Nitrosation of Amines in Nonaqueous Solvents. 3. Direct Observation of the Intermediate in Cyclohexane

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The reactions of *N*-methylaniline (MeAn) with 2,2-dichloroethylnitrite (DCEN) and 2,2,2-trichloroethylnitrite (TCEN) in cyclohexane, and *N*-methylmethoxyamine (MMA) with TCEN in the same solvent, all gave the expected *N*-nitrosamines. Spectrophotometric monitoring of the MeAn/DCEN and MMA/TCEN reactions showed accumulation of the reaction intermediate. These are the first nitrosations of amines by alkyl nitrites in which observation of the intermediate has been possible; this is attributed to the low basicity of these amines (a) having effectively eliminated the possibility of the intermediate decomposing by base catalysis and (b) having decreased the rate of spontaneous decomposition of the intermediate more than the rate of its formation. Because of the scant capacity of cyclohexane to stabilize charge, it is assumed that both the formation and decomposition of the intermediate occur via concerted mechanisms with four-center transition states: formation through nucleophilic attack by the amine on the nitroso group accompanied by transfer of the amine proton to this group, decomposition through simultaneous cleavage of the N−O bond, and protonation of the alkoxide leaving group.

Introduction

In a recent kinetic study of the nitrosation of the strongly basic amines pyrrolidine, piperidine, dimethylamine, *N*-methylpiperazine, and morpholine by alkyl nitrites in nonaqueous solvents, we found that the reaction mechanism is strongly dependent on the medium.[1,2] We concluded that, upon decreasing the polarity of the solvent, or its capacity to act as a proton donor in hydrogen bond formation, the concerted mechanism observed in aqueous media[3] is gradually replaced by a stepwise mechanism, apparently because the decreased solvation of the alkoxide leaving group introduces an energy barrier that delays cleavage of the RO−N bond. The mechanism thus becomes analogous to the mechanism generally accepted for the aminolysis of carboxylic esters.[4] Specifically, we suggested that the formation of a tetrahedral intermediate (I), via a hydrogen-bonded complex (HBC) between amine and alkyl nitrite, is followed by its decomposing either spontaneously or with the catalytic assistance of a second amine molecule (Scheme 1), the rate-controlling step being the formation of (I) at high amine concentrations and its decomposition at low amine concentrations. However, we were unable to obtain direct evidence of the accumulation of the intermediate, and thus to determine the kinetics of all the individual steps of the mechanism.

In principle, it might be thought that the intermediate would be most easily observable in a reaction in which the nitrosating agent is highly activated and has a poor leaving group, and the amine is strongly nucleophilic. However, Bernasconi et al.[5−7] have shown that in nucleophilic vinylic substitution reactions in which the

Scheme 1
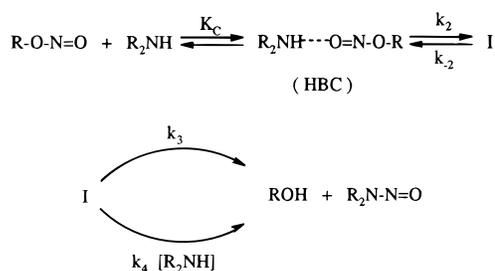
nucleophile is an amine, lowering the nucleophilicity of the amine increases the observability of the intermediate, because the ensuing reduction in the rate of expulsion of the leaving group outweighs the loss of reactivity of the amine. We therefore decided to seek the intermediate of amine nitrosation reactions in nonaqueous solvents using poorly basic amines and activated alkyl nitrites.

Decreasing the basicity of the amine, and hence its nucleophilicity, reduces the rate of formation of the intermediate.[1] It may also be expected to decrease the rate at which the intermediate evolves to the nitrosamine, in which the nitroso group withdraws charge from the amine nitrogen atom (as is shown by the involvement of both the resonance forms **1** and **2**,[8] where
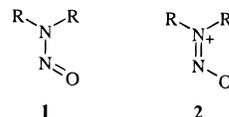
the true structure is the resonance hybrid). Furthermore, for poorly basic amines $k_4[R_2NH]$ may be treated as

(1) García-Río, L.; Leis, J. R.; Iglesias, E. *J. Org. Chem.* **1997**, *62*, 4701.
(2) García-Río, L.; Leis, J. R.; Iglesias, E. *J. Org. Chem.* **1997**, *62*, 4712.
(3) García-Río, L.; Iglesias, E.; Leis, J. R.; Peña, M. E.; Rios, A. *J. Chem. Soc., Perkin Trans. 2* **1993**, 29.
(4) Menger, F. M.; Smith, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 3824.

