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The Alkaline Hydrogen Peroxide Oxidation  
of Phenyl-2-Propanones

Drexel D. Jones

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THE ALKALINE HYDROGEN PEROXIDE OXIDATION  
OF PHENYL-2-PROPANONES

A thesis submitted by

Drexel D. Jones

B.S. 1962, State University  
College of Forestry at  
Syracuse University

M.S. 1964, Lawrence University

in partial fulfillment of the requirements  
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Appleton, Wisconsin

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## SUMMARY

The alkaline hydrogen peroxide oxidations of phenyl-2-propanones have been investigated. Comprehensive product analysis and kinetic studies of the phenyl-2-propanones and related compounds were made to determine the mechanism of the oxidation. Gas chromatography constituted the principal method of qualitatively and quantitatively investigating the volatile reaction products. The aromatic acids from the oxidations were quantitatively isolated and characterized. Satisfactory product analysis and kinetics were obtained for most of the ketones. The noted exceptions were those compounds having strong electron-releasing substituents, i.e., p-hydroxyl and p-dimethylamino substituents.

Extensive studies showed that the phenyl-2-propanones were being oxidized by two competitive mechanisms. The primary reaction involved cleavage to a benzaldehyde and acetic acid. The slow competitive cleavage produced the benzyl alcohol and acetic acid. The primary oxidation, which is unique to the phenyl-2-propanones, was the reaction of principal interest in this study. The oxidation was first order with respect to both oxidant and substrate. Hydroperoxide anion was shown to be the reactive peroxide species from studies of sodium hydroxide concentration and peroxide species concentration on reactivity.

Considerable indirect evidence suggested that the enol tautomer was the reactive substrate. The decreased reactivity of the phenyl-2-propanones in the presence of excess sodium hydroxide was attributed to the conversion of the reactive enol to an enolate anion. The most convincing evidence for the enol being the reactive substrate was obtained by studying the effect of structure modification on reactivity. The addition of another methylene group between the ring and the carbonyl group eliminates ring conjugated enolization and reaction by the primary mechanism. Addition of an alpha methyl group drastically reduces the reactivity of phenyl-2-propanone. Such a significant decrease in reactivity would be expected

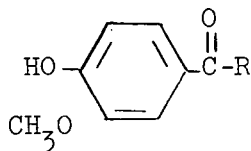
only if attack is occurring at the alpha position. The other aspects of the investigation were also consistent with attack of the hydroperoxide anion on the enol tautomer being the rate-determining step of the reaction.

A mechanism consistent with the experimental observations was postulated. The first step involves attack of the hydroperoxide anion on the enol. The cleavage is considered to occur by a concerted addition of a second mole of peroxide to the original carbonyl carbon.

## INTRODUCTION

Alkaline hydrogen peroxide has achieved wide utility as a commercial bleaching agent for wood pulps. It is utilized as one of several stages of multistage bleaching processes, and the brightness of high-yield pulps can be significantly increased accompanied by only a small decrease in yield.

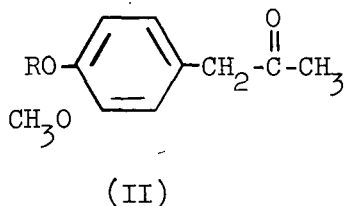
Numerous studies have been made to determine those conditions which are most suitable for effectively bleaching wood pulps. Such studies, while satisfying their immediate objectives, cannot disclose any information concerning what portions of the lignin structure are susceptible to alkaline peroxide oxidation and the mechanisms by which these structures are reacting. In an effort to answer some of these questions, Reeves (1) has recently completed an investigation of the products obtained from the alkaline peroxide oxidation of sixteen lignin-related model compounds. Identifiable reaction products were obtained from eight of these. The compounds studied were primarily oxygenated disubstituted phenylpropane structures, having hydroxyl and methoxyl substituents at the three and four positions of the ring. The reactions were carried out at 25°C. using equivalent amounts of substrate and sodium hydroxide and a slight excess of hydrogen peroxide. Several ketones having the general structure shown in (I) were



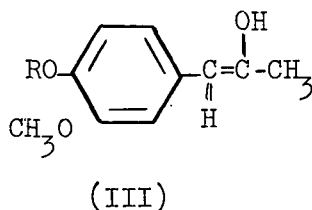
(I)

cleaved to methoxyhydroquinone. Similar structures in which the hydroxyl group was replaced by a methoxyl group were found to be unreactive. These results are those expected on the basis of the early work by Dakin (2). The reactivity of several other structures was investigated, the results of which will be discussed in later sections in conjunction with similar work.

In addition to the structures of type (I), Reeves (1) studied the reactivity of ketones in which the carbonyl group was separated from the ring by a methylene group (II). Reeves found that structures of this type were reactive for R being



either H or CH<sub>3</sub>. These results indicated that the important characteristics of this reaction were quite different from those of the Dakin reaction of α-carbonyl compounds. A significant characteristic of the β-ketones is the stabilization of the enol tautomer (III) by conjugation with the aromatic ring. The enol



content of pure phenyl-2-propanone is nearly 3%, 2 x 10<sup>4</sup> times as high as that for acetone (3). Although the enol content for this ketone is reduced to approximately one percent in a 5% solution, the enol content would still be much higher than that of simple ketones.

Recognizing the unique aspects of the phenyl-2-propanones, Reeves (1) suggested that the oxidation of these ketones proceeded through the enol form. The mechanisms for the oxidation of these compounds were apparently different, since 3,4-dimethoxybenzoic acid and 3,4-dimethoxybenzaldehyde were obtained as reaction products from 3,4-dimethoxyphenyl-2-propanone (II, R=CH<sub>3</sub>), while 4-hydroxy-3-methoxybenzoic acid was the only product obtained from 4-hydroxy-3-methoxyphenyl-2-propanone (II, R=H). If 4-hydroxy-3-methoxybenzaldehyde was the initial product of the

reaction, no 4-hydroxy-3-methoxybenzoic acid would be produced; the aldehyde would be converted to methoxyquinone (2). The purpose of this thesis was to attempt to elucidate the mechanism of oxidation of the phenyl-2-propanones. The techniques used for this investigation involved obtaining complete product analysis and extensive kinetic investigations of phenyl-2-propanones and related compounds.

#### ALKALINE HYDROGEN PEROXIDE SYSTEMS AND REACTION MECHANISMS

In aqueous alkaline solutions free hydrogen peroxide is in equilibrium with its hydroperoxide anion, Equation (1).



The hydroperoxide anion is considered to be the reactive species in many reactions of hydrogen peroxide, and observed base catalysis is often cited to indicate participation of this species.

Several instances have been encountered in which the hydroperoxide anion has been demonstrated to be an extremely strong nucleophile. Wiberg (4) has shown that hydrogen peroxide is more than  $10^4$  times as reactive as hydroxide ion in assisting the hydrolysis of benzonitrile to benzamide. A similar difference was noted by Jencks and Carriuolo (5) when a comparison was made of the attack upon p-nitrophenylacetate by hydroperoxide and hydroxide ions. Several other instances have been cited where similar but less dramatic effects have been observed (6). Bunton (7) has stated that the rate of such reactions is a function of the decomposition of the intermediate as well as its formation. The possibility that the reactions may be reversible suggests that the comparison of nucleophilicity made on the basis of such reactions is subject to some uncertainty.

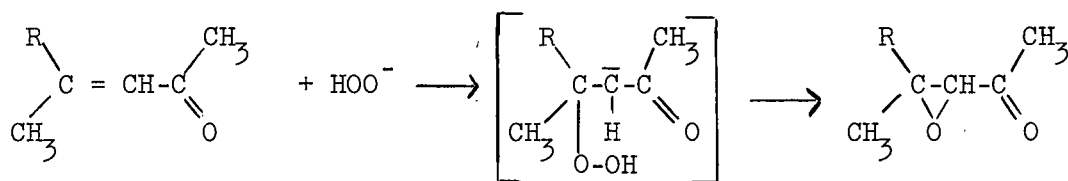
Edwards and Pearson (8) have recently considered the factors which determine nucleophilic reactivity and have offered an explanation for some of the observations concerning hydrogen peroxide reactions. Two factors which are important in determining nucleophilic reactivity are basicity and polarizability. The importance of these two quantities in determining the rate of nucleophilic displacement is dependent on the substrate. Basicity is most important for highly charged systems. Polarizability of the nucleophile will be most important when the substrate has a negligible positive charge and has a large number of electrons in the outer shell which obstruct the approach of the nucleophile. These aspects of nucleophilicity fail to explain the higher reactivity of hydroperoxide ion compared to hydroxide ion especially when the high basicity of the latter is considered.

Another aspect of nucleophilicity which is important, irrespective of the substrate, is termed the alpha effect by Edwards and Pearson (8). This term refers to the presence of an electronegative atom containing one or more pairs of unshared electrons adjacent to the nucleophilic atom. The nature of the effect is conceded to be poorly understood (8), but these authors suggest that it is related to the ability of the adjacent electronegative atom to receive a positive charge.

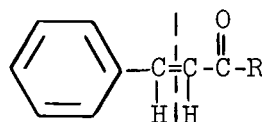
Such an effect is thought to be responsible for the anomalous reactivity of some nucleophiles such as hydroperoxide anion, hypochlorite ion, hydroxylamine, hydrazine, etc. The reactivity of the substrate can also be enhanced by such an effect, i.e., activated esters, nitriles, and activated double bonds.

The unique aspects of hydrogen peroxide and its anion are helpful in understanding the mechanism of alkaline hydrogen peroxide reactions. Many of the reactions of alkaline peroxide involve the displacement of an existing group or a pair of electrons from an electrophilic center, i.e., substitution or addition to carbon (7). The majority of the reactions which have been studied involve the latter,

addition to unsaturated carbon. Considerable attention has been given to the attack of activated  $\alpha,\beta$ -unsaturated compounds by alkaline hydrogen peroxide. Weitz and Scheffer (9) studied the oxidation of several  $\alpha,\beta$ -unsaturated carbonyl compounds and found that the primary products were epoxides. Bunton and Minkoff (10) studied the mechanism of oxidation of two  $\alpha,\beta$ -unsaturated ketones and established that the hydroperoxide anion was the attacking species. The postulated mechanism involves attack at the  $\beta$ -carbon with the ultimate formation of the epoxide. The reaction



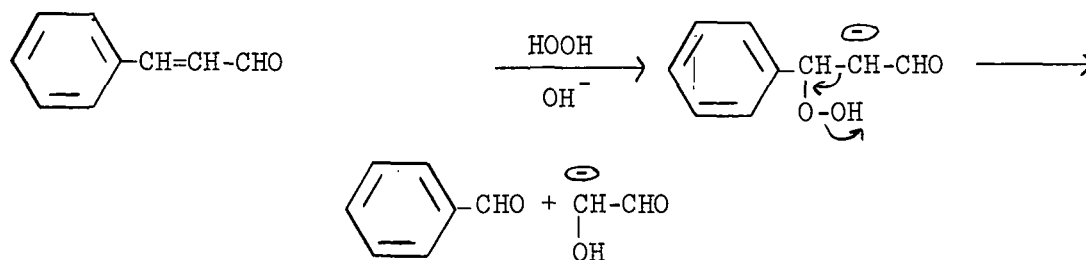
rate was found to be 5.6 times as fast with  $\text{R}=\text{H}$  compared to  $\text{R}=\text{CH}_3$ , supporting the contention that attack is occurring at the  $\beta$ -carbon. Southwick, *et al.* (11) found that compounds of the type (IV) did not produce stable epoxides but were cleaved at the double bond with alkaline hydrogen peroxide.



(IV)

Payne (12) prepared the epoxide of an  $\alpha,\beta$ -unsaturated ester, but the appropriate epoxide could not be obtained when the free  $\beta$ -hydrogen was replaced with a methyl group. These results are in accord with those of Bunton and Minkoff (10) which indicate that the attack is initiated at the  $\beta$ -carbon. Zimmerman, *et al.* (13) have reviewed and studied the stereochemistry of alkaline peroxide epoxidations. Yang and Finnegan (14) studied the alkaline *t*-butylhydroperoxide epoxidation of acrylonitrile and methyl acrylate. The reaction was considered to proceed by the method suggested by Bunton and Minkoff (10). The oxidation of  $\alpha,\beta$ -unsaturated aldehydes often results in cleavage at the carbon-carbon double bond. Payne

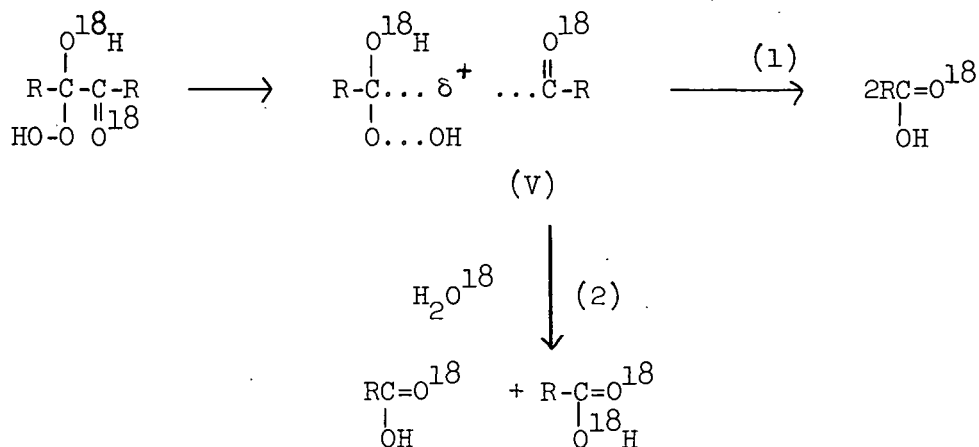
successfully prepared the epoxide of acrolein (15) using alkaline hydrogen peroxide, but only an unidentified organic peroxide was obtained in an attempt to prepare the epoxide of the aromatic aldehyde, cinnamaldehyde. The desired epoxide was, however, prepared using alkaline *t*-butylhydroperoxide (16). Reeves (1) found only the cleavage products, aromatic aldehyde and aromatic acid, when 3,4-dimethoxycinnamaldehyde and cinnamaldehyde were oxidized with alkaline hydrogen peroxide. Reeves considered that the initial attack occurred at the  $\beta$ -carbon and suggested two possibilities for the cleavage. The first involved formation of the epoxide with subsequent cleavage, and the second a direct decomposition of the  $\beta$ -hydroperoxyaldehyde to the aromatic aldehyde. The second suggestion would appear to be more feasible on the basis of the observations of Payne (16), Reeves (1) and those of Southwick, *et al.* (11).



Apparently, the formation of epoxides using alkaline hydrogen peroxide is not favorable when the  $\alpha,\beta$ -unsaturated system is adjacent to the aromatic ring. Such epoxides are stable since they can be prepared using organic peroxides (16). In contrast to the reactivity of other  $\alpha,\beta$ -unsaturated carbonyl compounds,  $\alpha,\beta$ -unsaturated acids were found to be stable in alkaline hydrogen peroxide (1).

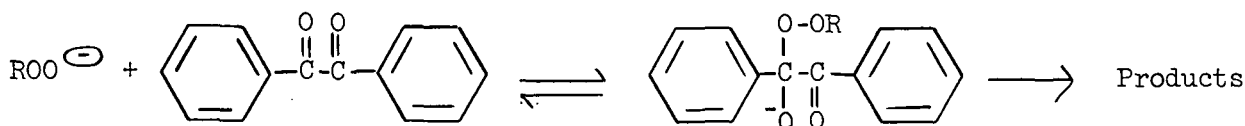
A general reaction of alkaline hydrogen peroxide is the cleavage of  $\alpha$ -diketones. Bunton (7,17) has studied these reactions for several diketones, and has discussed the mechanism of the oxidation of benzil equilibrated with  $\text{H}_2\text{O}^{18}$ . The benzoic acid obtained from the oxidation was found to be 56% enriched

indicating that intermolecular decomposition is not a feasible mechanism. The suggested mechanism for the decomposition involves the concerted fission of the O-O and C-C bonds to give an intermediate (V) which can decompose intramolecularly (1) or by attack of an external water molecule (2).



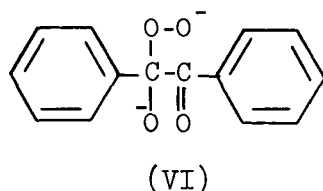
Kwart and Wegemer (18) investigated the oxidation of benzils over a wide pH range by various peroxides: peroxyacetic acid, t-butylhydroperoxide, and hydrogen peroxide. The reaction was found to be first order with respect to oxidant and substrate. For hydrogen peroxide and t-butylhydroperoxide the reaction showed a first-order dependence on hydroxide ion concentration between pH 7.4 and 10.3. Further addition of hydroxide increased the reactivity but at a slower rate for the hydrogen peroxide oxidations. No such break in the pH - rate plot was observed when t-butylhydroperoxide was used as the oxidant. A rate - pH profile was also determined for the oxidation of p-methoxybenzil. No break in the curve was found for a pH as high as 11.5 for this benzil. The peroxyacetic acid was not sufficiently stable for rate determinations at these higher hydroxyl ion concentrations.

A mechanism was proposed which involved the equilibrium attack of the peroxide anion on the carbonyl group. The rate-determining step was considered to be the decomposition of the peroxide intermediate. The discontinuity of the pH-rate



profile with hydrogen peroxide and the absence of such an effect with t-butylhydroperoxide suggested that the decomposition was the rate-determining step.

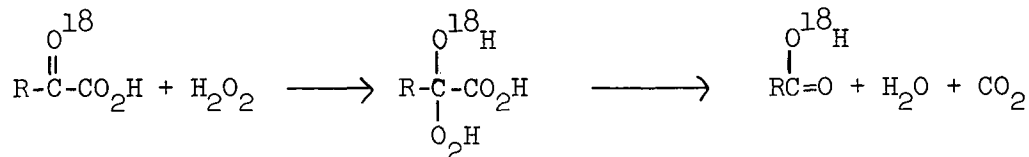
When R = H the hydroperoxide intermediate can exist as a dianion (VI) which would decompose less readily than the monoanion or the neutral molecule.



The relative reactivities of the three peroxides were consistent with these results. Peroxyacetic acid effected the cleavage 2000 times more readily than hydrogen peroxide, and hydrogen peroxide was ninety times as effective as t-butylhydroperoxide. Peroxyacetate ion is a much weaker nucleophile than the hydroperoxide or t-butylhydroperoxide ion, but the acetate ion is a much better leaving group than hydroxide or t-butoxide ion. The proposed mechanism adequately explains the data, but the arguments would be more convincing if the acidity of the intermediate hydroperoxide were known, and the comparison of the reactivities of the peroxides had been made on a comparable basis. The comparative reactivity of hydrogen peroxide and peroxyacetic acid is not accurate unless the concentrations of the peroxide anion provide the basis for comparison.

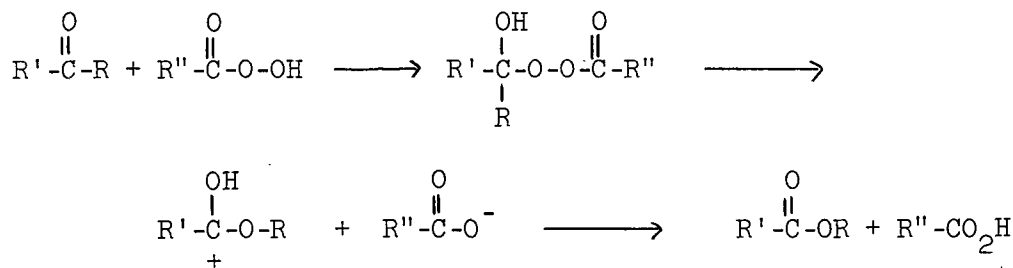
Activation parameters were determined for the alkaline peroxide cleavage. The values determined were  $\Delta H = 4.4 \text{ kcal. mole}^{-1}$  and  $\Delta S = -34.0 \text{ kcal. deg.}^{-1} \text{ mole}^{-1}$ . The values of the activation parameters were interpreted to indicate a relatively stable equilibrium complex between benzil and hydrogen peroxide. The magnitude and sign of  $\Delta S$  suggested that the cleavage was a concerted one.

The decarboxylation of  $\alpha$ -keto acids is another characteristic reaction of alkaline hydrogen peroxide. This reaction was studied using  $\text{H}_2\text{O}^{18}$  (17). The suggested mechanism



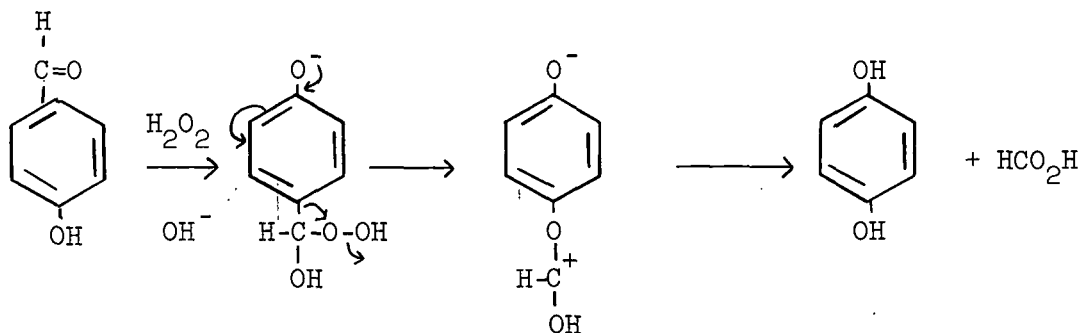
involved attack of the carbonyl carbon of the ketone by hydroperoxide anion, with subsequent decomposition. Vysotskaya and Brodskii (19) have apparently made a similar study. These investigations indicate that rearrangement occurs before cleavage. Reeves (1) observed the decarboxylation of (3,4-dimethoxyphenyl)-pyruvic acid.

The reactions which have been considered previously involved the attack of hydroperoxide anion upon activated unsaturated carbon. Direct attack of isolated carbonyl compounds is a general reaction for organic peroxides. The course of the reaction of peroxyacids in acid solutions, often referred to as a Baeyer-Villiger reaction, is shown below. Recent studies by Hawthorne and Emmons (20) and



Hawthorne, Emmons, and McCallum (21) have shown that the rate-determining step of the reaction involves the decomposition of the intermediate adduct. A comprehensive review of Baeyer-Villiger reactions has been given by Hassall (22).

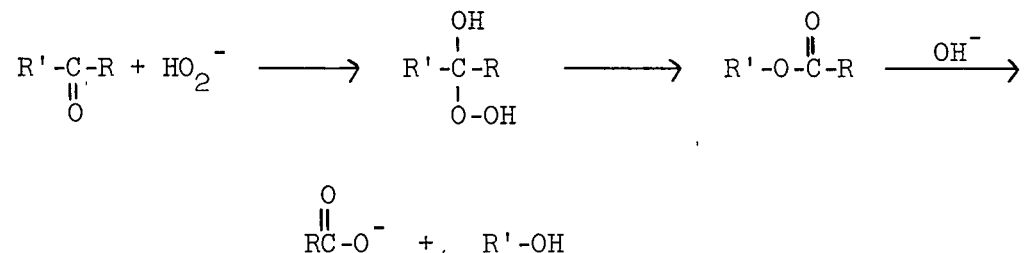
Aromatic aldehydes or ketones having an ortho or a para-hydroxyl group cleave to the corresponding diphenolic compounds in the presence of alkaline hydrogen peroxide. Dakin (2) in 1909 reported extensive studies of this reaction for a large number of hydroxy-substituted aldehydes and ketones. The cleavage, often referred to as the Dakin reaction, is generally conceded to involve the attack of hydrogen peroxide at the carbonyl carbon with subsequent rearrangement and decomposition to the phenolic products. The objection to several postulated mechanisms for the cleavage (7,23), is the inadequacy in explaining the specificity of these reactions. Davies (24) and Hine (25) have suggested a mechanism for the cleavage which requires the presence of a phenoxy anion.



The strongly electron-releasing phenoxy anion "synartetically" assists the fission of the oxygen-oxygen bond (24). Reeves (1) has postulated a similar mechanism with the inclusion of an epoxy-quinoid intermediate. Both of these mechanisms suggest that the rate-determining step of the reaction is decomposition of the intermediate. These mechanisms are consistent with the observed products, and a more thorough investigation might yield further support for their validity.

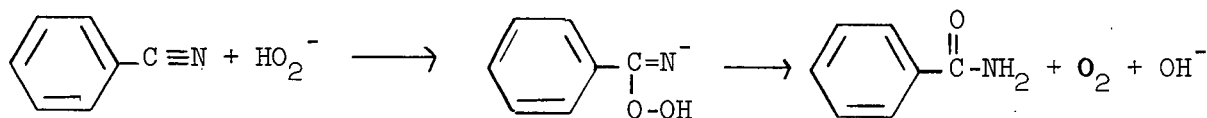
The cleavage of simple ketones by alkaline hydrogen peroxide is quite slow, with the exception of the Dakin reaction. However, under more severe conditions simple ketones react with alkaline hydrogen peroxide in a manner comparable to the Baeyer-Villiger reaction of peroxy acids. House and Wasson (26) have studied the

reaction of alkaline peroxide with several simple ketones. The products obtained were acids and alcohols. A mechanism for the cleavage was suggested which involves attack of hydrogen peroxide, rearrangement to an intermediate ester, and hydrolysis to an acid and an alcohol. Several instances have been cited of the cleavage of simple cyclic ketones (27a-d).

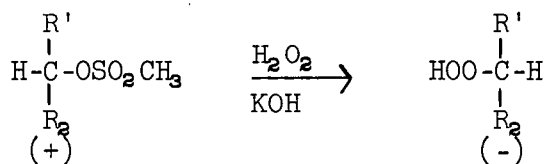


Treindl and Palackova (28) have studied the oxidation of cyclohexanol and cyclohexanone by hydrogen peroxide in neutral solutions. The kinetics of the reaction were followed using oscillographic polarography. Activation parameters were determined for the reaction. The activation energy and entropy for the alcohol and the ketone were, respectively, 8.2 kcal./mole and -42.6 cal. deg.<sup>-1</sup> mole<sup>-1</sup> and 9.8 kcal. mole<sup>-1</sup> and -37.8 cal. deg.<sup>-1</sup> mole<sup>-1</sup>.

Wiberg (4) has studied the effect of hydrogen peroxide upon the alkaline hydrolysis of benzonitrile to benzamide. The rate-determining step of the reaction is attack of hydroperoxide anion on the nitrile.



Williams and Mosher (29) studied the mechanism of alkylation of hydrogen peroxide by optically active 2-heptylmethane sulfonate. The resulting peroxide was characterized



by reduction to the corresponding alcohol. The reaction product showed a 95% inversion of configuration indicating that the displacement proceeded by a simple  $S_N2$  mechanism.

#### OXIDATION OF KETONES BY OTHER OXIDANTS

The oxidation of simple ketones by inorganic oxidants is generally conceded to involve the enol form with 2-electron oxidants. Recently, Green, *et al.* (30) studied the enolization and mercuric perchlorate oxidation of cyclohexanone. The rate of enolization, determined by the rate of bromination and iodination, were found to correspond to the rate of oxidation. To substantiate their observations, kinetics of enolization and oxidation were obtained using the deuterated and tritiated ketone. Large kinetic isotope effects were found indicating proton transfer was involved in the rate-determining step of the reaction.

Littler (31) studied the oxidation of cyclohexanone under acid conditions using three oxidants, mercuric perchlorate, thallic perchlorate, and potassium permanganate. These oxidations were all found to be first order with respect to the ketone and zero order with respect to the oxidant. From these data and the correlation of enolization rate with oxidation rate, Littler concluded that the rate of enolization was the rate-determining step in the reaction.

It also has been proposed that oxidations of ketones involving nitric and nitrous acid involve the enol form of the ketone. Stewart (32) suggests that the nitrosonium ion,  $NO^+$ , is important in the nitrous acid oxidations of ketones. Nikrolenko and Karpova (33) have concluded in a recent study of nitric acid oxidations that the reactive species are the enol and the nitronium ion.

The oxidations of ketones by at least two other reagents are proposed to occur through the enol form. Ichikawa and Yoshiteru (34) concluded that the oxidation of acetone and several acetophenones by lead tetraacetate involves enolization since the rates of enolization and oxidation were the same, and the reaction order with respect to the oxidant was zero. Best, Littler, and Waters (35) studied the chromic acid oxidation of cyclohexanone. The rate of oxidation was slower than the rate of enolization. It was concluded that the oxidation involved enolization on the basis of solvent isotope studies.

The mechanism of the oxidation of ketones by selenium dioxide has received considerable attention. Melnikov and Rokitskaya (36) concluded that the oxidation involves the enol form, but Duke (37) refuted this contention since he found the reaction to be first order with respect to oxidant. Corey and Schaeffer (38) made an extensive study of the oxidation of deoxybenzoins by selenium dioxide. The reaction was found to be catalyzed by both acid and base. Mechanisms for the oxidation under the influence of catalysts were formulated both of which involved the formation of an enol selenite ester by direct attack of the carbonyl group. Waters (39) concludes from the data of Corey and Schaeffer (38), that a more consistent interpretation would involve a rapid concerted attack of the oxidant on the enol to give the selenite ester. Barton, *et al.* (40,41) considered enolization to be important in the selenium dioxide oxidation of ketones and also suggested the possibility of a concerted mechanism. Contrary to Waters (39), Stewart (32) prefers the explanation of Corey and Schaeffer (38).

The oxidations of the ketones which have been discussed previously were made under acid conditions. Very few investigations of the mechanism of alkaline oxidations have been made, but the importance of enolization has been stressed in these oxidations. Kravchenko (42) studied the oxidation of phenyl-2-propanone

by alkaline permanganate. On the basis of the observed increase in reactivity from neutral to basic solutions, Kravchenko concluded that the reaction occurred through the enol.

Speakman and Waters (43) studied the alkaline ferricyanide oxidation of various aldehydes and ketones. These authors found the oxidations to be first order in ketone and hydroxyl ion concentration and variable order, zero to one, in oxidant. The proposed mechanism involved the formation of a complex between the enol anion and the ferricyanide anion.

The previous discussions demonstrate that almost all homolytic oxidations of ketones involve enolization or processes very closely related to them. Enolization is of questionable importance in reactions of ketones with one-electron oxidants. Speakman and Waters (43) suspected that the mechanism of the alkaline ferricyanide oxidations would proceed by a free radical mechanism. Stewart (32) presents some arguments to support this contention.

The oxidations by manganic pyrophosphate, another one-electron oxidant, have been considered to involve enolization. Drummond and Waters (44) studied the oxidations of several simple aliphatic and cyclic ketones whose rates of oxidation were slower than or comparable to their rates of enolization. More recent investigations by Littler (45) and Hoare and Waters (46) have shown that manganic and cobaltic ions can oxidize ketones at a rate of more than 300 times the enolization rate. The possibility of the enol form being involved is excluded.

Stewart (32) indicates that ceric ion is another one-electron oxidant which degrades ketones at a rate much higher than that of enolization. This is in opposition to the conclusions from the earlier work of Shorter and Hinshelwood (47) and Shorter (48).

This review of the oxidation of ketones by various inorganic oxidants demonstrates the importance of enolization in these oxidations. Two-electron oxidants are considered to attack the ketone almost exclusively through the enol form. The only oxidations of ketones which cannot be explained with reference to enolization are the rapid oxidations characteristic of some of the one-electron oxidants, and the oxidation of 1,2-diketones by periodic acid (49,50).

