

1972

The Mechanism of the Reaction of Lead(IV) Acetate, Thallium(III) Acetate and Mercury(II) Acetate with Ketones

Su Hsiung Tsung

Eastern Illinois University

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THE MECHANISM OF THE REACTION OF LEAD(IV) ACETATE,
THALLIUM(III) ACETATE AND MERCURY(II) ACETATE WITH KETONES
(TITLE)

BY

Su Hsiung Tsung
Bachelor of Science
Chung Yuan Christian College of
Science and Engineering, Chung Li
June, 1967

THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF

Master of Science

IN THE GRADUATE SCHOOL, EASTERN ILLINOIS UNIVERSITY
CHARLESTON, ILLINOIS

1972

YEAR

I HEREBY RECOMMEND THIS THESIS BE ACCEPTED AS FULFILLING
THIS PART OF THE GRADUATE DEGREE CITED ABOVE

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Thesis Approved :

Thesis Adviser

ACKNOWLEDGEMENTS

I am indebted to the entire faculty in the department of chemistry, especially to the guidance of Dr. Ellis. This study would have been impossible without his contributions.

I express my gratitude to my parents and brother for their continued support and understanding.

In addition, I would thank Miss. Chu-Chieh Huang for the encouragement to enable me to complete this work.

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Chapter I

Introduction

It is a well known fact that many routes to prove mechanisms of chemical reactions exist. Identification of products, isotope labeling, trapping of intermediates, stereochemical studies and evidence from reaction catalysis are frequently used to study reaction mechanisms. One of the most general and powerful methods of determining the mechanisms of reactions involves the use of kinetics.

Lead tetraacetate (LTA) has been used as a versatile oxidant for many years.¹ Most mechanisms of reactions involving LTA are still largely an enigma except the cleavage of diols. The mechanism of this oxidation has been widely studied.

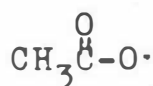
Many analogies as well as many differences have been found among lead tetraacetate, thallium triacetate (TTA), mercury acetate (MA) oxidation reactions. TTA exhibits properties in between those of LTA and MA. The main purpose of this work was to study the mechanism of the reaction of these metal acetates with ketones.

Historical Review

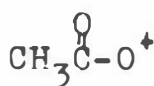
Various kinds of species have been suggested for the oxidation reaction with LTA. Acetoxy radicals (1) have been regarded as intermediates in many LTA oxidations.

Acetoxy cations (2) have been postulated as an active species in the LTA oxidation of organic acids.²

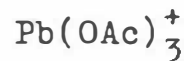
Many reactions can be understood by assuming that LTA loses an acetate ion forming 3.³



1



2

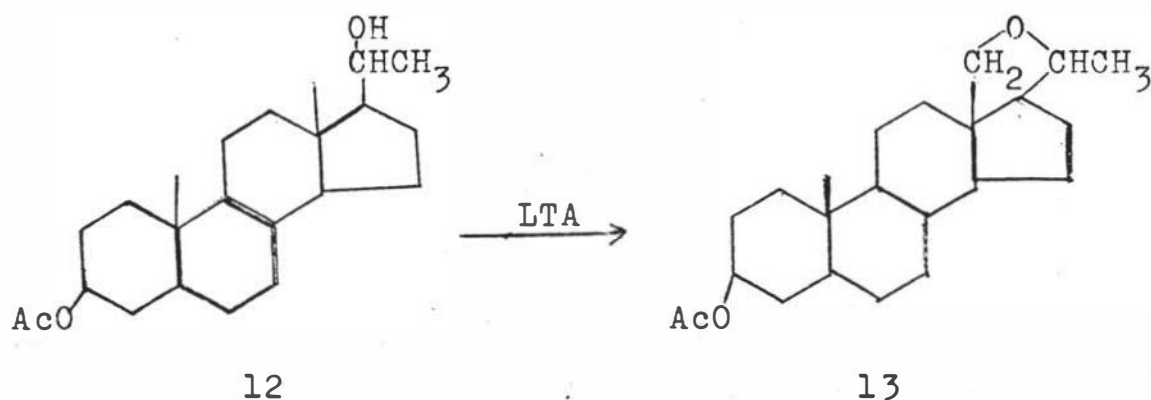


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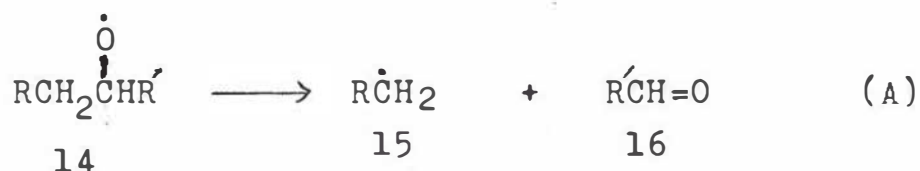
In 1952 two Japanese chemists, Ichikawa and Yamaguchi⁴, listed evidence suggesting that the rate of acetoxylation is dependent only on the concentration of the ketone. This implies that enolization of the ketone is the rate determining step in acetoxylation. Henbest⁵ and associates observed that the oxidation of ketones is strongly accelerated by boron trifluoride. They concluded that acceleration is probably due to catalysis by boron trifluoride to increase the rate of the enolization step.

Different mechanisms for the LTA oxidation have been reported in the literature.

Cavill and Solmon⁶ proposed that the oxidation of carbonyl compounds by LTA is free radical in nature. The mechanism postulated is shown below :

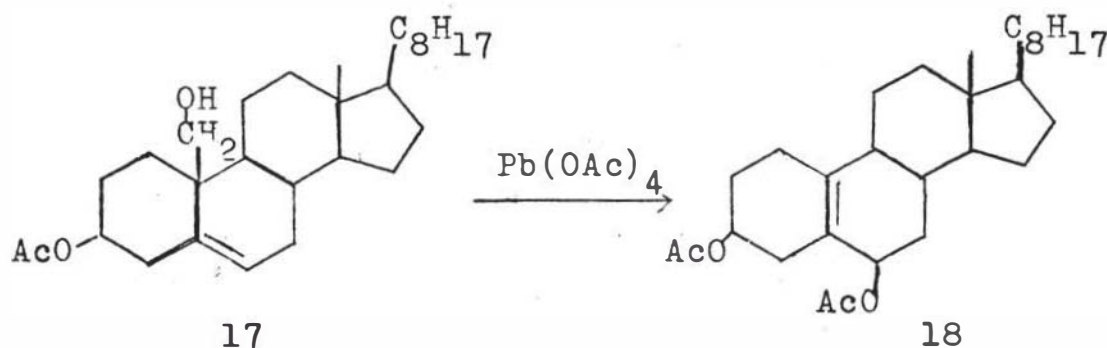


The mechanism was considered to go through the oxyradical which was formed from the hydroxyl group by LTA, then the hydrogen atom on the C-18 methyl could be abstracted intramolecularly. Once an oxygen radical has been produced by oxidation with LTA, fragmentation can take place as equation (A). The amount of cleavage that occurs increases with the stability of the alkyl radical formed.

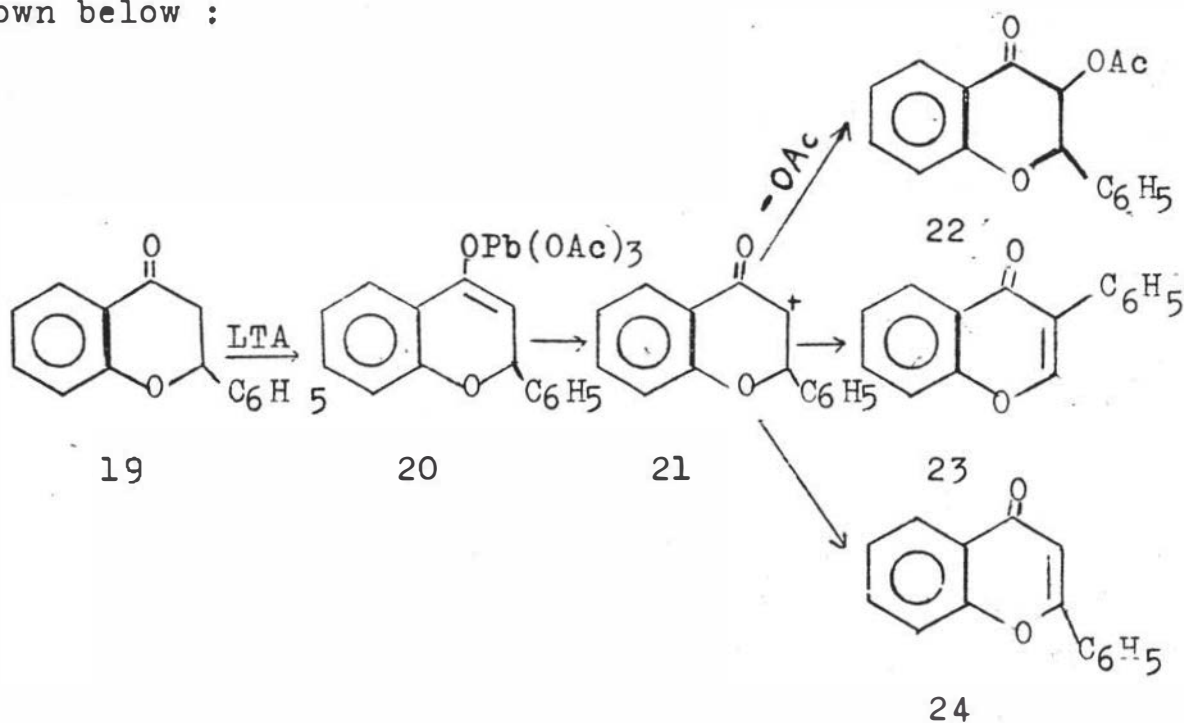


Some other factors can also influence the course of this reaction. Kaufman and Morand⁸ reported that the LTA oxidation of 3 β -acetoxycholest-5-en-19-ol (17) results in oxidative fragmentation with loss of the hydroxymethyl group at C-10, yielding as a product 3 β , 6 β -diacetoxy-19-nor-cholest-5-ene (18). The concerted

intramolecular transfer of an acetoxy group from the C-19 lead ester to C-6 in the resulting acetoxy group was postulated.

