

A STUDY OF THE CONDENSATIONS OF ALDEHYDES
WITH AROMATIC RINGS AND WITH ALCOHOLS
BY MEANS OF AN AZEOTROPIC METHOD

By

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PART I

A STUDY OF THE CONDENSATION OF ALDEHYDES WITH AROMATIC RINGS

INTRODUCTION

The reaction of aldehydes with aromatic compounds to form substituted di- or triphenylmethanes have been known for many years. In 1872 and 1873 Adolf Baeyer reported that formaldehyde, chloral, or bromal could be condensed with aromatic compounds such as benzene, toluene, mesitylene, diphenyl, chlorobenzene, and bromobenzene in the presence of concentrated sulfuric acid and glacial acetic acid.^{1,2} The condensation of acetaldehyde and benzene, chloral and thymol, chloral and phenol, formaldehyde and anisole were also described.³ The products were well-defined crystalline solids whose compositions indicated that they were formed by the elimination of a molecule of water from one molecule of the aldehyde and two molecules of the aromatic compound. Thus formaldehyde and benzene yielded diphenyl methane; chloral and toluene gave 1-trichloro-2,2-ditolylethane. A generalized equation may be written for the reaction:



R- may be one of a wide variety of aliphatic or aromatic groups and Z- may be a hydrogen or halogen atom or an alkyl, aryl, alkoxy, hydroxy, amino, or substituted amino group. Disubstituted aromatic compounds have also been used.

The reaction is generally carried out by letting the

reactants stand at room temperature in the presence of sulfuric acid or other catalyst. In some cases agitation and heat are necessary. Due to the pioneering work of Baeyer the reaction now bears his name.

It is of interest to note that in this early research of Baeyer, published seventy-five years ago, the preparation of 1-trichloro-2,2-bis(p-chlorophenyl)ethane was described. Many years were to pass before the high insecticidal activity of this substance, now known as "DDT", was discovered.

Soon after the first publication by Baeyer many other investigators as well as Baeyer himself explored further the scope of this condensation reaction. Thus Goldschmiedt in 1873 described the sulfuric acid catalyzed reactions of chloral and bromal with benzene to give substituted diphenyl ethanes⁴ and in 1878 it was reported that acetaldehyde would condense with phenol to give the expected dihydroxydiphenylethane.⁵

To indicate further the scope of the Baeyer Reaction, many more examples can be cited from the later literature. The following paragraphs will summarize some of the typical applications.

The condensation of paraldehyde and thymol has been studied by Steiner.⁶ Otto Fischer, using zinc chloride as a catalyst, condensed salicylaldehyde, vanillin, p-hydroxybenzaldehyde, and p-nitrobenzaldehyde with dimethylaniline and obtained the expected triphenylmethanes in all cases.^{7,8} Boessneck described the zinc chloride catalyzed condensation

of p-dimethylaminobenzaldehyde with dimethylaniline yielding crystal violet.⁹ In 1886 the condensation of p-chlorobenzaldehyde with dimethylaniline and diethylaniline was described.¹⁰ In the same year, it was reported that benzaldehyde could be condensed with even such unreactive aromatics as benzene and toluene by carrying out the reactions in a sealed tube at temperatures ranging from 250-400°.¹¹

In 1888 Tschacher observed that a nitro group substituted meta to the carbonyl group of benzaldehyde increased the reactivity of the aldehyde to such an extent that it would condense quite readily with benzene and toluene in an open vessel in the presence of concentrated sulfuric acid.¹² That the p-nitro substituted benzaldehyde was also quite active, was demonstrated by Baeyer and Loehr who reacted this aldehyde with benzene in the presence of concentrated sulfuric acid.¹³ The condensations of benzaldehyde with phenol and thymol were described in 1889.¹⁴ Hanzlick and Bianchi have condensed p-methylbenzaldehyde with dimethylaniline in the presence of zinc chloride to give the expected substituted triphenylmethane.¹⁵

Baeyer in 1902 described the condensation of benzaldehyde and p-methoxybenzaldehyde with anisole in glacial acetic acid using concentrated sulfuric acid as a catalyst.¹⁶ The expected products were obtained in each case. In the same year Feuerstein described the condensation of benzaldehyde with the disubstituted aromatic compounds: para- and ortho-methoxy toluene, and p-hydroxy toluene.¹⁷ The expected tri-

phenyl methanes were obtained in all three of these reactions.

In 1906 it was reported that *o*-, *m*-, and *p*-methylbenzaldehydes would condense with dimethylaniline in the presence of aqueous hydrochloric acid and zinc chloride.¹⁸ The *o*-, *m*-, and *p*-chloro substituted benzaldehydes were also successfully condensed with dimethylaniline under the same conditions. A series of substituted malachite greens have been prepared by the zinc chloride catalyzed condensations of anisaldehyde, *p*-ethoxybenzaldehyde, and piperonal with dimethylaniline.¹⁹

Frankforter found that aluminum chloride could be used as an effective catalyst in condensing chloral with phenol, anisole, and phenetole.²⁰ Later Harris and Frankforter extended these studies and found that chloral could be satisfactorily condensed with benzene, toluene, and *p*-cresyl methyl ether using the same catalyst.²¹ Bromal was also condensed with these aromatic compounds. Baekland has condensed butyraldehyde and phenol to give 1,1-bis(*p*-hydroxyphenyl)butane.²² Butyraldehyde has also been condensed with dimethylaniline in the presence of aqueous hydrochloric acid to yield 1,1-bis(*p*-dimethylaminophenyl)butane.²³

Many ketones have also been found to undergo condensation in a manner analogous to the Baeyer aldehyde condensations. Thus von Braun found that cyclohexanone reacted with aniline in the presence of concentrated hydrochloric acid to give 1,1-bis(*p*-aminophenyl)cyclohexane.²⁴ As a by-product there was also obtained 1-*p*-aminophenylcyclohexene. Acetone also reacted with aniline under the same conditions to give

2,2-bis(aminophenyl)propane. Some of the corresponding unsaturated amine was again found. Acetophenone, when reacted with dimethylaniline under the influence of zinc chloride, gave a 20% yield of crude 1,1-bis(dimethylaminophenyl)-1-phenylethane. Again some of the unsaturated compound, formed by splitting out of a molecule of amine, was found.²⁵ The reaction of acetophenone with phenol was quite analogous to the dimethylaniline reaction yielding 10% of 1,1-bis(hydroxyphenyl)-1-phenylethane and also some of the unsaturated compound 1-hydroxyphenyl-1-phenylethylene.²⁶

The synthetic value of most of the Baeyer reaction procedures given in the literature is difficult to evaluate due to the failure of the investigators to state their yields. The products obtained on condensing chloral with chlorobenzene have, however, been investigated in some detail because of their remarkable insecticidal activity.²⁷ The crude mixture of reaction products was found to contain upwards of 70% of 1-trichloro-2,2-bis(p-chlorophenyl)ethane, which proved to be the most potent insecticidal component. The principal impurity was the isomeric 1-trichloro-2-o-chlorophenyl-2-p-chlorophenylethane. Much smaller amounts of twelve other organic substances were found and their presence explained on the basis of side reactions and reactant impurities.

Baeyer and other early investigators did not indicate the exact structure of their products since they did not know if the condensation involved the ortho, meta, or para

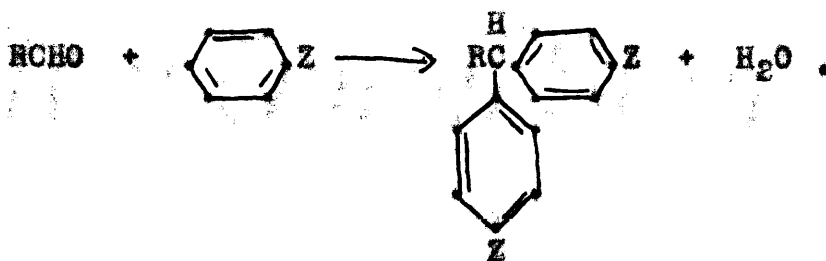
hydrogen of monosubstituted aromatic compounds. Different methods of synthesis later showed, however, that the condensation occurs principally at the para positions. Thus Ehrlich in 1903 showed that the addition of p-dimethylaminophenylmagnesium bromide to p,p'-dimethylaminobenzophenone yielded the color base of crystal violet, a dye that is also obtained by the oxidation of the Baeyer reaction product from p-dimethylaminobenzaldehyde and dimethylaniline.²⁸ Ehrlich also determined the positions of the dimethylamino groups in malachite green by the addition of 2 moles of p-dimethylaminophenylmagnesium bromide to methyl benzoate. The resulting substituted triphenylcarbinol was the same as the product obtained on oxidation of the leuco base obtained in the Baeyer reaction of benzaldehyde and dimethylaniline. Two years later Kliegl reported that addition of p-tolylmagnesium bromide to methyl benzoate and subsequent reduction of the carbinol gave the same product as the Baeyer reaction of benzaldehyde and toluene in concentrated sulfuric acid.²⁹ The condensation of benzaldehyde with anisole has been shown to give the di-para substituted triphenylmethane. This fact was demonstrated by Kauffman and Pannwitz who showed that the product was identical to one obtained by addition of p-methoxyphenylmagnesium bromide to p-methoxybenzophenone and subsequent reduction.³⁰ Votocek prepared the isomeric methoxy malachite greens by condensation of p-, o-, and m-methoxybenzaldehydes with dimethylaniline.³¹ These three products were then shown to be identical with the

products produced by the addition of p-, o-, and m-methoxyphenylmagnesium bromides to Michlers ketone and subsequent reduction. Votocek further characterized the positions of the dimethylamino groups by degradation of the leuco base obtained from p-methoxybenzaldehyde and dimethylaniline.³² The degradation, carried out with concentrated hydrochloric acid in a sealed tube at 140°, gave a mixture of methyl chloride, phenol, and 4,4'-dimethylaminobenzophenone. The formation of this latter substance offers further evidence that the Baeyer condensation involved the para positions of the dimethylaniline.

More recent work on the condensation products of chloral with chlorobenzene indicates again that the condensation occurs predominately at the para position.²⁷ This fact was established by dehydrohalogenating the 1-trichloro-2,2-bis(p-chlorophenyl)ethane with alcoholic potassium hydroxide to 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene. This latter compound was then oxidized to p,p'-dichlorobenzophenone, a known compound. The chloral condensation also yielded a smaller amount of a lower-melting isomer which on dehydrohalogenation and oxidation gave p,o'-dichlorobenzophenone indicating that the isomer was 1-trichloro-2-o-chlorophenyl-2-p-chlorophenyl ethane.

In view of all these investigations, it is evident that condensation in the Baeyer reaction results predominately in the formation of carbon-carbon bonds, joining the carbonyl carbon of the aldehyde and the para carbon atoms of the

aromatic component. Thus the general equation may be written in the more specific forms:



The more important applications of the Baeyer reaction are the preparation of DDT and the related insecticide, 1-trichloro-2,2-bis(p-methoxyphenyl)ethane. Also of great importance are the reactions of aromatic aldehydes with aromatic amines yielding substituted triphenylmethanes, which on oxidation give valuable dyes and indicators. Malachite green and crystal violet are typical examples of dyes that are readily obtained by the Baeyer reaction.

A survey of the literature has shown that no systematic study has been made of the relative reactivity of various aldehydes and aromatic compounds in the Baeyer reaction. This deficiency is understandable, however, when it is considered that the Baeyer reaction, as ordinarily carried out with large amounts of sulfuric acid or other acid catalyst, does not readily lend itself to studies of reaction rates.

The main objective of this investigation was to study the factors influencing the Baeyer reaction in order to gain an insight into the reaction mechanism. In order to accomplish this objective a series of rate studies was proposed employing a wide variety of aldehydes and aromatic compounds.

The purpose of these rate studies was twofold: first, to establish the effect on the reaction rate of the substitution of various groups on both the aldehyde and aromatic components, and second, to obtain the data necessary to calculate the kinetic order of the reactions. It was also hoped that the reaction could be improved from the synthetic standpoint.

A possible experimental method of following these reactions was suggested by some investigations of Draper. He found that acid catalyzed etherification reactions could be conveniently followed by carrying out the reaction in benzene at the reflux temperature.³³ As the water was formed in the reaction, it was readily removed since it forms a minimum boiling azeotrope with benzene. The water was collected in a graduated moisture trap so that the rate at which it collected measured the rate of the reaction.

Preliminary experiments showed that a similar procedure could be used in carrying out a wide variety of Baeyer reactions in which organic groups were substituted in both the aldehyde and aromatic components. In addition, an accurate comparison of the changes in reaction rates due to these substituents has been possible. This information has proved of great value in postulating a mechanism for the reaction. The synthetic method, in itself, is of considerable interest as it offers a simple and convenient procedure for carrying out many Baeyer condensations with good yields of pure products.

DISCUSSION

PRELIMINARY STUDY OF THE SCOPE AND
LIMITATIONS OF THE AZEOTROPIC METHOD

The Baeyer reactions carried out in the course of this research were run in an inert solvent in the presence of an acid catalyst. A constant temperature was maintained throughout the course of a given reaction by maintaining the solution of reactants at the reflux temperature. In addition the refluxing solvent effected a continuous removal of the water generated during the reaction interval and also protected the aldehyde in the reaction flask from air oxidation. Round bottom flasks fitted with thermometer wells and with capacities double that of the total solution volumes were employed in all reactions. Graduated Dean-Stark moisture traps were inserted between the reaction vessels and the reflux condensers. All pieces of glass apparatus were fitted with standard taper joints.

Reactant and catalyst concentrations were chosen so that the rates of reaction could be conveniently followed. Excessive catalyst concentrations caused water to be formed at such a rapid rate that the refluxing solvent could not remove it as rapidly as formed making it impossible to obtain accurate rate data. With too little catalyst, on the other hand, many days were required to effect complete reaction. Some of the slower reactions, as carried out, did require excessive reaction times due to the desirability of com-

paring them with other faster reactions under the same conditions of concentration and temperature.

By use of the procedure outlined above it was possible to compare the effect on the reaction rate of a wide variety of substituents on both the aldehyde and aromatic components. The rate observations also supplied the data needed in calculating the order of the reactions.

A solvent suitable for carrying out the Baeyer condensations, as outlined in the previous section, must fulfill a number of requirements. Obviously the solvent must not undergo any side reaction with either of the reactants or the catalyst under the experimental conditions employed. In addition the water solubility of the solvent must be very limited in order that the water formed during the reaction may be efficiently separated in the Dean-Stark moisture trap. The solvent should also dissolve a sufficient quantity of catalyst so that the reaction time will not be unduly prolonged. It is also desirable that the boiling point of the solvent be well below that of either of the reactants so that they do not distill from the reaction vessel. If a solvent which boils below 100° is to be used it must be one which forms a minimum boiling azeotrope with water so that the water will be rapidly and completely removed. And finally, one solvent should be suitable for a wide variety of aldehydes and aromatic compounds. Preliminary experiments showed that benzene fulfilled admirably all of these requirements for most of the reactions considered here. Benzene forms an azeotrope

with water which boils 11° below benzene itself.

The catalysts which have been used most commonly in conventional Baeyer reactions are sulfuric acid, zinc chloride, and aqueous hydrochloric acid. A suitable catalyst for use in the proposed research, however, must satisfy a number of requirements in addition to being a strong acid. Thus it is essential that the catalyst be non-volatile to prevent losses from the refluxing mixture during the period of reaction. Since the rate of the reactions are to be measured, any such losses would invalidate the data obtained. In addition the catalyst must be pure and of such a nature that definite, reproducible amounts are available for all reactions. Since the reactions are to be carried out in benzene it is necessary that the catalyst have a considerable solubility in this solvent. Obviously the catalyst should cause a minimum of charring and other side reactions. The only readily available catalyst that meets all of these requirements is p-toluene-sulfonic acid. This acid is available in a pure form as the monohydrate and has proved to be most satisfactory for carrying out the Baeyer reactions in this investigation.

In order to study the changes in reaction rates caused by substitution in the aromatic component it was necessary to select a standard aldehyde for use in all the reactions. The selection was limited somewhat by the low boiling point of many aldehydes. Fortunately, however, a variety of important aldehydes, both aliphatic and aromatic, were available having boiling points above 100° . Benzaldehyde proved to be

very satisfactory, reacting readily with anisole and dimethylaniline. The fact that this aldehyde is readily available and has been widely used in the conventional Baeyer reactions reported in the literature made it an especially desirable aldehyde with which to make the rate studies.

The selection of a standard aromatic compound to be used for comparing different aldehydes, on the other hand, was not so easily made. Preliminary experiments were performed in which benzaldehyde was reacted with aniline, methylaniline, phenol, anisole, and dimethylaniline. All of these reactions with the exception of the one with aniline went smoothly to completion with the formation of the theoretical amount of water. Benzaldehyde and aniline reacted rapidly to give an anil with very rapid liberation of water. The substituted triphenylmethane obtained from benzaldehyde and methylaniline is a non-crystallizable oil, difficult to purify. The condensation with phenol proceeded smoothly but gave a disappointingly small yield of crystalline reaction product. By thorough investigation of reaction conditions and product isolation the yield of product could possibly have been increased, but further work with phenol was discontinued when dimethylaniline was found to be very satisfactory. The condensation with anisole proceeded smoothly to give *p,p'*-dimethoxytriphenylmethane in good yield. The product was contaminated, however, with a smaller amount of lower melting isomer which was probably the isomeric *p,o'*-dimethoxytriphenylmethane. Anisole would probably have served satisfactorily as the standard aromatic compound for the study of various aldehydes

but was not used because dimethylaniline was found to be superior in several respects. The greatest advantage that this amine had over the other substances tried was the consistently excellent yields that could be obtained, ranging from 75% to 90% of pure products after recrystallization.

