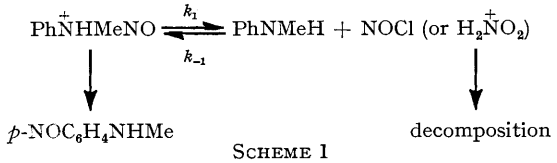
Kinetics and Mechanism of the Fischer–Hepp Rearrangement. Part III.[1] Rearrangement and Denitrosation in the Presence of Urea and Other Nucleophiles

By **D. Lyn H. Williams** * and **John A. Wilson**, Department of Chemistry, Durham University, Durham

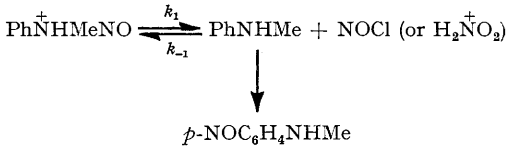
Rate measurements and product analyses have been carried out for the reaction of *N*-methyl-*N*-nitrosoaniline in both hydrochloric and sulphuric acid in the presence of added urea, sulphamic acid, sodium azide, and aniline. From the variation of the observed first-order rate coefficient (k_{obs}) with urea *etc.*, added *N*-methylaniline, added salts, and the changing acidity of the medium, together with the deuterium solvent isotope effect, a rate equation is established which is derived from a reaction mechanism involving concurrent rearrangement and (reversible) denitrosation. Features of the denitrosation reaction have been determined for the first time. In the presence of chloride (or bromide) ions the immediate product of denitrosation is *N*-methylaniline and nitrosyl chloride (or bromide) which then reacts rapidly with the added nucleophiles. The same mechanism, but involving the nitrous acidium ion $H_2\overset{+}{N}O_2$, is found for reaction in sulphuric acid. There is no evidence for a direct transnitrosation which does not involve the intermediacy of a free nitrosating agent either in hydrochloric or in sulphuric acid.

In earlier papers of this series [1,2] we have reported kinetic measurements and product analyses for the reaction of *N*-methyl-*N*-nitrosoaniline (NMNA) in hydrochloric acid solution. It was established that rearrangement to give *N*-methyl-*p*-nitrosoaniline and denitrosation to give *N*-methylaniline (NMA) took place in two separate concurrent reactions of the protonated form of the reactant (see Scheme 1). It was possible to isolate the



Scheme 1

rearrangement, by allowing reaction to take place in the presence of added NMA in sufficient excess to suppress denitrosation completely. Part II [1] describes mechanistic features of rearrangement (Fischer–Hepp) obtained in this way. Thus the previously generally accepted mechanism for this rearrangement [3] (see Scheme 2),



Scheme 2

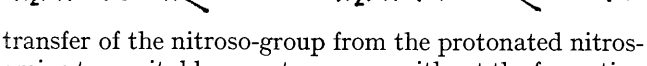
which was based completely on product analyses, and which involved denitrosation *followed by* *C*-nitrosation of the amine formed, was shown to be incorrect. One piece of evidence quoted [4] in support of the early intermolecular mechanism is the observation [5] that in the presence of excess urea *N*-methyl-*m*-nitro-*N*-nitrosoaniline undergoes complete denitrosation with no trace

[1] Part II, T. D. B. Morgan, D. L. H. Williams, and J. A. Wilson, *J.C.S. Perkin II*, 1973, 473.
[2] T. D. B. Morgan and D. L. H. Williams, *J.C.S. Perkin II*, 1972, 74.
[3] See for example, H. J. Shine, ' Aromatic Rearrangements,' Elsevier, Amsterdam, 1967, pp. 231—235.
[4] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' Bell, London, 1969, 2nd edn., p. 901.
[5] W. Macmillen and T. H. Reade, *J. Chem. Soc.*, 1929, 585.

of rearrangement. However, this nitrosoamine has never, so far as we are aware, been shown to undergo any rearrangement even in the absence of urea. No doubt this is as a result of the deactivating effect of the *m*-nitro-group which reduces the rate of rearrangement greatly [1] whilst having only a relatively small effect (if any) upon the rate of denitrosation.

