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THE UNIVERSITY OF ALBERTA

THE POTASSIUM PEROXYDISULFATE PROMOTED OXIDATIVE
DECARBOXYLATION OF CARBOXYLIC ACIDS

BY



SOAD ABDEL AZIZ OSMAN

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES IN
PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE
OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

SPRING, 1970

UNIVERSITY OF ALBERTA
FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and
recommend to the Faculty of Graduate Studies for acceptance, a
thesis entitled: THE POTASSIUM PEROXYDISULFATE PROMOTED
OXIDATIVE DECARBOXYLATION OF CARBOXYLIC ACIDS
submitted by SOAD ABDEL AZIZ OSMAN in partial fulfilment of the
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TO MY PARENTS

ABSTRACT

The oxidative decarboxylation reaction of carboxylic acids with potassium peroxydisulfate has been examined. The mechanism of the decarboxylation of substituted phenylacetic acids and a series of secondary alkylcarboxylic, tertiary alkylcarboxylic and allylcarboxylic acids has been studied as an approach to a resolution of the conflicting opinions on the nature of the transition state during one-electron transfer process from carboxylic acids. The relative rates of the decarboxylation of meta- and para-substituted phenylacetic acids, relative to radioactive phenylacetic acid-1-C¹⁴, were fitted to the Hammett equation and were found to show a good correlation with the σ^+ values of the substituents and only a fair correlation with the σ^- values. This infers a direct resonance interaction of the substituents with the incipient benzyl radical, influenced to some extent by the polar characters of the transition state i.e. $\text{ArCH}_2^+\text{CO}_2^-\text{SO}_4^{2-}$. It was found that the relative rates of the decarboxylation depended upon the structure of the acting acids. The order of reactivity was found to be primary alkylcarboxylic < secondary alkylcarboxylic < tertiary alkylcarboxylic < allylcarboxylic < benzylcarboxylic acids. This dependence of the relative rates on the structure of the acids indicates that there is a degree of carbonyl bond breakage associated with the transfer of an electron from the carboxylate anion.

Substitution of methyl and phenyl groups on the methylene carbon of phenylacetic acid decreased the rate of decarboxylation.

The retarding effect of the alpha-substituents on the rates of the decarboxylation is believed to be a result of their interference with the solvation of the polar transition state . This effect outweighed the enhancing electronic effect of the substituents which should provide extra stability to the radicals produced upon decarboxylation.

The competitive rates of decarboxylation of anti- and syn-7-norborn-2-enecarboxylic, and exo-2-norborn-5-enecarboxylic acids were determined. There was no noticable difference in the rates of the decarboxylation of the three acids. These findings excluded any appreciable assistance by the double bond in the decarboxylation process and hence any possibility of the involvement of nonclassical norbornenyl radicals.

The relative rate of the decarboxylation of 1-adamantane-carboxylic acid was found to be lower than that of pivalic acid. This indicated that the stability of the tertiary bridge-head radical is lower than that of the normal tertiary alkyl radical.

ACKNOWLEDGEMENTS

I would like to express my profound indebtedness and appreciation to my research director Dr. D. D. Tanner without whose constant assistance, guidance and encouragement this work would not have been completed.

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PART I

THE MECHANISM OF THE POTASSIUM PEROXYDISULFATE
PROMOTED DECARBOXYLATION OF CARBOXYLIC ACIDS

INTRODUCTION

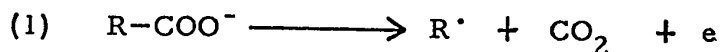
Several methods of electrochemical and chemical oxidative decarboxylation reactions of carboxylic acids are known. These reactions involve the transfer of one electron from the carboxylate group to either the electrode surface or to an oxidizing agent. Oxidative decarboxylation by the classical Kolbe electrolysis is a useful method of producing symmetrical alkanes. A number of side-products are also produced e.g. alcohol, alkenes, esters, olefins and rearranged products.

The mechanism of the reaction has been discussed at some length by Corey,¹ Weedon,² Lippincott³ and others. They based their discussions on the three theories, which have previously been advanced, concerning the mechanism of the electrolysis in aqueous media, the discharged ion theory, the acyl.peroxide theory and the hydrogen peroxide theory.

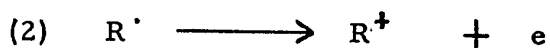
The discharged ion theory was proposed by Brans and Walker.⁴ The important steps in this mechanism are the direct oxidation of the carboxylate anion and the subsequent decomposition of the acyloxy radical formed. The nature of the Kolbe product, as well as product studies in the presence of trapping agents, indicate a radical mechanism. Gild and Smith^{5,6} showed that, the Kolbe electrolysis may serve as a useful source of free-radicals in solution which will add to dienes and cause vinyl polymerisation. They isolated over 20 compounds from the electrolysis of potassium acetate in the presence of butadiene. All of these products could be

rationalized by a radical mechanism. The formation of 4-phenylpyridine, and 4-phenylbenzoic acid during the electrolysis of benzoic acid in pyridine,⁷ and of diphenylmethane when diphenylacetic acid is electrolysed in methanol-pyridine,⁸ can be explained by a free-radical mechanism. The failure of aryl carboxylic acids to undergo the Kolbe reaction to any significant extent, is in accord with the known tendency of aryl radicals to attack solvent molecules and to give polymers rather than dimers.⁹

The calculation of the standard potentials for a number of electrode processes possibly involved in the anodic oxidation of salts of carboxylic acids led to the conclusion that the primary electrode process is best represented by (1), the direct discharge



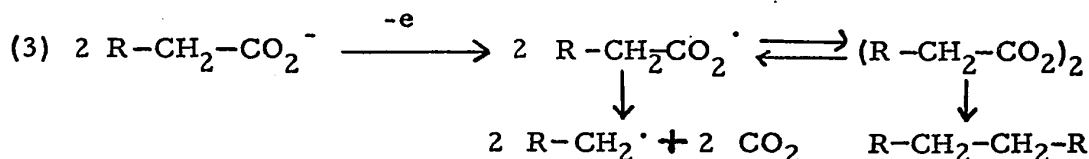
of the carboxylate ion to the alkyl radical.¹⁰ This can be followed by a further oxidation of the radical to a carbonium ion (2) in cases



where the ionization potential is lower than 8 ev. Eberson^{11,12} found that cyanoacetic, isopropyl, *t*-butyl, cyclohexyl and dimethylcyanoacetic acids on electrolysis in methanolic solution gave good yields of coupling products. The behaviour of the anodically generated α -cyanoalkyl radicals was very similar to that of α -cyanoalkyl radicals generated in homogenous solution. Thus the

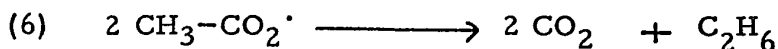
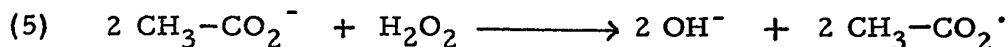
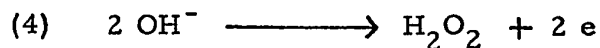
proportion of the C-C and C-N products as well as the ratio of meso- and dl- dialkylsuccinonitril from the C-C coupling were the same in the two reactions.

The acyl peroxide theory proposed by Fichter¹³ in 1924 is illustrated by the following scheme:-



He proposed that the electrode process is not a direct oxidation of the organic acid but, that a diacyl peroxide is the intermediate which gives rise to the observed products. The isolation of dihexanoyl peroxide¹⁴ in the electrolysis of potassium hexanoate at -20° and the formation of acetyl peroxide in the electrolysis of potassium acetate, reported by Glasstone and Hickling,¹⁵ were taken in support of this theory.

The hydrogen peroxide theory proposed by Glasstone and Hickling¹⁶ in 1934 can be represented by the following equations:



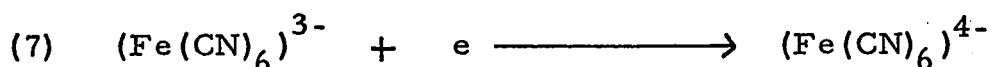
According to this concept hydrogen peroxide or hydroxyl radicals initiate the decomposition. An important objection to this theory was based on the fact that hydrogen peroxide gave oxygen instead of

the Kolbe product when added to the electrolyte under reaction conditions.¹⁷

A mechanism for the Kolbe reaction that consists of direct discharge of the anion with the possibility of reversible acyl peroxide formation explains the majority of experimental results.

The one-electron transfer to the electrode surface which takes place in Kolbe electrolysis can be achieved by transfer to a suitable oxidising agent. It is therefore possible to generate alkyl and aryl radicals by direct chemical oxidation of the appropriate carboxylic acids, and a number of reagents have been used in this manner.

Alkaline ferricyanide is one of the reagents used to effect a one-electron transfer. The oxidising species is a readily reduced complex ion. It has been used in the oxidation of phenols,

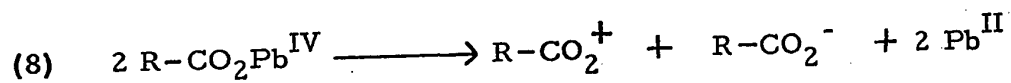


glycols, hydroxylamines, hydrocarbons and ethers. In oxidative decarboxylation, alkaline ferricyanide seems to attack a carboxylate ion to give rise to a carboxylate radical, which loses a molecule of carbon dioxide. Lahous¹⁸ and later, Fieser and Haddadin¹⁹ reported the synthesis of p-terphenyl by the oxidative decarboxylation of the corresponding dicarboxylic acid. Walker and Scott²⁰ have used the alkaline ferricyanide for the decarboxylation of dihydro-naphthalene-1,2- and 1,4-dicarboxylic acids. The reaction seems to be successful when the loss of carbon dioxide yields a highly

conjugated free-radical which ultimately leads to an aromatic system.

Lead tetraacetate is also used to effect the oxidative decarboxylation of aliphatic carboxylic acids as well as the bis-decarboxylation of 1,2-dicarboxylic acids.^{21,22} Lead (IV) carboxylate is converted to lead (II) carboxylate, carbon dioxide and the products from the oxidation of the alkyl moiety.

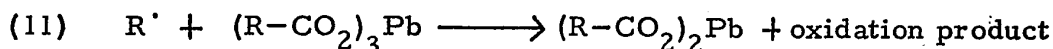
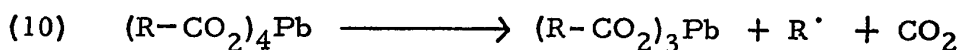
An investigation into the mechanism of the decarboxylation lead Mosher and Kehr^{23,24} to formulate a direct 2-equivalent process, based on the relative ease of decarboxylation of various carboxylic acids and the isolation from these reactions of the products characteristic of a carbonium ion intermediate. They postulated the direct formation of lead (II) esters and an acyloxonium intermediate which undergoes subsequent decarboxylation. The



possibility of a carbonium ion intermediate was further strengthened by the isolation of rearranged products. Partially racemized exo-2-norbornylacetate obtained by Corey and Casanova²² from optically active endo- and exo-norbornane-2-carboxylic acids, was attributed to the intermediacy of the 2-norbornyl cation. These workers concluded from their results that, as in the case of Kolbe electrolysis, cationic species can be produced by further oxidation of radicals formed in the decarboxylation using lead tetraacetate when the carbonium ion formed is of high stability. In certain

systems and under certain experimental conditions, cations and radicals may both give rise to the observed products. Watanobe, Furukawa and Oae²⁵ decarboxylated phenylacetic acid with lead tetraacetate in presence of oxygen and cupric oxide and suggested that the reaction proceeds through an ionic mechanism. The benzyl radical was excluded as an intermediate because toluene and diphenylethane could not be isolated as reaction products.

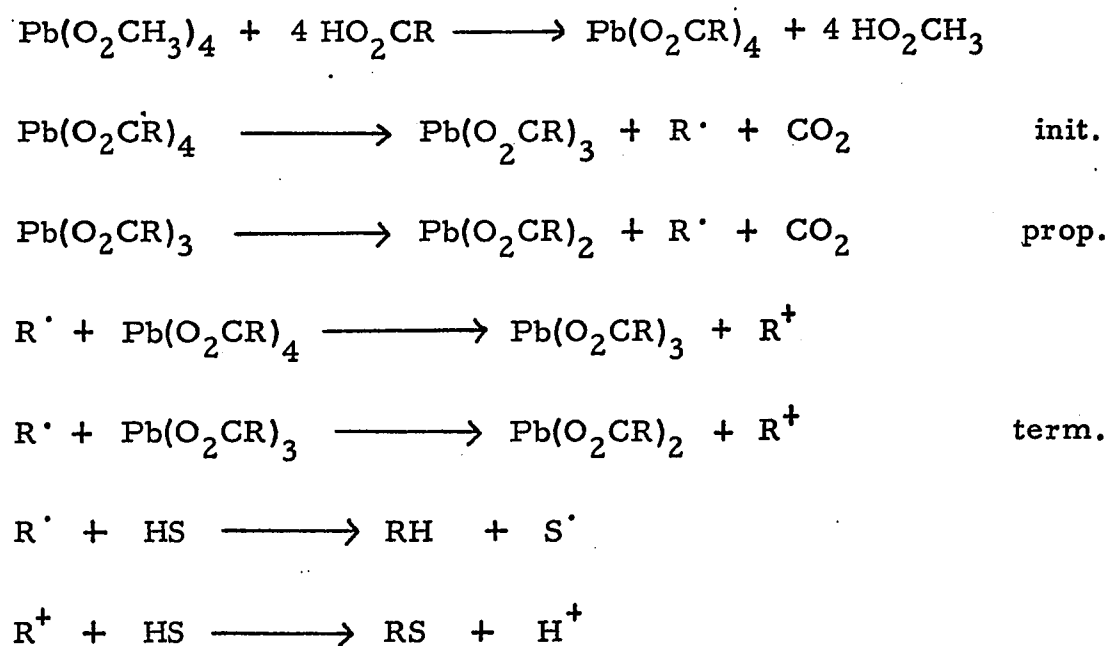
Kharasch²⁶ concluded that the decomposition of lead tetraacetate in glacial acetic acid proceeds via 1-equivalent changes and proposed lead (III) as an intermediate. It was not clear if the mechanism involved the direct formation of the carbonium ion in all or even most decarboxylations or if a radical mechanism (10-11) pertains.



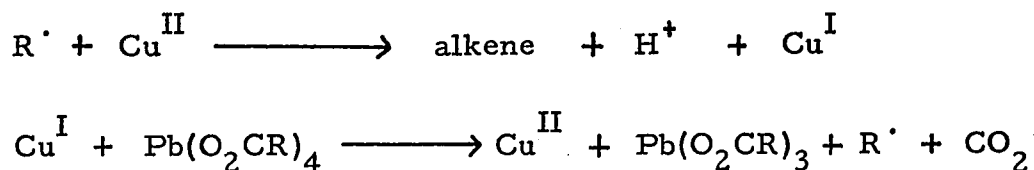
The participation of free-radicals in the oxidative decarboxylation of acids with lead tetraacetate was convincingly evident from the work of Kochi²⁷ on the decarboxylation of pentanoic acids. The marked inhibition by oxygen, the enhancement of the decarboxylation in the presence of a copper salt and valeryl peroxide, the nature of the products of decomposition, and the trapping of the radicals, as well as the initiation of the reaction photolytically,²⁸ strongly support the involvement of a free-radical chain process. Further work supporting the radical mechanism was carried out by a

number of investigators using 4,4,4-triphenylbutyric,²⁹ butyric, isobutyric, pivalic³⁰ and N-acetylamino acids.³¹

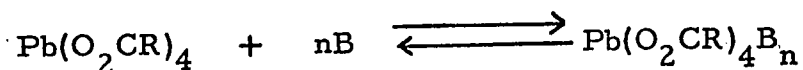
Lead (III) is implicated as an intermediate in this mechanism. The following sequence was proposed:



The catalysis by copper is as follows:

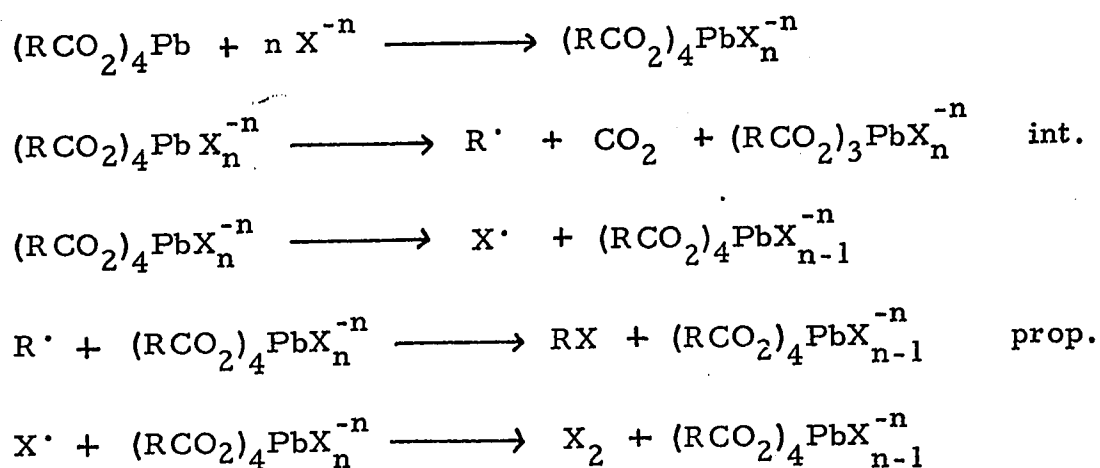


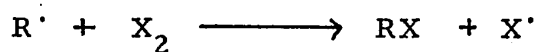
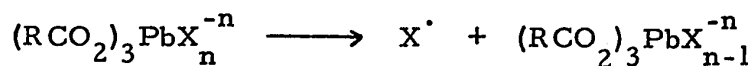
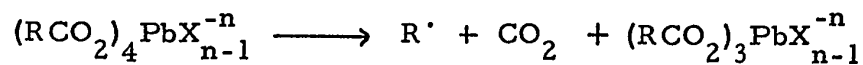
In benzene solution the decarboxylation is induced by acetate salts as well as bases such as pyridine and trialkylamines.²¹ The catalysis by these nucleophilic reagents has been attributed to the formation of highly coordinated lead (IV) species e.g.



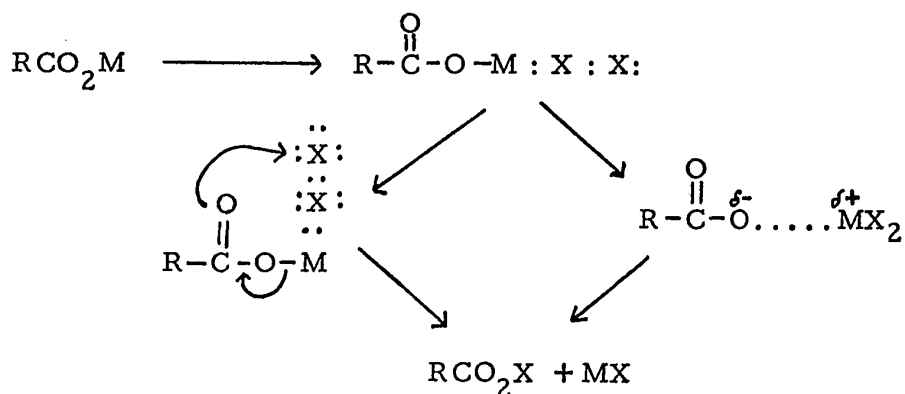
B = pyridine, R_3N , O_2CR

It has been suggested that complexes such as above are more susceptible to homolysis than the parent lead(IV) esters. It was also found that halides, thiocyanate and cyanide anions help rapid decomposition of lead(IV) esters.^{32,33} In the presence of acetate and pyridine, oxidative decarboxylation takes place, while in the presence of halide salts halodecarboxylation proceeds to give alkyl halides. Both reactions show similar behaviour towards oxygen inhibition. A radical chain mechanism similar to that for oxidative decarboxylation was proposed for the halodecarboxylation. The difference arises mainly in the nature of the propagation steps. In the latter reaction alkyl radicals are oxidized by ligand transfer, while in the former reaction, the radicals are oxidized by electron transfer. The proposed mechanism for halodecarboxylation which includes alkyl radicals and lead(III) species as intermediate is formulated in the following scheme:

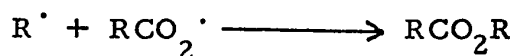
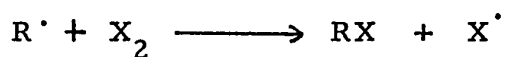
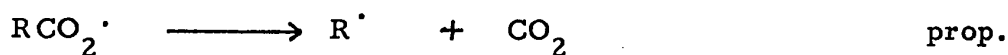
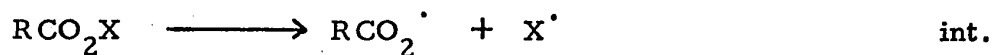




Halodecarboxylation of carboxylic acids is also achieved by the Hunsdiecker reaction which involves treatment of salts of carboxylic acids with a molecular halogen. The reaction is most efficient when the silver salt of the carboxylic acid is employed. The reaction has been used widely in preparation of halocompounds. The extensive applications and limitations to the Hunsdiecker reaction have been reviewed by Johnson and Ingham³⁴ and also by Wilson.³⁵ A free-radical mechanism has been proposed for the reaction. The first stage involves formation of an acyl hypohalide and metallic halide. The acyl hypohalide was suggested to be formed through one of the following two paths:³⁴



The sequence of Hunsdiecker reaction was suggested by Price,³⁶ and then modified by Berr³⁷ as represented below:

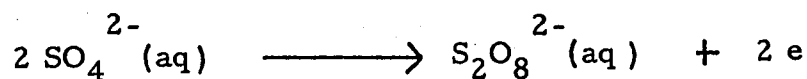


The isolation of coupling products in the bromination of silver picolinate and 2-pyridinecarboxylic acid³⁴ supports this mechanism. The catalysis by light,^{38,39} the production of racemic halides from optically active carboxylic acids,^{37,40,41,42} and the equilibration of geometrical cis- and trans-halides from each of the pure isomers of t-butyl cyclohexylcarboxylic acid,⁴³ also suggest a free-radical mechanism.

Cristol and Firth^{44,45} modified the reaction to get better yields of the halides by treating the acid with mercuric oxide and halogen. From the nature of the products in the original Hunsdiecker and modified Cristol-Firth reactions, a common acyl hypohalide intermediate was proposed.

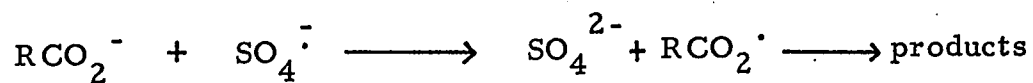
Carboxylic acids could also be oxidized by one-electron transfer using peroxydisulfate ion, which is considered one of the strongest oxidizing agents known in aqueous solution. The standard

oxidation-reduction potential for the reaction



is estimated to be -2.01 volts.⁴⁶

The oxidation of aliphatic and aromatic carboxylic acids by peroxydisulfate leads to the formation of alkyl or aryl radicals and the products obtained simulates those formed by Kolbe electrolysis. Fichter⁴⁷⁻⁵⁰ found that when potassium acetate was heated with aqueous potassium peroxydisulfate, the products included methane, ethylene, carbon dioxide and succinic acid, all of which are formed when diacetyl peroxide is heated in acetic acid. This result is consistent with the formation of acetoxy radicals which would arise from acetate ions and as proposed, the oxidation would be affected by one-electron transfer from a carboxylate anion to a sulfate radical anion. This work was later confirmed by Glasstone



and Hickling.¹⁶ On oxidation of toluene with potassium peroxydisulfate, Bacon⁵¹ obtained a 20% yield of bibenzyl as the coupling product of the benzyl radical formed. Oxidation of phenylacetic acid with peroxydisulfate lead to rapid and almost quantitative decarboxylation and the products were benzaldehyde and bibenzyl, the latter in 25% yield. Thomson⁵² obtained little biphenyl and biphenyl-4-carboxylic acid when sodium benzoate was heated with an aqueous solution of potassium peroxydisulfate. In the presence of

pyridine, oxidation of benzoic acid led to the formation of a mixture of phenylpyridines. Thomson also reported that the oxidation of phenylacetic acid and diphenylacetic acid gave the coupling product bibenzyl and 1,1,2,2-tetraphenylethane respectively.

The formation of aryl radicals during the oxidation of aromatic acids with peroxydisulfate was demonstrated in the formation of fluorenones from o-benzoylbenzoic acid⁵² and coumarin and 3,4-benzcoumarin from cis-cinnamic and biphenyl-2-carboxylic acids respectively.⁵³

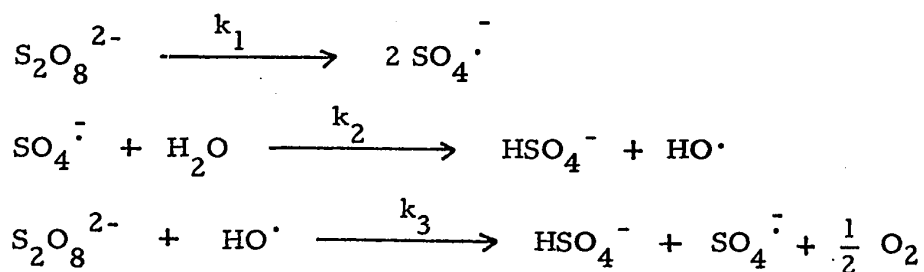
In a recent publication, Eberson⁵⁴ compared the electrolytic and peroxydisulfate oxidations of ethyl t-butyl malonate ion, t-butyl cyanoacetate ion and t-butyl malonate ion with respect to product distribution under almost identical conditions. The distribution of the coupling products are closely similar in the two reactions. No products derived from cationic intermediates are detected in the peroxydisulfate reaction. Needles^{31,55} found similarity in the products obtained when acylamino acids react with aqueous peroxydisulfate at 85-90° and the products from the reaction of the same acids with lead tetraacetate at 25° in dimethyl formamide.

