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of

MIN-MIN WEI

B.Sc., The University of British Columbia
1961

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          S. H. Zbarsky

External Examiner: Harold Shechter
          Department of Chemistry
          Ohio State University
          Columbus, Ohio

A STUDY OF THE MECHANISM OF THE PERMANGANATE
OXIDATION OF AMINES

ABSTRACT

The mechanism of the permanganate oxidation of benzylamine and benzylamine-α-d2 has been investigated in the pH region 2 to 14. The deuterium isotope effect, k_H/k_D, was found to be 7.0 from pH 8 to 10.7. The absence of salt effects and the observation that the oxidation rate followed the ionization process of the benzylammonium ion show that benzylamine is oxidized via the neutral molecule.

Beyond pH 12 the rate of oxidation was found to be directly proportional to the hydroxyl ion concentration.

A study of 11 meta- and para-substituted benzylamines shows excellent Hammett correlation with σ^+ for 8 of the compounds, with the p-nitro, m-nitro, and m-trifluoromethyl derivatives deviating considerably from the Hammett plot. ρ^+ was -0.28. The correlation with σ^+ and the very negative $\Delta S^{\ddagger}$ values obtained for the oxidation reaction show that the transition state must be an ionic one involving extensive charge separation. The rate-determining step is consistent with hydrogen transfer from benzylamine to permaganate but the choice of a hydride ion transfer mechanism or a hydrogen atom transfer mechanism cannot be unequivocally made from the results.

For the oxidations in the highly alkaline regions beyond pH 12, termolecular mechanisms are suggested.

Whereas 0-alkylation protects alcohols from oxidation by permanganate, N-alkylation greatly increases the oxidation rate of amines. However, N-acylation tends to protect the amine from oxidation.

Limited studies of the kinetics of permanganate oxidation of ammonia, cyclohexylamine, N,N-dimethylbenzylamine, and (-)-α-methylbenzylamine were carried out to compare their rates of oxidation with those for benzylamine.

The mechanism of the permanganate oxidation of t-butylamine to t-nitrobutane was studied from pH 8 to 12. As in the benzylamine oxidation t-butylamine is oxidized via its neutral molecule. The absence of an α-hydrogen and the absence of a substantial isotope

effect in t-butylamine-ND_2 suggest that the mechanism involves an oxidative attack on the nitrogen by permanganate.

The formation of a quaternary hydroxylamine derivative between t-butylamine and permanganate has been proposed for the rate-determining step.

The kinetics of permanganate oxidation of benzylamines at $-10°$ in frozen H_2O and D_2O has been investigated from pH 7.5 to 9.3. The reaction order remains unchanged from that at $25°$. The rates of oxidation are more than 10 times greater in ice at $-10°$ than in liquid water at $-10°$, and this acceleration increases with decreasing pH.

An apparent $pK_{BH}+$ of 8.70 was obtained for benzylamine at $-10°$ in ice. No change in the rate was observed when the oxidation was carried out in frozen D_2O and when the ionic strength of the medium was increased.

The accelerating effects observed in the frozen systems are discussed in terms of pH, concentrating effect of the freezing, and the orientating effect of the ice structure.

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MECHANISM OF PERMANGANATE OXIDATION

OF ALIPHATIC AMINES

by

MIN-MIN WEI

B.Sc., University of British Columbia, 1961

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF

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in the Department

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We accept this thesis as conforming to the

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ABSTRACT

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Beyond pH 12 the rate of oxidation was found to be directly proportional to the hydroxyl ion concentration.

A study of 11 meta- and para-substituted benzylamines shows excellent Hammett correlation with σ^+ for 8 of the compounds, with the p-nitro, m-nitro, and m-trifluoromethyl derivatives deviating considerably from the Hammett plot. ρ^+ was -0.28. The correlation with σ^+ and the very negative $\Delta S^{\ddagger}$ values obtained for the oxidation reaction show that the transition state must be an ionic one involving extensive charge separation. The rate-determining step is consistent with hydrogen transfer from benzylamine to permanganate but the choice of a hydride ion transfer mechanism or a hydrogen atom transfer mechanism cannot be unequivocally made from the results obtained in this thesis.

For the oxidations in the highly alkaline regions beyond pH 12, termolecular mechanisms are suggested.

Whereas O-alkylation protects alcohols from oxidation by permanganate, N-alkylation greatly increases the oxidation rate of amines. However, N-acylation tends to protect the amine from

oxidation.

Limited studies of the kinetics of permanganate oxidation of ammonia, cyclohexylamine, N,N-dimethylbenzylamine, and (-)-α-methylbenzylamine were carried out to compare their rates of oxidation with those for benzylamine.

The mechanism of the permanganate oxidation of t-butyl-amine to t-nitrobutane was studied from pH 8 to 12. As in the benzylamine oxidation t-butylamine is oxidized via its neutral molecule. The absence of an α-hydrogen and the absence of a substantial isotope effect in t-butylamine-ND_2 suggest that the mechanism involves an oxidative attack on the nitrogen by permanganate.

The formation of a quaternary hydroxylamine derivative between t-butylamine and permanganate has been proposed for the rate-determining step.

The kinetics of permanganate oxidation of benzylamines at -10° in frozen H_2O and D_2O has been investigated from pH 7.5 to 9.3. The reaction order remains unchanged from that at 25°. The rates of oxidation are more than 10 times greater in ice at -10° than in liquid water at -10°, and this acceleration increases with decreasing pH. For p-nitrobenzylamine there is only a 3-fold increase in rate in going from liquid to frozen water at -10°.

An apparent pK_{BH^+} of 8.70 was obtained for benzylamine at -10° in ice. No change in the rate was observed when the oxidation was carried out in frozen D_2O and when the ionic strength of the medium was increased.

The accelerating effects observed in the frozen systems are discussed in terms of pH, concentrating effect of the freezing,

and the orientating effect of the ice structure.

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And finally, I would like to thank the National Research Council for the financial assistance.

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INTRODUCTION

Permanganate has been extensively used for the oxidation
of organic compounds. The mechanisms by which these oxidations oc-
cur are usually complex; and, depending on the acidity of the medium
in which they take place, the extent of oxidation may vary quite
considerably. In highly alkaline solutions, permanganate is re-
duced via a one-equivalent change to manganese(VI); in alkaline,
neutral and weakly acidic solutions permanganate is reduced to man-
ganese(IV); and in strongly acidic solutions permanganate may be re-
duced by certain reducing agents to manganese(II). Manganese(III)
and manganese(V) are important intermediates of permanganate oxida-
tions, but since they undergo rapid disproportionation to higher and
lower valencies, they are rarely observed in these reactions. They
have been prepared under special conditions, however, and their chem-
istry has been studied.

The properties of each manganese species and their reac-
tions have been reviewed by Stewart (1) and only a brief summary will
be presented here.

Manganese(VI) is stable in solutions of pH 13 or above. In
more acidic media it disproportionates to manganese(VII) and mangan-
ese(IV), the rate of disproportionation increasing with increasing
acidity (2). Except in the case of aromatic aldehyde oxidations (3)
manganate oxidations are usually much slower than the corresponding
permanganate oxidations (4,5). Studies with manganate have been made
on 1,2-diols, phenols and olefinic acids (6).

The potassium salt of hypomanganate, manganese(V), was

first prepared by Lux (7). Pode and Waters (6) found that hypomanganate is stable in solutions more basic than 10N alkali, but below 8N alkali it disproportionates to manganese(VI) and manganese(IV). Hypomanganate is a much weaker oxidizing agent than manganate. It can slowly oxidize primary and secondary alcohols, but does not react with unsaturated acids, tertiary alcohols or phenols (6).

In alkaline and weakly acidic media manganese dioxide is the reduction product of permanganate. The use of phosphate buffers can delay the precipitation of manganese dioxide in solution by forming a complex with it. Heterogeneous reactions with manganese dioxide dispersed in organic solvents are often used for the oxidation of various alcohols, amines, and diarylmethanes (8,9,10,11,12,13,14). Such reactions of manganese dioxide seem to follow radical mechanisms.

The manganic ion (Mn^{III}) is stable in concentrated sulfuric acid solutions. In less acidic media it easily disproportionates to manganese(II) and manganese(IV), unless it is complexed by fluoride or pyrophosphate ions (15,16). In concentrated perchloric acid solutions (1-6M) manganic ions can be generated through anodic oxidation of manganese(II) (17). Recent studies of oxidations by manganese(III) have been made on malonic acid (18), pinacol (19), formaldehyde and formic acid (20).

Manganous ions are end-products of permanganate oxidation in acidic media when strong reducing agents such as iodide, ferrous ions or oxalic acid are used as substrates. The well-known Guyard reaction between manganous and permanganate ions occurs in weakly acidic or neutral solution:

$$2 \, MnO_4^- + 3 \, Mn^{+2} + 2 \, H_2O \rightleftharpoons 5 \, MnO_2 + 4 \, H^+ \qquad (1)$$
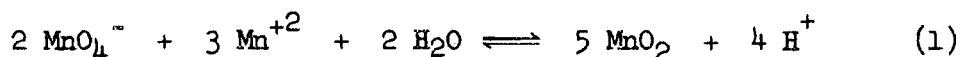
Mechanistic studies on this reaction have been reviewed by Ladbury and Cullis (21).

PERMANGANATE OXIDATIONS OF ORGANIC SUBSTRATES

The reactions of many different classes of substrates with permanganate have recently been examined. A selection of those reactions whose mechanisms have been studied in aqueous solutions and which are pertinent to the present investigation will be reviewed here.

Oxidation of aromatic aldehydes

The oxidation of benzaldehydes from pH 5 to 13 has been studied by Wiberg and Stewart (3). Two mechanisms were proposed for the oxidation: one for the reaction in acidic medium and one for the reaction in basic medium.

In basic solutions from pH 11 to 13 the rates increased with increasing pH, and were subject to specific hydroxyl ion catalysis according to the expression:

$$- \frac{d[MnO_4^-]}{dt} = k \ [PhCHO] \ [MnO_4^-] \ [OH^-]^{1/2} \qquad (2)$$

A negligible deuterium isotope effect was observed for PhCDO, and most of the oxygen in the product came from the solvent. A large, positive rho was obtained from the Hammett plot. For the reaction in the basic solutions, a free radical chain mechanism was suggested.

From pH 6.8 to 11 the rates levelled off and did not change with changing pH. The lowest second order rate constant in this region was 0.370 l.mole^{-1}sec^{-1}.

In more acidic solutions the rates gradually increased again, although the rate of increase was not nearly so great as that in the

basic region. The reactions were general-acid catalyzed, and an iso-
tope effect of 7 was found for PhCDO. The Hammett reaction constant,
ρ, for the reaction was small and negative. The mechanism for the
oxidation in acid solutions involves a fast ester formation between
the aldehyde hydrate and permanganate, followed by rate-determining
proton removal from the aldehydic hydrogen.

In solutions below pH 5 an autocatalytic reaction takes place
between permanganate and benzaldehyde.

Oxidation of alcohols

From the observations of a positive salt effect, a large ne-
gative entropy of activation, and hydroxyl ion catalysis, Stewart con-
cluded that benzhydrol was being oxidized through the benzhydrylate ion
(22). Oxygen-18 studies showed no oxygen transfer from permanganate to
substrate, and an isotope effect of 6.6 for PhCDOHPh showed C-H bond
breaking in the rate-determining step. The following mechanism was
proposed:

$$Ph_2CHOH \ + \ OH^- \ \rightleftharpoons \ Ph_2CHO^- \ + \ H_2O$$

$$Ph_2CHO^- \ + \ MnO_4^- \ \longrightarrow \ Products \qquad\qquad (3)$$
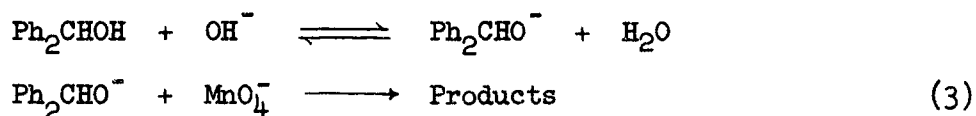
Stewart's proposed hydride transfer mechanism for benzhydrol
led Mocek to study the electronic requirements for this reaction (4).
Experimental difficulties prevented conclusive results, but it appeared
that both electron-withdrawing and electron-donating substituents ac-
celerated the oxidation rate.

Stewart and Van der Linden (23) observed that the rates of
oxidation of aryl trifluoromethyl carbinols followed their ionization
curves, which could be easily determined in the pH region. Observations

of positive salt effects, linear rate versus alkoxide ion dependence, and large entropies of activation support Stewart's previous assumption that the alkoxide ion is responsible for the oxidation with permanganate. An unusually large isotope effect of 16 was found for the 1-deuterio compound, but there was no solvent deuterium isotope effect. The evidence points to a hydride ion transfer mechanism, but substituent effects showed the reaction to be rather insensitive to electronic changes at the reaction site. Various explanations were offered for the latter observation.

Oxidation of fluoral hydrate

Stewart and Mocek (24) studied the permanganate oxidation of fluoral hydrate from 46% sulfuric acid to pH 14. In this wide range of acidities fluoral hydrate manifests itself as the monoanion, the dianion, and the neutral molecule with the relative oxidation rates of these species being as follows:

$$F_3C-\underset{\underset{O^-}{|}}{\overset{\overset{O^-}{|}}{C}}-H \quad \gg \quad F_3C-\underset{\underset{OH}{|}}{\overset{\overset{O^-}{|}}{C}}-H \quad \gg \quad F_3C-\underset{\underset{OH}{|}}{\overset{\overset{OH}{|}}{C}}-H$$
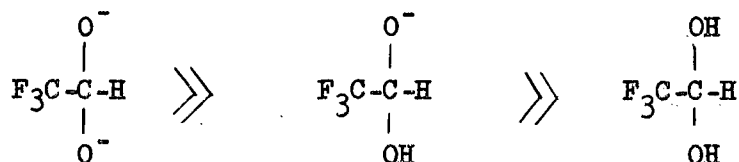
In the highly acidic solutions - up to 46% sulfuric acid - the rate of oxidation was dependent upon the H_- function. This was interpreted as the reaction between permanganic acid and the neutral fluoral hydrate.

In the oxidation of 1-deuterio fluoral hydrate, normal isotope effects were observed for the oxidation of the dianion and neutral species, but as with the fluoro alcohols, a large isotope effect, $k_H/k_D=10$, was obtained for the monoanion. All of the above results appear to favor

a hydride ion transfer mechanism. However, only a four-fold increase in rate was observed for $CF_3CH_2O^-$ compared with $(CF_3)_2CHO^-$, whereas in a hydride transfer mechanism one would expect a much greater difference in rate since the groups $-CF_3$ and $-H$ differ so greatly in their respective inductive effects. The following radical mechanism was also suggested:

$$F_3C-\underset{\underset{OH}{|}}{\overset{\overset{O^-}{|}}{C}}-H \; + \; MnO_4^- \; \longrightarrow \; F_3C-\underset{\underset{\downarrow \text{fast, } Mn^{VI} \text{ or } Mn^{VII}}{}}{\overset{\overset{O^- \quad OH}{\diagdown \; |}}{C_\bullet}} \; + \; HMnO_4^- \qquad (4)$$

$$F_3CCOOH$$
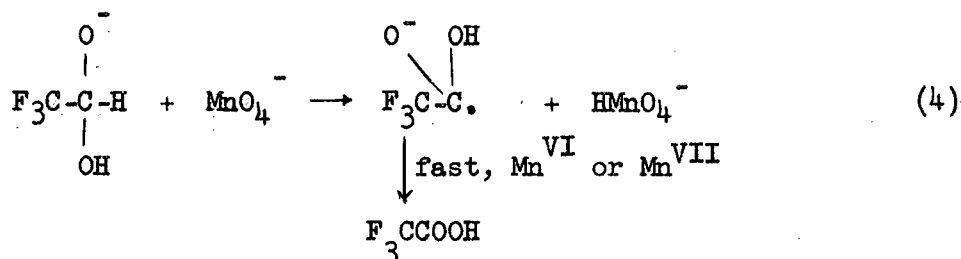
In a recent paper, Kurz (25) examined the results of the oxidation of fluoral hydrate and observed that the kinetic terms for each of the four processes, i.e. the oxidation of neutral fluoral hydrate by permanganic acid, the oxidation of the monoanion by permanganate, the oxidation of neutral fluoral hydrate by permanganate, and the oxidation of the dianion by permanganate, differ only in the extent of protonation of the reactants, so that he was able to calculate, from previously derived equations (26), the three successive $pK_a^{\ddagger}$'s corresponding to the equilibria between the four transition states. From these parameters, which must satisfy the required condition that their values lie between the pK_a of the reactants (zero bond formation) and the pK_a of the products (complete bond formation), he was able to estimate the structures of the various transition states, and to give upper and lower limits to bond-making and bond-breaking in these transition states. He found that if all the mechanisms of fluoral hydrate oxidation involved hydride ion transfer, then the calculated $pK_a^{\ddagger}$'s

satisfied the necessary requirement that their values be between the estimated pK_a's for the initial and final states of the reactants. On the other hand, if hydrogen atom transfers are assumed to be taking place in the four reactions, then the required condition was not satisfied. If two reactions containing nonadjacent total numbers of protons in the reactants proceed by hydrogen atom transfer and the other two proceed by hydride transfer, the required condition for $pK_a^{\ddagger}$ can still be met.

The question of whether a hydrogen atom transfer or a hydride ion transfer mechanism is taking place in a reaction arises in the oxidation of alcohols and fluoral hydrate. The strongest evidence in favor of hydride ion removal is the fact that the rate-controlling step in the oxidation of alcohols is between the anion and permanganate. Moreover, in the fluoral hydrate oxidation large increases in rate are encountered with each additional ionization of the hydrate molecule.

A hydride ion transfer mechanism should be favored by electron-donating substituents; and in the case of the fluoroalcohols, $ArCHOHCF_3$, one would expect a large negative Hammett ρ value (27). Most reactions that are known to involve hydride ion transfers are complicated by pre-equilibrium steps (28) so that the rho for such reactions is not representative of the hydride removal step alone. However, rho values of approximately +2.6 have been obtained for the addition of hydride ion to carbonyl groups (1, 29). For the fluoro alcohol oxidation rho was approximately zero at pH 13, where pre-equilibria are unimportant.

Structural changes should also have a pronounced effect in a hydride transfer mechanism. As mentioned before, only a four-fold difference in rate was observed for $(CF_3)_2CHOH$ and CF_3CH_2OH.

Swain et al (30) have suggested that, due to the nature of the bonding in the transition state of a hydride transfer reaction, deuterium isotope effects should not vary too much with different substituents on the reacting molecule. However, the observed isotope effects for Ph_2CDOH (22), $PhCDOHCF_3$ (23), and $(CF_3)_2CDOH$ (24) are 7:1, 16:1, and 19:1, respectively, at 25°.

A hydrogen atom transfer mechanism should also be considered. Taking the fluoro alcohols as an example, the following mechanism is suggested by Stewart (31):

$$\begin{array}{c} O^- \\ | \\ Ar-\underset{H}{C}-CF_3 \ + \ MnO_4^- \ \longrightarrow \ Ar-\overset{O^-}{\underset{\bullet}{C}}-CF_3 \ + \ HMnO_4^- \end{array} \qquad (5)$$

$$\downarrow \ \text{fast, } Mn^{VII} \text{ or } Mn^{VI}$$

$$Ar-\overset{}{\underset{O}{\overset{\|}{C}}}-CF_3$$
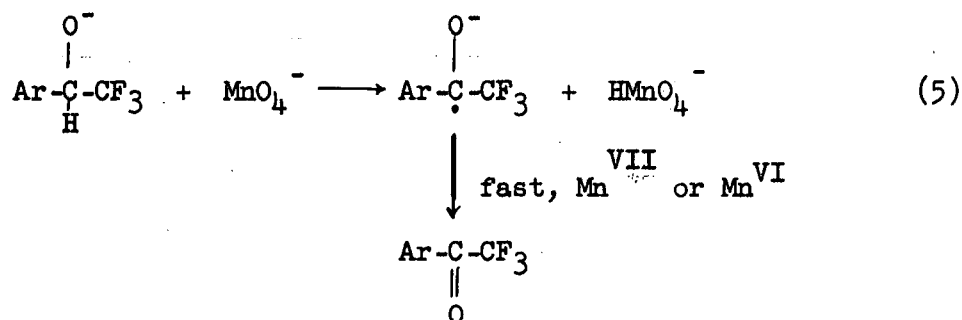
At first glance it is difficult to see why there should be such large differences in rate of hydrogen atom removal from the anion and the neutral molecule. An examination of the probable transition states of the hydrogen atom transfer reaction may help clarify the situation.

$$\begin{array}{ccc} H & & \\ | & & \\ Ph-\underset{Ph}{C}-OH & \longrightarrow [Ph_2\overset{\bullet}{C}-OH] & \quad A \\ & I & \end{array}$$

$$\qquad\qquad\qquad (6)$$

$$\begin{array}{ccc} H & & \\ | & & \\ Ph-C-O^- & \longrightarrow [Ph_2\overset{\bullet}{C}-O^-] & \quad B \\ | & & \\ Ph & II & \end{array}$$
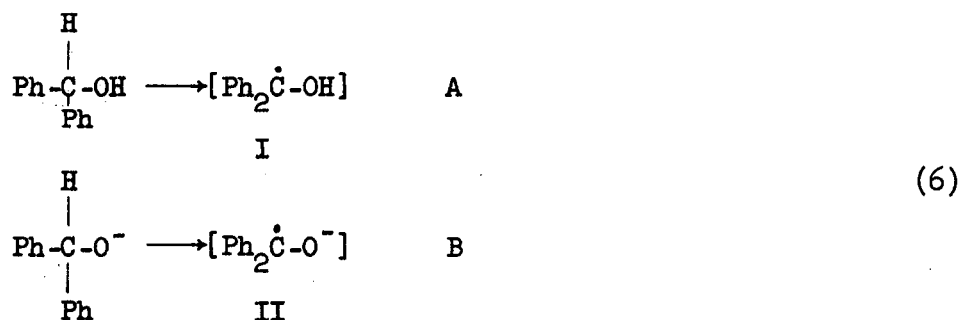
Recently, it was shown by Porter and Wilkinson (32) that the ketyl, $Ph_2\overset{\bullet}{C}$-OH, has a pK near 9, which makes it at least 10^6 times more acidic

than benzhydrol, Ph_2CHOH. This means that the ketyl radical anion (II) must be much more stable with respect to the ketyl radical (I) than is the benzhydrylate ion with respect to benzhydrol. It follows then, that reaction B must be much more energetically favorable than reaction A. Similar arguments can be applied to the case of fluoral hydrate oxidation.

Oxidation of formatopentaammine cobalt(III)

Recently Halpern and Candlin (33) reported the observation that formatopentaammine cobalt(III) can be oxidized by permanganate in a stepwise mechanism in which the first step involves hydrogen atom removal from the formato ligand to give a radical ion intermediate.

The similarity of isotope effects and activation parameters for the above reaction to those for the oxidation of formic acid in aqueous solution (34, 35) led the authors to suggest that the reaction of formate ion with permanganate may also proceed by hydrogen atom transfer rather than hydride ion transfer.

Oxidation of tertiary hydrogens

In the oxidation of S-(+)-4-methylhexanoic acid to R-(+)-4-hydroxy-4-methylhexanoate lactone by permanganate, Wiberg and Fox (36) observed a 42% retention of configuration in the lactone at pH 7 and a 35% retention at pH 13. However, in the oxidation of optically active p-sec-butyl benzoic acid to α-hydroxy-p-sec-butylbenzoic acid there was 100% racemization at pH 7 and only 6% retention at pH 13.

Oxygen-18 studies showed oxygen transfer not only from the permanganate but also from the carboxyl group to the tertiary carbon center. A hydride transfer mechanism was dismissed on account of the

small rate differences between the two substrates. Wiberg and Fox proposed the following hydrogen atom transfer mechanism, followed by three different modes of decomposition to give the observed stereochemistry in the products and to account for the oxygen transfers:

$$R_3CH \; + \; MnO_4^- \; \longrightarrow \; [R_3C \cdot MnO_4 \text{-}H]^- \; \longrightarrow \qquad (7)$$
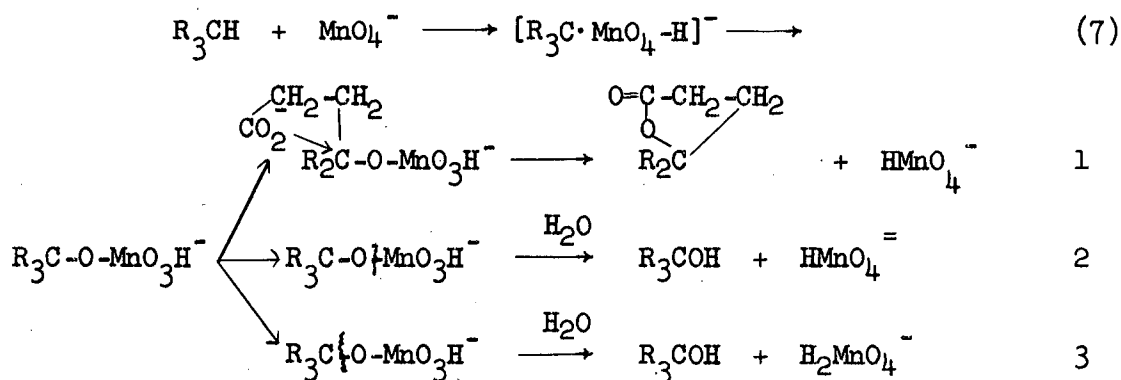
The above mechanism assumes that the C-O-Mn bond is formed while the products are still in the solvent cage. Step 1 in the subsequent decomposition of the manganese ester involves the attack of the carboxylate group on the tertiary carbon, which accounts for the oxygen transfer from carboxyl group and results in 100% inversion of configuration. Step 2 shows the cleavage of the Mn-O bond by hydrolysis to give complete retention and oxygen transfer from permanganate to product. In step 3 the intermediate undergoes an S_N1 reaction to give the carbonium ion which subsequently reacts with water to give the product. This step involves no oxygen transfer. In the case of p-sec-butylbenzoic acid step 3 must be favored since the carbonium ion could be stabilized by the phenyl group. This was shown in the observed decrease in retention of configuration and the decrease in oxygen transfer.

PERMANGANATE OXIDATION OF AMINES

Primary aliphatic amines are usually rapidly oxidized by per-

manganate to give aldehydes and acids (37). Benzylamine is oxidized by
alkaline permanganate to give benzaldehyde, benzoic acid and benzamide
(38). Kornblum and Clutter (39) found that t-butylamine can be oxid-
ized in good yield to t-nitrobutane. The reaction was slow, however,
and required heating.

Secondary dialkylamines are often oxidized to a variety of
products. Permanganate oxidizes diethylamine to ethanol, ammonia,
acetic acid and acetohydroxamic acid (40).

It was found by Labriola et al (41) that tribenzylamine is
oxidized by acidic permanganate to benzaldehyde and benzoic acid, but
that N,N-dimethylbenzylamine is resistant to this type of oxidation.

The parent compound, ammonia, is oxidized by alkaline perman-
ganate to the nitrite ion, and by acidic permanganate to the nitrate
ion (42) Both reactions occur extremely slowly, and the latter reac-
tion requires a high concentration of the ammonium ion.

Hydrazine can be exhaustively oxidized by acid permanganate
to give nitrogen (43), but controlled oxidation of 1,2-disubstituted
hydrazines in acetone solution give high yields of the 1,2-disubstituted
azo compounds (44). Under similar conditions, 1,1-disubstituted hydra-
zines are oxidized to tetrazenes by permanganate (45).

Although permanganate has often been used in the oxidation of
amines, the detailed mechanism of reaction has received little study.

Recently, Shechter, Rawalay and Tubis (46,47) made a systema-
tic study of the products of permanganate oxidation of primary, second-
ary, and tertiary amines in neutral aqueous t-butyl alcohol solutions,
and discussed the possible mechanisms for the various reactions. They
found that using an excess of permanganate, o-, m-, and p-substituted

benzylamines are rapidly oxidized to the corresponding substituted

N-[α-(benzylidene-amino)-benzyl]-benzamides,(I), and N,N'-(imino-

dibenzylidene)-bis-[benzamides], (II), as well as to benzoic acids and

ammonia.

$$Ar-CH=N-CH-NH-C-Ar \qquad (I)$$
$$\overset{|}{Ar} \quad \overset{\parallel}{O}$$

$$Ar-C-NH-CH-NH-CH-NH-C-Ar \qquad (II)$$
$$\overset{\parallel}{O} \quad \overset{|}{Ar} \quad \overset{|}{Ar} \quad \overset{\parallel}{O}$$
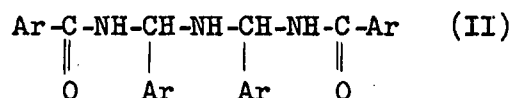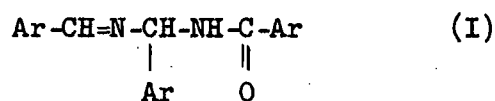
The precise mechanism for the formation of these complex molecules was

not known but it was assumed that benzalimines are the immediate pro-

ducts of the oxidation of benzylamines and that condensation of these

imines with the parent benzylamines together with further oxidation by

permanganate takes place to give (I) and (II).