Russian workers [6] and we [2] have observed separately the formation of rearranged product in the presence of quite large excesses of urea or sulphamic acid. Since these materials are generally thought of as being very reactive towards nitrous acid or nitrosyl chloride (*i.e.* are good ' nitrite ' traps), these qualitative experiments were taken to support the intramolecular nature of the rearrangement. The Russian workers proposed further that the rearrangement was in fact part *intra*- and part *inter*-molecular having assumed that the reaction in the presence of urea completely suppressed the reverse step of denitrosation, *i.e.* steps k_{-1} in Schemes 1 and 2. This does not accord with our kinetic results,[1] particularly those for reaction carried out with added NMA where that part of the reaction leading to rearrangement can be isolated. Further information regarding the denitrosation process would be forthcoming from a detailed kinetic study of the reactions of NMNA in the presence of urea and other ' nitrite ' traps. The results of such a study are presented and discussed in this paper.

It has been suggested recently [2,7] that a direct nitrosation (a transnitrosation) of the type shown in equation (1) might be operative in these situations. Here the



(1)

transfer of the nitroso-group from the protonated nitrosamine to a suitable acceptor occurs without the formation of free nitrous acid (or its protonated form) or a nitrosyl halide. We would expect to discover from a detailed kinetic study of the reactions of the nitrosoamine with urea *etc.*, whether such a mechanistic pathway exists in these systems.

EXPERIMENTAL

Materials.—NMNA was prepared and purified as previously described.[2] NMA was purified by distillation; urea, sulphamic acid, and sodium azide were recrystallised from water. AnalaR aniline was used without further purification. Solutions of DCl in D_2O were prepared by adding D_2O cautiously to PCl_5 and absorbing the DCl gas in D_2O. It was necessary to introduce three traps at $-60°$ to remove other products of the reaction. D_2SO_4 was obtained commercially.

Kinetic Measurements.—All the reactions were followed directly in a Unicam SP 8000 recording spectrophotometer in a cell block which was thermostatted at 31°. Ususally a convenient range of the spectrum (*e.g.* 250—300 nm) was scanned at appropriate intervals. When rearrangement occurred rate coefficients were obtained either from the decreasing optical density due to the reactant at 275 nm or from the appearance of the product peak (protonated) at 340 nm. Both methods agreed to within ±5%. For some runs readings of the optical density at a fixed wavelength were continuously recorded. When a reliable infinity value was obtained the first-order rate coefficients were determined from the integrated first-order rate equation; otherwise the method of Guggenheim was used. Again there was very good agreement between the two methods. A typical run is shown in Table 1.

TABLE 1

Typical rate data for the reaction of 1×10^{-4}M-NMNA and $1{\cdot}8 \times 10^{-3}$M-NaN_3 in 4·75M-H_2SO_4

t (units of 1·786 min)	0	1	2	3	4	5
Optical density (at 270 nm)	0·939	0·828	0·727	0·643	0·570	0·508
$10^4k_{obs}/s^{-1}$		13·9	14·1	14·1	14·1	14·0
t (units of 1·786 min)	6	7	8	9	10	11
Optical density (at 270 nm)	0·455	0·407	0·368	0·330	0·300	0·275
$10^4k_{obs}/s^{-1}$	14·0	14·1	14·0	14·2	14·2	14·2
t (units of 1·786 min)	12	13	14	15	16	17
Optical density (at 270 nm)	0·253	0·237	0·220	0·208	0·196	0·186
$10^4k_{obs}/s^{-1}$	14·2	14·1	14·2	14·0	14·0	14·0
t (units of 1·786 min)	18	19	20	∞		
Optical density (at 270 nm)	0·177	0·170	0·165	0·135		
$10^4k_{obs}/s^{-1}$	14·0	14·0	13·8			

