Intermediates in Nucleophilic Aromatic Substitution. II.[1] Temperature-Jump Study of the Interaction of 1,3,5-Trinitrobenzene with Aliphatic Amines in 10% Dioxane–90% Water. Concurrent Nucleophilic Attack on the Aromatic Carbon and on the Nitro Group?[2]

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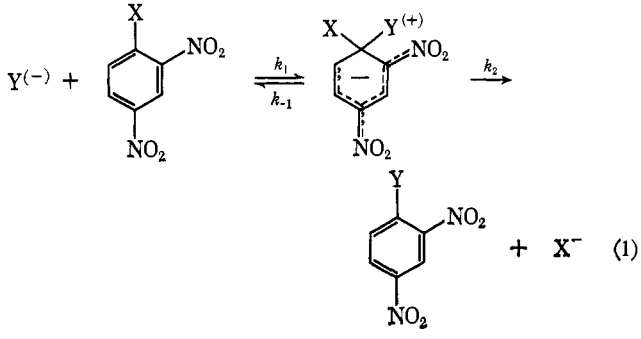
Abstract: Solutions of 1,3,5-trinitrobenzene and *n*-butylamine, piperidine, or pyrrolidine in 10% dioxane–90% water are characterized by three relaxation times. It is shown that τ_1 arises from Meisenheimer complex formation (XH and X^-) between 1,3,5-trinitrobenzene and the amine, τ_2 most probably from an oxyhydroxylamine (YH and Y^-), and τ_3 from a Meisenheimer complex formation (Z^-) between 1,3,5-trinitrobenzene and the hydroxide ion. Various rate coefficients and equilibrium constants involving the different complexes are evaluated. The relative rates of formation of a Meisenheimer complex by the three amines conform to the familiar reactivity pattern in nucleophilic aromatic substitution reactions by these amines. The rates of Meisenheimer complex decomposition are practically the same for the three amines; intramolecular hydrogen bonding to one or both *o*-nitro groups is believed to be mainly responsible for this result. The pK values of the Meisenheimer complexes formed by piperidine and pyrrolidine are very close to the pK of the respective amine; in the case of *n*-butylamine the pK of the complex is significantly lower. The general reactivity pattern in the oxyhydroxylamine series is similar to the one in the Meisenheimer complex series and is interpreted along similar lines. The various rate and equilibrium constants vary with amine and amine hydrochloride concentration and depend also on whether the compensating electrolyte is NaCl or $(CH_3)_4NCl$.

Conventional kinetic studies have provided us with considerable insight into the general mechanism of activated nucleophilic aromatic substitution reactions.[3] The main feature is that the nucleophile attacks the aromatic substrate—generally activated by one or several nitro or other electron-withdrawing groups—to form a high-energy intermediate, often referred to as a Meisenheimer complex, which can either proceed to products in a second step or revert to reactants, as illustrated in eq 1.



(1)

As far as reactivities are concerned, the amount of information which can be derived from conventional kinetic studies is limited. When the nucleophile is an anion, k_1 is the only rate coefficient of the three elementary steps which may be determined separately provided that $k_2 \gg k_{-1}$, a condition which has to be inferred indirectly.[4,5] When the nucleophile is a primary or secondary amine, it is sometimes possible to determine also the ratios k_2/k_{-1} and k_3^B/k_{-1}, provided that $k_2/k_{-1} < 1$;[6] k_3^B refers to the base-catalyzed decomposition of the intermediate to products. But k_{-1} and k_2 (k_3^B) can never be determined separately by following over-all steady-state kinetics.

The knowledge of these individual rate coefficients would not only give us a much more detailed picture of the whole reaction path and its energy profile, but it is also of considerable interest with respect to the general problems of (a) the stability of Meisenheimer complexes[1,3e,7-9] and (b) the reactivities of leaving groups from aromatic compounds, a field in which no systematic studies have been carried out to date.

In this paper we report a temperature-jump[10] study of the reversible formation of the Meisenheimer complexes, henceforth abbreviated MC, arising from the attack of *n*-butylamine, piperidine, and pyrrolidine on the 2 position of 1, 3, 5-trinitrobenzene, in 10% dioxane–90% water solution. Addition of 10% dioxane to the aqueous solution was necessary in order to increase the solubility of 1, 3, 5-trinitrobenzene, hence-

(1) Part I: C. F. Bernasconi, *J. Amer. Chem. Soc.*, 90, 4982 (1968).

(2) This investigation has been supported in part by Public Health Service Research Grant GM 14647 from the National Institute of General Medical Sciences.

(3) For reviews on the subject, see (a) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 49, 273 (1951); (b) J. F. Bunnett, *Quart. Rev.* (London), 12, 1 (1958); (c) J. Sauer and R. Huisgen, *Angew. Chem.*, 72, 294 (1960); (d) S. D. Ross, *Progr. Phys. Org. Chem.*, 1, 31 (1963); (e) E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev.* (London), 22, 123 (1968).

(4) J. F. Bunnett, E. W. Garbisch, and K. M. Pruitt, *J. Amer. Chem. Soc.*, 79, 384 (1957).

(5) C. F. Bernasconi and P. Schmid, *J. Org. Chem.*, 32, 2953 (1967).

(6) (a) J. F. Bunnett and J. J. Randall, *J. Amer. Chem. Soc.*, 80, 6020 (1958); (b) J. F. Bunnett and R. H. Garst, *ibid.*, 87, 3897 (1965); (c) J. F. Bunnett and C. F. Bernasconi, *ibid.*, 87, 5209 (1965); (d) C. F. Bernasconi, *J. Org. Chem.*, 32, 2947 (1967); (e) C. F. Bernasconi and P. Schmid, *ibid.*, 32, 2953 (1967); (f) A. J. Kirby and W. P. Jencks, *J. Amer. Chem. Soc.*, 87, 3217 (1965); (g) C. F. Bernasconi and H. Zollinger, *Helv. Chim. Acta*, 50, 3 (1967); (h) F. Pietra and D. Vitali, *J. Chem. Soc., B*, 1200 (1968).

(7) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, 16, 61 (1966).

(8) J. Miller, *J. Amer. Chem. Soc.*, 85, 1628 (1963).

(9) D. L. Hill, K. C. Ho, and J. Miller, *J. Chem. Soc., B*, 299 (1966).

(10) M. Eigen and L. DeMaeyer in "Technique of Organic Chemistry," Vol. VIII, Part 2, Interscience Publishers, New York, N. Y., 1963, p 895.