The reviews of alkaline peroxide reaction mechanisms and the oxidation of ketones by various other inorganic oxidants have demonstrated several general relationships. The reactions of alkaline peroxide almost always involve the nucleophilic attack of the hydroperoxide anion upon unsaturated carbon. Peroxides represent one of the few oxidants which can directly attack the carbonyl carbon. Essentially all the oxidations of ketones except those which involve free radical mechanisms are postulated to proceed through the enol form of the ketone. This pathway has been suggested regardless of whether the oxidations are made in acid or alkaline solutions, i.e., the attacking agent is neutral, electrophilic, or nucleophilic. Waters (39) has been able to explain most of the oxidations in acidic solutions on the basis of concerted reactions involving the enol form in the rate-determining step.

## EXPERIMENTAL PROCEDURES

### PREPARATION AND PURIFICATION OF COMPOUNDS

All of the ketones which were investigated had been prepared previously. Some of the compounds were commercially available, but most were prepared by general or specific literature methods. Since most of the ketones were liquids, the primary method of purification was fractional distillation. Either a Nester-Faust 18-inch or a 24-inch spinning band distillation column was used for these purifications. When only small amounts of materials were available, final purification was accomplished using an Aerograph Model A-700 preparative gas chromatograph.

The boiling points of the ketones and the melting points of the semicarbazones were used to verify the identity of the ketones. For the ketones which were crystalline at room temperature, their melting points were also used for identification. Literature values were available for comparison. The infrared spectra<sup>1</sup> of all the ketones were determined. Although reference spectra were seldom available, these spectra were helpful in verifying the identity of the ketones. Melting points were determined using total immersion thermometers calibrated by the National Bureau of Standards.

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<sup>1</sup>The infrared spectra were determined using a Perkin Elmer Model 21 spectrophotometer. The spectra for the liquids were determined as films between NaCl windows and the solids run in KBr pellets.

ORGANIC REACTANTS

4-Hydroxy-3-methoxyphenyl-2-propanone

This compound was prepared by the method of Pearl and Beyer (51) and West and Hibbert (52). The method involves condensation of the appropriate benzaldehyde with nitroethane to form the corresponding 1-phenyl-2-nitro-1-propene which is then reduced to the oxime and hydrolyzed to the ketone. Monsanto technical-grade vanillin was combined with the required amounts of nitroethane, methylamine hydrochloride, and sodium carbonate. The reaction mixture was allowed to stand at room temperature for two weeks. The nitropropene was then precipitated from solution by the addition of water. The recrystallized nitropropene was reduced with iron and hydrochloric acid in the presence of ferric chloride. The crude ketone was obtained by ether extraction and distilled on the spinning band column. The resulting light yellow viscous oil was obtained in a yield of 26.9%, boiling point 120-121° at 0.54 mm. [Lit. 115° at 0.15 mm. (52)]. The semicarbazone melting point was 157.2-157.8° [Lit. 155-158° (52)].

p-Hydroxyphenyl-2-propanone

This compound was prepared by the same method described for 4-hydroxy-3-methoxyphenyl-2-propanone (51,52) using Eastman white label p-hydroxybenzaldehyde. The yield of the ketone was 33.6%. After sufficient purification on the spinning band column, the boiling point of the clear viscous oil was found to be 117° at 0.27 mm. The purest fractions of the oil solidified, but several attempts to recrystallize the ketone from a solvent system were unsuccessful. The m.p. of the crystalline material was found to be 39.7-40.6° [Lit. 35.5° (52)]. The semicarbazone m.p. was 211.8-212.5 [Lit. 213° (53,54)].

p-Methoxyphenyl-2-propanone

This ketone was prepared by the method previously described (51,52), but a yield of only 19.3% was obtained. Heinzelman (55) describes a similar preparation; however, the condensation is accomplished in a few hours using a refluxing organic solvent. The nitropropene is not isolated but reduced directly with iron and hydrochloric acid. Using this method, p-methoxybenzaldehyde (K & K Laboratories) was condensed with redistilled nitroethane (Eastman white label) in the presence of n-butylamine. The resulting nitropropene was reduced and hydrolyzed, and the crude ketone was obtained by steam distillation. An accurate value of the yield could not be obtained since 30 g. of 1-(p-methoxyphenyl)-2-nitro-1-propene was added prior to the reduction. The estimated yield was 40-50%. The pale yellow ketone had a b.p. of 65° at 0.07 mm. [Lit. 82-82.5° at 0.8 mm. (56)]. The semicarbazone m.p. was 173.6-174.3° [Lit. 174° (56); 172-173° (57)].

3,4-Dimethoxyphenyl-2-propanone

This compound was obtained from Dr. I. A. Pearl, Lignin Group, The Institute of Paper Chemistry. The pale yellow oil was distilled on the spinning band column, b.p. 105° at 0.25 mm. [Lit. 110° at 0.4 mm. (1), 135° at 0.8 mm. (51)]. The semicarbazone m.p. was 175.2-176.2° [Lit. 175-177° (1,58)].

p-Chlorophenyl-2-propanone

This ketone was prepared by the method of Overberger and Bilech (59). An excellent description of a similar preparation is given in Organic Syntheses (60). p-Chlorophenylacetonitrile (Aldrich Chemical Company) in ethyl acetate was added to sodium ethoxide. The resulting  $\alpha$ -(4-chlorophenyl)acetoacetonitrile was then hydrolyzed and decarboxylated (60) to give the desired ketone in a yield of 49.4%. The b.p. of this pale green oil was 82° at 0.60 mm. [Lit. 100-101° at 3 mm. (59)]. The semicarbazone m.p. was 190.2-190.8° [Lit. 188-9° (59)].

p-Nitrophenyl-2-propanone

This ketone was also prepared by a method described by Overberger and Bilech (59). p-Nitrophenylacetyl chloride was prepared from p-nitrophenylacetic acid using thionyl chloride. This chloride was combined with the magnesium salt of diethyl malonate. The resulting complex was subsequently hydrolyzed and decarboxylated. Although a yield of 58% was reported (59), less than 5% yield was obtained. The light yellow-brown plates had a m.p. of 62.8-63.3° [Lit. 62-63° (59)].

p-Methylphenyl-2-propanone

This compound was prepared by the method of Heinzelman (55). The nitropropene produced from the condensation of p-methylbenzaldehyde (K & K Laboratories) with nitroethane was reduced and hydrolyzed with iron and hydrochloric acid, and the crude ketone was obtained by steam distillation. After successive fractional distillations the yield of the colorless oil was 36.4%. A careful distillation of the other fractions should have increased the yield to 50-60%. The ketone b.p. was 107° at 5 mm. [Lit. 92-94°, 3 mm. (61)]. The semicarbazone m.p. was 152.4-152.7° [Lit. 155-156° (61)].

p-Dimethylaminophenyl-2-propanone

The preparation of this compound was also attempted by the general method of Heinzelman (55). Although the reaction was slow, the condensation of p-dimethylaminobenzaldehyde with nitroethane was successful. The reduction was made in the usual manner using iron and hydrochloric acid. Steam distillation of the residue yielded very little crude oil. The purest fraction obtained from distillation of the crude oil was further purified by preparative gas

chromatography. Sufficient material for limited investigation was obtained. The infrared spectrum was consistent with that of a p-substituted aromatic material containing a nonconjugated carbonyl group. The identification of the ketone must be considered tentative.

#### Phenyl-2-propanone

This ketone was obtained from K & K Laboratories. Although gas chromatography showed the presence of no volatile impurities, it was distilled using the spinning band column, b.p. 105° at 11.5 mm. The commercial ketone had a definite green color whereas the freshly distilled material was very pale yellow-green.

#### 4-Phenyl-2-butanone

This ketone was obtained from K & K Laboratories. The ketone was purified by distillation on the spinning band column, b.p. 108.5° at 14 mm. The resulting oil was pale green.

#### 3-Methyl-3-phenyl-2-butanone

The ketone was prepared by the method of Jonsson (62) which involves the potassium t-butoxide catalyzed alkylation of phenyl-2-propanone with methyl iodide. The potassium t-butoxide was prepared from potassium metal and t-butyl alcohol (63). The preparation involved two successive additions of methyl iodide and potassium t-butoxide to phenyl-2-propanone. A crude oil was obtained in more than 90% yield by ether extraction. Two major products were shown to be present by gas chromatography. 3-Methyl-3-phenyl-2-butanone comprised about 60% of the crude oil. After collecting 24 fractions from the spinning band column, several grams of 3-methyl-3-phenyl-2-butanone were obtained which were over 95% pure. The other product was collected by preparative gas chromatography. A semicarbazone

was prepared, and the product was identified as 3-phenyl-2-butanone. The 3-phenyl-2-butanone was retained for further investigation. The 3-methyl-3-phenyl-2-butanone b.p. was 89-90° at 8 mm. [Lit. 98-101° at 11 mm. (62)]. The semicarbazone m.p. was 187.6-188.2° [Lit. 185.5-186.5° (64)].

### 3-Phenyl-2-butanone

Additional 3-phenyl-2-butanone was prepared by the method of Suter and Weston (64). This method is quite similar to the method described for the preparation of 3-methyl-3-phenyl-2-butanone except that sodium isopropoxide was used rather than potassium *t*-butoxide. The alkylation of phenyl-2-propanone was accomplished in a single step using methyl iodide. A crude oil was recovered in almost quantitative yield, but gas chromatography showed that approximately 10% of the oil was phenyl-2-propanone. After several unsuccessful attempts to obtain pure 3-phenyl-2-butanone by distillation on the spinning band column, some of the ketone was collected on the Aerograph A-700 gas chromatograph using the DEGS<sup>1</sup> preparative column. The semicarbazone m.p. was 170.7-171.4° [Lit. 169-170° (65)]. The 3-phenyl-2-butanone isolated from this preparation had a b.p. of 84-85° at 8.5 mm. [Lit. 103-106° at 22 mm. (64)].

### Deoxybenzoin

This ketone was obtained from Matheson Coleman and Bell. The recrystallized material had a m.p. of 54.9-55.7°.

### p-Chlorodeoxybenzoin

This ketone, prepared by the general method described for related deoxybenzoins by Clark, *et al.* (66), was obtained from Sobieski (67). The m.p. of the recrystallized ketone was 106.1-107.2° [Lit. 107.5° (68)].

<sup>1</sup>Diethyleneglycol succinate on acid-washed Chromosorb W 60/80; column 3/8 in. x 5 ft.

p'-Chlorodeoxybenzoin

This compound was prepared by the procedure of Clark, et al. (66). The method involves reacting p-chlorobenzylmagnesium chloride with benzamide. The resulting complex is then hydrolyzed with dilute sulfuric acid. After numerous recrystallizations from ethanol-water, white flakes were obtained which had a m.p. of 137.4-138.1° [Lit. 132° (66); 138° (68)].

HYDROGEN PEROXIDE

Eight liters of a peroxide solution were prepared by diluting Baker, A. R. 30% hydrogen peroxide with triple distilled water. The 1.1M hydrogen peroxide solution was stored in a two-gallon polyethylene bottle.

SODIUM HYDROXIDE

The sodium hydroxide used for the various oxidations was Baker, A. R. pellets. Four liters of a solution approximately 2.5N were prepared using triple distilled water. The exact concentration of the hydroxide was determined using 0.500N HCl prepared from standard volumetric concentrates. Triplicate analysis showed the concentration of the sodium hydroxide to be 2.477N. The sodium hydroxide solution was stored in a tightly closed two-gallon polyethylene bottle.

POTASSIUM CHLORIDE

One liter of a 2.00M potassium chloride solution was prepared using Matheson, Coleman, and Bell, A. R. chemical and triple distilled water. This reagent was prepared for use in those kinetic investigations which required added electrolyte to maintain a constant ionic strength or when the effect of added electrolyte was being investigated.

#### TRIPLE DISTILLED WATER

Water to be used in the oxidations was purified by three distillations. Distilled water from a Barnstead still was passed through a two-stage distillation, the first stage containing alkaline potassium permanganate and the second dilute sulfuric acid.

#### ORGANIC SOLVENTS

The solvent for the kinetics and most of the product analysis was a mixed ethanol-water system. A mixed solvent of 95% ethanol-water was used in some of the earlier product analysis studies; however, all the kinetics were determined using a mixture of absolute ethanol and water. The 95% ethanol was purified by distillation through a Vigreux column. The absolute ethanol was purified by a method suggested by Weissberger, et al. (69) for purifying methanol. Five grams of magnesium turnings and 0.5 g. of iodine were added to a liter of absolute ethanol. After the red color of the iodine had disappeared, the solution was refluxed for three to four hours. The ethanol was then distilled through the 40-cm. Vigreux column and stored in one-liter polyethylene bottles. Solvent was prepared as required during the course of the investigations.

#### TITANIUM SULFATE

A supply of titanium sulfate reagent was required for the spectrophotometric method used to follow hydrogen peroxide. The reagent was prepared according to the method of Satterfield and Bonnell (70). The titanium sulfate (titanium sulfate, pure, basic, E. D. Mackay Co., distributed by Matheson Scientific) was digested with  $3N$   $H_2SO_4$ . The most successful method of clarification involved an initial centrifugation to remove most of the excess titanium sulfate. The supernatant liquid was then filtered at least once through a fine fritted glass filter

funnel. When this reagent was required for kinetic investigations, it was diluted with twenty volumes of 4N sulfuric acid.

#### SODIUM THIOSULFATE

Eight liters of approximately 0.1N sodium thiosulfate were obtained from Russell (71). The thiosulfate was prepared by the method suggested by Spalding (72). The solution was standardized with potassium iodate according to the method given by Kolthoff and Sandell (73). The concentration of the thiosulfate was found to be 0.09169N.

#### CLEANING OF GLASSWARE AND POLYETHYLENE CONTAINERS

It was quite important to reduce the decomposition of the alkaline peroxide solutions to a minimum.<sup>1</sup> To remove trace impurities and to passivate the various containers which would contact any constituents of the alkaline peroxide solutions, they were cleaned by a suitable procedure (74e). The procedure involved:

1. Degreasing with an alkaline detergent - Alconox
2. Distilled water wash
3. 15-Minute soak in 1-1/2% sodium hydroxide
4. Distilled water wash
5. 45-Minute soak in 35% nitric acid
6. Distilled water wash
7. Twelve-hour soak in 30% hydrogen peroxide
8. Distilled water wash.

After such treatment these containers were rinsed only with distilled water or distilled 95% ethanol.

<sup>1</sup>The techniques suggested by Edwards (74b) for obtaining stable hydrogen peroxide solutions were unsatisfactory. The stabilizer, EDTA (ethylenediaminetetraacetic acid), consumed hydrogen peroxide. Purification of the base using phenyl-2-pyridyl ketoxime was also unsuccessful.

## PROCEDURES FOR PRODUCT ANALYSIS

### REACTION VESSEL

A small polyethylene wash bottle having a capacity of 125 ml. was the reaction vessel for all of the alkaline peroxide oxidations. The top of the bottle was provided with two polyethylene lines one of which extended to the bottom of the vessel. The entry having the extension connected the vessel to tank nitrogen by means of tygon tubing. The other entry was provided with a short rigid polyethylene fitting to which could be attached a 4-inch condenser the inner surface of which was a section of tygon tubing. The function of the condenser was primarily to contain any liquid or vapors entrapped by the nitrogen stream.

### p-METHOXYPHENYL-2-PROPANONE

The alkaline hydrogen peroxide oxidation of p-methoxyphenyl-2-propanone was studied extensively in order to establish the stoichiometry of the reaction. A large number of preliminary qualitative oxidations were made to determine that all of the stable products which were being produced had been detected. After completion of the qualitative investigations, several oxidations were made in order to establish suitable techniques for quantitative analysis. Comprehensive product analysis for p-methoxyphenyl-2-propanone was then possible.

### Initiating the Reaction

The method of initiating the reaction was modified to accommodate the difficulties arising from the spontaneous decomposition of the alkaline hydrogen peroxide solutions. An alkaline peroxide solution of appropriate specifications was prepared, transferred to the polyethylene reaction vessel, and a sample removed. The reaction vessel was placed in the thermostated bath, and the air

condenser and the nitrogen line attached. The concentration of the hydrogen peroxide solution was then followed intermittently by iodometric titration. The approximate amount of the ketone required for the oxidation was transferred to a 25-ml. volumetric flask using a graduated pipet. After determining the amount of the ketone added, the flask was sealed with Parafilm, placed in the thermostated bath, and the reactants combined.

### Analysis of Reactants and Products

#### Hydrogen Peroxide

Duplicate estimates of the residual hydrogen peroxide were made in order to establish peroxide consumption and to determine the sodium bisulfite required to quench the aliquots for the other analyses. The method used for determining hydrogen peroxide was essentially that described by Sulley and Williams (75) for the analysis of mixtures of peroxyacetic acid and hydrogen peroxide. Several modifications of this procedure were made since only hydrogen peroxide was being determined. A sample which would provide a sufficient titer was added to a 250-ml. Erlenmeyer flask which contained 100 ml. of 0.1N acetic acid and 15 ml. of a 15% potassium iodide solution. Four drops of an ammonium molybdate catalyst (76) were added to the solution, and the liberated iodine was titrated to the disappearance of the iodine color. It was determined in preliminary investigations that the organic materials present in the reaction mixture did not have a significant effect upon the determination of residual hydrogen peroxide.

#### Quantitative Gas Chromatography

The method chosen for quantitative chromatography was internal standardization (79). This method involves selecting an appropriate reference material and obtaining an accurate estimate of the response factor for the compound of

interest. After obtaining the required data, the response factor can be determined from the following equation:

$$F = (C_r/C_u)(V_r/V_u)(A_u/A_r) \quad (2)$$

where  $\underline{F}$  = response factor  
 $\underline{C}_r$  = initial concentration of the reference, w/v % (weight/volume %)  
 $\underline{C}_u$  = initial concentration of the unknown, w/v %  
 $\underline{V}_r$  = initial volume of the reference  
 $\underline{V}_u$  = initial volume of the unknown  
 $\underline{A}_u$  = area of the unknown, determined by triangulation  
 $\underline{A}_r$  = area of the reference.

The response factor is a reflection of the relative response of an equal weight of the unknown compared to an equal weight of the reference. The areas under the peaks corresponding to the various compounds were determined by triangulation.

A good estimate of the concentration of the various unknowns was available from preliminary investigations. Therefore, response factors could be determined using solutions which would give relative responses similar to those obtained from the oxidations. This procedure provided the most accurate estimate of the response factor. By solving Equation (2) for  $\underline{C}_u$ , it is possible to determine the concentration of the unknown in the solution knowing the response factor and the other parameters of the equation.

Acetic acid. Preliminary investigations showed that acetic acid was a primary product of the reaction. The most successful method of analysis was found to be quantitative gas chromatography. The determination of this material was particularly troublesome, the primary problems being attributed to the presence of water in the system. A thermal conductivity detector was impractical because

inadequate separation of acetic acid and water peaks could not be achieved. This problem was alleviated by using a chromatograph having a hydrogen flame detector which is insensitive to water.

The Aerograph Model A-600B Hy-FI gas chromatograph was used for the quantitative determinations of acetic acid. One of the columns suggested by Aerograph (77) for detecting low molecular weight organic acids was used for these investigations. The 1/8 inch x 5 ft. column, packed with Carbowax 4000 terminated with terephthalic acid on 60/80 Chromosorb W treated with HMDS (hexamethyldisilazane), gave satisfactory results.<sup>1</sup> The accuracy of the quantitative determinations was estimated to be  $\pm 7\%$ .

The samples for which a quantitative estimate of acetic acid was to be made were quenched with the appropriate amount of 3M sodium bisulfite, and sufficient 4N sulfuric acid was added to adjust the pH to 2-3. The appropriate amount of reference propionic acid in 50% ethanol - water was added and four to five injections made for the quantitative estimates. The response factor for the acetic acid was determined using prepared solutions of acetic and propionic acids of known concentration in 50% ethanol - water.

In an effort to obtain an independent estimate of acetic acid, an analytical method was developed which involved converting acetic acid to ethyl acetate, distilling the ester, and determining the amount of sodium hydroxide required to saponify it. The technique was considered to give a less accurate estimate of the acetic acid than quantitative gas chromatography, so a comprehensive discussion of the technique will not be given.

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<sup>1</sup>During the course of these investigations, it was necessary to obtain a second column identical to the first. As the column aged two problems were encountered: adsorption of the acids and double peak formation. Such problems have previously been encountered (78).

Volatile aromatic materials. The volatile aromatics were determined by quantitative gas chromatography using 1/8 inch x 5 ft. column packed with 5% diethyleneglycol succinate polyester - 30% Carbowax 20M on acid-washed 60/80 Chromosorb W. The Aerograph Model A-600B chromatograph was used for these determinations.

The concentrations of p-methoxyphenyl-2-propanone, p-methoxybenzaldehyde, and p-methoxybenzyl alcohol were determined by this method. The concentration of the aldehyde and the ketone were determined by direct comparison with an internal standard. The benzyl alcohol had a tendency to split into two peaks after quenching and acidification. To accommodate this problem, the concentration of the alcohol was determined by comparison of the relative areas of the alcohol to the ketone just prior to quenching the reaction. The areas of the two peaks resulting from the alcohol after quenching were comparable to that of the single alcohol peak prior to quenching. Similar behavior was observed for known p-methoxybenzyl alcohol.

Appropriate response factors for the three volatile aromatic materials were determined using phenylacetonitrile as the internal standard. The retention time of this reference compound was excellent for comparative purposes coming between the aldehyde and the ketone. The concentrations of the unknowns were determined using Equation (2), and the appropriate recoveries were calculated as mole percent yield based on the original ketone. The estimated accuracy of the quantitative determinations were  $\pm 4\%$ .

#### Aromatic Acid

The aromatic acid was determined by isolating the crystalline acid from an aliquot of the reaction mixture. The sample was quenched with 3M sodium bisulfite, and the solution was acidified with 4N sulfuric acid. After refrigeration for

several hours, the white needles which separated were filtered and washed several times with water and cold ethanol - water. The crystals were dried in a vacuum oven at 50°C. overnight, and the dry weight determined. After the filtrate was concentrated on the rotary evaporator, the residual aqueous solution was extracted with ether. The ether was extracted several times with sodium bicarbonate, and the bicarbonate extracts were acidified with 4N sulfuric acid. An ether extraction of the acidified bicarbonate extracts yielded the additional organic acids. The ether extracts were taken to dryness on the rotary evaporator, and the resulting material was extracted with ether. After removing the ether, the remaining aromatic acid was obtained by recrystallization from a small amount of ethanol - water. The yield was determined, and the acid was characterized by its melting point and mixed melting point.

#### PHENYL-2-PROPANONES

Product analyses for the other phenyl-2-propanones were less comprehensive than that for p-methoxyphenyl-2-propanone. For these ketones only quantitative determinations of the aromatic materials were made. Since no attempt was made to determine the amount of peroxide being consumed, these oxidations were made at higher temperatures, and the reactions were allowed to go almost to completion. This simplified the quantitative analysis since the primary determination was that of the aromatic acid. Since some volatile aromatic materials were still present, quantitative gas chromatography was utilized. Quantitative estimates were made using an appropriate standard, but response factors were not determined. The assumption of a weight response factor of 1.0 does not introduce a significant error in these analyses since the sum of the volatile aromatic materials seldom constituted more than 10-15% of total product.

The isolation of the aromatic acid was accomplished by a procedure similar to that described for p-methoxybenzoic acid. The residual hydrogen peroxide was quenched with sodium bisulfite and the solution was acidified with sulfuric acid. The aromatic acids, with the exception of p-chlorobenzoic acid, did not readily crystallize from the mixed solvent system. To remove most of the aromatic acid, the ethanol - water solution was extracted twice with large quantities of ether. These extractions removed some water and most of the organic material, including the ethanol. The ether extracts and the aqueous residue were both concentrated on the rotary evaporator. The residue from the original ether extracts and the original aqueous residue were extracted with ether. These ether extracts were combined and the aromatic acid was separated from the neutral aromatic materials by extraction with sodium bicarbonate. The bicarbonate extracts were washed several times with ether to insure removal of any neutral organic materials. After acidification, the bicarbonate extracts were extracted with ether and washed with distilled water to remove any residual salts. The ether extracts were evaporated to dryness, the residue extracted with a small amount of ether, and the extracts transferred to a tared weighing bottle. After removing the excess solvent, the contents were dried in the vacuum oven at 50°C. The weight and melting point of the aromatic acid was obtained. The aromatic acid was then recrystallized from ethanol - water, and another melting point was obtained. Melting points of appropriate references were obtained at the same time.

The procedure for initiating the reaction was the same as that described for p-methoxyphenyl-2-propanone, with one exception. No estimate of the decomposition of hydrogen peroxide was made. The reactants were combined, and the reaction was allowed to proceed in the thermostated bath. The samples were quenched, neutralized, and the various determinations made. The quantitative gas chromatographic investigations were made using a quenched, neutralized aliquot of the reaction mixture.

To determine if acetaldehyde was a product of the reactions, an oxidation of phenyl-2-propanone at 25° was made. The oxidation mixture was checked at 15-minute intervals by gas chromatography using a Carbowax 20M TPA column on the Hy-FI gas chromatograph.

#### PHENYL-2-BUTANONES

The product analysis of the phenyl-2-butanones required only quantitative gas chromatography since no aromatic acids were obtained as products of these oxidations. Internal standardization was used for establishing the product analysis of the most reactive butanone, 4-phenyl-2-butanone. Response factors were determined for the residual ketone and the primary product.

A quantitative determination of the products from the less reactive phenyl-2-butanones was obtained using internal normalization (79). In this technique, the total area under the peaks corresponding to the products and the residual starting material are summed. The concentration of a single component was determined by dividing the area for that peak by the total area of the volatile aromatic components, assuming equimolar response for each of the components.

The samples were quenched and neutralized. The quantitative estimates were then obtained using the methods which have been discussed. The possible production of aromatic acids was investigated. Attempts were made to isolate the acid from an aliquot of the reaction using the procedure discussed for the phenyl-2-propanones, but none was found.

#### DEOXYBENZOINS

Product analysis procedures for the deoxybenzoins were quite similar to those described for the phenyl-2-propanones. In these oxidations two moles of aromatic acids were produced. This complication provided no difficulty in the

analysis of the products for deoxybenzoin since both fragments are the same acid. For the two unsymmetrical deoxybenzoin, an equimolar amount of different aromatic acids is produced. To simplify the investigation, conditions for the oxidations of unsymmetrical deoxybenzoin were chosen such that the reaction would go essentially to completion. The yield of aromatic acids was calculated using the average molecular weight of the two acids.

The isolation of the aromatic acids was accomplished using the procedure described for the phenyl-2-propanones. Melting points were determined for the aromatic acid obtained from deoxybenzoin. To demonstrate that the aromatic acids isolated from the unsymmetrical deoxybenzoin contained only the two expected acids, paper chromatography was utilized. A butanol - aqueous ammonia developer provided adequate separation and maintained compact spots. The chromatograms were allowed to dry and were then sprayed with a solution of 4% alcoholic formaldehyde. After drying, the chromatograph was sprayed with an indicator, (Eastman Dye no. 1954) 4-(4-dimethylamino-1-naphthylazo)-3-methoxybenzene sulfonic acid (80). The acids immediately appeared as purple spots on an orange background. The spots were outlined since fading occurred upon standing.

An estimate of the volatile aromatic materials were made using quantitative gas chromatography. Internal standardization was used, but response factors were not determined since almost all of the aromatic materials were converted to acids. These estimates were made using the ether extracts of the neutral material obtained during isolation of the aromatic acids. These modifications of the more rigorous quantitative gas chromatographic methods introduced no significant errors since the quantity of volatile aromatic materials was low, essentially negligible in some instances.

## PROCEDURES FOR KINETIC MEASUREMENTS

No direct unambiguous method was available for following the kinetics of the system. The method chosen for following the oxidation involved indirectly monitoring the concentration of the hydrogen peroxide. One obvious criterion for using such a method requires that the spontaneous decomposition of hydrogen peroxide does not interfere. Proper cleansing of the reaction vessel and the various containers used in preparing the components of the reaction mixture reduced such decomposition to a minimum. Complete elimination of decomposition was not possible, however. To account for this decomposition, the peroxide was monitored prior to addition of the ketone. An appropriate corrected concentration was then used for the kinetics calculations.

An important consideration in kinetic investigations is the ratio of reactants which is utilized. The most satisfactory method for the present investigations involved using approximately equimolar amounts of the two reactants. A significant advantage of this technique is that the conditions for the kinetics are quite similar to those used for product analysis. An alternative procedure involves using a large excess of the substrate. Advantages of this procedure are that the kinetic expressions are simplified, and the importance of subsequent reactions are minimized. A significant disadvantage is that small amounts of contaminants can adversely affect the kinetic results. This problem is particularly important in the current instance since the decomposition of the peroxide is especially sensitive to the presence of trace impurities.

## SPECTROPHOTOMETRIC RATE DETERMINATIONS

### Determination of Hydrogen Peroxide with Titanium Sulfate

The most satisfactory method for following the hydrogen peroxide concentration involved using titanium sulfate to complex the hydrogen peroxide. The yellow

color of the complex was used to follow the concentration of the hydrogen peroxide. This procedure provides an accurate, sensitive method for determining hydrogen peroxide (81).

#### Flow System for Determining Hydrogen Peroxide

The concentration of the yellow complex was followed using a Model 15 Cary spectrophotometer adapted to accommodate a flow system. The reaction vessel, contained in a thermostated bath, was continuously sampled. The sample was combined with a reagent stream using a Technicon<sup>1</sup> proportioning pump. The pumping action of this apparatus involves passing rollers perpendicular to the fixed flow tubes. Two rollers are in contact with the tubes at all times forcing the liquid through the flow lines. Air is continuously added to the flow stream to assure adequate mixing. By varying the diameter of the flow tubes, the ratio of the liquid streams can be varied. The important aspect of the pump is that although slight variations in the total flow rate may occur, the proportion of each stream is always constant. A representation of the flow system is given in Fig. 1.

The flow line from the reaction mixture and that from the reagent stream pass through the proportioning pump after which the streams are combined. Proper combination of these streams is essential to obtain uniform sample distribution. Adequate stream combination was obtained using a Technicon H3 fitting which is equipped with a platinum side arm. Air was introduced through the platinum fitting, and the reagent stream passed through the primary entry. The sample line was introduced into the system by means of a polyethylene tube, one end of which was inserted in the exit end of the flow tube and the other through the side arm of the fitting. The end of the tube was positioned so that it extended just past the air inlet. The combined streams were then passed through the double mixer. Using tygon tubing

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<sup>1</sup>  
Technicon Controls Corporation, Chauncey, New York.

