitrosating agents have been identified, *viz.* NO^+, $H_2N^+O_2$, NOCl, NOBr, NOSCN, *etc.* For a given reaction the choice of reagent is governed by the acidity, the concentration of nitrous acid, and the concentration of any added nucleophiles such as Cl^-, Br^-, or SCN^-. These reactions are usually carried out in aqueous acid solution, where the amines are extensively protonated. However, it is believed that generally reaction occurs between the nitrosating agent and the free base present in equilibrium concentration. An exception [2] to this occurs in moderate acidities, in the absence of any added nucleophiles, when reaction occurs between $H_2N^+O_2$ and the protonated form of the amine, possibly by way of an intermediate ring-bonded species. Rate measurements by Schmid and his co-workers [3] for the diazotisation of some aniline derivatives in hydrochloric acid (0.2 and 0.4M) gave values for the second-order rate constants for the reaction between nitrosyl chloride and the free base form of the anilines, in the range 1—3×10^9 l mol^{-1} s^{-1}, for aniline, *o*-, *m*-, and *p*-chloroanilines, and *o*-, *m*-, and *p*-toluidines. Although the calculation of these rate constants required some approximations, it is reasonable to assume from their magnitude and little variation with substituent, that the reaction rates are indeed diffusion-controlled,[4] although the original authors attempted to relate the rate constants to the basicities of the amines.

In earlier papers we have been concerned with the mechanism of the denitrosation reaction (the reverse of *N*-nitrosation of secondary amines) of nitroso-amines, which occurs in moderately acidic solutions. As part of this work, we developed a method [5] for the determination of the relative rate constants for the nitrosation of any species X (so long as it undergoes nitrosation irreversibly) by a variety of nitrosating agents. Scheme 1 represents the mechanism of the denitrosation process (normally reversible in the absence of X) brought about

$$\mathrm{PhNMeNO} \underset{}{\overset{\mathrm{H^+}}{\rightleftharpoons}} \mathrm{Ph\overset{+}{N}HMeNO} + \mathrm{Cl^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{PhNMeH} + \mathrm{NOCl}$$

$$\mathrm{NOCl} + \mathrm{X} \xrightarrow{k_2} \text{various products}$$

SCHEME 1

in this case by chloride ion. The observed first-order rate constant k_0 (defined by $-\mathrm{d}[\mathrm{PhNMeNO}]/\mathrm{d}t = k_0[\mathrm{PhNMeNO}]$) is given in equation (i). This assumes a

$$k_0 = k_1Kh_0[\mathrm{Cl^-}]k_2'[\mathrm{X}]/(k_{-1}[\mathrm{NMA}] + k_2'[\mathrm{X}]) \quad \text{(i)}$$

Hammett acidity dependence for the initial protonation of the nitrosoamine (and the equilibrium constant is *K*). Both X (the aniline derivatives) and NMA (*N*-methylaniline) exist very largely as the protonated form, so that $k_2' = k_2K_\mathrm{X}/h_0$ and $k_{-1}' = k_{-1}K_\mathrm{NMA}/h_0$, where K_X and K_NMA are the acid dissociation constants for X and NMA, respectively. If a constant excess of X is maintained at a fixed acidity and [Cl$^-$], then $1/k_0$ should be directly proportional to [NMA] added. The ratio k_{-1}'/k_2' is then easily obtained from the slope of the line (and hence k_{-1}/k_2) since $k_1Kh_0[\mathrm{Cl^-}]$ is the limiting value of k_0 at high [X]. This method has been used [5] to establish the reactivity of a number of species X such as urea, hydroxylamine, sulphamic acid, hydrazine, and hydrazoic acid towards nitrosation in acid solution by nitrosyl chloride, nitrosyl bromide, $H_2N^+O_2$, and more recently [6] nitrosyl thiocyanate and the unstable $NO{-}S^+C(NH_2)_2$ ion. These results agree reasonably well with those of Stedman and his co-workers,[7] who measured the rate constants for some of these reactions directly. In particular, the same reactivity sequence of species X was found, and the relative behaviour of the nitrosyl halides was also similar. The indirect method lends itself to the determination of the relative rate constants for the nitrosation of aniline and substituted anilines by any of these nitrosating species. We present in this paper results for the reactions of aniline and its

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[1] J. H. Ridd, *Quart. Rev.*, 1961, 418.