Studies of the oxidation of benzhydrylamine, dibenzylamine,

and N-phenylbenzhydrylamine with neutral permanganate all follow the

same pattern in that the initial step involves dehydrogenation to the

Schiff base which then rapidly condenses with the parent amine. Taking

N-phenylbenzhydrylamine as an example, the reaction sequence is as

follows:

$$Ph_2CH-NHPh \; + \; MnO_4^- \xrightarrow{-H_2O} Ph_2C=NPh$$

$$\xrightarrow{Ph_2CHNHPh} Ph_2C-\overset{\overset{\textstyle Ph}{|}}{N}-CHPh_2 \qquad (8)$$
$$\underset{NHPh}{|}$$
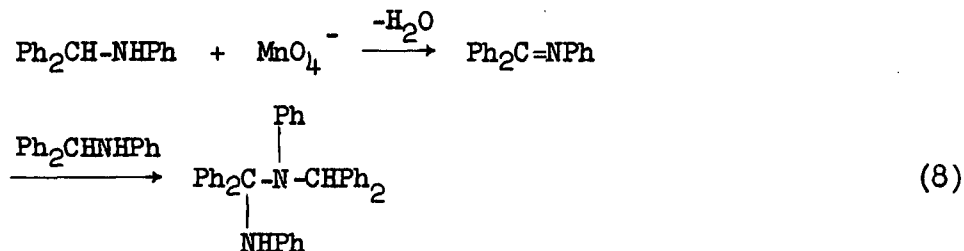
The products, N,N-dibutylformamide, N,N-dibutylbutyramide,

dibutylamine, butyraldehyde, and butyric acid from the oxidation of the

tertiary amine, tributylamine, suggest that the reaction initially

yields the enamine, which then reacts with water to form the precursor

to the observed products:

$$Bu_2NCH_2CH_2CH_2CH_3 \xrightarrow{MnO_4^-} [Bu_2NCH=CHCH_2CH_3] \xrightarrow{H_2O}$$

$$[Bu_2N-CH(OH)-CH_2CH_2CH_3]$$

$$\nearrow Bu_2NH + CH_3CH_2CH_2CHO$$

$$\xrightarrow{MnO_4^-} Bu_2N-\overset{O}{\overset{\|}{C}}-CHCH_2CH_3$$

(9)
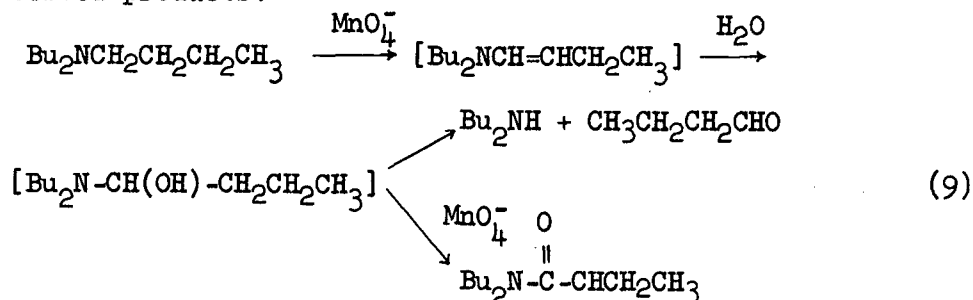
When tribenzylamine, which could not give an enamine intermediate, was oxidized by permanganate, the usual products, benzaldehyde and benzoic acid, are obtained.

OXIDATION OF AMINES BY OTHER OXIDIZING AGENTS

Oxidation by t-butyl hydroperoxide

The reactions of t-butyl hydroperoxide and alkylamines have been extensively studied by De La Mare et al (48,49) and all the evidence support a radical chain mechanism. The reactions may be summarized as follows:

(1) Primary amines

$$RCH_2NH_2 + tR'OOH \longrightarrow RCH=NH + tR'OH + H_2O \qquad (10)$$

(2) Secondary amines

$$(RCH_2)_2NH + tR'OOH \longrightarrow RCH=NCH_2R + tR'OH + H_2O \qquad (11)$$

(3) Tertiary amines

$$(RCH_2)_3N + tR'OOH \longrightarrow RCHO + (RCH_2)_2NH + tR'OH \qquad (12)$$
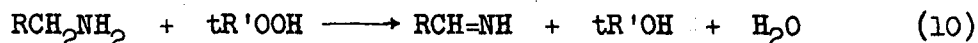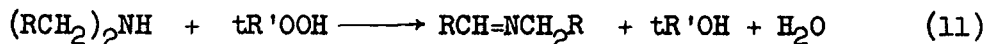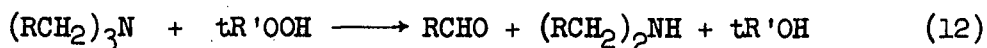
(4) When there are no α-hydrogens adjacent to the amino function, the reaction becomes extremely slow and proceeds by an oxidative attack on the nitrogen to give the nitro compound.

Electron paramagnetic studies showed that an amine oxide free

radical, RR'-CH-NO-CHR'R, is produced in these reactions (49). A mechanism in which this radical takes part in the chain transfer steps to produce other radicals which lead to the products was proposed by De La Mare.

Oxidation by di-t-butyl peroxide

Henbest and Patton (50) observed that the reaction of t-butoxy radicals with dimethylaniline gives tetra-N-substituted 1,2-diamines. Presumably the reaction proceeds by hydrogen atom abstraction from the α-carbon by the t-butoxy radical to give the following alkyl radical (I),

$$Ph-N\underset{CH_3}{\overset{CH_3}{}} + (CH_3)_3C-O\cdot \longrightarrow Ph-N\underset{CH_3}{\overset{CH_2\cdot}{}} + (CH_3)_3COH \qquad (13)$$
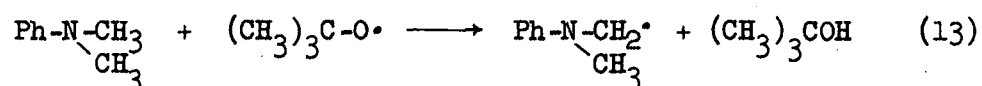
$$I$$

which then dimerizes to give the diamine.

Oxidation by hydrogen peroxide

Tertiary aliphatic amines are oxidized by hydrogen peroxide to amine oxides. It was suggested by Wieland (51) that the reaction occurs by the addition of hydrogen peroxide to the amine to form an ammonium peroxide. Subsequent decomposition yields the amine oxide and water. Oswald and Guertin (52) confirmed this course of reaction from infrared studies but found that the adducts are hydrogen-bonded complexes, not ammonium salts.

Oxidation by benzoyl peroxide

Recently a detailed study was made by Fayadh et al (53) on the reaction of dimethylaniline and benzoyl peroxide. They isolated and characterized the product, N-(p-dimethylaminobenzyl)-N-methylaniline,

(I), and use the previously suggested mechanism by Walling and Indictor (54) to interpret its formation.

$$[Ph-NMe_2O-COPh]^+PhCO_2^- \longrightarrow [Ph-\overset{+}{N}=CH_2 \longleftrightarrow Ph-\overset{+}{N}-CH_3]PhCO_2^-$$
$$\underset{CH_3}{\quad} \quad III \quad \underset{\overset{+}{C}H_2}{\quad}$$
$$II$$
$$+ PhCOOH \qquad (14)$$
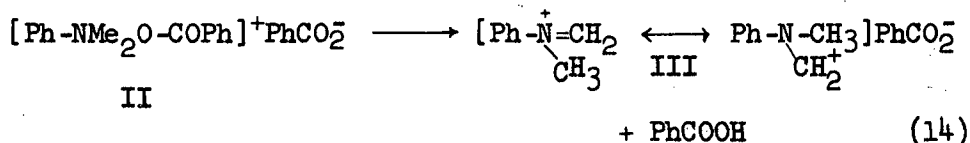
The rate-determining step involves a nucleophilic displacement on the benzoyl peroxide by dimethylaniline to give a quaternary hydroxyl-amine derivative (II), which then decomposes by homolytic N-O bond cleavage and hydrogen atom abstraction from the N-methyl group. The product, (I), arises from a substitution reaction of ion III on dimethylaniline.

Oxidation by Ozone

According to Horner et al (55) formation of N-oxides from tertiary amines in chloroform or methanol occurs by electrophilic attack by ozone on the nitrogen atom, followed by loss of oxygen.

$$R_3N + O_3 \longrightarrow R_3N-\overset{\frown}{O}-O-\overset{\frown}{O^-} \longrightarrow R_3N^+-O^- + O_2 \qquad (15)$$
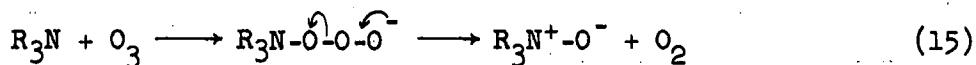
In hydrocarbon solvents, however, Henbest and Stratford (56) found that tri-n-butylamine with ozone gave mainly di-n-butylamine at -78°, and N,N-di-n-butylformamide at 15°. They suggested that an intermediate carbinolamine, (I), is formed which hydrolyzes to di-n-butylamine and butanol in the working-up with water; at higher temperatures it is dehydrated to the enamine, (II), which then reacts with ozone to give N,N-di-n-butylformamide.

$$Bu_2NCH=CHEt \rightleftharpoons Bu_2NCH(OH)-Pr \overset{H_2O}{\longrightarrow} Bu_2NH + PrCHO \qquad (16)$$
$$\underset{\downarrow O_3}{\quad II}$$

$$Bu_2NCHO + EtCHO$$
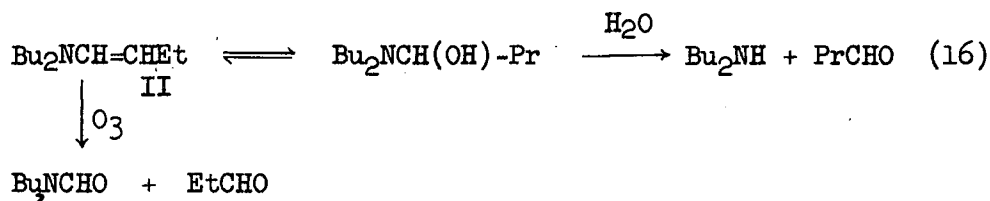
Oxidation by Chromium(VI)

Oxidations of aliphatic primary amines by potassium dichromate usually yields the corresponding aldehydes or acids (57). Bottini and Olsen (58) found that N-alkyl-2,4-dinitroanilines are oxidized by chromic acid to the corresponding carbonyl compounds and 2,4-dinitroanilines. They found no isotope effect when the α-hydrogen on the alkyl group was substituted with tritium.

Oxidation by OF_2

Primary aliphatic amines and ammonia are easily oxidized by oxygen difluoride to the nitroso or oxime compounds at -42° (59). The oxime is formed if there are hydrogens geminal to the amino group. The greatest reactivity is found with t-carbinamines. Aromatic amines are oxidized slowly to give polymeric products, and aromatic and aliphatic amides are unreactive. Presumably the reaction occurs by oxidative attack on the nitrogen and not on the α-hydrogen, since the products are oximes and nitroso compounds. Merritt and Ruff proposed the following mechanism for the oxidation of primary amines by OF_2:

$$R-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{N}}: \; + \; \overset{\overset{F}{}}{\underset{\underset{F}{}}{O}} \longrightarrow \left[R-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{N}}-OF\right]^{+} F^{-} \longrightarrow RN{=}O \; + \; 2\; HF \qquad (17)$$

$$\overset{or}{\searrow} \left[R-\overset{}{\underset{\underset{H}{|}}{N}}-OF\right] \; + \; HF$$
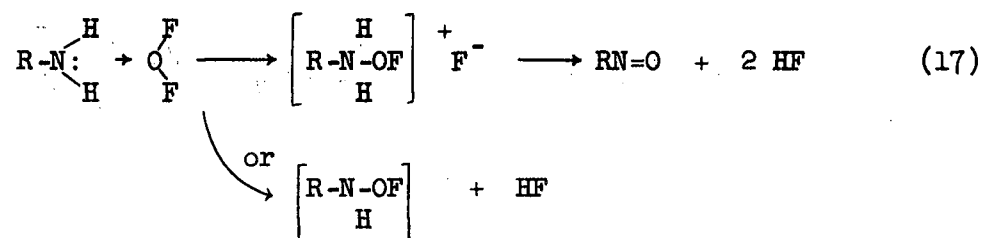
The amine reacts by a nucleophilic attack on the oxygen of OF_2, which is made electropositive by the strongly electron-withdrawing fluorine atoms. Elimination of HF gives the nitroso product.

Oxidation by manganese dioxide

Oxidation of primary aromatic amines with active manganese dioxide produces azobenzenes (13). It was suggested that two amine molecules are first adsorbed onto adjacent "active sites" on the surface of the MnO_2 polymer before being oxidized. It was observed that the more basic amines are preferentially adsorbed. No oxidation was found for nitroanilines and aminobenzoic acids, and it was suggested that this may be due to the preferential adsorption of the nitro and carboxyl groups on the manganese dioxide, which prevents the oxidation of the amino groups.

Recently Pratt and McGovern (60) studied the oxidation of N-alkylanilines to benzalanilines by manganese dioxide. They interpret the observed lack of correlation and small differences in rate with respect to substituent effects as evidence for a radical mechanism.

$$RCH_2NHR' + O=Mn=O \longrightarrow RCH\overset{\cdot}{N}R' + HO-Mn=O$$

$$RCH_2\overset{\cdot}{N}R' + HO-Mn=O \longrightarrow RCH=NR' + HO-Mn-OH$$

$$HO-Mn-OH \longrightarrow H_2O + MnO_2 \tag{18}$$
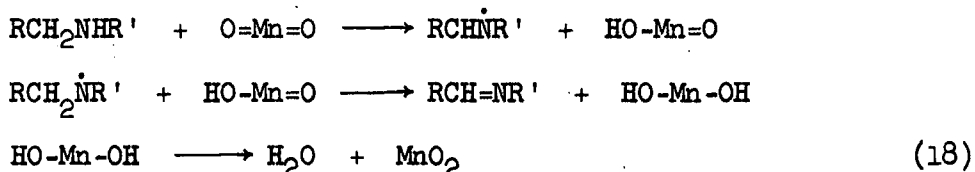
Further support for this mechanism arises from the observations that N-benzylaniline is oxidized more rapidly than dibenzyl and more slowly than hydrazobenzene, and from the fact that effects from substituents are more pronounced when they are attached to the anilino group of N-benzylaniline.

Reactions in Frozen Systems

Studies by Grant et al (61) in 1961 showed that the imidazole-catalyzed hydrolysis of various penicillins proceeds with greater speed

in ice between -5° and -30° than in liquid water. The rates in frozen H_2O were twice those in frozen D_2O.

Recently, kinetic studies on various bimolecular reactions in frozen systems at -10° were carried out by Butler and Bruice (62). They found large rate enhancements over the same reactions in liquid water and suggested that this increase in rate may be due to a concentration of the reactants in liquid pockets between the ice crystals. To test the validity of this assumption, Bruice and Butler (63) studied a typical third order reaction which should give an even more pronounced rate enhancement effect. The observed increases in rate for the general acid and general base catalyzed reactions of thiolactones with morpholine were about 6-7 x 10^3-fold on freezing. A solvent deuterium isotope effect was found to be 1.6. However, freezing changed the reaction mechanism from third order to second order. This last observation does not reconcile with the concentration mechanism suggested formerly, and it was suggested that the enhanced rates may, in fact, be due to a phenomenon which involves the ice structure itself in promoting the acceleration.

SCOPE OF PRESENT RESEARCH

Studies of the oxidation of fluoro alcohols and benzhydrol by permanganate have shown that the reaction takes place between the alkoxide ion and permanganate. As an extension to the work on alcohols it was decided to study the oxidation of a structurally similar class of compounds, aryl alkyl amines.

The initial purpose was to determine whether the oxidative attack occurs at nitrogen or at carbon. If, as in the case of alcohols, oxidation occurs via hydrogen removal from the alpha-carbon, it would be pertinent to determine whether it is removed as a proton, a hydrogen atom or a hydride ion.

Benzhydrylamine is the logical analogue of benzhydrol, but because of its very low solubility in water, a thorough study could not be made on it. Benzylamine was chosen for its much greater solubility in water, and because substituted benzylamines can be prepared without too much difficulty. It was important to determine whether amines are oxidized through the neutral molecule or through the corresponding anion or cation.

The effect of substituents was not too illuminating in the case of alcohols. The ease of preparation of substituted benzylamines and their greater solubility in water would provide a much larger range of substituents that could be examined.

Tertiary carbinamines are known to react very slowly with alkaline permanganate to give the corresponding nitro compounds (39). This is clearly a case of oxidative attack on the nitrogen. The problem was to determine whether this oxidative route is general for all

amine oxidations or whether it is chosen because in this case there are no alpha-hydrogens to be removed.

Another aspect of this research was to examine the effect of N-alkylation or N-acylation on the oxidation, to observe whether it protects the amine from oxidation as O-alkylation of the alcohol does.

Recently, various reactions have been found to proceed much more rapidly in frozen systems than in corresponding liquid systems (61,62,63). One of the theories advanced by Bruice and Butler (63) was that the ice structure may assist in orientating the reactants in such a way as to make the approach of the attacking species more facile.

It was decided to study the oxidation of benzylamines in ice to determine if there might be some orientation of the amino protons by the ice structure in such a way as to facilitate the reaction. Furthermore, since the oxidation process involves hydrogen removal from the substrate, the interaction of the ice lattice and the protons of the substrate might have a profound effect on the reaction.

PART I: OXIDATION OF BENZYLAMINES AND RELATED COMPOUNDS

EXPERIMENTAL

A. Synthesis, purification and identification of amines and related compounds.

1. Synthesis of benzylamine-α-d$_2$

Following the method of Halevi (64) dry benzonitrile (2.22g.) in 20 ml. dry ether was added dropwise to a stirred solution of lithium aluminum deuteride (0.86 g.) in 30 ml. dry ether. The mixture was refluxed for one hour, and decomposed with 20 ml. of 20% sodium potassium tartrate solution. The ethereal solution was separated and dried with sodium sulfate. After removal of the ether, a yellow oil was obtained (1.12 g., 97.5%). The liquid was vacuum distilled and its purity was checked on the Aerograph model A-90 gas chromatograph from which a single sharp peak was obtained.

The ultraviolet spectrum of benzylamine-α-d$_2$ in water gave a sharp peak at 250 mμ and a shoulder at 256 mμ. Benzonitrile in 1% ethanol solution gave peaks at 270 mμ, 278 mμ and a shoulder at 263 mμ. The infrared spectrum showed C-D stretching and bending frequencies and complete absence of C-H and -C≡N absorptions.

2. Synthesis of m-methylbenzylamine, m-methoxybenzylamine and m-chlorobenzylamine by LiAlH$_4$ reduction of the corresponding amides.

A typical procedure was carried out as follows: 23.4 g. m-chlorobenzoic acid and 28 g. thionyl chloride were refluxed in a 200 ml. Erlenmeyer flask over the steam bath for one hour. The condenser was then removed and heating continued until all the excess thionyl chloride had been expelled. The flask was then immersed in an

ice bath and 120 ml. concentrated ammonia solution was cautiously added. The resulting solid was filtered and washed with ice-water. Recrystallizations in aqueous ethanol gave white needles, m p., 134°; lit. 134.5° (65).

Following the method of Micovic and Mihailovic (66) 4 g. m-chlorobenzamide was placed in the thimble of a 100 ml. Sohxlet extractor and 50 ml. dry ether was added. In a 250 ml. round bottom flask below the extractor was placed 5.7 g. LiAlH$_4$ and 150 ml. dry ether. With vigorous stirring the reaction mixture was refluxed for 85 hours, after which time all the benzamide had dissolved. While the flask was cooled in ice the reaction mixture was quenched with 6 ml. water, 8 ml. 20% sodium hydroxide solution and 20 ml. water, successively. The ethereal part was separated from the white granular part by decantation and the latter was washed several times with ether. All the washings were combined and dried with sodium sulfate. Removal of the ether gave approximately 3 ml. of the crude m-chlorobenzylamine. It was possible to purify the acetate and hydrochloride salts by successive sublimations.

Physical properties and analyses

(a) m-chlorobenzylamine

Acetate salt: m.p. 81-2°; calculated for C$_9$H$_{12}$ClNO$_2$: C, 53.59; H, 5.96; N, 6.95; Found: C, 53.69; H, 5.88; N, 6.87.

(b) m-methylbenzylamine

Acetate salt: m.p. 92-4°; calculated for C$_{10}$H$_{15}$NO$_2$: N, 7.73. Found: N, 7.65.

(c) m-methoxybenzylamine

Hydrochloride salt: m.p. 141-2° (lit. 165.5-166.5° (67)); calculated

for $C_8H_{12}ClNO$: N, 8.07. Found: N, 8.16.

Acetate salt: m.p. 94-6°; calculated for $C_{10}H_{15}NO_3$: N, 7.11;

H, 7.62; C, 60.90. Found: N, 7.02; H, 7.89; C, 60.92.

3. Synthesis of p-nitro, m-trifluoromethyl, m-nitro, and p-ethyl

derivatives of benzylamine by a modified Sommelet method (68).

A typical method was carried out as follows: a mixture of 14 g.

finely ground hexamethylene tetramine, 200 ml. chloroform and 17.2 g.

p-nitrobenzyl chloride was refluxed for two hours. The resulting white

salt was filtered and dried in air. To the salt a solution of 17 ml.

concentrated ammonium hydroxide solution and 78 ml. water was added;

the resulting mixture was refluxed for one hour, during which time an

orange syrup formed. The condenser was removed and the mixture was

heated on a steam bath for another hour, during which time the syrup

solidified. The supernatant liquid was decanted and 100 ml. dilute

hydrochloric acid (1:10 dilution of concentrated acid) was added and

the mixture heated over the steam bath until all the liquid had eva-

porated. The p-nitrobenzylamine hydrochloride was recrystallized from

95% ethanol. M.p. 252°d; lit. 250° (69).

Base was added to part of the hydrochloride salt and the re-

sulting amine was quickly extracted with ether. Glacial acetic acid

was then added to the ethereal extract and the resulting acetate salt

was sublimed twice.

Physical properties and analyses

(a) p-nitrobenzylamine

Acetate salt: m.p. 145-7°; calculated for $C_9H_{12}N_2O_4$: C, 50.94;

H, 5.66; N, 13.21. Found: C, 50.75; H, 5.91; N, 13.20.

Hydrochloride salt: m.p. 252°d; lit. 250° (69).

Sulfate salt: m.p. 219-220°; lit. 232° (48, uncorrected value).

(b) m-nitrobenzylamine

Sulfate salt: m.p. 151-2°; calculated for $C_7H_{10}N_2O_6S$: N, 11.15.
Found: N, 10.80.

(c) p-ethylbenzylamine

Hydrochloride salt: m.p. 202-5°d; calculated for $C_9H_{14}ClN$:

Cl, 20.7. Found: Cl, 20.3.

The starting compound, p-ethylbenzyl chloride,was synthesized

according to the method given by Vogel (70), b.p. 92-100° at 15 mm.

(d) m-trifluoromethylbenzylamine

Calculated for $C_8H_8F_3N$: C, 54.83; H, 4.62; N, 8.00. Found:

C, 54.94; H, 4.83; N, 8.11.

Because of the anomalous oxidation rate found for this compound

(see Results section) further checks on the identity of m-trifluoro-

methylbenzylamine were carried out. A single sharp peak was obtained

by vapor phase chromatography. A weighed sample of the liquid amine

dissolved in water to a known volume agreed with its concentration ob-

tained by titration with standard acid to within 4%. A solution of

the amine was oxidized with basic permanganate, and the intermediate,

m-trifluoromethylbenzaldehyde, was isolated as its 2,4-dinitrophenyl-

hydrazone derivative, m.p. 262°; lit. 259-60° (71). Yield, 91.1%.

Further oxidation by basic permanganate produced m-trifluoromethylbenzoic acid which could be recrystallized from carbon tetrachloride. M.p. 100-2°; literature, 103-104.5°. (72).

The infrared spectra of the acetate salt of benzylamine (m.p. 97°; lit. 97.5-98.5° (73)) and of p-nitrobenzylamine were were very similar in that both had broad peaks from 3000 to 2500 cm^{-1} and from 1575 to 1525 cm^{-1}, which were assigned to the protonated amino group. The substituted compound had two very strong peaks at 1523 and 1342 cm^{-1} which were assigned to the nitro group.

An attempted synthesis of p-cyanobenzylamine was carried according to the modified Sommelet method described earlier. No product was obtained. An attempt was made to exchange the bromine in p-bromobenzylamine for the cyano group according to the method described by Friedman and Shechter (74). The yield was very low and infrared studies of the product showed incomplete exchange.

The following amines were obtained from commercial sources: p-methylbenzylamine (Columbia Organic Chemical Co.), DL- ∝-methylbenzylamine, benzylamine, p-methoxybenzylamine, t-butylamine, N,N-dimethylbenzylamine, hexamethylene tetramine (Eastman Organic Chemical Co.), p-chlorobenzylamine (Matheson).

B. Kinetic methods

Aqueous solutions were prepared from freshly distilled amines and distilled water, which had been boiled and saturated with nitrogen in all cases except p-nitrobenzylamine and m-nitrobenzylamine. The acetate salts of these two amines were weighed and solutions were made up in volumetric flasks. The concentrations of all other amines were

determined by titration with standard hydrochloric acid, using methyl red as indicator.

1. Standardization of potassium permanganate solutions

Aliquots of 0.1 N sodium oxalate solution, prepared according to Vogel (75), were titrated with the permanganate solution until just before the end point. Then concentrated sulfuric acid (7.5 ml.) was added to the flask, and titration was completed to a pink end point.

2. Iodometric method

A typical run was carried out as follows: in a 125 ml. stoppered red Erlenmeyer flask were mixed 10 ml. of 1 M disodium hydrogen phosphate buffer, 0.15 ml. of 2.6 M potassium hydroxide, 3.94 ml. of 0.0253 M benzylamine and 33.83 ml. of water. The solution was thermostated at $25.0 \pm 0.02°$ for one hour. The reaction was initiated by injecting, from a 10 ml. syringe, fitted with a Chaney adapter, 2.08 ml. of 0.0319 M potassium permanganate solution. The aliquots were withdrawn with a fast delivery pipet and passed into a quenching solution containing 10 ml. 3M sulfuric acid and 3 ml. 5% sodium bicarbonate solution containing an excess of potassium iodide. The liberated iodine was titrated with an appropriate thiosulfate solution using Thyodene as indicator.

For very slow reactions, the aliquots were delivered at the start of the reaction into stoppered volumetric flasks which were covered with aluminum foil and individually thermostated. At appropriate times the entire content of the flask was quenched and titrated as before.

For reactions from pH 12 to 14 no buffer was used, since the

hydroxyl ion concentration is high enough to act as a buffer.

From pH 2 to 10.8 the ratio of substrate to permanganate used was 3:2. This corresponds to the three equivalent change from Mn(VII) to Mn(IV) and the two equivalent change of the substrate. It was found that from pH 11 to 11.8 this same ratio could still be used to give linear rate plots, although in this region the stoichiometric ratio of substrate to permanganate is difficult to determine since the dispro- portionation of any manganate that is formed is not instantaneous but is time and pH dependent. In addition the imine and aldehyde interme- diates are possibly subject to oxidation by permanganate and manganate. For these reasons only initial rates up to 30% reaction were taken. Above pH 12 manganate is stable and the stoichiometric ratio of sub- strate to permanganate used was 1:2.

For the 3:2 ratio of substrate to permanganate, the following integrated second order rate expression was used (3):

$$k_2 = \frac{1}{[\text{amine}]_o t} \times \frac{V_o - V_t}{V_t - \frac{2}{5} V_o}$$

where V_o = volume of thiosulfate at t=0

V_t = volume of thiosulfate at time t

$\frac{2V_o}{5}$ = volume of thiosulfate at infinite time (calculated)

t in minutes

$[\text{amine}]_o$ = amine concentration at t=0

For the alkaline region from pH 12 to 14, the ratio of substrate to permanganate of 1:2 was found to be in error since in this region the oxidation of the amine by manganate was quite appreciable and since the intermediate, benzaldehyde, is rapidly oxidized by permanganate and

manganate to benzoic acid. Accordingly a 3:4 ratio would be required. However, the following integrated expression (see derivation in the Appendix) correcting for the excess permanganate was used with satisfactory results:

$$k_2 = - \frac{4.60}{[\text{amine}]_o \, t} \log \left(\frac{V_t - \frac{3}{5} V_o}{V_t - \frac{2}{5} V_o} \right)$$

The plot of $\left(V_o - V_t / V_t - \frac{2}{5} V_o \right)$ and $\log \left(V_t - \frac{3}{5} V_o / V_t - \frac{2}{5} V_o \right)$ versus time gave straight lines.

