Kinetic Study of the Phenylurea–Nitrous Acid Reaction: Evidence for an *O*-Nitrosation Initial Step

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The kinetics of the reaction between phenylurea (PhU) and nitrous acid in aqueous perchloric acid solution at 25 °C have been studied spectrophotometrically over the acidity range pH 2.2—4.0 (μ 0.20 mol dm^{-3}) by the initial-rate method and over the range $[H^+]$ 0.50—3.00 mol dm^{-3} (μ 2.0 mol dm^{-3}, except for $[H^+]$ 3.0 mol dm^{-3}) by the integration method. The proposed reaction mechanism for both weakly and strongly acidic media involves the rapid formation of an *O*-nitroso compound (**I**) followed by two separate reaction paths, the rate-controlling step in both cases being the loss of a proton by (**I**). In this step (**I**) is transformed to either of two conjugate bases, one of which subsequently undergoes rearrangement to secondary *N*-nitrosophenylurea (PhUNO) and the other to the unstable primary *N*-nitrosophenylurea, which a series of fast steps converts into benzenediazonium ion (PhN_2^+). These fast steps involve the nitrosating agent, which explains the stoicheiometry of the reaction ([PhU] : $[HNO_2]$ 1 : 2). The ratio between the formation constants of benzenediazonium ion and *N*-nitrosophenylurea is 0.3 in the absence of base catalysis. In keeping with the nature of the rate-controlling step, general base catalysis was found to be exerted in weakly acid media by both nitrite ion and the carboxylate anions of the buffers used, but not by halide ions.

Many *N*-nitrosoureas and similar compounds are powerful carcinogens and have been used to investigate the formation of tumours in animals. Such studies have shown that unlike *N*-nitrosamines, which are typically organ-specific, *N*-nitrosoureas generally act directly on the tissue to which they are applied.[1–6] Nevertheless, in spite of the undoubted interdisciplinary interest in the reactions by which *N*-nitrosoureas are formed, their kinetics have been much less thoroughly examined than those of *N*-nitrosamines because their mechanisms have been assumed to be analogous to those of the latter. This assumption has been questioned recently in view of indications to the contrary by Yamamoto *et al.*[7] and because of the differing biological effects of the two classes of nitroso compound (which are probably due to the greater instability of *N*-nitrosamides and *N*-nitrosoureas,[8] making their enzymatic decomposition unnecessary).

Whereas the nitrosation of amines may be of first and/or second order with respect to nitrous acid,[9,10] depending on whether the slow step involves attack on substrate by $H_2NO_2^+$–NO^+ or N_2O_3, only first-order reactions have been found for amides or ureas.[11,12] Moreover, Yamamoto *et al.*[7] have reported that the nitrosation of ureido derivatives is subject to catalysis by organic acids but not by halides, exactly the contrary to what occurs in the case of amines. The absence of nucleophilic catalysis in the nitrosation of methylurea has likewise been reported by Hallett and Williams,[13] who stated the slow step of the reaction to be the transfer of a proton from the protonated nitroso compound to the medium. This mechanism has recently been confirmed by Casado *et al.*, who obtained the slope of the Brønsted correlation for general base catalysis and isotopic effects for the nitrosation of both *N*-methylurea[14] and *N*-methylacetamide.[15]

This paper reports a study of the reaction between nitrous acid and phenylurea (over a wide range of acidity), which was chosen as substrate in order to discover whether its benzene ring affects the reaction mechanism in any way (it should be remembered that the diazotization of aromatic amines in highly acid media appears to take place *via* the protonated form of the amine as reactive species).[16,17] *N*-Nitrosophenylurea is known to be carcinogenic to animals.[18] In a previous paper[19] we have studied the denitrosation and hydrolysis reactions of *N*-nitrosophenylurea and some ring derivatives, which are relatively fast processes. The last one, leading to the benzenediazonium ion, could be of importance in arylation reactions.

Experimental

Merck phenylurea was recrystallized from ethanol–water. Sodium nitrite and sodium perchlorate solutions were made up from Merck products and perchloric acid solutions from Merck $HClO_4$ (70% by weight; density 1.67 g cm^{-3}). Other reagents used were Merck CH_3CO_2H, CCl_3CO_2H, NaOH, CH_2ClCO_2H, and $CHCl_2CO_2H$. *N*-Nitrosophenylurea synthesized as per Walter and Wlodkovsky[20] was thermolabile and was identified by mass spectrometry and by the formation of an azo dye on reaction with 2-naphthol.[21]

Kinetic measurements and u.v.–visible spectra were performed in 1 cm pathlength rectangular quartz cells using a KONTRON Uvikon 820 spectrophotometer with a cell carrier maintained at 25.0 ± 0.1 °C by water flow from a HETO 03T623 thermostat. The pH of weakly acid media was measured using a Radiometer pHM 26 pH-meter with a GK 2401C combined electrode.

In weakly acid media the kinetics of the formation of products were followed spectrophotometrically at 265 nm by the initial-rate method. Linear absorbance–time data were ensured by using data for no more than 2% of the reaction, and the results of duplicate experiments agreed to within 3%. The agreement between the expected value for the absorbance at time $t = 0$ and the experimental one ensures that r_0 (see Results and Discussion) is the real initial reaction rate.