The use of an amine has the further advantage of maintaining a constant effective acid concentration throughout the reaction. Thus the ability of an acid to catalyze a reaction is dependent on the concentration of any other basic substances present, which will tie up the acid as a salt. If, during the course of such a reaction, any of the basic components are removed the effective acidity will increase. This effect was very pronounced in some alkylation reactions carried out in this laboratory by Preston.³⁴ He found that when benzene was alkylated with benzyl alcohol with excess boiling benzene as the solvent and with p-toluenesulfonic acid as the catalyst, the rate of reaction did not fall off appreciably over the first part of the reaction as the concentration of benzyl alcohol decreased. This effect is plausible when it is considered that at the beginning of the reaction the only atoms present with basic tendencies are the oxygen atoms in the benzyl alcohol. As the reaction proceeds these oxygen atoms are removed from the system combined in the form of water so that, at the completion of the reaction, there will be present nothing but hydrocarbons and catalyst. These considerations indicate that it is desirable to have a quantity of basic material present in the reaction mixture at all times

so that the removal of the water will not alter the effective acidity of the catalyst.

THE EFFECT OF VARYING THE GROUP
SUBSTITUTED IN THE PARA POSITION OF BENZALDEHYDE

Preliminary experiments showed that a specific set of reaction conditions could most profitably be used in studying the various substituted benzaldehydes.

The standard amount of aldehyde used was 0.125 mole. This amount of aldehyde yielded, on complete reaction, 2.25 ml. of water, a volume that could be read with sufficient accuracy in a 5 ml. graduated Dean-Stark moisture trap. A 150% excess of dimethylaniline was used since the amine should be present in twice the molar amount of aldehyde plus enough to convert the catalyst to the amine salt. The excess amine also caused the reaction to proceed in shorter time. A much more important reason for selecting this concentration of amine was the fact that only at this concentration were first order constants obtained for the reactions. Higher or lower concentrations caused the "constants" to drift to higher and lower values respectively, as the reaction proceeded.

The lowest amount of catalyst which could be used without decreasing the rates too much was 0.064 mole (12.16g.) The reactants were diluted to a volume of only 250 ml. with benzene because larger amounts of solvent were found to decrease the concentration of reactants to such an extent that the reaction proceeded too slowly. Smaller amounts, on the other hand, caused too great a difference in boiling points of the

various reaction mixtures in which different aldehydes were employed. After the reactions were completed the benzene solutions were extracted with a 5% potassium hydroxide solution to remove the acid catalyst and then washed several times. The benzene was distilled off at atmospheric pressure and the dimethylaniline was distilled off in vacuo. The reaction products were then either distilled or crystallized.

Under the standard conditions given above, the benzaldehydes with the following para substituents were reacted: O_2N- , $Cl-$, CH_3- , CH_3O- , Me_2N- , and $H-$. In all cases the volume of water evolved was between 98 and 102% of theory. The half-reaction times varied from 175 minutes to 4 days. The yields of pure substituted triphenylmethanes ranges from 77% to 89%. The melting points of the products were in agreement with the values reported in literature.

The temperatures of the reaction mixtures were recorded whenever readings of the volume of water were made. It was found that the temperatures dropped about two degrees over the first 80% of the reaction. This temperature drop is not surprising when it is considered that the total concentration decreases from 3.46 molar to 2.46 molar over the same range of reaction. The average temperature for each reaction was $92.2 \pm 0.4^\circ$.

The yields could not be compared to those obtained by the conventional methods of carrying out the Baeyer reaction because of the failure of previous workers to state their yields. Some idea of the efficiency of the method can be

gained, however, by comparing the yield of malachite green obtained to that found in a laboratory procedure given in "The Fundamental Processes of Dye Chemistry".³⁵ This manual describes a synthesis of leuco malachite green by reaction of benzaldehyde, dimethylaniline, and aqueous hydrochloric acid with vigorous mechanical stirring at the reflux temperature. After 12 hours sodium carbonate was added to neutralize the acid, the excess dimethylaniline blown off with steam, and the residual leuco base separated by cooling. The residue was washed with water and dried. The crude yield of leuco malachite green was 72%. This same leuco base, when prepared by the azeotropic method, was distilled in 95% yield and after recrystallization was obtained as pure white crystals in an 85% yield. It seems probable that the yields obtained by methods in the literature for compounds other than malachite green were often considerably below 72%.

The details concerning this series of condensations and the corresponding rate tables are given in the experimental part of this thesis.

The experimental rate data obtained for the reaction of the six substituted benzaldehydes with dimethylaniline were found to fit the first order rate equation very satisfactorily. The integrated form of this equation can be written:

$$k = \frac{2.303}{t} \log \frac{a}{a-x}$$

For the application of this equation to the work reported here, a was the original number of moles of the benzaldehyde and a-x was the number of moles of aldehyde remaining after

the reaction time t had elapsed.

In order to treat the experimental data from all the reactions in a uniform manner, the following calculation method was adopted. First, a graph was made for each experiment in which reaction time versus per cent of reaction completion was plotted. Then a smooth curve was drawn in such a manner that any deviations of points from the curve were averaged. Over the 20% to 80% portion of these plots, however, none of the points were off more than 1%, and only a very few showed even this much deviation. In fact, the experimental readings taken directly from the rate chart without graphing, gave substantially the same rate constants as those obtained from the curve. All runs were repeated to ascertain reproducibility of results with the exception of the one with p-methylbenzaldehyde. No more of this aldehyde was available and because of the satisfactory checks obtained with the other five aldehydes it was not deemed necessary to prepare more of this aldehyde for use in a check run.

From the graphs the reaction times were read at 10 per cent intervals over the 20% to 80% portion of the reaction. Calculations for the first and last 20% of reaction were omitted because the experimental error is relatively large in these ranges. These reaction times including those for the duplicate runs are summarized in Table I .

TABLE I

Reaction Time in Minutes at
10 Per Cent Intervals

	<u>20%</u>	<u>30%</u>	<u>40%</u>	<u>50%</u>	<u>60%</u>	<u>70%</u>	<u>80%</u>
$p\text{-NO}_2\text{C}_6\text{H}_4\text{CHO}$	1	52	86	124	170	222	293
	2	57	89	127	171	229	302
$p\text{-ClC}_6\text{H}_4\text{CHO}$	1	145	230	325	450	600	790
	2	145	231	340	475	640	840
$p\text{-HC}_6\text{H}_4\text{CHO}$	1	185	300	436	600	803	1045
	2	180	290	415	575	775	1020
$p\text{-CH}_3\text{C}_6\text{H}_4\text{CHO}$	1	270	430	630	860	1140	1480
$p\text{-CH}_3\text{OC}_6\text{H}_4\text{CHO}$	1	450	740	1070	1470	1950	2550
	2	430	730	1070	1500	2000	2620
$p\text{-(CH}_3)_2\text{NC}_6\text{H}_4\text{CHO}$	1	1510	2600	3900	5420	7300	9550
	2	1600	2800	4300	5900	7750	9900

In the course of all these reactions there is produced 0.125 mole or 2.25 ml. of water. At any stage of reaction completion, therefore, the corresponding amount of water is known. This information at the different intervals is summarized in Table II. Since the rate of appearance of the water is equal to the rate of disappearance of the aldehyde the moles of the aldehyde present at any time is equal to the original number of moles of aldehyde minus the moles of water formed by that time. This information and values for the appropriate concentration function, $\log \frac{a}{a-x}$ are also given in Table II.

TABLE II

Standard Data for Rate Calculations

Per cent Reaction Completed	x	$a-x$	$\frac{a}{a-x}$	$\log \frac{a}{a-x}$
20%	.0250	.1000	1.250	.097
30%	.0375	.0875	1.429	.155
40%	.0500	.0750	1.667	.222
50%	.0625	.0625	2.00	.301
60%	.0750	.0500	2.50	.398
70%	.0875	.0375	3.33	.523
80%	.1000	.0250	5.00	.699

The first order reaction rate constants were then determined by use of the data given in Tables I and II. These values, calculated at 10% intervals, are listed in Table III. An examination of this latter table shows that, in any run, the deviation from the mean is less than 4% with the exception of the dimethylaminobenzaldehyde run where the deviation is somewhat larger. If the values are omitted at 20% reaction, where experimental error is the largest, the deviations from the mean are even smaller. No values were discarded, however, in determining the averages.

It must be pointed out at this time that these first order rate values, although remarkably constant over a wide range of reaction, are not true constants since they are not obtained at different reactant concentrations. Experiments showing the drift in these constants will be discussed later

TABLE III

Effect of Varying the Para Substituent
on the First Order Rate Constants^a

	<u>20%</u>	<u>30%</u>	<u>40%</u>	<u>50%</u>	<u>60%</u>	<u>70%</u>	<u>80%</u>	<u>Ave.</u>	<u>Ave. Two Runs</u>	<u>Yield of Pure Products</u>
p-NO₂C₆H₄CHO										
1	392	401	403	405	400	398	402	400	408	89%
2	429	415	412	408	413	411	420	415		
p-ClC₆H₄CHO										
1	154	155	158	154	153	152	153	154	151	83%
2	154	154	150	146	143	143	144	146		
p-HC₆H₄CHO										
1	121	119	117	115	114	115	118	117	119	85%
2	124	123	123	120	118	118	118	121		
p-CH₃C₆H₄CHO										
1	82.7	83.0	81.0	80.5	80.3	81.3	79.7	81.2	81.2	80%
p-CH₃OC₆H₄CHO										
1	49.7	48.2	47.7	47.1	47.0	47.2	48.8	48.0	47.9	85%
2	51.9	48.9	47.7	46.2	45.8	45.9	47.9	47.8		
p-Me₂NC₆H₄CHO										
1	14.8	13.7	13.1	12.8	12.5	12.6	13.0	13.2	12.8	77%
2	13.9	12.7	11.9	11.8	11.8	12.2	12.8	12.4		

^a Constants given in $\text{min}^{-1} \times 10^5$

under the section on the reaction mechanism. Under the standard conditions adopted for the study of para substitution, however, constants were obtained, and they have proved to be of considerable value in comparing the effect of substituent groups on the rate of reaction.

By examination of the rate constants in Table III, it is observed that electron-attracting groups, i.e. groups which withdraw electrons from the benzene ring, speed up the reaction. Electron-releasing groups, on the other hand, slow down the reaction. It is of interest to note that this effect of the para substituents is the exact opposite of that found in the alkylation of aromatic rings by para substituted benzyl alcohols.⁵⁴

The rate data obtained from this series of experiments shows that the ability of the para substituent to alter the reaction rate is a quantitative function of the electron attracting power of that group. This relationship can be most easily expressed by the method of Hammett in which the logarithms of the rate constants of a series of reactions involving side chains of aromatic compounds differing only in the para substituent are plotted against a function of the logarithms of the ionization constants of the corresponding para substituted benzoic acids.⁵⁶ Plots made in this manner have been shown by Hammett to show a linear relationship for a large number of side-chain reactions of para substituted benzene derivatives. As a result of these observations Hammett has concluded that the substituents exert their in-

fluence by an internal electron displacement. The values required for making a graph of this type, utilizing the data obtained in this investigation can be found in Table IV. The corresponding plot is given in Figure I.

TABLE IV

Functions Plotted in Figure 1

	<u>k</u>	<u>Log k</u>	<u>K^a x 10⁻⁵</u>	<u>$\frac{K}{K^0}$</u>	<u>Log $\frac{K}{K^0}$</u>
p-NO ₂ C ₆ H ₄ CHO	408	2.611	37.6	6.00	+0.778
p-ClC ₆ H ₄ CHO	151	2.179	10.5	1.67	+0.225
p-HC ₆ H ₄ CHO	119	2.076	6.27	1	0
p-CH ₃ C ₆ H ₄ CHO	81.2	1.909	4.24	0.676	-0.170
p-CH ₃ OC ₆ H ₄ CHO	47.9	1.681	3.38	0.539	-0.268
p-(CH ₃) ₂ NC ₆ H ₄ CHO	12.8	1.107	0.85	0.135	-0.870

K⁰ is the ionization constant of Benzoic Acid

a. Ionization constant of corresponding Benzoic Acid.

The ionization constants of the substituted benzoic acids were obtained by Dippy et al,³⁷ and are the same as those used by Hammett. Dippy did not determine an ionization constant for p-dimethylaminobenzoic acid, however, and the value given in Table IV was obtained from the International Critical Tables.

The linear relationship shown in Figure I is by no means perfect but is not inferior to many of those discussed by Hammett.³⁸ It is of interest to note that the relationship found by Hammett holds true for these Baeyer reaction rate

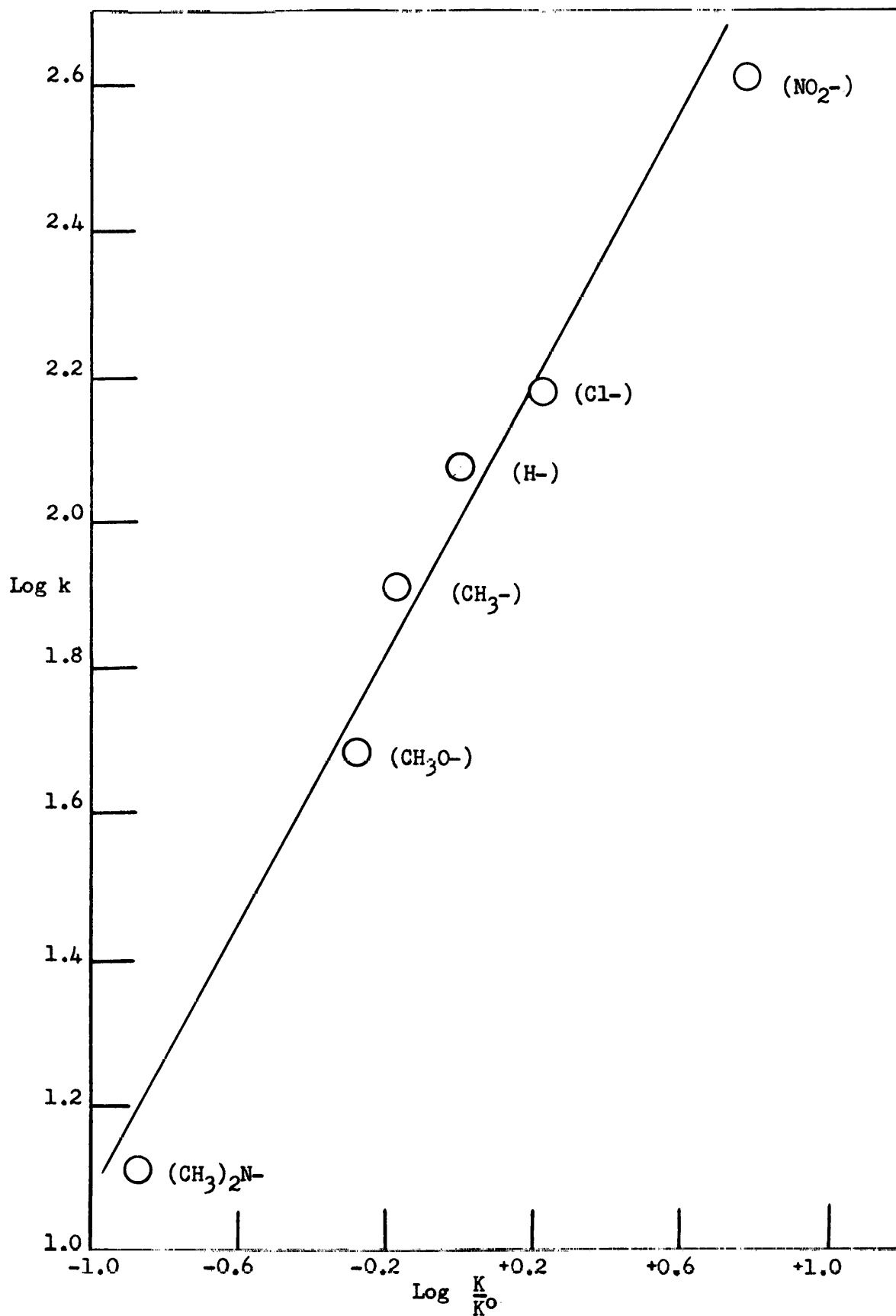


Figure 1 - A Comparison of the Reaction Rates of Para Substituted Benzaldehydes with Dimethylaniline to the Ionization Constants of the Corresponding Benzoic Acids.

constants even though these constants are known to drift at other reactant concentrations.

In any case, however, it has been clearly demonstrated that the rate of the Baeyer reaction is directly related to the internal electron displacements brought about by substituents in the para position. This fact, demonstrated experimentally for six different para substituted benzaldehydes, has been most useful in the discussion of a reaction mechanism which is given in a later section.

The reaction of dimethylaniline and benzaldehyde was also carried out in an equal volume of toluene in order to obtain an estimate of the temperature coefficient of the reaction. For this study 0.125 mole of benzaldehyde, 0.625 mole of dimethylaniline, and 0.064 mole of p-toluenesulfonic acid in 250 ml. of toluene solution were reacted in the usual manner. The half-time of reaction was 135 minutes as compared to 600 minutes for the similar run in benzene at the same concentrations. The yield of pure malachite green was 85%.

