SPECTROPHOTOMETRIC ANALYSIS FOR CARBANIONS AS A
METHOD OF STUDYING PROTON TRANSFER RATES

by

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Abstract

The direct spectrophotometric analysis for carbanions was considered as a method for measuring the kinetics of proton transfer reactions. It was applied to the reaction of 2-nitropropane with piperidine in water and 50% acetonitrile-water solvents. A large solvent effect on the equilibrium was found. Deuterium isotope effects in both solvents were measured and a correlation with the work of Bell and Goodall\(^{19}\), which says that \(^\frac{k_H}{k_D}\) should be a maximum when \(\Delta pK\) is zero, was shown.

This method was considered to be useful over a very wide range of reactivities, but with the disadvantage that a very large number of kinetics runs are required to obtain a rate constant for one reaction.
Table of Contents

Introduction 1
Reactions of Nitroalkanes 15
Results and Discussion 20
Experimental 38
Summary 41
References 42
Appendix 44

Index to Tables and Figures

Table 1  Second-Order Rate Constants for the Reaction of 2-Nitropropane with Piperidine in Water at 30°C 23
Table 2  Second-Order Rate Constants and Isotope Effect for Reactions of Nitro Compounds with Piperidine in Water at 30°C 25
Table 3  Second-Order Rate Constants and Isotope Effect for Reactions of Nitro Compounds with Piperidine in 50% Acetonitrile-Water at 30°C 26
Table 4  Ratios of Ionized to Unionized 2-Nitropropane at Various Buffer Ratios 27
Figure 1  Guggenheim Plot of 2-Nitropropane-Piperidine Reaction in 50% Acetonitrile-Water, \([B_T] = 0.01\) M 31
Figure 2  Guggenheim Plot of 2-Nitropropane-Piperidine 33
Reaction in 50% Acetonitrile-Water, \([B_T] = 0.057\) M

Figure 3
Plots of \(k_{obsd}\) vs \([B_T]\) for Reaction of 2-Nitropropane with Piperidine in 50% Acetonitrile-Water at 3 Buffer Ratios
Introduction

There are several methods which have been used to follow the kinetics of proton transfers from carbon, including halogenation, isotopic exchange, racemization, direct photometric analysis, and others. Of these methods, that which has been used most widely is halogenation.

This method is very useful because of the choice available for studying the kinetics. Rate measurements are often made by following the disappearance of bromine or iodine spectrophotometrically. In the case of base-catalyzed halogenation of aliphatic nitro compounds, the mechanism is:

$$
\begin{align*}
R_2CHNO_2 + B & \underset{k_1}{\overset{k_2}{\rightleftharpoons}} R_2C^-NO_2 + BH^+ \\
R_2C^-NO_2 + X_2 & \overset{k_2}{\longrightarrow} R_2CXNO_2 + X^-.
\end{align*}
$$

The reaction rate depends on concentrations of nitro compound and base, since the first step is rate-limiting, but is independent of the halogen used and its concentration.

Equation 1 gives the rate of disappearance of halogen:

$$
\text{Eq. 1} \quad - \frac{dX_2}{dt} = \frac{k_1k_2(RNO_2)(B)(X_2)}{k_2(X_2) + k_{-1}(BH^+)}
$$

When $k_2(X_2) \gg k_{-1}(BH^+)$, as is the case for normal halogen concentrations, equation 1 becomes:

$$
\text{Eq. 2} \quad - \frac{dX_2}{dt} = k_1(RNO_2)(B).
$$
Under conditions of large excesses of both nitro compound and base, the disappearance of $X_2$ is pseudo-zero-order, and $k_1$ can be determined as shown in equation 3.

$$\text{Eq. 3} \quad k_1 = \frac{(X_2)_{t_1} - (X_2)_{t_2}}{(RNO_2)_0 (B)_0 (t_2 - t_1)} = \frac{OD_{t_1} - OD_{t_2}}{\epsilon (RNO_2)_0 (B)_0 (t_2 - t_1)},$$

where $(RNO_2)_0$ and $(B)_0$ are the initial concentrations of nitro compound and base, $t$ is time, $(X_2)$ is concentration of halogen, OD is optical density and $\epsilon$ is the extinction coefficient of halogen.

One difficulty in applying this formula is that the apparent extinction coefficient of the halogen changes during the course of the reaction due to the formation of $X_3^-$: $X_2 + X^- \rightleftharpoons X_3^-$. Adding excess $X^-$ initially prevents this change, since the concentration of $X_3^-$ will then remain essentially constant throughout the reaction. This approach, suggested by Lewis and Johnson, can introduce another problem, however. The added $X^-$ may react with the nitro compound, depending on the system being studied. For example, Funderburk was unable to use this technique because of the slight reversibility of the reaction:

$$(\text{CH}_3)_2\text{C}^-\text{NO}_2 + I_2 \rightleftharpoons (\text{CH}_3)_2\text{CINO}_2 + I^-$$

Instead he constructed charts for converting optical density to iodine concentration, successfully avoiding these difficulties.

Equation 3 is applicable to other carbon acids than nitro compounds, and it has been used by Allen for determining rates of iodination of nitro compounds and of acetate catalyzed bromination of phenyl alkyl ketones.
Emmons and Hawthorne also used the spectrophotometric method for studying acid- and base-catalyzed reactions of phenyl cyclopentyl and phenyl cyclohexyl ketones with bromine.

One drawback of the spectrophotometric method of following halogenation rates is that very slight impurities in the reactants can invalidate results. In many cases only the first 5% or less of the reaction is followed, so the presence of any contaminant which may react with halogen must be avoided. Careful analysis of starting materials is required when this method is used.

Impurities can become particularly important in the determination of kinetic isotope effects by this method. Any undeuterated material, RH, present in the reaction of RD with halogen and basic catalysts could cause a large error in the rate determined for the ionization of RD. The impurity, RH, would be ionized first, and when only the first 5% of reaction is being followed, the error caused by a small amount of impurity becomes quite large.

Pearson and Williams used a conductometric method to determine rates of iodination of nitroethane catalyzed by pyridine bases in aqueous ethanol.

Bell, Everett, and Longuet-Higgins used a titrimetric method to determine the rate of bromination of diethyl malonate. At various times during the course of reaction, they added allyl alcohol to the reaction mixture to remove excess Br₂, then added potassium iodide, which reacts with the ethyl dibromo malonate formed in the reaction, giving off iodine. The iodine can then be titrated with sodium thiosulfate. The usefulness of this method is limited, apparently by side reactions which cause erratic results.

One possible difficulty arises in studying halogenations of substrates
having more than one acidic proton. In these cases the stoichiometry of the reaction must be known, since the substitution of one halo-atom for a hydrogen can lead to the ionization of the second proton at a faster rate than that of the first. Bell and Lidwell\textsuperscript{7} reported the rates of chlorination of each of the three protons of acetone with a variety of catalysts. For catalysis by hydroxide ions the rates were:

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Base</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH\textsubscript{3}COCH\textsubscript{3}</td>
<td>1.5 x 10</td>
</tr>
<tr>
<td>CH\textsubscript{3}COCH\textsubscript{2}Cl</td>
<td>5.6 x 10\textsuperscript{3}</td>
</tr>
<tr>
<td>CH\textsubscript{3}COCHCl\textsubscript{2}</td>
<td>2.7 x 10\textsuperscript{4}</td>
</tr>
</tbody>
</table>

This increase in rate with increasing substitution by halogen was observed with all catalysts studied. Allen\textsuperscript{3} has studied the reactivities of acetophenone and the mono- and dibromo- compounds. He found that the rate constants do not show nearly as large an increase with increasing halogen content, so that the formation of the monobromo ketone can be studied without difficulty.