(5) Bernasconi, C. F.; Leyes, A. E.; Rappoport, Z.; Eventova, I. *J. Am. Chem. Soc.* **1993**, *115*, 7513.
(6) Bernasconi, C. F.; Schuck, D. F.; Ketner, R. J.; Weiss, M.; Rappoport, Z. *J. Am. Chem. Soc.* **1994**, *116*, 11764.
(7) Bernasconi, C. F.; Leyes, A. E.; Rappoport, Z.; Eventova, I. *J. Am. Chem. Soc.* **1995**, *117*, 1703.

Scheme 2
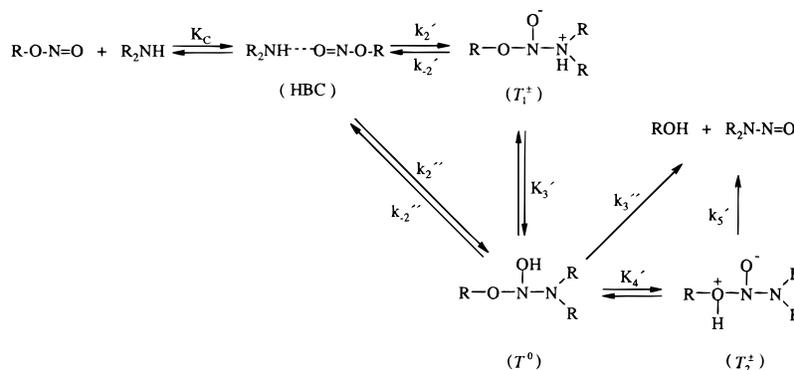
negligible in comparison with k_3, since reducing the basicity of the amine means increasing the acidity of R_2N H_2^+ and (I) by similar amounts, and hence that the rate of spontaneous decomposition of (I) increases while the rate of its decomposition by base catalysis, which depends on the difference in pK_a between $R_2NH_2^+$ and (I), remains constant.

In a weakly polar solvent it is unlikely that there can be any accumulation of the zwitterionic species previously postulated[1] as the intermediate resulting from nucleophilic attack on the alkyl nitrite by the amine ($T_1^{\pm}$ in Scheme 2): because of the poor capacity of such media to stabilize charges, $T_1^{\pm}$ must immediately be transformed, either into the reaction products or into a nonzwitterionic form. The $T_1^{\pm}$ intermediate can undergo a direct transformation into products through a direct pathway from $T_1^{\pm}$ involving intramolecular acid catalysis of RO^- departure by the NH^+ proton. However, accumulation of $T_1^{\pm}$ is unlikely because of the poor capacity of cyclohexane to stabilize charges. A further modification that must be made to Scheme 1 (in addition to the suppression of the k_4 step) is to consider a fast intramolecular proton transfer by which $T_1^{\pm}$ is converted into the nonzwitterionic form T^0.

In fact, the instability of $T_1^{\pm}$ may be such that the formation of T^0 from the HBC takes place via a concerted mechanism involving the four-center transition state **3** (the k_2'' step in Scheme 2). In either case, it is T^0 that must accumulate before the barrier to its conversion into the final products can be overcome. This conversion, too, may occur either directly, by a concerted mechanism involving the four-center transition state **4** (the k_3'' step
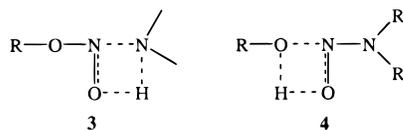
in Scheme 2), or by a stepwise mechanism in which a further intramolecular proton transfer affords the zwitterionic intermediate $T_2^{\pm}$ (the spontaneous decomposition of $T_2^{\pm}$, unlike that of $T_1^{\pm}$, does not involve an ionic leaving group).

In the work described here we sought experimental evidence of the existence of T^0 by studying the kinetics of the nitrosation of *N*-methylaniline (MeAn; $pK_a^{R_2NH_2^+}$

in water 4.85) and *N*-methylmethoxyamine (MMA; $pK_a^{R_2NH_2^+}$ in water 4.75) by the activated alkyl nitrite 2,2,2-trichloroethylnitrite (TCEN), and that of MeAn by 2,2-dichloroethylnitrite (DCEN), all these reactions being carried out in cyclohexane at 25 °C.