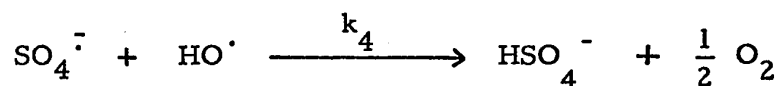
The kinetics of the oxidation of acids, alcohols, phenols, ketones, aldehydes and other organic compounds with peroxydisulfate have been studied. Sulfate free-radicals are generally produced in the decomposition of peroxydisulfate. This is evident from the fact that in polymerization studies using peroxydisulfate labelled with sulfur-35 polymer fragments containing radioactive sulfate

groups were isolated.⁵⁶⁻⁶⁰ The breakdown into free radicals was proposed by House⁶¹ to be irreversible, on the basis of an assumption that sulfate free-radicals would exchange electrons with sulfate ions at a rate comparable with their recombination to peroxydisulfate ions, and that no exchange of sulphur-35 between sulfate and peroxydisulfate ions has been observed under the kinetic experiments.⁶²⁻⁶⁵

The oxidation of various substrates can be catalyzed with metal ions. Silver and cupric ions are the most effective and most widely used. No absolute agreement was found, in the reported cases of the oxidation of the various substrates with peroxydisulfate, regarding the dependence of the rate of the oxidation reaction on the concentration of the reducing substrate. The lack of agreement was also noticed for the dependence of the rate on the peroxydisulfate and the metal ion catalyst concentrations in the catalyzed reactions. Yet, schemes for the catalyzed and uncatalyzed reactions were given to represent the mechanism of the reactions and to account for the generally observed rate laws.⁶¹

For the uncatalyzed reactions the scheme given for neutral, alkaline or slightly acidic solutions is as follows:



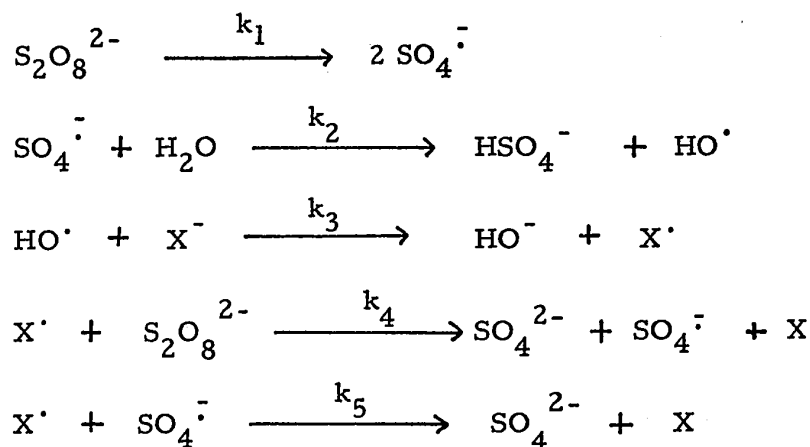


Using the steady state approximation for the radicals, a rate law was obtained as shown in equation (12). When an organic substrate

$$(12) \quad -d(\text{S}_2\text{O}_8^{2-})/dt = (k_1 k_2 k_3 / k_4)^{\frac{1}{2}} (\text{S}_2\text{O}_8^{2-})$$

is present it will compete with the water for the sulfate radical ion and with the peroxydisulfate ion for the hydroxyl radical.

It is generally assumed that the interaction of peroxydisulfate and organic compounds is initiated by the sulfate radical ion, but the possibility of the oxidation of carboxylate anion by hydroxyl radical cannot be excluded especially at elevated temperatures. Wiberg⁶⁶ showed that the peroxydisulfate oxidation of 2-propanol is initiated by hydroxyl radical. Thus, in the presence of a substrate X^- , the scheme given is represented below.



The observed rate law follows as (13)

$$(13) \quad -d(\text{X}^-)/dt = -d(\text{S}_2\text{O}_8^{2-})/dt = k_0 (\text{S}_2\text{O}_8^{2-})$$

The peroxydisulfate decomposed in the first and fourth steps leading to the rate expression

$$(14) \quad -d(X^-)/dt = k_1(S_2O_8^{2-}) + k_4(X^\cdot)(S_2O_8^{2-})$$

$$= [k_1 + k_4(X^\cdot)] (S_2O_8^{2-})$$

From equations (13) and (14)

$$(15) \quad k_o = k_1 + k_4(X^\cdot)$$

Using the steady state assumption, the concentration of the radical (X^\cdot) is constant and its value can be derived as in (16) (see appendix I).

$$(16) \quad (X^\cdot) = \left[-k_1 \pm (k_1^2 + 4 k_1 k_2 k_4 / k_5)^{\frac{1}{2}} \right] / 2 k_4$$

Substituting for the value of (X^\cdot) in equation (15)

$$(17) \quad k_o = k_1 + \frac{1}{2} \left[-k_1 \pm (k_1^2 + 4 k_1 k_2 k_4 / k_5)^{\frac{1}{2}} \right]$$

From equations (13) and (17)

$$(18) \quad -d(X^-)/dt = k_1 + \frac{1}{2} \left[-k_1 \pm (k_1^2 + 4 k_1 k_2 k_4 / k_5)^{\frac{1}{2}} \right] (S_2O_8^{2-})$$

Although the value of the rate of oxidation is not dependent on the concentration of the reducing substrate, it will vary from one system to the other according to the variation of the values of k_4 and k_5 which are different for different substrates.

Most of the kinetic work carried out on organic acids was on the oxidation of oxalic acid. Reports have also been given for formic and lactic acids. The stoichiometric equation for the oxidation of oxalate ion by peroxydisulfate has a simple form,

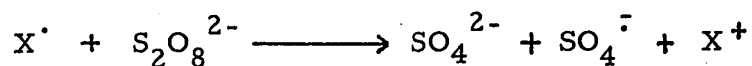
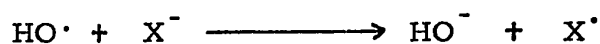


but the kinetics show all the characteristics of a complex chain reaction. The reaction shows an induction period when not deaerated. It is inhibited by oxygen and is catalysed by silver and cupric ions.⁶⁷⁻⁷⁵ All workers have agreed that the rate of the oxidation is not dependent on the oxalate concentration and is first order with respect to the peroxydisulfate ion concentration.

Recently Kumar and Saxena⁷⁶ studied the kinetics and the mechanism of the oxidation of lactic acid by peroxydisulfate. The rate was found to be first order in peroxydisulfate and independent of the reductant concentration. Hydrogen ion and oxygen catalyse the reaction. The system reduced Hg^{++} to Hg^+ , suggesting the production of transient free-radicals. A chain mechanism in which a radical-ion chain carrier participates and which is similar to the general scheme given previously for the uncatalysed reaction in neutral, alkaline and slightly acidic solution, accounts for the rate law.

Eberson studied the kinetics of oxidation of acetate, t-butyl malonate, t-butyl cyanoacetate and t-butyl malonate ions.^{11,12} The reactions exhibit the characteristics of many

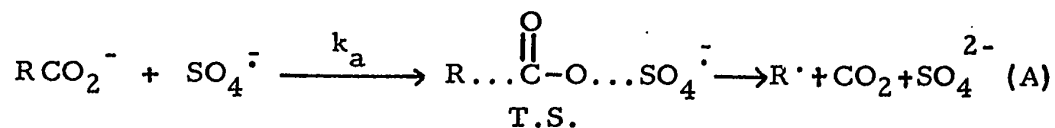
other peroxydisulfate oxidations in that, the reaction is first order in peroxydisulfate ion concentration and zero order in the substrate concentration. Nevertheless, the rate constant in the presence of the substrate is appreciably larger than that observed for the decomposition of peroxydisulfate in water alone. For the oxidation of acetate, Eberson excluded the possibility of having the hydroxyl radical as the oxidizing species as would be represented in the following equations.



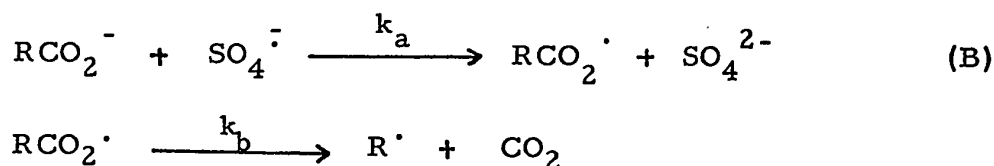
He based this conclusion on the fact that no products resulting from a carbonium ion intermediate could be isolated. Also, no coupling products were observed when t-butyl cyanoacetate ion was treated with Fenton's reagent, a known hydroxyl radical generating species. Thus Eberson concluded that the sulfate radical ion in all probability is the oxidizing species in the peroxydisulfate oxidation of carboxylate ions and, since no products derived from carbonium ions are observed, the radical $\text{X}\cdot$ cannot propagate a chain reaction as represented by the above equations.

An indefinite aspect in the mechanism of oxidative decarboxylation by one-electron transfer is whether the transfer of the electron from the carboxylate ion and the removal of the carbon dioxide molecule occur simultaneously (A) or there are two discrete steps involving the intermediacy of an acyloxy radical (B). In the

case of peroxydisulfate decarboxylation, the two alternatives are presented in the following equations.



or



Skell⁷⁷ measured the relative rate constants for the electrolysis of potassium alkylcarboxylates. He found that within a given molecular weight group, the nature of the alkylcarboxylate exerts little influence on the magnitude of the rate constant. Also, in water as solvent, a carboxylate with a higher molecular weight has a larger rate constant than a lower molecular weight carboxylate. In methanol all carboxylates are discharged at the same rate. This lead him to conclude that the nature of the alkyl radical generated, whether primary, secondary, or tertiary, exerted little influence on the rate of electrolysis and was taken as evidence for carboxylate radical intermediacy. Eberson⁷⁸ criticized Skell's results on the basis that using a competitive method to determine the relative rates of decarboxylation of the alkylcarboxylate was not a proper procedure when applied to the electrode process, a heterogenous system. The diffusion and adsorption effects on the rate of decarboxylation have to be taken into account. Moreover, it has long been recognized that

the alkaline media in which the electrolysis was performed, favor the formation of carbonium ions. Since no product studies were performed and the mechanism of the carbonium ion formation is still largely unknown, it is difficult to establish whether or not the relative rate values relate to the formation of radicals by the anodic oxidation of the carboxylate ions. The validity of using the observed relative rate constants as the actual rate constants of the rate-determining steps was also questioned. Further information about the standard potentials of the electrode processes involving the two competing alkylcarboxylate anions is needed and could be calculated only from appropriate thermodynamic data which are not available for most of the reactions studied by Skell.

The stepwise decarboxylation mechanism was also favored by other workers who studied the electrolysis of carboxylic acids. Dickinson and Wynne-Jones⁷⁹ in a theoretical discussion about Kolbe electrolysis supported the idea of the intermediacy of the acyloxy radical. Conway^{80,81} showed that trifluoroacetic acid decarboxylated on electrolysis in two separate steps. In representing the mechanism of Kolbe electrolysis, he proposed that the radical species absorbed on the electrode are the alkyl and acyloxy radicals. Fleishmann, Jonse and Kuhn⁸² represented the mechanism of the decarboxylation of formic acid on electrolysis as proceeding in a stepwise manner.

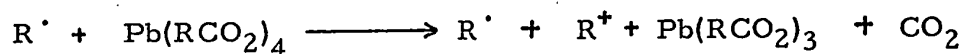
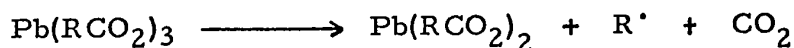
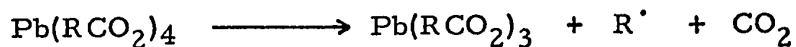
In support of the concerted mechanism, Eberson¹⁰ calculated the standard potential for a number of electrode processes 1-5, which could possibly take place at the anode in Kolbe electrolysis

of carboxylic acids, using thermodynamic data. He found that

1. $\text{RCO}_2^- \longrightarrow \text{RCO}_2^\cdot + e$
2. $\text{RCO}_2^\cdot \longrightarrow \text{R}^\cdot + \text{CO}_2$
3. $\text{R}^\cdot \longrightarrow \text{R}^+ + e$
4. $\text{RCO}_2^- \longrightarrow \text{R}^\cdot + \text{CO}_2 + e$
5. $\text{RCO}_2^\cdot \longrightarrow \text{R}^+ + \text{CO}_2 + e$

with acetate ion in aqueous solution the theoretically most favorable potential-determining step is an irreversible one-electron transfer with simultaneous bond breaking (step 4), thus favoring a concerted rather than a stepwise decarboxylation process for the carboxylate anion.

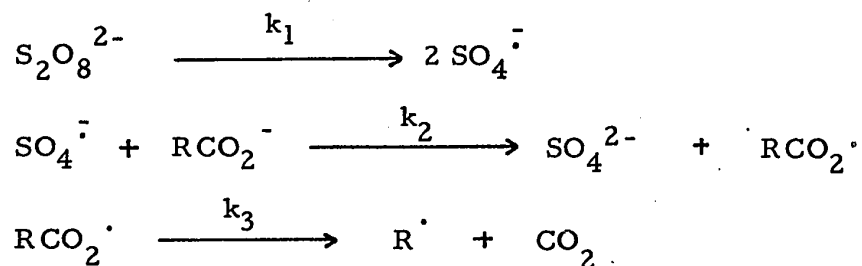
Kochi²⁷ in a study of the oxidative decarboxylation of pentanoic acid with lead tetraacetate postulated that the fragmentation of the carboxylate lead species, lead(IV) and lead(III) in the initial and propagation steps involves simultaneous two bond cleavage to generate lead(III) and lead(II), carbon dioxide and the alkyl radical directly rather than via a simple homolysis to an acyloxy radical intermediate as represented by the following scheme.



The homolysis of the lead carboxylate is favored when the alkyl radicals produced are of great stability.

The present work was aimed at resolving the conflict regarding the nature of the transition state during the one-electron transfer process from the carboxylate ion in the potassium peroxydisulfate promoted decarboxylation of carboxylic acids, and possibly to give some insight into the mechanism of the other decarboxylation reactions mentioned earlier.

The partial mechanism for the decarboxylation in concentrated aqueous base is best represented by the following scheme which is consistent with the results reported by various investigators.



Using the partial mechanism given above, the rate of disappearance of the carboxylate ion is given by (17).

$$(17) \quad -d(\text{RCO}_2^-)/dt = k_2 (\text{RCO}_2^-) (\text{SO}_4^{\cdot -})$$

The rate of formation of carbon dioxide is given by (18).

$$(18) \quad d(\text{CO}_2)/dt = k_3 (\text{RCO}_2^{\cdot})$$

Assuming a steady state concentration of the acyloxy radicals,

$$(19) \quad -d(\text{RCO}_2^{\cdot})/dt = k_3 (\text{RCO}_2^{\cdot}) - k_2 (\text{RCO}_2^-) (\text{SO}_4^{\cdot-}) = 0$$

From equation (19), the value of (RCO_2^{\cdot}) is given by (20).

$$(20) \quad (\text{RCO}_2^{\cdot}) = k_2/k_3 (\text{RCO}_2^-) (\text{SO}_4^{\cdot-})$$

Substituting the value of (RCO_2^{\cdot}) in equation (18)

$$(21) \quad d(\text{CO}_2)/dt = k_2 k_3 / k_3 (\text{RCO}_2^-) (\text{SO}_4^{\cdot-})$$

From equations (17) and (21)

$$(22) \quad -d(\text{RCO}_2^-)/dt = d(\text{CO}_2)/dt$$

Integrating (22) between t and 0 time

$$(23) \quad \int_0^t -d(\text{RCO}_2^-)/dt = \int_0^t d(\text{CO}_2)/dt$$

$$(24) \quad -(\text{RCO}_2^-)_t + (\text{RCO}_2^-)_0 = (\text{CO}_2)_t - (\text{CO}_2)_0$$

$$\text{As } (\text{CO}_2)_0 = 0$$

$$(25) \quad (\text{CO}_2)_t = (\text{RCO}_2^-)_0 - (\text{RCO}_2^-)_t = (\text{RCO}_2^-)_u$$

where the subscript (0) indicates the amount of either the carboxylate anion or carbon dioxide at 0 time, (t), the amount present at time t and (u), the amount used at time t .

To relate the rate of electron abstraction to the stability of the radicals formed, two different acids were decarboxylated in the same solution. Competitive rates of decarboxylation would give a correlation between the structures and the reactivities of the

acids decarboxylated.

Rearranging equation (17) and dividing the resultant rearranged equations for two acids, I and II, followed by integration between t and 0 time, over the total time t .

$$(26) \quad \frac{\int_0^t \frac{-d(\text{RCO}_2^-)^I}{(\text{RCO}_2^-)^I}}{\int_0^t \frac{-d(\text{RCO}_2^-)^{II}}{(\text{RCO}_2^-)^{II}}} = \frac{k_2^I (\text{SO}_4^{\cdot-})/dt}{k_2^{II} (\text{SO}_4^{\cdot-})/dt}$$

$$(27) \quad \frac{\ln \frac{(\text{RCO}_2^-)_0^I}{(\text{RCO}_2^-)_0^I - (\text{RCO}_2^-)_u^I}}{\ln \frac{(\text{RCO}_2^-)_0^{II}}{(\text{RCO}_2^-)_0^{II} - (\text{RCO}_2^-)_u^{II}}} = \frac{k_2^I}{k_2^{II}}$$

Substituting for $(\text{RCO}_2^-)_u$ by $(\text{CO}_2)_t$ from equation (25) and changing \ln to \log by multiplying by 2.303.

$$(28) \quad \frac{\log \frac{(\text{RCO}_2^-)_0^I}{(\text{RCO}_2^-)_0^I - (\text{CO}_2)_t^I}}{\log \frac{(\text{RCO}_2^-)_0^{II}}{(\text{RCO}_2^-)_0^{II} - (\text{CO}_2)_t^{II}}} = \frac{k_2^I}{k_2^{II}}$$

The quantities $(\text{CO}_2)^{\text{II}}$ and $(\text{CO}_2)^{\text{I}}$ can be differentiated when the competition reaction involves a carboxylic acid labelled with C^{14} on the carboxylate group and another nonradioactive acid. The former will give radioactive carbon dioxide, while the later will give nonradioactive carbon dioxide.

RESULTS

A number of para-, meta-, ortho-, and alpha-substituted phenylacetic acids and a series of secondary, tertiary, and allylic acids were subjected to oxidative decarboxylation with potassium peroxydisulfate in potassium hydroxide solution at 74.3° . The decarboxylation of the various acids was performed in competition with phenylacetic acid. The carbon dioxide liberated from both of the competing acids was measured using a high vacuum technique.⁸³ To differentiate between the carbon dioxide evolved from either of the acids being decarboxylated, the phenylacetic acid was labelled with carbon-14 in the carboxylate group. This gave a mixture of radioactive and non-radioactive carbon dioxide from the competitive decarboxylation reactions.

About 0.047 M solutions of the potassium salts of the acids were prepared by dissolving exact amounts of the acids in approximately 0.25 M potassium hydroxide solution. The reaction mixtures were prepared by mixing the required amount of the solutions of the potassium salts of the acids with the aqueous potassium peroxydisulfate solution in deoxygenated break seals. In competitive decarboxylation, the concentration of the acids in the mixture ranged from 0.013 to 0.015 M and that of peroxydisulfate was about 0.067 M. The carbon dioxide evolved was absorbed in the alkaline medium and was liberated upon acidification.

Phenylacetic acid-1-C¹⁴ was decarboxylated alone. The radioactive carbon dioxide evolved at various time intervals was

absorbed in a scintillation solution of ethanolamine, ethylene glycol monomethyl ether, toluene and the scintillator (PPO) after being quantitatively measured in the vacuum line. The radioactivity of the carbon dioxide was measured using the liquid scintillation counting techniques.⁸⁴ A linear relation was obtained between the molarity of the absorbed carbon dioxide and the number of counts as is shown in Figure I which was plotted from data in Table I.

In conjunction with the oxidative decarboxylation of phenylacetic acid, it is possible that benzoic acid could be formed during the reaction which would then undergo decarboxylation resulting in a greater amount of carbon dioxide than expected from phenylacetic acid alone. This possibility was eliminated because the addition of small amounts of benzoic acid to the reaction mixtures containing phenylacetic acid failed to produce any additional amounts of carbon dioxide.

Competitive Decarboxylation.

Competitive decarboxylation reactions between phenylacetic acid- 1-C^{14} and non-radioactive acids were carried out by mixing the acid solutions and the peroxydisulfate solution in the break seals as previously described. Quantitative yields of labelled and unlabelled carbon dioxide were obtained at 20 kinetic half-lives for the decarboxylation reaction. The total amount of carbon dioxide evolved from the two acids at any time interval was measured in the vacuum line. The carbon dioxide was absorbed in the scintillation solution and the radioactivity was determined.

The amount of carbon dioxide evolved from the phenylacetic acid-1-C¹⁴ was obtained graphically from Figure I. The carbon dioxide from the non-radioactive acid was obtained by subtraction from the total amount of the gas measured. Using the derived equation

$$\frac{k^I}{k^{II}} = \frac{\log \frac{(RCO_2^-)^I}{(RCO_2^-)^I - (CO_2)^I}}{\log \frac{(RCO_2^-)^I}{(RCO_2^-)^I - (CO_2)^{II}}}$$

the relative rate constants for the competitive decarboxylation reaction were calculated. In the above equation, k^I/k^{II} is the ratio of the rate constant of the decarboxylation of the non-radioactive acid to that of phenylacetic acid-1-C¹⁴. The starting concentrations of the acids in mol/l is represented by (RCO_2^-) and the number of mole/l of the carbon dioxide liberated at interval of times is represented by (CO_2) . The subscripts I and II indicate the non-radioactive and radioactive acids respectively.

Constant values for the relative rate constants ($\pm 4\%$) for the competitive decarboxylation of the two competing acids were obtained at varying percentage of the reaction throughout each run. Repeated runs gave reproduceable results as will be shown by the case of p-phenoxyphenylacetic acid and o-tolylacetic acid.

In Tables II to IX are reported the data for the derivation of the rate constants for the potassium peroxydisulfate promoted decarboxylation of para- and meta-substituted phenylacetic acids at

TABLE I

DECARBOXYLATION OF PHENYLACETIC ACID-1-C¹⁴ AT 74.3±0.10°.
 THE RELATION BETWEEN THE NUMBER OF MOLES OF CARBON
 DIOXIDE EVOLVED AT INTERVAL OF TIME AND THE NUMBER OF
 COUNTS CORRECTED FOR BACK GROUND SCINTILLATION.

phenylacetic acid-1-C¹⁴ (1.74×10^{-4} mol; 859 cpm/mg)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm
14.9	0.160	18882
24.1	0.305	33919
34.8	0.417	46639
40.7	0.432	50609
59.8	0.747	87326
79.9	0.918	100980
95.0	1.035	122538
112.4	1.138	131000
130.1	1.200	140773
150.2	1.353	150965
1800	1.797	197462

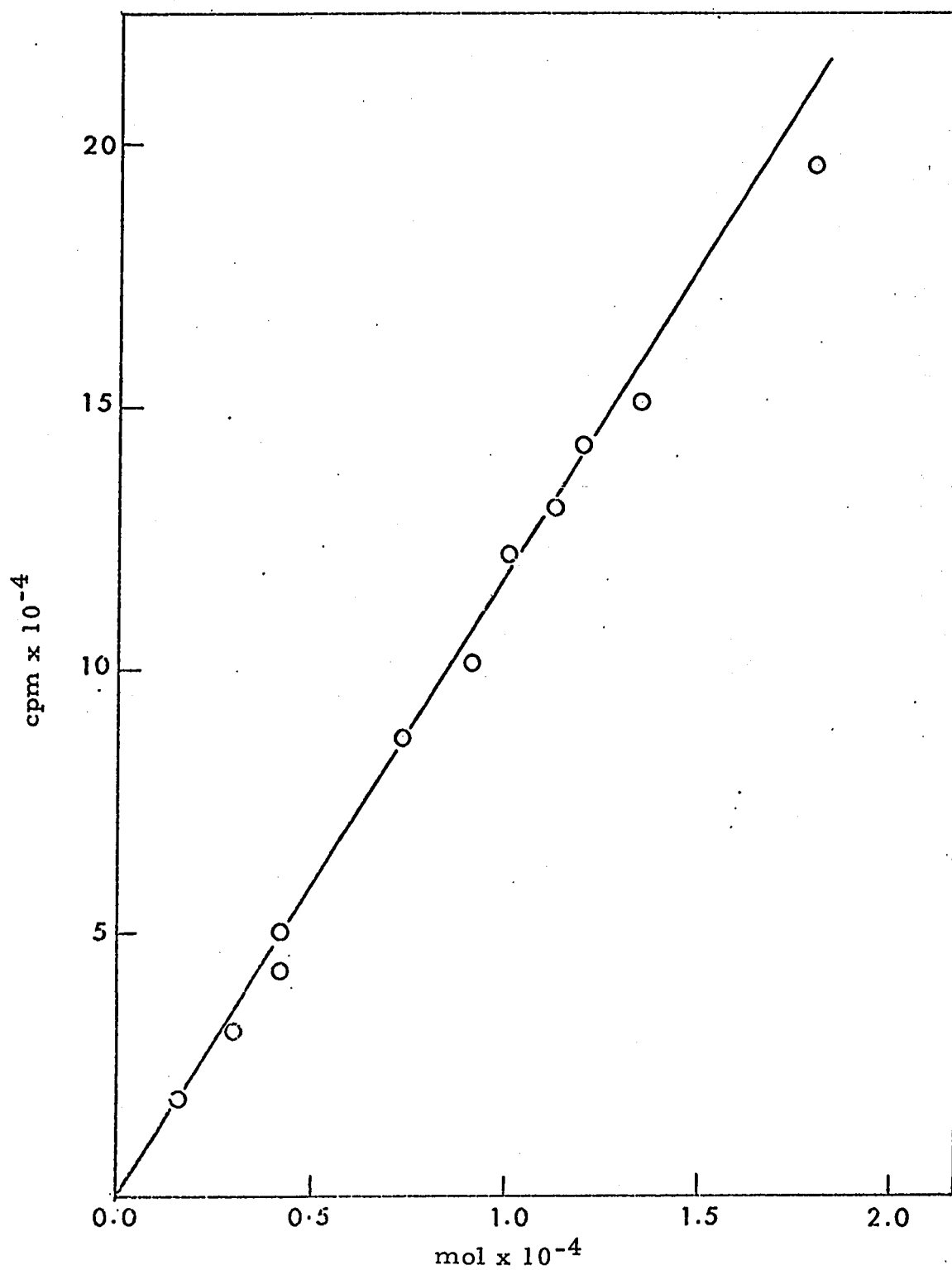


FIGURE I THE RELATION BETWEEN THE NUMBER OF MOLES OF CARBON DIOXIDE AND THE NUMBER OF COUNTS/MIN.