The major limitations of the halogenation method is that of side reactions of the halogen used. In many cases the halogen will react with the solvent or the base rather than the carbanion. In such cases an alternate route for kinetic study must be found.

There are instances in which halogen reacts so rapidly with carbon acids that the rate cannot be determined by any of these techniques. For example, Funderburk\textsuperscript{2} attempted to follow the rate of bromination of 2-nitropropane in 50% aqueous pyridine titrimetrically, but the reaction proceeded too rapidly. Iodination could not be used in this case because a precipitate of N-iodopyridinium triiodide was formed.
The examples presented here do not represent a complete survey of the halogenation method, by any means. The technique is very old, and has been used too often for all the examples to be cited.

A second method useful for obtaining information about the kinetics of proton transfers from carbon is isotopic exchange. Hsü, Ingold, and Wilson used isotopic exchange along with other techniques to demonstrate that the base-catalyzed halogenation, racemization, and exchange reactions of ketones shared a common, rate-determining ionization step. Having shown in earlier work that the rates of halogenation and racemization were equal (see p. 8), they measured the rates of racemization and exchange of the ketone \( \text{C}_2\text{H}_5\text{CH-C-}^{\text{H}}\\text{H}_3\text{C} \) in D_2O-dioxane solution with sodium deuter-oxide. The two rates were equal, and the investigators concluded that the rates of halogenation, racemization, and isotopic exchange with basic catalysts are controlled by the ionization of the \( \alpha \)-hydrogen.

Swain and co-workers used an interesting combination of isotopic exchanges to determine the identity of the attacking nucleophile in certain enolization reactions of ketones. They prepared DL-\( \alpha \)-phenyl-isocaprophenone-\( \alpha \)-d, \( \text{C}_6\text{H}_5\text{-CD-CH}_2\text{CH(CH}_3)\text{2} \), and the \( \alpha \)-tritium analog, and followed the reaction of each compound with acetic acid-sodium acetate in aqueous solutions. At various times reaction mixtures were worked up to give products which were then analyzed for deuterium or tritium content. The rate of the same reaction for the protiated ketone was determined by racemization of the optically active compound, so that \( k_H/k_D \) and \( k_H/k_T \) could be compared. The results gave experimental agreement with Swain's equation, \( k_H/k_T = (k_H/k_D)^{1.442} \).

Lewis and Robinson determined the tritium isotope effect in
2-nitropropane by following the loss of tritiated compound. The method they used was not strictly a direct exchange, because the exchange is complicated by side reactions, such as the Nef reaction. Weighed samples of 2,4,6-trimethylpyridine and 2-nitropropane-2-T were allowed to react in thermostatted aqueous t-butanol solutions, with aliquots removed at 2 to 6 week intervals. The products were purified and assayed by isotopic dilution analysis using solution scintillation counting.

There is an obvious limitation to this technique. The reaction is one in which $k_H$ is small and $k_H/k_T$ is large, so that several months of continuous reaction are required to obtain the rate constant, $k_T$. The question of the experimental practicality of maintaining constant reaction conditions for such periods of time must be taken into consideration for any reactions of a similar nature.

Jones$^{11}$ used a very similar experimental technique to determine $k_T$ for the much faster detritiation of 2-carbethoxycyclopentanone-2-T,

![Chemical Structure](image)

in D$_2$O, water, and in monochloroacetate and fluoride buffers.

Warkentin and Tee$^{12}$ followed rates of isotopic exchange of 2-butanol by nmr spectroscopy. To determine the kinetic data a deuterium exchange reaction was run in the nmr probe, with the appropriate proton peak integrated at various reaction times. The difficulty in controlling the temperature of the nmr probe accurately contributes to a larger experimental error than in many of the other methods discussed here.

Isotopic exchange is a very reliable method of measuring ionization rates of proton transfers unless the carbanion undergoes other reactions,
or unless intimate ion pairs are involved. In that case the original isotope may return to the anion without exchanging, so that the rate of exchange does not equal the rate of ionization. This has been illustrated by Cram \(^\text{13}\) in the following reaction scheme.

\[
\begin{align*}
\text{CH} & \rightleftharpoons \text{CH}^+ & \text{H}^+ & \rightarrow \text{CH}^+ & \rightarrow \text{CD} + \text{B} \\
k_1 & \quad k_2 & \quad k_{-1} & \quad DB & \quad \text{DB}
\end{align*}
\]

In this scheme \(k_1\) will be much less than \(k_{-1}\) or \(k_2\), so the steady state approximation applies, and the observed rate constant is given by the following equation:

\[
k_{\text{obsd}} = \frac{k_1 k_2}{(k_{-1} + k_2)}
\]

If \(k_2 \gg k_{-1}\), the rate expression reduces to

\[
k_{\text{obsd}} = k_1,
\]

and the rate measured will indeed be the rate of ionization. But if \(k_{-1} \gg k_2\),

\[
k_{\text{obsd}} = \frac{k_2 k_1}{k_{-1}} = k_2 K,
\]

and the observed rate constant is the product of an equilibrium constant and a rate constant for a process that does not involve ionization.

In 1936 Hsu and Wilson \(^\text{14}\) published the first experimental data comparing rates of base-catalyzed halogenations and racemizations of
ketones. The ketone studied was d-2-carboxybenzyldin-l-one,

![Chemical structure](image)

The rates of halogenation and racemization of this compound were found to be the same. This result supported the idea that ionization of the \( \alpha \)-hydrogen was the rate-determining step in the base-catalyzed halogenation of ketones, and showed that the carbanion formed did not retain its configuration.\(^\text{15}\)

It was mentioned earlier that Swain and co-workers\(^\text{9}\) used a racemization technique to determine the rate of enolization of D(+)\(\alpha\) phenylisocaprophenone in acetic acid-sodium acetate solutions. At various times samples were taken from the reaction vessels for polarimetric readings.

The first order rate constant in this type experiment is calculated by the equation

\[
k_{1t} = 2.303 \log \frac{\alpha_0 - \alpha_\infty}{\alpha - \alpha_\infty},
\]

where \( \alpha \) is observed rotation at time \( t \), \( \alpha_\infty \) is the rotation at infinite time, and \( \alpha_0 \) is the initial rotation. With complete racemization, \( \alpha_\infty = 0 \), and

\[
k_{1t} = 2.303 \log \frac{\alpha_0}{\alpha}.
\]

There is a limitation to the usefulness of racemization as a general
technique for studying rates of ionization. It is analogous to that discussed previously for isotopic exchange. If the initial loss of a proton yields an ion pair which can undergo internal return, the observed rate of racemization will not be equal to the rate of ionization, since the ion pair formed is returning to optically active material. In Cram's notation,\textsuperscript{16} an illustration of this is as follows:

\[
\begin{align*}
\text{optically} & \quad \text{optically} \\
\text{active} & \quad \text{racemic} \\
\text{active} & \quad \text{racemic}
\end{align*}
\]

Applying the steady state approximation,

\[
k_{\text{obsd}} = k_1 \frac{k_2}{(k_{-1} + k_2)}.
\]