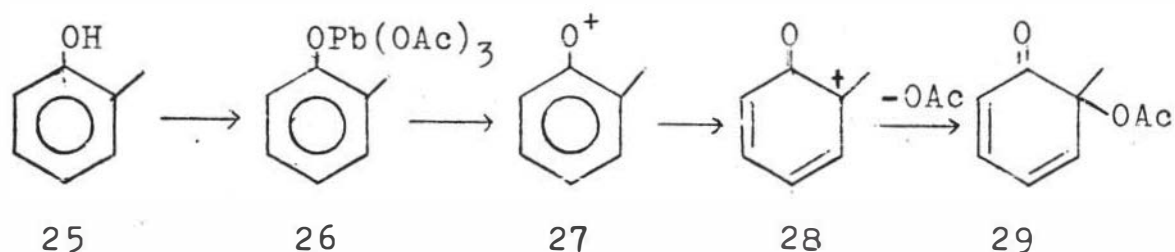


However, other workers reported that air oxidation was probably responsible for the observed radicals.⁹ In acetoxylation of flavanones by LTA, Criegee¹ suggested that an ionic mechanism seemed to be more probable as shown below :

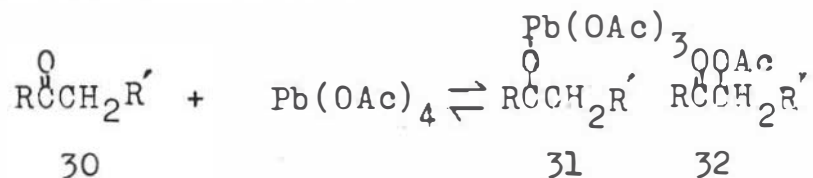


The products formed depend not only on the stability of the carbonium ion but also on the migratory aptitude of the substituent group.

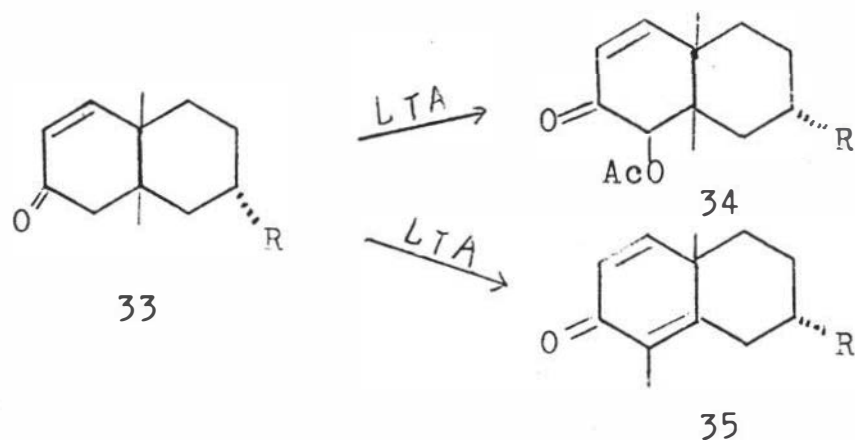
Criegee¹ also proposed from his work on phenols, that the acetoxylation resulted from the formation of a lead triacetoxy phenol derivative such as 26, followed by rearrangement of the lead ester to the product.



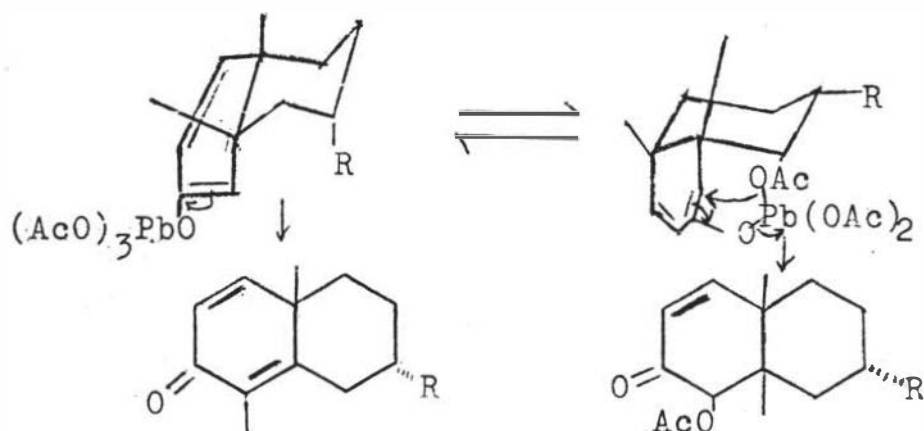
Corey¹⁰ reported the α -acetoxylation of ketones by LTA may involve the formation of an enol-lead triacetate 31 directly from the ketones followed by subsequent internal rearrangement and elimination.



A rearrangement was found to occur in the reaction of one unsaturated ketone with LTA. In addition to an α -acetoxyketone, a dienone 35 was also obtained.¹¹

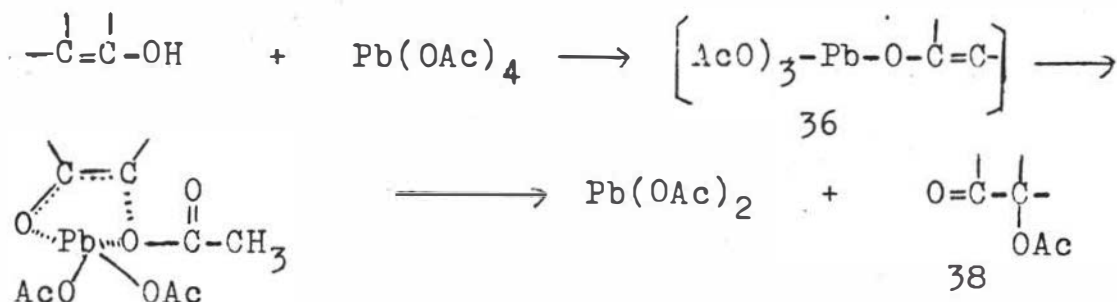


The Corey mechanism was applied to this reaction as follows :

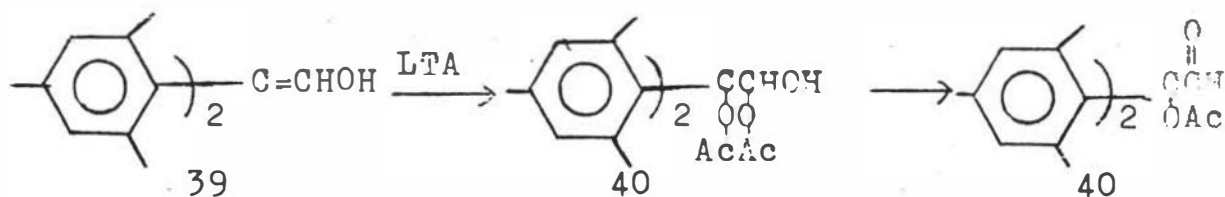


In this case steric effects retard the usually favored attack by acetate on the double bond thereby enabling methyl migration to occur. The disparity of the yield as the substituent changes from methyl to propyl was understood in terms of the stereoelectric effect.

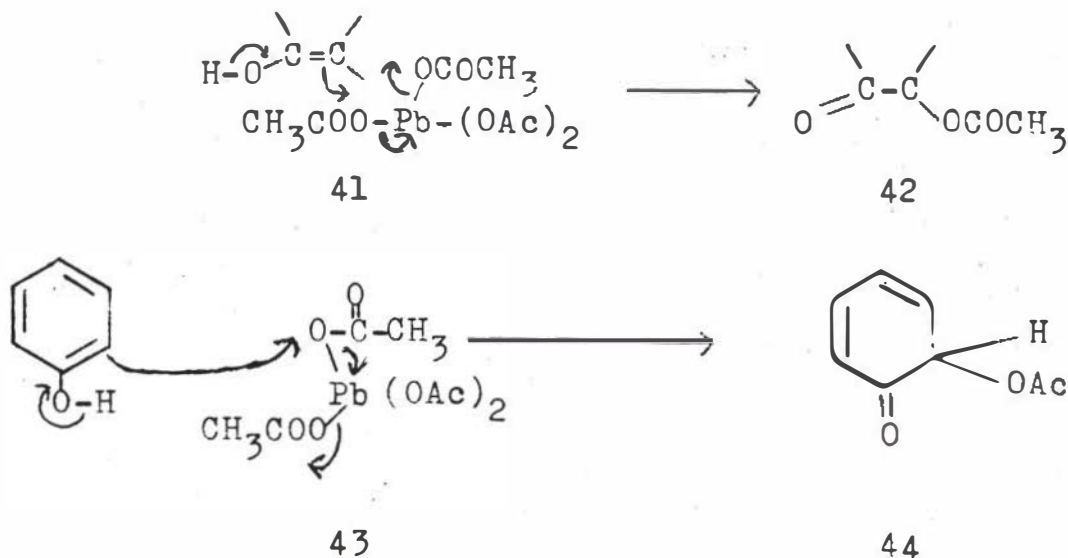
Fieser¹² rationalized that the delocalized transition state was involved in the reaction of ketones with LTA.