In strongly acid media, the integration method was used to follow the reaction at 262 nm, at which wavelength there is maximum absorption by the benzenediazonium ion. Preliminary experiments showed that PhN_2^+ was stable enough for its decomposition not to affect the kinetic measurements, and that the decomposition of nitrous acid (at acidities employed all nitrite was present as HNO_2) was never greater than 5%, even in the most unfavourable case. The kinetic curves obtained in these media exhibited initial induction periods, but in all cases fitted biexponential equations characteristic of consecutive processes [equation (1) where A_t and A_∞ are the absorbances at

$$A_t = A_\infty + B[\exp(-\lambda_1 t) - \exp(-\lambda_2 t)] - (A_\infty - A_0)\exp(-\lambda_2 t) \quad (1)$$

times t and ∞, A_0 is the absorbance when the first measurement is obtained, and the parameters B, λ_1, and λ_2 were computed by non-linear optimization [22] on a UNIVAC 1108 computer].

Barnett and O'Connor [23] published a value of -1.30 for the pK_{BH^+} of the protonation equilibrium of phenylurea [equation (7)] for aqueous sulphuric acid media. In our experimental conditions a considerable concentration of protonated phenylurea could exist, and we have determined spectrophotometrically a new value of pK_{BH^+} for aqueous perchloric acid media using equation (2) where A_B and A_{BH^+} are the absorbances of,

$$H_A = pK_{BH^+} - \log(A_B - A)/(A - A_{BH^+}) \quad (2)$$

respectively, the free and protonated forms of phenylurea and H_A is the acidity function for amides.[24] Since the experimental determination of A_{BH^+} would require very high concentrations of acid, the non-linear optimization algorithm of Davies *et al.*[25] was used to fit equation (2) to the experimental data. The acidity function H_A was proved to be the most satisfactory one since it leads to a slope of 1.05 ± 0.02. Values of ε_{BH^+} 5 432 dm^3 mol^{-1} cm^{-1} (λ 234 nm, maximum in the u.v. spectrum for free PhU) and pK_{BH^+} -0.88 ± 0.02 were obtained.

Results and Discussion

The spectrophotometric study for the phenylurea–nitrous acid reaction in the acidity range 0.50—3.0 mol dm^{-3} $HClO_4$ shows the following features.

(1) When the reaction is complete the u.v. spectrum (Figure 1) exhibits an absorption band centred at 262 nm (log ε 4.08), which agrees well with published values for the benzenediazonium ion (Table 1). Similar experiments were carried out with some substituted phenylureas (3-Me, 4-Me, 3-Br, 4-Br, 3-OEt, and 4-OEt) because the complexity of the reaction mixture prevented isolation and identification of the product by other techniques. We have found in all cases acceptable agreement of the spectrophotometric parameters with those corresponding to benzenediazonium ions (Table 1).

Table 1. Spectrophotometric parameters of substituted benzenediazonium ions in water solution

Substituent	$(\lambda_{max.})_{exp}$	$(\log \varepsilon)_{exp}$	$(\lambda_{max.})_{lit}$	$(\log \varepsilon)_{lit}$	Ref.
H	262	4.08	262	4.09	26
4-CH_3	278	4.16	282	4.21	27
3-CH_3	270	3.88	272	4.07	27
4-Br	292	4.03	293	4.18	28
3-Br	268	3.80	268.5	3.63	29
4-OC_2H_5	315	4.24			
3-OC_2H_5	274	3.78			
4-OCH_3			315	4.28	28
3-OCH_3			273.5	3.98	29

(2) The 262 nm absorbance data in Figure 1 also show an induction period in the reaction, as reflected in Figure 2. This behaviour, which was found under all the strongly acid conditions employed, shows that the reaction involves significant concentrations of three of the participant species. Until kinetic profiles reach the inflexion point there is no well defined isosbestic point (242 nm in this case; Figure 1).

Owing to the characteristics of the reaction and the fact that PhUNO is a highly reactive compound,[19] we deduced that it acts as an intermediate in the process, accounting for the above

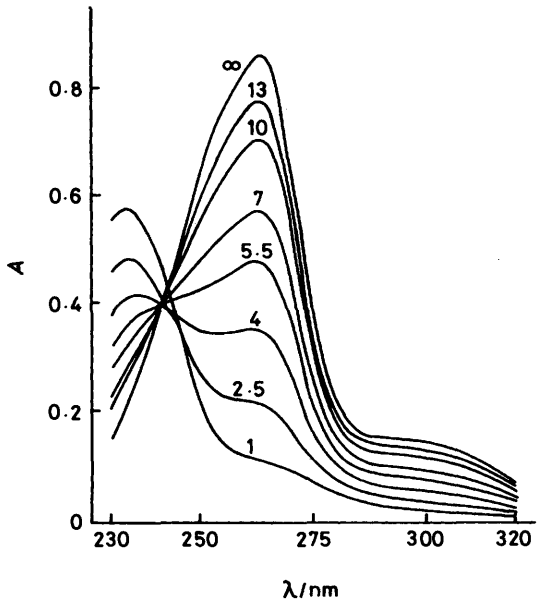


Figure 1. Spectra of the reaction between PhU and nitrous acid ([PhU] 7.15 × 10^{-5} mol dm^{-3}, [HNO_2] 4.25 × 10^{-3} mol dm^{-3}, [H^+] 2.00 mol dm^{-3}, T 25.0 °C, and μ 2.0 mol dm^{-3}). Scans were effected at the times shown in minutes in the Figure

