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   Chemistry, organic

Some synthetic applications of

vinyl- and arylmercuric chlorides

by

John Christian Bernhardt

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I. INTRODUCTION

Vinyl- and arylmercuric chlorides are now readily available from simple starting materials and their usefulness in organic synthesis has been the focus of increased research interest.

Vinylmercuric chlorides are obtained by the hydroboration of acetylenes using either dicyclohexylborane (1) or catecholborane (2) to generate a vinylborane. The vinylborane is mercurated by mercuric acetate and converted to the chloride with aqueous sodium chloride. Arylmercuric chlorides are obtained by electrophilic substitution of the corresponding arene, usually under acidic conditions (3, pp. 71-121; 4, pp. 28-59).

Prior to 1972 most of the synthetic applications of organomercurials were limited to transmetallation reactions (3, pp. 384-400), electrophilic cleavage of the carbon-mercury bond (5), and elimination of metallic mercury to form vinyl derivatives (6). Some isolated carbon-carbon bond forming reactions (7-11) were also reported, most notably the palladium catalyzed reactions reported by Heck (12-15).

Since 1972 the Larock group has been investigating the application of organomercurials to organic synthesis. As a part of this study I have investigated the synthesis of α,β-unsaturated ketones, symmetrical 1,3-dienes and biaryls, and 1,4-dienes from vinyl- and arylmercuric chlorides. The next two chapters of this thesis will provide a discussion

of the preparation of various organomercury reagents (Chapter II) and prior synthetic methods utilizing vinyl- and aryl-mercurials (Chapter III). Subsequent chapters will discuss the synthesis of α,β-unsaturated ketones (Chapter IV), symmetrical 1,3-dienes and polyenes (Chapter V), symmetrical biaryls (Chapter VI), and 1,4-dienes (Chapter VII). The concluding chapter (Chapter VIII) will provide a brief conclusion summarizing the results of these studies.

II. SYNTHESIS OF ORGANOMERCURIALS

Recently a number of new methods for the synthesis of organomercurials have been reported which allow the convenient preparation and isolation of these compounds and increase their value in organic synthesis. These routes have recently been reviewed (3, 4, 16) and are discussed only briefly here.

The most common route to organomercurials involves the transmetallation of Grignard and lithium reagents (3, pp. 16-35). Organosodium (17), -silver (18), -zinc, -aluminum (3, pp. 40-43), or -boron (3, pp. 249-254) reagents have also been used (Eq. 1). However, since the Grignard and lithium

$$R-M + HgX_2 \longrightarrow R-HgX + M-X$$

$$(1)$$

$$2\ R-M + HgX_2 \longrightarrow R_2Hg + 2\ M-X$$
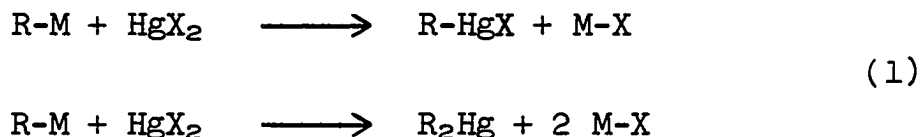
reagents are more reactive than the corresponding organomercurials, the organomercurials thus derived have not found extensive use in organic synthesis.

Until recently the usual route to organoboranes was through the corresponding Grignard or lithium reagents. However, with the development of the hydroboration reaction by H. C. Brown, organoboranes have become directly accessible and their use has been investigated in the synthesis of a number of organomercurials. For example, alkenes can be converted to alkylmercuric salts (Eq. 2 (19); Eq. 3 (20)). By proper choice of the hydroboration reagent and stoichiometry,

$$R\text{-}CH=CH_2 \quad \xrightarrow{\begin{array}{l}1.\ BH_3\\2.\ Hg(OAc)_2\\3.\ NaCl\end{array}} \quad RCH_2CH_2HgCl \qquad (2)$$

$$3\ \bigcirc \xrightarrow{\ BH_3\ } \xrightarrow[n=1\ or\ 2]{Hg_n(OR)_2} 2\ \bigcirc\!\!-HgOR \qquad (3)$$
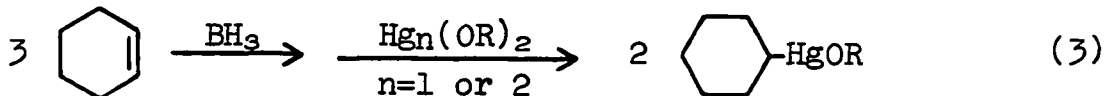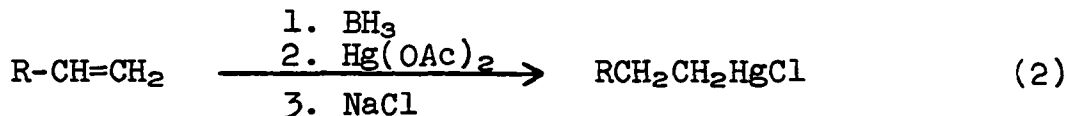
either vinylmercuric salts (1, 2) or dimercurated hydrocarbons

(21) may be obtained from acetylenes (Scheme 1). The hydro-

Scheme 1
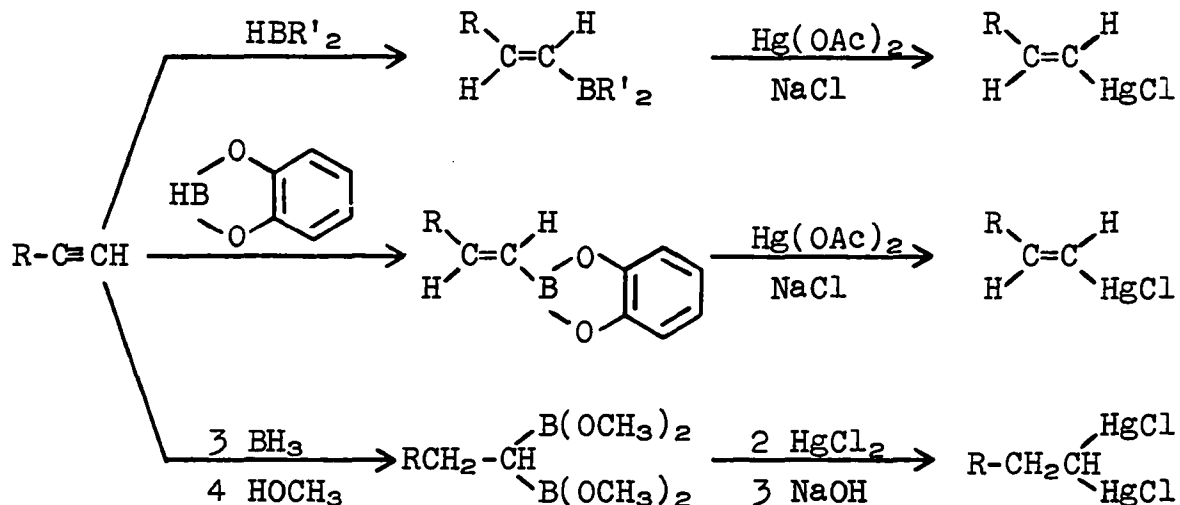
boration sequence tolerates functionality, such as nitriles

and esters, that are not stable to Grignard or lithium

reagents.

The hydroboration-mercuration of acetylenes produces

vinylmercuric chlorides that, by necessity, contain a hydrogen

atom cis to the mercury. However, if alkyl substitution cis

to mercury is desired, this may be accomplished by the use of

organocopper reagents (Scheme 2) (22).

Scheme 2

$$R'MgBr + CuBr \longrightarrow R'Cu \cdot MgBr_2$$

$$R'Cu \cdot MgBr_2 + R-C\equiv CH \longrightarrow \begin{array}{c} R \\ \diagdown \\ R' \diagup \end{array} C=C \begin{array}{c} \diagup H \\ \diagdown Cu \cdot MgBr_2 \end{array}$$

$$\begin{array}{c} R \\ \diagdown \\ R' \diagup \end{array} C=C \begin{array}{c} \diagup H \\ \diagdown Cu \cdot MgBr_2 \end{array} + HgBr_2 \longrightarrow \begin{array}{c} R \\ \diagdown \\ R' \diagup \end{array} C=C \begin{array}{c} \diagup H \\ \diagdown HgBr \end{array}$$
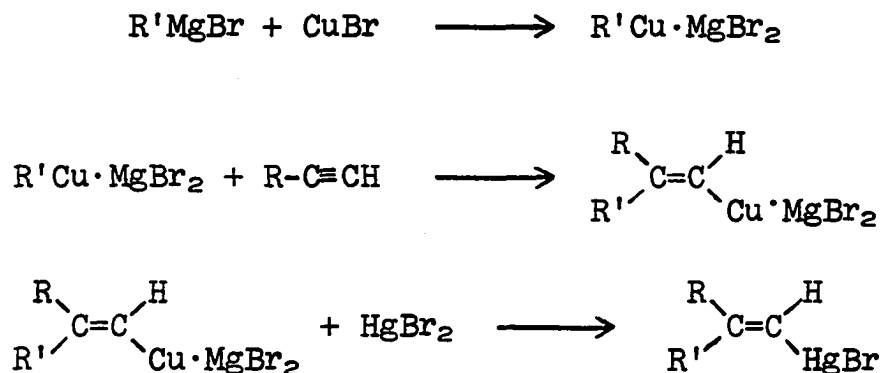
There are a number of reports of the direct synthesis of organomercurials. Olefins undergo direct mercuration by mercury(II) salts in the presence of compounds containing acidic hydrogens (Eq. 4) (4, pp. 130-192) resulting in an

$$RCH=CH_2 + HgX_2 + HY \longrightarrow \overset{Y}{\underset{|}{R-CH}}-CH_2HgX + HX$$

$$\overset{Y}{\underset{|}{RCH}}-CH_2HgX \xrightarrow{\text{NaBH}_4} \overset{Y}{\underset{|}{RCH}}-CH_3 \qquad (4)$$
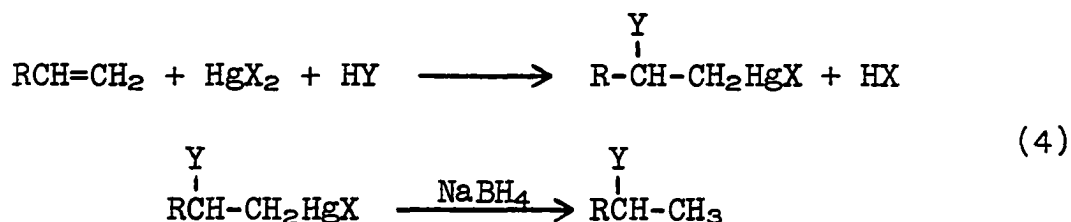
organomercurial substituted on the β-carbon. Most commonly these organomercurials are demercurated directly by sodium borohydride, although they can be isolated and purified.

