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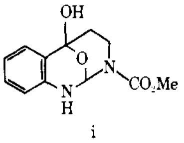

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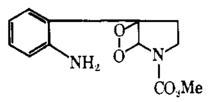

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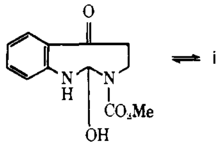

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Reaction Pathways in the Formation of the 1,3,5-Trinitrobenzene-Anilide σ Complex from Aniline and the 1,3,5-Trinitrobenzene-Methoxide σ Complex

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Abstract: The reversible reaction between the 1,3,5-trinitrobenzene-methoxide σ complex ($TNB{\cdot}OMe^-K^+$) and aniline in dimethyl sulfoxide-methanol solutions, yielding the 1,3,5-trinitrobenzene-anilide σ complex ($TNB{\cdot}NHPh^-K^+$), has been studied spectrophotometrically and found to obey a rate law which is of first order with respect to aniline, but of complex order with respect to $TNB{\cdot}OMe^-K^+$. An additional feature of this system is that whereas TNB and aniline alone undergo no reaction in Me_2SO-methanol, in the presence of methoxide ion a rapid reaction occurs to give the $TNB{\cdot}OMe^-$ complex, which then undergoes a slow reversible conversion to the $TNB{\cdot}NHPh^-$ complex. In both cases the kinetic data for the conversion of the methoxide complex (S) to the anilide complex (P) require a dissociative mechanism (Scheme IV) in which the interconversion of free TNB (I) and the protonated anilide complex (PH) constitutes the rate-determining step. Although the kinetic data do not rule against the intermediacy of the protonated methoxide complex (SH), the presence of this intermediate along the reaction pathway is considered unlikely. Further variations on the proposed dissociation mechanism (Scheme II), as well as displacement mechanisms (Scheme I) and a mechanism involving anilide ion (Scheme III), can be eliminated on kinetic grounds (cf. Table V and Figure 3). On the basis of the results of the present study, it is proposed that the lack of σ-complex formation between TNB and aniline in the absence of strong base is due to a thermodynamic, rather than kinetic, factor.

The σ complexes formed between polynitro aromatic compounds and bases[1-7] have been used as models of the reaction intermediates which are considered to be formed in activated nucleophilic aromatic substitution reactions.[8,9] Aliphatic primary and secondary amines have played a central role in such studies of S_NAr processes,[10-16] since they offer the possibility of base catalysis in the deprotonation of the initially formed zwitterionic intermediates (eq 1) and thereby provide kinetic evidence of the existence of such species.

Recent studies in this area have focused on the stable σ complexes formed between a number of nitroaromatic compounds and primary or secondary aliphatic amines, and on the catalytic processes involved in their formation and decomposition.[16-18] Such studies have led to a reconsideration of current

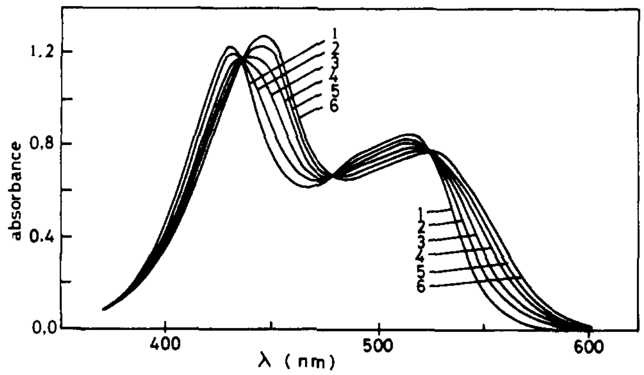
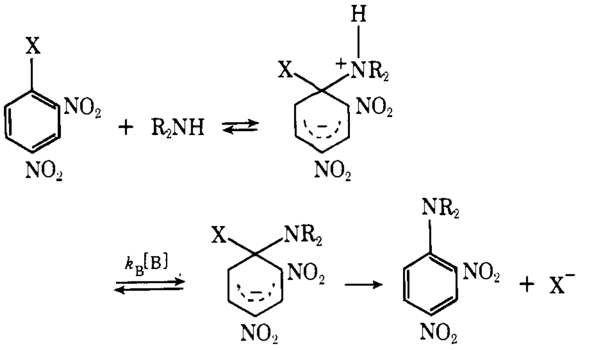


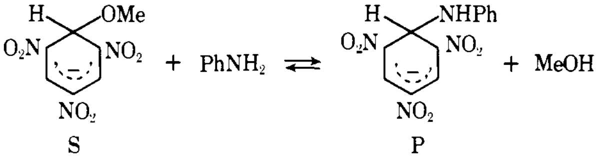
Figure 1. Illustration of spectral changes occurring during conversion of TNB·OMe$^-$K$^+$ (4 × 10^{-4} M) to TNB·NHPh$^-$K$^+$ by reaction with aniline (0.4 M) in 90:10 mol % Me_2SO-methanol at 25 °C. Scan 1 taken after 1 min reaction time; scan 2 after 5 min; scan 3 after 14 min; scan 6 after 90 min.



(1)

ideas regarding the mechanism of base catalysis in S_NAr systems.

It remained a puzzling problem that aromatic primary or secondary amines were not reported to yield stable σ complexes with polynitroaromatics such as 1,3,5-trinitrobenzene (TNB). Only the relatively weak π complexes[19,20] were found to be formed in such systems.[21,22] We observed, however, that the trinitrobenzene-methoxide σ complex reacts with aniline in dimethyl sulfoxide (Me_2SO)-methanol solution to yield the trinitrobenzene-anilide σ complex (eq 2).[23] Subsequently a number of substituted aromatic amines were used in this reaction and the structures of the resulting anilide complexes were investigated by NMR spectroscopy.[24,25]



(2)

In the present study we report the results of a kinetic investigation of the reaction between the TNB-methoxide σ complex and aniline in Me_2SO-methanol media. Complex kinetic behavior has been observed for this reaction and the detailed consideration thereof has led to a complete description of the reaction pathway.

Results

Spectral Characteristics of the Reaction. The reaction between aniline and the TNB·OMe$^-$K$^+$ σ complex (S), yielding the TNB·NHPh$^-$K$^+$ σ complex (P), can readily be followed by ultraviolet-visible spectrophotometry since σ complexes of trinitrobenzene have characteristic electronic absorption bands in the visible spectrum.[1-4] It was found after preliminary examination that the reaction proceeds smoothly in 90:10 mol % Me_2SO-methanol and most of our data refer to that medium, although moderate changes in medium composition have also been evaluated.

Table I. Equilibrium Data for Formation of TNB·NHPh$^-$K$^+$ from TNB·OMe$^-$K$^+$ and Aniline at 25 °C in 90:10 mol % Me_2SO-Methanol[a]

[Aniline], M	$A_e - A_0$[b]	$(A_e - A_0)$/[aniline]
0.0496	0.298	6.01
0.0496	0.294	5.93
0.0496	0.293	5.96
0.0984	0.380	3.86
0.0982	0.385	3.92
0.0980	0.390	3.98
0.198	0.459	2.32
0.196	0.470	2.40
0.392	0.490	1.25

[a] $[TNB·OMe^-K^+]_0 = 4 \times 10^{-4}$ M. [b] A_e and A_0 are absorbance values at equilibrium and at $t = 0$, respectively (λ 450 nm, l = 1 mm).

TNB itself does not undergo reaction with aniline, as shown by the absence of color development which would be characteristic of σ-complex formation on mixing the two reagents in Me_2SO-methanol. It was found, however, that in the presence of potassium methoxide the interaction between aniline and TNB leads to an instantaneous development of red color. The resulting spectrum corresponds quantitatively to that of the methoxide complex, TNB·OMe$^-$K$^+$. This spectrum is not stable under the reaction conditions and in time undergoes changes due to the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$. The spectral changes are reproduced exactly when the reaction is performed using TNB·OMe$^-$K$^+$ and aniline as the reactants. In Figure 1 are shown the spectral changes occurring as a function of time for a given experiment between TNB·OMe$^-$K$^+$ and aniline.[26]

