Isotope Effect of Solvent on the Equilibrium of Formation of the Nitrosonium/Nitrous Acidium Ion

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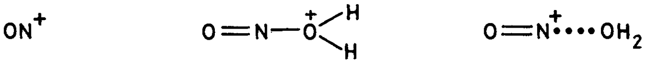
By using two different substrates under various experimental conditions, the value K_D/K_H = 2.55 ± 0.28 has been found for the solvent isotope effect on the equilibrium of formation of the nitrosonium/nitrous acidium ion over the pH range 1—5.

One of the most powerful of nitrosating agents is the ion thought by some[1–3] to be nitrosonium (**A**) (the existence of which in strongly acid media has been proved[4]); however it has also been suggested[5–9] that in dilute media the effective nitrosating agent is the nitrous acidium ion (**B**). A recent theoretical investigation[10] of this question concluded that the effective agent is an ion (**C**) in which the nitrosyl cation is bound electrostatically to a water molecule. This conclusion had been preceded by the suggestion[11,12] that the electrophile responsible for nitrosation is a species intermediate between the forms (**A**) and (**B**), the contribution of (**A**) increasing (and the strength of the nitrosyl–water bond decreasing) with increasing acidity.



(A) **(B)** **(C)**

In establishing the nature of the rate-controlling step of nitrosation reactions it is common practice to determine the isotope effect of the solvent,[13,14] which enables diffusion-controlled processes such as those involved in the nitrosation of amines[9] to be distinguished from proton transfers (as occur in the nitrosation of amides[15]); in calculating these effects it is necessary to know the isotope effect on the equilibrium of formation of the nitrosating agent. In the case of the nitrosonium/nitrous acidium ion, the value most frequently used for this latter effect is 2.2, found by Challis[16] for the reaction of nitrous acid with iodide ions at low acidities; but since approximate values of 2.19 and 2.98 have recently been obtained in our studies of the nitrosation of naphthylamines[17] we have now carried out a systematic investigation of the isotope effect on the equilibrium (1) using two different substrates and at acidities covering the pH range 1—5.

$$HNO_2 + H^+ \rightleftharpoons ON^+ + H_2O\,(\text{or } H_2NO_2^+) \qquad (1)$$

Experimental

All chemicals were of the highest purity available. Nitrite solutions were made up daily. Heavy water was supplied by the Spanish Nuclear Energy Board; its isotope content was determined by density measurements.

Acidity was measured by using a Radiometer pHM-84 pH meter equipped with a GK-2401-C combined electrode and calibrated using buffers of pH 3 (at 25 °C) and 6.98 (at 25 °C). The acidities of deuteriated media[18] were calculated by using equation (2), in which n represents the atomic fraction of deuterium in the solvent.

$$pH = pH_{\text{obs.}} + 0.3314n + 0.0766n^2 \qquad (2)$$

Table 1. Influence of the concentration of piperazine on its initial rate of nitrosation[a]

10^2[Pip]/M	$10^{-5}v_0[H^+]^{-2}$/dm^3 mol^{-1} s^{-1}
0.112	1.61
0.449	1.59
1.011	1.49
1.291	1.48

[a] T = 25.0 °C, I = 0.28M, $[NaNO_2]$ = 0.1050M, pH = 5.45.

All reactions were performed in a Perkin-Elmer 554 u.v. spectrophotometer with a thermostatically controlled cell carrier. The nitrosation of piperazine at low acidities (pH ⩾ 5) was studied by the initial-rate method; the formation of mononitrosopiperazine was monitored at 265 nm until at most 2% of the reaction had taken place. For the nitrosation of piperazine in the presence of bromide ions, the formation of mononitrosopiperazine was monitored at 249 nm and the integration method was used. The integration method was likewise employed to study the kinetics of nitrosation of sulphanilic acid, the reaction being monitored at 265 nm. Both 249 nm and 265 nm are isosbestic points of the nitrous acid/nitrite system. All experiments were carried out at 25 °C in solutions the ionic strength of which was controlled with sodium perchlorate. All experiments were duplicated, and the corresponding experimental rate constants always agreed to within 3%.