Table I. Solvent Dependence of τ_1 and τ_2 in the Piperidine–TNB System

Solvent	[Pip], M	[NaOH], M	$10^3 \times$ [TNB]$_0$ M	[NaCl], M	pH[a]	τ_1^{-1}, sec^{-1}	τ_2^{-1}, sec^{-1}
1% dioxane	0.05	0.05	0.25	0.45	12.46	836 ± 50	44.6 ± 2.5
1% dioxane	0.10	0.05	0.25	0.45	12.46	912 ± 60	55.1 ± 2.7
1% dioxane	0.15	0.05	0.25	0.45	12.46	980 ± 80	58.5 ± 3.0
1% dioxane	0.20	0.05	0.25	0.45	12.46	1072 ± 90	63.2 ± 3.5
20% dioxane	0.02	0.025	0.20	0.475	12.57	218 ± 15	
20% dioxane	0.05	0.025	0.16	0.475	12.57	314 ± 20	49.2 ± 3.5
20% dioxane	0.10	0.025	0.16	0.475	12.57	520 ± 40	46.6 ± 4.0
20% dioxane	0.15	0.025	0.12	0.475	12.57		49.9 ± 4.5

[a] Adjusted to the desired value by addition of a few drops of 5 *M* NaOH or 5 *M* HCl solution.

forth abbreviated TNB. TNB was chosen mainly for two reasons: (a) it is known to form relatively stable, though not too stable, MCs with a large group of nucleophiles; this allows the study of reactivity in an extended series.[11] (b) It has no displaceable leaving group;[12] hence the complexity of the kinetic schemes is reduced and thus the interpretation of the relaxation spectra facilitated.

In the course of this investigation it was found that the interaction of TNB with aliphatic amines produces another species which was not expected when this study was started. Thus considerable attention is devoted to the question of what this new species is.

Experimental Section

Materials. 1,3,5-Trinitrobenzene (Eastman White Label) was recrystallized twice from ethanol, mp 123°. *n*-Butylamine, piperidine, and pyrrolidine were refluxed over sodium for 8 hr and distilled. Middle fractions were taken and stored in the dark. It was found necessary to distill and store the pyrrolidine under nitrogen in order to avoid oxidation.[13] 1,4-Dioxane was purified by the method of Fieser[14] and was stored over lithium aluminum hydride, from which it was distilled as needed. Tetramethylammonium chloride (Matheson Coleman and Bell) was titrated potentiometrically with silver nitrate for determination of the concentration of stock solutions.

Measurement of Relaxation Times. Reaction solutions were prepared in volumetric flasks by combination of appropriate volumes of standard stock solutions of the several ingredients such as TNB, amine, hydrochloric acid, sodium chloride,t etramethylammonium chloride, sodium hydroxide, and dioxane. The pH value of each solution was determined by means of a Corning Model 12 pH meter at 25°. By adding a few drops of concentrated HCl or NaOH the pH could easily be adjusted to a value which was very close (±0.02 pH units) to the desired one, without significantly altering the concentration of the other ingredients through dilution. Through extrapolation the relaxation time was then adjusted to the desired pH value if necessary.

It is realized that the pH so measured in a medium which is not 100% aqueous gives not a strictly correct value for the hydrogen ion concentration. Nevertheless, due to the fairly low dioxane content, no great error is likely to be introduced by equating pH with $-\log [H^+]$, which was the basis of calculating apparent acid dissociation constants.

The relaxation times were measured with a temperature-jump transient spectrometer from Messanlagen Studiengesellschaft, Göttingen, Germany. The solutions were subjected to temperature jumps of 1 to 2°; the temperature of the preequilibrated solutions was chosen such as to be 25° after a jump. Relaxation curves were recorded at wavelengths beween 390 and 550 mμ; a wavelength for the determination of a particular relaxation time in a particular solution was chosen where the signal-to-noise ratio was high and the interference by adjacent relaxation curves was minimal. The relaxation times were calculated as the average value from 4 to 6 relaxation curves, generated from the same or often from two separately prepared solutions on different days. Due to the decomposition of TNB, especially at high aminehydrochloride concentrations, the *amplitudes* of the relaxation processes diminished with time, making it often impossible to determine all three relaxation times in the same solution. This slow decomposition did not have any effect on the relaxation *times* however, because these latter do not depend on the TNB concentration under the conditions used throughout, *i.e.* with a large excess of amine over TNB.

As seen below, the estimated error associated with each relaxation time varies from ±4% to ±11%. Several factors contribute to the experimental uncertainty, but not all are equally important under various conditions. Apart from errors in concentrations, including in particular the pH value, which may account for uncertainties in the range of ±1.5%–2.5%, there are essentially 3 sources of error: (1) temperature fluctuations in the cell and variation in jump height account for ±2.5%–3.0% error. This has to be taken into account for all relaxation times. (2) The signal-to-noise ratio. which becomes low (a) at very short times; (b) at amine concentrations, where complex formation is nearly complete; and (c) under conditions where decomposition of TNB is fairly rapid reducing the amplitude appreciably from the very beginning. (3) Though relaxation times are separated from each other by a factor of 10 or more in most cases, there was some influence by slower relaxation processes on relaxation curves with faster times. This effect was corrected for by a graphical procedure, but where interference between two relaxation curves was strong due to a high amplitude of the slower relative to the faster, some additional uncertainty may have been introduced in the values of various relaxation times.

Results

Relaxation Times.[15] Upon mixing of TNB with *n*-butylamine, piperidine, or pyrrolidine in 10% dioxane–90% water, there is an immediate red color formation which is characteristic for the interaction of bases with nitroaromatics.[3e] Chemical relaxational behavior of such solutions was studied by the temperature-jump method in the spectral region of 390–550 mμ, as a function of amine concentration and of pH at 25°. In a typical set of runs, the total concentration of an amine–aminehydrochloride buffer of constant buffer ratio was varied. The concentration of TNB was always much smaller than the amine concentration, so that pseudo-first-order conditions prevailed throughout. Several sets of buffer ratios were chosen for studying the pH dependence as well. The ionic strength was kept constant at 0.5 *M* in all runs by adding appropriate amounts of sodium chloride or tetramethylammonium chloride.

(11) Work on the interaction of TNB with several other nucleophiles is currently in progress at this laboratory.

(12) The formation of an isomeric MC through nucleophilic attack on 1 position would allow displacement of a nitrite ion in a subsequent step; this possibility will be extensively considered in the Discussion.