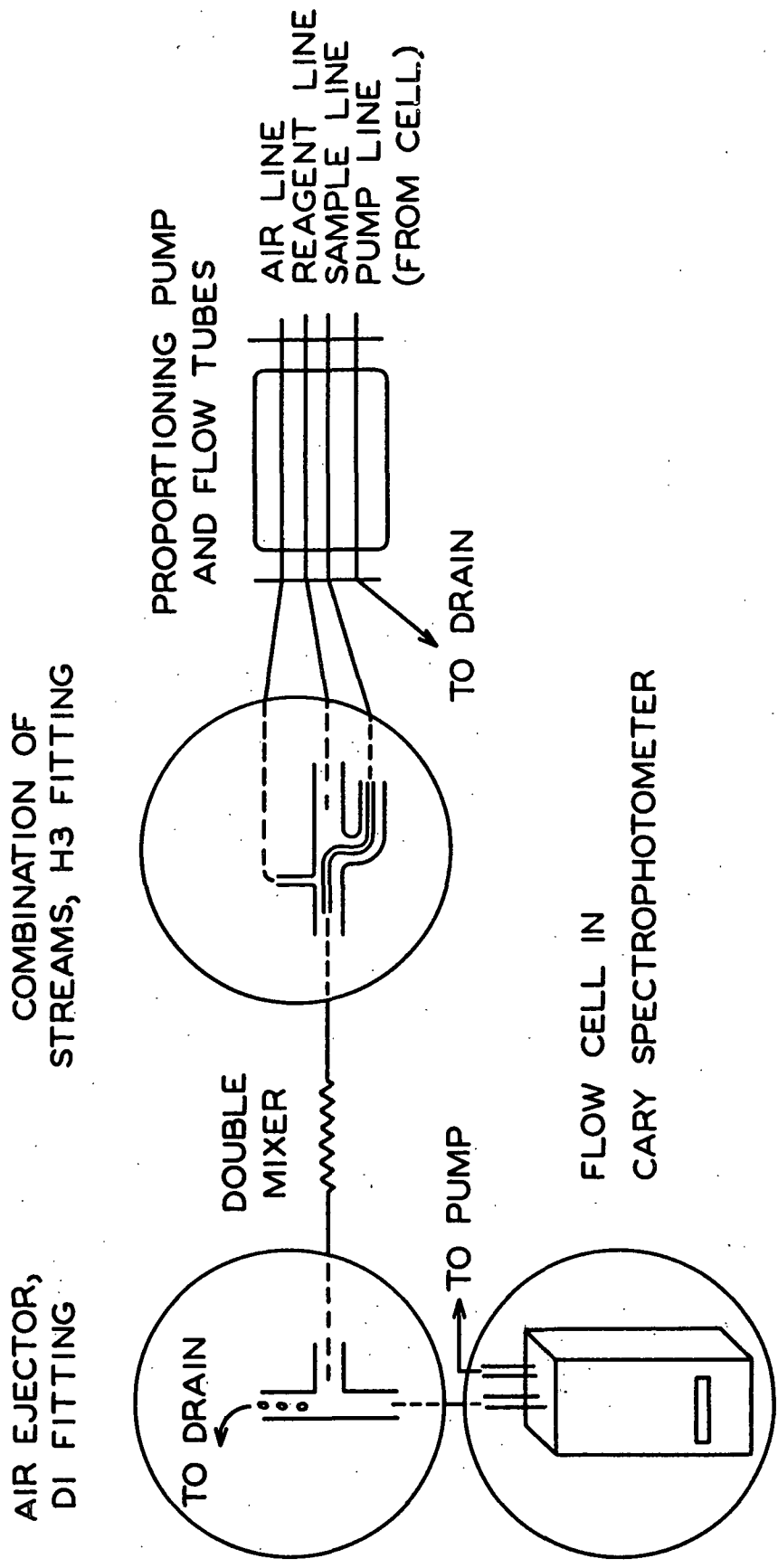


Figure 1. Schematic Diagram of Flow Sampling System

the stream was taken to a D1 fitting fixed in an upright position. The air bubbles and some of the liquid stream pass to the drain through a 1/4 x 1/16-inch tygon tube. The rest of the liquid stream passes to a Beckman microaperture Flow Cell No. 97290 in the cell compartment of the Cary Model 15 recording spectrophotometer. The flow cell was contained in a Cary thermostatable cell adapter 1444300. Water was circulated through the cell holder and the jacketed cell compartment from a thermostated bath maintained at  $25.0 \pm 0.1^\circ\text{C}$ . A special cover for the cell compartment was required. The cover was made of two sections, the small section provided with entry ports for the flow lines. The other section of the cover was removable for easy access to the cell compartment.<sup>1</sup>

Operation of the flow system was in general satisfactory. Most operating difficulties could be traced to the small flow tube which sampled the reaction mixture. This line was replaced several times during the course of the investigations, but the larger flow tubes required little or no replacement. The average deviation of the integrated rate constants was 4-5%. The uncertainty of the rate constants was least for those oxidations where decomposition was a small or insignificant fraction of the total peroxide consumption.

#### Preparation and Combination of Reactants

The first step in initiating a kinetic run involved preparing the alkaline peroxide solution. As previously mentioned, large quantities of the required inorganic constituents of the reaction mixture were prepared in concentrations convenient for the kinetic determinations. The required amounts of hydrogen peroxide and sodium hydroxide were added consecutively from 5-ml. capacity burets (0.01-ml. div.) to a 50-ml. volumetric flask. These burets had teflon

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<sup>1</sup>The cover was designed and fabricated by the Engineering Department, The Institute of Paper Chemistry.

stopcocks and were provided with reservoirs and side arm entry for easy filling. The required amount of potassium chloride was added using a graduated pipet, and the solution was diluted with 10-15 ml. of water. Twenty-five milliliters of absolute ethanol were added, and the solution was brought to volume with triple distilled water.

The solution was placed in the thermostated bath which could be controlled within  $\pm 0.1^{\circ}\text{C}$ . The nitrogen line and the condenser were attached. The base line on the spectrophotometer was set for the flowing stream using the titanium reagent and distilled water in the sample line. The sample line was transferred to the reaction vessel. The time lag from introduction of the sample line to the initial response was 100-120 sec. Within an additional 90 seconds the response was within 98% of maximum absorbance. However, three to six minutes were required before the maximum absorbance was obtained. The reference compartment contained an empty cell similar to that in the sample compartment.

The concentration of hydrogen peroxide was monitored for at least thirty minutes. During this time the approximate amount of ketone was transferred with a 0.01-ml. graduated buret to a tared 25-ml. volumetric flask. The exact weight of the ketone was determined; the flask was sealed with Parafilm and placed in the thermostated bath for five minutes. The flask and the reaction vessel were removed from the bath, and the contents of the flask diluted to volume with the alkaline peroxide solution. The residual alkaline peroxide solution was retained in a polyethylene flask. The contents of the volumetric flask were agitated and transferred back to the reaction vessel. The vessel was placed in the bath, and the sample line, nitrogen line, and the condenser replaced. The time lag between combination of the reactants and resumed sampling was thirty to forty seconds.

Duplicate determinations of initial hydrogen peroxide concentration were made on the residual solution using the iodometric method previously outlined. An initial pH was also determined for some of the runs. All pH determinations were made using a Beckman Model H2 pH meter using a calomel electrode, 39170, and a blue tip glass electrode, 41260, appropriate for measuring the pH of alkaline solutions. The pH was recorded directly; no attempt was made to convert the values obtained in 50% ethanol - water to those to be expected in a pure aqueous system.

The reaction was allowed to continue for a minimum of one and one-half hours. At the end of that time the final pH was determined for those reactions which required this measurement.

The procedure for determining the reaction rate of acetaldehyde was modified. The aldehyde was combined volumetrically at 0°C. with the reaction mixture. The solution was then transferred to the thermostated bath and the determinations made.

#### TITRIMETRIC RATE DETERMINATIONS

The continuous procedure described in the previous paragraphs was used for all kinetic investigations except those of the deoxybenzoin. These compounds were so insoluble that essentially all of the ketone precipitated when the sample stream was combined with the aqueous reagent stream. This made continuous sampling impossible since the flow lines plugged, and the suspended solids interfered with the spectrophotometric determinations. To obtain adequate kinetic data, 2-ml. samples were removed through the polyethylene sample line at six-minute intervals and titrated iodometrically.

The method of initiating the reaction had to be modified for the sparingly soluble deoxybenzoin. The alkaline peroxide solution of the desired concentration

was prepared and placed in the thermostated bath. The required amount of the deoxybenzoin was weighed into a 25-ml. volumetric flask and dissolved in 5 ml. of absolute ethanol with heating. After conditioning the solution of the ketone at 45° for five minutes in the thermostated bath, the solution was diluted to 25 ml. with the prepared alkaline peroxide reagent. The solution was transferred to the reaction vessel. The vessel was returned to the thermostated bath and sampling initiated. The nitrogen line and the condenser were replaced, and the reaction was allowed to proceed for an hour, sampling as required.

### EVALUATION OF THE KINETIC DATA

#### DETERMINATION OF INITIAL RATES

The initial rate approximation was used to determine the reaction order with respect to the reactants. This procedure involves maintaining the concentration of one reactant constant while varying the concentration of the other reactant. An initial rate was estimated using the pseudo first-order rate expression:

$$dx/dt = k_1 A^{\frac{n}{a}} B^{\frac{n}{b}} = k_2 A^{\frac{n}{a}} \quad (3)$$

An estimate of the initial reaction rate is obtained by making the approximation that  $\Delta x/\Delta t = dx/dt$ . Frost and Pearson (82) suggest that the use of such increments should not exceed 10% reaction.

The order of the reaction with respect to the reactant being varied can be conveniently determined using the following form of the expression:

$$\ln(\Delta x/\Delta t) = \ln k_2 + n_a \ln A \quad (4)$$

The slope of the plot of  $\ln(\Delta x/\Delta t)$  versus  $\ln A$  gives the reaction order with respect to A.

This technique was used for establishing the order with respect to hydrogen peroxide and the ketone and in distinguishing the reactive peroxide species. The data were evaluated over a range of approximately ten percent reactivity. In these calculations the apparent reaction rate was corrected for the decomposition of hydrogen peroxide.

#### INTEGRATED SECOND-ORDER RATE CONSTANTS

The results of the initial rate experiments enabled an integrated form of the second-order rate expression to be used. The differential form of the relationship is shown in Equation (5):

$$dc/dt = k A B \quad (5)$$

where  $\underline{c}$  = concentration of reactant,  $\underline{M}$   
 $\underline{A}$  = concentration of hydrogen peroxide,  $\underline{M}$   
 $\underline{B}$  = concentration of ketone,  $\underline{M}$   
 $\underline{t}$  = time, min.

For the oxidation of the phenyl-2-propanones, the stoichiometry of the reaction is given by  $2\underline{A} + \underline{B} \rightarrow$  products. Let  $\underline{x}$  be the number of moles per liter of hydrogen peroxide which react in time,  $\underline{t}$ . Then the concentration of hydrogen peroxide at time  $\underline{t}$  is  $\underline{a-x}$ , and the concentration of ketone is  $\underline{b-0.5x}$  where  $\underline{a}$  and  $\underline{b}$  are, respectively, the initial concentration of hydrogen peroxide and ketone. Making the proper substitutions:

$$dx/dt = k(a-x)(b-0.5x) \quad (6).$$

Integrating between appropriate limits, the following expression is obtained.

$$t = [1/k(a-0.5b)] \ln[b(a-x)/a(b-0.5x)] \quad (7)$$

This expression can be evaluated by plotting  $\ln[b(a-x)/a(b-0.5x)]$  as a function of  $t$ . The rate constant is then evaluated by dividing the slope of the line by  $(a-0.5b)$ .

A computer program was developed to determine the pseudo second-order rate constants.<sup>1</sup> The required input data included the initial concentrations of the reactants, the estimate of the decomposition, and the raw data (absorbance at specific time intervals). The decomposition of the peroxide, which averaged 3% per hour, was assumed to be first order; and a revised estimate of the decomposition was made for each data point. The program was designed to give a least squares fit of the data. The output included the correlation coefficient and the calculated second-order rate constant. The data used in these calculations were arbitrarily selected to include those data points between 10 and 60 minutes. The data from the first ten minutes were not used since the response of the flow system is not instantaneous, and a finite time is required for the system to reach thermal equilibrium.

The calculations, as developed in the previous expressions, were applicable to oxidation of the phenyl-2-propanones where initially two moles of the hydrogen peroxide are consumed per mole of ketone. In several instances the stoichiometry of the reactions of interest required initially only one mole of oxidant per mole of substrate. The integrated form of the equation for these instances is given in Equation (8).

$$t = [1/k(a-b)] \ln[b(a-x)/a(b-x)] \quad (8)$$

Only minor modifications of the computer program previously mentioned were required to obtain second-order rate constants. The IBM 1620<sup>II</sup> Computer was used

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<sup>1</sup>The second-order constant is a pseudo constant since the sodium hydroxide concentration is not included in Equation (5).

in all instances, and the programs were written for AFIT Fortran.

In several instances the slope and correlation coefficients were required for linear relationships. These were all calculated using Utility Program 903A available in the computer laboratory of The Institute of Paper Chemistry.

#### CALCULATION OF THE ACTIVATION PARAMETERS

The effect of temperature on reactivity was evaluated using the Arrhenius equation (82).

$$k = Z \exp(-E_a/RT) \quad (9)$$

where  $\underline{k}$  = rate constant  
 $\underline{E}_a$  = Arrhenius activation energy, cal. mole<sup>-1</sup>  
 $\underline{R}$  = gas constant, 1.987 cal. deg.<sup>-1</sup> mole<sup>-1</sup>  
 $\underline{T}$  = absolute temperature  
 $\underline{Z}$  = a constant

The relationship was evaluated in the logarithmic form by plotting  $\ln k$  as a function of  $1/\underline{T}$ . The activation energy

$$\ln k = \ln Z - E_a/RT \quad (10)$$

was determined by dividing the slope by  $\underline{R}$ . The enthalpy of activation,  $\Delta H^\ddagger$ , can then be determined from Equation (11).

$$E_a = \Delta H^\ddagger + RT \quad (11)$$

Transition state theory provides a theoretical relationship between the rate constant and the entropy and enthalpy of activation (83), Equation (12)

$$k = k_B T/h \exp(-\Delta H^\ddagger/RT) \exp(\Delta S^\ddagger/R) \quad (12)$$

where  $k$  = rate constant, liter mole<sup>-1</sup>  
 $k_B$  = Boltzmann constant,  $1.3803 \times 10^{-16}$  erg deg.<sup>-1</sup>  
 $h$  = Planck's constant,  $6.624 \times 10^{-27}$  erg-sec.  
 $\Delta S^\ddagger$  = entropy of activation, cal. deg.<sup>-1</sup> mole<sup>-1</sup>

By combining Equations (11) and (12), substituting for  $k_B$ ,  $h$ , and  $e$  the base of the natural logarithms, and taking the natural logarithm of the expression, the entropy of activation can be determined as a function of  $E_a$ ,  $k$ , and  $T$  (83).

$$\Delta S^\ddagger = R(\ln k - 24.76 - \ln T + E/RT) \quad (13)$$

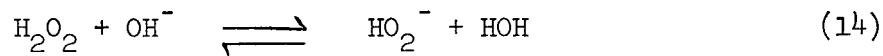
The value of  $\Delta S^\ddagger$  was calculated using the second-order rate constant, the Arrhenius activation energy, and the absolute temperature.

#### SPECTROPHOTOMETRIC DETERMINATION OF HYDROPEROXIDE ANION

For one series of investigations it was necessary to determine hydroperoxide anion concentration in a 50% ethanol - water system as a function of total hydrogen peroxide at constant added sodium hydroxide. Ultraviolet spectrophotometry provided a convenient method for determining this relationship. Muhammad and Rao (84) have used this method to determine the ionization constant of hydrogen peroxide in aqueous media.

Appropriate solutions were prepared for determining the molar absorptivity of the two peroxide species and for establishing the relationship between hydroperoxide concentration and free hydrogen peroxide. An identical solution without hydrogen peroxide was used in the reference cell for each determination. Each solution was prepared, and its absorbance immediately determined on the Cary Model 15 Recording Spectrophotometer. All determinations were made at a wavelength of 315  $\mu\text{m}$ . and at 25°C.

In order to determine the equilibrium concentration [Equation (14)] of the hydroperoxide anion, it was necessary to determine the molar absorptivity of the



hydroperoxide anion and the undissociated hydrogen peroxide. The absorbance of the two species in the solution is described by the following equation:

$$A = (\epsilon_{\text{F}} C_{\text{F}} + \epsilon_{\text{D}} C_{\text{D}}) b \quad (15)$$

where

- $A$  = total absorbance of the solution
- $b$  = cell path length, cm.
- $\epsilon_{\text{F}}, \epsilon_{\text{D}}$  = molar absorptivity of undissociated and dissociated hydrogen peroxide
- $C_{\text{F}}, C_{\text{D}}$  = concentration, M of undissociated and dissociated hydrogen peroxide

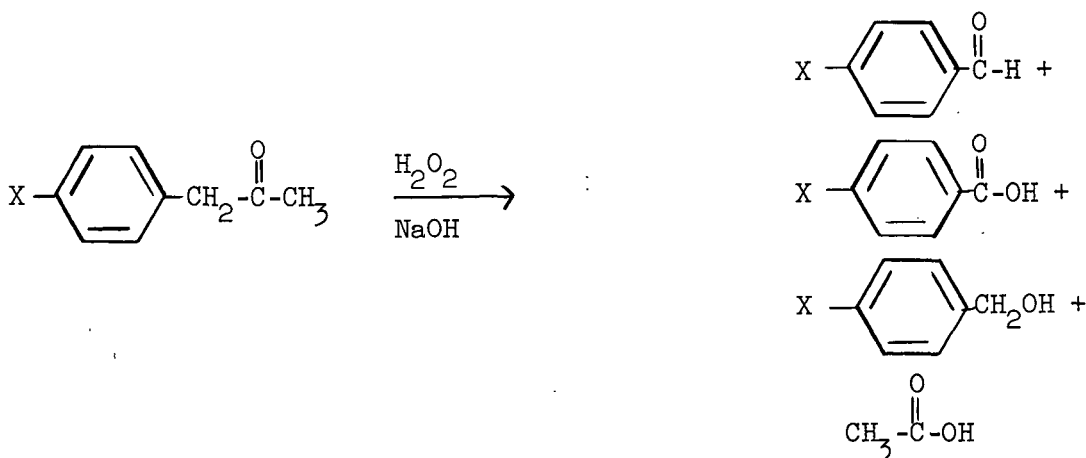
Knowing  $\epsilon_{\text{F}}, \epsilon_{\text{D}}$ , and  $C_{\text{D}} = \text{HO}_2^- = \text{H}_2\text{O}_2 \text{ (total)} - \text{H}_2\text{O}_2 \text{ (free)}$ , and substituting into Equation (15), the hydroperoxide anion concentration can be determined.

RESULTS AND DISCUSSION

PHENYL-2-PROPANONES

PRODUCT ANALYSIS AND REACTION STOICHIOMETRY

The oxidation of phenyl-2-propanones, by alkaline hydrogen peroxide has been shown to give several products. All the products which were obtained, aromatic aldehyde, acid, alcohol, and acetic acid, indicate that cleavage of the ketone always occurs to the ring side of the carbonyl group. The general course of the reaction is shown below. Thorough product analysis was necessary to insure that



the identified products and the recovered starting materials adequately accounted for the apparent stoichiometry of the reaction. To investigate this aspect comprehensive product analysis was made of the alkaline peroxide oxidation of p-methoxyphenyl-2-propanone. The conditions selected for these investigations were necessarily a compromise between low temperatures and short reaction times and high temperatures and long reaction times. The former is necessary to obtain an estimate of peroxide consumption without the interference of excessive decomposition, whereas the latter would be desirable so that the primary quantitative technique would be the gravimetric determination of the aromatic acid. The conditions,

(Table XI, Appendix III) selected for the oxidations were a three to one molar ratio of hydrogen peroxide and sodium hydroxide to ketone with the oxidation proceeding at 45° for four hours. The results of the two oxidations made for this purpose are shown in Table I. The recovery of aromatic materials and acetic acid was close to 90% for both oxidations. These results indicate that all of the primary products have been determined and that acetic acid is the two-carbon fragment of the cleavage.

The data relating to the consumption of hydrogen peroxide were also consistent. Slightly more than half of the original amount of peroxide was consumed. Peroxide consumption was estimated assuming that one, two, and three molar equivalents of peroxide per mole of ketone were required, respectively, to produce each mole of aromatic alcohol, aldehyde, and acid. The calculated consumption was approximately 20 to 25% lower than the observed consumption. This discrepancy is consistent since the estimated decomposition over the four-hour period of the oxidation would be approximately 20%.

To substantiate the identity of the volatile products, the materials having retention times which corresponded to p-methoxybenzyl alcohol and p-methoxybenzaldehyde were collected on the Aerograph A-700 "Autoprep" Gas Chromatograph using a preparative DEGS column.<sup>1</sup> The infrared spectra of the collected materials were almost identical to those of the known aldehyde and alcohol. The melting point of the isolated p-methoxybenzoic acid was 183.0-183.9°, mixed melting point 183.3-184.0°. The melting point of known p-methoxybenzoic acid was 184.1-184.9°.

<sup>1</sup>The 3/8 inch x 5 ft. column was packed with 30% DEGS (diethylene glycol succinate) on acid-washed Chromosorb W, 60/80.

TABLE I

COMPREHENSIVE PRODUCT ANALYSIS FOR TWO OXIDATIONS  
OF p-METHOXYPHENYL-2-PROPANONE

Product or Reactant	Oxidation 2417-11a, mole percent yield <sup>a</sup>	Oxidation 2417-15a, mole percent yield
Recovery of aromatics		
Residual ketone	26.3	15.6
<u>p</u> -Methoxybenzaldehyde	20.4	20.8
<u>p</u> -Methoxybenzyl alcohol	16.0	19.6
<u>p</u> -Methoxybenzoic acid	<u>25.2</u>	<u>32.1</u>
Total recovery of aromatics	<u>87.9</u>	<u>88.1</u>
Recovery of acetic acid		
Acetic acid	62.9	74.5
Residual ketone	<u>26.3</u>	<u>15.6</u>
Total recovery of acetic acid	<u>89.2</u>	<u>90.3</u>
	Percent Consumption	Percent Consumption
Hydrogen peroxide		
Peroxide consumed	53.2	61.7
Calculated peroxide consumption	41.2	50.8

<sup>a</sup>All yields of organic products were converted to a molar basis and presented as a mole percent of the original ketone concentration.

To determine the relationship between the aromatic products, two oxidations were made in which samples were taken at various times and the concentrations of the volatile aromatic materials were determined by gas chromatography. These results indicated that the aldehyde was produced quite rapidly during the early stages of the reaction, reached a maximum and then decreased as the oxidation proceeded. During this time the concentration of the alcohol slowly increased. These results indicate that both the alcohol and the aldehyde are primary cleavage products of the oxidation and that the aldehyde is oxidized to the acid. Exploratory investigations showed that alkaline hydrogen peroxide effected essentially a quantitative conversion of p-methoxybenzaldehyde to p-methoxybenzoic acid. Similar studies showed that p-methoxybenzyl alcohol could be converted very slowly to p-methoxybenzaldehyde.

To substantiate that the alcohol and aldehyde were produced by competitive mechanisms, a comparison was made of the rates of oxidation of p-methoxybenzaldehyde and p-methoxybenzyl alcohol. The conditions for these oxidations are given in Table XII. At 45° the average second-order rate constant for the oxidation of the aldehyde was  $0.163\text{M}^{-1} \text{min.}^{-1}$  while that for the alcohol was  $0.0033\text{M}^{-1} \text{min.}^{-1}$ . If the entire reaction was proceeding through the alcohol, the conversion of the aldehyde to the acid would be so rapid compared to the conversion of alcohol to aldehyde that less than 2% aldehyde would accumulate (82). This is contrary to the observations and confirms that the aromatic alcohol and aldehyde are being produced by competitive mechanisms.

The oxidative cleavage can best be represented as a combination of competitive and consecutive reactions with the primary reaction involving cleavage to the aldehyde and acetic acid.



TABLE II

OXIDATIONS OF PHENYL-2-PROPANONES FOR PRODUCT ANALYSIS

Experiment Number	Ketone	Aromatic Acid, mole percent	Residual Ketone, mole percent	Aromatic Aldehyde, mole percent	Aromatic Alcohol, mole percent <sup>a</sup>	Total Recovery
2417-124a	<u>p</u> -chloro	88.6	Trace	0.9	5.8	95.3
2417-126a	<u>p</u> -chloro	87.0	Trace	1.0	5.9	93.9
2417-122a	<u>p</u> -H	80.2	1.1	2.9	7.8	92.0
2417-129a	<u>p</u> -H	74.9	2.5	2.4	9.1	88.9
2417-121a	<u>p</u> -methyl	69.5	4.4	16.3	9.7	98.9
2417-128a	<u>p</u> -methyl	78.6	1.6	6.3	6.6	93.1
2417-125a	<u>p</u> -dimethyl-amino <sup>d</sup>	17.3	--	--	--	--
2373-113b	<u>p</u> -hydroxy	6.2	(63.1) <sup>b</sup>	--	--	(69.3) <sup>c</sup>
2373-118a	<u>p</u> -hydroxy	20.4	15.4	--	--	35.8
2373-119a	<u>p</u> -hydroxy	19.4	19.4(32.4)	--	--	38.8(51.8)

<sup>a</sup>Reference materials were not available for p-methylbenzyl and p-chlorobenzyl alcohol. The retention times for these compounds relative to the parent ketone were similar to those for which the alcohols were available, benzyl and p-methoxybenzyl alcohol.

<sup>b</sup>Estimates of residual ketone in parentheses refer to determinations on the quenched, neutralized reaction mixture. Those without refer to determinations made on the ether extracts.

<sup>c</sup>Quantitative estimates of acetic acid for 2373-113b, 118a, and 119a were 46.3, 102, and 96 mole percent on the basis of the original ketone.

<sup>d</sup>If a numerical estimate is not given the product was not detected. Under the gas chromatographic conditions utilized, volatile components would have been noted in a yield of less than one mole percent.

found was p-hydroxybenzoic acid. The acid accounts for considerably less than half of the consumed ketone in all instances. The reaction mixture was searched by gas, paper, and thin-layer chromatography for such products as hydroquinone, p-hydroxybenzaldehyde, and p-hydroxybenzyl alcohol, but no evidence of these products was found. The presence of phenol was noted, but this compound was produced from p-hydroxybenzoic acid by decomposition on the gas chromatography column. Thermal decarboxylation of the acid to phenol has been shown previously (85). The disubstituted ketone, 4-hydroxy-3-methoxyphenyl-2-propanone, was also investigated with equally poor results. A minimum of twenty preliminary oxidations was made under a variety of conditions in an effort to obtain satisfactory product analysis for the two hydroxylated phenyl-2-propanones, all with unsatisfactory results. Only the aromatic acid and residual ketone were found.

#### KINETIC INVESTIGATIONS

Properly characterizing the kinetics of a reaction is one of the most effective methods of investigating its mechanism. A knowledge of the order of the reaction with respect to the various reactants is often fundamental to making any conclusions concerning the mechanism. A determination of the activation parameters and the effect of an added electrolyte upon reactivity can also be helpful. A study of electronic effects on the reaction site, free energy relationships, are particularly effective in rigid systems where systematic interpretations of reactivity can be made. Kinetic investigations of these various aspects of the alkaline peroxide oxidation of p-methoxyphenyl-2-propanone and phenyl-2-propanone were made.

#### Order With Respect to the Reactants

The order of the reaction with respect to the ketone at 45.0° was determined for phenyl-2-propanone and p-methoxyphenyl-2-propanone. For p-methoxyphenyl-2-propanone, duplicate oxidations (Table XIII) at three ketone concentrations were

made. Six oxidations at variable ketone concentrations (Table XIV) were investigated for phenyl-2-propanone. The oxidation was found to be first order with respect to substrate for both the ketones. The slope of the initial rate plot, Fig. 2, was 1.02, corr. (correlation coefficient) = 0.98, for p-methoxyphenyl-2-propanone. Figure 3 shows the similar relationship for phenyl-2-propanone. The slope of this relationship was 0.99, corr. = 0.97.

The order with respect to hydrogen peroxide was determined by holding the ketone concentration constant and varying the hydrogen peroxide and sodium hydroxide concentrations. The difference in ionic strength was compensated by using potassium chloride. Five oxidations at different total hydrogen peroxide concentrations (Tables XV and XVI) were used to determine the order with respect to peroxide for phenyl-2-propanone and p-methoxyphenyl-2-propanone at 45.0°. These relationships are presented in Fig. 4 and 5. The slope for the oxidations of p-methoxyphenyl-2-propanone was 1.04 (corr. = 0.99) and that for phenyl-2-propanone was 1.01 (corr. = 0.99).

The results of the initial rate studies indicate that the reaction is first order with respect to both substrate and oxidant. First-order kinetics with respect to the substrate was anticipated and indicates that the substrate participates in the reaction during or prior to the rate-determining step. That the oxidation is first order in peroxide is of considerable mechanistic significance. The possibility that the reaction involves rate-controlling enolization is eliminated; zero-order kinetics with respect to peroxide would have been observed. Since two moles of peroxide are consumed before the ketone is cleaved, there was a possibility that the reaction would be second order in hydrogen peroxide. The rate-determining step occurs prior to the addition of the second mole of peroxide, indicating that initial attack of the peroxide is probably rate controlling.