[2] E. C. R. de Fabrizio, E. Kalatzis, and J. H. Ridd, *J. Chem. Soc.* (*B*), 1966, 533.

[3] H. Schmid and E. Hallaba, *Monatsh.*, 1956, **87**, 560; H. Schmid and M. G. Fouad, *ibid.*, 1957, **88**, 631; H. Schmid and C. Essler, *ibid.*, p. 1110.

[4] Ref. 1, p. 427.

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

[6] D. L. H. Williams, *J.C.S. Perkin II*, 1977, 128.

[7] G. Stedman, private communication.

p-OMe, -Me, -CO_2H, and -NO_2 derivatives with both nitrosyl chloride and nitrosyl thiocyanate.

RESULTS AND DISCUSSION

Two sets of conditions were chosen for the kinetic experiments: (*a*) 4.75M-hydrochloric acid and (*b*) 3.45M-sulphuric acid containing potassium thiocyanate (4×10^{-3}M). Values of the equilibrium constants for the formation of nitrosyl chloride and nitrosyl thiocyanate from nitrous acid and chloride or thiocyanate ion are well established. It has been calculated that any free nitrous acid is almost quantitatively converted into nitrosyl chloride in 4.5M-hydrochloric acid.[8] From the much larger value of the equilibrium constant for nitrosyl thiocyanate formation, it is to be expected that small quantities of added thiocyanate ion would produce large accelerations. For example[9] 1×10^{-3}M-thiocyanate increases the rate constant for the *N*-nitrosation of *N*-methylaniline by a factor of *ca.* 10^4. Earlier work by us[10] has shown that under the conditions (*a*) and (*b*) used in the present work the rate constant for the uncatalysed denitrosation (by the solvent) is negligible compared with that for the Cl^- and SCN^- reactions, suggesting (by the principle of microscopic reversibility) that the reverse reactions of *N*-nitrosation occur almost entirely by way of nitrosyl chloride and nitrosyl thiocyanate, respectively, with very little contribution from $H_2N^+O_2$. In all the experiments carried out at constant [X], [Cl^-] (or [SCN^-]), and acidity, the first-order rate constant k_0 decreased as expected on adding NMA. More quantitatively there was a linear dependence of $1/k_0$ upon [NMA] as predicted by equation (i).

TABLE 1

Variation of k_0 with [NMA] for denitrosation of PhNMeNO in 4.75M-HCl containing p-MeO·C_6H_4·NH_2

10^4[NMA]/M	$10^4k_0/s^{-1}$	k_0^{-1}/s
0	95.8	104
8.23	62.8	159
16.46	47.2	212
24.7	36.4	275
32.9	31.4	318

TABLE 2

k_{-1}'/k_2' Values

Aniline derivative	Cl^- reaction	SCN^- reaction
p-H	0.90	1.78
p-Me	0.77	2.15
p-OMe	0.59	1.71
p-CO_2H	0.082	1.52
p-NO_2	0.049	0.38
m-OMe	0.24	—

Table 1 shows some typical results for k_0 as a function of [NMA] in 4.75M-hydrochloric acid with a constant excess of *para*-methoxyaniline. Values of k_{-1}'/k_2' obtained from the slopes of $1/k_0$ *vs.* [NMA] plots are given in Table 2 for both the chloride and the thiocyanate ion catalysed reactions. This ratio represents the relative bulk reactivities of the various substituted anilines and *N*-methylaniline in each case towards the particular nitrosating agent. It is easy then to obtain the bulk reactivities of the anilines relative to aniline itself, *i.e.* the values of $(k_2')_X/(k_2')_H$. These are given in Tables 3 and 4 together with the values of $(k_2)_X/(k_2)_H$ for reaction *via* the free amine (Scheme 2) obtained from $(k_2')_X/(k_2')_H$ and the pK_a values of aniline and the substituted anilines.[11]

TABLE 3

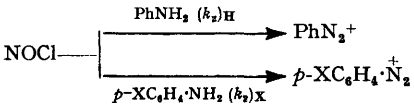
Relative reactivities for the chloride ion catalysed diazotisations