(13) I am indebted to Dr. Doris Hermann for carrying out the purification of pyrrolidine.

(14) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 284.

(15) Material supplementary to this article in the form of tables listing relaxation times in function of the experimental variables has been deposited as Document No. NAPS-00604 with the ASIS National Auxiliary Publication Service, c/o CCM Information Service Inc., 22 West 34th St., New York, N. Y. 10001. A copy may be secured by citing the document number and by remitting $1.00 for microfiche or $3.00 for photocopies. Advance payment is required. Make checks or money orders payable to: ASIS-NAPS.

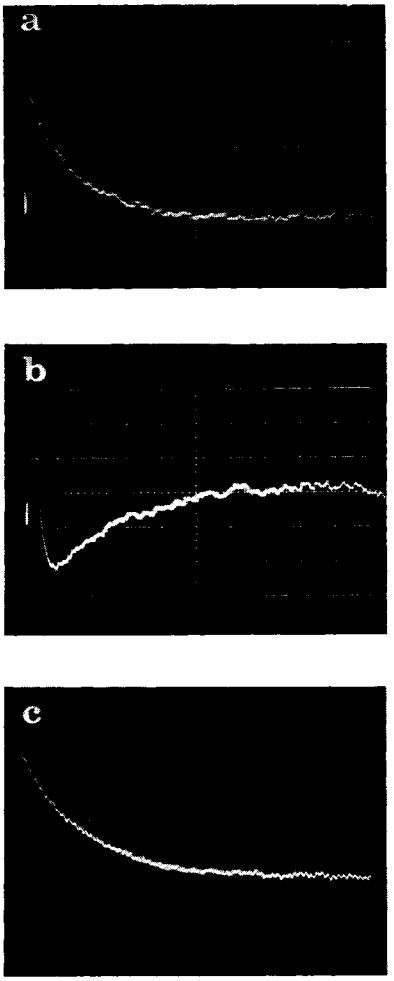


Figure 1. Representative oscilloscope traces of the piperidine–TNB system, at λ 407 mμ: a–c, [Pip] = 0.09 *M*, $[TNB]_0 = 5 \times 10^{-4}$ *M*, pH 11.95; a, τ_1, 0.5 msec/horiz division; b, τ_2, 5 msec/horiz division; c, τ_3, 100 msec/horiz division.

Within the ranges of amine concentrations and of pH indicated in Figures 1–10 below, each amine–TNB system is characterized by three relaxation times, which henceforth will be designated by τ_1, τ_2, and τ_3. τ_1 is the fastest process in all three systems, under all conditions. In the piperidine and pyrrolidine systems, τ_2 is always the second fastest and τ_3 the slowest; in the *n*-butylamine system τ_2 becomes slower than τ_3 under certain conditions. Figure 1a–c shows typical oscilloscope traces of τ_1, τ_2, and τ_3 for the piperidine–TNB system under a representative set of conditions. Under the experimental conditions chosen the amplitudes (percentage change in optical density) of the three relaxational processes are of comparable magnitude. This is not generally the case. At low pH and/or high amine concentration, the amplitude of τ_3 becomes very small and eventually nondetectable, so that τ_3 could only be studied in a limited range of conditions. τ_1 is observable under the broadest range of conditions, whereas τ_2 has a large amplitude mainly at high pH values and relatively high amine concentrations.

τ_1 and τ_2 are both strongly dependent on the pH and, except for τ_1 in the butylamine system, on the amine concentration. τ_3 depends only on the pH but not on the amine concentration in any of the three systems. As a matter of fact, τ_3 is present also in the absence of amine.

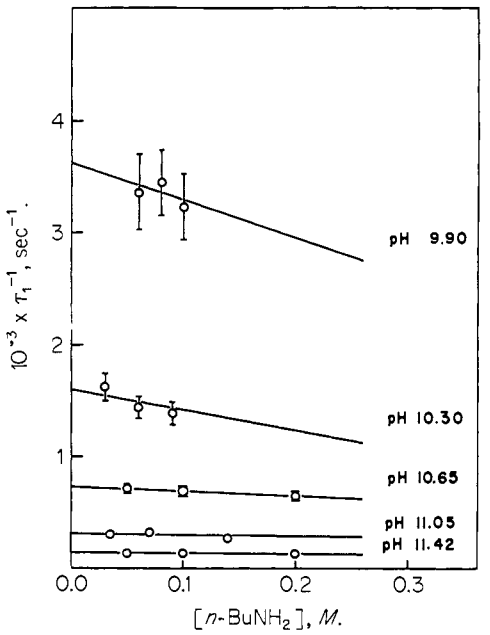


Figure 2. System *n*-butylamine–TNB with NaCl; τ_1^{-1} as function of amine concentration and pH.

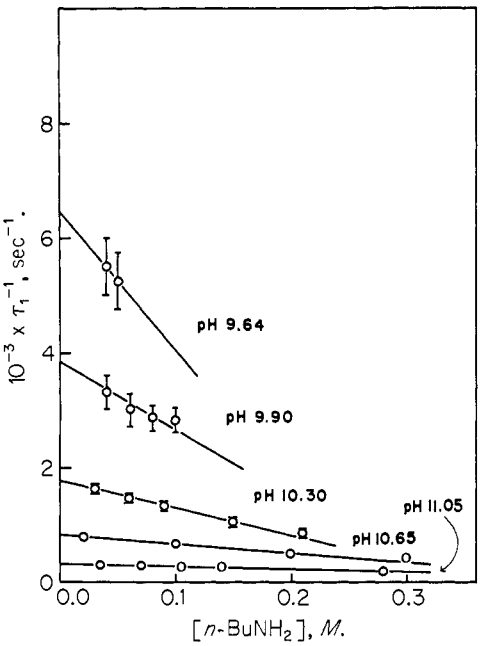


Figure 3. System *n*-butylamine–TNB with $(CH_3)_4NCl$. τ_1^{-1} as function of amine concentration and pH.

Figures 2–5 and 6–8 show plots of τ_1^{-1} and τ_2^{-1} *vs.* the amine concentration at different pH values.