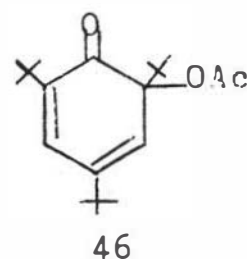
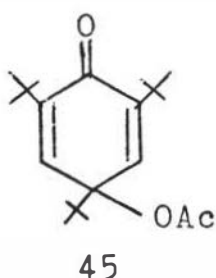
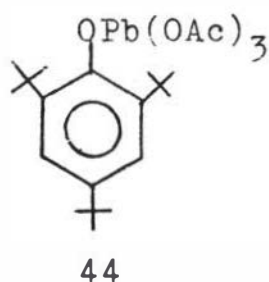
However, Fieser¹² presumed that the reaction of LTA with dimesitylvinyl alcohol (39) proceed via diacetoxy addition, followed by the elimination of acetic acid. This mechanism is similar to that proposed for the addition of LTA to olefins.¹²



Waters¹³ has suggested a concerted mechanism for both the enol form of ketones, such as 41, and phenols for example :

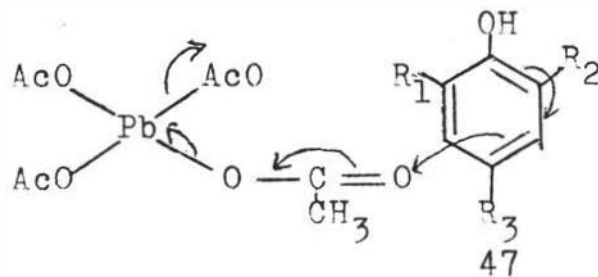


Norman¹⁴ recently explained the mechanism of oxidation of 2,4,6-tri-t-butylphenol with LTA from essentially the same point of view. The formation of the triacetoxylead ester 44 was then followed by a two electron transfer instead of one electron transfer to the product.

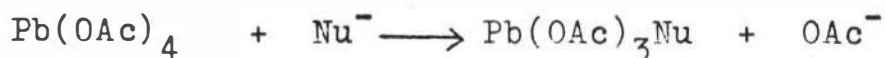


Wessely¹⁵ proposed a mechanism involving a one electron oxidation of the phenol to the corresponding aryloxy radical but Criegee¹⁶, Waring¹⁷ and Norman¹⁸ have mustered extensive evidence against free radical mechanism and proposed variants of a heterolytic mechanism which essentially amounts to nucleophilic displacement by acetate ions on a postulated intermediate aryloxy lead triacetate.

Bubb¹⁹ rationalized this as an electrophilic substitution. To obtain supporting evidence for this mechanism, the relative reactivity of a number of 2,4,6 trisubstituted phenols was examined. It was found that electron donating substituents accelerate and electron withdrawing groups retard the reaction.

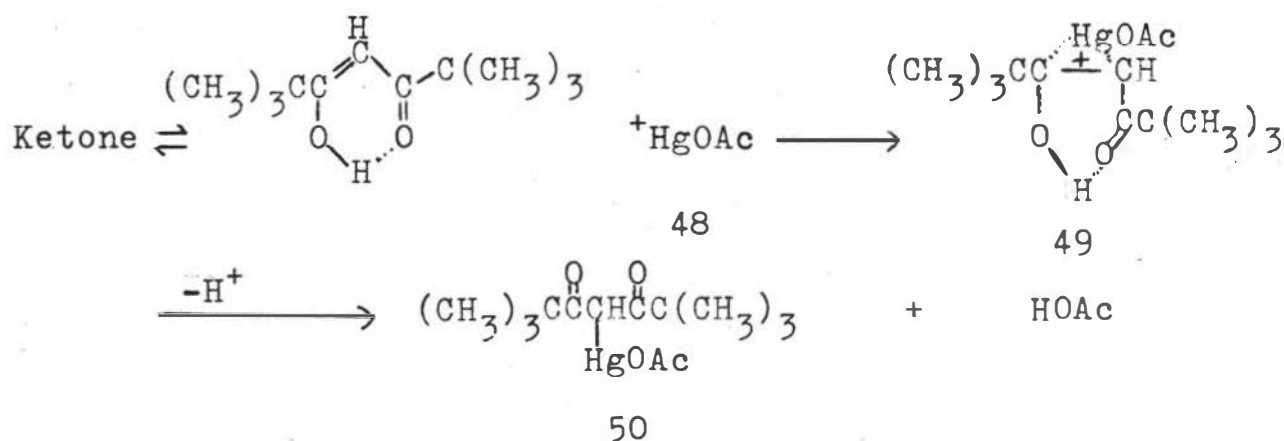


It also has been reported that LTA exchanges with nucleophiles very rapidly,¹ thus the formation of the lead ester is quite likely.



The oxidation of ketones and phenols by TTA and MA have rarely been investigated. In 1962 Hecker⁹ reported the use of TTA to oxidize p-alkylphenols to p-quinol acetate. This reaction is catalyzed by BF_3 . Treibs²⁰ found that ketones could be acetoxylated by MA at higher temperatures. Cyclohexanone afforded a small amount of the α -acetoxy derivative along with considerable tar and phenyl acetate.

Fish and Lundin²¹ suggested that mercury (II) differs from the other metals. When MA used to react with ketones, mercury is bonded to carbon instead of oxygen. The mechanism can be rationalized as below :



The mechanism is analogous to the addition of mercuric acetate to 1-butene or 2-butene, where allylic mercuricals are formed by addition of 48 to the double bond followed by loss of a proton.

Ouellette^{22, 23, 24} studied the kinetics of the cleavage of arylcyclopropane with MA. The cleavage reaction was postulated to involve electrophilic attack of these metal acetates on the cyclopropane ring. TTA has a similar action, but the reaction by TTA is complicated by double salt formation between $\text{Tl}(\text{OAc})_3$ and TlOAc .

Approach to Reaction Mechanism Studies

The two routes which were selected to study the reaction mechanism in this investigation were product analysis²⁵ and kinetic measurements.²⁶ The most fundamental basis for the mechanistic speculation is the identification of reaction products, for without such identification we can not be sure which reaction is actually under

consideration. Thus, when bromine is added to cyclohexene the products is trans-1,2-dibromo-cyclohexane, and any mechanism proposed for this reaction must account for trans addition.

Transition states and intermediates are two important parts of many mechanisms. For each step in a mechanism the molecular configuration at the point of highest energy is named the transition state. Transient species of variable stability are formed in most chemical reactions. These chemical species are called intermediates.²⁷

Although the empirical rate law does not give information about the geometry or structure of the transition state, the constitution and electric charge of the transition state for the rate determining step may sometimes be obtained from the empirical law. Non-integral orders in homogeneous reactions indicate that an important part of the mechanism is the splitting of a molecule. A more familiar type of reaction with non-integral order is the free radical chain mechanism.

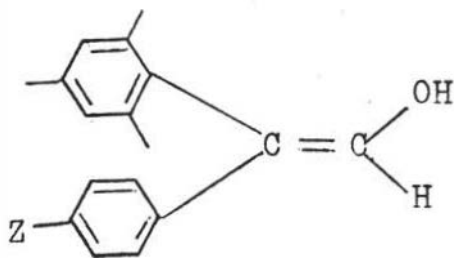
It has been previously discussed²⁶ in a qualitative way how changes in the structure can affect the chemical reactivity. Hammett first derived an equation (B) which relates structure-reactivity relationships in a more

quantitative manner. This equation is applied to meta and para substituted aromatic systems.

$$\log \frac{k_Z}{k_H} = \rho \sigma \quad (B)$$

In the Hammett equation k_Z and k_H are specific rate constants which are obtained from the rate law of this reaction, σ is a measure of the electron donating or electron withdrawing ability of the group Z on the benzene ring, and ρ reflects the sensitivity of a particular reaction to electron donation or electron withdrawal by Z .

If a compound such as 51 were chosen for the kinetic study,



51

various substituents Z could be used where $Z = -CH_3$, $-OCH_3$, $-Br$, etc. The value and sign of ρ would indicate the sensitivity of the reaction and the charge on the transition state. This could give very useful information about the mechanism.

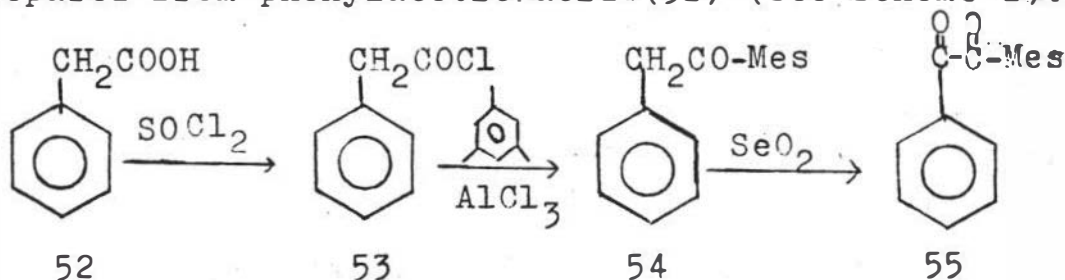
CHAPTER II

RESULTS and DISCUSSION

1. Kinetic Study

Since enolization is the rate determining step of the LTA oxidation with ketones, it is desirable to use a compound which is 100% enolized as a substrate for the kinetic study to determine the reaction mechanism. By doing this, the enolization step is bypassed so that the rate law might tell something about the next step.

If the reaction rate is taken into consideration, the low reactivity of the stereochemically hindered enol is expected. The enol, 2-mesityl-2-phenylvinyl alcohol (51, Z=H) was selected for this study. This compound was first prepared by R.C. Fuson, W. Rabjohn and D. T. Byers ²⁸ using high pressure hydrogenation for the reduction of mesitylphenyldiketone (55) which was prepared from phenylacetic acid (52) (see Scheme I).

