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Some reductions of substituted benzalacetophenones by aluminum isopropoxide and lithium aluminum hydride

Calvin Lyndall Fisher

SOME REDUCTIONS
OF
SUBSTITUTED BENZALACETOPHENONES
BY
ALUMINUM ISOPROPOXIDE AND LITHIUM ALUMINUM HYDRIDE

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THESIS

Presented in Partial Fulfillment of the Requirements for the Degree of Master of Science in\the Graduate Department of the University of Richmond

BY

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Approved by

J. Gillespie, Jr.

TABLE OF CONTENTS

INTRODUCTION

While the literature contains a large volume of material on the reduction of carbonyl compounds, the historical section of this thesis will be chiefly concerned with the reduction of α ,β - unsaturated carbonyl compounds by catalytic hydrogenation, metal combinations, aluminum alkoxides and by lithium aluminum hydride.

The purpose of this thesis is to study the effect various substituents have on a conjugated system when the system is undergoing reduction by lithium aluminum hydride.

CATALYTIC HYDROGENATION

The number and the nature of the publications on catalytic hydrogenation are so numerous that no critical or comprehensive survey of the field will be attempted in this section.

Sabatier has given a general historical development of catalytic hydrogenation (1). In various publications Ellis (2), Ipatieff (3), and Adkins (4) have discussed the wide application of catalytic hydrogenation in organic chemistry. Hence, this section shall be limited to a brief

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(1) Sabatier, P. - Reid, Catalysis in Organic Chemistry, D. Van Nostrand Company, New York (1922).

(2) Ellis, Hydrogenation of Organic Substances, D. Van Nostrand Company, New York (1930).

(3) Ipatieff, Catalytic Reactions at High Pressures and Temperatures, The Macmillan Company, New York (1936).

(4) Adkins, Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalysts, University of Wisconsin Press, Madison (1937).

discussion of the hydrogenation of α,β- unsaturated carbonyl compounds employing such catalysts as nickel and platinum in order to ascertain whether reduction by this method involves 1,2 or 1,4-addition to the compound.

Nickel: The most common nickel catalyst today is Raney nickel, which was prepared by Murray Raney and patented in 1927 (5). Since that time numerous hydrogenations of unsaturated compounds employing Raney nickel as a catalyst have been reported.

It has been said by Fuson (6) that nickel is more active catalytically for carbon-to-carbon double bond hydrogenations than it is toward carbonyl groups. For example. crotonaldehyde is converted to butyraldehyde (7)

$$CH_3CH = CHCHO \xrightarrow[Ni]{H_2} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$$

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(5) Raney, Murray, U.S. Patents, 1,628,190, (May, 1927).

(6) Fuson, R. C., Advanced Organic Chemistry, John Wiley and Sons, New York (1950), p. 256.

(7) Distillers Co. Ltd., Britain 595, 941 (Dec. 23, 1947).

and mesityl oxide is converted to isobutyl methyl ketone (8) by hydrogenation using a nickel catalyst.

$$CH_3-\overset{CH_3}{\overset{|}{C}}=CHCOCH_3 \xrightarrow[Ni]{H_2} CH_3CHCH_2COCH_3$$

Further evidence in support of this generalization is given by Baker and Weiss (9) who hydrogenated O-ethylbenzoylacetone, I, employing nickel as a catalyst. They have shown several plausible courses which the reaction might take. Of the two routes to the saturated ethoxy-carbinol, III, evidence was presented to show that the preferred one was through the ethoxyketone, II, by limiting the addition of hydrogen to one mole. However, the presence of IV could not be discounted, for its presence was indicated by tests for unsaturation.

$$\begin{array}{lccc}
\text{(II)} & C_6H_5COCH_2\overset{CH_3}{\overset{|}{C}}HOC_2H_5 & \xrightarrow[Ni]{H_2} & C_6H_5\overset{OH}{\overset{|}{C}}HCH_2\overset{CH_3}{\overset{|}{C}}HOC_2H_5 \quad \text{(III)} \\
 & \uparrow Ni & & \uparrow Ni \\
\text{(I)} & C_6H_5COCH=\overset{CH_3}{\overset{|}{C}}-OC_2H_5 & \xrightarrow{Ni} & C_6H_5CH(OH)-CH=\overset{CH_3}{\overset{|}{C}}-OC_2H_5 \quad \text{(IV)}
\end{array}$$

The statement of Fuson that nickel is more active catalytically for carbon-to-carbon double bond hydrogenations than it

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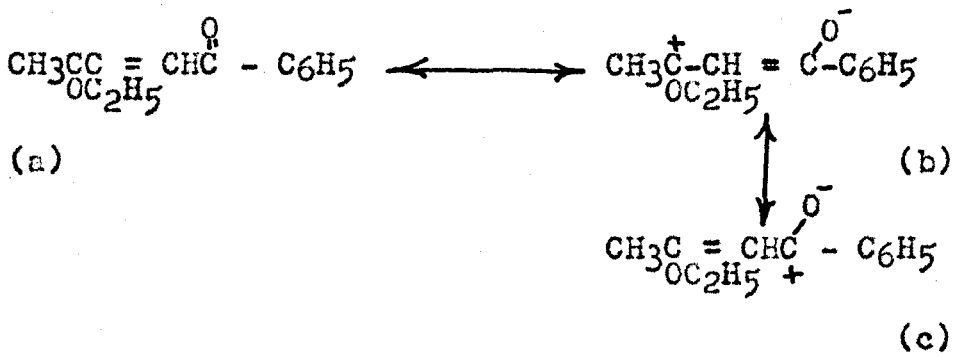
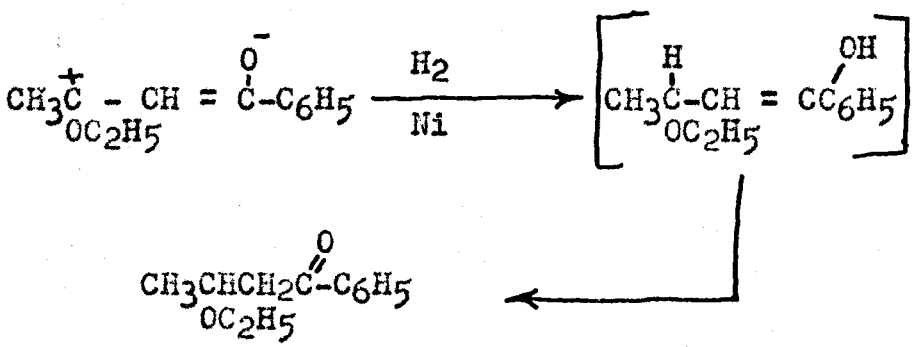
(8) Dupont, G., Bull. Soc. Chim. (5), 3, 1021-30 (1936).

(9) Baker, R. H. and P. C. Weiss, J. Am. Chem. Soc., 66, 343, (1944).

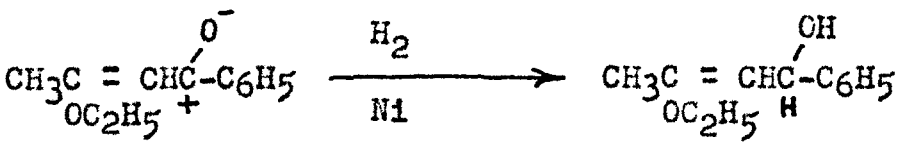
is toward carbonyl groups is true if end results are considered. However, if resonance structures of O-ethylbenzoylacetone are considered as pictured below, then it may be shown that hydrogenation may have proceeded 1,2 or 1,4 to the conjugated system.



If resonance structure (b) is considered, reduction may proceed 1,4 as pictured below.



If resonance structure (c) is considered, reduction may proceed 1,2 as shown by the equation below.



The presence of the enolic compound above was demonstrated by

tests for unsaturation as mentioned already. Since the enol was present only in minute amounts, the preferential attack of hydrogen to a conjugated system when nickel is employed may be said to be at the olefinic linkage.

Other examples showing preferential attack of hydrogen at the olefinic linkage when nickel is employed are given by Wojcik and Adkins who hydrogenated many unsaturated esters and acids employing nickel as a catalyst (10).

The carbonyl group of α,β- unsaturated carbonyl compounds has been hydrogenated also using nickel as a catalyst and varying the experimental conditions. It has been reported by Palfrey and Sabetay (11) that the catalytic hydrogenation of cinnamaldehyde employing Raney nickel resulted in almost quantitative yields of γ-phenylpropanol-1 at 105°C.

$$C_6H_5CH = CHCHO \xrightarrow[105^\circ]{Ni} C_6H_5CH_2CH_2CH_2OH$$

Delepine and Hanegraaf have studied the order of the addition of hydrogen in the hydrogenation of cinnamaldehyde employing Raney nickel as a catalyst (12). They have reported

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(10) Wojcek and Adkins, ibid., 56, 2424 (1934).

(11) Palfrey, L., S. Sabetay, and B. Ganthier, Compt. rend., 218, 553-5 (1944).

(12) Delepine, M. and C. Hanegraaff, Bull. soc. chim., (5), 4, 2087-93 (1937). C.A., 32, 2520 (1938).

that reduction took place simultaneously at the double bond and the CHO group but that addition to the double bond proceeded more rapidly.

It may be said that when proper conditions are employed, nickel may be used to hydrogenate selectively at the olefinic linkage or may be used to hydrogenate completely.

Platinum: Perhaps the most widely used catalyst in hydrogenation procedures has been platinum. There are numerous articles in the literature on the hydrogenation of unsaturated carbonyl compounds employing platinum.

Hans Weidlick and Roger Adams are two outstanding men who have done much work on the catalytic hydrogenation of unsaturated compounds employing platinum.

Weidlick has made a comprehensive study of the catalytic hydrogenation of α,β- unsaturated carbonyl compounds and has reported that the products of catalytic hydrogenation of α,β- unsaturated carbonyl compounds in acid medium can be interpreted as resulting from 1,2-addition to the C=O or C=C bond and those in alkaline medium as resulting from 1,4 addition to the conjugated system (13). For example, chalcone when hydrogenated in acid medium gave C_6H_5CH = CHCH (OH) C_6H_5

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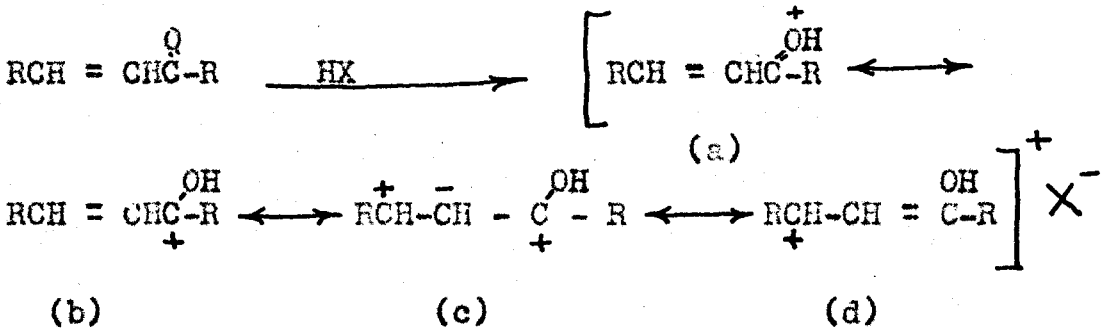
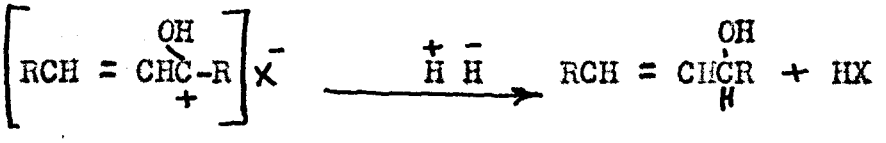
(13) Weidlick, H. A. and M. Meyer, Delius, Ber., 74B, 1195-1212 (1941). C.A., 36, 4805 (1942).

almost quantitatively, but when hydrogenated in alkaline medium gave the saturated ketone, $C_6H_5CH_2CH_2COC_6H_5$. The conversion of cinnamaldehyde to γ-phenylpropionaldehyde in alkaline medium further supports the generalization formulated by Weidlick. Other examples have been reported which support the above generalization.

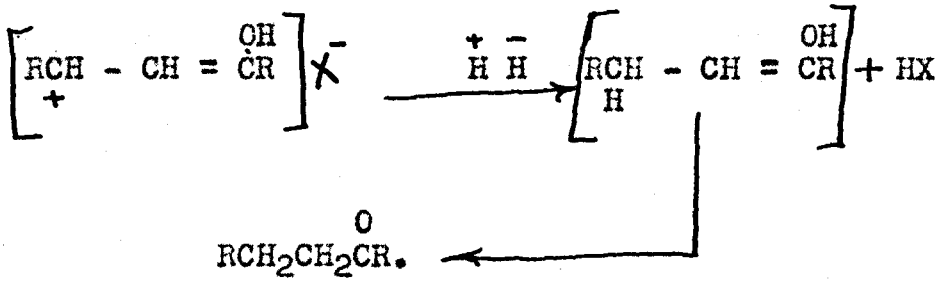
Weidlick has proposed two conceivable mechanisms for hydrogenation employing platinum. In acid medium, the course of the reaction may be formulated thus;



with which the hydrogen reacts as $\overset{+}{H}\ \overset{-}{H}$. The H anion may combine with any of the above resonance forms; the H cation always combines with X^- to form HX. If the H anion combines with resonance form (a), it will only replace the H already present and no change in the resonance form will be effected. If the H anion combines with the carbonium C of formula (b), the unsaturated alcohol will result. The reaction may be pictured as below:



If the H anion combines with the carbonium C of formula (d), the saturated ketone will result. The reaction may be pictured as below.

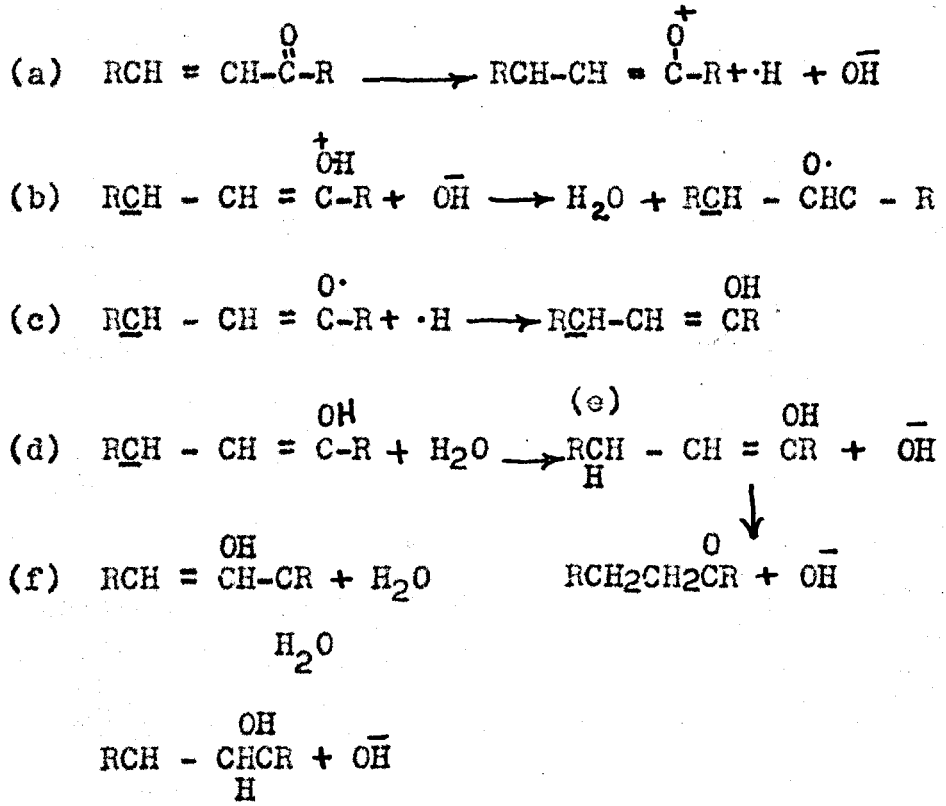


Weidlick has stated that in the course of the hydrogenation in acid medium only form (b) seems to be responsible, (d) being the determining factor only in exceptional cases. However, he has further stated that (b), by polarization of the double bond induced by the charge on the carbonium C atom, may react as follows:

This means that in acid medium there should be formed in addition to the saturated ketone, RCH_2CH_2CRO, a carbinol, RCH = CHC(OH)R, depending on the mechanism which has been followed and on the stability of the intermediate formed during

the course of the reaction.

The course of the reaction in alkaline solution proposed by Weidlick may be formulated as pictured below. He has proposed that the OH anion of the alkaline liquid takes possession of an H atom with the formation of water, while the election of the H atom is taken up by the electrophilic O of the carbonyl group as shown in equations (a) and (b).



Weidlich further proposed that a second H atom combines with the radical-like anion, equation (c), and depending on the relative stability of resonance forms, yields a carbinol,

RCH = CHC(OH)R, equation d→f, or an enol RCHCHC = C(OH)R equation d→e which can rearrange into the saturated ketone. The course most likely taken is shown by equation d→e, the saturated ketone being the final product.

Adams and co-workers have reported many catalytic hydrogenations of α,β- unsaturated carbonyl compounds. They have shown that platinum may catalyze the hydrogenation of α,β- unsaturated compounds selectively. For example, benzalacetophenone was converted to benzylacetophenone and benzalacetone was converted to benzylacetone by hydrogenation employing a platinum catalyst (14). Another example was the conversion of mesityl oxide to isobutyl methyl ketone. Adams has reported that unsaturated ketones are hydrogenated rapidly, whereas the hydrogenation of unsaturated acids and esters proceeds rather slowly.

Before Adams made his systematic study of catalytic hydrogenation of organic compounds, it had been impossible to hydrogenate α,β- unsaturated aldehydes selectively. In almost every instance the ultimate product of the hydrogenation of an unsaturated aldehyde was the corresponding saturated alcohol. Hence, the ultimate product of catalytic hydrogenation of cinnamaldehyde was phenylpropyl alcohol (15). However, Adams

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(14) Adams and Shriner, J. Am. Chem. Soc., 45, 2171 (1923) Vorkees and Adams, ibid., 44, 1347 (1 22);"Organic Syntheses", Collective Vol. I, John Wiley and Sons, New York (1932), p. 452.

(15) Adams, J.W.Kern and R. Shriner, J.Am.Chem. Soc., 47, 1047 (1925

was able to convert cinnamaldehyde to cinnamyl alcohol (16) by adding a trace of ferrous salt to promote reduction of the aldehyde group and also a trace of zinc acetate to inhibit the reduction of the olefinic linkage.

$$C_6H_5CH = CHCHO \xrightarrow[Fe^{++}\ Zn^{++}]{H_2(pt)} C_6H_5CH = CHCH_2OH$$

In this manner, Adams also accomplished the conversion of citral to geraniol (17).

$$CH_3\overset{CH_3}{\overset{|}{C}} = CHCH_2CH_2\overset{CH_3}{\overset{|}{C}} = CHCHO \xrightarrow[Fe^{++}\ Zn^{++}]{H_2(pt)} CH_3\overset{CH_3}{\overset{|}{C}} = CHCH_2CH_2\overset{CH_3}{\overset{|}{C}} = CHCH_2OH$$

The selective reduction of the olefinic double bond in unsaturated aldehydes employing platinum has not yet been accomplished.