Though no systematic investigation on the solvent dependence of the various kinetic parameters was attempted in this study, a few relaxation times were measured in 1% dioxane–99% water, in 20% dioxane–80% water, and in 50% dioxane–50% water mixtures for the piperidine–TNB system. This gave us some valuable preliminary information as to how the different processes involved are influenced by a change in solvent and helped a great deal in assigning the second relaxation time (see Discussion). These data are summarized in Table I. Figures 9 and 10 show plots of τ_1^{-1} and τ_2^{-1},

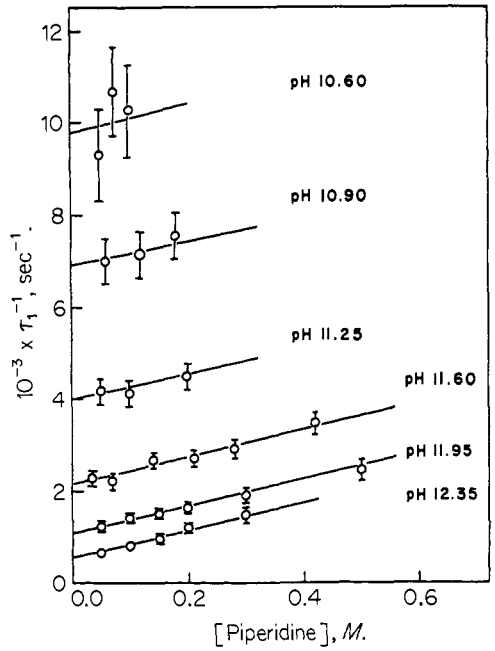


Figure 4. System piperidine–TNB with NaCl. τ_1^{-1} as function of amine concentration and pH.

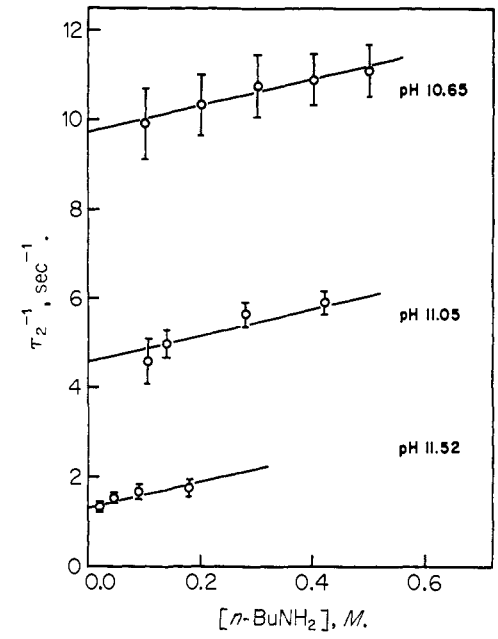


Figure 6. System *n*-butylamine–TNB with $(CH_3)_4NCl$. τ_2^{-1} as a function of amine concentration and pH.

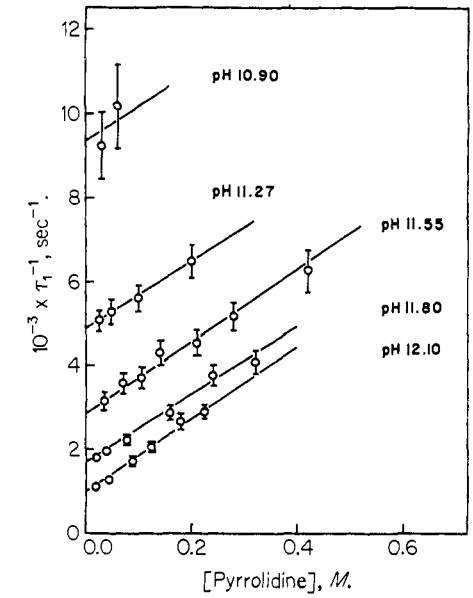


Figure 5. System pyrrolidine–TNB with NaCl. τ_1^{-1} as function of amine concentration and pH.

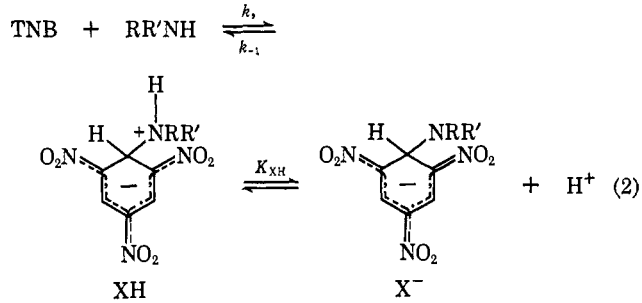
respectively, as a function of amine concentration in two different solvent mixtures.

Discussion

The red color which immediately appears upon mixing of TNB with aliphatic amines in a variety of solvents, has generally been associated with the formation of a MC.[3e,7] The most direct structural evidence has come from nmr studies.[16]

Though an nmr study in the solvent chosen for this investigation is precluded because of the low solubility of TNB, it is nevertheless most reasonable to assume that the interaction between TNB and the amines giving rise to the red color is indeed a MC. The kinetic data fully support this assumption as will be shown in the next paragraph; the question of the formation of radical anions and charge-transfer complexes as possible side reactions will be taken up below.

First Relaxation Time, τ_1. The dependence of τ_1^{-1} on pH and amine concentration as seen in Figures 2–5 for the three systems studied is consistent with the reaction scheme formulated in eq 2. The equilibrium process K_{XH} is a fast proton transfer reaction with the



participation of solvent and all acids and bases present; it is too fast for the temperature-jump technique.

The relation between τ_1^{-1} and the amine and hydronium ion concentration is given in eq 3. This is a simplified equation omitting the concentration of TNB, because under all conditions [RR'NH] ≫ [TNB]. K_{XH} is defined as the stoichiometric acid dissociation constant of XH. Equation 3 predicts plots of τ_1^{-1} *vs.* amine concentration to consist of a series of straight lines of equal slopes (k_1) and intercepts which increase in a nonlinear fashion with increasing hydrogen ion concentration. Figures 4 and 5 show this to be the case for the piperidine and pyrrolidine systems. In the *n*-butylamine case, Figures 2 and 3, one apparently deals with the limiting situation, where k_1 [$BuNH_2$] ≪ k_{-1}-

$$\frac{1}{\tau_1} = k_1[\mathrm{RR'NH}] + k_{-1}\frac{[\mathrm{H^+}]}{[\mathrm{H^+}] + K_{XH}} \qquad (3)$$

(16) M. R. Crampton and V. Gold, *J. Chem. Soc., B*, 23 (1967).