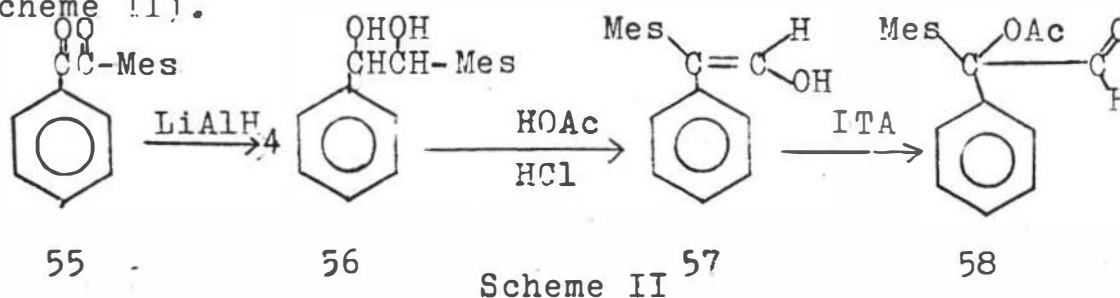


Scheme I

Since high pressure hydrogenation equipment was unavailable, lithium aluminum hydride was studied as a reagent to reduce 54 to 1-mesityl-2-phenylethylene glycol

(55). After a number of reactions were run, conditions were found where the glycol could be formed in about 40% yield. The glycol was rearranged to 51 ($Z=H$) in strong acid. The structure was confirmed by nmr.

Fuson²⁹ and coworkers reported that the enol (51, $Z=H$) reacted with LTA at 40° to produce the expected product 2-acetoxy-2-mesitylacetaldehyde (58) (see Scheme II).



Therefore the enol 51 ($Z=H$) seemed to meet all the requirements; it was 100% enolized, gave the α -acetoxy product, and judging from the 40° temperature reported by Fuson²⁹, should have a convenient reaction rate. Based on this information preliminary kinetic studies were undertaken.

Analysis of the lead (IV) content of the solution was accomplished by addition of aliquots of the reaction mixture to excess aqueous 5% potassium iodide. The resulting triiodide generated was titrated with standard sodium thiosulfate in the presence of a starch indicator.

The end point was a yellow heterogeneous mixture of lead diiodide. At 25° enol oxidation however took place rapidly and was complete in an extremely short period of time. Thus, the standard titration methods of analysis were not applicable.

The solvent can influence both the rates and mechanisms of reactions, but a solvent can change a rate without changing the mechanism by changing the force between reacting particles and hence altering the readiness with which they approach each other. Anhydrous tetrahydrofuran, glyme and dichloromethane were tried as solvents. However, the reaction rate was not decreased by changing the solvent.

Reactions which are fast at room temperature can be slowed down by cooling so that the rate can be determined by a conventional method.³⁰ A solution of 50% glacial acetic acid and 50% tetrahydrofuran was selected as a solvent. The reaction could not be run lower than -50° because of the limitation of the solubility of the LTA at lower temperatures. The rate constant was still too high to use conventional analytical techniques.

Sometimes high rate constants can be determined simply by using low concentrations of reactants. The

absorption due to the enol could be followed at 260 nm using ultraviolet spectroscopy at approximately 1.0×10^{-5} M concentration of each reactant. The reaction was complete in less than 3 seconds under these conditions. Having exhausted the available techniques and in the face of having to purchase expensive stopped flow equipment, other metal acetates were considered.

The reaction of $\text{Hg}(\text{OAc})_2$ with enol was attempted, but only starting material was observed. Apparently, lead(IV) acetate reacts extremely fast and MA not at all.

In view of these facts it was decided to try TTA since it is between Pb and Hg in the periodic table.

Indeed, when TTA was used to oxidize the enol in acetic acid at room temperature, 2-acetoxy-2-mesityl-acetaldehyde was obtained in about 65% yield. The reaction was slower than the reaction using LTA.

The kinetics of the decomposition of TTA in acetic acid have been reported at different temperatures. The decomposition of TTA was found to be sufficiently slow, so as not to interfere with the kinetic study.²⁴

Analysis of acetic acid solutions of TTA was accomplished by using potassium iodide and standard sodium thiosulfate solution. The rate of disappearance

of TTA by iodimetry was reflected in the volume of sodium thiosulfate which corresponds to the total concentration of thallium (III) species in the solution.

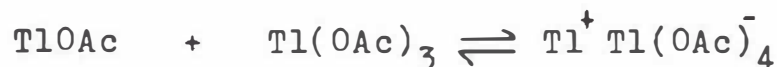
The rate law considered for this reaction is given as equation (C).

$$\frac{dx}{dt} = k (A-2x) (B-x) \quad (C)$$

Where A is the initial concentration of TTA, B is the initial concentration of enol, x is the amount of reactant which has reacted at time t. An integrated rate expression which was used to calculate the data is shown as equation (D).

$$\frac{2.303}{2B-A} \log \frac{A(B-x)}{B(A-2x)} = kt \quad (D)$$

In the reaction of TTA with enol (51, Z=H), a double salt, $Tl_2(OAc)_4$ was formed :



where $TlOAc$ was obtained from the oxidation. In order to derive a rate expression, it was assumed that equilibrium constant is very large in the direction of the double salt.²³ The equilibrium constant changes as a function of temperature. In addition, it was assumed that thallium (I) acetate is produced rapidly after the reaction. The total thallium (III) species as indicated by titration must be separated into free thallium (III) acetate and

the thallium (I), (III) acetate double salt. The free TTA is equal to $A-2x$.

If the double salt reacts with enol, then a possible rate law and integrated expression are shown as equation (E) and (F).

$$\frac{dx}{dt} = k (A-x) (B-x) \quad (E) \quad \frac{2.303}{B-A} \log \frac{A(B-x)}{B(A-x)} = kt \quad (F)$$

The rate varied with temperature such that a temperature of about 20° gave convenient reaction times. Only some preliminary kinetic studies were made by using two different concentrations of reactants. So any conclusions must be considered tentative.

As can be seen from Figure I-III, although the curves seem to fit second order expression (F) approximately, the rate constant k , or the slope, varies with concentration. One can conclude that although it is not a simple second order reaction, it is susceptible to kinetic analysis. Subsequently, more refined and reproducible data would help confirm those conclusions.