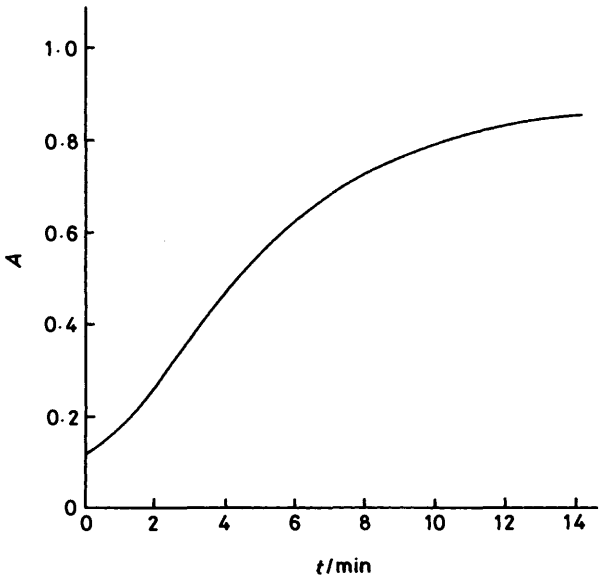


Figure 2. Absorbance–time graph of the reaction between PhU and nitrous acid at a wavelength of 262 nm ([PhU] 7.14 × 10^{-5} mol dm^{-3}, [HNO_2] 4.33 × 10^{-3} mol dm^{-3}, [H^+] 2.00 mol dm^{-3}, T 25.0 °C, and μ 2.0 mol dm^{-3})

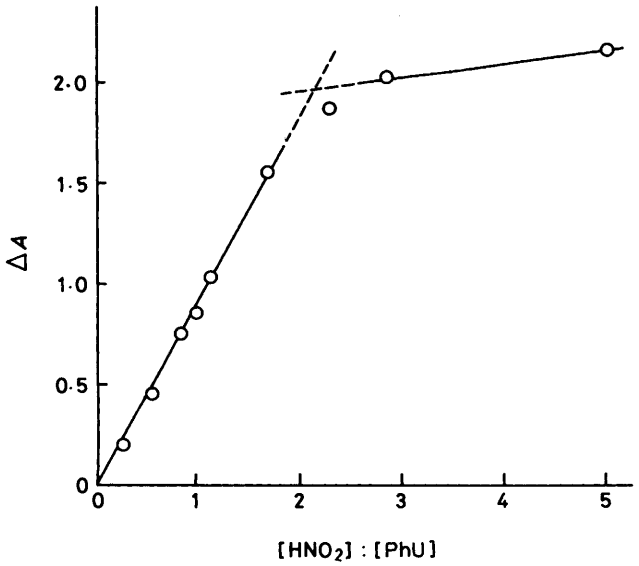


Figure 3. Increase in the absorbance [recorded at 300 nm (the high concentration of PhU not allowing the wavelength of maximum absorption of the benzenediazonium ion to be used)] of the reaction between PhU and nitrous acid for various values of $[HNO_2]$:[PhU] ([PhU] 1.14×10^{-3} mol dm^{-3}, $[H^+]$ 2.00 mol dm^{-3}, T 25.0 °C, and μ 2.0 mol dm^{-3})

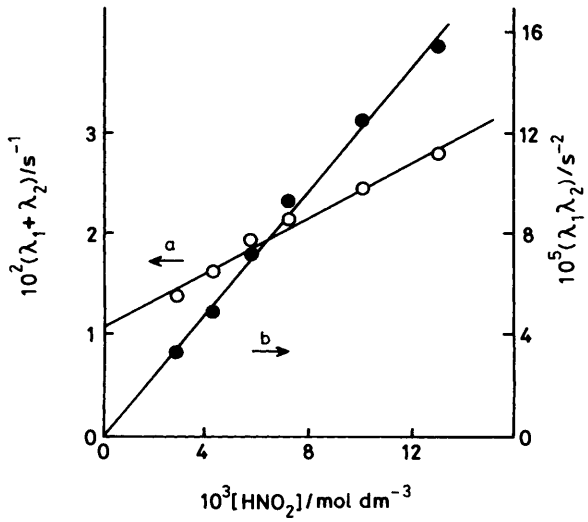


Figure 4. Influence of the concentration of nitrous acid on $\lambda_1 + \lambda_2$ (a) and $\lambda_1\lambda_2$ (b) (T 25.0 °C, μ 2.0 mol dm^{-3}, and $[H^+]$ 2.00 mol dm^{-3})

behaviour. This hypothesis is confirmed by reacting *N*-nitrosophenylurea with excess of nitrous acid under acid conditions. The fact that the reaction data also show sigmoid profiles and fit the biexponential equation (1) supports that point of view, against a possible autocatalytic process.