Addition of mercury salts directly to acetylenes are also known. 2-Butyne can be mercurated to give either cis- or trans-3-acetoxy-2-butenylmercuric chloride (Eq. 5) (23). Diphenylacetylene can also be mercurated in a similar manner to give the cis-β-acetoxystilbenylmercuric chloride (Eq. 6) (24).

$$CH_3\text{-}C=C \begin{array}{c} CH_3 \\ HgCl \end{array} \quad \overset{CH_3CO}{\underset{O}{||}} \longleftarrow CH_3C\equiv CCH_3 \longrightarrow \overset{O}{\underset{||}{CH_3CO}}\text{-}C=C\begin{array}{c} CH_3 \\ HgCl \end{array} \quad (5)$$

$$PhC\equiv C\text{-}Ph \longrightarrow \overset{Ph}{\underset{CH_3CO}{\underset{||}{O}}}C=C\begin{array}{c} Ph \\ HgCl \end{array} \quad (6)$$
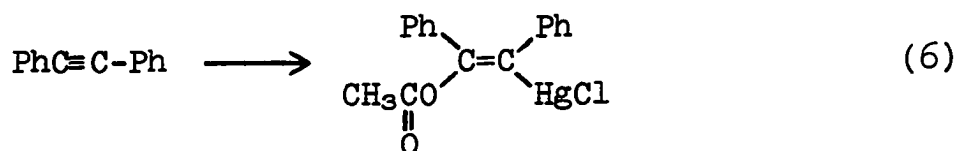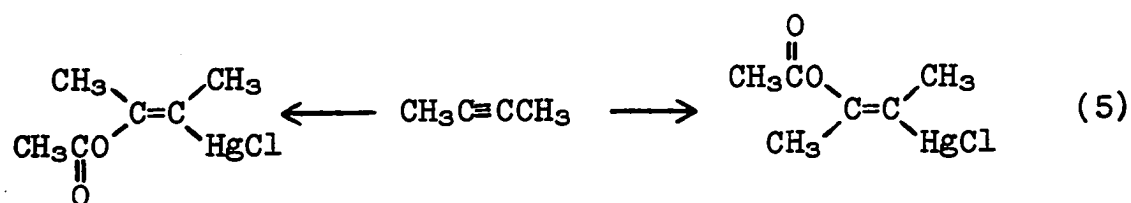
Mercuric chloride has been found to add across the acetylenic bond of propargylic alcohols (Eq. 7) (25). The reaction has

$$R\text{-}\overset{R}{\underset{OH}{|}}C\text{-}C\equiv CH \quad \xrightarrow{HgCl_2} \quad \overset{Cl}{R}C=C\begin{array}{c} H \\ HgCl \end{array}\underset{R}{\overset{R}{C}}\text{-}OH \quad (7)$$

$$R\text{-}\overset{R}{\underset{OH}{|}}C\text{-}C\equiv C\text{-}\overset{R}{\underset{OH}{|}}C\text{-}R \quad \xrightarrow{HgCl_2} \quad \overset{Cl}{R}C=C\begin{array}{c} R \\ OH \\ HgCl \end{array}\underset{R}{\overset{R}{C}}\text{-}OH$$
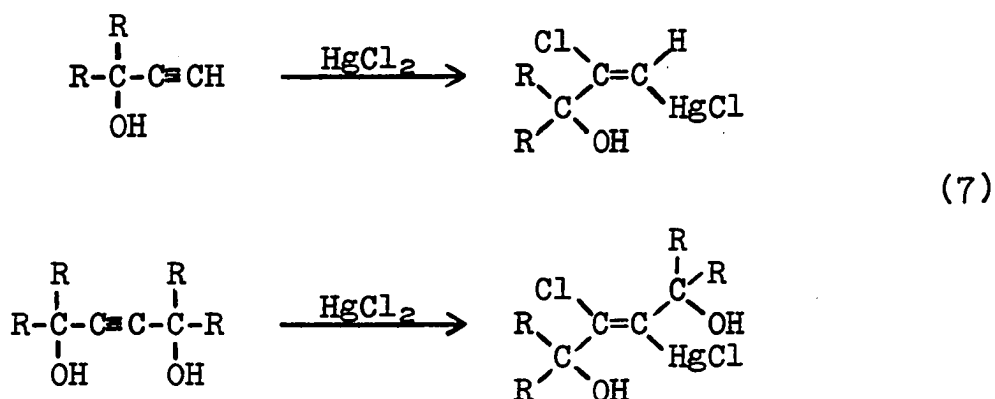
been found to work well only for primary or tertiary alcohols (26). Propargylic amines undergo a reaction similar to that observed for the alcohols (Eq. 8) (27). Acetylenes conju-

$$R\text{-}\overset{R}{\underset{NR'_2}{|}}C\text{-}C\equiv CH + HCl + 2 \ HgCl_2 \longrightarrow \overset{ClHg}{R}C=C\begin{array}{c} H \\ Cl \end{array}\underset{R}{\overset{R}{C}}\overset{+}{\underset{R'\overset{|}{R'}}{NH/_2}} \ HgCl_4^{-2} \quad (8)$$
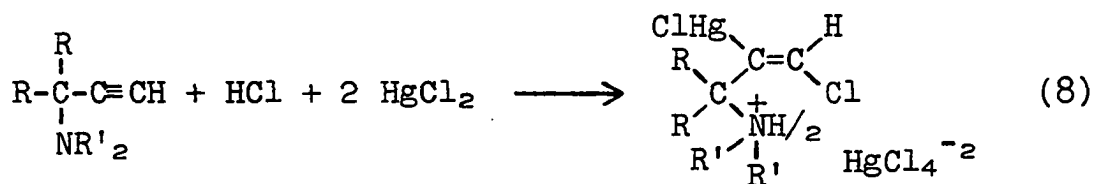
gated with esters, acids, or ketones have also been observed to add mercuric chloride (Eq. 9) (28).

$$R-C\equiv C-\overset{\overset{\displaystyle O}{\|}}{C}X \quad \xrightarrow{\text{HgCl}_2} \quad \overset{Cl}{\underset{R}{}}C=C\overset{\overset{\overset{\displaystyle O}{\|}}{C}X}{\underset{HgCl}{}} \qquad (9)$$

R=H, Ph, or CH$_3$ X=OH, OCH$_3$, OCH$_2$CH$_3$, or CH$_3$
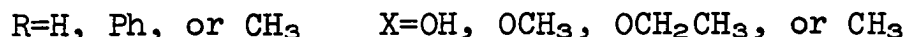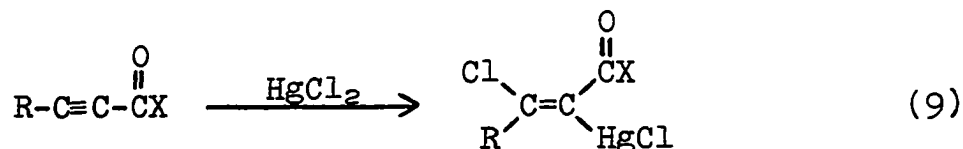
Under the influence of light, certain organic halides have been observed to insert metallic mercury into the carbon-halogen bond producing an organomercuric salt. Reactions with benzyl- (29), methyl- (29), methylene- (30), propargyl- (31), and allylic halides (32), and β-iodo-α,β-unsaturated ketones (33) have all been reported.

A wide variety of arenes can be mercurated directly by electrophilic substitution, usually under acidic conditions (Eq. 10) (3, 4). A mixture of isomers is usually obtained but
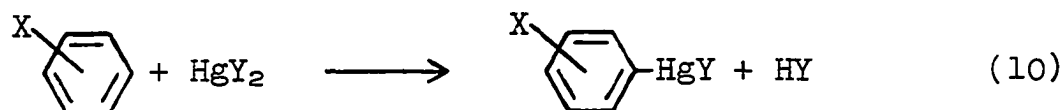
stereochemically pure materials can be readily obtained by re-crystallization.

While these are the most common methods for the preparation of organomercurials, there are also reports that alkyl- and arylhydrazines and aryl diazonium salts may be converted to organomercurials. Thus the hydrazone of cyclohexanone can be converted to 1-cyclohexenylmercuric acetate (Eq. 11) (34) by treatment with mercuric acetate in the presence of catalytic amounts of cupric acetate. Similarly, aromatic hydra-

$$\text{N-NH}_2 \text{ (cyclohexanone hydrazone)} + \text{Hg(OAc)}_2 \longrightarrow \text{HgOAc (cyclohexenyl)} \qquad (11)$$
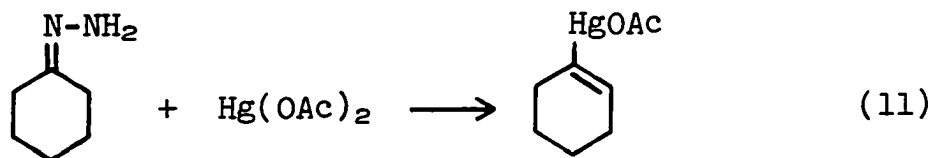
zines are readily converted to the aromatic mercurial by treatment with mercuric acetate in the presence of cupric acetate (Eq. 12) (35).

$$\text{ArNHNH}_2 + \text{Hg(OAc)}_2 + \text{Cu(OAc)}_2 \longrightarrow \text{ArHgOAc} \qquad (12)$$
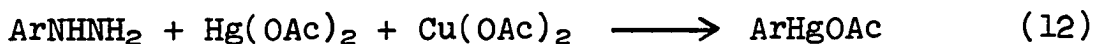
A variety of other methods for converting aromatic diazonium salts to mercurials have also been reported. Treatment with metallic copper (Eq. 13) (36) generates the cuprous

$$\text{ArN}_2\text{X} \cdot \text{HgX}_2 + 2 \text{ Cu} \longrightarrow \text{ArHgX} + 2 \text{ CuX} + \text{N}_2 \qquad (13)$$

$$\text{ArN}_2\text{X} \cdot \text{HgX}_2 + 6 \text{ Cu} \xrightarrow{\text{NH}_3} \text{Ar}_2\text{Hg} + 6 \text{ CuX} + \text{Hg} + 2 \text{ NH}_3 \qquad (14)$$

$$\text{ArN}_2\text{Cl} + \text{HgCl}_2 + \text{Cu}_2\text{Cl}_2 \longrightarrow \text{ArHgCl} + 2 \text{ CuCl}_2 + \text{N}_2 \qquad (15)$$
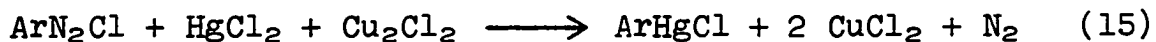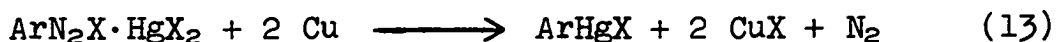
halide and nitrogen gas. Carrying the same reaction out in ammonia results in the formation of ammonia and diarylmercury (Eq. 14) (37). Cuprous chloride has also been used to generate the mercurial, nitrogen, and cupric chloride (Eq. 15) (38).

The vinylmercuric chlorides used in this study were prepared via the corresponding vinyldicyclohexylboranes (R'= cyclohexyl in Scheme 1) or directly from the acetylene (Eq. 5). The arylmercuric chlorides were prepared directly by electrophilic substitution (Eq. 10) and are referenced individually in the experimental section of Chapter VI.

A wide variety of methods for the preparation of organo-
mercurials have been described in the literature. Organo-
mercurials can be prepared from other organometallic com-
pounds, from hydrazines and diazoderivatives, or directly
from various arenes, alkenes, alkynes, or halides. The next
chapter will discuss synthetic methods utilizing organomer-
curials which were described prior to the work described in
this thesis.

III. PREVIOUS SYNTHETIC APPLICATIONS
OF VINYL- AND ARYLMERCURIALS

Organomercurials have been known for over a century and their chemistry has been of interest for some time. Early interest was centered mainly around their medicinal uses. The earliest uses of organomercurials in organic synthesis were as precursors for other organometallic reagents by metal exchange reactions. While there were some early reports of carbon-carbon bond forming reactions utilizing organomercurials, this field has only recently been studied systematically.

In discussing previous synthetic applications of organo-mercurials I will limit myself to those involving vinyl- and arylmercurials. Reactions related specifically to areas of my work are discussed in the appropriate chapters of this thesis.

A. Vinylmercurials

Prior to 1970 few reports of synthetic applications of vinylmercurials appeared in the literature. The main effort was on the transmetallation reaction (Eq. 16) (3, pp. 384-400).

$$R_2Hg + M \longrightarrow R_2M + Hg$$

$$R_2Hg + MX_2 \longrightarrow R_2M + HgX_2$$

(16)
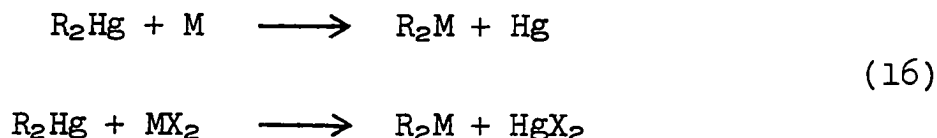
Some studies were also reported on the electrophilic substitution reaction, protic acids and halogens being the most

common electrophiles studied (5).