Experimental Section

Cyclohexane (nominal purity >99.9%, water content <0.01%, from Aldrich) was used as supplied. Published data for the solubility of water in this solvent[9] indicated that no special precautions would be necessary in the kinetic experiments. *N*-Methylaniline (Aldrich) was of the highest commercially available purity and was distilled under argon shortly before use. *N*-Methylmethoxyamine was obtained from its hydrochloride (Aldrich) by reaction with aqueous NaOH and subsequent repeated fractional distillation in a 20 cm Vigreux column (at least three runs), followed by drying over calcium hydride; the dried product was again distillated shortly before use.

The alkyl nitrites were prepared by a standard procedure involving reaction of the corresponding alcohol with sodium nitrite in an acid medium,[10] and were stored over 3 Å molecular sieves pending use. Solutions in cyclohexane were made up daily to avoid the risk of decomposition.[11]

In all the kinetic experiments the nitrosating agent was in deficit, its concentration generally lying in the range $(1-2) \times 10^{-4}$ M. Reaction kinetics were studied by monitoring absorbance in Varian Cary 1-Bio or Milton Roy 3000 array spectrophotometers, the wavelength being 320 nm for MeAn/TCEN, 335 nm for MeAn/DCEN, and 275 nm for MMA/TCEN. Pseudo-first-order rate constants were calculated by nonlinear regression analysis of the kinetic data using Marquardt's algorithm.[12] All kinetic and spectroscopic experiments were carried out at 25 °C.

Results

In reactions of MMA with TCEN, there was first a rapid increase and then a slower decline in absorbance by the amine at 275 nm (Figure 1). The difference between the initial and final ($t = \infty$) absorbances corresponded to the quantitative formation of *N*-nitroso-*N*-methylmethoxyamine. Hence, the intervening rise in absorbance indicates the accumulation of an intermediate with a greater molar absorptivity than the *N*-nitrosamine at the working wavelength. Figure 2 shows the [amine] dependence of the pseudo-first-order rate constants of the

(8) (a) Looney, C. E.; Phillips, W. D.; Reilley, E. L. *J. Am. Chem. Soc.* **1957**, *79*, 6136. (b) Karabastsos, G. J.; Taller, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4373.

(9) Sorensen, J. M.; Arlt, W. *Liquid–Liquid Equilibrium Data Collection*; Dechema: Frankfurt, 1979.
(10) Noyes, W. A. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 108.
(11) (a) Iglesias, E.; García-Rio, L.; Leis, J. R.; Peña, M. E.; Williams, D. L. H. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1673. (b) Oae, S.; Asai, N.; Fujimore, K. *J. Chem. Soc., Perkin Trans. 2* **1978**, 571.
(12) Marquardt, D. W. *J. Soc. Ind. Appl. Math.* **1963**, *11*, 431.
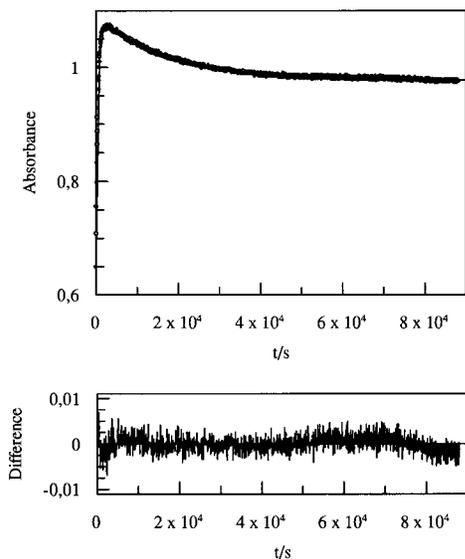
Figure 1. Time dependence of absorbance at 275 nm in the nitrosation of *N*-methylmethoxyamine (0.197 M) by 2,2,2-trichloroethylnitrite in cyclohexane at 25 °C.
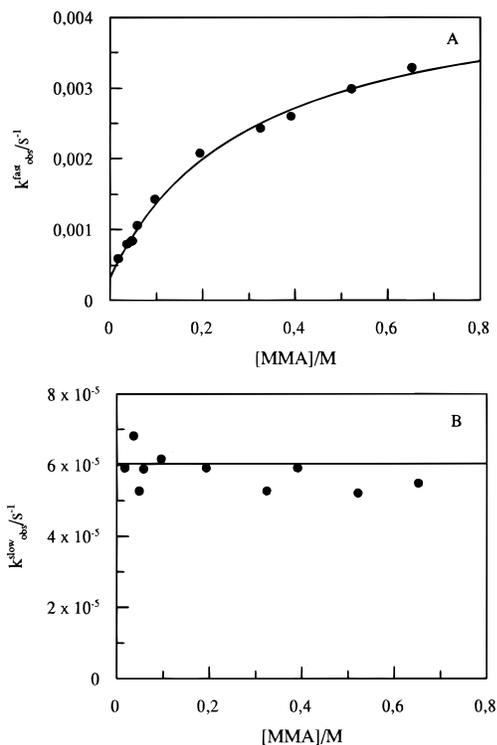
Figure 2. [Amine] dependence of the pseudo-first-order rate constants of the fast (A) and slow (B) processes observed in the nitrosation of *N*-methylmethoxyamine by 2,2,2-trichloro-ethylnitrite in cyclohexane at 25 °C.