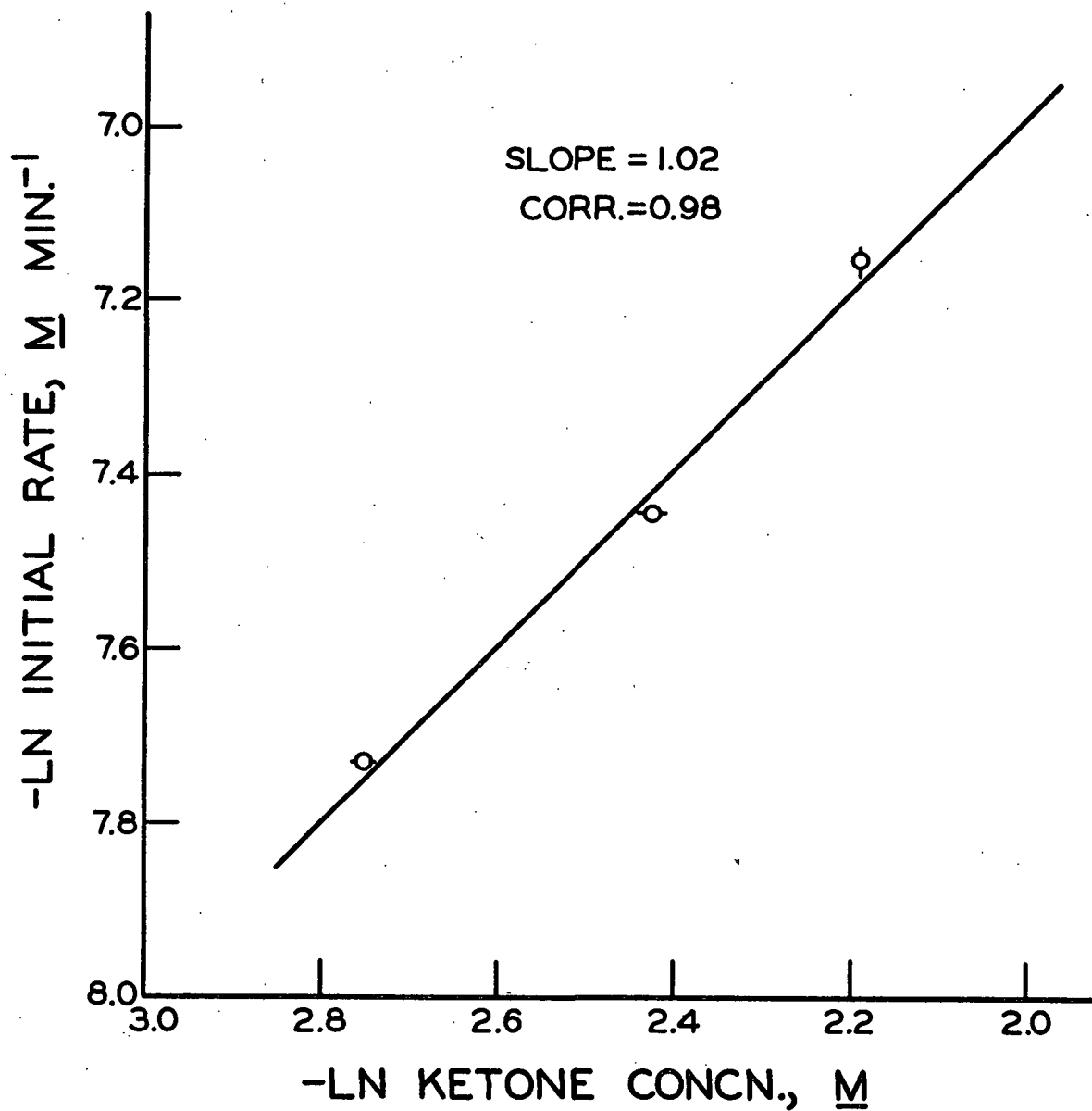


Figure 2. Oxidation of p-Methoxyphenyl-2-propanone:  
Effect of Substrate

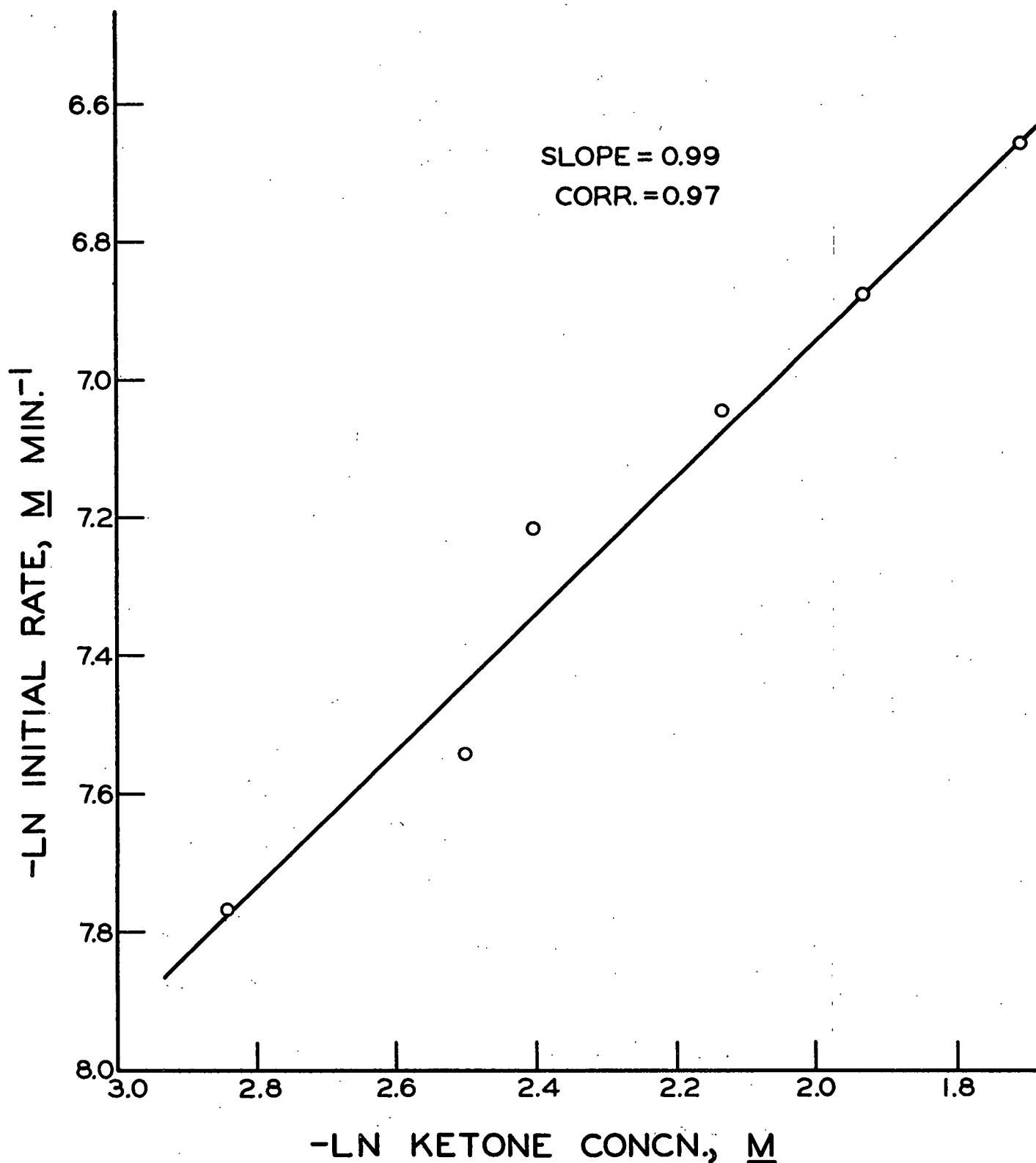


Figure 3. Oxidation of Phenyl-2-propanone:  
Effect of Substrate

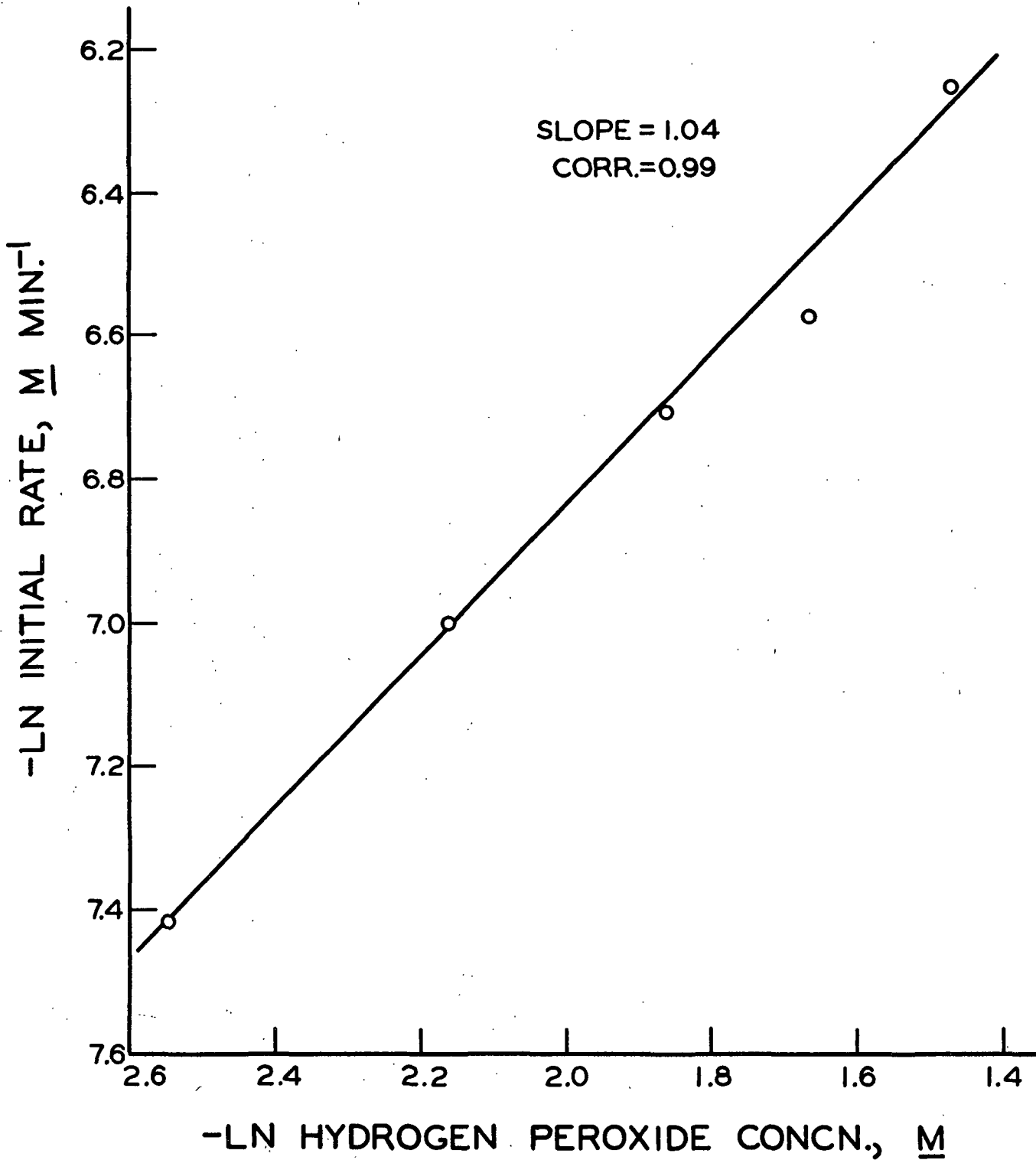


Figure 4. Oxidation of p-Methoxyphenyl-2-propanone:  
Effect of Total Peroxide

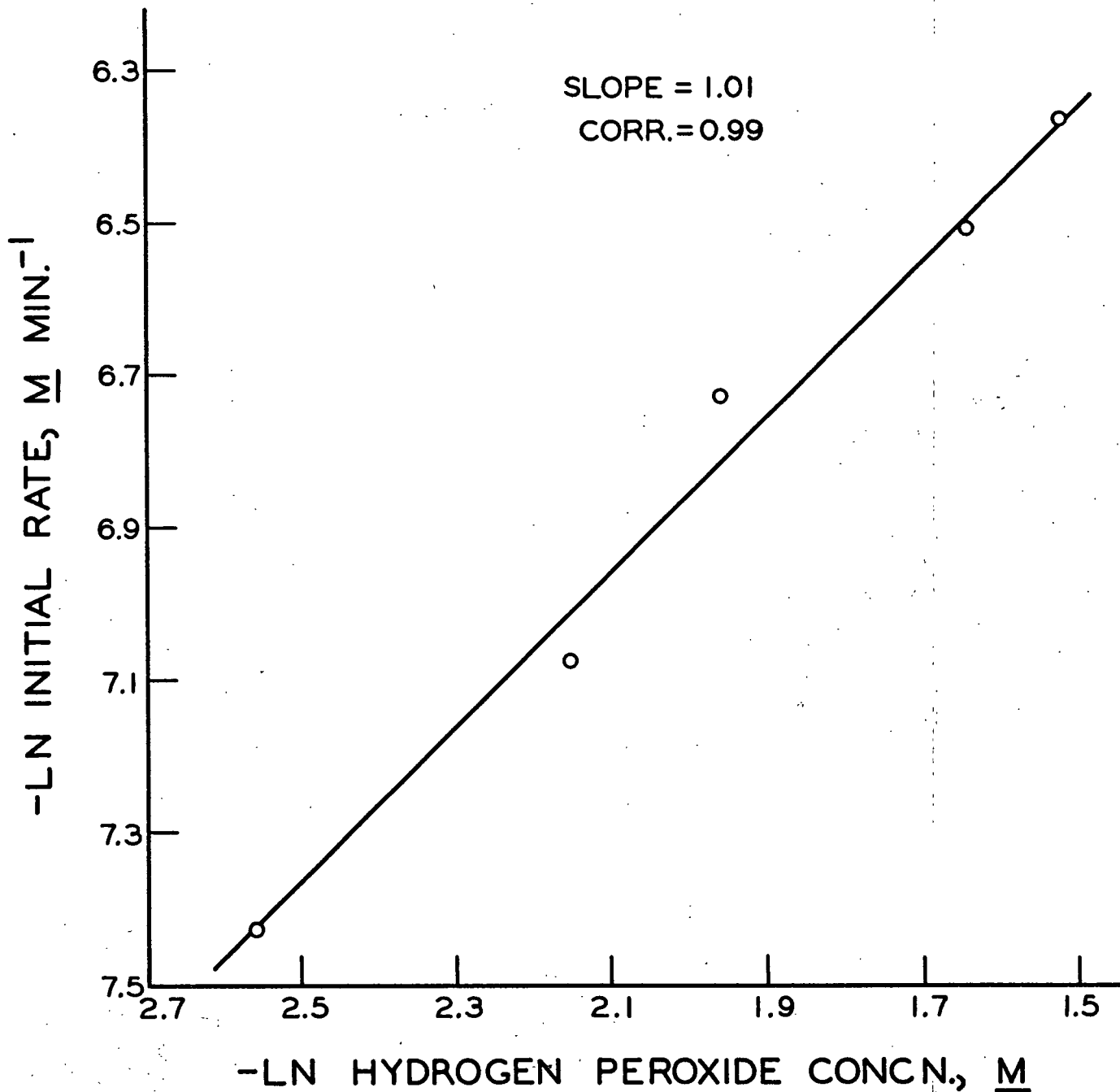


Figure 5. Oxidation of Phenyl-2-propanone:  
Effect of Total Peroxide

### Effect of Sodium Hydroxide

Having established that the reaction order was unity for peroxide and ketone for both of the phenyl-2-propanones, the effect of varying the sodium hydroxide concentration was studied. These investigations were made in an effort to provide some indication of the reactive species in the system. The oxidations of the phenyl-2-propanones were found to be first order with respect to both reactants from initial rate studies. However, the conditions for the oxidations were such that it was not possible to distinguish the reactive peroxide species. The concentration of both the peroxide species and the aromatic species are dependent upon the concentration of the base.

The effect of sodium hydroxide concentration on the reactivity of p-methoxyphenyl-2-propanone was studied by varying the sodium hydroxide concentration from 0.6 to 0.02N (Table XVII). Constant ionic strength was maintained with potassium chloride. The plot of the second-order rate constants against added sodium hydroxide is given in Fig. 6. The maximum rate is obtained when the added sodium hydroxide concentration equals that of the added hydrogen peroxide. The reactivity drops quite rapidly when either more or less base is added. The drop in reaction rate that occurs when the concentration of the base is lower than that of hydrogen peroxide is attributed to the corresponding decrease in hydroperoxide anion concentration. These results indicate that hydroperoxide anion is the peroxide species participating in the rate-determining step of the reaction.

When the concentration of added base exceeds that of the hydrogen peroxide, the rate also rapidly decreases but levels off at a sodium hydroxide concentration of about 0.3N to a reaction rate about half that of the maximum value. The decreased reaction rate in the presence of excess base is related to the distribution of the three aromatic species in the system. At lower pH the keto-enol

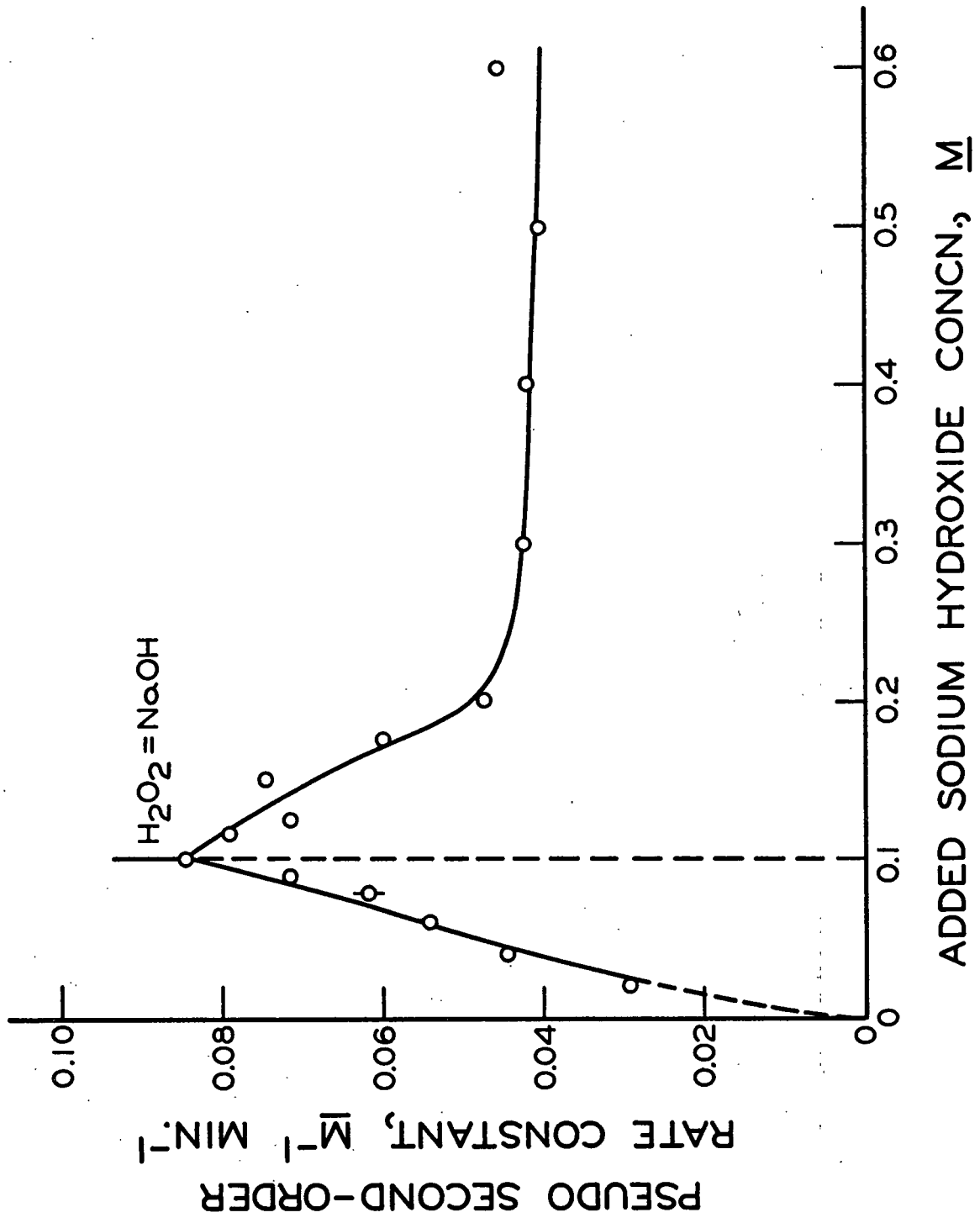


Figure 6. Oxidation of p-Methoxyphenyl-2-propanone:  
Effect of Sodium Hydroxide

equilibrium is important and the concentration of the enol anion is negligible, whereas the concentration of the enol anion is significant at higher alkalinities. The decrease in reactivity is considered to be a result of converting more of the substrate to the enol anion. The attack of the nucleophilic hydroperoxide anion would be repressed if a reactive neutral substrate was converted to a negatively charged one. This indicates that the reactive aromatic species is a neutral molecule. These data, however, cannot distinguish between direct attack on the carbonyl, direct attack at the methylene group adjacent to the carbonyl, or attack on the enol tautomer.

A similar investigation was made to determine the effect of sodium hydroxide upon the reactivity of phenyl-2-propanone. The conditions for these oxidations are given in Table XVIII. The results given in Fig. 7 show essentially the same trends as those of Fig. 6 for the oxidation of p-methoxyphenyl-2-propanone.

#### Determining the Reactive Peroxide Species

The investigations of the effect of sodium hydroxide on reactivity indicate that the hydroperoxide anion is the reactive peroxide species. To investigate this proposition, a series of oxidations of phenyl-2-propanone were made in which the total hydrogen peroxide was varied, and the added base was maintained constant.

To interpret these results it was necessary to have an estimate of the hydroperoxide anion concentration for each solution in the mixed solvent system. A correlation of hydroperoxide anion concentration as a function of total hydrogen peroxide was determined spectrophotometrically. The molar absorptivity of hydrogen peroxide and the hydroperoxide anion were determined using 0.08M hydrogen peroxide solutions. The first solution was prepared using a pH 7 buffer and the second was 0.5N in NaOH. Seven additional solutions (Table XIX) from 0.02 to 0.2M in hydrogen peroxide were prepared. The added sodium hydroxide was maintained constant at 0.08

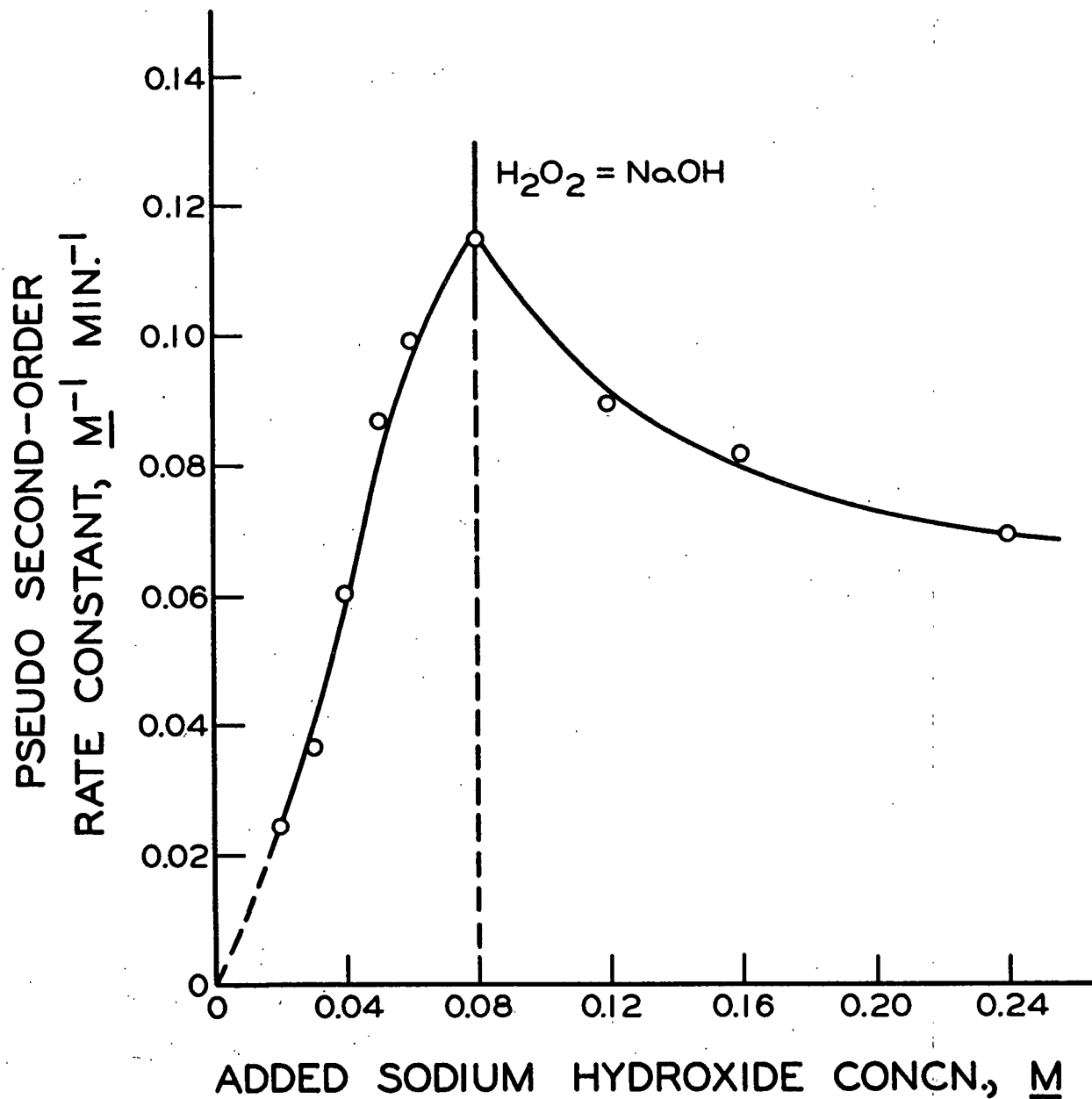


Figure 7. Oxidation of Phenyl-2-propanone:  
Effect of Sodium Hydroxide

M. Spectrophotometric measurements from these solutions were used to establish the relationship between hydroperoxide anion concentration and total hydrogen peroxide which is shown in Fig. 8.

Having a suitable method for determining the distribution of peroxide species, oxidations were made over a wide range of hydrogen peroxide concentrations (Table XX). The hydroperoxide anion concentration was determined by referring to Fig. 8 and the free hydrogen peroxide by difference.

The relationships between initial rate and the peroxide species concentration are shown in Fig. 9a. These data indicate that the reaction rate is definitely not dependent upon either total peroxide or undissociated hydrogen peroxide since the reaction rate is insensitive to free hydrogen peroxide at high peroxide concentrations. However, the relationship observed for the hydroperoxide anion is consistent with its being the reactive peroxide species. A continuous relationship was obtained between hydroperoxide anion concentration and reactivity; and excess hydrogen peroxide over that which can be converted to hydroperoxide anion is ineffective in increasing the reaction rate.

If these data reflected only the effect of peroxide species concentration on reactivity, a linear relationship between the logarithmic initial rate and the logarithmic reactive peroxide species concentration would be expected. However, excess sodium hydroxide has a significant effect on reaction rate (Fig. 6 and 7, pages 61 and 63). The predicted apparent reaction order would be higher than unity because of the adverse effect on the reaction rate for those runs having a large excess of base. The double logarithmic plot of initial rate versus peroxide species concentration should be curvilinear, since the addition of hydrogen peroxide would have two effects: increase in the reactive peroxide species concentration and a decrease in the excess base.

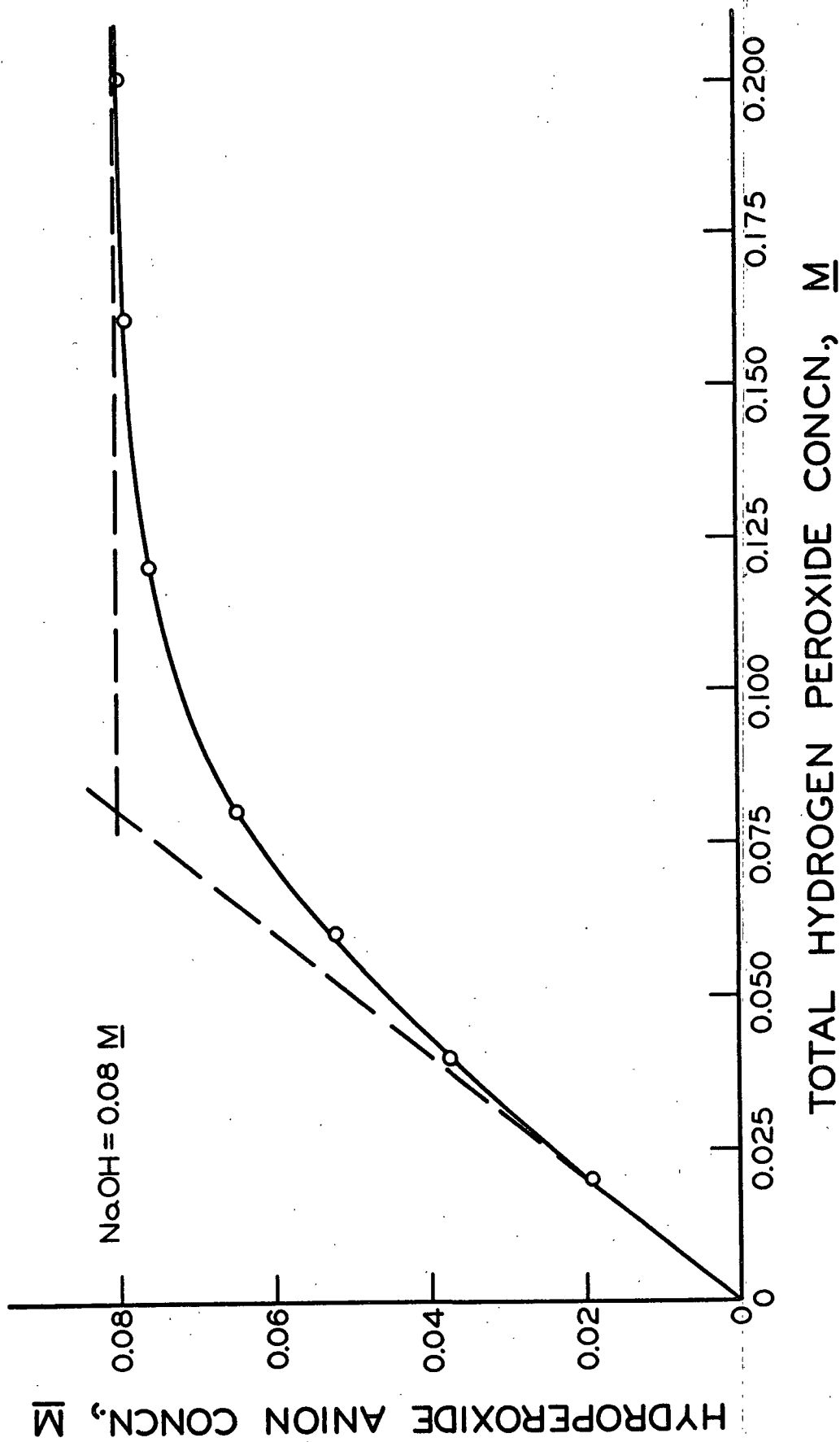
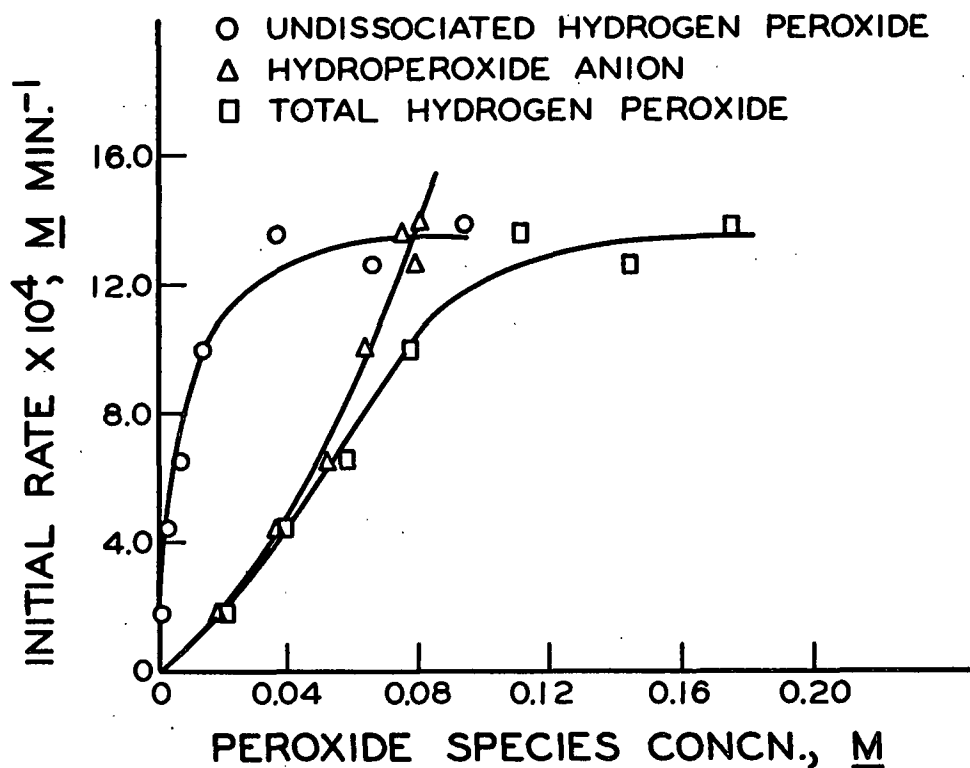
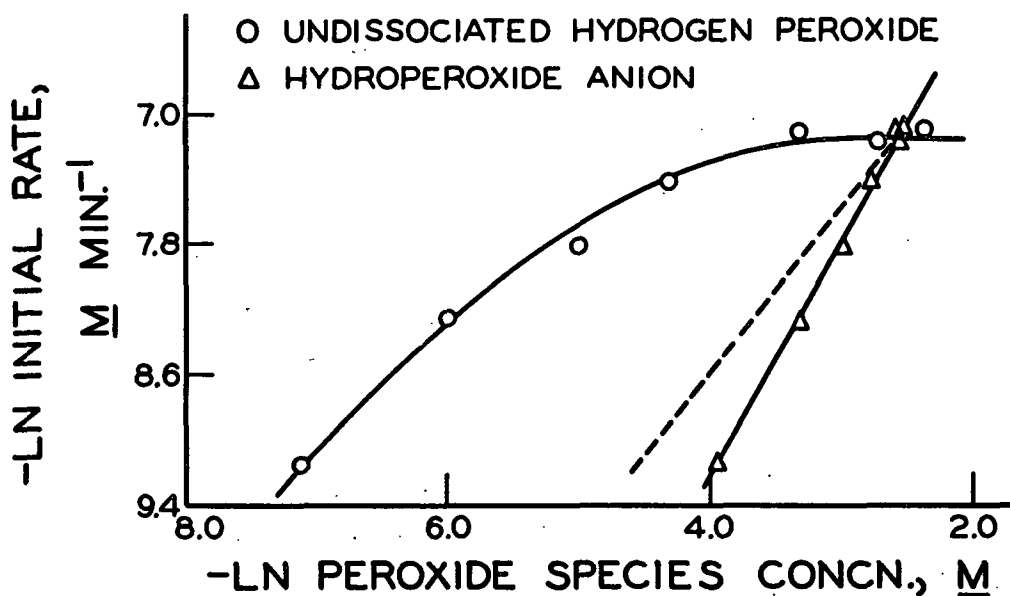


Figure 8. Hydroperoxide Anion Concentration in Various Hydrogen Peroxide Solutions Containing 0.08M Sodium Hydroxide



(a) REACTION RATE AS A FUNCTION OF PEROXIDE SPECIES



(b) LOGARITHMIC RELATIONSHIP, REACTION RATE VS. PEROXIDE SPECIES

Figure 9. Oxidation of Phenyl-2-propanone: Effect of Hydrogen Peroxide Species

The observed relationships are shown in Fig. 9b. The relationship for hydroperoxide anion is essentially that expected for the reactive peroxide species. The data best follow a straight line rather than the expected curve. However, the apparent reaction order was found to be 1.46, the deviation being in the direction expected. The dotted line in Fig. 9b is the relationship expected if the data were dependent only upon hydroperoxide anion concentration. The difference between the theoretical line of slope 1.0 and the actual correlation reflects the effect of excess base on the reaction.

