Kinetics and Mechanism of the Fischer–Hepp Rearrangement and Denitrosation. Part V.[1] The Mechanism of Denitrosation

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Rate measurements have been carried out for the reaction of *N*-methyl-*N*-nitrosoaniline in hydrochloric acid solution (0·4—5M) containing an excess of sulphamic acid, urea, or sodium azide. Under these conditions denitrosation (to form *N*-methylaniline) occurs irreversibly and without formation of any significant amounts of the rearrangement product except at low chloride ion concentrations. The first-order rate coefficient is proportional to the product $h_0[Cl^-]$; this is interpreted as rate-determining nucleophilic attack by chloride ion on the protonated form of the nitrosamine. Similar results are obtained for reaction in sulphuric acid containing sodium chloride and also other nucleophiles. The reaction is very sensitive to the nature of the nucleophile: the following increasing order of reactivity is observed, Cl^-, Br^-, SCN^-, I^-; 1 : 54 : 5300 : 15,000. This contrasts with the corresponding reactions of $H_2\overset{+}{N}O_2$, which discriminates very little between these nucleophiles. Denitrosation also occurs in sulphuric acid solution containing no added nucleophiles. The rate is now proportional to $h_0^{1·6}$, and there is no evidence of any significant attack by the hydrogen sulphate ion. These results are interpreted in terms of two concurrent mechanisms, one involving denitrosation brought about by a water molecule and the other which becomes more important at high acidity, where the reacting entity is H_3O^+. These mechanisms are discussed with reference to the reverse reaction, *i.e.* *N*-nitrosation of aromatic amines.

It is well known that aliphatic (and presumably aromatic) nitrosamines $>N-NO$ can be converted almost quantitatively into the corresponding secondary amines and nitrous acid (or nitrosyl chloride) by boiling with hydrochloric acid.[2] Denitrosation apparently occurs more readily if the nitrous acid is removed, either by passing a stream of gas through the reaction mixture, or by the addition of urea[3] (a well known nitrite scavenger) or of a mild reducing agent such as ferrous ion,[4] which converts the nitrous acid into nitric oxide. Presumably, the mechanism involves nucleophilic attack by chloride ion on the protonated nitrosamine, although this has apparently never been demonstrated quantitatively nor has the effect of other nucleophiles been examined. The reaction has a certain formal similarity to the first stage of the Orton rearrangement[5] of *N*-chloroanilines, where dechlorination is brought about by chloride ion attack on the protonated substrate. In that case a second-order dependence of the rate upon hydrochloric acid concentration has been obtained,[6] *i.e.* rate $\propto [H^+][Cl^-]$. Russian workers[7] have examined the denitrosation of aromatic nitrosamines and have shown that reaction is faster in hydrochloric acid solution than in sulphuric acid. It was claimed that two mechanisms were operating, one involving nucleophilic attack by the anion HSO_4^- or Cl^- on a hydrogen-bonded complex of the nitrosamine and the acid HA, whilst the other requires unimolecular fission of such a complex to give the secondary amine and free NO^+. It was further claimed that the effects of *para*-substituents support such mechanisms. A later paper[8]

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[1] Part IV, D. L. H. Williams, *Internat. J. Chem. Kinetics*, in the press.

[2] P. A. S. Smith, 'The Chemistry of Open-chain Organic Nitrogen Compounds,' Benjamin, New York, 1966, vol. II, p. 473.

[3] W. G. Macmillan and T. H. Reade, *J. Chem. Soc.*, 1929, 585.

[4] E. C. S. Jones and J. Kenner, *J. Chem. Soc.*, 1932, 711.

[5] H. J. Shine, 'Aromatic Rearrangements,' Elsevier, Amsterdam, 1967, pp. 221—230.

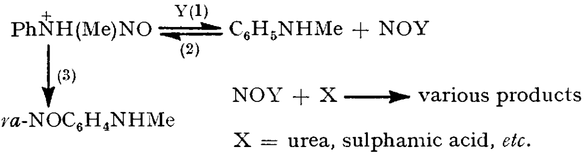
[6] F. G. Soper, *J. Phys. Chem.*, 1927, **31**, 1192; F. G. Soper and D. R. Pryde, *J. Chem. Soc.*, 1927, 2761.

[7] B. A. Porai-Koshits, E. Y. Belyaev, E. Szadowski, and V. I. Zaionts, *Doklady Akad. Nauk S.S.S.R.*, 1964, **157**, 629; B. A. Porai-Koshits, E. Y. Belyaev, and J. Szadowski, *Reakts. spos. org. Soedinenii*, 1964, **1**, 10; E. Y. Belyaev and B. A. Porai-Koshits, *ibid.*, p. 204.