The thermolysis of a wide variety of vinylmercuric salts has been shown to result in the elimination of metallic mercury and the formation of substituted vinyl derivatives (Eq. 17) (6). These thermolyses generally require relatively

$$CH_2=CH-HgX \xrightarrow{\Delta} CH_2=CH-X + Hg^0 \qquad (17)$$

$$X=O-\overset{O}{\overset{\|}{C}}R, \ -OAr, \ -SAr, \ -SR, \ -OTs, \ -SCN, \ -S\overset{O}{\overset{\|}{C}}OR, \ -O\overset{O}{\overset{\|}{S}}\!\!-\!\!\langle\bigcirc\rangle\!\!-\!\!CH_3,$$

$$-ON=C(CF_3)_2, \ -O\overset{O}{\overset{\|}{P}}(OR)_2, \ -O\overset{O}{\overset{\|}{P}}\!\!-\!\!OR, \ -S\overset{S}{\overset{\|}{P}}(OR)_2, \ -OSO_2F$$
$$\qquad\qquad\qquad\qquad\qquad\;\; \overset{|}{CH_3}$$
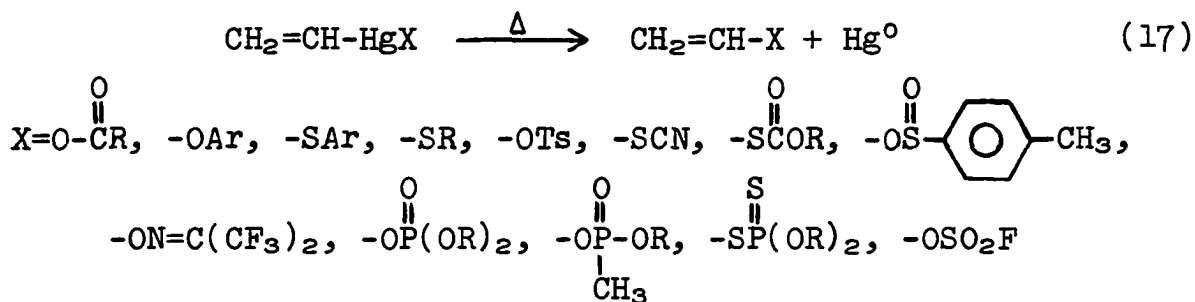
high temperatures. More recently it has been observed that vinyl acetates may be obtained at room temperature by the use of palladium acetate (Eq. 18) (26). Other researchers have ob-

$$\begin{array}{c}(CH_3)_3C\\ \diagdown\\ H\diagup\end{array}\!\!C\!=\!C\!\!\begin{array}{c}\diagup H\\ \diagdown HgCl\end{array} \xrightarrow{Pd(OAc)_2} \begin{array}{c}(CH_3)_3C\\ \diagdown\\ H\diagup\end{array}\!\!C\!=\!C\!\!\begin{array}{c}\diagup H\\ \diagdown O\overset{}{\underset{\|}{C}}CH_3\\ \;\;\overset{\|}{O}\end{array} \qquad (18)$$
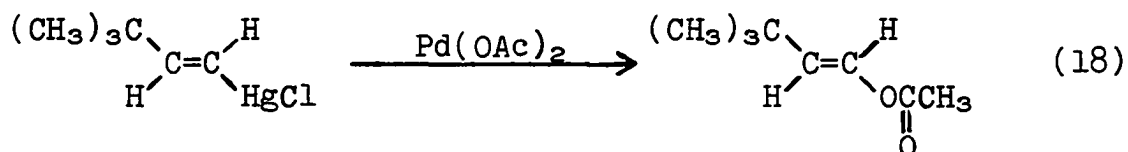
served that cyclohexanone can be obtained by treating cyclo-hexenylmercuric hydroxide with perchloric acid (Eq. 19) (39).

$$\text{(structure: cyclohexene-HgOH)} \xrightarrow[H_2O]{HClO_4} \left[\text{(cyclohexene-OH)} \right] \longrightarrow \text{(cyclohexanone, =O)} \qquad (19)$$
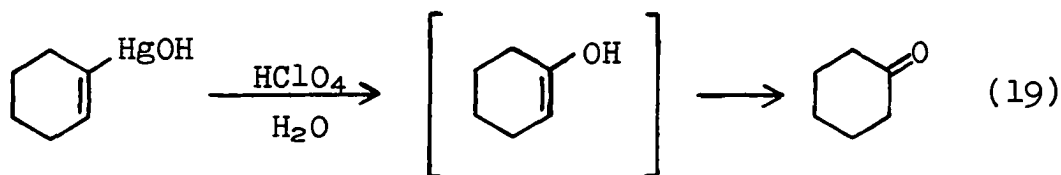
During a study of the cleavage of cis-2-butenylmercuric bromide by bromine, Casey, Whitesides and Kurth observed that

the product obtained depended on which solvent was used for
the reaction (Eq. 20) (40). In polar solvents, such as pyridine

$$\underset{\text{pyridine}}{\overset{\displaystyle CH_3\diagdown_{C=C}\diagup^{CH_3}_{H}\diagup\diagdown_{Br}}{\xleftarrow{\hspace{1em}Br_2\hspace{1em}}}}\quad CH_3\diagdown_{C=C}\diagup^{CH_3}_{H}\diagup\diagdown_{HgBr}\quad \overset{Br_2}{\underset{CS_2}{\xrightarrow{\hspace{1em}}}}\quad CH_3\diagdown_{C=C}\diagup^{Br}_{H}\diagup\diagdown_{CH_3}\quad (20)$$
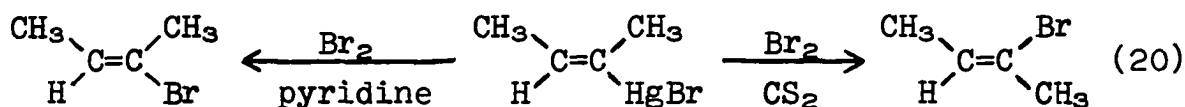
dine, the mercurial was found to under conventional electro-
philic cleavage with the expected retention of stereochemistry.
In non-polar solvents, such as carbon disulfide, the product
was the one resulting from inversion of stereochemistry. This
wss explained by invoking trans-addition across the olefin,
rotation, and then trans-elimination of mercuric bromide to
generate the product of inverted stereochemistry (Scheme 3).

Scheme 3
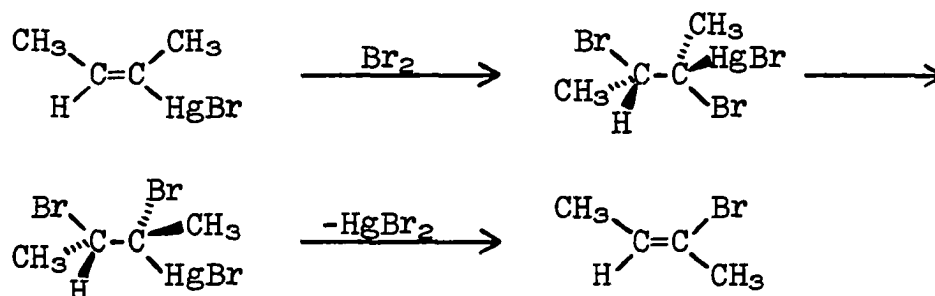
Other researchers observed that under ionic conditions either
cis- or trans-β-chlorovinylmercuric chloride was found to
generate trans-1-chloro-2-iodoethylene (Eq. 21) (41).

$$\underset{\text{cis or trans}}{ClCH=CHHgCl}\quad\xrightarrow{I_2}\quad Cl\diagdown_{C=C}\diagup^{H}_{H}\diagup\diagdown_{I}\quad (21)$$
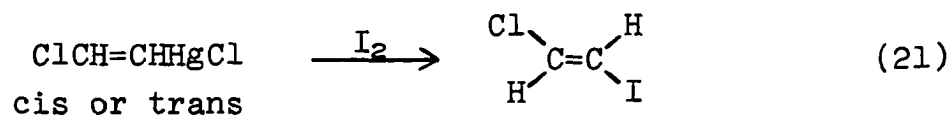
Recently, a number of carbon-carbon bond forming re-
actions have been developed in the Larock group. The complex
obtained by the addition of two equivalents of methyl iodide
to Wilkinson's catalyst has been shown to methylate the
carbon-mercury bond of vinylmercuric chlorides (Eq. 22) (42).

$$2\ CH_3I\ +\ ClRh(PPh_3)_3\ \longrightarrow\ CH_3RhClI(PPh_3)_2 \cdot CH_3I$$

(22)
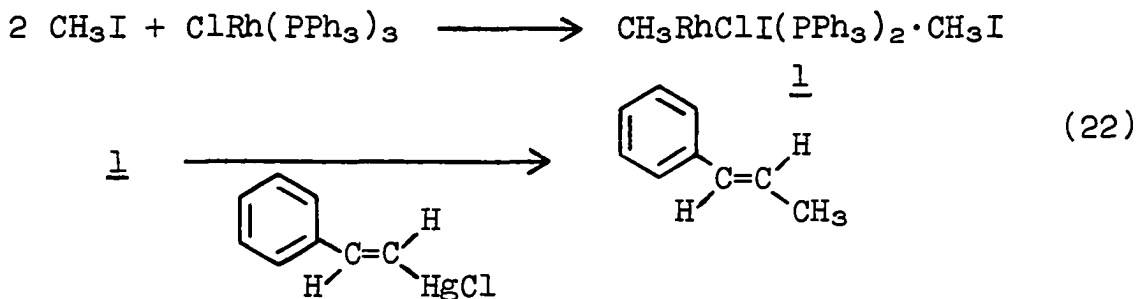
In a highly solvent dependent reaction, palladium
chloride has been found to cause the formation of either
symmetrical (43) or unsymmetrical (26) dienes from the corre-
sponding vinylmercuric chlorides (Eq. 23).

(23)
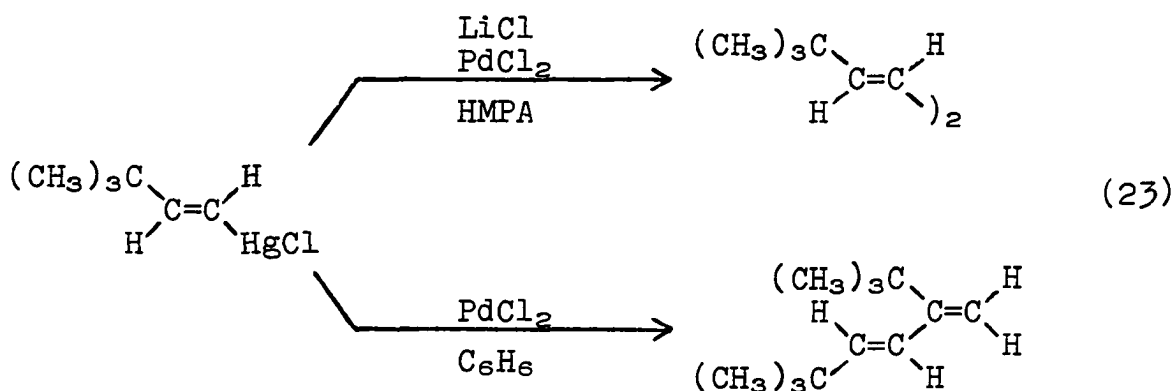
Carbonylation of vinylmercuric chlorides in the presence
of alcohols at low temperatures results in the formation of
esters, while the use of wet tetrahydrofuran (THF) results in
formation of the corresponding acids (Eq. 24) (44). In like

$$R\!\!\diagdown\!\!_{C=C}\diagup^H_{HgCl} \quad \xrightarrow[\text{Li}_2\text{PdCl}_4]{\text{CO, R'OH}} \quad R\!\!\diagdown\!\!_{C=C}\diagup^H_{COOR'}$$

$$\xrightarrow[\text{1-5\% H}_2\text{O/THF}]{\text{CO, Li}_2\text{PdCl}_4} \quad R\!\!\diagdown\!\!_{C=C}\diagup^H_{COOH}$$

(24)
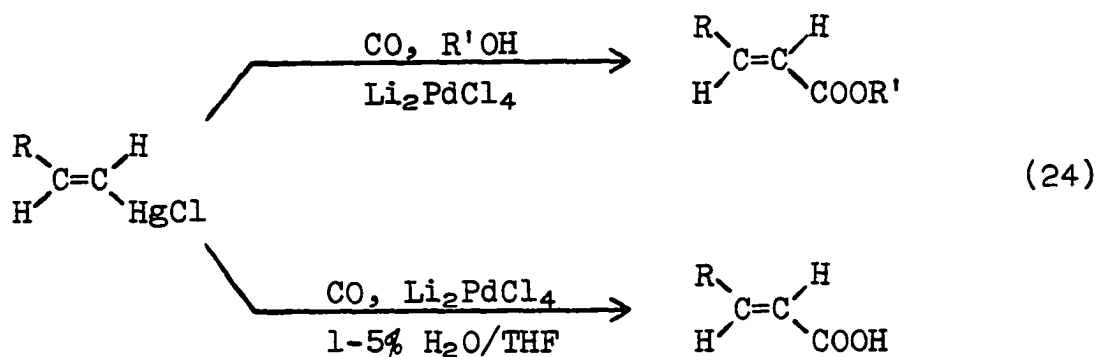
manner, organomercurials derived from propargylic alcohols have been carbonylated to generate β-chlorobutenolides (Eq. 25) (45). These carbonylations can be made catalytic

$$\xrightarrow{\text{HgCl}_2} \xrightarrow[\text{Li}_2\text{PdCl}_4]{\text{CO}}$$

(25)
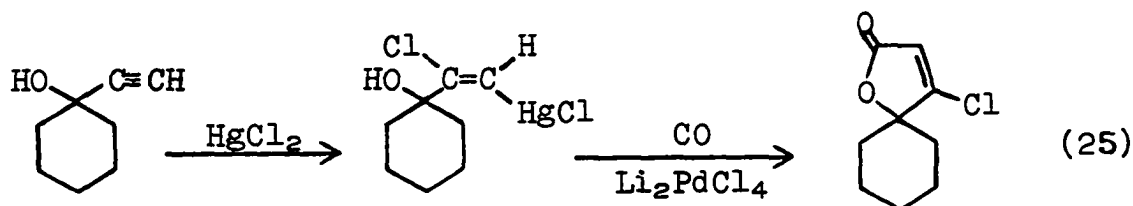
by the addition of cupric chloride. Butenolides are of interest for their biological activity.

