# Kinetics and Mechanism of the Fischer–Hepp Rearrangement.  Part II.[1] Separation of Rearrangement and Denitrosation

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The composite observed first-order rate coefficient ($k_{obs}$) for the reaction of $N$-methyl-$N$-nitrosoaniline in hydrochloric acid was found to decrease with added $N$-methylaniline to a limiting value while the yield of rearrangement product increased accordingly. This limiting value ($k_2$) is taken to be the rate coefficient for the rearrangement process alone. The results accord with a previously suggested scheme involving concurrent rearrangement and denitrosation. There was a linear dependence of log $k_2$ upon $H_0$ (slope $-1\cdot2$) between 3M- and 6·5M-acid, above which the rate levelled off, and a ring deuterium isotope effect $(k_2)_H : (k_2)_D$ of 2·4. Substituent (*meta*) effects confirmed the electrophilic nature of the rearrangement and supported the idea of concurrent rearrangement and denitrosation. A more detailed reaction mechanism is suggested for the rearrangement, involving the reversible formation of two intermediates, a σ-complex and probably a π-complex.

In Part I [1] the reaction of $N$-methyl-$N$-nitrosoaniline in hydrochloric acid at 31 °C was shown to yield the product of rearrangement, $N$-methyl-$p$-nitrosoaniline, together with the product of denitrosation, $N$-methylaniline. The overall reaction was shown to be of the first order in both the reactant and $h_0$, and there was a solvent isotope effect $(k_{obs})_{D_2O} : (k_{obs})_{H_2O}$ of 2·1. Rearrangement took place even in the presence of large amounts of the ' nitrite ' trap, urea.[1,2] These facts were considered to be inconsistent with the generally accepted mechanism [3] (based only on product analyses) for the rearrangement, whereby the secondary amine and nitrosyl chloride are reversibly formed and then react further by $C$-nitrosation to give the *para*-nitroso-rearrangement product. If this mechanism were operative then one might expect a second-order dependence on the hydrochloric acid concentration as was observed [4] in the Orton rearrangement of $N$-chloroanilides. It has recently been shown [5] that the rate of the rearrangement reaction is independent of the chloride-ion concentration. On the basis of these results it was suggested [1] that rearrangement and denitrosation were separate concurrent processes deriving from a common intermediate, the protonated $N$-nitrosoamine, as set out in Scheme 1. Rearrangement was said to occur by some intramolecular process. In order to examine further the rearrangement it is necessary to separate it from the denitrosation. It is difficult to determine the individual rate coefficients from Scheme 1 as it stands, in the absence of information concerning the decomposition and other side reactions of the ' nitrite ' species at these

relatively high acid concentrations. Accordingly we have set out to examine features of the rearrangement alone by attempting to suppress the denitrosation completely. It was hoped to achieve this by carrying

SCHEME 1
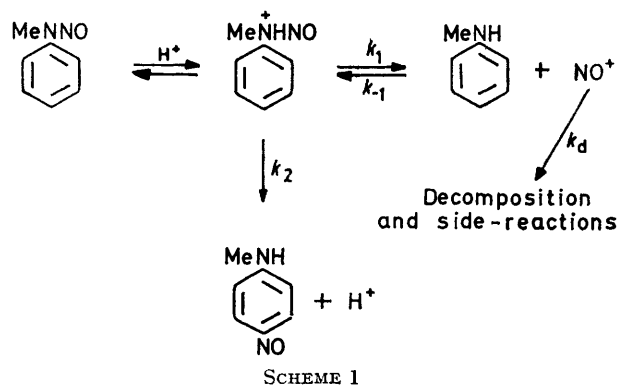
out the reaction in the presence of a large excess of $N$-methylaniline, thereby increasing the rate of $N$-nitrosation (step $k_{-1}$) such that the denitrosation (step $k_1$) becomes relatively unimportant. The results are presented and discussed. A preliminary account has appeared.[6]

## EXPERIMENTAL

*Materials.*—Some details of the preparations have been described.[1] $m$-Chloro-$N$-methylaniline was prepared by methylation of $m$-chloroaniline with dimethyl sulphate and the $N$-nitroso-derivative was obtained by nitrosation in dilute acid solution with sodium nitrite. After recrystallisation from ethanol it had m.p. 35 °C (lit.,[7] 34—35 °C).