(3) Experiments carried out using quantities of nitrous acid in excess of, equimolar with, and slightly deficient with respect to the quantity of phenylurea showed that the rise in the absorbance due to the reaction, *i.e.* $A_\infty - A_0$, increased with the ratio $[HNO_2]$:[PhU] (Figure 3). This suggests that the stoicheiometry of the reaction is 2:1 and that the nitrous acid is involved in two steps of the reaction. For this reason, and also to facilitate the use of the integration method, all kinetic experiments were carried out using a considerable excess of nitrous acid with respect to phenylurea.

λ_1 and λ_2, found by fitting equation (1) to the experimental data, comply with relations (3)—(6) where the acidity function

Table 2. Values of λ_1 and λ_2 [equation (1)] for various acidities (T 25.0 °C, $[HNO_2]$ 5.67 × 10^{-3} mol dm^{-3}, and μ 2.0 mol dm^{-3})

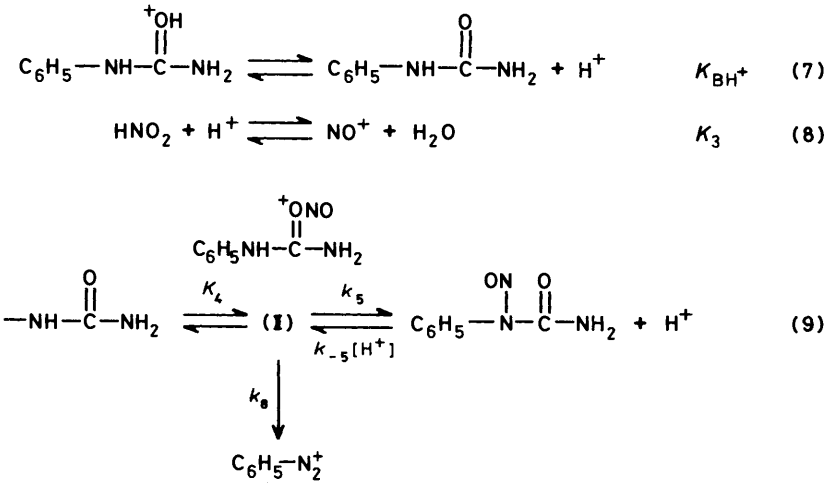
$[H^+]$/mol dm^{-3}	$10^2\lambda_1$/s^{-1}	$10^3\lambda_2$/s^{-1}
0.50	1.09 ± 0.03	1.313 ± 0.002
0.75	1.08 ± 0.01	2.041 ± 0.003
1.00	1.18 ± 0.02	2.551 ± 0.006
1.25	1.26 ± 0.02	2.894 ± 0.007
1.50	1.38 ± 0.03	3.384 ± 0.017
1.75	1.39 ± 0.03	3.632 ± 0.018
2.00	1.55 ± 0.04	4.158 ± 0.023
3.00	2.31 ± 0.06	7.739 ± 0.049

$$\lambda_1 + \lambda_2 = a + b[HNO_2] \quad (3)$$

$$\lambda_1 \cdot \lambda_2 = c[HNO_2] \quad (4)$$

$$\lambda_1 + \lambda_2 = d + e \cdot h_0 \quad (5)$$

$$\lambda_1 \cdot \lambda_2 = f \cdot h_0 \quad (6)$$



Scheme 1.

h_0 has been corrected for an ionic strength of 2.0 mol dm^{-3}.[30] The values of a and d deduced from Figure 4a and Table 2 are quite similar.

In order to interpret the results we must bear in mind the following facts. (a) At the acidities used, all nitrite would have to exist as nitrous acid, and protonation of phenylurea must be considered. (b) As we have mentioned above, *N*-nitrosophenylurea is an intermediate of the reaction and in our experimental conditions its denitrosation must be taken into account.[19] (c) The benzene diazonium ion is the only final product of the reaction.

These considerations lead to the provisional reaction mechanism shown in Scheme 1, where the steps have been numbered leaving room for other processes taking place in weakly acid media (see below).

$$[\mathrm{PhU}] = [\mathrm{PhU}]_0\left[\frac{k'_{-5}-\lambda_1}{\lambda_2-\lambda_1}\exp(-\lambda_1 t) + \frac{k'_{-5}-\lambda_2}{\lambda_2-\lambda_1}\exp(-\lambda_2 t)\right] \quad (10)$$

$$[\mathrm{PhUNO}] = K'_4k_5\left[\frac{\exp(-\lambda_1 t)}{\lambda_2-\lambda_1} + \frac{\exp(-\lambda_2 t)}{\lambda_1-\lambda_2}\right][\mathrm{PhU}]_0 \quad (11)$$

$$[\mathrm{PhN_2^+}] = [\mathrm{PhU}]_0\left\{1 - \left[\frac{k'_{-5}-\lambda_1}{\lambda_2-\lambda_1}\exp(-\lambda_1 t) + \frac{k'_{-5}-\lambda_2}{\lambda_1-\lambda_2}\exp(-\lambda_2 t)\right] - K'_4k_5\left[\frac{\exp(-\lambda_1 t)}{\lambda_2-\lambda_1} + \frac{\exp(-\lambda_2 t)}{\lambda_1-\lambda_2}\right]\right\} \quad (12)$$

$$\lambda_1,\lambda_2 = \frac{k'_{-5} + K'_4(k_5+k_8) \pm [(k'_{-5} + K'_4(k_5+k_8)^2 - 4K'_4k'_{-5}k_8]^{\frac{1}{2}}}{2} \quad (13)$$