3. Oxidation by manganate

Manganate was produced _in situ_ by adding an equivalent amount of sodium sulphite to a solution of permanganate at pH 13. Benzylamine was added to the resulting manganate solution and the rate of reaction was followed iodometrically. The following integrated second order expression employed by Stewart for manganate oxidations of benzaldehydes (3) was used:

$$k_2 = \frac{1}{[\text{amine}]_o \, t} \times \frac{V_o - V_t}{V_t - \frac{1}{2} V_o}$$

Initial rates were taken since the intermediate, benzaldehyde, is rapidly oxidized by manganate.

4. Oxidations in deuterium oxide

Separate 25 ml. stock solutions of the following compounds were prepared in water and in D_2O: potassium permanganate (0.11852 g.), dipotassium hydrogen phosphate (0.43555 g.), and benzylamine (0.12225 g.). The reaction vessel consisted of 10 ml. of amine solution, 10 ml. of

phosphate buffer, 20 ml. water or D_2O, and 10 ml. potassium permangan-
ate solution. The rate measurements were carried out at 25.0 $\pm$ 0.02°
in the usual manner. The ratio of exchangeable deuterons and protons
in the amine-buffer-deuterium oxide system above is 1:2800, meaning
that the substrate is approximately 99.9% $PhCH_2ND_2$.

5. Oxidation of (-)- α -methylbenzylamine

Optically active (-)- α -methylbenzylamine was prepared by
converting the racemic starting compound to its salt with d-tartaric
acid (76). Fractional recrystallization yielded the (-)-isomer which
was then regenerated with base and distilled. Rotations were taken
on an ETL-NPL automatic polarimeter, type 143A, with a 0.5 dm. cell.
The amine obtained from this method gave an optical purity of 33%.

The rate of oxidation of (-)- α -methylbenzylamine was fol-
lowed iodometrically on a solution consisting of: 10 ml. of 1 M phos-
phate buffer, 25 ml. of (-)- α -methylbenzylamine solution (0.0295 M),
11 ml. of water, 0.34 ml. of 2 M potassium hydroxide, and 3.66 ml. of
0.134 M potassium permanganate. Another solution was allowed to react
for 0.95 minutes at which time a 25 ml. aliquot was withdrawn and
passed into a quenching solution of 5 ml. of 5% sulfuric acid and 5 ml.
of 0.5 M sodium bisulfite solution. A 25 ml. aliquot from a blank using
the same reactants but substituting the potassium permanganate with
water was quenched in the same manner. The rotations of the two
quenched solutions were then taken.

C. Benzylamine product analysis

1. Determination of ammonia

Into a 250 ml. round bottom flask equipped with dropping funnel and reflux condenser were placed 10 ml. of 1 M phosphate buffer, 10 ml. of 0.0412 M benzylamine, 1 ml. of 1 N sodium hydroxide, 12 ml. of water, and 17 ml. of 0.0323 M potassium permanganate. The pH of the solution was 10.32. After the solution had stood for two hours and 32 minutes (the calculated time for 98% reaction), 8 ml. of 0.5 N sodium bisulfite was added via the dropping funnel. This addition was followed by 4 ml. of 10 M sodium hydroxide and 40 ml. of water. The apparatus was immediately set up for distillation. The distillate was collected in an ice-cooled volumetric flask containing 25 ml. of 0.15 N sulfuric acid. After more than half of the reaction solution had distilled the contents in the receiver were titrated with standard base, using methyl red as indicator.

2. Determination of benzaldehyde

The same reaction as described above was carried out at pH 10.43 for 16 minutes. The solution was quenched with an acidic sodium bisulfite solution. After cooling in an ice bath, 15 ml. of 0.04 M 2,4-dinitrophenylhydrazine solution was added and the mixture was stored overnight in the refrigerator. The 2,4-dinitrophenylhydrazone was filtered onto a weighed crucible, dried for four hours in a 60° oven, cooled in a vacuum desiccator over phosphorous pentoxide and weighed. The corresponding aldehydes from the substituted benzylamines were analyzed in the same manner.

RESULTS

Stoichiometry

In the pH region below 12 permanganate is reduced via a three-equivalent change to manganese dioxide. Benzylamine is initially oxidized by permanganate to benzalimine, which then condenses with the parent benzylamine to form various polymers (47). The stoichiometry for the first part of the reaction between permanganate and benzylamine can be represented as:

$$3 \text{ PhCH}_2\text{NH}_2 + 2 \text{ MnO}_4^- \longrightarrow 3 \text{ PhCH=NH} + 2 \text{ MnO}_2 + 2 \text{ H}_2\text{O} + 2 \text{ OH}^-$$
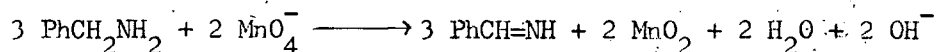
$$(19)$$

In the acidic solutions the imine is rapidly hydrolyzed to benzaldehyde (77) and the reaction is then complicated by the subsequent oxidation of benzaldehyde. Since benzaldehyde oxidation is very much faster in acid solutions than that of benzylamine, two equivalents of permanganate were used, thus converting the amine to the carboxylic acid.

Product analysis

As stated in the Experimental section the benzaldehyde or benzalimine was isolated as the 2,4-dinitrophenylhydrazone derivative. Since both the imine and the aldehyde give the same derivative, and since the imine cannot be isolated, the aldehyde will henceforth be shown as the product.

Table I

Product Study of the Oxidation of Benzylamines

Amine	% X-C$_6$H$_4$CHO (a)	M.p.	M.p. (lit.)
C$_6$H$_5$CH$_2$NH$_2$	94.8	235-239°	237° (65)
m-CF$_3$C$_6$H$_4$CH$_2$NH$_2$	91.1	262°	259-260° (71)
(CH$_3$)$_2$NCH$_2$C$_6$H$_5$	94.8	234-238°	237° (65)

(a) Isolated as the 2,4-dinitrophenylhydrazone derivative

After 98% reaction, a yield of 93% ammonia was obtained from the oxidation of benzylamine.

Order of the reaction

Using stoichiometric quantities of permanganate and benzylamine the rate data were found to fit second order integrated rate expressions used by Stewart (3), using iodometric titration methods of analysis (Figure 1). The rate plots were linear in most cases up to at least 50% reaction before levelling off. In very acidic solutions the rate plots are linear for approximately 20% reaction and then rise sharply in an autocatalytic manner. This latter phenomenon was partly subdued when enough permanganate was added to oxidize the benzaldehyde (see Figure 2). But it must be pointed out that the permanganate oxidation of benzaldehyde itself becomes autocatalytic in acid regions (3).

Effect of ionic strength

Oxidations of benzylamine at pH 10.43 with increasing concentrations of potassium sulfate (μ varied from 0.4 to 1.2) showed no ionic strength effect on the rate of reaction.

FIG. 1

OXIDATION OF BENZYLAMINE

TYPICAL RATE PLOT

pH = 9.90

$$[C_6H_5CH_2NH_2]_o = \frac{3}{2} [MnO_4^-]_o = 8.24 \times 10^{-3} \text{ M}$$

TIME IN MINUTES

33
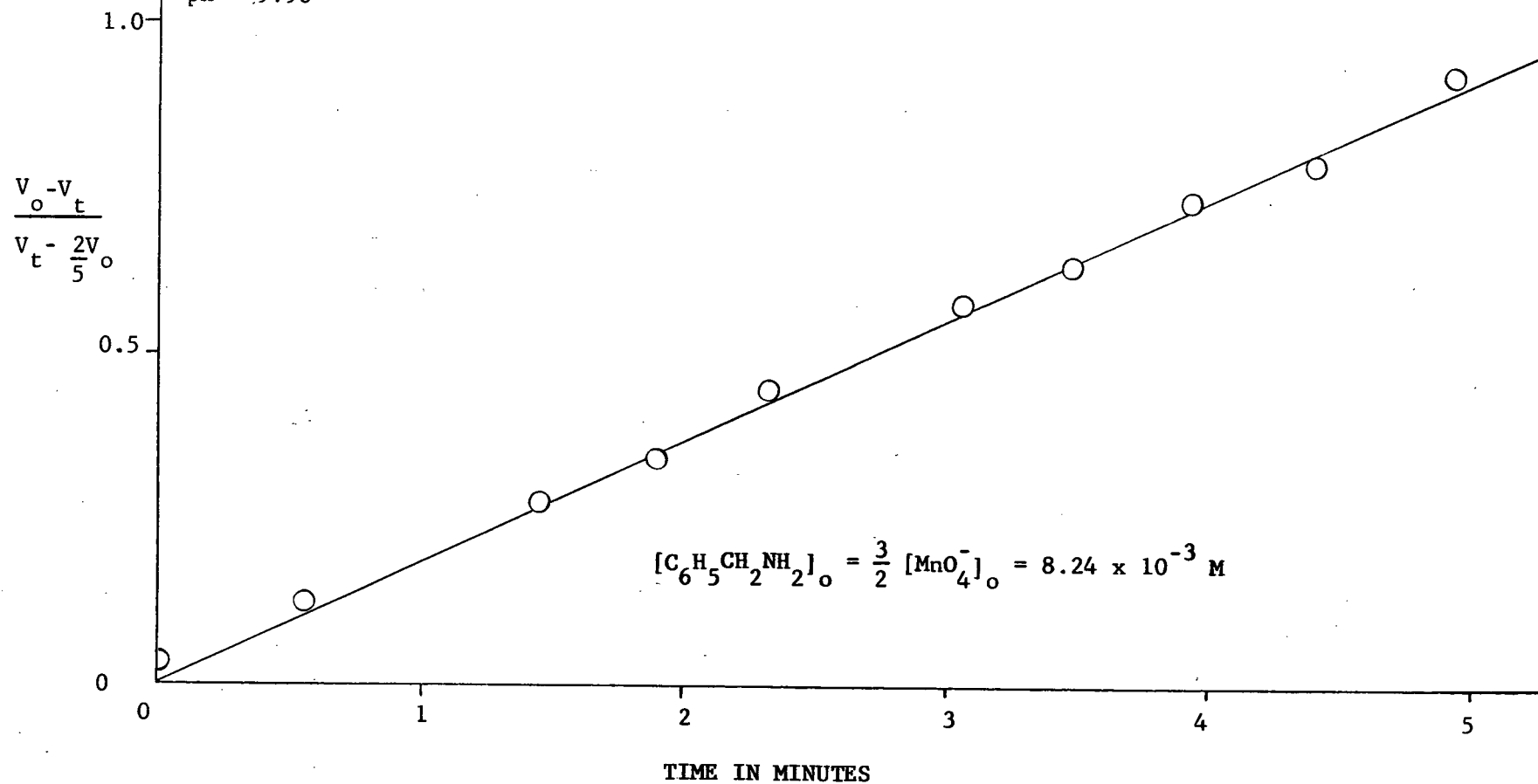
FIG. 2

OXIDATION OF BENZYLAMINE

TYPICAL RATE PLOT

pH = 7.62

$\dfrac{V_o - V_t}{V_t - \frac{2}{5}V_o}$

$[C_6H_5CH_2NH_2]_o = \frac{3}{4} \, [MnO_4^-]_o = 8.24 \times 10^{-3} \, M$

TIME IN MINUTES

34
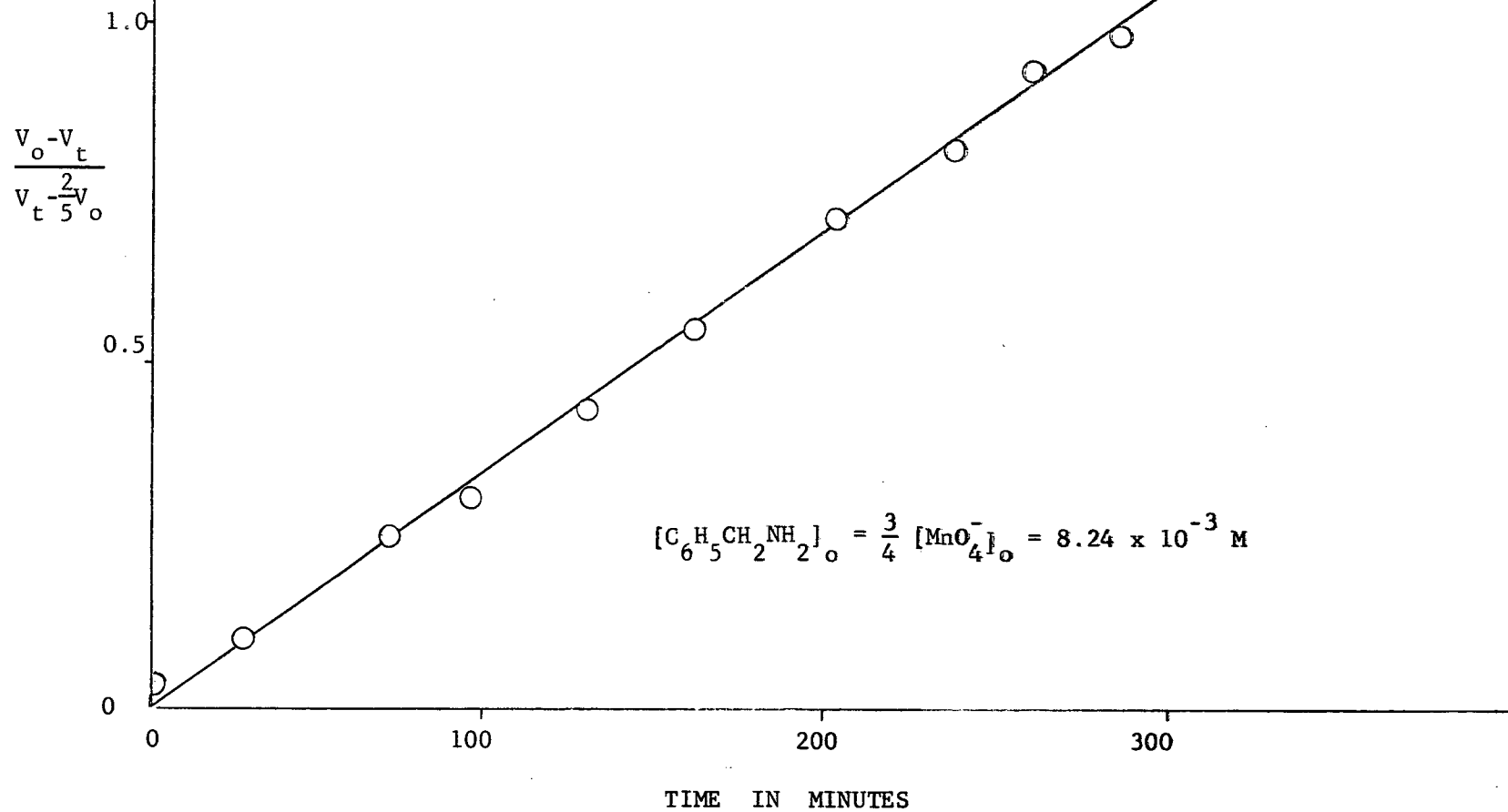
pH-Rate Profile

The rate of benzylamine oxidation increases with increasing pH, but the dependence is not linear (see Table 2). A plot of the rate constant versus pH produced a typical ionization curve (Figure 3) Since the concentration of permanganic acid in this region is negligible (78,4) the rate must be following the ionization process of benzylamine.

If the ionization is indeed that of benzylamine and if in the following relation

$$pK_{BH}^+ = pH + \log \frac{\alpha}{1-\alpha} \qquad (20)$$

where α = fraction of unionized benzylamine, one substitutes the identity

$$\log \frac{\alpha}{1-\alpha} \equiv \log \frac{\frac{k_2}{max}}{k_2^{max} - k_2}$$

then the plot of $\log \left(k_2/k_2^{max} - k_2 \right)$ versus pH, where k_2^{max} is read from the graph, should give a straight line of unit slope whose intercept is the pK_{BH}^+ of the benzylammonium ion. Figure 4 shows that this relation is indeed obeyed, and the pK_{BH}^+ of benzylamine is 9.28. This value is very slightly lower than the literature value of 9.34 (79). Although Mocek found a lowering of the pK_a of fluoral hydrate with increasing ionic strength (4), it is not certain how ionic strength will affect the ionization of substituted ammonium ions. In the former case, ions are produced from a neutral molecule, whereas in the latter case, there is no net change in charge upon dissociation.

Consider the following acid-base equilibrium:

$$A_1 + B_2 \rightleftharpoons A_2 + B_1 \qquad (21)$$

FIG. 3
OXIDATION OF BENZYLAMINE
RELATION BETWEEN RATE CONSTANT
AND pH

FIG. 4

OXIDATION OF BENZYLAMINE

LINEAR RELATION BETWEEN pH

AND LOG $\dfrac{k_2}{k_2^{max} - k_2}$

SLOPE = 1.0
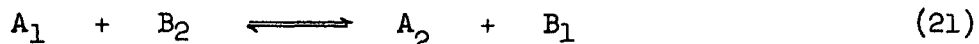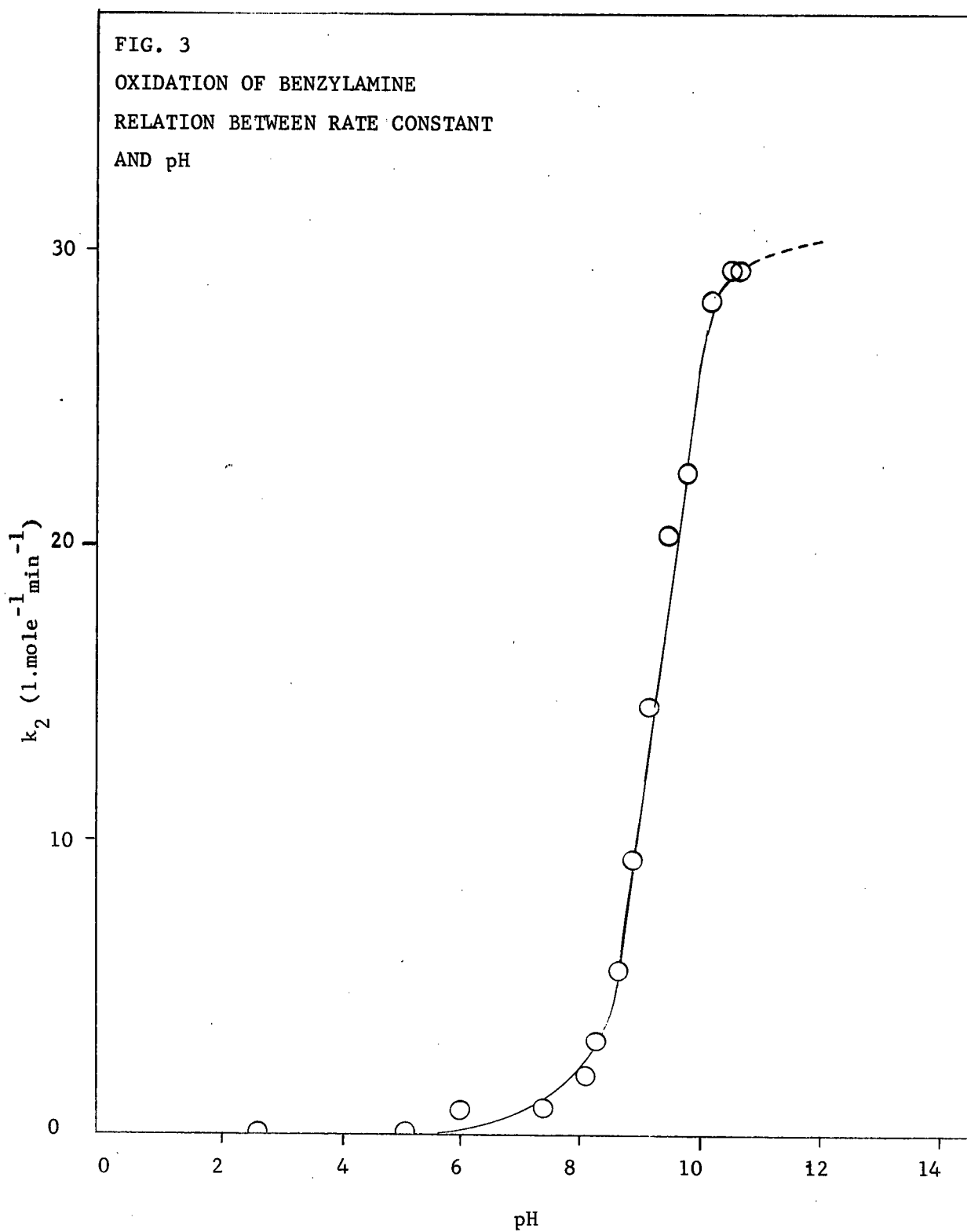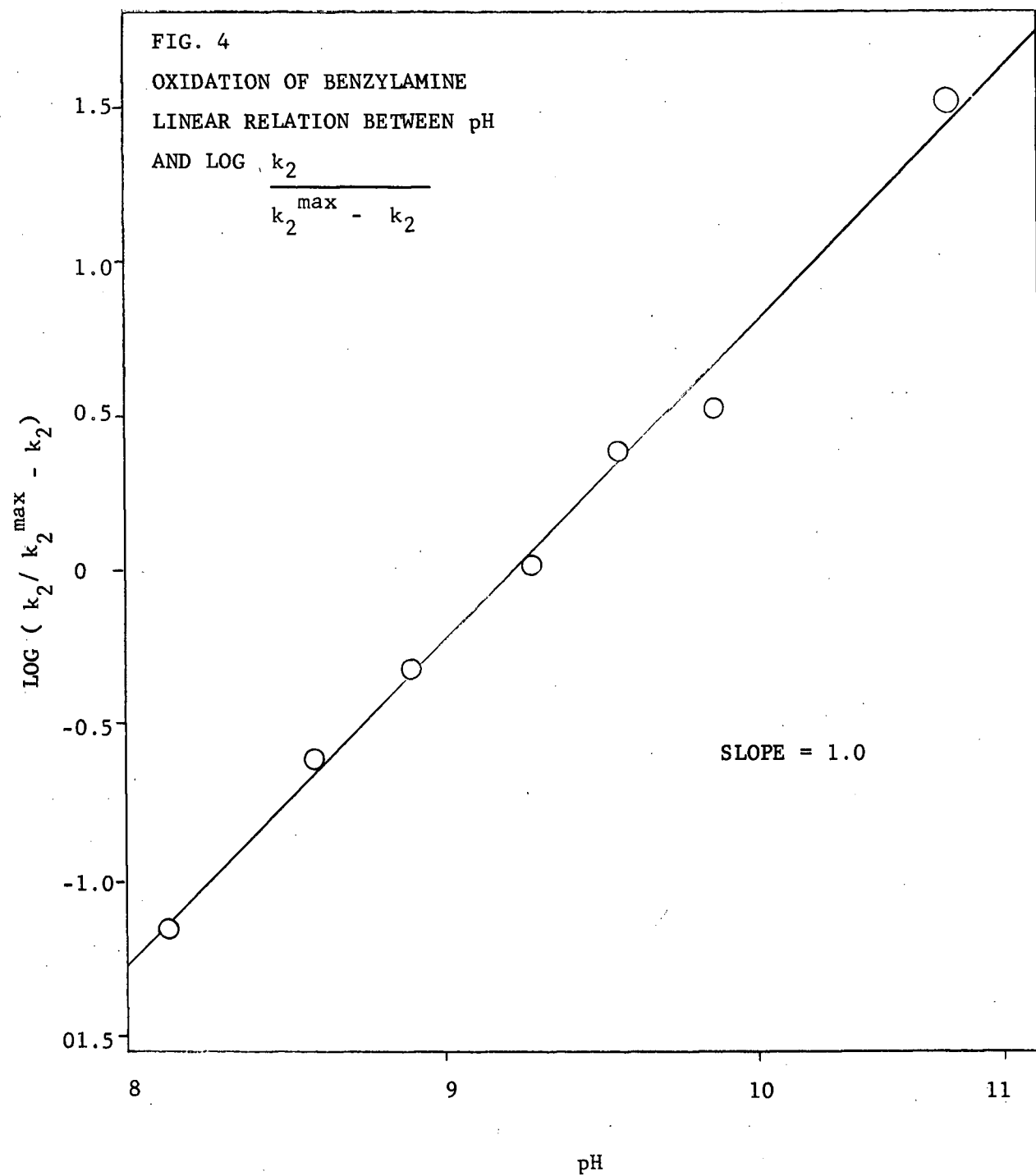
Table II

Oxidation of Benzylamine in the Region pH 2 to 14

Variation of the Rate Constant with pH

pH	k_2 (l.mole^{-1}min^{-1})	pH	k_2 (l.mole^{-1}min^{-1}
2.62	0.033 (a)	10.32	28.3 (a)
5.12	0.0147	10.65	29.0
5.87	0.0491	10.70	29.2
5.99	0.0638	8.25	2.95 (b)
6.52	0.0900	10.21	32.8
7.40	0.691	11.19	32.3 (c)
7.53	0.350	11.42	33.3
7.62	0.142	11.77	33.0
8.12	1.77	12.04	32.6 (d)
8.60	5.39	13.00	35.3
8.92	9.10	13.78	50.1
9.31	14.5	14.00	61.2
9.59	20.2		
9.90	22.3		

(a) [Benzylamine]$_o$ = $\frac{3}{2}$ [MnO$_4^-$]$_o$ = 0.00824 M

(b) [Benzylamine]$_o$ = $\frac{3}{2}$ [MnO$_4^-$]$_o$ = 0.00199 M

(c) [Benzylamine]$_o$ = $\frac{3}{2}$ [MnO$_4^-$]$_o$ = 0.00197 M

(d) [Benzylamine]$_o$ = $\frac{1}{2}$ [MnO$_4^-$]$_o$ = 0.000663 M, no buffers used

Temperature = 25.0 $\pm$ 0.02°

μ = 0.6

If K_0 is the equilibrium constant in water and K is the equilibrium

constant in any other solvent, then

$$\frac{K}{K_0} = \frac{f^{\circ}_{A_1} \; f^{\circ}_{B_2}}{f^{\circ}_{A_2} \; f^{\circ}_{B_1}} \tag{22}$$

where f° is the activity coefficient in water. Equation 22 expresses

the relative strengths of A_1 and A_2 in water and in any other solvent.

In order for these relative strengths to be the same, the function,

$f^{\circ}_{A_1} f^{\circ}_{B_2} / f^{\circ}_{A_2} f^{\circ}_{B_1}$ must be unity. In the case where the equilibrium is re-

presented by the following equation

$$R_1NH_3^+ \;+\; R_2NH_2 \;\rightleftharpoons\; R_2NH_3^+ \;+\; R_1NH_2 \tag{23}$$
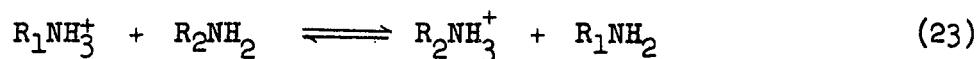
Bell (80) predicts that the function,

$$f^{\circ}_{R_1NH_3^+} \; f^{\circ}_{R_2NH_2} \; / \; f^{\circ}_{R_2NH_3^+} \; f^{\circ}_{R_1NH_2}$$

will not deviate too greatly from unity, such that the relative

strengths of K and K_0 will be constant over a wide range of solvents.

Analogously, the ionization of benzylammonium ion in water can be re-

presented by the following equation:

$$PhCH_2NH_3^+ \;+\; H_2O \;\rightleftharpoons\; PhCH_2NH_2 \;+\; H_3O^+$$
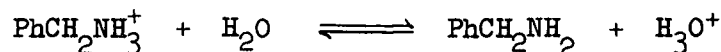
where H_2O replaces R_2NH_2 in equation 23. If the same assumption holds

for the benzylammonium ion ionization, i.e. that the ratio of the acti-

vity coefficients be unity over a wide range of concentrations, then

it is not surprising that the $pK_{BH}+$ value obtained in the solutions

used for the present kinetic studies, where the ionic strength ap-

proaches unity, agrees so closely with the value obtained in water (79).

The preceding results suggest that the rate is dependent on

the free amine. Since the $pK_{BH}+$ is already determined the concentra-

tion of the free amine for each pH can be easily calculated using the

relation,

$$[B] = \frac{[B]^+ [BH^+]}{1 + x} \qquad (24)$$

where [B] = concentration of free amine

[BH$^+$] = concentration of benzylammonium ion

x = [BH$^+$]/[B]

log x = pK_{BH}+ - pH

the plot of k_2 versus [B] is linear (Figure 5) and the plot of log k_2 versus log [B] is also linear giving a slope of 1.0 (Figure 6). This clearly shows that the oxidation is dependent on the first power of the free amine as well as on the first power of the permanganate.

Although the rate-pH profile for the oxidation of benzylamine levelled off in the region pH 11 to 12 as all the ammonium ion was converted to free amine, a further increase in rate occurred in strongly basic media. The rates from pH 12.04 to 14 were found, in fact, to increase linearly with increasing hydroxyl ion concentration (see Figure 7). The extrapolated rate constant at [OH$^-$] = 0 was 32 l.mole^{-1}min^{-1} which corresponded approximately to the rate constant obtained at the maximum of the ionization curve of the benzylammonium ion. A typical rate plot is shown in Figure 8 for the rates in the highly basic region.