TABLE II

DECARBOXYLATION OF p-METHOXYPHENYLACETIC ACID
 (1.35×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

p-methoxyphenylacetic acid (0.880×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.956×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k ^I /k ^{II}
29.9	0.660	24597	0.221	0.439	2.63
35.2	0.815	32516	0.292	0.523	2.47
43.4	0.862	34504	0.313	0.549	2.46
50.2	0.924	40145	0.355	0.569	2.24
61.9	1.191	50331	0.474	0.721	2.50
2204	1.879	108894	0.952	0.920	

Average k^I/k^{II} = 2.46 ± 0.09

TABLE III
 DECARBOXYLATION OF p-PHENOXYPHENYLACETIC ACID
 (1.41×10^{-2} M) AND PHENYLACETIC ACID-1- C^{14} (1.47×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

p-phenoxyphenylacetic acid (0.953×10^4 mol)
 phenylacetic acid-1- C^{14} (0.916×10^4 mol)
 potassium Peroxydisulfate (3.70×10^4 mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
35.0	0.718	28232	0.247	0.471	2.17
40.1	0.816	32149	0.285	0.531	2.18
47.3	0.920	36954	0.326	0.594	2.22
55.1	0.993	41360	0.366	0.627	2.11
63.5	1.114	47070	0.417	0.697	2.16
1710	1.864	107561	0.983		

Average $k^I/k^{II} = 2.17 \pm 0.02^*$

* A repeated run of this reaction gave an average of $k^I/k^{II} = 2.15 \pm 0.10$

TABLE IV

DECARBOXYLATION OF p-TOLYLACETIC ACID (1.48×10^{-2} M)
AND PHENYLACETIC ACID- l -C 14 (1.47×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

p-tolylacetic acid (0.960×10^{-4} mol)

phenylacetic acid- l -C 14 (0.934×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO $_2$ (mol $\times 10^4$)	cpm	Active CO $_2$ (mol $\times 10^4$)	Inactive CO $_2$ (mol $\times 10^4$)	k I /k II
30.0	0.422	19639	0.173	0.249	1.46
35.0	0.516	24161	0.214	0.302	1.46
42.1	0.635	30276	0.270	0.365	1.40
50.1	0.721	33779	0.299	0.422	1.50
1690	1.884	107446	0.940	0.944	

$$\text{Average } k^I/k^{II} = 1.46 \pm 0.02$$

TABLE V

DECARBOXYLATION OF p-BROMOPHENYLACETIC ACID
 (1.36×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.36×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

p-bromophenylacetic acid (0.882×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.882×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
49.1	0.602	35956	0.306	0.296	0.959
56.0	0.666	39770	0.338	0.328	0.963
65.1	0.772	46531	0.393	0.379	0.952
78.4	0.884	52683	0.447	0.438	0.972
1844	1.818	104123	0.910	0.908	

$$\text{Average } k^I/k^{II} = 0.961 \pm 0.008$$

TABLE VI

DECARBOXYLATION OF p-CHLOROPHENYLACETIC ACID
 (1.45×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

p-chlorophenylacetic acid (0.940×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.954×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
30.5	0.389	21955	0.196	0.193	0.996
34.0	0.514	29842	0.262	0.252	0.972
43.4	0.556	32198	0.287	0.269	0.942
52.5	0.745	43704	0.385	0.359	0.931
61.5	0.992	57676	0.520	0.472	0.885
2145	1.839	108738	0.950	0.884	

Average $k^I/k^{II} = 0.944 \pm 0.03$

TABLE VII

DECARBOXYLATION OF m-FLUOROPHENYLACETIC ACID
 (1.37×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

m-fluorophenylacetic acid (0.893×10^{-4} mol)
 phenylacetic acid-1-C¹⁴ (0.953×10^{-4} mol)
 potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
30.0	0.435	26821	0.237	0.198	0.877
43.0	0.623	37962	0.338	0.285	0.877
50.0	0.752	45885	0.406	0.346	0.883
58.1	0.895	55029	0.486	0.409	0.859
2800	1.806	105587	0.926	0.880	

Average k^I/k^{II} = 0.875 ± 0.007

TABLE VIII

DECARBOXYLATION OF m-BROMOPHENYLACETIC ACID
 (1.35×10^{-2} M) AND PHENYLACETIC ACID-1- C^{14} (1.35×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

m-bromophenylacetic acid (0.879×10^{-4} mol)

phenylacetic acid-1- C^{14} (0.886×10^{-4} mol)

potassium peroxydisulfate (3.68×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
50.7	0.621	38535	0.337	0.284	0.814
60.0	0.739	47266	0.399	0.340	0.819
69.9	0.838	53271	0.453	0.385	0.804
88.0	0.973	61319	0.518	0.455	0.825
1414	1.781	103755	0.907	0.874	

Average k^I/k^{II} = 0.817 ± 0.008

TABLE IX

DECARBOXYLATION OF m-CHLOROPHENYLACETIC ACID
 (1.35×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.36×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

m-chlorophenylacetic acid (0.880×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.882×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k ^I /k ^{II}
39.8	0.507	33644	0.286	0.221	0.737
45.0	0.564	36311	0.311	0.253	0.778
55.6	0.689	44318	0.376	0.313	0.790
65.6	0.806	51973	0.438	0.368	0.789
74.9	0.917	57241	0.487	0.430	0.834
1780	1.788	101998	0.894	0.894	

Average k^I/k^{II} = 0.786 ± 0.02

74.3°. A minimum of four or five determinations of each ratio of the relative rate constants was determined at varying percentages of completion of the reaction. An average value for every relative rate is also calculated.

The relative rate constants obtained for the para- and meta-substituted phenylacetic acids were fitted into the Hammett equation

$$\log k^I/k^{II} = \rho\sigma \text{ (or } \sigma^+)$$

where ρ is the reaction constant and σ (or σ^+) is the substituent constant. The plots of the logarithm of the relative rate constants vs. the substituent(s) constants are shown in Figure II for σ^+ values and in Figure III for σ values. The values σ and σ^+ for the substituents are listed with the relative rate constants of the corresponding acids in Table X.

The values of the σ constants were taken from data of McDaniel and Brown.⁸⁵ The σ^+ constants were taken from data of Okomoto and Brown⁸⁶ except for the p-phenoxy substituent for which the value was taken from data of Russell and Williams,⁸⁷ and Kennedy and Brown.⁸⁸ The following linear free energy correlations⁸⁹ were obtained from the data in Table X by the least square calculation. See appendix II.

$$\log k^I/k^{II} = -0.601\sigma + 0.11 \quad s = 0.068 \quad r = 0.936$$

$$\log k^I/k^{II} = -0.430\sigma^+ + 0.08 \quad s = 0.039 \quad r = 0.981$$

where (r) is the correlation coefficient and (s) is the standard deviation.

TABLE X

Substituent	k^I/k^{II}	$\log k^I/k^{II}$	σ	σ^+
<u>p</u> -methoxy	2.46	0.3909	-0.268	-0.778
<u>p</u> -phenoxyphenyl	2.17	0.3361	-0.320	-0.570
<u>p</u> -methyl	1.46	0.1631	-0.170	-0.311
H	1.00	0.0000	0.000	0.000
<u>p</u> -bromo	0.961	-0.0173	0.232	0.150
<u>p</u> -chloro	0.944	-0.0250	0.227	0.114
<u>m</u> -fluoro	0.875	-0.0580	0.337	0.352
<u>m</u> -bromo	0.817	-0.0878	0.391	0.405
<u>m</u> -chloro	0.786	-0.1046	0.373	0.399

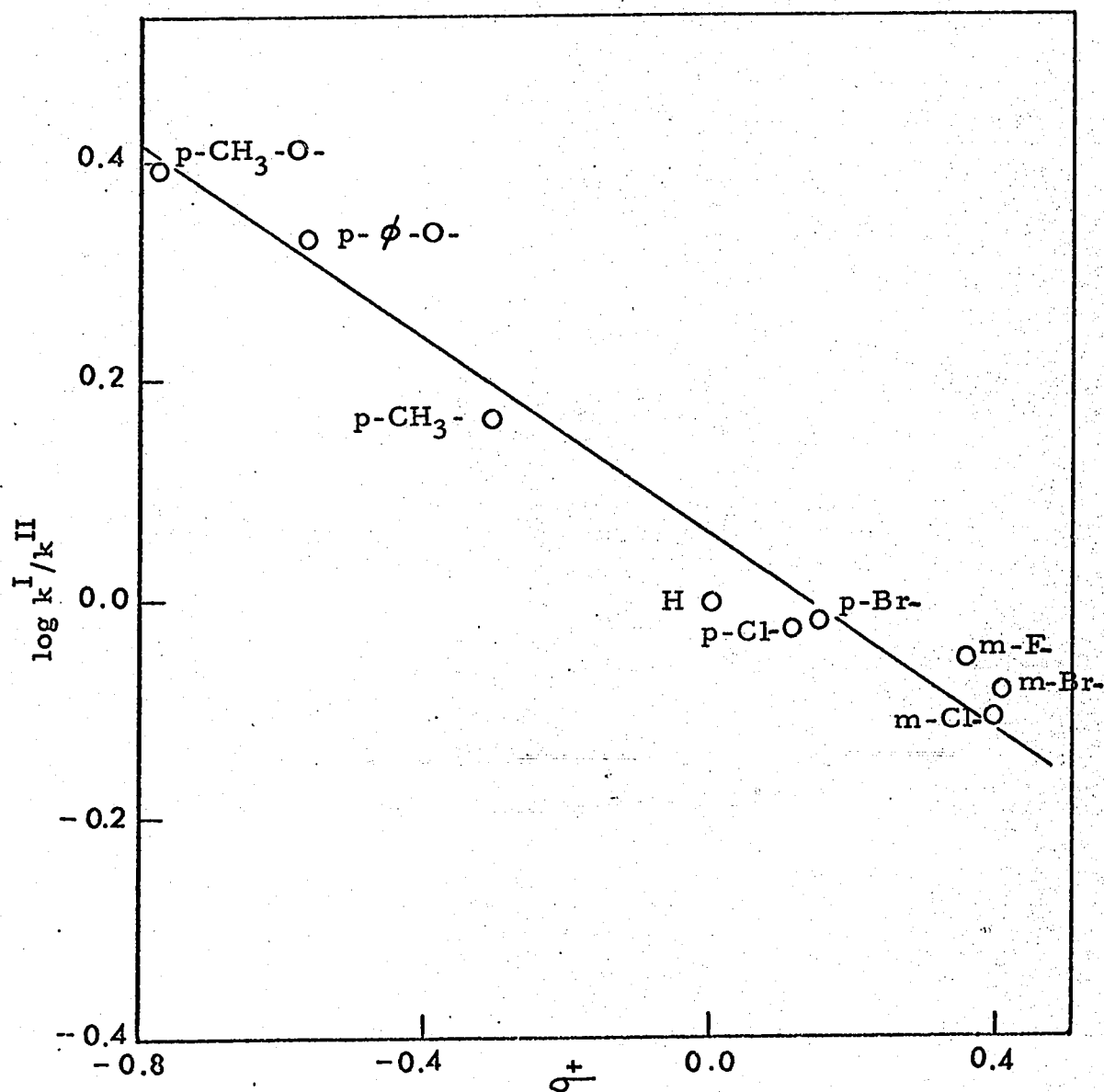


FIGURE II THE RELATION BETWEEN THE RELATIVE RATES OF DECARBOXYLATION OF meta- AND para-SUBSTITUTED PHENYLACETIC ACIDS AND THE SUBSTITUENT(S) CONSTANTS σ^+ .

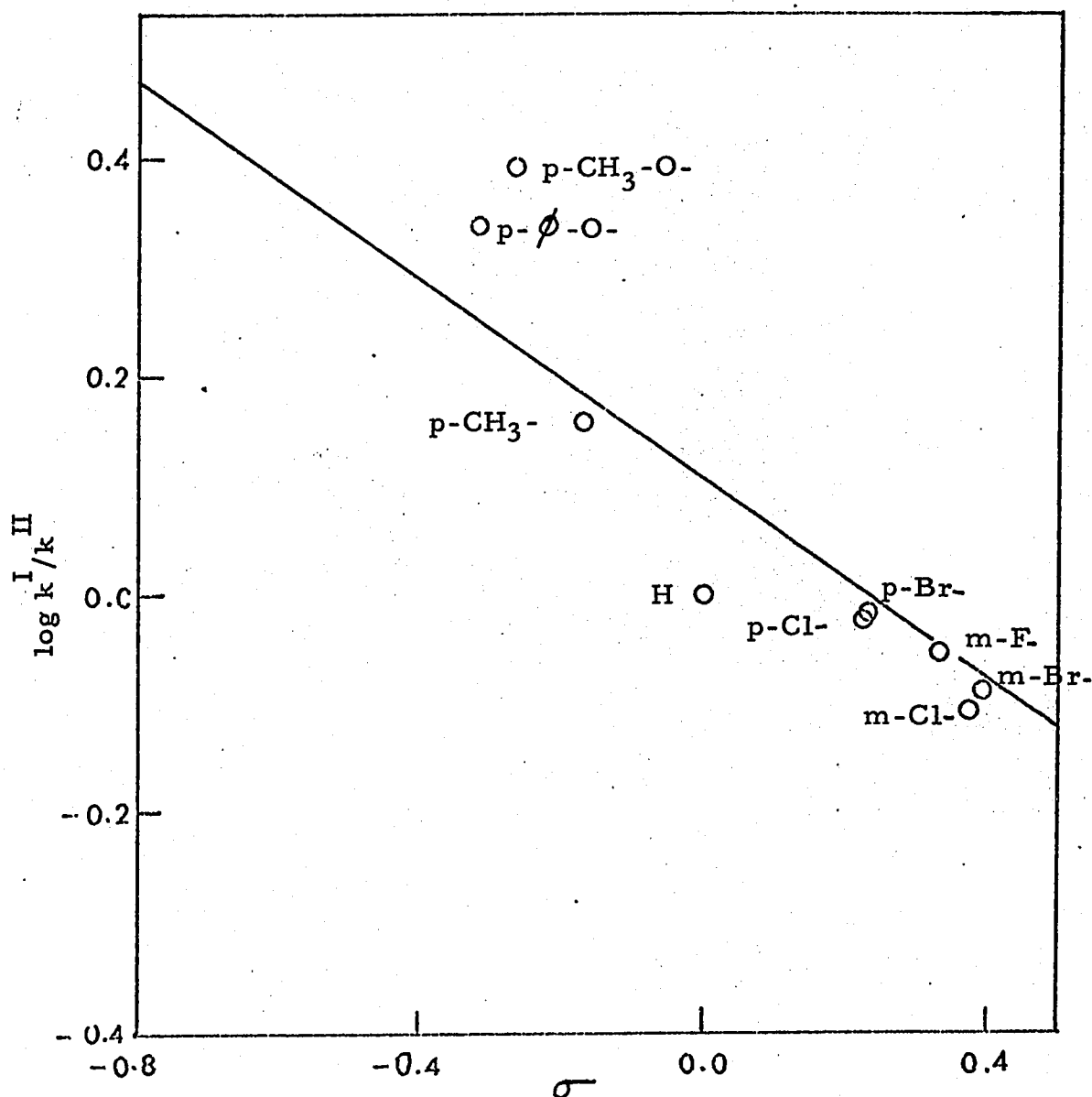


FIGURE III THE RELATION BETWEEN THE RELATIVE RATES OF DECARBOXYLATION OF meta- AND para-SUBSTITUTED PHENYLACETIC ACIDS AND THE SUBSTITUENT(S) CONSTANTS σ .

In Tables XII to XV are reported data for the derivation of the rate constants for the peroxydisulfate promoted decarboxylation of a number of secondary, tertiary and allylic acids relative to the benzylic acid, phenylacetic acid. Tables XVI to XXII list the data for the derivation of the relative rate constants for the decarboxylation of some alpha- and (or) ortho-substituted phenylacetic acids.

TABLE XI

DECARBOXYLATION OF MANDELIC ACID (1.45×10^{-2} M) AND
 PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M), AT $50.05 \pm 0.10^\circ$.

mandelic acid (0.942×10^{-4} mole)

phenylacetic acid-1-C¹⁴ (0.953×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (hr)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
10.0	0.633	45444	0.402	0.231	0.513
11.5	0.796	56143	0.498	0.298	0.515
14.0	0.935	64823	0.575	0.360	0.520
17.5	1.045	72261	0.639	0.406	0.508
23 days	1.839	109450	0.956	0.883	

$$\text{Average } k^I/k^{II} = 0.509 \pm 0.004$$

TABLE XII

DECARBOXYLATION OF ISOBUTYRIC ACID (1.38×10^{-2} M) AND
 PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

isobutyric acid (0.895×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.954×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
35.3	0.4122	48554	0.4120	0.0002	0.0004
39.2	0.4360	51026	0.4330	0.0030	0.0005
45.8	0.4800	56222	0.475	0.0050	0.0008
78.1	0.7463	86500	0.7280	0.0183	0.0014
25 days	1.836	108812	0.952	0.903	

$$\text{Average } k^I/k^{II} = 0.0008 \pm 0.0003$$

TABLE XIII

DECARBOXYLATION OF CYCLOHEXANECARBOXYLIC ACID
(1.47×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M),

AT $74.3 \pm 0.10^\circ$.

cyclohexanecarboxylic acid (0.953×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.953×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k ^I /k ^{II}
35.6	0.4590	52541	0.4470	0.0126	0.0021
40.2	0.5095	58581	0.4961	0.0134	0.0019
50.0	0.5640	62597	0.5311	0.0329	0.0042
60.0	0.6334	73359	0.6194	0.0140	0.0014
25 days	1.881	108276	0.951	0.930	

Average k^I/k^{II} = 0.0024 ± 0.0009

TABLE XIV

DECARBOXYLATION OF CYCLOHEXENE-3-CARBOXYLIC ACID
(1.47×10^{-2} M) AND PHENYLACETIC ACID-1- C^{14} (1.47×10^{-2} M),

AT $74.3 \pm 0.10^\circ$.

cyclohexene-3-carboxylic acid (0.957×10^{-4} mol)

phenylacetic acid-1- C^{14} (0.960×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO_2 (mol $\times 10^4$)	cpm	Active CO_2 (mol $\times 10^4$)	Inactive CO_2 (mol $\times 10^4$)	k^I/k^{II}
40.0	0.558	45278	0.385	0.173	0.385
46.1	0.599	50690	0.419	0.180	0.365
54.0	0.732	58450	0.506	0.226	0.359
61.6	0.790	64507	0.547	0.245	0.347
74.7	0.906	73631	0.623	0.283	0.335
2860	1.880	109824	0.957	0.923	

Average $k^I/k^{II} = 0.359 \pm 0.014$

TABLE XV

DECARBOXYLATION OF PIVALIC ACID (1.46×10^{-2} M) AND
 PHENYLACETIC ACID-1-C¹⁴ (1.46×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

pivalic acid (0.952×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.953×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
22.0	0.253	25173	0.214	0.039	0.165
28.0	0.328	32687	0.278	0.050	0.157
31.1	0.363	35916	0.306	0.057	0.160
35.5	0.427	42064	0.358	0.069	0.163
41.8	0.501	48742	0.414	0.087	0.169
70.0	0.757	72520	0.614	0.137	0.150
14 days	1.892	110500	0.965	0.927	

Average k^I/k^{II} = 0.161 ± 0.005

TABLE XVI

DECARBOXYLATION OF DIPHENYLACETIC ACID (1.45×10^{-2} M)
AND PHENYLACETIC ACID-1- C^{14} (1.47×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

diphenylacetic acid (0.946×10^{-4} mol)

phenylacetic acid (0.946×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
35.0	0.535	29152	0.253	0.282	1.34
40.0	0.581	29850	0.260	0.320	1.28
47.4	0.750	40129	0.356	0.394	1.14
55.0	0.850	45389	0.402	0.448	1.24
65.1	0.977	52902	0.468	0.509	1.13
1685	1.825	106882	0.938	0.887	

$$\text{Average } k^I/k^{II} = 1.19 \pm 0.06$$

TABLE XVII

DECARBOXYLATION OF TRIPHENYLACETIC ACID (1.48×10^{-2} M)
AND PHENYLACETIC ACID-1- C^{14} (1.47×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

triphenylacetic acid (0.960×10^{-4} mol)

phenylacetic acid-1- C^{14} (0.953×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
32.1	0.650	31062	0.277	0.373	1.43
36.2	0.769	36598	0.324	0.445	1.50
41.7	0.847	41929	0.371	0.476	1.40
49.2	0.931	45390	0.402	0.529	1.46
60.2	1.187	60012	0.532	0.655	1.40
2035	1.903	109645	0.956	0.947	

$$\text{Average } k^I/k^{II} = 1.44 \pm 0.03$$

TABLE XVIII

DECARBOXYLATION OF o-TOLYLACETIC ACID (1.47×10^{-2} M)
AND PHENYLACETIC ACID-1-C¹⁴ (1.49×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

o-tolylacetic acid (0.959×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.953×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
35.7	0.523	26565	0.226	0.297	1.37
41.9	0.718	38033	0.322	0.396	1.29
50.0	0.772	40063	0.346	0.426	1.30
58.1	0.770	39627	0.346	0.424	1.29
66.5	0.973	53079	0.441	0.532	1.30
2220	1.887	111587	0.964	0.923	

Average $k^I/k^{II} = 1.31 \pm 0.02^*$

* A repeated run of this reaction gave an average of $k^I/k^{II} = 1.30 \pm 0.08$

TABLE XIX

DECARBOXYLATION OF HYDRATROPIC ACID (1.47×10^{-2} M) AND
 PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M), AT $74.3 \pm 0.10^\circ$.

hydratropic acid (0.953×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.955×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
35.5	0.602	41703	0.354	0.248	0.651
42.3	0.758	52331	0.444	0.314	0.639
50.2	0.816	55981	0.474	0.342	0.648
56.9	0.927	62811	0.534	0.393	0.649
65.5	0.985	66714	0.565	0.420	0.669
2320	1.887	108945	0.952	0.937	

Average k^I/k^{II} = -0.651 ± 0.007

TABLE XX

DECARBOXYLATION OF α -METHYLHYDRATROPIC ACID(1.46 x 10⁻² M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47 x 10⁻² M),

AT 74.3 ± 0.10°.