The Equilibrium between TNB·OMe$^-$K$^+$ and TNB·NHPh$^-$K$^+$. The spectral changes resulting from variation of the concentration of aniline while keeping the concentration of TNB·OMe$^-$K$^+$ constant were indicative of the occurrence of an equilibrium process. This was apparent from the gradual shift to longer wavelengths of the absorption maxima, as well as the changing absorbance values of the peaks characteristic of the reaction product, as the concentration of aniline was increased. This trend may be expected from the following $\lambda_{max}(\epsilon)$ values:[25] TNB·OMe$^-$K$^+$, 430 nm (28 900 M^{-1} cm^{-1}), 512 nm (20 000 M^{-1} cm^{-1}); TNB·NHPh$^-$K$^+$, 446 nm (30 400 M^{-1} cm^{-1}), 522 nm (17 700 M^{-1} cm^{-1}). The apparent equilibrium constant, K_{app}, for the overall reaction in eq 2 could be obtained from the absorbance data by using the Foster-Hammick-Wardley equation[27] with adjustment for overlap of absorption bands due to the two spectral species as suggested by Ketelaar et al.[28] The relationship requires that a plot of $(A_e - A_0)/[PhNH_2]$ vs. $(A_e - A_0)$ should be linear with slope = $-K_{app}$ and intercept = $-K_{app}[S]_0(\epsilon_p - \epsilon_s)l$, where $(\epsilon_p - \epsilon_s)$ is the difference in extinction coefficients of the two species at the given wavelength and l is the cell path length. The results, listed in Table I, lead to a reasonably good linear plot, yielding $K_{app} = 23.2 \pm 1.7$ M^{-1} and ϵ_p (450 nm) = 29 500 ± 500 M^{-1} cm^{-1}. At the standard aniline concentration of 0.1 M the equilibrium composition is given by $[TNB·NHPh^-]/[TNB·OMe^-] = K_{app}[PhNH_2] = 2.3$.

Kinetic Behavior of the Conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$. 1. Order of Reaction with Respect to TNB·OMe$^-$K$^+$. A series of kinetic runs were performed at 25 °C in 90:10 mol % Me_2SO-methanol with TNB·OMe$^-$K$^+$ and aniline as the reactants. The concentrations of both reactants were varied while keeping the aniline concentration in large excess. To maintain a constant electrolyte concentration the

Table II. First-Order Rate Constants k_{ψ_1} for the Formation of TNB·NHPh$^-$K$^+$ in the Reaction of TNB·OMe$^-$K$^+$ with Aniline (0.098 M) in 90:10 mol % Me$_2$SO-MeOH[a]

10^4[TNB·OMe$^-$K$^+$]$_0$, M	$10^4 k_{\psi_1}$,[b] s^{-1}	$10^5 k_{\psi_1}$[TNB·OMe$^-$K$^+$]$_0^{1/2}$, M$^{1/2}$ s^{-1}
2.05	9.97	1.43
3.84	6.92	1.36
3.84	6.75	1.32
4.18	6.90	1.41
8.32	4.90	1.41
24.6	2.88	1.43
25.4	2.75	1.39

[a] All kinetic runs performed at 25 °C in the presence of 0.098 M Et$_4$NClO$_4$. [b] k_{ψ_1} values obtained from the initial approximately linear portions of plots of log ($A_e - A_t$) vs. reaction time.

Table III. Analysis of the Kinetic Data[a] for the Conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ on the Basis of the Differential Rate Equation $-\mathrm{d[S]}_t/\mathrm{d}t = k([\mathrm{S}]_t - [\mathrm{S}]_e)/[\mathrm{S}]_t^{1/2}$

10^4[TNB·OMe$^-$K$^+$]$_0$, M	$10^4 k_\delta$,[b] s^{-1}	10^4[S]$_e$,[c] M	$10^5 k_\delta$[S]$_e^{1/2}$, M$^{1/2}$ s^{-1}
2.05	15.2	0.626	1.20
3.84	10.0	1.17	1.08
4.18	10.5	1.27	1.18
8.32	6.88	2.54	1.10
24.6	4.17	7.51	1.14
25.4	3.85	7.73	1.07

[a] All runs performed at 25 °C in 90:10 mol % Me$_2$SO-methanol with [PhNH$_2$] = [Et$_4$NClO$_4$] = 0.098 M. [b] k_δ values obtained from the slopes of plots of $2\delta_S^{1/2} + \ln((\delta_S^{1/2} - 1)/(\delta_S^{1/2} + 1))$ vs. reaction time; slope = $-k_\delta$ (see eq 5). [c] [S]$_e$ = [TNB·OMe$^-$K$^+$]$_e$ = [TNB·OMe$^-$K$^+$]$_0$/(1 + K_{app}[PhNH$_2$]), with K_{app} = 23.2 M^{-1}.

runs were performed in the presence of ca. 0.1 M Et$_4$NClO$_4$. The conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ was followed spectrophotometrically by repeated scanning over the region 375–650 nm.

The absorbance data from the kinetic runs were at first analyzed by the normal procedure for reversible first-order reactions,[29] i.e., by performing plots of log ($A_e - A_t$) vs. t, where A_e is the equilibrium value of the absorbance and A_t is the value at time t. These plots have been found to exhibit reasonable linearity for about 1 half-life, followed by an increase in slope as the reaction proceeds to equilibrium.

However, the observed first-order rate constants (k_{ψ_1}) obtained from the slopes of these plots were found to vary considerably with the concentration of TNB·OMe$^-$K$^+$ (Table II). A plot of log K_{ψ_1} vs. log [S]$_0$, where [S]$_0$ is the initial concentration of TNB·OMe$^-$K$^+$, was found to be linear with a slope of −0.51, and a linear plot with zero intercept was obtained between $1/k_{\psi_1}$ and [S]$_0^{1/2}$. The results of these plots are equivalent to the constancy of the k_{ψ_1} [S]$_0^{1/2}$ values given in Table II. This kinetic behavior indicates a rate law of the approximate form given by

$$-\frac{\mathrm{d[S]}_t}{\mathrm{d}t} = k_{\psi_1}([\mathrm{S}]_t - [\mathrm{S}]_e) \simeq \frac{k}{[\mathrm{S}]_0^{1/2}}([\mathrm{S}]_t - [\mathrm{S}]_e) \quad (3)$$

during the early stages of the reaction. Such an apparent rate law, as well as the moderate increases (with increasing t) in the slopes of the first-order plots, suggested that the true rate law for the reaction was that given in

$$-\frac{\mathrm{d[S]}_t}{\mathrm{d}t} = k_{\psi_1}([\mathrm{S}]_t - [\mathrm{S}]_e) = \frac{k}{[\mathrm{S}]_t^{1/2}}([\mathrm{S}]_t - [\mathrm{S}]_e) \quad (4)$$

Early in the reaction, when $[\mathrm{S}]_t^{1/2} \sim [\mathrm{S}]_0^{1/2}$, eq 4 would lead to the approximate rate law given in eq 3, and in addition eq 4 predicts an increase in k_{ψ_1} (i.e., in $k/[\mathrm{S}]_t^{1/2}$), and hence an increase in the slope of a first-order plot, as the reaction proceeds to equilibrium. The assumed differential rate expression in eq 4 is readily integrated[30] to give

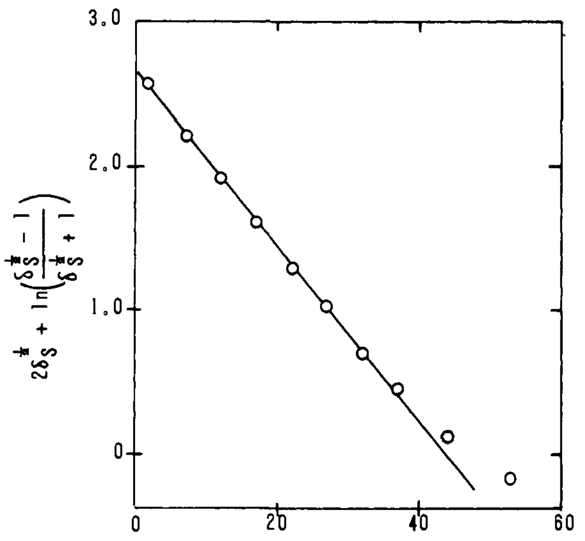


Figure 2. Plot according to the integrated equation (eq 5) for the rate law $-\mathrm{d[S]}_t/\mathrm{d}t = k([\mathrm{S}]_t - [\mathrm{S}]_e)/[\mathrm{S}]_t^{1/2}$. Reaction conditions: [TNB·OMe$^-$K$^+$]$_0$ = 3.84 × 10^{-4} M, [PhNH$_2$] = 0.10 M, 90:10 mol % Me$_2$SO-methanol, 25 °C (50% reaction at 17 min).

$$2\delta_S^{1/2} + \ln\left(\frac{\delta_S^{1/2} - 1}{\delta_S^{1/2} + 1}\right) = 2\left(\frac{[\mathrm{S}]_0}{[\mathrm{S}]_e}\right)^{1/2} + \ln\left(\frac{([\mathrm{S}]_0/[\mathrm{S}]_e)^{1/2} - 1}{([\mathrm{S}]_0/[\mathrm{S}]_e)^{1/2} + 1}\right) - k_\delta t \quad (5)$$

in which $\delta_S = [\mathrm{S}]_t/[\mathrm{S}]_e$ and $k_\delta = k/[\mathrm{S}]_e^{1/2}$. According to eq 5, a plot of the function $2\delta_S^{1/2} + \ln[(\delta_S^{1/2} - 1)/(\delta_S^{1/2} + 1)]$ vs. reaction time should be linear, with slope = $-k_\delta = -k/[\mathrm{S}]_e^{1/2}$. The kinetic data for the approach to equilibrium in the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ were fully in accord with these predictions. As shown in Figure 2, the plots performed according to eq 5 were linear as required. Also, as required by the relationship $k_\delta = k/[\mathrm{S}]_e^{1/2}$, the values of $k_\delta[\mathrm{S}]_e^{1/2}$ (Table III) were constant (average deviation of ±5%), and a plot of k_δ vs. $1/[\mathrm{S}]_e^{1/2}$ was linear, passing through the origin.