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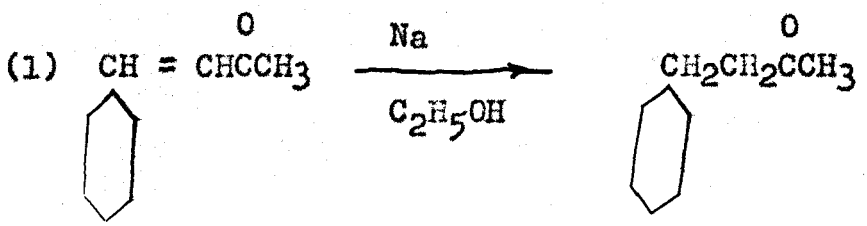
(16) Vavon, Compt. rend., 154, 359 (1912); Skita, Ber., 48, 1685 (1915); Armstrong and Hilditch, Chim. Ind., 12, 211 (1924).

(17) Adams and W. Tuley, J. Am. Chem. Soc., 47, 3061 (1925).

REDUCTIONS BY METAL COMBINATIONS

There have been numerous examples of reduction of unsaturated carbonyl compounds by various metal combinations reported in the literature; however, only a few representative examples of some of the more common metal combinations will be considered in this section.

Alkali Metal and Alcohol: Perhaps the first reduction of carbonyl compounds by an alkali metal and an alcohol was performed by Klages and Allendorf in 1898, when they reported the reduction of many aryl alkyl ketones by sodium and ethanol (1). Since that time many reductions of α,β- unsaturated carbonyl compounds by an alkali metal and an alcohol have been reported. Several examples of reduction of unsaturated carbonyl compounds by this method appear below.

(1) 

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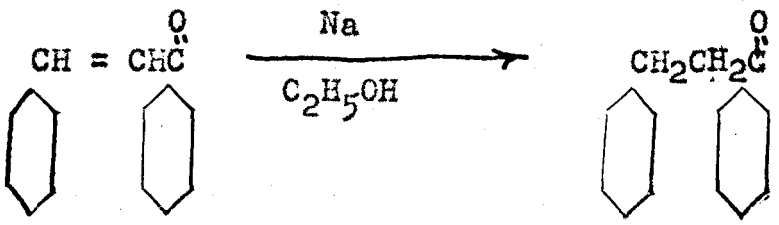
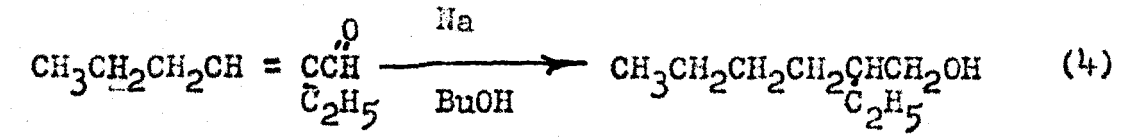
(1) Klages, and Allendorf, Ber., 31, 1003, (1898).

(2) 

(2)

(3) Cinnamic Acid Derivatives → Dihydrocinnamic Acid Derivatives (3)

(4) 

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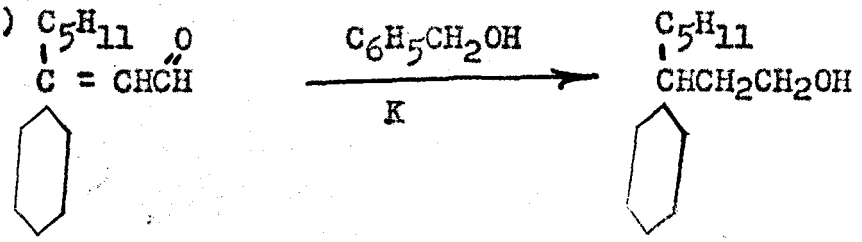
(5) 

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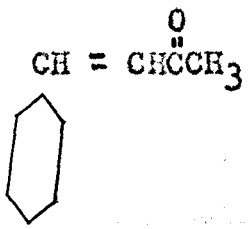
(2) Frederick, Dippy and Lewis, Rec. Trav. Chim., 56, 1000-6 (1937); C.A., 32, 5215 (1938)

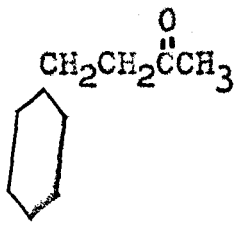
(3) Weygand, Organic Preparations, Interscience Publishers, Inc., New York. p. 5.

(4) Weismann, Sulzbacher, and Bergmann, J. Chem. Soc., (1947), 851.

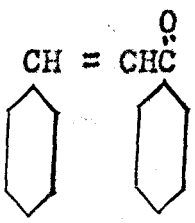
(5) Mostagli, Pierre, Am. Chim., 10, 281-377 (1938); C.A., 33, 1292.

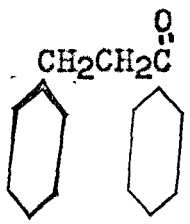
It has been proposed by Kohler and Thompson (6) that reduction of α,β- unsaturated ketones by metal combinations involves 1,4-addition to the conjugated system. For example, benzalacetone is reduced to benzylacetone (2)





and benzalacetophenone to benzylacetophenone (2).





The reduction of cinnamylideneacetone to γ - phenylpropylacetone by sodium and ethanol further supports this generalization. Further evidence in support of this generalization as well as exceptions will be discussed later.

Amalgams: There has been widespread use of various metal amalgams in reduction of unsaturated carbonyl compounds. The

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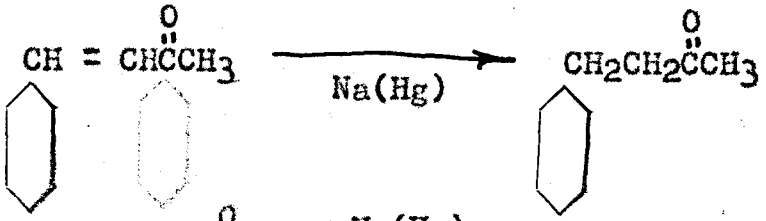
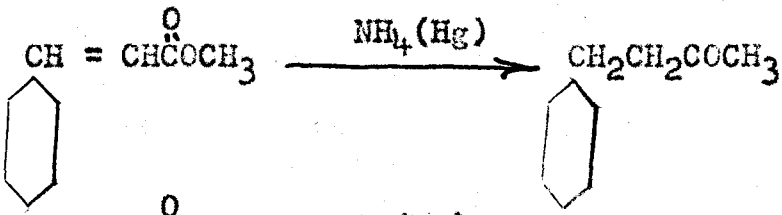
(6) Kohler, E. P. and R. B. Thompson, J. Am. Chem. Soc., 59, 890 (1937).

most common metal amalgams reportedly used are sodium amalgam, magnesium amalgam, ammonium amalgam, and aluminum amalgam. Several representative types of α,β- unsaturated carbonyl compounds reduced by metal amalgams appear below.

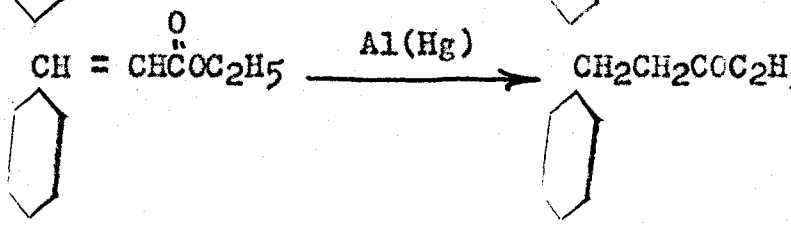
1. 

(7)

2. $CH_3CH = CHCOH \xrightarrow{Na(Hg)} CH_3CH_2CH_2COOH$ (3)

3. 

(8)

4. 

(3)

In this category there are many examples of reduction of α,β- unsaturated ketones by metal amalgams reported which support the generalization of Kohler and Thompson mentioned

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(7) Higginbottom, Lucy, and Lapworth, J. Chem. Soc., 1923, 1618.

(8) Takaki and Ueda, J. Pharm. Soc. Japan, 58, 427-30 (1937), C.A., 32, 6636^3 (1938).

previously. However, it is also in this category that numerous exceptions to that generalization are found. It has been reported (9) that α,β- unsaturated ketones and esters undergo bimolecular reduction in which the two simple molecules are joined at position 4 when certain amalgams are used. Hence, reduction of ethyl ethylidenemalonate by sodium amalgam yields the bimolecular product as pictured by the equation below (7),

$$2CH_3CH = C(COOC_2H_5)_2 \xrightarrow{Na(Hg)} \begin{matrix} CH_3CH(COOC_2H_5)_2 \\ | \\ CH_3CH(COOC_2H_5)_2 \end{matrix}$$

and methyl cinnamate yields methyl β,γ- diphenyladipate with aluminum amalgam.

$$2C_6H_5CH = CHCOOCH_3 \xrightarrow{Al(Hg)} \begin{matrix} C_6H_5CHCH_2COOCH_3 \\ | \\ C_6H_5CHCH_2COOCH_3 \end{matrix}$$

Also sodium amalgam and aluminum amalgam react with benzalacetone and benzalbenzylacetone yielding 1,6-diketones (7). Furthermore it is reported ethyl cinnamate yields ethyl β,γ- diphenyladipate as well as the normal dihydroderivative (7). Sorenson has reported that only rarely is bimolecular reduction of an aldehyde encountered.

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(9) Fuson, Advanced Organic Chemistry, John Wiley and Sons, Inc., New York, p. 482.

Higginbottom has proposed that the mechanism of the bimolecular reductions takes a free radical path (7). Such a mechanism failed to explain why the bimolecular reduction products were formed only when metals in certain forms were used as reducing agents. Higgenbottom evaded this difficulty by assuming that the carbonyl compounds were absorbed on the surface of the metal setting up conditions which would permit coupling of the molecules.

Metal + Acid: Perhaps the most widely used of all metal combinations in reduction of unsaturated compounds have been the metal-acid combinations. It was through a study of this combination that Kohler and Thompson proposed their generalization that reduction of α,β- unsaturated ketones with metal combinations involves 1,4- addition to the conjugated system. Several examples of reduction of unsaturated carbonyl compounds by various metal-acid combinations appear below.

(1) $$CH_3-\overset{CH_3}{\underset{|}{C}}=CHCOCH_3 \xrightarrow[AcOH]{Mg \text{ or } Zn} CH_3CHCH_2COCH_3 \qquad (11)$$

(2) $$(C_6H_5)_2C=CHCOC_6H_2(CH_3)_3 \xrightarrow[AcOH]{Zn} (C_6H_5)_2CHCH_2COC_6H_2(CH_3)_3$$

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(11) Weimann and Glacet, Compt. Rend., 226, 923-25 (1948); C.A., 42, 5416g (1948).

$$(3)\quad CH_3CH = CHCOOH \xrightarrow[H_2SO_4]{Zn} CH_3CH_2CH_2COOH \qquad (3)$$

The above examples involve 1,4- addition to the conjugated system. However, there are examples of bimolecular reduction and also ring formation when certain compounds are reduced by metal-acid combinations. It has been reported by Finch and White (12) that reduction of chalcone by zinc and acetic acid resulted in the bimolecular product,

$$C_6H_5CH = CHCOC_6H_5 \xrightarrow[AcOH]{Zn} \begin{matrix} C_6H_5CHCH_2COC_6H_5 \\ | \\ C_6H_5CHCH_2COC_6H_5 \end{matrix}$$

When Glacet and Wiemann (13) reduced acrolein with magnesium in acetic acid, they obtained a mixture of 4-hydroxy-5-vinyltetrahydro-furan and 2-hydroxy-5-vinyltetrahydrofuran.

$$CH_2CH = CHO \xrightarrow[HOAc]{Mg} \begin{matrix} CH_2- & CHOH \\ | & | \\ CH_2 & CHCH = CH_2 \\ & \diagdown\ \diagup \\ & O \end{matrix} + \begin{matrix} CH_2 & - & CH_2 \\ \downarrow & & | \\ HOCH & & CHCH = CH_2 \\ & \diagdown\ \diagup \\ & O \end{matrix}$$

An attractive mechanism for metal combination reductions has been suggested by Fuson (9). He has proposed that the metal functions by ceding an electron to the carbonyl compound.

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(12) Finch, L. R. and D. E. White, J. Chem. Soc., 1950, 3367 (1950).

(13) Glacet and Wiemann, Compt. rend., 208, 1323-5 (1939); C.A., 33, 4490[4] (1939).

This results in the formation of a free radical that may be represented by two different structures, I and II. He then proposes that

$$\underset{\text{I}}{RCH = \dot{C}H\overset{R}{\overset{|}{C}}OM} \longleftrightarrow \underset{\text{II}}{R\dot{C}H = CH = \overset{R}{\overset{|}{C}}OM}$$

if a second atom of the metal reacts with the free radical as structure I and the product treated with water, the carbinol would result.

$$RCH = \dot{C}H\overset{R}{\overset{|}{C}}OM \xrightarrow{H_2O} RCH = CH\overset{R}{\overset{|}{C}}OH$$

However, if the second atom of the metal reacts with the free radical of structure II, the product of hydrolysis would be the saturated carbonyl compound.

$$RCH\underset{M}{CH} = \overset{R}{\overset{|}{\dot{C}}}OM \longrightarrow RCH_2CH = \overset{R}{\overset{|}{C}}OH \longrightarrow RCH_2CH_2COR$$

Furthermore, Fuson has stated that the free radical may undergo coupling also, yielding either a pinacol, corresponding to structure I, or a bicarbonyl compound, corresponding to structure II.

$$2RCH = \dot{C}H\overset{R}{\overset{|}{C}}OM \longrightarrow \begin{matrix} RCH = CH\overset{R}{\overset{|}{C}}OM \\ RCH = CH\overset{R}{\overset{|}{C}}OM \end{matrix} \xrightarrow{H_2O} \begin{matrix} RCH = CH\overset{R}{\overset{|}{C}}OH \\ RCH = CH\overset{R}{\overset{|}{C}}OH \end{matrix} \qquad (I)$$

$$2RCHCH=\underset{}{\overset{R}{COM}} \longrightarrow \begin{matrix} RCHCH=\overset{R}{COM} \\ | \\ RCHCH=COM \end{matrix} \xrightarrow{H_2O} \begin{matrix} RCHCH_2COR \\ | \\ RCHCH_2COR \end{matrix} \qquad (II)$$

It has been shown that all three types of products are favored, the amalgams being perhaps the best reagents for bringing about bimolecular reduction.

ALUMINUM ALKOXIDE REDUCTION
(Meerwein - Ponndorf - Verley Reduction)

Aluminum alkoxides have been used extensively in the reduction of aldehydes and ketones. An excellent review of reduction with aluminum alkoxides, the Meerwein-Ponndorf-Verley reduction, has appeared in Organic Reactions, Vol. II, p. 178 ff. (1). The tables immediately following have been abstracted for the most part from data given in Organic Reactions, and show the results obtained in a great many reductions of α,β-unsaturated aldehydes and ketones.

Most of the reductions listed appear to proceed specifically 1,2 to the carbonyl group. The one exception in which conjugate reduction may have occurred, if the final product only is considered, is the reduction of quinone to hydroquinone. This has been explained (2) in terms of 1,2 reduction at one carbonyl followed by 1,5- enolization at the other.

Campbell and Khanna (3) reported that aluminum isopropoxide reduction of dibenzoylethylene and nuclear-substituted dibenzoyl-

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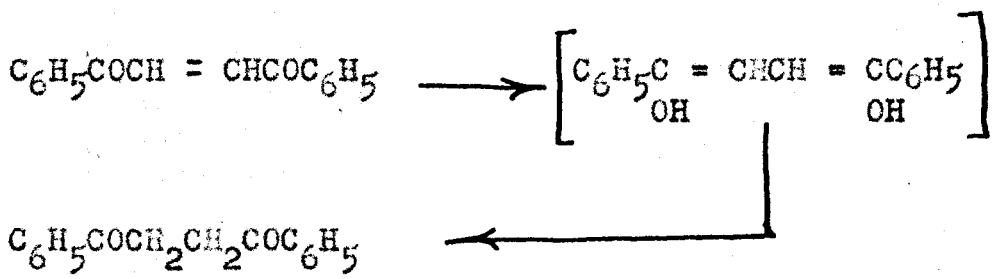
(1) Adams, et al., Organic Reactions, Vol. II, John Wiley and Sons, New York, P. 178 ff.

(2) Lutz and Gillespie, ~~ibid.~~ J. Am. Chem. Soc., 72, 344 (1950).

(3) Campbell and Khanna, Nature, 161, 54 (1949).

ethylenes gave the corresponding saturated diketones in good yield. They interpreted their reduction as being 1,6- reduction, following a mechanism that was proposed by Lutz and co-workers. (4).



Lutz, however, has reported (2) results for the same reaction which are in disagreement with that described above. Whereas Campbell and Khanna reported they obtained the saturated diketone in the reduction of dibenzoylethylene by aluminum isopropoxide, Lutz and Gillespie reported they were not able to obtain the saturated diketone even after many repetitions. They reported instead, the trans-unsaturated glycol (III) in yields as high as 34%. Lutz and Gillespie found the aluminum isopropoxide in low concentration caused cis-trans inversion of dibenzoylethylene but in higher concentration caused reduction to the trans-unsaturated glycol (III). A summary of the reactions just discussed appear below.

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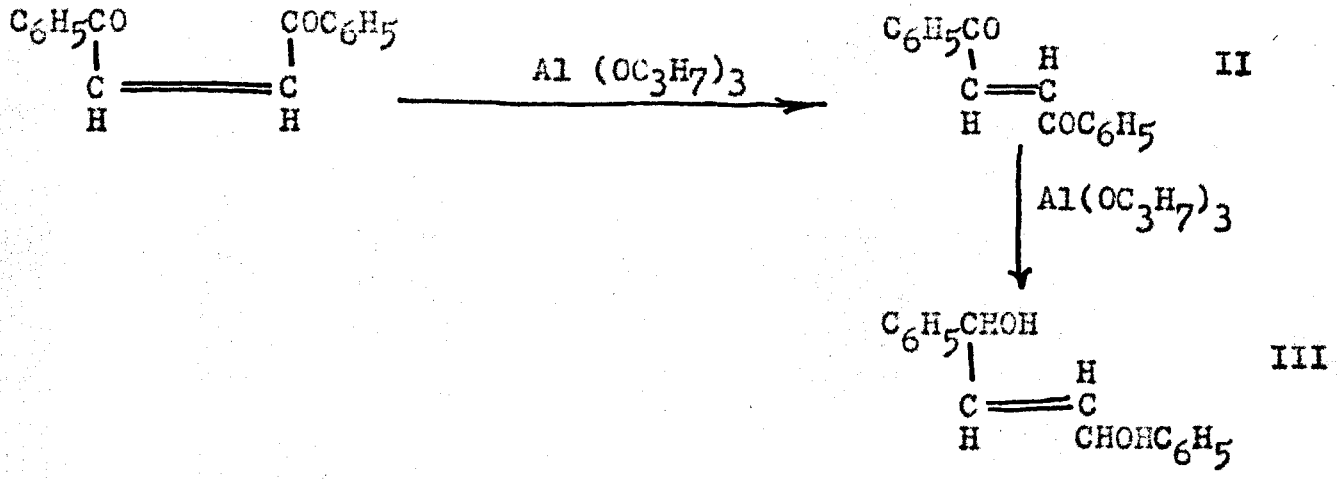
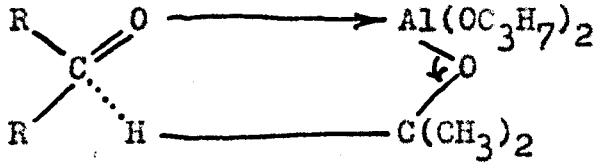
(4) Lutz and co-workers, J. Am. Chem. Soc., 45, 1047 (1923); 51, 3008.