[8] E. Y. Belyaev, T. I. Nikulicheva, and B. A. Porai-Koshits, *Zhur. org. Khim.*, 1965, **5**, 2141 (English translation).

by these authors discusses the denitrosation in sulphuric acid in terms of reaction *via* a singly protonated and a doubly protonated form of the nitrosamine, although there appears to be no compelling evidence for this. More recently Challis and Osborne[9] have measured the rates of a number of nitrosation reactions brought about by *N*-nitrosodiphenylamine. For some nucleophiles reaction appears to involve prior denitrosation, whilst for others it is claimed that the nitroso-group is transferred directly to the nucleophile without the intermediate formation of a free nitrosating agent. It is not clear how the choice of mechanism is governed by the nature of the nucleophile.

Earlier papers in this series[1,10,11] have been concerned with the rearrangement and denitrosation of *N*-methyl-*N*-nitrosoaniline in aqueous acid solution. It has been demonstrated that the rearrangement occurs intramolecularly and concurrently with the normally reversible denitrosation (Scheme 1). Details of reaction (3), *i.e.* leading to rearrangement, were obtained when reaction was carried out with a sufficient excess of added *N*-methylaniline. This increases the rate of *N*-nitrosation [reaction (2)] to such an extent that denitrosation (1) is completely suppressed. Relevant features of the mechanism of reaction (3) obtained in this way have been discussed.[10] Similarly, another limiting condition of Scheme 1 occurs when a sufficient quantity of a nitrite trap X is added to suppress reaction (2) completely. This ensures that reactions (1) and (3) occur concurrently, but it has been shown[11] that for Y = Cl^-, the rate of rearrangement (3) is negligibly small compared with denitrosation (1) except for very low [Cl^-], when a small amount of rearrangement does occur. The nitrite traps urea, sulphamic acid, hydroxylamine, aniline, and hydrazoic acid have all been used. So long as a certain minimum amount of X is present the reaction is zero order in X. Similar results have been found for reaction in sulphuric acid where Y is now the water molecule. It is thus possible to study the denitrosation reaction without complications either from reversibility or from a competing rearrangement reaction. The mechanisms of *N*-nitrosation of aromatic amines [reaction (2)] are well established mainly owing to the work of Ridd.[12] It is obviously of interest to determine the detailed mechanism of denitrosation and to note any comparison with the reverse reaction under comparable experimental conditions. This paper describes the results obtained for a variety of nucleophiles.



SCHEME 1

EXPERIMENTAL

N-Methyl-*N*-nitrosoaniline was prepared and purified by the standard method.[13] Kinetic measurements were carried out in a Pye–Unicam SP 8000 spectrophotometer at 31°. Typical reaction concentrations were *N*-methyl-*N*-nitrosoaniline 1·2 × 10^{-4}M and sulphamic acid 1·0 × 10^{-3}M. The reaction was followed by noting the decrease in absorbance at 275 nm corresponding to the reactant. In most cases the wavelength range 350—250 nm was scanned at suitable intervals, but for the faster reactions absorbances were recorded at fixed wavelength, 275 nm. Good first-order behaviour was found over 90% reaction, either from a measured infinity value or from a Guggenheim plot. Duplicates usually agreed to within ±5%.

RESULTS AND DISCUSSION

Table 1 gives the variation of the first-order rate coefficient k_0 (defined by $-d[I]/dt = k_0[I]$ where I is *N*-methyl-*N*-nitrosoaniline) with the concentration of hydrochloric acid. Most of the results were obtained for reaction with 10^{-3}M-sulphamic acid, but over this acidity range the reaction is independent of the concentration of sulphamic acid (so long as it exceeds some minimum value) and the same k_0 values were obtained with other nitrite scavengers X. No rearrangement occurs under these conditions except for *ca.* 2% at the lowest acidity studied. Up to 4·95M-HCl the plot of log k_0 against H_0 is linear with slope −1·62. This

TABLE 1

Variation of rate of denitrosation with [HCl]

[HCl]/M	H_0	$10^6k_0/s^{-1}$
0·42	0·28	8·75
0·70	0·02	26·2
1·37	−0·41	121
1·49	−0·46	148
1·86	−0·64	300
2·13	−0·73	437
3·05	−1·06	1600
3·61	−1·26	3340
4·14	−1·45	6075
4·95	−1·74	12,600