The k_{-5} step explains the induction period observed in the kinetics, since it means that for some time PhU, PhUNO, and PhN_2^+ must all be present in significant quantities.

Solving the differential equations controlling the concentrations of the species involved in Scheme 1 leads to the relations (11)—(13) where $k'_{-5} = k_{-5}h_A$ and $K'_4 = K_3K_4[HNO_2]h_0K_{BH^+}/(K_{BH^+} + h_A)$. We have used h_A for the protonation of PhUNO since it may be expected that this protonation were similar to that one of PhU, and h_0 for the equilibrium of formation of the nitrosating agent from nitrous acid[31] [equation (16)].

The absorbance at time t is accordingly given by equation (14) where the ε values are coefficients of molar absorptivity.

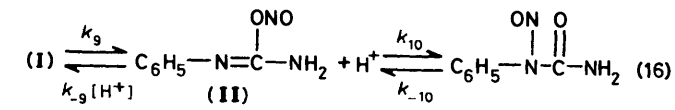
$$A_t = A_\infty + \frac{[\mathrm{PhU}]_0}{\lambda_1-\lambda_2}\{[(\varepsilon_{\mathrm{PhN_2^+}} - \varepsilon_{\mathrm{PhU}})(k'_{-5}-\lambda_1) + K'_4k_5(\varepsilon_{\mathrm{PhN_2^+}} - \varepsilon_{\mathrm{PhUNO}})]\exp(-\lambda_1 t) - [(\varepsilon_{\mathrm{PhN_2^+}} - \varepsilon_{\mathrm{PhU}})(k'_{-5}-\lambda_2) + K'_4k_5(\varepsilon_{\mathrm{PhN_2^+}} - \varepsilon_{\mathrm{PhUNO}})]\exp(-\lambda_2 t)\} \quad (14)$$

This equation, which is of the same form as (1), was fitted by the experimental data, and λ_1 and λ_2 were obtained by non-linear optimization as described in the Experimental section.

Equation (13) implies that (15) holds in agreement with the

$$\lambda_1 + \lambda_2 = k'_{-5} + K'_4(k_5 + k_8) \quad (15)$$

experimental equation (3) at constant acidity. However, equation (15) agrees with the experimental results [equation (5)] only if k'_{-5} deduced from Scheme 1 were independent of the acidity of the medium, which is not the case. Furthermore, the value of a/h_A implied by the results differs from that obtained on studying the denitrosation of *N*-nitrosophenylurea[19] by much more than is reasonable, attributable to the slightly weaker acidities used in the latter study (0.035—0.36 mol dm^{-3} $HClO_4$, with μ 1.0 mol dm^{-3}). These two facts suggest that the k_5,k'_{-5} steps of Scheme 1 are more complex comprising both the loss of a proton and subsequent internal rearrangement of the nitroso group, as demonstrated for nitrosation of several amides and ureas.[32] This mechanism (Scheme 2) means that the intermediate (**I**) must be taken to be the *O*-nitroso compound.



(16)

Scheme 2.

Solving the system of differential equations obtained when Scheme 2 is substituted for the k_5,k_{-5} steps in Scheme 1 and the intermediate (**II**) is assumed to be in the steady state now leads to relations (17) and (18) where $k'_{-9} = k_{-9}h_A$.

$$\lambda_1 + \lambda_2 = \frac{k'_{-9}k_{-10}}{k'_{-9}+k_{10}} + K'_4\frac{k_9k_{10} + k_8(k'_{-9}+k_{10})}{k'_{-9}+k_{10}} \quad (17)$$

$$\lambda_1 \cdot \lambda_2 = \frac{K'_4k'_{-9}k_{-10}k_8}{k'_{-9}+k_{10}} \quad (18)$$

Since $k'_{-5} = k'_{-9}k_{-10}/(k'_{-9} + k_{10})$ there exist two limiting possibilities. At low acidities the rate-limiting step for the denitrosation would be the protonation of PhUNO and k_{-5} should depend linearly on the acidity (h_A), but at high acidities the rate-limiting step would be the internal rearrangement, k_{-10}, independent of the acidity. These facts are in agreement with all the experimental results.