Mean $k_{obs} = 14{\cdot}1 \times 10^{-4}$ s^{-1}

RESULTS AND DISCUSSION

Both rearrangement and denitrosation occurred when *N*-methyl-*N*-nitrosoaniline was allowed to react in hydrochloric acid in the presence of an excess of urea. Table 2 shows the variation in the yields of the products

TABLE 2

Variation of product yields and k_{obs} with [Urea]

10^3[Urea]/M	Rearrangement (%)	Denitrosation (%)	$10^4k_{obs}/s^{-1}$
0	28	69	5·1
3·4	19	75	7·2
10·0	12	81	11·8
18·2	9	83	15·3
29·2	6	84	23·6

All at 5·90M-HCl, [NMNA] = $3{\cdot}0 \times 10^{-4}$M, at 31°.

of both reactions as a function of the initial urea concentration, together with the first-order rate coefficient k_{obs}. Clearly denitrosation is favoured as the urea concentration is increased, at the expense of rearrangement. This is associated with a markedly increasing value of k_{obs}. However at very high urea concentrations, where no rearrangement occurs, k_{obs} levels off to a limiting value at *ca.* 14×10^{-4} s^{-1} in 3·05N-HCl. These results are shown in Table 3 together with data for various concentrations of added sodium azide, sulphamic acid, and aniline. These refer to reactions in 3·05M-HCl since the rates are inconveniently high at the acidity to which the results in Table 2 refer. Within experimental error the same limiting value for k_{obs} is obtained for all the added nucleophiles. (The decreasing value in the case of urea at very high concentrations is probably due to the

[6] T. I. Aslapovskaya, E. Y. Belyaev, V. P. Kumarev, and B. A. Porai-Koshits, *Reakts. spos. org. Soedinenii*, 1968, **5**, 465, and later papers.

[7] B. C. Challis and M. R. Osborne, *Chem. Comm.*, 1972, 518.

TABLE 3

Limiting rate data for added urea, sodium azide, aniline, and sulphamic acid in HCl

[Urea]/M	$10^4k_{obs}/s^{-1}$	10^3[Azide]/M	$10^4k_{obs}/s^{-1}$
0·01	6·25	1·0	16·6
0·05	11·7	3·0	17·3
0·10	14·4	5·0	16·4
0·25	12·9	5·0 (0·52M added Cl^-)	23·0
0·25 (D_2O)	32·1	5·0 (0·52M added Br^-)	176
0·65	10·1	5·0 (4·47M total H^+)	32·3
		5·0 (D_2O)	49·0

10^3[Aniline]/M	$10^4k_{obs}/s^{-1}$	10^3[Sulphamic acid]/M	$10^4k_{obs}/s^{-1}$
1·0	13·9	3·0	16·7
3·0	13·8	5·0	16·9
5·0	13·7	5·0 (D_2O)	48·3
3·0 (0·52M added Cl^-)	23·8		
3·0 (0·52M added Br^-)	175		

All at 3·05M-HCl, [NMNA] = 1·2 × 10^{-4}M, at 31°.

effect on the acidity.) This limiting-rate reaction is subject to both chloride ion and hydrogen ion catalysis and gives a solvent isotope effect $k_{D_2O} : k_{H_2O}$ of *ca.* 2·8 for all the nucleophiles. Under these circumstances it appears that we are measuring the rate of a reaction which does not involve the added nucleophile. The results are qualitatively in agreement with the reaction

$$\mathrm{PhNMeNO} + \mathrm{H^+} \underset{}{\overset{K}{\rightleftharpoons}} \mathrm{Ph\overset{+}{N}HMeNO}$$

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

$$\mathrm{Ph\overset{+}{N}HMeNO} \xrightarrow{k_2} p\text{-}\mathrm{NOC_6H_4NHMe}$$

$$\mathrm{NOCl} + \mathrm{X} \xrightarrow{k_3} \text{Products (series of fast steps)}$$

