May 29, 1959

To the Graduate Council:

I am submitting herewith a dissertation written by Billy Lee Stump entitled "Part I: A Study of the Catalytic Hydrogenation of Hydroxybenzenes Over Platinum and Rhodium Catalysts; Part II: The Kinetics of the Acid-catalyzed Hydrolysis of the Dimethyl Esters of Cyclohexanedicarboxylic Acids." I recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Chemistry.

Hilton A. Smith
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and recommend its acceptance:

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Dean of the Graduate School

PART I: A STUDY OF THE CATALYTIC HYDROGENATION OF HYDROXYBENZENES OVER PLATINUM AND RHODIUM CATALYSTS

PART II: THE KINETICS OF THE ACID-CATALYZED HYDROLYSIS OF THE DIMETHYL ESTERS OF CYCLOHEXANEDICARBOXYLIC ACIDS

A DISSERTATION

Submitted to
The Graduate Council
of
The University of Tennessee
in
Partial Fulfillment of the Requirements
for the Degree of
Doctor of Philosophy

---

by

Billy Lee Stump

June, 1959

ACKNOWLEDGEMENT

The author wishes to express his sincere appreciation to Professor Hilton A. Smith for the generous and thoughtful guidance and encouragement he has given during the course of this work. Thanks are also due to Mr. Paul P. Hunt for his help in preparing some of the dimethyl cyclohexanedicarboxylates used and to Mr. Kenneth G. Scrogham for the use of some of his data for the monomethyl esters of the cyclohexanedicarboxylic acids.

He would like to thank his wife, Phyllis, for her patience and understanding and his Mother and Father for their encouragement and support.

He is grateful to the Chemistry Department of the University of Tennessee for a Graduate Assistantship and to the Petroleum Research Fund of the American Chemical Society for the support of this research.

457755

To Phyllis and Vicki

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PART I

A STUDY OF THE CATALYTIC HYDROGENATION OF HYDROXYBENZENES OVER PLATINUM AND RHODIUM CATALYSTS

CHAPTER I

INTRODUCTION: HISTORICAL AND THEORETICAL

A. Hydroxybenzene Hydrogenations

It has been recognized for many years that when phenol undergoes hydrogenation, the product may be predominantly cyclohexanol, benzene, or cyclohexane, depending on the catalyst employed and the conditions of the reaction. The two courses of the reaction are represented by the equations:

1. $C_6H_5OH + 3H_2 \longrightarrow C_6H_{11}OH$

2. (a) $C_6H_5OH + H_2 \longrightarrow C_6H_6 + H_2O$

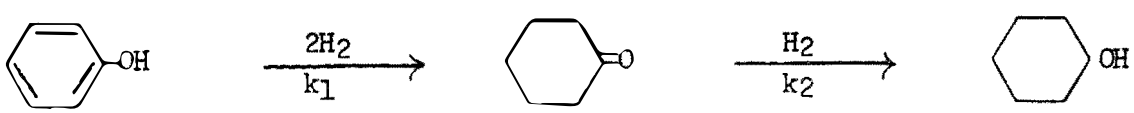
   (b) $C_6H_6 + 3H_2 \longrightarrow C_6H_{12}$

Under certain conditions and with specific catalysts, cyclohexanone may be isolated during the course of the reaction, and the role of this compound as an intermediate has been investigated. A detailed review of the catalytic hydrogenation of phenol and substituted phenols is given by Smith in Volume V of "Catalysis."[1] A portion of the work outlined in this review is presented here.

The first to isolate cyclohexanone as an intermediate in the hydrogenation of phenol were Vavon and Bertin.[1,2] They hydrogenated phenol and the cresols over platinum black and isolated cyclohexanone by reaction of the ketone with semicarbazide and isolation of the semicarbazone formed. It was proposed that cyclohexanone is the first product of the reaction and is desorbed. It later returns to the catalyst and there transfers hydrogen to phenol. Grignard and Mingasson[1,3] studied the

hydrogenation of phenol in the solvent cyclohexanol over pumice-supported nickel (from the hydroxide) as catalyst and at temperatures up to 300°. For each pressure investigated they observed a critical temperature at which cyclohexanol is dehydrogenated to cyclohexanone; e.g., 155° at around 20 mm. and 180° at 760 mm. They suggested that the non-contiguous double linkages of the phenol are first hydrogenated to form the enol of cyclohexanone, and that this enol is tautomerized when cyclohexanone is isolated but absorbs hydrogen to give cyclohexanol if the hydrogenation is prolonged.

Coussemant and Jungers[4] made a thorough study of the kinetics of catalytic hydrogenation of phenol over Raney nickel. By combining information on hydrogen absorbed plus refractive index, it was possible to ascertain the percentages of phenol, cyclohexanol, and cyclohexanone present at any stage of the reaction. It was found that cyclohexanone concentration reaches a maximum during the reaction, and that the fraction present at this maximum depends on the temperature. They concluded that the mechanism of the nickel-catalyzed reaction was



These authors made a complete kinetic analysis of this reduction which has general application to two-step catalytic reactions.

Zil'berman[1,5] studied the free energy changes accompanying the hydrogenation of phenol to cyclohexanone and cyclohexanol and set up equations relating such free energy changes to reaction temperature. Most of

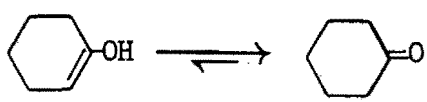
the other workers who have studied the catalytic hydrogenation of phenol and cresols have used some form of nickel catalyst to give cyclohexanols, although cobalt, copper, and mixed nickel and cerium oxide catalysts have been used to some extent.

In more recent work, Tutumi, Tsutsumi, Yoshijima, Akatsuka, and Nagao[6] have found that the nickel-aluminum and copper-aluminum alloys which are used as the raw materials for the preparation of Raney catalysts have a noticeable catalytic activity. Phenol is hydrogenated easily to cyclohexanol in water or diluted caustic soda solution, using 20 per cent alloy and 20 per cent water with 50 atmospheres hydrogen pressure and a temperature of about 200°. Rosenblatt[7] suspended phenol in water with 5 per cent rhodium-alumina catalyst. This mixture was shaken at room temperature and atmospheric pressure in an atmosphere of hydrogen, and the reaction proceeded with a uniform rate of .067 liters $minute^{-1}$ to the end of the reaction.

Sasa[8] hydrogenated phenol at 160° and 15 atmospheres hydrogen pressure in 6.3 hours to cyclohexanol, over the nickel catalyst obtained from nickel formate. When the reaction catalyst was used again (up to four times), the reaction time was shortened. Yeh, Chen, Chu, Hsu, Chang, and Hsiu[9] hydrogenated phenol over nickel-kaolin catalyst at 140° and 80 atmospheres hydrogen pressure to give a quantitative yield of cyclohexanol. Vandenheuvel[10] prepared a catalyst containing 14 per cent platinum by supporting platinum oxide on silicic acid. This catalyst is reported to be 2.5 times as active as Adams platinum. It is effective in catalyzing the hydrogenation of the benzene ring in phenol, but in phenol

ethers the ring is left intact. Phenol passed continuously over a mixture containing hydrogen in the presence of a complex silicate ($2H_2SiO_3 \cdot NiO \cdot 4H_2O$) at 140-180° is completely transformed to cyclohexanol for a period of one hundred twenty hours.[11]

Thompson[12] hydrogenated phenol to 26 per cent completion at 146° and 1500 p.s.i. initial hydrogen pressure over rhodium (oxide) catalyst and found 24 per cent ketone in the reaction mixture. He concluded that the formation of this ketone can be explained by a partial hydrogenation of the benzene ring to 1-hydroxycyclohexene-1, which is the tautomeric form of cyclohexanone:



The effect of the hydroxyl group on the rate of hydrogenation of the benzene ring was investigated by Gilman and Cohn[13] by comparing the reaction rates of benzene, phenol, hydroquinone, and pyrogallic acid. Their hydrogenations were carried out in aqueous solution over 5 per cent rhodium-alumina catalyst. Under comparable conditions, the hydrogenation rate decreases in the following order: benzene, toluene, benzyl alcohol, phenylethyl alcohol. The hydroxyl group depresses the hydrogenation rate somewhat more than an added alkyl group. It also seems that its effect is more pronounced when it is more distant from the ring.

Ungnade and McLaren[1,14] studied the effect of aqueous sodium hydroxide on the catalytic reduction of phenols over Raney nickel and were able to reduce substituted phenols and obtain high yields of the corresponding cyclohexanols. These reactions did not occur to an appreciable

extent without the addition of the base. Ungnade and Nightingale[1,15] hydrogenated the cresols and found the ease of hydrogenation to be *para* > *meta* > *ortho*, and the *trans* isomer was always produced by the reduction.

Barney and Haas[1,16] studied the hydrogenation of thymol over Raney nickel and investigated the influence of temperature and pressure on the formation of the ketone intermediate. They found that both increasing pressure and increasing temperature decrease the per cent of ketones present in the reaction mixture. Whitaker[1,17] prepared a number of substituted cyclohexanones and cyclohexanols by controlled hydrogenation of polyalkylphenols.

Wicker[18] hydrogenated *o*-, *m*-, and *p*-cresol and the corresponding methylcyclohexanones in acetic acid over Adams platinum catalyst at 20°. He reasoned that if phenol or the cresols hydrogenate *via* a cyclohexanone intermediate, then one should obtain the same per cent stable stereoisomer of cyclohexanol whether one starts with the cresol or the corresponding methylcyclohexanone. The results obtained were not in accordance with this prediction:

Compound	Stable Isomer (%)	Compound	Stable Isomer (%)
o-Cresol	75	2-Methylcyclohexanone	30
m-Cresol	51	3-Methylcyclohexanone	75
p-Cresol	61	4-Methylcyclohexanone	53

As was mentioned earlier, Vavon and Bertin[2] assumed that each molecule is hydrogenated to the ketone, which is then desorbed back into solution

where it competes with the remaining phenol for hydrogen. To interpret his results, Wicker assumed that the transition occurs, not only as Vavon and Bertin suggest, but also *via* the enolic form of the ketone; the reduction of the enol may occur while the compound is still adsorbed on the active centers of the catalyst. Hence the proportions of stereoisomers produced when the cresols are hydrogenated will differ from those obtained when the corresponding methylcyclohexanones are reduced, since these exist essentially in the ketonic form.

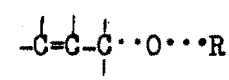
Benzene rings containing more than one hydroxyl substituent have also been reduced to the corresponding cyclohexanepolyols.[1] The catalyst used in most of these hydrogenations was some form of nickel, but copper chromite, platinum, and palladium have been used. Especially interesting is the hydrogenation of resorcinol in the presence of alkali over Raney nickel at 50° and 1000 to 1500 p.s.i. hydrogen pressure to form the diketone, dihydroresorcinol, in high yields.[1,19]

Gilman and Cohn[13] hydrogenated the isomeric dihydroxybenzenes, catechol, resorcinol, and hydroquinone, over 5 per cent rhodium-alumina catalyst. The hydrogenation rates of the *ortho*-, *meta*-, and *para*-isomers differ from each other in sharp contrast to the uniformity observed with the xylenes. In studying the rates of hydrogenation of the dihydroxybenzenes, a peculiar anomaly was observed. These compounds were hydrogenated at constant rate until approximately five-sixths of the theoretical amount of hydrogen was absorbed. At this point, the rate increased abruptly and markedly until the theoretical end point was reached with a sudden cessation of hydrogen uptake. In a typical example, 200 mg. of hydro-

quinone were hydrogenated over 150 mg. of 5 per cent rhodium on alumina in 100 ml. of water. Hydrogen was being consumed at 4.4 ml. $min.^{-1}$ till almost five-sixths of the reaction was complete; then the rate increased abruptly to 6.8 ml. $min.^{-1}$. The rate anomaly was observed with hydroquinone, resorcinol, and catechol. This different behavior of the dihydroxy compounds which might throw some light on the reaction mechanism is at the present unexplained.

B. Hydroxy-group Cleavages

The fission of the carbon-oxygen bond in ether linkages under a number of conditions has been known for many years. In molecules in which a carbon-oxygen ether bond is β with respect to a carbon-carbon double bond, cleavage is quite easy. Such a linkage is shown below:

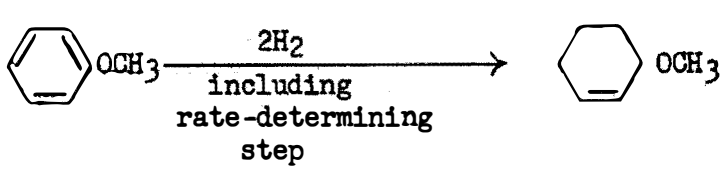


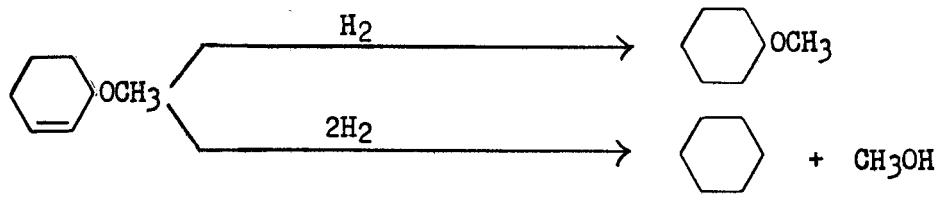
The double bond may be a part of an aromatic ring as in benzyl alkyl ethers. That such an ether bond is labile is in agreement with the well-known fact that a double bond in the β-γ position weakens carbon-oxygen, carbon-nitrogen, carbon-halogen, and other bonds throughout a wide series of compounds. Such a bond for aromatic ethers may be catalytically cleaved under conditions too mild for ring hydrogenation. For example, alkyl ethers of benzyl alcohol may be cleaved quantitatively to toluene and alkyl alcohols by use of palladium in alcohol solution.[20] It is of interest to note that hydrogenolysis of a p-methoxybenzyl ether, using palladium in alcohol solution, gives only p-methoxytoluene and an alkyl alcohol.[21] The methoxyl group on the aromatic ring is not cleaved under these conditions--

conditions which are also too mild for ring hydrogenation.

Thompson[12] has pointed out that the catalytic hydrogenolysis which has received less attention is that involving cleavage of methoxyl (or hydroxyl and alkoxyl, in general) groups from aromatic nuclei during the hydrogenation or ring saturation of these compounds. He studied the catalytic hydrogenation of methoxybenzenes and other aromatic methoxyl compounds. Hydrogenation of the aromatic ring was usually accompanied by some cleavage of the methoxyl groups. This cleavage occurred predominantly upon the carbon-oxygen bond adjacent to the aromatic ring, and the cleavage reaction was found to occur only as a part of the aromatic hydrogenation process. Platinum led to extensive methoxyl cleavage while rhodium catalyzed ring saturation with little cleavage. Reaction temperature and acid concentration were found to influence the extent of cleavage also.

A mechanism for the cleavage reaction was proposed.[12] The methoxybenzene, anisole for example, is adsorbed on the catalyst surface. With the approach of hydrogen to the catalyst surface, hydrogenation takes place to give methoxycyclohexene as a short-lived intermediate. This intermediate may then undergo cleavage to give cyclohexane and methanol or ring hydrogenation to give methoxycyclohexane. These reactions will probably occur simultaneously until the double-bonded molecules are saturated.





Phenols may be reduced to form aromatic hydrocarbons, cyclohexanone, and aliphatic compounds resulting from ring cleavage.[1] The hydroxybenzene to be reduced has generally been treated with hydrogen at 300 to 500° and pressures of from 50 to 150 atmospheres. Molybdenum sulfide has been used as the catalyst, although molybdenum oxide alone or in the presence of oxides of aluminum, silicon, chromium, and barium, as well as ammonium molybdate have been employed. Other catalysts include tungsten oxide and sulfide, cobalt oxide and sulfide and nickel oxide.

Lozovoi, Vol'Epshtein, and Senyavin[22] report the hydrogenation of phenol to benzene using three fresh samples of the principal vapor-phase catalysts, tungsten disulfide, tungsten disulfide plus nickel sulfide plus alumina, and tungsten disulfide plus aluminosilicates. A continuous laboratory installation employing 50-200 atmospheres hydrogen pressure at 350° was used. Klimov and Bogdanov[23] hydrogenated phenol with tungsten disulfide and reported the cleavage of the hydroxyl group from the ring to give benzene and water as products.

With these catalysts, cleavage is the expected and desired result. The catalytic hydrogenolysis which has received less attention is that involving cleavage of hydroxyl groups from aromatic nuclei during the hydrogenation or ring saturation of these compounds. Most literature articles simply relate that an hydroxyl group of a certain compound was cleaved during hydrogenation.

Amatatsu[1,24] found that hydrogenation of the dimethyl ether of catechol yielded several products and compared the distribution of these with those obtained by reduction of catechol and the dimethyl ether of 1,2-cyclohexanediol. His reductions were carried out over nickel at pressures of 50 to 60 atmospheres and temperatures of 140-200°. He also hydrogenated safrol to propylcyclohexanol. On the basis of his experiments, he concluded that the velocity of splitting of the oxygen-phenyl bond was in the order

$$-OH < -OCH_3 < -O-CH_2-O \ .$$

Levin and Pendergrass[25] have studied the effect of acidic and basic media on the cleavage of hydroxyl and methoxyl groups. For p-hydroxybenzoic acid and p-methoxybenzoic acid in alcohol solution, at room temperature and over platinum catalyst, they observed 38 and 74 per cent cleavage, respectively, during the hydrogenation. In weakly acidic ethanol, the hydroxyl compound exhibited 47 per cent cleavage, while only 22 per cent occurred in alkaline ethanol. The cleavage was also found to be greater in acetic acid than in ethanol. The cleavage product was cyclohexanecarboxylic acid in each case. These workers also report that the low-pressure hydrogenation of ethyl p-hydroxybenzoate in ethyl acetate over palladium-on-strontium carbonate as catalyst resulted in a mixture of reduction products containing about 25 per cent of the ethyl cyclohexanecarboxylate and 75 per cent ethyl 4-hydroxycyclohexanecarboxylate. However, high-pressure hydrogenation gave a quantitative yield of the hydroxy-ester. These experiments are claimed to indicate that hydrogenation and hydrogenolysis are competing reactions, with increased pressure favoring hydrogenation.

Reduction of the hydroxybenzoic acids has been reported by several authors. Balas and Srol[1,26] reduced ortho-, meta-, and para-hydroxybenzoic acids in alcohol over platinum black as catalyst and recovered the cis forms of the corresponding hydroxycyclohexanecarboxylic acids. Edson[1,27] reduced the same acids in water solution over platinum oxide catalyst and obtained mixtures of the hydroxycyclohexanecarboxylic acids with cyclohexanecarboxylic acid. The splitting of the hydroxyl group was about 80 per cent for the para acid, 50 per cent for the meta acid, and 15 per cent for the ortho acid.

Lukes, Trojanek and Blaha[28] made a systematic investigation of the reduction and hydrogenolysis of hydroxyl groups in the isomeric hydroxybenzoic acids. They used platinum oxide in aqueous suspension at 21 to 25° with about 740 mm. hydrogen pressure. Hydrogenolysis increased in the order ortho (20.8 per cent) < meta (67.8 per cent) < para (84.5 per cent). Wicker[18] reported 20-25 per cent cleavage of the hydroxyl groups when he hydrogenated o-, m-, and p-cresol over Adams platinum in acetic acid at 20°.

Further evidence that hydrogenolysis of methoxyl and hydroxyl groups does not occur when conditions are too mild for ring hydrogenation is furnished by the work of Williams.[29] Acetylhydroquinone was hydrogenated in the presence of pre-reduced copper chromite catalyst at 70-80° and 3800 to 4000 p.s.i. hydrogen pressure and found to give 2,5-dihydroxyphenylmethylcarbinol. Raising the temperature to 110-130° resulted in the cleavage of the carbinol hydroxyl group to give ethylhydroquinone, but the hydroxyl groups attached to the aromatic nucleus were not cleaved.

C. Supported Catalysts

The work of Thompson[12] represents the first study of supported catalysts in this laboratory. A detailed review of the functions of a catalyst support or carrier is given in Volume I of "Catalysis."[30] A catalyst support is defined by Innes as "a major catalyst constituent that serves as a base, support, carrier, or binder for the active constituent but which by itself has little, if any, catalytic activity." Some of the functions of a support are given below: (1) It serves as a framework for the catalytic component. The support may reduce shrinkage, lend physical strength, etc. in this capacity. (2) It may prevent sintering of the catalyst surface during a reaction by dissipating the heat of reaction over a much larger area than that of the active metal itself. (3) It may prevent catalyst poisoning during a reaction by selective adsorption of species which would cover the active metal. (4) It may increase the activity per unit weight of catalytic metal. This increase may be due to an increase in the number of available active sites or to a change in the electronic or crystal structure of the active constituent.

The nature of the support itself may vary widely depending upon the particular property desired in the final catalyst. Examples of widely used supports are alumina, silica, carbon, pumice, diatomaceous earths, and bauxite.

Little, if any, work has been done on the relative merits of supported and unsupported catalysts for phenol hydrogenations. The work of

Grignard and Mingasson[3] using pumice-supported nickel was referred to earlier. D'Or and Orzechowski[1,31] made a series of mixed nickel and cerium oxide catalysts and studied the reduction of phenol to cyclohexanol. They measured the actual nickel surface of these catalysts by adsorption of hydrogen at 180° and 1 atmosphere pressure. (Only nickel adsorbs hydrogen under these conditions.) For the most active catalysts, the activity per unit nickel area is equivalent to that of pure nickel. For the inactive catalysts of low nickel content, the fraction of the surface occupied by nickel is much too high, indicating an inactive form of sub-amorphous nickel.

Duzee and Adkins[32] state that supported catalysts are much better than the corresponding unsupported ones for catalytic hydrogenation without hydrogenolysis. Thompson[12] has shown that this is not necessarily true but depends on the nature of the support and other reaction conditions. For example, acidic supports such as silica promote dehydration or cleavage during high-temperature hydrogenations. Taylor, Rose, and Alderson[33] have reported that acidic supports lead to hydrogenolysis during the dehydrogenation of cyclohexanol to phenol.

D. Rhodium Catalysis

A review of the great amount of research done on the catalytic hydrogenation of aromatic compounds using platinum catalysts is beyond the scope of this work. However, the use of rhodium for reduction of aromatic rings is relatively new, and a summary of the work with this catalyst has been given by Thompson.[12] Portions of his review are included

here, together with more recent work with rhodium catalysts.

Zelinski and Pollak[12,34] were the first to report that rhodium is adapted to hydrogenation of the benzene ring. They worked with platinum, rhodium, ruthenium, and iridium catalysts supported on asbestos. The activity of the rhodium appeared to be about the same as that of platinum, and it was found that platinum and rhodium were superior to ruthenium and iridium with respect to sintering at high reaction temperatures. Of the series platinum, rhodium, iridium, ruthenium, and palladium, only platinum and rhodium continued to catalyze the hydrogenation of benzene at 300-310°.

Zenghelis and Stathis[12,35] have reported that colloidal rhodium is superior to colloidal platinum for the reduction of many unsaturated molecules. They further stated that the rhodium-catalyzed reduction did not require an acidic medium, while for some of the platinum hydrogenations such a medium was necessary. Minacher[12,36] has found that 1 per cent rhodium on alumina and on carbon have about the same activity with respect to hydrogenation of benzene as do the corresponding platinum catalysts. Recently, workers at Baker and Company[12,37] (supplier of commercial catalysts) have shown that 5 per cent rhodium on alumina is effective for the reduction of many substituted aromatic and heterocyclic compounds. This catalyst was shown to be somewhat more active than 5 per cent platinum on alumina.

Hernandez and Nord,[12,38] who worked with colloidal rhodium and rhodium on carbon, have some evidence that the mechanism for rhodium reductions may be different from that in platinum and palladium reductions.

With rhodium supported on colloidal polyvinyl alcohol, they found that the rate of reduction of nitro groups attached to aromatic nuclei was dependent upon the electronic nature of other substituents on the aromatic ring. Also, the rate of hydrogenation of nitrobenzene over the colloidal rhodium was sensitive to pH; the reaction was not sensitive to pH when carried out over colloidal palladium. Emmett[39] has repeated the work of Hernandez and Nord and found their results to be in error. His results indicate that the mechanisms for rhodium and platinum reductions are the same.

Thompson[12] has made an extensive study of the utility of various rhodium compounds as catalysts for the hydrogenation of the benzene nucleus. Five per cent rhodium on alumina was found to catalyze readily the hydrogenation of the benzene nucleus at room temperature and ordinary pressures. With this catalyst anisole absorbed 3.06 moles of hydrogen per mole, corresponding to only 6 per cent cleavage. The hydrogenation of 1,4-dimethoxybenzene was carried out using Adams platinum, 5 per cent platinum on alumina, rhodium black, and 5 per cent rhodium on alumina. The rates of hydrogenation were measured, as well as the amounts of cleavage.

It was found that about 50 per cent of the methoxyl groups were cleaved during hydrogenation with the platinum catalysts, while only about 12 per cent underwent cleavage when rhodium was employed. It appears to be an intrinsic metal property that governs the amount of cleavage rather than a difference in surface properties of the catalyst. Supported and unsupported catalysts for each metal led to about the same amount of cleavage.

On a total weight basis, the pure metal catalysts were found to be more active in each case. Adams platinum is almost six times as active as platinum on alumina; rhodium black is over twice as active as rhodium on alumina. On the basis of weight of catalytic metal, however, the supported catalysts are much superior.

Thompson did some hydrogenation work with commercially obtained rhodium oxide. This material did not catalyze the hydrogenation of benzoic acid in glacial acetic acid at room temperature. Heating the rhodium oxide in a high-pressure bomb under a hydrogen pressure of 1200 p.s.i. caused reduction at about 125°. The catalyst thus obtained was active in hydrogenating benzoic acid at room temperature and low pressures. Thompson hydrogenated anisole, p-dimethoxybenzene, m-methoxybenzoic acid, and phenol in the high-pressure bomb at temperatures of 125-150° and pressures of 1200-1600 p.s.i. It was found that rhodium (oxide) is not nearly as active a catalyst as are Adams platinum and 5 per cent rhodium on alumina.

Reference to the research of Gilman and Cohn[13] with 5 per cent rhodium on alumina catalyst has been made earlier in this work. They studied the rate of hydrogenation of benzene and the influence of substitution of alkyl-, hydroxyl-, and carboxyl-groups. All substitutions were found to decrease the hydrogenation rates. Upon introducing methyl groups directly in the ring, the hydrogenation rate decreases exponentially with an increasing number of methyl groups. With other alkyl groups and hydroxyl and acid groups, no simple correlation to the hydrogenation rate has been found. The hydrogenation is stoichiometric, and no indication for cleavage from the ring of the groups substituted was found.

E. Purpose of Present Research

1. Hydroxyl Cleavage

As previously mentioned, the hydrogenation of methoxybenzenes over platinum catalyst is accompanied by cleavage of the methoxyl groups from the benzene ring to a much greater extent than when rhodium is used as a catalyst. Thompson[12] has pointed out that most of the work which has been published on the cleavage of aromatic ethers does not deal with the ultimate nature of the phenomenon and the factors influencing it. There are sufficient data available for one to realize that the problem is complex and that both the existence and extent of cleavage are influenced by many factors. It was the purpose of this research to extend Thompson's methoxybenzene studies to include the hydroxybenzenes, with the hope that further understanding of the cleavage reaction could be gained. Effects of temperature were to be considered, as well as the structure of the compound being hydrogenated and the nature of the catalyst itself.