 α -methylhydratropic acid (0.947 x 10⁻⁴ mol)phenylacetic acid -1-C¹⁴ (0.954 x 10⁻⁴ mol)potassium peroxydisulfate (3.70 x 10⁻⁴ mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
32.4	0.481	30869	0.272	0.209	0.742
36.1	0.539	34690	0.308	0.231	0.719
43.1	0.615	38030	0.338	0.277	0.785
50.2	0.747	54300	0.422	0.325	0.718
60.1	0.876	54970	0.485	0.391	0.746
1845	1.877	109128	0.957	0.920	

Average k^I/k^{II} = 0.743 ± 0.017

TABLE XXI

DECARBOXYLATION OF o-METHYLHYDRATROPIC ACID
 (1.46×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

o-methylhydratropic acid (0.950×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.953×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
35.1	0.573	32759	0.278	0.295	1.08
42.2	0.683	39562	0.335	0.348	1.05
49.9	0.812	47470	0.402	0.410	1.03
57.2	0.828	48494	0.412	0.416	1.02
66.3	0.960	55198	0.468	0.492	1.08
1845	1.870	106034	0.930	0.940	

Average k^I/k^{II} = 1.05 ± 0.02

TABLE XXII

DECARBOXYLATION OF p-METHYLHYDRATROPIC ACID
 $(1.50 \times 10^{-2} \text{ M})$ AND PHENYLACETIC ACID- 1-C^{14} $(1.48 \times 10^{-2} \text{ M})$,

AT $74.3 \pm 0.10^\circ$.

p-methylhydratropic acid $(0.975 \times 10^{-4} \text{ mol})$

phenylacetic acid- 1-C^{14} $(0.960 \times 10^{-4} \text{ mol})$

potassium peroxydisulfate $(3.70 \times 10^{-4} \text{ mol})$

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
31.0	0.550	31410	0.266	0.284	1.06
34.9	0.578	32200	0.272	0.306	1.13
40.1	0.649	37429	0.317	0.332	1.04
50.1	0.748	42889	0.366	0.382	1.04
60.1	0.868	49774	0.422	0.446	1.06
2030	1.908	107105	0.939	0.969	

Average $k^I/k^{II} = 1.06 \pm 0.02$

MEASUREMENT OF pK_a OF ACIDS.

To correlate the acidity of the substituted phenylacetic acids with their structures, data on the dissociation constants of the acids was needed. The pK_a values for some acids were obtained from the reported values of their dissociation constants in aqueous solution, K_a .⁹⁰ The pK_a values for the unreported acids were obtained from the measurement of their pH in aqueous solution. The dissociation constant of an acid AH is given by equation (1).

$$(1) \quad K_a = \frac{a_{H^+} \cdot a_{A^-}}{a_{AH}} = \frac{\gamma_{H^+} \cdot \gamma_{A^-}}{\gamma_{AH}} \times \frac{[H^+][A^-]}{[AH]}$$

where a is the activity, γ is the activity coefficient and the brackets represent the concentrations. If the activity coefficient term is neglected, the dissociation constant of the acid, K_a will be given by equation (2).

$$(2) \quad K_a = \frac{[H^+][A^-]}{[AH]}$$

The hydrogen ion concentration is obtained by rearranging equation (2).

$$(3) \quad [H^+] = K_a \times \frac{[AH]}{[A^-]}$$

and

$$(4) \quad -\log [H^+] = -\log K_a + \log \frac{[A^-]}{[AH]}$$

or

$$(5) \quad pH = pK_a + \log \frac{[A^-]}{[AH]}$$

When the acid is half-neutralized, $[A^-] = [AH]$ and the second term on the right-hand side of equation (5) will be zero. The pK_a of the acid can then be taken as equal to the pH of its half-neutralized solution.

The pH measurements were taken on a pH meter adjusted to the known pH of the half-neutralized phenylacetic acid aqueous solution. The pK_a values for a number of acids whose dissociation constants are known were measured on the adjusted pH meter. There was a deviation between the values reported and the values observed. This deviation resulted from the fact that the activity coefficient term in equation (1) was neglected. The reported dissociation constants were based on conductivity data which accounted for the activity coefficients of the acids and the ions.

By plotting the observed values of the pK_a vs the reported ones, a straight line was obtained which was used as a correction in the measurements of the pK_a of the unreported acids. The correction was found to give good agreement between the observed and the reported values of pK_a for a number of other reported acids. The plot of the relation is shown in Figure IV which is based on the data in Table XXIII.

The pK_a value for p-phenoxyphenylacetic acid was not measured due to the insolubility of the acid in water. Measurement in a dioxan-water mixture, in which the acid is soluble, failed to give any correlation with the reported data. The dissociation constant of this acid was obtained from the plot of the $-\log$ of the dissociation constants of the meta- and para-substituted phenylacetic acids vs the corresponding substituents' constants (σ).

TABLE XXIII

Acid	pK_a reported	pK_a observed
phenylacetic	4.31	4.31
<u>p</u> -tolylacetic	4.37	4.38
<u>m</u> -chlorophenylacetic	4.14	4.13
pivalic	5.05	5.07

TABLE XXIV

THE RELATIVE RATES OF DECARBOXYLATION OF THE ACIDS
WITH THE CORRESPONDING DISSOCIATION CONSTANTS (AT 25°).

Acid	k^I/k^II	K_a	pK_a
<u>p</u> -methoxyphenylacetic	2.46	$4.36 \times 10^{-5*}$	4.36
<u>p</u> -phenyloxyphenylacetic	2.17	$3.93 \times 10^{-5**}$	4.40
<u>p</u> -tolylacetic	1.46	$4.27 \times 10^{-5*}$	4.37
phenylacetic	1.00	$4.88 \times 10^{-5*}$	4.31
<u>p</u> -bromophenylacetic	0.961	$6.43 \times 10^{-5*}$	4.19
<u>p</u> -chlorophenylacetic	0.944	$6.45 \times 10^{-5*}$	4.19
<u>m</u> -fluorophenylacetic	0.875	7.08×10^{-5}	4.15
<u>m</u> -bromophenylacetic	0.817	7.39×10^{-5}	4.14
<u>m</u> -chlorophenylacetic	0.786	$7.24 \times 10^{-5*}$	4.14
cyclohexanecarboxylic	0.0024	$1.26 \times 10^{-2*}$	4.90
isobutyric	0.0008	$1.32 \times 10^{-5*}$	4.86
pivalic	0.161	$8.91 \times 10^{-6*}$	5.05
cyclohexene-3-carboxylic	0.359	2.90×10^{-5}	4.54
diphenylacetic	1.19	$1.15 \times 10^{-4*}$	3.94
triphenylacetic	1.44	$1.09 \times 10^{-4*}$	3.96
<u>o</u> -tolylacetic	1.31	4.47×10^{-5}	4.45

continued . . .

TABLE XXIV - Continued

Acid	k^I/k^{II}	K_a	pK_a
hydratropic	0.651	3.89×10^{-5} *	4.41
<u>α</u> -methylhydratropic	0.743	3.02×10^{-5}	4.52
<u>o</u> -methylhydratropic	1.05	3.80×10^{-5}	4.42
<u>p</u> -methylhydratropic	1.06	3.55×10^{-5}	4.45

* Values taken from the data on the dissociation constants of organic acids in aqueous solution reported in the International Union of Pure and Applied Chemistry.⁹⁰

** Value obtained from the plot of the log of the dissociation constants of meta- and para-substituted phenylacetic acids vs the corresponding substituent constant (σ).

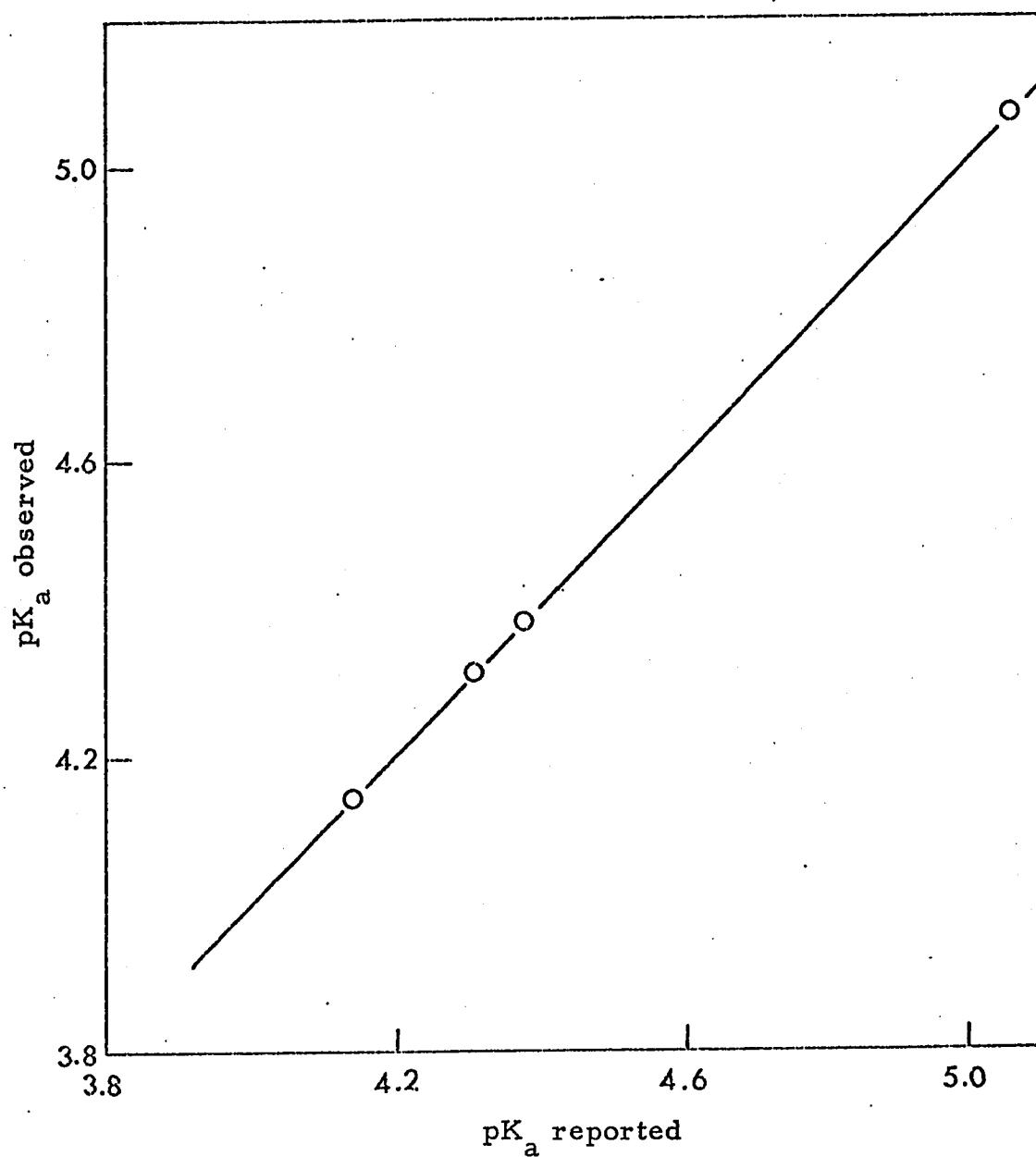


FIGURE IV THE RELATION BETWEEN THE REPORTED AND THE OBSERVED pK_a 'S FOR PHENYLACETIC ACID, p-TOLYLACETIC ACID, m-CHLOROPHENYLACETIC ACID AND PIVALIC ACID.

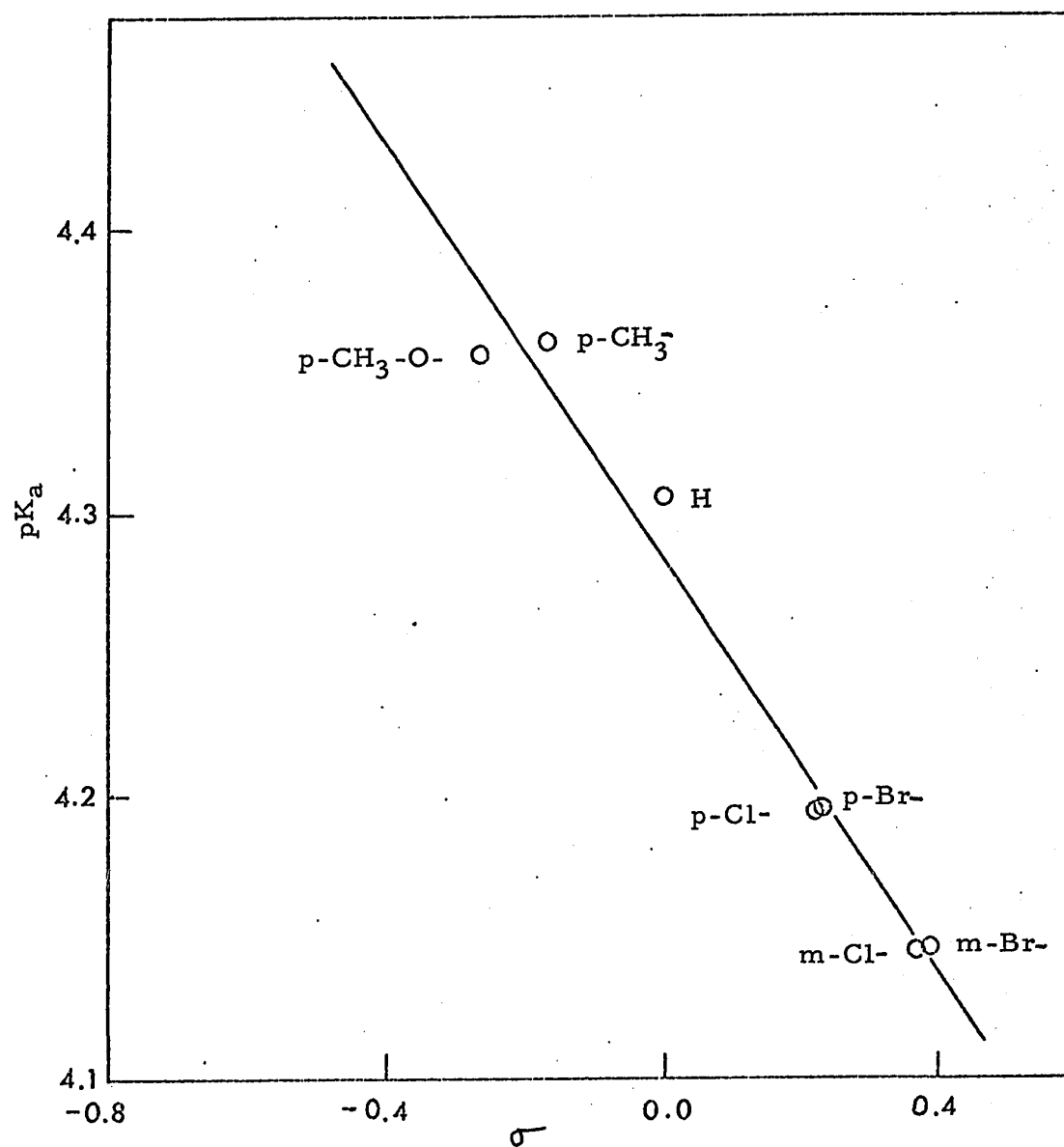


FIGURE V THE RELATION BETWEEN THE DISSOCIATION CONSTANTS OF THE meta- AND para-SUBSTITUTED PHENYLACETIC ACID AND THE SUBSTITUENT(S) CONSTANTS σ .

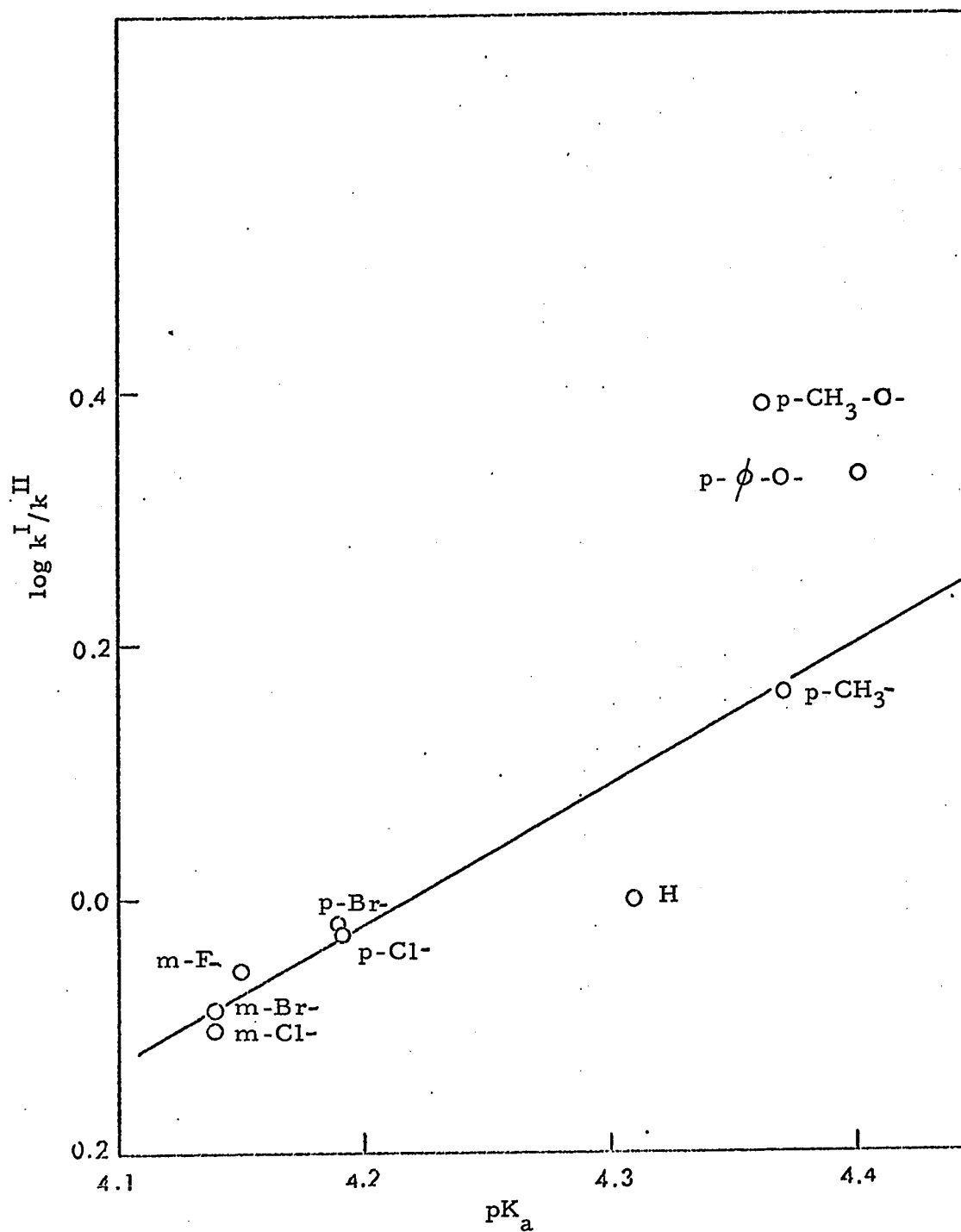


FIGURE VI THE RELATION BETWEEN THE RELATIVE RATES OF DECARBOXYLATION OF meta- AND para-SUBSTITUTED PHENYLACETIC ACIDS AND THEIR CORRESPONDING pK_a 'S.

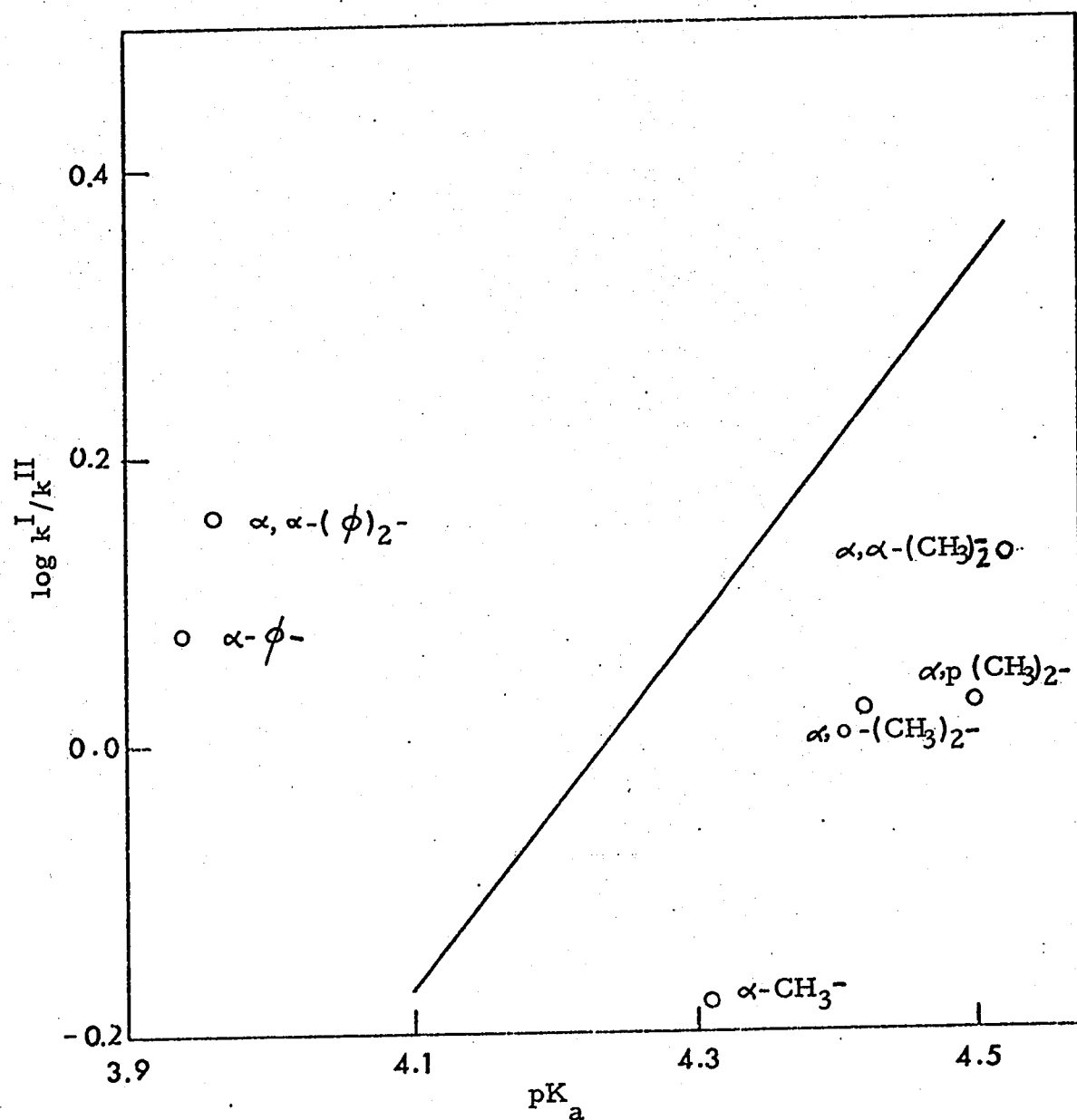


FIGURE VII THE RELATION BETWEEN THE RELATIVE RATES OF DECARBOXYLATION OF alpha-SUBSTITUTED PHENYLACETIC ACIDS AND THEIR CORRESPONDING pK_a 'S.

The products from the reaction of phenylacetic acid and potassium peroxydisulfate run to infinity were analysed by glpc. Freon-112 was used as an internal standard. The reaction mixture was extracted with ether. An insoluble polymeric material was left behind. The yellow solid polymer was isolated, washed with ether and water repeatedly and dried. It was insoluble in the common organic solvents (n-pentane, benzene, toluene, acetone, carbon tetrachloride, methylene chloride, chloroform, methyl alcohol and ethyl alcohol). It dissolved in dimethyl formamide and dimethyl sulfoxide. The average molecular weight of the polymer is 1400 and the elemental analysis shows, C, 63.26%; H, 4.31%; O, 20.19%; S, 2.33%. Its spectrum shows a strong hydroxyl band (3440 cm^{-1}) and a weak carbonyl band (1700 cm^{-1}). An approximate molecular formula for the polymer was calculated to be $\text{C}_{72}\text{H}_{60}\text{O}_{17}\text{S}_1$.

The products from the decarboxylation of phenylacetic acid with varying concentration of potassium peroxydisulfate are reported in Tables XXV-XXVII. The Tables also list the percentage of the products relative to the initial amount of phenylacetic acid.