$\mathrm{X} = \mathrm{CO(NH_2)_2}$, $\mathrm{NH_2SO_3H}$, $\mathrm{HN_3}$, or $\mathrm{PhNH_2}$

SCHEME 3

sequence in Scheme 3, where rearrangment and denitrosation arise by separate reactions of the protonated nitrosoamine, denitrosation occurring by chloride ion attack to form nitrosyl chloride which then reacts rapidly with the added nucleophile X. This scheme leads to the general rate equation given in equation (2). At sufficiently high concentrations of X equation (2) is simplified

$$-\mathrm{d[NMNA]}/\mathrm{d}t = k_2K[\mathrm{NMNA}][\mathrm{H^+}] + \frac{k_1k_3K[\mathrm{NMNA}][\mathrm{H^+}][\mathrm{Cl^-}][\mathrm{X}]}{k_{-1}[\mathrm{NMA}] + k_3[\mathrm{X}]} \quad (2)$$

if $k_3[X] \gg k_{-1}[NMA]$ so that the first-order rate coefficient k_{obs} is given by equation (3). At 3·05M-HCl k_2

$$k_{obs} = k_2K[\mathrm{H^+}] + k_1K[\mathrm{H^+}][\mathrm{Cl^-}] \quad (3)$$

is negligibly small compared with $k_1[Cl^-]$ (no rearrangement is observed) so that k_{obs} in effect gives the rate coefficient for the reaction of the protonated form of the nitrosamine with chloride ion. We would expect this to show the observed chloride ion, bromide ion, and hydrogen ion catalysis together with a solvent isotope effect $k_{D_2O} > k_{H_2O}$.

Challis and Osborne [7] observed similarly a limiting value of the rate coefficient for the reaction of *N*-nitrosodiphenylamine in 0·18M-HCl with both *N*-methylaniline and hydrazoic acid which they interpreted as a rate-limiting proton transfer to the nitrosoamine from the solvent, together with, in the case of *N*-methylaniline, a direct transnitrosation. Under the conditions of our experiments the results are consistent only with the formation of nitrosyl chloride which then acts as the nitrosating agent towards X. We would, of course, not be able to observe by our kinetic method the direct transnitrosation of *N*-methylaniline itself. It does however appear that this is unlikely under our conditions, since there is no transnitrosation to the other added nucleophiles which are present in comparable concentrations and which show about the same, or in some cases greater, reactivityt owards other nitrosating agents.

Scheme 3 predicts another limiting form of the general rate equation [equation (2)] at high concentrations of added NMA. Under these conditions *i.e.* if $k_{-1}[NMA] \gg k_3[X]$,k_{obs} is given by equation (4), denitrosation now

$$k_{obs} = k_2K[\mathrm{H^+}] \quad (4)$$

giving way exclusively to rearrangement. Data showing the variation of k_{obs} and the % rearrangement at constant urea concentration as a function of added NMA are shown in Table 4. It is obvious that k_{obs} tends

TABLE 4

Variation of k_{obs} and % rearrangement with [NMA]

10^3[NMA]/M	$10^4k_{obs}/s^{-1}$	Rearrangement (%)
0	5·33	8
0·20	2·61	22
0·40	1·95	30
0·60	1·70	39
0·80	1·49	44
1·00	1·35	65
2·00	1·16	67
5·00	1·05	72

[NMNA] = 1·16 × 10^{-4}M, [Urea] = 5 × 10^{-3}M, [HCl] = 4·51M.

towards a limiting value of *ca.* 1 × 10^{-4} s^{-1} and also the % rearrangement increases towards 70—80. Thus we have the same behaviour when an excess of NMA is added in the presence of urea as was observed [2] for reaction in the absence of urea. The limiting value should be the same in both cases; at this acidity the interpolated value for $k_2K[H^+]$ for no added urea is 0·8 × 10^{-4} s^{-1} which agrees well with the limiting value from Table 4. Qualitatively then, urea does not compete at all effectively with NMA for capture of the nitrosyl chloride formed, so that it cannot be assumed that even in the presence of a large excess of urea all the nitrosyl chloride (or other nitrite species) will be removed.