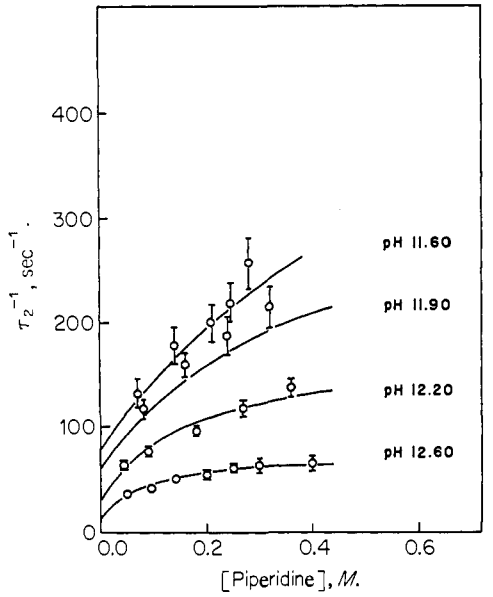


Figure 7. System piperidine–TNB with NaCl. τ_2^{-1} as function of amine concentration and pH. Curves are calculated by means of eq 6 as described in the Discussion.

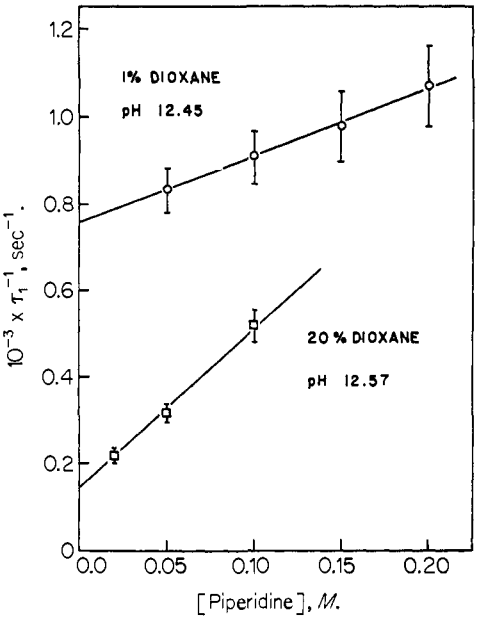


Figure 9. System piperidine–TNB with NaCl. Solvent dependence of τ_1^{-1}.

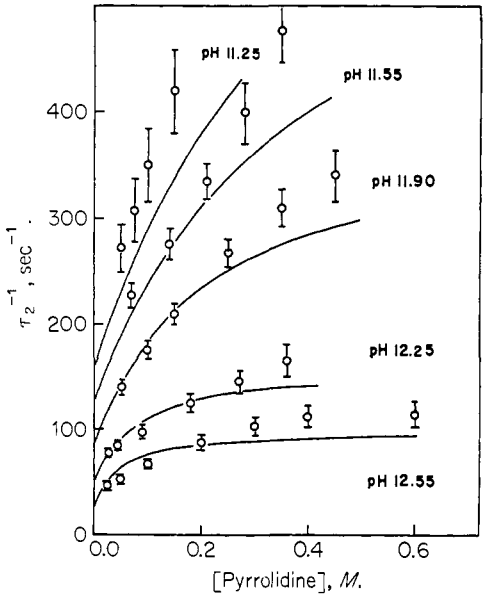


Figure 8. System pyrrolidine–TNB with NaCl. τ_2^{-1} as function of amine concentration and pH. Curves are calculated by means of eq 6 as described in the Discussion.

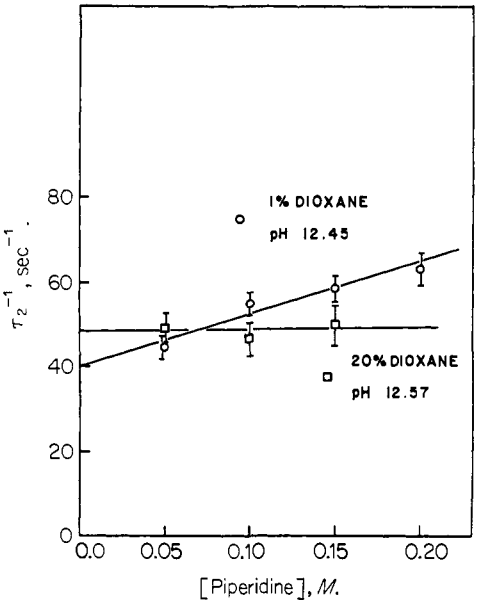


Figure 10. System piperidine–TNB with NaCl. Solvent dependence of τ_1^{-1}.

$[H^+]/([H^+] + K_{XH})$; some medium effect which will be dealt with below even produces negative slopes.

The present data allow the direct evaluation of k_1 for the piperidine and pyrrolidine reaction, but not for the butylamine reaction; the average of the slopes of the various lines in Figures 4 and 5 has been taken. k_1 for the *n*-butylamine system was estimated from spectroscopic equilibrium measurements coupled with the kinetically determined k_{-1} and K_{XH} values. k_{-1} and K_{XH} can be determined for all three systems from the intercepts by means of an inversion plot, *i.e.*, by plotting the reciprocal values of the intercepts *vs.* the reciprocal hydrogen ion concentrations (not shown). Equation 4 shows that the new intercepts of the resulting straight lines are equal to $1/k_{-1}$, the slopes K_{XH}/k_{-1} so that both k_{-1} and K_{XH} can be evaluated. It is realized that there is some degree of arbitrariness in drawing the best line through the points at the lowest pH values in Figures 4

$$\frac{1}{\text{Intercept}} = \frac{1}{k_{-1}} + \frac{K_{XH}}{k_{-1}[H^+]} \qquad (4)$$

and 5, which will be reflected in the intercepts and thus in the inversion plots. A rather generous uncertainty limit has therefore been allowed for the k_{-1} and K_{XH} values derived from the inversion plots. Rate and equilibrium constants are summarized in Table II.