TABLE XXV

PRODUCTS FROM THE REACTION OF PHENYLACETIC ACID
(2.94×10^{-2} M) AND POTASSIUM PEROXIDISULFATE (3.80×10^{-2} M),

AT $74.3 \pm 0.10^\circ$.

phenylacetic acid (5.73×10^{-4} mol; 0.078 g)

potassium peroxydisulfate (7.40×10^{-4} mol)

Product	Mol $\times 10^4$	% of phenylacetic acid
CO ₂	5.73	100
toluene	0.018	0.313
benzaldehyde	0.048	0.845
bibenzyl	0.399	13.93
polymer (0.047 g)		

TABLE XXVI

PRODUCTS FROM THE REACTION OF PHENYLACETIC ACID
 (2.94×10^{-2} M) AND POTASSIUM PEROXYDISULFATE (5.70×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

phenylacetic acid (5.73×10^{-4} mol; 0.078 g)

potassium peroxydisulfate (11.13×10^{-4} mol)

Product	Mol $\times 10^4$	% of phenylacetic acid
CO ₂	5.73	100
toluene	0.057	1.49
benzaldehyde	0.178	4.42
bibenzyl	0.412	10.86
polymer (0.051 g)		

TABLE XXVII

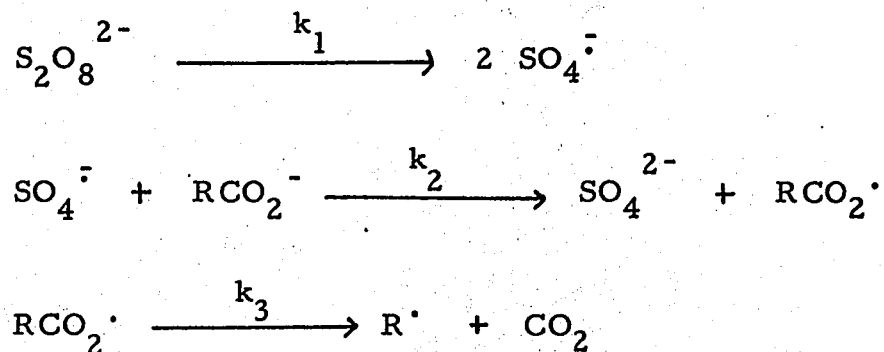
PRODUCTS FROM THE REACTION OF PHENYLACETIC ACID

 $(2.94 \times 10^{-2} \text{ M})$ AND POTASSIUM PEROXYDISULFATE $(9.47 \times 10^{-2} \text{ M})$,AT $74.3 \pm 0.10^\circ$.phenylacetic acid $(5.73 \times 10^{-4} \text{ mol; } 0.078 \text{ g})$ potassium peroxydisulfate $(18.46 \times 10^{-4} \text{ mol})$

Product	Mol. $\times 10^4$	% of phenylacetic acid
CO ₂	5.73	100
bibenzyl	0.953	33.40
polymer (0.033 g)		

DISCUSSION

A partial mechanism for the potassium peroxydisulfate promoted decarboxylation of carboxylic acid in concentrated aqueous base was presented at the end of the introduction section, in a scheme which is consistent with reported results. The scheme follows as shown below.



It was assumed that a steady concentration of the acyloxy radicals is reached at an early stage in the reaction. Based on the above scheme and the steady state assumption, a derivation of the relative rate of the electron abstraction in a reaction where two acids are competing was obtained as represented below.

$$k_2^{\text{I}}/k_2^{\text{II}} = \frac{\log \frac{(\text{RCO}_2^-)^{\text{I}}}{(\text{RCO}_2^-)^{\text{I}} - (\text{CO}_2)^{\text{I}}}}{\log \frac{(\text{RCO}_2^-)^{\text{II}}}{(\text{RCO}_2^-)^{\text{II}} - (\text{CO}_2)^{\text{II}}}}$$

In all cases investigated in this work, the relative rate constants in the competitive reactions with radioactive phenylacetic acid were obtained utilizing the above equation. It was found that the relative rates were constant in at least four or five determinations at varying percentages of completion of the reaction. These constant values for the relative rate constants of the electron abstraction from the pair of anions were taken as an evidence in support of the scheme proposed for the mechanism of the reaction.

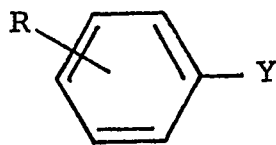
The results of the competitive decarboxylation reactions between phenylacetic acid-1-C¹⁴ and nonradioactive meta- and para-substituted phenylacetic acids were represented collectively in Table X. The rate of the electron transfer was found to decrease with the decreasing electron density at the benzylic carbon. This trend is opposite to that observed in the effects of the substituents on the dissociation constants for substituted phenylacetic acids. The relative rates of decarboxylation for the p-methoxy, p-phenoxy, p-methyl, p-chloro, p-bromo, m-fluoro, m-bromo, and m-chlorophenylacetic acids with the corresponding dissociation constants of the acids are listed in Table XXIV. The values of the dissociation constants were either measured in the present work or taken from data in the literature. Substituents in phenylacetic acid which gave an increased pK_a had the effect of decreasing the rate of decarboxylation of the acid as indicated by the data in Table XXIV. The effect of the substituents on the dissociation constants reflects the stabilization or the destabilization of the carboxylate anion. The

opposite effect of the same substituents on the rate of the electron transfer is consistent with substituent stabilization leading to electron transfer from a carboxylate anion.

Hydrogen atom abstraction from the methylene group of phenylacetic acid could possibly be taking place to give a radical which would give a sulfate ester by coupling with a sulfate radical ion or by displacement on a peroxydisulfate anion. The sulfate ester would then undergo hydrolysis to give mandelic acid. The latter acid, if formed in this way, would complicate the measurements of the relative rate constants for the decarboxylation of the phenylacetic acids. This possibility was excluded by decarboxylating mandelic acid in competition with phenylacetic acid- $l\text{-C}^{14}$. It was found that mandelic acid decomposes much slower than phenylacetic acid. The relative rate is (0.514). With this value, any intervention of mandelic acid would result in inconsistent values for the rates throughout every run, which was not observed.

The effect of the substituents was further employed to investigate whether the electron transfer from the carboxylate group is a concerted process with the loss of the carbon dioxide molecule or the latter is a distinct and separate step. The data in Table X, the relative rate constants and the corresponding substituent constants, were fitted to the Hammett equation.

The Hammett equation is a general quantitative linear free energy relationship between the substituent R and the reactivity of the side chain in the structure below.

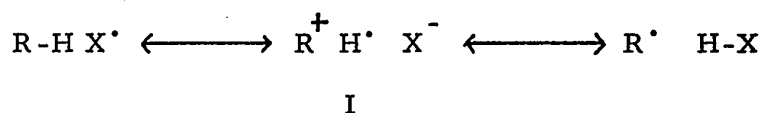


This relation is applied in the form; $\log (k/k^0) = \rho\sigma$, where k and k^0 are rates or equilibrium constants for reactions of the substituted and the unsubstituted compounds, respectively. The substituent constant, σ , depends solely on the nature and position of the substituent R and the reaction constant, ρ , depends on the reaction, the condition under which it takes place, and the nature of the side chain Y . The validity of the Hammett equation is restricted to substituents in the meta- and para-positions of the benzene ring. This equation was tested by Hammett⁹¹ on fifty-two reaction series and was found to correlate a large body of experimental data with a mean deviation of about $\pm 15\%$. Since then many additional reactions which permit the application of the equation have been investigated. The standard deviation (s) which is proportional to the probable error, and the correlation coefficient (r) are the two parameters chosen as the measure of the precision of the fit of the data to the Hammett equation. The significance of these parameters has been outlined by Jaffe⁸⁹, in an arbitrary scale, who considered $r > 0.99$ to indicate excellent, $r > 0.95$ satisfactory, and $r > 0.90$ fair fit to the Hammett equation. If $r < 0.90$ but > 0.80 when $\rho > 1.0$, and if $r < 0.80$ when $\rho > 0.50$, the data is considered as not being adequately represented by the equation. Reactions are considered to violate the Hammett equation if (s) exceeds certain values for

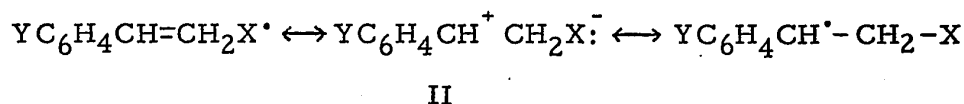
certain ranges of ρ as follows: $s > 0.4$ for all ρ , $s > 0.3$ for $\rho > 3$, $s > 0.25$ for $\rho > 2$ and $s > 0.2$ for $\rho > 1$. In the equation originally proposed by Hammett the sigma-values were defined in terms of the relative acidities of the benzoic acids. Powerful direct conjugative interaction between para-substituents and some reaction centers were recognized by Hammett as a major cause of failure of the equation. Subsequent investigations of reaction series, having powerful resonance requirements of aliphatic and aromatic systems, have yielded a number of specialized sigma values. One of these is the σ^+ which is an enhanced value of the substituent constant for direct conjugation in an electron demanding reaction. The values of σ^+ were based on the solvolysis of substituted t-cumyl chloride. Brown and Okamoto⁸⁶ used the calculated value of the reaction constant to estimate a total of 41 electrophilic substituent constants. Additional values have also been estimated.⁹²

Variations in the rates of free-radical reactions with substituents are expected whenever the radical formed can be stabilized by delocalization. However many free-radical reactions show significant electronic changes in their transition state leading to a dependence upon polar effects. Consequently the application of the Hammett equation to these reactions is possible. The competitive photochlorination of a series of substituted toluenes was studied by Walling and Miller.⁹³ The reactivities of the substituted toluenes were correlated with the sigma-values of the substituents.

Russell and Williamson⁸⁷ found that the attack of chlorine atoms upon substituted toluenes and of peroxy radicals upon substituted cumenes show a polar effect best correlated by σ^+ constants. This polar effect was attributed to contribution of resonance structure I to the transition state.



A similar resonance structure, II is responsible for the polar effect which was found in the autooxidation of substitute styrenes.



The relative rates for hydrogen abstraction from substituted toluenes by a bromine atom show an excellent fit to the Hammett correlation when σ^+ values are used.⁹⁴ Ingold and Kennedy⁸⁸ reported that σ^+ gave a better correlation than σ with the relative rates of hydrogen atom abstractions from substituted toluenes by t-butoxy radicals in carbon tetrachloride. The relative rates of the reaction of eleven meta- and para-substituted phenols with styrylperoxy radical have been measured by Howard and Ingold⁹⁵ and have been shown to give excellent correlation with the electrophilic substituent constants σ^+ . Relative rates of abstraction by t-butoxy radicals of an α -hydrogen atom from an alkyl side-chain, attached to aromatic nuclei, were studied by Johnson and Williams⁹⁶ and were found to correlate with σ values of the nuclear substituents. A kinetic

study of the thermal decomposition of t-butyl perbenzoate and four para-substituted peresters has been accomplished by Blomquist and Bernstein.⁹⁷ They observed that the rates of the decomposition of all of the peresters studied were correlated by the Hammett equation. The correlation followed the σ^- values of the substituents. Bartlett and Ruchardt⁹⁸ measured the decomposition rate of t-butyl phenylperacetate and its p- and m-methoxy, p-methyl, p- and m-chloro and p-nitro derivatives at a series of temperatures. They found that the rate constants fit the Hammett equation using σ^+ rather than σ^- values.

The present results on the relative rates of decarboxylation of the meta- and para-substituted phenylacetic acids when fitted to the Hammett equation showed the following linear free energy correlations. Using Jaffe's criteria for the correlation, it is

$$\log (k^{\text{I}}/k^{\text{II}}) = -0.601\sigma^- + 0.11 \quad s = 0.068 \quad r = 0.936$$

$$\log (k^{\text{I}}/k^{\text{II}}) = -0.430\sigma^+ + 0.08 \quad s = 0.039 \quad r = 0.981$$

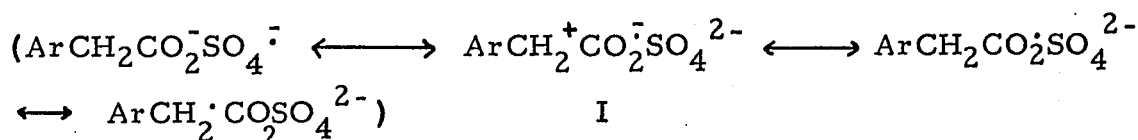
obvious that there is a good correlation with σ^+ values while there is only a fair fit with σ^- substituent constants.

The values of the dissociation constants of the meta- and para-substituted phenylacetic acids measured by Dippy and Watson,⁹⁹ were correlated by Jaffe.⁸⁹ The dissociation constants of 14 acids in aqueous solution at 25° gave the following parameters when fitted in the Hammett equation.

$$\rho = 0.439 \quad s = 0.033 \quad r = 0.981$$

The opposite sign of ρ for the dissociation and the decarboxylation reactions of the substituted phenylacetic acids is in accord with a substituent stabilization effect on the formation of the carboxylate anion in the first reaction and an electron transfer from the carboxylate anion in the second reaction.

There is a large difference between the σ^+ and σ^- values for the p-phenoxy group (-0.320 and -0.570 respectively) and for the p-methoxy group (-0.268 and -0.778 respectively). The applicability of the σ^+ values rather than the σ^- values for these substituents shows that the fragment being stabilized is not a phenylacetoxo group but a benzyl group, for it is only by resonance delocalization of a positive charge in the benzene ring that the p-methoxy and p-phenoxy groups show a correlation with σ^+ . The presence of the methylene group between the benzene ring and the carboxylate group will insulate the conjugative effect of the two groups if the stabilized center is on the carboxylate group. These results support the view that the electron transfer from the carboxylate anion is a concerted process to some extent with the loss of carbon dioxide during the rate determining step. The direct resonance interaction of the substituent with the benzyl radical being formed is attributed to the importance of the resonance structure I in the proposed transition state for the electron transfer.



In the decarboxylation of the series of acids, phenylacetic acid, cyclohexene-3-carboxylic acid, pivalic acid, cyclohexanecarboxylic acid and isobutyric acid, whose relative rates are summarized in Table XXVIII, there is distinct evidence that the radical formed in the transition state is not the carboxylate radical.

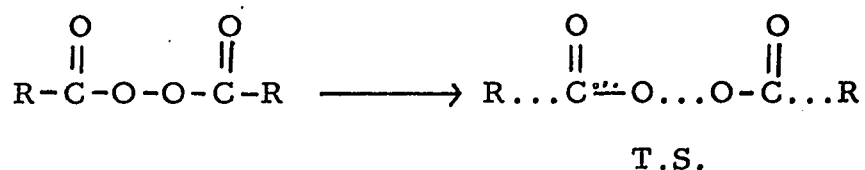
TABLE XXVIII

RELATIVE RATES OF DECARBOXYLATION OF SECONDARY, TERTIARY, ALLYLIC AND BENZYLIC ACID SERIES.

Acid		Relative rate
benzylic	: phenylacetic	1.000
allylic	: cyclohexene-3-carboxylic	0.359
tertiary	: pivalic	0.161
secondary	: cyclohexanecarboxylic	0.0024
secondary	: isobutyric	0.0008

The widely varied rates of decarboxylation follows the relative stabilities expected from benzylic, allylic, tertiary and secondary radicals. A similar case is found in the decomposition of acyl peroxides reported by Pryor,¹⁰⁰ who collected data on the rate of the decomposition of diacyl peroxides, RCO-O-O-COR , and dialkyl

peroxides, ROOR. Pryor stated that in the decomposition of alkyl peroxides, the nature of the R group has very little effect on the rate of the dissociation. The peroxides decompose at similar rates whether R is ethyl, propyl, isopropyl or t-butyl. However, in acyl peroxides the nature of the R group has a very pronounced effect on the rate of the dissociation. The stability of the R group as a free-radical influences the rate of the decomposition of the acyl peroxide. This implies that there is some C-CO bond stretching in the transition state as well as O-O bond stretching.



In the case of peresters, RCO-O-O-R =, those which are derived from acids with R groups that would form relatively stable radicals undergo a synchronous scission of two bonds to split out a molecule of carbon dioxide. In this way, some of the odd electron



density is delocalized on the R group in the transition state, and the stability of the R group correlates with the rates of the decomposition of the peresters. Table XXIX shows the data of Bartlett and Hiatt¹⁰¹ on the rates of the decomposition of the t-butyl peresters.

TABLE XXIX

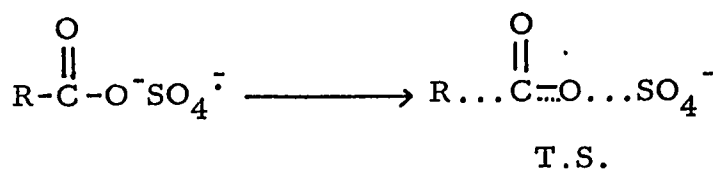
PERESTERS AND THE HALF-LIVES OF THEIR DECOMPOSITION
REACTIONS.

R in $t\text{-Bu-O-O-CO-R}$	Half-life at 60° , min.
$\text{CH}_3\text{-}$	5×10^5
$\text{C}_6\text{H}_5\text{-}$	3×10^5
$\text{C}_6\text{H}_5\text{-CH}_2\text{-}$	1.7×10^3
$(\text{CH}_3)_3\text{C-}$	300
$(\text{C}_6\text{H}_5)_2\text{-CH-}$	26
$\text{C}_6\text{H}_5\text{-(CH}_3)_2\text{C-}$	12
$(\text{C}_6\text{H}_5)_2(\text{CH}_3)\text{C-}$	6
$\text{Cl}_3\text{C-}$	970

Bartlett and Hiatt reported that when the R group of the acid part of the perester forms a radical of low stability e.g. methyl or phenyl, the perester decomposes in a stepwise manner. The cleavage of the O-O bond only takes place in the transition state of the rate determining step. As evident from the table given above, the rates of the decomposition of t -butyl peracetate and perbenzoate are about the same.

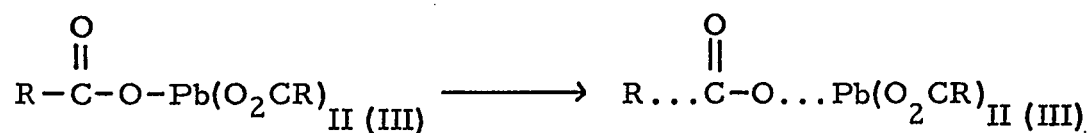
In the peroxydisulfate promoted decarboxylation of carboxylic acids, it is evident that the stability of the R groups of the acids correlates with their rates of decarboxylation. The difference in rates of the benzylic, the allylic, the tertiary alkylcarboxylic and the secondary alkylcarboxylic acids is significant. The rates of the decarboxylation shown by the secondary alkylcarboxylic, primary alkylcarboxylic and benzoic acids relative to that of phenylacetic acid were extremely small. Consequently, the accurate determination of these relative rates, to see if they exhibit a significant change was not possible.

The ρ value in the correlation of the rates of decarboxylation of the meta- and para-substituted phenylacetic acids with the substituent constants is rather small (-0.43). As the value of ρ reflects the degree of the involvement of the polar structure in the transition state of the reaction, the large dependence of the rate of decarboxylation on the structure of R indicates the participation, to a certain degree, of a concerted two-bond breakage in the rate determining step. This concerted mechanism allows for the delocalization of the odd electron on the R group in the transition state.



Similar effects of the R group on the rate of decomposition of compounds involving transition states similar to the one shown

above for the decarboxylation reaction, are reported in the case of homolysis of lead IV esters,²⁷ and in the thermal decomposition of azo compounds.¹⁰² In these two cases the transition state places

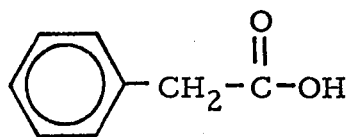


some of the odd electron density on the R group.



According to the argument presented above concerning the influence of the stability of the free-radical produced on the decarboxylation of acids, one would predict that substitution of the hydrogen atoms of the methylene group of the benzyl moiety by methyl and phenyl groups, should increase the rate of the decarboxylation as a result of the increase of the stability of the radical produced. The decarboxylation of a number of alpha-substituted phenylacetic acids, did not substantiate this prediction. The relative rates of decarboxylation of the alpha- and ortho-substituted phenylacetic acids are shown in Table XXX.

The relative rates of decarboxylation of phenylacetic acid, I, diphenylacetic acid, II, and triphenylacetic acid, III, increases

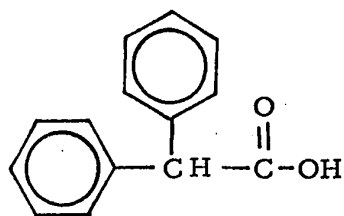


I

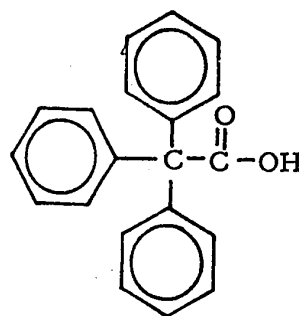
TABLE XXX

RELATIVE RATES OF PEROXYDISULFATE PROMOTED
DECARBOXYLATION OF alpha- AND ortho-SUBSTITUTED
PHENYLACETIC ACIDS AT $74.3 \pm 0.10^\circ$.

Acid	Relative rate
phenylacetic	1.00
diphenylacetic	1.19
triphenylacetic	1.44
hydratropic	0.651
<u>alpha</u> -methylhydratropic	0.743
<u>o</u> -tolylacetic	1.31
<u>o</u> -methylhydratropic	1.05
<u>p</u> -methylhydratropic	1.06



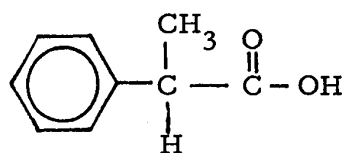
II



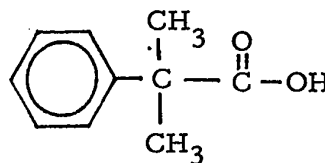
III

in the order of 1.00 : 1.19 : 1.44 . This is a comparatively small increase if we consider that the rate of the decarboxylation reflects the stability of the radical produced on the loss of a carbon dioxide molecule. A comparison with the results reported by Walling¹⁰³ in the study of the relative reactivity of hydrocarbons towards t-butyl hypochlorite indicates that substitution of the methylene hydrogen of the benzyl radical with one or two phenyl groups would be expected to increase the stability of the latter radical by four or nine folds, respectively. Walling found that the relative rates of hydrogen atom abstraction from toluene, diphenylmethane and triphenylmethane by t-butoxy radicals are in the order of 1 : 4.7 : 9.5. These results must depend to an extent on the stability of the radical formed.

Hydratropic acid, IV and α -methylhydratropic acid, V,



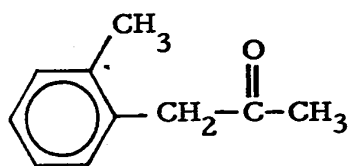
IV



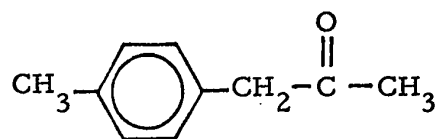
V

gave relative rates of decarboxylation which were lower than that of phenylacetic acid, although the radical produced should have enhanced stability due to the hyperconjugative effect of the methyl groups.

o-Tolylacetic acid, VI, showed a relative rate of decarboxylation almost the same as that of its isomer, p-tolylacetic acid, VII, (1.46)



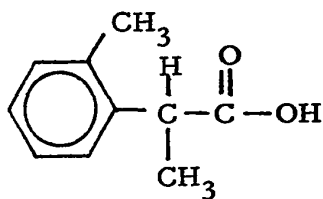
VI



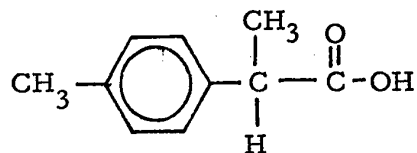
VII

indicating that substitution on the ortho-position does not have the pronounced retarding effect as substitution in the alpha-position.

o-Methylhydratropic acid, VIII, and p-methylhydratropic acid, IX, consequently have the expected relative rates of decarboxylation resulting from the additivity of the enhancing effect of substitution



VIII

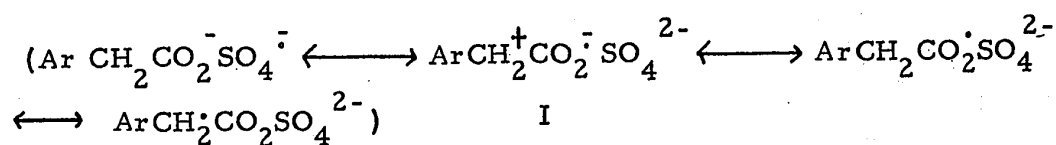


IX

of a methyl group in the ortho- or para-positions and the retarding effect of substitution of a methyl group in the alpha-position of the parent phenylacetic acid.

The effect of the alpha-substitution on the rate of the decarboxylation of phenylacetic acid could be rationalized by

considering the electronic effect of the substituents as well as their influence on the solvation and the conformation of the transition state of the decarboxylation reaction. The transition state proposed earlier for the peroxydisulfate promoted decarboxylation of phenylacetic acid and the substituted phenylacetic acids shows the importance of the resonance structure I. This transition state showing a polar character is expected to be stabilized by solvation.



Any factor that hinders this solvation will result in decreasing the rate of the decarboxylation. It was also proposed that the transition state allows the delocalization of the odd electron on the benzene ring. This delocalization should be most effective when the benzene ring and the C-O bond of the carbonyl group are coplanar. When the benzene ring is shifted from coplanarity in the transition state, the delocalization of the odd electron and consequently the rate of decarboxylation should decrease. Thus there are three possible effects on the rate of the decarboxylation of alpha-substituted phenylacetic acids. The electronic effect of the substituents would result in enhancing or retarding the rate by stabilizing or destabilizing the radicals formed. The solvent effect would result in retarding the rate if the solvation of the transition state is hindered. The conformation effect would result in retarding the rate if the benzene ring is shifted in the transition state from the position of coplanarity with the carbonyl group of phenylacetic acid.