2. Ketone Intermediates in the Hydrogenation of Phenols

A study of the role played by cyclohexanone in the hydrogenation of phenol has claimed the interest of various investigators over the years, and a review of these studies has been given earlier in this work. It was of interest to extend such studies to include the hydrogenation of the isomeric dihydroxybenzenes, catechol, resorcinol, and hydroquinone, to find out whether ketones or diketones are formed during the course of the reaction, and, if so, in what amounts. This might lead to interesting

conclusions concerning the mechanism of the hydrogenation of the benzene nucleus, as well as provide an advantageous method for the preparation of cyclic ketones and diketones.

3. Effect of Substitution on Reaction Rates

This laboratory has been active for many years in the study of the effect of substituents and substitution on the platinum-catalyzed hydrogenation of the benzene nucleus, and in more recent years this study has been extended to include various other catalysts, particularly rhodium. It was desired to extend these data to include various hydroxyl substituted benzenes. Of particular interest was a comparison of the rates of hydrogenation of hydroxybenzenes with the corresponding methoxybenzenes.

CHAPTER II

EXPERIMENTAL

A. Materials

1. Adams Platinum Catalyst

Commercial preparations of platinum oxide were used as obtained from the American Platinum Works, Newark, New Jersy, and from the Goldsmith Brothers, Chicago, Illinois. Each sample of catalyst was standardized by hydrogenation with benzoic acid in order that all rate constants might be referred to a standard catalyst. The standard which has been chosen for the work in this laboratory gives the value of 0.1120 liters $gram^{-1}$ $minute^{-1}$ for k_{30} for the hydrogenation of benzoic acid in glacial acetic acid with Adams platinum.

2. Five Per Cent Rhodium on Alumina and 5 Per Cent Platinum on Alumina

These catalysts were used as obtained from Baker and Company, Inc., Newark, New Jersey. All catalysts were stored in glass bottles which were kept in a desiccator.

3. Acetic Acid

Glacial acetic acid, used as solvent in most of the hydrogenations, was obtained by fractionation of du Pont C. P. glacial acetic acid through an 8-ft. Vigreux column and the fraction boiling between 116.7-116.9°/740 mm. was collected.

4. Methanol

Fisher Certified Reagent methyl alcohol was used without further purification as solvent in some hydrogenations.

5. Benzoic Acid

Eastman white label (sublimed) benzoic acid was used without further purification.

6. Hydrogen

Commercial hydrogen obtained from the National Cylinder Gas Company was used without further purification. This hydrogen has been shown previously to be satisfactory for use in catalytic hydrogenations.

7. Phenol

Matheson (Coleman and Bell Division) phenol was fractionated through a 2-ft. Vigreux column and the fraction boiling at 181.6°/745.8 mm. was collected. The colorless product was stored in a brown bottle in the dark.

8. Catechol

Eastman white label catechol, m.p. 106-106.2°,* was purified by recrystallization from benzene. The recrystallized catechol melted at 108.5°.

9. Resorcinol

Matheson (Coleman and Bell Division) resorcinol, m.p. 111.2-111.6°, was recrystallized from toluene. Recrystallization produced no change in the melting point.

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*All melting points were taken on an aluminum melting point block using Anscheutz thermometers.

10. Hydroquinone

Merck hydroquinone, m.p. 175.0-176.8°, was purified by dissolving the material in a minimum amount of acetone and adding an excess of benzene to the solution. The crystals of hydroquinone obtained in this manner melted at 175.4-176.6°.

11. Phloroglucinol

Eastman white label phloroglucinol, m.p. 219°, was used without further purification.

12. Pyrogallol

Baker Chemical Company pyrogallol, m.p. 136°, was recrystallized from an ethanol-benzene mixture. Recrystallization produced no change in the melting point.

13. Cyclohexanone

Eastman white label cyclohexanone was used without further purification.

B. Low-pressure Hydrogenations

1. Apparatus and Procedure

A low-pressure Parr apparatus containing certain modifications which allowed more accuracy in the determination of reaction rates was used. The hydrogen pressure gauge employed was graduated to the nearest quarter of a pound, and accordingly pressures could be estimated to be nearest tenth of a pound. The standard hydrogen tank provided was replaced

with a smaller tank so that small samples could be hydrogenated with a relatively large drop in pressure. The volume of the system used in this work, including reaction bottle and connections, was 1.14 liters.[40] The general procedure for carrying out a hydrogenation was the same as that previously described.[41]

The initial hydrogen pressures for each hydrogenation were about 50 p.s.i.g. The changes in pressure during the course of the reactions were of the order of 5-15 p.s.i.

The reaction bottle of the apparatus was enclosed in a metal jacket through which water from a constant-temperature bath was circulated. This bath was maintained within $\pm$ 0.1° of the desired reaction temperature. The rate of the water circulation was large enough that the temperature drop of the water returning to the bath was negligible. For the runs at 20°, 40°, and 50°, the solvent and reaction bottle were brought to the approximate temperature of that run before the bottle was placed in the apparatus. Then an additional time of five to ten minutes was allowed for thermal equilibrium while the bottle was being evacuated and filled with hydrogen. In almost every case shaking of the heterogeneous reaction mixture and timing began immediately after the vessel was filled with hydrogen. However, no pressure drop was noted when the apparatus was allowed to stand ten to twenty minutes before shaking.

Unless otherwise specified, 25 ml. of glacial acetic acid was used as the solvent in all runs. The weights of catalyst and acceptor were of the order of 0.05-0.5 g. and 1.0-2.0 g., respectively. All of the compounds used were completely soluble in the acetic acid solvent with the exception of hydroquinone and phloroglucinol.

2. Calibration

In order that the amount of hydrogen absorbed in each hydrogenation might be determined, it was necessary to calibrate the hydrogenation apparatus. This was done by hydrogenating several weighed samples of benzoic acid which is known to absorb three moles of hydrogen for every mole of benzoic acid. The pressure drop for the absorption of one mole of hydrogen, as calculated from the benzoic acid hydrogenations, was 321.2 pounds. Thus the ΔP for any hydrogenation could be related to the number of moles of hydrogen required to complete the reaction. Simple hydrogenation of any benzene nucleus would require 3.0 moles of hydrogen per mole of aromatic compound, while complete cleavage of the hydroxyl groups at the carbon-oxygen bond, in addition to ring saturation, would require 4.0, 5.0, and 6.0 moles for mono-, di-, and tri-hydroxybenzenes, respectively. For a given hydrogenation run on an hydroxybenzene, ring saturation is always complete; cleavage of the hydroxyl group is usually not complete. Thus a value of 3.40 for phenol indicated complete ring hydrogenation accompanied by cleavage of 40 per cent of the hydroxyl groups.

In order to allow for variation in catalyst activity for various batches of Adams platinum catalyst obtained, each batch was standardized as mentioned previously with benzoic acid and referred to a common basis. Smith, Alderman, and Nadig[42] prepared several batches of Adams catalyst and measured the rate of hydrogenation of benzoic acid for each batch. The average value for the rate constant was 0.1120 l. $min.^{-1}$ which was taken as the standard. For the other catalysts, a single batch was used for the entire work.

In the determination of rate constants in heterogeneous catalysis, it is important to remember that for a given shaking rate the amount of catalyst can only be varied over a limited range for which equilibrium exists. Otherwise, the rate of reaction is no longer proportional to the catalyst weight. The same is true, of course, for the choice of shaking rates with a given quantity of catalyst. In this work, the rate of hydrogenation for each compound was found to be proportional to the catalyst weights used (0.05-0.1 g. for platinum; 0.05-0.5 g. for rhodium) at a shaking speed of about 212 cycles per minute.

C. Calculations

As was shown previously for the hydrogenation of benzene and various substituted benzenes, the kinetics for the reduction of hydroxybenzenes were found to be first order with respect to hydrogen pressure, zero order with respect to concentration of hydrogen acceptor, and directly proportional to catalyst weight. These kinetics were obeyed for both the platinum and rhodium catalysts. For a heterogeneous reaction obeying these kinetics, the rate is given by:

$$-\frac{dn}{dt} = k'P \qquad (1)$$

where n is moles of acceptor, t is time, P is pressure, and k' is a constant. For the ideal gas law:

$$P = \frac{nRT}{V} \qquad (2)$$

where R, T, and V are the gas constant, the absolute temperature, and volume, respectively.

For constant temperature and volume,

$$\frac{dP}{dt} = \frac{dn}{dt} \frac{RT}{V} . \qquad (3)$$

Substituting the value of dn/dt from equation (3) into equation (1) and rearranging:

$$- \frac{dP}{dt} = \frac{k'' RT P}{V} \qquad (4)$$

where k'' is now the specific rate constant in moles atm.$^{-1}$ time^{-1}.

In order to compare the rate constants obtained with those previously calculated for various hydrogenations, specific rate constants were calculated from the expression given by Fuzek and Smith[40] in which RT is absorbed in the constant where k is now given in liters time^{-1}.

$$- \frac{dP}{dt} = \frac{k}{V} P \qquad (5)$$

This expression is correct when one is working at a constant and specified temperature, but it is in slight error when used for comparison of rate constants at different temperatures and for calculation of activation energies. The error in an activation energy calculated from k is well within experimental error when one is dealing with short temperature ranges and when most of the hydrogen remains at room temperature even though the temperature of the reaction flask is changed.

Integration of (5) above gives:

$$\log P = \frac{-kt}{2.303 V} + \log P_o . \qquad (6)$$

To obtain values of k, the slope of the straight line obtained by plotting log P *versus* t was multiplied by -2.303 V. All rate constants were referred to 1.0 gram of catalyst ($k_{1.0}$) by dividing k by the catalyst weight.

Figure 1 shows a typical hydrogenation plot. In most cases a drift from linearity was observed after about 60-80 per cent reaction. This was due to catalyst poisoning which reduced the number of "active" spots. Catalyst poisoning was not as pronounced for the supported rhodium on alumina catalyst as for Adams platinum. Rate constants calculated from the slope of the linear portion were usually reproducible within 5 per cent.

The Arrhenius equation, relating the change in rate constant with temperature is:

$$k = A\, e^{-\Delta H_a/RT} \quad . \tag{7}$$

Taking the logarithm of this equation,

$$\log k = \frac{-\Delta H_a}{2.303\ RT} + \log A \tag{8}$$

where ΔH_a is activation energy, A is a constant, and the other symbols are as previously defined. Activation energies were determined from the slopes of the lines obtained by plotting log k versus 1/T. The reaction rates for these plots were determined at temperatures of 20°, 30°, 40°, and 50°. For a heterogeneous reaction, true activation energies are obtained only for a zero order reaction. Since the reactions studied here are dependent upon hydrogen pressure, only apparent activation energies (and, indeed, rate constants) can be calculated. However, the deviation in true and apparent activation energies here involves only the heat of adsorption of hydrogen, which should be approximately the same for a given catalyst regardless of the compound studied. Hence the relative activation energies for a series of compounds on a given catalyst should be the same as for a zero order reaction.

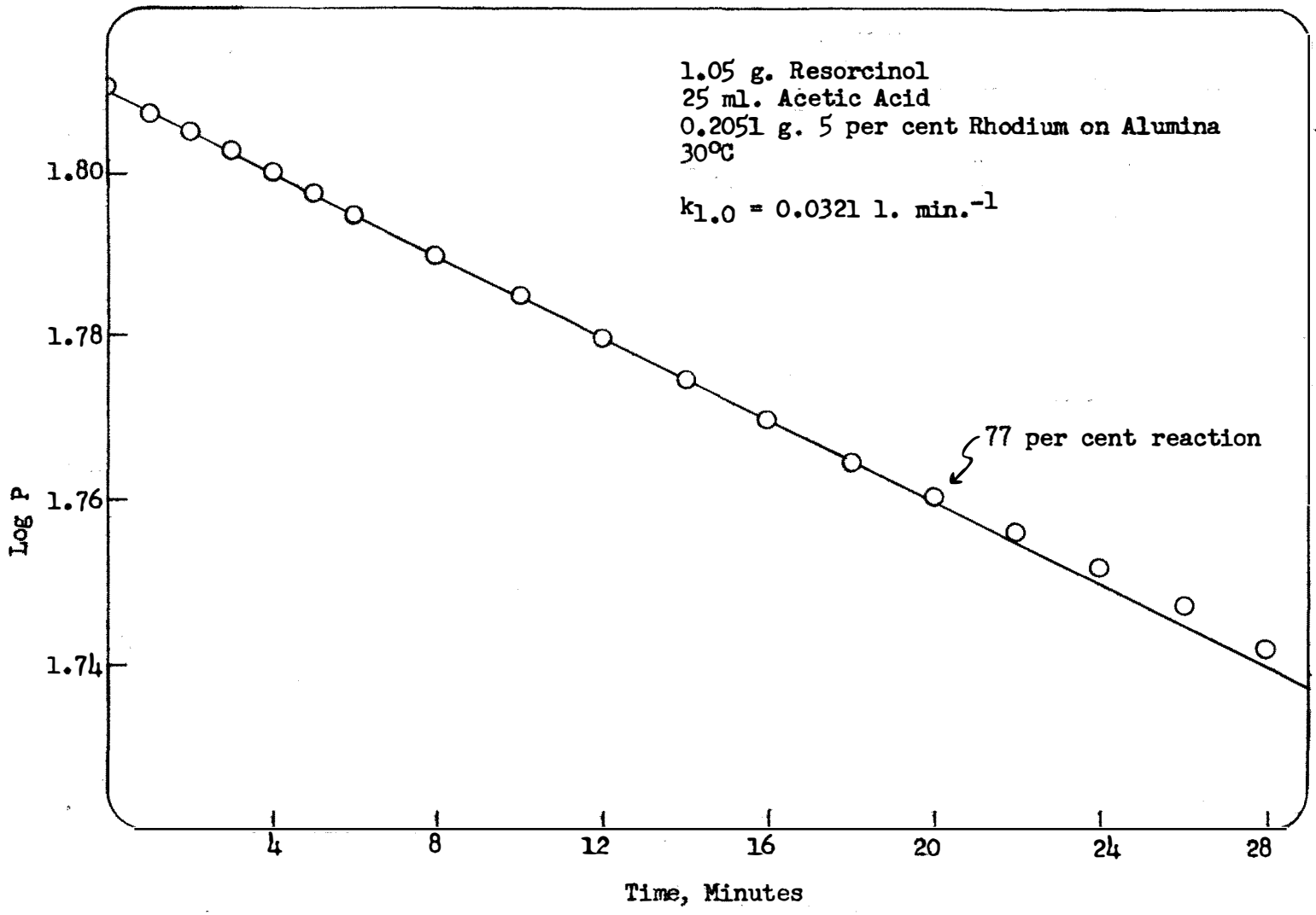


Figure 1. Typical low-pressure hydrogenation plot.

CHAPTER III

RESULTS AND DISCUSSION

A. Cleavages of Hydroxybenzenes

1. Effect of Catalyst

As has been pointed out previously in this work, the methoxyl group may be split from an aromatic nucleus during catalytic hydrogenation. The extent of cleavage is quite large when Adams platinum catalyst is employed. In the hydrogenation of phenol using rhodium (oxide) catalyst, Thompson[12] found from the moles of hydrogen absorbed per mole of phenol (3.09) and the refractive index of the products that some cleavage to cyclohexane and water occurred. Coussemant and Jungers[4] indicated that in the hydrogenation of phenol with Raney nickel a slight deviation of the refractive index was observed toward the end of the reaction, and they attributed this to "dehydration." The temperatures of their reactions varied between 113-174°, however, and it is not surprising that "dehydration" was observed at these higher temperatures.

At 30°, phenol over platinum absorbed 3.22 moles of hydrogen per mole of phenol which corresponded to 22 per cent cleavage of the hydroxyl group. Catechol is cleaved to the extent of about 32 per cent, while resorcinol and hydroquinone are cleaved about 50 per cent. Approximately 23 per cent of the hydroxyl groups are cleaved in the hydrogenations of phloroglucinol and pyrogallol.

Five per cent rhodium on alumina was found to catalyze readily the hydrogenation of the dihydroxybenzenes and trihydroxybenzenes at room temperature and ordinary pressures. With this catalyst phenol, catechol, and phloroglucinol show no appreciable cleavage at 30°, while resorcinol, hydroquinone and pyrogallol undergo cleavage to the extent of 7-9 per cent. These results are further proof that the nature of the catalyst is very important in determining the amount of cleavage and illustrate the fact that 5 per cent rhodium on alumina serves as an excellent catalyst for the hydrogenation of the benzene nucleus at room temperature and ordinary pressures without cleavage of groups substituted on the ring.

Thompson,[12] working with either platinum or rhodium, has shown that supported (on alumina) and unsupported catalysts led to about the same amount of cleavage, i.e., it appears to be an intrinsic metal property that governs the amount of cleavage rather than a difference in surface properties of the catalyst. As was pointed out, however, it is possible for these particular catalysts that the alumina surfaces are covered with active metal so that each active surface is essentially the same for the supported and unsupported catalysts. He found, also, that on a total weight basis the pure metal catalysts are more active in each case, i.e., Adams platinum was found to be almost six times as active as platinum on alumina and rhodium black was over twice as active as rhodium on alumina. However, when one compares the rates of hydrogenation on the basis of weight of catalytic metal, supported catalysts were found to be very much superior.

2. Effect of Temperature

The amount of cleavage of phenol, the dihydroxybenzenes, and the trihydroxybenzenes (phloroglucinol and pyrogallol) has been determined as a function of temperature over the range 20-50°. Tables I and II include the cleavage data for hydroxyl-compound hydrogenations over Adams platinum and 5 per cent rhodium on alumina, respectively. Plots of amount of hydrogen absorbed per mole of hydroxyl compound as a function of temperature are shown in Figures 2 and 3. It is of interest to note that the amount of cleavage over platinum is a linear function of temperature, increasing as the temperature increases. Figure 3 is included to point up the fact that cleavage of the hydroxyl group over 5 per cent rhodium on alumina does not appear to be a linear function of temperature. This is in contrast to the results obtained by Smith and Thompson[43] for methoxyl group cleavages over this catalyst. Actually, the extent of cleavage over rhodium is so small as to be almost within experimental error.

The data on the cleavage of hydroxyl compounds is of great value in organic synthesis. In some cases, the organic chemist wishes to hydrogenate an organic compound with loss of one or more hydroxyl groups, but more often he wishes to hydrogenate an hydroxyl compound and retain the group. The results obtained in this research add support to the results of Smith and Thompson,[43] i.e., a high temperature and use of platinum oxide promotes cleavage, while low temperatures and the use of rhodium on alumina combine to retard cleavage during hydrogenation.

TABLE I

CLEAVAGE OF HYDROXYL GROUPS OVER ADAMS PLATINUM
AS A FUNCTION OF TEMPERATURE

Compound	Temperature 20°	30°	40°	50°	T coeff.[a]
Phenol	3.19[b]	3.22	3.31	3.38	0.19
Catechol	3.61	3.63	3.66	3.68	0.07
Resorcinol	3.91	4.00	4.03	4.07	0.11
Hydroquinone	3.95	3.97	4.05	4.05	0.10
Phloroglucinol	3.28	3.48	3.54	3.64	0.29
Pyrogallol	3.57	3.70	3.72	3.83	0.26

[a]Change in moles of hydrogen absorbed per mole of acceptor for temperature change from 20 to 50° as determined from plots (Figure 2).

[b]Values are given in moles of hydrogen absorbed per mole of acceptor.

TABLE II

CLEAVAGE OF HYDROXYL GROUPS OVER 5 PER CENT RHODIUM ON ALUMINA AS A FUNCTION OF TEMPERATURE

Compound	Temperature			
	20°	30°	40°	50°
Phenol	3.04[a]	3.01	2.99	3.04
Catechol	3.04	2.94	3.10	3.13
Resorcinol	3.07	3.16	3.16	3.16
Hydroquinone	3.29	3.18	3.14	3.21
Phloroglucinol	2.78	2.85	2.88	2.81
Pyrogallol	3.12	3.22	3.24	3.24

[a]Values are given in moles of hydrogen absorbed per mole of acceptor.

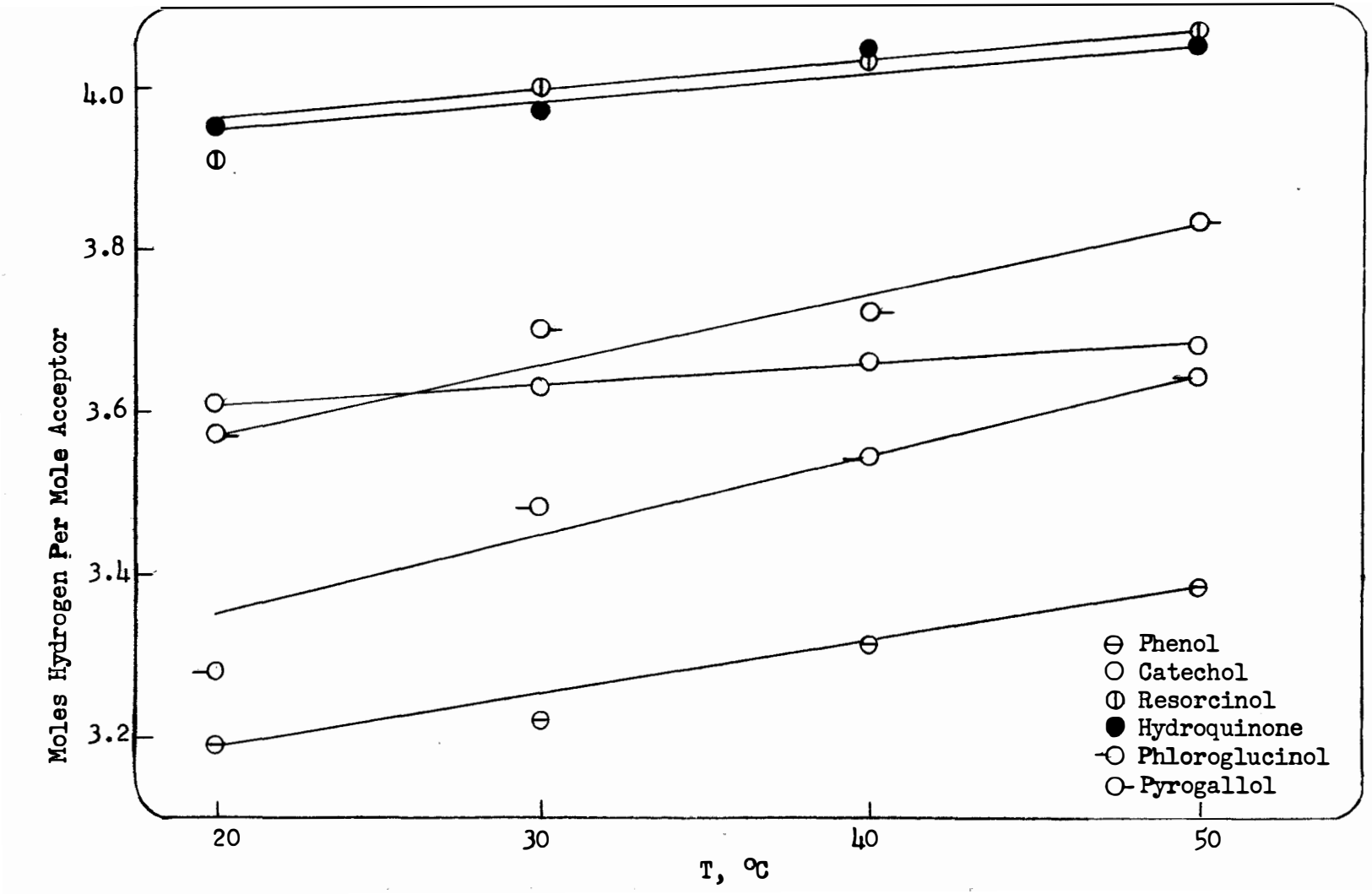


Figure 2. Cleavage of hydroxybenzenes as a function of temperature for hydrogenations over Adams platinum.

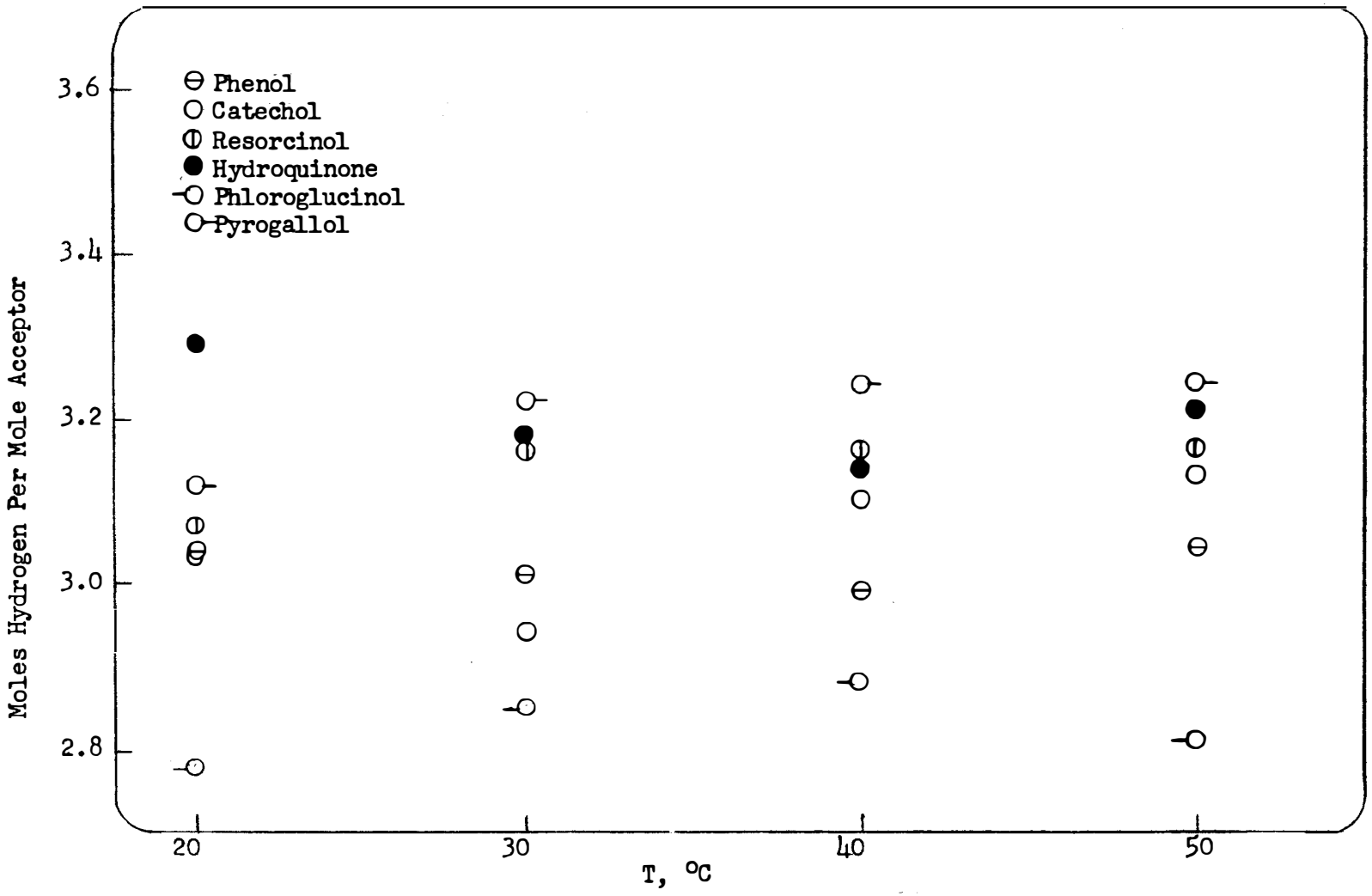


Figure 3. Cleavage of hydroxybenzenes as a function of temperature for hydrogenations over 5 per cent rhodium on alumina.