The first order reaction rate constants calculated over the 20% to 80% portion of the reaction were found to be constant within $\pm 3\%$ of the mean as were the constants for the previously described reaction in benzene. The average rate constant was 505×10^{-5} reciprocal minutes. A repeat run gave a constant of 483×10^{-5} . The average first order rate constant was 494×10^{-5} at a temperature of $123.2 \pm 0.7^\circ$ whereas the same run in benzene showed an average rate constant of 119×10^{-5} at a temperature of $91.6^\circ \pm 1.0$.

If it is assumed that any solvent effects of toluene and benzene are the same, it is possible to estimate the energy of activation for the reaction by means of the Arrhenius equation. This relation can be expressed in the integrated form,

$$\log \frac{k_2}{k_1} = \frac{E}{2.3R} \frac{T_2 - T_1}{T_1 T_2}$$

where k is the reaction rate constant and T the absolute temperature at which that rate was observed. On substitution of the values of k found at the two temperatures, a value of 14 kcal. is obtained for the activation energy. Since the reaction rate "constants" have been shown to vary on changing the concentration of the aldehyde, this value obtained for the activation energy cannot be considered absolute. It is, however, probably sufficiently accurate to show that this reaction has an activation energy within the normal range.

In order to determine the effect of acid catalyst concentration on the reaction rate, the run in toluene was repeated using one-half the amount of p-toluene sulfonic acid. Toluene was chosen as the solvent instead of benzene because of the shorter reaction time required to complete the run. This reaction, employing 0.125 mole benzaldehyde, 0.625 mole dimethylaniline, and 0.032 mole of catalyst in 250 ml toluene solution, was found to have a half-reaction time of 200 minutes as compared to 135 minutes for the run in the presence of 0.064 mole catalyst. Comparison of these half-reaction times shows that the reaction rate is not directly propor-

tional to acid concentration, but instead, doubling the amount of catalyst increases the rate about 50%

In order to ascertain whether any of the catalyst reacted with the solvent or either of the reactants an excess of standard alkali was added to the mixture after completion of one of the above experiments carried out in toluene. The solution was shaken thoroughly in a separatory funnel, the aqueous layer separated, and the benzene extracted once with water. The excess alkali was then back titrated with standard acid, and it was found that 99% of the catalyst originally added could be accounted for. It follows, therefore, that since the catalyst did not react with toluene or the reactants it also would not give any side reactions in the runs carried out in benzene at lower temperatures.

THE EFFECT OF OTHER CHANGES IN THE CARBONYL CONSTITUENT

In addition to the para substituted benzaldehydes, a number of other carbonyl compounds were studied to further determine the scope and applicability of the azeotropic method.

The two aliphatic aldehydes, n-heptaldehyde and 2-ethylbutyraldehyde, were condensed with dimethylaniline under exactly the same conditions of reactant and catalyst concentration as were the substituted benzaldehydes previously discussed. The n-heptaldehyde reacted smoothly giving the theoretical amount of water. The rate data obtained did not

fit the first order rate equation but the "constants" drifted rapidly to lower values. The rate of the reaction was considerably slower than that of the corresponding benzaldehyde run. The half-reaction times were 930 and 600 minutes respectively. The reaction product, 1,1-bis(p-dimethylamino-phenyl)heptane, was distilled in a 79% yield and after recrystallization gave 69% of pure material.

With the 2-ethylbutyraldehyde the time required for the reaction was considerably increased. In fact, the reaction was only 50% complete after a period of 3 days. Due to the excessive time required the reaction was shut down after 60% completion and the product worked up. A search of the literature revealed that the product, 1,1-bis(dimethylamino-phenyl)2-ethylbutane, had not been previously reported. The yield of this compound was 50% of impure crystalline product. A purified sample gave the proper analyses. Some more volatile material was obtained suggesting that aldol-type condensation products of the aldehyde were also formed. This reaction was repeated at double the catalyst concentration. Unfortunately, however, there was only a slight increase in reaction rate, the time for half reaction being reduced from 3 days to 6 days. The crude product was isolated in 70% yield.

In another attempt to speed up the reaction it was carried out in toluene as the solvent, thus raising the temperature. The higher boiling point of toluene also made it desirable to switch to an aldehyde with a higher boiling

point. For this experiment 2-ethylhexaldehyde was used and, as expected, the reaction proceeded at a considerably faster rate. Unfortunately, however, the higher temperature increased the rate of the side reaction even more, and very little of desired reaction product was obtained.

The observation that these aldehydes branched on the alpha carbon react much slower than the straight chain aldehydes is consistent with the relative rates of reaction found for the series of para substituted benzaldehydes. It is a well known fact that alkyl groups exert a positive inductive effect, i.e. they have a greater tendency to release electrons to a neighboring group than do hydrogen atoms. One manifestation of this inductive effect is the necessity of using especially strong bases as condensing agents for Claisen reactions involving alpha-branched aldehydes. Since electron-releasing groups substituted in benzaldehyde have been shown to retard the rate of reaction, the alpha alkyl groups of aliphatic aldehydes would be expected to show a similar effect.

Attempts were also made to condense chloral and cinnamaldehyde with dimethylaniline under the standard reaction conditions. Although 90% of the theoretical amount of water was removed in both cases, the experiments failed because of predominance of side reactions. The mixture containing the chloral turned very dark and, as the reaction proceeded, considerable amounts of black, tarry material separated from the benzene solution. The reaction involving the cinnamaldehyde, on the other hand, appeared to proceed quite normally,

but apparently the high acid concentrations caused polymerization at the double bonds as no product could be crystallized or distilled from the reaction residues.

Preliminary experiments showed that the application of the azeotropic method to similar condensations involving ketones would not be feasible. Thus methyl n-amyl ketone, when treated with dimethylaniline under the standard reaction conditions, reacted only very sluggishly. The amount of water removed indicated that only 12% reaction had occurred after three days. No attempt was made to isolate any reaction product.

THE EFFECT OF VARIATIONS IN THE AROMATIC CONSTITUENT

In order to obtain more information concerning the scope of the Baeyer reaction a variety of mono- and di-substituted benzenes was reacted with a standard aldehyde. For reasons already set forth in the section on Preliminary Study benzaldehyde was selected as the standard with which to make this investigation. The aromatic compounds employed can most profitably be discussed by dividing them into three classes: (1) aromatic amines: aniline, methyl aniline, and dimethylaniline (2) alkyl phenyl ethers: anisole, phenetole, and n-butyl phenyl ether (3) other aromatic compounds: phenol, toluene, mesitylene, p-xylene, and hydroquinone dimethyl ether.

When 0.125 mole benzaldehyde was added to 0.625 mole

of aniline and 0.008 mole catalyst in 250 ml. of boiling benzene, there resulted a vigorous reaction with the rapid evolution of water. On working up the reaction mixture no triphenylmethane derivative was found. A 36% yield of pure benzalaniline was isolated. Apparently the anil will not rearrange and react further to give a triphenylmethane derivative under the conditions employed. Even if it did, however, the rate study would be meaningless because of the initial rapid formation of water.

The condensation of methylaniline under exactly the same conditions as used for aniline proceeded half way to completion in 105 minutes. This reaction was very rapid compared to the corresponding dimethylaniline reaction described in the preceding section which showed a half-time of 600 minutes under the same conditions except that the concentration of catalyst was eight times as high. On working up the product from the methylaniline reaction there was obtained a very viscous brownish-red oil. It could not be made to crystallize by trituration with solvents. This compound is described in the literature as a viscous non-crystallizable oil.³⁹ A nitroso derivative was prepared which on recrystallization from alcohol melted at 180-184°; the literature value, however, is 149° with decomposition. Possibly in one case an N-nitroso compound and in the other case a ring nitroso compound was obtained. Analyses for carbon, hydrogen, and nitrogen agreed with that calculated for the expected product, 4,4'-bis(methylamino)triphenylmethane. In view of

the poorly defined product no further rate studies were made on this reaction.

The standard amounts of reactants selected for the study of the three phenyl alkyl ethers were 0.125 mole benzaldehyde, 0.625 mole of ether, and 0.064 mole of p-toluene-sulfonic acid. There was a much larger variation in the grams of reactants added in the different runs than for the series of experiments in which the aldehyde component was varied. In order to maintain the temperature approximately the same in the three runs it was necessary to increase the amount of benzene solution from 250 to 500 ml.

Anisole and benzaldehyde were found to react smoothly with the liberation of the theoretical amount of water. The half-time for this reaction was 365 minutes. After working up the reaction mixture the product was distilled in 70% yield. Crystallization of this distillate gave 60% of p,p'-dimethoxytriphenylmethane. From the mother liquor there was obtained a smaller amount of lower melting crystalline product that could not be purified by recrystallization. This substance melting from 68-87° is, no doubt, the isomeric p,o'-dimethoxytriphenylmethane (lit. m.p. 94°)

The reaction of anisole with benzaldehyde was also studied when excess anisole was used as the solvent. The yield of pure product obtained was significantly higher (76%). When anisole and benzaldehyde were reacted in equivalent amounts in benzene solution, the yield of pure product was much smaller (25%). A large amount of non-distillable

residue was formed.

Phenetole was found to act in a manner very similar to anisole when treated with benzaldehyde in benzene solution. The reaction was significantly faster, however, showing a half-time of 250 minutes compared to 365 for anisole. The product was distilled in a 77% yield but could not be made to crystallize. A literature search showed that the expected product, diethoxytriphenylmethane, had not been previously reported. To make sure that the reaction conditions employed did not split the ether linkages the product was extracted with hot alcoholic potassium hydroxide. The aqueous layer on separation and neutralization was found to contain no phenolic compound. It is possible that this compound would not crystallize because of contamination with the isomeric *p,o'*-diethoxytriphenylmethane. The product analyzed satisfactorily.

The third aromatic ether studied, butyl phenyl ether, reacted even more rapidly with benzaldehyde than did phenetole under the same conditions of reactant and catalyst concentrations. The half-time for this reaction was 175 minutes. The reaction product was distilled in a 70% yield, but, like the product from the phenetole run, could not be crystallized. This compound which has not been reported in the literature was found to analyze satisfactorily.

The first order rate constants for all three of these alkyl phenyl ethers drifted somewhat toward higher values. This drift never amounted to more than 20% for the 20% to 80%

portion of the reactions.

Phenol was found to react much more readily with benzaldehyde in benzene solution than any other aromatic compound studied. After the theoretical amount of water had formed, further reaction ceased. The first order rate constants drifted to about the same extent as did those for the alkylphenyl ethers. On working up the product, however, it was not possible to obtain more than about 10% of crude crystalline reaction product. In view of the discouragingly small yields, further work with phenol was abandoned in favor of other aromatic compounds.

Toluene will undergo the Baeyer type of condensation but with not near the vigour of the aromatic amines and the alkyl phenyl ethers. In order to make the reaction feasible with respect to the time required it was necessary to make the run using an excess of toluene as a solvent. The benzaldehyde (0.125 mole) was added to 2.57 moles of boiling toluene containing 0.128 mole of *p*-toluene sulfonic acid. The reaction proceeded very slowly even under these conditions, reaching the half-way mark only after 60 hours of refluxing. A plot of time versus per cent reaction gave a straight line over 90% of the reaction. The yield of product, which distilled over a one degree range as a water-white viscous liquid, amounted to 74% of theory. Only one-half of this material could be crystallized, however, as *p,p'*-dimethyltriphenylmethane. The balance of the product was probably the isomeric *p,o'*-dimethyltriphenylmethane.

The condensation reaction with mesitylene was complicated by the fact that some decomposition occurred merely on heating the mesitylene with the catalyst before the aldehyde was added. Because of this observation, plus the fact that no definite reaction product was obtained, no further investigations were made with mesitylene. The reaction with p-xylene was also unsatisfactory as this hydrocarbon also turned black in color on heating with the catalyst. The reaction resulted in the formation of 125% of the theoretical amount of water. Apparently the catalyst had reacted. On treatment of the distilled product with ligroin white crystals formed. These crystals were found to contain sulfur. A small second crop of large, well formed crystals which contained no sulfur apparently was not the expected reaction product, 2,5,2',5'-tetramethyltriphenylmethane. Although p-toluenesulfonic acid reacted in this run to give a product containing sulfur it was found that this acid would not react appreciably with boiling p-xylene when the aldehyde was omitted.

Hydroquinone dimethyl ether, was found to react much slower than the monosubstituted anisole. The reaction did not lead to the expected 2,5,2',5'-tetramethoxytriphenylmethane, but gave instead a small amount of amorphous solid material with a wide range in melting point.

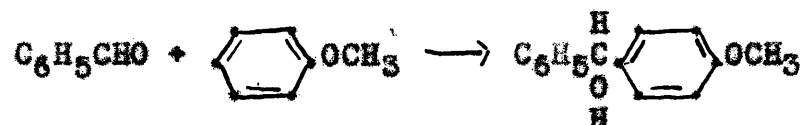
The foregoing experiments show that close comparison of the rates of reaction of benzaldehyde with all aromatic compounds cannot be made because of the widely different reac-

tivity of the aromatic constituents which made it impractical to carry out the reactions under identical conditions. Another important factor that must be born in mind in making comparison is that the deactivating effect of the various aromatic compounds on the catalyst will vary widely. In spite of these drawbacks, a qualitative comparison may be made in the rates. In general it has been observed that the rates are proportional to the ability of the substituent in the aromatic ring to release electrons by an inductive or by an electromeric shift. It will be noted that this effect is the exact converse of the effect found for substituents in the para position of benzaldehyde, where electron releasing groups slowed down the rate of reaction. Thus a methoxy group when substituted for the para hydrogen in benzaldehyde retarded the reaction considerably, but when substituted for hydrogen in the aromatic component (anisole) a much faster reaction rate was observed. With phenetole, there is an additional positive inductive effect over that of anisole due to the extra $-CH_2-$ in the alkoxy side chain which causes a somewhat greater electron release to the ring and a correspondingly faster reaction. Butyl phenyl ether likewise reacts faster than phenetole. Phenol can ionize to some extent and exist in part as the phenolate ion. This ion can then undergo a shift of electrons giving a relatively high electron density at the para position resulting in a much faster rate of reaction. Aromatic compounds such as toluene,

on the other hand, in which the electron release of the substituent group is much smaller, undergo the Baeyer condensation very slowly.

THE REACTION MECHANISM

The mechanism to be presented for the Baeyer reaction will indicate that a benzhydryl is formed as an intermediate. Thus, benzaldehyde and anisole would give p-methoxybenzhydryl:



According to a previous disclosure in the literature by Julius von Braun a benzhydryl cannot be an intermediate in this condensation. Before going on with a more detailed discussion of the mechanism, it will be necessary to examine in some detail this work of von Braun.⁴⁰ To support his contention he pointed out that the reaction of one mole of benzaldehyde with two moles of dimethylaniline was significantly faster than the reaction of one mole of p-dimethylaminobenzhydryl with one mole of dimethylaniline under the same conditions of catalyst concentration and temperature.

This observation is rather surprising, especially in view of the great reactivity of benzhydryls in Friedel-Craft types of reaction.⁴¹ The aminohydryl used by von Braun should be even more reactive than benzhydryl due to the greater ease of carbonium ion formation as discussed below. These anomalous results are clarified, however, when it is

considered that von Braun carried out the reactions in aqueous solution using one molecule of acid catalyst for each amine group present in the reaction mixture. Under these conditions the slow reaction of p-dimethylaminobenzhydrol with dimethylaniline is not surprising since the hydrol is actually present as the amine salt and not as the active free aminohydrol. This amine salt, in direct contrast to the free amine, would hinder carbonium ion formation and greatly decrease the rate of reaction. The condensation of benzaldehyde with dimethylaniline would also be expected to proceed very slowly, if at all, in the presence of acid catalyst equivalent to the amine. In carrying out either of these reactions, however, if slightly less than an equivalent amount of acid catalyst was present there would be at all times some free amine groups present allowing a much greater rate of reaction. If von Braun had used more dimethylaniline or less acid catalyst in his two runs, the relative rates he reported would undoubtedly have been reversed.

Direct evidence that the benzhydrol alkylation proceeds more rapidly than the corresponding aldehyde condensation is obtained by a comparison of some alkylation studies of Preston³⁴ with studies of the Baeyer reactions reported here. The reaction of benzaldehyde with anisole was found to require considerably more catalyst than the similar reaction carried out by Preston in which benzhydrol was reacted with anisole. Methoxybenzhydrol, the probable intermediate in the benzaldehyde reaction, should be even more reactive than

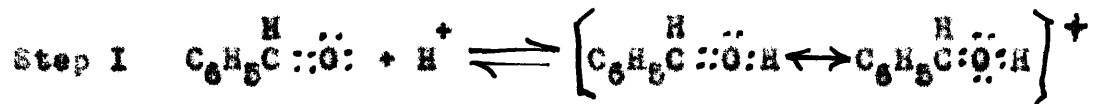
the unsubstituted benzhydrol studied by Preston.

In order to obtain still further evidence regarding the rates of these two reactions, p-methoxybenzhydrol, the active intermediate of the benzaldehyde-anisole condensation, was synthesized.