It appears that benzylamine is oxidized in the highly basic region to benzoic acid, since the intermediate, benzaldehyde, is rapidly degraded to benzoic acid by both permanganate and manganate under the conditions. Oxidation of benzylamine by manganate at pH 13 gave a second order rate constant of 15.3 l.mole^{-1} min^{-1}, which is about 2/5 as fast as the rate of oxidation of benzylamine by permanganate at the

FIG. 5

OXIDATION OF BENZYLAMINE

RELATION BETWEEN RATE CONSTANT AND

NEUTRAL BENZYLAMINE CONCENTRATION

k_2 (1. mole^{-1} min^{-1})

k_2^{max}

$[C_6H_5CH_2NH_2] \times 10^3$ M

41

FIG. 6
OXIDATION OF BENZYLAMINE
RELATION BETWEEN LOG k_2 AND
LOG $[C_6H_5CH_2NH_2]$

LOG k_2

SLOPE = 1.0

LOG $[C_6H_5CH_2NH_2]$

FIG. 7
OXIDATION OF BENZYLAMINE IN
ALKALINE SOLUTIONS
RELATION BETWEEN RATE CONSTANT AND
$[OH^-]$
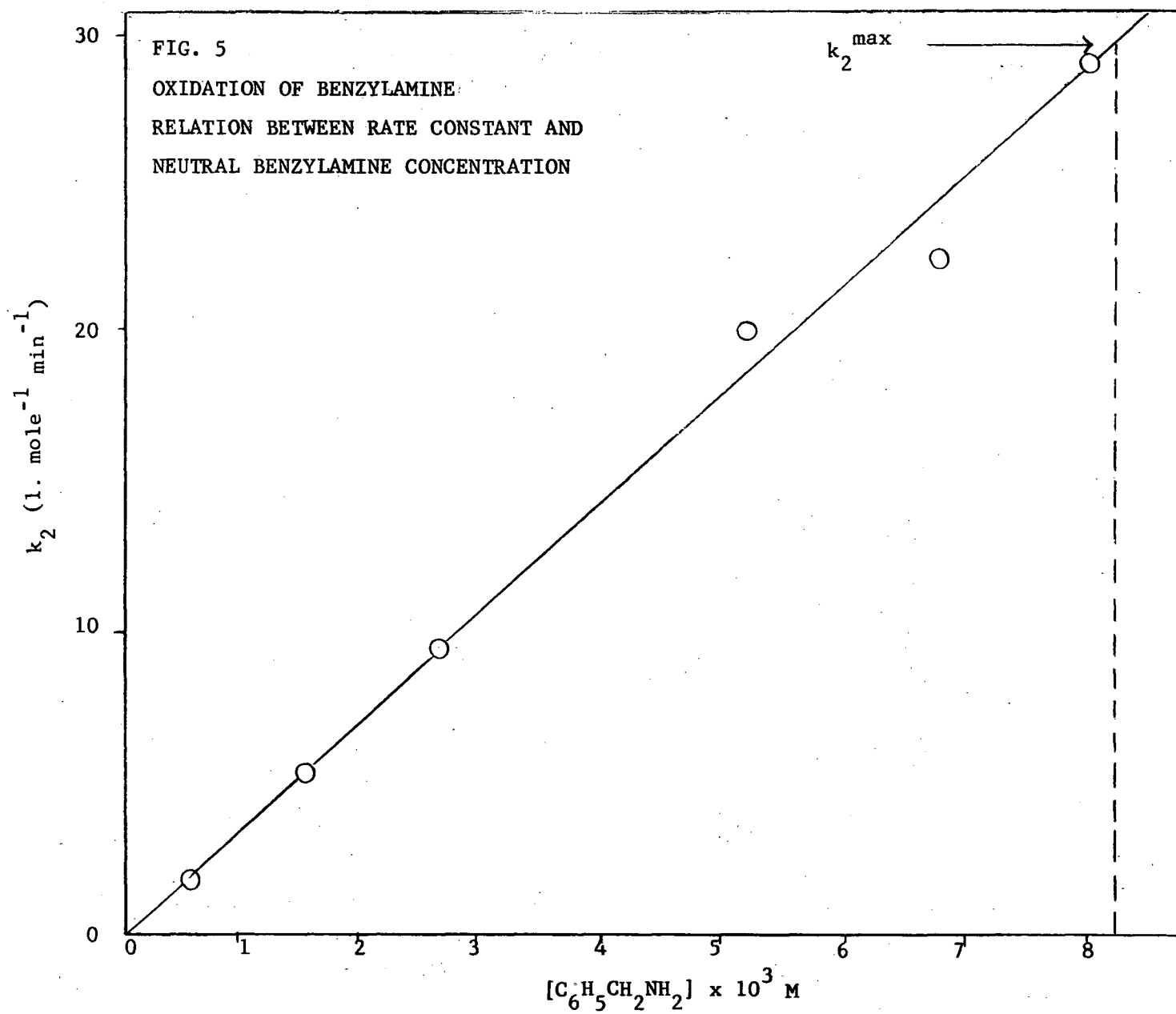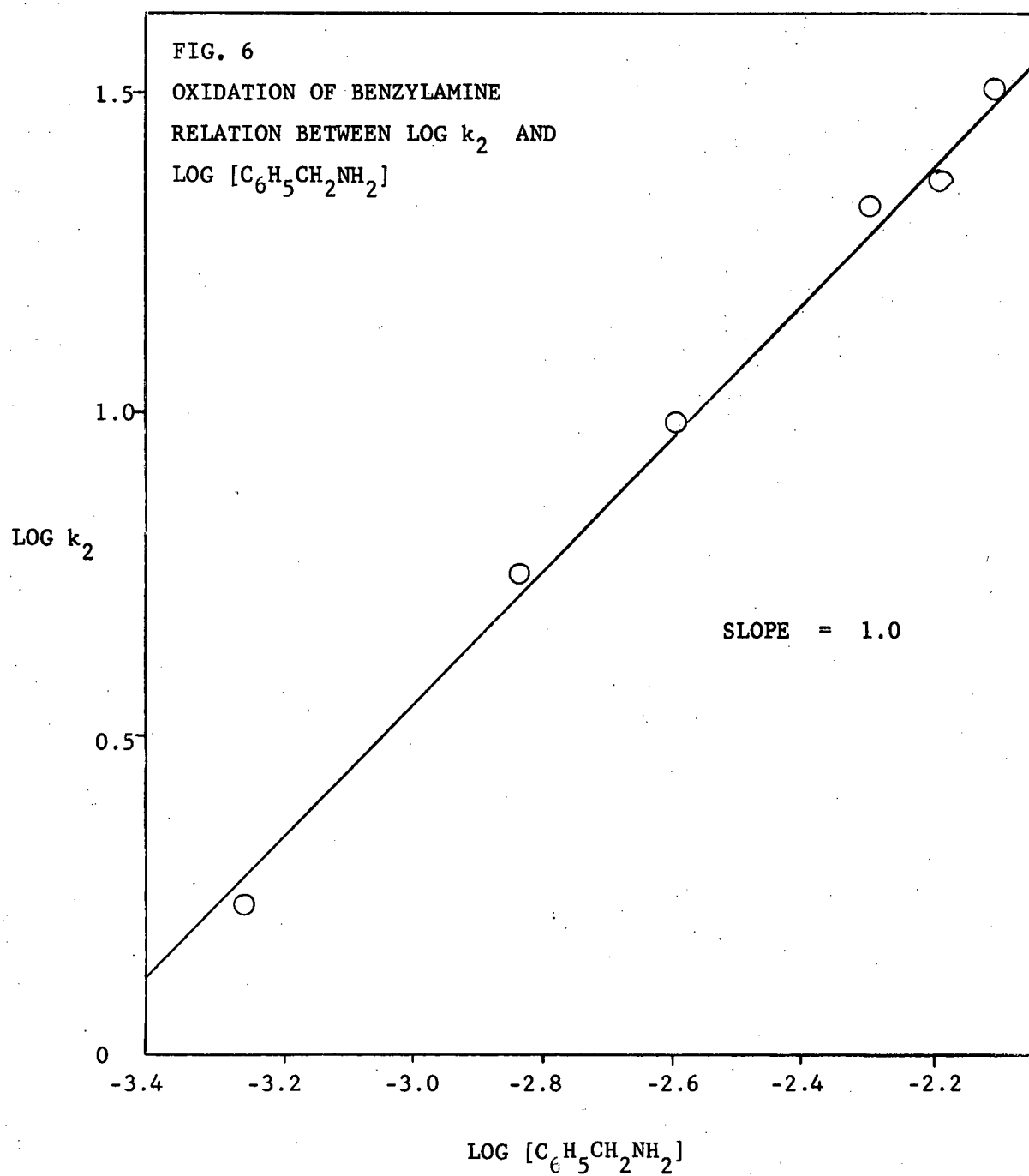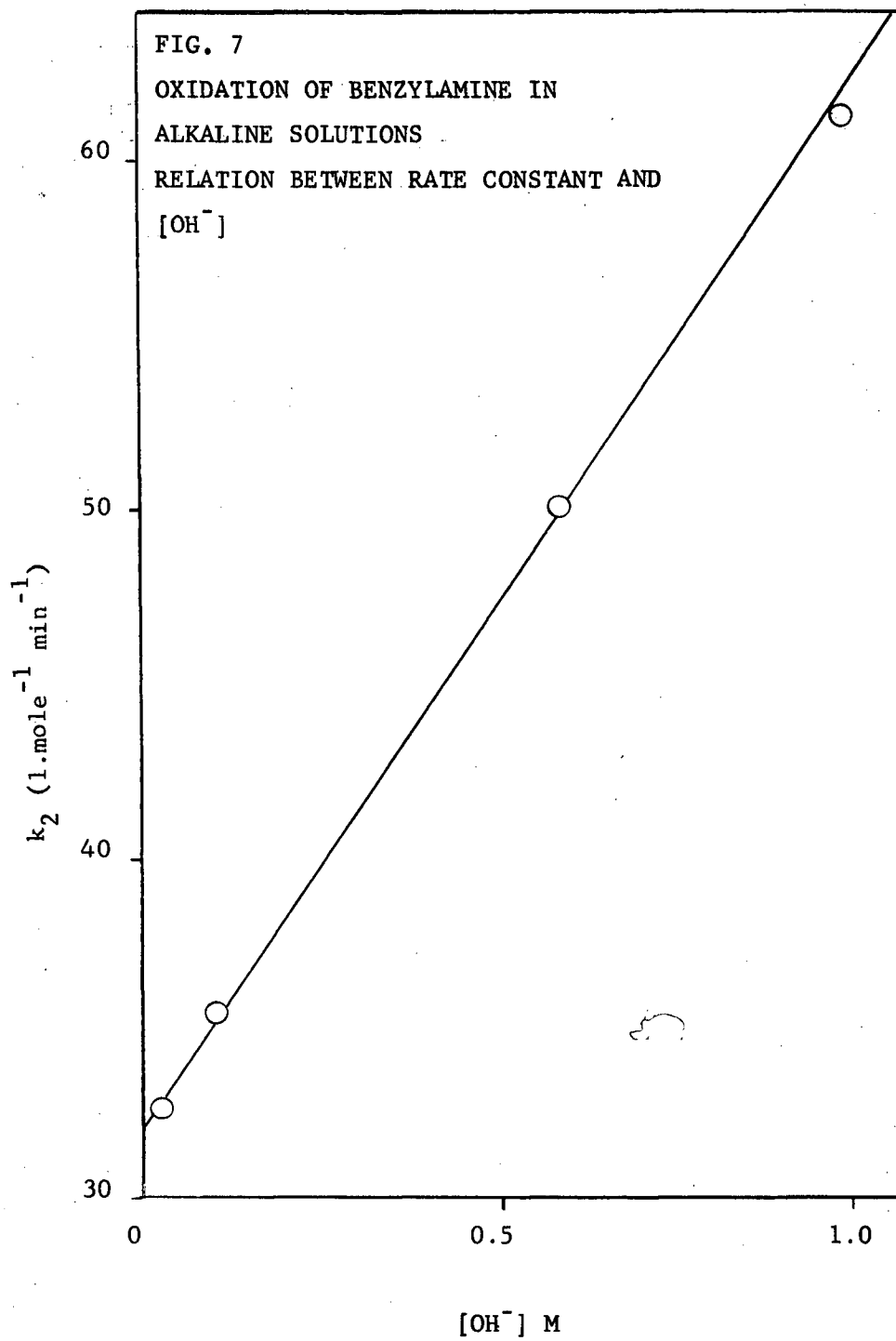
FIG. 8

OXIDATION OF BENZYLAMINE

TYPICAL RATE PLOT

pH = 13.78

$LOG \dfrac{V_t - \frac{3}{5} V_o}{V_t - \frac{2}{5} V_o}$

$[C_6H_5CH_2NH_2]_o = \dfrac{1}{2} [MnO_4^-] = 6.63 \times 10^{-4} M$

TIME IN MINUTES
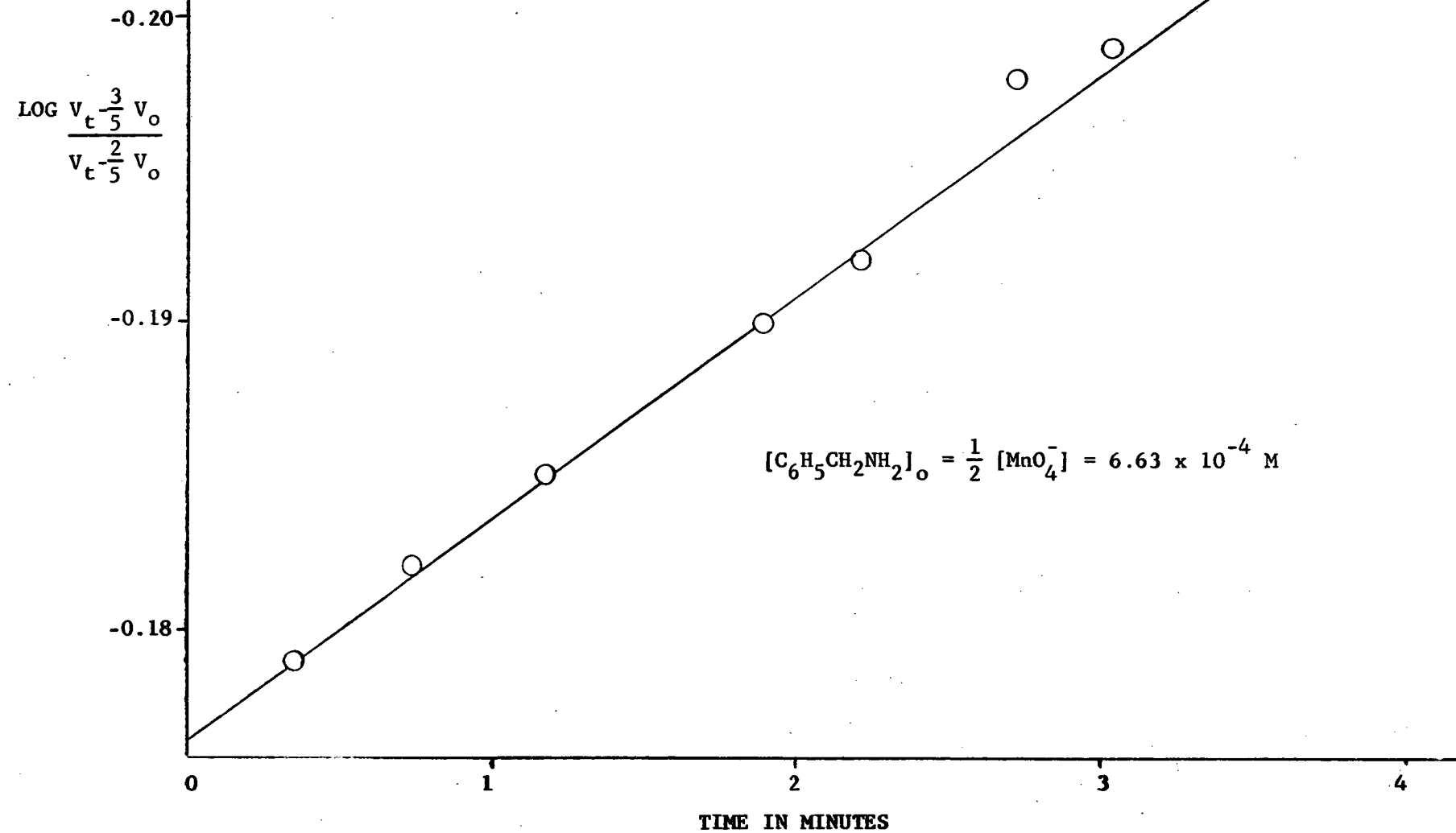
same pH. The correct ratio of substrate to permanganate on this basis is 3:4. The actual ratio used in the kinetic runs was 1:2, and a rate expression correcting for the presence of excess permanganate was derived (see Appendix).

$$k_2 = \frac{-4.60}{[\text{amine}]_o t} \log\left(\frac{V_t - \frac{3}{5} V_o}{V_t - \frac{2}{5} V_o}\right) \tag{25}$$

The rate plots of $\log\left(\dfrac{V_t - \frac{3}{5} V_o}{V_t - \frac{2}{5} V_o}\right)$ versus time were linear (Figure 8).

If one assumes that at pH 11.77, where the ratio of 3:2 for substrate:permanganate was used, the benzylamine is oxidized to benzoic acid instead of to the imine, then a rate expression can also be derived to account for the presence of excess amine (See Appendix).

$$k_2 = \frac{4.60}{[\text{amine}]_o t} \log\left(\frac{2 V_t}{\frac{5}{3} V_t - \frac{2}{5} V_o}\right) \tag{26}$$

The plot of $\log\left(\dfrac{2 V_t}{\frac{5}{3} V_t - \frac{2}{5} V_o}\right)$ versus time was linear, but the rate constant was 25.2 l. mole^{-1}min^{-1}, which is lower than the value of 33.0 l. mole^{-1}min^{-1} obtained when one assumes benzylamine is oxdized only as far as the imine. It must be pointed out that in the pH region 11 to 12, the stoichiometry of permanganate reactions cannot be predicted with certainty since the disproportionation of manganate is very much dependent on the time of reaction and the pH of the solution. The assumptions accompanying the use of the 3:2 ratio seem to be correct in the pH 11.77 reaction since the resulting rate constant, $k_2 = 33.0$ l.mole^{-1}min^{-1}, agrees with those obtained in the region pH 10.5 to pH 10.7.

Activation parameters

A series of kinetic runs were performed at pH values chosen at or near the maximum of the ionization curve so that the ionization process would not interfere with measurements of the activation process. The activation energy was obtained from a plot of log k_2 versus $1/T$ (Figure 9) and the enthalpy and entropy of activation were obtained from a plot of log $\frac{k_2}{T}$ versus $1/T$ (Figure 10). The data for benzylamine, m-trifluorobenzylamine, p-nitrobenzylamine, and p-methyl-benzylamine are presented in Table III.

Table III

Oxidation of Benzylamines

Activation Parameters

$X-C_6H_4CH_2NH_2$	E_a (kcal/mole)	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (e.u.)
p-CH$_3$	12.3	11.7 (11.3)	-20.6 (-21.6)
H	11.6	11.0	-22.5
m-CF$_3$	11.9	11.3 (11.7)	-21.4 (-21.9)
p-NO$_2$	11.0	10.4	-24.8

The values in the brackets are those corrected for incomplete ionization and temperature effects thereon.

The activation parameters were determined at pH values where the amines were largely unprotonated in order to reduce interference from the temperature effect on the ionization process. The corrections for the latter were made as follows: Table IV gives the measured pH changes

FIG. 9.
OXIDATION OF p-METHYLBENZYLAMINE
VARIATION OF RATE CONSTANT WITH
TEMPERATURE

FIG. 10

OXIDATION OF p-METHYLBENZYLAMINE

VARIATION OF LOG $\frac{k_2}{T}$ WITH
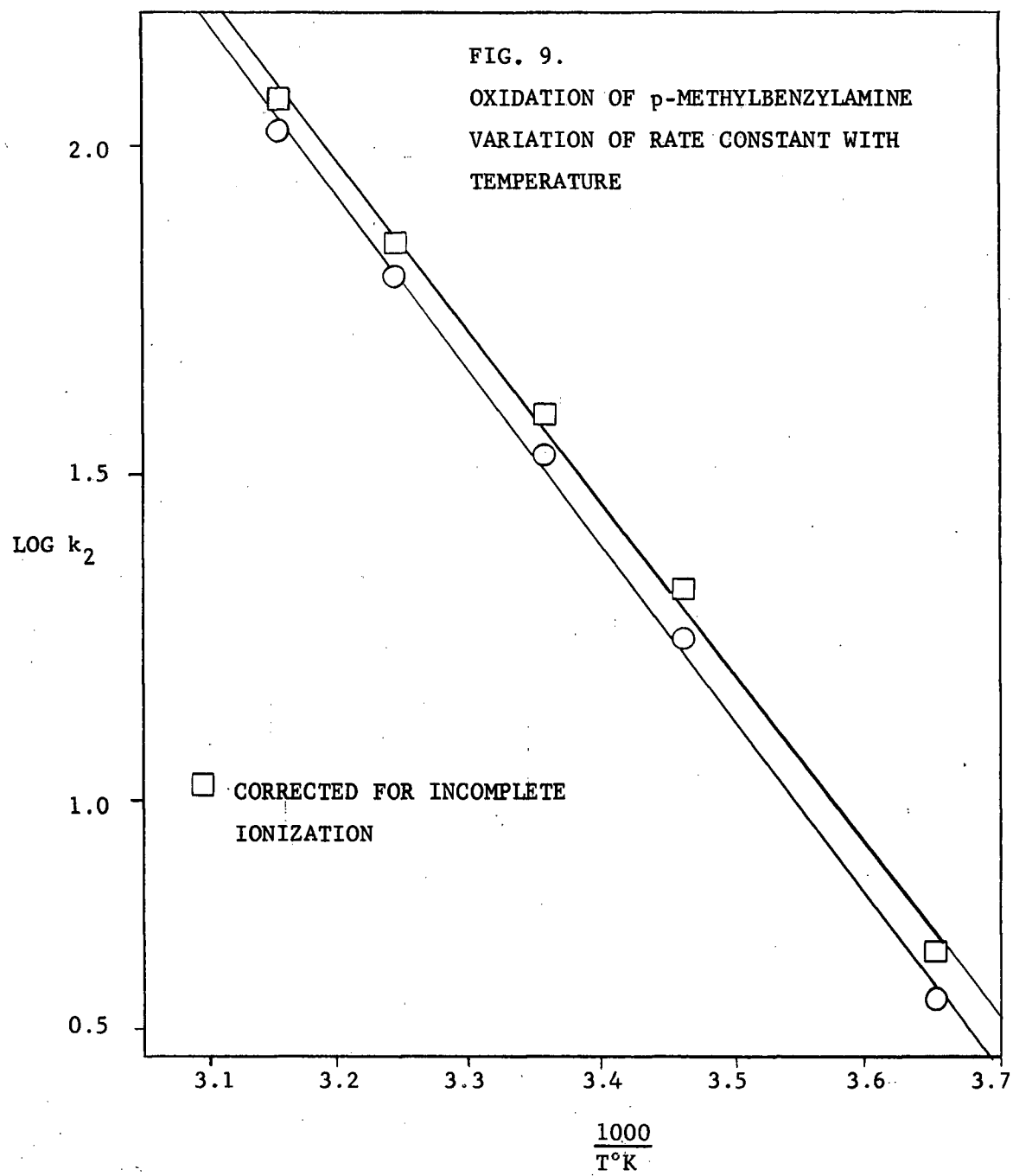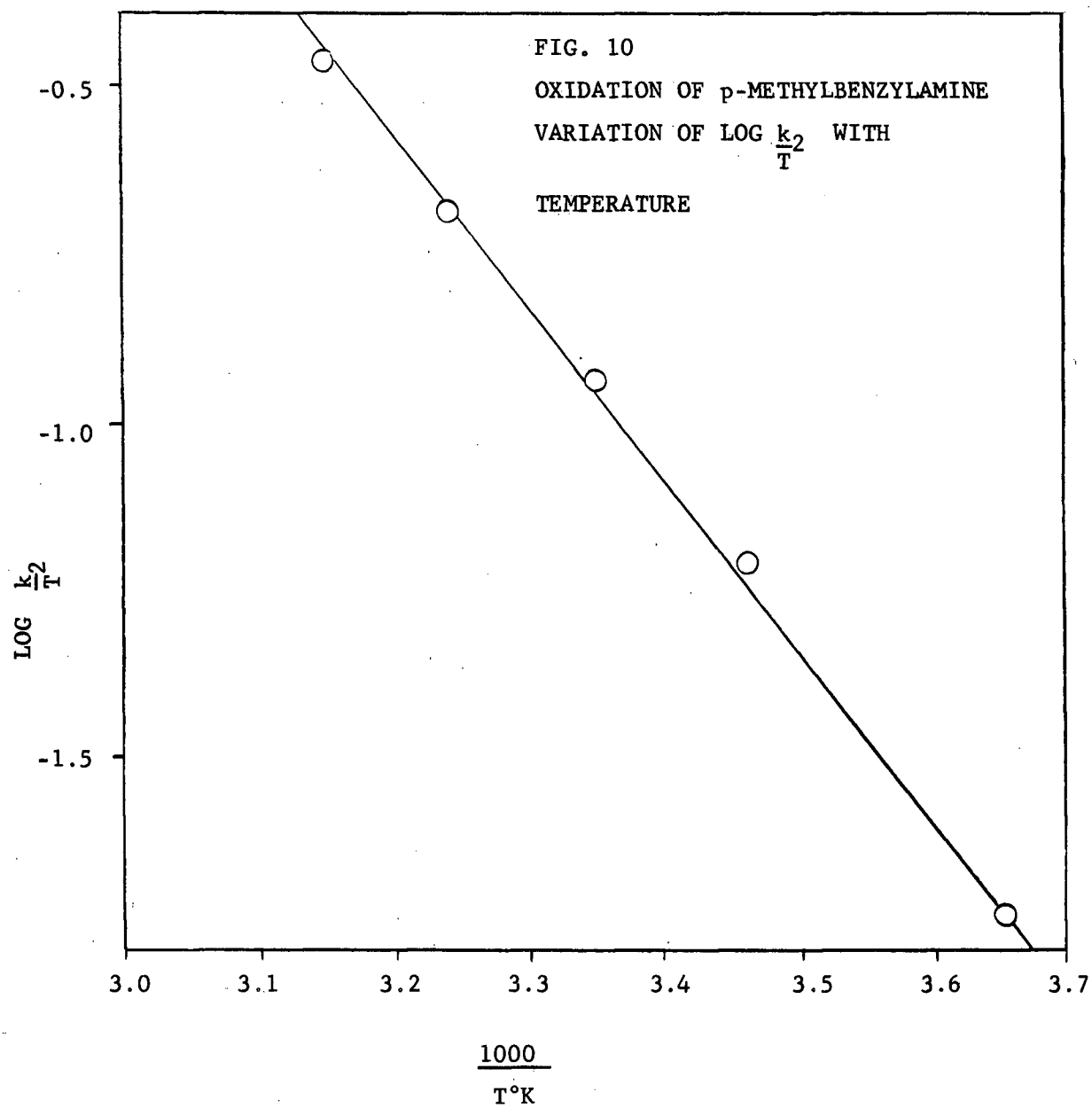
TEMPERATURE

of the phosphate buffer with temperature.

<center>Table IV</center>

<center>pH Variance of Phosphate Buffer with Temperature</center>

Temperature, °C	pH
23.00	10.68
26.90	10.61
30.70	10.53
35.70	10.47
40.00	10.37
15	10.33*
20	10.28
25	10.20
30	10.12
35	10.06
40	10.00

*The second set of values are taken from the Ph.D. thesis of M.M. Mocek (4).

The corrections for the variation of pK_{BH^+} with temperature were taken from Perrin's paper (81). In the case of m-trifluoromethylbenzylamine, whose calculated pK_{BH^+} at 25° was 8.96, a value of 0.025 was chosen for $-d(pK_{BH^+})/dT$.

Using the corrected pK_{BH^+} and pH values, and correcting for incomplete ionization, the rate constants for m-trifluoromethylbenzyl-amine were recalculated and replotted to give the corrected activation

10

parameters. A comparison of the corrected activation parameters with the original ones in Table III showed very little change in the actual values, thus corroborating the original assumption that if the activation parameters were determined at fairly high pH, then there would be little interference from the ionization process.

Isotope effects

Benzylamine-α-d_2 was oxidized in the pH range 8 to 11 and the plot of k_2 versus pH also gave a typical ionization curve. A unit slope was obtained from a log $(k_2/k_2^{max}-k_2)$ versus pH plot, and the intercept gave a pK_{BH^+} of 9.41. Table V gives a comparison of the rate constants for the protio and deuterio compounds. The average isotope effect, k_H/k_D, was found to be 7.0.

<div align="center">Table V</div>

<div align="center">Oxidation of Benzylamine, Protio and Deuterio Analogues</div>

<div align="center">in the Region pH 8 to 11</div>

<div align="center">Deuterium Isotope Effect</div>

pH	$k_2(H)(1.mole^{-1}min^{-1})$	$k_2(D)(1.mole^{-1}min^{-1})$	k_H/k_D
10.60	32.8	4.78	6.87
10.38	32.2	4.73	6.81
9.95	26.4	3.72	7.10
9.48	18.6	2.50	7.44
8.68	5.80	0.788	7.36
8.33	2.90	0.445	6.53

Mean = 7.0

Halevi et al (64) measured a $\Delta pK_{BH}+$ for benzylamine and benzylamine-α-d_2 of 0.054, while the oxidation results gave a $\Delta pK_{BH}+$ of 0.14. However, it must be pointed out that Halevi's method was the more precise one, and it would be sufficient to note that in both cases deuteration caused a decrease in the acid strength of the benzylammonium ion.

