amino-2-azidoazobenzene and ran some of the kinetics on this compound.

Registry No.—11 isomer 1, 67661-60-3; 11 isomer 2, 67661-61-4; 4'-dimethylamino-2-azidoazobenzene, 16675-41-5; nitrosobenzene, 586-96-9; 4-methoxycarbonylnitrosobenzene, 13170-28-0; 4-acetylnitrosobenzene, 31125-05-0; 4-nitrosobenzene, 4485-08-9; 4-nitrosobenzenesulfonamide, 2990-12-7; 4-acetamidonitrosobenzene, 67661-55-6; 4-methylnitrosobenzene, 623-11-0; 4-chloronitrosobenzene, 932-98-9; 4-cyanonitrosobenzene, 31125-07-2; 2-azidoaniline, 1005-07-8; methyl 4-nitrobenzoate, 619-50-1; 4-methylnitrobenzene, 99-99-0; 4-nitrobenzonitrile, 619-72-7; 4-nitrobenzenesulfonamide, 6325-93-5; *N*-(4-nitrophenyl)acetamide, 104-04-1; 4-nitroacetophenone, 100-19-6; *p*-nitroaniline, 100-01-6; *N*-(2-nitro-3,4,6-trimethylphenyl)phthalimide, 67661-56-7; 2-nitro-3,4,6-trimethylaniline, 41571-53-3; phthalic anhydride, 85-449; *N*-(2-amino-3,4,6-trimethylphenyl)phthalimide, 67661-57-8; *N*-(2-azido-3,4,6-trimethylphenyl)phthalimide, 67661-58-9; 2-azido-3,4,6-trimethylaniline, 67661-59-0; *N*,*N*-dimethylaniline, 121-69-7; 2-azido-6-methylaniline, 17537-14-3; 4-methyl-2-(4'-dimethylaminophenyl)benzotriazole, 67661-62-5.

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Kinetics and Mechanism of Aliphatic Transnitrosation

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The kinetics and mechanism of nucleophile-catalyzed transnitrosation by alicyclic nitrosamines are discussed. Transnitrosating agents used included 4-methyl-1-nitrosopiperazine, 2,6-dimethyldinitrosopiperazine, 3,5-dimethyl-1-nitrosopiperazine, and 3-methyl-4-nitroso-2-phenylmorpholine (nitrosophenmetrazine). In all cases morpholine was the recipient amine and thiocyanate ion the nucleophilic catalyst. The transnitrosation reaction was found to be first order in donor nitrosamine and thiocyanate ion, and to be acid dependent. The recipient amine entered into the kinetic rate equation only at low concentrations.

Transnitrosation, which we will define as the transfer of a nitroso group from a nitrosamine to another amine, is a well-known characteristic reaction of aromatic nitrosamines such as diphenylnitrosamine,[1] nitrosocarbazole,[2] and *N*-nitroso-*N*-methylaniline.[3,4] Challis suggested that transnitrosation might be a reaction of aliphatic nitrosamines,[5] but it was only recently demonstrated that certain aliphatic nitrosamines are in fact capable of facile transnitrosation under appropriate conditons,[6] i.e., the presence of a nucleophilic catalyst and appropriate hydrogen ion concentration.

Nitrosation[7] and transnitrosation[6] generally are reversible reactions, but nitrosotransfer to a compound which then decomposes to gaseous products provides an uncomplicated method for studying the kinetics of nitrosotransfer. Challis studied this form of transnitrosation with aromatic nitrosamines and nitrosomorpholine.[3,5] Williams also used this type of reaction in connection with his studies of the Fischer–Hepp rearrangement.[4,8,9] Challis[5] and Boyland[10] found that denitrosations are catalyzed by nucleophiles such as chloride, bromide, and thiocyanate in the same manner that nitrosations are catalyzed by these species.[11,12]

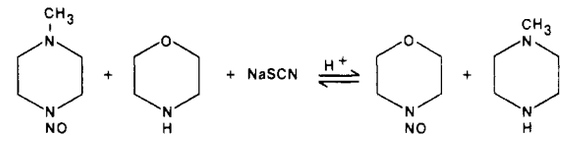
We recently reported the first examples of facile transnitrosation by alicyclic nitrosamines in which both donor and recipient amines were aliphatic.[6,13] We now report the detailed kinetics and mechanism of this reaction.