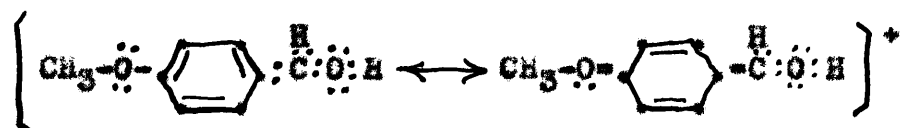
This hydrol (0.125 mole) was then reacted with 0.500 mole of anisole and the rate of reaction compared to that of 0.125 mole of benzaldehyde with 0.625 mole of anisole under the same conditions. The hydrol reaction was half-completed within 5 minutes whereas the corresponding benzaldehyde reaction required 365 minutes to reach the same stage of completion. The yields and reaction products obtained from these two runs proved to be identical in all respects. These experiments show conclusively that the rate of reaction of p-methoxybenzhydrol with anisole is much more rapid than the overall reaction of benzaldehyde with anisole. There is no reason to believe that these relative rates would be reversed by the use of any other aromatic compound. It is apparent, therefore, that contrary to the findings of von Braun an intermediate hydrol may be formed in the Baeyer reaction.

Further evidence that a hydrol is the intermediate is indicated by the fact that benzaldehyde and dimethylaniline react in a twenty-fold excess of aqueous hydrochloric acid to give p-dimethylaminobenzhydrol.⁴² The excess acid present ties up this hydrol as the amine salt and apparently retards its further reaction.

The first step of the Baeyer condensation has been expressed by Hammett as the formation of an ion by the aldehyde and acid catalyst:⁴³



The ion formed is a resonance hybrid between the oxonium and carbonium ions as shown. Since the next step in the reaction will involve the carbonium ion any factors which affect the stability of this ion will also have an influence on the rate at which the reaction proceeds, if, as is indicated in the discussion below, the carbonium ion is involved in the rate controlling step. Thus, a substituent on the para position of the phenyl group that can release or attract electrons from the ring would be expected to exert an influence on the stability of the carbonium ion. Consider, for example, the carbonium ion produced in the case of anisaldehyde.

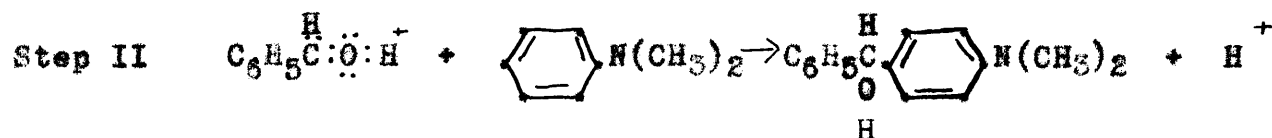


The electrons from the methoxyl oxygen can undergo an electro-meric shift to give still another resonance structure as shown, decreasing the contribution of the carbonium ion to the resonance hybrid. In other words, groups of the electron releasing type might be expected to slow up the rate of reaction. Conversely, substituents that withdraw electrons

from the ring, such as the nitro group, should increase the contribution of the carbonium ion to the resonance hybrid and lead to a more rapid rate of reaction. Inductive electron shifts of substituents such as alkyl groups will similarly affect the stability of the carbonium ion and the reaction rate.

The effect of substituents in the para position of benzaldehyde on the rates of reaction discussed in an earlier section have been found to fit this picture exactly. The six substituents tested can be arranged in the following order according to their tendency to release electrons: $(\text{CH}_3)_2\text{N}- > \text{CH}_3\text{O}- > \text{CH}_3- > \text{H}- > \text{Cl}- > \text{NO}_2-$. This is the same order as experimentally found for these groups in decreasing the rate of the Baeyer reaction. The very slow rate of reaction shown by alpha branched aliphatic aldehydes is another example of the retardation of rate brought about by the positive inductive effect of alkyl groups.

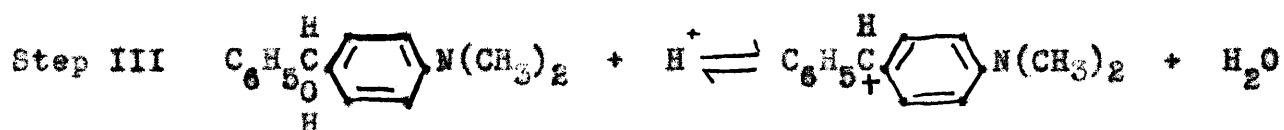
After the carbonium ion has been formed it may react with certain aromatic compounds, such as dimethylaniline, to give an intermediate benzhydrol. The equation for this second step may be written:



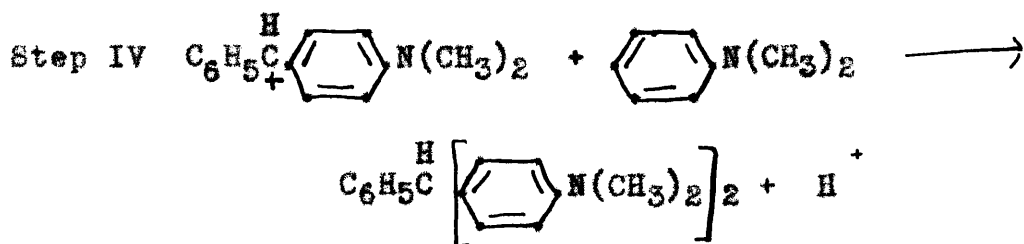
The rate at which this step occurs will depend on the effective concentrations of the carbonium ion and also on the electron density of the carbon atom para to the dimethylamino

group. Substituted aromatic compounds which have a high density at the para position due to electrometric or inductive shifts will, of course, be expected to show the fastest rate of reaction. Experimentally it has been found, as discussed earlier, that toluene is relatively inactive. Compounds in which electromeric shifts are possible, on the other hand, such as anisole, phenetole, and dimethylaniline, react at a much faster rate.

The intermediate benzhydryl formed in Step II is a very reactive type of carbinol and under the acid conditions employed will give a carbonium ion:



The active carbonium ion then reacts with more of the dimethylaniline to give the final product as in Step IV.



This four step mechanism is essentially the same as that given in an incomplete form by Hammett.⁴⁵ This author, however, does not give any experimental evidence but has inferred the mechanism from his knowledge of other carbonium ion reactions.

The comparative rate studies made during the course of this research have also made it possible to suggest which step in the above mechanism is rate controlling. As already ex-

plained, electron releasing substituents on the benzaldehyde should decrease the effective concentration of the carbonium ion formed in Step I, and cause Step II to proceed at a slower rate. These same electron releasing substituents are known to greatly increase the tendency of benzhydrols to form carbonium ions (Step III) resulting in very rapid alkylations (Step IV).⁴¹ Experiment has shown that electron releasing substituents in the carbonyl constituent decrease the rate of the overall reaction, i.e., Step I through IV, and that furthermore, this retardation is a function of the electron releasing power of the substituent. On the basis of these considerations it can be stated that Step II is the most probable rate controlling step in the reaction under the experimental conditions used. Since Step I is a simple acid-base reaction involving no rupture of bonds it appears to be a rapid one, but the possibility that it also is slow enough to affect the overall rate has not been eliminated.

The rate data obtained in this research has also made possible the calculation of the kinetic order of the various reactions. As pointed out earlier in the discussion, first order rate constants with respect to the aldehyde were obtained for the condensation of benzaldehyde with dimethylaniline under one set of reactant concentrations throughout the 20% to 80% portion of reaction. These constants apparently do not have any absolute significance for as was discussed above the nature of the aromatic compound greatly affects the rate of reaction.

It was found furthermore, that the first order rate constants drifted markedly on carrying out the reactions at different aldehyde concentrations. Three runs were carried out in which 0.0625, 0.125, and 0.250 mole of benzaldehyde were reacted with 0.625 mole of dimethylaniline in the presence of 0.032 mole of p-toluenesulfonic acid. All three reactions were run in 500 ml. of toluene solution. Tables showing the rates at which these runs proceeded are given in the experimental section. From the data in these tables the moles of aldehyde present at various times were calculated and these values substituted in the first order rate equation. The 0.125 mole benzaldehyde run, in which the reactant ratio is the same as that in the standard runs, gave first order constants that did not vary from the mean more than 3% over the 20% to 80% portion of the reaction. When the aldehyde concentration was doubled to 0.250 mole, however, the rate constants calculated in the same manner were found to drift markedly toward lower values indicating a higher order. On the other hand, the lower aldehyde concentration (0.0625 mole) gave constants which drifted to a higher value over the same portion of the reaction.

As discussed above Step II appears to be rate-controlling so that it becomes possible to calculate second order constants. The ordinary second order equation must be modified somewhat because the amine is consumed in both rate and non-rate controlling steps. The rate of Step II may be expressed:

$$\frac{dx}{dt} = k (\text{conc. carbonium ion})(\text{conc. amine})$$

The concentration of the carbonium ion is proportional to $a-x$, the amount of aldehyde present at any time t . Where b is the original amine concentration, the concentration of the amine will be $b-2x$ at any time t since for every mole of amine used in Step II there will be another mole used in the rapid Step IV. The differential rate equation may then be written:

$$\frac{dx}{dt} = k(a-x)(b-2x)$$

It should be pointed out that this k incorporates the equilibrium constant from Step I. Upon integration the above equation takes the form:

$$k = \frac{2.3}{t(2a-b)} \log \frac{b(a-x)}{a(b-2x)}$$

When the data from the three runs were substituted into this expression and the rate constants calculated over the various reaction intervals for the runs with 0.0625 and 0.125 mole of aldehyde the constants were found to drift to higher values. The constants for the 0.250 mole run, however, were fairly good showing some change toward a higher order.

To complete the picture substitution of the rate data into a third order equation was also carried out. The equation used expresses the time-concentration relationship in which the rate is proportional to the concentration of the aldehyde and the square of the concentration of the dimethylaniline. The integrated form of this equation is:

$$k = \frac{1}{t(b-2a)^2} \left[\frac{2x(2a-b)}{b(b-2x)} + \ln \frac{a(b-2x)}{b(a-x)} \right]$$

When the data from the three runs were substituted into this equation the rate constants were found in all cases to drift considerably toward higher values. The rate data calculations for the three different orders are summarized in Table V.

TABLE V

Effect of Changes in Aldehyde Concentration
on First, Second, and Third Order Constants

<u>Run</u>	<u>Moles Aldehyde</u>	<u>First Order</u>	<u>Second Order</u>	<u>Third Order</u>
1	0.0825	30% increase	50% increase	55% increase
2	0.125	constant within $\pm 3\%$	25% increase	40% increase
3	0.250	50% decrease	13% decrease	55% increase

Three more runs were made in which the concentrations of the reactants were varied. These experiments were carried out in 250 ml. of benzene instead of 500 ml. toluene and twice as much catalyst (0.064 mole) was used. Calculation of the rate constants for the different orders showed the same sort of drifts as did the corresponding runs in toluene just discussed.

These experiments on the condensation of benzaldehyde with dimethylaniline have shown that none of the common kinetic equations will express the rate at which the reaction proceeds under varying conditions of aldehyde concentration. This failure to obtain an integral order might indicate that

there is no single rate controlling step in the reaction. It must be remembered, however, that all of these order calculations were made by the substitution of molar concentrations into the different rate equations. Actually, of course, the rate of the various steps are proportional to the activities of the reactants and not the molar concentrations. The activities are dependent on the activity coefficients and these coefficients in turn are dependent on the ionic strength of the solution.

The actual rate equation that should be used to express the rate of this reaction if Step II controls the rate is:

$$\frac{dx}{dt} = k_1 a(\text{carbonium ion}^+) a(\text{amine})$$

Equilibrium in Step I can be expressed by

$$K = \frac{a(\text{carbonium ion}^+)}{a(\text{aldehyde}) a_{\text{H}^+}}$$

On substitution into the above rate equation we obtain:

$$\frac{dx}{dt} = k_1 K a(\text{aldehyde}) a(\text{amine}) a_{\text{H}^+}$$

and since the activity is equal to the molar concentration times the activity coefficient (γ) this may be converted to:

$$\frac{dx}{dt} = k_1 K c(\text{aldehyde}) c(\text{amine}) c_{\text{H}^+} \text{ times} \\ \gamma(\text{aldehyde}) \gamma(\text{amine}) \gamma_{\text{H}^+}$$

Unfortunately there is no way in which these activity coefficients can be evaluated, particularly at the relatively high concentration of reactants and catalyst employed experimentally. An inspection of this differential rate equation

does show, however, that even small changes in the activity coefficient during the course of the experiment could cause considerable drifts in the rate constant.

Although the rate studies have not been very helpful in the determination of an integral order for the reaction they have been instrumental in determining the effect on the reaction rate of substituents in both the aldehyde and aromatic components. The reaction mechanism was postulated on considerations arising from these relative reaction rates and not from the kinetic orders. The similarity of the kinetic data obtained for the various para substituted aldehydes indicates that these reactions proceeded by the same mechanism and therefore the determination of relative reactivities has a sound basis.

EXPERIMENTAL^a

STANDARD PROCEDURE

After preliminary experiments showed that benzaldehyde could be condensed with a variety of aromatic compounds a uniform method of carrying out the reactions was adopted. This standard procedure was used unless otherwise stated.

First, the desired amount of p-toluenesulfonic acid monohydrate was weighed out to 0.02 g. and placed in a round bottom flask fitted with a thermometer well. The aromatic compound was then weighed out to the nearest decigram and sufficient solvent added to bring the solution to a standard volume of 250 ml. or 500 ml. minus the volume of the aldehyde to be added. The flask was then heated by means of a "Glas Col" electric heating mantle. A "Variac" adjustable transformer was used to control the temperature of the mantle and cause a rapid reflux of solvent. After all the water from the catalyst had been driven off and collected in the moisture trap, the reaction vessel was opened momentarily and a glass vial containing the liquid aldehyde was dropped in. The solid aldehydes were simply brushed in from a piece of glazed paper. In all experiments the aldehyde was weighed out to the nearest centigram. After the addition of the aldehyde to the refluxing benzene solution, the flask was swirled manually to insure a rapid and thorough mixing of the reactants. This whole operation from the time the flask

a. Microanalyses by Mrs. Mary Aldridge and Mr. Byron Baer.

was opened was accomplished within 10 to 15 seconds insuring an accurate zero-time for the reactions.

Before each run the moisture traps were treated with sulfuric acid-potassium dichromate cleaning solution and then thoroughly washed. When this cleaning was omitted the water formed in the reaction had a tendency to cling tenaciously to the walls of the moisture trap making accurate readings impossible. When the traps were clean it was found that the water clinging to the walls and in the condenser could be readily shaken loose by agitation of the liquid in the trap with a length of copper wire operated from the top of the condenser. In an effort to obtain a cleaner water separation one of the traps was treated with a silicone water-proofing compound. A trial experiment using this trap was then carried out. The water separating in the trap had no tendency to cling to the walls but unfortunately the meniscus curvature varied so much that accurate readings were impossible. Because of the failure of the silicone treatment, the trap was treated with alcoholic potassium hydroxide to remove the water proofing layer and conventional cleaning methods were adopted.

In practically all the runs made, benzene or toluene was used as the solvent. Both of these compounds are useful solvents for the reaction because they form minimum boiling azeotropic mixtures with water resulting in a rapid and efficient removal of water from the reaction mixture. The benzene used was the thiophene-free product of the Jones and

Laughlin Steel Corporation. It was distilled before use, discarding the first and last 15%. The fraction collected distilled at 80.0-80.1^ob (lit., 80.1^o); $n_D^{25} = 1.4982$, (lit., $n_D^{25} = 1.4981$). A purified grade of toluene obtained from the J. T. Baker Chemical Company was used. It was also distilled before use, and the cut boiling at 109.9-110.2^o (lit. 110.8^o) was collected; $n_D^{25} = 1.4939$ (lit., $n_D^{25} = 1.4937$).

The acid catalyst used throughout this research was p-toluenesulfonic acid. This compound is supplied in a pure form by the Eastman Kodak Co. as a monohydrate; m.p. 105-106^o (lit., 106-107^o). In order to ascertain the purity of the acid, two weighed samples were taken directly from the bottle without drying, dissolved in water, and titrated with standard alkali. Neutral equivalents of 190.5 and 190.1 were obtained. The theoretical value for $p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_3\text{H}\cdot\text{H}_2\text{O}$ is 190.2

THE REACTIONS OF PARA SUBSTITUTED BENZALDEHYDES WITH DIMETHYLANILINE

Using the standard procedure described in the previous section, 0.125 mole of various para substituted aldehydes was reacted with 0.625 mole dimethylaniline in the presence of 0.064 mole catalyst in 250 ml. of benzene solution. The dimethylaniline used was Eastman's pure grade. It was distilled before use, b.p. 85.0-85.1^o/13 mm; $n_D^{21.5} = 1.5696$,

- b. All melting points and boiling points given in this thesis except those measured in vacuo are corrected.
c. All distillations in vacuo carried out in this research were conducted in a nitrogen atmosphere.

(lit., $n_D^{20} = 1.5702$). After the reactions reached completion they were all worked up in a similar manner. First, the benzene solutions were extracted with 100 ml. of 5% potassium hydroxide solution to remove the catalyst as the potassium salt. The benzene layer was then washed with 100 ml. portions of water until the washings showed no alkalinity. Three washings were generally required. The benzene was then distilled off and finally the excess dimethylaniline was removed under reduced pressure. The reaction products were then either crystallized from the residue or distilled under reduced pressure.