Results and Discussion

Nitrosation of Piperazine at Low Acidities.—As Table 1 shows, the initial rate of nitrosation of piperazine at pH ⩾ 5.4 was independent of the concentration of amine. The reaction was of order two with respect to the concentration of protons (Figure 1). The complex influence of the concentration of nitrite on the initial reaction rate is shown in Figure 2. Equation (3)

$$v_0 = \frac{[\text{Nit}]_0^2\,[H^+]^2}{a + b[\text{Nit}]_0} \qquad (3)$$

was shown to describe the experimental results satisfactorily by fitting it in linearized form to the combined data {[Nit] is the analytical concentration of nitrite and $[H^+]$ = antilog(−pH)}; the values obtained for a and b are listed in Table 2.

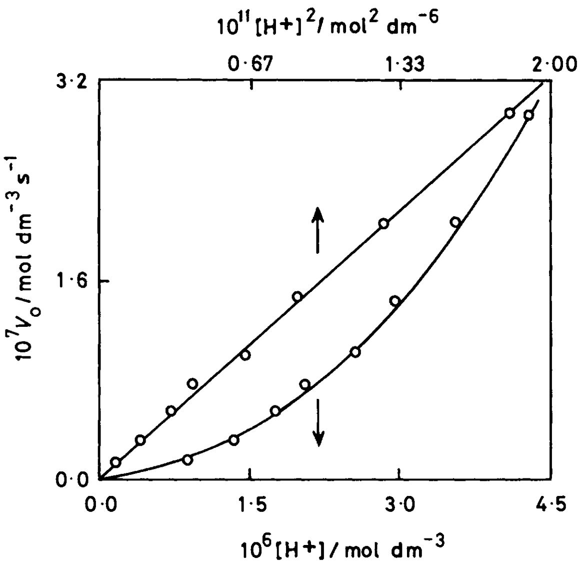


Figure 1. Influence of acidity on the initial rate of nitrosation of piperazine at 25 °C; $I = 0.28$M, [Nit] = 3.00 × 10^{-2}M, [Pip] = 1.12 × 10^{-2}M

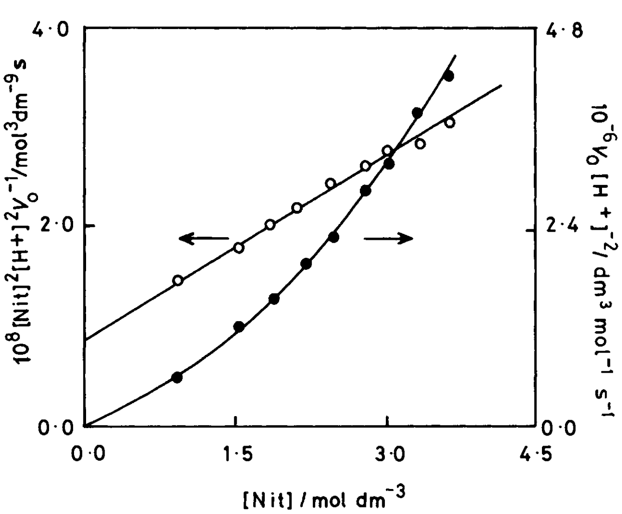


Figure 2. Influence of the concentration of nitrite on the initial rate of nitrosation of piperazine at 25 °C; $I = 0.37$M. Reaction in heavy water ($n = 0.99$); [Pip] = 1.12 × 10^{-2}M, pH = 5.60

Table 2. Values of the experimental rate equation parameters obtained by fitting the linearized equations to the experimental data by least squares

	H_2O	D_2O	Reaction
10^8a	5.22 ± 0.18	0.95 ± 0.05	Nitrosation of piperazine
10^7b	1.46 ± 0.13	0.56 ± 0.03	at pH ⩾ 5.4
10^{-7}a	4.23 ± 1.02		Nitrosation of piperazine
10^3b	1.96 ± 0.02	1.02 ± 0.01	at pH *ca.* 5.0
10a	1.33 ± 0.04	0.965 ± 0.029	Nitrosation of piperazine
10^4b	1.36 ± 0.05	0.600 ± 0.025	in the presence of Br^-
b	4.59 ± 0.03	3.07 ± 0.10	Nitrosation of sulphanilic acid at $[H^+] = 0.10$M

Table 3. Values of k_3 and k_3/K_2 in various reactions

Reaction	k_3/dm^3 mol^{-1} s^{-1}	$10^{-7}k_3/K_2$
NO_2^-–H_2O_2[a]	2 916	7.32
Diazotisation[b] of aniline	2 167	5.44
NO_2^-–N_3^-[c]	2 900	7.26
NO_2^-–$S_2O_3^{2-}$[d]	2 800	7.03
NO_2^-–$PipH^+$[e]	5 011	6.31

[a] Ref. 1. [b] H. Schmid and A. Woppmann, *Monatsh. Chem.*, 1959, **90**, 903. [c] F. Seel and E. Z. Schwaebel, *Z. Anorg. Allg. Chem.*, 1953, **274**, 169. [d] F. Seel and E. Degener, *Z. Anorg. Allg. Chem.*, 1956, **284**, 101. [e] $T = 25.0$ °C, $I = 0.28$M, [Pip] = 1.12 × 10^{-2}M, pH ⩾ 5.40, 0.03M < [$NaNO_2$] < 0.27M.