If \( k_{-1} \gg k_2 \) and the asymmetrically solvated carbanion is formed in an equilibrium step followed by a racemization associated with \( k_2 \), the rate constant is given by

\[
k_{\text{obsd}} = \frac{k_1 k_2}{k_{-1}} = k_2 K.
\]

For the rate of ionization and the rate of racemization to be equal, \( k_2 \) must be much greater than \( k_{-1} \) so that

\[
k_{\text{obsd}} = k_1.
\]

For two of the most common types of carbon acids, racemization may occur through tautomers of the substrate. The well known keto-enol
tautomerism is readily catalyzed by bases. Formation of the enol would result in the loss of optical activity.

\[
\begin{align*}
R-\overset{\text{H}}{\overset{\text{C}}{\overset{\text{C}}{R}}} & \rightarrow R-\overset{\text{C}}{\overset{\text{C}}{\overset{\text{C}}{R}}} \\
R'' & \leftrightarrow R-\overset{\text{C}}{\overset{\text{C}}{\overset{\text{C}}{R}}} \\
\text{ketone} & \rightarrow \text{enol} & \text{ketone} \\
\text{optically active} & \leftrightarrow \text{optically inactive}
\end{align*}
\]

The aci-nitro compound is similar to the enol in that it is a tautomeric form of a carbon acid, and its formation from optically active nitroalkane results in loss of optical activity.

\[
\begin{align*}
R'^{-} & \overset{\text{C}}{\overset{\text{N}}{\overset{\text{O}}{R}}} & \overset{+}{\overset{\text{O}}{\overset{\text{H}}{R}}} & \overset{H}{\overset{+}{\overset{\text{C}}{\overset{\text{N}}{\overset{\text{O}}{R}}}}} \\
\text{nitro compound} & \rightarrow \text{aci-nitro compound} & \text{nitro compound} \\
\text{optically active} & \rightarrow \text{optically inactive}
\end{align*}
\]

Among other methods which have been used to follow proton transfer rates is one in which the change in electrical conductivity is monitored throughout a reaction. This method was used by Bell and Norris\textsuperscript{17} to study the reaction of nitroethane with sodium hydroxide in aqueous methanol at low temperatures. In this type experiment the initial conductance of the basic solution is observed; then the decrease in this reading as the base is protonated is monitored to give the necessary kinetic data.

Wynne-Jones\textsuperscript{18} used a very similar method to study isotope effects by reacting nitroethane with hydroxide ions in D\textsubscript{2}O and H\textsubscript{2}O.
This technique is limited to a rather narrow range. It is practical in the above cases because a hydroxide ion has a mobility much greater than that of any other ion in the system, so that the experimental readings are actually a measure of the disappearance of hydroxide. However, this method is not applicable to the reaction of nitroethane with hydroxide at ordinary temperatures. This reaction proceeds too rapidly to be measured by conductivity methods.

Bell and co-workers developed two other methods specifically for the reactions of nitroalkanes with hydroxide ions. One method employed a pH stat, in which a glass electrode monitored the pH and controlled the addition of base, so that the pH remained constant. By automatically recording the amount of base added as a function of time, this instrument produced all the necessary kinetic data. The second of these is a thermal method, which depends on measuring very small changes in temperature (<0.1°C) caused by the reaction while maintaining essentially isothermal kinetics.

None of the methods discussed previously is suitable for kinetic studies of very fast reactions. Because of difficulties of mixing, reactions whose half lives are smaller than about 1 msec cannot be studied by flow techniques. Many proton transfers from oxygen or nitrogen, and some from carbon, occur at very high rates. These may be studied by relaxation methods.

As explained by Laidler, when relaxation methods are used, a reaction is allowed to reach equilibrium, and is then disturbed in some way. The approach to a new equilibrium is then followed by high-speed techniques. A quantity known as relaxation time is calculated from these measurements. The relaxation time is related to the rate constants in
various ways, depending on the order of the reaction. 22

In the simplest situation,

\[ A \xrightarrow{k_1} X, \xleftarrow{k_{-1}} \]

where the reactions in both directions are of the first order, the kinetic expression is

\[ \frac{dx}{dt} = k_1 (a_0 - x) - k_{-1} x, \]

where \( a_0 \) is the initial concentration of A and X, and \( x \) is the concentration of X. The relaxation time, \( t^* \), for this reaction can be determined to be

\[ t^* = \frac{1}{k_1 + k_{-1}}. \]

Therefore, determining \( t^* \) experimentally gives the value of \( k_1 + k_{-1} \). Since \( \frac{k_1}{k_{-1}} \) is an equilibrium constant, that quantity can also be determined, and the individual rate constants can be calculated. For reactions of a higher order the expression for \( t^* \) is more complicated, but readily gives values for \( k_1 + k_{-1} \).

The experimental determination may be carried out by a variety of experimental methods. The perturbation from equilibrium may be accomplished by changing the pressure or temperature very rapidly. These are known as pressure-jump and temperature-jump methods, and are suitable for reactions requiring a perturbation time of no less than \( 10^{-5} \) sec. For shorter times high electric fields or ultrasonic vibrations are effective for disturbing the equilibrium of the system. Various
techniques have been employed to observe the response of the system to the perturbation and calculate the relaxation time. Spectrophotometric methods are often used for this purpose.

Although these methods have been applied to a number of systems, the author has not found any examples in the area of fast proton transfers from carbon acids using relaxation techniques.

The final method to be discussed here is direct spectrophotometric analysis for carbanions. Consideration of a special problem – the kinetics of reactions of nitro compounds with phenoxide and aniline bases – brought attention to this method. These bases would cover an enormous range of steric requirements and reactivity. This method had been used by Gregory and Bruice\textsuperscript{23} and by Ritchie and Uschold\textsuperscript{24} to investigate proton transfers of widely differing rates. The work of Gregory and Bruice included rate constants in the range of $10^{-3} \text{ M}^{-1} \text{ sec}^{-1}$, while Ritchie and Uschold used essentially the same method to measure rate constants as large as $10^{3} \text{ M}^{-1} \text{ sec}^{-1}$. The widely differing conditions to which this method had been applied made it appear very useful in considering the special problem mentioned.

Other methods appeared to be more difficult to apply here, because of their limited range. The halogenation method could not be used for this problem because halogens would react with phenoxide bases to give the halo-substituted phenoxides.

The technique as described by Gregory and Bruice is essentially the method used in this investigation. Solutions of various buffers of known pH are thermostatted in the cell compartment of a spectrophotometer. The buffer concentration is kept at large excess over the concentration of nitro compound, so that the reaction follows pseudo-first-order kinetics.
Rate constants are obtainable from the slopes of plots of log \( \left( \text{OD}_\infty - \text{OD}_t \right) \) vs. time, \( t \). By running the same reaction at several buffer concentrations and pH's, one obtains the second-order rate constants for the forward and reverse reactions of nitro compound with base.\(^{23}\)
Reactions of Nitroalkanes

Consideration of the chemistry of nitroalkanes points out the importance of carbanion formation in the reactions of these compounds.