Condensation of Benzaldehyde: Paragon's chlorine free benzaldehyde was washed with 5% sodium carbonate solution, dried over calcium chloride, and distilled just before use. Later, however, a titration of the acid in the benzaldehyde showed that the carbonate washing was unnecessary. Thereafter, the aldehyde was distilled directly, b.p. 178.0-179.0° (lit., 179°); $n_D^{20} = 1.5458$, (lit., $n_D^{20} = 1.5430$). Within three minutes after the distillation of the benzaldehyde it was weighed out and added to the reaction mixture. The rate data for the reaction are given in Table VI. A check run showed substantially the same rate of reaction. The temperature of the reaction mixture dropped from 92.9° to 90.9° over the first 80% of the reaction. The product was worked up in the standard fashion. The dark colored reaction residue remaining after removal of the benzene and excess amine was dissolved in 400 ml. of hot ethanol and permitted to cool

TABLE VI

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
80	0.14	610	1.14
125	0.30	655	1.21
190	0.44	770	1.33
250	0.58	850	1.40
310	0.67	1025	1.57
335	0.82	1210	1.68
430	0.88	1390	1.81
485	0.94	1570	1.91
560	1.08	3070	2.23

slowly. After standing overnight, a copious yield of white crystalline material had formed. These crystals were filtered, washed and dried. There was obtained 27.0 g. of product, m.p. 93.3-94.1° (lit., m.p. for leucomalachite green is 93°). From the mother liquor there was obtained 5.6 g. of a crystalline material which melted at 97-101.8°. This substance proved to be an allotropic form of leucomalachite green, (lit., m.p. 102°). When this higher melting form was recrystallized rapidly from hot alcohol, it was converted to the lower melting form. The total yield was 32.6 g. or 79% of theory. In subsequent runs it was found that the leucomalachite green could be more efficiently isolated by distillation from the reaction residues, b.p. 236-250°/1.5-2.0 mm. On recrystallization of the 97% yield of distillate from 200 ml. ethanol, there was obtained an 85% yield of pure product, m.p. 99.5-101°. The mother liquors were not worked up.

In order to gain some idea of the temperature coefficient of reaction, the benzaldehyde-dimethylaniline reaction was repeated at the same concentration using toluene instead of

benzene as a solvent. The reaction was carried out using the standard experimental procedure. The rate at which the water collected is given in Table VII.

TABLE VII

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
10	0.07		193	1.37	497
20	0.16		223	1.57	473
30	0.29		283	1.67	478
40	0.39		313	1.77	492
50	0.47	470	343	1.84	496
60	0.55	468	383	1.92	
78	0.70	476	443	2.02	
93	0.82	488	543	2.12	
108	0.92	486	873	2.20	
128	1.03	478	1083	2.21	
148	1.14	480	1413	2.21	
168	1.25	483			

The temperature decreased from 124.0° to 122.4° over the first 80% of reaction. This product was worked up in a manner identical to that described for leuco malachite green in the section on the reactions of para substituted benzaldehyde. The yield of pure crystalline product was 85%, m.p. 99.6-101.1°. A repeat experiment showed approximately this same rate of reaction, giving an average rate constant of 505 x 10⁻⁵ reciprocal minutes. After this duplicate run had reached completion, 50 ml. of a 1.471 N sodium hydroxide solution (0.0735 mole) was added to the reaction mixture and the solution shaken in a separatory funnel for several minutes. The aqueous layer was withdrawn and the benzene solution extracted once with 40 ml. water. The excess alkali in the combined

water layers was then titrated using phenolphthalein as an indicator with 1 N hydrochloric acid solution, 10.1 ml. being required to reach the end point. This titration accounted for 0.0735 minus 0.0101 or 0.0634 mole. Since 0.0640 mole of catalyst had been added originally, the titration showed that 99% of this acid was still present at the end of the reaction.

In order to determine the effect of catalyst concentration on the reaction rate, the above experiment was repeated using one-half as much catalyst. The reaction was carried out in the standard fashion by adding 0.125 mole of benzaldehyde to 0.625 mole of dimethylaniline in the presence of 0.032 mole catalyst in 250 ml. of benzene. The rate data are given in Table VIII. The first order rate constants are also included.

TABLE VIII

TIME (min.)	VOLUME (ml. H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml. H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
20	0.09		350	1.59	351
50	0.30	286	395	1.67	347
75	0.45	297	440	1.73	334
115	0.66	302	515	1.87	345
145	0.82	312	590	1.96	
170	0.98	336	785	2.12	
200	1.11	340	1325	2.27	
245	1.25	331	1460	2.27	
290	1.40	344			

Condensation of p-Chlorobenzaldehyde: The purified product of the Paragon Testing Laboratories was used directly in this reaction, m.p. 46.5-47.5°, (lit., m.p. 47.5°). The standard amount of aldehyde was weighed out and added to the refluxing reaction mixture. An examination of Table IX shows that a

more rapid rate was obtained than in the case of benzaldehyde itself.

TABLE IX

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
50	0.15	800	1.34
100	0.30	820	1.60
145	0.44	1090	1.83
190	0.58	1375	2.03
235	0.70	1615	2.13
290	0.82	2030	2.21
380	1.05	2290	2.26
430	1.10	2780	2.27

A check run showed that this experiment was closely reproducible. Over the first 80% of reaction, the temperature of refluxing mixture decreased from 93.1° to 91.0°. On completion of reaction, the mixture was worked up in the standard fashion and the leuco base distilled in vacuo. The product distilled at 235-245°/0.5 mm giving 40.9 g. of a light yellow distillate. This oil was crystallized by dissolving it in 400 ml. of hot ethanol followed by slow cooling. There was obtained 37.6 g. of white crystalline p-chloromalachite green m.p. 105-106° (lit., 98-99°).⁴⁴ The yield was 83% of theory. It was found that when the leuco base was crystallized directly from the residues, omitting the distillation step, the m.p. of the product was 97-99°.

Condensation of p-Dimethylaminobenzaldehyde: Eastman Kodak's pure grade of p-dimethylaminobenzaldehyde was found to have a melting point of 72.0-74.0° (lit., m.p. 74°). This product, however, was yellowish in color and was rather amorphous in appearance. To further purify this aldehyde, 100 g.

was dissolved in 700 ml. of 5% hydrochloric acid giving a dark colored solution. This solution was filtered, diluted with an equal volume of water and a 15% solution of sodium hydroxide was added slowly with vigorous mechanical stirring. The precipitated aldehyde was filtered, washed thoroughly and dried. The dried material was distilled from a 250 ml. Claisen type flask, b.p. 151-152°/5 mm. The distillate was dissolved in 100 ml. ethanol and then 400 ml. of water added slowly with stirring. The product came down as white granular crystals with a melting point of 73.5-74.5°. Fifty-five grams was obtained.

The standard amount of this aldehyde was weighed out and added to the refluxing mixture of catalyst, dimethylaniline and benzene in the standard fashion. This aldehyde showed the slowest reaction time of all the para substituted benzaldehydes studied. The rate data is given in Table X.

TABLE X

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
60	0.10	8,580	1.42
190	0.17	10,020	1.58
720	0.28	11,460	1.72
1,470	0.42	12,780	1.82
2,250	0.57	14,040	1.93
2,910	0.69	15,480	2.01
3,600	0.80	16,920	2.11
4,290	0.89	18,780	2.21
5,790	1.10	20,220	2.22
7,140	1.27	21,900	2.23

A repeat experiment duplicated the one above very satisfactorily. The temperature of the reaction mixture decreased

from 93.6° to 91.6° over the first 80% of reaction. On completion of the reaction, the mixture was worked up in the usual manner. No attempt was made to distill this product, however. Instead, 100 ml. of hot toluene was added to the residue after the excess dimethylaniline had been distilled off under reduced pressure. To this toluene solution was added 250 ml. of hot absolute alcohol. As the solution cooled a copious yield of crystals was obtained. After standing in the refrigerator for 24 hours, the solution was filtered giving 36.1 g. (77% of theory) of white crystals with a purplish tint. Melting point of product 166-171°, (lit. m.p. for leucocrystal violet 172-173°).⁹ This leuco base oxidized rapidly in air taking on a purplish color.

Condensation of Anisaldehyde: A purified grade of product of the Paragon Testing Laboratories was distilled in vacuo just before use, b.p. 91.0-91.4/17 mm; $n_D^{20} = 1.5781$ (lit., $n_D^{20} = 1.5731$).

The reaction with this aldehyde was found to proceed considerably slower than the similar reaction with benzaldehyde. The rate of reaction observed for this experiment is shown in Table XI. The rate data for a duplicate run were substantially the same. The temperature of the reaction mixture decreased from 92.9° to 92.0°. The solution after reaction completion was worked up in the standard fashion and distilled in vacuo from the residue. There was obtained 42.5 g. of distillate, b.p. 246-265°/0.5 mm. The light yellow distillate was crystallized from 200 ml. of hot ethanol and

TABLE XI

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
60	0.05	1815	1.27
95	0.11	2125	1.43
185	0.20	2255	1.48
260	0.28	2705	1.62
385	0.38	3075	1.74
550	0.53	3555	1.86
775	0.69	4245	2.00
955	0.82	4705	2.10
1165	0.95	5065	2.13
1405	1.09	5665	2.19
1595	1.20	7105	2.21

gave 88.2 g., 85% yield, of white crystalline leuco-p-methoxymalachite green, m.p. 104.6-106.1°, (lit., m.p. 106°).¹⁹

Condensation of p-Tolualdehyde: This aldehyde was prepared by R. Erickson, a student at this University. He synthesized it by a Gatterman-Koch synthesis from toluene, carbon monoxide, and hydrogen chloride in the presence of cuprous chloride and aluminum chloride.⁴⁵ Before this product was used, it was necessary to purify it via the bisulfite addition product, which was then thoroughly washed and decomposed with a suspension of sodium carbonate. The aldehyde was extracted with ether, dried and distilled just before use, b.p. 94.3-95.0°/20 mm, $n_D^{20} = 1.5448$ (lit., $n_D^{20} = 1.5454$). The p-tolualdehyde condensed with dimethylaniline under the standard conditions at a rate shown in Table XII. The temperature decreased uniformly from 93.1° to 91.1° over the first 80% of the reaction.

The product was worked up in the usual fashion and recrystallized from 450 ml. of ethanol. There was obtained

A repeat experiment duplicated this rate almost exactly.

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
15	0.14	215	1.32
25	0.21	255	1.47
30	0.42	285	1.55
65	0.54	345	1.69
85	0.65	395	1.83
105	0.73	450	1.93
120	0.93	545	2.06
155	1.06	695	2.18
185	1.19	1380	2.28

TABLE XIII

(see Table XIII).

Condensation of p-Nitrobenzaldehyde: The aldehyde used in this experiment was the pure grade supplied by the Eastman Kodak Co. This product, m.p. 106-106.5° (lit., m.p. 106.5°) was used without further purification. The experiment was carried out using the standard conditions, and was found to give a faster rate of reaction than any other aldehyde studied.

m.p. 94-96° (lit., m.p. 93-94°).¹⁵

an 80% yield (34.4 g.) of leuco-p-methylmalachite green,

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
60	0.11	955	1.20
120	0.22	1165	1.37
180	0.30	1350	1.50
240	0.40	1575	1.62
290	0.47	1830	1.73
380	0.60	2070	1.82
460	0.70	2750	2.00
540	0.79	3390	2.10
660	0.92	4320	2.18
780	1.05	6750	2.20

TABLE XII

The temperature decreased uniformly from 92.6° to 91.1° .

The product was worked up in the usual manner. The crude reaction mixture was taken up in 100 ml. of toluene and 125 ml. of hot ethanol added. On cooling a copious yield of brilliant golden-yellow crystals formed. The product was filtered and dried giving a 89% yield (41.6 g.), m.p. $182-183^{\circ}$, (lit., m.p. $178-177^{\circ}$).⁷

THE REACTIONS OF OTHER ALDEHYDES WITH DIMETHYLANILINE

In addition to the para substituted benzaldehydes a number of other aldehydes were reacted with dimethylaniline under the same standard reaction conditions.

Condensation of n-Heptaldehyde: A practical grade of heptaldehyde supplied by Paragon Testing Laboratories was fractionated through a 40 cm. column packed with glass helices at a reflux ratio of 5 to 1. The cut distilling from 152.0° - 155° was collected (lit., b.p. 152.8°); $n_D^{20} = 1.4125$, (lit., $n_D^{20} = 1.4131$). The standard amount of aldehyde (0.125 mole) was added to a refluxing solution of dimethylaniline and catalyst in benzene. The reaction started at about the same rate as the similar benzaldehyde run but decreased appreciably as the reaction progressed. The rate at which the water collected is shown in Table XIV. Values for the first and second order rate constants are also given. The reaction mixture was worked up in the usual manner and distilled in vacuo. An 80% yield of light yellow distillate was obtained,

TABLE XIV

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANTS	
		1st ORDER	2nd ORDER
10	0.12		
15	0.19		
30	0.26		
90	0.36	194	321
160	0.46	144	241
265	0.59	115	194
375	0.72	103	177
440	0.77	95	164
570	0.88	87	153
750	1.01	77	138
930	1.12	74	133
1245	1.27	67	123
1600	1.36	58	108
1810	1.45	57	108
2235	1.55	52	102
2820	1.66	47	73
3300	1.72	44	67
4280	1.77		
5700	1.83		
7140	1.87		
8580	1.88		

b.p. 206-218°/0.5 mm. On trituration with 40 ml. of ethanol crystallization started. The white crystalline 1,1-bis-(p-dimethylaminophenyl)heptane obtained amounted to 69% of theory, m.p. 58.5-59.0°, (lit., 59.5°).⁴⁶

The Condensation of Alpha-Branched Aliphatic Aldehydes

A practical grade of 2-ethylbutyraldehyde (Eastman Kodak Co.) was distilled slowly through a column packed with 8 inches of glass helices. The cut boiling at 116.3-116.4° was collected (lit., b.p. 116-117°); $n_D^{21} = 1.4010$, (lit., $n_D^{20} = 1.4025$). The standard amount of aldehyde was weighed out and the reaction with dimethylaniline carried out in the usual manner. The rate of collection of water was much slower than that in the corresponding n-heptaldehyde experi-

ment. The rate at which the reaction proceeded is shown in Table XV. The first order rate constants are also included.

TABLE XV

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANTS 1st ORDER x 10 ⁻⁵
15	0.06	
75	0.15	
205	0.20	
440	0.24	
1600	0.39	118
2235	0.43	95.8
2820	0.50	90.6
4280	0.63	75.9
5700	0.74	70.3
7140	0.85	66.8
8580	0.93	62.4
10,460	1.05	59.8
11,940	1.12	57.6
13,140	1.18	56.4
15,780	1.29	54.0
17,445	1.34	51.8

The reaction was shut down after reaching 60% completion because of excessive time requirements. The resulting reaction mixture was worked up in the standard fashion and the crude product distilled. There was obtained a 6 g. forerun, b.p. 95-105°/0.6 mm. This substance could not be any of the starting materials or the expected Baeyer condensation product. In all probability it is an aldol condensation product of the 2-ethylbutyraldehyde. It was not further identified. The main fraction amounted to 20.3 g., bp. 175-205°/0.5 mm and distilled as a pale yellow liquid. It crystallized readily from ethanol giving 20.0 g. of white crystalline solid, m.p. 60-85°. Recrystallization from 70 ml. of ethanol gave 13.0 g. of product which melted at 86-97°. Five grams

of the material was recrystallized three times to a constant melting point yielding 3.7 g. of pure product, m.p. 103.1-104.6°. A literature search revealed that this product 1,1-bis(p-dimethylaminophenyl)-2-ethylbutyraldehyde was a new compound.

Anal. Calcd. for $C_{22}H_{32}N_2$: C, 81.43; H, 9.93; N, 8.64.
Found: C, 81.70; H, 10.21; N, 9.07.

The condensation with 2-ethylbutyraldehyde was repeated using 0.128 mole of catalyst, double that used in the experiment above, in an attempt to speed up the rate of reaction. This increased catalyst concentration, however, resulted in only a slight increase in the rate of reaction, the half time being reduced from 8 to 6 days. After two weeks the reaction reached 90% completion and was still proceeding very slowly. At this point, however, the reaction was shut down and product worked up as before giving 29.2 g. of distillate, b.p. 180-212°/0.8 mm. This crude product amounted to 72% of theory and was not further purified.

Since the rate of condensation of 2-ethylbutyraldehyde in benzene solution was so slow, a higher boiling solvent, toluene, was substituted. It was also necessary to use an alpha-branched aliphatic aldehyde with a higher boiling point because the aldehyde used in the above experiment would distill from the reaction vessel in which toluene was the solvent. For this purpose, 2-ethylhexaldehyde was selected, b.p. 162.5-163°; $n_D^{22.5} = 1.4154$, (lit., b.p. 163°, $n_D^{20} = 1.4160$).

The experiment was carried out using 0.125 mole of aldehyde, 0.625 mole dimethylaniline, and 0.064 mole catalyst in 250 ml. of toluene solution. As expected, the reaction proceeded much more readily reaching the half-way point in 24 hours. The reaction reached 94% completion in 4 days. Unfortunately, it was found on working up the product in the usual manner and distilling the product, that no sharply defined fraction could be obtained. The distillation temperature rose steadily from 97 to 200°/0.6 mm. Crystallization could not be induced by trituration with ethanol. Apparently the higher temperature has increased the rate of the aldol-condensation side reaction more than it has the desired Baeyer condensation.