3. Ketone Hydrogenations

Two ketones, cyclohexanone and 1,3-cyclohexanedione, were hydrogenated at 30° in acetic acid over Adams platinum and 5 per cent rhodium on alumina catalysts. The rates of hydrogenation, as well as the amounts of cleavage, were measured. These data are compared with the data for phenol and resorcinol hydrogenations in Tables III and IV.

The extent of cleavage of the hydroxyl group is nearly twice as great in the hydrogenation of phenol as it is in the hydrogenation of cyclohexanone. If phenol hydrogenates via cyclohexanone as an intermediate, one would expect the per cent cleavage to be the same in each case. Two explanations can be advanced for these results. Wicker[18] postulated that phenol and the cresols hydrogenate not only via a ketone intermediate but also through the enol form of the ketone. Thus a difference in the per cent stable stereoisomer formed on hydrogenation is expected and observed, starting with a cresol or the corresponding methylcyclohexanone. A similar situation might exist in the hydrogenation of phenol and cyclohexanone. Phenol could hydrogenate via the enol form of cyclohexanone as well as through the keto form, and a difference in per cent cleavage might be expected for the two different reaction routes. The important point, however, is that cyclohexanone cannot be an intermediate in the general sense in the hydrogenation of phenol on the basis of Wicker's results and from the information obtained from hydroxyl-group cleavage in this work.

A more favorable explanation evolves from the mechanism proposed by Thompson[12] for the cleavage of methoxyl groups during hydrogenation.

TABLE III

COMPARISONS OF RATE CONSTANTS AND CLEAVAGES AT 30° FOR HYDROGENATIONS OF HYDROXYBENZENES AND KETONES OVER PLATINUM

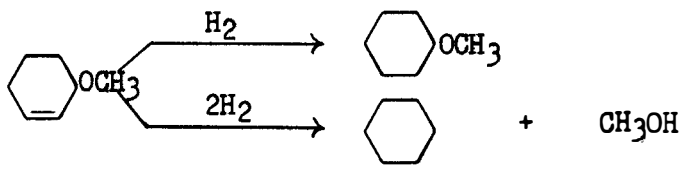
Compound	$k_{1.0}$	Moles H_2 / Mole Compound	Moles H_2 / Mole Hydroxyl Groups
Phenol	0.1620	3.22	0.22
Cyclohexanone	0.1937	1.12	0.12
Resorcinol	0.1611	4.00	0.50
1,3-Cyclohexanedione	0.1949	3.13	0.56

TABLE IV

COMPARISONS OF RATE CONSTANTS AND CLEAVAGES AT 30° FOR HYDROGENATIONS OF HYDROXYBENZENES AND KETONES OVER RHODIUM

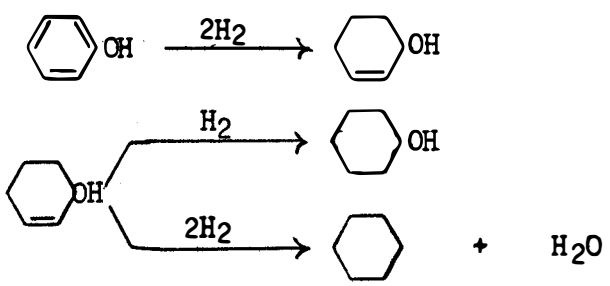
Compound	$k_{1.0}$	Moles H_2 / Mole Compound	Moles H_2 / Mole Hydroxyl Groups
Phenol	0.0687	2.96	0.00
Cyclohexanone	0.0452	0.92	0.00
Resorcinol	0.0311	3.16	0.08
1,3-Cyclohexanedione	0.1081	2.13	0.07

He postulated the formation of a cyclohexene intermediate with the double bond β-γ to the methoxyl group, which could react in one of two ways:

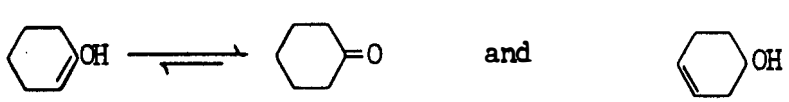


Simple hydrogenation would lead to methoxycyclohexane while hydrogenolysis and hydrogenation combined would lead to cyclohexane and methanol. These two reactions do not take place independently but compete with each other, and this competition accounts for the fact that hydrogenolysis is never 100 per cent.

With phenol the reaction could take place as follows:

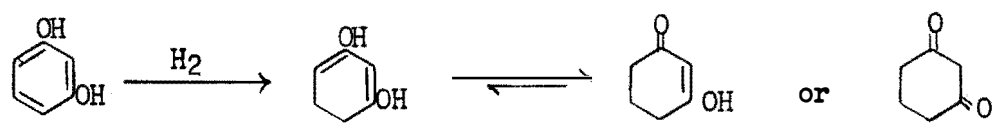


The competition between hydrogenation and hydrogenolysis of the hydroxycyclohexene would determine the per cent cleavage of the hydroxyl group. To account for the formation of cyclohexanone, one could picture the formation of 1-hydroxycyclohexene-1 and 4-hydroxycyclohexene-1 as well as 3-hydroxycyclohexene-1 as intermediates:

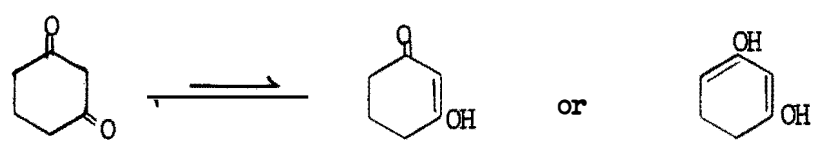


The 1-hydroxycyclohexene-1 would very probably tautomerize to the keto form. The extent of cleavage would be expected to be different for the three cyclohexenes and the hydrogenation of phenol should then lead to a different per cent cleavage than would be observed for cyclohexanone. A more detailed comparison between the hydrogenations of phenol and cyclohexanone is presented in a later portion of this work.

In contrast to the behavior of cyclohexanone and phenol, 1,3-cyclohexanedione undergoes cleavage of the hydroxyl groups to a greater extent than does resorcinol over Adams platinum. Actually, the difference in per cent cleavage obtained for resorcinol and 1,3-cyclohexanedione is almost within experimental error, especially over rhodium. This is not inconsistent with the modified Thompson mechanism proposed above for the hydrogenation of phenol. The reaction of resorcinol could be visualized as follows:



Starting with 1,3-cyclohexanedione in glacial acetic acid solution, the reaction might conceivably proceed as



This points up the fact that the reaction intermediates could be the same, starting with either resorcinol or 1,3-cyclohexanedione. Results of experiments will be presented later which indicate that ketones are not formed in

the hydrogenation of resorcinol. This seems to indicate that a cyclohexene or cyclohexadiene is the reaction intermediate in the hydrogenation of this compound.

4. Effect of Acetic Acid

Thompson[12] has shown that cleavage is very definitely a function of acid concentration in the hydrogenation of methoxybenzenes, increasing as the acid concentration increases. This behavior is logical since acidic media are known to promote ether cleavages. Reference was made earlier to the work of Levin and Pendergrass.[25] They observed that in the hydrogenation of p-hydroxybenzoic acid over Adams platinum a mixture of cyclohexanecarboxylic acid and 4-hydroxycyclohexanecarboxylic acid was obtained. Acidic reagents were found to increase the amount of cyclohexanecarboxylic acid while basic reagents reduced it.

Glacial acetic acid was used as the solvent in each of the hydrogenations in this work. Hence differences in per cent cleavage are not attributable to acid concentration.

5. ffect of Structure

Tables V and VI show the amount of cleavage at 30° of hydroxyl groups during the hydrogenation of phenol, catechol, resorcinol, hydroquinone, phloroglucinol and pyrogallol. It is apparent from these data that the catalyst is far more important in determining the extent of cleavage than the structure of the molecule hydrogenated. For each compound, the cleavage reaction was of considerable importance when the hydrogenation-hydrogenolysis was catalyzed by platinum; the cleavage reaction was of

minor importance in the case of rhodium on alumina.

It has been shown[12] that there is little or no electrical influence of substituents on cleavage. Rather, the relative size of the substituents involved seems to be an important factor. It can be seen from the data in Tables V and VI that the ortho isomer undergoes less cleavage than the meta or para isomers. This may be due to a slight steric inhibition of cleavage for the ortho isomer. However, if steric inhibition of cleavage were the prime factor, one might expect o-dimethoxybenzene to cleave less readily than o-dihydroxybenzene. A comparison of the data given in Table VII does not show this to be the case.

As was mentioned previously, Amatatsu[24] hydrogenated aromatic compounds containing the hydroxyl and methoxyl groups and the $-OCH_2O-$ linkage (as in safrole) over nickel at pressures of 50-60 atmospheres and at temperatures of 140-200°. He concluded that the ease of cleavage of the carbon-oxygen bond is:

$$-OCH_2O- > -OCH_3 > -OH \quad .$$

This would account for the fact that o-dimethoxybenzene cleaves to a greater extent than does o-dihydroxybenzene and anisole to a greater extent than phenol. The methoxyl groups in 1,2,3-trimethoxybenzene cleave to a greater extent than do the hydroxyl groups in 1,2,3-trihydroxybenzene. With the meta and para isomers, the dihydroxybenzenes and dimethoxybenzenes cleave to about the same extent.

Amatatsu's postulate is even more closely followed when one compares the extent of cleavage for these compounds over 5 per cent rhodium on alumina catalyst, Table VIII. In each instance, the methoxyl compound

TABLE V

CLEAVAGE OF HYDROXYL GROUPS AT 30° FOR LOW-PRESSURE HYDROGENATIONS OVER PLATINUM

Compound	Moles H_2 / Mole Compound	Moles H_2 / Mole Hydroxyl Groups
Phenol	3.22	0.22
Catechol	3.63	0.32
Resorcinol	4.00	0.50
Hydroquinone	3.97	0.49
Phloroglucinol	3.48	0.16
Pyrogallol	3.70	0.23

TABLE VI

CLEAVAGE OF HYDROXYL GROUPS AT 30° FOR LOW-PRESSURE HYDROGENATIONS OVER 5 PER CENT RHODIUM ON ALUMINA

Compound	$\frac{\text{Moles } H_2}{\text{Mole Compound}}$	$\frac{\text{Moles } H_2}{\text{Mole Hydroxyl Groups}}$
Phenol	3.01	0.01
Catechol	2.94	0.00
Resorcinol	3.16	0.08
Hydroquinone	3.18	0.09
Phloroglucinol	2.85	0.00
Pyrogallol	3.22	0.07

TABLE VII

COMPARISON OF CLEAVAGE OF METHOXYL AND HYDROXYL GROUPS AT 30°
FOR LOW-PRESSURE HYDROGENATIONS OVER ADAMS PLATINUM

Compound[a]	Moles H_2 / Mole Methoxyl Groups	Compound	Moles H_2 / Mole Hydroxyl Groups
Anisole	0.40	Phenol	0.22
o-Dimethoxybenzene	0.48	Catechol	0.32
m-Dimethoxybenzene	0.50	Resorcinol	0.50
p-Dimethoxybenzene	0.52	Hydroquinone	0.49
1,2,3-Trimethoxybenzene	0.44	Pyrogallol	0.23

[a]Data for these compounds obtained from Smith and Thompson.[43]

TABLE VIII

COMPARISON OF CLEAVAGE OF METHOXYL AND HYDROXYL GROUPS AT 30° FOR LOW-PRESSURE HYDROGENATIONS OVER 5 PER CENT RHODIUM ON ALUMINA

Compound[a]	Moles H_2 / Mole Methoxyl Groups	Compound	Moles H_2 / Mole Hydroxyl Groups
Anisole	0.06	Phenol	0.01
o-Dimethoxybenzene	0.08	Catechol	0.00
m-Dimethoxybenzene	0.18	Resorcinol	0.08
p-Dimethoxybenzene	0.10	Hydroquinone	0.09
1,2,3-Trimethoxybenzene	0.11	Pyrogallol	0.07

[a]Data for these compounds obtained from Smith and Thompson.[43]

shows a greater extent of cleavage than does the corresponding hydroxyl compound.

It is interesting to note that the symmetrical 1,3,5-trihydroxybenzene, phloroglucinol, undergoes cleavage to a lesser extent than does 1,2,3-trihydroxybenzene, pyrogallol. These results are obtained both with Adams platinum and with 5 per cent rhodium on alumina. This would indicate that the suppression of hydrogenolysis by steric crowding cannot be of major importance. One would certainly anticipate that the steric crowding provided by the three adjacent hydroxyl groups in pyrogallol would decrease the extent of cleavage of these groups. Ketone intermediates could play a more active role in the hydrogenation of pyrogallol than in the hydrogenation of phloroglucinol, however, and this could account for the difference in per cent cleavage of the hydroxyl group with these two compounds.

B. Ketone Intermediates in Phenol Hydrogenations

1. Phenol

As was mentioned previously, various investigators have obtained results which indicate that cyclohexanone is an intermediate formed during the catalytic hydrogenation of phenol. A mechanism for the hydrogenation of phenol has been proposed which involves cyclohexanone as an intermediate. Cyclohexanone was not isolated when phenol was hydrogenated over Adams platinum in this work, but Vavon and Bertin[2] reported the isolation of cyclohexanone when they hydrogenated phenol over platinum black.

In this work, 1.02 g. of phenol was hydrogenated over 0.0901 g. of platinum oxide in 25 ml. of acetic acid and in the presence of 1.21 g. of semicarbazide hydrochloride. After the catalyst was removed by filtration and the acetic acid solvent was evaporated in vacuo, an oil-like residue was obtained which gradually crystallized. After recrystallization from an ethanol-ethyl ether mixture, 0.40 g. of a white crystalline solid was obtained which melted at 175-176°. Elemental analysis showed that the material was not cyclohexanone semicarbazone. However, associating two molecules of water with the cyclohexanone semicarbazone gives the following result:

Anal.* Calcd. for $C_7H_{17}N_3O_3$: C, 43.96; H, 8.96; N, 21.97.

Found: C, 43.2; H, 8.8; N, 22.17.

When this material was mixed with known cyclohexanone semicarbazone a depression in the melting point was observed, a definite indication that the material is not unhydrated cyclohexanone semicarbazone.

There is no evidence that cyclohexanone semicarbazone forms a dihydrate. Indeed, the two molecules of water could be tied into the semicarbazone molecule in some form other than that of a hydrate. The material has a sharp melting point which does not change with recrystallization, an indication that it is a pure compound. Waser[44] reported the isolation of cyclohexyl semicarbazide, m.p. 182-183°, when he hydrogenated phenol over platinum black in an acetic acid-water solution and in the presence of semicarbazide hydrochloride. He neutralized the reaction mixture with ammonia before attempting to isolate the semicarbazide. No such neutrali-

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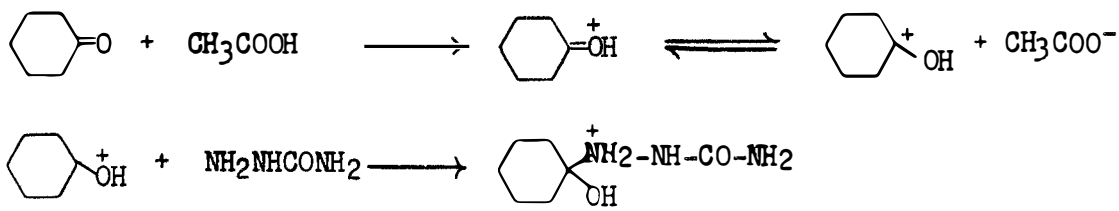
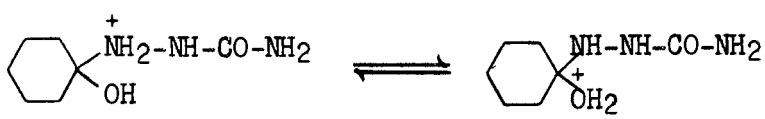
*All elemental analyses were performed by Weiler and Strauss Microanalytical Laboratory, Oxford, England.

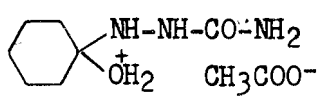
zation was made in this work, and this provides a possible explanation for the derivative obtained. Consider the mechanism for semicarbazone formation:



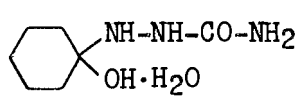
A proton would be expected to be removed at this point, but the possibility exists that in the glacial acetic acid system used in this work a situation such as the following might predominate:



Evaporation of the solvent would leave the acetate salt. Recrystallization



of this material from aqueous ethanol could easily lead to a derivative such as



which is in agreement with an elemental analysis obtained. 1,2-Cyclohexanediol forms a dihydrate,[45] so the association of a molecule of water with the hydroxyl group in the derivative above is not unusual, especially since various possibilities exist for the formation of hydrogen bonds. Regardless of the actual structure of the derivative obtained, some idea of the per cent ketone formed during the course of the reaction is gained

from the experiment.

The 0.40 g. of this material corresponds to 19.3 per cent ketone formed during the course of the reaction. The mixture absorbed 3.07 moles hydrogen per mole acceptor in comparison to 3.22 moles hydrogen per mole acceptor when no semicarbazide hydrochloride was present. If the 19.3 per cent ketone formed during the reaction were removed as the semicarbazone, then the reaction mixture would be expected to absorb 3.22 - 0.193 or 3.03 moles hydrogen per mole acceptor, which compares favorably (within experimental error) with the 3.07 moles hydrogen absorbed.

Semicarbazide hydrochloride (1.0 g.) was hydrogenated in 25 ml. of acetic acid over 0.0845 g. of platinum oxide. The hydrogen absorbed in excess of the amount required to reduce the platinum oxide was insignificant.

The formation of ketones during the hydrogenation of phenol over rhodium was not studied in this work. Thompson[12] has shown that ketones are formed in this reaction. He hydrogenated phenol over rhodium (oxide) catalyst and found 23 per cent ketone in the reaction mixture.

2. Catechol

a. Hydrogenation over 5 per cent rhodium on alumina catalyst. Catechol (8.0 g.) was hydrogenated in 20 ml. of acetic acid over 1.269 g. of 5 per cent rhodium on alumina until one-third of the theoretical amount of hydrogen had been absorbed. The catalyst was filtered from the solution and the acetic acid solvent was evaporated in vacuo. The oil-like residue which remained was dissolved in a small amount of boiling benzene. Chilling this solution produced white crystals, 0.34 g., m.p. 97-98°. Catechol melts at 104-105°.[46] A small amount of the white crystalline material was

dissolved in water and treated with ferric chloride solution.[47] A dark-green color was produced which was identical to the color produced by a known sample of catechol under the same conditions.

The benzene solution from which the white crystals above were obtained was distilled in vacuo to remove the benzene solvent. The residue which remained was dissolved in water and treated with an aqueous solution of phenylhydrazine and acetic acid.[47] An oil separated from the solution almost immediately. The oil gradually began to crystallize, and when the solution was chilled in the refrigerator yellow crystals formed, 0.14 g., m.p. 143°. Urion[45] reported that the diphenylhydrazone of 1,2-cyclohexanedione melts at 143°, while Pritzkow[48] reported that the phenylosazone of 2-hydroxycyclohexanone melts at 148-150°. An elemental analysis of the material as 1,2-cyclohexanedione diphenylhydrazone was made:

Anal. Calcd. for $C_{18}H_{20}N_4$: C, 73.94; H, 6.90; N, 19.16.

Found: C, 73.6; H, 7.02; N, 19.2.

The product obtained could be either 1,2-cyclohexanedione diphenylhydrazone or 2-hydroxycyclohexanone phenylosazone.

Catechol (2.0 g.) was hydrogenated in 30 ml. of acetic acid over 0.555 g. of 5 per cent rhodium on alumina until one-half the theoretical amount of hydrogen had been absorbed. The reaction mixture was filtered several times to remove all traces of catalyst and the acetic acid solvent was evaporated in vacuo. The residue which remained was dissolved in about 20 ml. of water and treated with 1 ml. of phenylhydrazine.[47] Yellowish-white crystals formed immediately, 0.86 g., m.p. 105.2-105.8°. Recrystallization from an ethanol-water mixture produced crystals which melted at

117.4-118°. Pritzkow[48] reported that 2-hydroxycyclohexanone phenylhydrazone melts at 119-120°. An elemental analysis of the material as 2-hydroxycyclohexanone phenylhydrazone was made:

Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.72.

Found: C, 70.72; H, 7.99; N, 13.44.

It appears, then, that 2-hydroxycyclohexanone is formed in the hydrogenation of catechol, rather than 1,2-cyclohexanedione. On the basis of the weight of the phenylhydrazone formed, there was 23.2 per cent ketone in the reaction mixture.

It has been observed that when researchers wished to synthesize ketones by means of catalytic hydrogenation, they carried out their reactions in basic media.[16,17,19] In the work reported here, glacial acetic acid was employed as solvent. This suggested the possibility that tautomerization of the enol to the keto form of the reaction intermediate was being suppressed by the acidic medium. Several hydrogenations of catechol were made in methanol over 5 per cent rhodium on alumina, and the per cent ketone present was studied as a function of per cent reaction. This was accomplished by stopping the hydrogenations at various degrees of completion, removing the catalyst and solvent, and treating the residue which remained with phenylhydrazine.[47] 2-Hydroxycyclohexanone phenylhydrazone was isolated in each case. The results of this study are shown in Figure 4. The per cent ketone present in the reaction mixture reached a maximum of 15.9 at 50 per cent reaction. From the shape of the curve, it seems that there is a steady build-up of ketone in the reaction mixture. For purposes of comparison, catechol was hydrogenated to 50 per cent

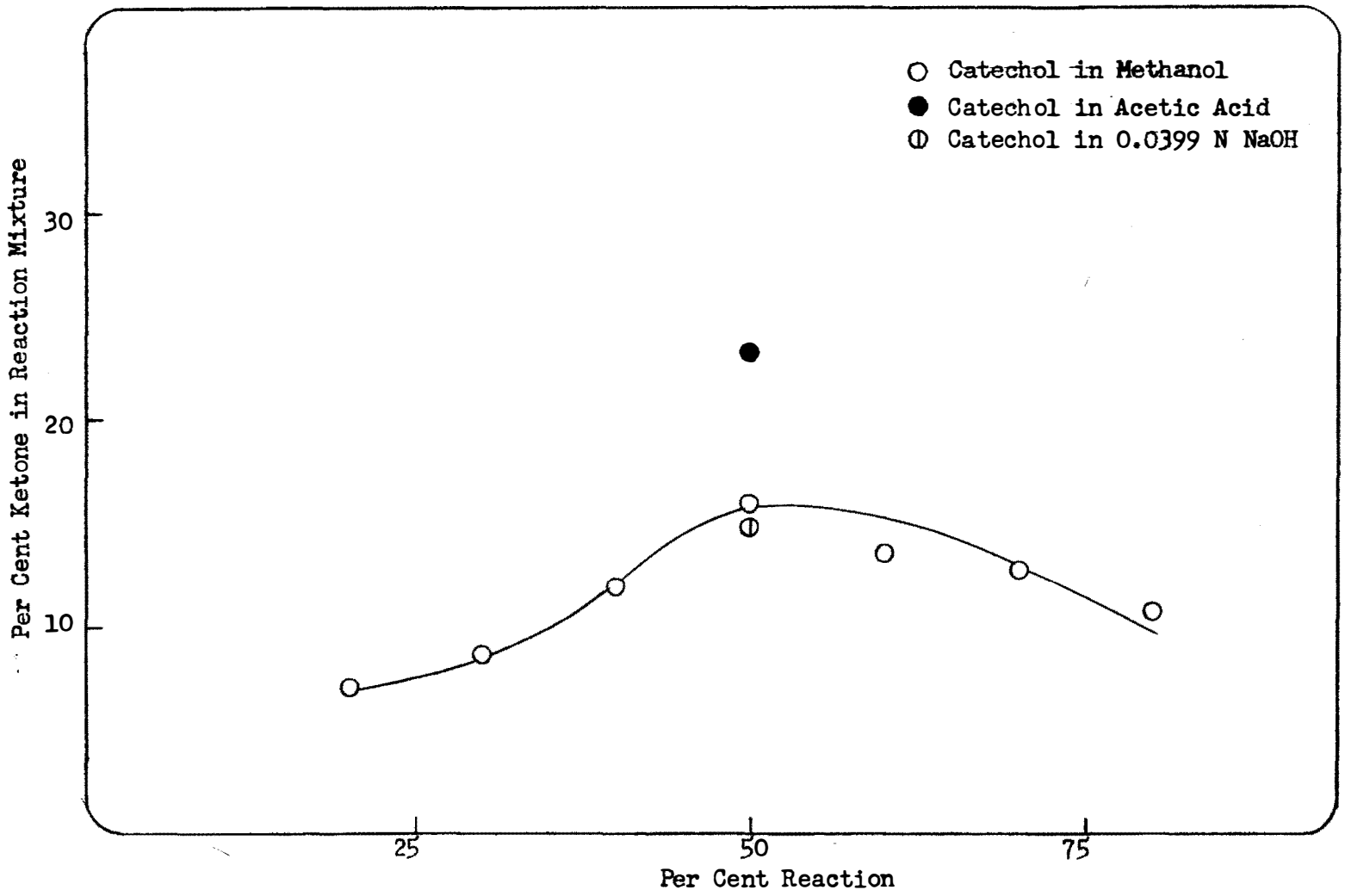


Figure 4. The per cent ketone present in the reaction mixture as a function of per cent reaction for the hydrogenation of catechol at 30° over 5 per cent rhodium on alumina.

completion in acetic acid over 5 per cent rhodium on alumina and found to contain 23.2 per cent ketone in the reaction mixture. Again, catechol was hydrogenated to 50 per cent completion over 5 per cent rhodium on alumina in 0.0399 N sodium hydroxide solution and found to contain 14.8 per cent ketone intermediate in the reaction mixture.

It is obvious that the acidic medium does not suppress tautomerization of the enol to the keto form appreciably. The difference in per cent ketone present in the reaction mixtures can be attributed to a difference in reactivity of the ketone in the various solvents.

In an attempt to evolve a suitable synthetic method for the preparation of 2-hydroxycyclohexanone, the technique employed by R. B. Thompson[19] for the preparation of dihydroresorcinol by the high-pressure hydrogenation of resorcinol was adapted to catechol. Low pressure (50 p.s.i.g.) and 5 per cent rhodium on alumina catalyst were substituted for high pressure (1500 p.s.i.g.) and Raney nickel catalyst. Catechol (10.0 g.) in 20 ml. of water and 4.36 g. of sodium hydroxide was hydrogenated to two-thirds completion over 1.0 g. of 5 per cent rhodium on alumina. Attempts to isolate ketones from the resulting reaction mixture failed.