2. Order of Reaction with Respect to Aniline. A number of runs were carried out in 90:10 mol % Me$_2$SO-methanol at constant ionic strength ([Et$_4$NClO$_4$] ≃ 0.1 M) and with the concentration of TNB·OMe$^-$K$^+$ maintained at ca. 4 × 10^{-4} M, while the aniline concentration was varied over the range 0.05–0.2 M.

Analysis of the kinetic data by both first-order plots and by plots based on eq 5 gave the k_{ψ_1} and k_δ values listed in Table IV. Plots of k_{ψ_1} vs. [PhNH$_2$] and of k_δ vs. [PhNH$_2$] were both linear with positive intercepts. Hence the order with respect to aniline is approximately unity regardless of the assumed order with respect to the substrate.

3. The Effect of Added CH$_3$O$^-$K$^+$. Several experiments were performed in which a potassium methoxide solution was added to the reaction solution containing TNB·OMe$^-$K$^+$ (4 × 10^{-4} M), aniline (0.1 M), and Et$_4$NClO$_4$ (0.1 M) in Me$_2$SO-methanol (90:10 mol %). It was observed in these experiments that the rate of increase in absorbance due to TNB·NHPh$^-$K$^+$ was highly retarded and that competing decomposition processes set in (as shown by a gradual decrease in absorbance due to the TNB·OMe$^-$K$^+$ complex). This behavior persisted at MeO$^-$K$^+$ concentrations as low as were reliably preparable

Table IV. Effect of Aniline Concentration and Medium Composition on the Rate of Formation of TNB·NHPh$^-$K$^+$ from TNB·OMe$^-$K$^+$ and Aniline[a]

Me$_2$SO-methanol mole ratio	[PhNH$_2$], M	$10^4k_{\psi_1}$,[b] s^{-1}	10^4k_δ,[c] s^{-1}
95:5	0.0981	5.50	
	0.0981	5.03	
90:10	0.0496	3.47	4.12
	0.0496	3.30	4.58
	0.0980	6.75	10.0
	0.0984	6.90	10.5
	0.198	12.7	24.2
	0.196	12.9	23.3
85:15	0.0980	8.25	
	0.0980	8.83	

[a] All runs performed at 25 °C with [TNB·OMe$^-$K$^+$] = 4 × 10^{-4} M and [Et$_4$NClO$_4$] = 0.098 M. [b] As footnote *b* in Table II. [c] As footnote *b* in Table III.

by this method, and thus kinetic data for the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ could not be obtained in the presence of added methoxide ion. However, the fact that inhibition of the rate by added methoxide ion occurs would appear to be significant in itself (vide infra).

4. Effect of Variations in Solvent Composition. Runs were performed over the region 5–15 mol % methanol in Me$_2$SO. The initial concentrations of TNB·OMe$^-$K$^+$ and of aniline were 4 × 10^{-4} and 0.1 M, respectively, and the ionic strength was maintained at 0.1 M. The pertinent data are listed in Table IV and show that the first-order rate constant k_{ψ_1} increases with increasing methanol content (k_δ values were not obtained for the runs performed in 5 and 15 mol % methanol). A plot of k_{ψ_1} vs. mole percent methanol was approximately linear.

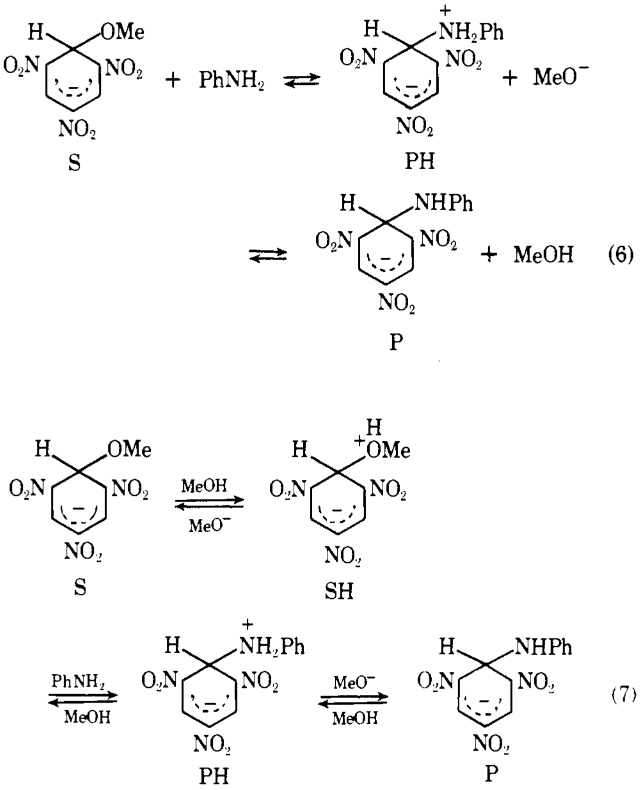
Kinetic Behavior of the TNB/PhNH$_2$/MeO$^-$K$^+$ System. The formation of TNB·NHPh$^-$K$^+$ was also studied by adding MeO$^-$K$^+$ to a mixture of TNB and aniline in 90:10 mol % Me$_2$SO-methanol containing 0.1 M Et$_4$NClO$_4$. The concentrations were [TNB] = [MeO$^-$K$^+$] $\sim$ 4 × 10^{-4} M and [PhNH$_2$] $\sim$ 0.1 M. The absorbance data showed the immediate quantitative formation of the TNB·OMe$^-$K$^+$ complex followed by the slow conversion of this complex to TNB·NHPh$^-$K$^+$. Of these two reaction stages, the formation of TNB·OMe$^-$K$^+$ was too rapid to be followed by our kinetic procedures. The subsequent conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ could, however, be followed, and the kinetic behavior and rate constants were in agreement within experimental error with those obtained when using TNB·OMe$^-$K$^+$ as the substrate.

Discussion

General Features of the Reaction. There are a number of unusual features associated with the formation of the anilide complex TNB·NHPh$^-$K$^+$ in the present system. (1) In the absence of added methoxide ion there is no reaction between TNB and aniline. (2) The addition of MeO$^-$K$^+$ to a TNB-aniline mixture results in the rapid formation of the methoxide complex TNB·OMe$^-$K$^+$ (S) followed by the slow formation of an equilibrium amount of the anilide complex TNB·NHPh$^-$K$^+$ (P). (3) The rate of conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ is decreased on the addition of MeO$^-$K$^+$. (4) The conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ is kinetically first order in aniline, but is not of a simple order in TNB·OMe$^-$K$^+$.

Both displacement[31] and dissociative[32] mechanisms have been proposed for the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$. These are examined here in the light of the observed features of the reaction outlined above. It is found that our kinetic data are best fitted by a dissociative mechanism involving rate-determining interconversion of free TNB and the protonated anilide complex.