Equation (18) can be expressed in the form (19). Plotting

$$\frac{h_0h_AK_{BH^+}}{\lambda_1\lambda_2(K_{BH^+}+h_A)} = \frac{k_{10}}{K_3K_4[HNO_2]k_8k_{-9}k_{-10}} + \frac{h_A}{K_3K_4[HNO_2]k_8k_{-10}} \quad (19)$$

$h_0h_AK_{BH^+}/\lambda_1\lambda_2(K_{BH^+} + h_A)$ against h_A (Figure 5) therefore enables $K_3K_4k_8k_{-10}$ and k_{-9}/k_{10} to be estimated from the ordinate at the origin and the slope of the graph [equations (20) and (21)]. The deviation of the experimental point for [H^+] 3.0 mol dm^{-3} in Figure 5 is attributable to the fact that the ionic strength at this acidity is different from that employed for the other data. Equation (18) also implies that $\lambda_1\lambda_2$ depends linearly on [HNO_2], and the value (1.0 ± 0.1) × 10^{-2} mol^{-1} dm^3 s^{-2} calculated for the slope of the corresponding graph using the values for $K_3K_4k_8k_{-10}$ and k_{-9}/k_{10} given in (20) and (21) agrees reasonably well with the value (1.23 ± 0.02) × 10^{-2} mol^{-1} dm^3 s^{-2} obtained directly by plotting $\lambda_1\lambda_2$ against [HNO_2] (Figure 4b).

$$K_3K_4k_8k_{-10} = (2.7 \pm 0.3) \times 10^{-3}\ \mathrm{mol^{-2}\ dm^6\ s^{-2}} \quad (20)$$

$$k_{-9}/k_{10} = 2.4 \pm 1.1\ \mathrm{mol^{-1}\ dm^3} \quad (21)$$

On the other hand, by using the ordinate at the origin of Figure 4a, and equations (17) and (21), (22) follows which with

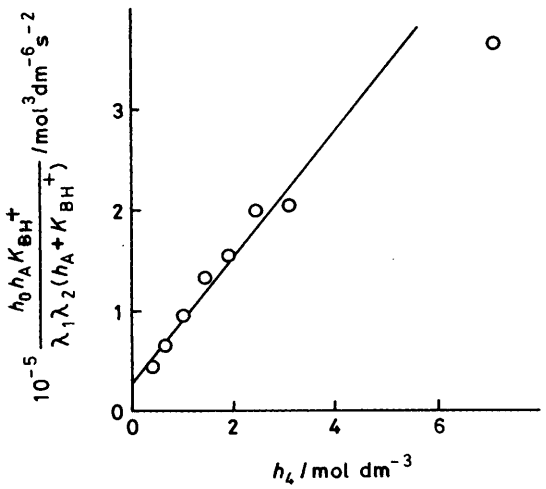


Figure 5. Influence of the acidity of the medium on $\lambda_1\lambda_2$ expressed in accordance with equation (19) (T 25.0 °C, μ 2.0 mol dm^{-3}, and [HNO_2] 5.67 × 10^{-3} mol dm^{-3})

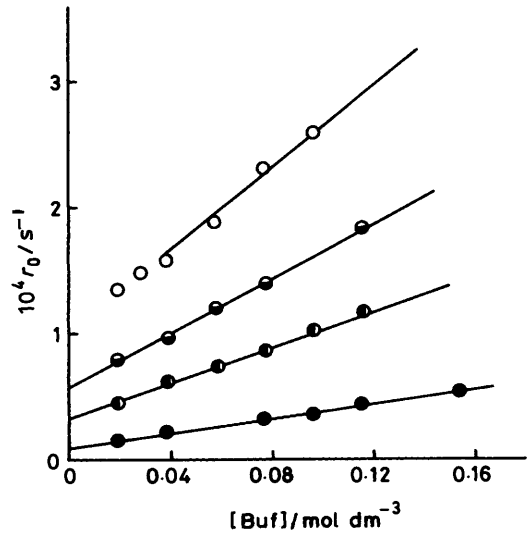


Figure 6. Influence of the concentration of monochloroacetate buffer on the initial reaction rate (defined as variation in absorbance with time) at 25.0 °C, μ 0.20 mol dm^{-3}, $[PhU]_0$ 1.0 × 10^{-3} mol dm^{-3}, and $[nit]_0$ 0.02 mol dm^{-3} (●), 0.05 mol dm^{-3} (◐), 0.08 mol dm^{-3} (◒), and 0.12 mol dm^{-3} (○)

$$k_{-10} = (1.2 \pm 0.1) \times 10^{-2}\ s^{-1} \quad (22)$$

$$K_3K_4k_8 = 0.23 \pm 0.03\ mol^{-2}\ dm^6\ s^{-1} \quad (23)$$

$$K_3K_4k_9 = 0.8 \pm 0.3\ mol^{-2}\ dm^6\ s^{-1} \quad (24)$$

(20) implies (23). Similarly, the slope of Figure 4a together with (21) and (23) now yields (24).

The value (2.92 ± 0.02) × 10^{-2} mol^{-1} dm^3 s^{-1} calculated for $k_{-9}k_{-10}/k_{10}$ from (21) and (22) agrees well with the value (2.44 ± 0.02) × 10^{-2} mol^{-1} dm^3 s^{-1} obtained[19] by studying the denitrosation reaction at an ionic strength of 1.0 mol dm^{-3} and acidities at which the rate-controlling step is k_{-9}. This agreement strongly supports the reaction mechanism now being proposed.