Attempts to hydrogenate catechol in acetic acid over 5 per cent rhodium on alumina and in the presence of semicarbazide hydrochloride failed. It is somewhat surprising that semicarbazide hydrochloride would poison rhodium catalyst and not poison Adams platinum. An attempt was made to hydrogenate catechol over 5 per cent rhodium on alumina in acetic acid to which 1 ml. of concentrated hydrochloric acid had been added. The reaction proceeded very slowly. Evidently, the poisoning of the rhodium is

a combination of both the semicarbazide and hydrochloride and could not be attributed to hydrogen chloride alone.

As was mentioned previously, Gilman and Cohn[13] hydrogenated the dihydroxybenzenes and observed a peculiar anomaly in the rate. These compounds hydrogenated at a constant rate until approximately five-sixths of the theoretical amount of hydrogen was absorbed. At this point, the rate increased abruptly and markedly until the theoretical end point was reached with a sudden cessation of hydrogen uptake. In an attempt to repeat the work of Gilman and Cohn, 0.5 g. of catechol was hydrogenated at 30° in 100 ml. of distilled water over 0.5 g. of 5 per cent rhodium on alumina. These conditions exactly duplicated those of Gilman and Cohn with the exception of the pressure. Their initial pressure was 1 atmosphere, while the initial pressure in this work was about 4.5 atmospheres. The result of this hydrogenation is shown in Figure 5. The reaction appears to occur in two steps, i.e., there is a change in the slope of the rate curve after the absorption of about 1.4 moles hydrogen per mole acceptor. However, the phenomenon observed by Gilman and Cohn was not apparent here. The result of this hydrogenation was verified by a second reaction carried out under similar conditions.

b. Hydrogenations over Adams platinum catalyst. In two different experiments, catechol (2.0 g.) was hydrogenated to 50 per cent completion in 25 ml. of acetic acid over 0.1089 g. of platinum oxide. After filtering off the catalyst and evaporating the solvent in vacuo, a residue remained which was dissolved in water and treated with phenylhydrazine.[47] A derivative was not formed, which indicated the absence of ketones in the reaction mixture.

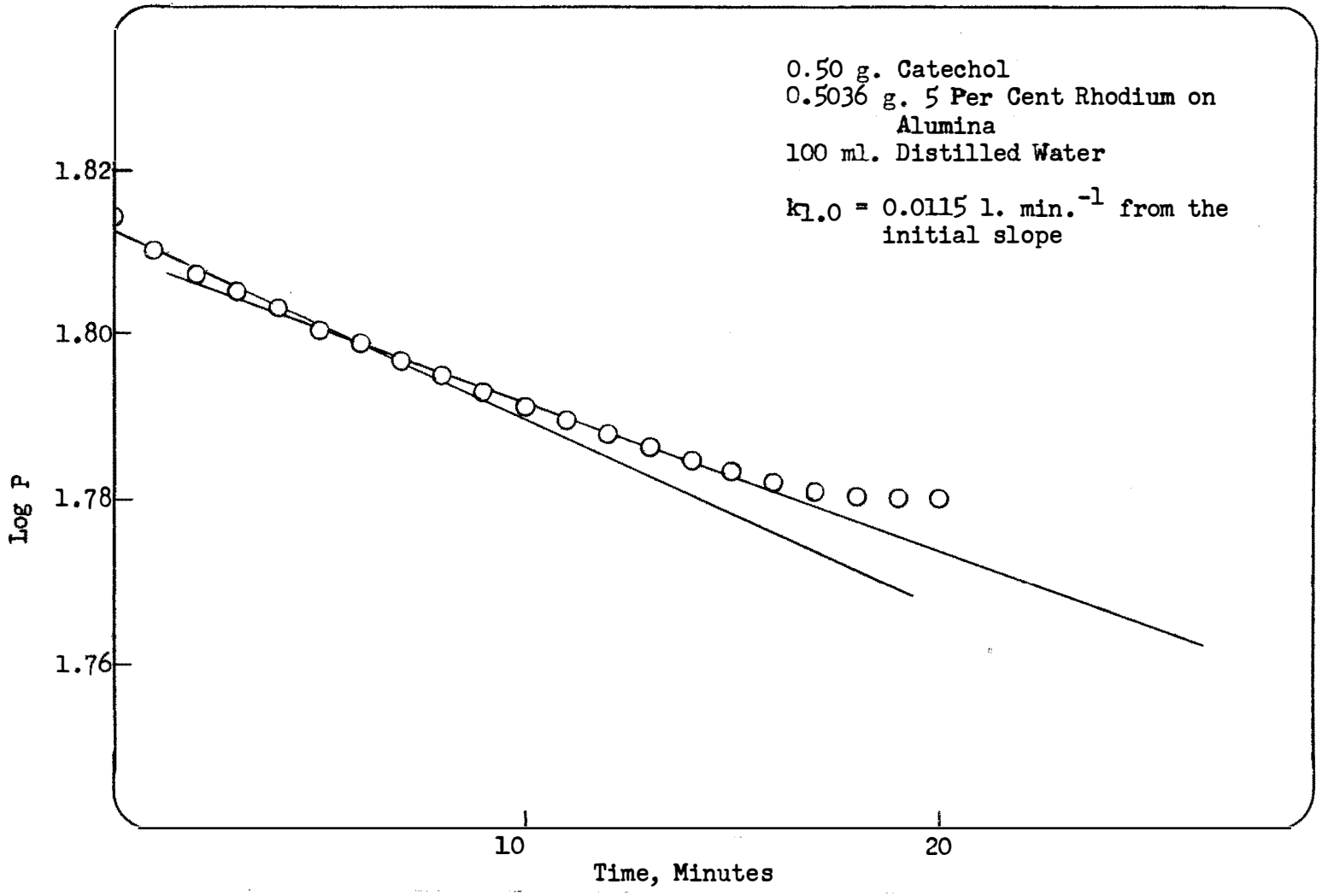


Figure 5. The hydrogenation of catechol at 30° in water over 5 per cent rhodium on alumina.

In another experiment, catechol (1.0 g.) was hydrogenated in 25 ml. of acetic acid in the presence of 1.4 g. of semicarbazide hydrochloride over 0.2239 g. of platinum oxide. A white insoluble solid was present in the reaction mixture at the conclusion of the reaction. Water was added to dissolve the white solid, and the solution which resulted was filtered to remove the catalyst. Solvent was evaporated *in vacuo* until the solution was of about 10 ml. of volume. A white solid precipitated from this solution, 0.45 g., m.p. 198-199°. An elemental analysis of this material was found to correspond to 2-hydroxycyclohexanone semicarbazone plus two molecules of water:

Anal. Calcd. for $C_7H_{17}N_3O_4$: C, 40.56; H, 8.27; N, 20.28.

Found: C, 40.6; H, 7.9; N, 20.42.

The amount of product obtained corresponds to 23.9 per cent ketone formed during the course of the reaction. The reaction mixture absorbed 3.77 moles hydrogen per mole acceptor in comparison to 3.63 moles hydrogen per mole acceptor absorbed when semicarbazide hydrochloride was not present. Since 23.9 per cent ketone was formed during the course of the reaction, the expected moles of hydrogen absorbed was 3.63 - 0.24 or 3.39. The only reasonable explanation which can be advanced for the fact that 3.77 moles of hydrogen was absorbed is that cleavage was greater in this particular reaction. It cannot be claimed that every molecule of ketone formed as an intermediate reacted with semicarbazide hydrochloride to form a semicarbazone, but it does seem logical to expect that more than 24 per cent of the ketone molecules would react with semicarbazide hydrochloride, if catechol hydrogenated completely *via* 2-hydroxycyclohexanone.

These results indicate that catechol hydrogenates by the same mechanism over both Adams platinum and 5 per cent rhodium on alumina. It seems significant that the 23.9 per cent ketone found in the hydrogenation above corresponds so closely to the 23.2 per cent ketone maximum determined by hydrogenating catechol to various degrees of completion over 5 per cent rhodium on alumina in acetic acid.

3. Resorcinol

a. Hydrogenations over 5 per cent rhodium on alumina catalyst. Resorcinol (2.0 g.) was hydrogenated to 40 per cent completion in 25 ml. of acetic acid over 5 per cent rhodium on alumina catalyst. The catalyst was removed from the reaction mixture by filtration and the filtrate was treated with 4 ml. of phenylhydrazine.[47] No phenylhydrazone derivative was isolated from the resulting solution.

Resorcinol (2.0 g.) was hydrogenated to 40 per cent completion in 25 ml. of acetic acid over 0.5 g. of 5 per cent rhodium on alumina. The catalyst was removed by filtration and the acetic acid solvent was evaporated in vacuo. The residue which remained was dissolved in water and treated with phenylhydrazine.[47] No phenylhydrazone derivative was isolated from the solution thus formed.

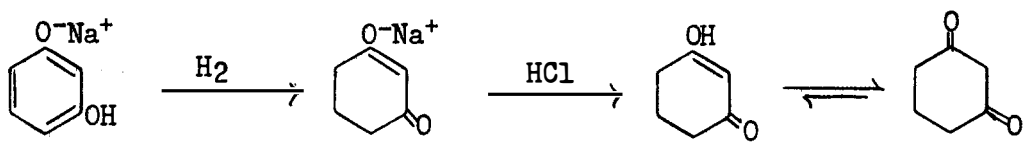
The hydrogenation was repeated using 2.0 g. of resorcinol and 25 ml. of acetic acid over 0.52 g. of 5 per cent rhodium on alumina. The reaction was stopped after 40 per cent completion, the catalyst was filtered off, and the acetic acid solvent was evaporated in vacuo. The residue remaining was dissolved in a small amount of water and the result-

ing solution was treated with an ethanol-water solution of sodium bisulfite.[47] No precipitate had formed in the reaction flask after it was left standing overnight. This indicated that ketone intermediates were not formed during the catalytic hydrogenation of resorcinol. This experiment was repeated using 2.0 g. of resorcinol and 25 ml. of acetic acid over 0.5 g. of 5 per cent rhodium on alumina. The reaction was stopped after one-third completion. After removing the catalyst and solvent, the residue which remained was treated with a solution containing 10 ml. of 40 per cent aqueous sodium bisulfite and 3 ml. of absolute ethanol.[47] No precipitate formed, even after the solution was left standing overnight.

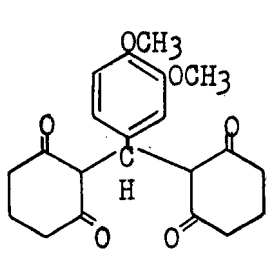
R. B. Thompson[19] prepared dihydroresorcinol (1,3-cyclohexanedione) by hydrogenating 55.0 g. of resorcinol at 50° in 100 ml. of water containing 24.0 g. of sodium hydroxide. He used 10 g. of Raney nickel catalyst and 1000-1500 p.s.i. hydrogen pressure. The reaction was stopped after 0.5 mole of hydrogen had been absorbed. Yields of dihydroresorcinol of 85-95 per cent were reported.

In this work, 1.0 g. (0.009 mole) of resorcinol was hydrogenated at 30° in 12 ml. of water containing 0.44 g. (0.0110 mole) of sodium hydroxide over 1.0 g. of 5 per cent rhodium on alumina. Hydrogen absorption ceased after 37 per cent reaction. The hydrogenation was repeated using 10.0 g. of resorcinol, 4.36 g. of sodium hydroxide, and 20 ml. of water over 2.0 g. of 5 per cent rhodium on alumina. The reaction again stopped after 37 per cent completion, which required about seventeen hours. The reaction mixture was filtered several times to remove completely all

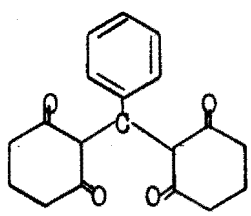
traces of catalyst. Concentrated hydrochloric acid was added to the filtrate until the solution was acidic to Congo red test paper. A small amount of solvent was evaporated in vacuo. Crystals formed when the solution was chilled in the refrigerator for a period of about one hour. The white crystalline material, 8.90 g., melted at 104-105°. 1,3-Cyclohexanedione melts at 105-106°.[46] Recrystallization from benzene was necessary to remove traces of sodium chloride from the solid, but the melting point was not raised. The 8.90 g. of solid corresponds to a yield of 87.4 per cent. The course of the reaction appears to be



To establish that the product formed was 1,3-cyclohexanedione, three derivatives were prepared. Veratraldehyde (1.1 g. or 0.0066 mole) was added to 1.5 g. of 1,3-cyclohexanedione (0.0132 mole) dissolved in a mixture of 10 ml. of ethanol and 10 ml. of water. To this solution was added 0.5 ml. of piperidine[49] and the mixture was warmed on the steam table for five minutes and cooled in the refrigerator for one hour. Scratching the sides of the beaker induced crystallization. The product was recrystallized from an ethanol-water mixture and found to melt at 164.6-165°. King and Felton[50] report a melting point of 163-164° for the expected derivative:



Benzaldehyde (0.7 g. or 0.0066 mole) was added to 1.5 g. (0.0132 mole) of 1,3-cyclohexanedione dissolved in a mixture of 10 ml. of ethanol and 10 ml. of water. Piperidine[49] (0.5 ml.) was added and the solution was heated on the steam table for five minutes. A crystalline product formed immediately, 1.21 g., m.p. 214-214.8°. The expected product[50] melts at 217-218°:



As a final check the dioxime was prepared by dissolving 1 g. of hydroxylamine hydrochloride in 4 ml. of water and adding to this solution 4 ml. of 10 per cent sodium hydroxide solution and 0.2 g. (0.00178 mole) of 1,3-cyclohexanedione.[47] The reaction mixture was heated on the steam table for ten minutes and cooled in the refrigerator. Crystals were obtained, 0.16 g., m.p. 155.4°. The dioxime of 1,3-cyclohexanedione melts at 154°.[51]

The use of 1,3-cyclohexanedione as an aldehyde reagent was illustrated above and has been described at length by King and Felton.[50] Dimedone (5,5-dimethyl-1,3-cyclohexanedione) usually serves the need but it is relatively expensive. The very easy low-pressure method for preparing 1,3-cyclohexanedione by hydrogenating resorcinol over 5 per cent rhodium on alumina, which has been developed in this work, should make the use of this diketone as an aldehyde reagent even more wide-spread. Thompson's method[19] has been used previously. However, not all organic laboratories are equipped with a high-pressure hydrogenation apparatus,

while most laboratories do possess at least one Parr low-pressure hydrogenator.

1,3-Cyclohexanedione (0.86 g.) was hydrogenated at 30° in 25 ml. of acetic acid over 0.2132 g. of 5 per cent rhodium on alumina. The rates of hydrogenation of this ketone and resorcinol are compared as Figure 6. As was shown in Table IV, 1,3-cyclohexanedione hydrogenated 3.5 times as rapidly as resorcinol. It is not surprising that ketone intermediates were not found in the hydrogenations of resorcinol described above. If such a ketone intermediate were formed, it would probably not accumulate as such to an appreciable extent in the reaction mixture, since it does hydrogenate so much more rapidly than resorcinol. It seems highly doubtful that any diketone forms during the course of the hydrogenation. If the reaction were to proceed through a ketone intermediate this would be expected to lead to complicated kinetics. For example, it can be seen in Figure 6 that 1,3-cyclohexanedione hydrogenates in a two-step manner. After the absorption of one mole of hydrogen, there is a slowing down of the reaction and the rate curve changes slope. The curve becomes linear again after the absorption of an additional one-half mole of hydrogen. The reaction was repeated using 1.0 g. of 1,3-cyclohexanedione in 25 ml. of acetic acid over 0.2122 g. of 5 per cent rhodium on alumina. Pressure readings were taken every fifteen seconds, and the results of this hydrogenation are shown in Figure 7. The reaction appears to take place in three distinct steps rather than two. There are three very definite linear portions to the rate curve, and each portion gives a reproducible rate constant. The rate constant for the first portion

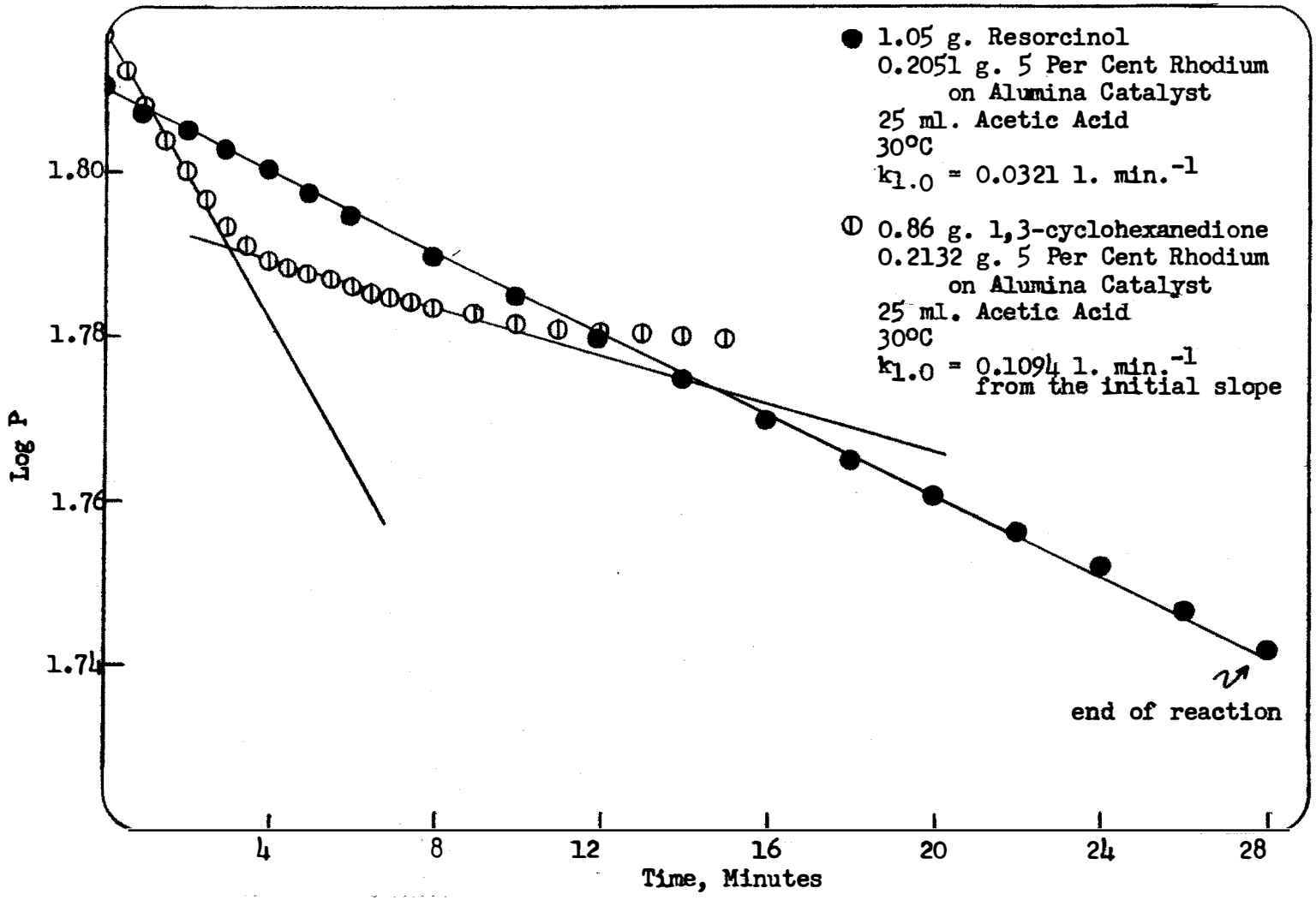


Figure 6. A comparison of the rate curves for the hydrogenation of resorcinol and 1,3-cyclohexanedione over 5 per cent rhodium on alumina.

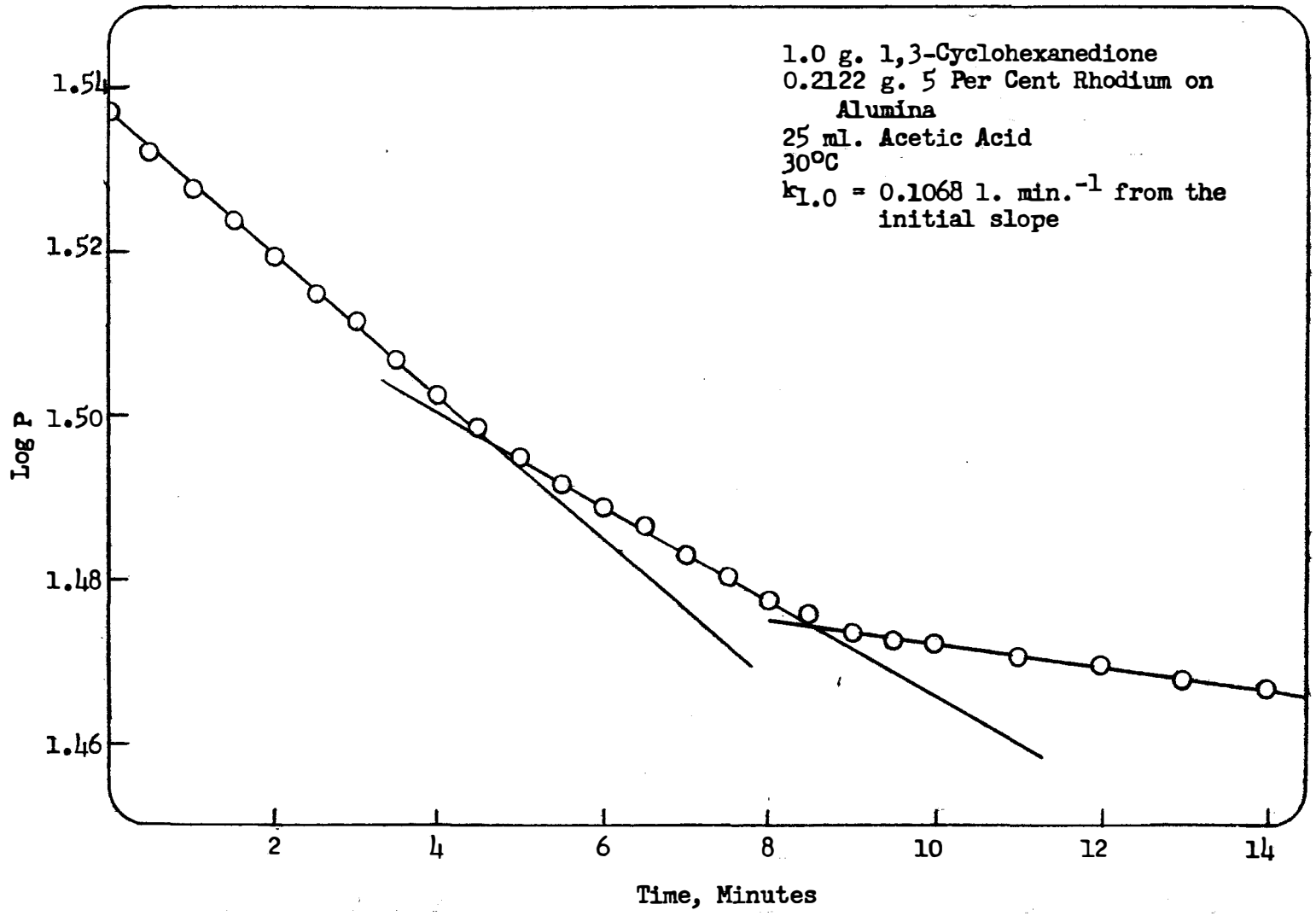
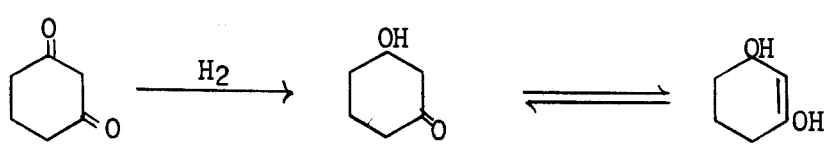
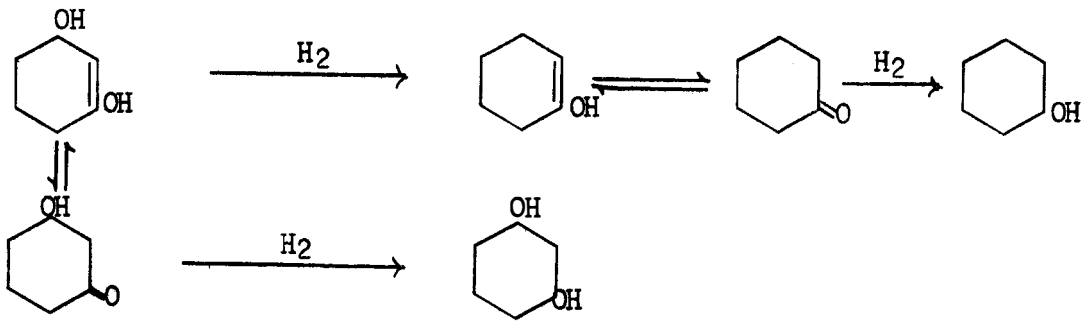


Figure 7. A plot of log pressure versus time for the hydrogenation of 1,3-cyclohexanedione over 5 per cent rhodium on alumina.

was calculated to be $k_{1.0}$ = 0.1068 l. min.$^{-1}$, for the second linear portion $k_{1.0}$ = 0.0733 l. min.$^{-1}$, and for the third linear portion $k_{1.0}$ = 0.01791 l. min.$^{-1}$. The two breaks in the curve or the changes in slope occur approximately at the points corresponding to the absorption of 1.0 and 1.6 moles of hydrogen, respectively. It could very well be that cleavage occurs during that portion of the reaction corresponding to the second linear part of the rate curve. An attempt was made to isolate a ketone intermediate in that portion of the reaction corresponding to the third linear part of the rate curve by hydrogenating 1.72 g. of 1,3-cyclohexanedione at 30° in 25 ml. of acetic acid over 0.210 g. of 5 per cent rhodium on alumina. The reaction was stopped after the absorption of 1.5 moles hydrogen per mole acceptor, the catalyst was removed by filtration, and the acetic acid solvent was evaporated in vacuo. The residue was dissolved in 20 ml. of water and divided into two 10-ml. portions. One portion was treated with 1.0 g. of semicarbazide hydrochloride and 1.5 g. of sodium acetate.[47] No semicarbazone had formed after two days. The second portion was treated with 1.1 g. of sodium hydroxide and 1.0 g. of hydroxylamine hydrochloride.[47] No oxime had formed after two days. It was thought that the reaction might be proceeding in the manner:



This ketone intermediate could react in two ways,



and these two competing reactions would account for the first change in slope of the rate curve.

The rate constant calculated from the slope of the first linear portion of the curve is approximately twice the rate constant for the hydrogenation of cyclohexanone, i.e., $k_{1.0} = 0.1068$ l. min.$^{-1}$ for 1,3-cyclohexanedione and $k_{1.0} = 0.0452$ l. min.$^{-1}$ for cyclohexanone. It might be expected that 1,3-cyclohexanedione would hydrogenate twice as rapidly as cyclohexanone since this molecule possesses two separated ketone groups to one for cyclohexanone. This indicated that the reaction corresponding to the first linear portion of the rate curve is the hydrogenation of one ketone group.