Condensation of Chloral: The use of chloral in carrying out the Baeyer reaction by the azeotropic method did not seem to be very promising in view of the low boiling point of chloral, its solubility in water, and the instability of many of the condensation products in presence of higher temperatures and acid concentrations. An experiment was made, however, in which chloral was reacted with dimethylaniline under the standard conditions used in studying the p-substituted benzaldehydes. The chloral, b.p. 96.7-97.2°(lit., b.p. 98°); $n_D^{22} = 1.4561$, (lit., $n_D^{20} = 1.4557$), was added to the refluxing reaction mixture and within an hour water had begun to collect in the moisture trap. The reaction proceeded smoothly for several hours acquiring a deep blue color. Soon after reaching the 50% completion mark, however, extensive decomposition began

to occur and a purplish-black tar deposited in the reaction vessel. After ten hours of reaction, a large amount of this viscous black tar had formed. No attempt was made to isolate any product.

The Condensation of Cinnamaldehyde: The cinnamaldehyde was distilled just before use, b.p. 185.0-185.5°/27 mm., $n_D^{22} = 1.6193$, (lit., $n_D^{20} = 1.6195$). The reaction, carried out in the usual manner, apparently proceeded in a normal fashion with liberation of 94% of the theoretical amount of water after 6 days. The reaction was half complete in about 20 hours but thereafter the rate fell off much more readily than for the similar experiment using benzaldehyde. The reaction mixture was worked up in the usual manner. No crystalline product could be obtained from the residue. On heating the residue to 310°/0.5-1.0 mm a small amount of black viscous distillate was obtained that could not be crystallized. The bulk of material, however, was not volatile even at this high temperature. Apparently polymerization had occurred.

THE REACTIONS OF VARIOUS AROMATIC COMPOUNDS WITH BENZALDEHYDE

Because of the wide variation in activity of various aromatic compounds in the Beeyer reaction, it was not possible to select one standard set of reactant and catalyst concentrations for all the reactions carried out. The same standard experimental procedure was used, however,

Condensation of Aniline with Benzaldehyde: Mallinckrodt's

pure grade of aniline was distilled in vacuo just before use, b.p. 90.0-90.8°/29 mm, n_D^{22} = 1.5840, (lit., n_D^{20} = 1.5863). The reaction was carried out by adding 0.125 mole of benzaldehyde to 0.625 mole of aniline and 0.008 mole of catalyst in 250 ml. of refluxing benzene solution. A rapid evolution of water occurred indicating anil formation. The reaction was 50% complete in less than 5 minutes. The reaction proceeded to 60% completion and stopped after a period of 8 hours. The product was worked up in the standard fashion. On distillation of the crude reaction product there was obtained 10.2 g. of yellow distillate b.p. 124-125°/1.8 mm. This distillate crystallized on cooling and on recrystallization from 20 ml. ethanol gave 8.0 g. (a 45% yield) of white crystalline benzalaniline, m.p. 52.0-52.5°, (lit., 51.0-52.0°). There was no higher boiling fraction and practically no distillation residue.

Condensation of N-Methylaniline and Benzaldehyde: A pure grade of methylaniline (Eastman Kodak Co.) was distilled before use, b.p. 196.5-197.0° (lit., b.p. 195.7°); $n_D^{21.5}$ 1.5696, (lit., $n_D^{21.5}$ = 1.5702). The reaction was carried out by adding 0.125 mole of benzaldehyde to 0.625 mole methylaniline and 0.008 mole catalyst in 250 ml. benzene solution. The reaction proceeded readily even with this small amount of catalyst. The rate at which water collected is shown in Table XVI. The first order rate constants based on the aldehyde are also given. The temperature of the reaction mixture decreased uniformly from 90.6° to 88.6° over the first 60% of reaction.

TABLE XVI

TIME (min.)	VOLUME (ml. H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml. H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
10	0.08		200	1.53	568
20	0.29		235	1.65	562
35	0.43		265	1.79	598
55	0.53	486	305	1.91	618
70	0.63	470	340	2.03	
105	0.96	528	400	2.07	
130	1.12	530	525	2.20	
155	1.26	530	625	2.25	
175	1.59	555	1530	2.27	

The mixture was worked up the standard fashion and the crude product distilled in vacuo, b.p. 225-242°/0.5 mm. The distillate amounted to 26.6 g. (70% of theory) of light yellow oil. The literature describes this compound, p,p'-bis(methylamino)triphenylmethane, as a very viscous noncrystallizable yellow oil.³⁹ A nitroso derivative was prepared by treatment of a hydrochloric acid solution of the amine with sodium nitrite in a freezing mixture. The solid material that formed was filtered, washed, and mixed with a small amount of water in an ice bath. Dilute sodium hydroxide solution was added slowly to alkalinity. The yellowish-green nitroso compound was extracted with ether, the ether evaporated and the residue recrystallized from ethanol. Yellow crystals were obtained which melted at 180-184°. The literature value, however, was 149° with decomposition. A sample of the aminotriphenylmethane was redistilled, b.p. 226-229°/0.5 mm., and submitted for analysis.

Anal. Calcd. for C₂₁H₂₂N₂: C, 83.40; H, 7.33; N, 9.27.

Found: C, 83.74; H, 7.45; N, 9.51.

The Condensation of Anisole with Benzaldehyde: A pure grade of anisole obtained from Paragon Testing Laboratories was distilled through an 8 inch column packed with glass helices. The cut distilling at 153-154° was collected, $n_D^{23} = 1.5180$ (lit., b.p. 153-154°; $n_D^{20} = 1.5179$). The condensation was carried out by adding 0.125 mole of benzaldehyde to 0.625 mole anisole and 0.064 mole p-toluenesulfonic acid in a total volume of 500 ml. of refluxing benzene. The rate at which the water collected is shown in Table XVII. The first order constants on the aldehyde are also given.

TABLE XVII

TIME (min.)	VOLUME (ml. H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml. H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
20	0.05		330	1.04	189
40	0.13		375	1.15	192
60	0.19	146	435	1.29	197
100	0.33	159	515	1.48	208
125	0.44	175	590	1.60	210
165	0.56	175	680	1.75	221
195	0.67	180	720	1.80	223
240	0.81	186	1350	2.18	
285	0.94	190	1575	2.23	
			1950	2.23	

A repeat experiment gave substantially the same reaction rate. The temperature of the reaction mixture decreased from 86.8° to 85.8° over the first 80% of the reaction. The acid catalyst was then removed by extraction with potassium hydroxide solution in the standard manner. The crude product was distilled in vacuo, b.p. 191-205°/0.8 mm., giving 26.6 g. (70% of theory) of a light pink distillate. There was left 8.0 g.

of a non-distillable residue. The distillate was crystallized from 25 ml. of a methanol-chloroform (1:1) mixture. The white crystalline material amounted to 23 g. (60%) of p,p'-dimethoxytriphenylmethane, m.p. 98-100.6°, (lit., 100-101°).¹⁷ From the mother liquor there was obtained 3 g. of white crystals which melted at 74-88°. Recrystallization of this material gave 1.5 g. of crystal, m.p. 85-96°. From the mother liquor of this latter crystallization there was obtained 1.1 g. of material which melted at 78-89°. This impurity is no doubt the isomeric p,o'-dimethoxytriphenylmethane, (lit., m.p. 94°).³⁰ The repeat experiment gave 28 g. (74% yield) of distillate.

The anisole-benzaldehyde condensation was also carried out using equivalent amounts of reactants, i.e., 0.125 mole of benzaldehyde and 0.250 mole of anisole, with 0.032 mole of catalyst in 250 ml. of benzene solution. This reaction reached 50% of completion in 20 hours and was complete in 3 days. Only a 30% yield of pure product was obtained upon distillation of the crude product. About one-half of the crude product was non-volatile refusing to distill at temperatures up to 250° at 0.5 mm. Since the yield of product was lowered by decreasing the concentration of anisole in the reaction mixture, another run was made using a large excess of anisole to ascertain the effect on the yield. This experiment was performed omitting the benzene and using excess anisole as the solvent. The aldehyde (0.125 mole) was added to 2.20 moles of anisole (238 g.) containing 0.032 mole of catalyst. This gave a total volume of 250 ml. exclusive of catalyst. The rate at

which the reaction proceeded is given in Table XVIII. The first order rate constants are also given.

TABLE XVIII

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
20	0.10	211	170	1.19	443
40	0.28	330	190	1.29	450
50	0.37	360	210	1.40	464
60	0.46	421	230	1.50	478
70	0.54	394	250	1.59	501
80	0.61	395	280	1.68	491
90	0.68	405	310	1.78	506
100	0.76	412	340	1.87	523
110	0.84	426	400	1.98	532
130	0.97	435	430	2.03	542
150	1.08	438	520	2.13	560
			1345	2.20	

It was found on distillation of the product that the yield was significantly increased over the reactions in which smaller amounts of anisole were used. There was obtained a 77% yield of *p,p'*-dimethoxytriphenylmethane, m.p. 99.6-101.1°.

Condensation of Phenetole with Benzaldehyde: A purified grade of phenetole (Eastman Kodak Co.) was distilled before use, b.p. 159.5-160.6 (lit., b.p. 172°) $n_D^{22} = 1.5062$ (lit., $n_D^{20} = 1.5080$). This reaction was carried out by the addition of 0.125 mole of benzaldehyde to 0.625 mole of phenetole and 0.064 mole of catalyst in 500 ml. of benzene. The rate at which the water collected is shown in Table XIX. A comparison of this table with Table XVII shows that phenetole reacts more rapidly than does anisole under the same conditions. The temperature decreased from 87.1° to 86.3° over the first

TABLE XIX

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
10	0.08		235	1.06	270
20	0.13		265	1.16	275
30	0.19		295	1.27	281
50	0.30	285	335	1.37	279
75	0.42	276	385	1.50	285
100	0.52	274	440	1.65	300
130	0.66	267	525	1.77	294
170	0.80	257	590	1.88	
200	0.92	263	635	1.90	
			1290	2.21	

80% of reaction. A duplicate experiment gave substantially the same rate of reaction.

The reaction mixture was worked up in the usual manner and the crude product distilled at reduced pressure. There was obtained 32.0 g. (77% of theory) of a light orange distillate, b.p. 196-204°/0.5 mm. The distillation residue was 5.9 g. The distillate could not be made to crystallize by tritubation with methanol-chloroform mixture. This same solvent mixture had brought about the rapid crystallization of the corresponding anisole condensation product. Treatment with other solvents such as ethanol, benzene, and ligroin also failed to bring about crystallization. The expected product *p,p'*-diethoxytriphenylmethane has not been previously reported in the literature. About 5 g. of the distillate was thoroughly shaken with hot 50% alcoholic potassium hydroxide solution. Apparently none of the oil dissolved. The aqueous layer was then withdrawn and divided into two parts. One of these solutions was neutralized by slow addition of

dilute hydrochloric acid and the other by saturation with carbon dioxide. In neither case did any organic material separate. Apparently none of the ethoxy groups split off under the acid conditions used to give phenolic type compounds. Another sample of distillate was redistilled for analyses, b.p. 196.0-196.1°/0.5 mm.

Anal. Calcd. for $C_{23}H_{24}O_2$: C, 83.10; H, 7.28. Found: C, 83.01, 83.11; H, 7.37, 7.33.

Condensation of n-Butyl Phenyl Ether: A pure grade of the Eastman Kodak Co.'s n-butyl phenyl ether was distilled before use, b.p. 207.4-208.0° (lit., b.p. 206°) $n_D^{26} = 1.4933$ (lit., $n_D^{26} = 1.5019$)⁴⁷. Because of the wide variation of the observed refractive index from the literature value, this ether was also prepared synthetically. The synthesis was carried out by N. Sharpless, a student at this University, by the reaction of sodium phenolate with butyl bromide in aqueous solution. This product had substantially the same physical constants as for the ether given above. They were b.p. 207.4-208.4°, $n_D^{26} = 1.4940$.

The condensation was carried out by the addition of 0.125 mole of benzaldehyde to 0.625 mole of the synthetic n-butyl phenyl ether and 0.064 mole catalyst in 500 ml. of benzene. This rate data and first order rate constants are given in Table XX. This rate was corroborated by a similar run. A comparison of the table with the corresponding ones for anisole and phenetol, XVII and XIX shows that n-butyl phenyl ether is the most reactive.

TABLE XX

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
10	0.05		175	1.11	389
20	0.13		200	1.24	412
30	0.21	330	230	1.35	398
40	0.30	357	260	1.48	413
50	0.35	341	290	1.61	433
60	0.45	372	320	1.74	463
80	0.56	359	350	1.83	482
100	0.69	368	490	2.07	
120	0.80	368	595	2.18	
150	0.98	382	640	2.22	

The temperature decreased from 87.3° to 86.8° over the first 80% of the reaction.

The reaction mixture was worked up in the standard manner and the crude product distilled. There was obtained 33.7 g. (70% of theory) of light orange distillate, b.p. 234-246°/1.0 mm. Like the similar product from phenetole it could not be made to crystallize by treatment with various solvents. A literature survey showed that this product, dibutoxytriphenylmethane had not been previously reported. It was redistilled for an analytical sample, b.p. 225-227°/0.5 mm.

Anal. Calcd. for C₂₇H₃₂O₂: C, 83.46; H, 8.30. Found: C, 83.39, 83.18; H, 8.31, 8.26.

Condensation of Phenol with Benzaldehyde: A chemically pure grade of phenol (Baker's) was distilled in vacuo before use, b.p. 72.0-72.5°/10 mm. After distillation it had a melting point of 41.0-41.1° (lit., m.p. 41°). The reaction was carried out by the addition of 0.125 mole of benzaldehyde to 0.625 mole

of phenol and 0.008 mole of catalyst in 500 ml. benzene. Phenol was found to react much more readily than any other aromatic compound studied. The rate data are given in Table XXI. The first order rate constant based on benzaldehyde are also given.

TABLE XXI

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
15	0.12		115	1.40	84.8
25	0.25		125	1.52	90.2
35	0.40		135	1.63	95.4
40	0.47	58.8	145	1.71	98.5
45	0.53	58.4	155	1.81	105
55	0.67	64.5	165	1.90	
65	0.80	68.0	175	1.97	
75	0.93	71.3	195	2.10	
85	1.06	75.1	215	2.21	
95	1.17	77.2	230	2.25	
105	1.30	82.3	230	2.25	

The reaction mixture was worked up in the usual manner. To the residue, after removing excess phenol, was added 40 ml. of chloroform. Crystals formed slowly over the course of three days. There was obtained 3.5 g. of orange-white crystals, m.p. 138-143°. From the mother liquor an additional 2.5 g. were obtained. No more solid product could be crystallized from the mother liquors. The two solid fractions, were recrystallized from 10 ml. chloroform yielding 4.9 g. (14% of theory) of white crystals, m.p. 157-159.5° (lit., m.p. 160-161°).¹⁴

The Condensation of Toluene with Benzaldehyde: Because of the low reactivity of this hydrocarbon in Baeyer type condensations

the reaction was carried out using excess toluene as a solvent. The benzaldehyde (0.125 mole) was added to 2.57 moles of refluxing toluene containing 0.128 mole of catalyst. The total volume was 250 ml. The rate at which the water collected and the first order rate constants are given in Table XXII.

TABLE XXII

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (1st ORDER x 10 ⁻⁵)
70	0.08		3130	0.96	178
130	0.10		4165	1.30	207
220	0.14		4615	1.44	221
340	0.18		5020	1.55	233
460	0.21		5560	1.73	263
1285	0.45	174	6040	1.85	286
1540	0.53	173	6490	1.96	
1750	0.59	175	7030	2.08	
2740	0.84	170	7735	2.20	

The temperature decreased from 115.9° to 115.2° over the first 80% of the reaction. The product was worked up in the usual fashion and distilled in vacuo, b.p. 156-157°/0.7 mm.

The yield amounted to 25.2 g. or 74% of the theoretical amount of dimethyltriphenylmethanes. After trying many different solvents, the product was finally crystallized from 150 ml. methanol. There was obtained 13 g. of p,p'-dimethyltriphenylmethane, m.p. 48-49° (lit., m.p. 52°, 54°). No more crystals could be obtained from the mother liquor. In all probability the rest of the product is the isomer, p,o'-dimethyltriphenylmethane.

Condensation of Other Aromatic Compounds. In addition to the condensation of the aromatic compounds already discussed,

several other reactions were carried out in which mesitylene, p-xylene, and hydroquinone dimethyl ether were condensed with benzaldehyde. None of these substances led to the expected products when condensed by this azeotropic method.

Mesitylene was reacted by adding 0.125 mole of benzaldehyde to 1.67 moles of refluxing mesitylene containing 0.128 mole catalyst. The total volume was 250 ml. The reaction was complicated by the fact that the catalyst apparently reacted with the mesitylene even before the aldehyde was added, turning the solution black in color. The reaction proceeded to completion, however, liberating the theoretical amount of water in 160 minutes. The mixture was worked up in the usual manner and the product distilled in vacuo. Only one fraction was obtained, b.p. 110-127°/0.6 mm. This amounted to about 10 g. of sulfur-free distillate of unknown composition. The rest of the product was non-distillable at temperatures up to 250°/0.6 mm. Apparently none of the expected hexamethyltriphenylmethane was formed in the reaction.