The solvent effect would have an influence on the rate of the dissociation of the alpha-substituted phenylacetic acids. The dissociation constant reflects the stability of the carboxylate anion, and is affected by the solvation as well as the inductive effect of the substituents. From the data in Table XXIV, it is clear that there is a small decrease in the dissociation constant of phenylacetic acid on introduction of one methyl group in the alpha-position, while the introduction of a second methyl group caused a relatively large decrease in the dissociation constant. A similar result is obtained with alpha-phenyl substitution. Diphenylacetic acid has a dissociation constant more than twice as high as that of phenylacetic acid, while triphenylacetic acid has a dissociation constant slightly lower than that of diphenylacetic acid. This data on the dissociation constants indicate the importance of the solvent effect on the dissociation of phenylacetic acids. Introduction of bulky groups in the alpha-position hindered the solvation of the anion and resulted in lower dissociation constants. From the data in Table XXIV, the relation between the relative rates of decarboxylation of meta- and para-substituted phenylacetic acids and their corresponding dissociation constants was plotted in Figure VI. Since the relative rates of the decarboxylation correlate with the σ^+ constants and the dissociation constants correlate with the σ^- constants, we expect that the correlation between the relative rates of the decarboxylation and the dissociation constants of the meta- and para-substituted phenylacetic acids would be only fair. The relation between the

relative rates of the decarboxylation of the alpha-substituted phenylacetic acids and their corresponding dissociation constants are plotted in Figure VII. Unlike the fair correlation between the rates of decarboxylation of the meta- and para-substituted acids and their dissociation constants, the lack of correlation in the alpha-substituted acids is quite apparent. This would exclude the possibility of the intermediacy of a carboxylate radical, $R-\overset{\overset{\text{O}}{\parallel}}{\text{C}}-\text{O}^{\cdot}$, which should be affected by solvation in a similar manner to the carboxylate anion.

In comparison with the dissociation of the acids, it is expected that the solvent effect would have a larger influence on the rate of the decarboxylation of the alpha-substituted phenylacetic acids. This is possibly due to the importance of the resonance structure $\text{ArCH}_2^+ \text{CO}_2^- \text{SO}_4^{2-}$ of the transition state with the positive charge localized on the methylene group, which would be greatly stabilized by solvation.

The distortion of the transition state from its favorable coplanarity position caused by alpha-substitution, does not seem to have an important influence on the rate of the decarboxylation as compared to the substituent effect. Table XXIX shows that o-tolylacetic acid and p-tolylacetic acid have almost the same rates of decarboxylation, indicating that the o-methyl group does not have an appreciable steric effect. More distinct evidence against the importance of the conformation effect in alpha-substituted phenylacetic acids is the fact that o-methylhydratropic acid and p-methylhydratropic acid decarboxylate at the same rate. If there is any

appreciable conformation effect, it would be very distinct in the case of o-methylhydrotropic acid, where there are two methyl groups in the ortho- and the alpha-positions.

The concerted decomposition of t-butyl peresters is a reaction which needs the same conformation requirements in the transition state as the decarboxylation reaction of the carboxylic acids. alpha-Substitution in the t-butyl peresters of phenylacetic acid affects the value of the entropy of activation, while it does not reduce the rate of the reaction significantly. Bartlett and Hiatt,¹⁰¹ in their study of the thermal decomposition of peresters showed that the perester derived from α-methylhydrotropic acid decomposed much faster than the perester derived from phenylacetic acid. The half-lives at 60° were 12 and 1700 min., respectively. Koenig and Wolf,¹⁰⁴ in a study of the concerted rate of decomposition of the peresters showed that perhydrotropate and α-methylperhydrotropate decompose faster than perphenylacetate. In isooctane, the rate of decomposition of perhydrotropate at 73.88° is $3.233 \times 10^{-4} \text{ sec}^{-1}$, that of α-methylperhydrotropate at 60.56° is $4.064 \times 10^{-4} \text{ sec}^{-1}$ and that of perphenylacetate at 84.98° is $1.080 \times 10^{-4} \text{ sec}^{-1}$.

From the above argument it can be concluded that the rate of the decarboxylation of the alpha-substituted phenylacetic acids can be influenced by two main factors. The electronic effect of the substituent which influences the stability of the resulting radicals and the solvent effect which results from the interference of the substituents with the solvation of the transition state. The second factor

seems to be more important than the first one. The effect of alpha-substituents on the conformation of the transition state and consequently on the rate of the decarboxylation would not be of the same importance as the other two factors.

The decomposition reaction of the peresters of the substituted phenylacetic acids has a ρ value (-1.09 at 90°) which is larger than the ρ value of the present decarboxylation reaction. This indicates that the transition state of the peresters decomposition has more polar character than the transition state of the decarboxylation reaction. It would thus appear that the solvent effect would have more importance in the decomposition of the peresters. Yet, from the results in Table XXIV, it seems that the electronic effect of the substituents is much stronger than the solvent effect in influencing the rates of the decomposition of the peresters of the alpha-substituted phenylacetic acids. This is possibly due to the fact that the decomposition reactions of the peresters were performed in solvents of low polarity e.g. isooctane and chlorobenzene.

In the present work, it was found that phenylacetic acid undergoes decarboxylation faster than pivalic acid. Yet, Bartlett and Simons,¹⁰⁵ and Koenig and Wolf¹⁰⁴ found that t-butyl perpivalate decomposed faster than t-butyl perphenylacetate. The difference in the rates of the decomposition of the two peresters was explained by Bartlett and Simons on the basis of the unfavourable entropy of activation in perphenylacetate, as there are conformations for the reacting esters which are unfavourable for producing the stabilized

benzyl radical itself. That is when the benzene ring is not coplanar with the C-O bond of the carboxylate group. No such restrictions exist for the perpivalate. In the case of the decarboxylation of acids and in the case of the decomposition of azo compounds which need the same requirements in the transition state for a concerted reaction, no such acceleration of the rates is observed when the resulting radical is the t-butyl radical rather than the benzyl radical. McGowen and Powell¹⁰⁶ measured the rates of the decomposition of azobis-phenylmethane and azobis-t-butane as, $-\log k (\text{C}_6\text{H}_5\text{CH}_2\text{N}=\text{N})_2 = 2.1$ and $-\log k [(\text{CH}_3)_3\text{CN}=\text{N}]_2 = 3.43$, from which the rates of decomposition can be calculated as 7.94×10^{-3} and 0.457×10^{-3} , respectively.

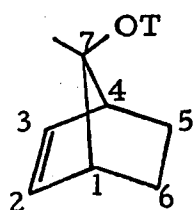
Bartlett and Simons¹⁰⁵ also pointed out that the benzyl radicals seem to have much less stabilization energy at the transition state than the t-butyl radical, but they did not offer any explanation for this.

The products formed during the oxidative decarboxylation of phenylacetic acid with potassium peroxydisulfate, were analysed and found to be in agreement with the previously reported results.⁵¹ Carbon dioxide was obtained quantitatively, not only from phenylacetic acid, but from all of the acids decarboxylated in the present work. The rest of the products of the decarboxylation of phenylacetic acid possibly arise from the reaction of the benzyl radical. Hydrogen abstraction by the radical gave toluene which was detected in a small amount. Coupling of the benzyl radical with the sulfate

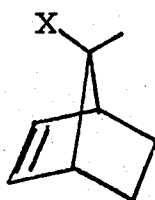
radical ion or the displacement of the benzyl radical on the peroxydisulfate ion to give a sulfate ester which on hydrolysis would yield benzyl alcohol. Yet, the latter alcohol was not detected in the reaction mixture probably due to its rapid oxidation to benzaldehyde, one of the reaction products. The absence of benzoic acid in the product mixture shows that further oxidation of benzaldehyde does not go to any appreciable extent. Coupling of the benzyl radicals gave rise to bibenzyl which was formed in fairly large amounts, especially when the concentration of the peroxydisulfate increased. The main product of the reaction was a polymeric yellow substance that may result from the polymerization of benzaldehyde.

PART II**NONCLASSICAL FREE-RADICALS**

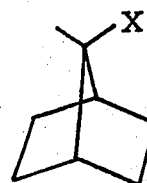
Very spectacular examples of anchimeric assistance by the π electrons associated with a C=C double bond has been noted in the reactions of anti-7-norbornenyl derivatives.^{107, 108} The anti-7-tosylate, I, is solvolysed over a billion times faster than its saturated analog III, and the ratio of the rates for ethanolysis of the corresponding chlorides is almost a million. As shown in IV, the electron lobes in the anti-7-norbornenyl derivatives lie near C₇



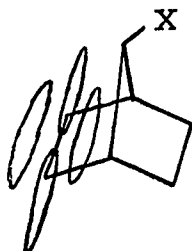
I



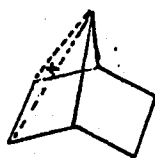
II



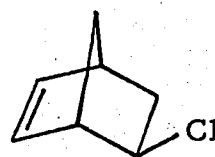
III



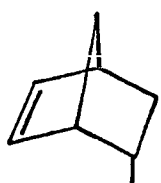
IV



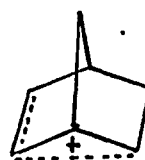
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VI



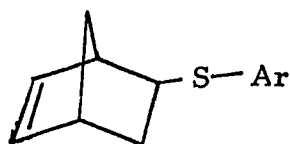
VII



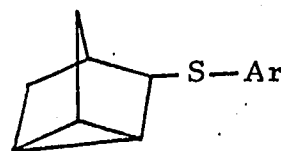
VIII

on the side opposite the leaving group. Not only may those electrons help the leaving group, but, with its departure, may help accommodate the positive charge on C_7 and its delocalization over three atoms as in the nonclassical carbonium ion V. Assistance by the π electrons requires that they lie opposite the leaving group. Thus, the syn-form of 7-norbornenyl halides and sulfonates, II, are solvolyzed more slowly than are the corresponding anti-form by a factor of more than 10^5 . The π electron lobes associated with the double bond between C_2 and C_3 in the norbornenyl system lie much nearer to C_7 than C_5 or C_6 . Such a double bond renders much less assistance to the ionization of substituents at C_5 or C_6 than to the ionization at C_7 . The exo-chloride VI undergoes solvolysis in 80% ethanol about 150 times more rapidly than the endo-chloride VII.^{109, 110}

In the case of radical producing reactions, some work was performed to examine if such nonclassical radicals analogous to the nonclassical carbonium ions V and VIII discussed above can exist. Cristol and coworkers¹¹¹ found that the free-radical addition of p-thiocresol to norbornadiene leads to a mixture of the exo-5-norbornene-2-yl aryl ether IX, formed by 1,2 addition and the 3-nortricyclyl aryl ether X, formed by homoconjugative addition. The ratio of the tricyclic product to the bicyclic product depends

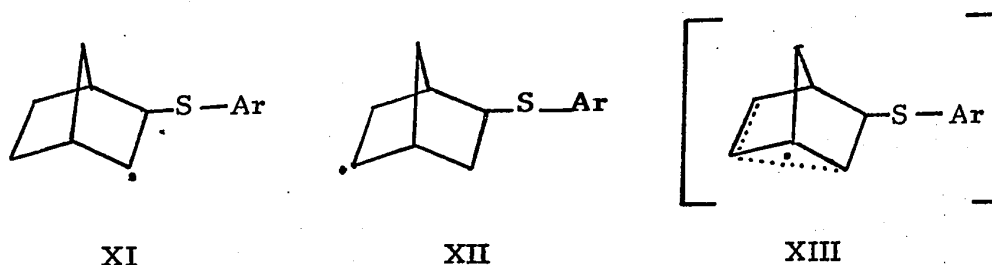


IX

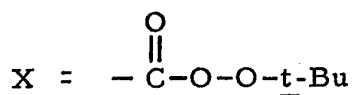
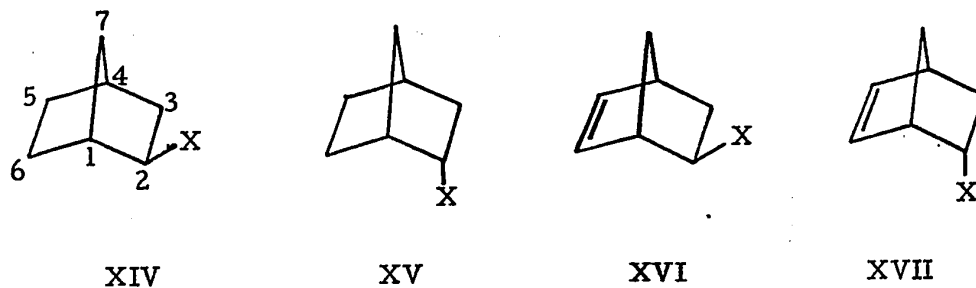


X

upon the initial concentration. This requires that there be present at least two interconvertible radical species which give rise to the products. The simplest assumption is that these are the two classical radicals XI and XII.



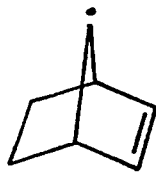
A similar observation was made in the free-radical addition of carbon tetrachloride, chloroform and bromotrichloromethane to 2-methylene-5-norbornene.¹¹² Thus, nonclassical radicals such as XIII have been proposed to be unimportant in the product-determining step in free-radical processes involving these ring systems. Martin and De Jong¹¹³ prepared a series of norbornane and norbornene peresters, XIV-XVII. On thermal decomposition of these peresters in cumene, the corresponding radicals are formed.



As shown by Winstein and Roberts, in the studies of the ionic reactions of similar compounds as those mentioned previously, participation by the C_1-C_6 single bond and of C_5-C_6 double bond is possible only when the departing group is exo. Hence, if non-classical radicals are formed, homolytic cleavage of an exo-group should be accelerated over that of an endo- one. Martin and De Jong found that all these series of compounds undergo concerted decomposition. Comparison of the activation parameters of each pair of exo- and endo-peresters showed that they are the same within the experimental error. Consequently, it was concluded that it is no more energetically favorable for an exo-bond to undergo homolytic scission than it is for an endo-bond.

Wilt and coworkers^{114, 115} suggested that the 7-norbornenyl radical and the 2,3-dibenzo-7-norbornenyl radical may be nonclassical, but the suggestion is based on qualitative and incomplete rate comparisons. Recently Warkentin and Sanford¹¹⁶ reported that 7-norbornenyl is a nonclassical radical. They generated the radical from either the syn- or anti-7-bromonorbornene with tri-n-butyltin deuteride in hexane. They reported that from both of the bromo compounds, the same 7-deuterionorbornene was produced in which the deuterium is anti to the double bond. A single classical radical, XVIII, or equilibrating radicals, XIX and XX, were ruled out to account for the stereochemical results. This was based on the fact that, for these radicals to accommodate the results, either a highly stereospecific reaction of the unhindered classical C_7

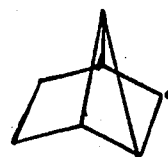
radical or reaction of the cyclopropylcarbinyl radical at a carbon which does not have radical character is required. The steric factor is too small and there is no precedent for a reaction of the other type. Warkentin and Sanford concluded that either the



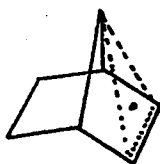
XVIII



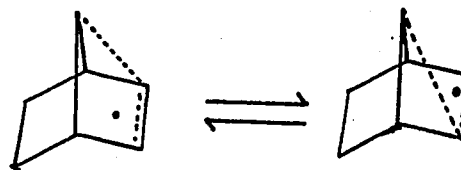
XIX



XX



XXI

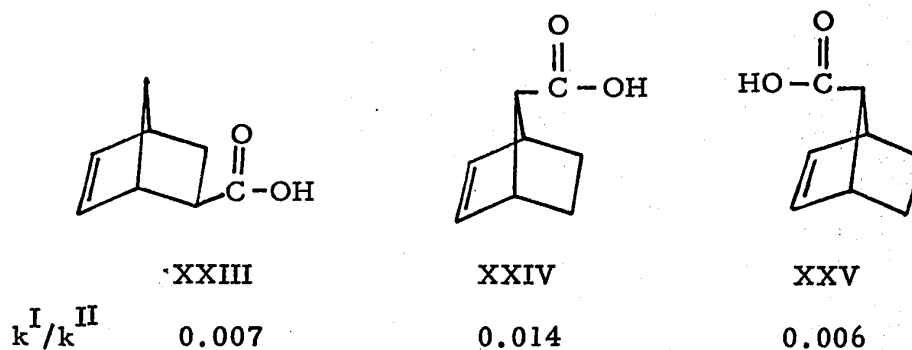


XXII

nonclassical radical, XXI, or the two equilibrating nonclassical radicals, XXII, can accommodate the results. In systems without a rigid framework, structures like XXI are expected to be favored, but rigid systems are also stabilized by introducing 1,4 along with 2,4 overlap.

In the present work we undertook to re-examine the nature of the radicals produced in the norbornene system. The exo-2-norborn-5-enecarboxylic acid, XXIII, the anti- and syn-7-norborn-2-enecarboxylic acids, XXIV and XXV, were prepared and subjected to potassium peroxydisulfate promoted decarboxylation. Their

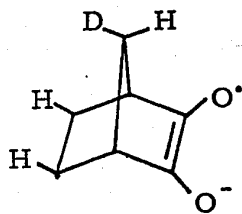
relative rates of decarboxylation with respect to phenylacetic acid- $l\text{-C}^{14}$ are given below. The relative rates given are very small



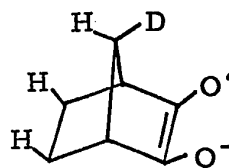
and contain a considerable amount of experimental error. More exact results would have been obtained if a less reactive acid had been used as the standard acid in this reaction. Nevertheless, the present data illustrates clearly the instability of the radicals produced. As was presented in an earlier part of this discussion, the rate of the decarboxylation should reflect, at least in a series of closely related compounds, the stability of the radical formed. It should also be noted that, by analogy to the carbonium ion, if any participation of the double bond exists in the transition state to accelerate the rate of decarboxylation, this should be possible when the 7-carboxylate group is in the anti-position to the double bond. The double bond participation would also be possible when the 5-carboxylate group is exo. From the present results it is apparent that the syn-7-norborn-2-enecarboxylic acid, its anti-isomer and the exo-2-norborn-5-enecarboxylic acid decarboxylate at nearly the same rate. These results are inconsistent with any appreciable acceleration by the double bond or any participation of nonclassical radicals such

as XXI.

During the progress of the present work, Russell and Lamson,¹¹⁷ and Cristol and Noreen¹¹⁸ independently reported results which gave evidences against the nonclassical structure XXI for the 7-norbornenyl radical. Russell and Lamson converted the products of the reaction of tri-butyltin deuteride with 7-syn- and 7-anti-bromonorbornene to the semidiones, a reaction which does not involve rearrangement, and examined the structure of the latter by esr spectroscopy. The semidiones produced from the products of either of the two bromocompounds were mixture of two semidiones, I and II. Analysis of the esr spectra revealed a I/II ratio



I



II

of the order 4.9 from both of the syn- and the anti-7-bromonorbornene. Cristol and Noreen carried the reduction of the syn- and the anti-7-bromobenzonorbornadiene with tri-n-butyltin deuteride in benzene in the presence of AIBN. Both isomers gave an identical mixture of syn- and anti-7-deutero-benzonorbornadiene. The product ratio of the two isomers in the mixture was determined by analysis of the nmr spectra of the Diels-Alder adducts of the deuterated benzo-norbornadiens with 1,3-diphenylisobenzofuran. The analysis

showed that anti and syn deuteration of each of the bromoisomers was 43 : 57. Cristol also reported that a rough analysis of the areas in the nmr spectrum published by Warkentin for the deuterated product of the reduction of the 7-bromonorbornenes suggests that tin hydride reduction of both syn- and anti-7-bromonorbornenes leads approximately to a 70 : 30 mixture of the anti- and syn-7-deuteronorbornenes.

TABLE XXXI

DECARBOXYLATION OF anti-7-NORBORN-2-ENECARBOXYLIC
ACID (1.46×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ ($1.46 \times$
 10^{-2} M), AT $74.3 \pm 0.10^\circ$.

anti-7-norborn-2-enecarboxylic acid (0.951×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.951×10^{-4} mol)

potassium peroxydisulfate (3.71×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
44.9	0.446	44615	0.379	0.067	0.014
55.1	0.566	56784	0.482	0.084	0.013
59.6	0.578	58036	0.491	0.087	0.013
64.5	0.615	61905	0.525	0.091	0.012
78.0	0.850	80265	0.680	0.170	0.016
30 days	1.865	110849	0.963	0.902	

Average k^I/k^{II} = 0.014 ± 0.001

TABLE XXXII

DECARBOXYLATION OF syn-7-NORBORN-2-ENECARBOXYLIC
ACID (1.45×10^{-2} M) AND PHENYLACETIC ACID-1- C^{14} ($1.46 \times$
 10^{-2} M), AT $74.3 \pm 0.10^\circ$.

syn-7-norborn-2-enecarboxylic acid (0.945×10^{-4} mol)

phenylacetic acid-1- C^{14} (0.951×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

Time (min)	Total CO ₂ (mol $\times 10^4$)	cpm	Active CO ₂ (mol $\times 10^4$)	Inactive CO ₂ (mol $\times 10^4$)	k^I/k^{II}
44.8	0.437	48670	0.395	0.042	0.008
50.0	0.480	52337	0.444	0.036	0.006
54.9	0.533	57719	0.488	0.045	0.007
62.1	0.563	62875	0.534	0.029	0.004
70.3	0.626	69470	0.587	0.039	0.004
77.9	0.690	75195	0.636	0.054	0.006
30 days	1.862	109053	0.953	0.909	

Average $k^I/k^{II} = 0.006 \pm 0.001$

TABLE XXXIII

DECARBOXYLATION OF 2-NORBORN-5-ENECARBOXYLIC ACID
 (1.46×10^{-2} M) AND PHENYLACETIC ACID-1-C¹⁴ (1.46×10^{-2} M),
 AT $74.3 \pm 0.10^\circ$.

2-norborn-5-enecarboxylic acid (0.952×10^{-4} mol)

phenylacetic acid-1-C¹⁴ (0.951×10^{-4} mol)

potassium peroxydisulfate (3.70×10^{-4} mol)

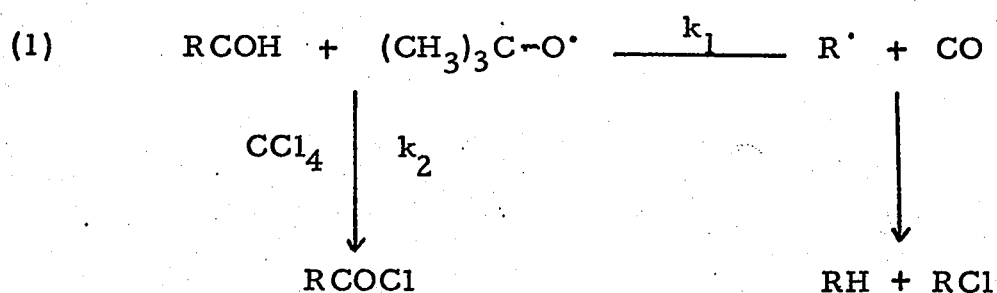
Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
44.8	0.360	38726	0.327	0.033	0.008
49.9	0.472	51171	0.434	0.038	0.007
54.6	0.514	56361	0.478	0.036	0.005
62.4	0.581	61496	0.519	0.062	0.009
70.1	0.649	67246	0.572	0.077	0.009
77.6	0.683	73655	0.624	0.059	0.006
30 days	1.868	108116	0.949	0.919	

Average $k^I/k^{II} = 0.007 \pm 0.001$

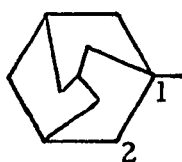
PART III

ON THE STABILITIES OF THE BRIDGE-HEAD RADICALS

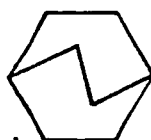
In an attempt to solve the problem of the preferred geometry for the aliphatic radical, a number of studies has been undertaken to generate bridge-head radicals and to determine their stabilities. Applequist and Kaplan¹¹⁹ studied the loss of the carbon monoxide from bridge-head acy radicals in ring systems having differing degrees of restriction of bridge-head planarity. The corresponding aldehydes were decarboxylated in carbon tetrachloride in the presence of *t*-butyl peroxide. Carbon tetrachloride served as an inefficient trap for the intermediate acy radicals (equation 1).



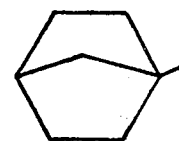
Assuming that the trapping efficiency deduced from the product ratios ($\text{RCOCl} : \text{RH} + \text{RCl}$) correlates with the stabilities of the alkyl radicals generated from the aliphatic aldehydes, the investigators reached the conclusion that the 1-adamantyl radical, I; and the 1-bicyclo(2.2.2)octyl radical, II, are slightly more stable than the *t*-butyl radical, while the 1-bicyclo(2.2.1)heptyl radical, III, is less



I

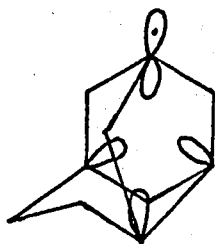


II



III

stable than the n-propyl radical. The investigators suggested that the extra stability of the 1-adamantyl radical may result from the possibility that the bridge-head radical has a low bending force constant. The stability could be a result of inductive stabilization or perhaps there is a special delocalization of the odd electron resulting from the overlap of the p-orbital lobe of the 1-adamantyl radical with the back-sides of the sp^3 orbitals of the three remaining bridge-head C-H bonds. This overlap would take place in the center of the molecule as represented in IV. Fort and Franklin¹²⁰ supported the idea of the greater stability of 1-adamantyl radical over that of

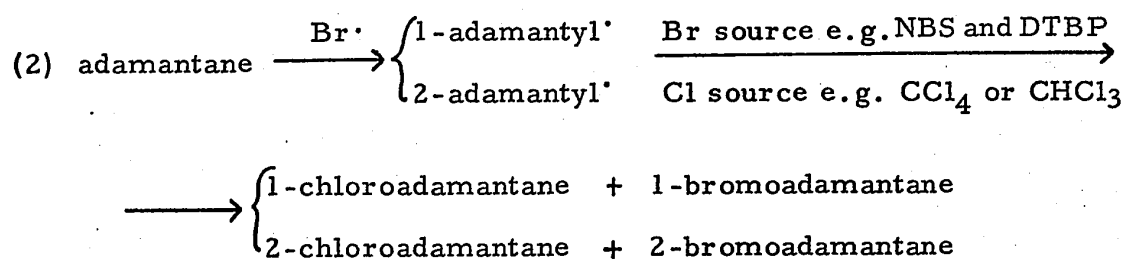


IV

the t-butyl radical as a result of measuring the rate of the decomposition of a series of t-butyl radicals including that of 1-adamantanecarboxylic acid and pivalic acid.