Finally, (23) and (24) imply that (25) holds, which means

$$k_9/k_8 = 3.6 \pm 1.5 \quad (25)$$

that both the formation of PhUNO path, k_9, and the formation of PhN_2^+ path, k_8, are significant, whatever the acidity of the medium.

To test this conclusion and the reaction mechanism itself we have studied the reaction at lower acidities (pH 2.2—4.0). In these conditions the reaction is very slow and the use of the initial-rate method is more appropriate. According to equation (25) the differential coefficient of molar absorptivity ε_{dif} is 4 287 mol^{-1} dm^3 cm^{-1} (see Appendix), which will be only valid when there is no additional catalysis.

However, we have found that in those conditions, the reaction is subject to base catalysis by nitrite ion and carboxylate anions of the buffers used (acetate and its chloro derivatives) but not by halides (Cl^-, Br^-). These results indicate that the rate-controlling step is the loss of a proton as occurs in the case of other ureas and amides.[14,15] Scheme 3 shows this mechanism together with the additional steps that lead to the benzenediazonium ion. As is shown in Figure 6, experimental results fit the theoretical kinetic law (26) deduced from the mechanism

$$r = \frac{[PhU][nit][H^+]^2}{K_1 + [H^+]}\left(\gamma + \delta\frac{[nit]}{K_1 + [H^+]} + \varepsilon\frac{[Buf]}{K_2 + [H^+]}\right) \quad (26)$$

where [nit] = [HNO_2] + [NO_2^-], [Buf] = [RCO_2H] + [RCO_2^-], $\gamma = K_3K_4(k_9 + k_8)$, $\delta = K_1K_3K_4(k_6 + k_{11})$, and $\varepsilon = K_2K_3K_4(k_7 + k_{12})$.

fast	$HNO_2 \rightleftharpoons NO_2^- + H^+$	K_1	(27)
	$RCO_2H \rightleftharpoons RCO_2^- + H^+$	K_2	(28)
	$HNO_2 + H^+ \rightleftharpoons NO^+ + H_2O$	K_3	
	$NO^+ + PhU \rightleftharpoons PhUNO^+$ (I)	K_4	
slow	(I) + H_2O → PhUNO + H_3O^+	k_9	
	(I) + NO_2^- → PhUNO + HNO_2	k_6	
	(I) + RCO_2^- → PhUNO + RCO_2H	k_7	(29)
	(I) + H_2O → PhN_2^+	k_8	(30)
	(I) + NO_2^- → PhN_2^+	k_{11}	(31)
	(I) + RCO_2^- → PhN_2^+	k_{12}	(32)

Scheme 3.

Since we do not know how catalysis by the different bases affects the various reaction pathways (29)—(32) δ and ε cannot be calculated. Therefore, we carried out some kinetic runs in the absence of such catalysis (*i.e.*, at low nitrite concentration and without buffers). A few experimental results are plotted in Figure 7. The value of ε_{dif} enables γ = 1.4 ± 0.1 mol^{-2} dm^6 s^{-1} to be calculated, and this is close to that obtained from equations (23) and (24) (1.1 ± 0.3 mol^{-2} dm^6 s^{-1}). Likewise, for the acidity constant of nitrous acid a value of K_1 = (1.29 ± 0.04) × 10^{-3} mol^{-1} dm^3 is obtained, which agrees well with published values.[33] All these facts support the reaction mechanism proposed.

The stoicheiometry of the reaction ([HNO_2]:[PhU] = 2:1) shows that nitrous acid must intervene at two different points of the reaction mechanism. The second intervention evidently affects the paths leading to the benzenediazonium ion, whose formation also remains to be explained. Consideration of (I) suggests that the loss of a proton may give rise not only to (II) [equation (16), Scheme 2], and hence eventually to the thermo-

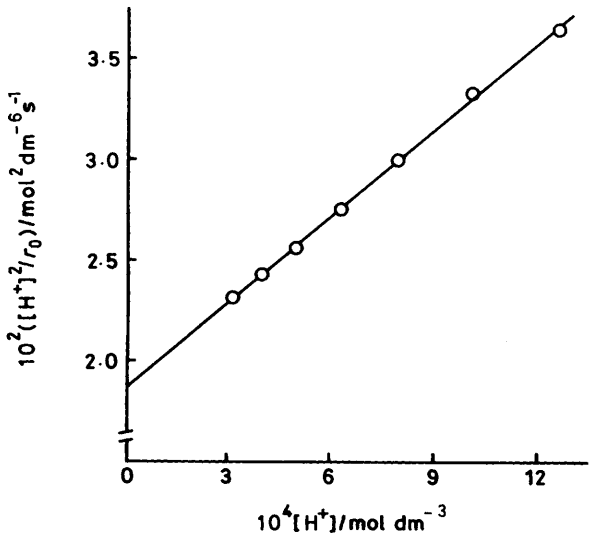
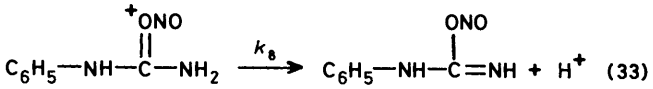