Results

The thiocyanate-catalyzed reaction between alicyclic nitrosamines and morpholine was chosen for study because of its importance to related in vivo carcinogenicity studies and because of the relative ease of analyzing for the principal products.

The kinetic reaction order of each reactant was determined by observing the change in the pseudo-first-order rate constant for appearance of product nitrosamine caused by varying the concentration of one reactant (the isolation method). The concentration of the reactant being studied was varied while all other reagents were kept at a constant, higher level. For a given set of reactions, the pH was held constant, in the range 1.5–1.8. This relatively low concentration of H^+ was necessary to retard the reaction rates for convenient study.

The reaction of *N*-nitroso-4-methylpiperazine with morpholine was found to be first order in thiocyanate. The results are given in Table I. The reaction was zero order in morpholine at high concentrations but approached first order at lower



(1)

concentrations (Table II). The pH dependence of the reaction shown in eq 1 was determined by one-point kinetics at 10 different pH's. The pH profile is shown in Figure 1.

The pH dependence of the rate of transnitrosation by nitrosophenmetrazine at three pH's was determined. In all cases good first-order plots were obtained, and the rate constants reflect a dependence on $[H^+]$. These reactions are run in 50%

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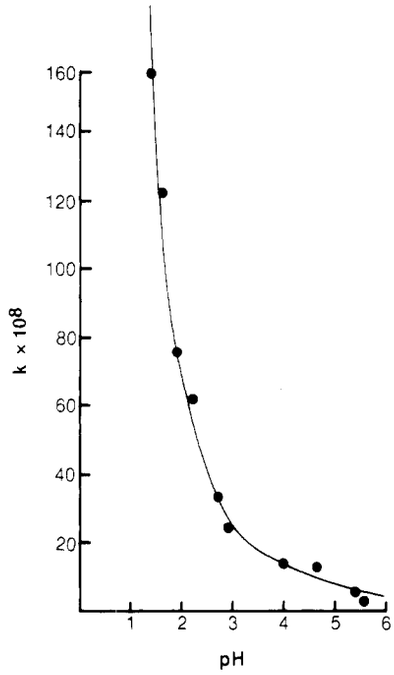


Figure 1. pH profile for the thiocyanate-catalyzed reaction of 4-methyl-1-nitrosopiperazine with morpholine.

Table I[a]

expt	[NaSCN], M	$k_{\psi 1}$, s^{-1}	expected for first order	found
A	0.1	4.39×10^{-5}		
B	0.01	4.15×10^{-6}	k_a/k_b 10	10.50

[a] Reaction conditions are as follows: 4-methyl-1-nitrosopiperazine, 0.5 M; morpholine, 0.5 M; pH 1.5 ($HClO_4$); 50 °C.

dioxane due to the limited solubility of the donor nitrosamine, and the presence of the organic solvent does affect the acidity of the solution. The changes in rate constants are not what would be anticipated for a first-order dependence on $[H^+]$, but in the presence of so many possible protonating species, general acid catalysis by one or more of the protonated amines is certainly possible.

Table III gives the results for the order of transnitrosation reaction in donor nitrosamine for four nitrosamines: 4-methyl-1-nitrosopiperazine 2,6-dimethyldinitrosopiperazine, 3,5-dimethyl-1-nitrosopiperazine, and nitrosophenemetrazine (3-methyl-4-nitroso-2-phenylmorpholine). The first-order plots for the latter are shown in Figure 2.

In the reaction of a nitrosamine with an amine

$$R_2NNO + R'_2NH \rightleftharpoons R'_2NNO + R_2NH \qquad (2)$$

the addition of a base, R_2NH, should inhibit the formation of R'_2NO by competing with R'_2NH for the nitrosating species. This was demonstrated for two examples: 1-methylpiperazine/4-methyl-1-nitrosopiperazine plus morpholine and 2,6-dimethyldinitrosopiperazine/3,5-dimethyl-1-nitrosopiperazine plus morpholine. In both instances, the reaction was slowed considerably by the addition of the base (Table IV).