Figure I

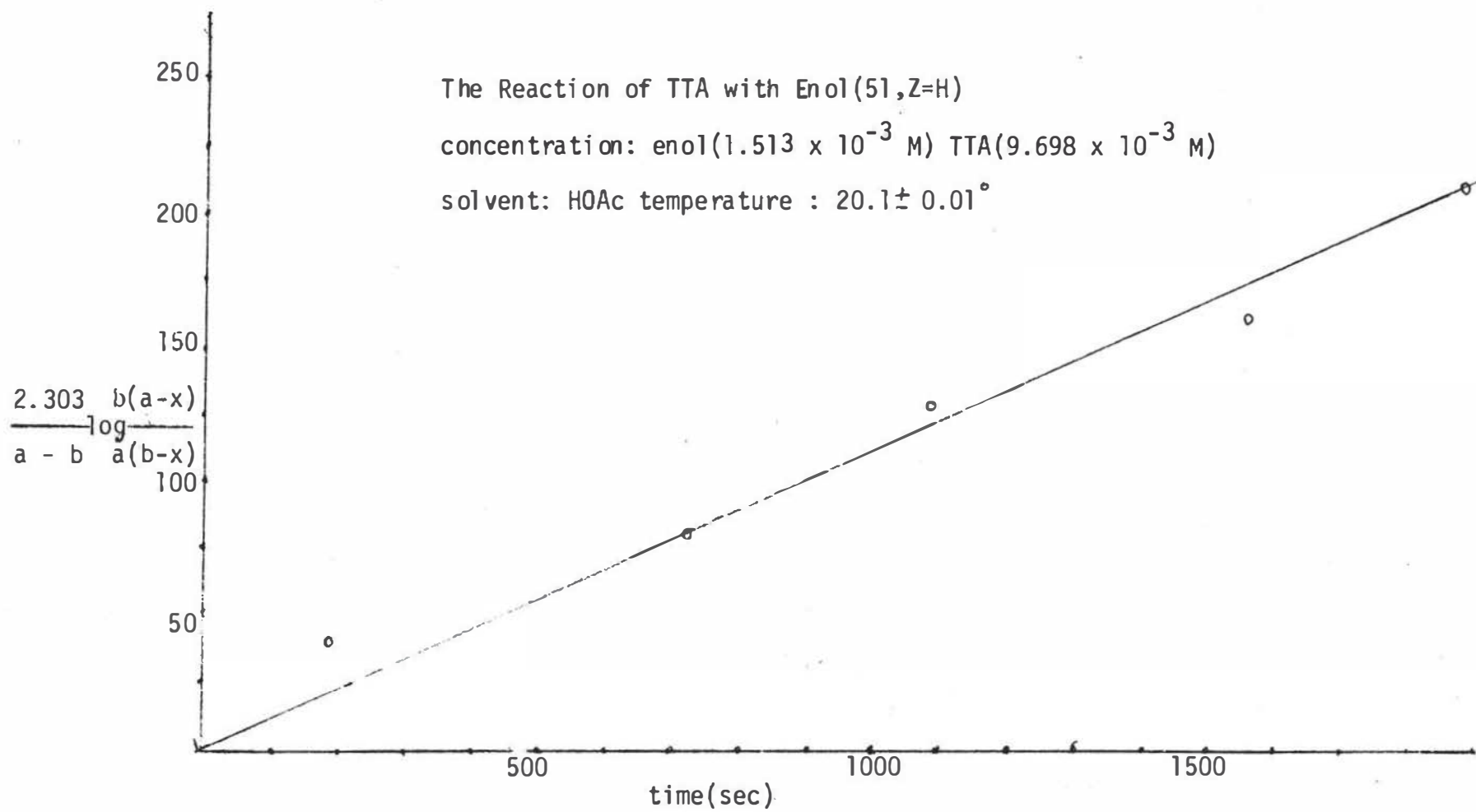


Figure II

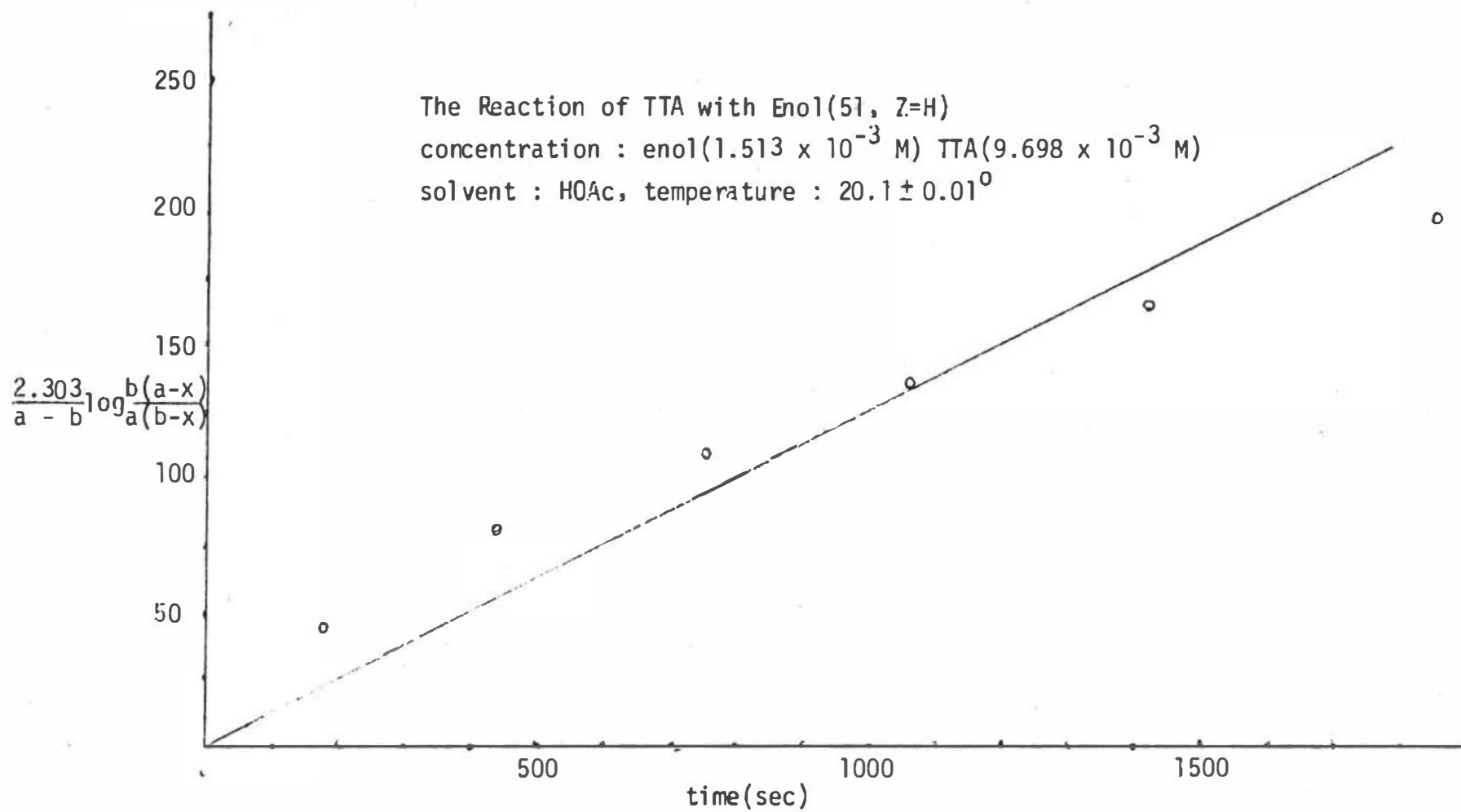
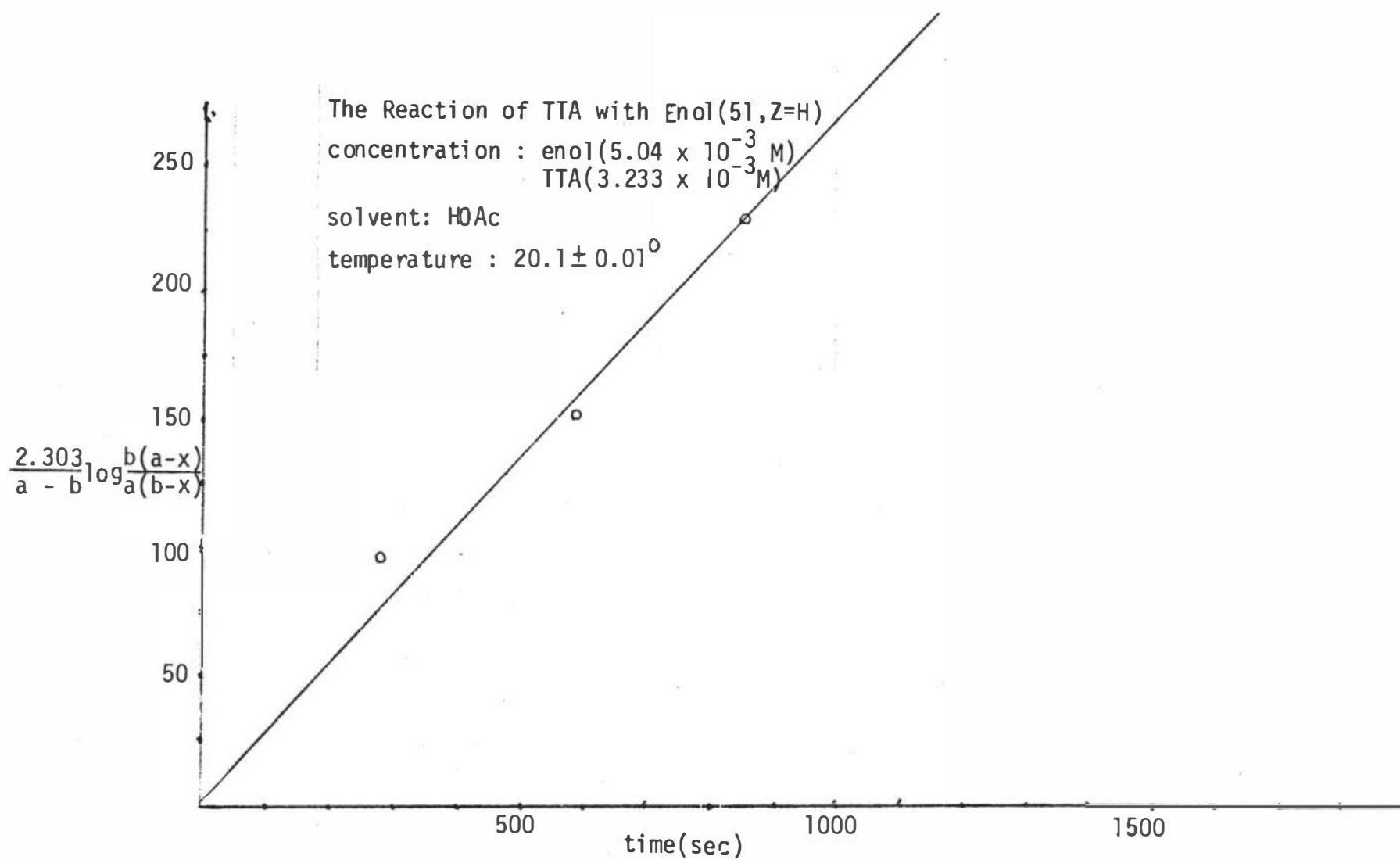


Figure III



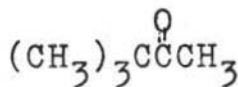
2. Product Analysis.

The mode of oxidations of ketones is dependent on the substrate and the reaction conditions. Acetoxiketones are the major products of this reaction. There have been numerous product studies about LTA oxidative processes which more or less provide insight into the nature of the reaction mechanism.

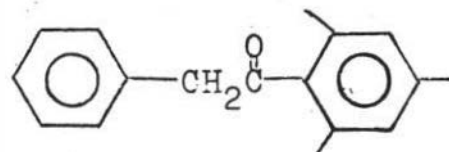
As mentioned earlier, Criegee explained the reaction of flavanone with LTA with ionic mechanism. Cavill preferred to interpret the reaction with 7-methoxyflavanone in terms of radicals instead of ions. On the basis of searching for additional evidence for the mechanism, several ketones were chosen which could easily rearrange if carbonium ions were involved. There were norcamphor (59), 3,3-dimethyl-2-butanone (60) and mesitylphenylketone (61).