The stability of the nitro carbanion is probably due to delocalization of the electron pair onto the more electronegative oxygen atom, as depicted by the resonance structures:

\[
\begin{align*}
R-CN^+O^- & \leftrightarrow R-CN^+O^- \\
R & \quad R
\end{align*}
\]

The fact that \((\text{CH}_3)_2\text{CHNO}_2\) is a stronger acid than \(\text{CH}_3\text{NO}_2\) lends support to the idea that the second structure shown makes a large contribution to the overall structure. The acyclic nitro carbanions are probably planar or almost planar, maximizing overlap between the p-orbital of the carbon and those on the nitro group.\(^{25}\)

Some representative reactions of nitroalkanes are listed below.

I. Condensations\(^ {26}\)

There are many variations of the condensation reactions of nitro compounds. Only three of these variations will be presented here, since the basic mechanistic features are common among these reactions.

\[
\begin{align*}
\text{CH}_3-\text{C-CH}_3 + \text{CH}_3\text{CH}_2\text{NO}_2 & \overset{\text{NaOH}}{\rightarrow} \text{CH}_3-\text{C-O-CH}_2\text{NO}_2 \\
\text{CH}_3-\text{CH}=\text{CH-CH}_2\text{O-OC}_2\text{H}_5 + \text{CH}_3\text{NO}_2 & \overset{\text{NaOH}}{\rightarrow} \text{CH}_3-\text{CH}-\text{CH}_2-\text{CH}_2-\text{OC}_2\text{H}_5 \\
& \quad \text{CH}_2-\text{NO}_2
\end{align*}
\]
Representative mechanism:

\[
\begin{align*}
\text{H-C-H} + \text{R}_2\text{NH} & \rightarrow \text{H-C-H} \\
\text{OH} & \rightarrow \text{OH}
\end{align*}
\]

\[
\begin{align*}
\text{R-CH}_2\text{NO}_2 + \text{OH}^- & \rightarrow \text{R-CH-NO}_2
\end{align*}
\]

\[
\begin{align*}
\text{H-C-H} + \text{R-CH-NO}_2 + \text{Sn}_2 & \rightarrow \text{H-C-H} + \text{OH}^- \\
\text{OH} & \rightarrow \text{R-CH-NO}_2
\end{align*}
\]

II. The Nef Reaction\(^\text{27}\) is the formation of carbonyl compounds from the salts of nitro compounds.
V. Halogenation of nitro compound has been discussed previously. The bromination of 2-nitropropane is given as an example.

\[
\text{CH}_3\text{-CHNO}_2\text{-CH}_3 \xrightarrow{\text{OH}^-} \text{CH}_3\text{-C-CH}_3 + \text{Br}^- \quad \xrightarrow{\text{Br}_2} \quad \text{CH}_3\text{-C-CH}_3 + \text{Br}^- \quad \xrightarrow{\text{NO}_2} \quad \text{CH}_3\text{-C-CH}_3 + \text{Br}^- \quad \xrightarrow{\text{NO}_2} \quad \text{CH}_3\text{-C-CH}_3 + \text{Br}^-.
\]

VI. Alkylation of nitro compound can be accomplished with a variety of alkylation agents, commonly alkyl halides.

\[
R'\text{-CH}_2\text{-NO}_2 + \text{Base} \rightarrow R'\text{CH-NO}_2 \xrightarrow{\text{R'X}} R'\text{-CH-NO}_2 + X^-.
\]

VII. Aliphatic diazonium coupling also proceeds through the anion.

\[
R'\text{-CH}_2\text{-NO}_2 + \text{Base} \rightarrow R'\text{CHNO}_2 \xrightarrow{\text{N=Ar}} R'\text{-CH-N=Ar} + \text{NO}_2 \quad \xrightarrow{\text{Ar}} \quad R'\text{-CH-N=Ar} + \text{NO}_2.\]

VIII. Reductions of nitro compounds occur under a variety of conditions.
A. Catalytic hydrogenation

\[
\text{H}_2 / \text{Pt} \\
\text{RNO}_2 \xrightarrow{\text{25}^\circ} \text{RNH}_2 \\
\text{or} \\
\text{H}_2 / \text{Ra-Ni}
\]

B. Lithium aluminum hydride reductions

\[
\text{CH}_3 \text{NO}_2 \xrightarrow{\text{LiAlH}_4, (\text{C}_2\text{H}_5)_2\text{O}} \text{CH}_3 \text{NH}_2 + \text{CH}_3 \text{NHCH}_3 + \text{CH}_3 \text{NH} + \text{CH}_3 \text{NHCH}_2 \text{OH}
\]

C. Dissolving metal reductions

\[
\text{RNO}_2 \xrightarrow{\text{Fe, HCl, H}_2\text{O}} \text{RNH}_2 \\
\text{C}_2\text{H}_5\text{OH} \xrightarrow{\Delta} \\
\text{Zn, NH}_4\text{Cl} \xrightarrow{\text{H}_2\text{O}} \text{RNH}_2 \xrightarrow{\Delta} \\
\text{Zn, NaOH} \xrightarrow{\text{H}_2\text{O}, \text{CH}_3\text{OH}} \text{R-N=N-R} \xrightarrow{\Delta}
\]

There is some experimental evidence, notably esr studies, that some of these reductions proceed through the formation of relatively stable
anion radicals. A possible reaction path is shown here.

\[
\begin{align*}
R-N^+\text{O}_2^- & \xrightarrow{\text{metal}} R-N^+\text{O}_2^- \xrightarrow{\text{H}^+} R-N^+\text{OH} \xrightarrow{\text{metal}} \\
R-N^+\text{OH} & \xrightarrow{\text{H}^+} R-N^+\text{OH} \xrightarrow{\text{metal}} R-N^+=\text{O} = \xleftarrow{\text{metal}} R-N^+\text{OH} \\
R-N^+\text{OH} & \xrightarrow{\text{H}^+} R-N^+\text{OH} \xrightarrow{\text{metal}} R-N^+\text{OH} \xrightarrow{\text{H}^+} R-N^+\text{OH} \\
\end{align*}
\]

Because of the predominance of the formation of carbanions in reactions of nitroalkanes, the study of the rates at which these anions are produced is of general importance to an understanding of nitroalkane chemistry.
Results and Discussion

For an analysis of the kinetics of the reaction of 2-nitropropane with piperidine, the reaction can be presented by

\[
AH + B \xrightleftharpoons[k_{2,A}]{k_{2,B}} BH^+ + A^- ,
\]

in the notation of Gregory and Bruice.\textsuperscript{23} The following treatment is similar to that of those authors. In this system \([B]\) and \([BH^+]\) are in large excess over \([(AH) + [A^-])\), so the equilibrium can be treated as

\[
AH \xrightleftharpoons[k_{2,A}[BH^+]]{k_{2,B}[B]} A^- ,
\]

The rate expression\textsuperscript{31} for (2) is

\[
-\ln \frac{[AH]_o - [AH]_e}{[AH] - [AH]_e} = (k_{2,B}[B] + k_{2,A}[BH^+])t ,
\]

where \([AH]_o\), \([AH]_e\), and \([AH]\) are concentrations of \(AH\) at \(t = 0\), at equilibrium, and at any time, \(t\). An absorption spectrum of the 2-nitropropane anion formed by the reaction of 2-nitropropane with 0.1 N NaOH in the sample cell of the spectrophotometer showed a broad, intense absorption band from 2500 Å down to less than 2150 Å. The formation of the anion was easily followed at 2300 Å in kinetic runs. In the spectrophotometric analysis for the anion, \((OD_\infty - OD_t)\) is proportional to
([AH] - [AH]_e), so that equation (3) can be written as

\[-\ln([AH]_o-[AH]_e)+\ln(OD_\infty-OD_t) = (k_{2,B}[B]+k_{2,A}[BH^+])t. \quad (4)\]