Kinetically speaking, cyclohexanone and 1,3-cyclohexanedione could be intermediates in the platinum-catalyzed hydrogenations since the rate constants for these ketones are greater than the rate constants for the corresponding hydroxyl compounds. This is obvious from the data in Table III presented earlier. However, the rate constant for cyclohexanone is two-thirds that of phenol for hydrogenation over 5 per cent rhodium on alumina (Table IV). This would rule out the possibility of cyclohexanone being an intermediate in the hydrogenation of phenol over this catalyst. A consideration of Figure 8, in which the rate curves for the hydrogenations of phenol and cyclohexanone are compared, adds further to the evidence that

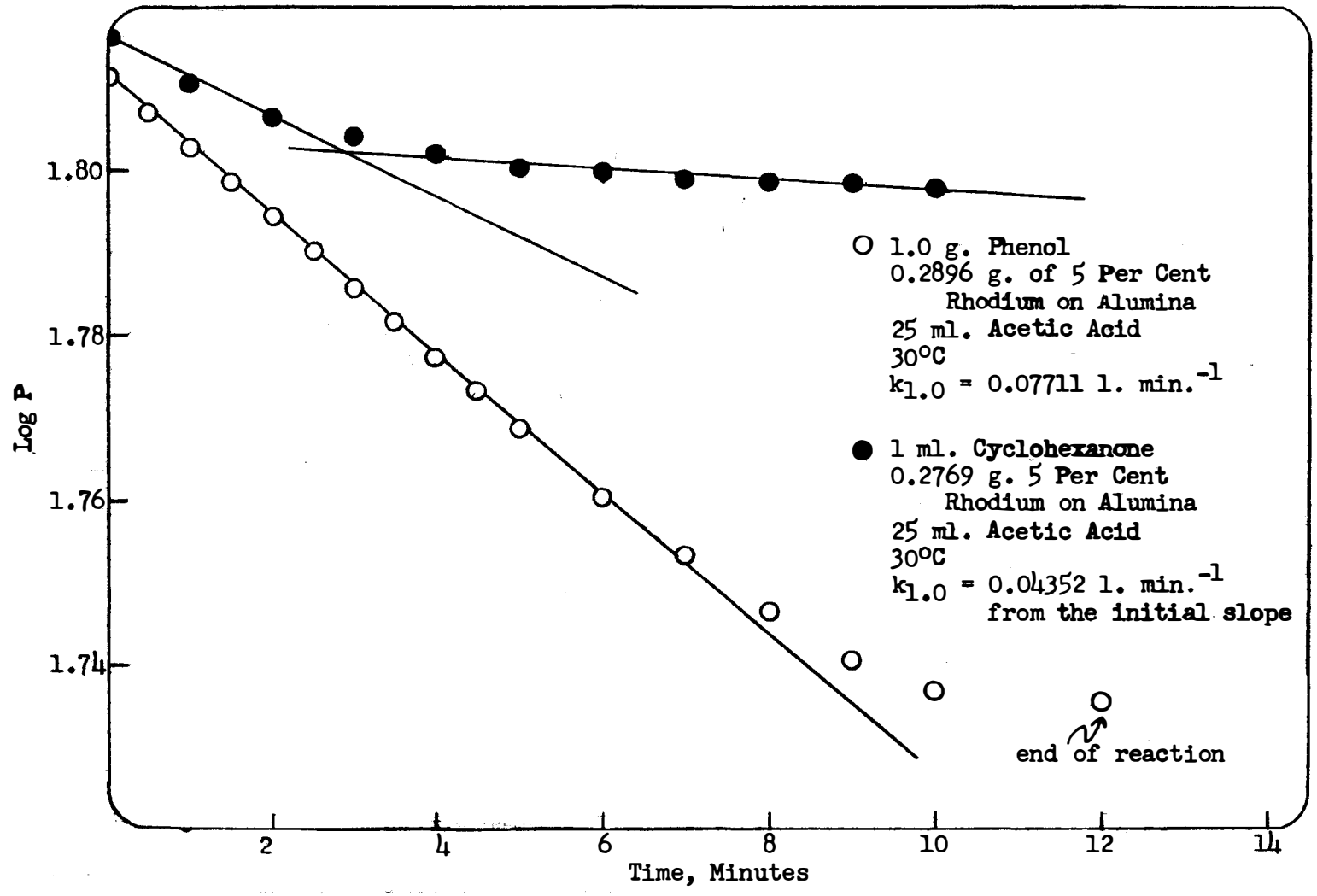


Figure 8. A comparison of the rate curves for the hydrogenation of phenol and cyclohexanone over 5 per cent rhodium on alumina.

cyclohexanone cannot be an intermediate. The ketone hydrogenates in a two-step manner, and the rate constants determined from the two slopes of the rate curve are both smaller than the rate constant for the hydrogenation of phenol.

Over rhodium, 1,3-cyclohexanedione could be an intermediate for resorcinol hydrogenations since the rate constant for this ketone is much greater than the rate constant for the hydroxyl compound. This was pointed out in Table IV. However, a consideration of Figures 6 and 7 shows that this ketone hydrogenates step-wise and the rate constant determined from the slope of the last portion of the curve is 1.8 times smaller than the rate constant for resorcinol. Too, the rate curve for the hydrogenation of resorcinol is linear over the major portion of the reaction. This rules out any possibility of 1,3-cyclohexanedione being an intermediate in this hydrogenation.

It will be shown later in this work that phenol and the dihydroxybenzenes hydrogenated at about the same rate as the corresponding methylbenzenes. If ketone intermediates played an appreciable role in the hydrogenation of these compounds, such agreement of data would not be expected.

b. Hydrogenations over Adams platinum catalyst. Resorcinol (2.0 g.) was hydrogenated at 30° in 25 ml. of acetic acid over 0.11 g. of platinum oxide and in the presence of 2.8 g. of semicarbazide hydrochloride. The reaction mixture absorbed 3.88 moles hydrogen per mole acceptor in comparison to 4.00 moles hydrogen per mole acceptor when semicarbazide hydrochloride was not present. The catalyst was removed and the acetic acid solvent was evaporated in vacuo. Attempts to isolate a semicarbazone derivative

from the residue which remained were unsuccessful. Obviously appreciable amounts of ketone are not formed during the course of this reaction.

1,3-Cyclohexanedione (0.50 g.) was hydrogenated in 25 ml. of acetic acid over 0.1 g. of platinum oxide. The reaction proceeded in a straightforward manner, i.e., the rate curve was linear for the major portion of the reaction, drifting from linearity only in the very last part of the reaction. Such a drift from linearity is observed with most platinum hydrogenations and is attributable to catalyst poisoning. It can be seen from the data in Table III that 1,3-cyclohexanedione hydrogenates only 1.2 times as rapidly as resorcinol, but the diketone does undergo cleavage to a greater extent than does the dihydroxybenzene. An attempt to explain this difference was included in an earlier section of this work.

4. Hydroquinone

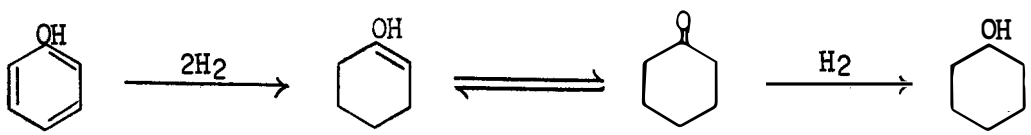
Hydroquinone (2.0 g.) was hydrogenated to 40 per cent completion at 30° in 25 ml. of acetic acid over 0.5119 g. of 5 per cent rhodium on alumina. The catalyst was removed by filtration and the acetic acid solvent was evaporated in vacuo. The residue which remained was dissolved in about 25 ml. of 95 per cent ethanol and to this solution was added 1.80 g. of 2,4-dinitrophenylhydrazine dissolved in a mixture of 9 ml. of concentrated sulfuric acid, 13.5 ml. of water, and 20 ml. of 95 per cent ethanol.[47] The solution was left standing at room temperature for one hour. Crystals were obtained, 0.96 g., m.p. 143-144°. After recrystallization from a methanol-water mixture, the crystalline material melted at 157°. The compound was analyzed as the 2,4-dinitrophenylhydrazone of 4-hydroxycyclohexanone.

Anal. Calcd. for $C_{12}H_{14}N_4O_5$: C, 48.98; H, 4.80; N, 19.04.

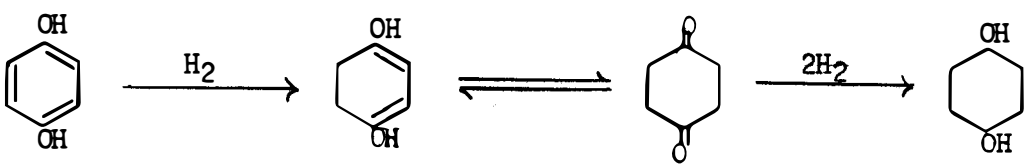
Found: C, 48.93; H, 4.71; N, 19.10.

The 0.96 g. of 2,4-dinitrophenylhydrazone derivative corresponds to 18 per cent ketone in the reaction mixture. This compound has not been reported in the literature previous to this work.

This reaction established the fact that 4-hydroxycyclohexanone rather than 1,4-cyclohexanedione is the ketone formed during the hydrogenation of hydroquinone. This could be taken as further evidence that phenol does not hydrogenate via cyclohexanone. If the one hydroxyl group in phenol offered sufficient protection to a double bond to cause this molecule to hydrogenate exclusively as



then the two hydroxyl groups in hydroquinone should offer sufficient protection to cause this compound to hydrogenate as



This reaction route would be even more feasible thermodynamically than would the cyclohexanone reaction route for phenol. However, results indicate that hydroquinone does not react by this mechanism.

C. Effect of Substitution on Reaction Rates

In the platinum-catalyzed hydrogenation of methylbenzenes by Smith and Pennekamp,[52] it has been shown that as the number of adjacent substituents increases, the rate constants decrease. For those compounds which have the same number of substituents, the one in which the arrangement is symmetrical has the highest rate, the vicinal isomer has the lowest rate and the unsymmetrical isomer has an intermediate rate. There exists an overlapping of these phenomena such that a symmetrical compound with a certain number of substituents has a higher rate than a vicinal compound with one less substituent. It has been shown that symmetrical substitution rather than molecular symmetry is actually the important factor in influencing the rate.

That a striking similarity exists between the rates of hydrogenation of methylbenzenes, methoxybenzenes, ortho-, meta-, and para-methoxytoluenes, and ortho-, meta-, and para-methoxybenzoic acids has been pointed out.[12] This comparison has been extended to include phenol, the ortho-, meta-, and para-dihydroxybenzenes, 1,2,3-trihydroxybenzene and 1,3,5-trihydroxybenzene.

1. Hydroxybenzenes

a. A comparison of rates of hydrogenation of hydroxybenzenes with those of methoxy- and methylbenzenes over Adams platinum. It may be seen in Tables IX and X that the rate constants of the dihydroxybenzenes and pyrogallol reveal the same effects of symmetry as for the methyl- and methoxybenzenes. The relative rates are not only in the same order, but

TABLE IX

COMPARISON OF RATE CONSTANTS AT 30° FOR HYDROGENATIONS OF HYDROXYBENZENES AND METHYLBENZENES OVER PLATINUM

Compound	$k_{1.0}$[a]	Compound[b]	$k_{1.0}$[a]	$\frac{k_{hydroxyl}}{k_{methyl}}$
Phenol	0.1620	Toluene	0.1800	0.90
Catechol	0.1330	o-Xylene	0.0932	1.43
Resorcinol	0.1611	m-Xylene	0.1434	1.12
Hydroquinone	0.2072	p-Xylene	0.1882	1.10
Pyrogallol	0.0951	Hemimellitene	0.042	2.26

[a]The $k_{1.0}$ is in l. $g.^{-1}$ $min.^{-1}$ and is given per unit weight of total catalyst.

[b]Data for these compounds obtained from Smith and Pennekamp.[52]

TABLE X

COMPARISON OF RATE CONSTANTS AT 30° FOR HYDROGENATIONS OF HYDROXYBENZENES AND METHOXYBENZENES OVER PLATINUM

Compound	$k_{1.0}$[a]	Compound[b]	$k_{1.0}$[a]	$\frac{k_{hydroxyl}}{k_{methoxyl}}$
Phenol	0.1620	Anisole	0.1588	1.02
Catechol	0.1330	o-Dimethoxybenzene	0.0843	1.58
Resorcinol	0.1611	m-Dimethoxybenzene	0.1013	1.59
Hydroquinone	0.2072	p-Dimethoxybenzene	0.1604	1.29
Pyrogallol	0.0951	1,2,3-Trimethoxybenzene	0.045	2.11

[a]The $k_{1.0}$ is in l. $g.^{-1}$ $min.^{-1}$ and is given per unit weight of total catalyst.

[b]The data for these compounds obtained from Smith and Thompson.[43]

fair quantitative agreement also exists. This is especially true with the hydroxybenzenes and methylbenzenes. The hydroxyl group would not be expected to be very much smaller than the methyl group, and one would expect little difference in the rates of hydrogenation of these compounds. This is found to be the case with the exception of the 1,2,3-trihydroxy- and 1,2,3-trimethylbenzenes. Here the hydroxyl compound hydrogenates about twice as rapidly as the methyl compound. The formation of ketone intermediates during the hydrogenation of the hydroxybenzene could probably account for this difference. It is interesting to note, too, that o-xylene and catechol are somewhat out of line. Any difference in steric factors would be expected to manifest itself with these two compounds. This very probably accounts for the different results observed here. The somewhat slower rates for the methyl compounds, in general, are probably attributable to the difference in size of the hydroxyl and methyl groups.

The agreement between hydroxy- and methoxybenzene rate constants is not as quantitative, however. This is especially pronounced with the o- and m-dihydroxy- and dimethoxybenzenes. The hydroxyl compounds hydrogenate about 1.6 times as rapidly as the methoxyl compounds. This difference in rates, again, is probably attributable to the difference in size of the hydroxyl and methoxyl groups, but ketone intermediates could play an important role here, also.

It is well to remember that for the methylbenzenes only aromatic hydrogenation occurred with the absorption of 3 moles of hydrogen per mole of acceptor in each case. However, for the hydroxy- and methoxybenzenes, the absorption of hydrogen indicated extensive cleavage of the hydroxyl

and methoxyl groups from the ring. It appears that for either series the symmetry and number of groups govern the rate of formation of activated complexes of catalyst, acceptor, and hydrogen. In the case of the hydroxy- and methoxybenzenes cleavage must then occur after the rate-determining step. The cleavage cannot take place to an appreciable extent before hydrogenation or a parallel between the behavior of methoxy-, hydroxy-, and methylbenzenes would not exist. It has been pointed out[12] that if cleavage preceded the hydrogenation of phenol, for example, the products would be benzene and water, and the rate of hydrogenation observed would then be that characteristic of benzene. Instead, phenol hydrogenates about one-half as rapidly as benzene, which is approximately the same ratio observed for the hydrogenations of toluene and benzene. The clear-cut kinetics of zero order with respect to acceptor and first order with respect to hydrogen pressure seem to indicate that independent simultaneous hydrogenation and hydrogenolysis reactions do not exist.

It is interesting to note that the relative rates for hydrogenations of hydroxy-, methyl- and methoxybenzenes, and methyl- or methoxybenzoic acids are in the order:

hydroxy > methyl > methoxy > methyl- or methoxybenzoic.

The decrease in rates here parallels the increase in size of the substituents.

b. Comparison of rates of hydrogenation of hydroxybenzenes with those of methoxybenzenes over 5 per cent rhodium on alumina. The rates of hydrogenation at 30° for the hydroxybenzenes using 5 per cent rhodium on alumina show the same general effect of symmetry as observed for the corresponding compounds with platinum. However, the differences in rates for

ortho-, meta-, and para-dihydroxybenzenes are not nearly as pronounced as for platinum.

Table XI shows a comparison of the rate constants of hydroxybenzenes with those of the methoxybenzenes for hydrogenations over 5 per cent rhodium on alumina. The relative rates are in the same order, and fair quantitative agreement also exists. The 1,2-dihydroxy- and 1,2-dimethoxybenzenes are somewhat out of line.

2. Activation Energies

Tables XII and XIII show the hydrogenation rates as a function of temperature for the hydroxybenzenes. The activation energy plots are shown as Figures 9 and 10. The activation energies were calculated from the "least-squares" slopes of activation energy plots. For each compound, the activation energy was greater for hydrogenation with the supported rhodium catalyst than for Adams platinum.

TABLE XI

COMPARISON OF RATE CONSTANTS AT 30° FOR HYDROGENATIONS OF HYDROXYBENZENES AND METHOXYBENZENES OVER 5 PER CENT RHODIUM ON ALUMINA

Compound	$k_{1.0}$[a]	Compound[b]	$k_{1.0}$[a]	$\frac{k_{hydroxyl}}{k_{methoxyl}}$
Phenol	0.0687	Anisole	0.0876	0.78
Catechol	0.0145	o-Dimethoxybenzene	0.0315	0.46
Resorcinol	0.0311	m-Dimethoxybenzene	0.0360	0.86
Hydroquinone	0.0363	p-Dimethoxybenzene	0.0362	1.00

[a]The $k_{1.0}$ is in l. $g.^{-1}$ $min.^{-1}$ and is given per unit weight of total catalyst.

[b]The data for these compounds obtained from Smith and Thompson.[43]

TABLE XII

REACTION RATES AND ACTIVATION ENERGIES OF HYDROXYBENZENES FOR HYDROGENATIONS OVER ADAMS PLATINUM

Compound	T, °C	$k_{1.0}$ (l. min.$^{-1}$)	ΔH_a (Kcal. mole^{-1})
Phenol	20	0.1361	
	30	0.1620	
	40	0.2050	
	50	0.2434	4.49
Catechol	20	0.1015	
	30	0.1330	
	40	0.1748	
	50	0.2281	4.62
Resorcinol	20	0.1177	
	30	0.1611	
	40	0.2129	
	50	0.2856	5.51
Hydroquinone	20	0.1571	
	30	0.2072	
	40	0.2611	
	50	0.3175	4.40
Phloroglucinol	20	0.0211	
	30	0.0378	
	40	0.0614	
	50	0.1001	9.67
Pyrogallol	20	0.0628	
	30	0.0951	
	40	0.1390	
	50	0.1687	6.54

TABLE XIII

REACTION RATES AND ACTIVATION ENERGIES OF HYDROXYBENZENES FOR HYDROGENATIONS OVER 5 PER CENT RHODIUM ON ALUMINA

Compound	T, °C	$k_{1.0}$ (l. min.$^{-1}$)	ΔH_a (Kcal. mole^{-1})
Phenol	20	0.0445	
	30	0.0687	
	40	0.1044	
	50	0.1249	6.61
Catechol	20	0.0102	
	30	0.0145	
	40	0.0211	
	50	0.0282	6.43
Resorcinol	20	0.0177	
	30	0.0311	
	40	0.0442	
	50	0.0633	7.84
Hydroquinone	20	0.0221	
	30	0.0363	
	40	0.0445	
	50	0.0653	6.49
Phloroglucinol	20	0.00471	
	30	0.00807	
	40	0.0150	
	50	0.0263	10.82
Pyrogallol	20	0.00463	
	30	0.00757	
	40	0.0116	
	50	0.0174	8.25

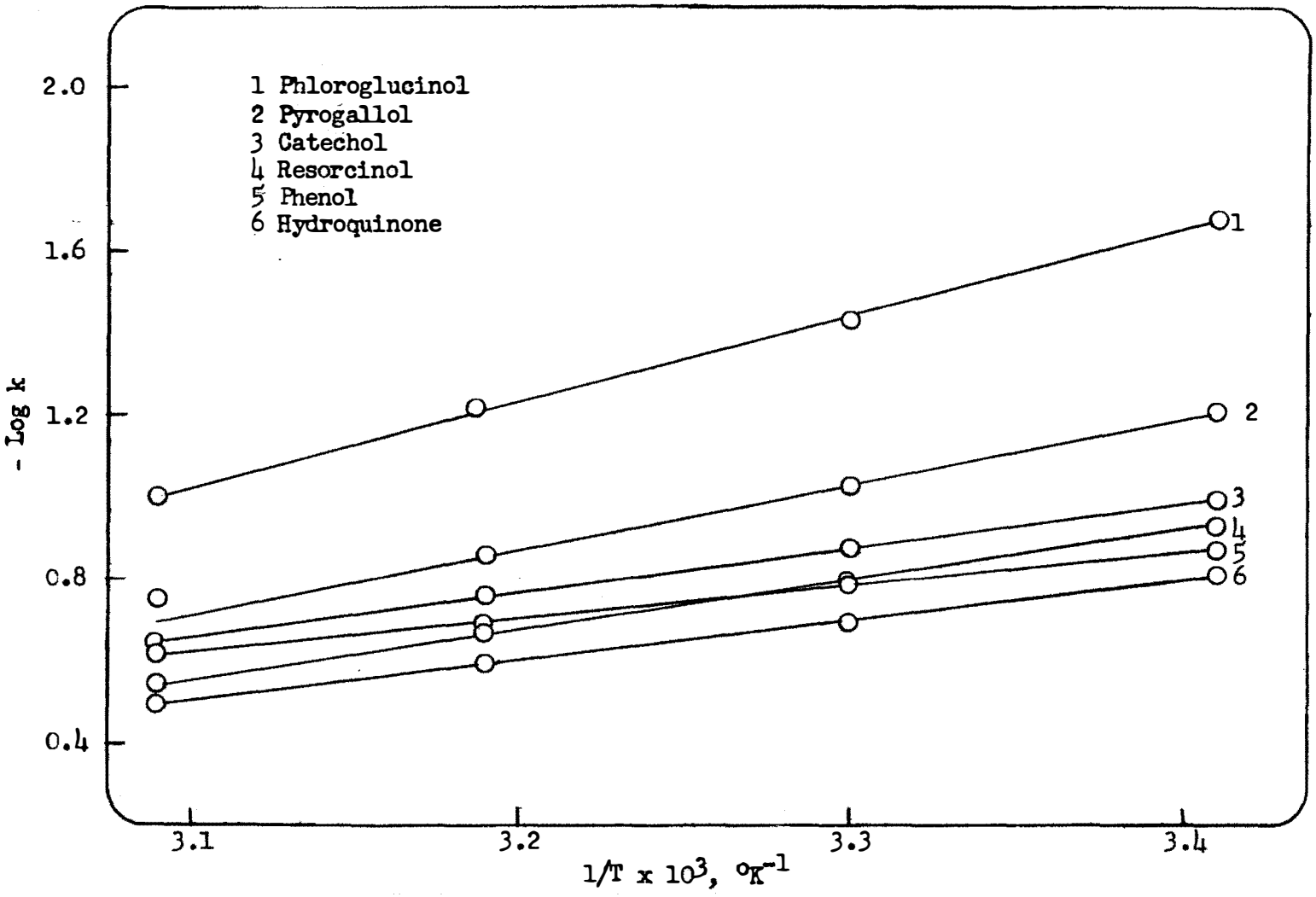


Figure 9. Activation energy plots for hydrogenations of hydroxybenzenes over Adams platinum.

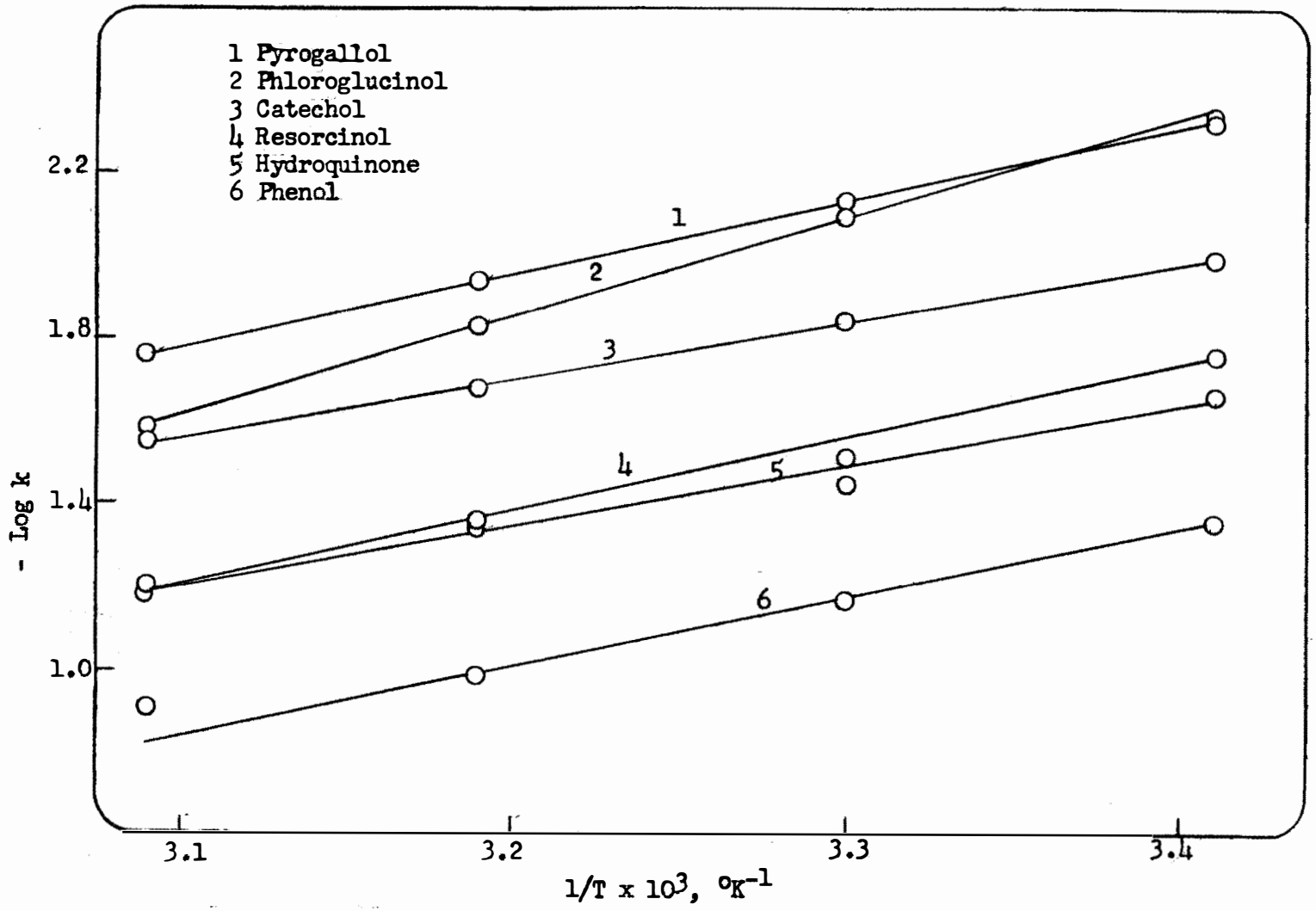
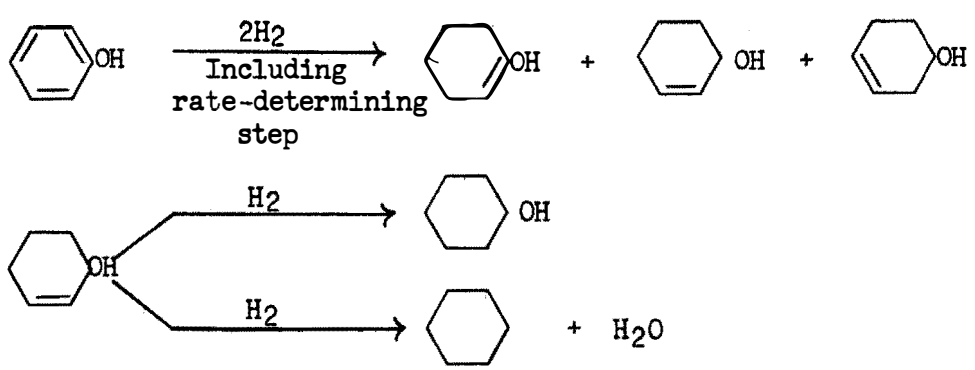


Figure 10. Activation energy plots for hydrogenations of hydroxybenzenes over 5 per cent rhodium on alumina.