A UV–vis spectrum was taken of a typical transnitrosation mixture (0.5 M nitrosamine, 0.5 M amine, and 1 M sodium thiocyanate in the region 500 to 400 nm). A peak of very low absorbance was observed at 460 nm (OD = 0.0575) which did not change throughout the course of the reaction. Stedman[14] has reported that nitrosyl thiocyanate has a red color, with an absorbance maximum at 460 nm and absorptivity equal to 100

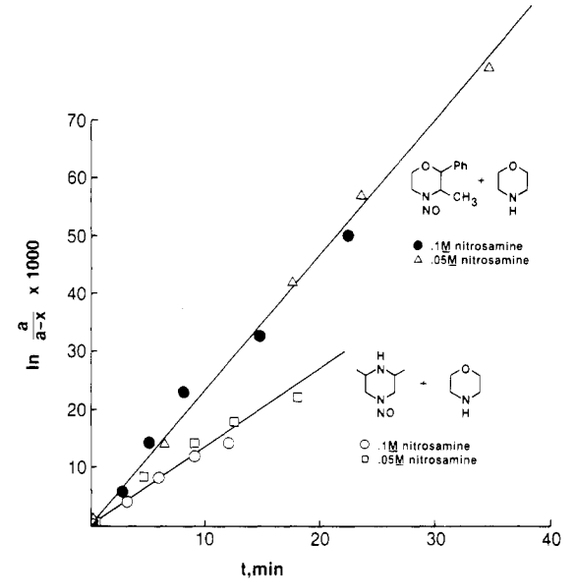


Figure 2. Transnitrosation by two nitrosamines at two concentrations plotted as first-order reactions.

Table II[a]

expt	[morpholine], M	$k_{\psi 1}$, s^{-1}	ratios of slopes: expected for first order	ratios of slopes: found
C	0.1	1.01×10^{-5}	k_c/k_d 2	1
D	0.05	9.69×10^{-6}	k_d/k_e 5	4.4
E	0.01	2.2×10^{-6}		

[a] Reaction conditions are as follows: 4-methyl-1-nitrosopiperazine, 0.5 M; NaSCN, 0.5 M; pH 1.5 ($HClO_4$); 50 °C.

± 5 L mol/cm. On the basis of his figure, the observed concentration of the species absorbing at 460 nm in the transnitrosation mixture would correspond to 5.75×10^{-4} mol/L of nitrosyl thiocyanate.

To determine whether any reaction would occur in a nonaqueous medium (which would be analogous to the behavior of diphenylnitrosamine), nitrosophenmetrazine was heated to 50 °C with morpholine in dioxane for 48 h; no reaction occurred. Similarly, there was no observed reaction when 1-nitrosopiperazine and 1-methylpiperazine were heated at reflux in $CHCl_3$.

In separate experiments, morpholine and *N*-methylpiperazine were reacted with NaSCN and $NaNO_2$ at pH 1.5 at concentrations approximating those used in transnitrosation reactions with the intent of measuring the rate of reaction. Reaction was complete on mixing, implying that this step is very rapid and therefore is not likely to be rate limiting in the sequence of transnitrosation reactions, except in the case where very low concentrations of morpholine are present.

Discussion

Transnitrosation by aliphatic nitrosamines does not occur at all unless a suitable nucleophilic catalyst is present. For example, reaction occurs in 3 N HCl, where chloride acts as a catalyst, but does not occur in 3 N $HClO_4$[6,13] since perchlorate is a very weak nucleophile.[15] There is no evidence for transnitrosation by aliphatic nitrosamines in aprotic solvents; when nitrosophenmetrazine was heated at 50 °C in dioxane with morpholine for 2 days, no nitrosomorpholine was detected. Diphenylnitrosamine would be expected to give a good yield of nitrosomorpholine in a similar reaction since aromatic nitrosamines can effect transfer by a direct uncatalyzed

Table III[a]

nitrosamine	registry no.	concn, M	$k_{\psi 1}$, s^{-1}
N-nitrosophenmetrazine	34993-08-3	0.1	3.64×10^{-4}
		0.05	3.43×10^{-4}
2,6-dimethyldinitrosopiperazine	55380-34-2	0.1	3.11×10^{-4}
		0.05	3.2×10^{-4}
3,5-dimethyl-1-nitrosopiperazine	67774-31-6	0.1	1.72×10^{-4}
		0.05	1.74×10^{-4}
4-methyl-1-nitrosopiperazine	10339-07-4	0.1	1.34×10^{-4}
		0.05	1.37×10^{-4}
		0.02	1.18×10^{-4}
		0.01	1.17×10^{-4}

[a] Reaction conditions are as follows: morpholine, 0.5 M; NaSCN, 0.5 M; pH 1.5 ($HClO_4$); 50 °C.