[1] T. D. B. Morgan and D. L. H. Williams, *J.C.S. Perkin II*, 1972, 74.
[2] T. I. Aslapovskaya, E. Y. Belyaev, V. P. Kumarev, and B. A. Porai-Koshits, *Reakts. sposobnost. org. Soedinenii*, 1968, **5**, 456.
[3] H. J. Shine, ' Aromatic Rearrangements,' Elsevier, Amsterdam, 1967, pp. 231—235.
[4] See ref. 3, pp. 221—228.
[5] B. T. Baliga, *J. Org. Chem.*, 1970, **35**, 2031.
[6] T. D. B. Morgan and D. L. H. Williams, *Chem. Comm.*, 1970, 1671.
[7] R. Stoermer and P. Hoffmann, *Ber.*, 1898, **31**, 2531.

Similarly, $m$-methoxy-$N$-methyl-$N$-nitrosoaniline and $m,N$-dimethyl-$N$-nitrosoaniline were obtained from $m$-anisidine and $m$-toluidine, respectively. They were purified by vacuum distillation and had b.p. 100 °C at 0·1 mmHg (lit.,[8] 98 °C at 0·1 mmHg) and b.p. 88—89 °C at 1 mmHg (lit.,[9] 89—90 °C at 1 mmHg). For each compound, the $p$-nitroso-derivative was obtained by carrying out the rearrangement in HCl–ethanol and was purified by column chromatography and recrystallisation. The u.v.–visible spectra of these derivatives in acid solution were recorded; they corresponded with the spectra obtained during the kinetic measurements.

*Kinetic Measurements.*—Runs were carried out at 31 °C in a recording u.v.–visible spectrophotometer, usually by scanning the wavelength range 450—250 nm at appropriate intervals. Some of the longer runs were carried out by recording the optical density at a fixed wavelength (usually 340 nm) over three half-lives of the reaction. Rate coefficients were determined for the appearance of the peak corresponding to the protonated form of the $p$-nitroso-rearrangement product. These values agreed with those determined for the disappearance of the reactant. Good first-order plots were obtained in all runs by use of the Guggenheim method for a reaction where the final reading is unknown, since there was some uncertainty regarding the ' infinity ' value owing to slow decomposition of the product.

## RESULTS AND DISCUSSION

Table 1 shows the variation of $k_{obs}$ and the yield of rearrangement product over a range of concentration of

TABLE 1

Effect of added $N$-methylaniline on the overall rate coefficient and yield of rearrangement product

| $10^3[N$-Methylaniline]/ M added | $10^4 k_{obs}/s^{-1}$ | Rearrangement (%) |
|---|---|---|
| 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 |

[$N$-Methyl-$N$-nitrosoaniline] $= 1·2 \times 10^{-4}$M in all cases.

added $N$-methylaniline for the reaction of $N$-methyl-$N$-nitrosoaniline in 5·9M-HCl. The rate coefficient decreases to a limiting value as the concentration of $N$-methylaniline is increased, whilst the yield of rearrangement product increases towards a maximum around 80%. Both sets of figures level off when there is $ca.$ 30-fold excess of the secondary amine present. If as a first approximation a steady-state treatment is carried out on the ' nitrite ' species, it can be shown that $k_{obs}$ will become equal to $k_2$ if $k_{-1}[N$-methylaniline$] \gg k_d$, $i.e.$, at high concentrations of added $N$-methylaniline, whilst at lower concentrations of $N$-methylaniline $k_{obs}$ will decrease with added $N$-methylaniline, $i.e.$, as observed experimentally. This method enables $k_2$ * to be measured directly by complete suppression of the denitrosation part of the reaction. The product analysis confirms this idea since the yield of rearranged product increases towards a maximum in the region of 80%.

* Values of $k_2$ determined this way necessarily include the equilibrium constant for protonation of the nitrosoamine.

The remaining 20% cannot be accounted for at present, but may represent some formation of, and possibly subsequent reaction of, the $o$-nitroso-isomer. No $ortho$-product has ever been isolated from the Fischer–Hepp rearrangement; indeed, $o$-nitrosoamines have only rarely been characterised as products from any reaction.[10]

Increased yields of rearrangement product brought about by the addition of sodium nitrite have been observed by early workers [11] and by us. This is readily explained by Scheme 1, since it is to be expected that added nitrite would have the same effect as added $N$-methylaniline, $i.e.$, to increase the rate of $N$-nitrosation. It is not, however, particularly convenient to carry out a kinetic study in the presence of added nitrite, since a substantial fraction of the nitrite is diverted along other pathways, $viz.$, decomposition and side-reactions, such as the $N$-nitrosation of the rearranged product. Further, the relatively large quantities of nitrite required would interfere with the analytical method employed in this work by producing a large absorption in the u.v. spectrum in the region where the $p$-nitroso-compound absorbs.