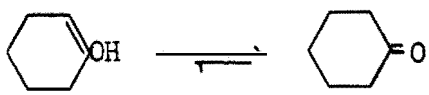
CHAPTER IV

A POSSIBLE REACTION MECHANISM

From the data which have been collected on the hydrogenation and hydrogenolysis of hydroxybenzenes, the following mechanism is postulated. The hydroxybenzene, phenol for example, is adsorbed on the catalyst surface. With the approach of hydrogen to the catalyst surface, hydrogenation takes place to give hydroxycyclohexenes as short-lived intermediates. These short-lived intermediates may or may not be desorbed from the catalyst, i.e., the hydroxycyclohexene may react with an additional mole of hydrogen to give a cyclohexanol without desorbing into the reaction mixture where it would compete with the unreacted phenol for adsorption and hydrogen. The intermediate hydroxycyclohexene may undergo cleavage to cyclohexene and water or ring hydrogenation to give cyclohexanol. These reactions will probably occur simultaneously until the double-bonded molecules are saturated.



Three hydroxycyclohexene intermediates are possible, and these are shown above. The 1-hydroxycyclohexene-1 is the tautomeric form of cyclohexanone:

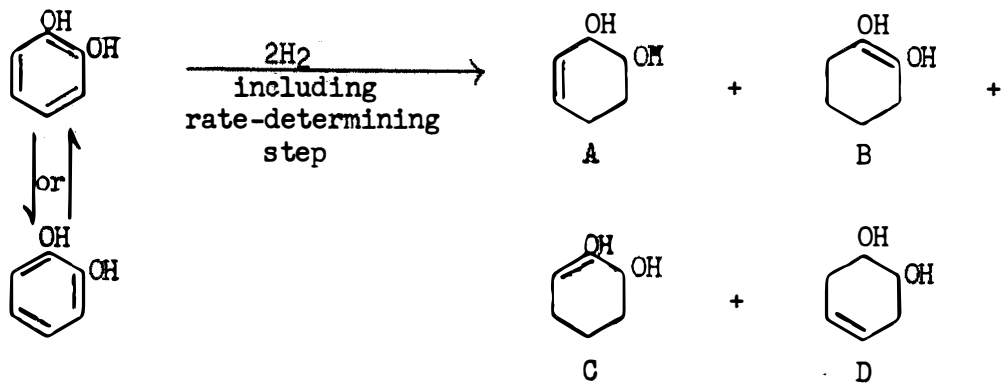


This tautomerization would be expected to take place when the 1-hydroxycyclohexene-1 desorbs from the catalyst surface, since the keto form is more stable than the enol form by about 18 kcal. $mole^{-1}$.[53] This accounts for the presence of ketones in the reaction mixture without claiming that cyclohexanone is a reaction intermediate in the usual sense.

This mechanism modifies to some extent the one postulated by Thompson[12] for the cleavage of methoxyl groups from aromatic nuclei during catalytic hydrogenation reactions. He felt that the cleavage reaction occurred in the 3-methoxycyclohexene-1 (3-hydroxycyclohexene-1 in this case), since the double bond in the β-γ position should make the carbon-oxygen bond labile to cleavage. Results obtained in this work with the hydrogenation of cyclohexanone indicate that cleavage occurs to an appreciable extent in this molecule, which probably hydrogenates either in the keto form or as 1-hydroxycyclohexene-1. Hence the carbon-oxygen bond does not have to be rendered labile by the β-γ double bond in order to undergo cleavage. The double bond in the β-γ position very probably does cause this intermediate (3-hydroxycyclohexene-1) to cleave to a greater extent than do the intermediates 1-hydroxycyclohexene-1 and 4-hydroxycyclohexene-1. Differences in per cent cleavage for various hydroxy-

benzenes can be explained as resulting from different proportions of the possible cyclohexenes being formed during the reaction. Too, hydrogenation and hydrogenolysis are competing reactions, and hydrogenolysis is very probably the slower reaction.

The proposed mechanism can be shown to account for the results obtained with the dihydroxybenzenes. Catechol reacts as follows:



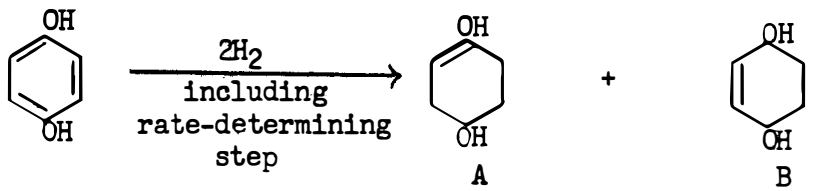
Intermediates B and C undergo tautomerization to 2-hydroxycyclohexanone when



desorbed from the catalyst into the reaction mixture. Experiments performed during this research have shown that 2-hydroxycyclohexanone is formed during the hydrogenation of catechol. Intermediate A has a double bond β-γ to a hydroxyl group and renders this group labile. Intermediate D very probably occurs to the least extent in the course of the reaction. If steric factors are important at all in determining the course of the reaction, intermediate B would be expected to predominate. This could account for the fact that catechol cleaves less readily than do resorcinol

and hydroquinone.

With hydroquinone two cyclohexene intermediates are possible:

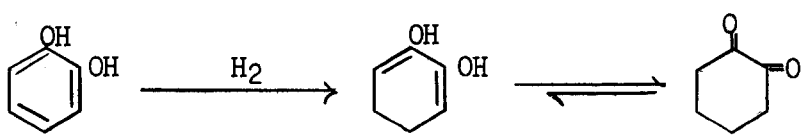


Intermediate A would undergo tautomerization when desorbed from the catalyst surface to give 4-hydroxycyclohexanone. The presence of this ketone



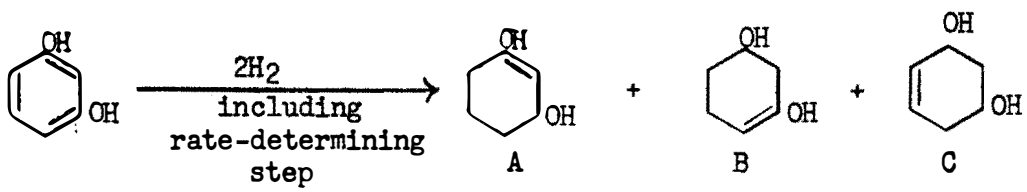
has been shown during the hydrogenation of hydroquinone. Intermediate B has a double bond β-γ to two hydroxyl groups, hence extensive cleavage of these groups is expected and observed during the hydrogenation of hydroquinone.

The fact that hydroxycyclohexanones rather than diketones are formed in the hydrogenations of catechol and hydroquinone adds support to the proposed mechanism. If phenol hydrogenated completely <u>via</u> cyclohexanone, as many investigators have claimed, this would mean that a combination of steric and thermodynamic factors makes such a reaction path feasible. With a diketone, catechol for example, such factors are even more favorable for ketone formation, yet diketones are not formed.



The difference in energies between the diketone and the dihydroxycyclohexadiene would certainly be sufficient to cause tautomerization of the enol to the diketone. The cyclohexadiene probably reacts with hydrogen on the catalyst surface to give an hydroxycyclohexene before desorption and tautomerization can take place.

The reaction of resorcinol follows the path



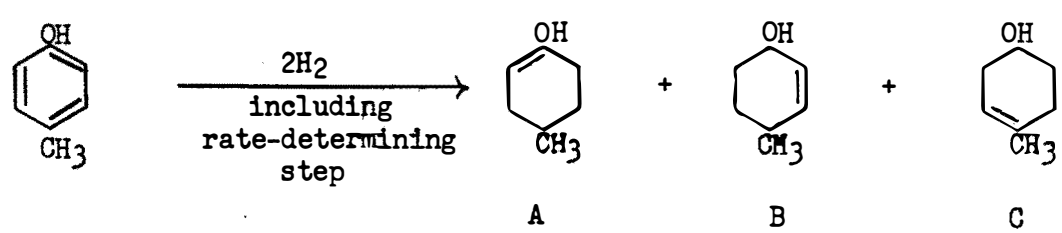
With both intermediates A and B, tautomerization to give an hydroxycyclohexanone is possible. Experiments performed during the course of this work indicate that such ketones are not formed. Evidently the cyclohexenes formed react with hydrogen before desorption from the catalyst surface can take place.

Cyclohexenes are thermodynamically-possible intermediates during the hydrogenation of benzene derivatives. In the hydrogenation of benzene it has not been possible to isolate cyclohexene as an intermediate. A possible explanation for this is that the molecule does not desorb from the catalyst until all the double bonds are hydrogenated. The mechanism proposed in this work does not require desorption of the substituted cyclohexene. Only the existence of the cyclohexene or some equivalent for a short time on the catalyst surface is necessary. In those cases where ketones are isolated, it is felt that desorption does take place prior to tautomerization. Thompson[12] found that cyclohexene hydrogenates

8.1 times as rapidly as benzene over Adams platinum. Hence the hydroxycyclohexene intermediates formed would be expected to hydrogenate rapidly and not accumulate in the reaction mixture. Stabilization of some of the hydroxycyclohexene intermediates by tautomerization to ketones would account for the presence of these during the course of the reaction. Cyclohexanone was found to hydrogenate only 1.2 times as rapidly as phenol.

It has been observed that 5 per cent rhodium on alumina gives little hydroxyl cleavage. Thompson[12] found that cyclohexene hydrogenates 20.4 times as rapidly as benzene over this catalyst. Thus any cyclohexene intermediate would be expected to have a shorter life with rhodium and therefore permit less cleavage.

The results obtained by Wicker[18] for the hydrogenation of the cresols and the corresponding methylcyclohexanones are readily explainable by the mechanism proposed here. He reasoned that if the cresols (and phenol) hydrogenated *via* a ketone intermediate, the same per cent stable stereoisomer should be formed by hydrogenation, whether the cresol or its corresponding methylcyclohexanone were used as the starting material. It has been shown earlier that such results were not obtained. By the mechanism proposed here, *p*-cresol (for example) would react as



With intermediate A tautomerization would give 4-methylcyclohexanone as an intermediate. Intermediates B and C would undergo hydrogenation to form 4-methylcyclohexanol. The hydrogenation of these three isomers would certainly be expected to lead to different amounts of stable stereoisomer product.

On the other hand, the hydrogenation of 4-methylcyclohexanone probably proceeds either through the ketone or 4-methyl-1-hydroxycyclohexene-1, and a difference in the per cent stable stereoisomer formed would be expected when the 4-methylcyclohexanone was used as starting material in place of p-cresol.

CHAPTER V

SUMMARY

The catalytic hydrogenation of hydroxybenzenes over Adams platinum and 5 per cent rhodium on alumina catalysts has been studied. The kinetics of the hydrogenation were found to be first order in hydrogen pressure, zero order in acceptor concentration and directly proportional to catalyst weight. Activation energies were determined using the integrated form of the Arrhenius equation.

Hydrogenation of the aromatic ring was usually accompanied by some cleavage of the hydroxyl groups. The amount of cleavage was found to be dependent upon the catalyst used. Platinum led to extensive hydroxyl cleavage while rhodium catalyzed ring saturation with little cleavage. Both the reaction temperature and the structure of the acceptor were found to influence the extent of cleavage.

A mechanism for the hydrogenation of hydroxybenzenes has been proposed. This mechanism involves the formation of hydroxycyclohexene intermediates. Tautomerization of the hydroxycyclohexene to the keto form accounts for the formation of ketones during the course of the reaction. The carbon-oxygen bond is labilized by the β-γ carbon-carbon double bond in the hydroxycyclohexene and cleaves easily under these conditions.

No kinetic evidence was found for the formation of ketone intermediates, but the role played by ketones in hydroxybenzene hydrogenations was investigated.

A simple method of preparation for 1,3-cyclohexanedione was developed using resorcinol, low pressures of hydrogen, and 5 per cent rhodium on alumina catalyst.

The preparation of the 2,4-dinitrophenylhydrazone of 4-hydroxycyclohexanone has not been reported previous to this work.

The effect of substitution and number of substituents on the rate of hydrogenation was found to be about the same for the various hydroxybenzenes as for the corresponding methyl and methoxy compounds.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. H. A. Smith in P. H. Emmett, "Catalysis," Vol. V, Reinhold Publishing Corp., New York, N. Y., 1957, p. 198.

2. G. Vavon and A. L. Berton, Bull. soc. chim., 37, 296 (1925).

3. V. Grignard and V. Mingasson, Compt. rend., 185, 1552 (1927).

4. F. Coussemant and J. C. Jungers, Bull. soc. chim. Belges, 59, 295 (1950).

5. E. N. Zil'berman, Khim. Prom., 1954, 152.

6. S. Tutumi and S. Nagao, J. Chem. Soc. Japan, 54, 165-7 (1951); C. A., 47, 1569 (1953); S. Tsutsumi, T. Yoshijima, H. Akatsuka, and S. Nagao, Technol. Repts. Osaka Univ., No. 74-92, 343-9 (1953); C. A., 49, 8177 (1955).

7. E. F. Rosenblatt, U. S. Patent 2,675,390; C. A., 48, 8258 (1954).

8. T. Sasa, J. Soc. Org. Synthetic Chem. (Japan), 11, 463-6 (1953); C. A., 49, 919 (1955).

9. P. Y. Yeh, C. T. Chen, C. C. Chu, H. C. Hsu, C. S. Chang, and C. L. Hsiu, Formosan Sci., 7, 27-30 (1953); C. A., 49, 3033 (1955).

10. F. A. Vandenheuvel, Anal. Chem., 28, 362-5 (1956); C. A., 50, 15991 (1956).

11. Belg. Patent 490,599; C. A., 50, 13336 (1956).

12. R. G. Thompson, "A Study of the Catalytic Hydrogenation of Methoxybenzenes Over Platinum and Rhodium Catalysts," Doctoral Dissertation, The University of Tennessee, Knoxville, 1956.

13. G. Gilman and G. Cohn, "Advances in Catalysis," Vol. IX, Academic Press, Inc., Publishers, New York, N. Y., 1957, p. 736.

14. H. E. Ungnade and A. D. McLaren, J. Am. Chem. Soc., 66, 118 (1944).

15. H. E. Ungnade and D. V. Nightingale, J. Am. Chem. Soc., 66, 1218 (1944).

16. A. L. Barney and H. B. Haas, Ind. Eng. Chem., 36, 85 (1944).

17. A. C. Whitaker, J. Am. Chem. Soc., 69, 2414 (1947).

18. R. J. Wicker, J. Chem. Soc., 1957, 3299.

19. R. B. Thompson, Organic Syntheses, 27, 21 (1947).

20. W. H. Hartung and R. Simonoff, "Organic Reactions," Vol. 7, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 263.

21. R. Baltzly and J. S. Buck, J. Am. Chem. Soc., 65, 1984 (1943).

22. A. V. Lozovoi, A. B. Vol'Epshtein, and S. A. Senyavin, Trudy Inst. Goryuch. Iskopaemykh, Akad. Nauk. S. S. S. R., Otdel. Tekh. Nauk., 6, 16-34 (1955); C. A., 50, 16086 (1956).

23. B. K. Klimov and I. F. Bogdanov, Trudy Inst. Goryuch. Iskopaemykh, Akad. Nauk. S. S. S. R., 3, 140-150 (1954); C. A., 50, 270 (1956).

24. R. Amatatsu, J. Chem. Soc. Japan, 52, 585 (1931).

25. R. H. Levin and J. H. Pendergrass, J. Am. Chem. Soc., 69, 2436 (1947).

26. F. Balas and A. Kosik, Casopis Ceskoslov. Lekarnictva, 7, 105 (1927); F. Balas and L. Srol, Collection Czechoslov. Chem. Communications, I, 658 (1929).

27. N. L. Edson, J. Soc. Chem. Ind., 53, 138 (1934).

28. R. Lukes, J. Trojanek, and K. Blaha, Chem. Listy, 49, 717-22 (1955); C. A., 49, 12368 (1955).

29. J. L. R. Williams, J. Org. Chem., 19, 1205-14 (1954).

30. W. B. Innes in P. H. Emmett, "Catalysis," Vol. 1, Reinhold Publishing Corp., New York, N. Y., 1945, p. 245.

31. L. d'Or and A. Orzechowski, Compt. rend., 235, 368 (1952).

32. E. M. Van Duzee and H. Adkins, J. Am. Chem. Soc., 57, 147 (1935).

33. A. W. C. Taylor, H. N. Rose, and T. Alderson, U. S. Patent 2,503,641; C. A., 44, 7877 (1950).

34. N. D. Zelinski and M. B. Turowa-Pollak, Ber., 58B, 1298 (1925).

35. C. Zenghelis and C. Stathis, Compt. rend., 206, 682 (1938); C. Zenghelis and C. Stathis, Monatsh. Chem., 72, 58 (1938).

36. K. M. Minachev, N. I. Schuikin, and I. D. Rozhdestvenskaya, Izvest. Akad. Nauk. S. S. S. R., Otdel. Khim. Nauk., 1954, 338, C. A., 48, 10259 (1954).

37. Baker and Company, Inc., Newark, New Jersey, Brochure #2, "Rhodium Catalysts for the Hydrogenation of Ring Compounds."

38. L. Hernandez and F. F. Nord, Experientia, 3, 489 (1947); C. A., 43, 27 (1949); L. Hernandez and F. F. Nord, J. Colloid Sci., 3, 363 (1948).

39. P. H. Emmett, Private Communication.

40. H. A. Smith and J. F. Fuzek, J. Am. Chem. Soc., 70, 3743 (1948).

41. H. A. Smith et. al., J. Am. Chem. Soc., 67, 272, 276, 279 (1945).

42. H. A. Smith, D. M. Alderman, and F. W. Nadig, J. Am. Chem. Soc., 67, 272 (1945).

43. H. A. Smith and R. G. Thompson, "Advances in Catalysis," Vol. IX, Academic Press, Inc., Publishers, New York, N. Y., 1957, p. 727.

44. E. Waser, H. Sommer, C. Landweer, and C. Gaza, Helv. Chim. Acta, 12, 418 (1929).

45. E. Urion, Compt. rend., 192, 1662-4 (1931).

46. "Handbook of Chemistry and Physics," 33rd ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1951.

47. R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948.

48. W. Pritzkow, Chem. Ber., 87, 1668-75 (1954); C. A., 50, 14575 (1956).

49. E. C. Horning and M. G. Horning, J. Org. Chem., 11, 95 (1946).

50. F. E. King and D. G. I. Felton, J. Chem. Soc., 1948, 1371.

51. K. Nakazawa and S. Matsuura, J. Pharm. Soc. Japan, 71, 802-4 (1951); C. A., 46, 8025 (1952).

52. H. A. Smith and E. F. H. Pennekamp, J. Am. Chem. Soc., 67, 276, 279 (1945).

53. R. H. Thomson, Quart. Revs. (London), 10, 27 (1956).

PART II

THE KINETICS OF THE ACID-CATALYZED HYDROLYSIS OF THE DIMETHYL ESTERS OF CYCLOHEXANEDICARBOXYLIC ACIDS

CHAPTER I

INTRODUCTION

A. Statement of Problem

A study of the kinetics of the acid-catalyzed hydrolysis of the dimethyl esters of the cyclohexanedicarboxylic acids was undertaken in this problem. It was hoped that an investigation of the relative reaction rates of the various esters would provide further information as to the predominant configurations of the compounds involved and add to the present knowledge of acid-catalyzed hydrolyses in general. It would also furnish an interesting comparison with the base-catalyzed hydrolyses of these same esters and the acid-catalyzed esterification of the corresponding acids. These reactions have been previously studied in this laboratory.

B. Previous Work

1. Acid-catalyzed Ester Hydrolysis

Many investigators have studied the rates of acid-catalyzed hydrolysis of various esters under widely different reaction conditions, and a complete review of the research in this field is beyond the scope of this work. Of particular interest has been the elucidation of the mechanism of this reaction. Day and Ingold[1] have pointed out that certain reactions which have usually been considered to be among the simplest in organic chemistry may pursue any of several mechanisms. Hence in ester hydrolysis there exists a reaction which is not altogether simple, and a number of distinct

mechanisms may be recognized. In order to distinguish between the various possible mechanisms, it is necessary to determine the position of rupture of the carbon-oxygen bond, i.e.,

$$R'\text{-}CO\cdots OR \qquad \text{or} \qquad R'\text{-}CO\text{-}O\cdots R\ ,$$

the acyl-oxygen bond or the alkyl-oxygen bond.

In acid-catalyzed hydrolyses, it is the acyl-oxygen linkage which is broken. This has been established fully by the normal methods for hydrolysis. This was first done by Holmberg[1,2] for acid hydrolysis by the method which seeks to detect any change of configuration in an alkyl group R which is asymmetric at its point of attachment in the ester. He showed that in the acid hydrolysis of O-acetyl malic acid, the asymmetric group completely retains its configuration.

Using isotopically distinguished oxygen in one of the interacting oxygen compounds and tracing its reappearance in one of the products has been applied to acid hydrolysis using methyl hydrogen succinate.[3] It was shown that isotopically-distinguished oxygen from the solvent (water) does not appear in the alcohol and, therefore, must enter into the acid produced by the acid hydrolysis of an ester. This method involves no assumptions and hence affords the most self-contained proof.

Ingold and Ingold[4] applied the method of choosing a form of R which, if liberated, would be mesomeric, and would accordingly lead to isomeric end-products. The esters α-methylallyl acetate and crotyl acetate were used, and no isomerization was observed.[3] All these results prove acyl-oxygen fission. This is also required by the principle of microscopic reversibility, since esterification involves the formation of this same bond.

Ingold and Ingold[4] summarized the possible mechanisms for acid-catalyzed hydrolyses with the following considerations. It is a known fact that the carbonyl oxygen atom has definite basic tendencies, which polarization of the carboxyl group, $O \overset{\curvearrowright}{-} C \overset{\curvearrowright}{=} O$, would be expected to enhance. Therefore hydrolysis might conceivably be initiated at the carbonyl oxygen atom, the complete reaction, in which the last stage is analogous to 'onium salt decomposition, being as follows:

$$R'\text{-}CO\text{-}OR + H^+ \longrightarrow R'\text{-}\overset{+}{C}OH\text{-}OR \longrightarrow R'\text{-}\overset{+}{C}OR\text{-}OH \longrightarrow R'COOH + R^+$$

$$R^+ + H_2O \longrightarrow ROH + H^+$$

Let this be known as mechanism A. The alternative hypothesis is that the reaction commences at the ethereal oxygen atom in conformity with the established basic character of singly-linked bicovalent oxygen. In this case, an 'onium structure would be produced which could lead to the products of hydrolysis by fission in either of two directions. Let these two directions be known as mechanisms B and C, respectively:

$$R'\text{-}CO\text{-}OR + H^+ \longrightarrow R'\text{-}CO\text{-}\overset{+}{O}HR \longrightarrow R'\text{-}CO\text{-}OH + R^+$$

$$R^+ + H_2O \longrightarrow ROH + H^+$$

$$R'\text{-}CO\text{-}OR + H^+ \rightleftharpoons R'\text{-}CO\text{-}\overset{+}{O}HR \underset{\rightleftharpoons}{\overset{\text{slow}}{\longrightarrow}} R'\text{-}\overset{+}{C}{=}O + ROH$$

$$R'\text{-}\overset{+}{C}{=}O + H_2O \longrightarrow R'\text{-}CO\text{-}OH + H^+$$

Both mechanisms A and B involve the cleavage of the alkyl-oxygen linkage, and it has been pointed out earlier that such cleavage does not take place. Hence mechanism C seems to be the only reasonable one.

Day and Ingold[1] have proposed still another mechanism which for purposes of discussion will be referred to as mechanism D:

$$R'\text{-}CO\text{-}OR + H^+ \underset{\rightleftharpoons}{\overset{\text{fast}}{\longrightarrow}} R'\text{-}CO\text{-}\overset{+}{O}HR$$

$$H_2O + R'\text{-}CO\text{-}\overset{+}{O}HR \overset{\text{slow}}{\rightleftharpoons} H_2\overset{+}{O}\text{-}CO\text{-}R' + ROH$$

$$H_2\overset{+}{O}\text{-}CO\text{-}R' \overset{\text{fast}}{\rightleftharpoons} R'\text{-}CO\text{-}OH + H^+$$

The main kinetic requirements of mechanism C are that the initial rate of hydrolysis should be proportional to the concentrations of acid catalyst and ester, and independent of the concentration of water. Mechanism D, however, requires the initial rate of hydrolysis to be proportional to the concentrations of acid catalyst, ester, and water. Proportionality of the rate of reaction to the water concentration could not be demonstrated as long as water was the solvent. However, Friedman and Elmore[5] have shown that, in acetone as solvent, the rate is, indeed, proportional to the concentration of water.

One other kinetic criterion may be mentioned. The first step of mechanism D consists of a preliminary reversible proton transfer. Bonhoeffer[6] and Reitz[7] have shown that, while the rates of aqueous reactions are usually reduced when ordinary solvent water is replaced by heavy water, this difference may become reversed in the case of reactions which proceed by a mechanism dependent on a pre-equilibrium involving a proton (or deuteron) transfer. Conversely, they assumed that the observation of a larger rate in heavy water may be taken as an indication that the mechanism does involve such a pre-equilibrium. Aqueous hydrolysis of esters does proceed faster in heavy water than in ordinary water.[8] Mechanism D evidently brings the rule of Bonhoeffer and Reitz and the observations into harmony.

Historically, the idea that the initial stage in the hydrolysis of an ester is the formation of a complex ion seems to have originated with

Kastle.[9] The idea was developed by various workers. Lapworth[10] suggested two alternative mechanisms for hydrolysis, one of which is identical to mechanism A above, while the other is related to mechanism C, differing from it in that the molecule of alcohol is assumed to be eliminated in two parts, alkoxide ion and hydrogen ion. The alkoxide ion is ejected from the (hydrated) ester molecule without prior formation of the complex cation. Stieglitz[11] advanced a mechanism which, after the first stage, becomes equivocal and may be regarded as a generalized representation covering both the possibilities B and C. Acree[12] formulated the intermediate cation in a manner which appears to leave open all three possibilities A, B, and C. Later, Lapworth[13] explained results he obtained with the acid-catalyzed hydrolysis of esters by assuming mechanism C to hold.