In contrast to these results, Lonard¹²¹ found that the t-butyl perester of 1-adamantanecarboxylic acid decomposes at the same rate as t-butyl perpivalate indicating that 1-adamantyl and t-butyl radicals are of essentially identical stabilities. Tabushi and coworkers¹²² presented the results of the free-radical substitution on adamantane, specially focusing upon a comparison of the reactivities of the 1- and 2-positions. They found that in the

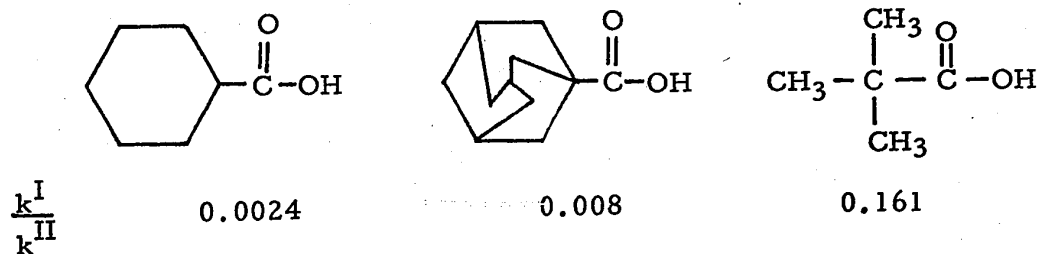
presence of a halogenating reagent, e.g. NBS and DTBP, and a halogenating solvent, e.g. carbon tetrachloride or chloroform, there is much less discriminating halogen abstraction by 1-adamantyl radical from carbon tetrachloride or chloroform than by 2-adamantyl radical (equation 2). 1-Adamantyl radical abstracted chlorine



predominantly, while 2-adamantyl radical abstracted bromine as a major reaction. This indicates that the bridge-head (sp^2) radical is less stable than the normal secondary radical (planar). The former is less selective and more reactive. When the modified Hunsdieker reaction was carried on 1- and 2-adamantanecarboxylic acids using the $\text{Br}_2\text{-CCl}_4\text{-HgO}$ system, it was found that the ratio of 1-chloroadamantane to 1-bromoadamantane is 10 : 1, while the ratio of 2-chloroadamantane to 2-bromoadamantane is 0.11 : 1. These product ratios show the greater reactivity of 1-adamantyl radical over the 2-adamantyl radical.

In the present work, we subjected the 1-adamantane-carboxylic acid to oxidative decarboxylation with potassium peroxydisulfate, a decarboxylation reaction in which the rate was proposed to reflect the stability of the radical produced. The results, as represented below for the rate of the decarboxylation relative to that

of phenylacetic acid-1-C¹⁴, show that 1-adamantanecarboxylic acid decarboxylates at a much slower rate than that of pivalic acid and at about the same order as that of cyclohexanecarboxylic acid.



This data is in support of Tabushi's findings that the 1-adamantyl radical is less stable than the t-butyl radical and is contrary to the conclusion reached from the decarbonylation studies¹¹⁹ and from the results of the perester decompositions.¹²¹

TABLE XXXIV

DECARBOXYLATION OF 1-ADAMANTANECARBOXYLIC ACID

(1.47 x 10⁻² M) AND PHENYLACETIC ACID-1-C¹⁴ (1.47 x 10⁻² M),

AT 74.3 ± 0.10°.

1-adamantanecarboxylic acid (0.954 x 10⁻⁴ mol)phenylacetic acid-1-C¹⁴ (0.951 x 10⁻⁴ mol)potassium peroxydisulfate (3.70 x 10⁻⁴ mol)

Time (min)	Total CO ₂ (mol x 10 ⁴)	cpm	Active CO ₂ (mol x 10 ⁴)	Inactive CO ₂ (mol x 10 ⁴)	k ^I /k ^{II}
44.9	0.552	58132	0.491	0.061	0.009
50.1	0.566	60001	0.509	0.057	0.008
54.8	0.632	67453	0.571	0.061	0.007
61.4	0.657	69568	0.587	0.070	0.008
79.8	0.801	83620	0.707	0.094	0.008
30 days	1.854	108154	0.948	0.906	

Average k^I/k^{II} = 0.008 ± 0.0005

EXPERIMENTAL

PHYSICAL MEASUREMENT

All melting and boiling points are uncorrected. Melting points were obtained using a Fisher-Johns melting point apparatus, except for sealed tube melting points for which a Mel-Temp. apparatus was used. Refractive indices were measured on a Bauch-Lomb refractometer.

SPECTRAL MEASUREMENTS

Infrared (ir) spectra were recorded on a Perkin-Elmer model 421 recording spectrophotometer. The proton nuclear magnetic resonance (nmr) spectra were determined using a Varian Associates A-60 nuclear magnetic resonance spectrometer. Chemical shifts are expressed in τ units and are relative to tetramethylsilane (TMS, τ , 10.000). Mass spectra were obtained on Metropolitan Vickers S₂ machine using an ionizing voltage of 70 ev.

GAS CHROMATOGRAPHY

Two instruments were used as described below.

1. Varian Aerograph model 202 with thermal conductivity detector and linear temperature programmer.
2. Varian Aerograph model 600-D with flame ionization detector.

LIQUID SCINTILLATION COUNTING

The Nuclear Chicago Model 724 scintillation spectrometer

system designed for counting soft-beta emitting isotopes such as carbon-14 and tritium was used. The system provides data listing of sample number, time and counts for each channel.

MICROANALYSIS

The microanalysis for carbon and hydrogen were performed in the Microanalytical Laboratory, Chemistry Department, University of Alberta, Edmonton. Sulfur and oxygen analysis were performed by the Galbraith Laboratories, Inc., Knoxville, Tennessee.

MOLECULAR WEIGHT DETERMINATIONS

Molecular weight determinations were performed by Galbraith Laboratories.

MATERIALS USED

A number of commercially available acids were purified as described below and their purity was checked by titration. An accurately weighed amount of each acid was dissolved in a standardized potassium hydroxide solution. Back-titration of the latter solution gave equivalent weights of the acids which indicated a 100% purity for all acids used.

Phenylacetic acid. The acid was crystallized from water. The shiny white leaflets of the pure acid melted at 75° (lit. ¹²³ mp 76°).

p-Methoxyphenylacetic acid. The acid was crystallized from water and gave shiny white leaflets, mp 84° (lit. ¹²⁴ mp 85°).

p-Tolylacetic acid. The commercial acid was dissolved in potassium hydroxide solution and the organic impurities were extracted with ether. The aqueous solution was filtered from the insoluble impurities and acidified with concentrated hydrochloric acid. The precipitated acid was filtered and crystallized from water. The white shiny leaflets of the pure acid melted at 91° (lit.¹²⁵ mp $90-91^{\circ}$).

p-Bromophenylacetic acid. The acid was purified by crystallization from a 1:1 mixture of ethyl alcohol and water. The pure acid was obtained as white small needles, mp 115° (lit.¹²⁶ mp 114°).

p-Chlorophenylacetic acid. The acid was crystallized twice from water and gave white small shiny needles, mp $105-106^{\circ}$ (lit.¹²⁶ mp $104-105^{\circ}$).

m-Fluorophenylacetic acid. The yellow sand-shaped commercial acid was crystallized twice from water. It gave white leaflets of pure acid, mp 45° (lit.¹²⁷ mp 45°).

m-Bromophenylacetic acid. The acid was crystallized from a 1:2 mixture of ethyl alcohol and water and gave white shiny leaflets, mp $100-101^{\circ}$ (lit.¹²⁶ mp $90-100^{\circ}$).

m-Chlorophenylacetic acid. The acid was purified by dissolving in potassium hydroxide solution and the organic impurities were extracted with ether. The aqueous solution was filtered from the insoluble impurities and acidified with concentrated hydrochloric acid. The precipitated acid was filtered and crystallized from 1:1 mixture of ethyl alcohol and water. The pure acid was obtained as

white shiny leaflets, mp $75-76^{\circ}$ (lit.¹²⁶ mp 76°).

Mandelic acid. The commercial acid was crystallized from benzene to give lustrous white plates, mp $119-120^{\circ}$ (lit.¹²⁸ mp 118°).

Isobutyric acid. The acid was purified by Distillation. The pure acid was obtained as a colorless liquid, bp 147 (690 mm) [lit.¹²⁹ bp $152-155^{\circ}$ (760 mm)].

Cyclohexanecarboxylic acid. The acid was distilled under reduced pressure. The pure acid was a colorless liquid, bp $121-122^{\circ}$ (15 mm) [lit.¹³⁰ bp 232 (760 mm)]. The acid solidified on cooling, mp $29-30^{\circ}$ (lit.¹³⁰ 29°).

Pivalic acid. The acid was distilled and gave a colorless liquid, bp 158° (694 mm) [lit.¹³¹ bp $162-165^{\circ}$ (760 mm)].

Hydratropic acid. The acid was purified by distillation on a teflon spinning band. The colorless acid distilled at 132° (17 mm) [lit.¹³² bp 155° (21 mm)], n_D^{25} 1.5209 (lit.¹³² n_D^{25} 1.5204).

α -Methylhydratropic acid. The acid was crystallized twice from n-pentane. The pure acid was obtained as white needles, mp 78° (lit.¹³³ mp $76-77^{\circ}$).

o-Tolylacetic acid. The acid was crystallized from water. It gave white needles, mp 87° (lit.¹²⁵ mp 88°).

Diphenylacetic acid. The acid was purified by crystallization from ethyl alcohol to give long white needles, mp 148° (lit.¹³⁴ mp 148°).

Triphenylacetic acid. The acid was dissolved in potassium hydroxide solution and the organic impurities were extracted with

ether. The aqueous layer was filtered from the insoluble impurities and acidified with concentrated hydrochloric acid. The precipitated acid was crystallized from ethyl alcohol. The shiny small needles of the pure acid melted at 267° (lit.¹³⁵ mp 267°).

1-Adamantanecarboxylic acid. The acid was crystallized from a 3:1 mixture of methyl alcohol and water and gave lustrous white leaflets, mp $175.5-176.5^{\circ}$ (lit.¹³⁶ mp $175-176^{\circ}$).

Phenylacetic acid-1-C¹⁴. The carboxyl labelled acid was obtained from the Tracerlab Division of International Chemical and Nuclear Corp. Watham, Mass. The purified phenylacetic acid (150 g) was dissolved in ethyl alcohol. To this solution was added 0.1 mc of phenylacetic acid-1-C¹⁴. The solution was thoroughly mixed and the alcohol was evaporated. The dilute radioactive acid was dried in a desiccator over phosphorous pentoxide. An accurately weighed amount of the acid (0.0123 g) was dissolved in a scintillation solution and its radioactivity determined using a scintillation counter. The scintillation solution was a mixture of 2-ethanolamine, ethylene glycol monomethyl ether, toluene and the scintillator, diphenyl-oxazole (PPO). The acid had an activity of 859 cpm/mg.

p-Phenoxyphenylacetic acid. The acid was prepared from diphenyl ether by the following sequence of reactions.

Acetylation of diphenyl ether. The acetylation of diphenyl ether (45 g; 0.265 mol) by acetyl bromide (30 g; 0.322 mol) was performed following a procedure by Kipper.¹³⁷ The crude p-phenoxyacetophenone was obtained in a yield of 30 g (33%) and was crystallized

from ethyl alcohol. The pure compound had a melting point of 45° (lit.¹³⁷ mp 45°).

Synthesis of *p*-phenoxyphenylacetamide. The compound was prepared from *p*-phenyloxyacetophenone (12 g; 0.057 mol) by the Willgerodt reaction following a procedure by Tomita and Hashimoto.¹³⁸ The crude *p*-phenyloxyphenylacetamide (9 g) was chromatographed on a silica gel column. The amide was dissolved in acetone and eluted with ethyl acetate. The final fraction was fairly colorless and pure. The deeply colored first fraction was neglected. The middle slightly colored fraction was collected and rechromatographed. The process was repeated a third time. The three final fractions were combined and crystallized three times from ethyl alcohol. A yield of 2.5 g (21%) of the pure amide was obtained, mp $172-173^{\circ}$ (lit.¹³⁸ mp 172°).

Hydrolysis of *p*-phenoxyphenylacetamide. The pure amide (2.5 g) was heated under reflux with 200 ml of 10% aqueous potassium hydroxide solution for 8 hr. The alkaline solution was acidified with concentrated hydrochloric acid. The precipitated acid was crystallized three times from *n*-pentane. Pure *p*-phenoxyphenylacetic acid was obtained as white shiny leaflets in a yield of 1.3 g (52%), mp 78° (lit.¹³⁸ 78°); nmr (CDCl_3), τ 7.1 (m, 9 H), 3.75 (s, 2H), -1.9 (s, 1H). The equivalent weight of the acid obtained by titration as described before (p. 112) is 228.

Cyclohexene-3-carboxylic acid. The acid was prepared by the reduction of benzoic acid (15 g; 0.123 mol) with 5% sodium amalgam in sodium hydroxide solution. The preparation was performed

following a procedure of Boorman and Linstead.¹³⁹ The crude acid obtained was purified by distillation under reduced pressure. The pure acid (7 g; 48%) boiled at 122-123° (11 mm) [lit.¹³⁹ bp 120° (10 mm)]; n_D^{25} 1.4847 (lit.¹³⁹ n_D^{25} 1.4814). The overall yield of the acid was 2.5 g (17%). The equivalent weight, obtained by titration as described before (p. 112), was 126.

Sodium amalgam (5 %). The compound was prepared from sodium metal (50 g; 2.17 mol) and mercury (950 g; 4.74 mol) by a procedure reported by Brosen and Hauser.¹⁴⁰

o-Methylhydratropic acid. The acid was prepared by the methylation of the methylene group of o-tolylacetic acid as described in the following sequence of reactions.

Esterification of o-tolylacetic acid. o-Tolylacetic acid (15 g; 0.1 mol) was mixed with 98% ethyl alcohol (50 ml) in a 500 ml round bottom flask. Concentrated hydrochloric acid (4 ml) was added slowly down the walls of the flask. The mixture was heated under reflux for 2 hr. The mixture was then cooled and transferred to a separatory funnel containing water (50 ml). The ester was extracted with ether (75 ml) and the ethereal solution was washed with water and then with 5% sodium carbonate solution to remove any unreacted acid. The ethereal solution was dried over anhydrous sodium sulfate and the ether was evaporated. The yield of the ethyl ester was 16 g (80%).

Methylation of the ethyl ester of o-tolylacetic acid. A general procedure for the alkylation of the methylene group of phenylacetic acids reported by Kenogen, Kaizer and Hauser¹⁴¹ was followed.

To a stirred suspension of sodamide (2.3 g; 0.059 mol) in liquid ammonia (250 ml) was added a solution of the ethyl ester of o-tolyl-acetic acid (16 g; 0.085 mol) in ether (50 ml), followed, after 15 min, by a solution of methyl bromide (5.2 ml; 0.1 mol) in ether (15 ml). After 2 hr, ammonium chloride (3 g) was added to the stirred mixture and the ammonia was allowed to evaporate to dryness with stirring. The residue was washed with saturated sodium carbonate solution, followed by saturated sodium chloride solution, and then combined with two ethereal washings of the original aqueous layer, treated in the same manner. The ethereal solution was dried over anhydrous sodium sulfate and the ether was evaporated. The crude ester was obtained in a yield of 16.5 g. The ester was distilled under reduced pressure and the major fraction, distilled at 114° (7 mm), was collected. The yield of the ester was 10.3 g (60%).

Hydrolysis of the ethyl ester of o-methylhydratropic acid. In a 1 l round bottom flask, a mixture of the ethyl ester of o-methylhydratropic acid (10.3 g) and 10% aqueous potassium hydroxide solution (500 ml) was heated under reflux for 14 hr. The unhydrolysed ester was removed by ether extraction. The aqueous solution was then acidified with concentrated hydrochloric acid, and the free acid was precipitated in a yield of 8.7 g (85%); nmr (CDCl_3), τ 2.23 (s, 3H), 3.55 (s, 2H), 7.10 (s, 4H), -1.9 (s, 1H). The nmr spectrum of the methylated acid showed that this acid was contaminated with the parent acid, nmr (CDCl_3), τ 1.43 (d, 3H), 3.93 (q, 1H), 2.30 (s, 3H),

7.12 (s, 4H), -2.13 (s, 1H). The o-methylhydratropic acid was purified by repeated crystallization. The purity was checked by the nmr spectra, through the disappearance of the bands of the aromatic methyl protons and the methylene protons of the parent acid. Four crystallizations from a 4 : 1 mixture of water and ethyl alcohol gave 6.2 g of 95% pure acid, mp 92-94°. Three further crystallizations from n-heptane gave 4.5 g (43%) of pure acid as indicated by the nmr spectrum. The melting point of the acid was 93-94° (lit.¹⁴² mp 92-94°). The equivalent weight obtained by titration as described before (p. 112) was 164.

Anal. Calcd. for C₁₀H₁₂O₂: C, 73.14; H, 7.36. Found: C, 72.14; H, 7.26.

p-Methylhydratropic acid. The acid was prepared by the methylation of the methylene group of the p-tolylacetic acid as described in the following sequence of reactions.

Esterification of p-tolylacetic acid. In a 500 ml round bottom flask, a mixture of p-tolylacetic acid (23 g; 0.153 mol), methyl alcohol (60 ml) and concentrated sulfuric acid (6.5 ml) was heated under reflux for 3.5 hr. After cooling, the mixture was transferred to a separatory funnel with 75 ml water. The ester was extracted with ether (150 ml). The ethereal layer was separated and washed with water and then 5% sodium carbonate solution to remove the unreacted acid. The ethereal solution was dried over anhydrous sodium sulfate and the ether was evaporated. The methyl ester was obtained in a yield of 23 g (98%), nmr (CCl₄), τ 7.02 (s, 4H), 3.50 (s, 3H),

2.22 (s, 2H), 3.42 (s, 2H).

Methylation of the methyl ester of *p*-tolylacetic acid. The general procedure for the alkylation of the methylene group of phenylacetic acids (mentioned previously)¹⁴¹ was followed. To a stirred solution of sodamide (3.5 g; 0.087 mol) in liquid ammonia (450 ml) was added a solution of the methyl ester of *p*-tolylacetic acid (22 g; 0.134 mol) in ether (80 ml). After 15 min a solution of methyl bromide (5 ml; 0.0983 mol) in ether (25 ml) was added. After 3 hr, ammonium chloride (3 g) was added and the ammonia was allowed to evaporate to dryness with stirring. The residue was transferred in water and ether to a separatory funnel and the layers were separated. The ethereal solution was washed with a saturated solution of sodium carbonate followed by a saturated solution of sodium chloride. Two ether extractions and washings were repeated as above. The combined ethereal solution was dried over anhydrous sodium sulfate and the ether was evaporated. The ester was obtained in a yield of 22.4 g; nmr (CCl₄), τ 7.12 (s, 4H), 3.52 (s, 3H), 2.24 (s, 3H), 3.55 (q, 1H), 1.38 (d, 3H). The singlet of the methylene protons of the parent ester appeared as a shoulder with the band of the methyl protons of the carbomethoxy group of the methylated ester and overlapping with the quartet of the methine proton of the latter ester. Estimation of the purity of the methylated ester was done by comparing the intensity of the doublet of the α -methyl protons to that of the singlet of the aromatic methyl protons. The methyl ester of *p*-methylhydratropic acid was found to be 85% pure. The ester

(5 g) was chromatographed on 150 g silica gel. The ester was eluted with n-pentane which was later mixed with increasing amounts of carbon tetrachloride. Carbon tetrachloride was then used alone as eluent, followed by chloroform. The separation gave 2.9 g of relatively pure ester. The fraction having the highest impurities was 91% pure.

Hydrolysis of the methyl ester of p-methylhydratropic acid. The ester (2.9 g) was hydrolysed by heating under reflux with 10% aqueous potassium hydroxide solution (150 ml) for 2 hr. The unreacted ester was extracted from the aqueous solution with ether. The alkaline aqueous solution was then acidified with concentrated hydrochloric acid. The precipitated acid was extracted with ether. The ethereal solution was dried over anhydrous calcium sulfate and the ether was evaporated. The p-methylhydrotrropic acid was crystallized three times from n-pentane. The pure acid was obtained in a yield of 1.7 g (63%), mp 40° (lit.¹⁴³ mp 39-40°); nmr (CCl₄), τ -2.40 (s, 1H), 7.80 (d, 4H), 1.38 (d, 3H), 2.24 (s, 3H), 3.55 (q, 1H). The equivalent weight obtained by titration as described before (p. 112) was 164.

Anal. Calcd. for C₁₀H₁₂O₂: C, 73.14; H, 7.36. Found: C, 73.45; H, 6.99.

exo-2-Norborn-5-enecarboxylic acid. The crude acid was prepared from cyclopentadiene (89 g; 1.35 mol) and methyl acrylate (130.3 g; 1.51 mol) by the Diels-Alder reaction followed by hydrolysis and isomerization of the endo-2-norborn-5-ene methylcarboxy-

late formed. The preparation followed a procedure of Roberts, Turnbull Jr., Bennett and Armstrong.¹⁴⁴ The preparation gave a mixture of the endo- and the exo-2-norborn-5-enecarboxylic acid in 71.5% yield (74.4 g), bp 112.5-113° (4.5 mm) [lit.¹⁴⁴ bp 103.5-104° (2.2 mm)]. The exo-acid was separated from the acid mixture (55.6 g) and purified following a procedure of Ver Nooy and Rondestvedt Jr.¹⁴⁵ The pure acid was obtained in 58% yield (28 g), mp 44° (lit.¹⁴⁵ mp 44-45°).

anti- and syn-7-norborn-2-enecarboxylic acids. The acids were prepared from norbornylene by the following sequence of reactions.

Bromination of norbornylene. A procedure reported by Joshel and Butz¹⁴⁶ for the preparation of 2,7-dibromonorbornane by the bromination of norbornylene (240 g; 2.53 mol) was followed. The dibromo compound was obtained in 36% yield (234 g), bp 75° (6.5 mm)-77° (7 mm) [lit.¹⁴⁶ bp 70° (2.5 mm)].

Dehydrobromination of 2,7-dibromonorbornane. The dehydrobromination reaction of 2,7-dibromonorbornane (233 g; 0.917 mol) was carried out following a procedure of Joshel and Butz,¹⁴⁶ where syn-7-bromonorbornene was obtained in 52.8% yield (84 g), bp 70° (13 mm) [lit.¹⁴⁶ bp 68-70° (13 mm)]; n_D^{25} 1.5269 (lit.¹⁴⁶ n_D^{25} 1.5260).

Preparation of the methyl ester of anti- and syn-7-norborn-2-enecarboxylic acids. The mixture of acids was prepared from syn-7-bromonorbornene (126 g; 0.729 mol) by the Grignard reaction

following a procedure of Sauers and Howkorn.¹⁴⁷ The acids were obtained as a deep colored oily mixture (32.4 g, 32%). Crystallization from n-pentane and cooling in dry ice gave a yellowish white powder. The product was divided into two portions and each was methylated by adding it slowly at 0° to an ethereal solution of diazomethane (120 ml) that contained approximately 3.6 g of diazomethane. To each of the methylated solutions was added a few drops of acetic acid to ensure complete removal of all the diazomethane. The combined ethereal solution of the methyl esters was filtered from the solid impurities and the ether was evaporated. The mixture was fractionated using 380 x 10 mm column packed with glass helices. A fraction (8.3 g) distilled at 88-90° (25 mm), a second fraction (2.8 g) distilled at 90-93° (25 mm), and a third fraction (5 g) distilled at 93-99° (25 mm). A dark tarry material was left in the flask. The first fraction was analysed by glpc on a 10' x 1/4" column of diethyl glycol succinate (DEGS) on a 100/80 Firebrick using a Varian Aerograph, 202 with thermal conductivity detector. The fraction consisted of anti- and syn-7-norborn-2-ene methyl carboxylate in the ratio of 4 : 3. The two esters were collected separately by injecting 3 g of the mixture using 50 μ l syringe. The anti-ester was obtained in a yield of 1.25 g, n_D^{25} 1.4710 (lit.¹⁴⁷ n_D^{25} 1.4705). The syn-ester was obtained in a yield of 1.1 g, n_D^{25} 1.4784 (lit.¹⁴⁷ 1.4688).