The fact that the initial rate is independent of the concentration of the amine implies that the rate-controlling step occurs prior to attack of the effective nitrosating agent on the substrate, and therefore formation of the nitrosating agent must be involved. At low concentrations of nitrite equation (3) becomes (4), showing that the rate-controlling step is the

$$v_0 \propto [\text{Nit}]_0^2\,[\text{H}^+]^2 \tag{4}$$

formation of N_2O_3 (Scheme 1), as is well documented.[19,20] The form taken by equation (3) at high nitrite concentrations, together with the accepted[21] mechanisms for the formation of N_2O_3, suggest that under these conditions the rate-controlling step is the formation of the nitrosonium/nitrous acidium ion.

$$\begin{aligned}
\text{PipH}_2^{2+} &\underset{}{\overset{K_1}{\rightleftharpoons}} \text{PipH}^+ + \text{H}^+\\
\text{HNO}_2 &\overset{K_2}{\rightleftharpoons} \text{NO}_2^- + \text{H}^+\\
\text{HNO}_2 + \text{H}^+ &\underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \text{ON}^+ + \text{H}_2\text{O}\,(\text{or H}_2\text{NO}_2^+)\\
\text{ON}^+/\text{H}_2\text{NO}_2^+ + \text{NO}_2^- &\xrightarrow{k_4} \text{N}_2\text{O}_3\\
\text{PipH}^+ + \text{N}_2\text{O}_3 &\xrightarrow[\text{fast}]{k_6} \text{products}
\end{aligned}$$

Scheme 1.

In view of these findings, we propose the reaction mechanism shown in Scheme 1. When the steady-state condition is applied to the nitrosonium/nitrous acidium ion, this implies the theoretical rate equation (5), which is of the same form as equation (3).

$$v_0 = \frac{[\text{Nit}]_0^2\,[\text{H}^+]^2}{K_2/k_4K_3 + K_2[\text{Nit}]_0/k_3} \tag{5}$$

The value $k_3 = 5\,011$ dm^3 mol^{-1} s^{-1} implied by the value of b in water and the ionization constant of nitrous acid[22] differs considerably from previously published values (Table 3). This discrepancy may be due to the acidities used by other authors having introduced systematic errors: instead of measuring acidity experimentally, they added mineral acid to sodium nitrite solutions the acidity of which they then calculated by using the value $pK_a = 3.40$, which is not always correct. The corresponding values of k_3/K_2, which are less affected by these systematic errors than k_3, agree satisfactorily with the present results (Table 3).

If K_3 is taken[23] to be 3 × 10^{-7}, then the value of *a* implies a value of 4.8 × 10^{10} dm^3 mol^{-1} s^{-1} for k_4, the rate constant for the attack of nitrosonium/nitrous acidium ion on the nitrite ion. This is similar to values observed in reactions the rates of which are generally accepted to be controlled by diffusion.[9]

In calculating the isotope effects k_{3H}/k_{3D}, k_{-3H}/k_{-3D}, and K_{3D}/K_{3H} it is necessary to take into account the isotope effects on K_2 (ref. 22) and k_4. Since k_4 is diffusion-controlled, the corresponding isotope effect is proportional to $\eta_H/\eta_D = 1.22$, where η_H and η_D are the viscosities of water and heavy water, respectively. Table 4 shows that there is no isotope effect on k_3,

Table 4. Observed isotope effects on the nitrosation of piperazine in weakly acid media (pH $\geqslant$ 5.4)[a]

k_{3H}/k_{3D}	1.15 ± 0.11
k_{-3H}/k_{-3D}	2.55 ± 0.20
K_{3D}/K_{3H}	2.23 ± 0.22

[a] In water: T = 25.0 °C, I = 0.28M, [Pip] = 1.12×10^{-2}M, pH = 5.4, 0.03M < [$NaNO_2$] < 0.27M. In heavy water (n = 0.99): T = 25.0 °C, I = 0.37M, [Pip] = 1.12×10^{-2}M, pH = 5.60, 0.09M < [$NaNO_2$] < 0.36M.