Various other mechanisms have been proposed, but most of them are variations of the four which have been presented here. Watson[14] has proposed a mechanism which is very similar to mechanism D above, but includes a carbonium ion as an intermediate:

$$R'\text{-}CO\text{-}OR + H^+ \rightleftharpoons R'\text{-}\overset{+}{C}\text{-}(OH)(OR) \underset{-H_2O}{\overset{+H_2O}{\rightleftharpoons}} R'\text{-}C\text{-}(OH)(\overset{+}{O}H_2)(OR).$$

Lowry[15] advanced a termolecular mechanism which requires that the approach of the proton to the ester molecule be reduced in speed until it keeps pace exactly with the approach of the water molecule. Roberts and Urey[16] advanced a mechanism which consists of bimolecular stages but makes a proton transfer the rate-determining stage. These ideas, however, are not at all in harmony with the modern idea that proton transfers between acidic and

basic oxygen are very rapid processes, and cannot in general be retarded to conform to any rate which is measurable at ordinary temperature.

In more recent work, Bell, Dowding, and Noble[17] made measurements on the kinetics of hydrolysis of ethyl acetate and methyl formate in 4 per cent concentration in solutions of hydrochloric and sulfuric acids up to 10 M and on the acidity function of concentrated hydrochloric acid solutions. Plots of log k vs. H_0 (the acidity function) were not linear, excluding a unimolecular mechanism for the hydrolysis and lending support to the bimolecular mechanism involving the slow step

$$RC\overset{+}{O}OHR' + H_2O \rightleftharpoons RC\overset{+}{O}OH_2 + R'OH$$

Bender,[18] using ethyl-, isopropyl-, and tert-butylbenzoates labeled with oxygen-18 in the carbonyl group, determined the kinetics of hydrolysis and the oxygen exchange accompanying hydrolysis. The fact that oxygen exchange occurs in every case between the carbonyl oxygen of the ester and the solvent during the process of hydrolysis strongly suggests that a true intermediate, in which the carbonyl oxygen participates in a reversible fashion, occurs during the hydrolysis. The most probable structure of this intermediate must include a contribution from the unionized hydrate of the ester, $RC(OH)_2OR$, since the intermediate must assume a symmetrical structure capable of exchange. The ratio $k_{hydrolysis}/k_{exchange}$ was determined for each ester. The similarity of this ratio for the three esters studied and the virtual identity of $k_{hydrolysis}/k_{exchange}$ for both the acid and alkaline hydrolysis of ethyl benzoate suggest a similar intermediate in all cases.

2. Dimethyl Esters of Cyclohexanedicarboxylic Acids

Although it had been prepared as a hydrogenation product of dimethyl phthalate contaminated by the trans isomer, dimethyl cis-1,2-cyclohexanedicarboxylate was not isolated and characterized until 1950, when Cope and Herrick[19] prepared it by the reduction of cis-dimethyl-Δ^4-tetrahydrophthalate as an intermediate in their study of derivatives of cyclooctatetraene. Baeyer,[20] in 1890, was the first to prepare the dimethyl ester of the trans-1,2 acid by esterification of the acid with methanol and hydrochloric acid. He was also the first to assign cis and trans configurations to these compounds.

Komppa[21] in 1933 was the first to report the preparation of the methyl esters of the 1,3-cyclohexanedicarboxylic acids, but he made no attempt to separate the cis and trans configurations. The next year Malachowski and Jankiewicsowna[22] prepared the cis-1,3 diester by treatment of the corresponding acid with diazomethane. In 1939, Skita and Rossler[23] made a study of the esters of the 1,3-cyclohexanedicarboxylic acids and prepared and characterized both the cis- and trans-1,3 diesters. They were prepared by reduction of dimethyl isophthalate in the presence of acetic acid over platinum-barium sulfate catalyst.

The cis- and trans-1,4 dimethyl esters were first prepared in 1888 by Baeyer[24] by treatment of the respective acid chlorides with methanol. In 1903 they were prepared by Knoevenagel and Bergdolt[25] by heating the dimethyl ester of trans-$\Delta^{2,5}$-dihydroterephthalic acid in a stream of carbon dioxide in the presence of palladium. Stoermer and Ladewig[26] made the trans isomer by treating a methanol solution of the trans-1,4 diacid

with ultraviolet light for a period of two weeks or more. In 1911, Zelinsky and Glinka[27] characterized the cis-1,4 diester prepared by the method of Knoevenagel. In 1938, Fichter and Holbro[28] prepared the trans-1,4 dimethyl ester by simple esterification of the acid with sulfuric acid and methanol.

CHAPTER II

THEORETICAL DISCUSSION

A. Introduction

The theoretical discussion which follows will be divided into two parts: the first deals with the various rate expressions and equations by means of which the experimental data were treated and the second involves theoretical considerations relative to the stereoisomerism of the derivatives of cyclohexane.

B. Kinetic Considerations

The acid-catalyzed hydrolysis of any ester of an organic acid can be described by the following equation:

$$RCOOR' + H_2O + H^+ \rightleftharpoons RCOOH + R'OH + H^+,$$

and the kinetics of the reaction by the following rate expression:

$$\frac{dA}{dt} = - k' A B C \qquad (1)$$

where

A = concentration of ester at time t

B = concentration of water at time t

C = concentration of acid catalyst at time t

k' = specific reaction rate constant.

To explain these kinetics, the following mechanism has been proposed:[29]

$$RCOOR' + H^+ \overset{\text{fast}}{\rightleftharpoons} RC\overset{+}{O}OHR'$$

$$H_2O + RC\overset{+}{O}OHR' \overset{\text{slow}}{\rightleftharpoons} RC\overset{+}{O}OH_2 + R'OH$$

$$RC\overset{+}{O}OH_2 \overset{\text{fast}}{\rightleftharpoons} RCOOH + H^+$$

According to the law of mass action this reaction should be bi-molecular and third order, with the rate dependent on the concentrations of ester, water, and acid catalyst. However, the hydrogen ion (acid catalyst) is not consumed in the reaction but merely catalyzes it and thus remains at the same concentration. Hence C in equation (1) becomes a constant.

In this work the concentration of the water is so great (the reactions were carried out in 70 per cent acetone in water solutions) that its change is negligible. Hence the concentration of water may be assumed to remain constant. If A_o and B_o represent the initial concentrations of ester and water, respectively, then $B_o - B = B_o$ since the concentration of water is constant. With both water and acid catalyst concentrations remaining constant, the hydrolysis reaction becomes pseudo-unimolecular[30] and equation (1) becomes

$$\frac{dA}{dt} = -(k'B_oC)\,A = -k_1 A \qquad (2)$$

where k_1 represents the rate constant determined in this work. In order to determine the specific reaction rate constant, k_1 would have to be divided by the concentrations of water and acid catalyst used, i.e.,

$$k' = \frac{k_1}{B_o\,C} \qquad (3)$$

The terms in this equation have been defined earlier.

Integration of equation (2) gives

$$\ln \frac{A_o}{A} = k_1 t \qquad (4)$$

or

$$\log A = \log A_o - \frac{k_1}{2.303} t \qquad (5)$$

which is the equation for a first order reaction. A plot of log A as a function of time gives a straight line with a slope equal to - $k_1/2.303$.

The obtaining of the rate constant for the hydrolysis of the first ester group in the dimethyl esters is complicated by the fact that hydrolysis of the second ester group becomes appreciable as the monomethyl ester accumulates in the reaction mixture. The observed kinetics then represent the sum of two processes, the hydrolysis of the dimethyl ester and the subsequent reaction of the monomethyl ester to yield the dicarboxylic acid. The situation may be represented by

$$R(COOR')_2 + H_2O \longrightarrow R(COOR')(COOH) + R'OH$$

$$R(COOR')(COOH) + H_2O \longrightarrow R(COOH)_2 + R'OH .$$

However, the rate of hydrolysis of the second ester group is so much smaller than that of the first that in the early stages of the reaction the kinetics follow, quite closely, the simple first order law. The rate constants were determined for the diesters in this work by following the concentration of the acid formed, assuming the monoester concentration to be neglible until about 30 per cent of the reaction was complete. The monomethyl ester concentration had become sufficient at this point to cause interference by hydrolysis of the second ester group.

In addition to the rate constants, the quantity most frequently determined in kinetic studies is the effect of temperature on reaction

velocity. The Arrhenius equation, written

$$k = A\, e^{-E/RT} \qquad (6)$$

where

k = specific reaction rate constant

E = activation energy

R = gas constant

T = absolute temperature

A = temperature independent constant,

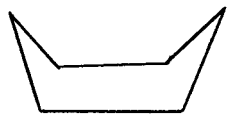
adequately represents the temperature dependence for most reactions. The activation energy may, in general, be assumed constant over a not too wide temperature interval. Taking the logarithm of the above expression, then, one obtains

$$\log k = \log A - \frac{E}{2.303\ RT} \cdot \qquad (7)$$

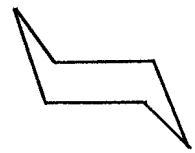
It is obvious that a plot of the logarithm of the rate constant as a function of reciprocal temperature yields a straight line graph with a slope of - E/2.303 R.

C. Stereoisomerism of Cyclohexane Derivatives

A six-membered alicyclic ring cannot assume a strain-free planar ring structure because of the tetrahedral valence structure of the carbon atom. However, two possible strainless ring forms are observed, and these are designated "boat" and "chair" forms, as indicated below.



Boat Form



Chair Form

Electron diffraction techniques have been applied to a study of the cyclohexane molecule.[31] While both strainless ring forms are equally probable, the ratio of the concentrations of the chair to the boat forms in the tautomeric equilibrium existing between the two is greater than 99-1 at room temperature. Actually, the energy difference between the two structures is only 5-10 kcal. $mole^{-1}$ in favor of the chair form.

The number of isomeric possibilities is increased when one or more of the hydrogen atoms on the cyclohexane ring is replaced by another substituent group. In this connection, a distinction must be made between the two different kinds of substituents on the cyclohexane ring. From a study of scale models, it becomes obvious that for each structure half of the substituents extend out from the cyclohexane ring, while the other half extend above and below the carbon ring. The first type of substituent is designated "equatorial" and the second "axial" ("polar").

In addition to the equilibrium which exists between the boat and chair forms, a further equilibrium is possible between the carbon atoms within these configurations. With substituted cyclohexanes, the position of the substituent may be either equatorial or axial and the individual substituents may move from one position to the other. Thus, different isomers of substituted cyclohexanes are theoretically possible. Isomers formed in this way have been designated as "inverted isomers."[32]

With disubstituted cyclohexanes in which both substituents are the same and on different carbon atoms, six separable isomers are possible. The substituent groups may be on adjacent carbon atoms or separated by one or two carbons. Within each of these groupings is the possibility of cis- and trans-isomerism. The inverted isomer possibilities for the chair and boat forms are listed in Table I.

It has been pointed out earlier that the derivatives are for all practical purposes exclusively in the "chair" form. Hence, it may be seen from the data in Table I that the substituents in the cis-1,2, trans-1,3, and cis-1,4 derivatives assume axial-equatorial positions. Experimental results indicate that substituents in the trans-1,2 derivative assume an axial-axial position, while in the cis-1,3 and trans-1,4 derivatives they assume an equatorial-equatorial position.

TABLE I

POSSIBILITIES FOR INVERTED ISOMERS FOR DISUBSTITUTED DERIVATIVES OF CYCLOHEXANE

	Chair Structure		Boat Structure	
	cis	trans	cis	trans
1,2-Derivative	ae	aa	ae	ae
		ee	aa	aa
			ee	ee
1,3-Derivative	aa	ae	ae	aa
	ee		ee	ee
			aa	ae
1,4-Derivative	ae	aa	aa	ae
		ee	ee	

The notation aa, ee, ae above indicates axial-axial, equatorial-equatorial, and axial-equatorial substituents, respectively.

CHAPTER III

EXPERIMENTAL PROCEDURE AND RESULTS

A. Temperature Control

Reactions were run in water baths maintained at 25°, 35°, 45°, and 55°. Maximum temperature deviations were ± 0.02° in the latter three cases and ± 0.04° in the first case. Temperature was controlled in each bath by a mercury expansion thermo-regulator, thyratron tube, and efficient stirring. A refrigeration unit was necessary to govern the temperature of the 25° thermostat.

B. Volumetric Apparatus

Kimble "Normax" brand glassware was used for all volumetric apparatus. The slow rate of the reactions (which required from one day to several months to be completed) and the volatility of the solvent made necessary the use of a special reaction flask which consisted of a three-inch length of 9 mm. Pyrex tubing attached to the rounded bottom of a 125-ml. Erlenmeyer flask, the mouth of which had been sealed in an oxygen-gas flame. A short piece of thick-walled rubber tubing was slipped over the narrow neck so that a glass plug could be inserted. In this manner, evaporation was reduced to a minimum; that is, the only solvent lost from a properly stoppered flask was that which escaped during the withdrawal of the samples. Sampling was accomplished by pipetting 10-ml. aliquots of the reaction mixture at appropriate time intervals. The pipettes

were heated prior to use to the temperature of the reaction mixture. They were calibrated only at 20°, however. Differences in the volume delivered from the glassware over the temperature interval would be smaller than the uncertainty as to the temperature of the solution in the pipette and the corresponding uncertainty as to the volume of the solution contained in the pipette at the reaction temperature. Calculations made from the thermal expansion coefficient for Pyrex glass indicate that the maximum error from this source would be about 0.03 per cent at 55°.

C. Preparation of Reagents

The preparation of the esters used in the various hydrolyses is described in detail in the appendices. The reaction medium in each case was a 70 volume per cent acetone-water solution. The acetone used was purified by fractionally distilling U. S. P. acetone from alkaline permanganate through an 8-ft. Vigreux column and collecting the distillate at constant head temperature.

Carbonate free alkali was assured by letting a 50 per cent solution of sodium hydroxide stand for a month, then filtering to remove the carbonate just before solution preparation. All alkali solutions were standardized by titration with Merck's primary standard potassium acid phthalate.

A stock solution of hydrochloric acid used as catalyst was prepared by diluting du Pont reagent grade concentrated hydrochloric acid with distilled water to the desired concentration. It was standardized by titra-

tion with the standard alkali solution.

For the rate experiments it was necessary to know the concentrations of the reacting species under the conditions of the reaction, and not just at room temperature. Acetone and acetone-water solutions have a considerable temperature coefficient of expansion, and if this were not taken into account when preparing the solutions, considerable error would occur. To determine this expansion, exactly 100 ml. of a 70 volume per cent acetone-water solution was placed in a 100-ml. volumetric flask at 25°. The volumetric flask had a graduated neck (similar to a burette) reading from 100.00 ml. to 110.00 ml. The level of the liquid was noted, and the flask was then placed consecutively in the 35°, 45°, and 55° thermostats, allowed to come to thermal equilibrium, and the new volume noted. The solution volume was plotted as a function of temperature as shown in Figure 1. From this graph, volume conversion factors were easily determined.

An additional correction factor must be applied to this system to account for the contraction in volume which occurs when acetone and water are mixed. To determine the contraction in volume which occurs, 70 ml. of acetone and 30 ml. of water were carefully measured into a 100-ml. volumetric flask from burettes. The contents of the flask were carefully mixed. Previously prepared 70 volume per cent acetone solution was then added from a burette to bring the volume up to 100 ml. From this a correction factor of 1.033 was calculated, i.e., 1.033 times as much acetone and water should be mixed as calculated in order to give the desired volume.

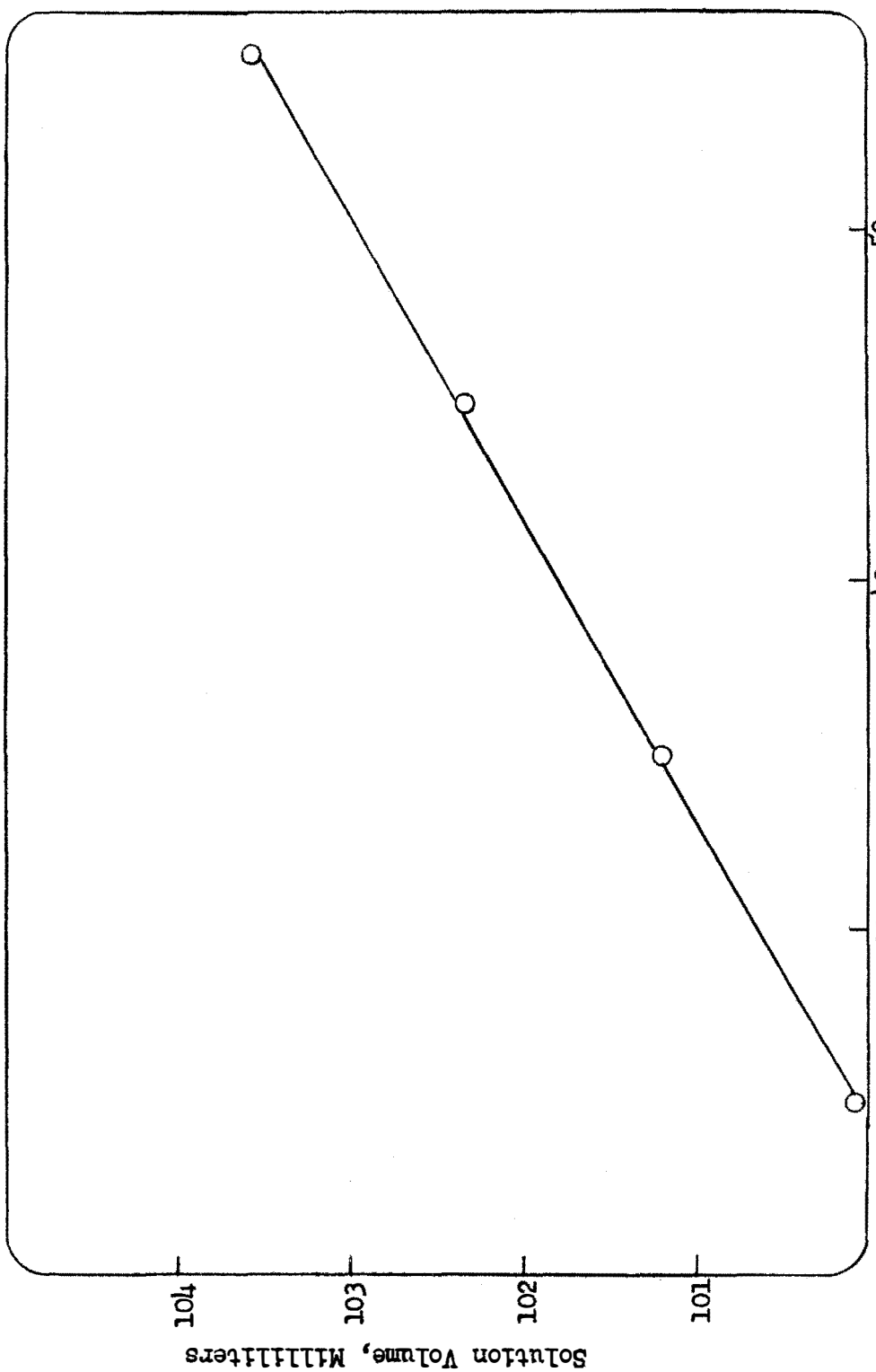


Figure 1. Thermal expansion for 70 per cent acetone.

The ester which is to be added to the reaction mixture also has a small but definite volume for which a correction must be applied. To determine this volume, a 1-g. sample of one of the diesters was added to exactly 100 ml. of 70 per cent acetone solution, thoroughly shaken, and the volume increase of the solution noted. Variation of the volume in solution of the esters over the temperature interval of concern was neglected.

From these data the starting concentrations of all the reactants can be calculated. This is illustrated in Table II. In all cases the initial concentrations of the acid and dimethyl ester were 0.100 and 0.050 M., respectively. Making the initial concentrations the same for each run greatly simplifies the subsequent calculations and negates the possibility of variations in the specific reaction rate constants due to differences in the ionic strengths of the solutions.

D. Experimental Procedure for Rate Determinations

The procedure for starting a run was the same for all the esters. Approximately 1 g. of ester was weighed into the reaction flask. To the ester in the flask were added the calculated amounts of acetone and water from burettes, and the solution was thoroughly mixed. The calculated amount of acid catalyst was added last, and the timing of the reaction was started with the addition of the acid catalyst. The reaction flask was then placed in the thermostat and allowed to come to thermal equilibrium. The first sample was removed and titrated with standard

TABLE II

PRELIMINARY CALCULATIONS FOR THE PREPARATION OF A SOLUTION TO BE 0.05 M. IN DIMETHYL ESTER AND 0.10 M. IN ACID AT 55°C

1. Solution temperature = 25°
2. Volume in solution of the dimethyl ester = 0.70 ml./g.
3. Volume conversion factor for 70 per cent acetone (55° to 25°) = 0.966
4. Grams of dimethyl ester in 100 ml. of 0.05 M. solution = 1.001
5. Grams of dimethyl ester used in this run = 1.0240
6. Volume of solution required at 55° to give a 0.05 M. solution of

   diester - $1.001/100 = 1.0240/x$

   $x = 102.30$ ml.
7. Volume of 70 per cent acetone solution required at 55°

   $102.30 - 0.70 = 101.60$ ml.
8. Volume of 70 per cent acetone solution required at 25°

   $(101.60)(0.966) = 98.15$ ml.
9. Volume of acetone required at 25°

   $(98.15)(0.70)(1.033) = 70.98$ ml.
10. Volume of water and acid required at 25°

    $(98.15)(0.30)(1.033) = 30.43$ ml.

    Volume of 0.5655 M. hydrochloric acid required at 25° to give a 0.10 M. acid solution at 55°

    $0.5655\ x = (102.30)(0.10)$

    $x = 18.90$ ml.

    Volume of water required

    $30.43 - 18.09 = 12.34$ ml.

alkali about fifteen minutes after the reaction flask was placed in the thermostat.

The reactions were followed by pipetting 10-ml. samples from the reaction mixture and discharging them into 125-ml. Erlenmeyer flasks. Phenolphthalein* indicator was added. The time of the sample was arbitrarily taken as the time when the pipetting of the sample was initiated. The amount of acid formed was determined by titration with standard carbonate free alkali.

The pipettes were cleaned between uses by wiping them with a tissue saturated with acetone, then rinsing three times by pulling acetone through them with the aid of an aspirator.

E. Treatment of Data

The kinetic expression for a simple first order reaction is shown in the previous chapter (equation 5) to be:

$$\log A = \log A_o - \frac{k_1}{2.303} t$$

where

A = concentration of diester at time $t = t$

A_o = concentration of diester at time $t = 0$

k_1 = reaction rate constant.

It is evident that a graph in which log A is plotted as a function of t should yield a straight line of slope equal to the rate constant

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*The indicator was composed of 1.0 g. of phenolphthalein dissolved in 99.0 g. of 95 per cent ethanol.

divided by 2.303, i.e., the rate constant is calculated by multiplying the slope of the straight line by 2.303. This method of calculation was used for all of the diesters as illustrated by Table III and Figure 2. All concentrations are listed in terms of moles per liter, and all times in minutes.

The rate constants obtained in this research are tabulated in Table IV. The units of k_1 in each case are minutes^{-1}. The activation energies listed were obtained from a least squares treatment of the slopes of the various temperature coefficient curves shown in Figure 3. All rate constants represent a compilation of data gained from at least two, and in many cases three, independent experimental determinations.

TABLE III

DATA AND CALCULATIONS FOR THE DIMETHYL ESTER OF THE
cis-1,3-CYCLOHEXANEDICARBOXYLIC ACID AT 55°C

Sample	Time (minutes)	Alkali Required[a] (ml.)	A Concentration of ester (M.)	- log A
1	17	30.31	0.04922	1.3078
2	33	30.68	0.04799	1.3189
3	52	31.13	0.04649	1.3327
4	72	31.78	0.04433	1.3533
5	98	32.52	0.04187	1.3781
6	133	33.17	0.03971	1.4011
7	161	33.80	0.03762	1.4246
8	185	34.37	0.03572	1.4471

[a]Normality of alkali = 0.03325.

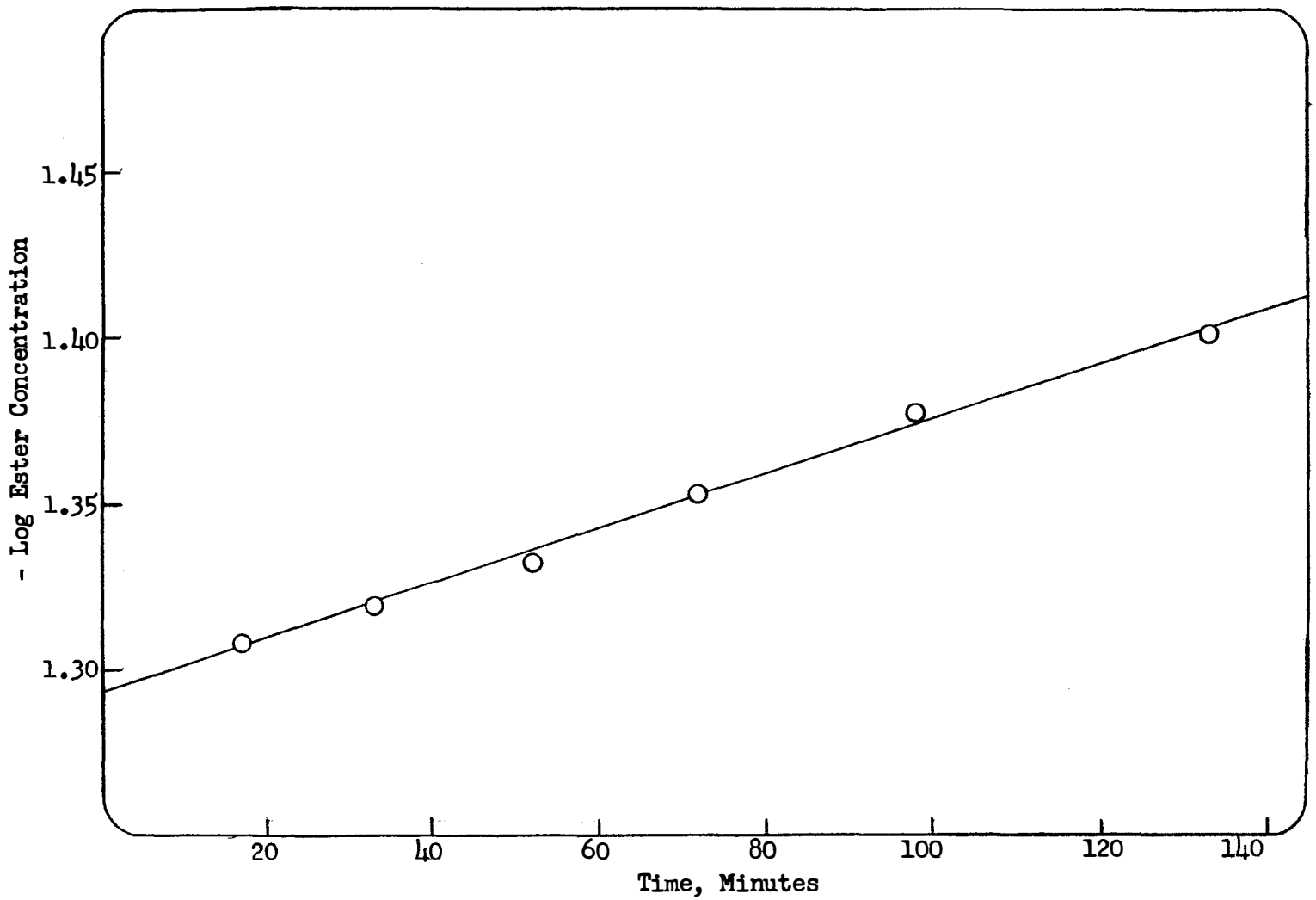

Figure 2. Kinetics plot for <u>cis</u>-1,3 diester at 55°.