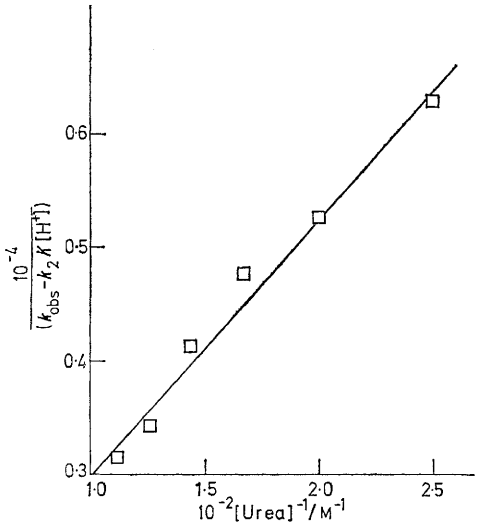
Apart from identifying two limiting forms of equation (2), we have demonstrated its validity when neither of the limiting forms applies. In general, k_{obs} can be written according to equation (5) which can be rearranged to

equation (6). At constant $[H^+]$, $[Cl^-]$, and [NMA], a plot of the left-hand side of equation (6) against 1/[X]

$$k_{obs} = k_2K[H^+] + \frac{k_1k_3K[H^+][Cl^-][X]}{k_{-1}[NMA] + k_3[X]} \quad (5)$$

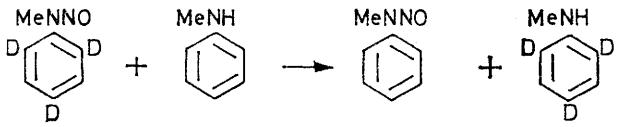
$$\frac{1}{k_{obs} - k_2K[H^+]} = \frac{k_{-1}[NMA]}{k_1k_3K[H^+][Cl^-][X]} + \frac{1}{k_1K[H^+][Cl^-]} \quad (6)$$

should be linear. Such a plot is shown for X = urea in the Figure.



Demonstration of the validity of the rate equation (2) for added urea by means of a plot of the left-hand side of equation (6) against $[Urea]^{-1}$

It is perhaps not surprising that we do not observe a direct transnitrosation [equation (1)] in the present system since the concentration of chloride ion is relatively high, very much favouring the reaction of the protonated nitrosoamine with chloride ion, rather than



with the weaker nucleophile X. We proposed such a direct transnitrosation earlier to account for the deuterium exchange observed in the reaction of 2,4,6-trideuterio-*N*-nitroso-*N*-methylaniline with *N*-methylaniline which took place rapidly even in the presence of a large excess of urea. It now appears from our present kinetic studies that this exchange could well have involved free nitrosyl chloride although this does not exclude the possibility of a direct transnitrosation. The experiments of Challis and Osborne were carried out in 0·18M-HCl. In order to establish whether such a direct transnitrosation is a possible mechanism in our system we have repeated our experiments in sulphuric acid, since it is generally believed that the sulphate ion does not form a covalently bonded nitrosating agent. The results are set out in Tables 5 and 6. For convenience in the actual determination of the rate coefficients, reactions were carried out at a higher acidity (4·75M-H_2SO_4; $H_0 = -2{\cdot}17$) than for the hydrochloric acid

TABLE 5

Variation of k_{obs} and % rearrangement with [Urea] in H_2SO_4

10^3[Urea]/M	$10^4k_{obs}/s^{-1}$	Rearrangement (%)
0	1·32	65
3·0	4·41	24
4·2	4·96	21
6·0	6·08	18
12	8·7	14
18	9·8	13
24	10·3	12
30	10·5	12
102	10·7	10

[NMNA] = 1·1 − 2·7 × 10^{-4}M, H_2SO_4 = 4·75M.