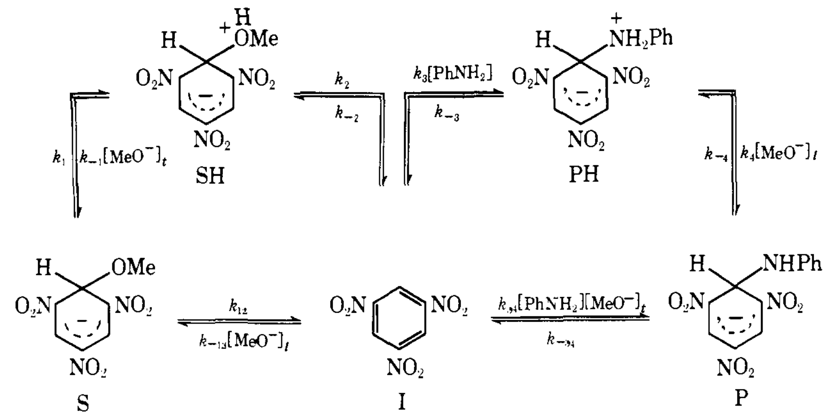
Scheme I



Displacement Mechanisms (Scheme I). Of the various possible pathways which can be formulated for the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$, probably the simplest, from the viewpoint of the number of elementary steps involved, is synchronous displacement of methoxide ion by aniline (eq 6) with subsequent (or concurrent) loss of a proton from the nitrogen of the zwitterionic species PH. This mechanism was actually proposed[31] following our initial report[23] on the formation of TNB·NHPh$^-$K$^+$ from TNB·OMe$^-$K$^+$ and aniline. Such a finding would be of considerable interest, as there appears to be no precedent for synchronous displacement at the sp^3 carbon center of a Meisenheimer type σ complex, likely as a result of hindrance to the rearward approach at the sp^3 carbon by the cyclohexadienate ring system. S$_{\text{N}}$2 displacements are, however, known to occur even in more sterically unfavorable situations.[33] In addition to the direct displacement mechanism (eq 6), one might also consider the possibility of an indirect displacement of methoxide ion by aniline, i.e., nucleophilic attack at C-3. Such a process could be termed S$_{\text{N}}$Ar2′ by analogy with the S$_{\text{N}}$2′ mechanism of allylic substitution.[34]

However, reaction by either of these mechanisms would lead to a rate law which is first order with respect to TNB·OMe$^-$K$^+$. In order to accommodate these displacement mechanisms to the observed rate law (eq 4) it would be necessary to introduce a rapid preequilibrium formation of the protonated methoxide complex SH, as is shown in eq 7 for the case of attack at C-1. However, since one would expect SH, once formed, to undergo a rapid loss of MeOH (yielding free TNB(I)), it is unlikely that the reaction in eq 7 (i.e., S → SH → PH → P) could compete effectively with the dissociative pathway S → SH → I → PH → P. Thus displacement mechanisms for the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ are found either to be inconsistent with the kinetic data (i.e., reaction as in eq 6) or to require unreasonable re-

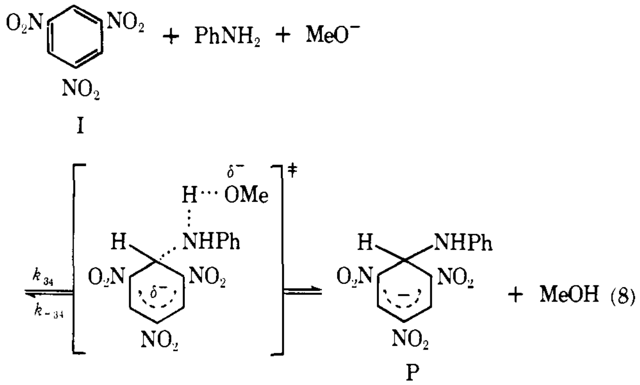
Scheme II



action characteristics (i.e. reaction as in eq 7, with SH → PH faster than SH → I → PH).

Dissociative Mechanisms (Scheme II). In Scheme II are summarized the various dissociative reaction pathways which might be invoked for the conversion of $\mathrm{TNB{\cdot}OMe^-K^+}$ to $\mathrm{TNB{\cdot}NHPh^-K^+}$ via the intermediacy of TNB.[35,36] Of the two zwitterionic species SH and PH (i.e., the protonated methoxide and anilide complexes), species such as the latter have been shown to be involved in the formation (and decomposition) of σ complexes between TNB and aliphatic amines.[17] The former species (SH) has been included in this discussion, although there is no requirement for the existence of such species in systems involving σ-complex formation between TNB and alkoxide ions in basic media[37-40] (see, however, ref 41).

Two distinct reaction pathways can be envisaged for the reaction process I ⇌ P in Scheme II. These are a concerted process, as shown in eq 8, or a stepwise process involving the



(8)

formation of anilide ion (as in Scheme III vide infra). In the present discussion, the reaction I ⇌ P will be treated kinetically according to the concerted process in eq 8.[42] Consideration will later be given to the stepwise reaction involving anilide ion.

Implicit in Scheme II are four distinguishable reaction pathways (eq 9-12), all involving the intermediacy of free TNB (I), but all differing with respect to the presence (or absence) of the zwitterionic intermediates SH and PH.

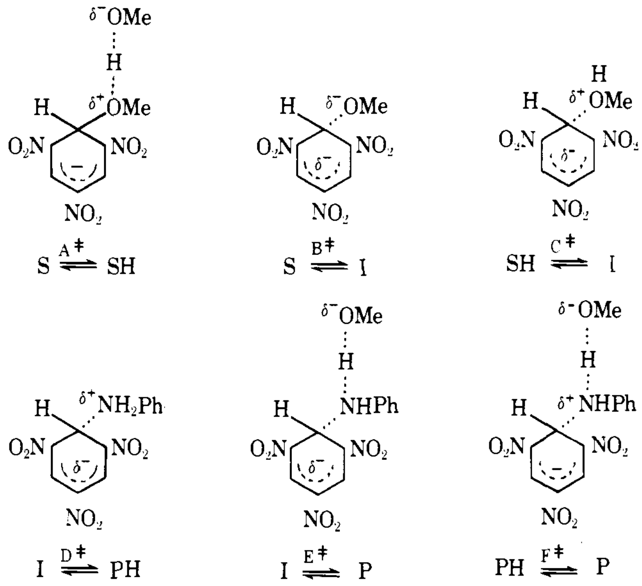
$$\mathrm{S} \underset{k_{-1}[\mathrm{MeO^-}]_t}{\overset{k_1}{\rightleftharpoons}} \mathrm{SH} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{I} \underset{k_{-3}}{\overset{k_3[\mathrm{PhNH_2}]}{\rightleftharpoons}} \mathrm{PH} \underset{k_{-4}}{\overset{k_4[\mathrm{MeO^-}]_t}{\rightleftharpoons}} \mathrm{P} \qquad (9)$$

$$\mathrm{S} \underset{k_{-12}[\mathrm{MeO^-}]_t}{\overset{k_{12}}{\rightleftharpoons}} \mathrm{I} \underset{k_{-3}}{\overset{k_3[\mathrm{PhNH_2}]}{\rightleftharpoons}} \mathrm{PH} \underset{k_{-4}}{\overset{k_4[\mathrm{MeO^-}]_t}{\rightleftharpoons}} \mathrm{P} \qquad (10)$$

$$\mathrm{S} \underset{k_{-1}[\mathrm{MeO^-}]_t}{\overset{k_1}{\rightleftharpoons}} \mathrm{SH} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{I} \underset{k_{-34}}{\overset{k_{34}[\mathrm{PhNH_2}][\mathrm{MeO^-}]_t}{\rightleftharpoons}} \mathrm{P} \qquad (11)$$

$$\mathrm{S} \underset{k_{-12}[\mathrm{MeO^-}]_t}{\overset{k_{12}}{\rightleftharpoons}} \mathrm{I} \underset{k_{-34}}{\overset{k_{34}[\mathrm{PhNH_2}][\mathrm{MeO^-}]_t}{\rightleftharpoons}} \mathrm{P} \qquad (12)$$

For each of these reaction pathways, the predicted kinetic behavior will depend on which of the constituent steps is rate determining, or alternatively on which of the activated complexes ($\mathrm{A^{\ddagger}}$ to $\mathrm{F^{\ddagger}}$) corresponds to the highest barrier in the reaction profile of that pathway.



In Figure 3 are shown the reaction profiles corresponding to the various possibilities outlined above. The profiles in Figure 3 have been arranged in rows corresponding (in descending order) to the reaction processes in eq 9-12. From left to right in each row the rate-determining step has been shifted from the reactant to the product side in each of eq 9-12. In other words, proceeding from left to right in Figure 3 the activated complex in each reaction pathway proceeds from $\mathrm{A^{\ddagger}}$ to $\mathrm{F^{\ddagger}}$.

In comparing the predicted kinetic behavior for each of the reaction profiles in Figure 3 with the actual kinetic behavior of the conversion of $\mathrm{TNB{\cdot}OMe^-K^+}$ to $\mathrm{TNB{\cdot}NHPh^-K^+}$, it is simplest to deal with the differential equation for a reversible first-order reaction.

$$-\frac{\mathrm{d}[\mathrm{S}]_t}{\mathrm{d}t} = k_{\psi_1}([\mathrm{S}]_t - [\mathrm{S}]_e]) \qquad (13)$$

For each of the profiles in Figure 3, an expression is obtained for k_{ψ_1} (defined by eq 13)[43] which can be compared with the observed behavior of k_{ψ_1} (i.e., $k_{\psi_1} = k/[\mathrm{S}]_t^{1/2}$). Such a comparison ((1) and (2) below) leads to the elimination of all but two of the reaction profiles in Figure 3.