Free hydrogen peroxide is certainly not the reactive peroxide species since the reaction rate becomes insensitive to undissociated hydrogen peroxide at higher concentrations. Although the study of reactive peroxide species is complicated by the presence of variable base, the data definitely indicate that hydroperoxide anion is the reactive peroxide species.

#### Effect of Added Electrolyte

The effect of potassium chloride upon the reactivity of p-methoxyphenyl-2-propanone and phenyl-2-propanone was studied. The conditions for these oxidations are given in Tables XXI and XXII. The results of these investigations, Fig. 10, indicate that a slight decrease in reactivity occurs in the presence of excess electrolyte, especially for p-methoxyphenyl-2-propanone. Increasing the polarity of the reaction medium would affect the equilibria in the system. The concentration of the enol tautomer would be decreased (86), but the dissociation of hydrogen peroxide would be expected to increase. If the enol tautomer and hydroperoxide anion are the reactive species, opposing effects would be encountered. This would explain the decrease in reactivity providing the keto-enol equilibria is the predominant factor. These arguments account for the observations, but since the effects are small, especially for phenyl-2-propanone, little significance can be attached to the results.

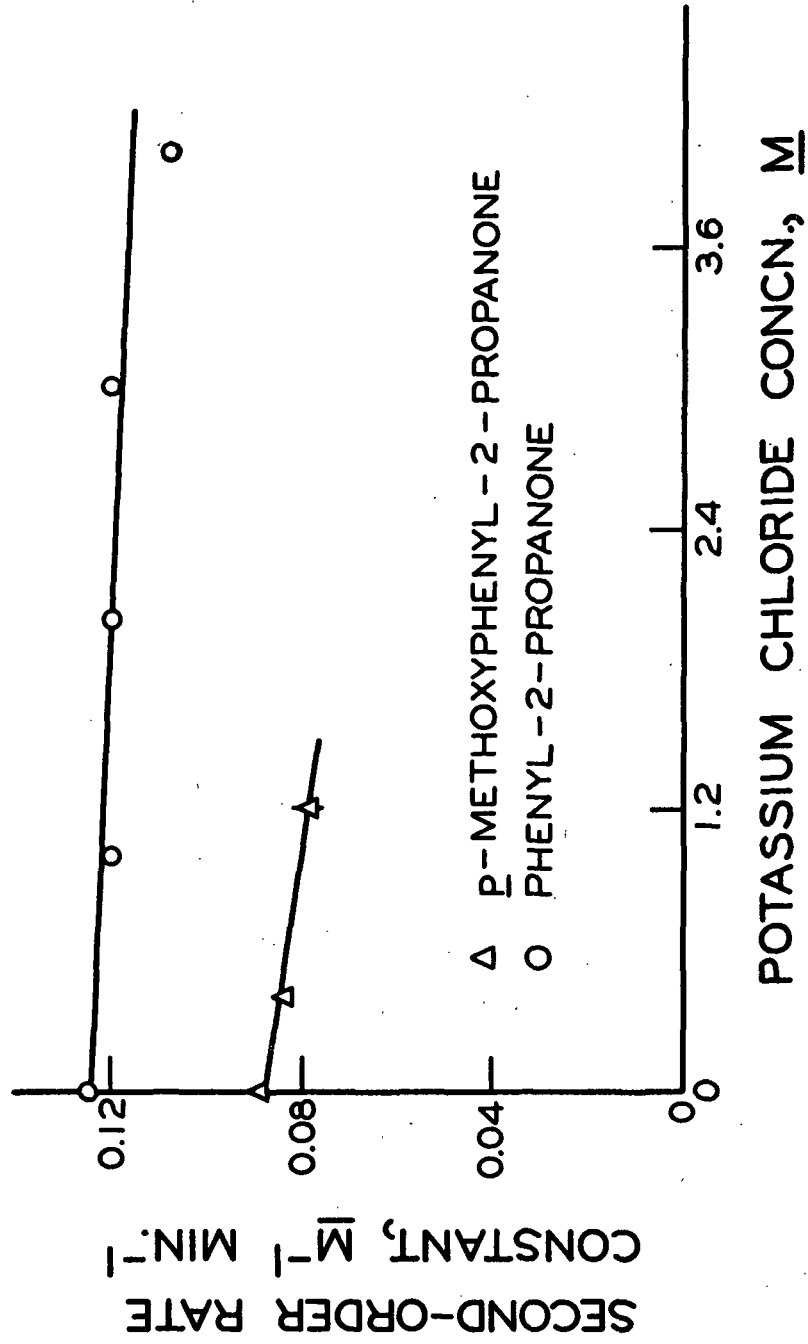


Figure 10. Oxidation of Phenyl-2-propanones:  
Effect of Added Electrolyte

### Temperature Dependence of the Reaction

The effect of temperature upon reactivity was studied for p-methoxyphenyl-2-propanone and phenyl-2-propanone. Duplicate oxidations (Tables XXIII and XXIV) were made at four different temperatures (26.5 to 65.0°) for each of the ketones. The relationships between the logarithm of the rate constant and reciprocal of the absolute temperature are shown in Fig. 11 and 12. A good linear relationship was found for phenyl-2-propanone, but the values at 35° fell off the linear correlation of the other data for p-methoxyphenyl-2-propanone. The energy of activation for p-methoxyphenyl-2-propanone was obtained using the slope of the line presented in Fig. 11. The calculated entropies and enthalpies of activation are given in Table III along with some activation parameters which have been reported for other alkaline peroxide reactions. The activation energy for the oxidation of p-methoxyphenyl-2-propanone was much lower than that for phenyl-2-propanone.

The activation parameters for the cleavage of benzil and the oxidations of the phenyl-2-propanones are of similar magnitude. The benzil cleavage involves attack of hydrogen peroxide on the carbonyl group with the rate-determining step considered to be decomposition of the intermediate hydroperoxide (18). Although this proposition has not been investigated for the alkaline peroxide cleavage of simple ketones, the rate-determining step in the Baeyer-Villiger reaction is also considered to be rearrangement of the intermediate  $\alpha$ -hydroxy peroxide (20). If the rate-determining step in the alkaline peroxide cleavage of simple ketones (the competitive reaction for the phenyl-2-propanones) is rearrangement of the hydroxyhydroperoxide, then the activation energy could be comparable to that observed for the benzils. If the competitive cleavage of p-methoxyphenyl-2-propanones has an activation energy which is considerably different than that of

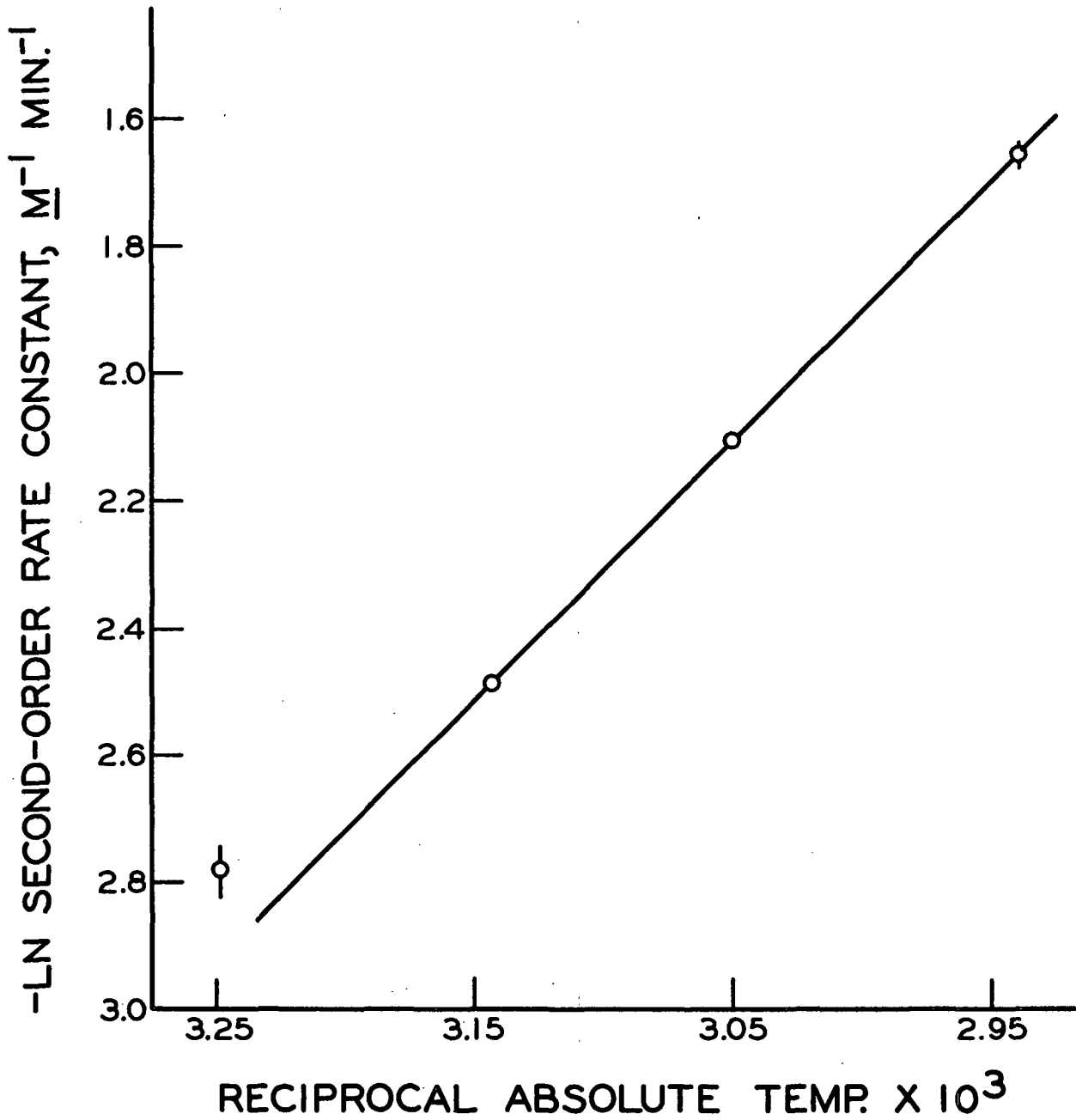


Figure 11. Oxidation of p-Methoxyphenyl-2-propanone:  
Effect of Temperature on Reaction Rate

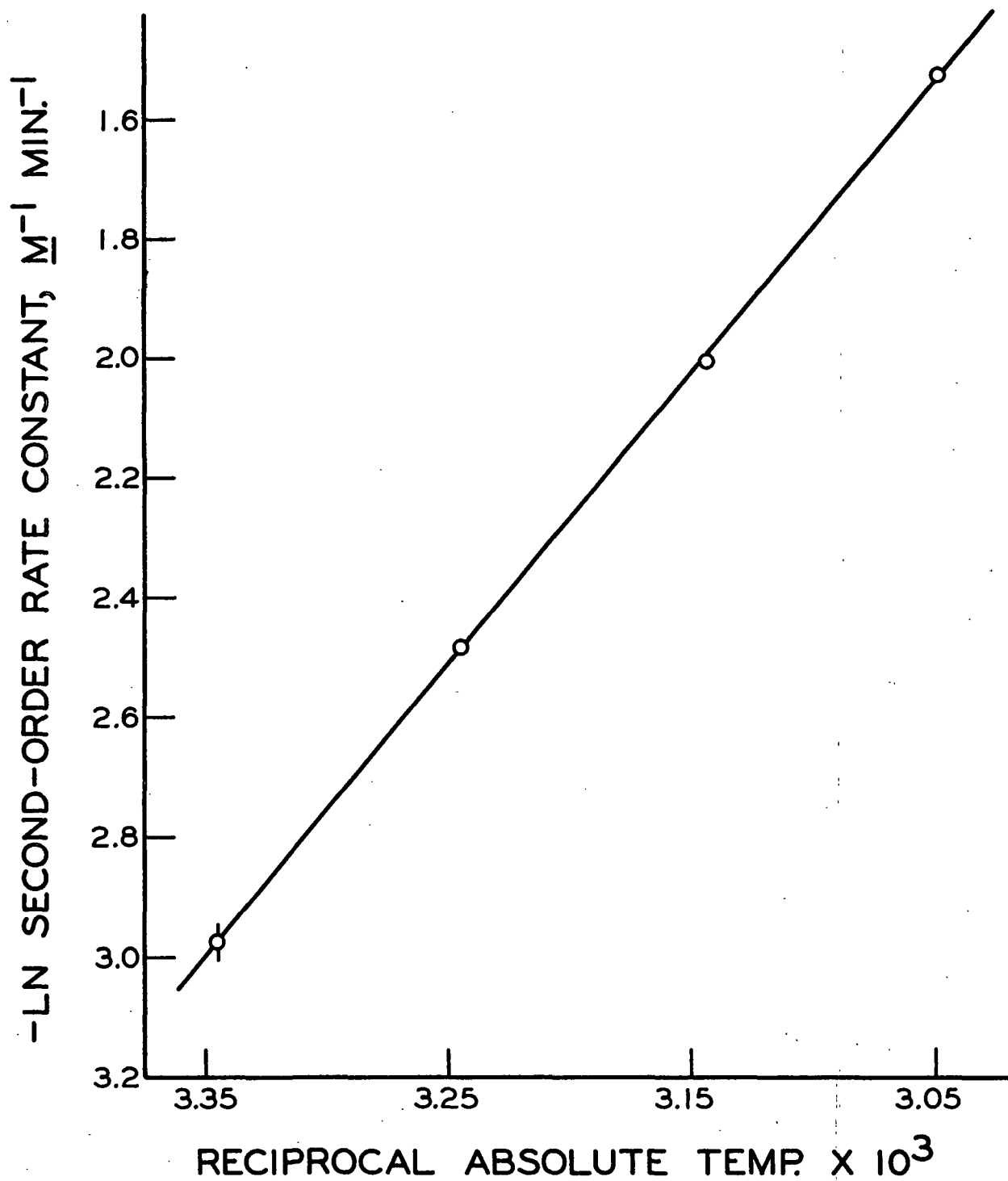


Figure 12. Oxidation of Phenyl-2-propanone:  
Effect of Temperature on Reaction Rate

the primary reaction, a curved Arrhenius plot would be obtained. It is quite possible that the Arrhenius plot for p-methoxyphenyl-2-propanone is curved and that the complexity of the reaction accounts for the curvature.

TABLE III

ACTIVATION PARAMETERS FOR REACTIONS OF  
ALKALINE HYDROGEN PEROXIDE

	$\frac{H^\ddagger}{kcal. mole^{-1}}$	$\frac{S^\ddagger}{cal. deg.^{-1} mole^{-1}}$
Hydrolysis of benzonitrile ( <u>4</u> )	22 ± 1	5 ± 4
Cleavage of benzil ( <u>18</u> )	4.4	-34.0
Cleavage of phenyl-2-propanones		
Phenyl-2-propanone	9 ± 2 <sup>a</sup>	-35 ± 6 <sup>a</sup>
<u>p</u> -Methoxyphenyl-2-propanone	7 ± 2	-49 ± 6

<sup>a</sup>The accuracy of these determinations was estimated as given by Friess, et al. (83).

Effect of Various Substituents on Reactivity

Several p-substituted phenyl-2-propanones were studied for the purpose of determining the effect of substituents on reactivity. A linear free energy relationship, the Hammett equation (25, 87), related reaction rates to two

$$\log k/k_0 = \rho\sigma$$

parameters. The substituent constant, sigma, represents the electron-withdrawing or electron-releasing ability of a substituent. Rho, the reaction constant, is an indication of the importance of electronic effects on reactivity. This parameter is constant for a reaction series for a particular solvent and temperature. Providing the reaction is sufficiently simple and all the compounds are reacting by

the same mechanism, a linear correlation should be obtained between the logarithm of the appropriate rate constant and a substituent constant,  $\sigma$ . The purpose of making such a study is to determine the significance of changes in electron density at the reaction site.

A total of nine para-substituted ketones were studied, ranging from the nitro ( $\sigma_{\text{NO}_2} = +0.778$ ) to the hydroxyl substituent ( $\sigma_{\text{O}^-} = -1.00$ ). The reactivity of these compounds was studied following the kinetic procedures described for p-methoxyphenyl-2-propanone. These procedures were applicable to all the ketones except the p-nitro compound. The reactivity of this ketone was extremely high, and an insoluble precipitate was formed when the sample was combined with the reagent stream. The precipitate clogged the flow lines and made continuous analysis impossible. No such problems were encountered for any of the other ketones. Duplicate determinations of the reactivity of the other ketones were made. The conditions for these oxidations are given in Table XXV.

The Hammett relationship found for the phenyl-2-propanones is presented in Fig. 13. Although a linear relationship was not obtained, the data for those ketones not having a hydroxyl or a p-dimethylamino substituent suggest that removal of electrons from the reaction center increase reactivity. The inconsistent behavior observed for some of the ketones can be explained by reference to their kinetic curves (Fig. 14). The oxidations were considered to be pseudo-second-order reactions in all instances. This does not appear to be a good assumption for several ketones. The initial rapid reaction and subsequent decrease observed for the p-hydroxy ketone, and to a lesser extent the 4-hydroxy-3-methoxy compound, is not characteristic of a simple second-order reaction. Product analysis of the p-hydroxyphenyl-2-propanone (Table I, p. 50) was also unsuccessful, indicating the reaction was not sufficiently specific or the products or intermediates sufficiently stable for meaningful kinetics to be obtained.

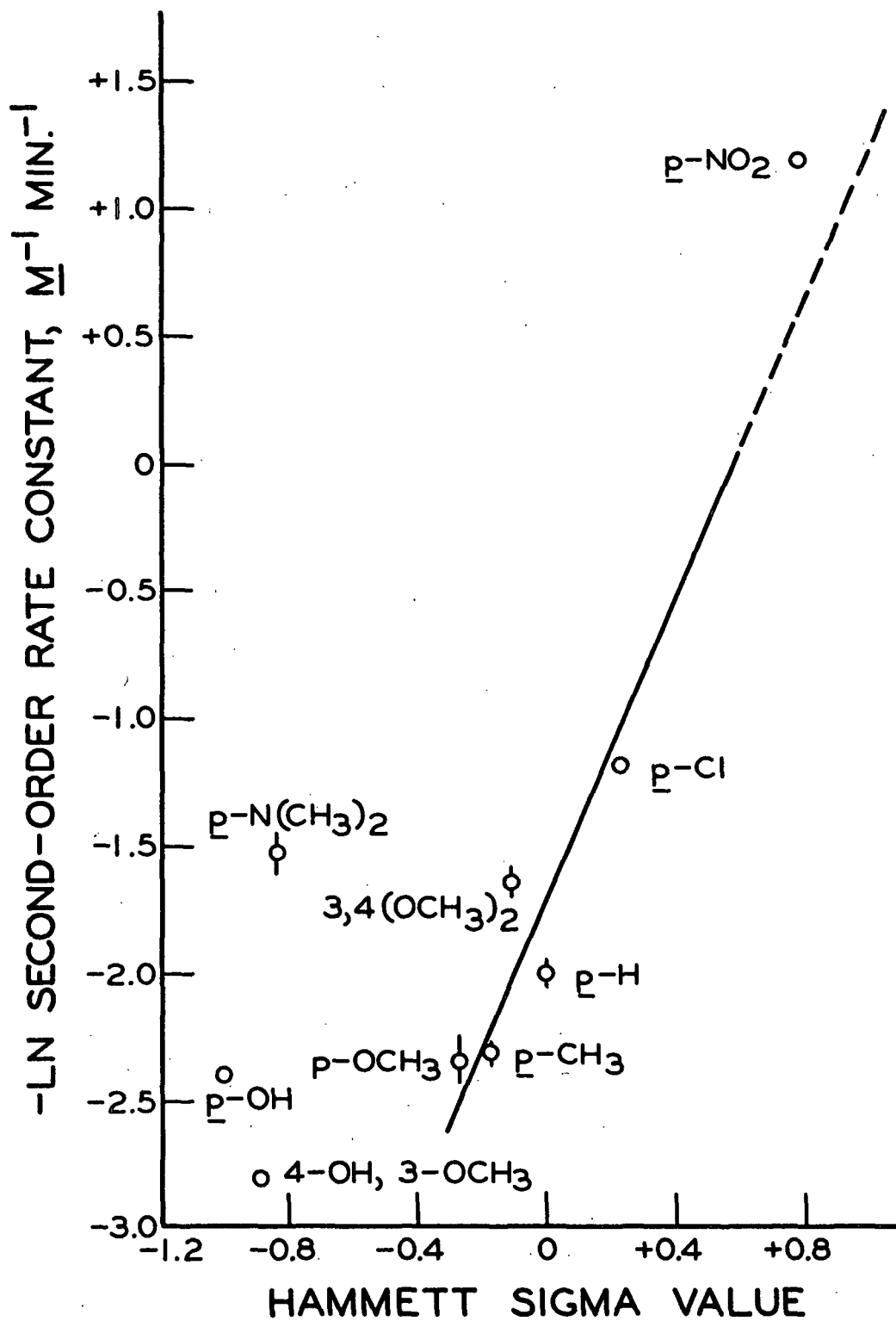


Figure 13. Oxidation of Phenyl-2-propanones:  
Effect of Substituents

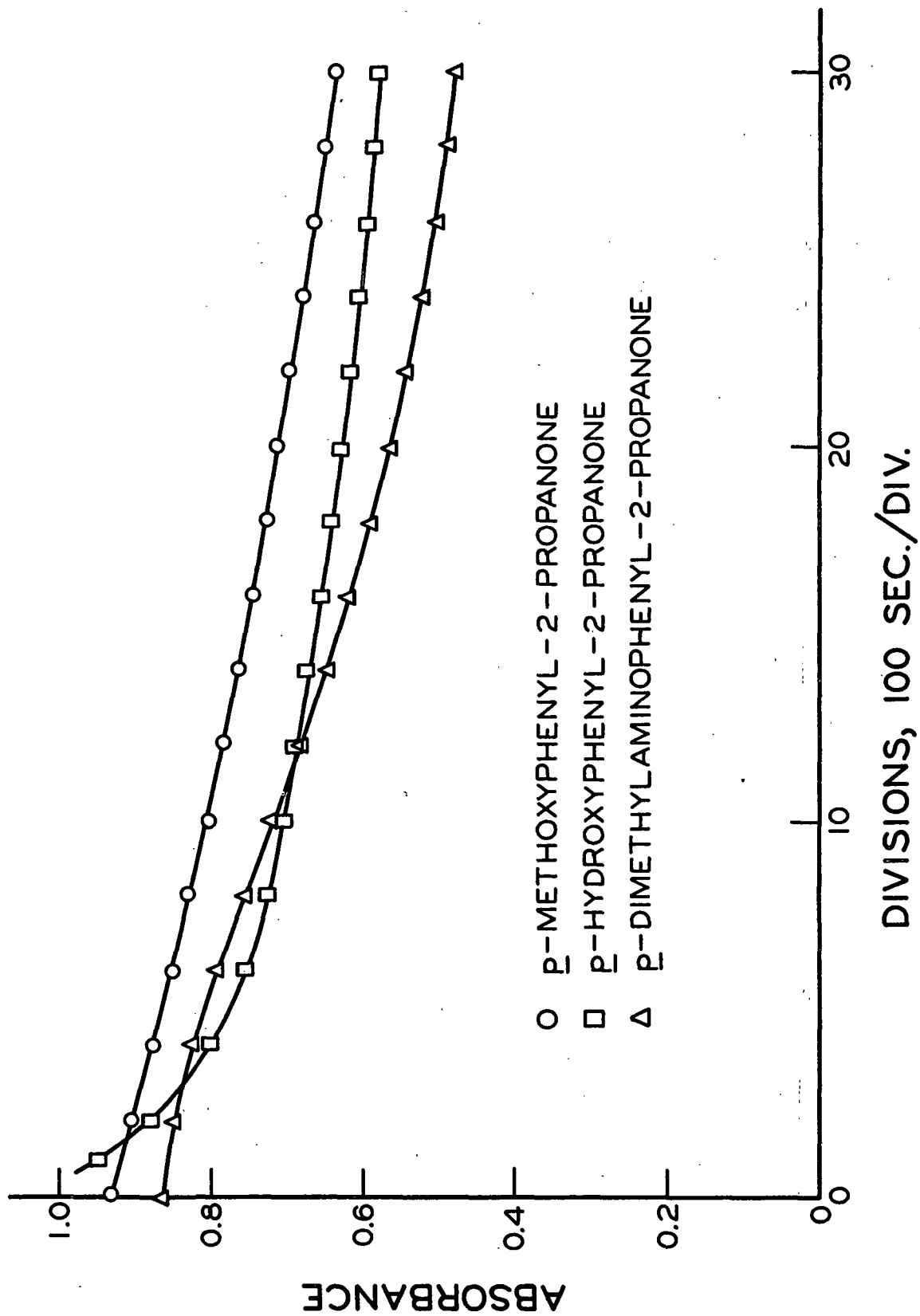


Figure 14. Kinetic Curves for Several Phenyl-2-propanones

The kinetic curve for the p-dimethylamino substituted ketone was also anomalous. The reaction was initially slow with the rate increasing after a short period of time. The product analysis of this compound (Table I) was also unsuccessful. Because of the anomalous kinetic curves and unsatisfactory product analysis, the derived rate constants cannot be considered representative of the reaction of interest for ketones having p-hydroxyl and p-dimethylamino substituents. The rate curves of these ketones compared to an oxidation of p-methoxyphenyl-2-propanone are shown in Fig. 14.

The kinetic behavior of the other phenyl-2-propanones was much more consistent. A linear correlation should be obtained between  $\ln \frac{b(a-x)}{a(b-0.5x)}$  and time if these oxidations obey pseudo-second-order kinetics. Typical relationships are shown in Fig. 15. The correlation with the expected rate expression was found to be satisfactory in all instances. The data for these oxidations are given in Tables XXXIII to XXXVIII.

Disregarding the points for the ketones having a hydroxyl or a p-dimethylamino substituent, the data definitely indicate that the oxidation is facilitated by electron-withdrawing substituents. To further investigate the reactivity of the four ketones for which satisfactory product analysis was obtained, a second series of oxidations was made under somewhat different conditions (Table XXVI). The results of this investigation (Fig. 16) were similar to those obtained in the earlier study. Discontinuous Hammett plots have previously been reported, the discrepancies being attributed to a change in reaction mechanism (87). Such an explanation is not considered the most likely one in this instance.