Lutz has said "Consideration of mechanisms of aluminum alkoxide reductions which have been put forward suggests that a coordinate complex between the carbonyl group and aluminum alkoxide is involved and is in fact requisite; the electrophilic aluminum may make the carbonyl group so positive that it can abstract a hydride ion from an alcohol molecule and at the same time it would activate the alkoxide - hydrogen in the sense of facilitating release of hydride hydrogen, all this occurring through a resonating transition state or six-membered quasi-ring phase such as that pictured below.



Such a mechanism would be consistent with the seeming limitation

of the reagent to 1,2 - reductions, and expressed in these terms it is analogous to that of 1,2 - reductions of ketones by alkylmagnesium halides, and 1,4 - reactions between the α, β-unsaturated ketone system and the Grignard reagent and lithium aluminum hydride" (2).

TABLE I

, - Unsaturated Compounds Reduced by Meerwein - Ponndorf - Verley Reduction

Compound Reduced	Product Formed	% Yield
Mesityl Oxide	4-Methylpentene-3-01-2	63
cis-Heptene-3-One-2 trans-Heptene-3-One-2	Heptene-3-01-2 (Both gave same isomer)	22-24
Cyclohexen-2-One-1	Cyclohexen-2-01-1	49-74
4-Isopropylcyclohexen-2-One-1	4-Isopropylcyclohexen-2-01-1	73-88
1-Menthen-4-One-3	cis and trans-1-Menthen-4-01-3	84
Axerophthylidene Acetone	Axerophthylidene Isopropyl Alcohol	-
Benzalacetone	Methylstyrylmethanol	35
Dibenzalacetone	Distyrylmethanol	58
Dibenzalcyclohexanone Dibenzalcyclopentanone Dicinnamyl Acetone Dicennamalacetophenone	Difficult to isolate the Pure Reduced Compounds	- - - -
Benzaldesoxybenzoin	1, 2, 3-Triphenyl allyl Alcohol	91
Cholesten-4-One-3	Cholesten-4-01-3 and Epi-Cholesten-4-01-3	52
Cholesten-8-One-7	Cholesten-8-01-7	44

Compound Reduced	Product Formed	% Yield
Cholestadien-4, 7-One-3	Cholestadien-4, 7-Ol-3(35%) - Epicholestadien-4, 7-Ol-3(49%)- Cholestadien-5, 7-Ol-3(15%) - Epicholestadien-5, 7-Ol-3(1%) -	
Ergostratrien-4,7,22-One-3	Ergostratrien-4,7,22-Ol-3(45%)- Epiergostatrien-4,7-22-Ol-3(35%)-	
Ergostratetraen-4,7,9(11), 22-One-3	Mixture of Ergostatetraen-Ols-3	73
4-Dehydrostigogenone-3	Epi-4-Dehydrotigogenal-3	22
2-Bromocholesten-4-One-3	Little Bromine in Product	-
Quinone	Hydroquinone	100
Androsten-4-Dione-3,17	cis and trans-Androsten-4-Ol-17-One-3	70
3-Enol Ethyl Ether of 16-Benzal Androsten-4-Dione-3,17.	16-Benzalandrosten-4-Ol 17-One-3 (isolated as acetate)	68
Androsten-4-Ol-17-One-3	Stereoisomers of Androsten-4-Diol-3,17.	95
16-(1-Methylpropylidine-) Androsten-5-Ol-3-One-17	16-Benzylidine Androstene 5-Diol-3,17.	52
Allopregnen-16-Ol-3-One-20	Allopregnene-16-Diol-3,20	40
Pregnadiene-5,16-Ol-3-One-20	Pregnadiene-5,16-Diol-3,20	-
3,17-Diacetoxyandrosten-5-One-7	Androsten-5-Triol-3,7,17	-
3-Acetoxycholesten-5-One-7	Stereoisomers of Cholesten-5-Diol-3,7	63
3-epi-Acetoxycholesten-5-One-7	Cholesten-5-Diol-3-Epi-7(35%); 7-(25%)	88
3-Acetoxysitosten-5-One-7	Stereoisomers of Sitosten-5-Diol-3,7	93
3-Acetoxystigmastadien-5, 22-One-7	Stereoisomers of Stigmastodien-5,22-Diol-3,7	68

Compound Reduced	Product Formed	% Yield
Ethyl-α-Benzylidene Acetoacetate	Ethyl-α-Benzylidene-Hydroxybutyrate (?)	-
Methyl Ester of ^{5}-7-Keto Cholenic Acid	^{5,7}-Choladienic Acid (after hydrolysis)	90
Methyl Octenyl Ketone (double bond not Specified)	$(CH_3)_3CCH = \begin{matrix} CCH_2CHOHCH_3 \\ 1 \\ CH_3 \end{matrix}$	-
	and $(CH_3)_3\ CCH_2C = \begin{matrix} CHCHOHCH_3 \\ 1 \\ CH_3 \end{matrix}$	
Trans-Dibenzoylethylene	Dibenzoylethone 1,4-diphenyl-2-butene-1, 4-Diol	70 34
cis-Dibenzoylethylene	Dibenzoylethone 1,4-diphenyl-2-butene-1, 4-Diol	60 34
Trans-Di-p-Toluylethylene	Di-p-Toluylethane	75
cis-Di-p-Toluylethylene	Di-p-Toluylethane	95
Trans-Di-p-Chlorobenzoylethylene	Di-p-Chlorobenzoylethane	80
cis-Di-p-Chlorobtnzoylethylene	Di-p-Chlorobenzoylethane	90
Trans-Di-p-Bromobenzoylethylene	Di-p-Bromobenzoylethane	75
cis-Di-p-Bromobenzoylethylene	Di-p-Bromobenzoylethane	90
d-Pulegone	d-Neoisopulegol	-

Compound Reduced	Product Formed	Reagent R in $Al(OR)_3$	% Yield
Crotonaldehyde	Crotyl Alcohol	$i\text{-}C_3H_7$	60-65
∝-Chlorocrotonaldehyde	2-Chloro-2-Butenol-1	C_2H_5	-
∝-Bromocrotonaldehyde	2-Bromo-2-Butenol-1	C_2H_5	-
2,4-Hexadienol-1	2,4-Hexadienol-1	$i\text{-}C_3H_7$	64
2,4,6-Octatrienol-1	2,4,6-Octatrienol-1	$i\text{-}C_3H_7$	70
2,4,6,8-Decatetraenal-1	2,4,6,8-Decatetraenol-1	$i\text{-}C_3H_7$	-
Citral	Geraniol (24%) Nerol (44%)	$i\text{-}C_3H_7$	83
Cyclocitral	Cyclo-Geraniol	$i\text{-}C_3H_7$	77-93
Axerophthal	Isomer of Vitamin A	$i\text{-}C_3H_7$	-
Rupenal	Pseudolupenol	$i\text{-}C_3H_7$	55
Cinnamaldehyde	Cinnamyl Alcohol	$i\text{-}C_3H_7$ and C_2H_5	45-86
∝-Chlorocinnamaldehyde	∝-Chlorocinnamyl Alcohol	C_2H_5	-
∝-Bromocinnamaldehyde	∝-Bromocinnamyl Alcohol	C_2H_5	-
2,3,or 4-,Nitrocinnamaldehyde	2,3, or 4-,Nitrocinnamyl Alcohol	C_2H_5	-
∝-Methylcinnamaldehyde	∝-Methylcinnamyl Alcohol	$i\text{-}C_3H_7$	-
11-Phenyl-2,4,6,8,10-Undecapentaenal-1	11-Phenyl-2,4,6,8,10-Undecapentaenol-1	$i\text{-}C_3H_7$	90

Compound Reduced	Product Formed	Reagent R in $Al(OR)_3$	% Yield
2-Styryl Benzaldehyde	2-Styryl Benzyl Alcohol	i-C_3H_7	95
3-Pyrenealdehyde	3-Pyrenylmethanol	i-C_3H_7	54

LITHIUM ALUMINUM HYDRIDE

Since it was first reported in May, 1947, by Finholt, Bond and Schlesinger (1), lithium aluminum hydride has proved to be extraordinarily useful as a reducing agent, and it is now commercially available.

Lithium aluminum hydride has been employed to reduce acids, esters, acid anhydrides, acid chlorides, aldehydes, and ketones to the corresponding alcohols (2), amides, nitriles, aldimines, aliphatic nitro compounds, and oximes have been reduced to amines. Aromatic nitro and azoxy compounds have been reduced to azo compounds (3). Other groups have also been reduced by lithium aluminum hydride but only the reduction of α,β- unsaturated carbonyl compounds by this reagent will be considered in this section.

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(1) Finholt, Bond and Schlesinger, J. Am. Chem. Soc., 69, 1197 (1947).

(2) Brown and co-workers, J. Am. Chem. Soc., 69, 2548, (1947).

(3) Brown and co-workers, ibid., 70, 3738 (1948).

Brown has said (6) that, normally, carbon-carbon double bonds are not attacked by lithium aluminum hydride even when they are in conjugation with the functional group undergoing reduction. For example, sorbic acid, $CH_3CH = CHCH = CHCOOH$, has been reduced to sorbyl alcohol, $CH_3CH = CHCH = CHCH_2OH$, (4) and crotonaldehyde, $CH_3CH = CHCHO$, reduced to crotyl alcohol using lithium aluminum hydride (2). Ethyl β-ionylidene acetate, a highly conjugated ester, has been reduced to β-ionylidene ethyl alcohol (5) in which the double bonds remained intact. The reduction of benzalacetophenone (7) to phenylstryrylcarbionol by lithium aluminum hydride has further supported this generalization. There are instances, however, which are exceptions to this. One class is represented by an ethylenic nucleus substituted on one side by a phenyl group and on the other side by a reducible group such as carboxyl, aldehyde, etc. In the normal reduction of these compounds at room temperature, the double bond is reduced. An excellent example of this class is cinnamaldehyde. Brown (8) has reported that at room temperature in the normal reduction

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(4) Brown and co-workers, ibid., 69, 2549 (1947).

(5) Milas and Harrington, J. Am. Chem. Soc., 69, 2247 (1947).

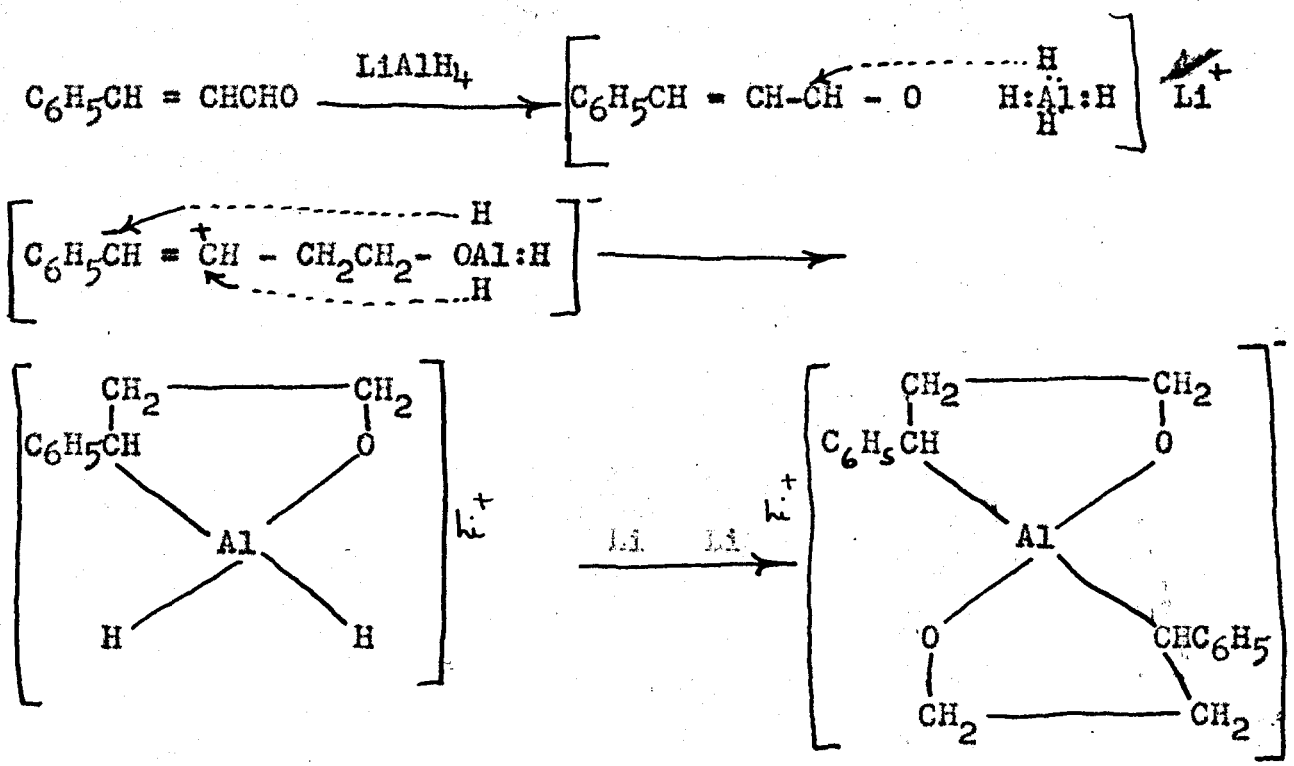
(6) Brown and co-workers, ibid., 69, 1197 (1947).

(7) Hochstein, J. Am. Chem. Soc., 71, 305 (1949).

(8) Brown and Hochstein, J. Am. Chem. Soc., 70, 3484 (1948).

procedure cinnamaldehyde is converted to hydrocinnamyl alcohol. However, the reverse mode of addition, carried out by adding the calculated amount of hydride solution to a solution of cinnamaldehyde at temperatures below 10°C, resulted in an excellent yield of cinnamyl alcohol. Cinnamyl alcohol in turn was found to be reduced at room temperature to hydrocinnamyl alcohol.

Brown has proposed that cinnamyl alcohol results from the formation of an intermediate metallo-organic complex which upon hydrolysis yields the unsaturated alcohol. Gillespie (9) has suggested a possible route to the complex which is pictured below.

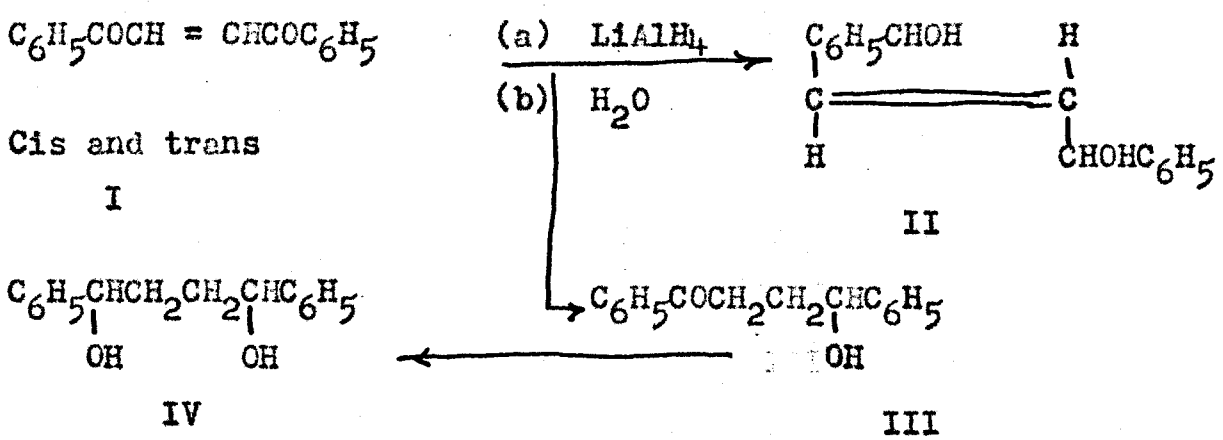


(9) Gillespie, Dissertation, Univ. of Virginia, June, (1949).

It should be noted that benzalacetophenone, a ketone which is comparable to cinnamaldehyde was reduced to phenylstyrylcarbinol at room temperature (7), but that no reduction of the double bond, analogous to that of cinnamaldehyde occurred.

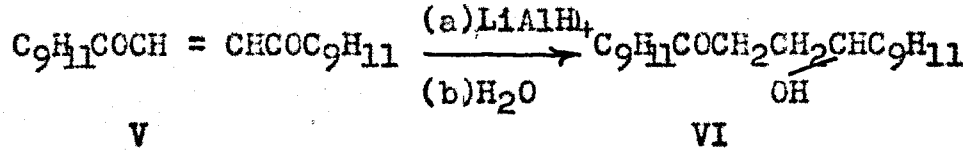
The reduction of unsaturated 1,4-diketones by lithium aluminum hydride has been studied by Lutz and co-workers (10) in order to ascertain whether the reagent would bring about 1,4- reductions analogous to 1,4- addition of the Grignard reagent.

When Lutz and Gillespie reduced cis and trans-dibenzoylethylenes with lithium aluminum hydride (10), they obtained as their main product, the partially reduced compound, 1,4-diphenyl-4-hydroxy-1-butanone. In addition, they also obtained the trans unsaturated glycol, 1,4-diphenyl-2-butene-1,4-diol.



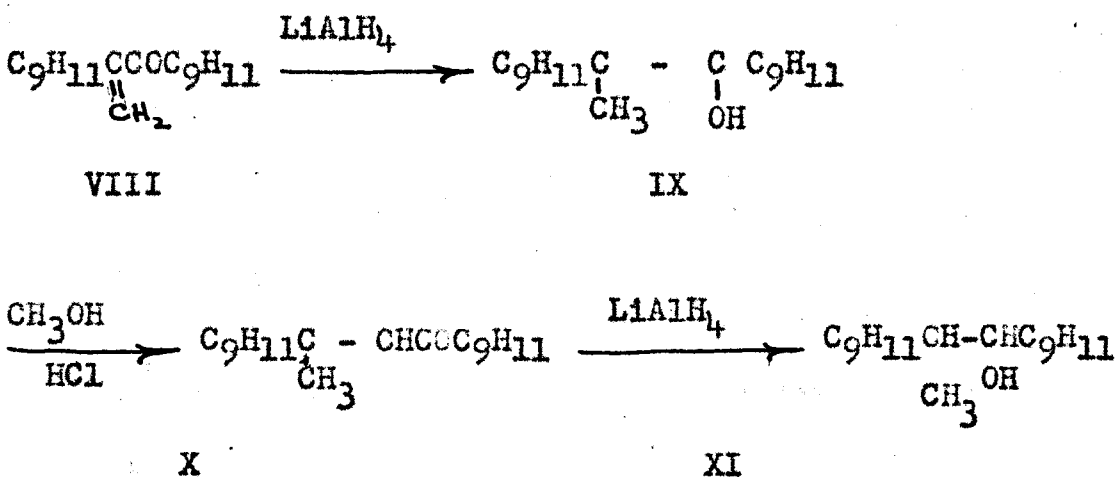
(10) Lutz and Gillespie, J. Am. Chem. Soc., 72, 2002 (1950).

In the reduction of trans-dimesitoylethylene by an excess of lithium aluminum hydride, Lutz reported only a single product, a saturated hydroxy ketone, VI.



V VI

Lutz has also reported the reduction of 1,2- dimesitoylpropenone (VIII) by lithium aluminum hydride (11). He obtained an enol IX, which was isolated and ketonized with methanolic hydrogen chloride to 1,2- dimesitoylpropanone X. He subsequently reduced the 1,2-dimesitoylpropanone to the corresponding alcohol XI.