K_{XH}, k_1, and k_{-1}. The zwitterionic form of the MC derived from *n*-butylamine is 25.3 times more acidic than the free butyl ammonium ion, whereas for piperidine and pyrrolidine the ratios $K_{XH}/K_{RR'NH}$ are only

Table II. Rate and Equilibrium Constants of the Various Processes Studied in 10% Dioxane–90% Water

Constant	n-$BuNH_2$	Piperidine	Pyrrolidine
k_1 ($1\ M^{-1}\ sec^{-1}$)	123 ± 20[a]	$3{,}000 \pm 200$	$8{,}100 \pm 500$
k_{-1} (sec^{-1})	$20{,}000 \pm 4{,}000$[d]	$14{,}900 \pm 2{,}000$	$25{,}000 \pm 3{,}000$
$K_1 = k_1/k_{-1}$ ($1\ M^{-1}$)	$6.17 \pm 2.1 \times 10^{-3}$[a]	0.201 ± 0.040	0.31 ± 0.060
K_{XH} (mol/l.$^{-1}$)	$5.28 \pm 1.2 \times 10^{-10}$[d]	$1.49 \pm 0.22 \times 10^{-11}$	$2.15 \pm 0.27 \times 10^{-11}$
$K_{RR'NH}$(mol/l.$^{-1}$)[b]	2.09×10^{-11}[c]	7.60×10^{-12}[c]	5.0×10^{-12}[c]
$K_{XH}/K_{RR'NH}$	25.3	1.96	4.30
k_2 ($1\ M^{-1}\ sec^{-1}$)	4.6 ± 1.0[d]	720 ± 150	$1{,}480 \pm 300$
k_{-2} (sec^{-1})	≥ 100[d]	167 ± 17	208 ± 20
$K_2 = k_2/k_{-2}$ ($1\ M^{-1}$)	≤ 0.046[d]	4.3 ± 1.3	7.12 ± 2.1
K_{YH} (mol/l.$^{-1}$)	$\geq 3.93 \times 10^{-10}$[d]	$2.47 \pm 0.30 \times 10^{-12}$	$1.80 \pm 0.20 \times 10^{-12}$
$K_{YH}/K_{RR'NH}$	≥ 18.8[d]	0.325	0.36

[a] From spectral data. [b] Acid dissociation constant of the ammonium ion in pure water. [c] D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solutions," Butterworths, London, 1965. [d] With $(CH_3)_4NCl$ instead of NaCl. With NaCl the uncertainty is very high: $k_{-1} = 25{,}000 \pm 10{,}000\ sec^{-1}$, $K_{XH} = 7.42 \pm 3.0 \times 10^{-10}$ mol/l.$^{-1}$

1.96 and 4.30 (Table II), respectively.[17] The rather close similarity between the pK values of the MC's and the free amines can be understood in terms of two main factors. The first is electronic in nature, arising from the withdrawing effect of the nitro groups and the distribution of the negative charge. Contrary to the common representation of these complexes, molecular orbital calculations and nmr data on similar systems suggest that there is no negative charge on the ring, but that there is some positive charge on it, which is compensated by more than one unit negative charge among the three nitro groups.[20] From this one expects the pK of the amine nitrogen to be lowered; this effect should depend little on the amine involved.

The second factor is intramolecular hydrogen bonding to the o-nitro group(s) in the zwitterionic form, which should have a weakening effect on the acid strength[21,22] and partially compensate for the electronic effect. The higher $K_{XH}/K_{RR'NH}$ ratio for butylamine compared to the secondary amines is difficult to interpret at the present time due to the limited amount of data.

The rates of nucleophilic attack, k_1, reflect the well-established reactivity pattern of these three amines in nucleophilic aromatic substitution reactions.[3a,6h,23-25]

Most interestingly the k_{-1} values are very nearly the same for the three amines, though one might have expected a considerably higher k_{-1} for the less reactive n-butylamine. This unexpected behavior may be due either to the fact that upon expelling the primary amine from the MC, two intramolecular hydrogen bonds have to be broken instead of only one for secondary amines. An alternative explanation could be that the bulkiness of the secondary amines should make them better leaving groups relative to primary amines of similar reactivity. The second hypothesis is less attractive on the grounds that k_{-1} for piperidine is slightly smaller than for pyrrolidine, though the former is less reactive and bulkier than the latter.

Second Relaxation Time, τ_2. As seen from the concentration dependence of τ_2^{-1}, the process responsible for τ_2 must be another interaction of TNB with the amine. This process is slower and hence coupled to the MC equilibrium, which explains the rather complex dependencies of τ_2^{-1} shown in Figures 7 and 8, though the situation seems more straightforward in Figure 6. The pH dependence of the intercepts further shows that the new species is also involved in an acid–base equilibrium like XH. Equation 5 represents the only reasonable extended reaction scheme which accounts for τ_1 and τ_2. K_{YH}, in analogy to K_{XH}, stands for a

$$\mathrm{TNB} + \mathrm{RR'NH} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{XH} \overset{K_{XH}}{\rightleftharpoons} \mathrm{X^-} + \mathrm{H^+} \qquad \mathrm{RR'NH} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{YH} \overset{K_{YH}}{\rightleftharpoons} \mathrm{Y^-} + \mathrm{H^+} \qquad (5)$$

rapid acid–base equilibrium between the unknown species YH and its conjugate base. For $\tau_2 \gg \tau_1$, which is the case in all our experiments, and again for [RR'NH] $\gg$ [TNB], the analytical expression for τ_2^{-1} can be derived according to standard procedures[10] and is given in eq 6. Consideration of two extreme situations

$$\frac{1}{\tau_2} = k_2[\mathrm{RR'NH}]\frac{k_{-1}\dfrac{[\mathrm{H^+}]}{K_{XH}+[\mathrm{H^+}]}}{k_{-1}\dfrac{[\mathrm{H^+}]}{K_{XH}+[\mathrm{H^+}]} + k_1[\mathrm{RR'NH}]} + k_{-2}\frac{[\mathrm{H^+}]}{K_{YH}+[\mathrm{H^+}]} \qquad (6)$$

shows that eq 6 indeed describes the experimental data adequately.

Case A. When the amine concentration is low and the hydrogen ion concentration high, so that $k_1[\mathrm{RR'NH}] \ll k_{-1}[\mathrm{H^+}]/(K_{XH} + [\mathrm{H^+}])$, then eq 6 simplifies to eq 7.

$$\frac{1}{\tau_2} = k_2[\mathrm{RR'NH}] + k_{-2}\frac{[\mathrm{H^+}]}{K_{YH}+[\mathrm{H^+}]} \qquad (7)$$

In this limiting case, a plot of τ_2^{-1} *vs.* [RR'NH] gives a straight line with the slope k_2, and a further decrease in pH will leave this slope unaffected. In the piperidine system eq 7 is approximately fullfilled at pH 11.60, the

(17) The acid dissociation constants of the free ammonium ions refer to aqueous solutions, at lower ionic strengths than used in our experiments. The change in solvent to 10% dioxane–90% water and the higher ionic strength is estimated to change them at most by 30%.[18,19]

(18) W. F. K. Wynne-Jones and G. Solomon, *Trans. Faraday Soc.*, 34, 1321 (1938).