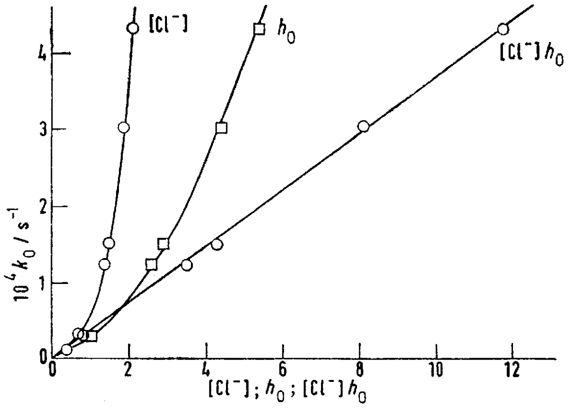


FIGURE 1 Variation of k_0 with [Cl^-], h_0, and [Cl^-]h_0 at low acidity

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[9] B. C. Challis and M. R. Osborne, *J.C.S. Perkin II*, 1973, 1526.

[10] T. D. B. Morgan, D. L. H. Williams, and J. A. Wilson, *J.C.S. Perkin II*, 1973, 473.

[11] D. L. H. Williams and J. A. Wilson, *J.C.S. Perkin II*, 1974, 13.

[12] J. H. Ridd, *Quart. Rev.*, 1961, **15**, 418.

[13] A. J. Vogel, 'Textbook of Practical Organic Chemistry,' Longmans, London, 1954, p. 547.

shows that not only hydrogen-ion catalysis is being observed. Figures 1 and 2 show that both hydrogen and chloride ion catalysis occur, as plots of k_0 against $[Cl^-]$ and h_0 both curve upwards, whereas k_0 against $h_0[Cl^-]$ is linear over the whole acid range studied. An alternative way of demonstrating this is to plot $\log k_0$ against $-H_0 + \log [Cl^-]$: this results in a straight line with slope very close to unity. The results are consistent with the mechanism set out in Scheme 2, where fast protonation of the nitrosamine (probably at the amino nitrogen) is followed by rate-determining nucleophilic attack by the chloride ion. The nitrosyl chloride is removed effectively as soon as it is formed by reaction with sulphamic acid or any other nitrite scavenger. There is no evidence of a direct reaction between sulphamic acid and the protonated nitrosamine, as the reaction is zero-order in sulphamic acid. The mechanism is supported by the observed solvent isotope effects $k_{D_2O} : k_{H_2O}$ of 2·9 at 3·05M-HCl and 3·2 at 1·55M-HCl, thus ruling out any rate-determining proton transfers. If we can assume a Hammett acidity dependence for the initial protonation, k_0 is given by $k_1K[Cl^-]h_0$. Unfortunately K is not known for aromatic nitrosamines because of their reactions in acid solution. There are indications[14] that a number of different protonated species exist at different acidities, and it is possible that we have over-simplified the situation by assuming reaction *via* the amino-protonated species. However the results yield a value of $0{\cdot}45 \times 10^{-4}$ l mol^{-1} s^{-1} for k_1K for the chloride reaction. Chloride ion catalysis has also been demonstrated by carrying out the reaction at one acidity in sulphuric acid containing varying quantities of sodium chloride. The results in Table 2 show the extent of catalysis by chloride, bromide, iodide, and thiocyanate, all in 2·52M-sulphuric acid at 31°. For each anion good straight lines were obtained for plots of k_0 against [Added salt]. The slopes of such lines should be k_1Kh_0. A summary of all the values of k_1K obtained for the different nucleophiles, and in some cases under different experimental conditions is given in Table 3. As expected k_1K is independent of the acidity of the medium and also of the nature and concentration of the added nitrite scavengers, so long as it exceeds a certain minimum value. Most of the results were in fact obtained using sulphamic acid in the concentration range 1—5 × 10^{-3}M. The trend of reactivity of the nucleophiles is very clear and is in the expected order $Cl^- < Br^- < CNS^- < I^-$, with relative rate constants for the denitrosation process of 1 : 54 : 5300 : 15,000. Denitrosation is thus very sensitive to the nature of the nucleophile, which is in marked contrast to the corresponding reactions of these nucleophiles with the nitrous acidium ion $H_2\overset{+}{N}O_2$,[15] where the rate constants change only by a factor of 1·5 over the range. This has been explained in terms of the rates being close to the diffusion controlled limit, so that no great discrimination between the various nucleophiles is to be expected. The application of the Swain–Scott equation[16] gives a good straight line (shown in Figure 3) for plots of $\log k_1K$ against n, the nucleophilic constant. The slope gives a value of 2·1 for s, the susceptibility constant. This compares with values of 0·7 for substitution reaction of ethyl tosylate and 0·9 for nucleophilic attack of