Thus, the slope of a plot of \(\log(OD_\infty-OD_t)\) vs. \(t\) is

\[k_{slope} = 0.434 \ (k_{2,B}[B]+k_{2,A}[BH^+]).\]

But the forward reaction is also catalyzed by hydroxide ion and the reverse reaction is catalyzed by the conjugate acid of hydroxide, water, so those terms must also be included in \(k_{obsd}^\prime\):

\[k_{obsd} = k_{2,B}[B] + k_{2,A}[BH^+] + k_{OH}[OH^-] + k_{H_2O}. \quad (5)\]

A plot of \(k_{obsd}^\prime\) vs. \([B] + [BH^+]\) is linear, of slope \(k_2^\prime\) and intercept \(k_{OH}[OH^-] + k_{H_2O}\), where

\[k_2^\prime = k_{2,B} \left(\frac{[B]}{[B]+[BH^+]}\right) + k_{2,A} \left(\frac{[BH^+]}{[B]+[BH^+]}\right). \quad (6)\]

Assuming that the activity coefficient is 1, \(a_H = [H^+]\), and \(\frac{[B][H^+]}{[BH^+]} = Ka'\), since \(Ka'\) is the equilibrium constant for the reaction \(BH^+ \rightleftharpoons B + H^+\).

Making these substitutions, equation (6) can be written as

\[k_2^\prime = k_{2,B} \left(\frac{Ka'}{(Ka'+a_H)}\right) + k_{2,A} \left(\frac{a_H}{(Ka'+a_H)}\right). \quad (7)\]
For most amines a plot of $k_2'(K_{a'} + a_H)$ vs. $a_H$ would be linear of slope $k_{2,A}$ and intercept $k_{2,B}K_{a'}$. But for piperidine, which has a high $pK_{a'} = 11.10$, the acid-catalyzed reverse rate constant, $k_{2,A'}$ is so small that $k_2'(K_{a'} + a_H)$ is, within experimental error, a constant equal to $k_{2,B}K_{a'}$. The values of $k_{2,B}$ calculated by this method are given in Table 1.

Equation (6) can also be expressed as

$$k_2' \left( \frac{[BH^+]}{[B]} + 1 \right) = k_{2,A} \frac{[BH^+]}{[B]} + k_{2,B},$$

or when $k_{2,A}$ is small,

$$k_{2,B} = k_2' \left( \frac{[BH^+]}{[B]} + 1 \right).$$

With equation (9), $k_{2,B}$ can be determined in solvents other than water. Values of $k_{2,B}$ determined by equation (9) and deuterium isotope effects are given in Tables 2 and 3.

There is some error in determining rate constants for the ionization of a deuteron by the above analysis. The extraction of $k_{2,B}$ and $k_{2,A}$ from the experimental data is based upon their being rate constants for reverse reactions. However, when deuterium has been substituted for the acidic proton, the two reactions of ionization and protonation are no longer reverses of each other. In the case of reactions with piperidine, the error introduced is very small, because the extent of protonation of the carbanion is so slight that $k_{2,A}$ is negligible.
Table 1

Second order rate constants for the reaction of 2-nitropropane with piperidine in water at 30°C

\[
a_H \quad k_{2,B} = \frac{k'(K_a' + a_H)}{K_a'} \quad \text{(mole}^{-1} \text{sec}^{-1})
\]

<table>
<thead>
<tr>
<th>(a_H)</th>
<th>(k_{2,B})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(3.98 \times 10^{-12})</td>
<td>0.1080</td>
</tr>
<tr>
<td>(5.01 \times 10^{-12})</td>
<td>0.1044</td>
</tr>
<tr>
<td>(7.94 \times 10^{-12})</td>
<td>0.1085</td>
</tr>
<tr>
<td>(2.75 \times 10^{-11})</td>
<td>0.1090</td>
</tr>
</tbody>
</table>

average \(k_{2,B} = 0.1075 \pm 0.0015\) M\(^{-1}\)sec\(^{-1}\)

\(^a\) Errors indicated in Tables 1, 2, and 3 are average deviations.
In water solution, Ka for 2-nitropropane is $1.82 \times 10^{-8}$, and for piperidinium ion Ka is $7.94 \times 10^{-12}$. Using RH and BH$^+$ to represent 2-nitropropane and piperidinium, respectively,

$$\frac{K_{a_{RH}}}{K_{a_{BH}^+}} = \frac{1.82 \times 10^{-8}}{7.94 \times 10^{-12}} = 2.3 \times 10^3.$$

To determine $\frac{K_{a_{RH}}}{K_{a_{BH}^+}}$ in 50% acetonitrile-water solution, excess concentrated sodium hydroxide was added to reaction mixtures after equilibrium had been reached. The absorbance readings gave the percentage of 2-nitropropane ionized at equilibrium.

$$\frac{[R^-]}{[RH]} = K \frac{[B]}{[BH^+]}, \quad (10)$$

where $K = \frac{K_{a_{RH}}}{K_{a_{BH}^+}}$. So plotting the ratio of ionized to unionized nitro compound vs. the inverse of the buffer ratio gives a straight line of slope K. The data for this plot is shown in Table 4.

A least squares analysis of these points gives a slope, $K = 1.067 \pm 0.3$, where the error shown is the probable error in the slope. So we can say that

$$K_{a_{RH}} = 1.067 K_{a_{BH}^+}.$$

The data in Tables 2 and 3 show that the rate of the forward reaction
Table 2

Second order rate constants and isotope effect for reactions
of nitro compounds with piperidine in water at 30°C

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Buffer ratio [BH⁺]/[B]</th>
<th>k₂,B = k₂([BH⁺] + 1) (\text{mole}^{-1} \text{sec}^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>((\text{CH}_3)_2\text{CHNO}_2)</td>
<td>0.50</td>
<td>0.1079</td>
</tr>
<tr>
<td></td>
<td>0.63</td>
<td>0.1042</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.1085</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>0.1098</td>
</tr>
<tr>
<td>average k₂,B</td>
<td></td>
<td>0.1076 ± 0.0017 mole⁻¹ sec⁻¹</td>
</tr>
<tr>
<td>((\text{CH}_3)_2\text{CDNO}_2)</td>
<td>0.63</td>
<td>0.0141</td>
</tr>
</tbody>
</table>

\(k_H/k_D = 7.4\)

\(^a\) Only one value of k₂,B was determined for 2-nitropropane-2-d in water, since it was known that k₂,A was negligible, and one direct comparison of rates at the same buffer ratio would be sufficient to determine \(k_H/k_D\).
Table 3

Second order rate constants and isotope effect for reactions of nitro compounds with piperidine in 50% acetonitrile-water at 30°C