Table IV[a]

donor nitrosamine	added amine	concn of added amine, M	$k_{\psi 1}$, s^{-1}
4-methyl-1-nitrosopiperazine	1-methylpiperazine	0	1.46×10^{-4}
		0.01	1.33×10^{-4}
		0.05	3.18×10^{-4}
		0.1	1.95×10^{-5}
2,6-dimethyl-*N*,*N*′-dinitrosopiperazine	3,5-dimethyl-1-nitrosopiperazine	0	2.9×10^{-4}
		0.05	2.15×10^{-5}

[a] Reaction conditions are as follows: morpholine, 0.5 M; NaSCN, 0.5 M; nitrosamine, 0.1 M; pH 1.5 ($HClO_4$); 50 °C.

mechanism in protic and aprotic solvents[3,5] depending on the nature of the recipient. The reactions involved in nucleophile-catalyzed transnitrosation may be summarized as in Scheme I.

Scheme I

$$R_2NNO + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_2NNOH^+ \quad (3)$$

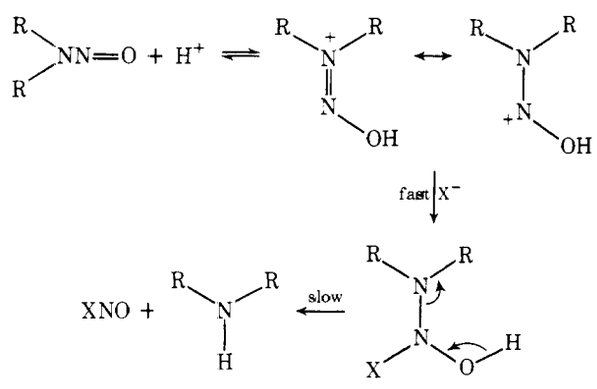
$$R_2NNOH^+ + X^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R_2NH + NOX \quad (4)$$

$$NOX + R'_2NH \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} R'_2NNO + H^+ + X^- \quad (5)$$

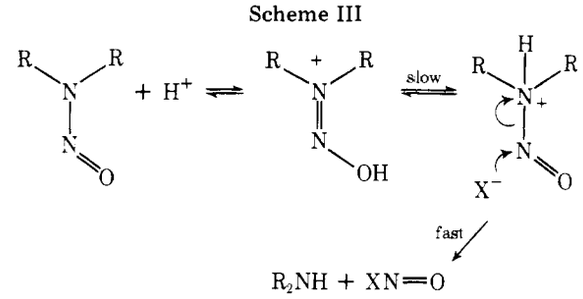
In this scheme it is assumed that the protonation of the nitrosamine is rapid, but most of the nitrosamine is unprotonated. Step 2 (eq 4) is the slow step, and the reaction of NOX with amine is rapid. Indeed, reaction of NOSCN (from $NaNO_2$ plus NaSCN) at pH 1.5 with morpholine or *N*-methylpiperazine is too rapid to measure conveniently.

There are at least two possible mechanisms for step 2. In one case, an addition–elimination type of mechanism could occur as shown in Scheme II. This mechanism involves rapid addition of the nucleophile to the protonated nitrosamine, followed by a slow decomposition of the adduct to amine and nitrosyl–X. The possibility that attack by X^- is the slow step and decomposition of the adduct is rapid is less likely since

Scheme II



Scheme III



reaction of two charged species would be expected to be very rapid.

The other possible mechanism for step 2 is shown in Scheme III. It involves a direct displacement of amine from N=O from the protonated nitrosamine by the nucleophile. In this case the slow step is tautomerization of the protonated nitrosamine to the *N*-protonated form. There is good evidence that the site of protonation in nitrosamines is on the oxygen,[16,17] but it is possible that tautomerization could occur to a sufficient extent to permit the reaction to proceed by the pathway shown in Scheme III.