TABLE IV

RATE CONSTANTS AND ACTIVATION ENERGIES FOR THE DIMETHYL ESTERS OF THE CYCLOHEXANEDICARBOXYLIC ACIDS

Ester	Rate Constants x 10^3 in Minutes^{-1}				E_A (cal. mole^{-1})
	25°	35°	45°	55°	
cis-1,2	0.00302	0.00962	0.0288	0.0746	2.09×10^4
trans-1,2	0.00332	0.00990	0.0350	0.0786	2.10×10^4
cis-1,3	0.137	0.336	0.822	1.79	1.68×10^4
trans-1,3	0.0695	0.180	0.440	1.04	1.76×10^4
cis-1,4	0.0820	0.194	0.534	1.28	1.81×10^4
trans-1,4	0.164	0.371	0.867	1.88	1.59×10^4

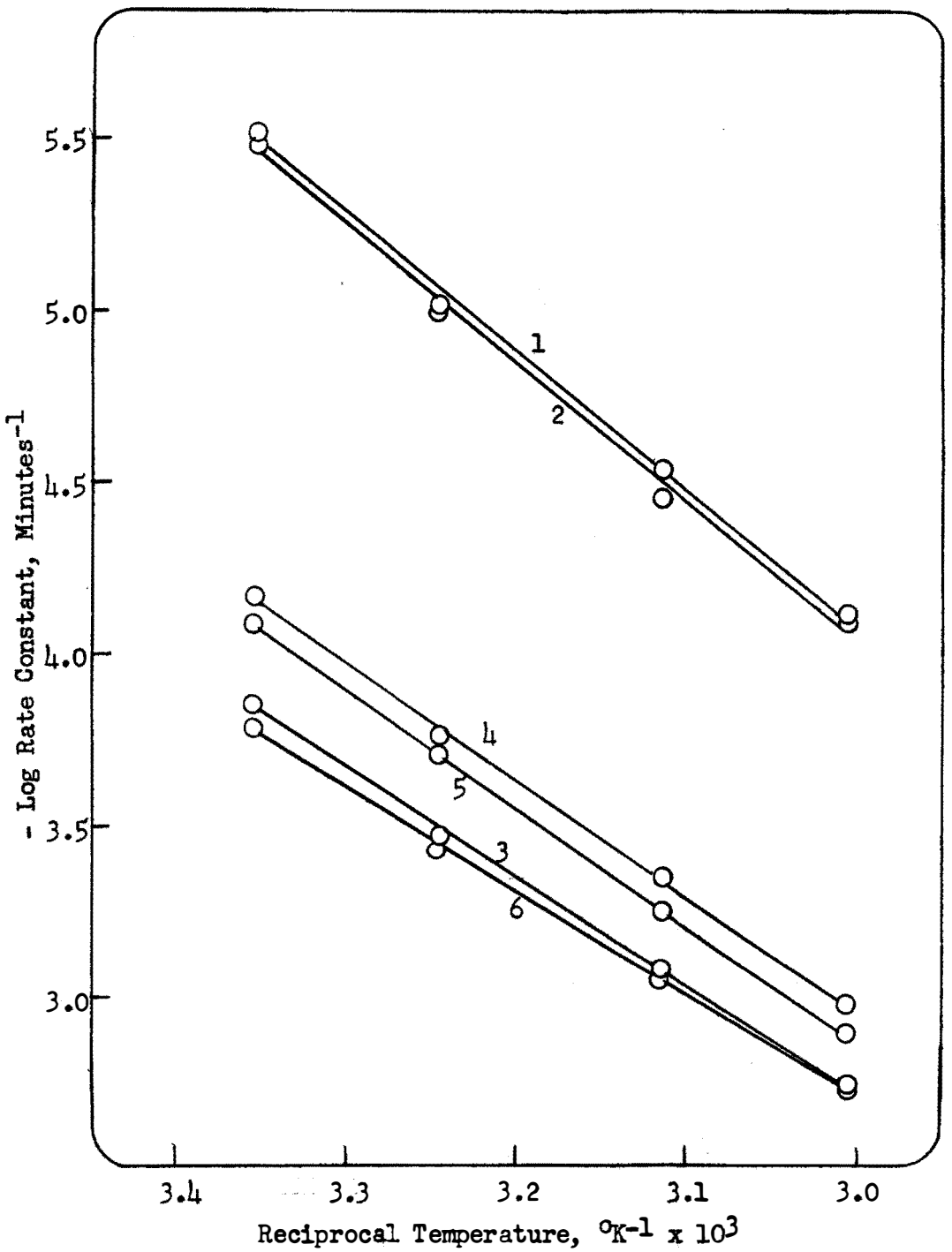

Figure 3. Rate constant-reciprocal temperature plots for the dimethyl esters of the cyclohexanedicarboxylic acids. (Esters are numbered in the order in which they appear in Table IV.)

CHAPTER IV

DISCUSSION OF RESULTS

A. Previous Considerations

Smith and Byrne[33] studied the kinetics of esterification of the cyclohexanedicarboxylic acids in dry methanol solutions with hydrochloric acid as catalyst. The rates of esterification of the 1,2-acids were slower than for the 1,3- and 1,4-acids. For the esterification of the diacids and monomethyl esters, the cis-1,3 and trans-1,4 configurations gave similar rate constants, which differed from those for the trans-1,3 and cis-1,4 forms. For the 1,2-acids, the cis isomer of the cyclohexanedicarboxylic acid esterified more rapidly but for the monomethyl esters the rate constant is greater for the trans form. These results were explained by assuming that the cyclohexane ring is almost entirely in the chair form, where two conformations of the chair structure are possible, axial-axial or equatorial-equatorial. The one yielding the greatest separation of substituents is predominant.

Smith and Fort[34] investigated the kinetics of the base-catalyzed hydrolysis of the monomethyl and dimethyl esters of the cyclohexanedicarboxylic acids in 85 per cent methanol-water solutions. The results obtained by them correspond favorably with those obtained by Smith and Byrne[33] for the 1,3- and 1,4-acids. The ratios of the rates of hydrolysis of the dimethyl esters compared to the monomethyl esters were found to vary from 6.3 for the trans-1,4 isomers to 104.6 for the esters of the

cis-1,2 acid. On the basis of the first and second rate constants determined for the esters, the separation of the two ester (or ester and acid) groups decreases in the following order: trans-1,4 > cis-1,3 > cis-1,4 > trans-1,3 > trans-1,2 > cis-1,2. This corresponds to the expected separation as shown by scale models. The fundamental difference in the acid catalyzed esterification and the base catalyzed hydrolysis lies in the fact that with esterification the monomethyl ester is in the form of an uncharged molecule and exerts no great influence on the approach of the positive charged ion in the reaction, while with hydrolysis the partially saponified ion is negatively charged and repels the attack of the negatively charged base. Steric hindrance accounts for the fact that the rate constants for hydrolysis of both the first and second ester groups are greater for the trans-1,2 than for the cis-1,2 forms.

Cavell, Chapman, and Johnson[35] have reported preliminary results of a study of the rates of base-catalyzed hydrolysis of the methyl esters of the cyclohexanedicarboxylic acids. Their work is similar to that of Smith and Fort. However, they used dioxane-water solvent (3:1 by volume) for their reactions. Results reported are in good general agreement with those of Smith and Fort.

Smith and Hunt[36] studied the rates of esterification of the cyclohexanedicarboxylic acids and their monomethyl esters with diphenyldiazomethane in absolute ethanol. The expected similarity of reaction for the diacids and the monomethyl esters of the cis-1,3 and the trans-1,4 configurations was obtained. Different from these but again similar were

the rates of reaction for the trans-1,3 and the cis-1,4 isomers. These results led to the conclusion that the equatorial position was the more favorable position for reaction.

The trans-1,2 acids were found to react more rapidly than any of the other isomers. Possible ring formation and polar effects were proposed to explain this increase in reaction rate. The rates for the cis-1,2 acids compared favorably with the cis-1,3 and trans-1,4 acids. Again, polar effects were proposed to explain the increase in reaction rate.

The kinetics of the acid catalyzed hydrolysis of the dimethyl esters of the cyclohexanedicarboxylic acids were studied in this work. This provides an interesting comparison with the base catalyzed hydrolysis of these same esters and the acid catalyzed esterification of the corresponding acids. Actually, a complete discussion of the results of this work demands data for the monomethyl esters of the cyclohexanedicarboxylic acids. This work is in progress in this laboratory at the present time.

B. The Diesters of the 1,2-Cyclohexanedicarboxylic Acids

Consider the 1,2-dimethyl esters, the trans in the equatorial-equatorial and the cis in the axial-equatorial conformation. The trans isomer reacts only about 1.1 times as fast as does the cis. This is in contrast to the behavior observed by Smith and Fort[34] for these esters. In the saponification reaction, the trans isomer reacts about twice as fast as does the cis, which indicates that one of the ester groups in the cis structure is essentially nonreacting. This difference was ex-

plained by the fact that the carbon on the axial carboxyl group of the cis isomer is so highly shielded by the ring, the other ester group, and the methoxy group attached to it that it is made almost invulnerable to the attack of a hydroxyl ion. Both equatorial carboxyls in the trans structure, on the other hand, are exposed and easily open to attack as is the carbon in the equatorial carboxyl group of the cis structure.

Smith and Byrne[33] found that the trans-1,2 monomethyl ester esterified about 1.4 times as rapidly as did the cis isomer. The slower rate observed for the cis isomer is explainable on the basis of the steric hindrance between the carboxyl and ester groups in axial and equatorial conformations.

As was mentioned above, it was found in this work that the cis isomer reacts but little slower than the trans configuration. Here the attacking species in the rate-determining step is a water molecule rather than the somewhat larger alcohol molecule involved in esterification. Hence, steric requirements would not be expected to create as large a difference in reaction rates for hydrolysis between the cis and trans configurations as was observed in esterification.

C. The Diesters of the 1,3-Cyclohexanedicarboxylic Acids

The cis configuration with both ester groups in equatorial positions shows no possibility of steric hindrance. Completely free rotation of both carboxyl groups is possible (no possibility of formation of any kind of fused ring) and it would be expected to be among the fastest reacting of the compounds studied, which is found experimentally to be the case.

The trans isomer, on the other hand, with one ester group in the equatorial and one in the axial position, reacts only about one-half as fast as does the cis. Here, again, the equatorial group present is free and its reaction should be uninhibited. The reaction of the axial group is slowed by two factors, however. In the first place, the carbon which is to be attacked by the water molecule is partly shielded by the ring and is not in as vulnerable a position as is that of the cis isomer. Too, examination of scale models shows that a six-membered ring may be formed by a hydrogen bond between the alpha hydrogen of the equatorial ester group and the carboxyl oxygen of the axial group. Both of these effects would slow its reaction.

Examination of models of the axial-axial cis-1,3 structure shows considerable shielding of both carboxyl groups. This structure could then not account for the very rapid reaction of the cis-1,3 isomer.

These, essentially, are the same arguments used by Smith and Byrne[33] to explain similar results obtained by them for the esterification of the cis- and trans-1,3 diacids and monomethyl esters, and by Smith and Fort[34] to explain similar results obtained by them for the saponification of these esters.

D. The Diesters of the 1,4-Cyclohexanedicarboxylic Acids

The trans-1,4 equatorial-equatorial structure, like the cis-1,3, has both ester groups in exposed positions vulnerable to attack, has no possibility of fused ring formation, and is among the fastest reacting of all the esters.

The cis-1,4 diester reacts about one-half as fast as does the trans. Again, the one axial ester group accounts for the difference. There is no possibility of fused ring formation here, but the puckering of the cyclohexane ring sterically blocks the carbon on the axial ester group which is to be attacked even more than it does in the case of the trans-1,3 diester. This accounts for the reduced reaction rate.

The trans-1,4 axial-axial structure shows considerable shielding of both carboxyl groups and would be expected to react slower than the cis isomer which has one exposed equatorial group. This for all practical purposes eliminates the axial structure from consideration. These results are completely in line with those obtained by Smith and Byrne[33] and Smith and Fort.[34]

E. Comparison of the Reaction Rates of the 1,2-, 1,3-, and 1,4-Diesters

For both the cis- and trans-1,2 diesters, the reaction rates are considerably lower than the corresponding 1,3 and 1,4 compounds. This is the familiar ortho effect and is, simply, the result of the shielding of one carboxyl group by the other.

The reaction rates of the trans-1,3 and cis-1,4 diesters are almost the same. This is the obvious result of their similar axial-equatorial structures.

The reaction rates of the cis-1,3 and trans-1,4 diesters are very comparable and are the fastest of the esters studied.

CHAPTER V

SUMMARY

The dimethyl esters of the isomeric 1,2-, 1,3-, and 1,4-cyclohexanedicarboxylic acids have been prepared and the rates of their acid catalyzed hydrolyses in 70 per cent acetone have been determined. All hydrolysis reactions were run at four temperatures, 25°, 35°, 45°, and 55°. The rate constants for the hydrolyses at each of these temperatures, along with the activation energies for the reactions, have been tabulated in Table IV.

The rates of hydrolysis of the cis-1,3 and trans-1,4 diesters were found to be almost identical. Similarly, the reaction rates of the trans-1,3 and cis-1,4 diesters were found to be nearly the same. The cis- and trans-1,2 diesters reacted at much slower rates.

The relative reaction rates which were determined for the various diesters were taken to be indicative of the predominant inverted isomeric possibilities of the compounds studied. An ester with an exposed carbomethoxyl group would be expected to react at a faster rate than a similar compound whose carbomethoxyl group was not so exposed.

Using this idea, and with the aid of scale models of the various compounds, the results obtained in this work were explained by assuming that in the conformational equilibrium which exists with all the cyclohexane derivatives, the predominant conformation with the cis-1,2, trans-1,3, and cis-1,4 diesters was the axial-equatorial, while with the cis-1,3, trans-1,4, and trans-1,2 diesters the equatorial-equatorial con-

formation predominated. These similar inverted isomeric states explain the similar reaction rates noted.

APPENDICES

APPENDIX I

PREPARATION OF THE DIMETHYL ESTERS OF THE 1,2-CYCLOHEXANEDICARBOXYLIC ACIDS

A. Preparation of cis-1,2-Cyclohexanedicarboxylic Acid

$$1,2\text{-}C_6H_4(COOH)_2 + 3H_2 \longrightarrow \underline{cis}\text{-} + \underline{trans}\text{-}1,2\text{-}C_6H_{10}(COOH)_2$$

Fifty grams of Eastman White Label phthalic acid was reduced in a Parr hydrogenator in the presence of 75 ml. of glacial acetic acid over 0.5 g. of platinum oxide catalyst. When the theoretical amount of hydrogen had been absorbed, the reaction mixture was transferred to a beaker, heated to boiling, and filtered to remove the catalyst. On cooling the filtrate to room temperature, the cis-1,2 acid precipitated; this was filtered and recrystallized once from water. Yield -- 45 g. Melting point -- 191°C. The highest literature melting point is 191.5-192.5°.[37]

B. Preparation of trans-1,2-Cyclohexanedicarboxylic Acid

$$\underline{cis}\text{-}1,2\text{-}C_6H_{10}(COOH)_2 \longrightarrow \underline{trans}\text{-}1,2\text{-}C_6H_{10}(COOH)_2$$

cis-1,2-Cyclohexanedicarboxylic acid (46.2 g.) was refluxed for twenty-four hours with 170 ml. of sulfuric acid (sp. g. 1.84) and 100 ml. of distilled water. The reaction mixture was then transferred to a beaker and cooled overnight in the refrigerator. The crystals which formed were collected on a fritted glass filter of coarse porosity and the filtrate was discarded. The precipitate was washed three times with cold water and was twice recrystallized from water after treatment with Norite decolorizing charcoal. The crystals were then refluxed four times for

ten-minute periods with 75-ml. portions of xylene; at the end of each period the xylene was decanted and discarded. The acid was then washed with cyclohexane and recrystallized once more from water, then air-dried. Melting point -- 227.5-229.4°. Yield -- 33.6 g. The highest literature melting point is 227.0-229.0°.[37]

C. Preparation of the Dimethyl Esters of *cis*- and *trans*-1,2-Cyclohexanedicarboxylic Acids

cis- or *trans*-1,2-$C_6H_{10}(COOH)_2$ + $2CH_3OH$ ⟶

cis- or *trans*-1,2-$C_6H_{10}(COOCH_3)_2$ + $2H_2O$

Thirty grams of *cis*- or *trans*-1,2-cyclohexanedicarboxylic acid was refluxed for four hours with 190 ml. of methanol and 2.3 ml. of sulfuric acid (sp. g. 1.84). The mixture was boiled to expel the excess methanol and then treated with a dilute sodium carbonate solution. This was extracted three times with ether. The ether was evaporated on the steam cone and the oily residue was dried in an evacuated desiccator over calcium chloride.

The dimethyl ester of the *cis* acid was purified further by fractionation through a 2-ft. Vigreux column. Ten milliliters of the middle fraction which distilled at 124.4° under a pressure of 12 mm. of mercury was chosen for the kinetic studies.

The dimethyl ester of the *trans* acid is a solid with a melting point a little above room temperature. It was placed in the coldest part of the refrigerator and allowed to stand for several days. The

crop of oily crystals which was obtained was purified by three recrystallizations from a 50 per cent methanol-water solution. The purified ester was dried in an evacuated desiccator over anhydrous calcium chloride. Yield -- 10 g. Melting point -- 30.2-30.8°. The highest listed literature melting point is 33°.[20]

APPENDIX II

PREPARATION OF THE DIMETHYL ESTERS OF THE 1,3-CYCLOHEXANE-DICARBOXYLIC ACIDS

A. Preparation of the cis-1,3-Cyclohexanedicarboxylic Acid

The cis-1,3-cyclohexanedicarboxylic acid used was prepared by P. P. Hunt.[38]

B. Preparation of the Dimethyl Ester of cis-1,3-Cyclohexane-dicarboxylic Acid

$$\text{cis-1,3-}C_6H_{10}(COOH)_2 + 2KOH \longrightarrow \text{cis-1,3-}C_6H_{10}(COOK)_2 + 2H_2O$$

$$\text{cis-1,3-}C_6H_{10}(COOK)_2 + 2AgNO_3 \longrightarrow \text{cis-1,3-}C_6H_{10}(COOAg)_2 + 2KNO_3$$

$$\text{cis-1,3-}C_6H_{10}(COOAg)_2 + 2CH_3I \longrightarrow \text{cis-1,3-}C_6H_{10}(COOCH_3)_2 + 2AgI$$

Thirty grams of pure cis-1,3 acid was mixed with a little water and neutralized to the phenolphthalein end point with concentrated potassium hydroxide solution. To this solution, while still warm, was added 60 g. of silver nitrate. After standing for two hours in the refrigerator, the precipitated silver salt was filtered and dried over calcium sulfate in an evacuated desiccator. The salt was then suspended in 400 ml. of absolute ether, and to it was added 80 g. of methyl iodide dissolved in 100 ml. of ether. The mixture was warmed on a water bath for four hours, and the silver iodide which precipitated was removed by filtration. The ethereal solution was extracted three times with a

2 per cent sodium carbonate solution and once with water. The ether was evaporated and the resulting oil was purified by fractional distillation in a 2-ft. Vigreux column at 10 mm. of mercury pressure. The sample used for kinetic measurements distilled at 130.6°.

C. Preparation of the Dimethyl Ester of trans-1,3-Cyclohexanedicarboxylic Acid

The dimethyl ester of trans-1,3-cyclohexanedicarboxylic acid was prepared by P. P. Hunt[38] by reduction of the dimethyl ester of isophthalic acid in a Parr hydrogenator and separation of the cis- and trans-dimethyl-1,3-cyclohexanedicarboxylates by fractionation through a 12-ft. Vigreux column.

APPENDIX III

PREPARATION OF THE DIMETHYL ESTERS OF THE 1,4-CYCLOHEXANE-DICARBOXYLIC ACIDS

A. Preparation of *cis*- and *trans*-1,4-Cyclohexanedicarboxylic Acids

$$1,4\text{-}C_6H_4(COOH)_2 + 3H_2 \longrightarrow \underline{cis}\text{-} + \underline{trans}\text{-}1,4\text{-}C_6H_{10}(COOH)_2$$

Two separate 50 g. samples of Eastman White Label terephthalic acid were reduced in a Parr hydrogenator in the presence of 75 ml. of glacial acetic acid over 1.0 g. of platinum oxide catalyst. After the theoretical amount of hydrogen had been absorbed, the catalyst was separated by filtration and the acetic acid solvent was evaporated *in vacuo*. The solid which formed was washed with cold water. After the residue was recrystallized twice from water, the pure *trans* acid was obtained. Yield -- 44 g. Melting point -- 312-313°. The highest literature melting point is 312-313°.[22]

The remaining solutions containing the mixed acids were combined in a beaker and the contents were evaporated on the steam cone until a light scum remained. The impure *cis* acid was dissolved in boiling water, and the mixture was quickly filtered through a preheated funnel. The filtrate was again transferred to a beaker, heated to boiling, and allowed to cool slowly to 50°. The precipitate was filtered and air-dried. This same process was repeated twice. Yield -- 15 g. Melting point -- 170-172°. The highest literature melting point is 171.3-172.3°.[33]

B. Preparation of the Dimethyl Ester of cis-1,4-Cyclohexanedicarboxylic Acid

$$\underline{cis}\text{-}1,4\text{-}C_6H_{10}(COOH)_2 + 2CH_3OH \longrightarrow \underline{cis}\text{-}1,4\text{-}C_6H_{10}(COOCH_3)_2 + 2H_2O$$

Thirty grams of cis-1,4-cyclohexanedicarboxylic acid was refluxed for four hours with 190 ml. of methanol and 2.3 ml. of sulfuric acid (sp. g. 1.84). The excess methanol was evaporated on the steam cone, and the residue was extracted twice with a cold, dilute sodium carbonate solution. The resulting oil was transferred to a 2-ft. Vigreux column and fractionated at 10 mm. of mercury pressure. Ten milliliters of the middle fraction, boiling at 131.0°, was chosen for the kinetic studies.

C. Preparation of the Dimethyl Ester of trans-1,4-Cyclohexanedicarboxylic Acid

$$\underline{trans}\text{-}1,4\text{-}C_6H_{10}(COOH)_2 + 2CH_3OH \longrightarrow \underline{trans}\text{-}1,4\text{-}C_6H_{10}(COOCH_3)_2 + 2H_2O$$

This compound was prepared just as was the corresponding cis ester, except that it is a solid and was purified by recrystallization rather than fractionation. The excess methanol was evaporated from the esterification product which was then cooled, filtered and washed, first with a cold sodium carbonate solution and then with water. The ester was recrystallized twice from a methanol-water solution. Yield -- 23 g. Melting point -- 69°. The literature melting point is 71°.[28]

BIBLIOGRAPHY

BIBLIOGRAPHY

1. J. N. E. Day and C. K. Ingold, Trans. Faraday Soc., 37, 686 (1941).

2. B. Holmberg, Ber., 45, 2997 (1912).

3. S. C. Datta, J. N. E. Day, and C. K. Ingold, J. Chem. Soc., 1939, 838.

4. E. H. Ingold and C. K. Ingold, J. Chem. Soc., 1932, 758.

5. H. B. Friedman and G. V. Elmore, J. Am. Chem. Soc., 63, 864 (1941).

6. K. F. Bonhoeffer, Trans. Faraday Soc., 34, 252 (1938).

7. O. Reitz, Z. Elektrochem., 44, 72 (1938).

8. J. C. Hornel and J. A. V. Butler, J. Chem. Soc., 1936, 1361; Schwarz, Z. Elektrochem., 40, 474 (1934).

9. J. H. Kastle, P. Murrill, and J. C. Frazer, Amer. Chem. J., 19, 894 (1897).

10. A. Lapworth in J. W. Mellor, "Chemical Statics and Dynamics," Longmans, Green, and Co., New York, N. Y., 1904, p. 289.

11. J. Stieglitz, Amer. Chem. J., 39, 166 (1908).

12. S. F. Acree, Amer. Chem. J., 38, 297 (1907).

13. A. Lapworth and J. Ferns, J. Chem. Soc., 101, 273 (1912).

14. H. B. Watson, "Modern Theories of Organic Chemistry," 2nd ed., Oxford University Press, London, 1941, p. 130.

15. T. M. Lowry, J. Chem. Soc., 1925, 1381; J. Chem. Soc., 1927, 2558; Trans. Faraday Soc., 24, 546 (1928).

16. I. Roberts and H. C. Urey, J. Am. Chem. Soc., 61, 2584 (1939).

17. R. B. Bell, A. L. Dowding, and J. A. Noble, J. Chem. Soc., 1955, 3106.

18. M. Bender, J. Am. Chem. Soc., 73, 1626 (1951).

19. A. C. Cope and E. C. Herrick, J. Am. Chem. Soc., 72, 983 (1950).

20. A. Baeyer, Ann., 258, 217 (1890).

21. G. Komppa, Ann. Acad. Sci. Fennicae, 37A, No. 6, 10 (1933).

22. R. Malachowski and J. Jankiewicsowna, Ber., 67B, 1783 (1934).

23. A. Skita and R. Rossler, Ber., 72B, 265 (1939).

24. A. Baeyer, Ann., 245, 173 (1888).

25. E. Knoevenagel and B. Bergdolt, Ber., 36, 2858 (1903).

26. R. Stoermer and H. Ladewig, Ber., 47, 1804 (1914).

27. N. Zelinsky and N. Glinka, Ber., 44, 2310 (1911).

28. F. Fichter and T. Holbro, Helv. Chim. Acta, 21, 141 (1938).

29. A. A. Frost and R. C. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 265.

30. C. F. Prutton and S. H. Maron, "Fundamental Principles of Physioal Chemistry," Revised edition, The MacMillan Company, New York, N. Y., 1951, p. 627.

31. H. Viervoll, Acta Chem. Scand., 1, 120 (1947).

32. K. Kojima, Kagaku, 21, 362 (1951).

33. H. A. Smith and F. P. Byrne, J. Am. Chem. Soc., 72, 4406 (1950).

34. H. A. Smith and T. Fort, Jr., J. Am. Chem. Soc., 78, 4000 (1956).

35. E. A. S. Cavell, N. B. Chapman, and M. D. Johnson, Chem. and Ind., 376 (1956).

36. H. A. Smith and P. P. Hunt, J. Am. Chem. Soc., 81, 590 (1959).

37. R. P. Linstead, S. B. Davis, and R. R. Whetstone, J. Am. Chem. Soc., 64, 2009 (1942).

38. P. P. Hunt, M. S. Thesis, The University of Tennessee, Knoxville, Tennessee, 1958.

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