The condensation of p-xylene with benzaldehyde was also complicated by an apparent reaction of the catalyst with the p-xylene. The reaction was carried out by addition of 0.125 mole benzaldehyde to the black-colored solution of 0.128 mole of catalyst in 1.91 moles of p-xylene. The total volume exclusive of catalyst was 250 ml.

The reaction proceeded readily giving 125% of the theoretical amount of water after 3 days. The acid catalyst apparently has condensed to give the excess water. The reac-

tion mixture was worked up the standard fashion and distilled in vacuo giving 28.3 g. of viscous white distillate, b.p. 150-182°/0.5 mm. This distillate was crystallized from 90 ml. of ligroin (90-100°) and yielded 15.0 g. of white crystals, m.p. 86-89°. A sodium fusion analysis showed a strongly positive test for sulfur. No further work was done on this fraction. From the mother liquor there was obtained an additional 6 g. of crystalline product, which contained no sulfur compounds, m.p. 88-99°. This product melts too high to be the expected *o,o',m,m'*-tetramethyltriphenylmethane which melts at 92.5°. The above experiment was repeated omitting the aldehyde, but no appreciable reaction of catalyst and *p*-xylene occurred within the period of 4 days. It seemed likely that a sulfone could be synthesized in this manner, since one somewhat similar method reported in the literature consists of blowing hot aromatic hydrocarbon vapors into molten benzene or toluene sulfonic acids at temperatures of 140-180°. ⁴⁸

The disubstituted aromatic compound, hydroquinone dimethyl ether, was also condensed with benzaldehyde. The reaction was carried out by adding 0.0625 mole of benzaldehyde to 0.3125 mole of hydroquinone dimethylether and 0.032 mole catalyst in a total of 125 ml. of benzene solution. The reaction was much slower than the corresponding reaction with anisole. The half-time of the reaction was about 24 hours. The theoretical amount of water was collected after a period of 3 days. The reaction mixture was worked up the usual manner. The crude residue was taken up in 70 ml. of methanol-

chloroform mixture giving a dirty green solution. The solution was evaporated to 35 ml., permitted to cool, and was placed in the refrigerator. After one day a small amount of greenish white solid material had formed. This substance melted over a wide range from 120-180°. The expected product, *o,o',m,m'*-tetramethoxytriphenylmethane has a melting point of 74°. The substance obtained in this reaction is obviously some other product.

ADDITIONAL EXPERIMENTS USED IN THE STUDY OF THE MECHANISM

The Effect of Varying the Ratio of Reactants: Three experiments were performed in which different amounts of benzaldehydes were condensed with 0.625 mole dimethylaniline in the presence of 0.032 mole catalyst in 500 ml. of toluene solution. The rate data for these three experiments are summarized in Table XXIII. The temperature for the three runs over the first 80% of the reaction were: Run 1, 117.7° to 116.7°; Run 2, 118.6° to 116.9°; Run 3, 119.3° to 118.3°. The data from this table was used in calculating first and second order rate constants as described in the discussion. The various order constants for all three runs at various times are given in Table XXIV.

The intermediate, *p*-methoxybenzhydrol was prepared by N. Sharpless, a student at this University. He synthesized it by a Friedel-Crafts reaction of anisole and benzoyl chlor-

TABLE XXIII

TIME (min.)	RUN 1	RUN 2	RUN 3
	0.0625 mole aldehyde	0.125 mole aldehyde	0.250 mole aldehyde
	VOLUME (ml.H ₂ O)	VOLUME (ml.H ₂ O)	VOLUME (ml.H ₂ O)
60	0.07	0.14	0.25
100	0.14	0.25	0.38
145	0.21	0.37	0.55
190	0.27	0.48	0.71
235	0.34	0.55	0.85
295	0.41	0.66	1.06
355	0.50	0.79	1.20
430	0.55	0.89	1.38
520	0.64	1.01	1.57
610	0.73	1.14	1.72
700	0.82	1.24	1.84
790	0.85	1.35	1.98
940	0.92	1.49	2.16
1120	0.98	1.65	2.36
1330	1.05	1.78	2.56
1525	1.08	1.89	2.75
1730	1.09	2.00	2.94
2140	1.11	2.10	3.18
2770	1.12	2.22	3.47
4360		2.22	3.96
6010			4.22
7450			4.34
8770			4.38

ide followed by a sodium amalgam reduction of the ketone formed. The product was obtained as white crystals which melted at 66.5-67.5° (lit., m.p. 68°).

Alkylation with p-methoxybenzhydrol: The reaction was carried out by adding 0.125 mole of p-methoxybenzhydrol to 0.500 mole anisole and 0.064 mole of catalyst in a total volume of 500 ml. benzene. A very rapid evolution of water ensued. See Table XXV.

TABLE XXV

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
2	0.16	7	1.49	16	2.14
3	0.48	8	1.65	20	2.20
4	0.90	9	1.74	30	2.25
5	1.14	11	1.86	45	2.25
6	1.34	13	2.03	90	2.25

The temperature increased from 83 to 85° during the course of reaction. This table should be compared to Table XVII where the rate data for the similar run with benzaldehyde is given. The mixture was worked up in the usual manner and distilled in vacuo, b.p. 170-196°/0.3 mm. On recrystallization from 40 ml. of a methanol-chloroform mixture there was obtained 26 g. (68% of theory) of p,p'-dimethoxytriphenylmethane, m.p. 99-100° (lit., m.p. 100-101°). From the mother liquor there was obtained almost a gram of a lower melting solid fraction, m.p. 79-89° which is probably the isomer, p,o'-dimethoxytriphenylmethane.

PART II

A STUDY OF THE FORMATION OF
BENZALDEHYDE ACETALS

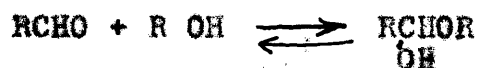
INTRODUCTION

Both aliphatic and aromatic aldehydes react readily with alcohols in the presence of acid catalysts to yield acetals. It is believed that an intermediate hemiacetal is initially formed, followed by further reaction with the alcohol to give the acetal. These hemiacetals have been isolated in a number of cases where they are solids. Thus equal molar amounts of chloral and cyclohexylalcohol will react at 2° to give a hemiacetal which crystallizes upon standing for three days.⁴⁹

There is some evidence that a hemiacetal forms instantly and almost quantitatively on mixing an aldehyde and alcohol. This possibility was demonstrated by Adkins and Broderick who mixed heptaldehyde and ethanol in various molar ratios and then measured the refractive indices.⁵⁰ They then plotted these indices versus the mole ratios and found that the maximum divergence from the ideal solution straight line was obtained at a molar ratio of one to one. It was concluded, therefore, that the aldehyde and alcohol reacted almost quantitatively to form a hemiacetal. The same result was obtained for the following aldehyde-alcohol pairs: acetaldehyde, isopropanol; acetaldehyde, ethanol. Four other alcohol systems were studied but they did not give curves diverging enough from the ideal curve to give any

conclusive results.

After concluding that aldehydes and alcohols did react rapidly and quantitatively to form hemiacetals, Adkins was able to treat acetal formation as a second order reaction involving the hemiacetal and alcohol.⁵¹ The first rapid step was expressed:



The second or rate controlling step was then:



By letting a equal the original concentration of hemiacetal, b the original concentration of alcohol, and x the concentration of acetal at any time t, a differential equation expressing the overall rate for the reaction was written:

$$\frac{dx}{dt} = k_1(a-x)(b-x) - k_2x^2$$

The equilibrium constant for the above reaction was : $K = \frac{k_1}{k_2}$.
Substituting in the above differential equation gives:

$$\frac{dx}{dt} = k_1(a-x)(b-x) - \frac{k_1x^2}{K}$$

The concentration of aldehyde at the various reaction intervals was determined by withdrawing an aliquot portion, adding a 10% solution of sodium sulfite, and titrating the alkalinity produced. The concentration of aldehyde at equilibrium was also determined and the equilibrium constant, K, evaluated. In this manner second order rate constants were determined for a variety of reactions employing different aldehydes and alcohols.

The "Constants" obtained in this manner, however, were found to drift rapidly toward lower values as the reaction progressed. Adkins was not able to satisfactorily explain these drifts but gave as one possibility the poisoning effect on the catalyst by the water formed in the reaction. By the use of an empirical equation, however, Adkins was able to obtain fairly good rate constants and thus was able to make rough comparisons of reaction rates when primary, secondary, and tertiary alcohols were reacted with a given aldehyde.⁵² In general, Adkins found that secondary alcohols reacted faster than primary alcohols and that tertiary alcohols reacted even faster. Thus the reaction of n-butyl, sec-butyl, and tert-butyl alcohols with acetaldehyde, gave experimental second order rate constants of 2.68, 4.64 and 11.34 respectively.

If the poisoning effect of water was responsible for Adkins inability to obtain rate-constants, the azeotropic method used in Part I of this thesis should eliminate this difficulty and perhaps demonstrate that the reaction is actually second order. Certain cyclic acetals have been prepared by carrying out the reactions in refluxing benzene and removing the water azeotropically but apparently, no attempt was made to utilize the method in making a comparison of reaction rates.⁵³

The object of this part of this investigation was twofold: first, to compare the effect of various alcohols on the rate of acetal formation, and second, to determine if

the rate data obtained would indicate that the reaction is second order.

Preliminary experiments showed that acetals could be prepared in relatively dilute benzene solution with very small amounts of acid catalyst. Other experiments designed to show the relative reactivity of various alcohols were then carried out and are described in the following section of this thesis.

DISCUSSION

A discussion of the general procedure and apparatus used in carrying out condensation reactions azeotropically was given in Part I of this thesis. The precautions that must be observed in making relative rate studies with regards to solvents, reactants, and catalysts were also discussed.

In one of the preliminary experiments carried out, 0.13 mole of benzaldehyde was added to 0.39 mole of n-butyl alcohol in the presence of 0.1 g. of p-toluenesulfonic acid in a total volume of 500 ml. of refluxing benzene solution. The initial rate of reaction was very rapid reaching the 50% completion stage within 55 minutes. Thereafter the reaction slowed considerably and then ceased at 81% reaction completed. Apparently the wet benzene flowing back into the reaction vessel from the moisture trap contained enough water to reverse the reaction and stop it. An eight inch column packed with porcelain saddles was then placed between the reaction flask and moisture trap to prevent the saturated benzene from reentering the flask. The reaction then proceeded to completion liberating the theoretical amount of water. After the reaction was completed, 15 mg. of metallic sodium was added to neutralize the acid catalyst. The benzene was distilled off and the excess butyl alcohol removed under reduced pressure. The acetal was then distilled in vacuo giving a 90% yield of product.

After it was demonstrated that acetals could be satis-

factorily prepared by the azeotropic method, a standard set of reaction conditions was selected for a study of the relative rates of reaction of six different alcohols with benzaldehyde. The standard amounts of reactants selected were: 0.125 mole of benzaldehyde, 0.375 mole of alcohol, 0.0005 mole of p-toluenesulfonic acid catalyst all dissolved in sufficient benzene to give 1 liter of solution. This large volume of benzene was used to insure a constant reaction temperature in the different runs. The use of the excess benzene also gave more dilute solutions thus resulting in a more suitable environment for a determination of the kinetic order of reaction.

In all reactions an eight inch column, packed with porcelain saddles was used between the reaction flask and the moisture trap. Under the standard conditions given above the following alcohols were reacted with benzaldehyde: n-butyl, n-hexyl, n-heptyl, n-decyl, iso-butyl and sec-butyl. It was found that all of the primary alcohols reacted at about the same rate throughout the whole course of reaction. The temperature of all of the refluxing solutions was $89.1^{\circ} \pm 1.5^{\circ}$ at all stages of reaction. The yields of acetal ranged from 88% to 95%. Secondary butyl alcohol, on the other hand showed a much slower rate of reaction and gave only a 35% yield. This observation is the opposite of that made by Adkins and discussed in the introduction. Tertiary butyl alcohol would not give an acetal under these conditions but instead dehydrated yielding isobutylene. A comparison of the

rates of reaction of all these alcohols (except tert-butyl) is given in Figure 2.

By assuming rapid hemiacetal formation it was possible to treat the reaction as a second order reaction of hemiacetal and alcohol. Since the water is removed as the reaction progresses, the reverse reaction was ignored in making the rate calculations. The equation used in making these calculations in an integrated form is:

$$k = \frac{2.3}{t(a-b)} \log \frac{b(a-x)}{a(b-x)}$$

In this equation a is the original concentration of aldehyde, b the original concentration of hemiacetal, and x the concentration of acetal at any time t. On substitution of the rate data from the reaction of the primary alcohols into the equation, it was found that the "constants" drifted markedly toward lower values. For a run with hexyl alcohol, for example, the "constants" fell from 0.045 to 0.010 over the 20% to 80% portion of the reaction.

One possible explanation of the failure to obtain better constants is that the reverse reaction of acetal and water is exerting an influence on the overall rate. In making the calculations, this reverse reaction was ignored, but if any water remained in the refluxing benzene mixture, an error could be introduced. That the reverse reaction is very rapid was demonstrated by adding a definite small quantity of water to one of the refluxing reaction mixtures after it had reached 99% completion. The water did not distill over immediately

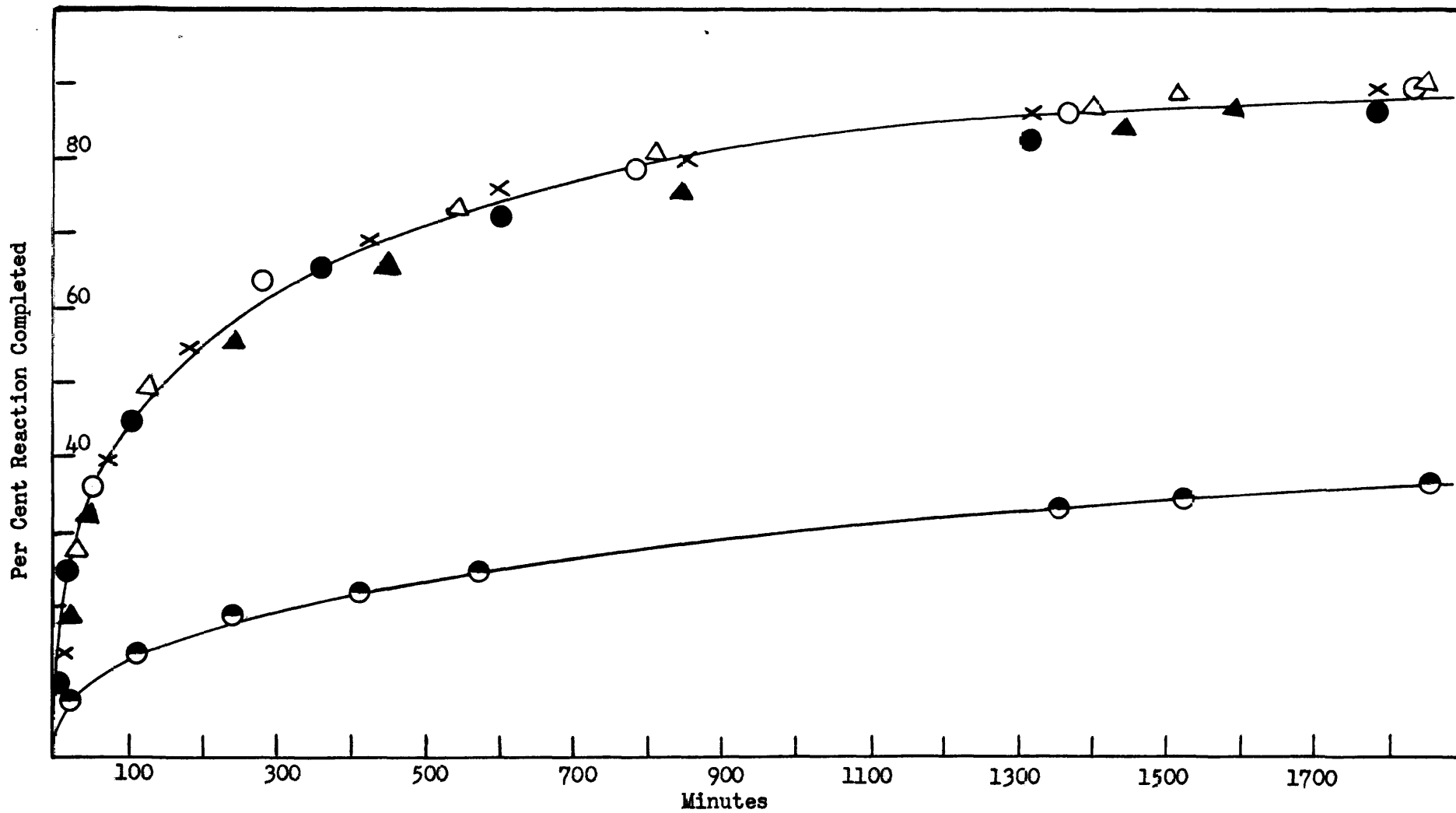


Figure 2 - Rate of Acetal Formation: ● n-butyl, × n-hexyl, ○ n-heptyl, △ n-decyl, ▲ iso-butyl, ○ sec-butyl.