The mechanisms shown in Schemes II and III are very similar to those proposed by Challis and co-workers.[3] As Challis observed, neither his nor our experimental data allows a choice between the two mechanisms.

In deriving a kinetic expression for transnitrosation, the use of a steady state approximation for the concentration of NOX may be supported by experimental evidence. In a typical reaction using thiocyanate as catalyst, a faint reddish-brown color appears immediately on mixing the reagents.

Stedman has reported that nitrosyl thiocyanate is a red substance, with a weak absorbance at 460 nm. He determined the equilibrium constant for formation of nitrosyl thiocyanate from NaSCN and HNO_2 at 25 °C to be ca. 80 at H^+ concentrations and ionic strengths of 0.4. Therefore, we may infer that the formation of nitrosyl thiocyanate is very rapid and a highly favored process. It is possible that the absorbance at 460 nm is due in part to a contribution from one of the adducts shown in Scheme II, e.g., the second adduct, but there is no unambiguous way to prove or disprove this. This color is most probably due to the presence of NOSCN,[14] and a UV spectrum

of this reaction mixture includes a weak absorption at 460 nm, in agreement with Stedman's characterization of NOSCN.[14] The absorbancy at 460 nm does not change during the course of the reaction, implying a steady state concentration of NOSCN. The rate expression for the formation of nitrosamine can be expressed by

$$\frac{d[R'_2NNO]}{dt} = \frac{k_2k_3[R'_2NH][SCN][R_2NNOH^+] + k_{-3}[R'_2NNO][H^+]}{k_{-2}[R_2NH] + k_3[R'_2NH]} - k_{-3}[R'_2NNO][H^+][SCN] \quad (6)$$

When the rate of reversal of nitrosamine formation is very small (e.g., the formation of a relatively stable nitrosamine), k_{-3} becomes very small and the k_{-3} terms may be disregarded. The concentration of protonated donor nitrosamine may be expressed in terms of the equilibrium constant $K_1 = k_1/k_{-1} = [R_2NNOH^+]/[R_2NNO][H^+]$. The rate expression can then be expressed by

$$\frac{d[R'_2NNO]}{dt} = \frac{k_2k_3K_1[R'_2NH][SCN^-][R_2NNO][H^+]}{k_{-2}[R_2NH] + k_3[R'_2NH]} \quad (7)$$

The first transnitrosation we studied was the reaction of 4-methyl-1-nitrosopiperazine with morpholine in the presence of thiocyanate ion and acid (eq 1). We chose this combination of reagents for the following reasons: (1) 4-methyl-1-nitrosopiperazine is a rapid nitrosotransfer agent[6] and is not carcinogenic;[19] (2) the product, nitrosomorpholine, is not as rapid of a nitrosotransfer agent as the donor nitrosamine;[6,13] and (3) thiocyante ion is an excellent catalyst for transnitrosation reactions[5,6] and has physiological importance since it occurs normally in saliva[6] and at elevated concentrations in the saliva of smokers.[6]

The initial step in the mechanism of transnitrosation probably is protonation of the nitroso group oxygen.[4,19] This should be rapid, but the equilibrium must favor the nitrosamine in dilute acid, pH 1.7. There is no literature data on the pK_a's of nitrosamines, but Williams estimates the pK_a value for *N*-nitroso-*N*-methylaniline to be ca. −2.[4]

The second step is the formation of nitrosyl-X through displacement of NO by the nucleophile. This is generally the rate-determining step. (If R'_2NH is present in a low concentration, the third step of the reaction, formation of the product nitrosamine, must become rate limiting.) The NOX then rapidly reacts with available amine and X^- is regenerated. In the early stages of the reaction, the concentration of recipient amine (R'_2NH) is much greater than the concentration of R_2NH formed in step 2 (eq 4), and the reaction proceeds on to form R'_2NNO with essentially no complication from the reversal of step 2. If the nitrosamine formed (R'_2NNO) is less susceptible to either protonation and/or denitrosation than the donor nitrosamine (R_2NNO), the reversal of step 3 will also not complicate the reaction until the concentration of R'_2NNO is relatively high. *N*-Nitrosomorpholine satisfies these criteria.