In an unexpected result, π-allylpalladium compounds were obtained when a vinylmercuric salt was allowed to react with ethyl acrylate in the presence of palladium chloride (Eq. 26) (46). A dienic ester was the expected product. This reaction

$$(CH_3)_3C\!\!\diagdown\!\!_{C=C}\diagup^H_{HgCl} + Li_2PdCl_4 + CH_2=CHCO_2Et \longrightarrow$$

(26)

$$(CH_3)_3C-C\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{\underset{PdCl)_2}{\overset{C}{|}}}}C-CH_2CO_2Et$$
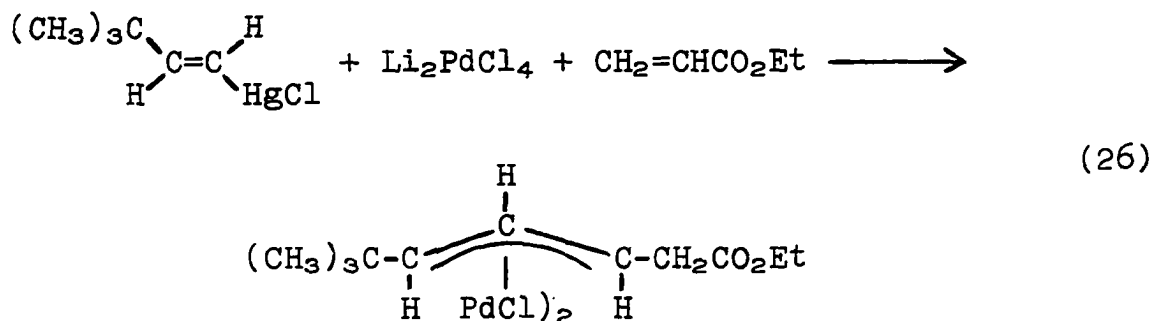
has been extended to a wide range of olefins and was found to be quite general.

B. Arylmercurials

Arylmercurials became readily available before vinylmercurials did and as a result the chemistry of arylmercurials has been more thoroughly studied. However, even in the case of arylmercurials many of their synthetic applications were only recently reported.

Seyferth has carried out extensive studies on the use of arylmercurials as carbene transfer agents (Eq. 27) and

$$\text{Ph-Hg-}\overset{\overset{\displaystyle X}{|}}{\underset{\underset{\displaystyle R}{|}}{C}}\text{-R'} \;+\; \overset{}{\underset{}{>}}\text{C=C}\overset{}{\underset{}{<}} \;\xrightarrow{\;\Delta\;}\; \text{PhHgX} \;+\; \overset{R\diagdown\;\diagup R'}{\underset{\diagup\;\diagdown}{C}} \tag{27}$$
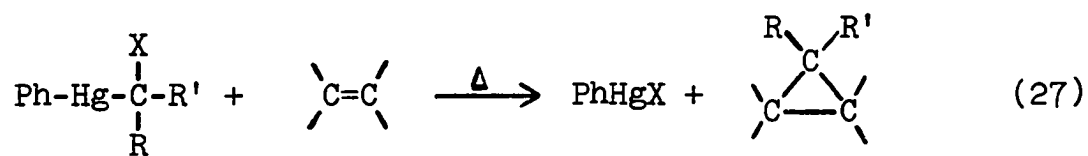
reviews have recently been published.(47, 48; 4, pp. 351-380). "X" is always a halogen. R and R' usually are halogens but other functionalities have also been reported. The migratory tendency was found to be I>Br>Cl>F.

There have been reports of the substitution of various heteroatoms for the mercury in arylmercurials. For example, o-chloromercuriphenol has been converted to o-iodophenol by the action of iodine (49). Similarly, N-iodosuccinimide converts ferrocenylmercuric chloride to iodoferrocene (Eq. 28) (50, 6c). There have also been a number of reports of the conversion of diarylmercurials to diarylsulfides (51-53). Arylboranes may be obtained by treating arylmercurials with di-

$$(28)$$
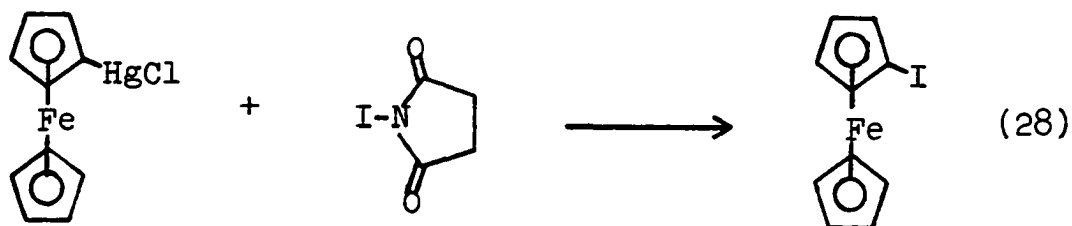
borane. The arylboranes are then converted to phenols by oxidation with alkaline hydrogen peroxide (54).

Early researchers reported isolated examples of the direct alkylation of arylmercurials by molecules containing reactive halides (Eq. 29 (7); Eq. 30 (8); Eq. 31 (9); Eq. 32

$$Ph_2Hg + BrCH_2CH_2Br \xrightarrow{180-200^{\circ}} Ph-CH_2CH_2Br \qquad (29)$$

$$Ph_2Hg + PhCHCl_2 \xrightarrow{150^{\circ}} Ph_3CH \qquad (30)$$

$$(31)$$

$$(32)$$
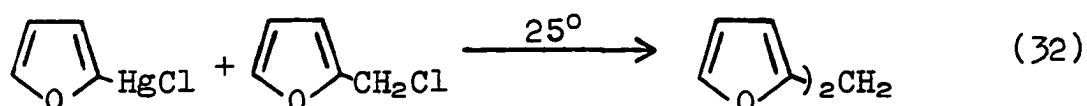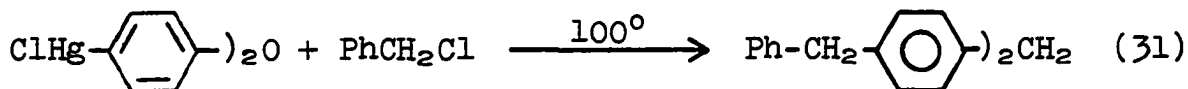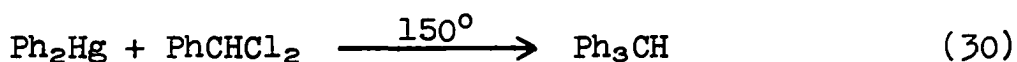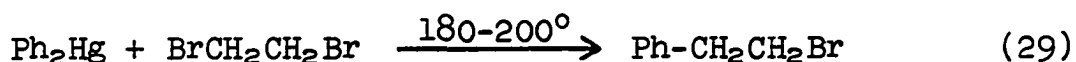
(10)). More recently aluminum bromide has been reported to catalyze the reaction of benzylic halides with dialkyl- or diarylmercury compounds (Eq. 33) (11).

$$ArCH_2X + Bu_2Hg \text{ or } Ar_2Hg \xrightarrow{AlBr_3} ArCH_2Bu \text{ or } ArCH_2Ar \qquad (33)$$
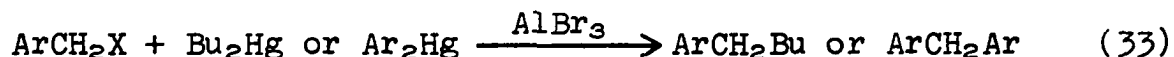
Heck has done extensive work on the palladium assisted conversion of organomercurials to olefins (Eq. 34 (12); Eq. 35

(13); Eq. 36 (14)). The use of cupric chloride as a reoxidant

$$\text{Ph}_2\text{Hg} + \underset{\underset{\underset{CH_3}{|}}{CH}}{CH\!\!\diagdown}\!\!\overset{CH_2}{\underset{CH}{\diagup}}\!\!\text{---PdCl} \longrightarrow \underset{CH_3}{\overset{\overset{\displaystyle H}{|}}{C}}\!\!\diagup\!\!\overset{\displaystyle C}{\underset{\underset{H}{|}}{\diagdown}}\!\!\text{CH}_2\text{Ph} \qquad (34)$$

$$\text{RHgX} + \text{PdX}_2 + \text{CH}_2\text{=CHY} \longrightarrow \text{R-CH=CHY} \qquad (35)$$

$$\overset{\qquad\qquad O}{\underset{\displaystyle R\text{=Ar-, RO-}\overset{\|}{C}\text{-, RCH}_2\text{-}}{}}$$

$$\text{ArHgCl} + \text{CH}_2\text{=CHR} + 2\ \text{CuCl}_2 \xrightarrow{\ \text{PdCl}_2\ } \text{ArCH}_2\overset{\overset{\displaystyle Cl}{|}}{CH}\text{-R} \qquad (36)$$
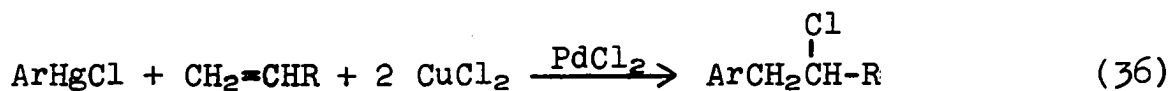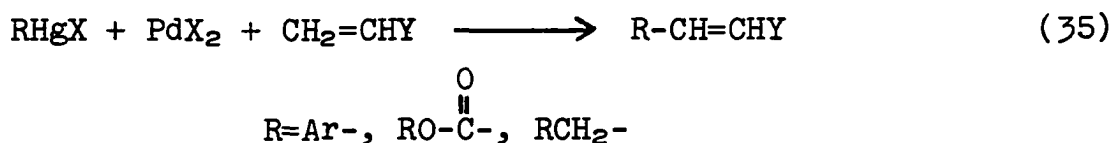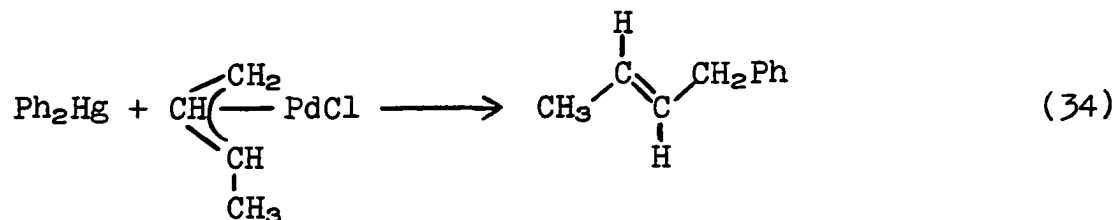
results in the formation of an alkyl chloride rather than an olefin. These reactions give mixtures of products if either the mercurial or olefin component have β-hydrogens capable of eliminating to form other olefins. In such cases more than one hydride elimination is possible and a mixture of products is obtained. The mechanism of this reaction is envisioned to involve formation of an arylpalladium complex which adds to the olefin and then eliminates a palladium hydride generating a new olefin (Scheme 4) (15).