All our data in Part I relate to measurements of the composite rate coefficient $k_{obs}$. We have now determined $k_2$ as a function of acidity by measuring, in each case, the limiting value of $k_{obs}$ with added $N$-methylaniline. The variation of log $k_2$ with $-H_0$ is shown in Table 2. Between 3M- and 6·5M-acid there is a linear dependence of log $k_2$ upon $-H_0$ with a slope of 1·2; above 6·5M-acid the rate levels off. This is the same

TABLE 2

Variation of the rate coefficient for rearrangement ($k_2$) with acidity

| [HCl]/M | $-H_0$ | $10^4 k_2/s^{-1}$ |
|---|---|---|
| 3·53 | 1·23 | 0·26 |
| 3·78 | 1·32 | 0·31 |
| 4·70 | 1·65 | 0·89 |
| 4·90 | 1·72 | 1·15 |
| 5·46 | 1·91 | 1·76 |
| 5·90 | 2·07 | 2·80 |
| 6·50 | 2·30 | 5·90 |
| 6·85 | 2·44 | 6·29 |
| 7·65 | 2·74 | 10·3 |
| 8·06 | 2·89 | 14·5 |
| 8·87 | 3·18 | 16·0 |

pattern as was observed for the variation of log $k_{obs}$ with $-H_0$, perhaps somewhat fortuitously, since $k_{obs}$ is a composite rate coefficient; it may well be that the denitrosation shows the same dependence on acidity if $N$-methylaniline is formed from the same protonated $N$-nitrosoamine intermediate. The slope of 1·2 is of the expected order for the protonation of a tertiary base. The levelling-off of the rate coefficient coincides with the change in the spectrum of the reactant from a maximum at 269 nm ($\varepsilon$ 7040) to a maximum at $ca.$ 240 nm with a much increased extinction coefficient. This is readily accounted for in terms of the formation, at these

[8] M. F. Millson and R. Robinson, *J. Chem. Soc.*, 1955, 3362.
[9] J. V. Braun, K. Heider, and E. Müller, *Ber.*, 1918, **51**, 279.
[10] D. W. Russell, *J. Chem. Soc.*, 1963, 894; 1964, 2829.
[11] J. Houben, *Ber.*, 1913, **46**, 3984.

acidities, of significant quantities of the protonated form. At higher acidities it is expected that the reactant will be completely in the protonated form.

Low yields of rearrangement product have been reported [12] for the Fischer–Hepp rearrangement in sulphuric acid. By carrying out the reaction in the presence of a 30-fold excess of $N$-methylaniline, we have been able to obtain yields of the rearrangement product of up to 80% in sulphuric acid. The kinetics of the reaction in sulphuric acid containing excess of $N$-methylaniline show the usual linear $H_0$ plot which levels off at high acidity. In the absence of complicating side reactions, there is no reason why this method should not give almost quantitative yields of the rearrangement product from any aqueous acidic medium. Such media have not in the past been considered the most favourable systems for producing high yields of rearrangement product.

In order to establish whether the substitution by the nitroso-group at the *para*-position is electrophilic or nucleophilic in character, we have examined the effects of three *meta*-substituents on the kinetics and products of the reaction. The results are in Table 3. Clearly,

TABLE 3

Substituent effects on the overall rate coefficient and yield of rearrangement product from $RC_6H_4N(Me)NO$

| R | $k_{obs}/s^{-1}$ | Rearrangement (%) |
|---|---|---|
| H | $3\cdot6 \times 10^{-5}$ | 55 |
| $m$-OMe | $1\cdot0 \times 10^{-3}$ | 92 |
| $m$-Me | $9\cdot1 \times 10^{-5}$ | 40 |
| $m$-Cl | $3\cdot7 \times 10^{-6}$ | 14 |

(At $H_0 = -1\cdot0$, *i.e.*, 3M-HCl).

both the electron-releasing substituents –OMe and –Me increase the rate of reaction whilst the electron-attracting –Cl substituent reduces $k_{obs}$ appreciably. It is conceivable that part or all of the rate changes may be due to the effect of the substituents on the protonation equilibria of the nitroso-amines. The $pK_a$ values of these have not been determined, presumably because reaction takes place in acid solution. The effect of *meta*-substituents on the $pK_a$ value of aniline may be usefully taken as a guide [13] ($NN$-dimethylaniline derivatives show similar behaviour). Both $m$-chloro- and $m$-methoxy-substituents decrease the base strength of aniline whilst a $m$-methyl substituent results in a small increase. So for both $m$-chloro- and $m$-methyl substituents the rate changes are in the direction expected, if the protonation of the nitroso-amine is the main factor concerned, although it seems to us unlikely that the relatively small changes expected in the $pK_a$ values could account completely for the observed results. However, in the case of the $m$-methoxy-substituent there is no doubt; the $pK_a$ value is *decreased*, presumably by the $-I$ inductive effect, whilst the rate coefficient is *increased* by a large factor. It is more likely that the substituent effects reflect the electrophilic nature of the substitution by $NO^+$. Similar rate data were obtained at higher acidities, where the degree of protonation of