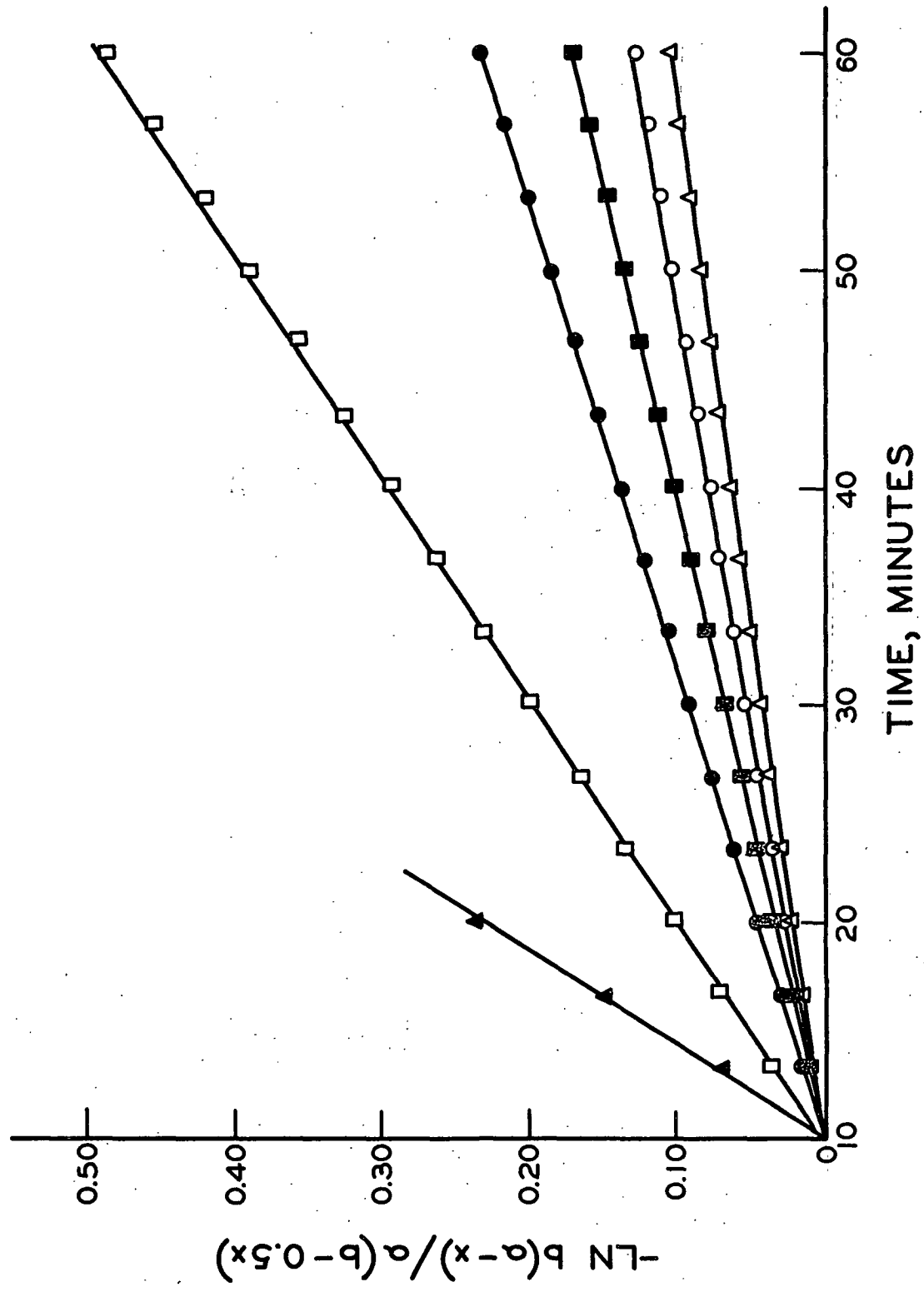


Figure 15. Typical Second-Order Reactions for Some Phenyl-2-propanones at 45°C.  
(▲ p-Nitro-, □ p-Chloro-, ○ p-H, ● 3,4-Dimethoxy-, △ p-Methyl-, ■ p-Methoxy-)

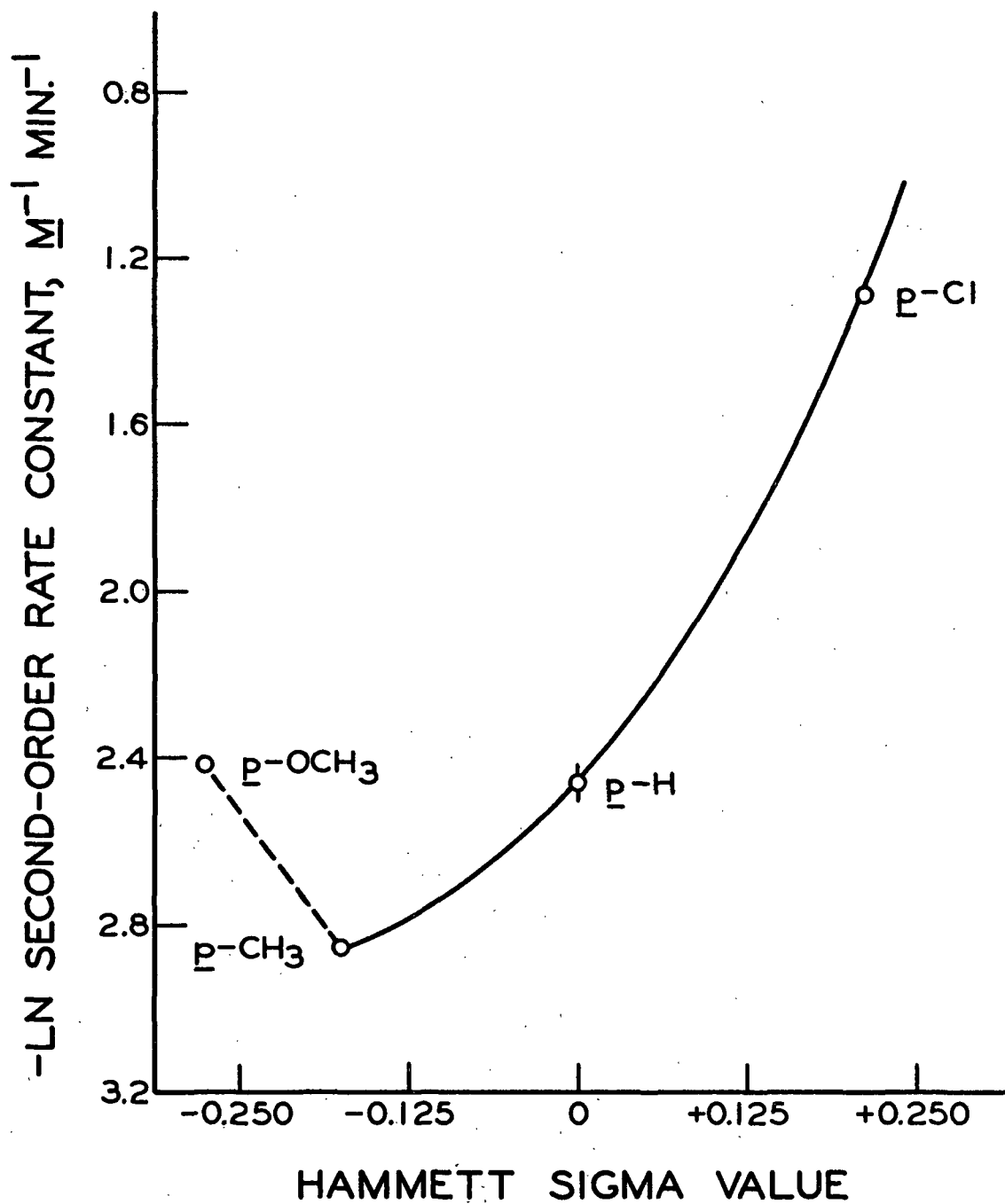


Figure 16. Oxidation of Phenyl-2-propanones with 0.05M  $H_2O_2$ :  
Effect of Substituents

The best explanation of the nonlinear correlation is related to the complexity of the system. The phenyl-2-propanones undergo oxidation by two different mechanisms. It is quite possible that the two competitive reactions have opposite rho values. The Baeyer-Villiger reaction, in which the rate-determining step is the decomposition of the peroxide intermediate, has been shown to have a rho value of -1.10 and -1.45 (20). Similar behavior in an alkaline system would explain the discontinuous Hammett relationship found in the present study. Another significant complication is the distribution of the aromatic species. The keto-enol-enolate ion equilibria are undoubtedly different for these compounds. Such relationships are critical in determining the apparent reactivity of the compounds, and would differ depending upon the conditions selected for comparison.

Even if the rate constants were determined under optimum conditions, the resulting plot would still reflect at least two effects. The substituent would determine the concentration of the reactive aromatic species, and it would reflect the effect of electron density upon the rate-determining step of the oxidation. The continuous, if not linear, increase in reactivity for three of the four ketones suggests that the rate-determining step of the reaction is accelerated by electron-withdrawing substituents. It is possible that the rho value for this reaction is large and positive, the estimated value from Fig. 13 being 1.3. A positive rho value for the oxidation would be consistent with the other more convincing investigations which indicate attack by the nucleophilic hydroperoxide anion.

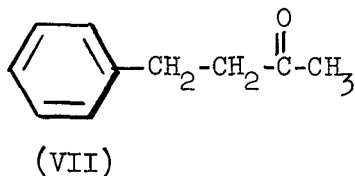
## RELATED KETONES

The hydroperoxide anion has been shown to be the active peroxide species in the oxidation of phenyl-2-propanones. The identity of the reactive aromatic species has not been demonstrated, however. It is not possible to determine the distribution of the various aromatic species, so an indirect method was utilized to elucidate the identity of the reactive substrate. The method chosen for these investigations was to study the effect of structure modification on products and reactivity.

### PHENYL-2-BUTANONES

#### 4-Phenyl-2-butanone

The most significant difference in the structure of phenyl-2-propanone and 4-phenyl-2-butanone (VII) is the elimination of ring conjugated enolization for the latter. Preliminary gas chromatographic investigations showed that the only significant product of the oxidation was the aromatic alcohol, phenethyl alcohol. Two oxidations were made for quantitative analysis (Table XXIX). After ten hours nearly 40% of the ketone had been converted to phenethyl alcohol, with the residual ketone comprising most of the remaining aromatic material. The only other products



detected were traces of acetaldehyde and an unknown compound. These results are presented in Table IV, p. 81, in conjunction with the product analysis of the other phenyl-2-butanones.

TABLE IV

PRODUCT ANALYSIS FOR PHENYL-2-BUTANONE OXIDATIONS<sup>a</sup>

Experiment Number	Butanone	Residual Ketone, %	Aromatic Alcohol, %	Carbonyl Product, %	Unknown, %	Total Recovery <sup>d</sup>
2417-134a	(4-phenyl-	56.0	39.0	3.3 <sup>b</sup>	2.5	100.8
2417-135a	2-)	55.3	38.4	2.9	1.3	97.9
2373-109a	(3-phenyl-	39.2	16.7	44.6 <sup>c</sup>	--	--
2373-112a	2-)	40.3	19.1	40.6	--	--
2373-111a	(3-methyl-	82.7	14.0	--	3.3	--
2373-122c	3-phenyl- 2-)	88.3	11.7	--	trace	--

<sup>a</sup>Internal normalization was used to determine the yields for the last two compounds. These values are thus weight percents. The values for the first compound are mole percent determined using a response factor and internal standardization.

<sup>b</sup>Phenyl acetaldehyde.

<sup>c</sup>Acetophenone.

<sup>d</sup>No evidence was found for the products which would be produced if cleavage on the other side of the carbonyl occurred.

The identity of the aromatic alcohol was verified by collecting some of the product using the DEGS column, p. 50, on the Aerograph Model A-700 Gas Chromatograph. The infrared spectrum corresponded to known phenethyl alcohol.

This ketone apparently reacts only by attack on the carbonyl group, the alkaline Baeyer-Villiger cleavage. For comparison, the effect of base on reactivity of 4-phenyl-2-butanone was studied. The conditions for the oxidations are given in Table XXVII. When less than equivalent amounts of base to hydrogen peroxide are present, the reaction rate increases with base, but excess base has little effect on the reactivity (Fig. 17). A decrease in reactivity was noted for both the phenyl-2-propanones in the presence of excess base (Fig. 6 and 7). The comparison of these results support the proposal that the decrease in reactivity in the presence of excess base for the phenyl-2-propanones is a result of shifting the keto-enol-enolate ion equilibria.

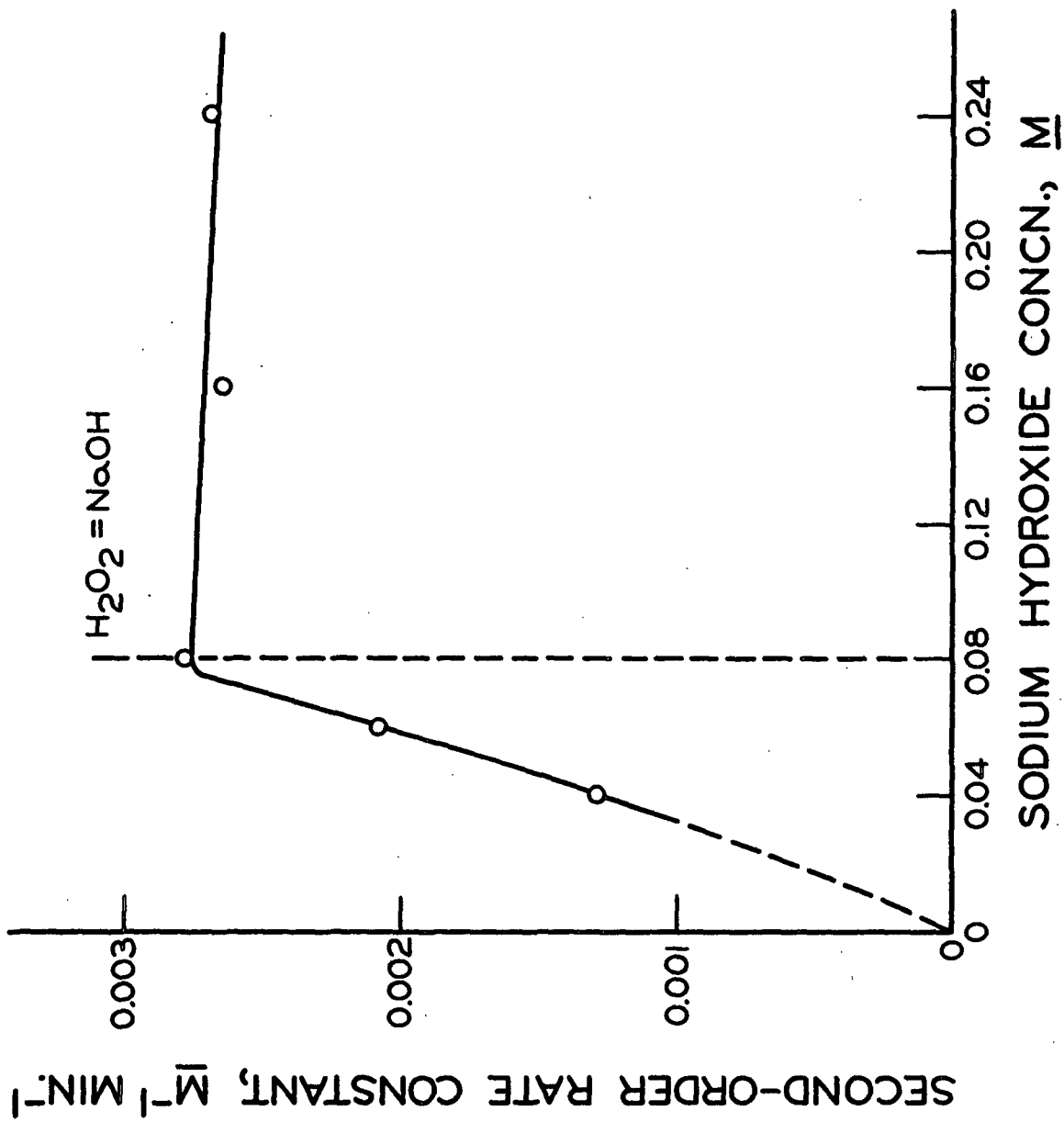
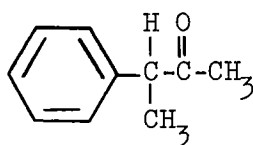


Figure 17. Oxidation of 4-Phenyl-2-butanone:  
Effect of Sodium Hydroxide

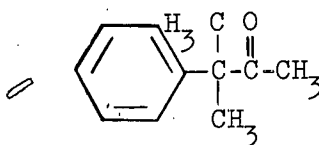
A comparison of the activation energies of the phenyl-2-propanones and 4-phenyl-2-butanone was also made. The conditions for these oxidations of 4-phenyl-2-butanone are given in Table XXVIII. Because of the low reactivity of this ketone and the excessive decomposition of hydrogen peroxide above 55°, oxidations were made at only three temperatures. A linear relationship was obtained when the logarithm of the pseudo-second-order rate constant was plotted as a function of reciprocal absolute temperature (Fig. 18). The calculated activation energy was 8.3 kcal. mole<sup>-1</sup>. This value is of a similar magnitude as that for the two phenyl-2-propanones. These results emphasize the low activation energies which have been observed for the attack of hydroperoxide anion on unsaturated systems.

3-Phenyl-2-butanone and 3-Methyl-3-phenyl-2-butanone

The effect of structure modification on products and reactivity were studied for two other propanones, 3-phenyl-2-butanone (VIII) and 3-methyl-3-phenyl-2-butanone (IX).



(VIII)



(IX)

Duplicate oxidations (Table XXIX) of each ketone were made for quantitative product analysis. The oxidations of 3-phenyl-2-butanone yielded two products, acetophenone and  $\alpha$ -phenethyl alcohol. After 28 hours (Table IV) 60% of the starting material had been converted to the two products, the yield of acetophenone

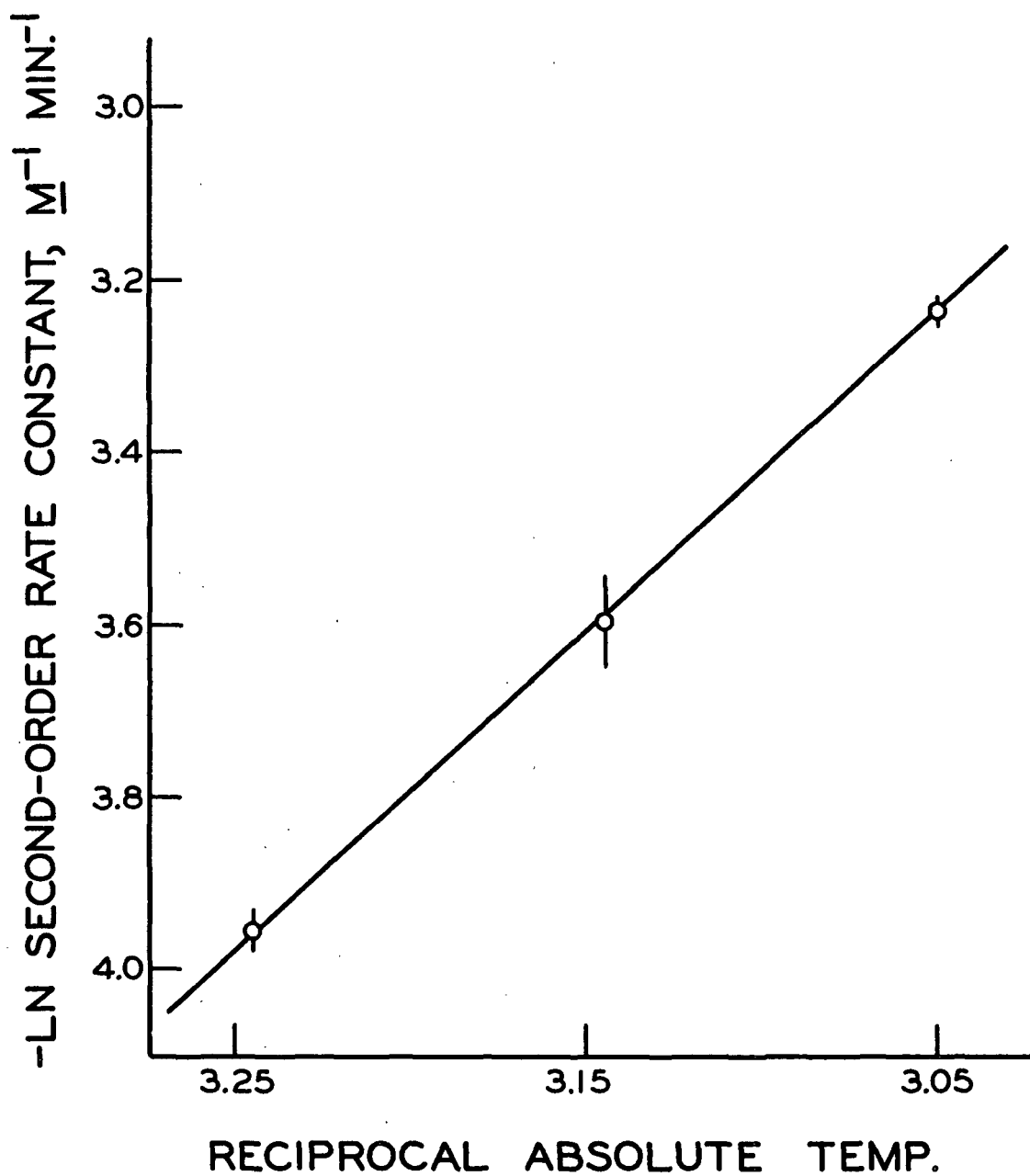


Figure 18. Oxidation of 4-Phenyl-2-butanone:  
Effect of Temperature

to alcohol being about two to one. To substantiate the identity of the products, they were collected on the Aerograph A-700 chromatograph using the DEGS column. The infrared spectrum of the alcohol was identical to that of  $\alpha$ -phenethyl alcohol. The infrared spectrum of the ketone was quite similar to that of acetophenone. To insure the identity of the ketone, a semicarbazone was prepared from the remaining oil. The semicarbazone readily separated; the clean white crystals gave a melting point of 199.6-200.0°, compared to a reported value of 198°C. (88).

The oxidation of 3-methyl-3-phenyl-2-butanone was quite slow. After 64 hours (Table IV) only 10-15% of the ketone had reacted yielding primarily a single product, 2-phenyl-2-propanol. By extending the reaction time, the oxidation proceeded sufficiently for the primary product to be collected using the gas chromatograph. The collected product differed drastically from Sadtler Spectrum 15283 for 2-phenyl-2-propanol. However, the spectrum of commercial 2-phenyl-2-propanol (Aldrich Research Chemicals) was identical to that of the collected product. A published infrared spectrum of 2-phenyl-2-propanol (89) was also quite similar to that of the collected product. It was concluded that the Sadtler Spectrum is incorrect, and the collected product is the expected compound, 2-phenyl-2-propanol.

A comparison of the reactivities of the three phenyl-2-butanones and phenyl-2-propanone was made. The conditions for these oxidations are given in Table XXX. The calculated second-order rate constants for these oxidations are given in Table V. Phenyl-2-propanone was found to be much more reactive than any of the phenyl-2-butanones. Of the two ketones for which the only reaction was the alkaline Baeyer-Villiger cleavage, 4-phenyl-2-butanone was the more reactive. This would be expected since House and Wasson (26) found that tertiary groups migrate less readily than secondary or long-chain primary groups.

TABLE V  
 COMPARATIVE REACTIVITY OF PHENYL-2-PROPANONE  
 AND THE PHENYL-2-BUTANONES

Experiment Number	Ketone	Second-Order Rate Constant, $M^{-1} \text{ min.}^{-1}$
2373-105a	(phenyl-2-propanone)	0.115
2373-93a		0.134
2373-93b	(4-phenyl-2-butanone)	0.030
2373-93c		0.027
2373-93d	(3-methyl-3-phenyl-2-	0.012
2373-94a	butanone)	0.012
2373-94b	(3-phenyl-2-butanone)	0.016
2373-94c		0.015
2373-100a		0.016

The replacement of a single alpha hydrogen with a methyl group had a significant effect on the reactivity. If the attack of the ketones is occurring at this position, a significant decrease would be expected in the reactivity of this compound. These comparative studies of products and reactivity provide a sound basis for proposing that the oxidation of the phenyl-2-propanones involves the enol tautomer.

#### DEOXYBENZOINS

The alkaline peroxide oxidation of three deoxybenzoins, p'-chloro-deoxybenzoin (X), deoxybenzoin (XI), and p-chlorodeoxybenzoin (XII), were studied. Preliminary investigations showed that the reaction products were the expected aromatic acids. Duplicate oxidations were made to obtain quantitative product analysis (Table XXI). The average recovery was 85-90% in all instances (Table VI).

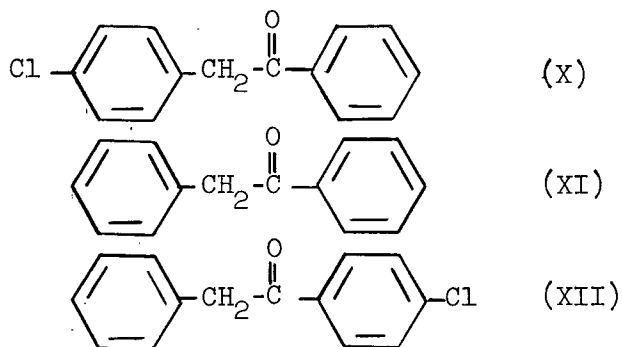


TABLE VI  
PRODUCT ANALYSIS OF DEOXYBENZOINS

Experiment Number	Ketone	Aromatic Acid, mole, %	Residual Ketone, mole, %	Unknown, %	Total Recovery
2417-111a	(p-chloro-deoxybenzoin)	86.2	trace	--	86.2
2417-118a		87.0	0.8	--	88.5
2417-116a	(p'-chloro-deoxybenzoin)	84.1	trace	--	84.1
2417-118b		85.1	1.1	0.7	86.8
2417-117a	(deoxybenzoin)	75.4	15.0	--	90.4
2417-119a		76.1	5.3	--	81.4

Using deoxybenzoins the effect of substituents on both the benzyl and the phenyl rings can be studied. Because of the sparse solubility of the ketones, the reaction could not be followed continuously. A titrimetric method was found to be suitable. Duplicate oxidations (Table XXXII) were made to determine the second-order rate constants for these reactions. A plot of titer versus time is given for one oxidation for each of the ketones (Fig. 19). The second-order rate constants, estimated from initial rates, for duplicate oxidations of the three ketones are given in Table VII. Although the accuracy of these constants is not comparable to those determined using the continuous system, the values are sufficiently different for valid comparisons to be made. A Hammett rho value was estimated based on the reactivity of compounds (X) and (XI). The value was 1.8, comparable to that determined for the phenyl-2-propanones. Both the p-chloro-

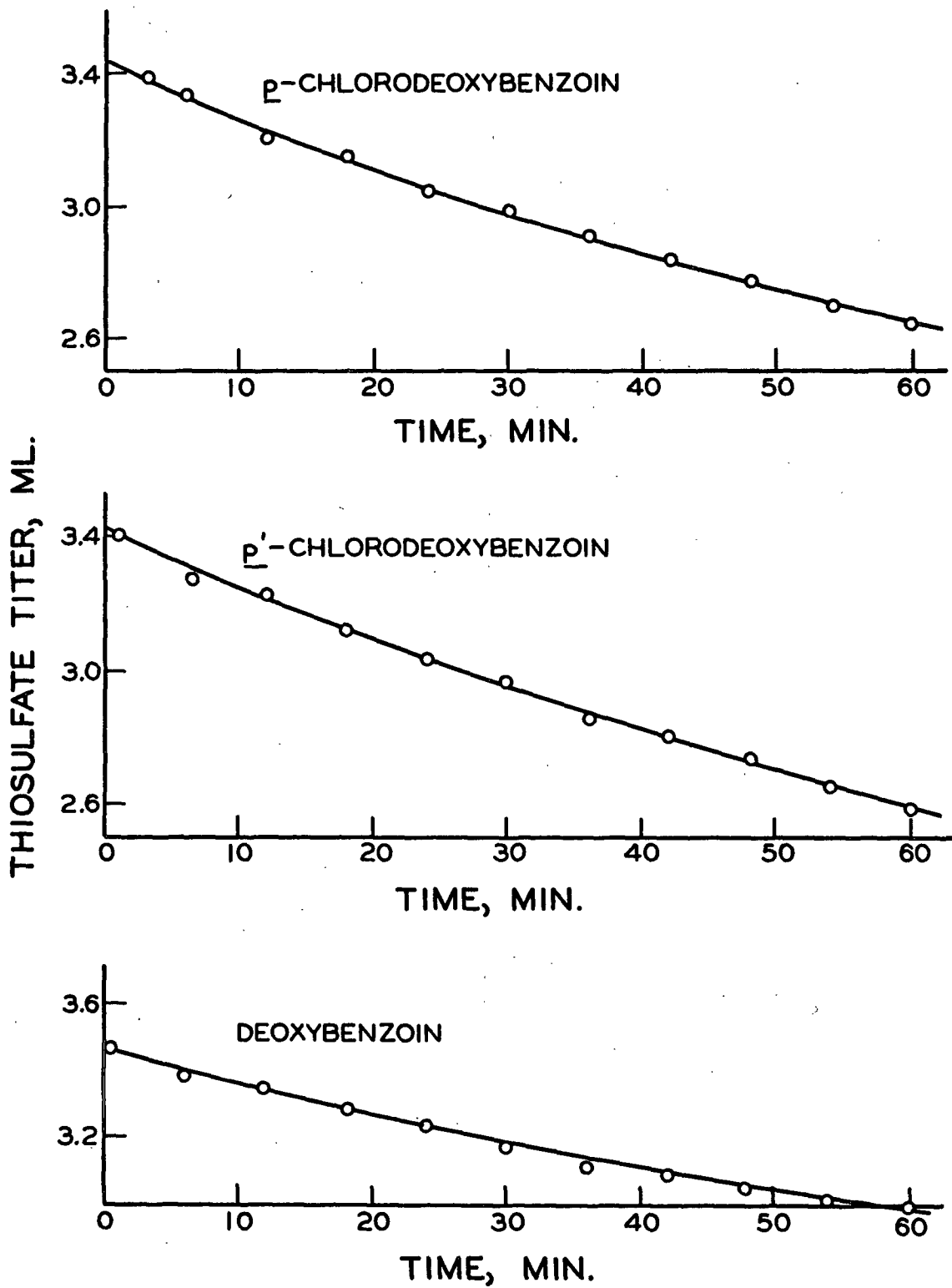


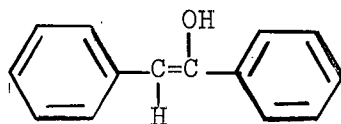
Figure 19. Kinetic Runs for the Deoxybenzoin

substituted deoxybenzoins are clearly much more reactive than the unsubstituted deoxybenzoin. This would be expected since the electron-withdrawing chloro substituent should facilitate attack by the hydroperoxide anion regardless of whether the substituent is in the phenyl or benzyl ring.

TABLE VII  
ESTIMATE OF THE SECOND-ORDER RATE CONSTANTS  
FOR OXIDATIONS OF THE DEOXYBENZOINS

Experiment Number	Ketone	Second-Order Rate Constant, $M^{-1} \text{ min.}^{-1}$
2417-153a	(p-chloro-deoxybenzoin)	0.395
2417-156a		0.390
2417-154a	(p'-chloro-deoxybenzoin)	0.497
2417-155a		0.483
2417-156b	(deoxy-benzoin)	0.132
2417-157a		0.168

The comparative reactivity of the two para-substituted compounds is significant. The benzyl-substituted ketone was found to react more readily than the phenyl-substituted one. If initial attack was occurring at the carbonyl group, the reverse would have been observed. A prediction of the reactivity of the two compounds is more complicated if the reaction mechanism involves attack upon the enol tautomer. At least two effects are anticipated. The electron-withdrawing chloro group would facilitate attack by the hydroperoxide anion, and the keto-enol equilibrium would be influenced. Of these two effects, the latter would probably be less significant. A para-substituent on either ring should be



(XIII)

equally as effective in stabilizing the enol tautomer (XIII) since each would be

equidistant from the active site. Assuming that the enol is the reactive form, the benzyl-substituted ketone (X) should be more reactive than the phenyl-substituted ketone if the substituent is electron-withdrawing. The ketone having the benzyl substituent was found to be more reactive than the phenyl-substituted ketone (XII). The study of the deoxybenzoins indicates that initial attack is probably occurring at the methylene carbon rather than at the carbonyl carbon.

#### MECHANISM OF OXIDATION OF THE PHENYL-2-PROPANONES

The product analysis and kinetic investigations of the phenyl-2-propanones and related compounds have provided considerable information from which a mechanism for the oxidation of these ketones can be postulated. Initial rate studies showed the reaction to be first order in hydrogen peroxide. Initial attack by the hydroperoxide anion was indicated from studying the effect of sodium hydroxide on reactivity. The study of peroxide species concentration on reactivity was also consistent with hydroperoxide anion being the reactive peroxide species.

The question of where the hydroperoxide anion attacked the substrate was less clearly answered. However, a comparison of the reactivity and products of the four ketones in Table VIII provide considerable evidence suggesting the initial step in the reaction is attack of the enol tautomer by hydroperoxide anion. Product analysis of the phenyl-2-propanones<sup>1</sup> showed these ketones to be reacting by two mechanisms: cleavage to the aromatic aldehyde and a slower competitive cleavage to the benzyl alcohol. The first reaction is unique to the phenyl-2-propanones. Cleavage to an alcohol and an acid, referred to as an alkaline Baeyer-Villiger reaction, is a slow cleavage which can be considered a general reaction of simple

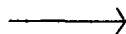
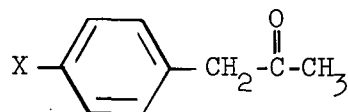
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<sup>1</sup>When this expression is used in the current discussion, it will refer to those ketones for which satisfactory product analysis was obtained. Those ketones having a hydroxyl substituent are not included.