Interest in the carbon-carbon bond forming reactions of organomercurials has increased in recent years and a number of useful reactions have been discovered. A number of these have been discussed in this chapter. The following chapters

Scheme 4
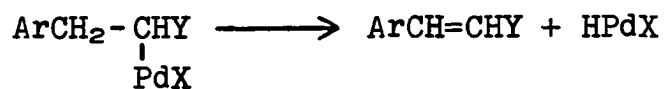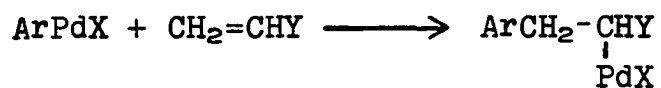
$$ArHgX + PdX_2 \longrightarrow ArPdX + HgX_2$$

$$ArPdX + CH_2\text{=}CHY \longrightarrow ArCH_2\text{-}\underset{\underset{PdX}{|}}{C}HY$$

$$ArCH_2\text{-}\underset{\underset{PdX}{|}}{C}HY \longrightarrow ArCH\text{=}CHY + HPdX$$

$$HPdX \longrightarrow Pd^0 + HX$$

will discuss the synthesis of α,β-unsaturated ketones, symmetrical 1,3-dienes and biaryls, and 1,4-dienes. Related reactions involving organomercurials will be discussed in the appropriate chapters.

IV. THE SYNTHESIS OF α,β-UNSATURATED KETONES

A. Introduction

1. <u>General syntheses of enones</u>

A variety of methods presently exist for the synthesis of α,β-unsaturated ketones. One important reaction is the Friedel-Crafts reaction of acid chlorides (55, 56), acids (56), or anhydrides (56) with olefins. The Friedel-Crafts reaction utilizes Lewis acids such as aluminum chloride or stannic chloride and olefins (Eq. 37) and proceeds by way of carbonium

$$RCH=CH_2 + R'COCl \xrightarrow[\text{acid}]{\text{Lewis}} R-CH=CHCR' \qquad (37)$$
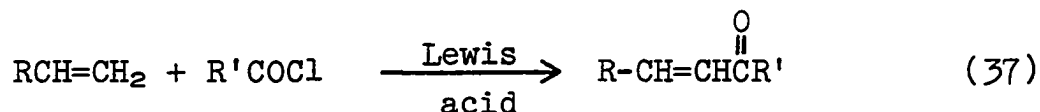
ions. As a result, the reaction is susceptible to carbonium ion rearrangements and is further limited by the requirement that the products be formed from the most stable carbonium ions.

The aldol condensation (57) is another important approach to the synthesis of α,β-unsaturated ketones. The aldol reaction can proceed in quite high yields when carried out as a self-condensation of aldehydes or ketones (Eq. 38) or the

$$2CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow{\text{base}} CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{OH}{\overset{|}{C}}H(CH_3)_2 \xrightarrow{-H_2O} CH_3\overset{O}{\overset{\|}{C}}CH=C(CH_3)_2 \qquad (38)$$
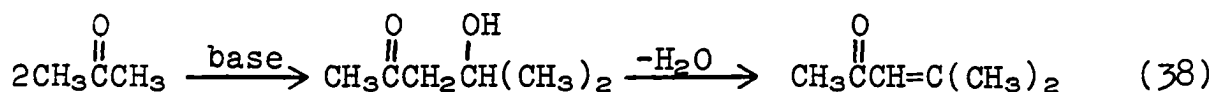
condensation of a ketone with the carbonyl group of an aldehyde. However, the aldol reaction will generate mixtures when the cross-condensation of two aldehydes or ketones is attempted, and fails when one attempts to condense aldehydes with the

carbonyl group of a ketone. Furthermore, unsymmetrical ketones lead either to mixtures when the two possible enolates are of equal energy or to products derived solely from the more stable enolate when the enolates differ in energy. Mixtures of cis- and trans-enones are also obtained. Self-condensation of aldehydes can be prevented by the formation of aldehyde imines (58) while kinetic enolates can be pre-formed by use of a hindered base before addition of the carbonyl component (59).

The acylation of vinylmercurials appeared to be a promising route to enones since vinylmercurials are readily available from acetylenes and the reaction was expected to proceed stereospecifically.

2. Mercury based syntheses of ketones

A number of reactions of organomercurials which lead to ketones have been reported previously, and will be discussed briefly here.

Mercury salts have been used to obtain ketones from alkenes (60, 61) or acetylenes (62) (Eqs. 39, 40). Alkenes are

$$RCH=CH_2 \xrightarrow[ROH]{Hg(OAc)_2} R-\underset{\underset{OR}{|}}{C}HCH_2HgOAc \longrightarrow R\overset{\overset{O}{\|}}{C}CH_3 \tag{39}$$

$$R-C\equiv CH \xrightarrow[cat. HgSO_4]{H_2O} \overset{H^+}{\longrightarrow} R\overset{\overset{O}{\|}}{C}CH_3 \tag{40}$$
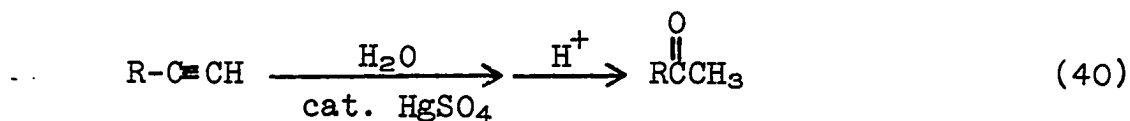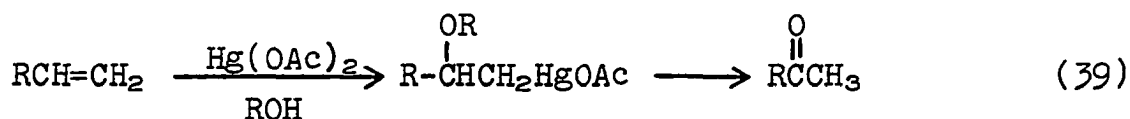
oxidized to ketones by oxymercuration and the use of either palladium chloride and cupric chloride, or chromium trioxide in sulfuric acid, while acetylenes are hydrolyzed directly to ketones. This reaction with acetylenes has found wide use in synthesis. Ketones have also been prepared from α-mercurated ketones and alkyl halides (Eq. 41) (63, 64).

$$\underset{\text{RCCH}_2\text{HgX}}{\overset{\text{O}}{\parallel}} + \text{R'X} \longrightarrow \underset{\text{RCCH}_2\text{R'}}{\overset{\text{O}}{\parallel}} \qquad (41)$$

A number of methods have been found to synthesize symmetrical diaryl ketones from diarylmercurials and transition metal carbonyls. Nickel tetracarbonyl (65), dicobaltoctacarbonyl (66), and $ClRh(CO)(PEt_3)_2$ in the presence of carbon monoxide (67) have all been used effectively.

There are only isolated examples of the direct reaction of acid chlorides with organomercuric chlorides(9, 10, 68, 69). Most of the examples involve the reaction of acid halides and activated arylmercuric chlorides and even some of these reactions require forcing conditions. One interesting reaction used mercuric chloride catalytically (Eq. 42) (9). Only one

$$(C_6H_5)_2O + C_6H_5COCl \xrightarrow[150\text{-}160^\circ]{HgCl_2} C_6H_5\overset{O}{\overset{\parallel}{C}}\!\!-\!\!\langle \text{—} \rangle\!\!-\!\!OC_6H_5 \qquad (42)$$
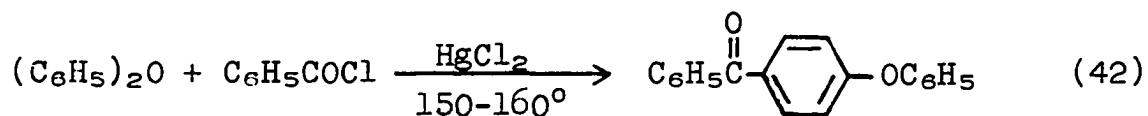
non-arylmercuric chloride, allylmercuric iodide, has been reported to react directly with an acid halide (Eq. 43) (70)

$$CH_2=CH-CH_2HgI + R\overset{O}{\overset{\|}{C}}X \longrightarrow R\overset{O}{\overset{\|}{C}}CH_2CH=CH_2$$

$$2\ CH_2=CH-CH_2HgI + RCH_2\overset{O}{\overset{\|}{C}}X \longrightarrow \begin{matrix} RCH=C-CH_2-CH=CH_2 \\ | \\ O-\underset{\underset{O}{\|}}{C}CH_2R \end{matrix}$$

(43)
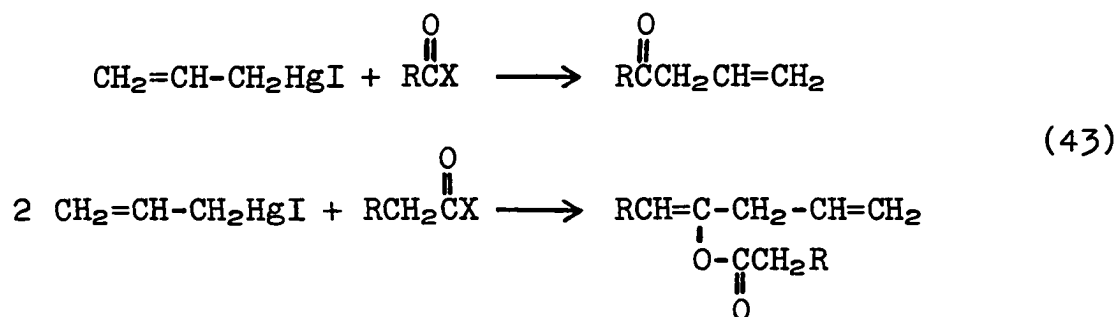
to produce ketones. An unexpected product was obtained when the acid halide has α-hydrogens. Its formation was explained by invoking an intermediate ketene (Scheme 5). The reaction

Scheme 5

$$RCH_2\overset{O}{\overset{\|}{C}}X \longrightarrow RCH=C=O \xrightarrow{\ IHgCH_2-CH=CH_2\ }$$

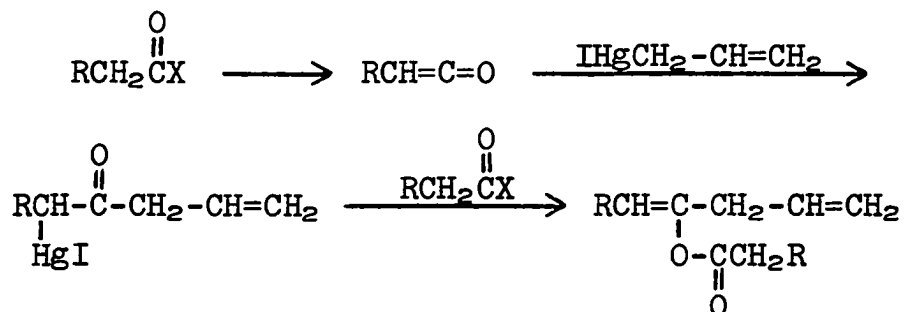$$\begin{matrix} RCH-\overset{O}{\overset{\|}{C}}-CH_2-CH=CH_2 \\ | \\ HgI \end{matrix} \xrightarrow{\ RCH_2\overset{O}{\overset{\|}{C}}X\ } \begin{matrix} RCH=C-CH_2-CH=CH_2 \\ | \\ O-\underset{\underset{O}{\|}}{C}CH_2R \end{matrix}$$

of α-mercurated ketones with acid halides has literature (64,71) precedent (Eq. 44). In both cases the reaction with the acyl

$$ClHgCH_2\overset{O}{\overset{\|}{C}}-R \underset{HgCl_2/KCl}{\overset{R'\overset{O}{\overset{\|}{C}}Cl}{\rightleftharpoons}} \begin{matrix} O\overset{O}{\overset{\|}{C}}R' \\ | \\ CH_2=C-R \end{matrix}$$

(44)
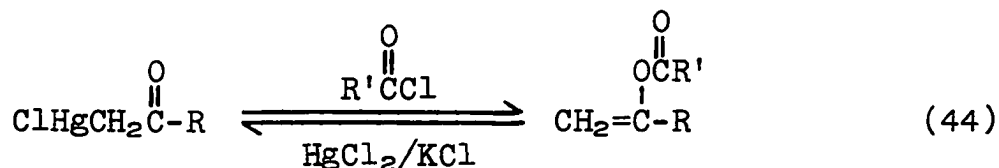
chloride occurs at oxygen rather than carbon.