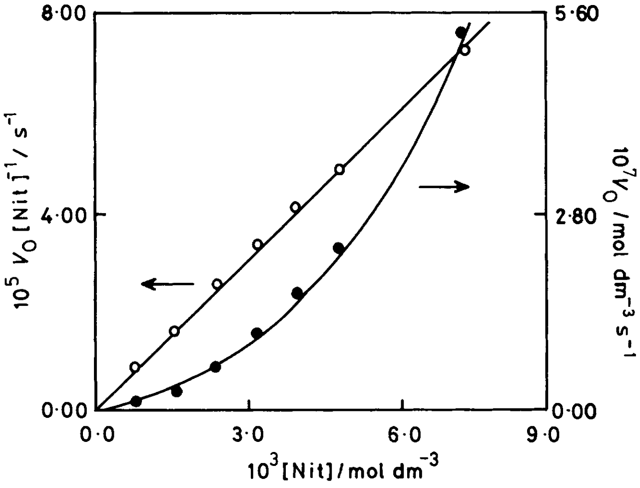


Figure 3. Influence of the concentration of nitrite on the initial rate of nitrosation of piperazine at 25 °C; I = 0.20M. Reaction in heavy water (n = 0.99), [Pip] = 1.11×10^{-2}M, pH = 5.01

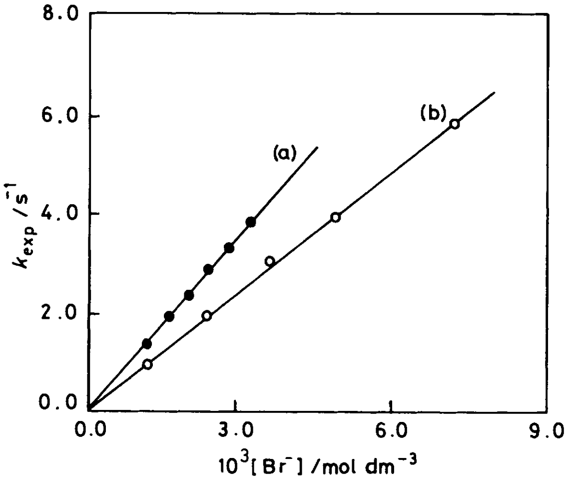


Figure 4. Influence of Br$^-$ on the first-order pseudo-constant for the formation of mononitrosopiperazine at 25 °C, I = 0.75M, [Pip] = 0.25M, [Nit] = 4.98×10^{-5}M, pH = 3.35; (a) D_2O (n = 0.98); (b) H_2O

whereas k_{-3} is affected. The final effect on K_3 agrees closely with that reported by Challis.[16]

It has been found[24] that at pH *ca.* 5 the initial rate of nitrosation of piperazine at constant amine concentration is given by an equation (6) with both first- and second-order terms

$$v_0 = \mathrm{a}[\mathrm{Nit}]_0 + \mathrm{b}[\mathrm{Nit}]_0^2 \qquad (6)$$

in nitrite concentration. Figure 3 shows that this equation is corroborated by the results of experiments carried out under these conditions in the present study, and Table 2 lists the corresponding values of a and b. The observed behaviour may be explained by adding the step (7) to Scheme 1. The reaction rate is now controlled by both the k_4 step (attack by the nitrosonium/nitrous acidium ion on the nitrite ion) and the k_a step (attack of the nitrosonium/nitrous acidium ion on the amine), and the corresponding theoretical rate equation is (8) which is of the same form as equation (6).