Hydrolysis of the methyl ester of anti-7-norborn-2-enecarboxylic acid.

The ester (1.25 g) was dissolved in methyl alcohol (11 ml) in a 50 ml round bottom flask. Potassium hydroxide (0.65 g) was added and the

solution was heated under reflux for 11 hr. The solution gradually darkened. After cooling, the methyl alcohol was evaporated, and water (11 ml) was added to dissolve the residue. The unreacted ester was extracted with ether and the aqueous layer was acidified with concentrated hydrochloric acid. On cooling, a brownish solid precipitated (1 g; 80%), mp 69-71°. The crude acid was crystallized three times from *n*-pentane by cooling in dry ice. The pure anti-7-norborn-2-enecarboxylic acid was obtained as white shiny leaflets. The yield was 0.65 g, mp 72-73° (lit.¹⁴⁷ mp 70-73°). The melting point did not change after the second crystallization.

Hydrolysis of the methyl ester of *syn*-7-norbornenecarboxylic acid.

The ester (1.1 g) was dissolved in methyl alcohol (13 ml) in a 50 ml round bottom flask. Potassium hydroxide (0.5 g) was added and the mixture was heated under reflux for 12 hr. The methanol was evaporated and water (7 ml) was added to dissolve the residue. The unreacted ester was removed by extraction with ether and the alkaline aqueous solution was acidified with concentrated hydrochloric acid to give 0.6 g (55%) of the crude acid. Crystallization of the acid from *n*-pentane and cooling in dry ice gave pure *syn*-7-norborn-2-enecarboxylic acid (0.35 g), mp 95-96° (lit.¹⁴⁷ mp 91-96°).

Nitrosomethylurea. The compound was prepared by nitrosation of *N*-methylurea using a mixture of urea (200 g; 3.36 mol), 24 % aqueous methylamine solution (13 g; 1.02 mol), 95% sodium nitrite solution (73 g; 1 mol) and concentrated sulfuric acid (66 g; 0.66 mol). The preparation followed a procedure by Arndt¹⁴⁸ and the nitrosomethylurea was obtained in 70% yield.

Diazomethane. A solution of diazomethane in ether was prepared from an ethereal solution of nitrosomethylurea (31 g; 0.30 mol) and 50% aqueous potassium hydroxide solution (90 ml) following a procedure of Arndt.¹⁴⁹ The estimation of the amount of diazomethane in a certain volume of the solution was done in the following way. To an aliquot of the solution (15 ml) was added accurately weighed benzoic acid (2.01 g). After the yellow color of diazomethane disappeared, the excess benzoic acid was titrated against standardized sodium hydroxide solution. It was found that 0.74 g of the acid was left unmethylated. From the amount of benzoic acid consumed, it was estimated that 15 ml diazomethane solution contained about 0.41 g diazomethane.

Potassium Peroxydisulfate. The reagent grade, commercially available potassium peroxydisulfate was used without any further purification.

PROCEDURE FOR THE COMPETITIVE DECARBOXYLATION OF THE ACIDS.

Preparation and mixing of the solutions. Approximately 4.75×10^{-3} mol of each acid was accurately weighed into a 100 ml volumetric flask and dissolved in a 0.25-0.26 M solution of potassium hydroxide. The concentration of the solutions, approximately 4.75×10^{-2} M were checked by titration against standardized hydrochloric acid. The solution containing triphenylacetic acid, due to its low solubility, was two-thirds of the above mentioned

concentration. Solutions of potassium peroxydisulfate were prepared by dissolving accurately weighed amounts of the salt in water to make solutions of approximately 0.185 M.

The above stock solutions were used to prepare reaction aliquots (6.5 ml) which were 1.32×10^{-2} - 1.48×10^{-2} M in phenylacetic acid-1-C¹⁴, 1.32×10^{-2} - 1.48×10^{-2} M in the non-radioactive acids, about 5.8×10^{-2} M in potassium peroxydisulfate and about 0.16-0.18 M in potassium hydroxide. The reaction aliquants were placed in break seals (Figure VIII) cooled in ice. The break seals were degassed and sealed.

Decarboxylation of the acids. The break seals were placed in an oil bath at $74.3 \pm 0.1^{\circ}$. At this temperature the half-life of potassium peroxydisulfate is 7 hr.¹⁵⁰ The flasks were removed from the bath at intervals and quenched in ice to stop the reaction. The reaction was followed to about 50% completion which is usually a period of approximately 1 hr. One flask was kept as a blank, while two others were run to infinity.

Isolation and collection of carbon dioxide. The carbon dioxide formed upon the decarboxylation of the acids was absorbed in the potassium hydroxide solution as potassium carbonate. It was liberated by addition of sulfuric acid. In order to measure the carbon dioxide produced, a high vacuum technique was used⁸³ where the break seals containing the carbon dioxide as carbonate were connected to a series of traps (Figure IX). A breakable ampule containing sulfuric acid was placed on the seal of the break seal

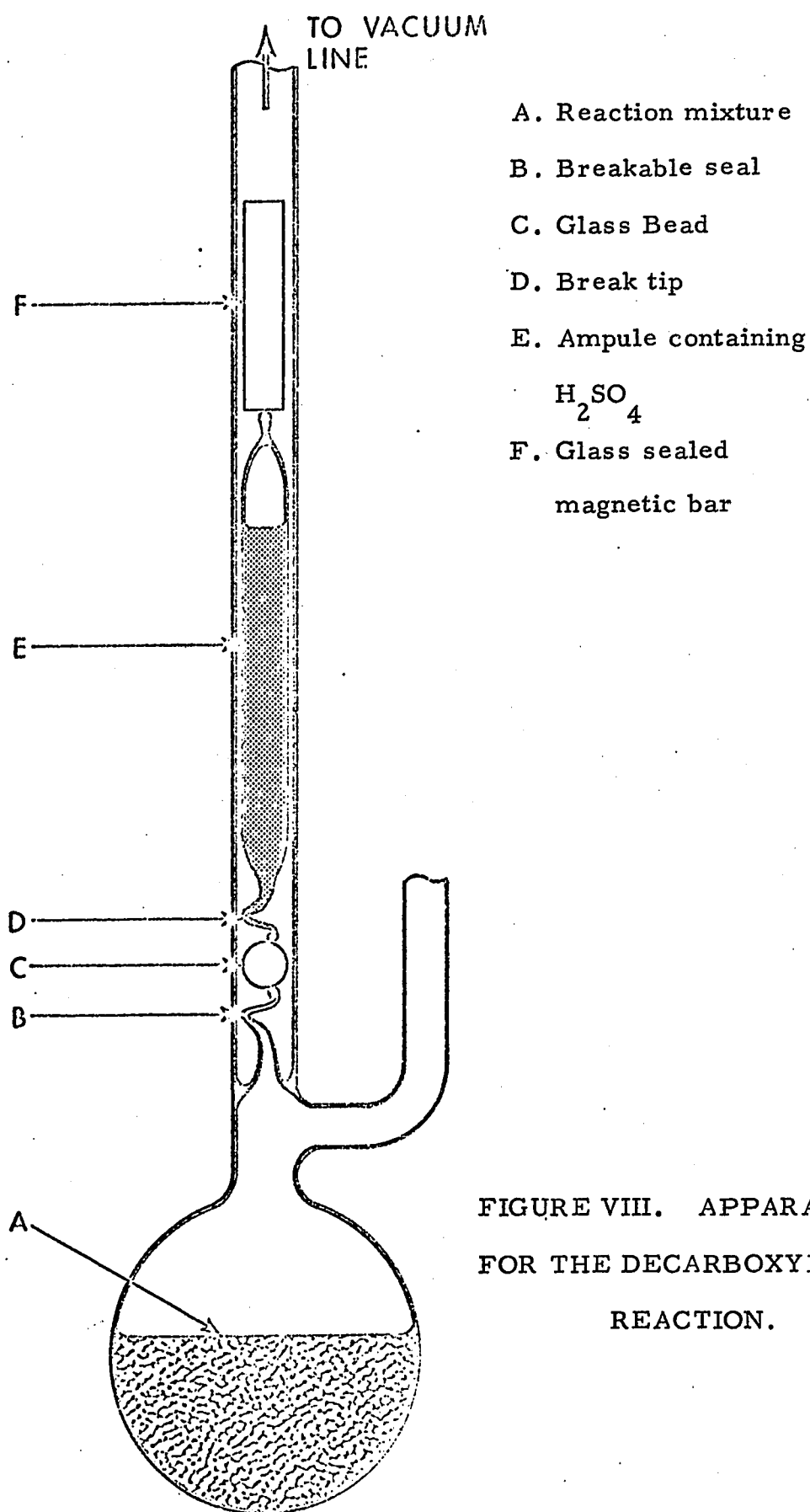
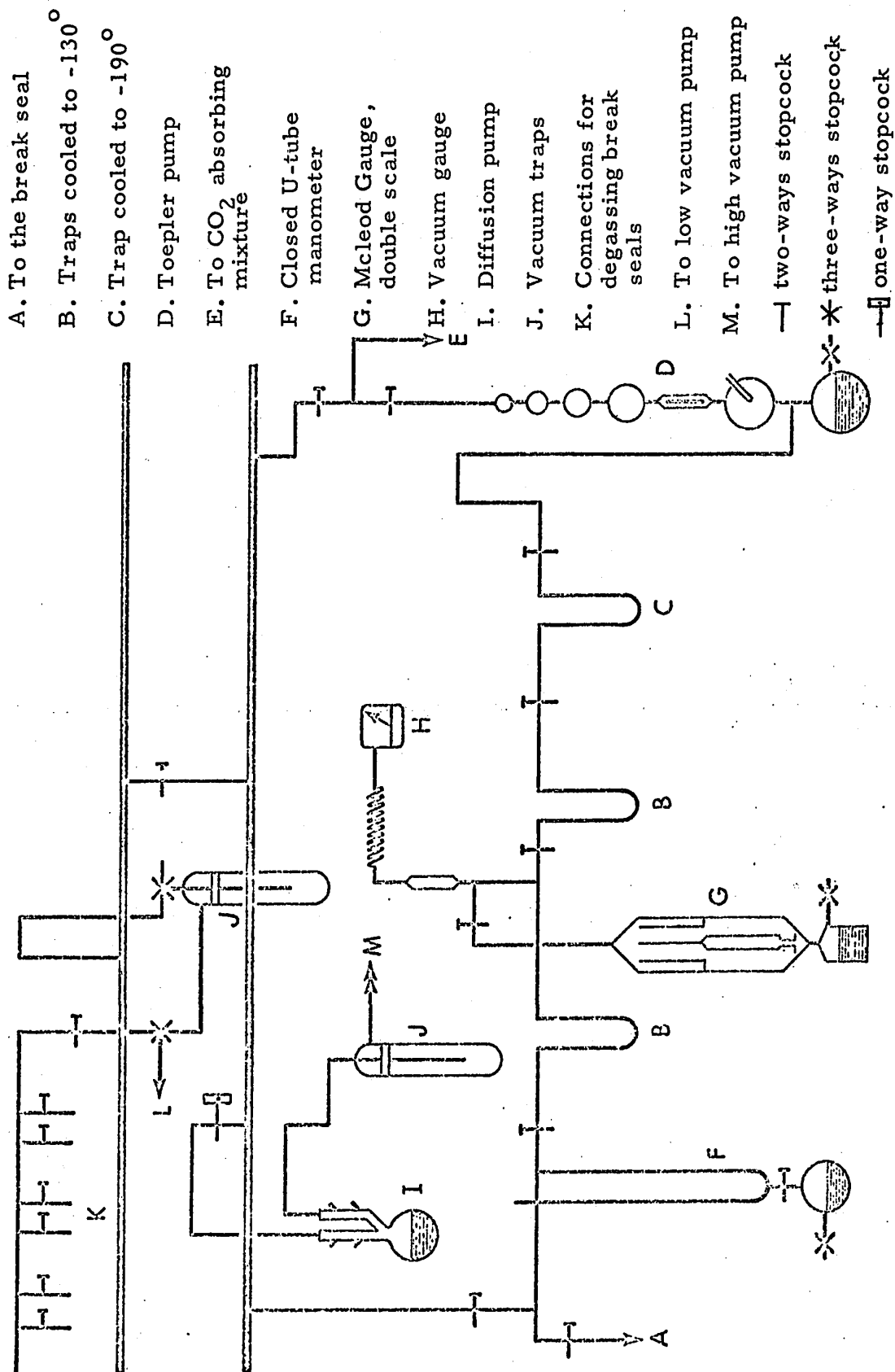


FIGURE VIII. APPARATUS
FOR THE DECARBOXYLATION
REACTION.

FIGURE IX. VACUUM LINE FOR THE ISOLATION AND COLLECTION OF CARBON DIOXIDE.



and a magnetic bar was placed on the top of the sulfuric acid ampule. The magnetic bar was raised using a magnet. When it was released, it broke the sulfuric acid ampule and the seal of the break seals, and the sulfuric acid was mixed with the reaction mixture. Sulfuric acid liberated the carbon dioxide from the potassium carbonate. Two traps were cooled with slushes of n-pentane (temp -130°) to condense the water, a third trap was cooled with liquid nitrogen (temp -196°) to condense the carbon dioxide. Any other residual noncondensable material contained in the vacuum line was distilled from the system. Carbon dioxide was distilled to a calibrated and evacuated Toepler pump where its volume and pressure were measured.

Absorption of the carbon dioxide in the scintillation mixture and the radioactivity counting. After it was measured, the carbon dioxide was absorbed in a scintillation solution and its radioactivity measured following a procedure by Jeffey and Alvary.⁸⁴

The trapping solution was a 1 : 2 mixture of 2-aminoethanol in ethylene glycol monomethyl ether. The scintillation solution was a 1 : 2 mixture of ethylene glycol monomethyl ether and toluene, to which was added the scintillator, 2,5-diphenyloxazole (PPO) (0.60 g/100 ml). The absorbing solution (3 ml) placed in a 25 ml round bottom flask connected to the vacuum line at an exit of the Toepler pump containing the measured gas. The absorbing mixture was cooled with liquid nitrogen and the exit of the pump was opened to let the carbon dioxide condense in the flask. The exit was closed and the

absorbing solution was brought to room temperature and stirred to dissolve all the carbon dioxide in the amine solution. A 2 ml portion of the amine carbonate solution was placed in a vial with 10 ml of the scintillation solution and the activity measured using the scintillation counter.

Upon the decarboxylation of phenylacetic acid- l -C¹⁴ alone, a linear relation was obtained between the amount of carbon dioxide measured at intervals of the decarboxylation reaction, from the first few minutes till infinity, and the numbers of counts/min (cpm) recorded on the scintillation counter. This linear relation plotted on a graph (Figure I) was used to relate the activity observed to the amount of radioactive gas evolved in the competitive decarboxylation reactions. On decarboxylation of a mixture of the active phenylacetic acid and any of the other inactive acids, the total amount of carbon dioxide evolved at any interval of the reaction was measured. The gas was absorbed in the scintillation mixture and its radioactivity obtained as cpm. From the number of counts obtained, the amount of the radioactive gas could be calculated. By subtracting this from the total amount of the mixed gas, the amount of the nonradioactive gas was determined.

The reaction, when run to infinity, 20 kinetic half-lives, gave quantitative yields of labelled and unlabelled carbon dioxide. The purity of the gas was confirmed by mass spectroscopic analysis.

pK_a MEASUREMENTS.

The pK_a's of the various acids were taken as the pH values of the half-neutralized aqueous solutions of the acids, measured with a Beckman Zeromatic II pH meter. An accurately weighed amount of phenylacetic acid was dissolved in potassium hydroxide solution of known concentration (approximately 0.1 M). The concentration of phenylacetic acid in this solution was calculated and checked by titrating an aliquot of the solution against a standardized hydrochloric acid solution. To 10 ml of the above mentioned solution, an amount of the standardized hydrochloric acid solution was added which was enough to neutralize all the potassium hydroxide and to liberate half of the phenylacetic acid from its potassium salt. A 10 ml portion of this half-neutralized solution of phenylacetic acid was placed in the pH meter cell. The pK_a value of phenylacetic acid, obtained from the reported dissociation constant,⁹⁰ was used to standardize the reading of the pH meter.

Similar half-neutralized solutions of p-tolylacetic acid, m-chlorophenylacetic acid, and pivalic acid were prepared and their pH values were measured on the standardized pH meter. The pK_a's for the acids were obtained from their reported dissociation constants.⁹⁰ It was found that there was a linear relation between the measured values of pH and the pK_a's reported. This relation was plotted as a straight line (Figure IV) and was used to correct for the readings of the pH's of the other unreported acids. This linear relation was checked using a number of other acids of known dissociation constants (p-bromophenylacetic acid, p-chlorophenylacetic acid and isobutyric

acid) and was found to give good agreement between the corrected and reported values of the pK_a 's.

Half-neutralized solutions of p-methoxyphenylacetic acid, o-tolylacetic acid, m-fluorophenylacetic acid, hydratropic acid, α -methylhydratropic acid, o-methylhydratropic acid, p-methylhydratropic acid and cyclohexene-3-carboxylic acid were prepared and their pH values measured and corrected using the linear relationship obtained earlier. The pK_a 's for all the other acids were obtained from their reported dissociation constants.⁹⁰

PRODUCT ANALYSIS FROM THE DECARBOXYLATION OF PHENYL-ACETIC ACID.

Aqueous solutions which were 2.94×10^{-2} M in phenylacetic acid, about 5.8×10^{-2} M in potassium hydroxide and 3.80×10^{-2} - 4.47×10^{-2} M in potassium peroxydisulfate were placed in break seals, degassed and sealed. The decarboxylation reactions were carried to infinity. After the completion of the reaction, the seal of each break seal was broken and the reaction mixture was transferred to a separatory funnel. The mixture was acidified with dilute sulfuric acid and saturated with potassium bromide. The organic material was extracted repeatedly with ether. The ethereal solution was separated leaving a yellow solid suspended in the aqueous layer.

Analysis of the ethereal solution was carried on by glpc using a 10' x 1/8" SE-30, 5% on 60/80 chromosorb W column on a

Varian Aerograph model 600-D with a flame ionization detector. Freon-112 was used as internal standard.

Calibration curves were made between Freon-112 and benzoic acid, benzylalcohol, benzaldehyde, bibenzyl and toluene, the expected soluble products from the decarboxylation reaction.

Very accurately weighed amounts of Freon-112 were added to the extract from each break seal and the mixture was injected in the gas chromatograph. The column temperature started at 40° and was programmed to 200°. From the weight of Freon-112 added, the area of peaks on the trace and the calibration curves, the amount of each component in the reaction mixture was calculated.

The insoluble polymeric material suspended in the aqueous layer was separated by centrifugation, repeatedly washed with water, and the solid was dried in a dessicator over phosphorous pentoxide at reduced pressure. The polymer was insoluble in the common organic solvents (n-pentane, benzene, toluene, carbon tetrachloride, methylene chloride, chloroform, methyl alcohol and ethyl alcohol). It dissolved in dimethyl formamide and dimethyl sulfoxide. Elemental analysis and molecular weight determination were carried out on the polymer to elucidate its structure. The average molecular weight of the polymer was 1400 and the elemental analysis showed, C, 63.26%; H, 4.31%; O, 20.19%; S, 2.33%. An approximate molecular formula for the polymer was calculated to be $C_{72}H_{60}O_{17}S_1$. The ir spectrum showed a strong hydroxyl band

(3340 cm^{-1}) and a weak carboxyl band (1700 cm^{-1}).

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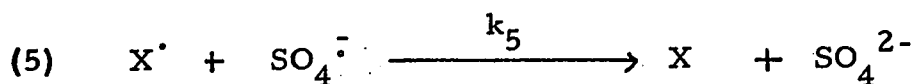
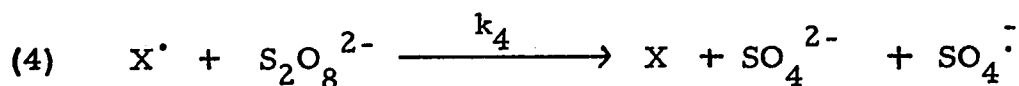
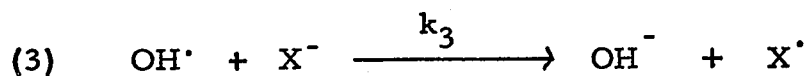
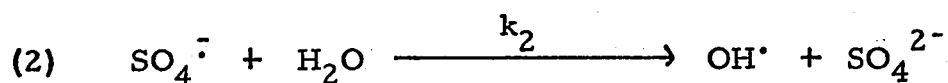
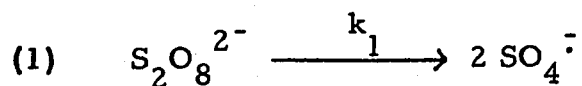
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APPENDIX I

DERIVATION OF THE VALUE OF THE RADICAL (X^\cdot) INVOLVED
IN THE MECHANISM OF THE UNCATALYSED OXIDATION OF THE
SUBSTRATE (X^-) WITH POTASSIUM PEROXYDISULFATE IN
NEUTRAL OR ALKALINE MEDIA.

The general scheme proposed for the above-mentioned
reaction is given in equations (1-5).



Several differential equations can be set up from this scheme.

$$(6) \quad -d(S_2O_8^{2-})/dt = k_1 (S_2O_8^{2-}) + k_4 (X^\cdot) (S_2O_8^{2-})$$

$$(7) \quad -d(X^-)/dt = k_3 (OH^\cdot) (X^-)$$

$$(8) \quad d(SO_4^{\cdot -})/dt = 2 k_1 (S_2O_8^{2-}) - k_2 (SO_4^{\cdot -}) + k_4 (X^\cdot) (S_2O_8^{2-}) \\ - k_5 (X^\cdot) (SO_4^{\cdot -})$$

$$(9) \quad d(X^\bullet)/dt = k_3(OH^\bullet)(X^-) - k_4(S_2O_8^{2-})(X^\bullet) - k_5(X^\bullet)(SO_4^{\cdot-})$$

$$(10) \quad d(OH^\bullet)/dt = k_2(SO_4^{\cdot-}) - k_3(OH^\bullet)(X^-)$$

By the steady state hypothesis, $(SO_4^{\cdot-})$, (X^\bullet) and (OH^\bullet) are constant, therefore:

$$(11) \quad d(SO_4^{\cdot-})/dt = d(X^\bullet)/dt = d(OH^\bullet)/dt = 0$$

Thus, from (10) and (11)

$$(12) \quad k_2(SO_4^{\cdot-}) = k_3(OH^\bullet)(X^-)$$

Substitution of (12) in (7) gives

$$(13) \quad -d(X^-)/dt = k_2(SO_4^{\cdot-})$$

and substitution of (12) in (9) gives

$$(14) \quad d(X^\bullet)/dt = k_2(SO_4^{\cdot-}) - k_4(X^\bullet)(S_2O_8^{2-}) - k_5(X^\bullet)(SO_4^{\cdot-}) = 0$$

Adding equations (8) and (14)

$$(15) \quad k_1(S_2O_8^{2-}) = k_5(X^\bullet)(SO_4^{\cdot-})$$

and subtracting equations (8) and (14)

$$(16) \quad k_2(SO_4^{\cdot-}) = k_1(S_2O_8^{2-}) + k_4(X^\bullet)(S_2O_8^{2-})$$

Thus, from equations (6), (13), and (16)

$$-d(S_2O_8^{2-})/dt = -d(X^-)/dt$$

Now, from equation (15)

$$(17) \quad (\text{SO}_4^{\cdot-}) = k_1(\text{S}_2\text{O}_8^{2-})/k_5(X^{\cdot})$$

and substitution of (17) in (16) gives

$$(18) \quad k_1 + k_4(X^{\cdot}) = k_1k_2/k_5(X^{\cdot})$$

Therefore

$$(19) \quad k_4(X^{\cdot})^2 + k_1(X^{\cdot}) - k_1k_2/k_5 = 0$$

Solving this quadratic gives

$$(20) \quad (X^{\cdot}) = \left[-k_1 \pm (k_1^2 + 4k_1k_2k_4/k_5)^{\frac{1}{2}} \right] / 2k_4$$

APPENDIX II

THE LEAST SQUARE CALCULATION.

For rate constants that are correlated by the Hammett equation, the reaction constant (ρ), the correlation coefficient (r) and the standard deviation (s) are obtained in the following way, where σ (or σ^+) are the substituent constant.

If (n) is the number of points on the graph or the number of relative rate constants and (y) is taken as the log of the relative rate constants k^I/k^{II} , then

$$\sum X^2 = \sum \sigma^2 - (\sum \sigma)^2/n$$

$$\sum XY = \sum (\sigma y) - (\sum \sigma)(\sum y)/n$$

$$\sum Y^2 = \sum y^2 - (\sum y)^2/n$$

$$\rho = \sum XY / \sum X^2$$

$$r = \left[(\sum XY)^2 / (\sum X^2)(\sum Y^2) \right]^{1/2}$$

$$s = \left\{ \left[(\sum Y^2) - (\sum XY)^2 / (\sum X^2) \right] / (n - 2) \right\}^{1/2}$$