The ketone forming reactions of organomercurials and acid chlorides previously discussed are not general reactions. The use of Lewis acids has been found to promote the reaction of organomercurials and acid chlorides. Skoldinov and Koschkov

used aluminum chloride to promote their reactions (Eq. 45)

$$(C_6H_5)_2Hg + C_6H_5\overset{O}{\overset{\|}{C}}Cl \xrightarrow[\text{CS}_2]{\text{AlCl}_3} C_6H_5\overset{O}{\overset{\|}{C}}C_6H_5$$

$$C_6H_5HgCl + C_6H_5\overset{O}{\overset{\|}{C}}Cl \xrightarrow[\text{neat}]{\text{AlCl}_3} C_6H_5\overset{O}{\overset{\|}{C}}C_6H_5$$

(45)
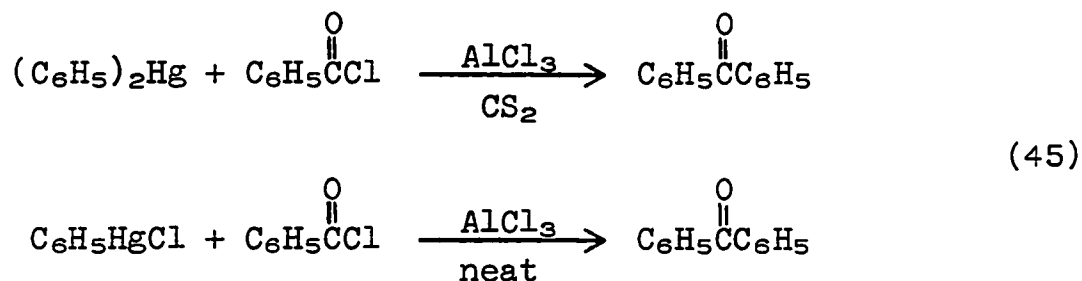
(72). The yield of benzophenone in carbon disulfide was 47% based on utilization of both phenyl groups. The reaction of phenylmercuric chloride was carried out in neat benzoyl chloride an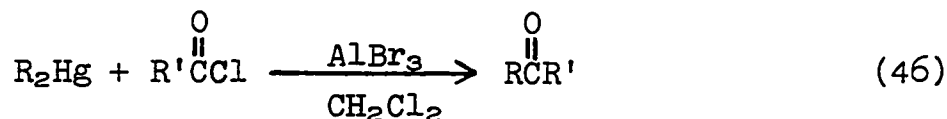d resulted in a 59% yield of benzophenone. Kurts and co-workers (73) used aluminum bromide in dichloromethane to prepare ketones (Eq. 46). Either dialkyl- or diarylmercury

$$R_2Hg + R'\overset{O}{\overset{\|}{C}}Cl \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{AlBr}_3} R\overset{O}{\overset{\|}{C}}R' \qquad (46)$$

compounds could be used with either aliphatic or aromatic acid halides. The reaction occurs very quickly, often in minutes, and appears to transfer one aryl or alkyl group from mercury to the acid halide.

One example of a transition metal catalyzed reaction of dialkyl- or diarylmercurials with acid bromides has appeared recently. Tetrakis-triphenylphosphine palladium(0) catalyzes the reaction of acid halides with organomercurials (Eq. 47)

$$R\overset{O}{\overset{\|}{C}}Br + R'_2Hg \xrightarrow[\text{HMPA}]{\text{Pd(PPh}_3)_4} R\overset{O}{\overset{\|}{C}}R' + R'HgBr \qquad (47)$$
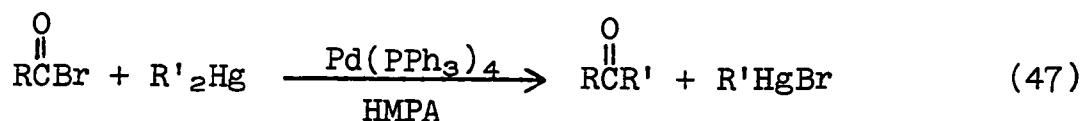
(74). The reaction requires the use of hexamethylphosphoramide (HMPA) and failed for alkyl-and arylmercuric chlorides.

I have developed the first synthesis of α,β-unsaturated ketones from vinylmercuric chlorides and acid chlorides. The reaction proceeds to give high yields of trans-α,β-unsaturated ketones greater than 95% stereochemically pure. The reaction works very well with aliphatic acid chlorides and moderately well with aromatic acid chlorides. Unfortunately, not all functional groups are tolerated and the reaction conditions, although relatively mild, tend to cause rearrangements in some isolated systems. With these limitations in mind, the reaction appears to be fairly general.

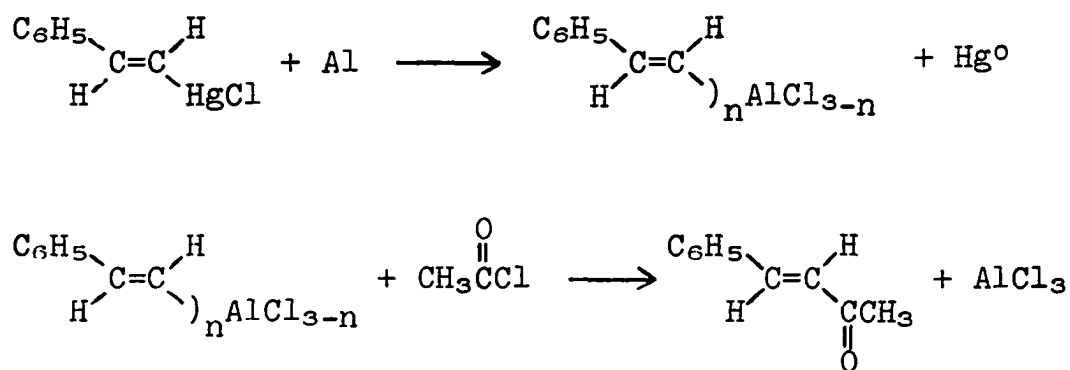## B. Results and Discussion

1. The reaction of styrylmercuric chloride with acetyl chloride

Reutov's report of the synthesis of ketones from diaryl-or dialkylmercurials (73) prompted me to study the reaction of vinylmercuric chlorides with acid chlorides. Trans-styrylmercuric chloride was chosen as a model system for study (Eq. 48). The results of this study are summarized

$$\tag{48}$$
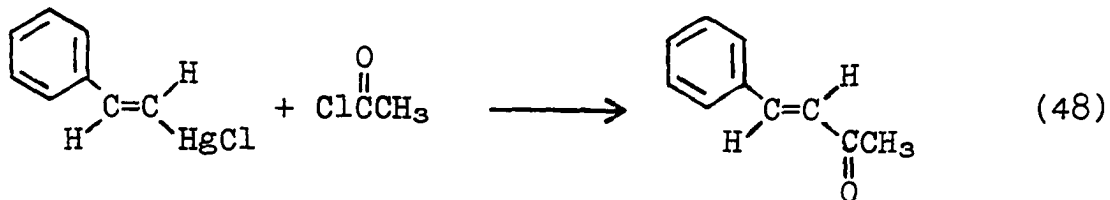
in Table I. Reutov's reaction conditions, aluminum bromide in dichloromethane at room temperature, were not successful in this system. Reutov reported that aluminum bromide gave the best yield of ketone of the Lewis acids studied. Therefore other Lewis acids were not tried. Metals tried were zinc, zinc-copper couple (prepared in situ from zinc and copper(II) sulfate), aluminum, aluminum/aluminum bromide, and magnesium/-aluminum bromide. Magnesium was added in an attempt to form distyrylmercury in situ which would then undergo reaction (75) with the acid chloride and aluminum chloride. Zinc and the zinc-copper couple might work through either transmetallation (3, p. 390) or symmetrization to distyrylmercury (76). Metallic aluminum is envisioned to proceed through trans-metallation to a vinylalane (Scheme 6). Excess aluminum was

Scheme 6

$$
\begin{array}{c}
C_6H_5 \\ \diagdown \\ H \diagup
\end{array}
C{=}C
\begin{array}{c}
\diagup H \\ \diagdown \\ HgCl
\end{array}
+ \text{ Al} \longrightarrow
\begin{array}{c}
C_6H_5 \\ \diagdown \\ H \diagup
\end{array}
C{=}C
\begin{array}{c}
\diagup H \\ \diagdown \\ )_n AlCl_{3-n}
\end{array}
+ \text{ Hg}^{\circ}
$$

$$
\begin{array}{c}
C_6H_5 \\ \diagdown \\ H \diagup
\end{array}
C{=}C
\begin{array}{c}
\diagup H \\ \diagdown \\ )_n AlCl_{3-n}
\end{array}
+ \overset{O}{\underset{\|}{CH_3\overset{}{C}Cl}} \longrightarrow
\begin{array}{c}
C_6H_5 \\ \diagdown \\ H \diagup
\end{array}
C{=}C
\begin{array}{c}
\diagup H \\ \diagdown \\ \underset{\underset{O}{\|}}{CCH_3}
\end{array}
+ \text{ AlCl}_3
$$

found to be necessary due to the formation of an amalgam. Four equivalents of aluminum powder in dichloromethane resulted in the best yield of enone. The substitution of distyrylmercury for styrylmercuric chloride was also found to result in a

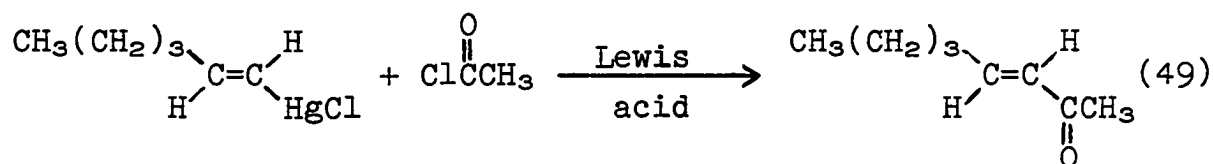Table I. The Reaction of Trans-styrylmercuric Chloride with
Acetyl Chloride

Solvent	Lewis Acid or Metal[a]	Temp. (°C)	Time (hr)	% Yield[b]
CH_2Cl_2	$AlBr_3$	25	24	0
$CHCl_3$				0
$C_6H_5NO_2$				0
DMF				0
THF				0
pentane	$Al/AlBr_3$	0	16	17[c]
CH_2Cl_2	$AlBr_3/Mg$	25	24	30
	Zn			6
	$Zn/CuSO_4$		0.5	19
	Al foil[d]		24	10
	Al powder[d]			42
	Al powder[d]		9	40
	Al powder[e]			48
THF	Al foil[d]		24	24
	Al powder[d]			21
DMF	Al foil[d]			0
	Al powder[d]			0

[a]One equivalent of Lewis acid or metal.

[b]GLC yield using an internal standard.

[c]Acetyl chloride and aluminum bromide added after four hours.

[d]Two equivalents of aluminum.

[e]Four equivalents of aluminum.

reasonably successful reaction, resulting in a 53% yield.
Distyrylmercury is significantly more soluble in dichloro-
methane than is the chloride. As a result, the success of
this reaction may be due to a combination of increased
reactivity and increased solubility of the distyrylmercury.
Both the aluminum powder and distyrylmercury reactions result
in utilization of roughly half of the styryl groups available
and therefore appear to be equally useful synthetically.

2. The reaction of trans-1-hexenylmercuric chloride with acetyl chloride

A new model system was then investigated to determine if
the difficulties encountered in the styryl system were unique
to that system or a general characteristic of all vinylmercuric
chlorides (Eq. 49). Trans-1-hexenylmercuric chloride was

$$CH_3(CH_2)_3 \diagdown C=C \diagup H \diagdown HgCl + Cl\overset{O}{\underset{\|}{C}}CH_3 \xrightarrow[\text{acid}]{\text{Lewis}} CH_3(CH_2)_3 \diagdown C=C \diagup H \diagdown \underset{\underset{O}{\|}}{C}CH_3 \quad (49)$$

treated with acetyl chloride and aluminum bromide in dichloro-
methane for one hour at 0°C. Analysis of the reaction mixture
by GLC showed an excellent yield of enone, although a mixture
of approximately equal quantities of cis- and trans-3-octen-2-
one were obtained.