Oxidation of benzylamine in D_2O

The kinetic runs were carried out at pH values where benzylamine was almost completely in the neutral amine form. Presumably in such a region the isotope effect on the ionization of the amine will have a negligible effect on the concentration of free amine. That there was no measurable isotope effect shows the oxidation does not involve a rate-determining N-H bond cleavage. Table VI gives the data for the kinetic runs in D_2O.

Table VI

Data for the Oxidation of Benzylamine in D_2O

pH = 10.42

$[PhCH_2NH_2] = 3/2\ [MnO_4^-] = 0.00913\ M$

$[K_2HPO_4] = 0.02\ M$

Temperature = 25.0 $\pm$ 0.02°

k (H_2O) = k (D_2O) = 32.4 l.mole^{-1}min^{-1}

Substituent Effects

To obtain information regarding the electronic requirements at the α-carbon, eleven meta and para substituted benzylamines were oxidized at pH values at or near their maximum ionization. The rate constants were then corrected for incomplete ionization using the pK_{BH^+} values calculated from the $\bar{\sigma}$ and ρ values derived by Blackwell et al (82) (see Table VII). Figure 11 illustrates the nonlinear Hammett relation that one obtains when log k was plotted against σ values (28).

Table VII

Data for the Hammett Plots

$X-C_6H_4CH_2NH_2$	pK_{BH^+}	σ (28)	$\bar{\sigma}$ (82)	σ^+ (83)	log k
p-CH$_3$O	9.39	-0.268	-0.11	-0.778	1.762
p-CH$_3$	9.42	-0.170	-0.14	-0.311	1.612
p-C$_2$H$_5$	9.43	-0.151		-0.295	1.616
m-CH$_3$	9.33	-0.069	-0.06	-0.066	1.565
p-H	9.28	0	0.01	0	1.549
m-CH$_3$O	9.16	0.115	0.10	0.047	1.513
p-Cl	9.02	0.227	0.24	0.114	1.515
m-Cl	8.89	0.373	0.36	0.399	1.442
m-CF$_3$	8.83	0.415		0.520	1.624
m-NO$_2$	8.53	0.710	0.70	0.674	1.448
p-NO$_2$	8.38	0.778	0.84	0.790	1.608

However, when log k was plotted against σ^+ values all the points fell

FIG. 11
OXIDATION OF BENZYLAMINES
HAMMETT PLOT
t = 25.0 ± 0.02°

53
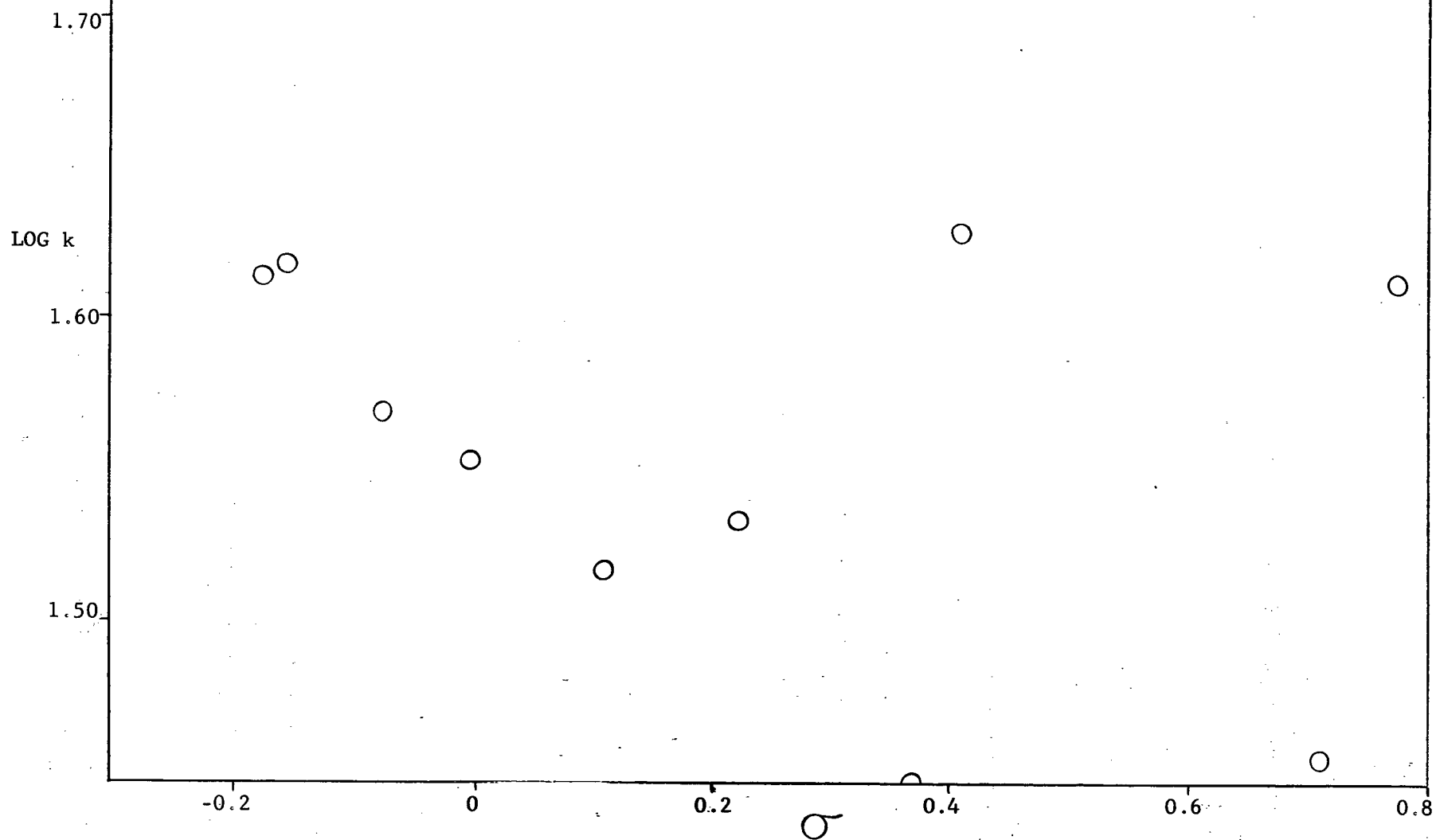
on a straight line with the exception of m-trifluoromethylbenzylamine,
m-nitrobenzylamine, and p-nitrobenzylamine (Figure 12). The slope of
the linear part of the graph was -0.28. A least squares treatment of
the same points (excluding the three "anomalous" ones) also gave a
slope of -0.28.

In reactions where the rates cannot be satisfactorily cor-
related with either the Hammett σ constants or the σ^+ constants,
Yukawa and Tsuno have derived a Hammett relation which involves a
linear combination of both constants (84):

$$\log k/k_o = \rho'(\sigma + r\Delta\sigma_R^+) \qquad (27)$$

where r is the reaction constant describing the extent of resonance in
the transition state and $\Delta\sigma_R^+$ is the substituent constant numerically
equal to $(\sigma^+ - \sigma)$. If one assumes that $(\sigma^+ - \sigma)$ is zero for meta
substituents, then a plot of $\log k/k_o$ versus σ for the meta-substituted
compounds may be used to evaluate ρ. Then r is obtained from the plot
of $\log k/k_o$ versus $\rho \Delta\sigma_R^+$. The ρ' in the Yukawa-Tsuno equation is ob-
tained from the plot of $\log k/k_o$ versus $(\sigma + r\Delta\sigma_R^+)$ (Figure 13).
Table VIII gives the data for Figure 13. The ρ' from Figure 13 is
-0.24, which agrees roughly with the value -0.28 obtained in Figure 12.
Of the three Hammett plots (Figures 11,12,13), the best fit is still
in Figure 13 where log k is plotted against σ^+.

To determine if the exalted rate for p-nitrobenzylamine
might be due to some condensation reaction between the amino and the
nitro groups prior to the oxidation step a pH 10.10 solution of equi-
molar amounts of benzylamine and nitrobenzene was oxidized with per-
manganate. No difference was found in the rates for the solution con-

FIG. 12

OXIDATION OF BENZYLAMINES

HAMMETT PLOT

t = 25.0 $\pm$ 0.02°
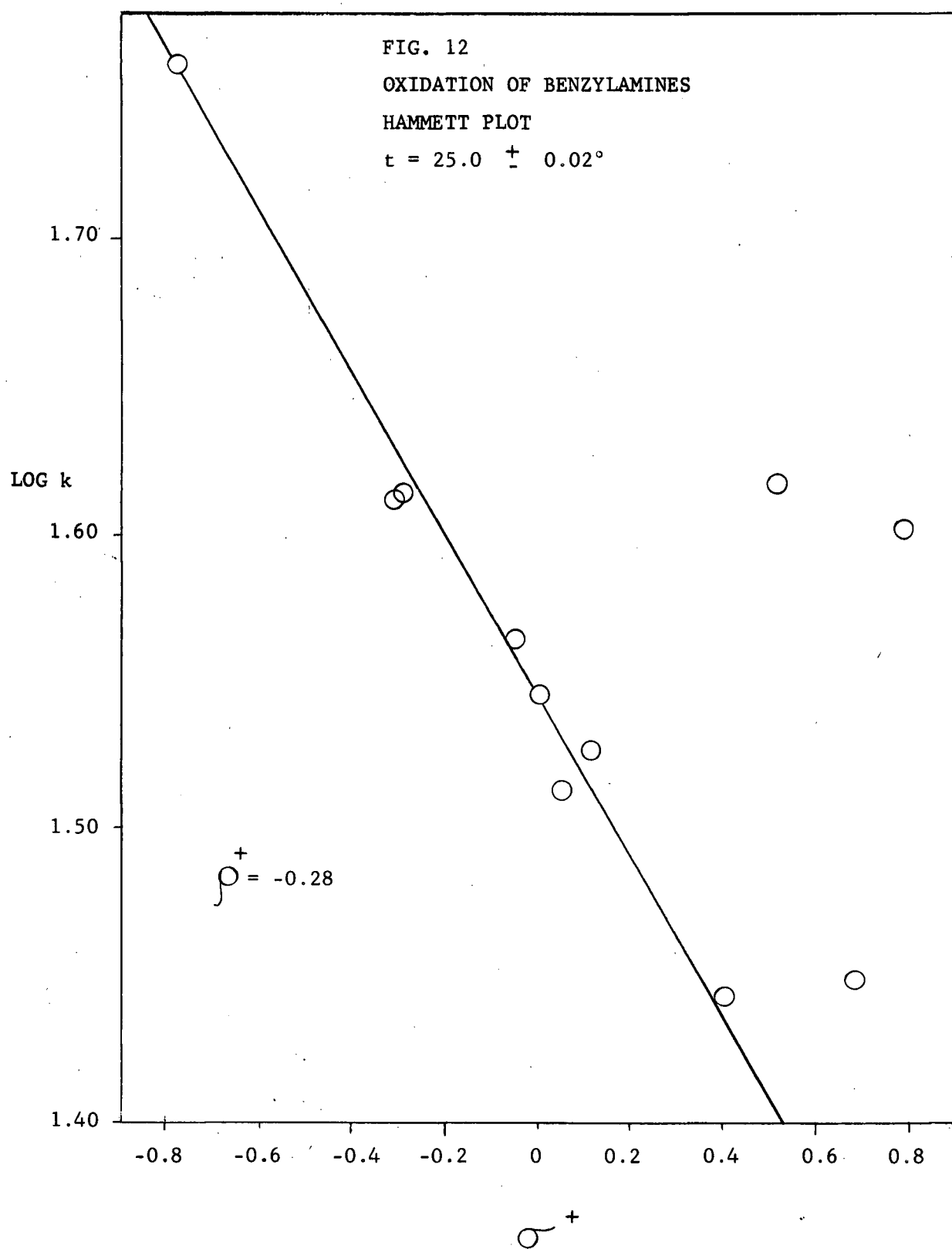
taining no nitrobenzene and that containing nitrobenzene.

A test was also carried out to determine whether the acetate ion might have any effect on the oxidation rates since the stock solutions of some of the amines were prepared from the amine acetate salts. No change in rate was again observed for benzylamine solutions containing no sodium acetate and for those containing equimolar amounts of sodium acetate at pH 10.10.

Table VIII

Data for the Hammett Plot Using the Yukawa-Tsuno Equation

$X-C_6H_4CH_2NH_2$	$\log k/k_o$	$\Delta\sigma_R^+ (85)$	$\rho\Delta\sigma_R^+ (a)$	$\sigma + r\Delta\sigma_R^+ (b)$
p-CH$_3$O	0.213	-0.496	0.144	-0.977
p-CH$_3$	0.063	-0.131	0.038	-0.357
p-C$_2$H$_5$	0.067	-0.141	0.041	-0.353
p-Cl	-0.034	-0.106	0.031	0.075
m-CH$_3$O	-0.036			
m-CH$_3$	0.016			
m-Cl	0.107			

(a) ρ = -0.29, obtained from a plot of $\log k/k_o$ versus σ for the meta-substituted benzylamines

(b) r = 1.43, obtained from a plot of $\log k/k_o$ versus $\rho\Delta\sigma_R^+$

FIG. 13

OXIDATION OF BENZYLAMINES

HAMMETT PLOT USING THE YUKAWA-TSUNO EQUATION

LOG $\frac{k}{k_o}$

$\rho' = -0.24$

$r \Delta\sigma^+ + \sigma$

57
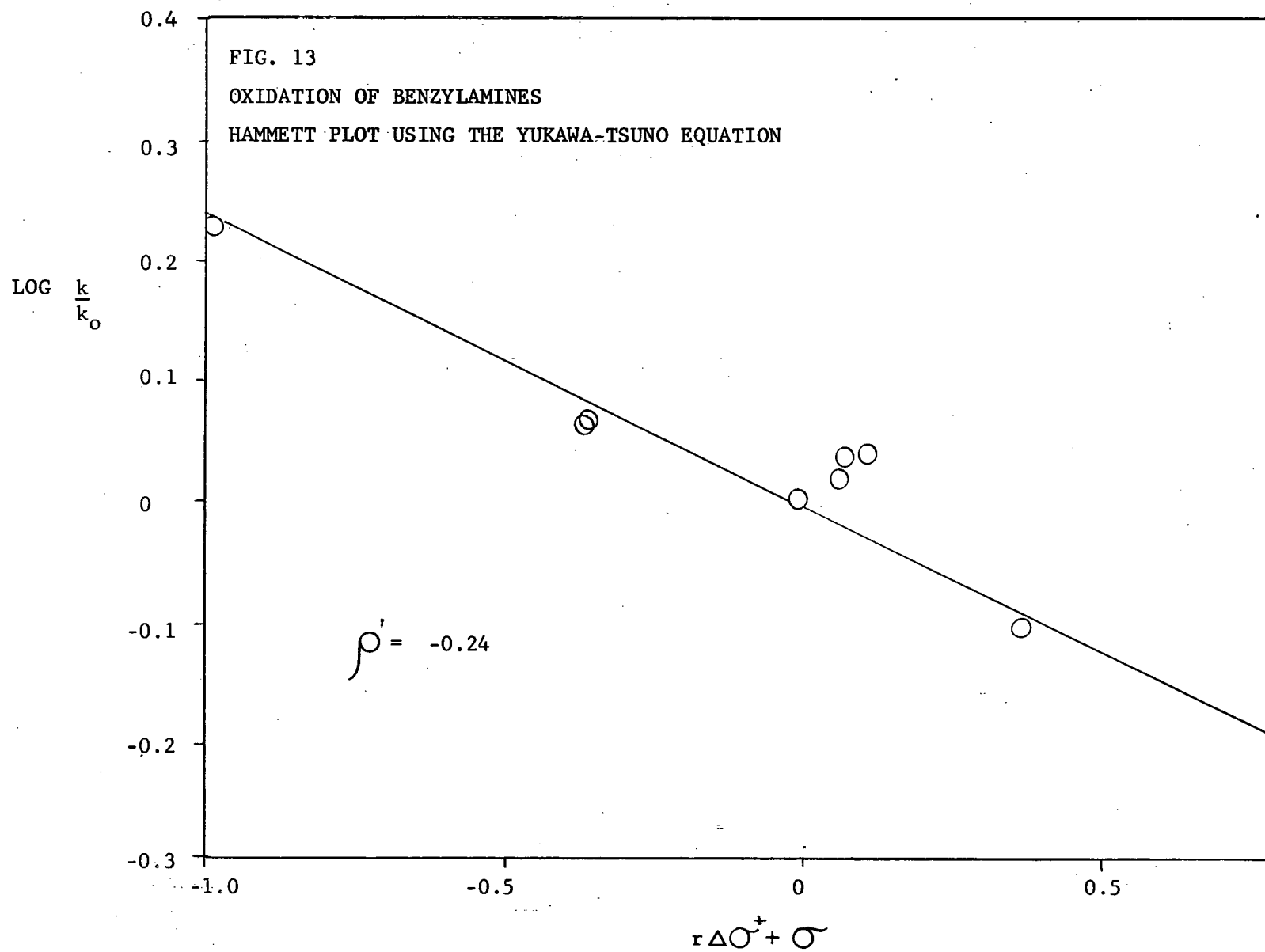
Oxidation of (-)- α -methylbenzylamine

Good second-order kinetics were observed for the reaction of (-)- α-methylbenzylamine with permanganate at pH 10.39. The calculated rate constant after 60% reaction was 32.2 l.mole^{-1}min^{-1}. In an identical run, the solution was quenched after 31% reaction had occurred. Polarimeter readings taken of this solution revealed a 74% loss of optical activity.

Table IX

Polarimeter Data for the Oxidation of (-)- α -methylbenzylamine

Rotation of (-)- α -methylbenzylamine, neat, $[\alpha]_D^{22}$	-40.3° (76)
Calculated rotation for 0.01M amine concentration	-0.024°
Rotation of blank solution	-0.0088°
Rotation after 31% reaction	-0.0021°
Temperature at which readings were taken	22 ± 1°

Miscellaneous reactions

(a) Oxidation of N,N-dimethylbenzylamine

Linear second order kinetics were observed to only 35% reaction before the plot curves upwards. The estimated rate constant for the linear portion was 115 l.mole^{-1}min^{-1}, which is approximately eight times as fast as the rate for benzylamine at the same pH (9.32) and about six times as fast as the rate for benzaldehyde (3).

(b) Oxidation of NH_3

Two pseudo first order kinetic runs were carried out on the oxidation of ammonia. The rates were very slow, but the plot of log V_t versus time was roughly linear in the time examined (Figure 14) and hence quantitative values for the rate constants were obtained.

Table X

Oxidation of Ammonia: Variation of Rate with pH

pH	k_2 (l.mole^{-1}hour^{-1})
11.63	0.107
8.54	0.00689

(c) Oxidation of cyclohexylamine

Good second order rate plots were obtained by using 3:2 molar ratios of cyclohexylamine to permanganate, up to pH 11. Beyond pH 11.2, the plots appear autocatalytic and no rate constants could be obtained from them. The rates are in general about one-tenth of the rates for benzylamine. Table XI gives the rate constants for four pH regions.

Table XI

Oxidation of Cyclohexylamine: Variation of Rate with pH

pH	k_2(l.mole^{-1}min^{-1})
7.46	0.0117
9.19	0.319
9.86	1.04
10.17	1.92

FIG. 14

OXIDATION OF NH_3
TYPICAL PSEUDO FIRST ORDER RATE PLOT

pH = 11.63

LOG V_t

TIME IN HOURS

60
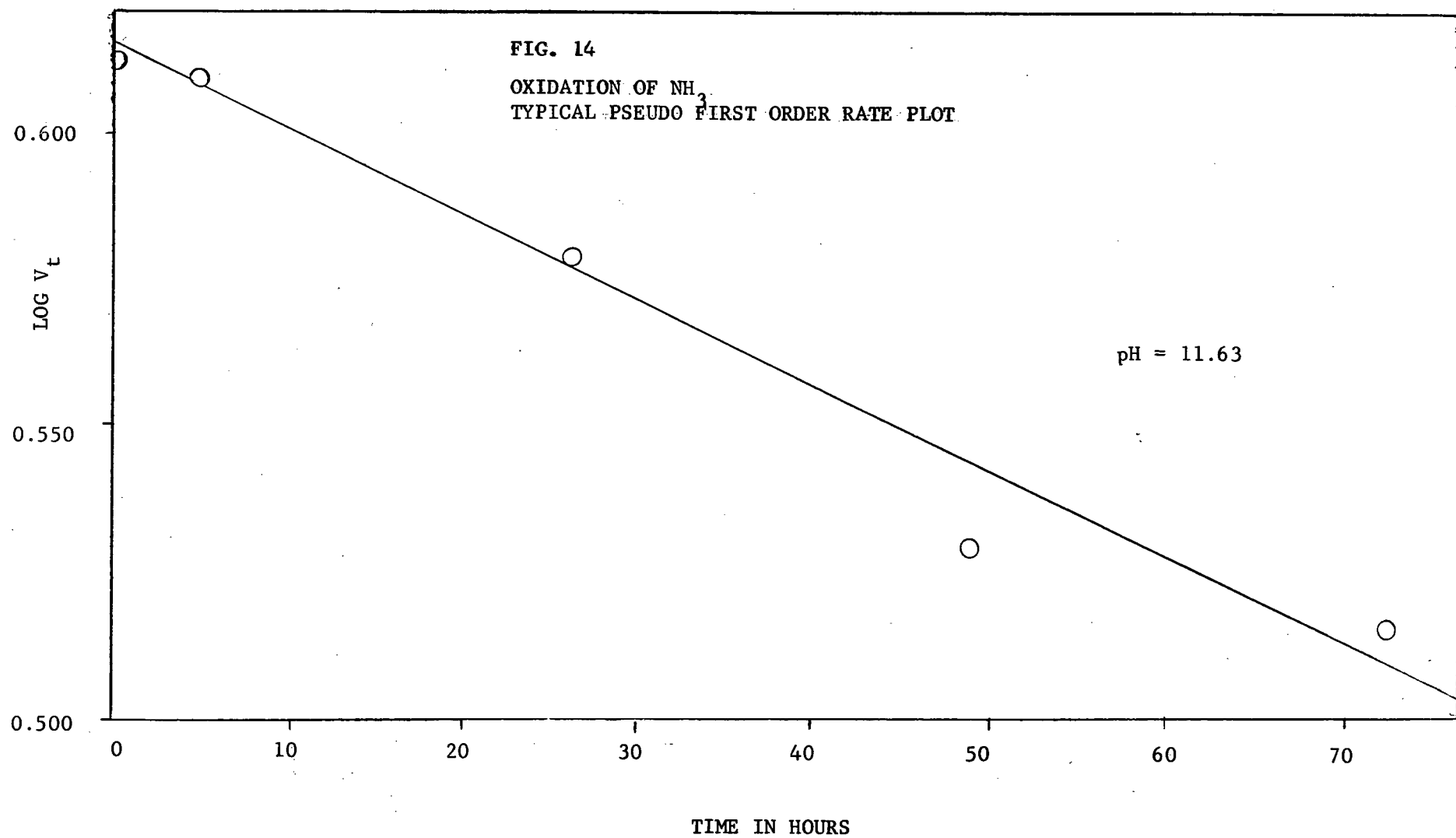
The plot of k_2 versus pH gave only what appears to be a part of an ionization curve.

Cyclohexanone at pH 9.33 and 11.29 oxidized at about the same rate as cyclohexylamine for about 10% of the reaction before the rate greatly speeded up in an autocatalytic manner.

(d) Oxidation of acetamide

Permanganate failed to oxidize acetamide after 30 hours of reaction both in acidic and basic solutions.

(e) Oxidation of N,N-dimethylformamide and N-benzylformamide

Both these compounds were slowly oxidized by permanganate at pH values higher than 13, but below pH 13, there appears to be no reaction during five or six hours.

(f) Oxidation of methylamine, dimethylamine, trimethylamine, t-butylamine, and tetramethylammonium hydroxide

In the qualitative reactions which were carried out on these compounds, it was observed that while methylamine, dimethylamine, and trimethylamine were almost instantaneously oxidized by permanganate, t-butylamine, whose kinetics has been studied in a later section, and tetramethylammonium hydroxide exhibited no appreciable reaction after three to four hours.

DISCUSSION

The stoichiometry of the initial reaction between permanganate

and benzylamine in the pH region investigated may be represented by the

following equation:

$$3 \ PhCH_2NH_2 + 2 \ MnO_4^- \longrightarrow 3 \ PhCH=NH + 2 \ MnO_2 + 2 \ H_2O + 2 \ OH^- \qquad (28) \quad 3)$$
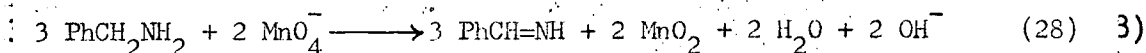
The highly reactive imine intermediate is never isolated from the reac-

tion mixture since in acidic and highly basic solutions it hydrolyzes

rapidly to benzaldehyde (77) and in neutral and weakly basic solutions

it reacts with benzylamine to produce condensation products (47).

These two reactions effectively limit the rate determinations to the

first 50% of reaction, since in acidic solutions benzaldehyde is ox-

idized autocatalytically by permanganate, and in neutral and weakly

basic solutions the condensation reactions tend to cause the rate

of oxidation of benzylamine to level off after about 40-50% reaction.

In strongly alkaline solutions, pH 12 to 14, the stoichiometry

changes.

$$3 \ PhCH_2NH_2 + 4 \ MnO_4^- \longrightarrow 3 \ PhCO_2^- + 3 \ NH_3 + H_2O + 4 \ MnO_2 + OH^- \qquad (29)$$
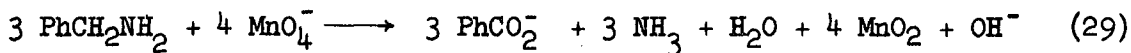
Benzoic acid is the final product in the highly basic region since the

chief oxidation intermediate of benzylamine, benzaldehyde, is rapidly

oxidized both by permanganate and by manganate to benzoic acid. Pre-

sumably the rates of the hydrolysis of the imine intermediate to ben-

zaldehyde far exceed the rate of condensation which occur at lower pH

regions between the imine and benzylamine. The reduction of Mn(VII) to

Mn(IV) is in accord with the observation that manganate rapidly oxidizes

benzylamine.

The overall kinetics of the oxidation of benzylamine is second order; in particular, it is first order in benzylamine and first order in permanganate. The intermediate manganese species, manganese(V) or manganese(VI), undergoes rapid disproportionation to yield MnO_2, which is stable in the entire pH region except in the highly basic solutions where $MnO_4^=$ tends to accumulate.

The dependence of the reaction rate on pH is graphically represented in the form of an ionization curve (Figure 3). The mid-point of this curve corresponds to an apparent $pK_{BH}+$ of 9.28, which agrees within 0.1 pK unit with the previously measured $pK_{BH}+$ of the benzylammonium ion (79).

No appreciable salt effects were observed for benzylamine oxidation at pH 10.70 and 25°.

The kinetics are consistent with a mechanism which involves the reaction of permanganate ion and the neutral amine in the rate-determining step.

$$C_6H_5CH_2NH_2 + H_2O \xrightleftharpoons{K} C_6H_5CH_2NH_3^+ + OH^- \qquad (30)$$

$$C_6H_5CH_2NH_2 + MnO_4^- \xrightarrow{k} \text{Products}$$
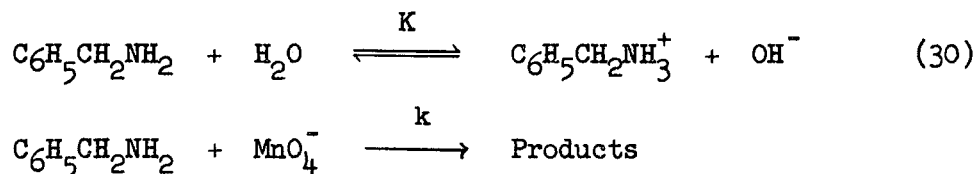
The rate law corresponding to this mechanism is:

$$- \frac{d[MnO_4^-]}{dt} = k\,[MnO_4^-]\,[C_6H_5CH_2NH_2] \qquad (31)$$

or

$$- \frac{d[MnO_4^-]}{dt} = \frac{k}{K}\,[MnO_4^-]\,[C_6H_5CH_2NH_3^+]\,[OH^-] \qquad (32)$$

$$\text{where } K = \frac{[C_6H_5CH_2NH_3^+]\,[OH^-]}{[C_6H_5CH_2NH_2]}$$

The experimental rate law was found to be:

$$- \frac{d[MnO_4^-]}{dt} = k_2 [MnO_4^-] [amine]$$

where $[amine] = [C_6H_5CH_2NH_2] + [C_6H_5CH_2NH_3^+]$

As the pH of the system is raised the concentration of benzylamine approaches the total amine concentration, k_2 approaches k, the rate constant of the rate-controlling step, and one observes a levelling-off of the rate.