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Buffer ratio</th>
<th>$k_{2,B} = k_2 ([\text{BH}^+]/[\text{B}]) + 1$ (mole$^{-1}$ sec$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$(\text{CH}_3)_2\text{CHNO}_2$</td>
<td>0.183</td>
<td>$3.123 \times 10^{-2}$</td>
</tr>
<tr>
<td></td>
<td>0.225</td>
<td>$2.854 \times 10^{-2}$</td>
</tr>
<tr>
<td></td>
<td>0.620</td>
<td>$3.490 \times 10^{-2}$</td>
</tr>
<tr>
<td></td>
<td>0.825</td>
<td>$2.920 \times 10^{-2}$</td>
</tr>
<tr>
<td></td>
<td>0.951</td>
<td>$3.063 \times 10^{-2}$</td>
</tr>
<tr>
<td>Average $k_{2,B}$</td>
<td></td>
<td>$3.090 \times 10^{-2} \pm 0.17 \times 10^{-2}$</td>
</tr>
<tr>
<td>$(\text{CH}_3)_2\text{CDNO}_2$</td>
<td>0.081</td>
<td>$3.600 \times 10^{-3}$</td>
</tr>
<tr>
<td></td>
<td>0.168</td>
<td>$3.422 \times 10^{-3}$</td>
</tr>
<tr>
<td></td>
<td>0.225</td>
<td>$3.381 \times 10^{-3}$</td>
</tr>
<tr>
<td></td>
<td>0.445</td>
<td>$3.295 \times 10^{-3}$</td>
</tr>
<tr>
<td>Average $k_{2,B}$</td>
<td></td>
<td>$3.425 \times 10^{-3} \pm 0.09 \times 10^{-3}$</td>
</tr>
</tbody>
</table>

$k_{H}/k_D = 8.9 \pm 0.1$
Table 4

Ratios of ionized to unionized 2-nitropropane at various buffer ratios

<table>
<thead>
<tr>
<th>[B]/[BH⁺]</th>
<th>[R⁻]/[RH]</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.67</td>
<td>5.56</td>
</tr>
<tr>
<td>4.45</td>
<td>6.11</td>
</tr>
<tr>
<td>3.44</td>
<td>2.86</td>
</tr>
<tr>
<td>1.62</td>
<td>2.05</td>
</tr>
<tr>
<td>1.21</td>
<td>1.63</td>
</tr>
<tr>
<td>1.05</td>
<td>0.835</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
in the equilibrium

\[
\begin{align*}
\text{CH}_3\text{C}^-\text{CH}_3 + \text{H} & \rightleftharpoons \text{H}_3\text{C}^-\text{CH}_3 + \text{NO}_2^- \\
\text{NO}_2^- & 
\end{align*}
\]

changes only by a factor of about 3.5 in changing solvents from water to 50% acetonitrile-water. Therefore, the rate of the reverse reaction must change by a factor of more than 650 to account for the overall equilibrium difference, which is a factor of almost 2300.

A comparison of the average deviations given in Tables 2 and 3 shows that the error in \(k_{2,B}\) in the mixed solvent is considerably higher than that in water. One probable reason for this is that \(k_{2,A}\) is assumed to be negligible in both systems. This assumption is justified in the case of Table 2 (water as solvent), but it is a poor assumption in Table 3 (50% acetonitrile-water). The data from the equilibrium determination in the mixed solvent indicates that \(k_{2,A}\) does make a measurable contribution and should be considered.

A least squares determination of the intercept and slope was run for the reactions of 2-nitropropane in 50% acetonitrile-water. These results give \(k_{2,B} = 3.049 \times 10^{-2} \text{ M}^{-1} \text{ sec}^{-1}\) and \(k_{2,A} = 0.14 \times 10^{-2} \text{ M}^{-1} \text{ sec}^{-1}\), but the errors are so high that the usefulness of these values is questionable.

Bell and Goodall\(^{19}\) have considered a relationship between the magnitude of isotope effects and the difference in pK's of acid and base reacting for a variety of ionizations of C-H bonds, based on the symmetry argument of Westheimer. The data considered had been obtained by several different experimentors, but all at 25°C in water solution. In plotting \(\log \frac{k_H}{k_D}\) against \(\Delta pK = pK_{\text{acid}} - pK_{\text{base}} + \text{a statistical correction}\), they
found at least qualitative evidence that $k_H/k_D$ is a maximum when $\Delta pK = 0$.

For the results presented in this thesis, in water at $30^\circ$C, $\Delta pK = -3.36$ and $\log k_H/k_D = 0.89$. In 50% acetonitrile-water at $30^\circ$C, $\Delta pK = 0$ and $\log k_H/k_D = 0.95$. These data would appear to agree with Bell's and Goodall's contention, even though there has been a change in solvent systems in the two values being compared. However, further experiments would be needed for any real test of this relationship in the system studied here.

Dixon and Bruice\(^{32}\) have used direct spectrophotometric analysis to determine values of $k_H/k_D$ for nitroethane ionizations catalyzed by primary amines in water and 50% dioxane-water. Their results also support the idea that $k_H/k_D$ reaches a maximum when $\Delta pK = 0$.

Data obtained spectrophotometrically were treated in the following manner. Optical density readings were plotted against time in the manner proposed by Guggenheim.\(^{33}\) In this method $\log (OD_t - OD_{t-\Delta t})$ is plotted against $t$, where $t$ is time and $\Delta t$ is some increment of time greater than two half lives of the reaction. Under pseudo-first-order reaction conditions, this plot is a straight line with slope = $0.434 k_{obsd}$. The value of $k_{obsd}$ was actually determined in a least squares computer program written by Peter J. Brown for the Burroughs B5500 time sharing computer system. This program is given in the appendix. The plots were usually reliable straight lines out to about 4 half lives. Figures 1 and 2 show two of these Guggenheim Plots. Figure 1 is an example of the best plots obtained by this method; Figure 2 is an example of the worst. Data for these plots are given in the accompanying tables.

Values of $k_{obsd}$ were then plotted against $[B_T] = [B] + [BH^+]$. At a constant pH, these plots are straight lines of slope $k_2'$ and intercept
Data for Figure 1

Solvent: 50% Acetonitrile-water

\[ [B_t] = 0.01 \text{ M piperidine} \]

\[ [BH^+] / [B] = 0.183 \quad k_{\text{obsd}} = 3.158 \times 10^{-4} / \text{sec} \]

\( \Delta t = 64 \text{ min.} \)

<table>
<thead>
<tr>
<th>t (min.)</th>
<th>(OD(<em>t) - OD(</em>{t-\Delta t}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>0.605</td>
</tr>
<tr>
<td>68</td>
<td>0.564</td>
</tr>
<tr>
<td>72</td>
<td>0.523</td>
</tr>
<tr>
<td>76</td>
<td>0.487</td>
</tr>
<tr>
<td>80</td>
<td>0.452</td>
</tr>
<tr>
<td>84</td>
<td>0.421</td>
</tr>
<tr>
<td>88</td>
<td>0.390</td>
</tr>
<tr>
<td>92</td>
<td>0.360</td>
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<tr>
<td>96</td>
<td>0.338</td>
</tr>
<tr>
<td>100</td>
<td>0.311</td>
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<td>104</td>
<td>0.290</td>
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<tr>
<td>108</td>
<td>0.268</td>
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<tr>
<td>112</td>
<td>0.248</td>
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<td>116</td>
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</tr>
<tr>
<td>120</td>
<td>0.211</td>
</tr>
<tr>
<td>124</td>
<td>0.197</td>
</tr>
<tr>
<td>128</td>
<td>0.183</td>
</tr>
<tr>
<td>132</td>
<td>0.168</td>
</tr>
<tr>
<td>136</td>
<td>0.156</td>
</tr>
<tr>
<td>140</td>
<td>0.144</td>
</tr>
<tr>
<td>144</td>
<td>0.133</td>
</tr>
<tr>
<td>148</td>
<td>0.125</td>
</tr>
</tbody>
</table>
Figure 1. Guggenheim Plot of 2-Nitropropane-Piperidine Reaction in 50% Acetonitrile-Water, \([B_T] = 0.01\) M. \(k_{obsd} = 3.158 \times 10^{-4}\) sec\(^{-1}\).
Data for Figure 2