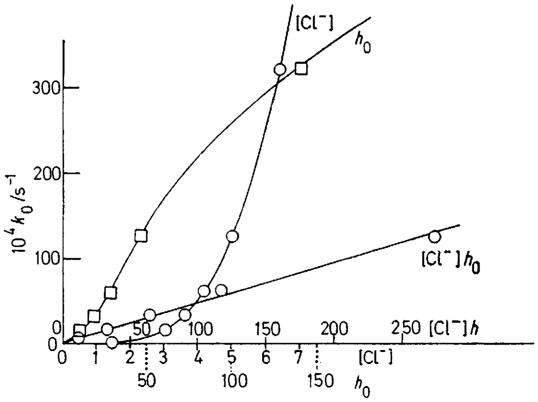

FIGURE 2 Variation of k_0 with $[Cl^-]$, h_0, and $[Cl^-]h_0$ at high acidity

$$PhN(Me)NO + H^+ \overset{K}{\rightleftharpoons} Ph\overset{+}{N}H(Me)NO$$

$$Ph\overset{+}{N}H(Me)NO + Cl^- \xrightarrow{k_1} PhNHMe + NOCl$$

$$NOCl + NH_2SO_3H \xrightarrow{\text{fast}} N_2 + SO_3 + H_2O + HCl$$

SCHEME 2

TABLE 2

Catalytic effect of added anions on denitrosation

[NaCl]/M	10^5k_0/s^{-1}	10^3[NaBr]/M	10^5k_0/s^{-1}
0	3·4	0	3·4
0·10	9·0	4·92	17·4
0·15	11·8	6·56	22·1
0·20	14·0	8·20	26·6
0·20	14·0	9·84	31·4
10^5[KI]/M	10^4k_0/s^{-1}	10^4[KCNS]/M	10^4k_0/s^{-1}
0	0·3	0	0·3
5·8	5·8	3·8	11·8
8·7	8·3	5·7	17·5
11·6	10·5	7·6	23·0
14·4	12·4	9·5	28·8

TABLE 3

Rate parameters for various nucleophiles and acids

Catalyst	[Acid]	k_1Kh_0	10^4k_1K
Cl⁻	2·52M-H_2SO_4	$55{\cdot}0 \times 10^{-5}$	0·41
Cl⁻	3·96M-H_2SO_4	$27{\cdot}8 \times 10^{-4}$	0·42
Cl⁻	4·75M-H_2SO_4	$72{\cdot}0 \times 10^{-4}$	0·43 *
Cl⁻	0·4—5·0M-HCl		0·45 †
Br⁻	2·52M-H_2SO_4	$2{\cdot}84 \times 10^{-2}$	21·1
Br⁻	3·96M-H_2SO_4	$1{\cdot}57 \times 10^{-1}$	23·8
CNS⁻	2·52M-H_2SO_4	2·99	2217
I⁻	2·52M-H_2SO_4	8·50	6300

* 1·0 × 10^{-3}M-NaN_3 used instead of NH_2SO_3H. † From the data in Table 1.

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[14] W. S. Layne, H. H. Jaffé, and H. Zimmer, *J. Amer. Chem. Soc.*, 1963, **85**, 1816.

[15] Ref. 12, p. 432 and references quoted therein.

[16] C. G. Swain and C. B. Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 141.

epichlorohydrin,[16] and shows that attack at the nitroso-nitrogen atom of protonated nitrosamines is strongly dependent upon the reactivity of the nucleophile.

The Non-catalysed Reaction.—Denitrosation also occurs in sulphuric acid containing no added salts, although reaction is now much slower than for the corresponding acidity in hydrochloric acid. Table 4 gives the variation of k_0 over a range of sulphuric acid concentration. Since the rate of denitrosation is now much reduced, rearrangement now competes more effectively than in hydrochloric acid. At 2·52M-sulphuric acid, for example, 19% rearrangement occurs.