Figure 7. Influence of $[H^+]$ on the initial reaction rate (defined as variation in absorbance with time) at 25.0 °C, μ 0.20 mol dm^{-3}, $[PhU]_0$ 1.0×10^{-3} mol dm^{-3}, and $[nit]_0$ 0.01 mol dm^{-3}

dynamically stable secondary *N*-nitrosophenylurea, but also to a third intermediate (**III**). Since the C=N bond in (**III**) is not conjugated with the ring as in (**II**), (**III**) must be the less stable



(**III**)

of the two. The formation of the benzenediazonium ion and the second nitrosation can be accounted for by its internal rearrangement to the unstable primary *N*-nitrosophenylurea, the deamination and subsequent decarboxylation of the *N*-nitrosourea to aniline, and the nitrosation of the aniline to the benzenediazonium ion. An alternative mechanism, once the rearrangement to the primary *N*-nitrosourea has taken place, might possibly consist in the nitrosating agent attacking the secondary nitrogen at the same time as the carbonyl C–N bond is split, giving diazohydroxide, whose equilibrium with the benzenediazonium ion is such that only the latter exists under the working conditions used in these experiments.[26] These two mechanisms are kinetically indistinguishable, but the second seems unlikely in view of the fact that no *N*-nitrosourea (including the secondary *N*-nitrosophenylurea formed *via* the k_9 step) has ever been observed to undergo a second nitrosation, even in the presence of excess of nitrous acid. It is clear, in any case, that the second nitrosation cannot take place prior to the rate-controlling step, for all current knowledge of nitrosation reactions indicates that if it did, the rate-controlling step would be either the attack by the nitrosating agent (as in the case of amines) or the subsequent loss of a proton by the conjugate acid of the *O*-nitroso compound (as for amides and ureas); in either case the second intervention of the nitrosating agent would show up in the rate equation, which it does not.

Finally, indirect proof for the transformation of (**I**) *via* the intermediates (**II**) and (**III**) is provided by the facts that the nitrosation reactions of 1-(2-chloroethyl)-3-cyclohexylurea[34] and 1-substituted 3-(3-pyridylmethyl)ureas[35] lead to mixtures of 1- and 3-nitrosated ureas, and that in the latter case the denitrosation of any of the products, which by the microreversibility principle must take place by the inverse mechanism, yields not only the denitrosated urea but also the isomeric *N*-nitrosourea. These findings are readily explained in terms of mechanisms like that proposed in the present article, the initial formation of an *O*-nitroso compound being followed by the loss of a proton leading to the two nitrosated isomers. Such a mechanism seems much more likely than an intramolecular rearrangement or the migration of the nitroso group from one nitrogen atom to the other.

Appendix

The absorbance at time t is $A_t = [PhU]\,\varepsilon_{PhU} + [PhUNO]\,\varepsilon_{PhUNO} + [PhN_2^+]\,\varepsilon_{PhN_2^+}$ or $A_t = ([PhU]_0 - x)\,\varepsilon_{PhU} + (x - y)\,\varepsilon_{PhUNO} + y\,\varepsilon_{PhN_2^+}$ where $x - y = [PhUNO]$, $y = [PhN_2^+]$, and the subscript 0 indicates initial concentration. Following Scheme 3, the ratio $[PhUNO]/[PhN_2^+]$ should be expressed by equation (A1) and therefore (A2) holds, from which the

$$\frac{x - y}{y} = \frac{k_9 + k_6[NO_2^-]_0 + k_7[RCO_2^-]}{k_8 + k_{11}[NO_2^-]_0 + k_{12}[RCO_2^-]} \equiv \frac{k_{NO}}{k_{N_2}} \quad (A1)$$

$$A_t = A_0 + x\left[\varepsilon_{PhUNO} - \varepsilon_{PhU} + \frac{k_{N_2}}{k_{NO} + k_{N_2}}(\varepsilon_{PhN_2^+} - \varepsilon_{PhUNO})\right] \quad (A2)$$

differential coefficient of molar absorptivity is deduced [equation (A3)]. In the absence of base catalysis, equation (A3)

$$\varepsilon_{dif} = (\varepsilon_{PhUNO} - \varepsilon_{PhU}) + (\varepsilon_{PhN_2^+} - \varepsilon_{PhUNO})\frac{1}{1 + (k_{NO}/k_{N_2})} \quad (A3)$$

is simplified to (A4). By taking into account equation (25) and

$$\varepsilon_{dif} = (\varepsilon_{PhUNO} - \varepsilon_{PhU}) + (\varepsilon_{PhN_2^+} - \varepsilon_{PhUNO})\frac{1}{1 + (k_9/k_8)} \quad (A4)$$

ε_{PhU} 755, ε_{PhUNO} 3 105, and $\varepsilon_{PhN_2^+}$ 12 050 mol^{-1} dm^3 cm^{-1}, a value of 4 287 mol^{-1} dm^3 cm^{-1} for ε_{dif} is deduced.

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