Solvent: 50% Acetonitrile-water

\[ [B_T] = 0.057 \text{ M piperidine} \]

\[ \frac{[BH^+]}{[B]} = 0.183 \quad k_{obsd} = 1.734 \times 10^{-3}/\text{sec} \]

\( \Delta t = 14 \text{ min.} \)

<table>
<thead>
<tr>
<th>t (min.)</th>
<th>OD (_t)</th>
<th>OD (_{t-\Delta t})</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>0.699</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0.563</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>0.452</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>0.363</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>0.293</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>0.237</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>0.193</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>0.156</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>0.126</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>0.103</td>
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</tr>
<tr>
<td>34</td>
<td>0.086</td>
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<tr>
<td>36</td>
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<tr>
<td>38</td>
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</tr>
<tr>
<td>44</td>
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</tr>
<tr>
<td>46</td>
<td>0.024</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>0.021</td>
<td></td>
</tr>
</tbody>
</table>
Figure 2. Guggenheim Plot of 2-Nitropropane-Piperidine Reaction in 50% Acetonitrile-Water, $[B_T] = 0.057 \text{ M}$, $k_{obsd} = 1.734 \times 10^{-3} \text{ sec}^{-1}$. 
Data for Figure 3

Solvent: 50% Acetonitrile-water

A. Points marked by $[\text{BH}^+] / [\text{B}] = 0.225$

\[
[\text{B}_T] \ (\text{M}) \quad k_{\text{obsd}} \times 10^4 \ (\text{sec}^{-1})
\]

<table>
<thead>
<tr>
<th>\text{M}</th>
<th>\text{sec}^{-1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.067</td>
<td>16.47</td>
</tr>
<tr>
<td>0.050</td>
<td>12.15</td>
</tr>
<tr>
<td>0.033</td>
<td>8.02</td>
</tr>
<tr>
<td>0.025</td>
<td>6.94</td>
</tr>
</tbody>
</table>

\[
\Rightarrow k_2' = 2.33 \times 10^{-2} \ \text{M}^{-1} \ \text{sec}^{-1}
\]

B. Points marked by $[\text{BH}^+] / [\text{B}] = 0.620$

\[
[\text{B}_T] \ (\text{M}) \quad k_{\text{obsd}} \times 10^4 \ (\text{sec}^{-1})
\]

<table>
<thead>
<tr>
<th>\text{M}</th>
<th>\text{sec}^{-1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.08</td>
<td>17.27</td>
</tr>
<tr>
<td>0.04</td>
<td>8.32</td>
</tr>
<tr>
<td>0.02</td>
<td>4.20</td>
</tr>
<tr>
<td>0.01</td>
<td>2.34</td>
</tr>
<tr>
<td>0.005</td>
<td>1.02</td>
</tr>
</tbody>
</table>

\[
\Rightarrow k_2' = 2.16 \times 10^{-2} \ \text{M}^{-1} \ \text{sec}^{-1}
\]

C. Points marked by $[\text{BH}^+] / [\text{B}] = 0.951$

\[
[\text{B}_T] \ (\text{M}) \quad k_{\text{obsd}} \times 10^4 \ (\text{sec}^{-1})
\]

<table>
<thead>
<tr>
<th>\text{M}</th>
<th>\text{sec}^{-1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.08</td>
<td>12.60</td>
</tr>
<tr>
<td>0.04</td>
<td>5.61</td>
</tr>
<tr>
<td>0.02</td>
<td>2.84</td>
</tr>
<tr>
<td>0.01</td>
<td>1.46</td>
</tr>
<tr>
<td>0.005</td>
<td>0.82</td>
</tr>
</tbody>
</table>

\[
\Rightarrow k_2' = 1.57 \times 10^{-2} \ \text{M}^{-1} \ \text{sec}^{-1}
\]
Figure 3. Plots of \( k_{\text{obsd}} \) vs \([\text{Br}]\) for Reactions of 2-Nitropropane with Piperidine in 50\% Acetonitrile-Water at 3 Buffer Ratios.
k_{OH}[^{[OH]^-}] + k_{H_2O}. k_2' was obtained from these graphs by least squares calculations done on a desk calculator. Figure 3 is a typical example of such a graph, showing the lines obtained at three buffer ratios, as explained in the table of data.

This method appears to be very useful for determining kinetic data of the type presented here. The values determined for k_{obsd} were generally found to be reproducible within 5% or less. The average deviations in the rate constants are less than 2%.

There are some limitations on the use of this method, of course. Although it can be used in a wide range of reactivities, as mentioned earlier, other difficulties arise. The main problems encountered in this investigation were with different solvent systems. Dimethylsulfoxide cannot be used as a solvent in studying the ionization of 2-nitropropane by this method because of the intense absorption of dimethylsulfoxide in the region in which the carbanion absorbs. A different problem was encountered in attempts to use a solvent mixture of N,N-dimethylphosphoramid and water. 2-nitropropane was insoluble in a 50% (v-v) mixture of the two, even though 2-nitropropane is quite soluble in both pure solvents.

Absorption of carbon dioxide in the solutions is a potential problem, but one that can easily be avoided. Any solutions that cannot be used on the day they are prepared should be stored under nitrogen.

The problem of determining k_D in a protic solvent has been discussed earlier. A small, but real, error is introduced in the value of k_D by this method.

An advantage of this method is that rate constants for both the forward and reverse reactions can be obtained. The disadvantage involved is the large number of kinetic measurements required for the determination
of the final rate constants. For example, if four points are considered adequate for the accurate determination of a straight line, sixteen kinetics runs must be made to obtain $k_{2,B}$ and $k_{2,A}$ for one reaction. It is obvious that determining isotope effects in various solvent systems becomes a task of considerable magnitude under these conditions.

The use of non-aqueous solvents introduces the need for some method of equilibrium measurement, as was discussed earlier. Alternatively an established pH scale in solvents other than water would be of considerable value when determining rate constants by this method. When equilibrium data are readily available, as when working in a system with a known pH scale, the problems in using this method are decreased considerably.

The precision of $k_{2,B}$ is questionable because of the number of algebraic manipulations required to obtain it. The plots of $k_{\text{obsd}}$ vs. $[B_T]$ give one measure of this precision with how near the points fall to a straight line. The error indicated by this measurement is 10% or less.

Other workers, previously cited, have successfully applied this method to other systems, so that its general usefulness has been demonstrated.
Experimental

Apparatus. Absorbance measurements were made on a Cary 14 spectrophotometer. Solutions were maintained at 30 ± 0.1°C by circulating water from a Haake circulator through both the sample and reference compartments. pH measurements were taken on a Beckman zeromatic pH meter, using glass and Calomel reference electrodes (Fisher).