Figure 3. Time dependence of absorbance at 335 nm in the nitrosation of *N*-methylaniline (5×10^{-2}M) by 2,2-dichloroet-hylnitrite in cyclohexane at 25 °C.
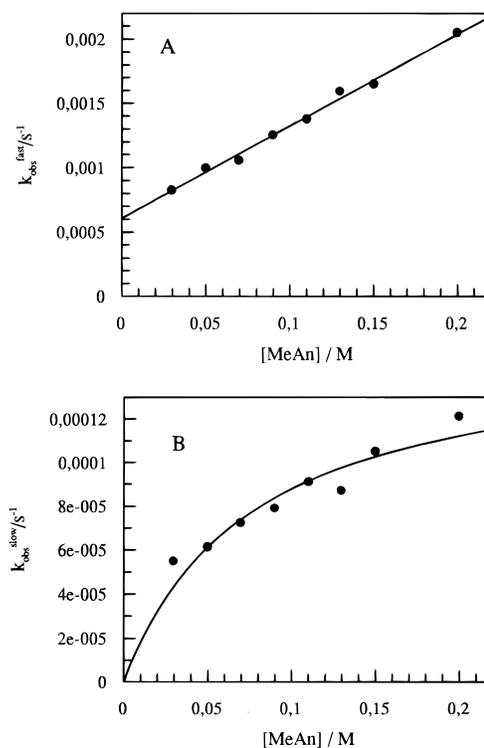
Figure 4. [Amine] dependence of the pseudo-first-order rate constants of the fast (A) and slow (B) processes observed in the nitrosation of *N*-methylaniline by 2,2-dichloroethylnitrite in cyclohexane at 25 °C.

fast, k_{obs}^{fast} (intermediate formation), and slow, k_{obs}^{slow} (intermediate decomposition), processes, as calculated by fitting the experimental absorbance—time data with a double exponential equation (Figure 1 shows an example).

The reactions of MeAn with DCEN had the same kind of kinetics as those of MMA with TCEN (Figure 3), and again the difference between the initial and final absorbances corresponded to the quantitative formation of *N*-nitrosamine. In this case, however, the rate constant

for the fast process increased linearly with amine concentration, while that of the slow process tended to a limit (Figure 4).

Unlike the above reactions, those of MeAn with TCEN had absorbance—time plots showing no indication of the accumulation of an intermediate. The overall observed rate constant for the formation of *N*-nitrosamine increased linearly with amine concentration between 5.00 $\times 10^{-3}$ and 0.90 M (Figure 5), with a rate constant of $(1.12 \pm 0.02) \times 10^{-2}$ M^{-1} s^{-1}.

Table 1. Rate and Equilibrium Constants for the Nitrosation of *N*-Methylmethoxyamine by 2,2,2-Trichloroethyl Nitrite and of *N*-methylaniline by 2,2-Dichloroethyl Nitrite in Cyclohexane