TABLE VIII

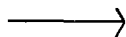
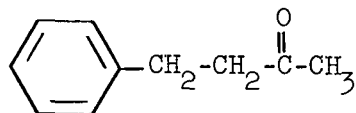
SUMMARY OF THE EFFECT OF STRUCTURE ON REACTION PRODUCTS

1. phenyl-2-propanones

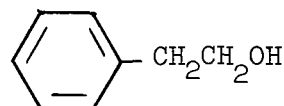


substituted benzaldehyde,  
substituted benzyl alcohol,  
and substituted benzoic  
acid

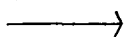
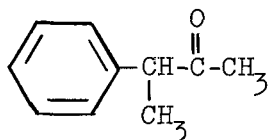
2. 4-phenyl-2-butanone



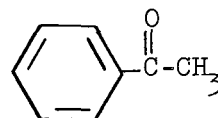
phenethyl alcohol



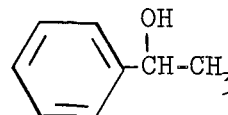
3. 3-phenyl-2-butanone



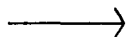
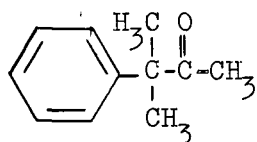
acetophenone



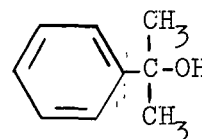
$\alpha$ -phenethyl alcohol



4. 3-methyl-3-phenyl-2-butanone



2-phenyl-2-propanol



ketones and alkaline hydrogen peroxide (26). The only aromatic product from the oxidation of 4-phenyl-2-butanone was phenethyl alcohol (Table VIII), the product expected from an alkaline Baeyer-Villiger reaction.<sup>1</sup> Only a trace of phenyl-acetaldehyde was obtained. These results constitute good evidence that the enol is the reactive form of the phenyl-2-propanones. Insertion of another methylene group between the carbonyl group and the aromatic ring eliminates the stabilization of the enol form by conjugation with the ring.

The results obtained from the investigation of the two other ketones, 3-phenyl-2-butanone, and 3-methyl-3-phenyl-2-butanone also support the contention that attack of the phenyl-2-propanones is occurring on the enol form. The oxidation of 3-phenyl-2-butanone yielded the products expected from oxidation by both the primary and the competitive mechanisms which were observed for the phenyl-2-propanones. The second-order rate constant for the oxidation of phenyl-2-propanone was 8.1 times as high as the corresponding constant for 3-phenyl-2-butanone. This represents a significant change in rate but is of the magnitude expected if the reaction involves the enol tautomer. Bunton and Minkoff (10) observed that the addition of a beta methyl group reduced the reactivity of alkaline hydrogen peroxide toward  $\alpha,\beta$ -unsaturated ketones by a factor of 5.6. Payne (12) found that the addition of a methyl group to the beta carbon of  $\alpha,\beta$ -unsaturated esters eliminated epoxide formation by alkaline hydrogen peroxide. The presence of the bulky methyl group would contribute to the decrease in reactivity, and the presence of an electron-releasing group at the site of the attack would repulse the nucleophilic hydroperoxide anion.

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<sup>1</sup>Methyl migration has been shown to be less favorable than that of other primary or secondary groups (26).

The presence of the alpha methyl group would exhibit an additional effect in inhibiting the reactivity of 3-phenyl-2-butanone. The apparent reaction rate would be decreased by a reduction of the enol content which would probably accompany the replacement of hydrogen by the electron-releasing methyl group. The combination of these factors adequately explains the reduced reactivity of 3-phenyl-2-butanone and indicates that attack is occurring on the enol form of the phenyl-2-propanones.

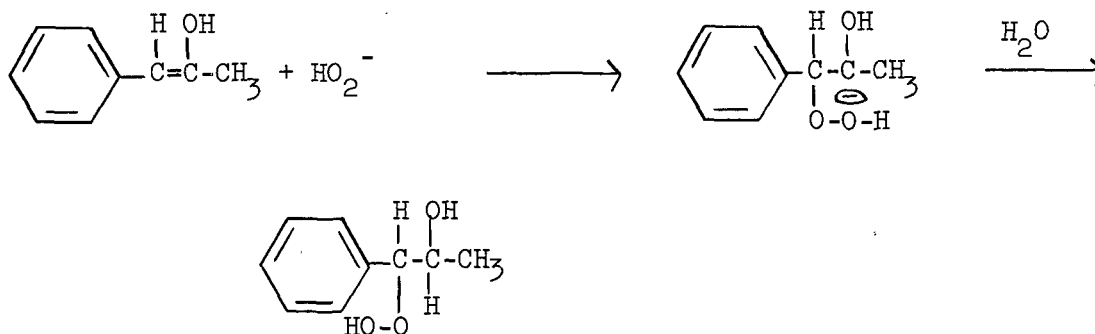
The only aromatic product obtained from the oxidation of 3-methyl-3-phenyl-2-butanone was 2-phenyl-2-propanol, a product of the alkaline Baeyer-Villiger reaction. The two  $\alpha$ -methyl substituents have eliminated entirely the possibility of ring conjugated enolization and have markedly reduced the reactivity of this ketone compared to phenyl-2-propanone.

Other aspects of the investigation are consistent with the rate-determining step of the reaction being attacked by hydroperoxide anion on the enol tautomer. The presence of an electron-withdrawing chloro group on the benzyl ring in deoxybenzoin was more effective in accelerating the reaction than the same substituent on the phenyl ring. The reactivity of the phenyl-2-propanones was adversely affected by the addition of excess alkali while the reactivity of 4-phenyl-2-butanone was hardly altered. A slight negative salt effect for the oxidations of the phenyl-2-propanones was observed. These relationships are all consistent with the enol being the reactive form for the phenyl-2-propanones.

The activation parameters are consistent with rate-determining attack of a charged species on an unsaturated system. The enthalpy of activation was low, comparable to the values (11-13 kcal. mole<sup>-1</sup>) for the alkaline hydrolysis of esters (90). The first step of the hydrolysis involves attack of a nucleophile,

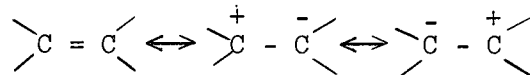
hydroxide ion, upon unsaturated carbon, the carbonyl group (91). The observed entropies of activation for oxidations of the phenyl-2-propanones were very large and negative. Such a trend would be expected for the reaction, such as addition to unsaturated carbon, since the total number of molecules in the system decreases (91). The large positive rho value, observed for both the phenyl-2-propanones and the deoxybenzoins, also support the postulation. Electron-withdrawing groups should facilitate attack of the hydroperoxide anion and increase enolization.

On the basis of extensive product analysis and kinetic investigations of the phenyl-2-propanones and related compounds, a satisfactory reaction mechanism for the primary reaction of the phenyl-2-propanones can be postulated. The rate-determining step in the reaction involves attack of the enol tautomer by the hydroperoxide anion to give an intermediate  $\beta$ -hydroxy-hydroperoxide anion which immediately picks up a proton. Such a suggestion requires the addition of a nucleophile to a

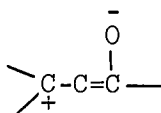


carbon-carbon double bond, a situation which is usually considered to be unfavorable. Hydrogen peroxide will not attack isolated double bonds, but the reactivity of activated double bonds,  $\alpha,\beta$ -unsaturated aldehydes, ketones, esters, nitriles, etc., has been widely noted. Edwards and Pearson (8) have cited the unexpectedly high reactivity of these compounds as examples of substrates subject to the "alpha effect." The conjugation of the electronegative oxygen with the reaction site enhances the reactivity of the double bond. The carbon-carbon

double bond has a high polarizability. The antibonding orbitals of the  $\pi$  system are mixed with the bonding orbitals, and a polar structure is created which contributes to the structure of the system (8).



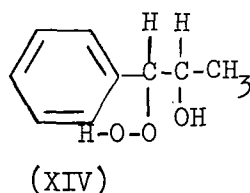
The following structure is a significant resonance contributor when there is a polar carbonyl group adjacent to the double bond. Such a structure would have an enhanced reactivity toward the hydroperoxide anion.



The enol tautomer is similar in some respects to the activated  $\alpha,\beta$ -unsaturated systems. The hydroxyl group is much less polar than the carbonyl group. However, the electronegative oxygen atom is directly attached to the carbon which is involved in the unsaturation. The inductive effect of the electron-withdrawing hydroxyl group would assist the attack of the hydroperoxide anion on the unsaturated system.

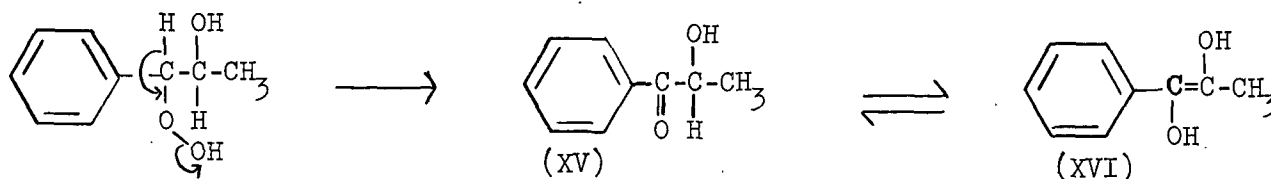
The attack of hydroperoxide anion upon the enol tautomer is similar to the attack of hypohalite ion on enolizable ketones. In alkaline solution the rate is quite rapid (91,92) compared to the cleavage of phenyl-2-propanones by hydrogen peroxide. These reactions both involve attack on the enol by a strong nucleophile. An activation energy of 13.4 kcal. mole<sup>-1</sup> was determined for the attack of hypobromite on acetone (92). This value is of a similar magnitude as that for attack of hydroperoxide anion on the phenyl-2-propanones.

Considering the pseudo-stable intermediate to be the  $\beta$ -hydroxyhydroperoxide (XIV), several possible routes for cleavage to the observed products are available. The intermediate could decompose to give benzaldehyde and acetaldehyde,



the acetic acid being produced by oxidation of the acetaldehyde. This possibility is eliminated since no evidence of acetaldehyde was ever found in the reaction mixture, and it reacts slow enough to be detected.<sup>1</sup>

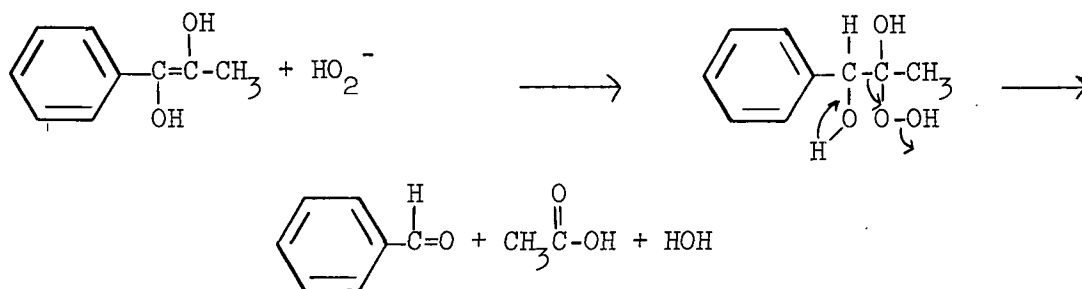
The production of the benzaldehyde and acetic acid as primary products requires that two moles of hydrogen peroxide are added to the system with the cleavage occurring during or after addition of the second mole of peroxide. Subsequent oxidation of the intermediate (XIV) can occur in two ways: (1) attack on a rearranged product of (XIV) or (2) by a direct attack on the intermediate. The intermediate could undergo intramolecular loss of water producing an  $\alpha$ -hydroxyketone (XV). The  $\alpha$ -hydroxyketone could then react through the enediol (XVI) to



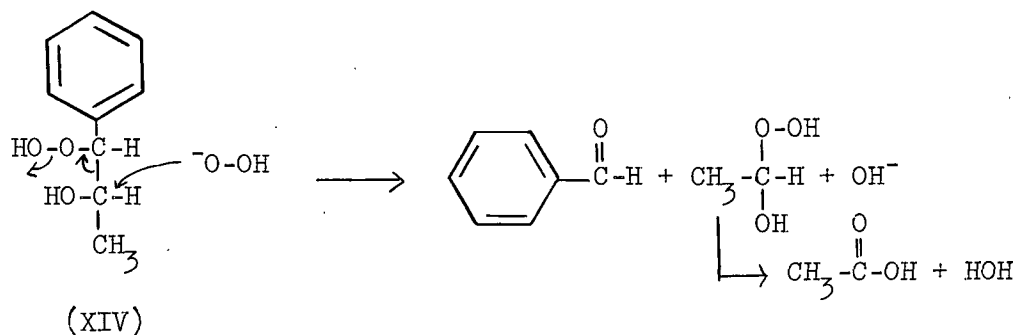
give benzaldehyde and acetic acid. Such a mechanism, however, could not account for the reactivity of 3-phenyl-2-butanone<sup>2</sup> since the presence of the alpha methyl group eliminates the possibility of forming an  $\alpha$ -hydroxyketone (XV).

<sup>1</sup>An oxidation of phenyl-2-propanone, checked at five different times during the course of the reaction, showed no trace of acetaldehyde. Acetaldehyde in as low as one mole percent could have been detected using this technique. The rate of oxidation of acetaldehyde was only 20% of that of phenyl-2-propanone under comparable conditions.

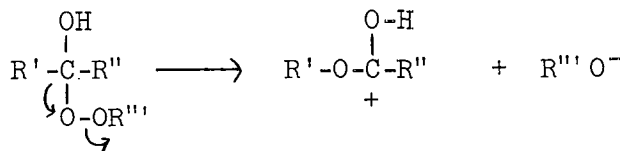
<sup>2</sup>The validity of the mechanism was also investigated by preparing 1-hydroxy-1-phenyl-2-propanone, the stable isomer of structure (XV) which in alkali would give the same enediol (XVI). Some aromatic aldehyde was produced, but the ketone rapidly consumed two moles of peroxide. Such behavior is inconsistent with the enediol being an intermediate since the consumption of the second mole of peroxide, conversion of the aldehyde to the aromatic acid should be much slower than the observed attack of (XV).



Direct attack of the  $\beta$ -hydroxyhydroperoxide (XIV) by the strongly nucleophilic hydroperoxide anion represents the most feasible mechanism of cleaving the ketone which is consistent with all of the experimental observations. The cleavage is considered to occur in a concerted manner in which the oxygen-oxygen bond and the carbon-carbon bond are broken concurrently with formation of the carbon-oxygen bond at the original carbonyl carbon. An analogous series of



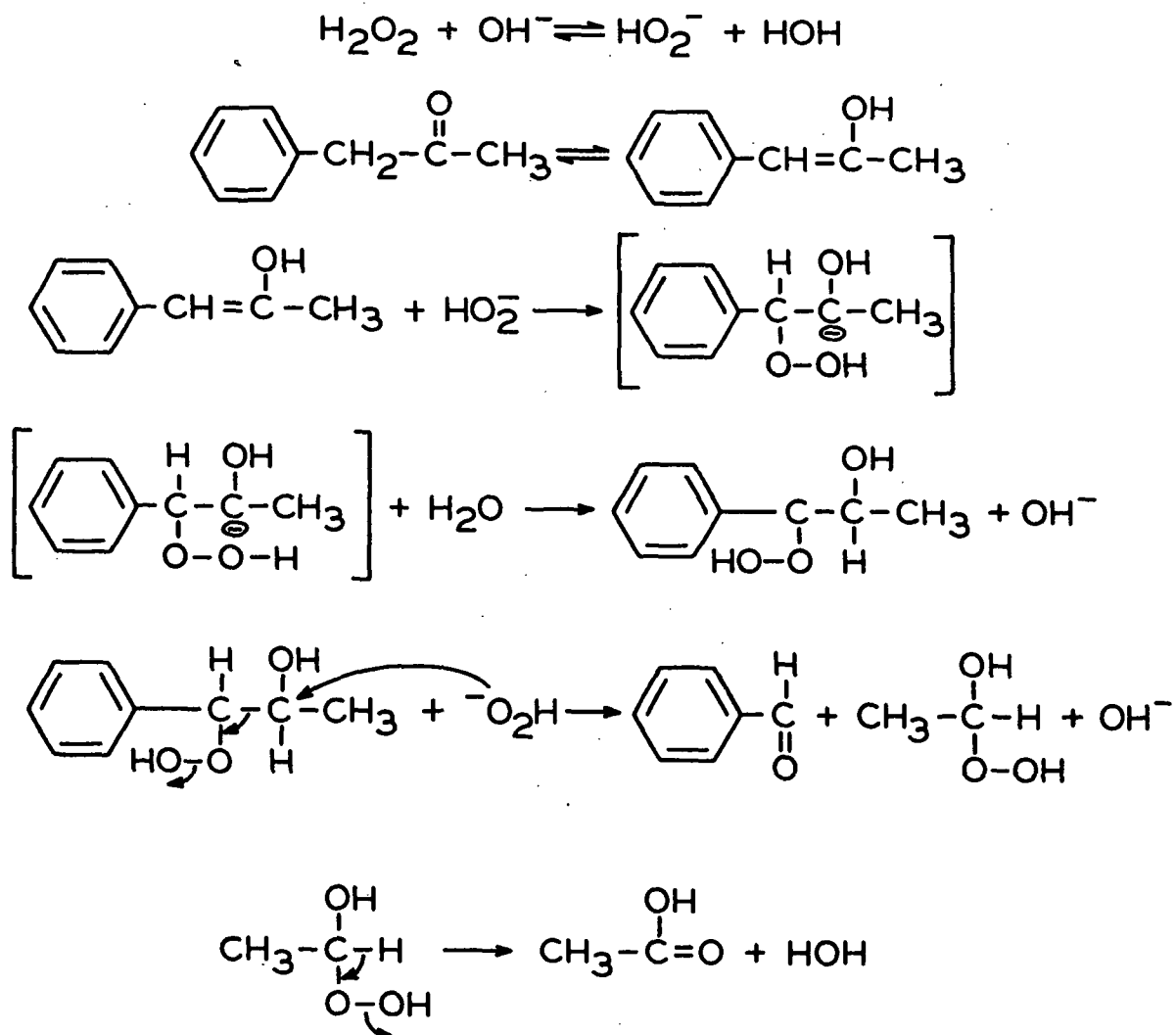
events are postulated to occur in the rearrangement of an  $\alpha$ -hydroxyhydroperoxide in the Baeyer-Villiger reaction.



A requirement of the cleavage is that it be faster than the rate-determining step of the reaction. In addition to the Baeyer-Villiger reaction, many of the mechanisms of peroxide reactions involve intramolecular decomposition of peroxide intermediates. The driving force for these reactions, with the exception of the Dakin reaction, is primarily the instability of the oxygen-oxygen

bond. The presence of a strong nucleophile such as the hydroperoxide anion could certainly assist this decomposition when there is a reactive site adjacent to the hydroperoxide. The presence of the polar hydroxyl group on the carbon adjacent to that containing the hydroperoxide provides a site for such attack of the nucleophile. Such a process would be expected to proceed at a faster rate than unassisted decomposition of similar intermediates.

A summary of the suggested mechanism for the primary oxidation of the phenyl-2-propanones by alkaline hydrogen peroxide is shown below.



The competitive cleavage of phenyl-2-propanones to a benzyl alcohol is an example of the Baeyer-Villiger reaction which is characteristic of ketones. The suggested mechanism (26) described on p. 13 is consistent with experimental observations: This mechanism postulates an intermediate ester which is rapidly hydrolyzed. No evidence of intermediate esters has been found. The concentration of such intermediates would be quite small. The second-order rate constant for the alkaline hydrolysis of benzyl acetate is  $0.070\text{M}^{-1} \text{sec.}^{-1}$  at  $24.9^\circ\text{C}$ . (90), whereas the second-order rate constant for the cleavage of the phenyl-2-propanones is only  $0.00085\text{M}^{-1} \text{sec.}^{-1}$  at  $26.5^\circ\text{C}$ . Since the competitive cleavage represents only a small fraction of the total reaction, the ratio of the rate constant for hydrolysis of the ester would be 500 to 1000 times as great as that of its production.

## CONCLUSIONS

The alkaline peroxide oxidation of phenyl-2-propanones occurs by two mechanisms. The slow competitive cleavage, analogous to the Baeyer-Villiger reaction of ketones in acidic media, produces the benzyl alcohol and acetic acid by direct attack of hydrogen peroxide on the carbonyl group. The primary cleavage is unique to the phenyl-2-propanones. The rate-determining step of the reaction involves attack of hydroperoxide anion on the relatively stable ring-conjugated enol. Considerable evidence for attack of the enol tautomer of the phenyl-2-propanones was obtained by studying related ketones.

The presence of an additional methylene group between the ring and the carbonyl group drastically reduces the equilibrium enol content and eliminates the cleavage considered to involve the enol tautomer. An electron-withdrawing benzyl substituent accelerates the reaction rate more than the same phenyl substituent. Various other aspects of this study indicate attack of the enol form including the observed activation parameters, the Hammett relationships, and the effect of electron-releasing substituents at the reaction site. After slow attack of the enol form, the cleavage occurs by a concerted nucleophilic attack of a second mole of peroxide. The second hydroperoxide anion attacks the intermediate  $\beta$ -hydroxyhydroperoxide at the original carbonyl carbon to give the observed products, a benzaldehyde and acetic acid.

ACKNOWLEDGMENTS

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LITERATURE CITED

1. Reeves, R. H. A study of the reaction products formed upon the alkaline peroxide oxidation of lignin-related model compounds. Doctor's Dissertation, Appleton, Wisconsin, The Institute of Paper Chemistry, 1964. See also Reeves, R. H., and Pearl, I. A., *Tappi* 48:121-5(1965).
2. Dakin, H. D., *Am. Chem. J.* 42:477-98(1909).
3. Gero, A., *J. Org. Chem.* 19:1960-70(1954).
4. Wiberg, K. B., *J. Am. Chem. Soc.* 77:2519(1955).
5. Jencks, W. P., and Carriuolo, J., *J. Am. Chem. Soc.* 82:1778(1960).
6. Pearson, R. G., and Edgington, D. V., *J. Am. Chem. Soc.* 84:4607(1962).
7. Bunton, C. A., In Edwards' "Peroxide reaction mechanisms," p. 11-27. New York, Interscience Publishers, 1962.
8. Edwards, J. O., and Pearson, R. G., *J. Am. Chem. Soc.*, 84:16(1962).
9. Weitz, E., and Scheffer, A., *Ber.* 54B:2327-44(1921).
10. Bunton, C. A., and Minkoff, G. J., *J. Chem. Soc.* 1949:665.
11. Southwick, P. L., Dimond, H. L., Moores, M. S., and Sappen, D. I., *J. Am. Chem. Soc.* 78:101(1956).
12. Payne, G. B., *J. Org. Chem.* 24:2048(1959).
13. Zimmerman, H. E., Singer, L., and Thyogarajan, B. S., *J. Am. Chem. Soc.* 81:108(1959).
14. Yang, N. C., and Finnegan, R. A., *J. Am. Chem. Soc.* 80:5845(1958).
15. Payne, G. B., *J. Am. Chem. Soc.* 81:490(1959).
16. Payne, G. B. *J. Org. Chem.* 25:275(1960).
17. Bunton, C. A., *Nature* 163:444(1949).
18. Kwart, H., and Wegemer, N. J., *J. Am. Chem. Soc.* 83:2746-55(1961).
19. Vysotskaya, N. A., and Brodskii, A. E., *Kerneigie* 5, no. 405:362-5(1962); *C.A.* 61:16005d.
20. Hawthorne, F. M., and Emmons, Wm. D., *J. Am. Chem. Soc.* 80:6398(1958).
21. Hawthorne, F. M., Emmons, Wm. D., and McCallum, K. S., *J. Am. Chem. Soc.* 80:6393(1958).
22. Hassall, C. H., *Organic reactions*. Vol. IX. p. 73-106. New York, John Wiley and Sons, 1957.

23. Wacek, A. V., and Eppinger, H. O., Ber. 73:644-51(1940).
24. Davies, A. G. Organic peroxides. p. 155. London, Butterworths, 1961.
25. Hine, J. Physical organic chemistry. p. 341. New York, McGraw-Hill, 1962.
26. House, H. O., and Wasson, R. L., J. Org. Chem. 22:1157(1957).
27. Fox, S. W., Polak, E. H., Bullock, M. W., and Kobayashi, Y., J. Am. Chem. Soc. 73:4979(1951); (b) Heial, H. W., and Jones, H., J. Am. Chem. Soc. 73:1361(1951); (c) Fling, M. Minard, F. N., and Fox, S. W., J. Am. Chem. Soc. 69:2466(1947); (d) Westerfield, W. W., J. Biol. Chem. 143:177(1942).
28. Treindl, L., and Palackova, E., Chem. Zvesti. 18:385-90(1964).
29. Williams, H. R., and Mosher, H. S., J. Am. Chem. Soc. 76:3495(1954).
30. Green, A. J., Kemp, T. J., Littler, J. S., and Waters, W. A., J. Chem. Soc. 1964:2722.
31. Littler, J. S., J. Chem. Soc., 1962:827.
32. Stewart, R. Oxidation mechanisms, applications to organic chemistry. p. 81, 110-11. New York, W. A. Benjamin, Inc., 1964.
33. Nikolenko, L. N., and Karpova, E. N., Zh. Obshch. Khim. 34, no. 1:358-9(1964).
34. Ichikawa, K., and Yoshiteru, Y., J. Chem. Soc. Japan, Pure Chem. Sect. 73:415-18(1952); C. A. 47:10474e.
35. Best, P. A., Littler, J. S., and Waters, W. A., J. Chem. Soc. 1962:822.
36. Melnikov, N. N., and Rokitskaya, M. S., J. Gen. Chem., USSR 14:1059-62(1944); C.A. 4:5780h and previous papers.
37. Duke, F. R., J. Am. Chem. Soc. 70:419(1948).
38. Corey, E. J., and Schaeffer, J. P., J. Am. Chem. Soc. 82:918-29(1960).
39. Waters, W. A. Mechanisms of oxidation of organic compounds. p. 90-9. London, Methuens and Co., Ltd., 1964.
40. Banerji, J. C., Barton, D. H. R., and Cookson, R. C., J. Chem. Soc. 1957:5041.
41. Barnes, C. S., and Barton, D. H. R., J. Chem. Soc. 1953:1419.
42. Kravchenko, A. I., Uchenge Zapiski Krasnoyarsk Gosudarst. Pedagog. Inst. 5:159-65(1956); C.A. 52:12754h.
43. Speakman, P. T., and Waters, W. A., J. Chem. Soc. 1955:40-5.
44. Drummond, A. Y., and Waters, W. A., J. Chem. Soc. 1955:497.
45. Littler, J. S., J. Chem. Soc. 1962:832.

46. Hoare, D. G., and Waters, W. A., J. Chem. Soc. 1962:971.
47. Shorter, J., and Hinshelwood, C., J. Chem. Soc. 1950:3276.
48. Shorter, J., J. Chem. Soc. 1950:3425.
49. Shiner, V. J., Jr., and Wasmuth, C. R., J. Am. Chem. Soc. 81:37-42(1949).
50. Bunton, C. A., and Shiner, V. J., Jr., J. Chem. Soc. 1960:1593.
51. Pearl, I. A., and Beyer, D. L., J. Org. Chem. 16:221-4(1951).
52. West, K. A., and Hibbert, H., J. Am. Chem. Soc. 65:1185-7(1943).
53. Kratzl, K., and Schweers, W., Chem. Ber. 89:186-92(1956).
54. La Brazidec, E., Bull. Soc. Chim. 31:255-65(1922).
55. Rabjohn, N. Organic syntheses. Col. Vol. IV. p. 573. New York, John Wiley and Sons, 1963.
56. Criegee, R., Dimroth, P., Noll, K., Simon, R., and Weis, C., Chem. Ber. 90:1070-81(1957).
57. Govdal, G. D., and Haworth, R. D., J. Chem. Soc. 1930:2482-7.
58. Muller, A., Lempert-Streter, M., and Karczag-Wilhelms, A. J., J. Org. Chem. 19:1533-47(1954).
59. Overberger, C. G., and Bilech, H., J. Am. Chem. Soc. 73:4880(1951).
60. Blatt, A. H. Organic syntheses. Col. Vol. II. p. 487, 391. New York, John Wiley and Sons, 1943.
61. Temnikova, T. I., and Viksler, V. I., Zh. Obshch. Khim. (J. Gen. Chem.) 19:1318-23(1949); C.A. 44:1056e.
62. Jonsson, A., Acta Chem. Scand. 8:1203-10(1954).
63. Reference 55, p. 132.
64. Suter, C. M., and Weston, A. W., J. Am. Chem. Soc. 64:534(1942).
65. Schultz, E. M., and Bicking, J. B., J. Am. Chem. Soc. 75:1128-9(1953).
66. Clark, M. T., Hendley, E. C., and Neville, O. K., J. Am. Chem. Soc. 77:3280-4(1955).
67. Sobieski, J. F. A polarographic study of the reduction of unsymmetrical benzils. Doctor's Dissertation in progress.
68. Jenkins, S. S., J. Am. Chem. Soc. 56:682-4(1934).

69. Weissberger, A., Prickauer, E. S., Riddick, J. A., and Topps, E. E., Jr., Organic solvents, techniques of organic chemistry. Vol. III. p. 334. New York, Interscience Publishers, Inc., 1955.
70. Satterfield, C. N., and Bonnell, A. H., Anal. Chem. 27:1174-5(1955).
71. Russell, N. A. A study of the initial phase of the aqueous chlorination of kraft pulp. Doctor's Dissertation. Appleton, Wisconsin, The Institute of Paper Chemistry, 1966.
72. Spalding, C. W. The absorption of chlorine into aqueous media in light of the penetration theory. Doctor's Dissertation. Appleton, Wisconsin, The Institute of Paper Chemistry, 1961.
73. Kolthoff, I. M., and Sandell, E. B. Textbook of quantitative inorganic analysis. 3rd ed. p. 593. New York, The Macmillan Co., 1963.
- 74a. Edwards, J. O., J. Am. Chem. Soc. 85:2263(1963).
- 74b. F.M.C. Corporation. The operation of a bench scale peracetic acid generator. New York, 1963.
75. Sulley, B. D., and Williams, P. L., The Analyst 87:653-7(1962).
76. Reference 73, p. 682.
77. Wilkens Instrument and Research, Inc. Gas chromatography. p. 4. Walnut Creek, California, 1964.
78. Ackman, R. G., and Burgher, R. D., Anal. Chem. 35:647-52(1963).
79. Pecsok, R. L. Principles and practices of gas chromatography. p. 136-50. London, Chapman and Hall, Ltd., 1959.
80. Pearl, I. A., and Beyer, D. L. J. Am. Chem. Soc. 76:6106(1954).
81. Snell, D. F., and Snell, C. T. Spectrophotometric methods of analysis. Volume IIa. p. 734. Princeton, New Jersey, D. Van Nostrand Co., Inc., 1959.
82. Frost, A. A., and Pearson, R. G. Kinetics and mechanism. 2nd ed. p. 23, 45, 169. New York, John Wiley and Sons, Inc., 1961.
83. Friess, S. L., Lewis, E. S., and Weissberger, A. Rates and mechanisms of reactions, techniques of organic chemistry. Vol. III. Part I. p. 199-202. New York, Interscience Publishers, Inc., 1961.
84. Muhammad, S. S., and Rao, T. N., J. Chem. Soc. 1957:1077-8.
85. Fieser, L. F., and Fieser, M. Organic chemistry. p. 663. New York, Reinhold Publishing Corp., 1956.
86. Murthy, A. S. N., Balasubramanian, A., and Rao, C. N. R., Can. J. Chem. 40: 2267-71(1962).

87. Wells, P. R., Chem. Rev. 63:171-219(1963).
88. Shriner, R. L., and Fuson, R. C. Identification of organic compounds. 3rd ed. p. 317. New York, John Wiley and Sons, Inc., 1948.
89. Philpotts, A. R., and Thain, W., Anal. Chem. 24:638-43(1952).
90. Tommilla, E., and Hinshelwood, C. N., J. Chem. Soc. 1938:1801-10.
91. Gould, E. S. Mechanism and structure in organic chemistry. p. 180-1. New York, Holt Reinhart and Winstrom, 1959.
92. Bartlett, P. D., J. Am. Chem. Soc. 56:967(1934).
93. Bell, R. P., and Longuet-Higgins, H. C., J. Chem. Soc. 1946:636.