VIII IX X XI

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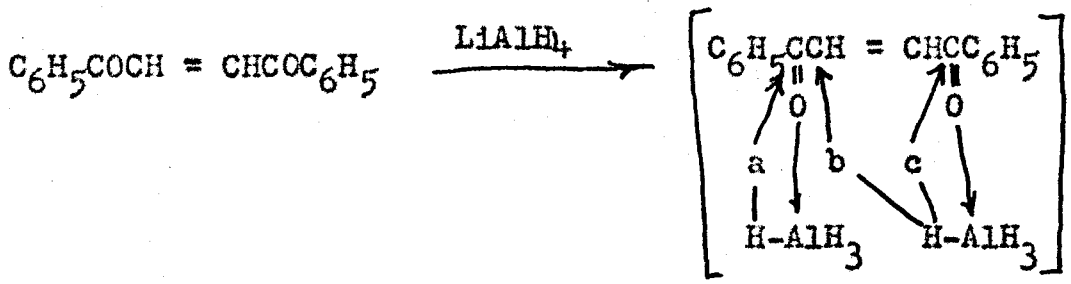
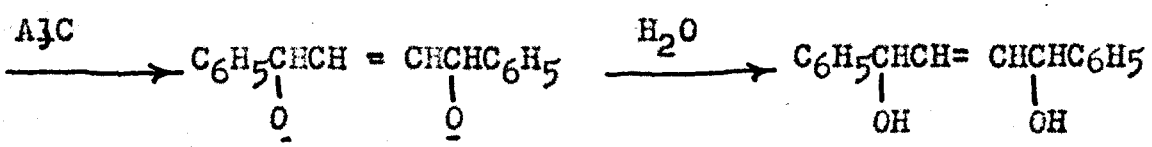
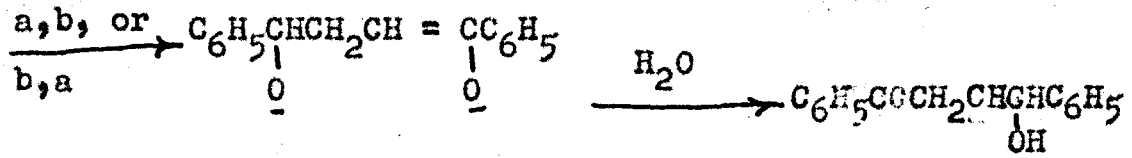
(11) Lutz and Hinkley, Ibid., 72, 4091 (1950).

The unsaturated 1,4-glycol (ii) formed when dibenzoylethylene was reduced by lithium aluminum hydride was the expected result of successive 1,2-reduction of the two carbonyl groups. Lutz has suggested that the hydroxyketone (III) must have been stabilized in the form of an enolate and liberated upon hydrolysis of the reaction mixture. The mechanism offered to explain this result involved 1,4 addition of the reagent to the α,β- unsaturated ketone system (cf. XII b) with prior or subsequent 1,2-reduction (XII a) independently of the other carbonyl group. These several possibilities are pictured in formulas XII - XIV below as three two-step paths,(A,c), (a,B), and (b,a).



XII





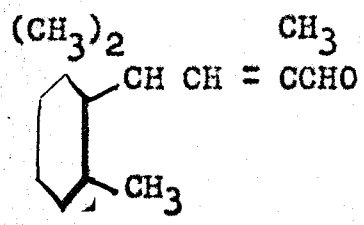
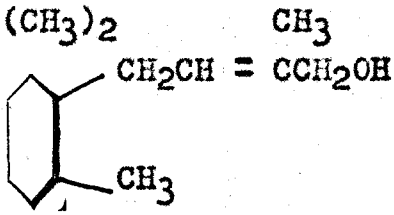
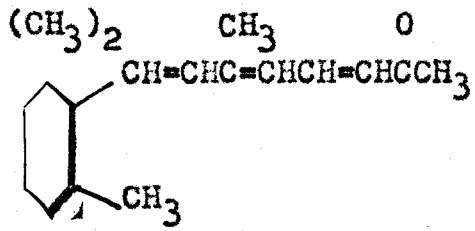
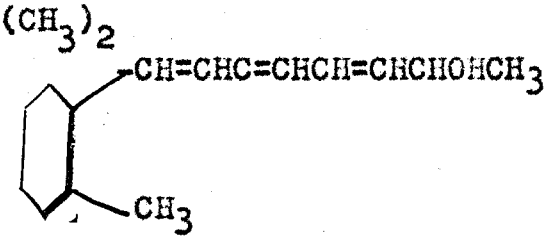
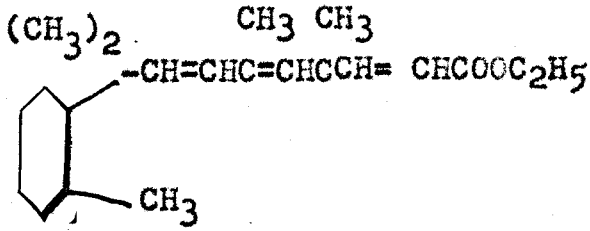
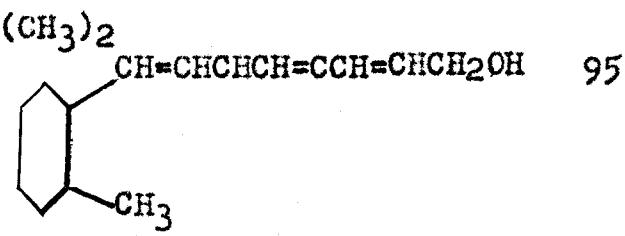
In the case of dimesitoylethylene Lutz has proposed that steric hindrance would diminish the facility of the 1,2 attack at the carbonyls, but would not affect the 1,4 addition. This he offered as the reason for just the one product, the hydroxyketone, III.

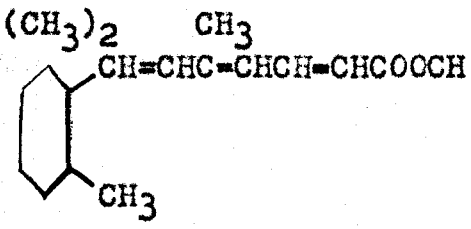
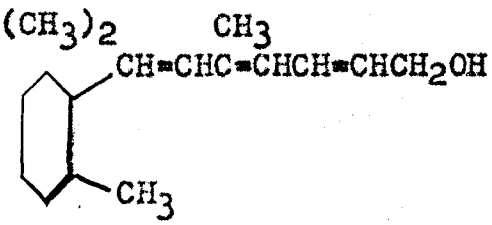
Lutz has rigorously demonstrated that 1,4- addition of lithium aluminum hydride to an α,β- unsaturated carbonyl system occurred when he reduced 1,2- dimesitoylpropenone VIII and isolated the enol IX.

Immediately following are several tables of α,β- unsaturated carbonyl compounds which have been reduced by lithium aluminum hydride. The tables are by no means complete since some examples doubtless have been overlooked.

LITHIUM ALUMINUM HYDRIDE REDUCTIONS

Compound Reduced	Product Formed	% Yield
Sorbic Acid	Sorbyl Alcohol	92
Cinnamic Acid	Hydrocinnamyl Alcohol	85
Ethyl- -Ionylidene Acetate	-Ionylidene Ethyl Alcohol	-
Crotonaldehyde	Crotyl Alcohol	70
Cinnamaldehyde	Cinnamyl Alcohol	90
Cinnamaldehyde	Hydrocinnamyl Alcohol	87
Maleic Anhydride	-	-
Sorbyl Chloride	Sorbyl Alcohol	98
p - Benzoquinone	Hydroquinone	70
Benzalacetophenone	Phenylatyrylcarbinol	65
1,2-Dimesitylpropenone	1,2-Dimesityl-1-Propene-1-Ol	90
Cis-Dibenzoylethylene	1,4-Diphenyl-4-Hydroxy-1 Butanone	-
	1,4-Diphenyl-2-Butene-1,4-Diol	-
trans-Dibenzoylethylene	1,4-Diphenyl-4-Hydroxy-1 Butanone	-
	1,4 Diphenyl-2-Butane-1,4-Diol	-
trans-Dimesitoylethylene	1,4-Dimesityl-4-Hydroxy-1-butanone	-
Coumarin	3-(O-Hydroxyphenyl)-Propanol	50
	O-Hydroxycinnamyl-alcohol	40

Compound Reduced	Product Formed	% Yield
		89
		-
Vitamin A Aldehyde	Vitamin A Alcohol	65
Ethyl 2-heptenoate	2-Heptenol	79
Ethyl 2-Nonenoate	2-Nonenol	-
Ethyl β -Ionylideneacetate	β - Ionylideneethyl alcohol	-
		95
^{4}-Androstene-3,17-dione,3-(-hydroxy-ethyl) -thioenol ether	Testoterone,3-(-hydroxy-ethyl) thioenol ether	66
^{4}-Androstene-3,17-dione,3-benzyl-thioenol ether	Testoterone,3-benzyl-thioenol ether	66
3-Δ^{4} - Cholestenone	Allocholesterol,epiallo- -cholesterol	-

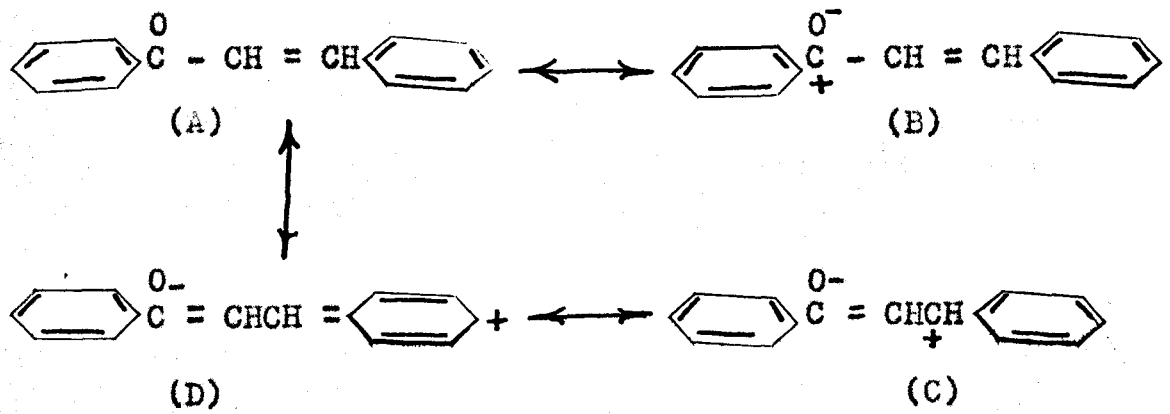
Compound Reduced	Product Formed	% Yield
		68
p-Methylcinnamic Acid	p-Methylcinnamyl alcohol	90
Fumaric acid	2-Butene-1,4-diol	78
Acrylic Acid	Allyl Alcohol	68
Propiolic Acid	Allyl Alcohol	85
c-Cyclohexene-1-yl hydroperoxide	3-cyclohexen-1-ol	83

DISCUSSION OF RESULTS

It has been shown in the Historical Section that reduction of α,β- unsaturated carbonyl compounds by aluminum alkoxides proceeds specifically 1,2 to the carbonyl group. It has also been shown that, when α,β- unsaturated carbonyl compounds are reduced by lithium aluminum hydride, the reduction may proceed either 1,2 or 1,4 to the carbonyl group.

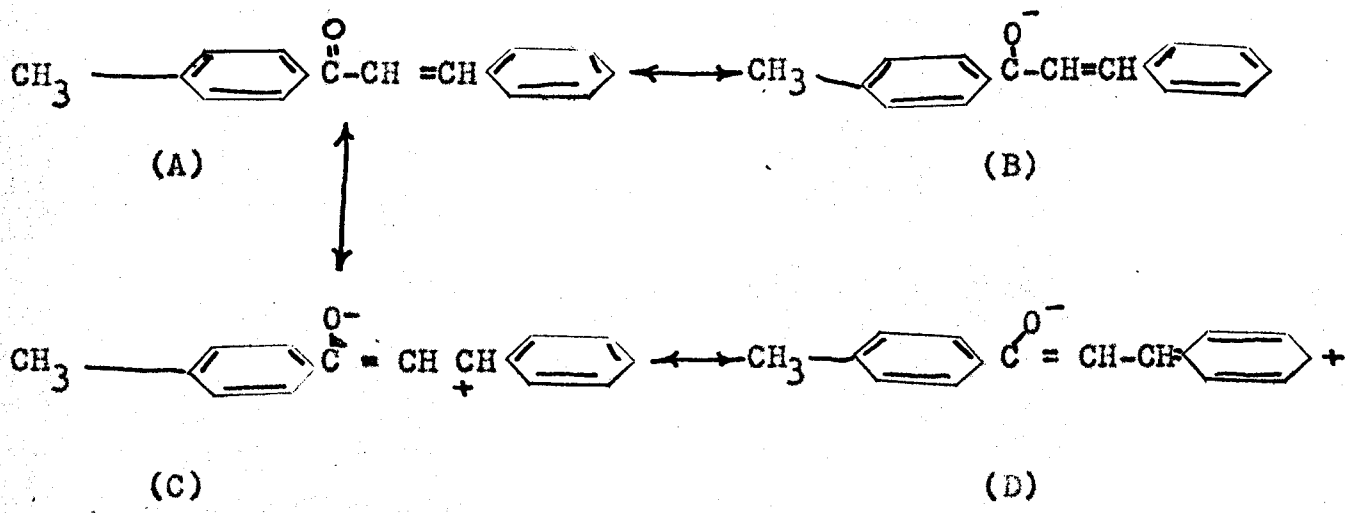
Benzalacetophenone and p,p' substituted derivatives were chosen for the lithium aluminum hydride reductions for this study because they could be easily prepared and particularly because they are simpler compounds than the diketones which were reduced by Lutz. The series of compounds were reduced by aluminum isopropoxide in order to compare the product obtained by this reduction with the product obtained by reduction with lithium aluminum hydride.

One can write several resonance forms of benzalacetophenone which can account for 1,4 or 1,2 reduction with lithium aluminum hydride.



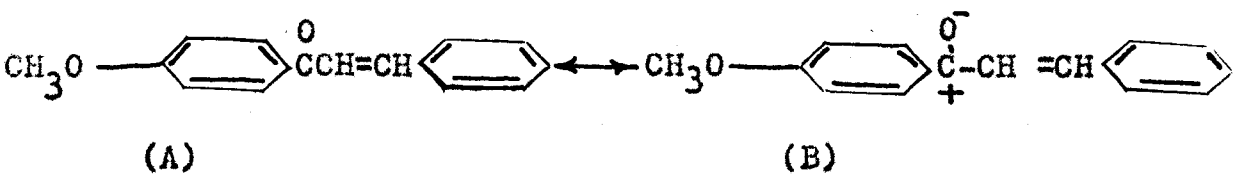
When benzalacetophenone was reduced by lithium aluminum hydride, phenylstyrylcarbinol was obtained. This was proven by comparing its ultraviolet absorption spectrum with the ultraviolet absorption spectrum of phenylstyrylcarbinol obtained by aluminum isopropoxide reduction of chalcone. Although it is not possible to predict which path reduction might have taken by examination of the resonance forms above, the reagent preferentially attacked 1,2 since the product obtained was phenylstyrylcarbinol.

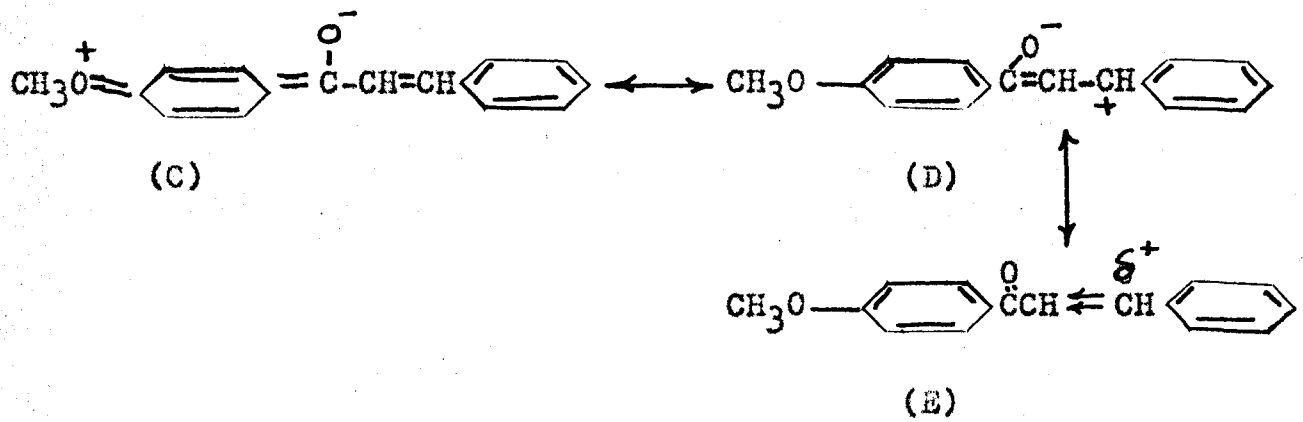
In the reduction of p'-methylbenzalacetophenone by lithium aluminum hydride, the unsaturated alcohol, 1-(p-methylphenyl)-3-phenyl-2-propen-1-ol, was obtained. This was proven by the ultraviolet absorption spectrum of the product. The resonance forms of p'-methylbenzalacetophenone are pictured below.



It is not possible to make a prediction which path reduction might have taken by examination of the resonance forms above, but the product obtained was the unsaturated alcohol, indicating that the reagent preferentially attacked 1,2.

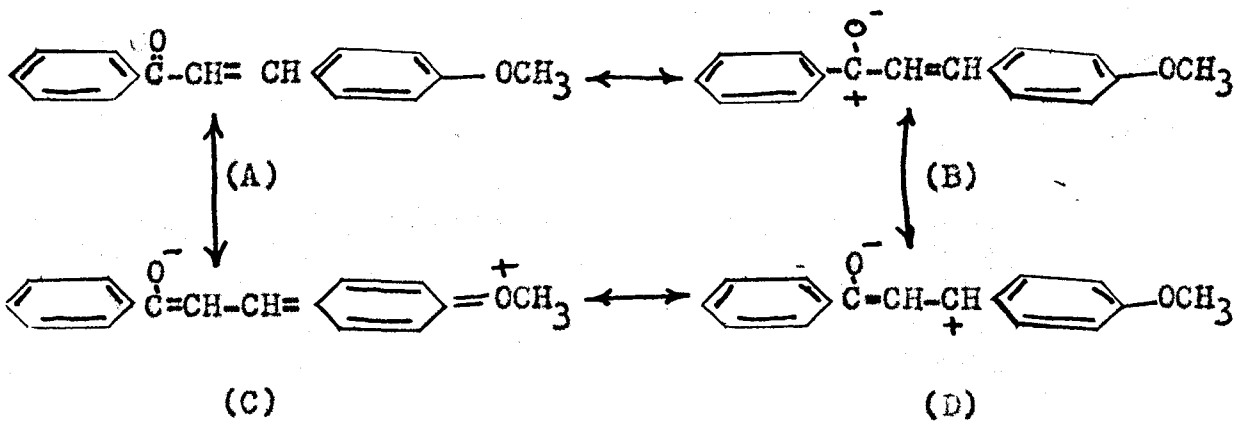
When p'-methoxybenzalacetophenone was reduced by lithium aluminum hydride, the product obtained was 1-(p-methoxyphenyl)-3-phenyl-2-propen-1-ol. This was proved by its ultraviolet absorption spectrum. Reduction must have proceeded 1,2 to the carbonyl group, since the product of reduction was the unsaturated alcohol. However, if the resonance forms pictured below are examined, it may be seen that conceivably the reduction could take a 1,4 path. Such, however, was not the result.