Aniline derivative	$(k_2')_X/(k_2')_H$	$(k_2)_X/(k_2)_H$
p-H	1	1
p-Me	1.18	3.6
p-OMe	1.5	8.6
p-CO_2H	11.0	9.0×10^{-2}
p-NO_2	18.5	5.6×10^{-3}
m-OMe	3.7	1.5

TABLE 4

Relative reactivities for the thiocyanate ion catalysed diazotisations

Aniline derivative	$(k_2')_X/(k_2')_H$	$(k_2)_X/(k_2)_H$
p-H	1	1
p-Me	0.83	2.5
p-OMe	1.04	6.0
p-CO_2H	1.17	9.5×10^{-3}
p-NO_2	4.72	1.4×10^{-3}



SCHEME 2

Since the anilines are almost completely in their protonated forms in these acid solutions, the $(k_2')_X/(k_2')_H$ values give the relative rate constants for reaction *via* the protonated forms. These values (Tables 3 and 4) are all (except the case of *p*-Me for the nitrosyl thiocyanate reaction) greater than one, *i.e.* both electron-attracting and -releasing substituents appear to activate the system; it is thus not easy to rationalise the results in terms of reaction *via* the protonated form of the anilines. On the other hand, the relative reactivities for reaction *via* the free base form, *i.e.* $(k_2)_X/(k_2)_H$ do fall into a discernible pattern, for both nitrosyl chloride and nitrosyl thiocyanate reactions, in that the electron-releasing *p*-Me and -OMe substituents increase the reactivity (relative to aniline itself), whereas the electron attracting *p*-CO_2H and -NO_2 substituents reduce the reactivity towards the nitrosating agents. The apparent greater bulk reactivity of *p*-nitroaniline (relative to aniline) for example is readily accounted for by its much smaller pK_a value. The true relative reactivities [$(k_2)_X/(k_2)_H$] have values expected for an

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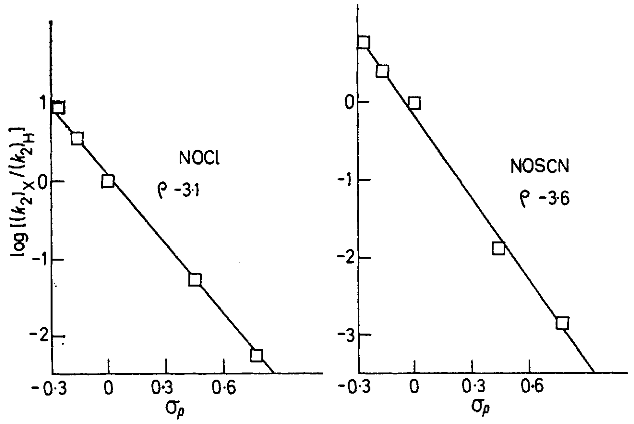
[8] H. Schmid and A. Maschka, *Z. phys. Chem.* (*B*), 1941, **49**, 171.

[9] E. Boyland and S. A. Walker, *Nature*, 1974, **248**, 601.

[10] I. D. Biggs and D. L. H. Williams, *J.C.S. Perkin II*, 1975, 107.

[11] D. D. Perrin, 'Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965; J. W. Smith, 'The Chemistry of the Amino Group,' ed. S. Patai, Interscience, New York, 1968, pp. 182, 188

electrophilic attack at the amino nitrogen atom, *i.e.* *p*-Me and -OMe are both activating whereas *p*-CO_2H and -NO_2 both reduce the reactivity towards *N*-nitrosation. In fact there is a surprisingly good correlation between $\log[(k_2)_X/(k_2)_H]$ and σ_P, as shown in the Figure, again for both nitrosating agents. The slope of the lines gives ρ values of *ca.* —3. This quite large range of reactivity from *p*-OMe to *p*-NO_2 argues against a situation where the reactions are so fast as to be diffusion-controlled. The same conclusion is reached from the k_{-1}'/k_2' values for aniline in Table 2. The true rate constant function k_{-1}/k_2 obtained by using the pK_a values of aniline and *N*-methylaniline are 1.6 for the nitrosyl chloride and 3.2 for the nitrosyl thiocyanate reaction. This activation by an *N*-methyl substituent is of the expected order for a substituent effect—Kalatzis and Ridd [12] found a similar activation effect in *N*-nitrosation by dinitrogen trioxide.