(1) Kinetic Order with Respect to $\mathrm{TNB{\cdot}OMe^-K^+}$. As described in the Results section, the first-order rate constant k_{ψ_1}

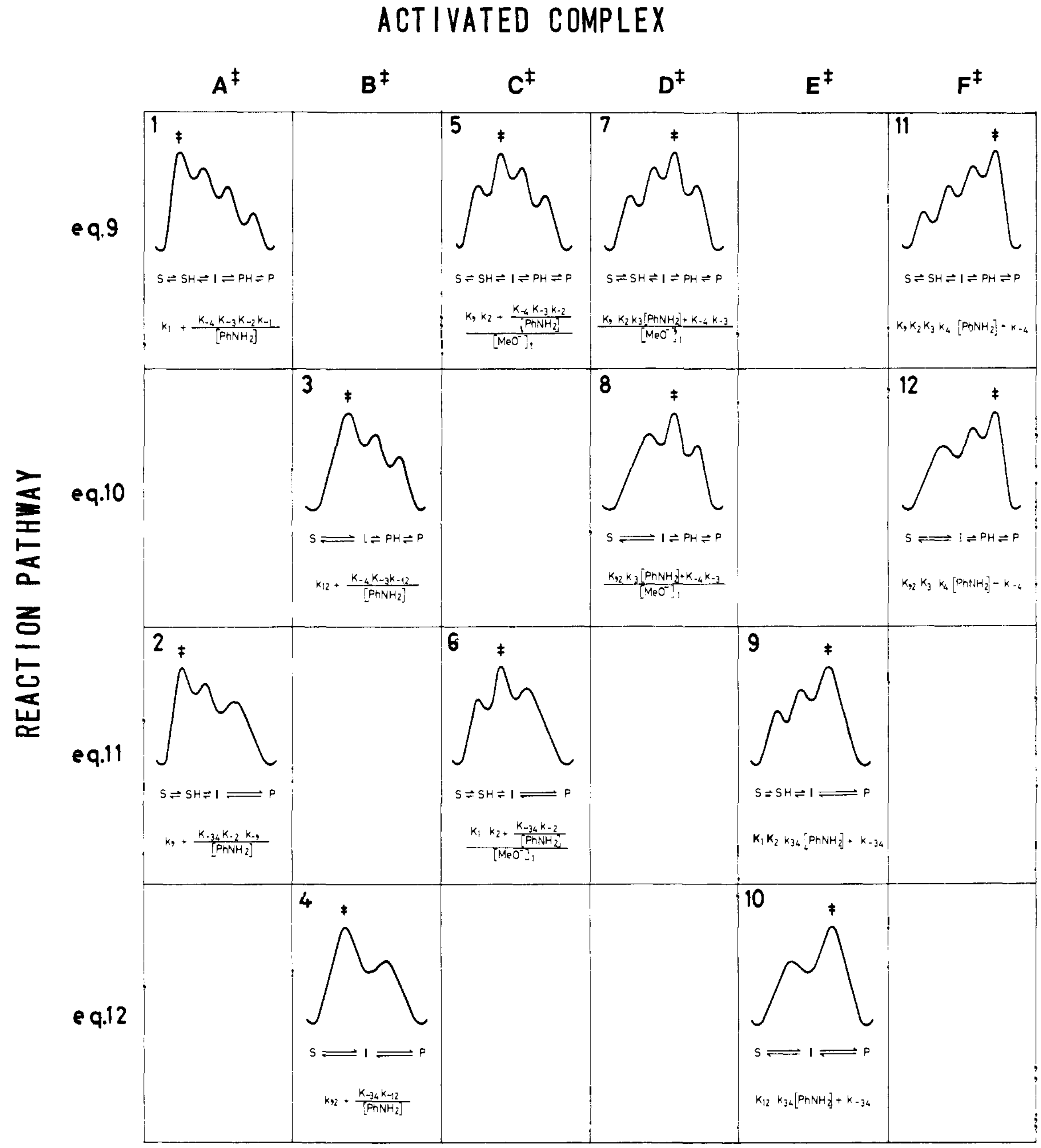


Figure 3. Reaction profiles and associated expressions for k_{ψ_1} for the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ via dissociative mechanisms.

for the approach to equilibrium in the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ exhibits inverse dependence on $[\mathrm{TNB{\cdot}OMe^-}]_t^{1/2}$. Thus, of the various reaction profiles in Figure 3, those for which k_{ψ_1} is predicted to be invariant (within a given run) are considered to be inappropriate. The only concentration terms which appear in the expressions for k_{ψ_1} are [PhNH$_2$] and $[\mathrm{MeO^-}]_t$. Of these two, [PhNH$_2$] will be constant within a given run, since aniline was always present in large excess over TNB·OMe$^-$K$^+$. However, since the reaction solutions in the present system were unbuffered, the concentration of methoxide ion (formed by the dissociation of TNB·OMe$^-$) is predicted to vary with $[\mathrm{TNB{\cdot}OMe^-}]_t$, i.e., with the extent of reaction. The predicted variations in $[\mathrm{MeO^-}]_t$ are considered in detail below. However, for the present it is seen that for eight reaction profiles (cases 1-4 and 9-12 in Figure 3) the expression for k_{ψ_1} does not contain the term $[\mathrm{MeO^-}]_t$. This group of profiles, associated with the activated complexes A‡, B‡, E‡, and F‡, can thus be eliminated.[44]

(2) Kinetic Order with Respect to Aniline and the Relative Rates of Formation of TNB·OMe$^-$K$^+$ and TNB·NHPh$^-$K$^+$ from TNB. Of the four remaining reaction profiles in Figure 3, two (cases 5 and 6) predict a decrease, with increasing [PhNH$_2$], in the rate of approach to equilibrium, which is contrary to the observed increase in rate with [PhNH$_2$] (Table IV). In addition, these two profiles (which involve the activated complex C‡) predict a rapid formation of TNB·NHPh$^-$K$^+$ from TNB, followed by a slow conversion of this complex to TNB·OMe$^-$K$^+$, when MeO$^-$K$^+$ is added to a mixture of TNB and aniline. This prediction is also contrary to the experimental behavior. *Thus only two reaction profiles (cases 7 and 8) are potentially consistent with the kinetic behavior of the reaction.*

The results of the above analysis of dissociative pathways are summarized in Table V. Of the four possible reaction pathways (eq 9-12) and the 12 associated reaction profiles (Figure 3), all but two pathways (eq 9 and 11), and all but one activated complex (D‡) have been eliminated. On consideration of the two remaining reaction pathways (cases 7 and 8 in Figure 3), it is seen that (with the possible exception of re-

Table V. Predicted Kinetic Behavior for the Formation of TNB·NHPh$^-$K$^+$ from TNB·OMe$^-$K$^+$ and Aniline via Dissociative Schemes

Assumed activated complex	Predicted form of k_{ψ_1}[a,b]	Predicted order with respect to TNB·OMe$^-$K$^+$	Predicted rate dependence on [PhNH$_2$]	Predicted relative rates of complex formation[c]
A‡ or B‡	$a + \frac{b}{[\mathrm{PhNH_2}]}$	First order	Decrease	$\mathrm{S} \xrightleftharpoons{\text{slow}} \mathrm{I} \xrightleftharpoons{\text{fast}} \mathrm{P}$
C‡	$\frac{a + \frac{b}{[\mathrm{PhNH_2}]}}{[\mathrm{MeO^-}]_t}$	Complex	Decrease	$\mathrm{S} \xrightleftharpoons{\text{slow}} \mathrm{I} \xrightleftharpoons{\text{fast}} \mathrm{P}$
D‡	$\frac{a[\mathrm{PhNH_2}] + b}{[\mathrm{MeO^-}]_t}$	Complex	Increase	$\mathrm{S} \xrightleftharpoons{\text{fast}} \mathrm{I} \xrightleftharpoons{\text{slow}} \mathrm{P}$
E‡ or F‡	$a[\mathrm{PhNH_2}] + b$	First order	Increase	$\mathrm{S} \xrightleftharpoons{\text{fast}} \mathrm{I} \xrightleftharpoons{\text{slow}} \mathrm{P}$
		Obsd behavior		
		Complex	Increase	$\mathrm{S} \xrightleftharpoons{\text{fast}} \mathrm{I} \xrightleftharpoons{\text{slow}} \mathrm{P}$

[a] k_{ψ_1} defined by $-\mathrm{d}[\mathrm{S}]_t/\mathrm{d}t = k_{\psi_1}([\mathrm{S}]_t - [\mathrm{S}]_e)$. [b] The constants a and b are various combinations (see Figure 3) of the rate and equilibrium constants in Scheme II. [c] These predictions apply to the procedure in which MeO$^-$K$^+$ is added to a mixture of TNB and aniline.

action by anilide ion considered below) the kinetic data for the reaction require the presence of the zwitterionic intermediate PH, but that the presence of SH in the reaction pathways is optional. Before analyzing these two reaction pathways in more detail, the question of the possible role of anilide ion in the reaction is considered.