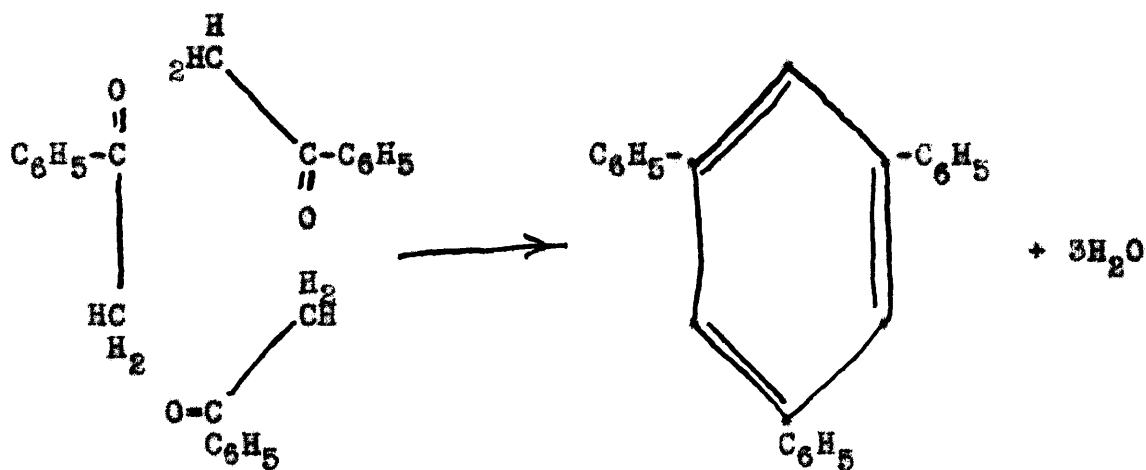
but apparently reacted with the acetal. The water was then collected slowly over a period of about 20 hours and the acetal was again formed. This experiment indicates that the reverse reaction of acetal and water cannot be ignored in determining reaction rate constants by this method.

Another possible reason for the failure to obtain rate constants is that a hemiacetal may not be formed quantitatively on mixing the aldehyde and alcohol as was postulated by Adkins. The evidence for this assumption, which was discussed in the Introduction, is not very conclusive. In order to test the validity of this basic assumption an experiment was carried out in which 0.25 mole of benzaldehyde was reacted with 0.25 mole of n-hexyl alcohol. If a hemiacetal is formed quantitatively as postulated by Adkins there should be no alcohol left to react with the hemiacetal and no reaction should occur. It is found, however, that acetal formation occurred readily liberating 90% of the theoretical amount of water. The yield of acetal obtained was 80% of the theory. The excess benzaldehyde was recovered.

This experiment indicates that a hemiacetal is not formed quantitatively simply on mixing an aldehyde and an alcohol at a temperature of 65°. In view of this fact the failure to obtain second order constants is not surprising. The failure of Adkins to obtain satisfactory constants may well be attributed to this same basic error. This complication together with the above demonstration that added water was removed only very slowly made it seem inadvisable to pur-

sue further the study of the order of the reaction by this method.

By means of the azeotropic method an acetal from benzaldehyde and crotyl alcohol was successfully prepared in an 82% yield without any polymerization. The rate was about the same as for the other primary alcohols. An attempt was also made to prepare a n-butyl ketal of acetophenone. Only a small amount of ketal was formed, however. A side reaction occurred in which the acetophenone condensed with itself to give sym-triphenyl benzene. The existence of this side reaction indicates that the azeotropic method may prove of value in carrying out still other types of condensation reactions. A run was made in which acetophenone was condensed with itself in the presence of acid catalyst but in the absence of any alcohol. A 68% yield of sym-triphenyl benzene was obtained.



EXPERIMENTAL

In all the following acetal experiments the same type of apparatus was used as that described in Part I except that a column, 8 inches in height and one-half inch in diameter, and which was packed with porcelain saddles was inserted between the reaction vessel and the moisture trap. When this column was not used the reaction would not proceed more than 80% to completion.

The Reaction of Primary and Secondary Alcohols with Benzaldehyde: In order to study the effect of chain length of the alcohol on the reaction rate, n-butyl, n-hexyl, n-heptyl and n-decyl alcohol in concentrations of 0.375 molar were reacted with 0.125 molar benzaldehyde in the presence of 0.0005 molar catalyst in a total volume of 1000 ml. of benzene solution. Sec-butyl alcohol was also reacted under these conditions in order to compare the rate of secondary alcohols to that of the primary alcohols. The rate at which the n-hexyl acetal was formed is shown in Table XXVI. The second order rate constants, calculated as described in the previous section are also given.

The other four primary alcohols gave very similar rate tables. A comparison of the rates has been given in Figure 2.

After the reaction of n-hexyl alcohol with benzaldehyde had reached 99% completion, 0.987 g. of water was weighed out in a small vial and dropped into the refluxing reaction mixture. This water did not immediately distill into the

TABLE XXVI

TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (2nd order)	TIME (min.)	VOLUME (ml.H ₂ O)	RATE CONSTANT (2nd order)
10	0.18		360	1.50	0.015
15	0.31		425	1.55	0.014
20	0.59	0.040	600	1.69	0.012
30	0.55	0.045	850	1.79	0.010
40	0.63	0.035	1320	1.93	0.0084
55	0.73	0.032	1735	2.00	0.0072
75	0.88	0.030	2205	2.03	
105	1.02	0.028	2775	2.10	
135	1.12	0.024	3225	2.13	
180	1.25	0.021	3685	2.15	
240	1.33	0.018	5645	2.20	
300	1.43	0.017	6355	2.22	

moisture trap. The only reasonable explanation of the disappearance of the water is that it has reacted rapidly with the acetal to give the hemiacetal and alcohol. This added water was then slowly removed by continued refluxing of the solution for many hours. At the end of 24 hours 80% of the added water had been removed and in another day 95% was collected. The product was then worked up by the standard procedure given below.

All of these acetals were isolated from the reaction mixtures in the same fashion. First the benzene was distilled off to a residual volume of 200 ml. at atmospheric pressure. This solution was then extracted once with 100 ml. of 5% sodium carbonate solution. The acetals were then separated from the remaining benzene and excess alcohol by distillation under reduced pressure.

A literature search revealed that all of these acetals were new compounds with the exception of the benzaldehyde

dibutyl acetal. A summary of the physical constants of the five primary alcohols used, the yields obtained and the analyses is given in Table XXVII.

The reaction with the sec-butyl alcohol was only 67% complete after 6 days. The rate curve for the first 37% of reaction is given in Figure 2. The yield of benzaldehyde di-sec-butyl acetal was only 39%, b.p. 72°/0.5 mm. Because of the poor yield, the acetal was not further characterized by analysis.

The Reaction of Tertiary Butyl Alcohol with Benzaldehyde:

The benzaldehyde (0.125 mole) was added to 0.375 mole of tert-butyl alcohol and 0.0035 mole of catalyst in 500 ml. of benzene solution. In this experiment a dry ice trap was connected to the top of the condenser to collect any volatile reaction products. Practically no reaction had occurred after a period of three hours. To speed up the rate of reaction, therefore, sufficient catalyst was added to give a total of 0.008 mole. Within two hours a considerable amount of water started to collect in the moisture trap and some volatile material was found in the dry ice trap. After two days a total of 6.53 ml. of water had collected. The theoretical amount of water for acetal formation is only 2.25 ml. whereas the dehydration of the tert-butyl alcohol would give 3.75 ml. of water. In the dry ice trap there was found 16.5 g. (80%) of isobutylene. On working up the product in the usual manner, there was recovered 91% of benzaldehyde. No acetal was found.

The Reaction of n-Hexyl Alcohol with Benzaldehyde in 1 to 1

TABLE XXVII

ALCOHOL	PHYSICAL CONSTANTS OF ALCOHOL	PHYSICAL CONSTANTS OF THE BENZALDEHYDE ACETALS	YIELDS	ANALYSIS
n-butyl	b ₂₈ 117.8-118.0° n _D ²⁵ 1.3980 (lit.) b ₂₈ 117.7° n _D ²⁵ 1.3974	b ₂₈ 85-87°/0.4 mm; n _D ²⁵ 1.4732 (lit.); b.p. 149-150°/14 mm; n _D ²⁵ 1.4790	89%	Calcd. for C ₁₉ H ₃₂ O ₂ : C, 78.03; H, 11.03. Found: C, 77.97, 78.27; H, 11.29, 11.30
n-hexyl	b ₂₈ 156.8-157.8° n _D ²⁵ 1.4174 (lit.) b ₂₈ 157.2° n _D ²⁵ 1.4176	b ₂₈ 139-140°/1.0 mm n _D ²⁵ 1.4744	95%	Calcd. for C ₂₁ H ₃₆ O ₂ : C, 78.84; H, 11.34. Found: C, 78.72; H, 11.41, 11.68.
n-heptyl	b ₂₈ 174.8-175.5° n _D ²⁵ 1.4225 (lit., b.p. 175; n _D ²⁵ 1.4222)	b ₂₈ 164.5-165.3°/1.3 mm n _D ²⁵ 1.4753	89%	Calcd. for C ₂₇ H ₄₈ O ₂ : C, 80.2; H, 11.97. Found: C, 80.12, 80.24; H, 12.19, 12.14
n-decyl	b ₂₈ 122-123/13 mm; n _D ²⁵ 1.4365 (lit., b.p. 120/12 mm; n _D ²⁵ 1.4368)	b ₂₈ 212-215°/1.0 mm n _D ²⁵ 1.4720	92%	Calcd. for C ₁₅ H ₂₄ O ₂ : C, 76.23; H, 10.23. Found: C, 75.84, 76.35; H, 10.20, 10.40
iso-butyl	b ₂₈ 107.0-107.9° n _D ²⁵ 1.3949 (lit., b.p. 107°; n _D ²⁵ 1.3939)	b ₂₈ 93-95°/0.4-0.7 mm n _D ²⁵ 1.4715	88%	

Molar Ratios: To 500 ml. of refluxing benzene solution containing 0.0005 mole catalyst and 0.250 mole n-hexyl alcohol was added 0.250 mole of benzaldehyde. The rate data for this reaction is given in Table XXVIII.

TABLE XXVIII

TIME (min.)	VOLUME (ml.H ₂ O)	TIME (min.)	VOLUME (ml.H ₂ O)
5	0.23	280	1.53
10	0.38	415	1.66
20	0.58	625	1.75
35	0.76	1360	1.92
80	1.11	1840	1.96
100	1.19	2800	2.04
165	1.33	3040	2.05

The product was worked up in the usual manner. Distillation of the residues gave 19 g. of forerun which was mostly benzaldehyde, b.p. 100-112°/22 mm. There was also obtained 82% (29.2 g.) the di-n-hexyl benzal acetal, b.p. 130-145°/0.5 mm.

The Reaction of Crotyl Alcohol with Benzaldehyde: This reaction was carried out by adding 0.125 mole benzaldehyde to 0.375 mole of crotyl alcohol and 0.0005 mole catalyst in 250 ml. benzene solution. The rate at which the acetal formed is shown in Table XXIX.

The product was worked up in the usual manner and distilled in vacuo, b.p. 94.0-95.5°/0.7 mm.; this relatively low boiling point indicated that no polymerization had occurred. The yield was 82%, $n_D^{27} = 1.4979$. A literature search revealed that this acetal had not been previously reported.

TABLE XXIX

TIME (min.)	VOLUME (ml. H ₂ O)	TIME (min.)	VOLUME (ml. H ₂ O)
5	0.28	145	1.58
10	0.48	175	1.67
20	0.75	220	1.76
30	0.97	335	1.97
40	1.09	670	2.08
55	1.22	1375	2.23
70	1.34	1525	2.26
85	1.40	1645	2.26
115	1.48	1855	2.26

Anal. Calcd. for C₁₅H₂₀O₂: C, 77.55; H, 8.68. Found: C, 77.65, 77.36; H, 8.88, 8.95.

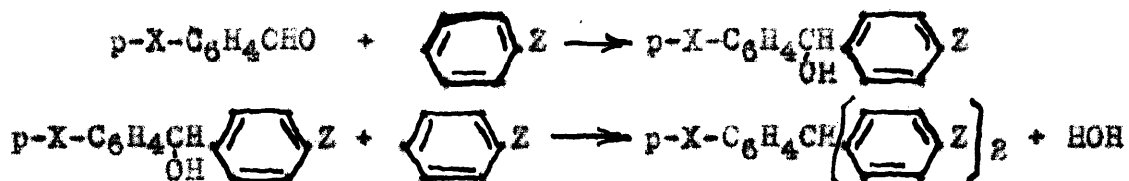
The Reaction of Acetophenone with n-Hexyl Alcohol: To 0.2 mole of n-butyl alcohol was added 0.1 mole of acetophenone and 5 g. of p-toluenesulfonic acid catalyst. An 8 inch column packed with glass helices inserted between the reaction flask and moisture trap was necessary to drive the reaction to more than 40% of completion. After a period of 3 days 92% of the theoretical amount of water was removed. On working up the product only a 35% yield was obtained of material distilling in the range of the expected ketal, 160-170°/1.5 mm. The pot residue on cooling solidified to a yellow-colored crystalline mass. On recrystallization from absolute alcohol, lustrous needle-like crystals were obtained. This substance melted at 171°, contained no sulfur, and was insoluble in concentrated sulfuric acid. It proved to be syn-triphenylbenzene, (lit., m.p. 171°).

Apparently the acetophenone has condensed with itself, cyclizing to give this hydrocarbon. With a view to improving

the yield of the sym-triphenylbenzene, 0.15 mole acetophenone was condensed in 50 ml. of benzene solution in the presence of 2 g. p-toluenesulfonic acid. After 2 days 92% of the theoretical amount of water had been removed. This reaction ordinarily would have taken a longer time to reach completion but the apparatus developed a slow-leak, some benzene was lost, and the temperature rose from 93° to 165°. The acid catalyst was removed by extraction once with sodium carbonate solution. The benzene was distilled off and the residue recrystallized from 150 ml. of ethanol. There was obtained a 66% yield of yellowish-white crystals, m.p. 168-171°.

SUMMARY

The first part of this investigation consisted of a study of the condensation of aldehydes with aromatic rings.



It was found that these reactions could be readily carried out in refluxing benzene solution in the presence of *p*-toluenesulfonic acid as a catalyst. The rate of the reactions could be accurately determined by noting the rate at which the water formed was collected in a trap inserted between the reaction mixture and the condenser.

When -Z in the above equation was -N(CH₃)₂ and -X was O₂N-, Cl-, H-, CH₃-, CH₃O-, or (CH₃)₂N-, the reactions proceeded readily to completion and the expected products were isolated in 77% to 89% yields. The order of decreasing reactivity as X- was varied was found to be that given above showing that electron releasing substituents in the aldehyde retarded the rate of reaction. Under the standard conditions used it was found that the reactions followed first order kinetics based on the aldehyde. In spite of the fact that changes in the reactant ratio from the standard caused drifts in the constants it was found that the relative reactivities could be quantitatively correlated by means of a graphical method developed by Hammett. A linear relation-

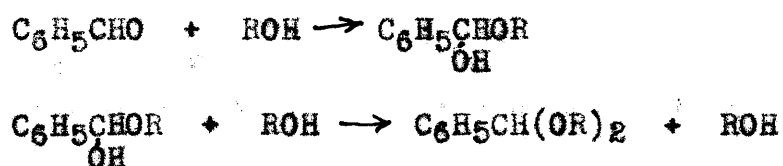
ship was found when logarithms of the rate constants were plotted against the logarithms of the ionization constants of the corresponding benzoic acids.

2-Ethylbutyraldehyde reacted less rapidly than heptaldehyde when these aldehydes replaced the benzaldehydes in the above equation. Both products were isolated in about 70% crude yields.

When -Z in the above equation was varied among $-\text{N}(\text{CH}_3)_2$, $-\text{NHCH}_3$, $-\text{OCH}_3$, $-\text{OC}_2\text{H}_5$, $-\text{OC}_4\text{H}_9$ and $-\text{CH}_3$ the corresponding products were obtained in 70% to 85% yields. Several polysubstituted benzenes did not react satisfactorily. In contrast to the effect noted above for X- it was found that the rate of the reaction increased as the electron-releasing ability of -Z increased.

The opposite effects of increasing electron-releasing ability of the X- and Z- groups together with the demonstration that the reaction probably proceeded via an intermediate hydrol as shown in the above equation made it possible to show that the second step of a four step mechanism was probably the rate-controlling one.

The formation of acetals was studied under the same general conditions and by the same method:



Before a kinetic study could be made of the acetal reaction, the equilibrium constant of the first step must

be known. Adkins had previously postulated that this first step proceeded rapidly and quantitatively. This assumption was disproved, however, when it was shown that an acetal could be prepared by using only one-half of the stoichiometric amount of ROH, showing that the hemiacetal underwent considerable reconversion into the aldehyde and alcohol. When it was also found that the acetal reacted very rapidly with water under these conditions it appeared to be inadvisable to attempt a determination of the mechanism by this method.

A number of new acetals of benzaldehyde and primary alcohols, including crotyl alcohol, were readily prepared in 82% to 95% yields by this method. It was found that n-butyl, n-hexyl, n-heptyl, n-decyl, iso-butyl, and crotyl alcohols reacted at about the same rate. Secondary alcohols were found to react much more slowly while tertiary alcohols underwent dehydration in preference to acetal formation.

Acetophenone, instead of forming the ketal, underwent self-condensation to give sym-triphenylbenzene in 63% yield.

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