	K_C	K_2'	$K_2'K_C$	K_{-2}'	K_2''	K_CK_2''	k_3''
MMA	3.6	4.14×10^{-3}	1.49×10^{-3}	3.0×10^{-4}	13.8	49.7	6×10^{-5}
MeAn	≤ 1		7.2×10^{-3}	6×10^{-4}		12	1.5×10^{-4}
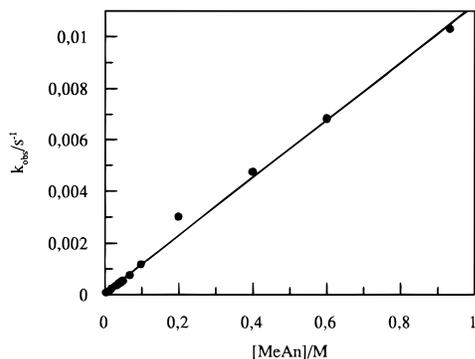
Figure 5. [Amine] dependence of the pseudo-first-order rate constant in the nitrosation of *N*-methylaniline by 2,2,2-trichloroethylnitrite in cyclohexane at 25 °C.

Discussion

Nitrosation of MMA by TCEN and MeAn by DCEN. Scheme 2 implies that the observed rate constants for the formation and decomposition of T^0 by the respective concerted mechanisms are given by

$$k_{obs}^{fast} = \frac{k_2''K_C[\text{amine}]}{1 + K_C[\text{amine}]} + K_{-2}' \qquad (1)$$

and

$$k_{obs}^{slow} = \frac{k_3'K_CK_2''[\text{amine}]}{1 + (K_C + K_CK_2'')[\text{amine}]} \qquad (2)$$

The corresponding expressions for the formation and decomposition of T^0 by the routes involving zwitterionic intermediates are

$$k_{obs}^{fast} = \frac{k_2'K_C[\text{amine}]}{1 + K_C[\text{amine}]} + \frac{K_{-2}'}{1 + K_3'} \qquad (3)$$

which becomes

$$k_{obs}^{fast} = \frac{K_{-2}'/K_3' + (K_{-2}'/K_3')K_C[\text{amine}]}{1 + K_C[\text{amine}]} \qquad (4)$$

if $K_3' \gg 1$ (a reasonable assumption for the equilibrium constant of a charge neutralization process), and

$$k_{obs}^{slow} = \frac{K_CK_2'K_3'K_4'K_5'[\text{amine}]}{1 + (1 + K_2' + K_2'K_3' + K_2'K_3'K_4')K_C[\text{amine}]} \qquad (5)$$

Although eqs 4 and 5 have the same form of [amine] dependence as eqs 1 and 2, respectively, the apolarity and nonproticity of cyclohexane, together with our earlier finding that both the formation and decomposition of the intermediate exhibit isotope effects indicative of proton transfer in the slow step,[1] suggest that contributions of the routes involving the zwitterionic species $T_1^{\pm}$ and $T_2^{\pm}$ must be negligible under the working conditions.

Fitting eq 1 to the data of Figure 2A under the assumption that the observed fast process is the forma-

tion of T^0 leads to the values $k_2'' = 4.14 \times 10^{-3}$ s^{-1}; $K_{-2}' = (3.0 \pm 0.6) \times 10^{-4}$ s^{-1} and $K_C = 3.6 \pm 0.9$ M^{-1} for the nitrosation of MMA by TCEN (Table 1). In view of the value of K_C and that of $K_2'' = k_2''K_{-2}'' = 13.8$, eq 2 reduces to

$$k_{obs}^{slow} = \frac{k_3''K_CK_2''}{K_C + K_2''K_C} \cong \frac{k_3''K_CK_2''}{K_2''K_C} \cong k_3'' \qquad (6)$$

which agrees with Figure 2B if $k_3'' = 6.0 \times 10^{-5}$ s^{-1} (Table 1).

The linear [amine] dependence of the rate of the fast process in the reaction of MeAn with DCEN (Figure 4A) suggests that K_C must be much smaller for this reaction than for that of MMA with TCEN, probably due to the steric hindrance of the aromatic ring of MeAn being much greater than that of the methoxy group of MMA. With this assumption, eq 1 reduces to

$$k_{obs}^{fast} = k_2''K_C[\text{amine}] + K_{-2}' \qquad (7)$$

Fitting this equation to the data of Figure 4A affords the values $K_{-2}' = (6.0 \pm 0.3) \times 10^{-4}$ s^{-1} and $k_2''K_C = (7.2 \pm 0.4) \times 10^{-3}$ M^{-1} s^{-1} (Table 1). Fitting eq 2 to the data of Figure 4B affords $k_3''K_CK_2'' = (2.0 \pm 0.3) \times 10^{-3}$ M^{-1} s^{-1} and $K_C(1 + K_2'') = 13 \pm 4$ M^{-1}; since the behavior of k_{obs}^{fast} means that K_C cannot be greater than unity, these values imply that $K_CK_2'' \approx 13 \pm 4$ M^{-1} and that $k_3'' \approx 1.5 \times 10^{-4}$ s^{-1} (Table 1). Note that the estimate of K_CK_2'' is compatible with that obtained from the k_{obs}^{fast}-based estimates of K_{-2}' and $(K_{-2}' + k_2'')K_C$ if it is taken into account that, given the accumulation of T^0, k_2'' must be much greater than K_{-2}'.