59



60

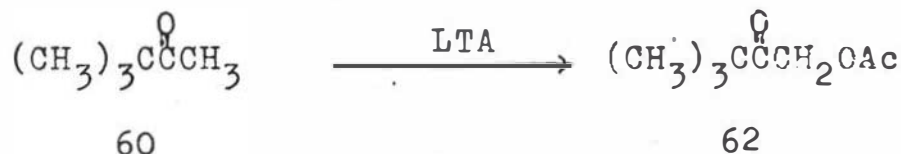


61

Norcamphor was refluxed without LTA in acetic acid for about 24 hours. Only starting material was isolated. No

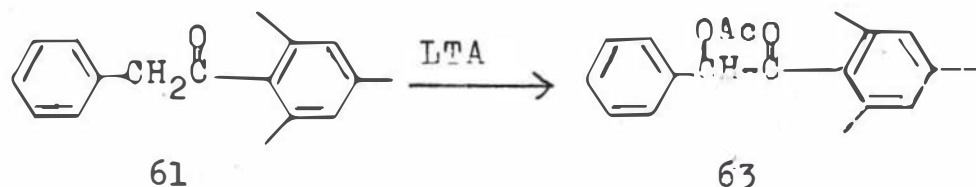
rearrangement occurred. If any products were obtained, they must be considered as the results of the LTA oxidation of norcamphor. Therefore 59 was allowed to react LTA in acetic acid at 70° for 24 hours, thin layer chromatography indicated the presence of product and starting material. The crude product could be separated from the reactants in 31% yield by distillation with a spinning band column. Gas chromatography of the distillate indicated three products and no starting material. Column chromatography was used in attempt to separate these products. Various absorbents (silica gel, Al_2O_3) and eluants (petroleum ether, benzene) were tried, but it was not possible to separate the individual components of the mixture. Although the spectra of the distillate indicated that some acetate was formed, no further information could be gained from this reaction.

When 3,3-dimethyl-2-butanone (60) reacted with LTA in acetic acid, gas chromatographic analysis showed starting material in addition to two products. The ratio of these two components was 6 to 1.



One of the products proved to be a monoacetate 62 from ir and nmr spectral data. This is the major product and its yield was determined as 36.7%. This compound has not been found in the literature. The other product may remain in the black tar and was not identified.

Mesitylphenylketone (61) also was allowed to react with LTA at about 50°. Although an aryl group could migrate to a positive center to give rearranged product, the only product that was detected was the α-acetoxylketone 63 which was isolated in 40.2% yield.

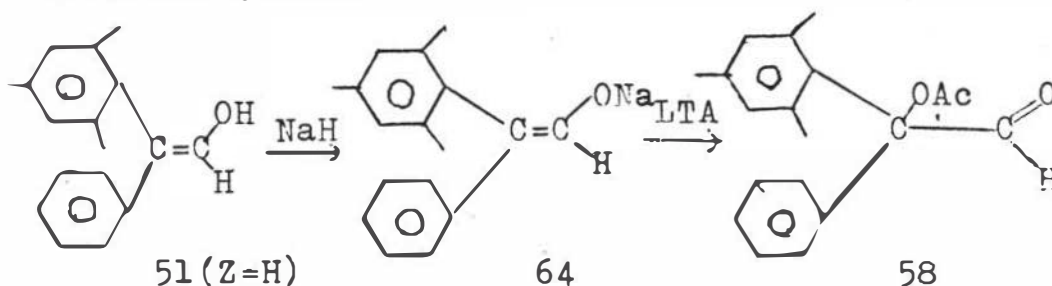


If the mechanism is that proposed by Corey¹⁰ for LTA, then the enol or enolate anion of a ketone ought to react faster and in a yield higher than the unenolized ketones.

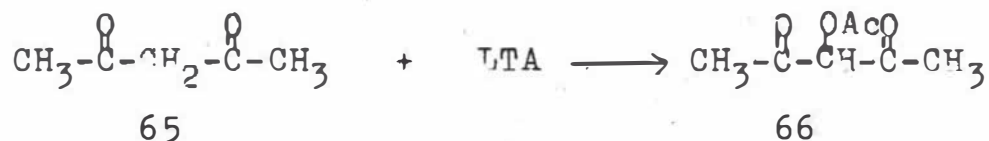
The magnesium enolate 51 (Z=H) was allowed to react with LTA in anhydrous benzene, the product 58 was obtained in 60% yield.²⁹

Different enolates were run with LTA in dry benzene in order to clarify this point. Sodium hydride was added to enol 51 (Z=H) to form the enolate which was allowed to

react with LTA. A trace of NaH was put into the benzene to assure that no acetic acid was present. After recrystallization from ethyl alcohol, the pure acetoxyaldehyde 58 was obtained in 12% yield.



After acetylacetone (65) was allowed to react with LTA at room temperature overnight, and the reaction mixture was worked up, gas chromatographic analysis showed the presence of one product. The crude product was distilled under reduced pressure gave a yellow oil in 21.5% yield. The spectral evidences indicated that acetoxkyetone was formed. No dimeric product was detected.

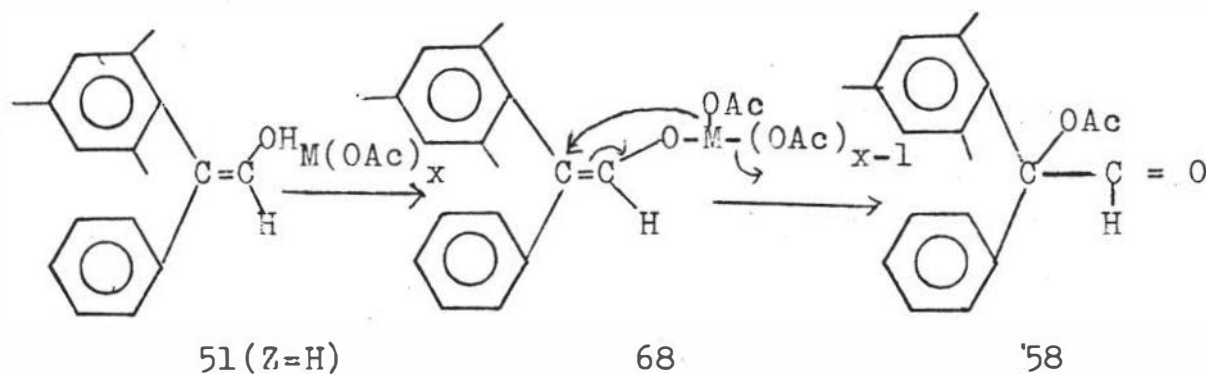


The sodium enolate of 65 was formed by adding small pieces of sodium metal to 65. In the reaction of 67 with LTA, the monoacetate was obtained in 21.6% yield which is identical to 66 from the ir, nmr evidence.



Although the fact norcamphor gave several products leaves the question open, there were no carbonium ions formed in the other reactions that were susceptible to rearrangement even though the selected compounds have easily rearranged.

It was previously mentioned, the arylcyclopropane cleavage reaction by these metal acetates in acetic acid is electrophilic substitution. Mercury(II) acetate and thallium (III) acetate can act as effective electrophiles. These two acetates have similar electrophilic reactivity. The order of reactivity of these metals probably is related to the higher oxidation state or nuclear charge of the metal elements. $\text{Pb}(\text{OAc})_3^+$ is assumed as an electrophile and results in the formation of organolead compounds. Hence LTA has more electrophilic properties than the other two metal acetates. This is consistent with the rates which were determined from the kinetic measurements. It was postulated that an organometallic derivative was formed and rearranged to the product. Then the mechanism of these reactions may follow Corey's mechanism.

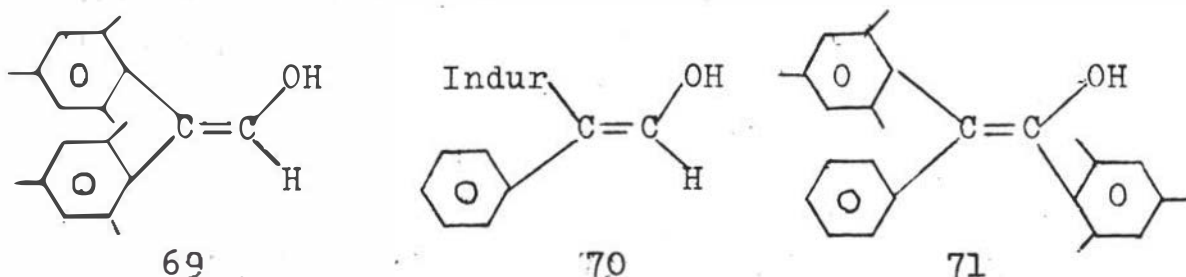


The reaction of the sodium enolate 67. with LTA in better yield than the reaction using unenolized ketone may support the above assumption. But the yield of the former reaction was not high. No firm conclusion could be reached.

Suggested Research

The rate of a chemical reaction is greatly affected by atoms or groups which are close to the reactive centers of the reagents molecules. The activation energy corresponds to the rate of the reaction. If the crowding is greater in the activated complex than it is in the original reagents, the activation energy must be increased and the rate of the reaction must be accordingly be decreased.^{31, 32}

The reaction rate of LTA with enol may be slowed down on the basis of this reason. A series of 100% enol compounds have been reported including β, β -dimesitylvinyl alcohol (69)³³, 2-isoduryl-2-phenylvinyl alcohol (70)³³ and 1,2-dimesityl-2-phenylvinyl alcohol (71).³³



The enol 71 is the most hindered alcohol among these compounds. The rate may be slower if 71 is used as a substrate to react LTA for the kinetic study, thus allowing conventional titration techniques to be used.

The rate of the reaction between TTA and enol 51 ($Z=H$) is slow enough to be determined by the conventional methods. Whether or not the $Tl_2(OAc)_4$ double salt reacts with enol needs to be established. More reproducible data needs to be obtained,

and the rate law firmly established. Then various enols (51, $Z = -NO_2, -Br, -CH_3$) could be used as reagents to react with TTA in order to work out the real character of the reaction. Since LTA has similar activity as TTA in the oxidation, the results of TTA kinetic studies may suggest some sort of mechanism about LTA oxidation with ketones.