A Dissociative Mechanism Involving Anilide Ion (Scheme III). In an earlier investigation it was found that TNB undergoes a rapid reaction with potassium anilide in Me$_2$SO to yield the TNB·NHPh$^-$K$^+$ σ complex.[25] Hence it is not unreasonable to consider the possibility in the present system that free TNB, formed by the dissociation of TNB·OMe$^-$, undergoes reaction with anilide ion formed in the equilibrium between aniline and free methoxide ion (Scheme III).

Scheme III

$$\mathrm{TNB \cdot OMe^-} \underset{k_{-12}}{\overset{k_{12}}{\rightleftharpoons}} \mathrm{TNB + MeO^-} \tag{14}$$

$$\mathrm{MeO^- + PhNH_2} \underset{k_{-3'}}{\overset{k_{3'}}{\rightleftharpoons}} \mathrm{MeOH + PhNH^-} \tag{15}$$

$$\mathrm{TNB + PhNH^-} \underset{k_{-4'}}{\overset{k_{4'}}{\rightleftharpoons}} \mathrm{TNB \cdot NHPh^-} \tag{16}$$

However, our present kinetic data do not appear to support such a proposal. Of the three reaction steps in Scheme III, either rate-determining dissociation of TNB·OMe$^-$ (eq 14) or rate-determining formation of TNB·NHPh$^-$ (eq 16) would result in first-order rate laws (eq 17 and 18, respectively).[45,46]

$$k_{\psi_1} = k_{12} + \frac{K_{-4'}K_{-3'}k_{-12}}{[\mathrm{PhNH_2}]} \tag{17}$$

$$k_{\psi_1} = K_{12}K_{3'}k_{4'}[\mathrm{PhNH_2}] + k_{-4'} \tag{18}$$

This leaves only the possibility of a rate-determining proton transfer in the formation of anilide ion (eq 15). In this case a complex rate law *is* obtained.

$$k_{\psi_1} = \frac{K_{12}k_{3'}[\mathrm{PhNH_2}] + K_{-4'}k_{-3'}}{[\mathrm{TNB}]_t} \tag{19}$$

Now due to the equilibrium in eq 14, the addition of MeO$^-$K$^+$ would reduce the concentration of free TNB ([TNB] = K_{12}[S]/[MeO$^-$]). Thus eq 19 predicts an increase in rate when MeO$^-$K$^+$ is added to the reaction medium, whereas the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$ was found to be retarded on the addition of MeO$^-$K$^+$.

From this analysis we consider that reaction of free TNB with anilide ion (to yield P directly) does not compete significantly in the present system with the reaction between free TNB and aniline (to form the zwitterion PH). It is not unreasonable that the present system and the TNB-potassium anilide system[25] should differ in this manner, as a result of the large difference in anilide ion concentrations in the two systems. In the previous study,[25] the stoichiometric anilide concentration was 0.4 M, whereas in the present system (with eq 15 as the only significant source of anilide ion) the anilide ion concentration can be estimated as $\sim 10^{-14}$ M.[47]

Detailed Kinetics of Scheme IV and the Relative Concentrations of the Intermediates SH, I, and PH. The elimination of reaction via anilide ion, and the earlier elimination of all but cases 7 and 8 in Figure 3, leaves the reaction pathways in eq 9 and 10 (with the step I $\rightleftharpoons$ PH rate determining) as the only viable processes for the conversion of TNB·OMe$^-$K$^+$ to TNB·NHPh$^-$K$^+$. These two reaction pathways are combined and given in full in Scheme IV.

It remains to be shown that this reaction scheme is indeed consistent with the observed kinetic behavior (i.e. the differential rate eq 4). With I $\rightleftarrows$ PH rate determining, the scheme gives the rate equation

$$-\frac{\mathrm{d}[\mathrm{S}]_t}{\mathrm{d}t} = \frac{K_{12}k_3[\mathrm{PhNH_2}] + K_{-4}k_{-3}}{[\mathrm{MeO^-}]_t}([\mathrm{S}]_t - [\mathrm{S}]_e) \tag{23}$$

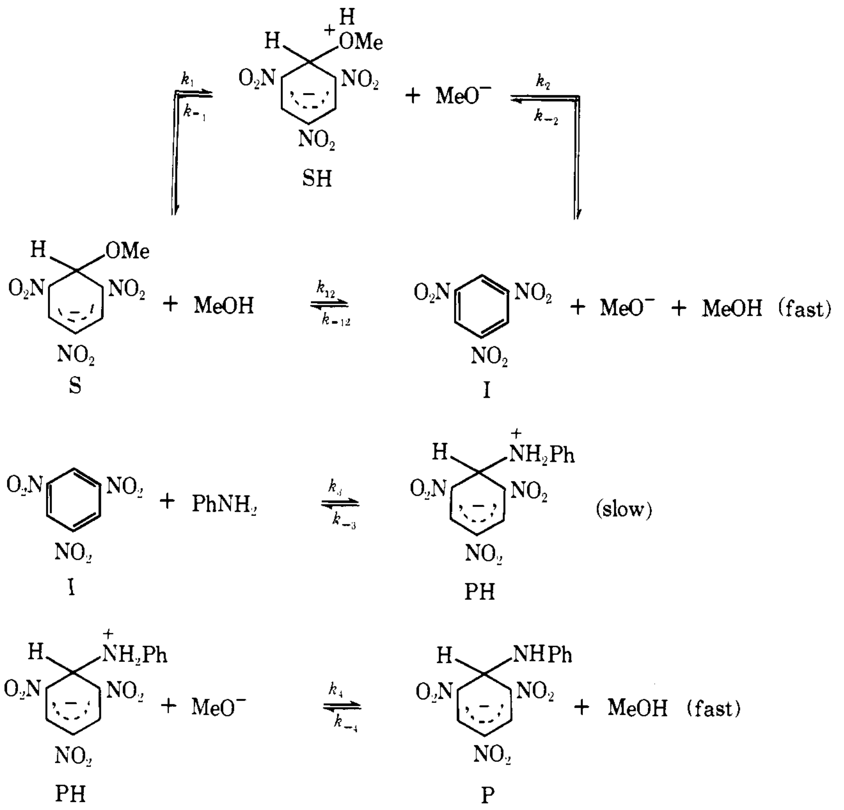
From the stoichiometry of the reaction steps, [MeO$^-$]$_t$ will be given by the sum of the concentrations of the three intermediate species SH, I, and PH. With respect to the relative concentrations of these three species, the only two kinetically distinguishable limiting cases are $[\mathrm{SH}]_t + [\mathrm{I}]_t \gg [\mathrm{PH}]_t$ and $[\mathrm{SH}]_t + [\mathrm{I}]_t \ll [\mathrm{PH}]_t$.[51] In the former case one obtains the expression $(K_1 + K_{12})^{1/2}[\mathrm{S}]_t^{1/2}$ for [MeO$^-$]$_t$, and substitution of this expression in eq 23 gives eq 24. *It is seen that eq 24 is equivalent to the observed rate law of eq 4, with the unspecified rate constant k in eq 4 being given by eq 25.* Note that eq 25 is also consistent with the observed linear increase in k_δ with [PhNH$_2$].[52]

$$-\frac{\mathrm{d}[\mathrm{S}]_t}{\mathrm{d}t} = \frac{K_{12}k_3[\mathrm{PhNH_2}] + K_{-4}k_{-3}}{(K_1 + K_{12})^{1/2}} \times \frac{([\mathrm{S}]_t - [\mathrm{S}]_e)}{[\mathrm{S}]_t^{1/2}} \tag{24}$$

$$k = k_\delta[\mathrm{S}]_e^{1/2} = \frac{K_{12}k_3[\mathrm{PhNH_2}] + K_{-4}k_{-3}}{(K_1 + K_{12})^{1/2}} \tag{25}$$

On the other hand, when one considers the other limiting case ($[\mathrm{SH}]_t + [\mathrm{I}]_t \ll [\mathrm{PH}]_t$), one obtains the expression

Scheme IV



(20)

(21)

(22)

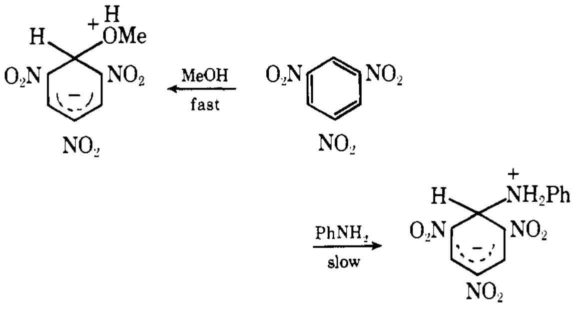
$K_{-4}^{1/2}[P]_t^{1/2}$ for $[MeO^-]_t$, and substitution of this expression in eq 23 will give the differential rate equation

$$-\frac{d[S]_t}{dt}=\frac{K_{12}k_3[PhNH_2]+K_{-4}k_{-3}}{(K_{-4})^{1/2}}\frac{([S]_t-[S]_e)}{[P_t]^{1/2}} \qquad (26)$$

which is inconsistent with the observed rate eq 4.