(C) (D) (E)

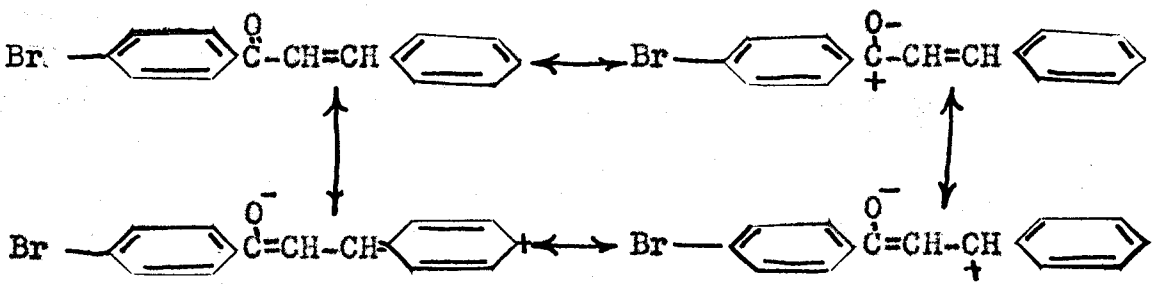
When the methoxyl group was shifted to the p position as in p-methoxybenzalacetophenone, the product of reduction by lithium aluminum hydride was still an unsaturated alcohol. In this instance, the product obtained was 3-(p-methoxyphenyl)-1-phenyl-2-propene-1-ol, which was proved by its ultraviolet absorption spectrum. The preferential attack by the reagent must have been 1,2 to the carbonyl group, although a possible 1,4 attack could have occurred as is shown by the resonance forms pictured below.



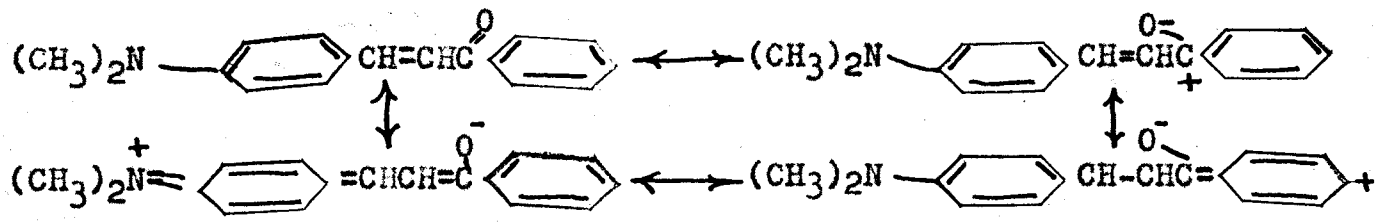
(A) (B) (C) (D)

The product of reduction of p'-bromobenzalacetophenone by lithium aluminum hydride was the unsaturated alcohol, 1-

(p-bromophenyl)-3-phenyl-2-propen-1-ol. This was proved by comparing its ultraviolet absorption spectrum with the absorption spectrum of the product obtained by aluminum isopropoxide reduction of p'-bromobenzalacetophenone. Although it is not possible to predict which path reduction might have taken by examination of the resonance forms pictured below, the reagent preferentially attacked 1,2 to the carbonyl group since the unsaturated alcohol was the product obtained.



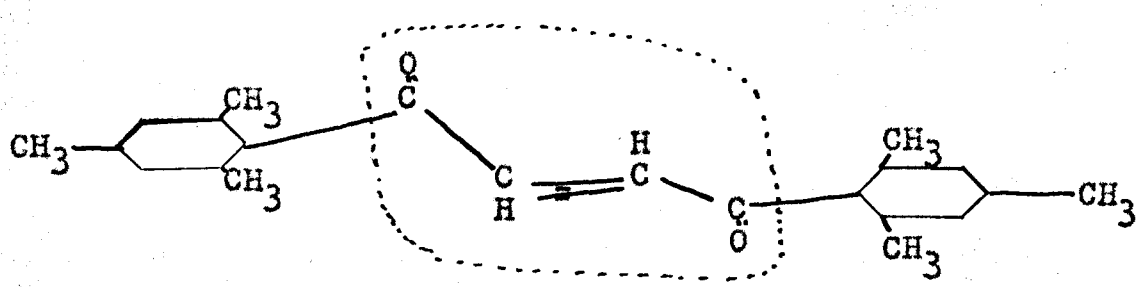
Nothing can be said of a definite nature about the product obtained when p-dimethylaminobenzalacetophenone was reduced by lithium aluminum hydride. The ultraviolet absorption spectrum did not indicate one definite and distinct product. It is not possible to predict whether the reagent will add 1,2 or 1,4 to the conjugated system if the resonance structures are considered as below.



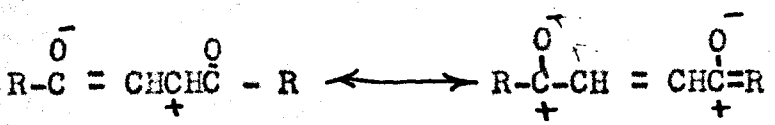
If the reagent ad s to the system 1,2 as it did in all instances thus far, the expected product of reduction would be 3-(p-dimethylaminophenyl)-1-phenyl-2-propen-1-ol.

In all instances where a definite product was obtained and identified, lithium aluminum hydride preferentially attacked 1,2 to the carbonyl group. There was no instance of conjugate reduction by the reagent as in the diketones of Lutz.

If one considers the resonance structures which are exhibited in the diketones of Lutz, consideration must be given to the spatial configuration of the compound in question. The benzene nuclei in dimesitoylethylene cannot be planar with the carbonyl groups because of the ortho substituents on the rings; hence the resonance structures which must be considered must arise from the encircled part pictured below.



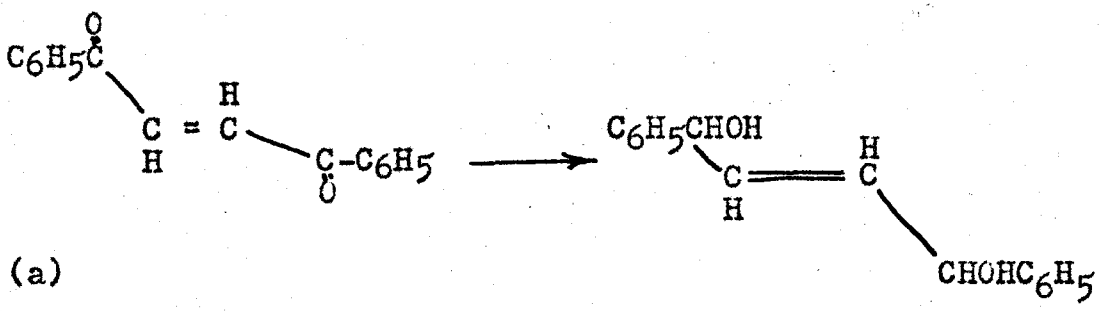
These resonance structures are pictured below where R = mesitoyl.



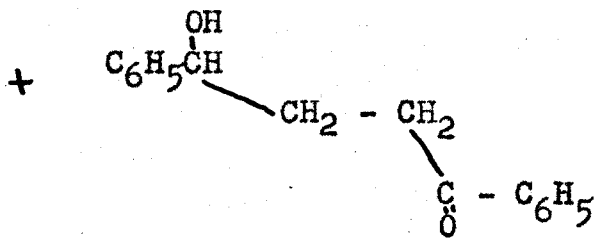
When Lutz reduced dimesitoylethylene, he obtained only the hydroxyketone, indicating that the preferential attack by

the reagent was 1,4. Steric hindrance must have diminished the facility of the 1,2 attack at the carbonyl group, but did not affect the 1,4 attack.

When Lutz reduced dibenzoylethylene he obtained the hydroxyketone, c, as the main product, but also obtained the unsaturated glycol (b).

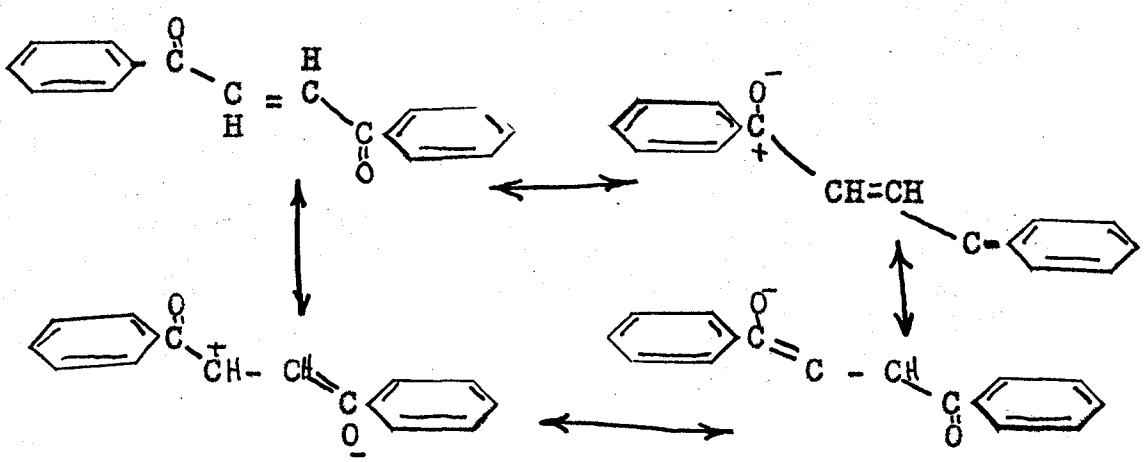


(a) (b)



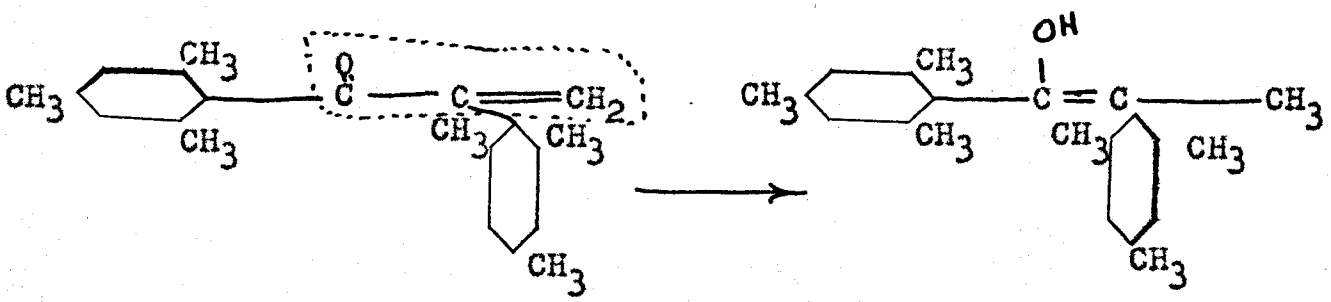
(c)

The benzene nuclei in dibenzoylethylene can be planar, hence they can be considered in the resonance forms.



Although the preferred path taken by the reagent in the above reduction was 1,4, there was 1,2 reaction at the carbonyls also as indicated by the presence of the unsaturated glycol, (b). Steric hindrance did not deminish the 1,2 attack at the carbonyl as in dimesitoylethylene.

Lutz repated that he obtained and isolated the unsaturated enol, (b) when he reduced 1,2-dimesitoylpropenone by lithium aluminum hydride.



(A) (B)

The compound above exhibits similar resonance formulae as did dimesitoylethylene. The benzene nuclei cannot be planar with the carbonyl group because of the ortho methyl groups on the ring, so that the resonance forms to be considered are as pictured below.

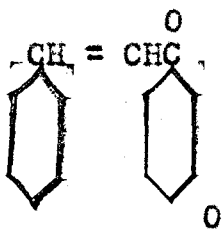
(C) (D)

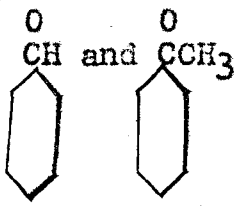
If mesityl group R_2 is planar in resonance formula D, then the structure will be further stabilized, and 1,4 attack by the reagent would be facilitated. Steric hindrance of mesityl group R_1, would diminish the 1,2 attack at the carbonyl group but would not affect the 1,4 attack.

In the reduction of the benzalacetophenones here reported several points should be noted. The conjugated system present in the compounds is somewhat different from that in the unsaturated compounds previously studied since it contains only one carbonyl group. The benzene nuclei are planar with the rest of the molecule and can therefore contribute to the resonance structures of the molecule. There is no steric hindrance to diminish a possible 1,2 addition of the reagent to the conjugated system. No instance of conjugate reduction by lithium aluminum hydride was found in the present study.

EXPERIMENTAL

Benzalacetophenone



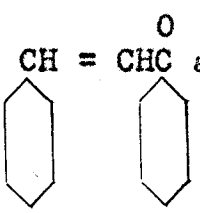
Reactants: 

A solution of 44 g. of chemically pure sodium hydroxide (1.1 mole) in 396 g. of distilled water and 245 ml. of 95% ethyl alcohol was introduced into a 2-liter flask fitted with a stirrer and a thermometer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 104 g. of acetophenone (0.86 mole) was poured, the flask was immediately surrounded by ice and the stirrer was started. Immediately afterwards 112 g. of benzaldehyde (1.05 mole) was added. The temperature was kept at approximately 25°C, and

was not allowed to go below 15°C nor above 30°C. Stirring was continued until the mixture thickened (about 3.5 hours); then it was placed in an icebox overnight. The mixture was filtered on a Buchner funnel and washed with cold water until the washings were neutral to litmus. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 50°C. The alcoholic solution was allowed to cool gradually, then placed in an ice bath at 0°C to complete the recrystallization.

Yield: 163.5 g.; 91.5% of theory.
M.p. 56-57.5°C.

Reduction Product of Benzalacetophenone by Aluminum Isopropoxide

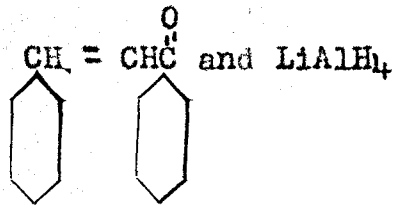
Reactants:  and $Al(OC_3H_7)_3$

A solution of 10 g. of benzalacetophenone (0.048 mole) was dissolved in 75 ml. of freshly distilled anhydrous isopropanol and introduced into a flask fitted with a still-head and heated by a heating mantle. A 50-ml. volume of hot 1.0M aluminum isopropoxide solution was added and the mixture was refluxed for 30 minutes. Acetone was evolved slowly.

The solvent was evaporated under reduced pressure. The residue was hydrolyzed in the cold with 100 ml. of 50% sodium hydroxide solution and extracted with three 100-ml. volumes of ether. The ether extract was washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which crystallized upon scratching the container and cooling it in an ice bath at 0°C. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 30°C. The alcoholic solution was placed in an icebox at 0°C to complete the recrystallization. The melting point of the product obtained agreed with the melting point of 1,3-diphenyl-3-hydroxy-1-propene, the expected product. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. Maximum absorption occurred at a wavelength of 255 mu, indicating the presence of a styryl radical which is present in 1,3-diphenyl-3-hydroxy-1-propene.

Yield: 8.8 g.; 88.0% of theory.
M.p. 55-56°C.

Reduction Product of Benzalacetophenone by Lithium Aluminum Hydride

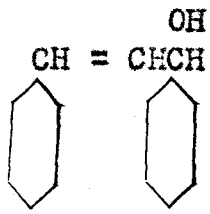
Reactants:  and $LiAlH_4$

A solution of 10 g. of benzalacetophenone (0.048 mole) dissolved in 100 ml. of anhydrous ether was slowly added to 2 g. of lithium aluminum hydride (0.052 mole) dissolved in 200 ml. of anhydrous ether. After all the ethereal benzalacetophenone solution had been added, the mixture was stirred for 10 minutes. The mixture was then cooled in an ice bath and hydrolyzed by dropwise addition of 100 ml. of water followed by 100 ml. of 10% sulfuric acid. The ether layer was extracted, washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure. An oil remained which did not solidify upon scratching the sides of the container or upon standing in an icebox at 0°C for two weeks. The oil was fractionally distilled, the largest fraction distilling over at 151-153°C and at 2 mm pressure. The distillate did not crystallize upon standing in an icebox at 0°C for six months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. The absorption spectrum of the product above was almost identical with the absorption

spectrum of the product obtained by reduction with aluminum isopropoxide, 1,3-diphenzl-3-hydroxy-1-propene.

Yield: 9.3 g.; 92.2% of theory.

Oxidation of 1,3-diphenyl-2-propen-1-ol to benzalacetophenone.

Reactants:  and CrO_3

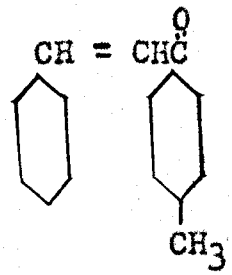
A solution of 2 g. of 1,3-diphenyl-2-propen-1-ol (0.01 mole) obtained by the reduction of benzalacetophenone with aluminum isopropoxide in 100 ml of glacial acetic acid was introduced into a flask fitted with a stirrer. A solution of 1.0 g. of chromium trioxide (0.01 mole) in 10 ml of 50% acetic acid was added dropwise over a period of 30 minutes with continued stirring for another 30 minutes. The acetic acid solution was then poured on ice. Crystals formed which were filtered on a Buchner funnel, washed with cold water, and recrystallized from 95% ethanol. The oxidation product gave no depression of melting point in mixture with benzalacetophenone.

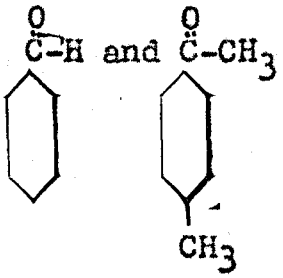
Yield: 1.3 g.; 62.8% of theory.

M.p. 56-57°C.

Similar oxidation of the oil obtained by lithium aluminum hydride reduction of benzalacetophenone gave only a resinous-like substance which could not be crystallized.

p'-Methylbenzalacetophenone



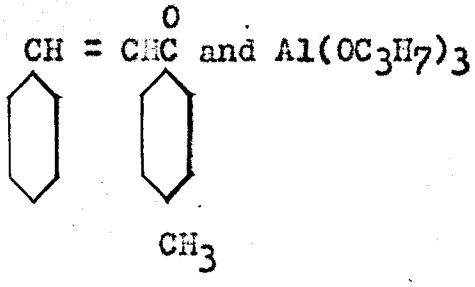
Reactants: 

A solution of 40 g. of chemically pure sodium hydroxide (1.0 mole) in 400 ml. of water and 245 ml. of 95% ethanol was introduced into a 2-liter flask fitted with a stirrer and a thermometer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 134 g. of methyl p-tolyl ketone (1.0 mole) was added, the flask was immediately surrounded by ice, and the stirrer was started. Immediately afterwards 106 g. of benzaldehyde (1.0 mole) was added. Stirring

was continued for 7 hours at 25°C after which the mixture was placed in an icebox overnight. The mixture was filtered on a Buchner funnel and washed with water until the washings were neutral to litmus. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 40°C. The alcholic solution was allowed to cool gradually, then placed in an ice bath at 0°C to complete the recrystallization.

Yield: 183.7 g.; 82.7% of theory.
M.p. 58-59°C.

Reduction Product of p'-Methylbenzalacetophenone by Aluminum Isopropoxide

Reactants:  and $Al(OC_3H_7)_3$

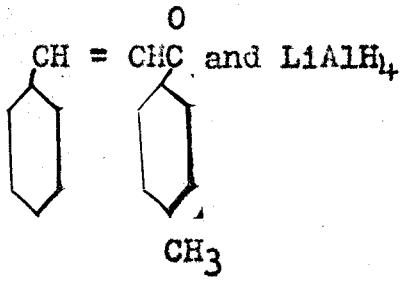
A solution of 11 g. of p'-methylbenzalacetophenone (0.049 mole) was dissolved in 75 ml. of freshly distilled anhydrous isopropanol and introduced into a flask fitted with a still-head and heated by a heating mantle. A 50-ml. volume of hot 1.0M aluminum isopropoxide solution was added

and the mixture was refluxed for 50 minutes. Acetone was evolved slowly. The solvent was evaporated under reduced pressure. The residue was hydrolyzed in the cold with 100 ml. of 50% sodium hydroxide solution and extracted with three 100-ml. volumes of ether. The ether extract was washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which crystallized upon scratching the container and cooling it in an ice bath at 0°C. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 40°C. The alcoholic solution was placed in an icebox at 0°C to complete the recrystallization. The product obtained by the above reduction and the product obtained by reduction with lithium aluminum hydride gave a mixture melting point of 73-74°C. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. The absorption spectrum of the product above was almost identical with the spectrum of the product obtained by reduction with lithium aluminum hydride, i.e., 1-(p-methylphenyl)-3-phenyl-2-propene-1-ol.