In an effort to improve the stereospecificity of the
reaction, studies on the effect of the Lewis acid (Table II)

Table II.   Effect of Lewis Acid on the Reaction of Trans-
1-hexenylmercuric Chloride with Acetyl Chloride

Lewis Acid[a]	Time (hr)	Yield of 3-Octen-2-one[b]		
		% Cis-	% Trans-	% Total
SbCl$_5$	.1	0	0	0[c]
SbCl$_3$	24	0	0	0
SnCl$_4$	1	0	0	0[c]
SbF$_3$	24	0	0	0
BF$_3$·Et$_2$O		6	7	13
ZnCl$_2$	6	7	5	12
BCl$_3$		0	3	3[c]
FeCl$_3$	.1	2	23	25[d]
Al powder	24	7	41	48
TiCl$_4$	.25	23	76	99
AlBr$_3$	.50	44	49	93
AlCl$_3$	.25	5	95	100

[a]One mmol each of Lewis acid, acetyl chloride, and trans-1-
hexenylmercuric chloride in 10 ml CH$_2$Cl$_2$ at ~25°C.

[b]GLC yield calculated using calculated correction factors.

[c]Transmetallation reaction possible.

[d]No products seen at -78°C.

and solvent (Table III) were carried out. Titanium tetra-
chloride, aluminum bromide, and aluminum chloride were found
to be the only synthetically useful Lewis acids. Antimony
pentachloride, stannic chloride, and boron trichloride showed
evidence of undergoing transmetallation reactions with the
vinylmercuric chloride although no ketone products were seen
by GLC. A precipitate, presumably mercuric chloride, is
observed in the successful reactions and a similar precipitate
was observed in these three non-ketone forming reactions.
Although it is not known exactly what is happening in these
reactions it is assumed that a transmetallation reaction
occurs leading to new vinylmetallics which do not provide
enone product.

As can be seen in Table III, dichloromethane was a signifi-
cantly better solvent for the reaction than any other solvent
tested. Polar solvents are necessary to dissolve the vinyl-
mercuric chloride, but solvents which are capable of co-
ordinating with the Lewis acid are undesirable since they
weaken the ability of the Lewis acid to promote acylation.
One difficulty with styrylmercuric chloride was its in-
solubility in dichloromethane, which probably explains its
lack of reaction under conditions where other vinylmercuric
chlorides react readily.

The effect of reaction temperature on the stereospecifi-
city of the three Lewis acid systems which were found to be
effective in this reaction was studied (Table IV). The stereo-

Table III. Effect of Solvent on the Reaction of Trans-1-
hexenylmercuric Chloride with Acetyl Chloride

Lewis Acid	Time (hr)	Solvent[a]	Yield of 3-Octen-2-one[b]		
			% Cis-	% Trans-	% Total
AlBr$_3$	24	DMF[c]	0.5	2	2.5
		HMPA[d]	0	4	4
	0.25	CHCl$_3$	9	6	15
		C$_6$H$_5$NO$_2$	13	13	26
		CH$_3$NO$_2$	trace	21	21
		CH$_2$Cl$_2$	44	49	93
AlCl$_3$	24	DMF[c]	0	0	0
		Et$_2$O	0	0	0
		HMPA[d]	0	2	2
	0.25	CHCl$_3$	0	4	4
	18	THF[e]	3	19	22
	0.25	C$_6$H$_5$NO$_2$	19	19	38
		CH$_3$NO$_2$	14	26	40
		CH$_2$Cl$_2$	5	95	100

[a]One mmol each of Lewis acid, acetyl chloride, and trans-1-

hexenylmercuric chloride in 10 ml solvent at ~25°C.

[b]GLC yield calculated using calculated correction factors.

[c]DMF = N,N-dimethylformamide.

[d]HMPA = hexamethylphosphoramide.
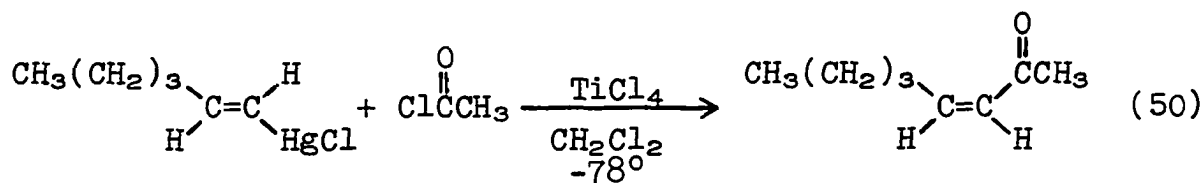
[e]THF = tetrahydrofuran.

Table IV. Effect of Temperature on Stereospecificity in the
Reaction of Trans-1-hexenylmercuric Chloride with
Acetyl Chloride

Lewis Acid	Temp (°C)	Time (hr)	Yield of 3-Octen-2-one[a]		
			% Cis-	% Trans-	% Total
AlBr$_3$	25	0.5	44	49	93
	0		35	64	99
	-22		37	61	98
	-78		16	84	100
AlCl$_3$	25	0.25	5	95	100
	0		8	86	94
	-22		8	92	100
	-78		5	88	93
TiCl$_4$	25		23	76	99
	-78		29	6	35
		3	91	3	94

[a]GLC yield calculated using calculated correction factors.

specificity observed with aluminum bromide was found to improve on lowering the temperature to -78°C. However the improvement never equalled the stereospecificity of the room temperature reaction of aluminum chloride. The stereospecificity observed with aluminum chloride was relatively insensitive to changes in reaction temperature.

An interesting effect was observed when the titanium tetrachloride reaction was carried out at -78°C. The product observed was that obtained from inversion of stereochemistry of the carbon-carbon double bond (Eq. 50). This reaction will

$$CH_3(CH_2)_3 \overset{H}{\underset{H}{\diagdown}}C=C\overset{H}{\underset{HgCl}{\diagup}} + Cl\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[\substack{CH_2Cl_2 \\ -78°}]{TiCl_4} CH_3(CH_2)_3 \overset{\overset{O}{\overset{\|}{C}CH_3}}{\underset{H}{\diagdown}}C=C\overset{}{\underset{H}{\diagup}} \quad (50)$$

be discussed in greater detail later in this chapter.

Studies to determine the optimum reaction time showed that the aluminum chloride reaction was complete in less than five minutes while aluminum bromide required thirty minutes to reach completion (Table V).

The report that Pd(PPh$_3$)$_4$ catalyzed the reaction of dialkyl- or diarylmercurials with acid bromides (77) led me to also try various transition metal catalysts on this system. The results of this study are summarized in Table VI. Only two systems proved to be of any utility, Pd(PPh$_3$)$_4$ in HMPA and [ClRh(CO)$_2$]$_2$ in dichloromethane. Neither of these systems worked as well as the aluminum chloride promoted reaction.

Table V. Effect of Time on the Reaction of Trans-1-hexenyl-
mercuric Chloride and Acetyl Chloride at 25°C

Lewis Acid	Time (min)	Yield of 3-Octen-2-one[a]		
		% Cis-	% Trans-	% Total
AlBr$_3$	1	18	41	59
	5	19	41	60
	20	23	42	65
	30	44	49	93
	1440	0	51	51
AlCl$_3$	1	5	86	91
	5	5	95	100
	15	5	95	100
	30	7	93	100
	60	6	94	100
	1440	10	90	100

[a]GLC yield calculated using calculated correction factors.

Table VI. Transition Metal Catalyzed Reaction of Trans-1-hexenylmercuric Chloride and Acetyl Chloride

Catalyst[a]	Solvent	Time (hr)	Temp. (°C)	Yield %Cis-	3-Octen-2-one[b] %Trans-	%Total
[(C$_6$H$_5$)$_3$P]$_2$Rh(CO)Cl	CH$_2$Cl$_2$	6	25	4	12	16
		0.5	0	7	7	14
	THF	24	25	0	7	7[c]
[(C$_6$H$_5$)$_3$P]$_3$RhCl				0	0	0
Pd[P(C$_6$H$_5$)$_3$]$_4$				0	0	0
	HMPA	6		0	45	45[d]
			60	0	58	58
				0	46	46[d]
			100	0	45	45[d]
[ClRh(CO)$_2$]$_2$[e]	CH$_2$Cl$_2$	1	25	0	24	24[f]
	THF	6		0	0	0[c]
	HMPA	1.5		0	0	0[g]

[a] 10% Catalyst based on vinylmercuric chloride.

[b] GLC yield calculated using calculated correction factors.

[c] The two major products were 1-acetoxy-4-chlorobutane and trans, trans-5,7-dodecadiene.

[d] 1% Palladium reagent.

[e] 5% Of the dimeric rhodium catalyst.

[f] Trans, trans-5,7-dodecadiene is also seen.

[g] Only trans, trans-5,7-dodecadiene is seen.

Some interesting observations were made however. Two reactions were observed when the rhodium catalysts were tried in THF, neither of which was expected. The acetyl chloride reacted with the solvent to give 1-acetoxy-4-chlorobutane (Eq. 51), while the vinylmercuric chloride reacted with itself to form a symmetrical 1,3-diene (Eq. 52). In HMPA only the sym-

$$\text{(furan ring)} + CH_3\overset{O}{\overset{\|}{C}}Cl \longrightarrow CH_3\overset{O}{\overset{\|}{C}}O(CH_2)_4Cl \qquad (51)$$

$$\underset{H}{\overset{CH_3(CH_2)_3}{\diagdown}}C=C\underset{HgCl}{\overset{H}{\diagup}} \longrightarrow \left(\underset{H}{\overset{CH_3(CH_2)_3}{\diagdown}}C=C\underset{}{\overset{H}{\diagup}}\right)_2 \qquad (52)$$
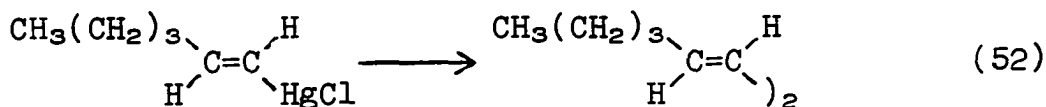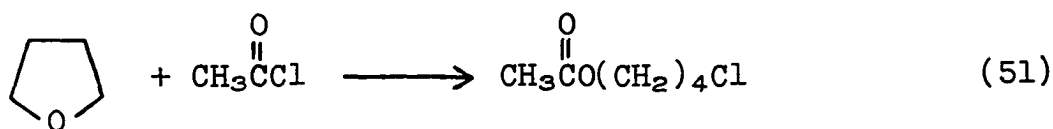
metrical-1,3-diene was observed. These reactions provided the basis for the work discussed in Chapter V of this thesis.

3. The synthesis of α,β-unsaturated ketones

Using our best reaction conditions, aluminum chloride in dichloromethane, we have examined the scope of this new α,β-unsaturated ketone synthesis. All reactions were carried out at room temperature for five minutes. A series of vinylmercurials and acid chlorides were examined. The results are summarized in Table VII. The isolated yields are generally greater than 95% with stereochemical purity also greater than 95% in most cases. Alkyl, aryl, and functionally substituted mercurials were all found to work well. Aliphatic, unsaturated, and aryl acid chlorides were also found to work satisfactorily. α,β-Un-

Table VII. Synthesis of α,β-Unsaturated Ketones

Vinylmercurial	Acid Chloride	Ketone	Isolated Yield(%)
$CH_3(CH_2)_3$, H / C=C / H, HgCl	$ClCCH_3$ (C=O)	$CH_3(CH_2)_3$, H / C=C / H, CCH_3 (C=O)	97
$CH_3(CH_2)_3$, H / C=C / H, HgCl	ClC(C=O)–C₆H₅	$CH_3(CH_2)_3$, H / C=C / H, C(=O)–C₆H₅	64[a]
$(CH_3)_3C$, H / C=C / H, HgCl	$ClCCH_3$ (C=O)	$(CH_3)_3C$, H / C=C / H, CCH_3 (C=O)	95
$(CH_3)_3C$, CH_3 / C=C / H, HgCl	$ClCCH_3$ (C=O)	$(CH_3)_3C$, CH_3 / C=C / H, CCH_3 (C=O)	99
cyclohexyl, H / C=C / H, HgCl	$ClC(CH_2)_2CH_3$ (C=O)	cyclohexyl, H / C=C / H, $C(CH_2)_2CH_3$ (C=O)	96
CH_3CH_2, CH_2CH_3 / C=C / H, HgCl	$ClCCHCl_2$ (C=O)	CH_3CH_2, CH_2CH_3 / C=C / H, $CCHCl_2$ (C=O)	89[b]

|		
(C6H5)(C6H5)C=C(H)(HgCl)	ClC(O)(CH2)2CH3	(C6H5)(C6H5)C=C(H)C(O)-(CH2)2CH3 — 72[c]
CH3OC(O)(CH2)8CH=CHHgCl	ClCCH3 (O)	CH3OC(O)(CH2)8CH=CHCCH3 (O) — 100[d]
CH3(CH2)7\C=C/(H)(HgCl)	ClCCH(CH3)2 (O)	CH3(CH2)7\C=C/(H)CCH(CH3)2 (O) — 97
CH3(CH2)2\C=C/(H)(HgCl)	ClC\C=C/(H)(CH3) (O)	CH3(CH2)2\C=C\C/(O)\C=C/(CH3)(H) — 97
CH3(CH2)2\C=C/(H)(HgCl)	ClCCH2CH=CH2 (O)	CH3(CH2)2\C=C\C/(O)\C=C/(CH3)(H) — 91