From the above analysis, as well as from the preceding discussions of displacement mechanisms and reactions via anilide ion, it is found that *only the dissociative mechanism in Scheme IV, with* $[SH]_t + [I]_t \gg [PH]_t$, *is in complete accord with the kinetic behavior exhibited by the conversion of TNB·OMe⁻K⁺ to TNB·NHPh⁻K⁺*. The features of this scheme which are required by our kinetic data are: (a) a rapidly established equilibrium between the TNB-methoxide complex (S) and free TNB (I); (b) a rate-determining interconversion of TNB (I) and the protonated anilide complex (PH); and (c) a rapidly established equilibrium between the protonated (PH) and unprotonated (P) anilide complexes. Thus, of the three possible intermediates initially proposed in Scheme II, only the protonated methoxide complex (SH) is not required by our data.

Reaction via SH has been included to this point in the discussion because our kinetic data do not rigorously exclude it. However, arguments can be presented which virtually eliminate it. It has been shown that our kinetic data require the condition [SH] + [I] ≫ [PH]. On the basis of the expected relative basicities of P and S, the conditions [PH] ≫ [SH] and hence [I] ≫ [PH] ≫ [SH] must apply. In fact, the high energy requirement for [SH] in our basic medium makes it extremely unlikely that it could be on the reaction pathway without its formation being rate determining. A similar argument against the presence of SH on the reaction pathway is provided by the result of the experiment using TNB, $PhNH_2$, and MeO⁻K⁺ as the reactants. If SH is an intermediate in the reaction pathway, then our data require the relative rates shown in eq 27. However, since aniline is a far more basic species than methanol, then to the extent that the rates of formation of σ complexes follow the basicity of the nucleophilic species, eq 27 is a totally unreasonable result for the relative reactivities of methanol and of aniline towards TNB. Thus it is considered



(27)

that of the two processes shown in Scheme IV for the interconversion of S and I, the one not involving the zwitterionic intermediate SH (i.e., the k_{12} route) predominates in the interconversion of TNB·OMe⁻K⁺ and TNB·NHPh⁻K⁺.

Concluding Remarks

As a summary of the preceding discussion, we have found that our kinetic data require the presence of TNB and aniline, but the absence of methoxide ion, in the activated complex for the conversion of TNB·OMe⁻K⁺ to TNB·NHPh⁻K⁺, and that there is no reasonable alternative to Scheme IV which meets these requirements.

Scheme IV can be considered to consist of two reaction stages, the first stage being the interconversion of the TNB·OMe⁻K⁺ complex and free TNB, and the second stage being the interconversion of free TNB and the TNB·NHPh⁻K⁺ complex. Our conclusion that the protonated methoxide complex SH is not involved in the first stage of the reaction is in accord with previous kinetic studies of σ-complex formation between nitroaromatics and oxygen bases in basic media,[37-40,53,54] and is also in accord with Jencks' work.[55] Our study gives no information as to the role of methanol in the dissociation of TNB·OMe⁻K⁺, i.e., whether or not it acts as a general acid.[40] Our findings with respect to the second stage of the reaction (viz., the initial formation of the zwitterionic species PH, which is subsequently deprotonated) suggest that in sufficiently basic media the formation of σ complexes from aromatic amines should follow closely the normal mechanism observed with the more strongly basic primary and secondary amines.[16-18,56-58] In this context it is worth noting that the *inverse* dependence of rate on base concentration (i.e., on [MeO$^-$]) in the present system is not a manifestation of some unusual property of the mechanism of formation of TNB·NHPh$^-$K$^+$. Rather, it is simply a consequence of the two factors: (1) that one complex (TNB·OMe$^-$K$^+$) is being converted into another (TNB·NHPh$^-$K$^+$); and (2) that base catalysis of the formation of TNB·NHPh$^-$K$^+$ from TNB occurs *after* the rate-determining step (in the forward direction).

The absence of σ-complex formation between nitroaromatics and aromatic amines has been well documented.[20,23] This contrast with the behavior of aliphatic amines is generally considered to be due to the different basicities of the two classes of amines. The results of the present study are in accord with this conclusion, and in addition indicate that the unreactivity of aromatic amines toward nitroaromatics is the result of a thermodynamic, rather than kinetic, factor. Considering the TNB-aniline system in the absence of a strong base, the failure to obtain the reaction in the equation

$$\mathrm{TNB} + 2\mathrm{RNH_2} \rightleftarrows \mathrm{TNB{\cdot}NH_2R^{\pm}} + \mathrm{RNH_2} \rightleftarrows \mathrm{TNB{\cdot}NHR^-} + \mathrm{RNH_3^+} \quad (28)$$

(with R = Ph) cannot be attributed to a slow rate of proton transfer in the second step.[59-61] Furthermore, the possibility that the first step of the reaction might be slow (as a result of the low basicity of aniline) can be discounted, since the reaction of the present study, which proceeds at a reasonable rate, has been shown to involve this step (Scheme IV). Thus the absence of reaction according to eq 28 cannot be due to a kinetic factor, but rather *must result from an unfavorable overall equilibrium, in contrast with the case for aliphatic amines, where a favorable overall equilibrium is generally observed.*

We have previously reported the formation of the TNB·NHPh$^-$K$^+$ σ complex from TNB and aniline in the presence of the added bases triethylamine or 1,4-diazabicyclo[2.2.2]octane (DABCO).[62] From consideration of Scheme IV and the above discussion, it is apparent that the tertiary amine takes the function of the methoxide ion in eq 22. It is expected that the more weakly basic tertiary amine will lead to a decrease in the k_4 term as compared to the present system. With the k_{-3} term being unaffected by the change in base, it is possible that the proton-transfer step (eq 22) may be made to be rate determining. This possibility is currently under investigation.[63]

Experimental Section

TNB, aniline, and Me$_2$SO were purified as described previously.[25] Anhydrous methanol was obtained by distillation from magnesium metal. Tetraethylammonium perchlorate (Eastman) was dried in vacuo at 60 °C. The preparation of TNB·OMe$^-$K$^+$ has been given.[25] The Me$_2$SO-methanol stock solvent was prepared by weight. Transfer of solutions and other manipulations were performed, when possible, in a drybox under nitrogen.

Rate measurements were performed on a Unicam SP800 spectrophotometer equipped with a scale expansion accessory and an external recorder. Cuvettes, varying in size between 0.1 and 1 mm, were placed in the thermostated block of the spectrophotometer and the temperature in the cells was measured by means of a thermocouple.

Reaction was initiated by adding a thermostated solution of TNB·OMe$^-$K$^+$ in Me$_2$SO-methanol, using a syringe and flasks fitted with silicone rubber serum caps, to the Me$_2$SO-methanol solution of aniline and tetraethylammonium perchlorate contained in a 10-mL volumetric flask. After mixing, an aliquot of the reaction solution was removed by syringe and placed into the cuvette, which was also fitted with a silicone rubber plug. The progress of the reaction was monitored by recording spectral scans as a function of time over the region 375–600 mm.

Runs evaluating the effect of added potassium methoxide on the rate of reaction of TNB·OMe$^-$K$^+$ with aniline were initiated by adding the MeOK/TNB·OMe$^-$K$^+$ solution in Me$_2$SO-MeOH to the solution of PhNH$_2$/Et$_4$NClO$_4$ in Me$_2$SO-MeOH. The experiment in which TNB was the substrate (rather than TNB·OMe$^-$K$^+$) was performed by adding the TNB solution in Me$_2$SO-MeOH to the MeOK/PhNH$_2$/Et$_4$NClO$_4$ solution in Me$_2$SO-MeOH; the final concentrations were [TNB] $\approx$ [MeOK] $\approx 4 \times 10^{-4}$ M (with TNB in excess by 5%), [PhNH$_2$] $\approx$ [Et$_4$NClO$_4$] $\approx$ 0.1 M. In all the kinetic runs the aniline was present in large excess (40–500-fold) over the TNB·OMe$^-$K$^+$.