APPENDIX I

CHARACTERIZATION OF PRODUCTS: GAS CHROMATOGRAPHIC RETENTION TIMES  
OF REACTANTS AND VOLATILE AROMATIC PRODUCTS AND MELTING  
POINTS OF THE AROMATIC ACIDS

Extensive use was made of gas chromatography for both quantitative and qualitative product analysis. Table IXA gives the column, conditions of the investigations, and the retention times of the various ketones and the products obtained from the alkaline hydrogen peroxide oxidations. These are typical conditions usually corresponding to those for quantitative determinations. All the gas chromatographic investigations were made on the Hy-FI Aerograph Model A-600B Gas Chromatograph using 1/8 inch by 5 ft. columns.

The melting points of the aromatic acids (Table IXB) from the oxidations were determined using N.B.S. calibrated total immersion thermometers.

TABLE IXA

## GAS CHROMATOGRAPHIC DATA FOR THE KETONES AND THEIR VOLATILE AROMATIC PRODUCTS

Ketone	Column	R.T. Original Ketone, min.	R.T. Aromatic Aldehyde, min.	R.T. Aromatic Alcohol, min.	R.T. Known Product, min.	R.T. Unknowns, min.	Conditions
p-Methoxyphenyl-2-propanone	5% DEGS - 30% Carbowax	15.4	7.7	21.8	--	--	200°C., 10 no. N <sub>2</sub>
p-Chlorophenyl-2-propanone	5% DEGS - 30% Carbowax	15.6	6.0	26.2	--	--	190°C., 10 no. N <sub>2</sub>
Phenyl-2-propanone	5% DEGS - 30% Carbowax	8.7	4.0	14.2	--	--	170°C., 10 no. N <sub>2</sub>
p-Methyl-phenyl-2-propanone	5% DEGS - 30% Carbowax	12.5	6.5	19.8	--	--	170°C., 10 no. N <sub>2</sub>
p-Dimethylaminophenyl-2-propanone	5% DEGS - 30% Carbowax	7.1	8.6	--	--	--	250°C., 10 no. N <sub>2</sub>
p-Hydroxyphenyl-2-propanone	FFAP	13.0	--	--	--	--	265°C., 10 no. N <sub>2</sub>
4-Hydroxy-3-methoxyphenyl-2-propanone	5% DEGS - 30% Carbowax 20M	10.4	--	--	--	--	250°C., 14 no. N <sub>2</sub>
p-Chlorodeoxybenzoin	5% DEGS - 30% Carbowax 20M	22.2	--	--	--	--	250°C., 10 no. N <sub>2</sub>
p'-Chlorodeoxybenzoin	5% DEGS - 30% Carbowax 20M	26.5	3.5	--	--	12.0	250°C., 14 no. N <sub>2</sub>
Deoxybenzoin	5% DEGS - 30% Carbowax 20M	12.2	--	--	--	--	250°C., 10 no. N <sub>2</sub>
4-Phenyl-2-butanone	5% DEGS - 30% Carbowax 20M	15.9	6.9	18.5	--	4.4	165°C., 10 no. N <sub>2</sub>
3-Methyl-3-phenyl-2-butanone	5% DEGS - 30% Carbowax 20M	19.0	--	21.2	--	12.1, 16.1	140°C., 10 no. N <sub>2</sub>
3-Phenyl-2-butanone	Carbowax 4000 TPA	20.7	--	--	--	--	145°C., 10 no. N <sub>2</sub>

(acetophenone)

TABLE IXB

MELTING POINTS OF AROMATIC ACIDS

Oxidation	Acid	Melting Points	
		Isolated Acid	Reference
2417-124a	<u>p</u> -Chloro	242.9-243.9	
2417-126a	Benzoic	243.3-244.0	243.1-244.3
2417-122a	Benzoic	121.4-122.4	
2417-129a	Benzoic	120.8-122.3	123.0-123.2
2417-121a	<u>p</u> -Methyl	180.3-180.8	
2417-128a	Benzoic	180.2-180.8	180.4-180.9
2417-125a	<u>p</u> -Dimethylamino- benzoic <sup>a</sup>	241 -242	242 -243
2373-118a	<u>p</u> -Hydroxybenzoic	209 -211	214 -215
2417-117a	Benzoic <sup>b</sup>	121.8-122.7	
2417-119a	Benzoic	122.2-123.1	123.0-123.2

<sup>a</sup>These melting points were determined with the Hoover Uni-Melt apparatus.

<sup>b</sup>These acids were the products of the oxidations of deoxybenzoin. All others are products of phenyl-2-propanone oxidations.

APPENDIX II

ANALYSES OF HYDROGEN PEROXIDE: INTERFERENCE OF ORGANICS

Two quantitative methods were used to determine hydrogen peroxide: (1) iodometric titration, and (2) a spectrophotometric method using titanium sulfate. To insure that these methods were satisfactory, the possibility of interference from the organic products and reactants was investigated. The iodometric titration was tested by titrating 5-ml. samples of 1.118M hydrogen peroxide in the presence of the 3,4-dimethoxy substituted compounds. There was no evidence of any interference (Table X). The spectrophotometric method was checked by determining the absorbance of  $0.5 \times 10^{-3}$  M hydrogen peroxide solutions in the presence of p-methoxy substituted compounds. These determinations were made using a Beckman DU Spectrophotometer. There was no interference from any of the organic materials (Table X).

TABLE X

DETERMINATION OF HYDROGEN PEROXIDE: EFFECT  
OF ORGANICS

Organic Added	Iodometric Method		Spectrophotometric Method	
	Organic Added, grams	Titer, ml.	Concn. Organic, <u>M</u>	Absorbance
Standard	None	11.15 <sup>a</sup> 11.19	None	0.335
Substituted phenyl-2-propanone	0.1 0.2	11.19 11.19	0.015 (30x) <sup>b</sup>	0.332
<u>p</u> -Methoxy benzyl alcohol	--	--	0.001 (2x)	0.329
Substituted benzoic acid	0.1 0.1	11.15 11.20	0.001 (2x)	0.321
Standard	--	--	None	0.280 <sup>c</sup>
Substituted benzaldehyde	0.1 0.1	11.19 11.16	0.001 (2x)	0.282
Acetic acid	--	--	0.002 (4x)	0.281

<sup>a</sup>The original concentration of the hydrogen peroxide used in these determinations was 1.118M.

<sup>b</sup>The numbers in parentheses refer to the ratio of the concentration of the organic substance to that of the hydrogen peroxide.

<sup>c</sup>A new peroxide solution was prepared for the last two comparisons. Decomposition of the hydrogen peroxide accounts for the slight decrease which is observed in the two previous determinations.

APPENDIX III

EXPERIMENTAL CONDITIONS AND RESULTS: PRODUCT ANALYSIS AND KINETICS

This appendix includes the experimental conditions for the oxidations which were made for product analysis and kinetics studies. Rate constants are given for those oxidations made for kinetic investigations. The data for the kinetic runs, absorbance as a function of time, presented in Fig. 14 are included. All the oxidations are given a code number which corresponds to the notebook number and page on which the data for the run were recorded. These same code numbers are used on the Cary Charts and the Computer Output.

TABLE XI

OXIDATIONS FOR PRODUCT ANALYSIS OF THE PHENYL-2-  
PROPANONES IN 50% ETHANOL<sup>a</sup>

Experiment Number	Ketone	Ketone Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Time, hours	Temp., °C.
2417-11a	<u>p</u> -Methoxy	0.1290	0.42	0.50	4	45.0
2417-15a	<u>p</u> -Methoxy	0.1300	0.41	0.50	4	45.0
2417-124a	<u>p</u> -Chloro	0.0898	0.40	0.40	4-1/2	55.0
2417-126a	<u>p</u> -Chloro	0.0967	0.40	0.40	4-1/2	55.0
2417-122a	<u>p</u> -H	0.1078	0.40	0.40	7	55.0
2417-129a	<u>p</u> -H	0.0910	0.40	0.40	6-1/2	55.0
2417-121a	<u>p</u> -Methyl	0.0922	0.40	0.40	6	55.0
2417-128a	<u>p</u> -Methyl	0.0861	0.40	0.40	9	55.0
2417-125a	<u>p</u> -Dimethyl amino	0.0644	0.40	0.40	11	55.0
2373-113b	<u>p</u> -Hydroxy	0.1122	0.50	0.50	1	45.0
2373-118a	<u>p</u> -Hydroxy	0.0782	0.50	0.50	4	45.0
2373-119a	<u>p</u> -Hydroxy	0.0760	0.50	0.50	2	45.0

<sup>a</sup>The solvent for Runs 2373-113b, 118a, and 119a was water.

TABLE XII

COMPARATIVE REACTIVITY OF p-METHOXYBENZALDEHYDE  
AND p-METHOXYBENZYL ALCOHOL IN 50%  
ETHANOL AT 45.0°C.

Experiment Number	Substrate	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Second-Order Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2373-121a	Alcohol	0.0729	0.0792	0.08	0.0021
2373-121b	Alcohol	0.0751	0.0801	0.08	0.0045
2373-122a	Aldehyde	0.0641	0.0794	0.08	0.1770
2373-122b	Aldehyde	0.0619	0.0796	0.08	0.1490

TABLE XIII

OXIDATION OF p-METHOXYPHENYL-2-PROPANONE: EXPERIMENTS  
FOR DETERMINING THE REACTION ORDER WITH RESPECT  
TO SUBSTRATE IN 50% ETHANOL AT 45.0°C.

Experiment Number	Ketone Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>	Initial pH	Corrected Initial Rate, <u>M</u> min. <sup>-1</sup>
2417-92a	0.1229	0.0754	0.08	12.92	0.00078
2417-92b	0.1270	0.0762	0.08	12.90	0.00077
2417-92c	0.0923	0.0759	0.08	12.88	0.00058
2417-92d	0.0899	0.0767	0.08	12.92	0.00058
2417-93a	0.0648	0.0759	0.08	12.99	0.00045
2417-93b	0.0657	0.0756	0.08	12.96	0.00044

TABLE XIV

OXIDATION OF PHENYL-2-PROPANONE: EXPERIMENTS FOR  
DETERMINING THE REACTION ORDER WITH RESPECT  
TO SUBSTRATE IN 50% ETHANOL AT 45.0°C.

Experiment Number	Substrate Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>	Corrected Initial Rate, <u>M</u> min. <sup>-1</sup>
2373-105a	0.0603	0.0794	0.08	0.00042
2373-106b	0.0840	0.0790	0.08	0.00052
2373-105b	0.0939	0.0795	0.08	0.00073
2373-105c	0.1260	0.0797	0.08	0.00087
2373-105d	0.1542	0.0794	0.08	0.00104
2373-106a	0.1930	0.0797	0.08	0.00127

TABLE XV

OXIDATION OF p-METHOXYPHENYL-2-PROPANONE: EXPERIMENTS FOR DETERMINING THE REACTION ORDER WITH RESPECT TO HYDROGEN PEROXIDE, IN 50% ETHANOL AT 45.0°C.

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Potassium Chloride Conc., <u>M</u>	Corrected Initial Rate, <u>M</u> min. <sup>-1</sup>
2417-149b	0.1006	0.2290	0.24	0.00	0.00193
2417-150a	0.1000	0.1890	0.20	0.04	0.00139
2417-150b	0.1018	0.1550	0.16	0.08	0.00123
2417-150c	0.1001	0.1154	0.12	0.12	0.00091
2417-150d	0.1030	0.0779	0.08	0.16	0.00060

TABLE XVI

OXIDATION OF PHENYL-2-PROPANONE: EXPERIMENTS FOR DETERMINING REACTION ORDER WITH RESPECT TO HYDROGEN PEROXIDE IN 50% ETHANOL AT 45.0°C.

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Potassium Chloride Conc., <u>M</u>	Corrected Initial Rate, <u>M</u> min. <sup>-1</sup>
2373-103b	0.0625	0.2187	0.24	0.00	0.00170
2373-104a	0.0617	0.1937	0.20	0.04	0.00146
2373-104b	0.0613	0.1418	0.16	0.08	0.00119
2373-104c	0.0608	0.1164	0.12	0.12	0.00084
2373-104d	0.0614	0.0775	0.08	0.16	0.00059

TABLE XVII

OXIDATION OF p-METHOXYPHENYL-2-PROPANONE: EFFECT OF  
SODIUM HYDROXIDE ON REACTION RATE IN 50% ETHANOL  
AT 45.0°C.

Experiment Number	Substrate Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>	Potassium Chloride Concn., <u>M</u>	Initial pH	Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2417-141a	0.0589	0.0903	0.60	0.00	--	0.0454
2417-141b	0.0612	0.0968	0.50	0.10	--	0.0407
2417-141c	0.0608	0.0937	0.40	0.20	--	0.0421
2417-142a	0.0599	0.0972	0.30	0.30	13.72	0.0424
2417-142b	0.0603	0.0988	0.20	0.40	13.62	0.0485
2417-142c	0.0600	0.0992	0.175	0.425	13.54	0.0603
2417-143a	0.0595	0.0996	0.150	0.450	13.47	0.0748
2417-143b	0.0606	0.1001	0.125	0.475	13.20	0.0714
2417-143c	0.0608	0.0980	0.115	0.485	13.12	0.0792
2417-144a	0.0596	0.1001	0.100	0.50	13.02	0.0848
2417-144b	0.0610	0.0969	0.09	0.51	12.81	0.0714
2417-144c	0.0603	0.0986	0.08	0.52	12.71	0.0633
2417-145a	0.0624	0.0996	0.08	0.52	12.75	0.0596
2417-145b	0.0595	0.0974	0.06	0.54	12.52	0.0559
2417-145c	0.0615	0.0980	0.04	0.56	12.17	0.0448
2417-146a	0.0603	0.0940	0.02	0.58	11.84	0.0297

TABLE XVIII

OXIDATION OF PHENYL-2-PROPANONE: EFFECT OF SODIUM  
HYDROXIDE ON REACTION RATE IN 50% ETHANOL AT  
45.0°C.

Experiment Number	Substrate Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>	Potassium Chloride Concn., <u>M</u>	Initial pH	Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2417-137a	0.0597	0.0756	0.24	0.00	13.4	0.0687
2417-137b	0.0593	0.0783	0.16	0.08	13.18	0.0814
2417-138a	0.0623	0.0797	0.12	0.12	13.08	0.0891
2417-138b	0.0598	0.0798	0.08	0.16	12.98	0.1012
2417-138c	0.0645	0.0755	0.08	0.16	--	0.1304
2417-138d	0.0619	0.0792	0.06	0.18	12.65	0.0996
2417-139a	0.0594	0.0791	0.05	0.19	12.51	0.0868
2417-139b	0.0645	0.0795	0.04	0.20	12.24	0.0598
2417-139c	0.0610	0.0793	0.03	0.21	12.08	0.0364
2417-139d	0.0618	0.0798	0.02	0.22	11.97	0.0237

TABLE XIX

SOLUTIONS FOR DETERMINING THE HYDROPEROXIDE ANION  
CONCENTRATION IN ALKALINE HYDROGEN PEROXIDE  
SOLUTIONS IN 50% ETHANOL

Solution Number	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Absorbance at 3150 A.
2373-124a	0.08	0.50	0.746
2373-124b	0.08	pH 7 buffer	0.031
2373-124c	0.20	0.08	0.791
2373-124d	0.16	0.08	0.766
2373-124e	0.12	0.08	0.724
2373-124f	0.08	0.08	0.609
2373-124g	0.06	0.08	0.491
2373-124h	0.04	0.08	0.350
2373-124i	0.02	0.08	0.179

TABLE XX

OXIDATION OF PHENYL-2-PROPANONE: EXPERIMENTS FOR  
DETERMINING THE REACTIVE PEROXIDE SPECIES IN  
ALKALINE PEROXIDE OXIDATIONS IN 50% ETHANOL  
AT 45.0°C.

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Corrected Initial Rate, <u>M min.<sup>-1</sup></u>
2373-136a	0.0646	0.1728	0.08	0.00083
2373-136b	0.0634	0.1430	0.08	0.00076
2373-136c	0.0675	0.1101	0.08	0.00081
2373-136d	0.0662	0.0763	0.08	0.00060
2373-137a	0.0657	0.0578	0.08	0.00039
2373-137b	0.0665	0.0385	0.08	0.00026
2373-137c	0.0660	0.0198	0.08	0.00011

TABLE XXI

OXIDATION OF p-METHOXYPHENYL-2-PROPANONE: EFFECT OF ADDED ELECTROLYTE ON REACTION RATE IN 50% ETHANOL AT 45.0°C.

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Potassium Chloride Conc., <u>M</u>	Initial pH	Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2417-93a	0.0648	0.0759	0.08	0.00	12.99	0.0880
2417-93b	0.0657	0.0756	0.08	0.00	12.96	0.0895
2417-93c	0.0657	0.0761	0.08	0.04	12.96	0.0381
2417-93d	0.0657	0.0757	0.08	0.12	12.95	0.0758
2417-93e	0.0638	0.0760	0.08	0.12	12.91	0.0816

TABLE XXII

OXIDATION OF PHENYL-2-PROPANONE: EFFECT OF ADDED SALT ON REACTION RATE IN 50% ETHANOL AT 45.0°C.

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Potassium Chloride Conc., <u>M</u>	Second-Order Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2373-93a	0.0607	0.0779	0.08	0.00	0.1346
2373-105a	0.0603	0.0794	0.08	0.00	0.1154
2373-106c	0.0671	0.0790	0.08	0.10	0.1195
2373-107a	0.0683	0.0790	0.08	0.20	0.1201
2373-107b	0.0678	0.0788	0.08	0.30	0.1200
2373-107c	0.0623	0.0791	0.08	0.40	0.1068

TABLE XXIII

OXIDATION OF p-METHOXYPHENYL-2-PROPANONE: EFFECT OF TEMPERATURE ON REACTIVITY IN 50% ETHANOL<sup>a</sup>

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Initial pH	Temp., °C.	Rate Constant <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2417-93f	0.0644	0.0668	0.08	12.99	65.0	0.1875
2417-93h	0.0646	0.0641	0.08	12.98	65.0	0.1938
2417-93g	0.0650	0.0753	0.08	12.98	55.0	0.1217
2417-93i	0.0654	0.0741	0.08	12.98	55.0	0.1215
2417-93c	0.0657	0.0761	0.08	12.96	45.0	0.0831
2417-93j	0.0638	0.0753	0.08	13.00	35.0	0.0599
2417-93k	0.0645	0.0756	0.08	12.99	35.0	0.0645

<sup>a</sup>Potassium chloride concentration constant at 0.04M for all runs of this series.

TABLE XXIV

OXIDATION OF PHENYL-2-PROPANONE: EFFECT OF TEMPERATURE ON REACTIVITY IN 50% ETHANOL

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Temp., °C.	Second-Order Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2373-95a	0.0606	0.0766	0.08	55.0	0.2166
2373-95b	0.0602	0.0774	0.08	55.0	0.2186
2373-93a	0.0607	0.0779	0.08	45.0	0.1346
2373-96b	0.0619	0.0793	0.08	35.0	0.0837
2373-96c	0.0605	0.0806	0.08	35.0	0.0832
2373-97b	0.0616	0.0804	0.08	26.5	0.0495
2373-97c	0.0653	0.0795	0.08	26.5	0.0527

TABLE XXV

OXIDATION OF PHENYL-2-PROPANONES: EFFECT OF SUBSTITUENTS  
ON REACTIVITY IN 50% ETHANOL AT 45.0°C.

Experiment Number	Phenyl-2-propanone	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Second-Order Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2417-103a	<u>p</u> -Nitro	0.0247	0.0642	0.065	3.320
2417-103b	<u>p</u> -Chloro	0.0310	0.0637	0.065	0.311
2417-103d	<u>p</u> -Chloro	0.0303	0.0799	0.08	0.317
2417-103e	<u>p</u> -H	0.0788	0.0814	0.08	0.131
2417-103f	<u>p</u> -H	0.0789	0.0806	0.08	0.141
2417-103g	<u>p</u> -Methyl	0.0719	0.0784	0.08	0.102
2417-103h	<u>p</u> -Methyl	0.0729	0.0786	0.08	0.095
2417-103i	3,4-Dimethoxy	0.0628	0.0814	0.08	0.209
2417-103j	3,4-Dimethoxy	0.0630	0.0811	0.08	0.184
2417-93a	<u>p</u> -Methoxy	0.0648	0.0759	0.08	0.088
2417-93b	<u>p</u> -Methoxy	0.0657	0.0756	0.08	0.090
2417-104a	<u>p</u> -Methoxy	0.0709	0.0806	0.08	0.108
2417-104b	<u>p</u> -Dimethyl-amino	0.0593	0.0805	0.08	0.235
2417-104c	<u>p</u> -Dimethyl-amino	0.0572	0.0816	0.08	0.200
2417-104d	4-Hydroxy-3-methoxy	0.0668	0.0800	0.15	0.061
2417-104e	<u>p</u> -Hydroxy	0.0682	0.0813	0.15	0.101
2417-104f	<u>p</u> -Hydroxy	0.0402	0.0802	0.15	0.192

TABLE XXVI

OXIDATIONS OF PHENYL-2-PROPANONES: EFFECT OF SUBSTITUENTS ON REACTIVITY IN 50% ETHANOL AT 45.0°C. USING 0.05M HYDROGEN PEROXIDE

Experiment Number	Ketone	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Second-Order Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2417-147a	<u>p</u> -Methoxy	0.0626	0.0499	0.05	0.091
2417-147b	<u>p</u> -Methoxy	0.0596	0.0506	0.05	0.086
2417-147c	<u>p</u> -Methyl	0.0601	0.0499	0.05	0.058
2417-148a	<u>p</u> -Methyl	0.0621	0.0502	0.05	0.057
2417-148b	<u>p</u> -H	0.0639	0.0502	0.05	0.082
2417-148c	<u>p</u> -H	0.0629	0.0503	0.05	0.090
2417-148d	<u>p</u> -Chloro	0.0597	0.0490	0.05	0.272
2417-149a	<u>p</u> -Chloro	0.0596	0.0497	0.05	0.281

TABLE XXVII

OXIDATION OF 4-PHENYL-2-BUTANONE: EFFECT OF SODIUM HYDROXIDE ON REACTIVITY IN 50% ETHANOL AT 45.0°C.

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Potassium Chloride Conc., <u>M</u>	Second-Order Rate Constant, <u>M</u> <sup>-1</sup> min. <sup>-1</sup>
2373-101a	0.0598	0.0791	0.24	0.00	0.0269
2373-102a	0.0628	0.0791	0.16	0.08	0.0264
2373-102b	0.0604	0.0783	0.08	0.16	0.0279
2373-102c	0.0610	0.0779	0.06	0.18	0.0209
2373-102d	0.0602	0.0767	0.04	0.20	0.0129

TABLE XXVIII

OXIDATION OF 4-PHENYL-2-BUTANONE: EFFECT OF TEMPERATURE  
ON REACTIVITY IN 50% ETHANOL

Experiment Number	Substrate Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Temp., °C.	Second-Order Rate Constant, <u>M<sup>-1</sup> min.<sup>-1</sup></u>
2373-95c	0.0591	0.0786	0.08	55.0	0.0393
2373-96a	0.0628	0.0761	0.08	55.0	0.0405
2373-93b	0.0606	0.0792	0.08	45.0	0.0297
2373-93c	0.0619	0.0793	0.08	45.0	0.0270
2373-96d	0.0601	0.0803	0.08	35.0	0.0184
2373-97a	0.0638	0.0801	0.08	35.0	0.0192

TABLE XXIX

OXIDATIONS FOR PRODUCT ANALYSIS OF PHENYL-2-BUTANONES IN 50% ETHANOL<sup>a</sup>

Experiment Number	Butanone	Butanone Conc., <u>M</u>	Hydrogen Peroxide Conc., <u>M</u>	Sodium Hydroxide Conc., <u>M</u>	Time, hr.
2417-134a	4-phenyl-2-	0.0395	0.40	0.40	10
2417-135a	4-phenyl-2-	0.0414	0.40	0.40	10
2373-109a	3-phenyl-2-	0.1075	0.40	0.40	28
2373-112a	3-phenyl-2-	0.1077	0.40	0.40	28
2373-111a	3-methyl-3-phenyl-2-	0.0626	0.40	0.40	64
2373-122c	3-methyl-3-phenyl-2-	0.0605	0.40	0.40	64

<sup>a</sup>The oxidations for the first compound were made at 55.0°C. whereas the last four were made at 45.0°C.

TABLE XXX

OXIDATIONS FOR COMPARING THE REACTIVITY OF PHENYL-2-  
 PROPANONE WITH THE PHENYL-2-BUTANONES IN 50%  
 ETHANOL AT 45.0°C.

Experiment Number	Ketone	Substrate Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>
2373-105a	Phenyl-2- propanone	0.0603	0.0794	0.08
2373-93a	Phenyl-2- propanone	0.0607	0.0779	0.08
2373-93b	4-Phenyl-2- butanone	0.0606	0.0792	0.08
2373-93c	4-Phenyl-2- butanone	0.0619	0.0793	0.08
2373-93d	3-Methyl-3- phenyl-2- butanone	0.0508	0.0794	0.08
2373-94a	3-Methyl-3- phenyl-2- butanone	0.0534	0.0744	0.08
2373-94b	3-Phenyl-2- butanone	0.0587	0.0798	0.08
2373-94c	3-Phenyl-2- butanone	0.0571	0.0794	0.08
2373-100a	3-Phenyl-2- butanone	0.0582	0.0797	0.08

TABLE XXXI

OXIDATIONS FOR PRODUCT ANALYSIS OF DEOXYBENZOINS  
IN 70% ETHANOL AT 55.0°C.

Experiment Number	Ketone	Ketone Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>	Time, hr.
2417-111a	(p-Chloro- deoxybenzoin)	0.0158	0.13	0.13	4
2417-118a		0.0150	0.13	0.13	4
2417-116a	(p'-Chloro- deoxybenzoin)	0.010	0.11	0.11	4
2417-118b		0.011	0.11	0.11	4
2417-117a	(Deoxybenzoin)	0.0231	0.22	0.22	6
2417-119a		0.0233	0.22	0.22	6

TABLE XXXII

OXIDATIONS OF DEOXYBENZOINS IN 60% ETHANOL AT 45.0°C.

Experiment Number	Ketone	Substrate Concn., <u>M</u>	Hydrogen Peroxide Concn., <u>M</u>	Sodium Hydroxide Concn., <u>M</u>
2417-153a	(p-Chloro- deoxybenzoin)	0.0200	0.0814	0.08
2417-156a		0.0138	0.0794	0.08
2417-154a	(p'-Chloro- deoxybenzoin)	0.0106	0.0783	0.08
2417-155a		0.0109	0.0784	0.08
2417-156b	(Deoxybenzoin)	0.0184	0.0786	0.08
2417-157a		0.0178	0.0794	0.08

The data in Tables XXXIII to XXXVIII present corrected absorbance-time data and a calculated logarithmic expression for several phenyl-2-propanones. The logarithmic expression is plotted as a function of time in Fig. 14.

TABLE XXXIII

REACTION OF p-NITROPHENYL-2-PROPANONE,  
OXIDATION 2417-103a

Divisions, 100 sec./div.	Absorbance	Corrected Absorbance	$\ln \frac{b(a-x)}{a(b-0.5x)}$
6	0.975	0.975	0.000
8	0.798	0.798	0.0679
10	0.667	0.667	0.1471
12	0.570	0.570	0.2363

TABLE XXXIV

REACTION OF p-CHLOROPHENYL-2-PROPANONE,  
OXIDATION 2417-148d

Divisions, 100 sec./div.	Absorbance	Corrected Absorbance	$\ln \frac{b(a-x)}{a(b-0.5x)}$
6	0.784	0.784	0.000
8	0.737	0.737	-0.0363
10	0.697	0.698	-0.0698
12	0.662	0.663	-0.1013
14	0.628	0.630	-0.1341
16	0.597	0.599	-0.1662
18	0.568	0.571	-0.1982
20	0.542	0.545	-0.2287
22	0.516	0.520	-0.2612
24	0.492	0.496	-0.2931
26	0.470	0.475	-0.3241
28	0.448	0.463	-0.3416
30	0.429	0.435	-0.3871
32	0.410	0.416	-0.4188
34	0.390	0.396	-0.4544
36	0.373	0.380	-0.4863

TABLE XXXV

REACTION OF 3,4-DIMETHOXYPHENYL-2-PROPANONE,  
OXIDATION 2417-103j

Divisions, 100 sec./div.	Absorbance	Corrected Absorbance	ln $\frac{b(a-x)}{a(b-0.5x)}$
6	0.769	0.769	0.000
8	0.740	0.740	-0.0135
10	0.712	0.713	-0.0273
12	0.685	0.685	-0.0415
14	0.662	0.664	-0.0543
16	0.638	0.641	-0.0684
18	0.616	0.619	-0.0821
20	0.596	0.600	-0.0952
22	0.576	0.581	-0.1090
24	0.558	0.563	-0.1220
26	0.541	0.547	-0.1349
28	0.523	0.529	-0.1492
30	0.506	0.513	-0.1634
32	0.490	0.497	-0.1775
34	0.473	0.480	-0.1932
36	0.458	0.466	-0.2077

TABLE XXXVI

REACTION OF PHENYL-2-PROPANONE, OXIDATION  
2417-148c

Divisions, 100 sec./div.	Absorbance	Corrected Absorbance	ln $\frac{b(a-x)}{a(b-0.5x)}$
6	0.877	0.877	0.0000
8	0.860	0.860	-0.0112
10	0.843	0.844	-0.0228
12	0.828	0.830	-0.0332
14	0.812	0.815	-0.0446
16	0.796	0.799	-0.0563
18	0.782	0.786	-0.0668
20	0.767	0.772	-0.0783
22	0.752	0.757	-0.0902
24	0.738	0.744	-0.1015
26	0.724	0.731	-0.1131
28	0.711	0.718	-0.1241
30	0.698	0.706	-0.1353
32	0.685	0.693	-0.1469
34	0.672	0.681	-0.1587
36	0.659	0.669	-0.1708

TABLE XXXVII

REACTION OF p-METHOXYPHENYL-2-PROPANONE,  
OXIDATION 2417-93b

Divisions, 100 sec./div.	Absorbance	Corrected Absorbance	$\ln \frac{b(a-x)}{a(b-0.5x)}$
6	0.905	0.905	0.0000
8	0.883	0.885	-0.0095
10	0.865	0.869	-0.0173
12	0.846	0.852	-0.0259
14	0.828	0.836	-0.0343
16	0.808	0.818	-0.0441
18	0.791	0.802	-0.0525
20	0.775	0.788	-0.0606
22	0.760	0.775	-0.0684
24	0.745	0.762	-0.0764
26	0.730	0.749	-0.0846
28	0.716	0.736	-0.0925
30	0.702	0.724	-0.1005
32	0.637	0.711	-0.1095
34	0.673	0.698	-0.1181
36	0.662	0.689	-0.1247

TABLE XXXVIII

REACTION OF p-METHYLPHENYL-2-PROPANONE,  
OXIDATION 2417-147c

Divisions, 100 sec./div.	Absorbance	Corrected Absorbance	$\ln \frac{b(a-x)}{a(b-0.5x)}$
6	0.910	0.910	0.0000
8	0.898	0.898	-0.0076
10	0.887	0.877	-0.0147
12	0.877	0.877	-0.0213
14	0.867	0.867	-0.0280
16	0.856	0.857	-0.0354
18	0.846	0.847	-0.0424
20	0.837	0.838	-0.0486
22	0.827	0.828	-0.0558
24	0.818	0.819	-0.0623
26	0.808	0.810	-0.0696
28	0.800	0.802	-0.0756
30	0.791	0.793	-0.0824
32	0.782	0.784	-0.0893
34	0.774	0.776	-0.0955
36	0.766	0.768	-0.1018