The oxidation of the benzylammonium ion is extremely slow, the rate of benzylamine oxidation exceeding that of benzylammonium ion oxidation by a factor of more than 10^3.

Alkoxide ions, produced by the ionization of alcohols in basic solution, are generally much more reactive than neutral amines towards permanganate. The maximum rates observed for the aryl trifluoromethyl carbinol oxidations are more than ten times higher than the maximum rates for the benzylamines. Benzhydrol ion oxidation rates appear to exceed those of benzylamine by an even greater extent.

The further increase in rate that is observed as the pH is raised from 12 to 14 indicates a second reaction exists. It seems most unlikely that the hydroxyl ion dependence is due to the ionization of the benzylamine molecule. The amino protons are far too weakly acidic to be sufficiently ionized at pH 14. Aniline has a pK_a of about 27 (86) and benzylamine should be an even weaker nitrogen acid. Hence if the reaction were even diffusion controlled, the concentration of the benzylamine anion, $C_6H_5CH_2NH^-$, would still not be nearly high enough to produce the observed rate.

It is also doubtful whether a proton can be removed from the α-carbon of benzylamine at pH 14. The half-life of the ionization of p-nitrobenzylamine is approximately 30 minutes at $H_- = 17.9$ (86), and one would expect the ionization of benzylamine to be much slower at pH 14. Hence the rise in rate beyond pH 12 cannot be due to the partial formation of the benzylamine carbanion. The following mechanisms are consistent with the experimental results for the oxidation of benzylamine from pH 12 to 14.

(1) Hydrogen atom transfer

$$\phi \text{-}\overset{\cdot}{C}H\text{-}\overset{-}{N}H \ + \ MnO_4^- \ \longrightarrow \ \text{Products} \tag{34}$$

(2) Hydride ion transfer

$$\phi\text{-}CH=NH \ \xrightarrow[\text{fast}]{\text{Mn(VII) or Mn(V)}} \ \text{Products} \tag{35}$$

(3) Electron transfer to permanganate

$$\phi \text{-}\overset{\cdot}{C}H\text{-}NH_2 \ \xrightarrow[\text{fast}]{\text{Mn(VII) or Mn(VI)}} \ \text{Products} \tag{36}$$

The rate law corresponding to mechanisms 1, 2, and 3 is:

$$- \frac{d \, [MnO_4^-]}{dt} = k \, [MnO_4^-] \, [OH^-] \, [PhCH_2NH_2] \qquad (37)$$

All three mechanisms are termolecular. In mechanism 1, permanganate removes a hydrogen atom from the α-carbon while the hydroxyl ion removes a proton from the amino group. In mechanism 2, permanganate removes the α-hydrogen as a hydride ion as the hydroxyl ion removes a proton from the amino hydrogen. In mechanism 3, the hydroxyl group removes the α-hydrogen as a proton while permanganate abstracts an electron from the nitrogen.

Activation parameters

The activation parameters for the oxidation of benzylamines were obtained in pH regions where the amine is almost completely in the neutral form. The small corrections which were required for incomplete ionization together with corrections for pH changes with temperature made only slight differences to the actual values of the parameters (see Table III).

The energies of activation are, on the whole, 1-2 kcal. higher than those observed for the fluoro alcohols. This is in accord with the slower rates observed for the amines.

The results for the entropies of activation for the benzylamines are somewhat unexpected. The very large negative $\Delta S^{\ddagger}$ values for the reaction of the neutral amine with permanganate are of the same order of magnitude as the $\Delta S^{\ddagger}$ values for anions with permanganate (23, 24, 34). In general, when two anions come together to form the activated

complex the resulting $\Delta S^{\ddagger}$ for the reaction is large and negative
(87,88). However, in this respect, previous studies of the reaction
of neutral molecules with permanganate have also revealed abnormally
negative entropies of activation. The $\Delta S^{\ddagger}$ for the reaction of MnO_4^-
and H_2 is -17 e.u. (89) and $\Delta S^{\ddagger}$ for the reaction of neutral formic
acid with permanganate is -19 e.u. (34). For all these reactions in-
volving a neutral substrate with permanganate, one can postulate an
ionic transition state which has extensive charge separation resulting
from the transfer of either electrons or hydride ions. In the case of
benzylamine the transition state may be represented by the following:

$$\phi - \overset{\overset{\displaystyle NH_2}{|}}{\underset{\underset{\displaystyle H}{|}}{C}} - H \; + \; MnO_4^- \;\longrightarrow\; \left[\delta^+ \left\langle \!=\!\!=\! \right\rangle \!\!=\!\! \overset{\overset{\displaystyle NH_2}{|}}{\underset{\underset{\displaystyle H}{|}}{C}} \!-\!-\!-\! \overset{\delta^-}{H} \!-\!-\!-\! \overset{-}{O}MnO_3 \;\longleftrightarrow\; \phi - \overset{\overset{\displaystyle NH_2}{|}}{\underset{\underset{\displaystyle H}{|}}{C}} \!-\!-\!-\! H \!-\!-\!-\! \overset{-}{O}MnO_3 \right]$$

$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad a \qquad\qquad\qquad I \qquad\qquad b$$

$$(38)$$
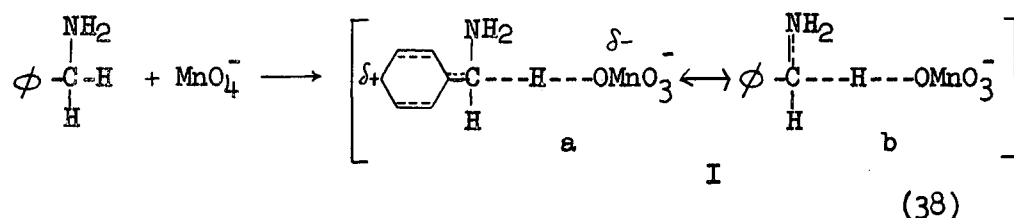
The mechanism represented by equation (38) involves a hydride ion trans-
fer from the amine to permanganate. Transition state I is a highly
ionic one and should be more hydrated than the reactants in the ground
state. Shown also is the participation of the amino group and the
phenyl group in the delocalization of the charge which develops at the
reaction center. However, results from studies of ring substituent
effects, which will be discussed in a later section, suggest that re-
sonance stabilization by the ring of any charge which develops at the
alpha-carbon, as shown in transition state I, is not a large factor
contributing to the stability of the transition state. Further evidences
showing the importance of the amino group in absorbing some of the charge
developed at the alpha-carbon are found in the studies of the oxidation
rate of benzylamine with different N-substituents. Alkyl groups, which

are electron-donating, increase the rate of oxidation, but acyl groups, which are electron-withdrawing, cause the rate to drop considerably. When benzylamines are protonated, the rates are greatly diminished, indicating the importance of structures such as I[b].

Of the four benzylamines whose activation parameters were measured, the nitro compound had the lowest activation energy and the most negative entropy of activation. The lowered energy of activation may be due to increased resonance interaction between the phenyl ring and the reaction center, although it is not clear how resonance effects can be important with the nitro group if hydride transfer were the mechanism.

If the mechanism of reaction for the nitro compound did, in fact, involve a hydrogen <u>atom</u> transfer, then the following equation shows how resonance can occur between the nitro group and the reaction center:

(39)
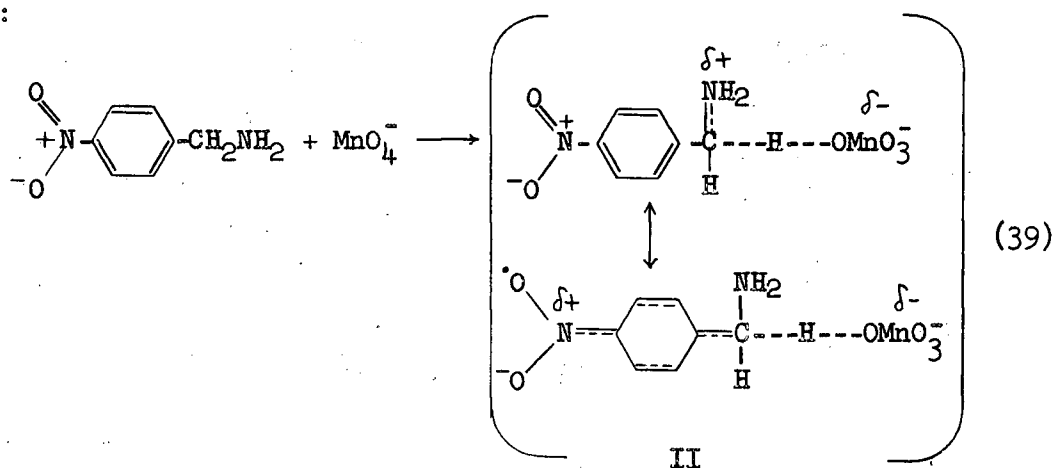
In structure II for the transition state there is even greater charge separation than in I, and as such, should be the most highly solvated species. This is in agreement with the more negative $\Delta S^{\ddagger}$ obtained for p-nitrobenzylamine.

An alternate explanation for the decrease in $\Delta S^{\ddagger}$ for p-nitrobenzylamine is that the ground state solvation of this compound is less than that of the other benzylamines since p-nitrobenzylamine had the lowest $pK_{BH}+$. This assumes that the extent of solvation of the amino protons is approximately the same for all the benzylamines and that differences lie chiefly in the extent of solvation of the amino nitrogen. If the above assumption is valid, then the more negative $\Delta S^{\ddagger}$ associated with p-nitrobenzylamine must be due to the larger difference between the solvation in the ground state and the solvation in the transition state.

Isotope effects

The manifestation of a rather large isotope effect for the benzylamine reaction, k $(PhCH_2NH_2)$/k $(PhCD_2NH_2)$ = 7.0, shows that the rate-determining step involves the cleavage of the C-H bond. The fact that the isotope effect remains constant throughout the pH range investigated suggests that the same mechanism must be operating in that range.

The absence of a solvent (H_2O/D_2O) isotope effect supports the proposed mechanism, which does not involve the amino hydrogens in the rate-determining step.

Substituent effects

Except for m-trifluoromethylbenzylamine, p-nitrobenzylamine and m-nitrobenzylamine, three compounds which have highly electron-withdrawing substituents, the logarithm of the rate constants for all the para- and meta-substituted benzylamines was found to correlate

better with σ^+ constants than with σ constants. The reaction constant, ρ^+, was -0.28, which is in accord with the proposed hydride transfer mechanism. The rather small value for ρ^+ shows that the reaction is not subject to large nuclear substituent effects, and that most of the positive charge in the transition state remains at the α-carbon or at the nitrogen atoms.

In the log k versus σ^+ plot, the three points corresponding to p-nitrobenzylamine, m-trifluoromethylbenzylamine and m-nitrobenzylamine all lay well above the straight line through the other points (Figure 12).

For p-nitrobenzylamine, a change in mechanism may be taking place, the most probable one being a hydrogen atom transfer mechanism since the activation parameters for the p-nitro compound are not too vastly different from those for benzylamine. The increased rate could be due to enhanced resonance interaction with the ring. However, this mechanism cannot explain the higher rates for m-trifluoromethylbenzyl-amine and m-nitrobenzylamine, since there can be no direct resonance with meta-substituents.

Another possible explanation for the high rates observed for the three "anomalous" benzylamines is based on the ionization at the α-carbon.

$$z\text{-}\langle\bigcirc\rangle\text{-}CH_2\text{-}NH_2 + OH^- \rightleftharpoons z\text{-}\langle\bigcirc\rangle\text{-}\overset{\ominus}{C}H\text{-}NH_2 + H_2O \qquad (41)$$
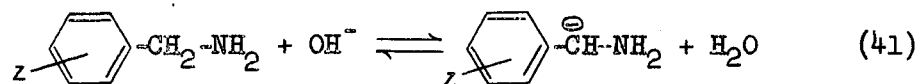
Presumably such an equilibrium must be shifted far to the left in the ordinary pH range. However, with strongly electron-withdrawing groups such as nitro and trifluoromethyl, the equilibrium might be shifted towards the right to such an extent that at pH 10, for example, even

a very small concentration of the anion could contribute to a large increase in rate. One assumes the anion is oxidized much more quickly than the neutral molecule. Qualitative studies in this laboratory (86) have shown that p-nitrobenzylamine appears to be only slightly ionized in 60% dimethylsulfoxide solution (H_- =-17.9). The ionization process was time dependent, however, the half-life at H_- =-17.9 being 33 minutes. This is slower than the oxidation rate and it is highly probable that in the lower pH regions, the ionization reaction would be even slower. Furthermore, it can be shown that involvement of the anion, $p-NO_2C_6H_4\overline{C}HNH_2$, in the rate-determining step would require the oxidation rate to be proportional to the square of the hydroxyl ion concentration in the region well below the pK of the amine, instead of the first order dependence that was observed.

Oxidation of (-)- α -methylbenzylamine

Studies of the oxidation of (-)- α -methylbenzylamine have provided some new insight into the oxidation mechanism for benzylamines.

The loss of 74% optical activity in the starting compound corresponding to only 31% reaction suggests that a racemization process may be occurring prior to the rate-determining step. Furthermore, this observation gives some information regarding the nature of the hydrogen that is transferred to the permanganate.

If a hydrogen atom transfer mechanism were taking place involving the transitory existence of a benzyl radical, then it is conceivable that there can be an exchange of the hydrogen atom between the radical and permanganate within the solvent cage before the atom is finally removed by the permanganate.

$$\underset{\overset{|}{CH_3}}{\overset{\overset{NH_2}{|}}{\phi-C-H}} + MnO_4^- \underset{slow}{\rightleftharpoons} \left[\underset{\overset{|}{CH_3}}{\overset{\overset{NH_2}{|}}{\phi-C\cdot}} HMnO_4^- \right] \underset{\text{Solvent cage}}{\longrightarrow} \underset{\overset{|}{CH_3}}{\overset{\overset{NH_2}{|}}{\phi-C\cdot}} + HMnO_4^- \quad (42)$$
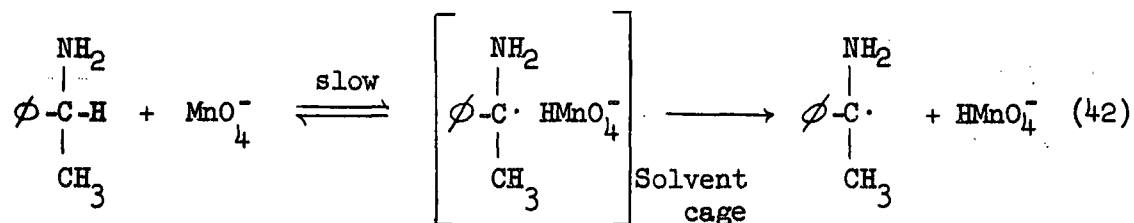
Although in most cases the escape from the solvent cage will be more rapid than the rotation of any molecule within the solvent cage, Leffler and Grunwald (83) state that there is evidence for rotation, although incomplete, of radicals within the solvent cage. For example, the product from the primary recombination of the alkyl and acyloxy radicals derived from the decomposition of optically active β-phenylisobutyryl peroxide was found to be 15% racemized. They point out that the results from the studies of the polar decomposition of decalyl perbenzoate and of p-methoxy-p'-nitrobenzoyl peroxide suggest that it is unlikely for caged <u>ions</u> to rotate before they recombine (90,91, 92) Such decompositions occur instead through an intimate ion-pair mechanism. It is likely, then, that rotation would not occur in the hydride ion transfer mechanism proposed for the oxidation of (-)-α-methylbenzylamine, but might occur, to a small extent, in the radical mechanism (equation 42).

Results from the oxidation of benzylamine-α-d_2 suggest that any hydrogen exchange in the transition state must occur between the radical and the permanganate, for if exchange occurred between the radical and the solvent, then one should observe an increase in the rate of reaction for the deuterated compound as the reaction proceeds since the deuterium would be exchanging for the protium. No such rise in rate was observed for benzylamine-α-d_2.

Summary

The transition state for the permanganate-benzylamine reaction has been shown to be the following:

$$\left[\begin{array}{c} \overset{NH_2}{\underset{H}{C_6H_5 - C}} \text{----} H \text{----} OMnO_3 \end{array} \right]^{-}$$
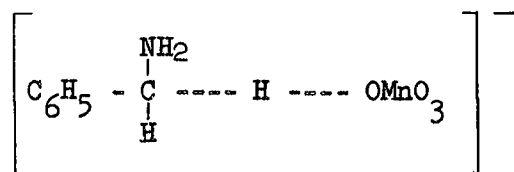
The way in which charge is distributed in this transition state is not known with certainty, however. That is, the choice of a hydride ion transfer mechanism or a hydrogen atom transfer mechanism for the oxidation of benzylamines cannot be unequivocally made from the results obtained in this thesis. It seems that the same predicament also exists in other permanganate oxidations (23,24,34), and it is not obvious whether a clear-cut differentiation for the two mechanisms will ever be possible.

The results from the oxidation of benzylamines seem to support both mechanisms. The direct correlation of the reactivity and σ^+ values for most substituents and the negative rho value of the reaction support the hydride transfer mechanism giving a carbonium ion in the transition state. Radical reactions have also been known to give good Hammett correlations with σ^+, and moreover, to give large, negative rho values (93,94,95) which indicate the importance of resonance effects in the transition state. For such reactions, transition states with some carbonium ion character have been postulated.

On the other hand, results from the study of (-)-α-methylbenzylamine and of p-nitrobenzylamine suggest a hydrogen atom transfer mechanism.

A mechanism which takes into account the properties of both hydride ion and hydrogen atom removal is presented below:

$$\phi\text{-CH}_2\text{-NH}_2 \ + \ \text{MnO}_4^-$$

$$\left[\begin{array}{c} \overset{\delta+}{}\text{NH}_2 \\ \phi\text{-}\overset{|}{\underset{|}{\text{C}}}\text{---H---OMnO}_3^- \\ \text{H} \end{array}\right] \qquad \left[\begin{array}{c} \text{NH}_2 \\ \phi\text{-}\overset{|}{\underset{|}{\text{C}}}\text{---H---OMnO}_3^- \\ \text{H} \end{array}\right]$$

$$\text{I} \qquad\qquad\qquad\qquad \text{II}$$

$$\phi\text{-}\overset{+}{\underset{\text{H}}{\text{C}}}\text{=NH}_2 \qquad\qquad \phi\text{-}\overset{\ominus\ \cdot}{\underset{\text{H}}{\text{C}}}\text{-}\overset{+}{\text{N}}\text{H}_2 \longleftrightarrow \phi\text{-}\overset{\cdot}{\underset{\text{H}}{\text{C}}}\text{-NH}_2$$

$$-\text{H}^+ \qquad\qquad\qquad \text{Mn(VII) or Mn(VI)}$$

$$\text{fast}$$

$$\phi\text{-CH=NH} \qquad\qquad\qquad\qquad\qquad (43)$$
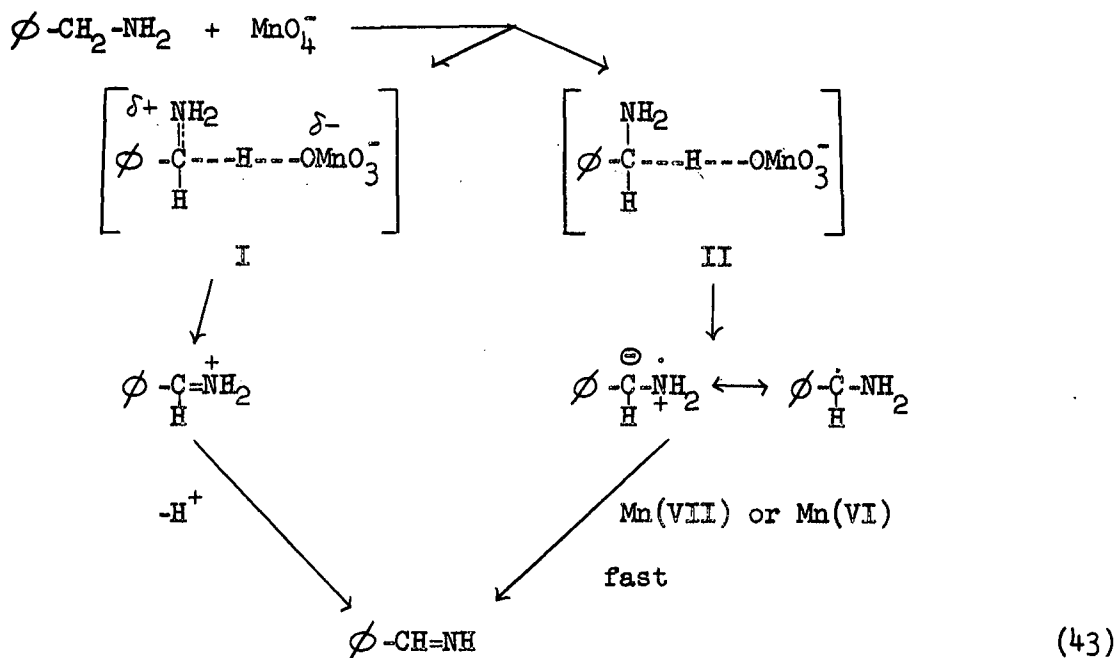
The transition states I and II in equation (43) may be of equal or nearly equal energy such that the choice of either one can be influenced by the nature of the groups attached to the alpha-carbon. The stabilities of benzyl carbonium ions and benzyl radicals lend support to the existence of both transition states. Depending on the particular nuclear substitution, transition state I or transition state II may be on the more favored pathway.

In general, electron-withdrawing substituents tend to stabilize benzyl radicals (96), but electron-donating substituents exert very little influence on their stability. The correlation of reactivity with σ^+ and the negative rho value for the oxidation of benzylamines with electron-donating and weakly electron-withdrawing substituents suggest that resonance stabilization of the carbonium ion may

be important in the transition state. On the other hand, the enhanced reactivity of the benzylamines with strongly electron-withdrawing substituents may be explained by the increased importance of the radical transition state II. It should be pointed out that I and II may, in fact, simply be different formulations of the same transition state since the only difference between them is the way in which electrons are distributed. To be sure, one leads to a radical intermediate and the other to a cation intermediate and this means that two distinct paths can be envisaged for the overall reaction. It is possible, however, that the decomposition of the activated complex to the two types of products is nicely balanced and can be influenced by many factors such as the electronic effect of ring substituents, vibrational effects in the transition state, etc. It may indeed be preferable to consider a common activated complex whose decomposition is normally controlled by a probability factor but which can be influenced by changes in the electron density at the reaction site, i.e.,

$$ArCH_2NH_2 \; + \; MnO_4^- \; \longrightarrow \; \left[Ar-\underset{H}{\overset{NH_2}{C}}\text{---H---}OMnO_3 \right]^- \; \longrightarrow \; ArCH=\overset{+}{N}H_2 \; + \; HMnO_4^=$$

$$\searrow \; Ar\dot{C}H=NH_2 \; + \; HMnO_4^-$$

$$\updownarrow$$

$$Ar\overset{..}{C}H-\overset{.}{\underset{+}{N}}H_2$$
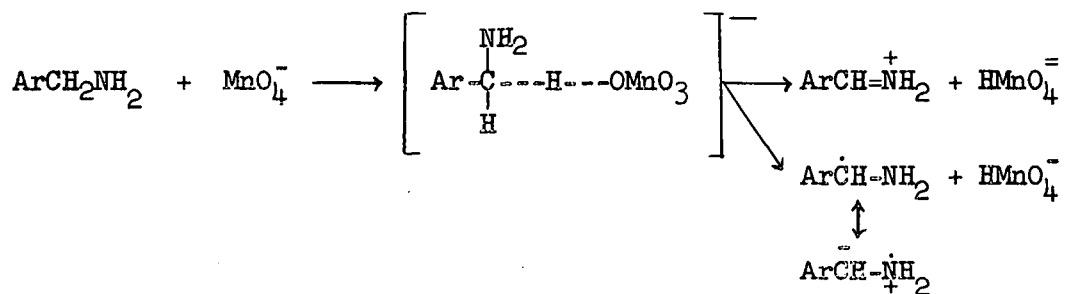
(44)

PART II: OXIDATION OF t-BUTYLAMINE

EXPERIMENTAL

A. Synthesis of Possible Oxidation Intermediates

1. Synthesis of t-butylhydroxylamine

Zinc dust (10.5 g.) was added to a stirred mixture of ammonium chloride (9.8 g.) and t-nitrobutane (23.5 g) in 300 ml. water over a period of 15 minutes. The temperature of the reaction was kept at 35° for 35 minutes. The zinc oxide was filtered and washed with 50 ml. warm water. The filtrate was saturated with sodium chloride and cooled in an ice bath. A small amount of unreacted t-nitrobutane crystallized out and was filtered with crushed ice. The filtrate was extracted with ether and dried with sodium sulfate. The ether was then distilled off under nitrogen and the residue was recrystallized in 30-60° petroleum ether. M.p. 61-62° (lit. 64-65°)(97). The oxalate salt of t-butylhydroxylamine was prepared by adding the latter to an ethereal solution of oxalic acid. The salt was recrystallized from water, m.p. 200° (lit. 200-202°) (98).

2. Synthesis of t-nitrosobutane

When air was bubbled through an aqueous solution of t-butyl-hydroxylamine blue t-nitrosobutane was produced. The ultraviolet spectrum of this solution showed the typical nitroso peak at 287 mμ (99).

B. Product Analysis

1. Synthesis of t-nitrobutane from t-butylamine

Following the method of Kornblum (39) 28.8 ml (0.274 mole) t-butylamine was slowly added to a stirred mixture of 130 g. (0.823 mole)

of potassium permanganate and 600 ml. water. The mixture was stirred at room temperature for nine hours, warmed to 60° for 16 hours, and then stirred without heating for 15 hours. The t-nitrobutane was separated from the reaction mixture by steam distillation and after acidification with dilute hydrochloric acid and cooling in ice, it crystallized in white lumps. The yield of the crude product was 23.5 g., or 83%.

2. Synthesis of t-nitrobutane from t-butylhydroxylamine

To an aqueous solution of t-butylhydroxylamine (3.5 g. dissolved in 10 ml. water) a solution of potassium permanganate (0.1M) was added until the solution turned purple. The compounds were allowed to react for 30 minutes, after which time the t-nitrobutane was removed by steam distillation. The distillate was slightly blue in color, presumably due to some traces of t-nitrosobutane. The yield of the t-nitrobutane was 1.9 g., or 47%, and its infrared spectrum was identical with the sample of t-nitrobutane synthesized previously by the Kornblum method.

C. Kinetic Studies

1. Buffers of high concentration

Since the permanganate t-butylamine reaction was so very slow the concentration of the components was greatly increased in order to give measurable rates. Since the final concentration of hydroxyl ion formed during the reaction will equal that of the initial permanganate (0.1M), the buffer concentration was raised to 1.2M. A stock solution of 2M dipotassium hydrogen phosphate was prepared and was diluted ac-

cordingly for the kinetic runs.

2. t-Butylamine

t-Butylamine was twice distilled and a middle fraction boiling at 44° was collected and used for the kinetic runs. Stock solutions were prepared from freshly distilled amine and distilled water which had been boiled and saturated with nitrogen. The concentrations were determined from titrations with standard·hydrochloric acid using methyl red as indicator.

The purity of the t-butylamine was checked by vapor phase chromatography and only one peak was observed.

3. Kinetic method

A typical run was carried out as follows: in a 125-ml red Erlenmeyer flask were mixed 30 ml. of 2M phosphate buffer, 5.96 ml. of 4M potassium hydroxide, 4.04 ml. of 0.615M t-butylamine. The solution was thermostated at $25.0 \pm 0.02°$ for one hour. The reaction was started when 10 ml. of 0.497M potassium permanganate was injected from a 10 ml. Chaney-adapted syringe into the solution. One ml. aliquots were immediately removed with a 2 ml. Chaney-adapted syringe and delivered into 5 ml. volumetric flasks. Each flask was wrapped with aluminum foil to exclude light and then thermostated at $25.0 \pm 0.02°$. The pH was 11.20. At appropriate times the contents of the entire flask was quenched with excess acidified potassium iodide. Analyses were carried out by iodometric titration.

Since the reactions were very slow the pH of the solutions were checked regularly and were found to vary by only ± 0.02 unit for all the solutions.

4. Studies in D_2O

Since the buffer concentrations must be very high, dipotassium hydrogen phosphate was replaced with tripotassium phosphate, in order to minimize the number of exchangeable protons. The most concentrated stock solution of tripotassium phosphate which could be prepared was 1.0M, however. Separate stock solutions of buffer, t-butylamine, and potassium permanganate were prepared in D_2O and H_2O. In each case the concentrations were identical. 0.5 ml. D_2SO_4 (approximately 10%) was used in the protio as well as the deuterio reaction solutions in order to bring the pH down to 11.50.