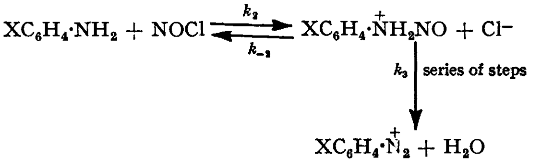


Plots of $\log[(k_2)_X/(k_2)_H]$ *vs* σ_p or diazotisations by nitrosyl chloride and nitrosyl thiocyanate

Whilst our results appear to differ from those of Schmid and his co-workers [3] on the question of selectivity, there is an interesting comparison with the findings of de Fabrizio, Kalatzis, and Ridd,[2] who obtained k_X/k_H values for the diazotisation of *para*-substituted anilines in 3M-perchloric acid as follows: *p*-Me 7.4, *p*-Cl 0.20, and *p*-OMe 9.5. Under these conditions the effective reagent is the nitrous acidium ion $H_2N^+O_2$, which attacks the *protonated* form of the amines. These results also show some discrimination amongst the substrates, with electron-releasing substituents activating and the electron-attracting substituent deactivating the system, giving a fair correlation with σ_p (ρ —3.6). It appears that our results (where nitrosation occurs through the free base) and those of Ridd and his co-workers [2] (where reaction takes place *via* the protonated species) show the same general pattern of *para*-substituent effects, suggesting that similar factors are involved. This is not unreasonable, as it is perhaps to be expected that one of the main factors governing the reactivity is the extent of π-electron donation from the aromatic ring, to the amino nitrogen atom if reaction occurs *via* the free base, and to the electrophile bonded to the aromatic ring [2] in the case of reaction *via* the protonated form.

It is not easy to explain the differences between our results and those of Schmid and his co-workers. The acidity is much higher in our case, although this should not appreciably affect the situation, unless a mechanism involving the nitrosation (by nitrosyl chloride and nitrosyl thiocyanate) of the *protonated* form of the amine becomes important at these acidities. Such a mechanism has been reported[2] for nitrosation by $H_2N^+O_2$, but *not* by the nitrosyl halides. Schmid's data are however limited to the effects of *p*-Me and *p*-Cl substituents only, and each rate constant was determined usually from two analytical points taken at an early stage of the reaction.

Preliminary results [13] have been obtained for the direct measurement (by a fast reaction technique) of the diazotisation of aniline derivatives at both low (0.2M) and high (5M) concentrations of hydrochloric acid. The results at high acidity agree well with those reported in this paper, which were obtained by an indirect method. There is clearly a greater discrimination by the substituents at higher acidity than at the lower acidity (Schmid's data). A probable explanation is that at high [Cl^-] the reverse step of *N*-nitrosation (denitrosation by Cl^-) becomes important, so that the observed rate constant is now a composite quantity including k_2, k_{-2}, and k_3 (from Scheme 3), each of which is likely to be affected by ring substitution. It is hoped to present a full account of this work shortly.



$$XC_6H_4{\cdot}NH_2 + NOCl \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} XC_6H_4{\cdot}\overset{+}{N}H_2NO + Cl^- \xrightarrow[\text{series of steps}]{k_3} XC_6H_4{\cdot}\overset{+}{N}_2 + H_2O$$

SCHEME 3

EXPERIMENTAL

Aniline and *N*-methylaniline were distilled and the *para*-substituted anilines recrystallised before use. The kinetic measurements were all carried out in water at 31 °C in the cell of a recording u.v.–visible spectrophotometer, by noting the appearance of an absorption (at fixed wavelength) due to the diazonium ion in the region 300—330 nm (not the maximum), depending upon the particular *para*-substituted aniline concerned. As the diazonium ion was not infinitely stable under these conditions, the infinity value after 10 half-lives was not considered reliable, so the Guggenheim method [14] for obtaining the first-order rate constant was employed throughout. Good first-order plots were obtained in all cases and duplicate runs agreed to within ±4%.

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[6/1060 *Received, 6th June,* 1976]

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[12] E. Kalatzis and J. H. Ridd, *J. Chem. Soc.* (*B*), 1966, 529.

[13] M. R. Crampton and D. L. H. Williams, to be published.

[14] E. A. Guggenheim, *Phil. Mag.*, 1926 **2**, 538.