Direct Observation of the Intermediate. The reaction of strong nucleophiles with activated substrates carrying poor leaving groups should yield the best conditions for observation of an intermediate. The conditions for detectability of T^0 are given by eq 8 ("thermodynamic condition") and eq 9 ("kinetic conditions"). An analysis

$$K_CK_2''[\text{amine}] > 1 \qquad (8)$$

$$\frac{k_2''K_C[\text{amine}]}{k_3''} > 1 \qquad (9)$$

of the possible reasons why T^0 could not be detected led to the conclusion that even though eq 8 is most likely met, eq 9 is not. Both conditions are fulfilled in the nitrosation of MeAn by Cl$_2$CHCH$_2$ONO ($K_2''K_C = 12$) and ($k_2''K_C/k_3'' = 48$) and in the nitrosation of MMA by Cl$_3$CCH$_2$ONO ($K_2''K_C = 49.7$ and $k_2''K_C/k_3'' = 952$).

Nature of the Transition States. Although both the formation and the decomposition of T^0 are assumed here to come about by concerted mechanisms in which proton transfer occurs simultaneously with N–N bond formation or N–O bond cleavage, the formation/cleavage and proton-transfer processes are unlikely to be synchronized. In the case of T^0 formation, our earlier results[1] showed (a) that increasing the number of charge-withdrawing groups in the alkyl nitrite increases the rate of interme-

Scheme 3
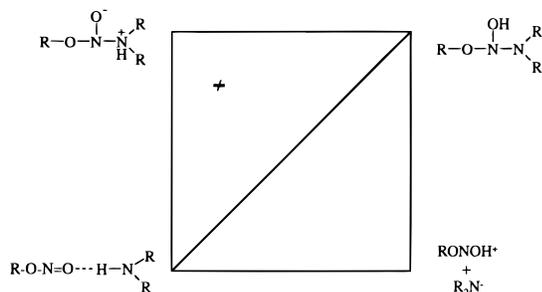
diate formation, k_2 (Scheme 1), $(k_2)_{\text{morpholine}}^{\text{TCEN}}/(k_2)_{\text{morpholine}}^{\text{DCEN}}$ = 6.46, $(k_2)_{\text{piperidine}}^{\text{DCEN}}/(k_2)_{\text{piperidine}}^{\text{BrCH}_2\text{CH}_2\text{ONO}}$ = 12.3, (b) that the relative values of k_2 for the amines pyrrolidine, piperidine, *N,N*-dimethylethylenediamine, *N*-methylpiperazine, diethylamine, and morpholine exhibit practically the same order as the reactivities of these amines with the N=O group in water, generally increasing with the basicity of the amine, and (c) that k_2 is nevertheless much less sensitive to amine basicity than is the reactivity in water, $k_2^{\text{amine}}/k_2^{\text{morpholine}}$ = 13:3.3:3.3:2.2:1.4:1, respectively, whereas in water $k_2^{\text{amine}}/k_2^{\text{morpholine}}$ = 167:32:28: 1.6:11.7:1, respectively.[3] Findings (a) and (b) suggest that in the transition state of T^0 formation, N—N bond formation must have progressed considerably more than proton transfer, although finding (c) implies that some degree of proton transfer has also occurred. Electron-withdrawing substituted alkyl nitrites increase the electrophilicity of the nitroso group and decrease the proton affinity of the nitroso oxygen, hindering the intramolecular proton transfer. In the same way increasing the basicity of the amine increases its nucleophilicity but decreases its proton donor ability. We have also reported that both the formation and decomposition of the intermediate exhibit isotope effects indicative of proton transfer in the slow steps.[1] These conclusions are summarized schematically in the More O'Ferrall diagram[13] shown in Scheme 3. Note that the HBC is shown in the bottom left-hand corner of this diagram as being formed via the nitroso oxygen of the alkyl nitrite, which is more negatively charged than the alkoxide oxygen due to the coexistence of the resonance structures **5** and **6**. Although
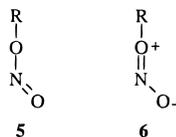
the stabilization of alkyl nitrites by resonance is limited by the scant capacity of oxygen to support positive charge, and is thus less intense than the stabilization of *N*-nitrosamines by resonance between **1** and **2**, it is sufficient to make the nitroso oxygen the preferred site for hydrogen bonding (which parallels the behavior of carboxylic esters[14]).