Materials. 2-Nitropropane (Eastman White Label) was washed with saturated sodium carbonate, sodium bisulfite, and concentrated sulfuric acid; then distilled (bp 120°) through a 9-in. Vigreux column onto type 4A molecular sieves. G. C. analysis showed the 2-nitropropane to be pure. The 2-nitropropane was diluted in a ratio of 1:250 with p-dioxane (Matheson, Coleman and Bell) which was purified of peroxides, for all non-deuterated solutions, by the method of partial freezing. 2-nitropropane-2-d was obtained with 80% deuterium in the 2-position from Dr. Sophia Wang. This material was refluxed with calcium oxide in deuterium oxide overnight and separated from the water. Fresh deuterium oxide and calcium oxide were added and the mixture was refluxed for 6 hours; then allowed to stand overnight. NMR analysis showed the 2-position to be more than 99% deuterated. The material was dried over magnesium sulfate and distilled, bp = 118°. 2-Nitropropane-2-d was also diluted 1:250 in dioxane which had been refluxed over calcium hydride for 6 hours, after partial freezing; then distilled from fresh calcium hydride and lithium aluminum hydride on a Nester Faust spinning band column. Addition of lithium aluminum hydride showed the distillate to be dry. Acetonitrile (Matheson, Coleman and Bell) was dried over potassium carbonate, then mixed with equal volumes of freshly distilled
water to make 50% acetonitrile-water solutions. Piperidine (Matheson, Coleman and Bell) was distilled from sodium. Some impurity was not completely removed, but was present at such low concentrations (less than 1% by gas chromatography) that it did not hinder the kinetic studies. Concentrated sodium hydroxide (British Drug House) of the type used for making up standard solutions was used undiluted in the equilibrium determination, and was carbonate free. Concentrated hydrochloric acid (Baker and Adamson) was used in making all buffer solutions of piperidine. Potassium chloride (Baker and Adamson) solutions of the appropriate concentration were made up in either water or 50% acetonitrile-water to maintain constant ionic strength in each series of reactions.

Kinetics. The rate of formation of the 2-nitropropane anion was followed by measuring the increase in absorbance at 230 nm. 2-nitropropane-dioxane solutions were added to the cell containing -3 ml. of buffer solution in such quantities (6-10 μl) that the reaction mixtures were approximately 10^{-5} M in 2-nitropropane. The buffer solutions were contained in both the sample and reference cells to compensate for any absorption of the buffer. The reactions were carried out in round cells with 1-cm. path length. Reactions were followed to at least four, and usually five or more, half lives. The temperature of the cells was determined by calibration with a galvanometer, which showed that maintaining the thermometer in the circulator at 30.4°C provided a temperature of 30.0°C in the cells. The measurement of \([R^-]/[RH]\) for determining the equilibrium ratio was made by adding 2-nitropropane-dioxane solution to the buffer in the sample cell as done for kinetic runs, allowing ample time in the thermostatted cell compartment for the system to reach equilibrium, then recording the absorbance of \([R^-]\). A drop of concentrated
sodium hydroxide was then added to the reaction mixture to convert the remaining 2-nitropropane to the anion and a second absorbance reading was taken. The value of this second reading minus that of the first gave $[\text{RH}]$. The ultraviolet absorption spectrum of 2-nitropropyl anion was taken by adding the 2-nitropropane solution to a 0.1 N sodium hydroxide solution in the sample cell, with 0.1 N sodium hydroxide in the reference cell. It showed one broad, intense absorption band from 250 nm, which continued with the absorbance increasing until 217 nm, at which point the slits of the spectrophotometer were completely open, so that $\lambda_{\text{max}}$ and $\epsilon$ could not be determined. The ultraviolet absorption spectrum of 2-nitropropane is very similar to that of the anion, showing only one absorption peak. It appears to be shifted slightly to lower wavelengths than that of the anion. The absorption begins at 245 nm and continues to rise sharply to 205 nm, where the slits of the Cary 14 were opened completely. At 230 nm the absorbance of the 2-nitropropyl anion is ~5 times as intense as that of 2-nitropropane.
Summary

The direct spectrophotometric analysis for carbanions was considered as a method for measuring the kinetics of proton transfer reactions. It was applied to the reaction of 2-nitropropane with piperidine in water and 50% acetonitrile-water solvents. A large solvent effect on the equilibrium was found. Deuterium isotope effects in both solvents were measured and a correlation with the work of Bell and Goodall\textsuperscript{19}, which says that $k_H/k_D$ should be a maximum when $\Delta pK$ is zero, was shown.

This method was considered to be useful over a very wide range of reactivities, but with the disadvantage that a very large number of kinetics runs are required to obtain a rate constant for one reaction.
References

27. Reference 26, p. 659.
30. Reference 29, pp. 4-9, 33-34, 73-74.
33. E. A. Guggenheim, Phil. Mag., 2, 538 (1926).
Appendix

Computer Program for Slope Determination by Least Squares

TYPE: FORTRAN

DIMENSION X(100), CONC(100), Y(100), RES(100), L(100)

PRINT 1
PRINT 2
PRINT 3
PRINT 17
READ 8, N
PRINT 4
PRINT 6
D0 301 I=1, N
READ 9, L(I)
301 X(I)=L(I)
PRINT 5
PRINT 7
D0 303 I=1, N
READ 10, CONC(I)
303 Y(I)=ALOG(CONC(I))
306 CALL LEAST(X, Y, N, A, B)
RATE = -1.0*B
PRINT 2
PRINT 2
PRINT 11, RATE
PRINT 2
PRINT 14
D0 230 I=1, N
RES(I)=Y(I)-B*X(I)-A
IF(X(I) .GE. 0) G0 T0 216
PRINT 9, I
G0 T0 230
216 PRINT 15, I, RES(I)
230 CONTINUE
PRINT 2
PRINT 2
PRINT 16
PRINT 17
READ 8,NBAD
IF (NBAD .EQ. 0) G0 T0 310
PRINT 18
PRINT 17
D0 246 J=1,NBAD
READ 8,I
246  X(I)=-1.0
     G0 T0 306
310  PRINT 12
     READ 13,TEST
     IF (TEST .EQ. 'YES') G0 T0 39
     ST0P
1   F0RMAT("    FIRST ORDER KINETICS")
2   F0RMAT(1H )
3   F0RMAT("HOW MANY POINTS")
4   F0RMAT("INPUT THE TIMES")
5   F0RMAT("INPUT THE CONCENTRATIONS")
6   F0RMAT(" XXXXX")
7   F0RMAT(" X.XXX")
8   F0RMAT(I2)
9   F0RMAT(I5)
10  F0RMAT(F5.0)
11  F0RMAT("K/(TIME) = ",1PE12.5)
12  F0RMAT("ANY MORE DATA")
13  F0RMAT(A3)
14  F0RMAT("POINT RESIDUAL")
15  F0RMAT(I5,F12.4)
16  F0RMAT("NO. OF BAD POINTS")
17  F0RMAT(" XX")
18  F0RMAT("INPUT THE BAD POINTS")
END
SUBROUTINE LEAST (X,Y,N,A,B)
DIMENSION X(100), Y(100)
N1 = N
SX = 0
SY = 0
SX2 = 0
SXY = 0
DO 431 I = 1, N
IF (X(I) .GE. 0) Go TO 411
N1 = N1 - 1
Go TO 431
411 SX = X(I) + SX
SY = Y(I) + SY
SX2 = X(I) * X(I) + SX2
SXY = X(I) * Y(I) + SXY
431 CONTINUE
B = (N1 * SXY - SX * SY) / (N1 * SX2 - SX * SX)
A = (SY - B * SX) / N1
RETURN
END