Yield: 9.8 g.; 89.3% of theory.

M.p. 73-74°C.

Reduction Product of p'-Methylbenzalacetophenone by Lithium Aluminum Hydride

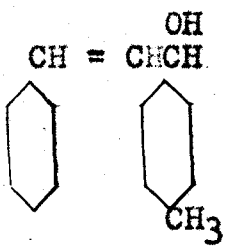
Reactants:  and $LiAlH_4$

A solution of 11 g. of p'-methylbenzalacetophenone (0.049 mole) dissolved in 100 ml. of anhydrous ether was slowly added to 4 g. of lithium aluminum hydride (0.104 mole) dissolved in 300 ml. of anhydrous ether. After all the ethereal p'-methylbenzalacetophenone solution had been added, the mixture was stirred for 20 minutes. The mixture was then cooled in an ice bath and hydrolyzed by dropwise addition of 100 ml. of water followed by 100 ml. of 10% sulfuric acid. The ether layer was extracted, washed twice with water and dried over sodium sulfate overnight. The ether was evaporated by reduced pressure employing no heat. An oil remained which crystallized upon scratching the container and cooling in an ice bath at 0°C. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 40°C. The alcoholic solution was placed in an icebox at 0°C to complete the recrystallization. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectro-

photometer. Maximum absorption occurred at a wavelength of 255 mu, indicating the presence of a styryl radical which is present in 1-(p-methylphenyl)-3-phenyl-2-propen-1-ol.

Yield: 9.3 g.; 84.7% of theory.
M.p. 73-74°C.

Oxidation of 1-(p-methylphenyl)-3-phenyl-2-propen-1-ol to p'-methylbenzalacetophenone.

Reactants:  and CrO_3

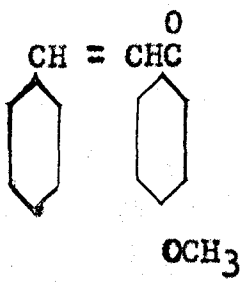
A solution of 2.2 g. of 1-(p-methylphenyl)-3-phenyl-2-propen-1-ol (0.01 mole) obtained by reduction of p'methylbenzalacetophenone with lithium aluminum hydride in 100 ml. of glacial acetic acid was introduced into a flask fitted with a stirrer. A solution of 1 g. of chromium trioxide (0.01 mole) in 10 ml. of 50% acetic acid was added dropwise over a period of 30 minutes with continued stirring for another 30 minutes. The acetic acid solution was then poured on ice. Crystals formed which were filtered on a Buchner funnel, washed with cold water and recrystallized from 95% ethanol. The oxidation

product above gave no depression of melting point in mixture with p'methylbenzalacetophenone.

Yield: 1.1 g.; 49.9% of theory.
M.p. 58-59°C.

Similar oxidation of 1-(p-methylphenyl)-3-phenyl-2-propen-1-ol obtained by aluminum isopropoxide reduction of p'-methylbenzalacetophenone gave the expected product, p'methylbenzalacetophenone.

p'-Methoxybenzalacetophenone



Reactants:  and 

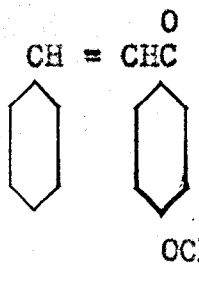
A solution of 40 g. of chemically pure sodium hydroxide (1.0 mole) in 400 ml. of water and 245 ml. of 95% ethanol was

introduced into a 2-liter flask fitted with a stirrer and a thermometer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 150 g. of p-methoxyacetophenone (1.0 mole) was added, the flask was immediately surrounded by ice, and the stirrer was started. Immediately afterwards 106 g. of benzaldehyde (1.0 mole) was added. The temperature was kept at 25°C ± 5°C. Stirring was continued for 3 hours, then the mixture was placed in an ice-box overnight. The mixture was filtered on a Buchner funnel and washed with cold water until the washings were neutral to litmus. The product was then recrystallized from boiling 95% ethanol. The alcoholic solution was allowed to cool gradually, then it was placed in an ice bath at 0°C to complete the recrystallization.

Yield: 191.7 g.; 80.6% of theory.

M.p. 107-108°C.

Reduction Product of p'-Methoxybenzalacetophenone by Aluminum Isopropoxide

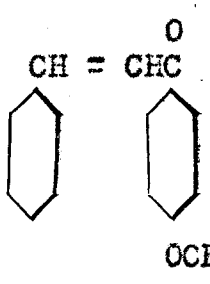
Reactants:  and $Al(OC_3H_7)_3$

A solution of 12 g. of p'-methoxybenzalacetophenone (0.050 mole) was dissolved in 100 ml. of freshly distilled anhydrous isopropanol and introduced into a flask fitted with a still-head and heated by a heating mantle. A 60-ml. volume of hot 1.0M aluminum isopropoxide solution was added and the mixture was refluxed for 75 minutes. Acetone was evolved slowly. The solvent was evaporated under reduced pressure. The residue was hydrolyzed in the cold with 100 ml. of 50% sodium hydroxide solution and extracted with three 100-ml. volumes of ether. The ether extract was washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which would not crystallize upon scratching the container and cooling it in an ice bath at 0°C. The product began to crystallize upon continued standing in an icebox, but would not crystallize completely. A white paste was obtained upon repeated scratching of the container and upon standing in

an icebox at 0°C for four months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. Maximum absorption occurred at a wavelength of 260 mu, indicating the presence of a styryl group. The absorption spectrum of the product above was almost identical with that of the product obtained by reduction with lithium aluminum hydride. The spectrum indicated that the product was 1-(p-methoxyphenyl)-3-phenyl-2-propen-1-ol.

Yield: 10.8 g.; 90.0% of theory.

Reduction Product of p'-methoxybenzalacetophenone by Lithium Aluminum Hydride

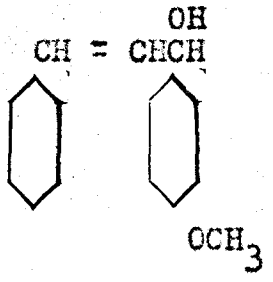
Reactants:  and $LiAlH_4$

A 12-g. sample of p'-methoxybenzalacetophenone (0.050 mole) was extracted from a Soxhlet thimble over a period of 5 hours by refluxing with a solution of 4 g. of lithium aluminum hydride (0.104 mole) dissolved in 500 ml. of anhydrous ether. This procedure was employed because the compound was difficultly soluble in ether. The mixture was cooled in an ice

bath and hydrolyzed by dropwise addition of 100 ml. of water followed by 100 ml. of 10% sulfuric acid. The ether was extracted, washed twice with water and dried over sodium sulfate overnight. The ether was evaporated employing no heat. An oil remained which would not crystallize upon scratching the sides of the container and upon continued standing in an icebox at 0°C. The oil was fractionally distilled, the largest fraction distilling over at 200-202°C and at 0.2 mm pressure. The distillate did not crystallize upon standing in an icebox at 0°C for eight months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. Maximum absorption occurred at a wavelength of 260 mu, indicating the presence of a styryl group. The absorption spectrum indicated that the product was 1-(p-methoxyphenyl)-3-phenyl-2-propen-1-ol.

Yield: 10.2 g.; 85.0% of theory.

Oxidation of 1-(p-methoxylphenyl)-3-phenyl-2-propen-1-ol to p'-methoxybenzalacetophenone.

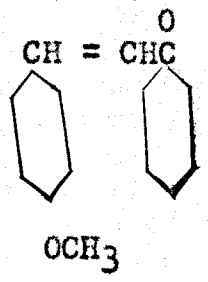
Reactants:  and CrO_3

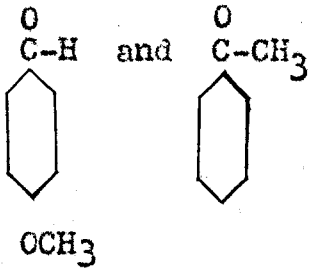
A solution of 2.4 g. of 1-(p-methoxyphenyl)-3-phenyl-2-propen-1-ol (0.01 mole) obtained by reduction of p'-methoxybenzalacetophenone with lithium aluminum hydride in 100 ml. of glacial acetic acid was introduced into a flask fitted with a stirrer. A solution of 1.0 g. of chromium trioxide (0.01 mole) in 10 ml. of 50% acetic acid was added dropwise over a period of 30 minutes, with continued stirring for another 30 minutes. The acetic acid solution was then poured on ice. Crystals formed which were filtered on a Buckner funnel. Not enough product was formed for recrystallization.

Yield: 0.7 g., 29.4% of theory.
M.p. 100-101 (crude).

Similar oxidation of the product obtained by reduction with aluminum isopropoxide gave a resinous product which could not be crystallized.

p-Methoxybenzalacetophenone



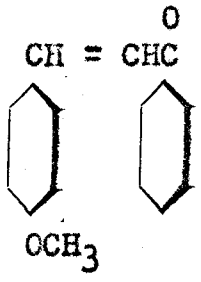
Reactants: 

A solution of 40 g. of chemically pure sodium hydroxide (1.0 mole) in 400 ml. of water and 245 ml. of 95% ethanol was introduced into a 2-liter flask fitted with a stirrer and a thermometer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 120 g. of acetophenone (1.0 mole) was poured, the flask was immediately surrounded by ice and the stirrer was started. Immediately afterwards 136 g. of anisaldehyde (1.0 mole) was added. The temperature was kept at approximately 25°C and was not allowed to go below 15° nor above 30°C. Stirring was continued until the mixture thickened, then it was placed in an icebox overnight. The mixture was filtered on a Buchner funnel and washed with cold water until the washings were neutral to litmus.

The product was then recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 50°C, since the product would separate as an oil at a higher temperature. The alcoholic solution was allowed to cool gradually, then it was placed in an ice bath at 0°C to complete the recrystallization.

Yield: 203.8 g.; 85.6% of theory.
M.p. 77-78°C.

Reduction Product of p-Methoxybenzalacetophenone by Aluminum Isopropoxide

Reactants:  and $Al(OC_3H_7)_3$

A solution of 12 g. of p-methoxybenzalacetophenone (0.050 mole) was dissolved in 150 ml. of freshly distilled anhydrous isopropanol and introduced into a flask fitted with a still-head and heated by a heating mantle. A 50-ml. volume of hot 1.0M aluminum isopropoxide solution was added and the mixture was refluxed for 60 minutes. The solvent was evaporated under reduced pressure. The residue was hydrolyzed

in the cold with 100 ml. of 50% sodium hydroxide solution and extracted with three 100-ml. volumes of ether. The ether extract was washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which would not crystallize upon scratching the container and upon standing in an icebox at 0°C for three weeks. The product was fractionally distilled, the largest fraction distilling over at 156-157°C and at 0.15 mm pressure. The distillate would not crystallize upon standing in an icebox at 0°C for 8 months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. The absorption spectrum obtained on the above product was almost identical with the spectrum of the product obtained by reduction with lithium aluminum hydride. The absorption spectrum indicated that the product was 3-(p-methoxyphenyl-1-phenyl-2-propen-1-ol.

Yield: 10.7 g.; 89.3% of theory.

Reduction Product of p-Methoxybenzalacetophenone by Lithium Aluminum Hydride

Reactants: $CH = CHC(=O)$ and $LiAlH_4$

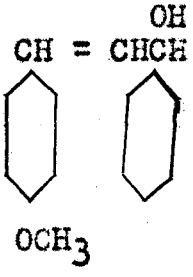
OCH_3

A solution of 12 g. of p-methoxybenzalacetophenone (0.050 mole) dissolved in 200 ml. of anhydrous ether was slowly added to 3 g. of lithium aluminum hydride (0.078 mole) dissolved in 250 ml. of anhydrous ether. After all the ethereal p-methoxybenzalacetophenone solution had been added, the mixture was stirred for 20 minutes. The mixture was then cooled in an ice bath and hydrolyzed by dropwise addition of 100 ml. of water followed by 100 ml. of 10% sulfuric acid. The ether layer was extracted, washed twice with water, and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which would not solidify upon scratching the sides of the container or upon standing in an icebox at 0°C for four weeks. The oil was fractionally distilled, the largest fraction distilling over at 167-160°C and at 0.2 mm pressure. The distillate would not crystallize upon standing in an icebox at 0°C for six months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectro-

photometer. Maximum absorption occurred at a wavelength of 260 mu, indicating the presence of a styryl group. The absorption spectrum indicated that the product was 3-(p-methoxyphenyl)-1-phenyl-2-propen-1-ol.

Yield: 10.6 g.; 88.3% of theory.

Oxidation of 3-(p-methoxyphenyl-1-phenyl-2-propen-1-ol.

Reactants:  and CrO_3

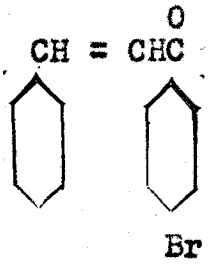
A solution of 2.4 g. of 3-(p-methoxyphenyl)-1-phenyl-2-propen-1-ol (0.01 mole) obtained by reduction of p-methoxybenzalacetophenone with lithium aluminum hydride in 100 ml. of glacial acetic acid was introduced into a flask fitted with a stirrer. A solution of 1.0 g. of chromium trioxide (0.01 mole) in 25 ml. of 50% acetic acid was added dropwise over a period of 40 minutes. The acetic acid solution was then poured on ice. Some crystallization was apparent, but when the product was filtered on a Buchner funnel, a resinous-like material appeared.

Yield: 0.8 g.; 33.6% of theory.

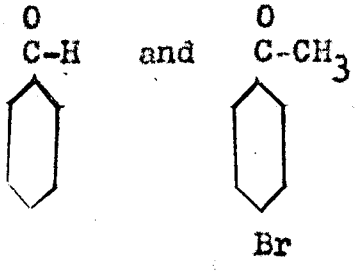
Similar oxidation of the product obtained by reduction with aluminum isopropoxide gave crystals which gave a mixture melting point of 76°C with p-methoxybenzalacetophenone. The product was, therefore, p-methoxybenzalacetophenone, thus proving that the double bond was not reduced in the aluminum isopropoxide reaction.

Yield: 1.2 g.; 50.4 % of theory.
M.p. 77°C.

p'-Bromobenzalacetophenone



Reactants:



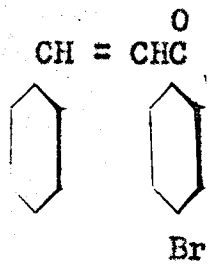
A solution of 10 g. of chemically pure sodium hydroxide (0.25 mole) in 100 ml. of water and 75 ml. of 95% ethanol was introduced into a 500-ml. flask fitted with a stirrer

and a thermometer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 50 g. of p-bromoacetophenone (0.25 mole) was placed, the flask was immediately surrounded by ice and the stirrer was started. Immediately afterwards 26.5 grams of benzaldehyde (0.25 mole) was added. Stirring was continued for 4 hours at 25±5°C, then the mixture was placed in an icebox overnight. The mixture was filtered on a Buchner funnel and washed with cold water until the washings were neutral to litmus. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 60°C. The alcoholic solution was allowed to cool gradually, then it was placed in an ice bath at 0°C to complete the recrystallization.

Yield: 60.8 g.; 84.7% of theory.

M.p. 99-100°C.

Reduction Product of p'-Bromobenzalacetophenone by Aluminum Isopropoxide

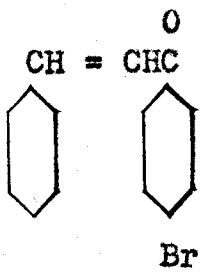
Reactants:  and $Al(OC_3H_7)_3$

A solution of 14 g. of p'-bromobenzalacetophenone (0.049 mole) was dissolved in 100 ml. of freshly distilled anhydrous isopropanol and introduced into a flask fitted with a still-head and heated by a heating mantle. A 60 ml. volume of hot 1.0M aluminum isopropoxide solution was added rapidly and the mixture was refluxed for one hour. The solvent was evaporated under reduced pressure. The residue was hydrolyzed in the cold with 100 ml. of 50% sodium hydroxide solution and extracted with three 100-ml. volumes of ether. The ether was washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which crystallized upon scratching the container and upon standing in an icebox at 0°C for three weeks. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 30°C. The alcoholic solution was placed in an icebox at 0°C to complete the recrystallization. The

ultraviolet absorption spectrum of the product was determined in a Beckman D U quartz spectrophotometer. The absorption spectrum of the above product and the spectrum of the product obtained by reduction with lithium aluminum hydride were almost identical. The spectrum indicated that the product was 1-(p-bromophenyl)-3-phenyl-2-propen-1-ol.

Yield: 10.8 g.; 76.0% of theory.
M.p. 46.5-47°C.

Reduction Product of p'-Bromobenzalacetophenone by Lithium Aluminum Hydride

Reactants:  and $LiAlH_4$

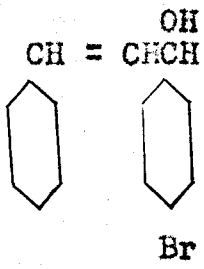
A solution of 14 g. of p'-bromobenzalacetophenone (0.049 mole) dissolved in 100 ml. of anhydrous ether was slowly added to 3 g. of lithium aluminum hydride (0.078 mole) dissolved in 300 ml. of anhydrous ether. After all the ethereal p'-bromobenzalacetophenone solution had been added, the mixture was stirred for 15 minutes. The mixture was then cooled in an ice bath and hydrolyzed by dropwise addition of

100 ml. of water followed by 100 ml. of 10% sulfuric acid. The ether layer was extracted, washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which would not crystallize upon continued standing in an icebox at 0°C. The oil was fractionally distilled, the largest fraction distilling over at 168-170°C and at 0.15 mm pressure. The distillate crystallized on standing at 0°C in an icebox for two months. The ultraviolet absorption spectrum of the product was determined on a Beckman DU quartz spectrophotometer. Maximum absorption occurred at a wavelength of 265 mu, indicating the presence of a styryl group. The absorption spectrum indicated that the compound was 1-(p-bromophenyl)-3-phenyl-2-propen-1-ol.

Yield: 12.8 g.; 90.1% of theory.

M.p. 46.5-47°C.

Oxidation of 1-(p-bromophenyl)-3-phenyl-2-propen-1-ol to p'-bromobenzalacetophenone

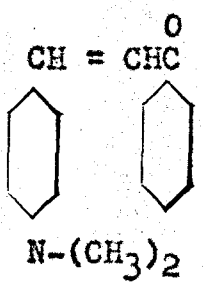
Reactants:  and CrO_3

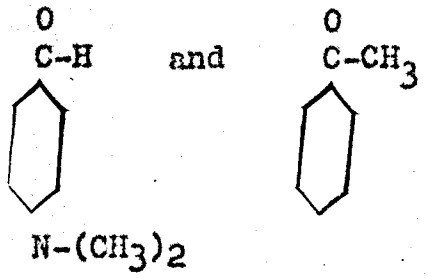
A solution of 2.8 g. of 1-(p-bromophenyl)-3-phenyl-2-propen-1-ol (0.01 mole) obtained by the reduction of p'-bromochalcone with lithium aluminum hydride dissolved in 100 ml. of glacial acetic acid was introduced into a flask fitted with a stirrer. A solution of 1 g. of chromic acid (0.01 mole) in 10 ml. of 50% acetic acid was added dropwise over a period of 30 minutes with continued stirring for another 30 minutes. The acetic acid solution was then poured on ice. Crystals formed which were filtered on a Buchner funnel, washed with cold water and recrystallized from 95% ethanol. The product gave no depression of melting point when mixed with p'-bromobenzalacetophenone.