As regards the decomposition of T^0, the nonaccumulation of intermediate in our earlier studies with more basic amines,[1,2] and the partial positive charge on the amine nitrogen of nitrosamines (as discussed in the

(13) (a) More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 274. (b) Jencks, W. P. *Chem. Rev.* **1972**, *72*, 705.

(14) (a) Nagy, J. B.; Nagy, O. B.; Bruylants, A. *Bull. Soc. Chim. Belg.* **1973**, *82*, 539. (b) Mukana, D.; Nagy, J. B.; Bruylants, A. *Bull. Soc. Chim. Belg.* **1974**, *83*, 201. (c) Nagy, J. B.; Muanda, M.; Nagy, J. B. *J. Phys. Chem.* **1979**, *83*, 1961.
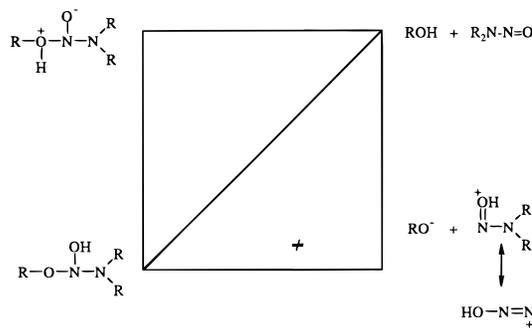
Scheme 4

Table 2. Qualitative Dependence of Constants in Scheme 2 on the Nature of the Amine and Alkyl Nitrite

	k_2''	k_{-2}''	K_2''	k_3''
increasing the electron-withdrawing groups on the RONO	↑	↓	↑	↑
increasing the amine basicity	↑	↑	↑↓	↑

Introduction), suggest that k_3'' must increase with the ability of the amine to support positive charge, and hence that the transition state of this step must lie below the diagonal of the More O'Ferrall diagram of Scheme 4. This location not only avoids the development of positive charge on the alkoxide oxygen that occurs above the diagonal, but is also supported by k_3'' apparently being increased in solvents with high proton donicity capable of stabilizing the development of negative charge on the alkoxide oxygen; in Cl$_3$CH, for example, the rate-controlling step is the formation of the intermediate at all amine concentrations in the range $(2-1000) \times 10^{-3}$ M.[2]

In view of the amine basicity argument justifying Scheme 4, the results listed in Table 1 for k_3'' have implications for the relative values of the $pK_a^{\text{R}_2\text{NH}_2^+}$ of MMA and MeAn in cyclohexane, which are not known. The fact that k_3'' is greater for MeAn/DCEN than for MMA/TCEN means that $pK_a^{\text{R}_2\text{NH}_2^+}$(MeAn) minus $pK_a^{\text{R}_2\text{NH}_2^+}$(MMA) must be large enough to outweigh TCEN's being better able to support negative charge on its alkoxide oxygen than DCEN. This suggests that the difference in $pK_a^{\text{R}_2\text{NH}_2^+}$ between MeAn and MMA is greater in cyclohexane than in water, in which they are quite similar (4.85 and 4.75, respectively).

Table 2 summarizes the qualitative influence of the natures of amine and alkyl nitrite on the constants involved in the formation and decomposition of T^0. We have already seen that k_2'' and k_3'' are increased both by increasing the basicity of the amine and by increasing the number or efficacy of the charge-withdrawing groups in the alkyl nitrite. Since increasing charge withdrawal in the alkyl nitrite reduces its stability, it must diminish K_{-2}'' and hence, given its effect on k_2'', increase K_2''. However, the positive charge on the amine nitrogen in the transition state of the k_{-2}'' process implies that this constant may be expected to increase with the basicity of the amine (leaving the response of K_2'' to amine basicity uncertain). Finally, K_C may be expected to be diminished both by increasing amine basicity and by increasing charge withdrawal in the alkyl nitrite (which reduces the negative charge on the hydrogen-bonding nitroso group).