N-Nitrosomorpholine can itself act as a transnitrosation agent, but five to ten times more slowly than the four nitrosamines used as donors.[13]

The transnitrosation reaction is first order in thiocyanate, as would be expected from the mechanism shown in Scheme I. The order of the reaction in morpholine, however, varies with concentration. There is no difference in the rates obtained at 0.05 and 0.1 M morpholine, but at concentrations ≤0.05 M the reaction appears to approach first order in morpholine. At high concentrations (>0.05 M), $k_3[R'_2NH] \gg k_{-2}[R_2NH]$ (particularly early in the reaction) and the rate expression can be expressed by

$$d[R'_2NNO]/dt = k_2K_1[SCN][R_2NNO][H^+] \quad (8)$$

i.e., zero order in recipient amine. At lower concentrations of R'_2NH, k_{-2} is not negligible; if $k_{-2}[R_2NH]$ were now $\gg k_3[R'_2NH]$, the kinetic expression would approach being first order in $[R'_2NH]$. When R'_2NH is at a low concentration, the amount of R_2NH present from denitrosation increases to a level comparable to the concentration of R'_2NH quickly, and it will compete effectively for available NOX. When the amine corresponding to donor nitrosamine was added, in two examples (Table IV), the reversal of NOX formation became the predominate reaction, as indicated by a slowing of appearance of product nitrosamine which was inversely proportional to the concentration of R_2NH added.

In addition to 4-methyl-1-nitrosopiperazine (**1**), three other donor nitrosamines were studied (Table III). These included *N*-nitrosophenmetrazine (**2**), a noncarcinogenic morpholine derivative, 2,6-dimethyldinitrosopiperazine (**3**), a potent carcinogen,[20] and a new compound synthesized by denitrosation of (**3**), 3,5-dimethyl-1-nitrosopiperazine (**4**). In all cases, transnitrosation was first order in donor nitrosamine. Compounds **2** and **3** are of particular interest because in both cases steric factors (the presence of methyl groups α to the nitroso function) accellerate denitrosation of **3**, which occurs exclusively at the 1-nitroso position to provide a facile synthesis of **4**.

The pH dependence of the transnitrosation reaction is of particular interest because of the possible physiological importance of the reaction. The pH profile shown in Figure 1 for the reaction of morpholine with 4-methyl-1-nitrosopiperazine shows that the reaction is rapid in the pH range 1–2, with the curve asymptotically approaching pH 1. The kinetics of reactions run at pH's lower than 0 are too rapid to follow and are accompanied by rapid decomposition of the thiocyanate. Therefore, it was not possible to maintain the $[H^+]$ at a level comparable to that of the other reactants. It is not possible to obtain a simple hydrogen ion dependence for the transnitrosation since there are many protonating species present in the reaction mixture, e.g., H^+, $R_2NH_2^+$, and $R'_2NH_2^+$. For example, in the case of 4-methyl-1-nitrosopiperazine, the protonated free amine nitrogen can also act as proton donor.

Conclusions

We have studied the kinetics of transnitrosation by aliphatic nitrosamines under conditions similar to those found in vivo, e.g., in the stomach. The fact that transnitrosation is a facile reaction of many aliphatic nitrosamines under appropriate conditions represents a significant new concept in nitrosamine chemistry and may well be of significance in relation to environmental exposure to nitrosamines. Even noncarcinogenic nitrosamines such as 4-methyl-1-nitrosopiperazine[19] could engage in transnitrosation reactions in the human stomach or saliva to give carcinogenic nitrosamines such as nitrosomorpholine.[21] (Some noncarcinogenic nitrosamines which can act as transnitrosating agents[6,13] occur in the human diet, e.g., nitrosoproline and 4-hydroxy-1-nitrosoproline.[23]) The mechanisms we have considered are similar to those tentatively proposed by Challis[3,22] for nucleophile-catalyzed transnitrosation by diphenylnitrosamine. Since we are dealing with a nitrosamine as the end product, complications can arise from the reversal of step 3, but this situation apparently does not occur until relatively late in the reaction.