A weakness in the enolate study is that it is not certain if enol or enolate is reacting. If the enolate is protonated, the enol thus produced will react to give products thereby confusing the results. Using an enolate of a less enolized ketone, i.e. cyclohexanone, could solve the problem.

Adsorption chromatography is considered practical for the separation of the components of the mixture that are otherwise resolved with difficulty. Though it failed to separate the mixture of norcamphor with liquid chromatography, some other polar solvents or different absorbents such as calcium carbonate or sucrose are worthwhile for trying to separate the mixture. Since much of the available knowledge in the field is empirical, the choice of absorbent and solvent for a given separation must often be made on a trial and error basis. Perhaps a more extensive survey of absorbents and eluants might reveal conditions that would allow separation to be accomplished. The use of preparative gas chromatography might solve the norcamphor problem.

CHAPTER III

EXPERIMENTAL

A Thomas-Hoover capillary melting point instrument was used and melting points were uncorrected. The infrared spectra were taken in potassium bromide or liquid cells on a Perkin-Elmer 337 Infrared Spectrometer and only characteristic strong bands were reported. The ultraviolet spectra were taken in a 1 cm cell on a Beckman model DB Spectrometer with a model SRL Sargent Recorder. A Varian T-60 Nuclear Magnetic Resonance Spectrometer with CCl_4 as a solvent and tetramethylsilane (TMS) as an internal standard was used. Chemical shifts are reported in parts per million (PPM) downfield from TMS with the parentheses designating the multiplicity of the signals: s, singlet; d, doublet; t, triplet; q, quartet and m, multiplet. The number immediately following the parentheses indicates the number of protons causing the signal.

Gas phase chromatographic analysis were made using a Sargent SR Recorder and a Perkin-Elmer Model 154 L gas chromatograph with a $\frac{1}{4}$ inch x 10 ft column of 4% neopentylglycol sebacate (npgs) on 60 to 90 mesh non-acid washed Chromosorb W. This column was run using a helium

flow rate of 60 ml/min. Thin layer chromatographic analysis (TLC) were obtained with the help of commercial silica with CHCl_3 solvent and developed by using iodine vapor. Solvents were dried before distillation. LTA was dried over KOH under reduced pressure prior to use. Potassium iodide and sodium thiosulfate were reagent grade. The $\text{Na}_2\text{S}_2\text{O}_3$ solution (0.3 N) was diluted with deionized water and standardized with iodine which was determined by arsenious oxide. A 5% KI solution was prepared by dissolving 5 g of KI in 95 ml of deionized water.

(A) Kinetic Studies.

(a) Material Used :

Preparation of 2-Mesityl-2-phenylvinyl alcohol (51, Z=H).

To lithium aluminum hydride (21.6 g, 0.565 mol) in 500 ml of tetrahydrofuran in a three neck flask, diketone 58 (28.5 g, 0.113 mol) in 100 ml of THF was added slowly. The mixture was stirred at room temperature. A 1 ml aliquot of the reaction mixture was worked up by adding the mixture to 5 ml of 0.1 M HCl, extracted with ether then dried with MgSO_4 . The TLC indicated only the glycol was present after 48 hours. The mixture then was poured into 1.0 l of

saturated NH_4Cl solution and extracted with ether five times. The combined ethereal extracts were light yellow and a light gray precipitate remained at the bottom of the solution. The mixture was filtered with suction and the solvent was evaporated on a hot plate until the crude product appeared on the top of the solution. The crude product was filtered and dissolved in petroleum ether and recrystallized from it to give 11.4 g (40%) of pure product : mp $142-144^\circ$ (lit.²⁸ mp 144°); ir(KBr) 1630 cm^{-1} , ($\text{C}=\text{C}$, aromatic ring), 3600 cm^{-1} (O-H); nmr δ (CCl_4) 7.36 (s, 5, aromatic protons), 6.76 (s, 2, aromatic protons), 4.95 (q, 2, CH), 2.44 (s, 3, CH_3 on benzene ring), 2.25 (s, 6, CH_3 on benzene ring), 1.56 (m, 2, OH).

A solution of glycol 56 (10 g, 0.039 mol) in 200 ml of glacial acetic acid and 50 ml of concentrated HCl was heated under reflux for about 1 hour, allowed to cool and poured into 1 liter of water. The colorless product which formed was removed by filtration and recrystallized from the petroleum ether. The pure white product was obtained : mp $112-114^\circ$ (lit.²⁹ mp 114°); ir(KBr) 1630 cm^{-1} ($\text{C}=\text{C}$) 3325 cm^{-1} (O-H); nmr δ 2.14 (s, 6, CH_3 on benzene ring), 2.30 (s, 3, CH_3 on benzene ring), 4.10 (d, 2, OH), 7.00 (m, 8, aromatic and vinylic protons); uv (CH_2Cl_2) λ_{max} 260 nm. ϵ 15400.

Preparation of Lead Tetracetate.

A 500 ml 3 neck flask was fitted with a thermometer and glass teflon stirrer. A mixture of 257 ml of glacial acetic acid and 83 ml of acetic anhydride was placed in the flask, and then, with stirring, 150 g of dry minimum was added over a period of a few minutes. The Pb_3O_4 was added in small portions to prevent caking. The remaining neck was fitted with a drying tube. The flask was cooled if necessary to insure that the temperature did not rise above 55° . The mixture, which contained a trace of unreacted Pb_3O_4 was cooled to approximately 15° with an ice bath. The product was filtered by suction from most of the mother liquor and transferred to a one liter Erlenmeyer flask. The material was mixed with approximately 450 ml of glacial acetic acid to which 30 ml of acetic anhydride had been added and the stirred mixture was heated to about 90° to complete solution. After cooling to room temperature the product was filtered to give approximately 70 g of $\text{Pb}(\text{OAc})_4$.

(b) Kinetic Procedure.

1. Lead Tetraacetate (LTA) as Reagent

In this experiment 0.443 g of LTA, 0.24 g of enol 51 ($\text{Z}=\text{H}$) were dissolved in 50 ml of glacial

acetic acid in volumetric flasks. These solutions were allowed to come to the same temperature in a constant thermostated water bath with a temperature $25 \pm 0.1^\circ$. All runs were run made by mixing equal amounts of the standardized solution of LTA with a solution of the enol (51, Z=H). Aliquots of 5 ml were then pipetted into 15 ml of 5% KI solution. The heterogeneous mixture became yellow immediately after it was titrated with $\text{Na}_2\text{S}_2\text{O}_3$ in the presence of a starch indicator.

For the runs at low temperature, 5.0 ml of (51, Z=H) solution (0.02 M) and 5.0 ml of LTA (0.02 M) then were diluted with 5.0 ml of THF respectively. Liquid nitrogen was used to cool the solution to -50° . These two solutions were mixed together after their temperature reached equilibrium. Under this condition, aliquots of the reaction mixture were added to 15 ml of KI solution with a starch indicator. The solution changed to yellow immediately.

For the runs using spectroscopy, acetonitrile with a trace of glacial acetic acid was used as a solvent. The procedure for sample preparation follows :

Enol (51, Z=H) (0.1 g) was dissolved in the solvent in 10 ml volumetric flask to give solution no 1. A 0.5 ml

aliquot of solution number 1 was diluted to 10 ml to give solution number 2. A 1.0 ml aliquot of solution number 2 was diluted to 10 ml to give solution number 3. The concentration of this enol solution number 3 was 4.2×10^{-5} M. The same procedure was applied to the acetoxy product 58 and LTA where 0.124 g of 58 and 0.185 g of LTA were used to prepare the corresponding solution number 1. Spectra were run with this concentration at 260 nm as an appropriate wavelength to determine the amount of enol remaining. The reaction was complete within 3 seconds since the absorbance decreased and was constant after 3 seconds.

2. Thallium (III) Acetate as Reagent.

Purity of Thallium (III) Acetate.

Commercial TTA (8.57 g) was dissolved in one liter of acetic acid in the volumetric flask. Aliquots of 5.0 ml of the solution was then pipetted into 10 ml of a 5% KI solution in the presence of a starch indicator. The green heterogeneous mixture were then titrated with $\text{Na}_2\text{S}_2\text{O}_3$ (0.00408 N). A total of 47.54 ml of $\text{Na}_2\text{S}_2\text{O}_3$ were required which corresponds to a concentration of 0.01936 N TTA. The purity of the purchased TTA was then calculated to be 86%.

Kinetic Measurements.

The procedure used was similar to that used with LTA except that the temperature was kept at $20.1 \pm 0.01^\circ$.

A 10 ml syringe was used for the convenience of handling aliquots of solution within short periods of time in some of these measurements. Several runs at various conditions were made. When one run was made at 46⁰, the reaction was complete in 8 minutes. Thus lower temperatures gave more convenient reaction times. The data are shown in Tables I, II and III.

Table I

Title : The Kinetic Data of the Reaction of TTA with Enol(51,Z=H)
at 20.1° in Glacial Acetic Acid.

Aliquot number	Time (sec)	Volume of $\text{Na}_2\text{S}_2\text{O}_3$ (ml)	$\frac{2.303}{a-b} \log \frac{b(a-x)}{a(b-x)}$	k
1.	188	30.3	35.7	0.190
2.	705	17.6	91.0	0.129
3.	1088	12.8	130.1	0.1156
4.	1558	9.3	164.3	0.1107
5.	1858	7.2	213.4	0.1149
6.	2196	5.8	250.0	0.1138
7.	2650	4.1	309.0	0.1166

concentration : TTA(9.698×10^{-3} M) Enol(1.513×10^{-3} M) $\text{Na}_2\text{S}_2\text{O}_3$ (4.08×10^{-3} M)

Aliquot volume : 10 ml

Table II

Title : The Kinetic Data of the Reaction of TTA with Enol (51, Z=H)
at 20.1⁰ in Glacial Acetic.