the substrate is much more extensive. In addition, the yield of rearrangement product is much increased for the methoxy-compound and much reduced for the chloro-compound. These *meta*-substituents would be expected to have a very small effect on the rate of denitrosation since they are some distance away from the breaking N–N bond. For rearrangement, however, it is to be expected that the $m$-methoxy-substituent would produce a rate enhancement with a corresponding rate reduction for the $m$-chloro-system since these substituents are now in a position to stabilise or destabilise the transition state for the step leading to rearrangement. These results are fully consistent with concurrent rearrangement and denitrosation as suggested in Scheme 1; $m$-methoxy-substitution so increases the rate of rearrangement that it is now virtually quantitative, whilst chloro-substitution reduces the rate of rearrangement sufficiently to make the denitrosation reaction dominant. The reactions of all the substituted $N$-nitrosoamines were subject to acid catalysis, giving a linear plot of log $k_{obs}$ against $-H_0$ with slope *ca.* $1\cdot2$ for most of the acidity range studied. All also showed the levelling-off effect of the rate coefficient at high acidity (around $6\cdot5$M-HCl) consistent with full protonation of the reactant at these acidities.

In Part I [1] a ring deuterium isotope effect of $1\cdot7$ $(k_H : k_D)$ was found (on $k_{obs}$) for the reaction of $N$-methyl-$N$-nitrosoaniline and its 2,4,6-trideuterio-analogue. We have now determined the deuterium isotope effect on the rearrangement alone $(k_2)$ by the method already described for suppressing denitrosation with added $N$-methylaniline, using in the case of the deuterium experiment 2,4,6-trideuterio-$N$-methylaniline. At $5\cdot9$M-HCl, $(k_2)_H : (k_2)_D$ was determined as $2\cdot4$. Similar isotope effects were found at several different acidities for the $m$-methoxy-compound where the rearrangement is virtually quantitative. As expected, this isotope effect is greater than that observed on $k_{obs}$ since the latter includes the denitrosation reaction which should not be subject to a primary ring isotope effect. A synchronous process involving direct transfer of the nitroso-group from the amino nitrogen atom to the *para*-position, together with proton loss from the ring, seems to us very unlikely because of the large distance involved. Thus the mechanism requires participation by the σ-complex (II) (in Scheme 2) from which proton loss is, at least in
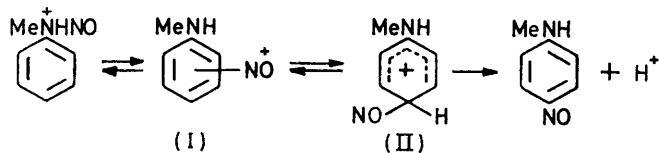
SCHEME 2

part, rate-determining. Since it is difficult, again, to envisage the direct formation of (II) from the protonated $N$-nitrosoamine, it seems reasonable to suggest that

[12] P. W. Neber and H. Rauscher, *Annalen*, 1942, **550**, 182.
[13] J. W. Smith in 'The Chemistry of the Amino-group,' ed. S. Patai, Interscience, New York, 1968, p. 183.

another intermediate is formed before (II). This intermediate (I) requires that the nitroso-group has become detached from the amino nitrogen but is still attached to the aromatic system. Since the process of substitution is likely to be electrophilic, as shown by substituent effects, the nitroso-group will become detached as $NO^+$. We have written (I) as some kind of π-complex, since it seems the most convenient and simple way of representing this intermediate. The existence of the ring isotope effect requires that the formation of both these intermediates is reversible. Primary isotope effects are well known [14] in the nitrosations of many aromatic compounds; the suggested mechanism includes rate-determining proton loss from intermediates such as (II). It may be that nitroso-σ-complexes of this type have some additional stability not generally found in σ-complexes formed in other electrophilic substitutions (where isotope effects are not usually observed). This may well account for the exclusive formation of the para-isomer in the Fischer–Hepp rearrangement.

[14] K. M. Ibne-Rasa, J. Amer. Chem. Soc., 1962, 84, 4962; B. C. Challis, R. J. Higgins, and A. J. Lawson, Chem. Comm., 1970, 1223.