(19) J. C. James and J. G. Knox, *ibid.*, 46, 254 (1950).

(20) P. Caveng, P. B. Fischer, E. Heilbronner, A. L. Miller, and H. Zollinger, *Helv. Chim. Acta*, 50, 848 (1967).

(21) M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, 3, 1 (1964), and references cited therein.

(22) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman and Co., San Francisco, Calif., 1960, p 181.

(23) (a) H. Suhr, *Ann.*, 687, 175 (1965); (b) H. Suhr and H. Grube, *Ber. Bunsenges.*, 70, 544 (1966).

(24) F. Pietra and A. Fava, *Tetrahedron Lett.*, 1535 (1963).

(25) C. F. Bernasconi and H. Zollinger, *Helv. Chim. Acta*, 49, 103 (1966).

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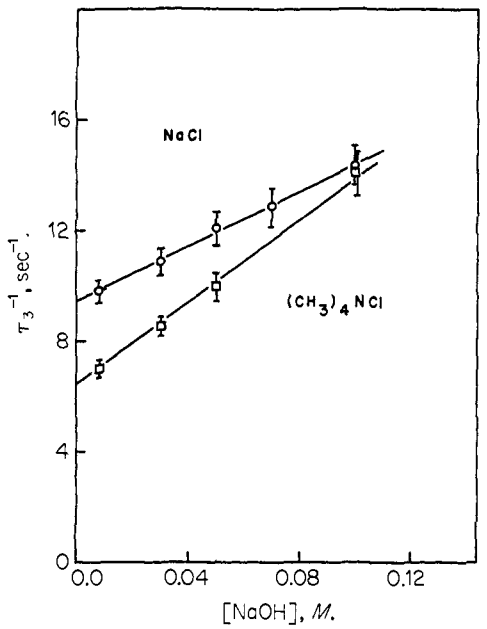


Figure 11. τ_3^{-1} as a function of [NaOH] in the absence of amine.

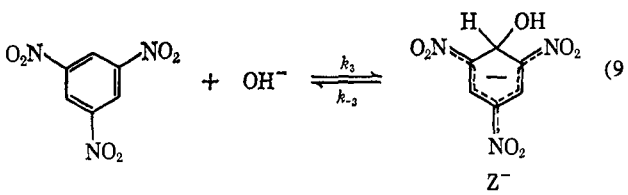
A more direct argument in favor of the oxhydroxylamine being responsible for τ_2 comes from a study of the solvent dependence of τ_1 and τ_2. If the 1-MC (I) gave rise to τ_2, a change in solvent composition is expected to influence k_2, k_{-2}, and K_{YH} in a comparable way as it does k_1, k_{-1}, and K_{XH}, because in both isomeric MC's the negative charge is delocalized. On the other hand, the oxyhydroxylamine, especially in its anionic form differs strongly from X^- with respect to the charge distribution. Thus k_2, k_{-2}, and particularly K_{YH} should display a markedly different solvent dependence from k_1, k_{-1}, and K_{XH}. The data in Table I and Figures 9 and 10, for the piperidine–TNB system, show that the change in solvent from 1% dioxane–99% water to 20% dioxane–80% water has in fact quite different effects on τ_1 and τ_2. The pH of the solutions in these experiments was such that $K_{XH} \gg [H^+]$, so that the intercepts in Figures 9 and 10 are approximately $k_{-1}[H^+]/K_{XH}$ and $k_{-2}[H^+]/K_{YH}$, respectively. For the same change in solvent $k_{-1}[H^+]/K_{XH}$ *decreases* by a factor of 5.6 whereas $k_{-2}[H^+]/K_{YH}$ *increases* by a factor of 1.3.[39] This represents quite a dramatic difference in behavior indeed considering the rather small change in solvent.

A question which might arise is why this species has not been found in other solvents, by other methods. The strong solvation requirements of the oxyhydroxylamine, particularly in its anionic form by a polar protic solvent, as borne out by these experiments, which show that even a slight modification of the solvent tips the balance of relative stabilities strongly in favor of the MC, may be the principal answer;[40] thus, water appears to be a unique solvent favoring oxyhydroxylamines.

K_{YH}, k_2, and k_{-2}. By similar reasoning as with the MC's, electronic effects on K_{YH} are expected to be comparable for the three oxyhydroxylamines and any difference among the amines should mainly reflect differences in intramolecular hydrogen bonding (Table II).

The k_2 values show the secondary amines to be more reactive than butylamine by a factor of over 100, whereas the k_{-2} values appear to be strictly comparable. This is again similar to the trend in k_1 and k_{-1}. Molecular models show that a steric factor seems even less likely to be responsible for the similarity between the k_{-2} values of the primary and secondary amines than it is for the k_{-1} values. Again the stronger stabilization of YH through two hydrogen bonds in the butylamine complex is believed to be the principal cause.

Third Relaxation Time, τ_3. τ_3 does not depend on the amine concentration, nor on the pH below 12. Even more revealing, the relaxation times does not disappear in complete absence of amine. Hence it cannot be due to an interaction of the amine with TNB, but arises from a Meisenheimer complex between TNB and the hydroxide ion, eq 9. When appreciable amounts of sodium hydroxide are added, τ_3 becomes



(9

shorter as expected on the basis of eq 10. This equation

$$\frac{1}{\tau_3} = k_3[OH^-] + k_{-3} \qquad (10)$$

pertains under pseudo-first-order conditions and in the absence of amine.[41] From Figure 11 the rate coefficients k_3 and k_{-3} were determined. With sodium chloride as compensating electrolyte, $k_3 = 48$ l. M^{-1} sec^{-1}, $k_{-3} = 9.55$ sec^{-1}, and thus the equilibrium constant for MC formation $K_3 = 5.02$ l. M^{-1}; with tetramethylammonium chloride, $k_3 = 70$ l. M^{-1} sec^{-1}, $k_{-3} = 6.5$ sec^{-1}, and $K_3 = 11.8$ l. M^{-1}. The different salt effect exerted by the two compensating electrolytes is noteworthy; it is in aggreement with findings by Bunton and Robinson on the reaction of 2,4-dinitrochlorobenzene with hydroxide ion.[42]

k_3 is seen to be so small that it cannot contribute significantly to τ_3 at pH < 12. This explains why τ_3 is not increased in the presence of amine[41] in the experiments reported.