Yield: 1.5 g.; 52.2% of theory.

M.p. 101-102°C.

p-Dimethylaminobenzalacetophenone



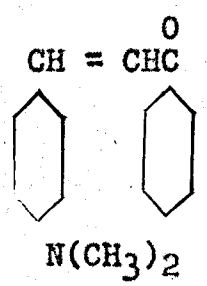
Reactants:  and

A solution of 20 g. of chemically pure sodium hydroxide (0.5 mole) in 200 ml. of water and 125 ml. of 95% ethanol was introduced into a 1-liter flask fitted with a stirrer and a thermometer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 75 g. of p-dimethylaminobenzaldehyde (0.5 mole) was added, the flask immediately surrounded by ice and the stirrer started. Immediately afterwards 60 g. of acetophenone (0.5 mole) was added. Stirring was continued for 8 hours at 25°C ± 5°, then the mixture was filtered on a Buchner funnel and washed with cold water until the washings were neutral to litmus. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above

60°C. The alcoholic solution was allowed to cool gradually, then it was placed in an ice bath at 0°C to complete the recrystallization.

Yield: 54.4 g.; 43.4% of theory.
M.p. 114-114.5°C.

Reduction Product of p-Dimethylaminobenzalacetophenone by Aluminum Isopropoxide

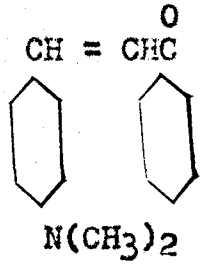
Reactants:  and $Al(OC_3H_7)_3$

A solution of 12.5 g. of p-dimethylaminobenzalacetophenone (0.050 mole) was dissolved in 75 ml. of freshly distilled anhydrous isopropanol and introduced into a flask fitted with a still-head and heated by a heating mantle. An 80-ml. volume of hot 1.0M aluminum isopropoxide solution was added and the mixture was refluxed for 2 hours. Acetone was evolved slowly. The solvent was evaporated under reduced pressure. The residue was hydrolyzed in the cold with 100 ml. of 50% sodium hydroxide and extracted with three 100 ml. volumes of ether. The ether extract was washed twice with

water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which would not solidify upon scratching the sides of the container or upon standing in an icebox at 0°C for four weeks. The oil was fractionally distilled, the largest fraction distilling over at 175-178°C and at 0.2 mm pressure. The distillate would not crystallize upon standing in an icebox at 0°C for eight months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. Maximum absorption occurred at wavelengths of 260 and 300 mu. The spectrum obtained indicated a probable mixture, but nothing of a definite nature can be said about the product or products obtained by the above reduction.

Yield: 11.2 g.; 88.8% of theory.

Reduction Product of p-Dimethylaminobenzalacetophenone by Lithium Aluminum Hydride

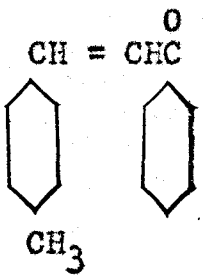
Reactants:  and $LiAlH_4$

A 12.5 g. sample of p-dimethylaminobenzalacetophenone (0.050 mole) was extracted from a Soxhlet thimble over a period of 6.5 hours by refluxing with a solution of 2 g. of lithium aluminum hydride (0.052 mole) dissolved in 500 ml. of anhydrous ether. This procedure was employed because the compound was difficultly soluble in ether. The mixture was cooled in an ice bath and hydrolyzed by dropwise addition of 100 ml. of water followed by 100 ml. of 10% sulfuric acid. The ether was extracted, washed twice with water and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure employing no heat. An oil remained which would not crystallize upon scratching the sides of the container and upon standing in an icebox at 0°C for eight months. The ultraviolet absorption spectrum of the product was determined in a Beckman DU quartz spectrophotometer. Maximum absorption occurred at 260 and 300 mu. The spectrum of the product above was similar to the spectrum of the product

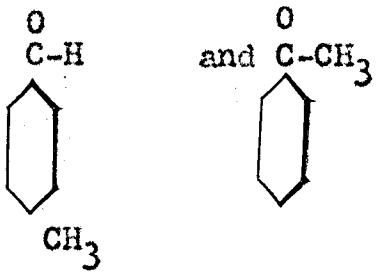
obtained by reduction with aluminum isopropoxide, but nothing of a definite nature can be said about the product or products obtained by the above reduction.

Yield: 10.7 g.; 84.9% of theory.

p-Methylbenzalacetophenone



Reactants:

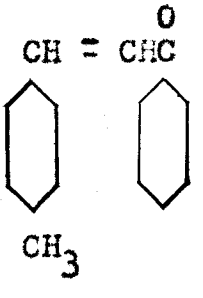


A solution of 40 g. of chemically pure sodium hydroxide (1.0 mole) in 400 ml. of water and 245 ml. of 95% ethanol was introduced into a 2-liter flask fitted with a stirrer and supported in a vessel which would permit cooling with ice. Into the alkaline solution 120 g. of acetophenone (1.0 mole) was added, the flask was immediately surrounded by ice and the stirrer was started. Immediately afterwards 120 g. of p-methylbenzaldehyde was added. The temperature

was kept at approximately 25°C, and was not allowed to go below 15°C nor above 30°C. Stirring was continued for 8 hours, then the mixture was placed in an icebox overnight. The mixture was filtered on a Buchner funnel and washed with cold water until the washings were neutral to litmus. The product was recrystallized from 95% ethanol. The temperature of the ethanol was not allowed to rise above 40°C. The alcoholic solution was allowed to cool gradually, then it was placed in an ice bath at 0°C to complete the recrystallization.

Yield: 179.6 g.; 80.9% of theory.
M.p. 55-56°C.

Reduction Product of p-Methylbenzalacetophenone by Lithium Aluminum Hydride

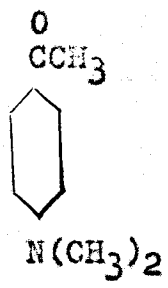
Reactants:  and $LiAlH_4$

A solution of 11 g. of p-methylbenzalacetophenone (0.050 mole) dissolved in 250 ml. of anhydrous ether was slowly added to 3 g. of lithium aluminum hydride (0.078 mole)

dissolved in 200 ml. of anhydrous ether. After all the ethereal p-methylbenzalacetophenone solution had been added, the mixture was stirred for 15 minutes. The mixture was then cooled in an ice bath and hydrolyzed by dropwise addition of 10[illegible] ml. of water followed by 100 ml. of 10% sulfuric acid. The ether layer was extracted, washed twice with water, and dried over sodium sulfate overnight. The ether was evaporated under reduced pressure. An oil remained which would not solidify upon scratching the sides of the container or upon standing in an icebox at 0°C for two weeks. Crystals began to form during the third week of standing in an icebox at 0°C. The product had not completely crystallized after standing for four months. The ultraviolet absorption spectrum was determined in a Beckman DU quartz spectrophotometer. Maximum absorption occurred at a wavelength of 255 and 315 mu. The absorption spectrum indicated the presence of a mixture of p-methylbenzalacetophenone and 3-(p-methylphenyl)-1-phenyl-2-propen-1-ol.

Yield: 8.9 g.; 79.4% of theory.

p-Dimethylaminoacetophenone

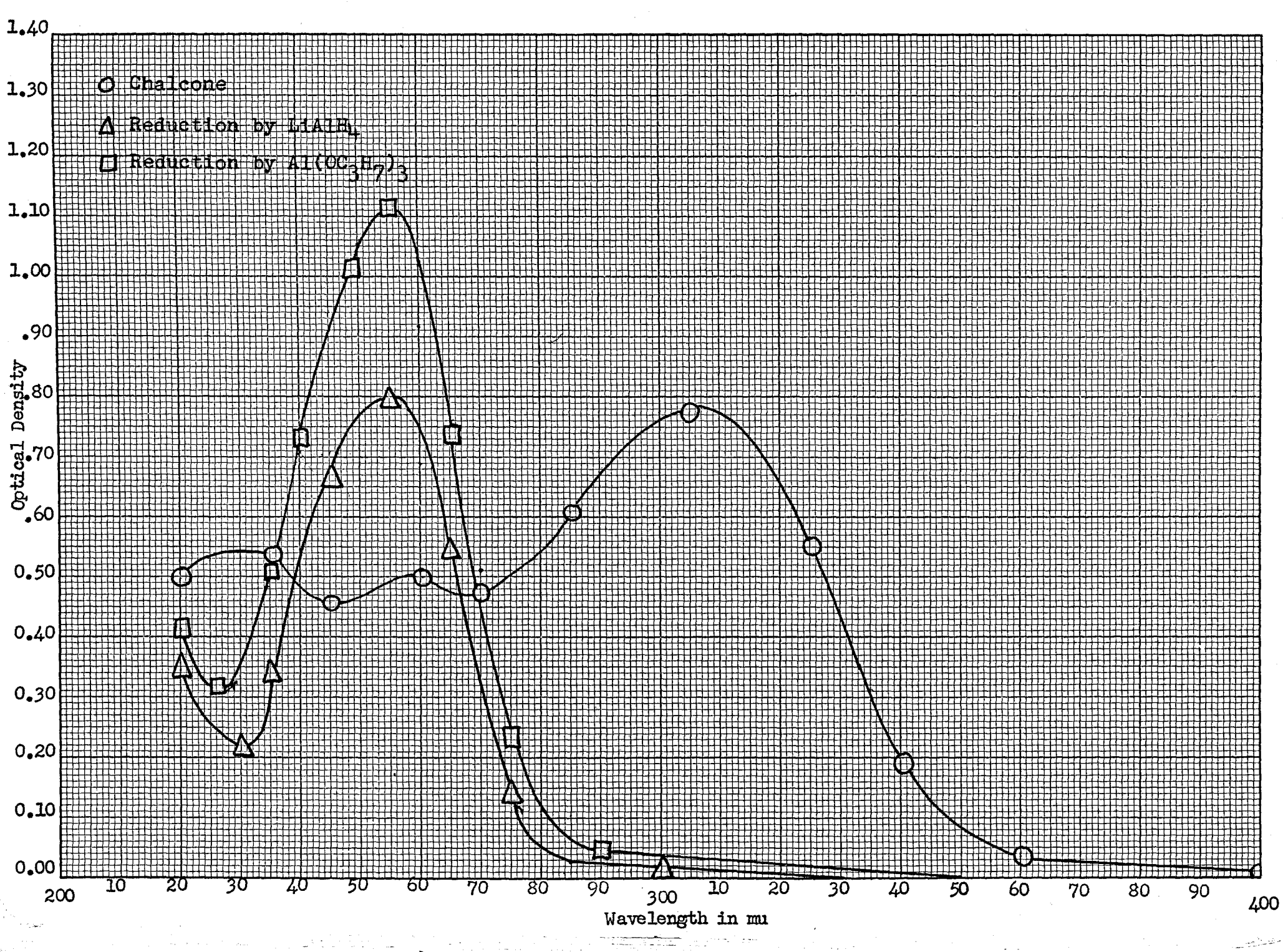


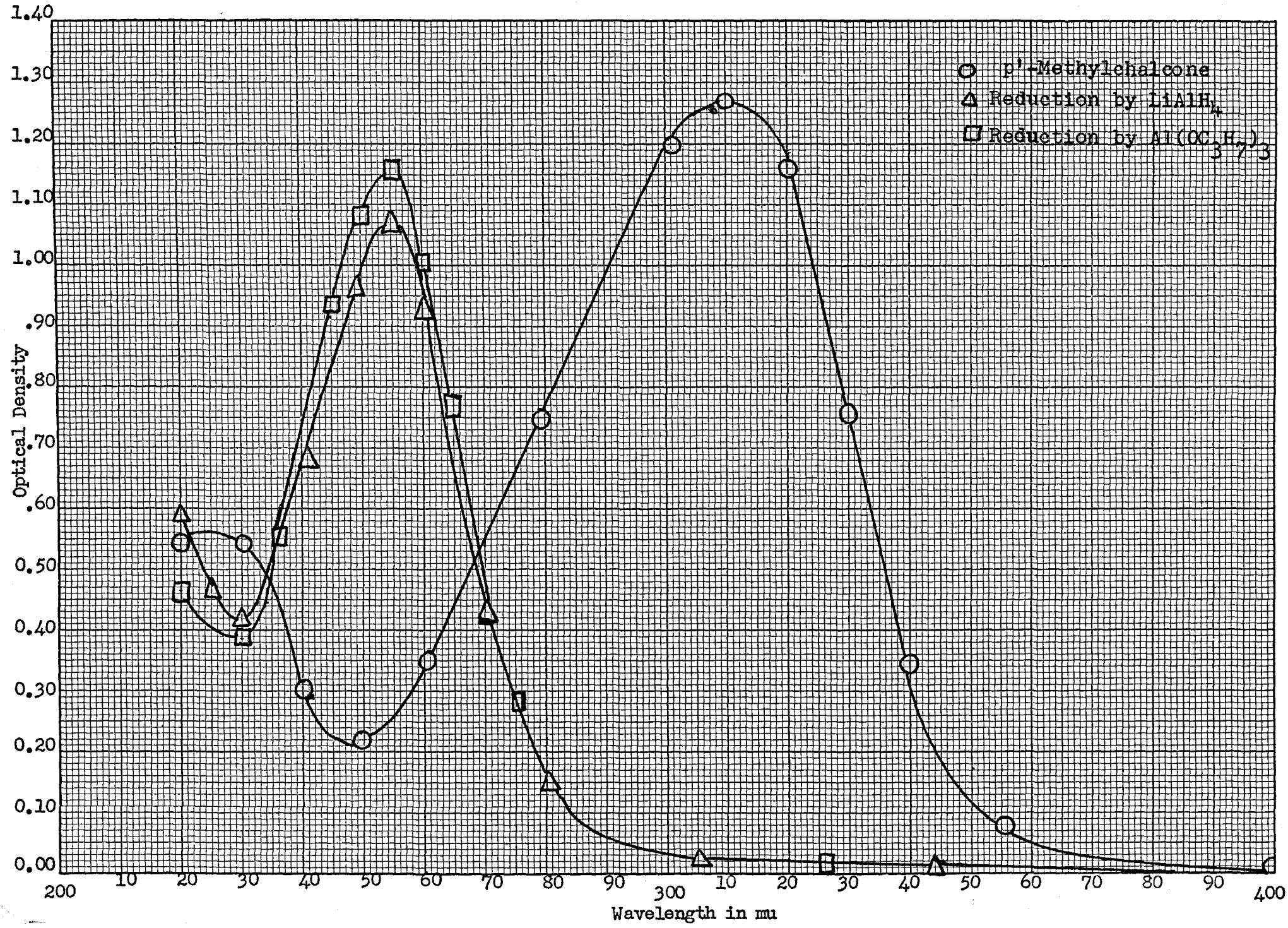
Reactants:  and $CH_3C(=O)-O-C(=O)CH_3$

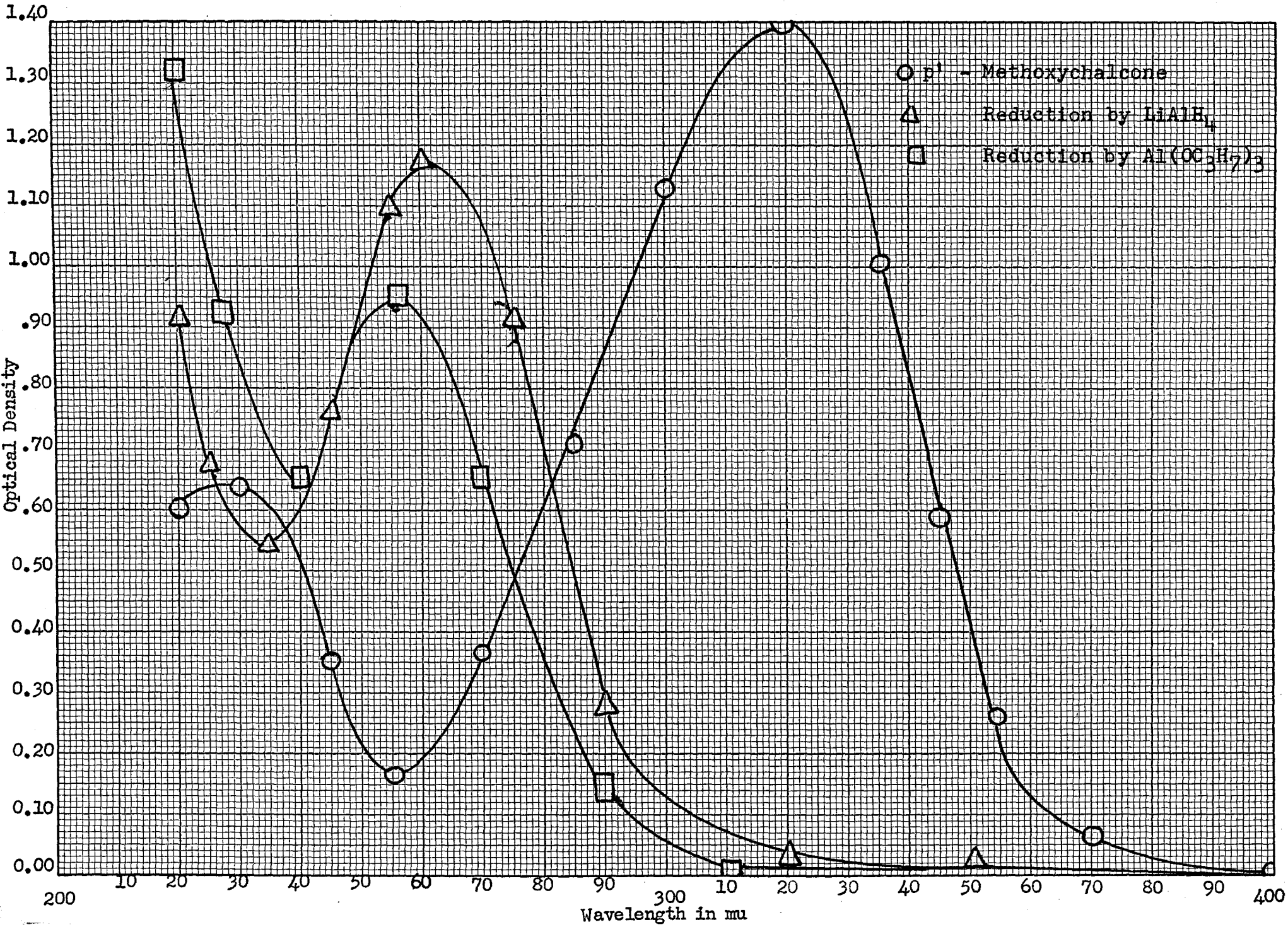
A solution of 89 g. of zinc chloride (0.65 mole) 70 g. of acetic anhydride (0.69 mole) and 50 g. of dimethylaniline (0.41 mole) was refluxed for four hours. A dark resinous material resulted which was extracted with three 200-ml. volumes of ether. The ether was evaporated, but no product remained.