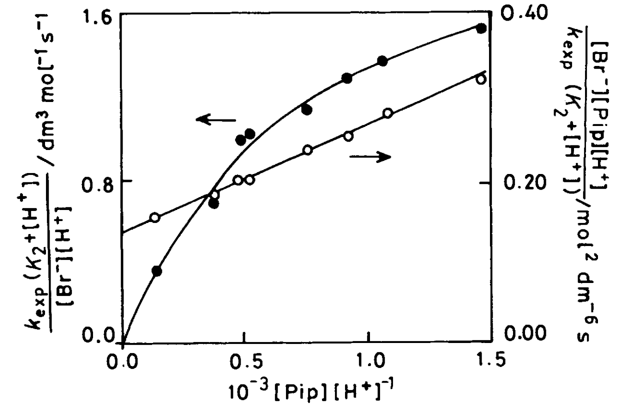


Figure 5. Influence of the concentration of piperazine on the first-order pseudo-constant for the formation of mononitrosopiperazine at 25 °C; I = 1.5M, [Nit] = 5.02×10^{-5}M, [Br$^-$] = 1.30×10^{-2}M, pH = 3.35, 0.05M < [Pip] < 0.5M

$$\mathrm{ON^+/H_2NO^+{}_2 + PipH^+ \xrightarrow{k_a} products} \qquad (7)$$

$$v_0 = \frac{k_a K_3 K_1 [\mathrm{H}^+]^2}{K_2(K_1 + [\mathrm{H}^+])}[\mathrm{Pip}]_0[\mathrm{Nit}]_0 + \frac{k_4 K_3}{K_2}[\mathrm{H}^+]^2[\mathrm{Nit}]_0^2 \qquad (8)$$

The value of b in water implies that $k_4 = 4.2 \times 10^{10}$ dm^3 mol^{-1} s^{-1}, which if the same assumptions as before are made regarding the isotope effects on k_4 and K_2 yields K_{3D}/K_{3H} = 2.27 ± 0.13. Both these values are compatible with those obtained at pH $\geqslant$ 5.4.

Nitrosation of Piperazine in the Presence of Bromide Ions at pH 3.4.—Like others,[25] we found that this reaction was of order one with respect to nitrite and Br$^-$ (Figure 4). The dependence of the first-order pseudo-constant on the concentration of piperazine is shown in Figure 5. The combined data may be described by equation (9); the experimental values of a and b in water and heavy water are listed in Table 2. As before, the existence of two limiting forms for the rate equation implies the presence of a species in the steady state, and on the basis of previous studies[25] this species may be assumed to be nitrosyl bromide. The reaction mechanism in Scheme 2 may therefore be proposed.

$$k_{exp} = \frac{[\mathrm{Pip}][\mathrm{H}^+][\mathrm{Br}^-]}{([\mathrm{H}^+] + K_2)(\mathrm{a} + \mathrm{b}[\mathrm{Pip}]/[\mathrm{H}^+])} \qquad (9)$$

$$\mathrm{PipH_2{}^{2+} \overset{K_1}{\rightleftharpoons} PipH^+ + H^+}$$
$$\mathrm{HNO_2 \overset{K_2}{\rightleftharpoons} NO_2{}^- + H^+}$$
$$\mathrm{HNO_2 + H^+ \overset{K_3}{\rightleftharpoons} ON^+ + H_2O\ (or\ H_2NO_2{}^+)}$$
$$\mathrm{ON^+/H_2NO_2{}^+ + Br^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} BrNO}$$
$$\mathrm{PipH^+ + BrNO \xrightarrow{k_c} products}$$

Scheme 2.

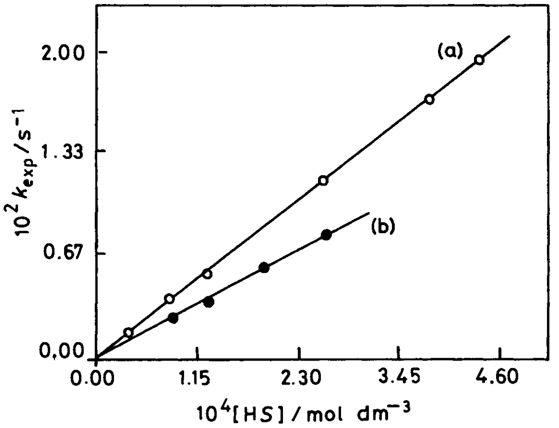


Figure 6. Influence of the concentration of sulphanilic acid on the first-order pseudo-constant for the diazotization of sulphanilic acid at 25 °C; $I = 0.10$M, [Nit] $= 1.7 \times 10^{-5}$M, $[H^+] = 0.10$M; (a) H_2O; (b) D_2O. $n = 0.99$

Table 5. Solvent isotope effects on the equilibrium of formation of the nitrosonium/nitrous acidium ion ($T = 25.0$ °C)

K_{3D}/K_{3H}	I/M	$[H^+]$/M
2.23[a]	0.28	$10^{-5.5}$
2.27[a]	0.20	$10^{-5.0}$
2.62[b]	0.20	$10^{-3.9}$
2.73[c]	1.50	$10^{-3.5}$
2.89[d]	0.10	$10^{-1.0}$

K_{3D}/K_{3H} (mean value) $= 2.55 \pm 0.25$

[a] Nitrosation of piperazine. [b] Ref. 16. [c] Nitrosation of piperazine in the presence of bromide ions. [d] Nitrosation of sulphanilic acid.