Experimental Section

Organic chemicals were obtained from Aldrich and were used as received. Inorganic chemicals were Fisher ACS reagent grade. Sol-

vents were either Fisher ACS reagent or Burdick and Jackson "Distilled in Glass".

4-Methyl-1-nitrosopiperazine and 2,6-dimethyldinitrosopiperazine were prepared by standard methods.[16,18] Nitrosophenmetrazine was provided by Dr. W. Lijinsky.

IR spectra were recorded on a Perkin-Elmer Model 297 spectrometer. UV spectra were obtained on a Beckman Acta IV spectrometer. High-pressure liquid chromatography (LC) was carried out on a Waters liquid chromatograph equipped with a Model 440 absorbance detector. Mass spectra were obtained on a Finnegan Model 3200 quadrupole mass spectrometer. NMR spectra were obtained on a Varian Associates XL-100 spectrometer equipped with a Nicolet 1080 FT computer.

3,5-Dimethyl-1-nitrosopiperazine (1). 2,6-Dimethyldinitrosopiperazine (5 g, 0.029 mol) was dissolved in 3 N HCl (250 mL) and warmed to 50 °C, and $NH_4SO_3NH_2$ (3.04 g, 0.026 mol) was added slowly with stirring. After 20 min, the reaction mixture was cooled in ice, basified with KOH pellets, and extracted with $CHCl_3$ (2 × 100 mL). The $CHCl_3$ extract was then extracted with 1 N HCl (2 × 100 mL). The aqueous extract was basified and extracted with $CHCl_3$ (2 × 100 mL). The $CHCl_3$ extract was dried (Na_2CO_3) and evaporated to give **1** (4.0 g, 96%): mp 54–57 °C; IR (KBr) 3290 (NH), 1408, 1050 (NN=O) cm^{-1}; MS (70 eV) *m/e* (relative intensity) 144 (2.5), 143 (M^+, 1), 128 (12), 113 (78), 70 (100).

Anal. Calcd for $C_6H_{13}N_3O$: C, 50.33; H, 9.31; N, 29.35. Found: C, 50.39; H, 9.15; N, 29.23.

Kinetics. All kinetic reactions were done in the following manner. Neutral stock solutions of the reagents were made up (NaSCN in H_2O, amines in $HClO_4$, and nitrosamines in $HClO_4$ or 50% dioxane–H_2O where necessary for solubility). Appropriate quantities were mixed and equilibrated at 50 °C, except in the case of 2,6-dimethyldinitrosopiperazine where the reaction was run at 23 °C. The reaction was initiated by adjusting the pH with 6 N $HClO_4$ so that all reactions in a given series were run at the same pH (1.5–1.7). At appropriate intervals, 200-μL aliquots were withdrawn and diluted with H_2O to 10 mL. These samples were then analyzed by LC using a Waters μBondapak C_{18} column with water–methanol or pH 3.4 acetic acid (10.4 mM)–methanol mixtures as eluent. When 4-methyl-1-nitrosopiperazine was used, a different procedure was followed because this compound interfered with the analysis; a 200-μL aliquot was added to CH_2Cl_2 (10 mL), mixed on a vortex mixer for 15 s, and filtered through $CaCl_2$ (8 mesh) to remove the aqueous layer. The CH_2Cl_2 extract was then shaken with 200 mg of Na_2CO_3 to remove traces of acid and filtered again. The 4-methyl-1-nitrosopiperazine plus morpholine reactions gave the best analysis on a Waters μBondapak-CN column with 20% 1-propanol–80% *n*-hexane as eluent at 2 mL/min.

Quantitation of analyses was accomplished with the use of a Hewlett Packard 3350 chromatographic computer.

Rates were determined by graphical analysis of the linear portion of the curve obtained from a plot of $\ln (a/a - x)$ vs. t, and a theoretical value for x_∞ was determined. All rate values were also calculated by a least-squares method of analysis.

pH Profile. Solutions that were 0.25 M in morpholine, 4-methyl-1-nitrosopiperazine, and sodium thiocyanate were adjusted to the desired pH's and left at 23 °C for 19 h. Samples were extracted and analyzed as described above.

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Registry No.—1-Methylpiperazine, 109-01-3; morpholine, 110-91-8.

References and Notes

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