Medium Effects. The negative slopes in Figures 2 and 3 and the observation that the calculated τ_2^{-1} curves in Figures 7 and 8 do not perfectly fit with the experimental results were suggestive for some medium effect operating. There appear to be three different factors influencing the kinetic parameters: the amine concentration, the amine hydrochloride, and the compensating electrolyte.

In general, relaxation kinetics is not a very amenable method for the study of medium effects except for limiting situations. The reason for this is that in equations such as 3 or 11 the rate coefficient of the forward and reverse reaction will generally be affected in an opposite way, so that medium effects tend to compensate

(39) The meaning of pH in 20% dioxane–80% water being uncertain, the intercepts rather than k_{-1}/K_{XH} or k_{-2}/K_{YH} values are compared directly here. This has no bearing on the argument however.

(40) In 50% dioxane–50% water, not even a trace of τ_2 can be detected, implying that the oxyhydroxylamine formation has become negligible relative to MC formation.

(41) In the presence of amine, k_3 has to be multiplied by a complex correction factor including all the equilibria.

(42) C. A. Bunton and L. Robinson, *J. Amer. Chem. Soc.*, 90, 5965 (1968).

each other in τ, unless one term is much larger than the other and solely determines τ. Thus τ_1 in the piperidine and pyrrolidine systems does not reveal any significant medium effect outside the limit of error, but τ_1 in the butylamine reaction does, because here $\tau_1^{-1} = k_{-1}[H^+]/(K_{XH} + [H^+])$, without contribution of k_1.

Interestingly, the medium effect is much more pronounced with tetramethylammonium chloride than with sodium chloride as compensating electrolyte (Figures 2 and 3). It is not clear whether the medium effect is inherently large but greatly compensated by sodium chloride in a certain concentration range, or if tetramethylammonium chloride introduces an effect of its own. Intuitively, the first hypothesis seems more reasonable because tetramethylammonium chloride is a better model for the amine hydrochloride and should be a more suitable compensating electrolyte. This is also consistent with data obtained by Bunton and Robinson[42] on the effect of a series of electrolytes on the reaction of aniline with 2,4-dinitrochlorobenzene.

Analysis of the data at different pH values, with $(CH_3)_4NCl$ compensating electrolyte, demonstrates that both the amine and the amine hydrochloride contribute about equally to a decrease in τ_1^{-1}, *i.e.*, both tend to stabilize the MC with respect to reactants.

Several nucleophilic aromatic substitution reactions by amines, in a variety of solvents, have been found to proceed faster in the presence of high amine concentrations,[3d,43] implying a stabilization of the intermediate relative to reactants.[44] The problem is very complex and there has been no agreement as to the precise nature of this stabilization.

The stabilization of the MC by the amine hydrochloride on the other hand might be due to hydrogen bonding to the rather strongly negatively charged nitro groups;[20] that *intra*molecular hydrogen bonding plays a role has been shown previously.

Acknowledgment. I wish to thank Professor J. F. Bunnett for criticism and discussion.

(43) See, *e.g.* (a) J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, 87, 3875 (1965); (b) H. Suhr, *Ber. Bunsenges.*, 67, 893 (1963); (c) C. F. Bernasconi and H. Zollinger, *Helv. Chim. Acta*, 49, 2570 (1966).

(44) This is to be differentiated from the occasional finding that the amine acts as a general base catalyst.[6b-h]

The Mechanism of Reduction of Alkyl Halides by Chromium(II) Complexes. Alkylchromium Species as Intermediates

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Abstract: Alkyl halides are reduced quantitatively to alkanes by an ethylenediaminechromium(II) reagent prepared *in situ* from chromous salts and ethylenediamine in aqueous dimethylformamide solutions. The reduction proceeds *via* an alkylethylenediaminechromium(III) intermediate, which is hydrolytically unstable. The kinetics of the formation of the alkylchromium species is first order each in the alkyl halide and the chromium(II) reagent. The mechanism is postulated to proceed in two steps: a rate-limiting transfer of a halogen atom from the alkyl halide to ethylenediaminechromium(II) followed by a rapid association of the resultant alkyl radical with a second chromium(II) species. The second-order rate constant for the latter reaction is estimated as 4×10^7 M^{-1} sec^{-1} based on competition studies of the cyclization of the ω-hexenyl radical to the cyclopentylmethyl radical. The absorption spectra of various alkylchromium complexes are also examined, and the rates of acetolysis to afford alkane are measured in DMF solutions.

A reagent useful for the facile reduction of alkyl halides to alkanes was presented in a preliminary report.[1] Chromium(II) perchlorate and ethylenediamine react rapidly in aqueous dimethylformamide (DMF) solutions to form ethylenediamine–chromium(II) complexes, which reduced even primary alkyl chlorides to alkanes and aryl bromides and iodides to arenes at room temperature. Indirect evidence suggested the formation of a metastable alkylchromium intermediate.[1] In this paper, we wish to delineate the scope of the reduction of alkyl halides by the ethylenediaminechromium(II) reagent, to establish the kinetics, to demonstrate the role of alkylchromium complexes[2] as intermediates, and to elaborate on the mechanism of the reduction.

Results

Reduction of Alkyl Halides to Alkanes by Cr^{II}(en). The chromous reagent was prepared *in situ* by simply treating a solution of chromous perchlorate with stoichiometric amounts of ethylenediamine(en) in aqueous DMF solutions in the absence of air. The organic halide was then added and the reduction allowed to proceed at room temperature.[3]

(1) J. K. Kochi and P. E. Mocadlo, *J. Am. Chem. Soc.*, 88, 4094 (1966).

(2) Other aralkylchromium complexes have been isolated: (a) R. G. Coombs, M. D. Johnson, and N. Winterton, *J. Chem. Soc.*, 7029 (1965); 177 (1966); *Chem. Commun.*, 251 (1965); (b) R. P. A. Sneeden and H. P. Throndsen, *ibid.*, 509 (1965). (c) Alkylchromium(III) complexes have also been obtained by metathesis: H. H. Zeiss and R. P. A. Sneeden, *Angew. Chem. Intern. Ed., Engl.*, 6, 435 (1967).

(3) Cr^{II} is used to denote chromous ion in aqueous solutions of DMF and other solvents. Hexacoordination with solvent is indicated but no attempt will be made to specify coordination unless pertinent to the discussion.