RESULTS

Stoichiometry

Studies carried out on t-butylhydroxylamine and t-nitrosobutane, which are probable intermediates in the oxidation of t-butylamine by permanganate, have shown that they are almost instantaneously oxidized by acidic or basic permanganate. Half-life of the reaction between permanganate and t-butylhydroxylamine at pH 8.86 and a hydroxylamine concentration of 2×10^{-2} M was less than 0.6 of a minute. Because o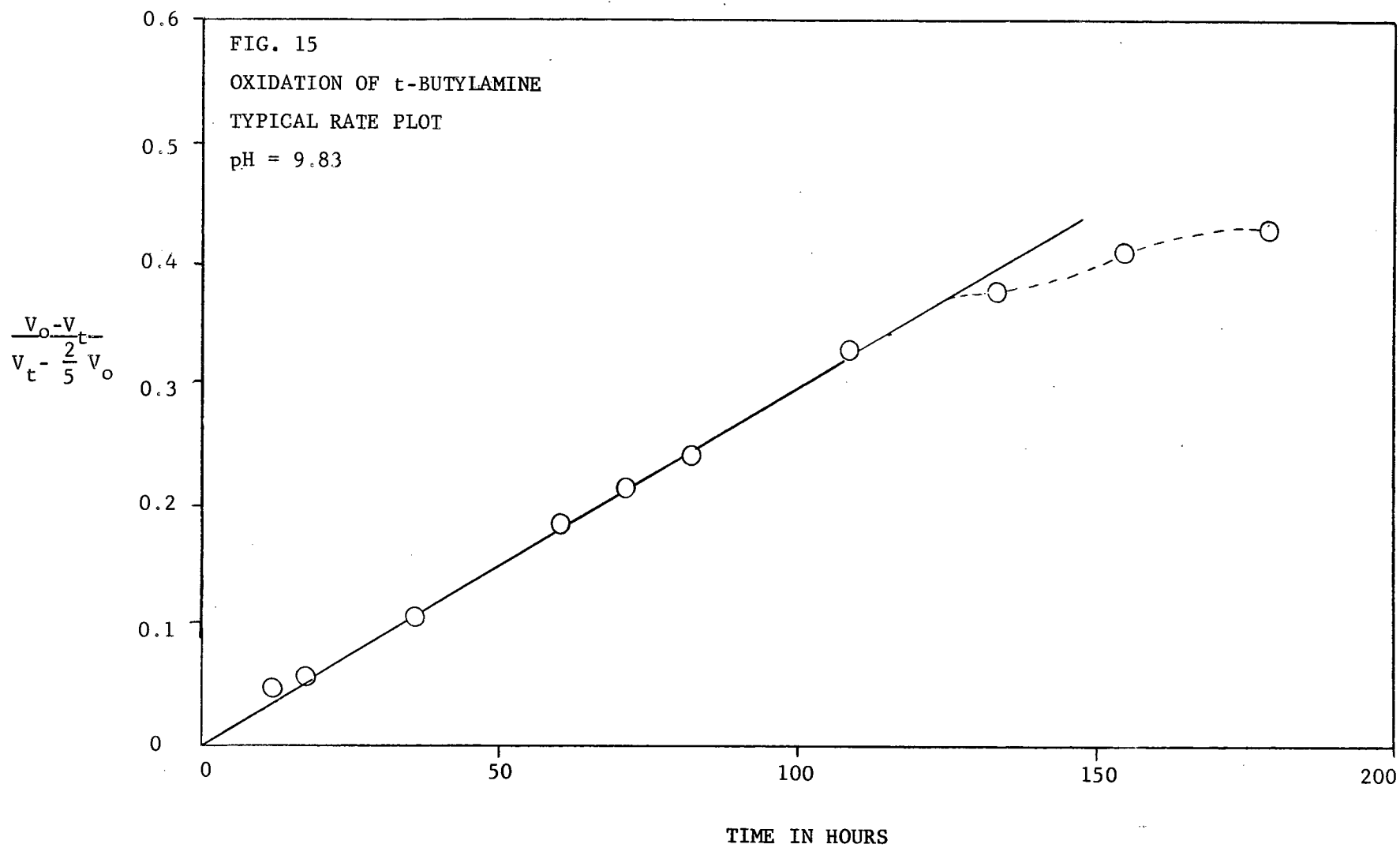f the rapidity with which these compounds are oxidized the stoichiometry of the much slower reaction between basic permanganate and t-butylamine can be expressed as follows:

$$2 \, MnO_4^- + RNH_2 \longrightarrow RNO_2 + 2 \, MnO_2 + 2 \, OH^- \qquad (45)$$
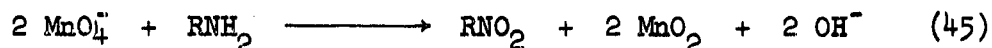
Order of reaction

The kinetic data gave good linear second order plots up to approximately 20-30% reaction, after which the points became scattered. (Figure 15). A possible explanation is that the cause of the erratic and reduced rate might be due to an accumulation of manganese dioxide. It was observed that after about 20-30% reaction there was visible precipitation of manganese dioxide in the reaction flask. It is known that the -OH group of alcohols can be oxidized by MnO_2 after being adsorbed onto the latter's surface (10). Correspondingly, it is possible that the amino group of t-butylamine can also be adsorbed by the precipitated MnO_2. Although the t-butyl group is not activating enough to cause the amino group to be oxidized by MnO_2, the adsorption

FIG. 15

OXIDATION OF t-BUTYLAMINE

TYPICAL RATE PLOT

pH = 9.83

$$\frac{V_o - V_t - \frac{2}{5} t}{V_t - \frac{2}{5} V_o}$$

TIME IN HOURS

process itself must serve to deactivate the amine to permanganate oxid-ation. To test this assumption, MnO_2, corresponding to 25% of the total Mn(VII) concentration, was generated in situ according to the equation (21):

$$3 \ Mn^{+2} + 2 \ MnO_4^- + 2 \ H_2O \longrightarrow 5 \ MnO_2 + 4 \ H^+ \qquad (46)$$
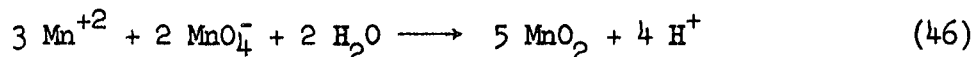
When this was done prior to the addition of the t-butylamine at pH 9.87 the resulting second order plot was erratic from the very begin-ning of the reaction (Figure 16).

Effect of pH on the oxidation rate

The plot of the rate constants versus pH gave a typical ion-ization curve (Figure 17). Table XII lists the data for Figure 17. The rate plots for pH 13 and higher were autocatalytic in character, and hence no rate constants were calculated from them.

To show that the ionization is due to that of t-butylamine, a plot of log $(k_2/k_2^{max} - k_2)$ versus pH was made, where k_2^{max} was es-timated from the graph. A slope of 1.1 was obtained and the intercept at zero gave the pK_{BH^+} of 10.98 for t-butylamine. The literature value for the pK_{BH^+} of t-butylamine was 10.45 (100).

Oxidations in D_2O

The rate in H_2O at pH 11.50 and 25.0 ± 0.02° was 0.886 1. mole^{-1}hour^{-1}, compared with 0.630 1. mole^{-1}hour^{-1} in D_2O. The isotope effect was 1.4.

FIG. 16

OXIDATION OF t-BUTYLAMINE

EFFECT OF Mn^{+4} ON THE OXIDATION

pH = 9.87

$\dfrac{V_o - V_t}{V_t - \frac{2}{5}V_o}$

TIME IN HOURS

83

FIG. 17

OXIDATION OF t-BUTYLAMINE

RELATION BETWEEN RATE CONSTANT AND pH
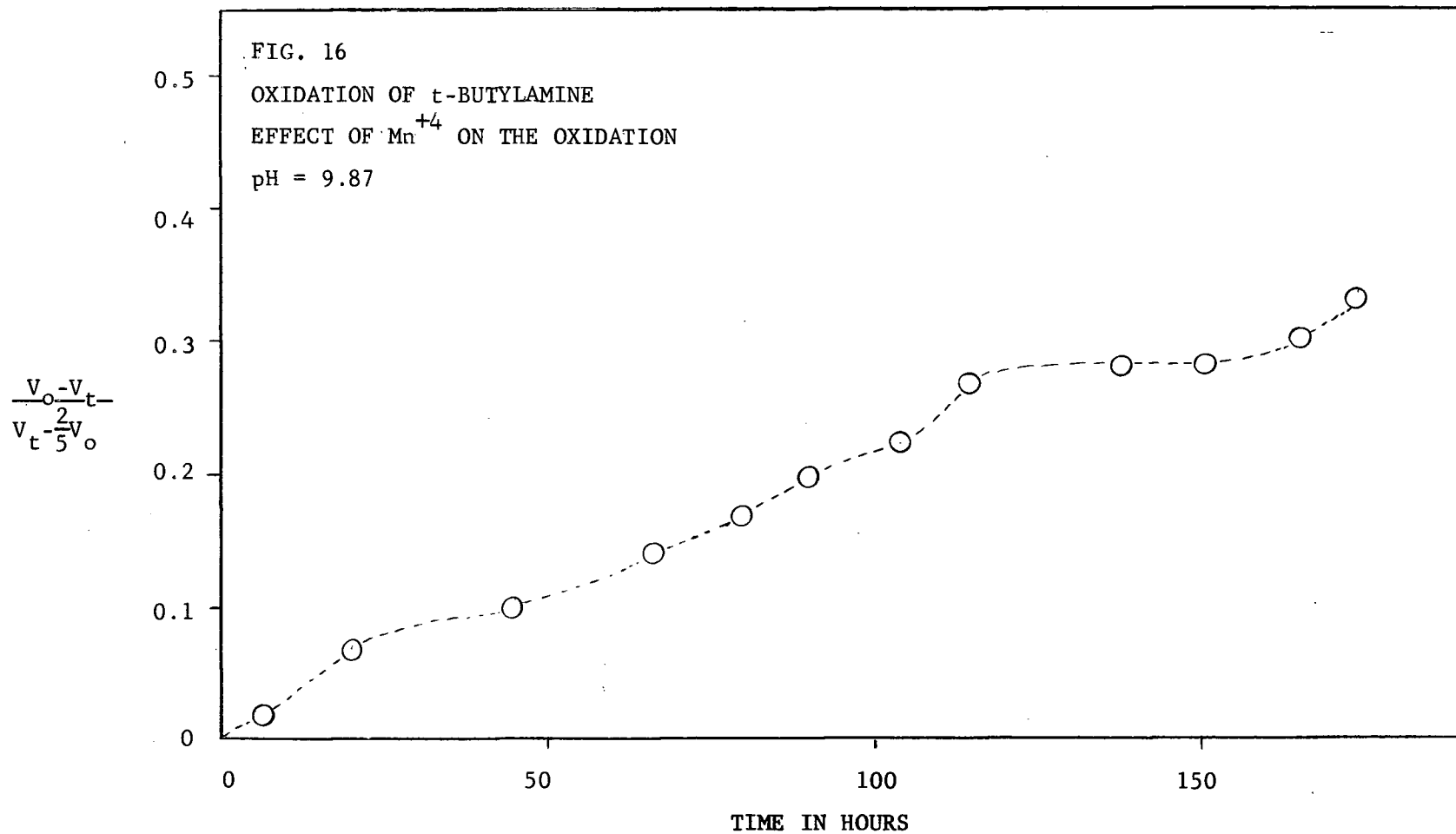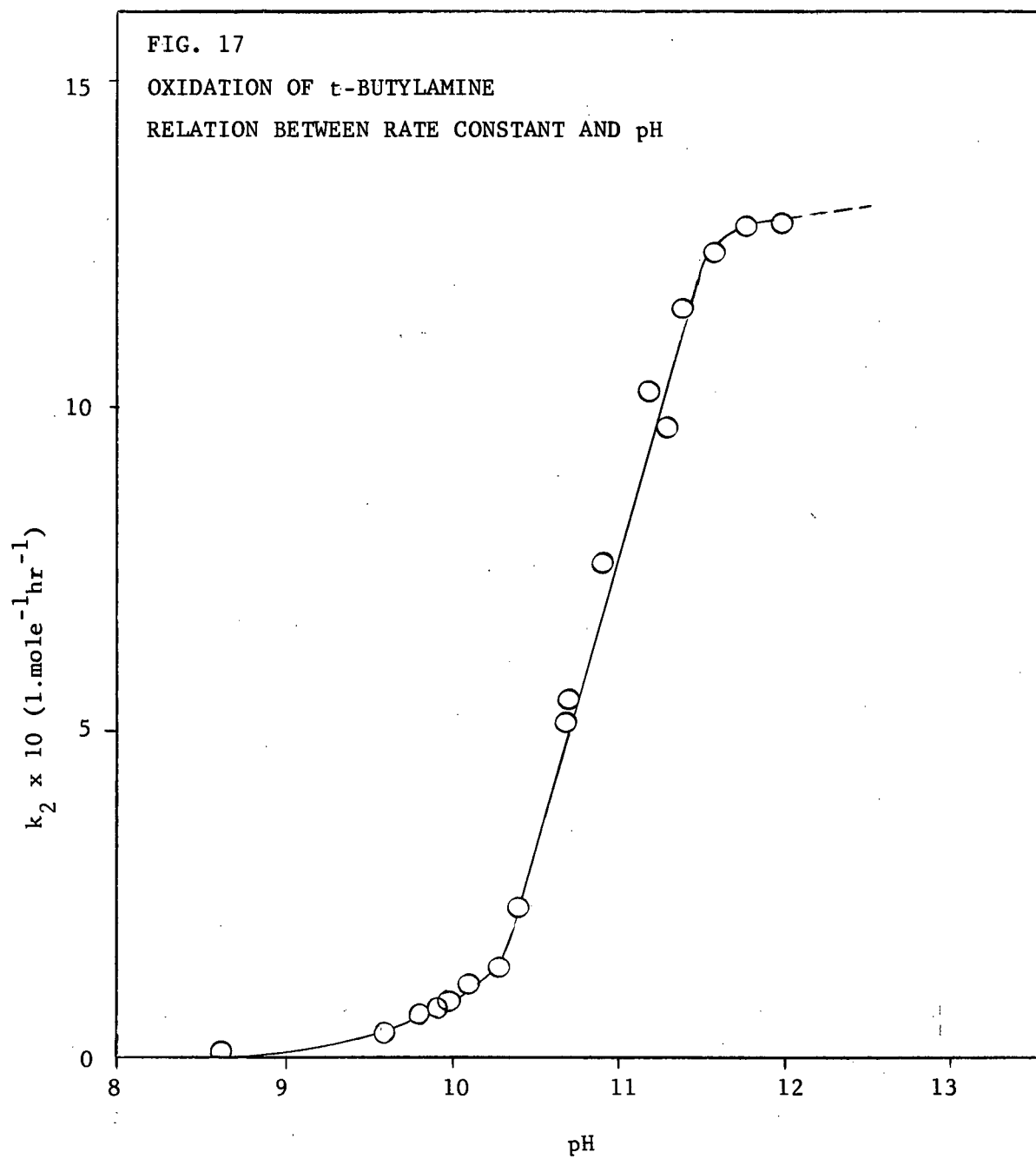
Table XII

Oxidation of t-Butylamine

Variation of Rate with pH

pH	k_2 (l.mole^{-1}hr^{-1})
8.62	3.28×10^{-3}
9.60	3.40×10^{-2}
9.83	5.81×10^{-2}
9.89	7.32×10^{-2}
9.99	7.55×10^{-2}
10.12	1.09×10^{-1}
10.26	1.34×10^{-1}
10.32	2.24×10^{-1}
10.40	2.26×10^{-1}
10.67	5.03×10^{-1}
10.68	5.42×10^{-1}
10.90	7.54×10^{-1}
11.20	1.02
11.34	9.57×10^{-1}
11.42	1.14
11.56	1.23
11.81	1.27
12.04	1.26

$$k_2^{max} = 1.30$$

DISCUSSION

The stoichiometry of the reaction between permanganate and t-butylamine may be represented in the following equation:

$$RNH_2 + 2\ MnO_4^- \longrightarrow RNO_2 + 2\ MnO_2 + 2\ OH^- \tag{45}$$
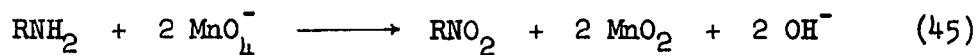
The product, t-nitrobutane, is not further attacked by permanganate and can be isolated in very good yields.

The kinetics of the oxidation of t-butylamine by permanganate is second order, first order in permanganate and first order in t-butylamine. As in the oxidation of benzylamine, the permanganate reacts with the neutral amine. Accordingly, a plot of the second order rate constant versus pH resembles an ionization curve (Figur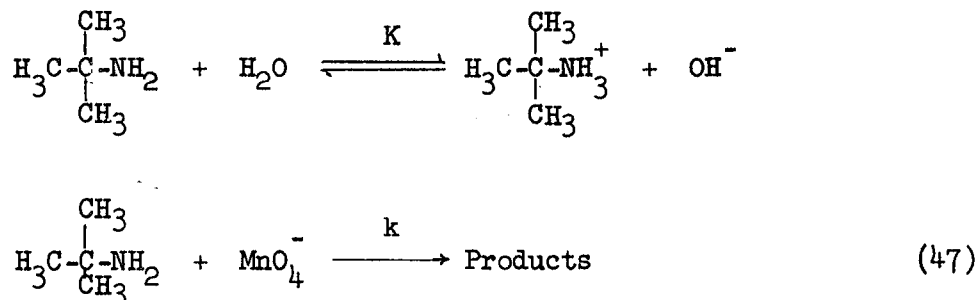e 17), the midpoint of which is 10.98. This value differs considerably from the reported pK_{BH}^+ of t-butylamine, 10.45 (100). However, it is possible that the pK_{BH}^+ is altered by the very high ionic strength (approaching 3.6) that was used.

The mechanism of the reaction can be expressed by the following equations:

$$
\begin{array}{c}
\quad CH_3 \\
\quad | \\
H_3C\text{-}C\text{-}NH_2 \\
\quad | \\
\quad CH_3
\end{array}
+ H_2O
\underset{\longleftarrow}{\overset{K}{\rightleftharpoons}}
\begin{array}{c}
\quad CH_3 \\
\quad | \\
H_3C\text{-}C\text{-}NH_3^+ \\
\quad | \\
\quad CH_3
\end{array}
+ OH^-
$$

$$
\begin{array}{c}
\quad CH_3 \\
\quad | \\
H_3C\text{-}C\text{-}NH_2 \\
\quad | \\
\quad CH_3
\end{array}
+ MnO_4^-
\xrightarrow{\ k\ }
\text{Products}
\tag{47}
$$

The rate law corresponding to the proposed mechanism is:

$$- \frac{d[MnO_4^-]}{dt} = k\ [MnO_4^-]\ [(CH_3)_3CNH_2]$$

$$= \frac{k}{K}\ [MnO_4^-]\ [(CH_3)_3CNH_3^+]\ [OH^-] \tag{48}$$

The rate of oxidation of t-butylamine is very much slower than that of benzylamine. Permanganate reacts 30 times more rapidly with benzylamine than with t-butylamine. Ammonia, on the other hand, is oxidized by permanganate at 1/10th the rate of the oxidation of t-butylamine.

The oxidation of t-butylamine in D_2O compared with the oxidation in H_2O at the same pH gives a solvent isotope effect, $k\ (H_2O)/k\ (D_2O)$ of 1.4. This value is not sufficiently large to suggest the cleavage of the N-H bond in the rate-controlling step. The only alternative pathway for permanganate to take in the oxidation process is an oxidative attack on the nitrogen, since in t-butylamine there is no α-hydrogen to react with.

The following mechanism is proposed to accommodate the observed results:

$$RNH_2 + MnO_4^- \xrightarrow{\text{r.d.s.}} R\overset{+}{\underset{H}{\overset{H}{N}}}\text{-O-}MnO_3^= \tag{I}$$

$$\xrightarrow{\text{fast}} R\overset{+}{N}H_2O^- \quad + \quad MnO_3^-$$

$$\downarrow \qquad\qquad\qquad \downarrow \text{Disproportionation}$$

$$RNHOH \qquad\qquad Mn(IV) + Mn(VII)$$

$$\text{Fast} \downarrow Mn(VII)$$

$$RNO_2 \tag{49}$$
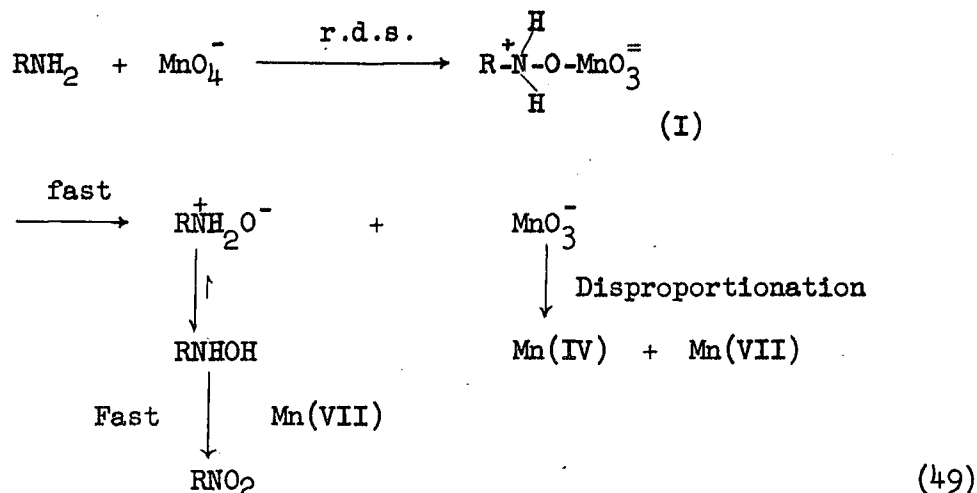
The rate-controlling step involves an electrophilic attack on the t-butylamine by permanganate to give a quaternary hydroxylamine deriva-tive (I). It seems doubtful that the formation of I could be rever-sible since the manganese is already in the oxidation state of +5 in this ion. Moreover, efforts made to detect the permanganate-t-butyl-amine (and NH_3) interaction spectrophotometrically in the visible and ultraviolet regions failed to show (1) any change in the original Mn(VII) spectrum and (2) any appearance of the manganese(V) species. If an equilibrium does occur it must be shifted very far to the left.

Since there is a small isotope effect, probably a solvent isotope effect, it seems likely that the formation of (I) is rate-controlling. Solvent isotope effects of similar magnitude (20-40%) as that observed for t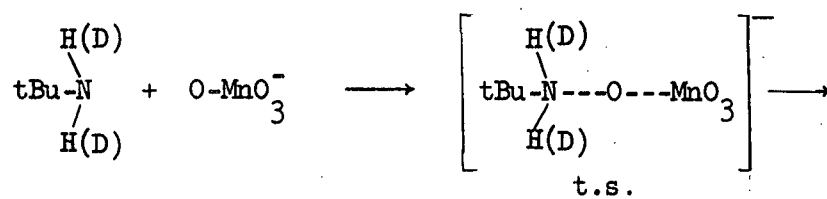-butylamine have been found for numerous reac-tions where decreases in rates were observed on changing the solvent from H_2O to D_2O (101,102,103,104). In all these cases the solvent does not take part in the actual reaction, but it is involved in the solvation of all the species which are in solution. The isotope effects which are observed must therefore be due to the difference in the sol-vating powers of H_2O and D_2O for the reactants or for the transition state. The similarity between the transition state for the hydrolysis of methyl bromide and the transition state for the permanganate oxida-tion of t-butylamine and their respective solvent isotope effects are compared below:

$$\begin{matrix} H \\ \diagdown \\ O \\ \diagup \\ H \end{matrix} \quad + \quad CH_3Br \quad \longrightarrow \quad \left[\begin{matrix} H & & H \\ \diagdown{\scriptstyle\delta+} & & | \\ O\text{---}C\text{---}Br\,{\scriptstyle\delta-} \\ \diagup & & | \\ H & & H\,H \end{matrix} \right] \quad \longrightarrow$$

t.s.

$$D{-}O{-}D \quad + \quad CH_3Br \quad \longrightarrow \quad \left[\begin{array}{c} D \\ \overset{\delta+}{O}{-}{-}{-}\overset{H}{\underset{H\,H}{C}}{-}{-}{-}\overset{\delta-}{Br} \\ D \end{array} \right] \quad \longrightarrow$$

t.s.

$$k(H_2O)/k(D_2O) \quad = \quad 1.25 \text{ at } 70° \quad (101)$$

$$\underset{H(D)}{\overset{H(D)}{tBu{-}N}} \quad + \quad O{-}MnO_3^- \quad \longrightarrow \quad \left[\underset{H(D)}{\overset{H(D)}{tBu{-}N}}{-}{-}{-}O{-}{-}{-}MnO_3 \right] \quad \longrightarrow$$

t.s.
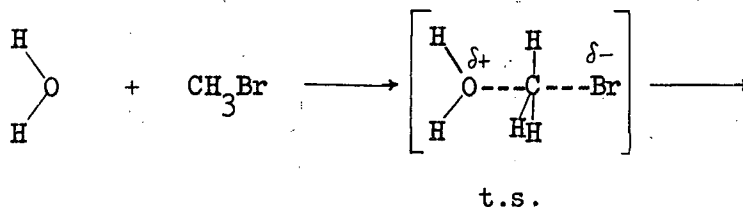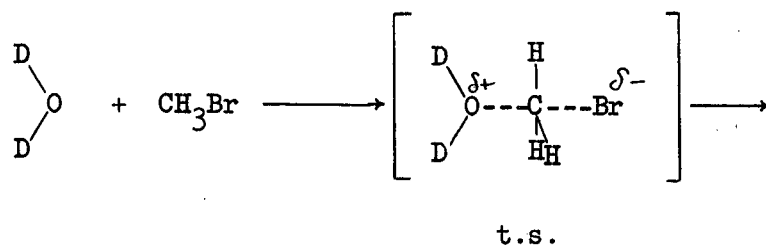
$$k(H_2O)/k(D_2O) \quad = \quad 1.40 \text{ at } 25°$$

PART III: OXIDATION OF BENZYLAMINES IN FROZEN SYSTEMS

EXPERIMENTAL

Oxidation of benzylamine in ice at -10°

A typical run was carried out as follows: a pH 9.31 solution
made up of   10 ml. of 1M buffer (K_2HPO_4)

3.94 ml. benzylamine (0.0253M)

33.98 ml. of water

2.08 ml. of potassium permanganate (0.0319M)

was prepared in a 125 ml. red Erlenmeyer flask which was cooled in an
ice water bath. Immediately after the last reagent, the permanganate,
was added, a 4 ml. sample was delivered into a 10 ml. screw-capped
bottle and immersed in a Dry Ice-acetone bath. This sample was used
for the blank. Eight more samples were then prepared and they were
all simultaneously placed undisturbed into the Dry Ice-acetone bath
for 4 minutes. During this solidification process, the blank was
warmed under hot tap water (ca. 50°), quenched with excess warm
acidic KI solution and transferred quantitatively into a 50 ml. flask
containing 10 ml. of 0.3M sulfuric acid. The contents were then
titrated with thiosulfate solution.

After four minutes the eight samples in the Dry Ice-acetone
bath were transferred to an ice-water bath for 1 minute, during which
time the temperature of the samples was found to rise to approximately
-10°. The samples were finally transferred to a salt-ice bath which had
been adjusted to $-10 \pm 0.2°$. The various baths were prepared in covered
Dewar flasks, so that temperatures were constant for the duration of the
entire experiment. Initial time was taken when the samples were placed

into the -10° bath. At appropriate intervals, the frozen samples were removed and warmed and analysed in the same manner as for the blank. The pH of the solutions were taken when the samples were at room temperature.

RESULTS

Table XIII compares the rates obtained for identical solutions in liquid and in frozen states.