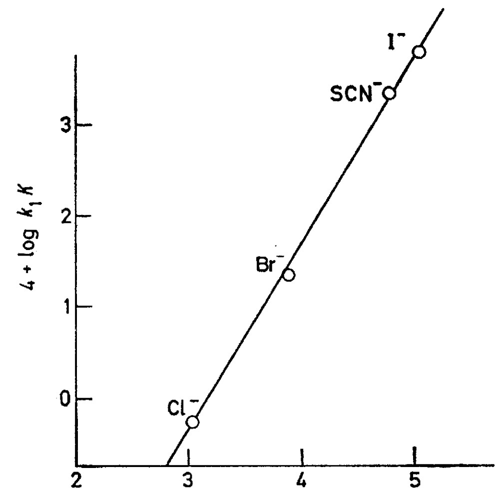


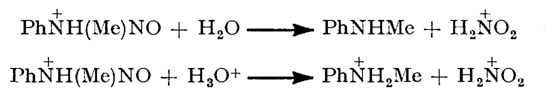
FIGURE 3 The Swain–Scott equation for the nucleophiles Cl⁻, Br⁻, SCN⁻ and I⁻

TABLE 4

Variations of k_0 and k_0' with [H_2SO_4]

[H_2SO_4]/M	H_0	10^6k_0/s^{-1}	$10^6k_0'$/s^{-1}
2·52	−1·13	34·1	27·6
3·23	−1·49	111	94
3·96	−1·82	363	323
4·66	−2·14	1180	1100
4·80	−2·20	1630	1530
5·08	−2·30	2540	2410
5·43	−2·49	4030	3870
5·67	−2·61	6370	6120
6·19	−2·86	13200	12800
6·41	−2·98	20800	20200
6·68	−3·14	38600	37900

The final column in Table 4, k_0', represents the rate constant for denitrosation only, having been ' corrected ' for rearrangement from the observed yield of rearrangement product. The plot of log k_0' against H_0 is linear but has a slope of −1·58. Apparently k_0' increases more rapidly than expected by a simple first-order h_0 dependence. There is no correlation between k_0' and $h_0 + h_0[HSO_4^-]$ which would be expected if nucleophilic attack by hydrogen sulphate ion were important. Further, only small increases in k_0 were observed (of the order of salt effects) when quite substantial quantities of sodium sulphate were added, *e.g.* at 2·52M-H_2SO_4 k_0 is increased from 0·34 × 10^{-4} to 0·43 × 10^{-4} and 0·44 × 10^{-4} s^{-1} respectively by the additions of 0·36M- and 0·71M-sodium sulphate. The best correlation that we can find takes the form $k_0 = Ch_0 + C'h_0^2$. This is shown in Figure 4 where k_0'/h_0 is plotted against h_0. Even here the situation is not straightforward since two discrete lines are obtained of different slopes with a sharp break occurring at *ca.* 5M-H_2SO_4. An explanation of this would be that at this acidity a change occurs in the nature and extent of solvation of H_3O^+, resulting in a different value of the rate constant for attack by H_3O^+ which is reflected in C'. Other explanations are of course possible. However, it seems to us, since catalysis by HSO_4^- is at best very small, that the results are best interpreted in terms of Scheme 3, where there are two concurrent reactions of the protonated nitrosamine, one with H_2O and the other with H_3O^+. Clearly the second reaction becomes more important at higher acidities. The reaction between two positively charged species seems a little unusual, but for the reverse reaction (the *N*-nitrosation of aromatic amines) it has been shown[17] that at higher acidities, a mechanism whereby the nitrous acidium ion $H_2\overset{+}{N}O_2$ attacks the protonated form of the amine does in fact occur. It is no surprise therefore to find that the reverse reaction, which should go through the same transition state, shows the same stoicheiometry. Rearrangement and denitrosation thus show somewhat different acidity dependences: the former is proportional to $h_0^{1·2}$ (ref. 10) and the latter to $h_0^{1·6}$. This explains the variation in the rearrangement : denitrosation product ratio observed as the acid concentration is changed. At 2·52M-H_2SO_4 there is 19% rearrangement, this decreases steadily to 11% at 3·96M, 7% at 4·66M, and 5% at 5·08M.



$$Ph\overset{+}{N}H(Me)NO + H_2O \longrightarrow PhNHMe + H_2\overset{+}{N}O_2$$

$$Ph\overset{+}{N}H(Me)NO + H_3O^+ \longrightarrow Ph\overset{+}{N}H_2Me + H_2\overset{+}{N}O_2$$

