Kinetics of the Fischer–Hepp Rearrangement

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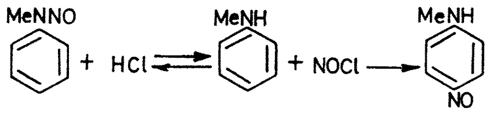
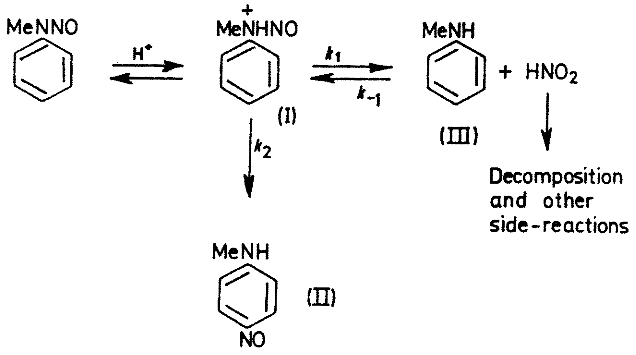
Summary The rate equation for the reaction of *N*-methyl-*N*-nitrosoaniline in aqueous hydrochloric acid is $v = k[\text{PhNMeNO}]h_0^{1\cdot17}$; this, together with the observed isotope effects and rate measurements in the presence of added *N*-methylaniline is inconsistent with the commonly accepted mechanism and shows that the rearrangement is intramolecular and takes place concurrently with reversible denitrosation.

The mechanism of the well known acid-catalysed rearrangement of aromatic *N*-nitroso-amines in the presence of hydrogen chloride[1] is widely believed[2] to involve reversible denitrosation producing nitrosyl chloride and the secondary amine, which then react to form the *C*-nitroso-product, usually the *para*-isomer, as shown in Scheme 1. The evidence for the formation of, and reaction *via* nitrosyl chloride is based solely on the fact that apparently better yields of rearranged product were obtained in hydrochloric acid than in other strong acids[3] and also that products have been isolated derived by transfer of the nitroso-group to an added amine or an olefin.[3] Nevertheless this mechanism has generally been accepted although Dewar[4] has pointed out that this evidence in fact does not specifically require this or any other mechanism.



Scheme 1,

We have determined the kinetics of the reaction of *N*-methyl-*N*-nitrosoaniline in aqueous hydrochloric acid spectrophotometrically at 31°. The reaction was strictly first-order in the nitroso-amine and log k_{obs} gave an excellent straight line of slope 1·17 when plotted against $-H_0$ in the acid range 2—6·5M. Above this acidity the rate became almost independent of the acidity. A solvent isotope effect $(k_{\text{obs}})(\text{D}_2\text{O}) : (k_{\text{obs}})(\text{H}_2\text{O})$ of 2·1 was found at *ca.* 4M acid. These results argue against the involvement of chloride ion (as in the Orton rearrangement of *N*-chloroacetanilides[5] where the rate was proportional to $[\text{HCl}]^2$) and hence of nitrosyl chloride but rather suggest that reaction takes place by unimolecular decomposition of the protonated form of the nitroso-amine (I) as in the case of the nitramine rearrangement.[6] This is supported by the fact that rearrangement takes place even in the presence of a vast excess of urea (known to react very rapidly with nitrous acid and species derived from it) which has also been demonstrated by Russian workers[7] who examined the rearrangement in sulphuric acid. We and many early workers have observed the concurrent formation of rearranged product (II) and that of dinitrosation (III). We suggest that both arise in parallel reactions from (I) as outlined in Scheme 2. Further support for this mechanism comes from the results of rate measurements in the presence of added (III). The observed rate coefficient k_{obs} is a function of k_1, k_2, and k_{-1}; Scheme 2 requires that added (III) should increase the yield of (II) whilst decreasing k_{obs}. Both of these effects are shown in the results in the Table. When a sufficiently large excess of (III) is added, the reaction leading to rearrangement is isolated and k_{obs} becomes equal to k_2. In sulphuric acid also, 80% of (II) is formed when a large excess of (III) is present.

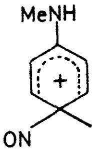


Scheme 2.

Variation of rate coefficient and yield of (II) *with added* (III)

[III] 10^3M	10^4k_{obs} (s^{-1})	Yield (II) (%)
0	5·07	28
0·44	3·74	54
0·94	3·61	60
3·08	2·80	76
3·96	2·78	78
5·71	2·84	80

As to the detailed mechanism of the rearrangement step, as yet we have no evidence apart from the observed isotope effect using 2,4,6-trideuteriated substrate, $(k_{\rm obs})_{\rm H} : (k_{\rm obs})_{\rm D}$ of 1·7 and $(k_2)_{\rm H} : (k_2)_{\rm D}$ of 2·4 at two acidities. This shows that proton loss from the σ-complex (IV) is rate-determining or conceivably that the transformation is a one-step process, which seems less likely. Rate-determining proton-transfer has been known in the nitrosation of phenols for some time[8] and has recently been demonstrated for a variety of other substrates.[9] Further work is in progress.

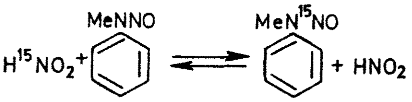


(IV)

Recently the rearrangement of *N*-nitrosodiphenylamine in methanol has been shown[10] to be first-order both in the substrate and in hydrogen chloride and almost independent of added chloride ion. A mechanism based on the formation of nitrosyl chloride and the free amine *via* a four-centred transition state was put forward. This is completely ruled out by our present results, *viz.* the H_0 correlation, solvent and ring deuterium isotope effects, effect of added *N*-methylaniline, and by the fact that reaction takes place in the presence of a large excess of urea.

Additionally we have shown by using 2,4,6-trideuteriated *N*-methyl-*N*-nitrosoaniline that the nitroso-amine can transfer the NO group to *N*-methylaniline (unlabelled) at a rate much greater than that of the rearrangement, without forming free nitrous acid or nitrosyl chloride. This reaction is acid-catalysed and shows that (I) can act as a primary nitrosating agent, thus accounting for the cross-nitrosations that have been observed.

In an earlier communication[11] we reported very little pick-up of ^{15}N in the rearranged product when reaction was carried out in the presence of $^{15}NO_2^-$ in aqueous ethanol. Repetition of this experiment in water and again in aqueous ethanol however shows that complete ^{15}N exchange occurs between the substrate and the labelled nitrite at a very early stage. We cannot explain the earlier incorrect result; possibly an impurity in the solvent destroyed the nitrite. The overall conclusion however remains that the rearrangement is an intramolecular process. ^{15}N experiments of this type cannot be used in this case to demonstrate this because of the equilibration reaction (Scheme 3).



SCHEME 3.

We have evidence that k_1 and k_2 are of the same order of magnitude, so the reversible denitrosation cannot account for the exchange.

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