Aliquot number	Time (sec)	Volume of Na ₂ S ₂ O ₃ (ml)	$\frac{2.303}{a-b} \log \frac{b(a-x)}{a(b-x)}$	k
1.	172	13.0	48.1	0.280
2.	446	9.5	79.6	0.178
3.	724	7.6	104.6	0.145
4.	1070	5.9	135.6	0.127
5.	1410	4.7	165.6	0.117
6.	1834	3.8	195.3	0.107
7.	2036	3.2	220.4	0.108
8.	2407	2.4	264.4	0.110

concentration : TTA (9.698×10^{-3} M) Enol (1.513×10^{-3} M) Aliquot volume: 5 ml
Na₂S₂O₃ (4.08×10^{-3} M)

Table III

Title : The Kinetic Data. of the Reaction of TTA with Enol (51, Z=H)

at 20.1⁰ in Glacial Acetic.

Aliquot number	Time (sec)	Volume of Na ₂ S ₂ O ₃ (ml)	$\frac{2.303}{a-b} \log \frac{b(a-x)}{a(b-x)}$	k
1.	274	15.3	98.8	0.3604
2.	553	12.5	152.4	0.2751
3.	835	10.8	230.3	0.2758
4.	1377	7.3	363.6	0.2641
5.	1767	6.5	427.0	0.2417
6.	2460	3.6	429.0	0.1744

concentration : TTA (3.233×10^{-3} M) Enol (5.04×10^{-3} M) Na₂S₂O₃ (1.36×10^{-3} M)

Aliquot volume : 10 ml

B. Product Analysis.

The Reaction of Norcamphor with Lead Tetraacetate in Glacial Acetic Acid.

To a 100 ml round bottom flask equipped with a reflux condenser and containing a magnetic stirrer was added 5 g (0.0454 mol) of norcamphor and 50 ml of glacial acetic acid. The mixture was stirred until all the norcamphor dissolved. A total of 20.1 g (0.0454 mol) of crystalline LTA was added to the solution in small portions. The temperature was maintained at approximately 70°. The color of the heterogeneous mixture gradually changed to yellow. At the end of 24 hours a negative starch-iodide test was obtained which indicated that all the LTA was consumed. The reaction mixture was then cooled, neutralized with solid NaHCO_3 , and extracted with ether four times. The combined ethereal solutions were concentrated by distillation through Vigreux column and dried with MgSO_4 . Analysis of the filtrate by TLC indicated the presence of some product in addition to starting material. The crude product was distilled with a spinning column at reduced pressure. Gas chromatography showed three components of the product with retention times of 5.6 min, 7.3 min, 9.0 min respectively at 160°. No starting material

was observed. Attempts to separate the mixture by vacuum distillation were unsuccessful. The mixture was dissolved in benzene poured onto a Silica Gel Column (2 cm x 60 cm) The column was eluted with petroleum ether, petroleum-benzene 1:1, and then the various fractions were evaporated with a rotary evaporator. Nothing was obtained. Aluminum oxide was also used to form the column. But the same result was observed.

The total yield of the product mixture was 2.4 g (31%)

The reaction of norcamphor in acetic acid was run under the same conditions as described above. Analysis of the concentrated reaction mixture by gas chromatography at 160° indicated no product formed.

Reaction of 3,3-dimethyl-2-butanone with Lead Tetraacetate in Glacial Acetic Acid.

A mixture of 5 g (0.05 mol) of ketone 60 and 30 ml of glacial acetic acid was stirred at room temperature. LTA (22.1 g, 0.05 mol) was added to the solution over a period of approximately 5 minutes. The solution was heated at reflux for 3 hours after which the color was yellow and iodide-starch indicator test was negative. The contents of the flask were allowed to cool and poured into 200 ml of deionized water. The mixture was neutralized with solid NaHCO_3 and the resulting solution extracted with

four 50 ml portions of ether. The ether was then distilled using a vigreux column and the concentrated ethereal solution was dried with MgSO_4 for 2 hours, filtered and distilled with a spinning band column at one atmosphere. The first five fractions were ether and starting material as evidenced from gas chromatographic analysis. The residue was subjected to same analysis. The peaks with retention times of 3.5 min, 6.6 min were different from the starting material. The residue was distilled at low pressure to give 2.9 g (36.7%) of a light yellow oil : bp. $44-46^\circ$ (0.2 mm); ir (film) 1040 cm^{-1} (C-O-C), 1375 cm^{-1} (C=O); nmr δ 1.18 (s, 9, t- CH_3), 2.05 (s, 3, COCH_3), 4.82 (s, 2, CH_2OAc).

Reaction of Mesitylphenylketone (61) with Lead Tetraacetate in Glacial Acetic Acid.

A mixture of 20.0 g (0.84 mol) of ketone 55, 100 ml of glacial acetic acid, 37.2 g (0.84 mol) of LTA, was heated in a 250 ml round-bottom flask and the temperature was maintained at approximately 40° . The solution gradually changed to yellow and after the contents were stirred 4 hours the potassium iodide-starch test was negative. The cool reaction mixture was poured into 150 ml of deionized water and solid NaHCO_3 was added to the solution until the solution was neutral. The mixture was extracted with five, 50 ml portions of ether, the combined ethereal extracts were concentrated and dried with MgSO_4 . Analysis by TLC

indicated starting material and product. The crude product was evaporated with a rotary evaporator to give a yellow oil from which the product crystallized after standing overnight. The crystals were filtered and recrystallized from the mixture of petroleum and ether to give 7.2 g (40. 2%) of white crystals. The product was dried under reduced pressure at 56° for approximately 1 hour. The material had the following properties : mp. $68 - 70^{\circ}$, ir (KBr) 1700 cm^{-1} (C=O ketone), 1740 cm^{-1} (acetate); nmr δ 1.9 (s, 9, CH_3), 2.2 (s, 3, OCCCH_3), 6.4 (s, 1, CH), 6.7 (s, 2, aromatic protons), 7.3 (s, 5, aromatic protons).

Reaction of the Enolate of 51 (Z=H) with Lead Tetraacetate in Benzene.

To 2 g (0.0084 mol) of enol 51 (Z=H) in dry benzene, 0.184 g (0.0081 mol) sodium metal was added to form the enolate. Then 3.6 g (0.0081 mol) dry LTA was added to the heterogeneous mixture. The mixture was stirred at room temperature until a negative starch-iodide test was observed. The solution was filtered by suction, concentrated with a rotary evaporator and subjected to gas chromatographic analysis. Some product in addition to starting material was observed. The concentrated solution was dried over MgSO_4 , filtered and then let stand at 0° . The product crystallized after standing overnight. The crystals were

recrystallized from the ethyl alcohol to give the pure white product which is identical to the compound obtained from the authentic enol (51, Z=H) with LTA. The melting point was 128° - 134° and the yield was 12%.

Reaction of Acetylacetone and the Sodium Enolate of Acetylacetone (65) with Lead Tetraacetate in Benzene.

To 5.0 g (0.05 mol) of acetylacetone in 175 ml of benzene, was added 22.1 g (0.05 mol) of LTA. The reaction mixture was stirred overnight at room temperature at which time negative iodide- starch test was observed. The light yellow solution was filtered and washed several times with water, dried over MgSO_4 , filtered and distilled at reduced pressure to give 1.7 g (21.5%) of a yellow oil : bp. $70-78^{\circ}$; ir (film) 1710 cm^{-1} (C=O ketone), 1745 cm^{-1} 1745 cm^{-1} (C=O acetate); nmr δ 1.9 (s, 3, C- CH_3), 2.2 (s, 6, CH_3), 5.4 (s, 1, CH).

Sodium enolate of acetylacetone (8.4 g, 0.0688 mol) was prepared by adding sodium to acetylacetone in 50 ml of benzene. LTA (31 g, 0.070 mol) was added to the enolate solution. The reaction mixture was stirred at room temperature. The color gradually changed to yellow. After all the LTA was consumed, the reaction mixture was filtered and evaporated using a rotary evaporator. The crude product was distilled at reduced pressure to give 2.35 g (21.6%)

of a yellow oil; bp 55-80° (0.4 mm). The spectral properties of this product are identical with those of the acetate prepared from the authentic acetylacetone.

Reaction of Enol (51, Z=H) with Thallium(III) Acetate and Mercury(II) Acetate in Acetic Acid.

To 1.0 g (0.0042 mol) of enol 51 (Z=H) was added 1.5 g (0.0038 mol) of TTA and 35 ml of glacial acetic acid. The mixture was heated and maintained at about 50°. Then the reaction mixture was stirred until all the TTA was consumed. The cool mixture was poured into 50 ml of deionized water and neutralized with NaHCO_3 . The solution was extracted with three 20 ml portions of ether. The extracts were collected and removed with a rotary evaporator. The concentrated solution was poured into 20 ml of petroleum ether. A white precipitate was formed. The precipitate was filtered and recrystallized from ethyl alcohol to give pure white crystals 0.81 g (65%). The spectral data confirmed that the product is identical to acetoxo product 58 prepared from using LTA and enol 51 (Z=H).

To 1.0 g (0.0042 mol) of enol 51 (Z=H) in 30 ml of glacial acetic acid was added 1.32 g (0.0041 mol) of MA in small portions. The reaction mixture was heated at reflux for about 14 hours. The color of the solution gradually changed to red. The solvent was removed at reduced pressure using

a rotary evaporator. Analysis of the concentrated reaction mixture by the comparison with the authentic material by TLC showed no product was formed.

CHAPTER IV
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