Nitrosation of MeAn by TCEN. For T^0 to accumulate, it must be generated faster than it is removed by either the backward (k_{-2}'') or forward (k_3') decomposi-

tion processes; i.e., the constants in Scheme 2 must satisfy the conditions given by eqs 8 and 9. With the amine concentrations used in this work, the values listed in Table 1 show both conditions to have been amply satisfied for the nitrosation of MMA by TCEN ($K_C K_2'' =$ 49.7, $k_2'K_C/k_3'' = 952$) and the nitrosation of MeAn by DCEN ($K_C K_2'' = 12$, $k_2'K_C/k_3'' = 48$). In view of this, Table 2 suggests that the failure to observe T^0 in the reaction of MeAn with TCEN must have been due to a large drop in K_C, resulting in nonsatisfaction of eq 8, and/or to a large drop in K_C and/or a large increase in k_3'' outweighing the expected rise in k_2'' and thereby causing nonsatisfaction of eq 9.

If nonaccumulation of the intermediate in the MeAn/TCEN reaction is due to a large increase in k_3'' outweighing the expected increase in k_2'', perhaps largely as the result of k_3'' being more sensitive to amine basicity than k_2'',[1] then the rate-limiting step of this reaction is the formation of T^0. Scheme 2 then implies

$$k_{\text{obs}} = \frac{k_2'' K_C[\text{amine}]}{1 + K_C[\text{amine}]} \qquad (10)$$

which, if $K_C < 0.1$, reduces to

$$k_{\text{obs}} = k_2'' K_C[\text{amine}] \qquad (11)$$

and is therefore compatible with the linear [amine] dependence observed in Figure 5. However, the linearity observed in Figure 5 is also compatible with control by T^0 decomposition under the same assumption that $K_C < 0.1$; for then the expression for k_{obs} implied by Scheme 2 under the assumption of control by T^0 decomposition

$$k_{\text{obs}} = \frac{k_2'' k_3'' K_C[\text{amine}]}{(k_3'' + k_{-2}'')(1 + K_C[\text{amine}])} \qquad (12)$$

reduces to the linear expression

$$k_{\text{obs}} = \frac{k_2'' k_3'' K_C}{k_3'' + k_{-2}''}[\text{amine}] \qquad (13)$$

The value of $k_2'' K_C$ obtained by fitting eq 11 to the data of Figure 5, $k_2'' = 1.12 \times 10^{-2}$, is greater than the upper limit of 1×10^{-2} obtained by fitting eq 13 to the Figure 5 data (which gives $k_2'' k_3'' K_C/(k_3'' + k_{-2}'') = 1.12 \times 10^{-2}$) and taking into account that $0 < k_3''/(k_3'' + k_{-2}'') < 1$. However, this comparison decides nothing, nor does comparison with the value of $k_2'' K_C$ for the MeAn/DCEN reaction, 7.2 $\times 10^{-3}$; although k_2'' is expected to be greater for MeAn/TCEN than for MeAn/DCEN, K_C is expected to be smaller under the hypothesis that T^0 decomposition is rate limiting (unless k_{-2}'' is much more sensitive to amine basicity than k_2'', and of this there is no independent evidence). We must conclude that the available data are insufficient to identify the rate-controlling step of the MeAn/TCEN reaction and thereby determine whether this reaction is or is not in keeping with our earlier conclusion[1] that the rate-controlling step is the formation of the intermediate at high amine concentrations but its decomposition at low amine concentrations.

Conclusions

The reactions of MeAn with DCEN and MMA with TCEN in cyclohexane are the first nitrosations of amines by alkyl nitrites in which the expression $k_2'' K_C/k_3''$ is large enough to allow the accumulation of detectable concentrations of the intermediate T^0. This finding is compatible with earlier indications[1] that, although both k_2'' and k_3'' increase with increasing amine basicity and with the charge-withdrawing capacity of the substituent groups of the alkyl nitrite, k_3'' is more sensitive to amine basicity than k_2''. The scant capacity of cyclohexane to stabilize charge suggests that in this solvent both the formation and the decomposition of T^0 must be concerted processes with four-center transition states. In the transition states of the formation and decomposition of T^0, proton transfer appears to have progressed less than N−N bond formation and N−O bond cleavage, respectively.