Since the steady-state condition is assumed to hold for nitrosyl bromide, Scheme 2 implies the theoretical rate equation (10), which is of the same form as the experimental equation (9).

$$v = \frac{[\mathrm{Pip}][\mathrm{H}^+][\mathrm{Br}^-][\mathrm{Nit}]}{([\mathrm{H}^+] + K_2)(1/k_c K_3 K_4 K_1 + [\mathrm{Pip}]/[\mathrm{H}^+]k_4 K_3)} \qquad (10)$$

If we use the value $K_3 = 3 \times 10^{-7}$, the value found for b in water implies that $k_4 = 2.4 \times 10^{10}$ dm^3 mol^{-1} s^{-1}, so that the rate of formation of nitrosyl bromide must be controlled by diffusion, and the corresponding isotope effect is inversely proportional to the ratio between the densities of water and heavy water. With this in mind, the results obtained in heavy water and water yield the value 2.73 ± 0.25 for the isotope effect (K_D/K_H) on the equilibrium of formation of the nitrosonium/nitrous acidium ion, close to the 2.62 obtained in our studies of the nitrosation of 2-naphthol at similar acidities.[26]

Nitrosation of Sulphanilic Acid at $[H^+] = 0.1$M.—The present experiments corroborate the findings of Williams and co-workers[27] that the nitrosation of sulphanilic acid (H*S*) is of order one with respect to both nitrite and substrate (Figure 6) [equation (11)]. The observed values of b are listed in Table 2.

$$v = \mathrm{b}[\mathrm{Nit}][\mathrm{H}S] \qquad (11)$$

This experimental behaviour is explained by the mechanism shown in Scheme 3, which implies the theoretical rate equation (12).

$$v = k_a K_3 K_1 [\mathrm{Nit}][\mathrm{H}S] \qquad (12)$$

The accepted[28] value of K_1 now implies that $k_a K_3 = 7.7 \times 10^3$ dm^6 mol^{-2} s^{-1}, a value similar to that found by Williams and co-workers,[27] and that $k_a = 2.6 \times 10^{10}$ dm^3 mol^{-1} s^{-1}, which suggests that attack of the nitrosonium/nitrous acidium ion on the sulphanilic acid molecule is diffusion-controlled. The results obtained in water and heavy water, together with the isotope effects on the ionization equilibrium of sulphanilic acid[29] ($K_{1H}/K_{1D} = 3.50 \pm 0.30$) and the diffusion-controlled k_a step, now yield a value of $K_{3D}/K_{3H} = 2.89 \pm 0.25$.

$$\mathrm{H}S \overset{K_1}{\rightleftharpoons} S + \mathrm{H}^+$$
$$\mathrm{HNO_2} + \mathrm{H}^+ \overset{K_3}{\rightleftharpoons} \mathrm{ON}^+ + \mathrm{H_2O}\ (\text{or } \mathrm{H_2NO_2}^+)$$
$$\mathrm{ON}^+/\mathrm{H_2NO_2}^+ + S \xrightarrow{k_a} \text{products}$$

Scheme 3.

Conclusion.—Table 5 lists the values obtained for the solvent isotope effect on the equilibrium of formation of the nitrosonium/nitrous acidium ion under the various conditions of acidity and ionic strength employed. Experimental error apart, the variability of the results may be due in part to differences in the working conditions employed. In all cases in which acidity was less than 0.1M the approximation pH $= -\log[H^+]$ was used, in view of the inaccuracy of activity coefficients at ionic strengths greater than 0.1M. The tendency for the isotope effect to increase with acidity is very small in comparison with the range of acidities used, and is insufficient to throw light on the nature of the effective nitrosating agent in dilute media. For practical purposes, it is suggested that the value 2.55 ± 0.28 for K_D/K_H may be used for the solvent isotope effect on the equilibrium of formation of the nitrosonium/nitrous acidium ion, *i.e.* the mean of the effects observed in the present study. This value is independent of whether or not a value of K_3 different from that used here is accepted.

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