TABLE 6

Limiting rate data for added azide, aniline, and sulphamic acid in H_2SO_4

10^3[Azide]/M	$10^4k_{obs}/s^{-1}$	10^3[Aniline]/M	$10^4k_{obs}/s^{-1}$
0·9	14·1	0·9	13·6
1·8	14·1	1·8	14·0
0·9 (D_2O solvent)	32·3		
		10^3[Sulphamic acid]/M	
1·0 (5·00M-H_2SO_4)	22·5	2·7	14·5
1·0 (4·45M-H_2SO_4)	9·0	5·4	14·3

[H_2SO_4] = 4·75M, [NMNA] = 1·1 × 10^{-4}M.

experiments (3·05M-HCl; $H_0 = -1{\cdot}06$) since reaction was very much slower in sulphuric acid. The pattern of the results is however similar to those obtained in hydrochloric acid, k_{obs} again increasing with increasing urea concentration towards a limiting value, this again being associated with a reduction in the yield of rearrangement product. The same limiting value of k_{obs} is again obtained when X is changed to sulphamic acid, aniline, or hydrazoic acid. Both hydrogen ion and chloride ion catalysis are observed (the latter is shown in Table 7) and the solvent isotope effect $k_{D_2O} : k_{H_2O}$

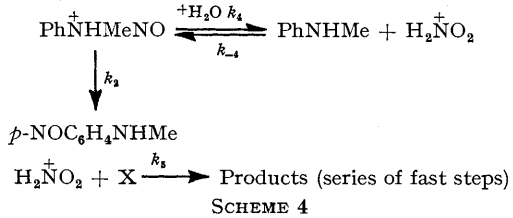
TABLE 7

Dependence of k_{obs} on $[Cl^-]$

[NaCl]/M	[Urea]/M	$10^4k_{obs}/s^{-1}$
0	0·25	7·9
0·16	0·25	13·8
0·40	0·25	25·8
0·98	0·25	63·5

[H_2SO_4] = 4·30M, [NMNA] = 2·1 × 10^{-4}M.

is 2·3. These results are wholly consistent with a mechanism involving concurrent rearrangement and denitrosation as before but in this case involving the formation of the nitrous acidium ion as shown in Scheme 4.



SCHEME 4

The limiting value of k_{obs} at high [X] is given by equation (7). Under these conditions k_2 is not negligible compared with $k_4[H_2O]$ so that at the limit for each X, *ca.*

$$k_{obs} = k_2K[H^+] + k_4K[H^+][H_2O] \qquad (7)$$

10% rearrangement product is formed. As expected there was no catalysis by added sodium sulphate.

For fairly strongly acidic solutions, with both sulphuric and hydrochloric acid, in the presence of sufficient quantity of the added nucleophile X, we are in effect measuring the rate constant for the denitrosation of the protonated form of the nitrosamine. In hydrochloric acid this involves direct attack by the chloride ion whereas in sulphuric acid it appears that a water molecule brings about the denitrosation and, as expected, the latter is a much less effective process, the rate constant being approximately one power of ten less, at the same acidity, than in hydrochloric acid. From our results it is possible to see that urea reacts with nitrosyl chloride (or the nitrous acidium ion) much more slowly than do sulphamic acid, aniline, or hydrazoic acid, *i.e.* urea is not a particularly good ' nitrite ' trap as we require a very large concentration of urea present before the rate of denitrosation becomes rate limiting. From the variation of this limiting rate coefficient k_{obs} with added NMA it is possible to determine quantitatively the ratio of rate coefficients for attack by nitrosyl chloride on NMA and X, *i.e.* k_{-1}/k_3 in Scheme 3 or k_{-4}/k_5 in Scheme 4 for the nitrous acidium ion. We hope to present the results of such an investigation shortly [8] when the reactivity of various nucleophiles X towards nitrosyl halides and the nitrous acidium ion will be compared and discussed.

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[8] D. L. H. Williams and J. A. Wilson, to be published.