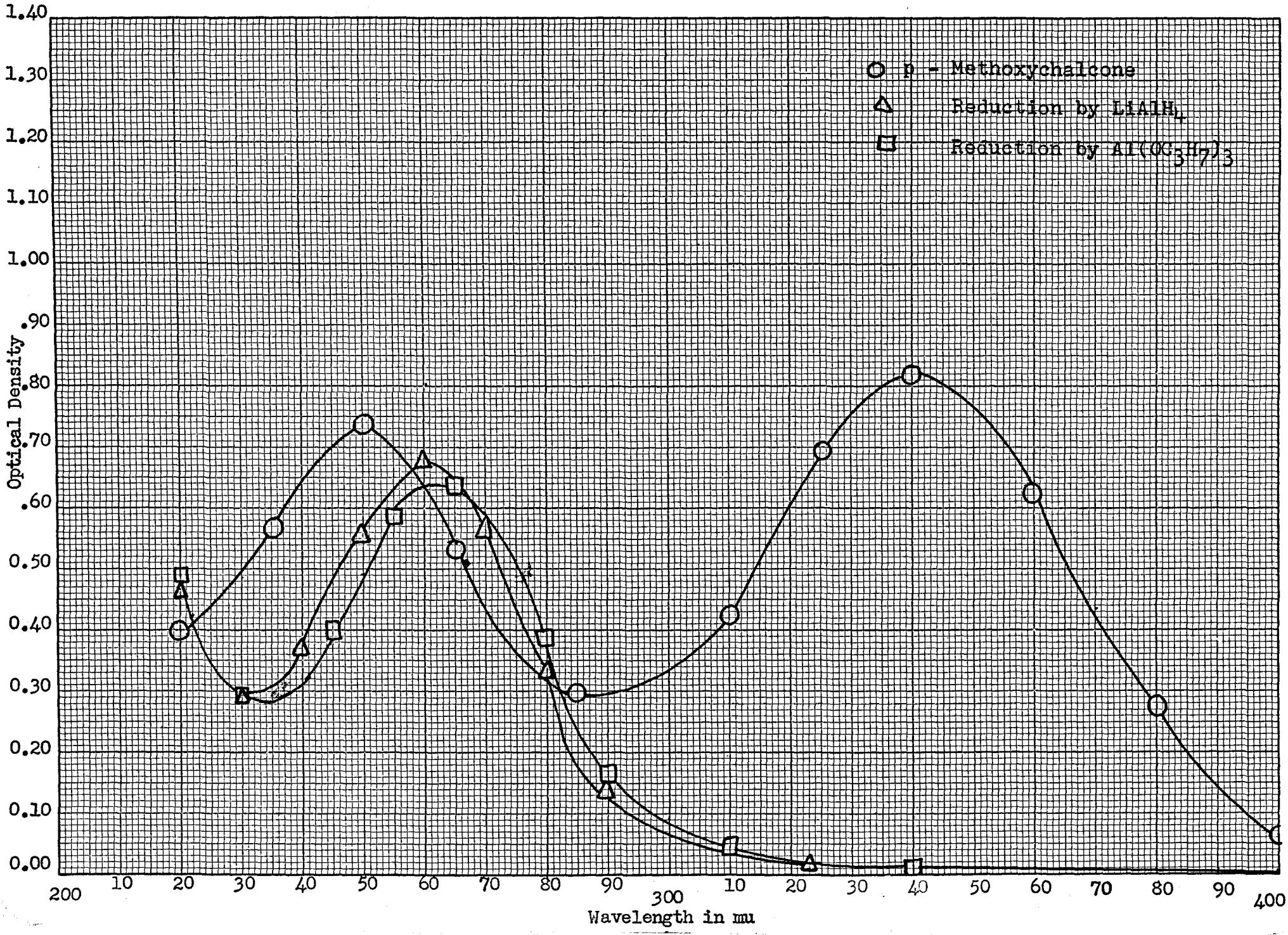
ABSORPTION SPECTRA DATA

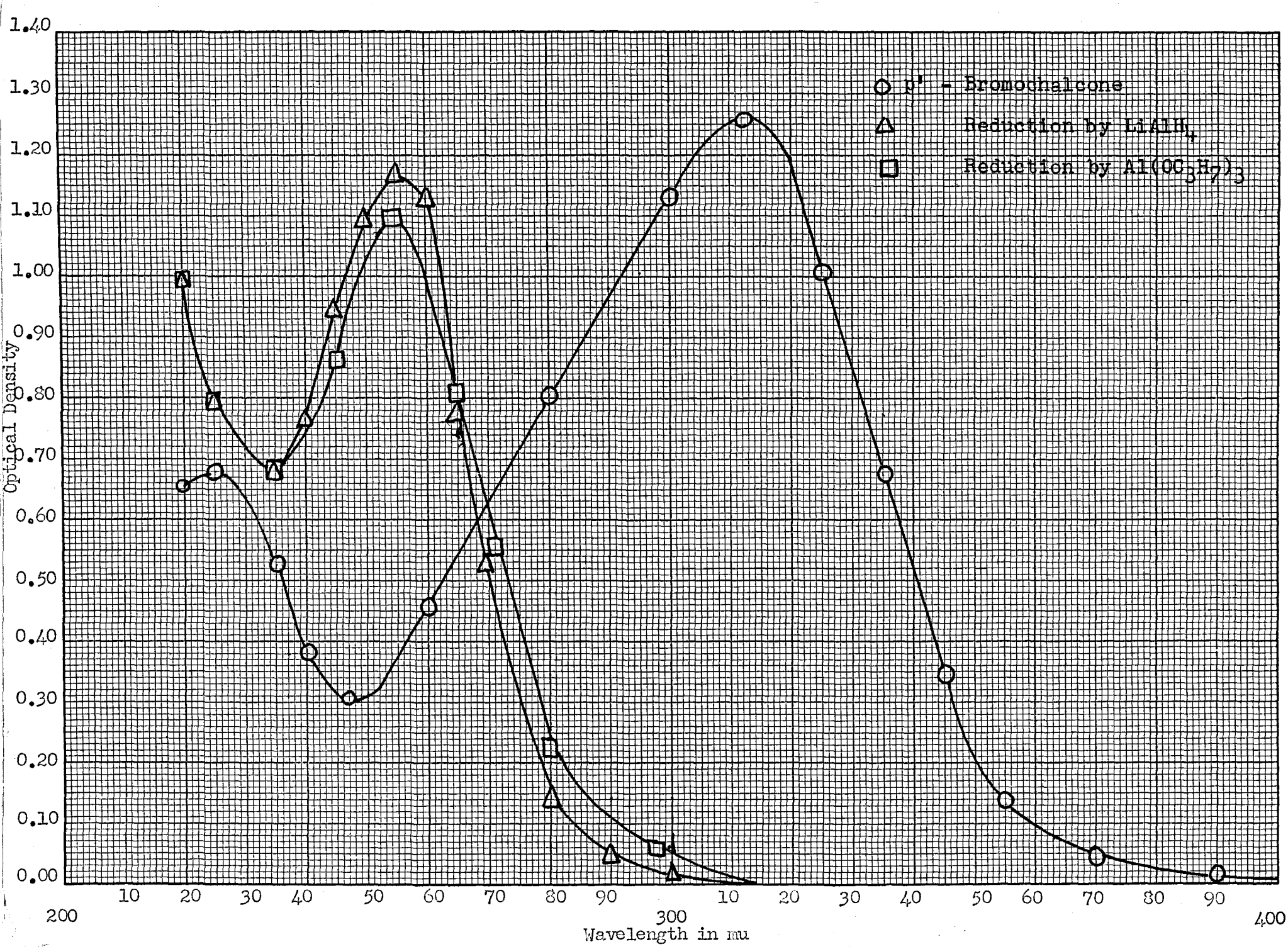
Compound		Wavelength max.	Wavelength min.	Extinction Coefficient max.	Extinction Coefficient min.
Benzalacetophenone		310	245	15620	9200
Phenylstyrylcarbinol		255	-	22400	-
p-Methoxybenzalacetophenone	(1) (2)	250 340	285	14460 16400	6040
3-(p-methoxyphenyl)-1-phenyl-2-propene-1-ol		260	-	12840	-
p'-methoxybenzalacetophenone		320	255	28000	3300
1-(p-methoxyphenyl)-3-phenyl-2-propen-1-ol		260	-	23600	-
p'-Methylbenzalacetophenone		310	245	25400	4320
1-(p-methylphenyl)-3-phenyl-2-propen-1-ol		255	-	51400	-
p-Methylbenzalacetophenone		315	-	24800	-
p'-Bromobenzalacetophenone		315	245	25200	6200
1-(p-Bromophenyl)-3-phenyl-2-propen-1-ol		255	-	22000	-
p-Dimethylaminobenzalacetophenone		265 420	340	16300 32000	3140

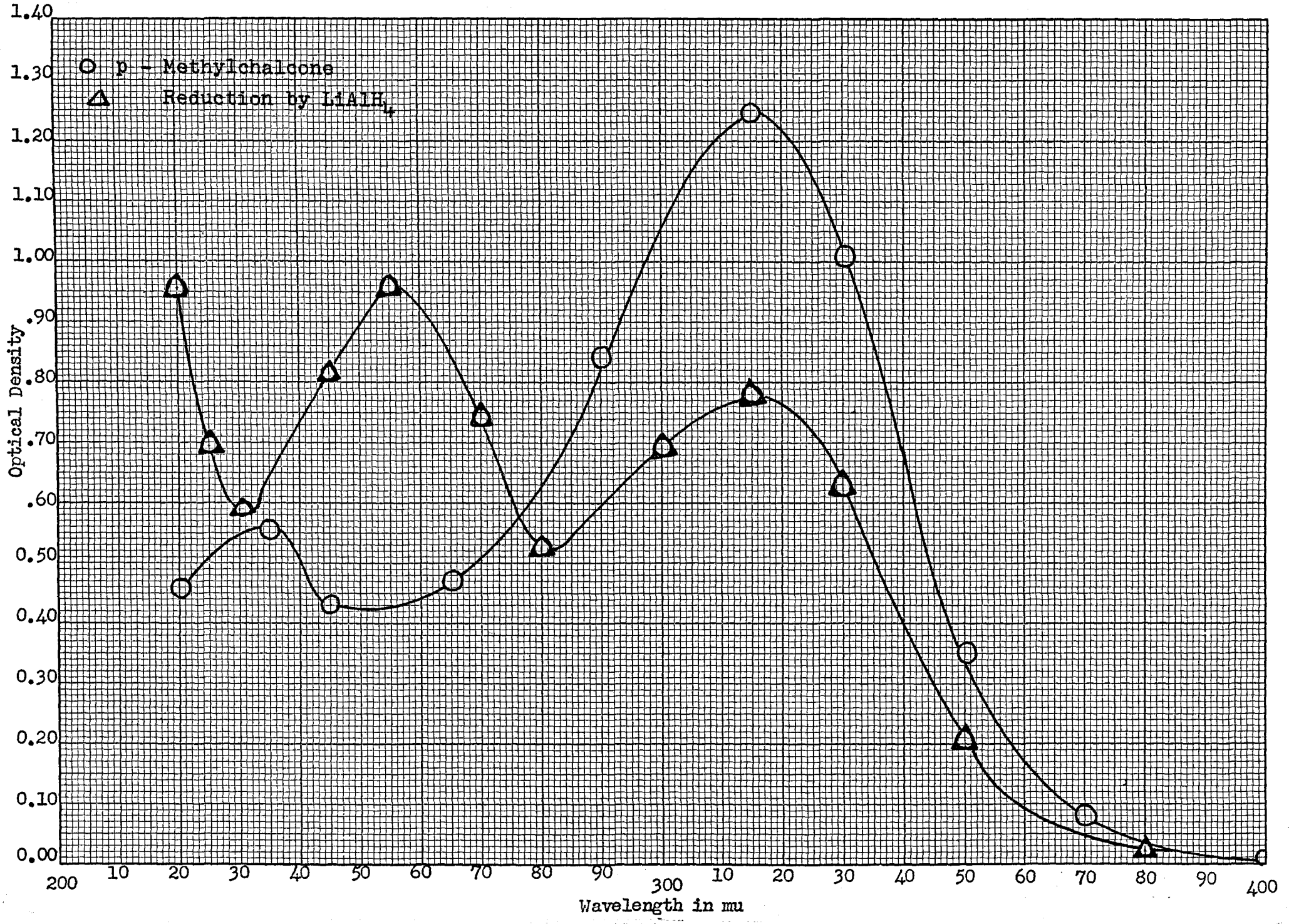

Chalcone
Reduction by $LiAlH_4$
Reduction by $Al(OC_3H_7)_3$
Optical Density
1.40
1.30
1.20
1.10
1.00
.90
.80
.70
.60
0.50
0.40
0.30
0.20
0.10
0.00
200
10
20
30
40
50
60
70
80
90
300
10
20
30
40
50
60
70
80
90
400
Wavelength in mu

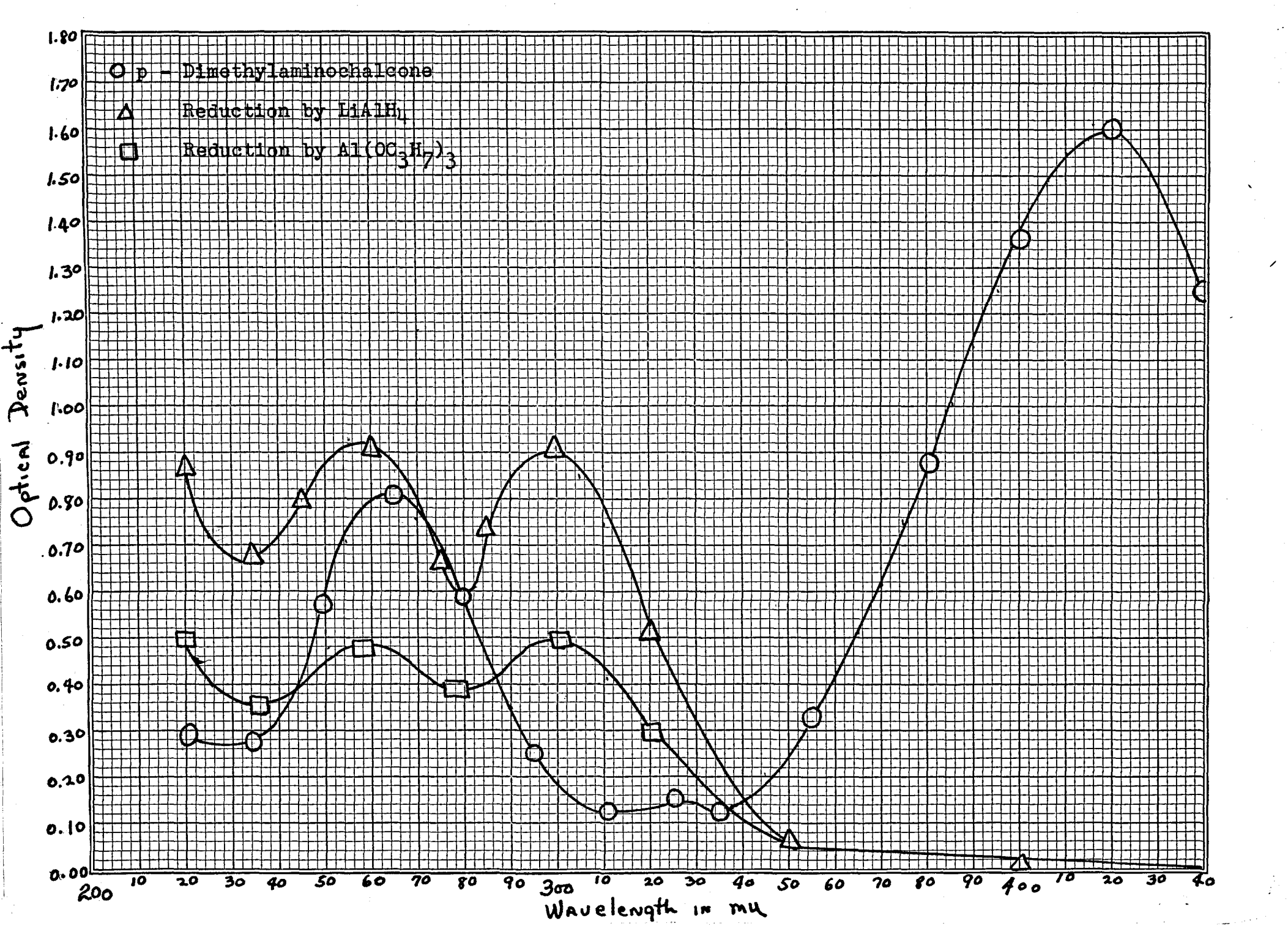

p'-Methylchalcone
Reduction by $LiAlH_4$
Reduction by $Al(OC_3H_7)_3$
Optical Density
1.40
1.30
1.20
1.10
1.00
.90
.80
.70
.60
0.50
0.40
0.30
0.20
0.10
0.00
200
10
20
30
40
50
60
70
80
90
300
10
20
30
40
50
60
70
80
90
400
Wavelength in mu


p' - Methoxychalcone
Reduction by $LiAlH_4$
Reduction by $Al(OC_3H_7)_3$
Optical Density
1.40
1.30
1.20
1.10
1.00
.90
.80
.70
.60
0.50
0.40
0.30
0.20
0.10
0.00
200
10
20
30
40
50
60
70
80
90
300
10
20
30
40
50
60
70
80
90
400
Wavelength in mu


p - Methoxychalcone
Reduction by $LiAlH_4$
Reduction by $Al(OC_3H_7)_3$
Optical Density
1.40
1.30
1.20
1.10
1.00
.90
.80
.70
.60
0.50
0.40
0.30
0.20
0.10
0.00
200
10
20
30
40
50
60
70
80
90
300
10
20
30
40
50
60
70
80
90
400
Wavelength in mu


p' - Bromochalcone
Reduction by $LiAlH_4$
Reduction by $Al(OC_3H_7)_3$
Optical Density
1.40
1.30
1.20
1.10
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
200
10
20
30
40
50
60
70
80
90
300
10
20
30
40
50
60
70
80
90
400
Wavelength in mu


○ p - Methylchalcone
△ Reduction by $LiAlH_4$
Optical Density
1.40
1.30
1.20
1.10
1.00
.90
.80
.70
.60
0.50
0.40
0.30
0.20
0.10
0.00
200
10
20
30
40
50
60
70
80
90
300
10
20
30
40
50
60
70
80
90
400
Wavelength in mu


p - Dimethylaminochalcone
Reduction by $LiAlH_4$
Reduction by $Al(OC_3H_7)_3$
Optical Density
1.80
1.70
1.60
1.50
1.40
1.30
1.20
1.10
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
200 10 20 30 40 50 60 70 80 90 300 10 20 30 40 50 60 70 80 90 400 10 20 30 40
Wavelength in mμ

SUMMARY

Some reductions of substituted benzalacetophenones by lithium aluminum hydride and aluminum isopropoxide are described. In all of the reductions described the product obtained was the corresponding unsaturated alcohol indicating a 1,2 reduction of the conjugated system. The ultraviolet absorption spectrum of each unsaturated alcohol is also given.

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AUTOBIOGRAPHY

I, Calvin Lyndall Fisher, was born on May 24, 1927, in Wilson, Virginia. When I was two years old, my father moved to Petersburg, Virginia, where I started my primary education. Due to the death of my father in 1935 I was placed in the Methodist Orphanage in Richmond, Virginia. I completed my primary education at Albert H. Hill Junior High School and in 1942 I entered Thomas Jefferson High School where I majored in general science. Upon graduation in 1945 I left the Orphanage and entered the United States Navy.

In 1947 I was honorably discharged from the Navy and entered the University of Richmond. There I majored in Chemistry and received the B.S. degree in 1949. I was awarded the Puryear Fellowship in Chemistry for the year 1951.

This thesis is submitted in partial fulfillment of the requirements for the M.S. degree for which I am an applicant.