Acknowledgment. We thank the National Research Council of Canada for financial support of this research.

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(35) Implicit in Scheme II are the assumptions that methanol is the only effective protonating species (e.g., the rate constant k_1 represents protonation of S by methanol) and that methoxide ion is the only effective deprotonating species, in the present reaction system. The rate constants for the conversion of S to SH, S to I, P to PH, and P to I could, in principle, include additional contributions due to H$^+$ (solvated) and PhNH$_3^+$. However, the contributions due to such terms are considered to be negligible under the basic conditions of this study. Similarly, for the reversal of the above reaction steps, contributions by the weak bases MeOH and PhNH$_2$ are considered to be negligible with respect to that by the strongly basic methoxide ion.
(36) The following identities hold for the rate and equilibrium constants in each of the reaction steps in Scheme II (the concentration terms refer to the equilibrium condition): S + MeOH $\rightleftharpoons$ SH + MeO$^-$, [SH][MeO$^-$]/[S] = $K_1 = k_1/k_{-1}$; SH $\rightleftharpoons$ I + MeOH, [I]/[S] = $K_2 = k_2/k_{-2}$; S $\rightleftharpoons$ I + MeO$^-$, [I][MeO$^-$]/[S] = $K_{12} = k_{12}/k_{-12}$; I + PhNH$_2$ $\rightleftharpoons$ PH, [PH]/[I][PhNH$_2$] = $K_3 = k_3/k_{-3}$; PH + MeO$^-$ $\rightleftharpoons$ P + MeOH, [P]/[PH][MeO$^-$] = $K_4 = k_4/k_{-4}$; I + PhNH$_2$ + MeO$^-$ $\rightleftharpoons$ P + MeOH, [P]/[I][PhNH$_2$][MeO$^-$] = $K_{34} = k_{34}/k_{-34}$. Additional identities are $K_{12} = K_1K_2$, $K_{34} = K_3K_4$ and K_{app} = [P]/[S][PhNH$_2$] = $K_1K_2K_3K_4$. Also, equilibrium constants for the re-

verse processes are designated $K_{-1} = 1/K_1$, etc. It should be noted that the rate constants k_1, k_{12}, k_2, k_{-2}, k_{-3}, k_{-34}, and k_{-4} are all first-order rate constants i.e., in those reaction steps in which methanol is involved, [MeOH] (~1 M in 90:10 mol % Me_2SO-methanol) does not appear in the rate equations which define the rate constants. This treatment leads to the relationships between rate and equilibrium constants as described above.

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(42) The concerted process in eq 8 and the stepwise process in eq 15 and 16 (Scheme III) are kinetically indistinguishable if the equilibrium in eq 15 is rapidly established relative to that in eq 16, but give rise to different kinetic forms if the proton transfer in eq 15 is a relatively slow process.

(43) The rate equations have been derived on the assumption of a single rate-determining step in each case. Analysis of the equations based on the steady-state assumption (for SH, I, or PH) ultimately leads to the same conclusions as those described in the text. Since the intermediates SH, I, and PH are not present in detectable quantities, the conditions $[S] \gg [SH] + [I] + [PH]$ and $[P] \gg [SH] + [I] + [PH]$ have also been used in deriving the equations.

(44) A simple relationship is evident between the predicted kinetic behavior and the species involved in the activated complex of the rate-determining step. Since non-first-order behavior derives in this system from the dissociation of $TNB{\cdot}OMe^-$ into TNB and MeO^-, then those reaction pathways for which the activation process involves recombination of TNB and MeO^- will be kinetically first order. This recombination occurs in $A^{\ddagger}$, $B^{\ddagger}$, $E^{\ddagger}$, and $F^{\ddagger}$, but not in $C^{\ddagger}$ and $D^{\ddagger}$.

(45) The rate and equilibrium constants in Scheme III have been defined in the same manner as in Scheme II. Thus, $K_{-4'} = 1/K_{4'} = [I][PhNH^-]/[TNB{\cdot}NHPh^-] = k_{-4'}/k_{4'}$. Also, $[PhNH^-]/[MeO^-][PhNH_2] = K_{3'} = k_{3'}/k_{-3'} = 1/K_{-3'}$ and $k_{-3'}$ is by definition a first-order rate constant.

(46) That the expressions for k_{ψ_1} in eq 17 and 18 must be similar to those in cases 3 and 12 (Figure 3), respectively, can be seen by comparing the activated complexes for the processes in eq 14 and 16 with the activated complexes $B^{\ddagger}$ and $F^{\ddagger}$, respectively.

(47) The estimated value is based on $K_{3'} \sim 6.3 \times 10^{-8}\ M^{-1}$ and $K_{12} \sim 10^{-8}$ M (which gives $[MeO^-] \sim 2 \times 10^{-6}$ M at $[TNB{\cdot}OMe^-K^+]_0 = 4 \times 10^{-4}$ M). The K_3' value is obtained by combining the H_- value[48] of 18.5 in 90:10 mol % Me_2SO–methanol containing 2.5×10^{-2} M CH_3ONa with the pK_a value[49] of 27.3 for aniline. The K_{12} value is obtained by extrapolation of the results in ref 50.

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(51) Since the position of the equilibrium between SH and I does not affect the methoxide ion concentration ($[I]_t/[SH]_t = K_2$), the further cases arising from $[SH]_t \gg [I]_t$ and $[SH]_t \ll [I]_t$ are not kinetically significant.

(52) According to eq 25, an estimate of the equilibrium constant K_{app} for the conversion of $TNB{\cdot}OMe^-K^+$ to $TNB\text{-}NHPh^-K^+$ can be made using the values obtained for the slope and the intercept of the plot of $k_\delta[S]_e^{1/2}$ vs. $[PhNH_2]$: the ratio slope/intercept $= K_{12}K_3K_4 = K_{app}$. Although a linear plot is in fact obtained, unfortunately the small magnitude of the intercept value obtained in the plot leads to considerable uncertainty in such a procedure. The value obtained for K_{app} was 86 M^{-1} as compared to the measured value 23.2 M^{-1}.

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Intramolecular Nondissociative Proton Transfer in Aqueous Solutions of Tautomeric Heterocycles: a Temperature-Jump Kinetic Study

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Abstract: The mechanism of tautomeric interconversion in some substituted pyridines, pyrimidines, and imidazoles in aqueous solution is investigated using the T-jump relaxation technique. It is found that when the tautomeric functional groups are remote, tautomeric interconversion occurs through intermediate ionization and dissociation followed by ion recombination. However, when these functional groups get close enough, such as in tautomeric α-substituted pyridines, a direct proton-transfer mechanism not involving intermediate ionic dissociation contributes efficiently to the interconversion rate. The contribution of this process is examined in terms of the nature and geometry of the tautomeric functional groups. Biological implications are discussed.

In aqueous solutions, proton transfers between an acidic -OH or -$^+$NH group and a basic -O$^-$ or -N group belonging to two independent molecules have been extensively studied[2] and shown[3,4] to be diffusion controlled when thermodynamically favorable. For "carbon" acids and bases such processes are usually much slower, whereas acids and bases involving a sulfur atom behave intermediately in this respect.

By contrast, little is known about the proton-transfer rate when the transfer occurs between two nitrogen atoms or between two oxygen atoms or between a nitrogen and an oxygen atom within the same molecule. In previous papers,[5,6] we used the temperature-jump relaxation method to investigate the mechanism of the tautomeric interconversion of some heterocycles such as the imidazole cycle of adenine,[5] and the pyrimidine cycles of cytosine[6] and 3-methylcytosine.[6] In these cases the tautomeric interconversion proceeds through intermediate ionization to the anionic or cationic form of the substrate, followed by neutralization, with the thermodynamically favorable acid-base reactions being diffusion controlled or nearly so: in any case, no direct or nondissociative proton-transfer mechanism was detected.

On the other hand, fluorescence data on the salicylate anion[7] indicate that the interconversion between the phenolate and the carboxylate forms of the molecule is far too fast to be interpreted by such a model, thereby suggesting that the exchanging proton can jump from one site to another without intermediate dissociation. Furthermore, Grunwald, Meiboom, et al.,[8] from NMR line bandwidth studies of acetic and benzoic