SCHEME 3

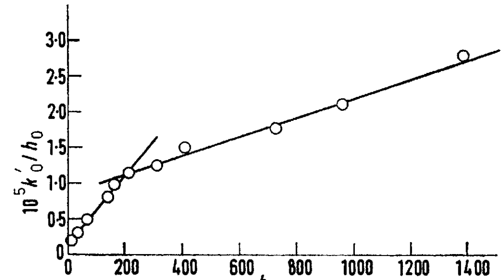


FIGURE 4 A plot of k_0'/h_0 against h_0 for denitrosation in H_2SO_4

The Russian workers[7] examined the effect of *para*-substituents on the rate of denitrosation of *N*-methyl-*N*-nitrosoaniline in sulphuric acid, and have presented their results in terms of a Hammett plot.[12] The curve obtained is explained in terms of a change of mechanism,[18]

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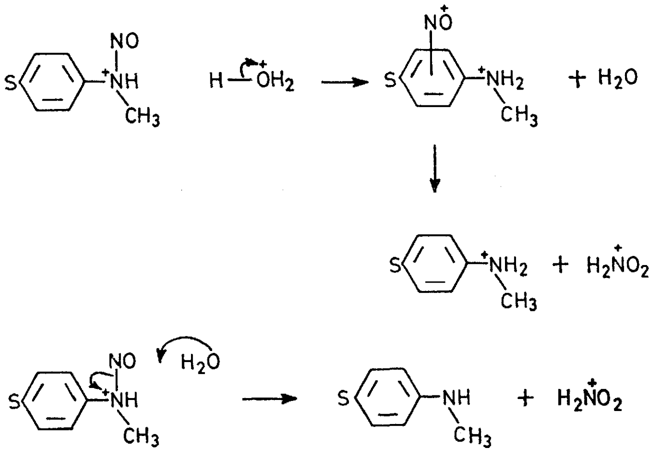
[17] E. Kalatzis and J. H. Ridd, *J. Chem. Soc.* (*B*), 1966, 529.

[18] J. Shorter in ' Correlation Analysis in Organic Chemistry—An Introduction to Linear Free-energy Relationships,' Clarendon Press, Oxford, 1973, p. 20.

although the details of such mechanisms are not clear. It does not seem to us appropriate to discuss substituent effects this way here, since it is probable that *para*-ring substituents will affect K, the equilibrium constant for the initial protonation and k_1 the rate constant for nucleophilic attack in opposing directions. The intervention of a step, as in Scheme **3**, where there is attack by H_3O^+ would further complicate the analysis, since nucleophilic attack by H_2O at the nitroso-group and a second proton transfer to the amino-nitrogen atom from H_3O^+ (Scheme 4) are likely to have different electronic requirements. Further work is in progress regarding the effect of substituents both in the aromatic ring and at the amino-nitrogen atom. In particular it is hoped that further evidence will be found for the mechanism of the non-catalysed reaction in moderately high acidity.



S = substituent

Scheme 4

We find no evidence of a direct reaction between the protonated nitrosamine and the various nitrite traps (X) added even though some of these species have substantial nucleophilic activity. The reason is quite simple; in strong acid solution very little of these species are present in the free base form, and presumably the nucleophilic activity of XH^+ is several orders of magnitude less. Aniline has a value of n, the nucleophilicity constant, of 4·49 which indicates that it lies between bromide ion and thiocyanate ion. If we assume that the direct reaction (sometimes called a transnitrosation) occurs between non-protonated aniline and the protonated nitrosamine, and that both bases act as Hammett bases, then the calculated value of k_0 for this reaction with total aniline concentration added of 10^{-3}M, is *ca.* 10^{-9} s^{-1}, which is not observable. Even if the total aniline (protonated + non-protonated) were 1M then the half-life of this reaction would be 6 days, whereas at the lowest acidity studied by us (2·52M-H_2SO_4) denitrosation brought about by the water molecule has a half-life of *ca.* 7 h. Similar considerations apply to azide ion and the other X species. It is therefore not surprising that we do not observe any direct reaction between the protonated nitrosamine and the X compounds chosen at these moderately high acidities. At very low acidities, it might be possible to observe the direct reaction with *e.g.* aniline, for at 0·1M-sulphuric acid k_0 for the water reaction is estimated at 3×10^{-8} s^{-1}. In 0·1M-hydrochloric acid however, the estimated value of k_0 for the chloride ion reaction is $0{\cdot}4 \times 10^{-6}$ s^{-1}, so that the aniline reaction would not dominate the chloride ion reaction until the total aniline concentration was of the order of 1M. Work on other nucleophiles is in progress.

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