Table XIII

Comparison of Rates for Benzylamine and p-nitrobenzylamine in Liquid and in Frozen Systems. k_2 in $l.mole^{-1}min^{-1}$

| Benzylamine	k_2 (25°)	k_2 (-10°, ice)
pH 9.31	14.50	15.11
8.25	2.96	5.02
7.53	0.350	0.834
p-Nitrobenzylamine		
pH 7.50	4.90	1.15

It was observed that whereas the second-order rate plots for the runs at 25° tended to curve downwards after about 35% reaction, those for the frozen systems were entirely linear (Figure 18). However, in most of the rate plots, the line did not pass through the origin. This is not observed in the identical solutions oxidized at 25°. Moreover, the departure from the origin increased as the pH of the solution increased. This may be due to the fact that during the preparation of the samples, which usually took about 3 minutes, the reaction was already occurring in the liquid state. This assumption is reasonable, since in the oxidation of benzylamine at 25°, pH 7.53, the % reaction at 3 minutes corresponded almost exactly to the % reaction at zero

FIG. 18
OXIDATION OF BENZYLAMINE
TYPICAL RATE PLOT AT -10.0° (IN ICE)
pH = 7.53 (22°)

$$\frac{V_o - V_t}{V_t - \frac{2}{5} V_o}$$

TIME IN MINUTES

93
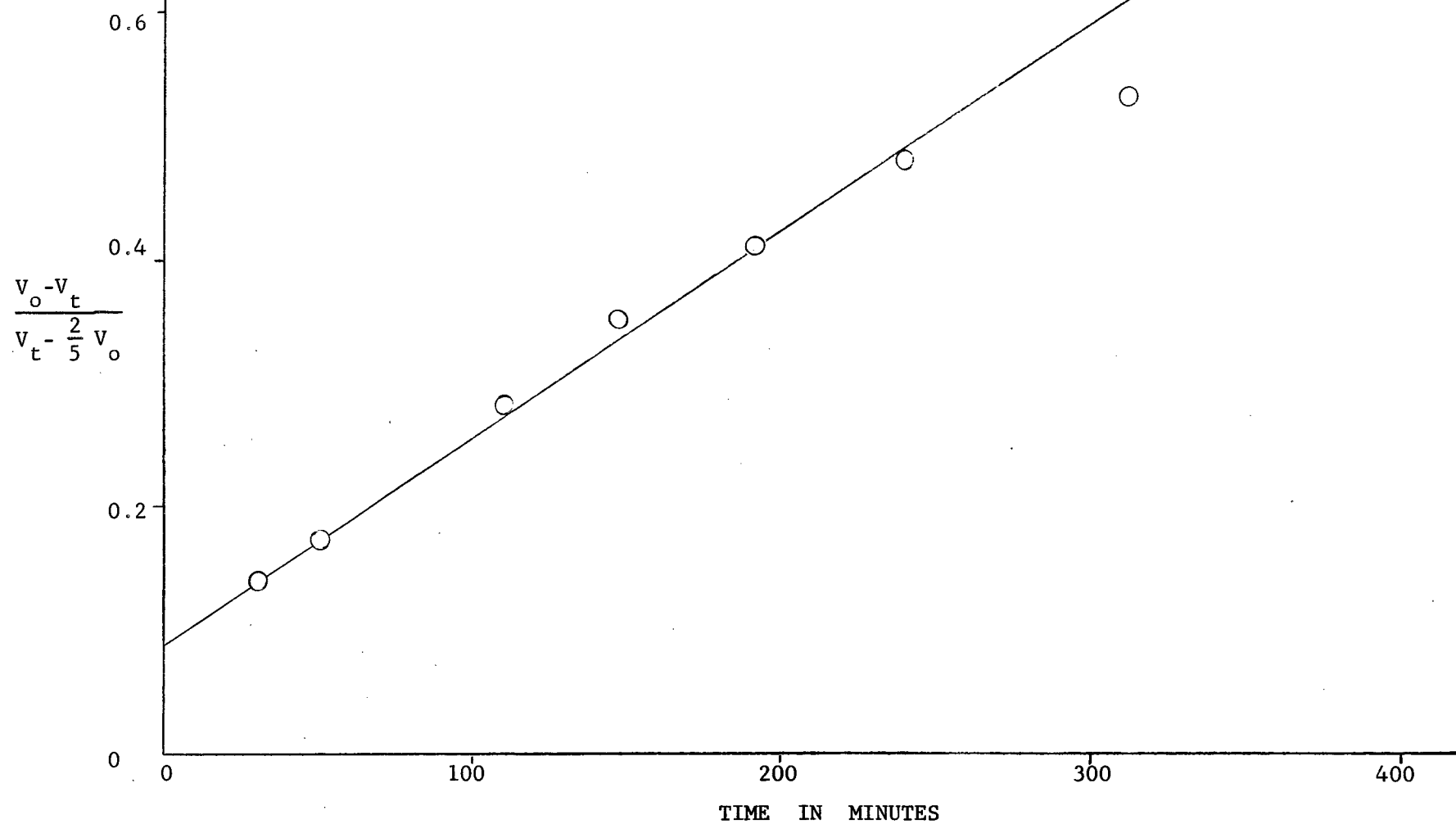
time for the frozen run.

Since these studies in the frozen systems are rather explor-
atory in nature, all the possible errors inherent in the technique have
not been entirely eliminated, although attempts to minimize them as
much as possible were made.

In the frozen systems, the oxidation rate also increased with
increasing pH, although the relationship was not a linear one (Figure 19).
To show that the rate is dependent on the free amine, a plot of
log (free amine) versus log k_2 was made (Figure 20) which was linear,
but with a slope of 1.37.

If one assumes that the rate law in the frozen systems is
unchanged from that in the liquid system, that

$$\text{Rate} = k \, [\text{MnO}_4^-] \, [\text{amine}],$$

then the reaction should be first order with respect to the amine.
It was found that if one used an "apparent" $pK_{BH}+$ of 8.70 for ben-
zylamine then the plot in Figure 20 assumed a unit slope.

It is not obvious at present whether the accelerated rates
obtained in the frozen systems are due to a reaction in the solid state
or to a concentrating of the reactants in pockets of liquid in the ice
lattice.

A kinetic run at pH 8.30 in which a large excess of sodium
sulfate was added (0.6M) showed no change in rate compared to the reac-
tion without added salt at the same pH.

Table XIV gives the rates obtained for the oxidations of ben-
zylamine in H_2O and D_2O. Unfortunately the pH of the solutions were
not identical, and hence in the third row the k_2' represents the calculated

FIG. 19

OXIDATION OF BENZYLAMINE AT -10.0° (IN ICE)

RELATION BETWEEN RATE CONSTANT AND pH

k_2 (1. mole^{-1} min^{-1})

pH (22°)
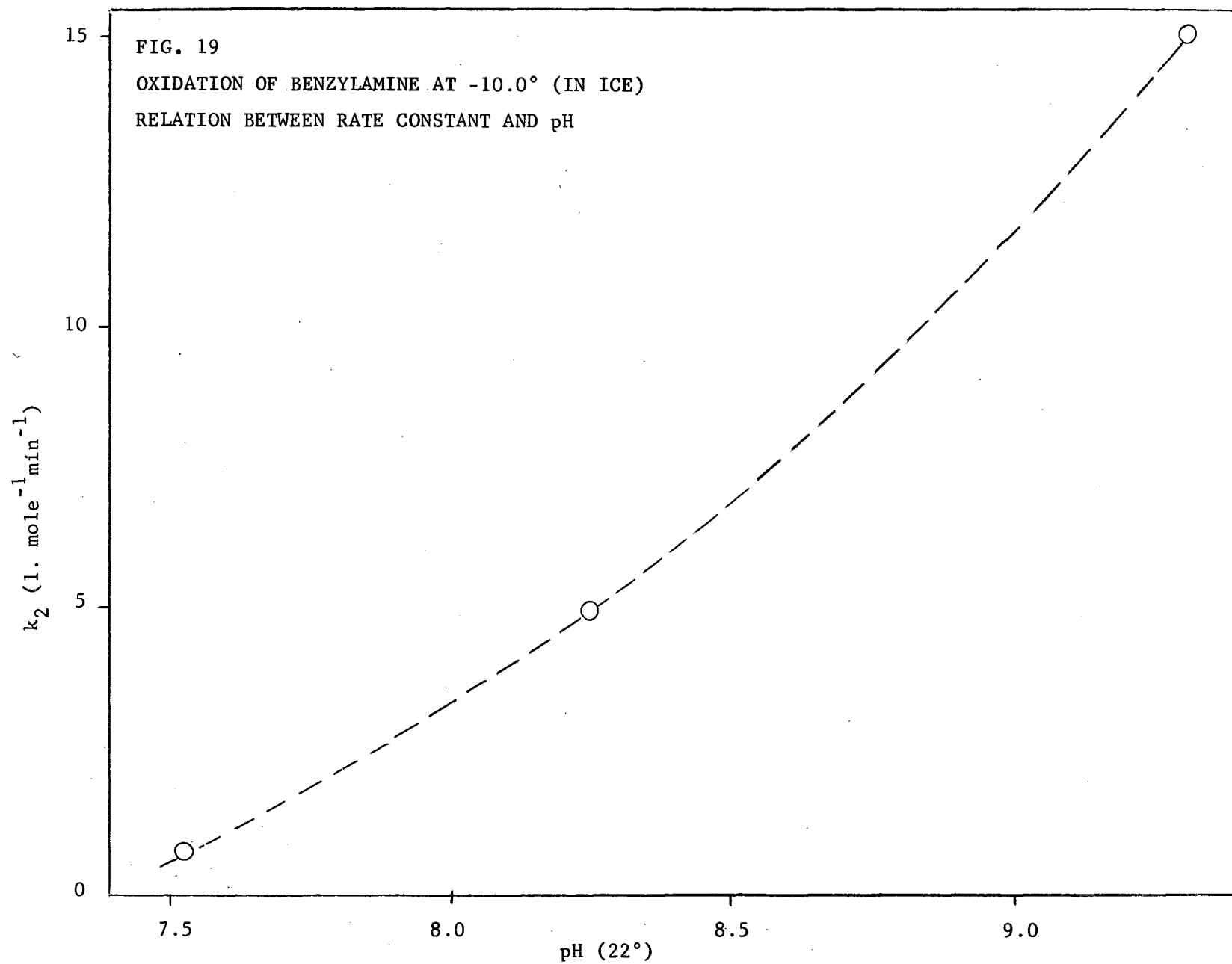
FIG. 20

OXIDATION OF BENZYLAMINE AT -10.0° (IN ICE)

RELATION BETWEEN LOG $[C_6H_5CH_2NH_2]$ AND LOG k_2

SLOPE = 1.4, USING $pK_{BH}+ = 9.28$

SLOPE = 1.0, USING APPARENT $pK_{BH}+ = 8.70$

LOG $[C_6H_5CH_2NH_2]$

LOG k_2
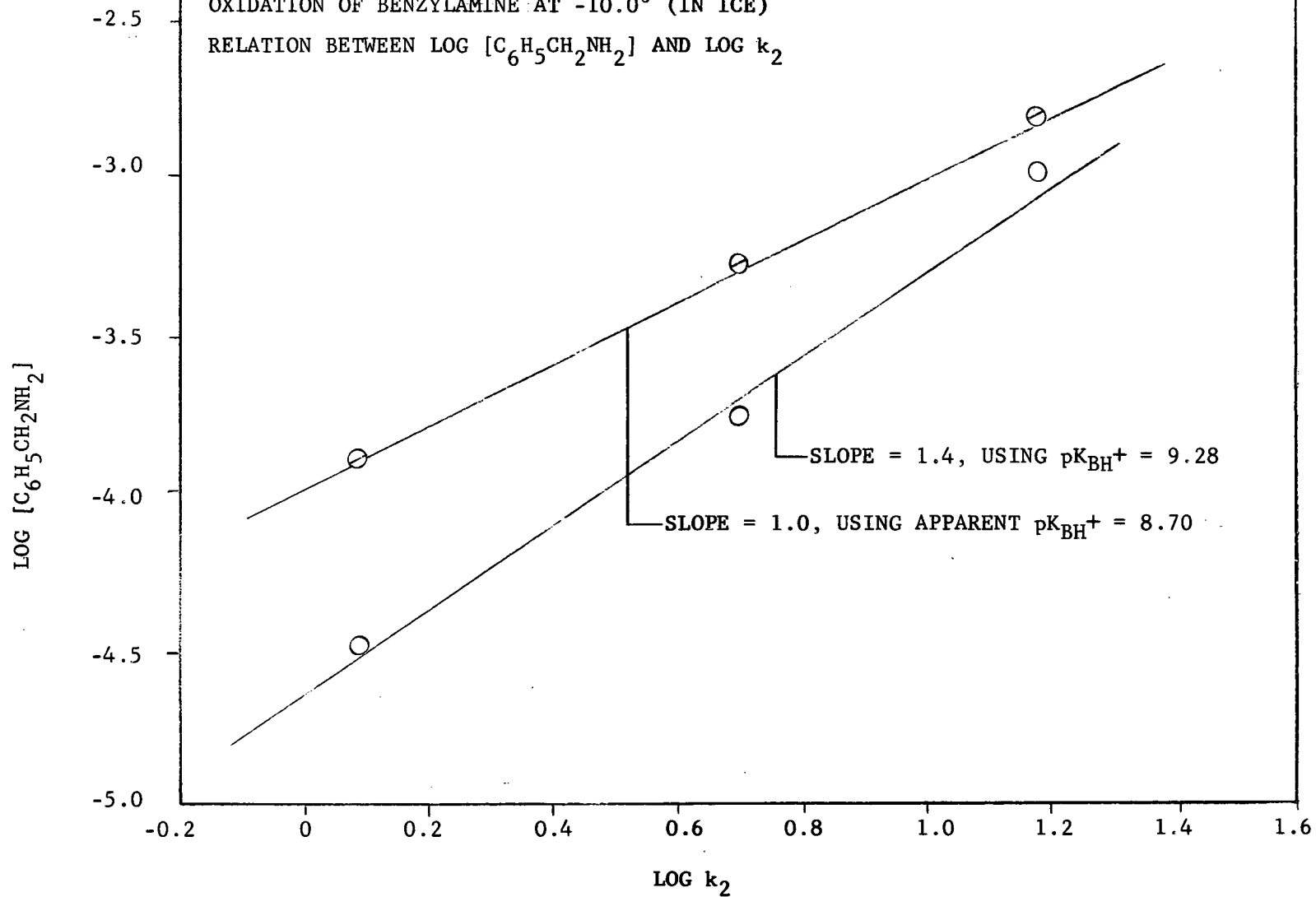
rate in D_2O if the pH were 8.99. To calculate k_2', the apparent $pK_{BH}{}^+$, 8.70, was used.

Table XIV
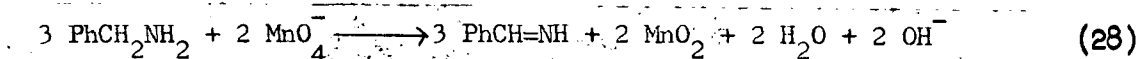
Rate Studies in H_2O and D_2O at -10°

(in ice)

Solvent	pH	k_2	k_2'	k_H/k_D
H_2O	8.99	17.01		
D_2O	9.23	24.10	20.60	0.83
D_2O	10.38	23.62	15.92	1.07

Mean = 0.95

It is puzzling that the rate in frozen H_2O at pH 8.99, k_2 = 17.01 l.mole^{-1}min^{-1}, did not agree with the extrapolated value obtained from Figure 19, k_2 = 11.8 l.mole^{-1}min^{-1}. The discrepancy might be partly due to the fact that in the former case, all the reagents are prepared by weight and in the latter case, all the reagents are standardized through titration.

DISCUSSION

There was no detectable change in the mechanism of permanganate oxidation of benzylamine when the reactions were carried out in frozen systems at -10°. The overall kinetics was second order: first in permanganate and first in benzylamine. The stoichiometry is still represented by the following equation:

$$3 \text{ PhCH}_2\text{NH}_2 + 2 \text{ MnO}_4^- \longrightarrow 3 \text{ PhCH=NH} + 2 \text{ MnO}_2 + 2 \text{ H}_2\text{O} + 2 \text{ OH}^- \qquad (28)$$

There was no marked solvent $(\text{H}_2\text{O}/\text{D}_2\text{O})$ isotope effect, and no salt effect.

Significant changes in the reaction rates were observed, however. In general, the rates from the frozen systems were higher than the corresponding rates from identical reactions at 25°. The difference in rates between the two systems increases with decreasing pH (Table XV).

Table XV

Relative Rates of Permanganate Oxidation between Reactions in Frozen Systems at -10° and those at 25° with Respect to pH

pH	k_2 (in frozen system)/k_2 (at 25°)
9.31	1
8.25	5/3
7.53	>2.5

Compared to the calculated rate constants for liquid systems at -10°, the rates from the frozen systems at -10° showed very large

accelerations which again increase with decreasing pH (Table XVI).

Table XVI

Comparison of Rate Constants between Liquid and Frozen Systems at -10°

| pH	k_2 (frozen, -10°)/k_2 (liquid, -10°)
9.31	10
8.25	21
7.53	40

The acceleration in rate is comparatively small for p-nitro-benzylamine in the frozen system. There was only a three-fold acceleration in going from the liquid (-10°) to the frozen (-10°) system.

The excellent linear second order plots which were obtained for the reactions in the frozen systems showed that the tendency for the imine to condense with benzylamine is minimized in these reactions at low temperature in ice.

Another significant change resulting from studies in the frozen systems is in the $pK_{BH}+$ of benzylamine. An apparent $pK_{BH}+$ of 8.70 was determined by benzylamine. Its $pK_{BH}+$ at 25° is 9.28. It is not known how the pH changes in these frozen systems. Kavanau (105) suggests that going from 25° to -10° (frozen system) there is a corresponding lowering of the activity of the hydrogen ion by a factor of approximately 10^3. This suggests a considerable increase in pH going from the liquid system to the frozen system.

It was originally thought that the ice lattice might affect

the amino hydrogens in some way so as to facilitate the removal of the

hydrogens in some way so as to facilitate the removal of the hydrogen

from the α-carbon by the permanganate. Such an effect would be par-

ticularly important in the oxidation of the benzylammonium ions, where

the transfer of an amino proton to the cavity walls might occur simul-

taneously with the removal of the hydrogen from the α-carbon by the

permanganate, viz.

$$\phi\text{-CH}_2\text{-NH}_3^+ \xrightarrow{\text{H}^+} \quad \text{ice wall}$$

$$\left(\text{H} \right.$$

$$\text{MnO}_4^-$$
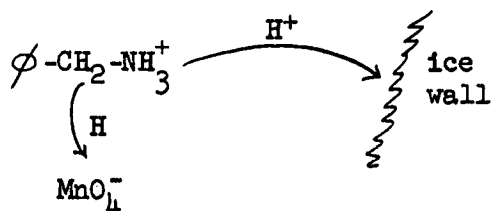
One is tempted to conclude that the lattice does remove a proton from

the benzylammonium ion since the relative rate, k(frozen)/k(liquid),

at $-10°$ does increase with decreasing pH. However, it must be pointed

out that the oxidation rate of benzylamine at pH 9.31 in ice is still

more than ten times faster than that of the benzylammonium ion in ice

at pH 7.53, and if a proton is removed by the lattice at the lower pH

values one would probably observe a much smaller difference between

the rates at pH 9.31 and 7.53.

Ordinary ice has been described by Kavanau as having an open

centrosymmetric structure similar to that of the hexagonal form of

silica, the tridymite structure (105). Each oxygen atom is tetra-

hedrally surrounded by four other oxygen atoms to which it is hydrogen-

bonded. The unit cell contains four water molecules, and the inter-

stitial regions are each bounded by six water molecules, the dimen-

sions of these regions between the coordinated tetrahedra being greater

than those of the water molecules. Because ammonium ions have tetra-
hedral structures resembling that of the water tetrahedron, they can
occupy the interstitial areas between the ice molecules and form hy-
drogen bonds with them without greatly disturbing the structural order
of the ice lattice. The greater accelerations in rate with decreasing
pH in ice may, therefore, be due to this special orientation of the
benzylammonium ions within the ice lattice by hydrogen bonding,
which is tantamount to removing some of the positive charge on
nitrogen, thus making the removal of the α-hydrogen by permanganate
much more facile.

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APPENDIX

Derivation of the rate expression for the kinetics in the basic region pH 12 to 14:

Assume the following stoichiometry:

$$3 \ RNH_2 \ + \ 4 \ MnO_4^- \longrightarrow 3 \ RCOOH \ + \ 4 \ MnO_2$$
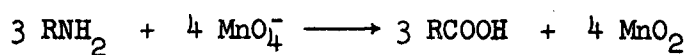
Let

$$y = [RNH_2]$$
$$x = [MnO_4^-]$$

Then

$$- \frac{dx}{dt} = kxy = k \left(\frac{3x^2}{4} \right)$$

Integrating:

$$- \int \frac{dx}{x^2} = \frac{3}{4} kt$$

$$\frac{3}{4} kt = \frac{1}{x_t} - \frac{1}{x_o}$$

$$\frac{3 x_o}{4} kt = \frac{x_o}{x_t} - 1$$

$$y_o kt = \frac{x_o}{x_t} - 1$$

If the ratio of $y_o:x_o$ were 1:2 instead of 3:4, then permanganate is in in excess, and

$$\text{at} \ \ t_\infty \ , \ x = x_o/3 \quad \text{and} \ y = 0$$

According to the 1:2 ratio used,

$$x = \frac{x_o}{3} + \frac{4y}{3} , \quad y = \frac{3x}{4} - \frac{y_o}{2}$$

The rate expression becomes

$$-\frac{dx}{dt} = kxy$$

$$= kx\left(\frac{3x}{4} - \frac{y_o}{2}\right)$$

$$= \frac{3\,kx}{4}\left(x - \frac{2y_o}{3}\right)$$

Integrating

$$\int \frac{dx}{x\;\;x - \frac{2y_o}{3}} = -\frac{3}{4}\,kt$$

$$\frac{3}{2y_o}\,\ln\left(\frac{x - 2/3\,y_o}{x}\right) = -\frac{3}{4}\,kt$$

$$\frac{1}{y_o}\,\ln\left(\frac{x - 2/3\,y_o}{x}\right) = -\frac{kt}{2}$$

Let $x_o = AV_o$, and $x = A[V_t - \frac{2}{3}(V_o - V_t)]$

where V_o = volume of standard thiosulfate solution

at $t=0$

V_t = volume of thiosulfate used at time t

A = constant of proportionality

Substituting

$$\ln\left(\frac{x - 2/3\,y_o}{x}\right) = \ln\left(\frac{x - 1/3\,x_o}{x}\right)$$

$$= \ln\left\{\frac{A\,[V_t - 2/3\,(V_o - V_t)] - 1/3\,AV_o}{A\,[V_t - 2/3\,(V_o - V_t)]}\right\}$$

$$= \ln\left\{\frac{V_t - 2/3\,V_o + 2/3\,V_t - 1/3\,V_o}{V_t - 2/3\,V_o + 2/3\,V_t}\right\}$$

$$= \ln \left(\frac{5/3\, V_t - V_o}{5/3\, V_t - 2/3\, V_o} \right)$$

$$= \ln \left(\frac{V_t - 3/5\, V_o}{V_t - 2/5\, V_o} \right)$$
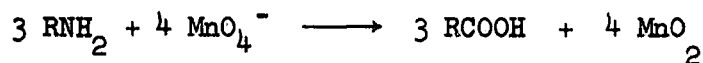
Hence

$$- y_o \frac{kt}{2} = \ln \left(\frac{V_t - 3/5\, V_o}{V_t - 2/5\, V_o} \right)$$

$$k = - \frac{4.60}{y_o t} \log \left(\frac{V_t - 3/5\, V_o}{V_t - 2/5\, V_o} \right)$$

At $t = 0$

$$\log \left(\frac{V_t - 3/5\, V_o}{V_t - 2/5\, V_o} \right) = \log (2/3)$$

Derivation of rate expression for the kinetics in the pH region 11.0 to 11.8:

Assume the following stoichiometry:

$$3\ RNH_2 + 4\ MnO_4^- \longrightarrow 3\ RCOOH + 4\ MnO_2$$

Let

$$y = [RNH_2]$$

$$x = [MnO_4^-]$$

According to the above stoichiometry: $y/x = 3/4$

If one used the ratio of $y:x = 3:2$, instead, then at $t = \infty$

$$x = 0$$

$$y = 1/2\, y_o$$

$$y = y_\infty + 3/4\, x$$

$$= \frac{y_o}{2} + 3/4\, \dot{x}$$

The rate expression becomes

$$- \frac{dx}{dt} = k \, xy$$

$$= kx \, (y_o/2 + 3x/4)$$

$$= kx \, (3x/4 + y_o/2)$$

$$= 3/4 \, kx \, (x + 2/3 \, y_o)$$

Integrating

$$- \int \frac{dx}{x(x + 2/3 \, y_o)} = \frac{3}{4} \, kt$$

$$- \frac{3}{2y_o} \ln \frac{2y_o/3 + x}{x} = - \frac{3}{4} \, kt$$

$$\frac{1}{y_o} \ln \left(\frac{2/3 \, y_o + x}{x} \right) = kt/2$$

Express in terms of V_o, V_t (defined as before)

$$\ln \left(\frac{2y_o/3 + x}{x} \right) = \ln \left(\frac{V_t - 2/3 \, (V_o - V_t) + 3V_o/2}{V_t - 2/3 \, (V_o - V_t)} \right)$$

$$= \ln \left(\frac{V_t - 2V_o/3 + V_t + 3V_o/2}{V_t - 2V_o/3 + 2V_t/3} \right)$$

$$= \ln \left(\frac{2 \, V_t}{5V_t/3 - 2V_t/3} \right)$$

$$k = \frac{4.60}{y_o \, t} \log \left(\frac{2 \, V_t}{5V_t/3 - 2 \, V_o/3} \right)$$

At $t = 0$,

$$\log \left(\frac{2 \, V_t}{5V_t/3 - 2V_o/3} \right) = \log 2$$

RATE CONSTANTS

Oxidation of Benzaldehyde

At pH 8.27: [PhCHO] = 3.75×10^{-3} M, $k_2 = 21.1$ l. mole^{-1} min^{-1}

[PhCHO] = [NH$_3$] = 3.75×10^{-3} M, $k_2 = 21.1$ l.mole^{-1} min^{-1}

Substituent Effects

X-C$_6$H$_4$CH$_2$NH$_2$	pH	k_2 (l.mole^{-1}min^{-1})
p-NO$_2$	9.24	30.8
p-NO$_2$	9.03	29.3
p-NO$_2$	10.21	40.9, 41.2
p-CH$_3$	9.19	12.5
p-CH$_3$	10.21	35.2
p-CH$_3$	9.73	23.6
p-CH$_3$O	8 88	13.6
p-CH$_3$O	10.21	50.25
m-CF$_3$	10.12	40.0
m-CF$_3$	10.15	40.0
p-Cl	10.21	31.7
m-CH$_3$	10.21	33.9, 30.9
m-NO$_2$	10.22	27.5
p-C$_2$H$_5$	10.21	35.4

Temperature Studies

| $X-C_6H_5CH_2NH_2$	pH	t° C	k_2(l.mole^{-1}min^{-1})
p-H	10.40	0.10	5.03
		14.75	16.7
		34.25	57.4
		45.40	112
p-NO$_2$	10.05	0.10	7.81
		13 50	17.9
		25.00	39.7
		38 60	89.2
m-CF$_3$	10.12	0.10	6.42
		16.00	21.8
		25.00	40.0
		35.20	81.1
		43.40	127
p-CH$_3$	10.19	0.10	4.88
		16.10	17.5
		25.25	33.5
		35.75	62.8
		44.35	106

SUGGESTIONS FOR FURTHER WORK

1. The kinetics of the permanganate oxidation of benzylamines in the
highly alkaline pH region requires further elucidation. All three
of the proposed mechanisms (equations 34-6) require the C-H bond
breaking in the rate-determining step. This could be easily
checked by studying the oxidation of benzylamine-α-d_2. Where-
as mechanisms 34 and 35 require hydrogen atom and hydride ion
removal respectively, mechanism 36 requires proton removal in
the rate-determining step. The first two mechanisms may be dif-
ferentiated from the last one by studying the substituent ef-
fects. Mechanisms 34 and 35 also suggest proton removal from
the nitrogen by the hydroxyl ion. Studies in D_2O should show a
substantial isotope effect for $PhCH_2ND_2$. It would also be in-
teresting to study the N-H proton removal step in frozen systems,
since studies of the oxidation of benzylamine in frozen systems
at lower pH regions suggest that the ice lattice might be re-
moving a proton from the nitrogen simultaneously as the perman-
ganate removes a hydrogen from the alpha carbon. In the previous
studies of the oxidation of benzylamine in frozen systems it was
not possible to decide whether the rate enhancements were due to
a concentrating effect of the freezing or to an orientating ef-
fect of the ice lattice. Since the oxidations in the highly al-
kaline region are termolecular, the concentrating effect of the
freezing should give much greater rate enhancements.

2. The study of the permanganate oxidation of p-trifluoromethyl-
benzylamine should shed some light on the anomalous behaviour

of the m-trifluoromethylbenzylamine.

3. The explanation suggested for the oxidation of p-nitrobenzylamine is that permanganate is removing a hydrogen atom from the amine and the enhanced rate that is observed is due to the extra sta- bilization of the resulting radical by the nitro group. Since the rate of racemization of (-)- α-methylbenzylamine is greater than its rate of oxidation, a radical mechanism has also been suggested in which the permanganate removes the alpha-hydrogen as a hydrogen atom. The permanganate oxidation of benzaldehyde and benzhydrol both show "normal" isotope effects when deu- terium is substituted in the alpha-position, while the perman- ganate oxidation of fluoral hydrate (monoanion) and aryl tri- fluoromethyl carbinols both exhibited very large isotope effects when deuterium is substituted in the alpha position. All of the above observations can be incorporated into one problem by studying the permanganate oxidation of optically active p-nitro- α-trifluoromethylbenzylamine, and its alpha-deuterio analogue,

$$O_2N-\langle\overline{\bigcirc}\rangle\overset{*}{\underset{H(D)}{\overset{CF_3}{\underset{|}{C}}}}-NH_2 \ ,$$
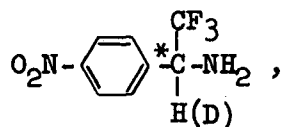
i.e. the two compounds can be used (1) to examine the unusually large isotope effects which have been observed with a $-CF_3$ group which is located alpha to a reaction center, and (2) to make a more thorough examination of the rate of racemization and compare it with the rate of oxidation.

It would be interesting to determine whether p-Nitro- α -

methylbenzylamine is acidic enough to ionize to the carbanion in the pH region. If it does ionize in the pH region, it should provide some interesting kinetics in its oxidation with permanganate. Its rate has been predicted to be much faster than that for the neutral molecule.