[a] GLC yield containing 14% cis-ketone.
[b] Ketone decomposes readily.
[c] Ketone separated from a mixture of cis- and trans-stilbene by column chromatography.
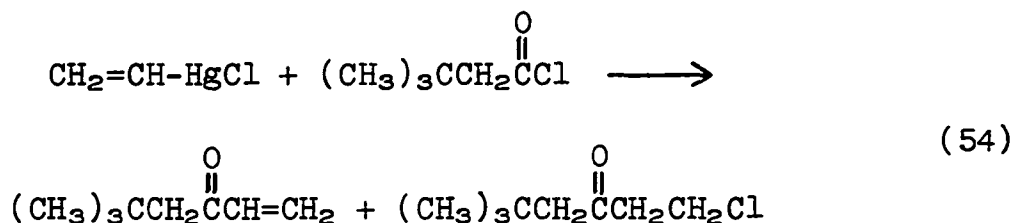[d] Both the vinylmercuric chloride and ketone are cis, trans-mixtures.

saturated acid chlorides reacted cleanly to produce fully

conjugated dienones in high yield. β,γ-Unsaturated acid

chlorides on the other hand react to produce the same dienones

as the α,β-isomers (Eq. 53). Esters are tolerated in the

$$
\begin{array}{c}
\text{O} \\
\| \\
\text{ClCCH}_2\text{CH=CH}_2
\end{array}
\tag{53}
$$
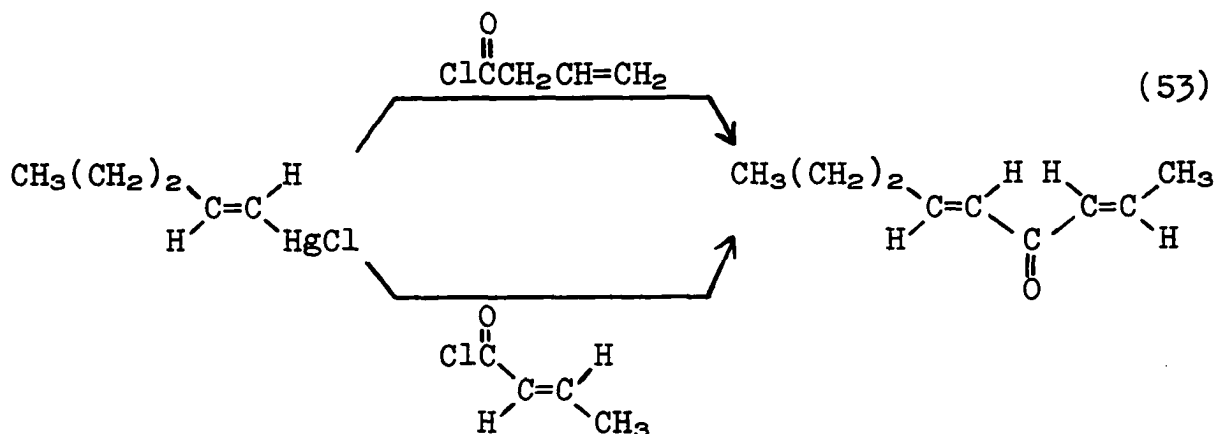
mercurial component and halides should be tolerated in either

component of the reaction.

Six systems were tried unsuccessfully. Pivaloyl chloride

decarbonylated under the influence of aluminum chloride before

the vinylmercurial, trans-cyclohexylethenylmercuric chloride,

could be added to the reaction flask. Gas evolution occurred

immediately on addition of the acid chloride to the flask

containing the solution of aluminum chloride. An nmr of the

reaction mixture showed a t-butyl group and cyclohexyl

hydrogens but no vinyl hydrogen pattern as expected for the

enone. Likewise, no carbonyl absorption was seen in the ir of

the product mixture. Levulinyl chloride and trans-cyclohexyl-

ethenylmercuric chloride gave ambiguous results. No precipi-

tate formed in the reaction indicating that no reaction

occurred, but the product mixture isolated was an oil (the

mercurial is a white crystalline solid) and its nmr showed

neither of the patterns expected for an enone or a vinyl-

mercurial, even though vinyl hydrogens were observed in the

nmr. The product(s) was not characterized further. Methyl

succinyl chloride [prepared from succinic anhydride (77)]

likewise did not react as desired with trans-cyclohexylethenyl-

mercuric chloride. Neither the enone pattern expected, nor

the methyl ester singlet were evident in the nmr of the

product mixture. The reaction was not examined further.

Vinylmercuric chloride reacted with 3,3-dimethylbutyryl

chloride to produce 5,5-dimethyl-1-hexen-3-one and 1-chloro-

5,5-dimethyl-3-hexanone (Eq. 54) in approximately equal yields.

$$CH_2=CH-HgCl + (CH_3)_3CCH_2\overset{\overset{\displaystyle O}{\|}}{C}Cl \longrightarrow$$

$$(CH_3)_3CCH_2\overset{\overset{\displaystyle O}{\|}}{C}CH=CH_2 + (CH_3)_3CCH_2\overset{\overset{\displaystyle O}{\|}}{C}CH_2CH_2Cl$$

(54)

Stirring the product mixture with 10% sodium hydroxide, either

as a two phase system with dichloromethane or without added

solvent, did not cause elimination of HCl from the β-chloro

ketone. E-3-acetoxy-2-chloromercuri-2-butene was reacted

with isobutyryl chloride, but the product mixture obtained

showed a nmr much too complex to be the desired product, which

should show only three singlets and an isopropyl group. The

product decomposed before further analysis could be carried out.

Two products, 2 and 3, were obtained when benzoyl chloride

was reacted with $\underline{E}$-2-chloromercuri-4,4-dimethyl-2-pentene

(Eq. 55). This reaction takes longer than with aliphatic

(55)
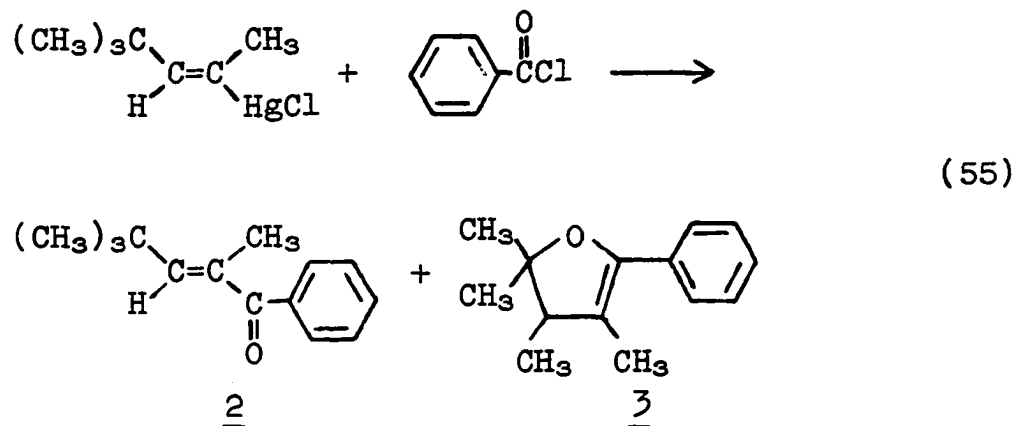
acid chlorides. Initially the two products are obtained in

approximately equal amounts, but by the time the reaction is

complete the dihydrofuran predominates. Further discussion

of this reaction will be put off until the mechanistic dis-

cussion.

4. The reaction with titanium tetrachloride

As indicated earlier, unusual stereochemical results were

found when examining the reaction of trans-1-hexenylmercuric

chloride, acetyl chloride, and titanium tetrachloride at -78°C.

When this reaction was scaled up to 10 mmol an isolated yield

of 78% cis-3-octen-2-one was obtained. A three hour reaction

was necessary and less than 3% of the trans-isomer was seen by

nmr.

Three acid chlorides were then tried with trans-1-decenyl-

mercuric chloride. 3,3-Dimethylbutyryl chloride and butyryl

chloride yielded only 1-decene after three hours at -78°C.

Likewise, acetyl chloride yielded only 1-decene after three hours. 1-Decene was identified, after quenching with water and working up in the usual way, by comparison with an nmr of an authentic sample. Only after one day was a 26% yield of cis-ketone obtained (GLC analysis). It appeared therefore that this mercurial is very unreactive in this system.

Trans-cyclohexylethenylmercuric chloride and acetyl chloride showed no evidence of enone after three hours at -78°C, as evidenced by lack of the relevant nmr resonances in the vinyl region. At -45°C the trans-isomer was the predominant product, as determined by GLC and nmr.

Trans-3,3-dimethyl-1-butenylmercuric chloride failed completely to react with acetyl chloride at -78°C after 3 hours. Only a symmetrical divinylmercurial was obtained after preparative GLC. Even after 48 hours at -78° no enone products were seen. Raising the reaction temperature to -45°C gave only the trans-enone. No yield was calculated.
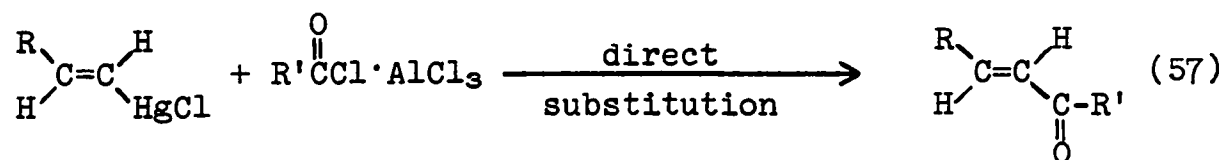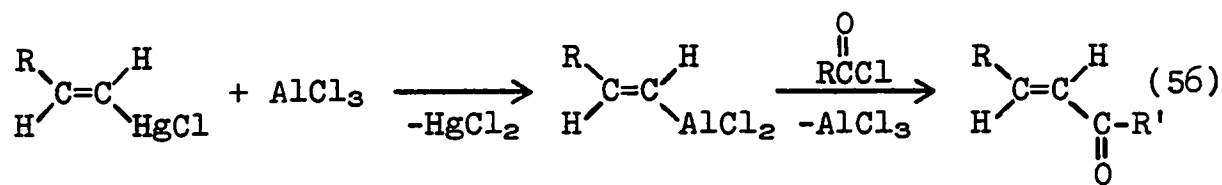
Three other acid chlorides were then tried with trans-1-hexenylmercuric chloride, butyryl chloride, 3-methylbutyryl chloride, and 3,3-dimethylbutyryl chloride. Butyryl chloride gave variable yields ranging from 73% cis- and 5% trans- to equal mixtures of cis- and trans-enones. 3-Methylbutyryl chloride gave a 40% trans- to 60% cis-ratio with no absolute yield obtained. 3,3-Dimethylbutyryl chloride gave the trans-isomer as the predominant product (nmr analysis). Results for all three systems were determined by GLC.

After these negative results trans-1-hexenylmercuric
chloride and butyryl chloride was chosen as a model system
for further studies. In studying this reaction the following
variables were investigated; reaction time (6 hours was
usually optimum), reaction temperature (warmer than -78°C
decreased the amount of cis-isomer seen), stoichiometry
(varying from 1:1:1, mercurial to TiCl$_4$ to butyryl chloride,
to two fold excesses of TiCl$_4$ and/or butyryl chloride, with
no discernible pattern), and the order and mode of addition
of the reagents (each of the reagents added last after
stirring for various lengths of time at room temperature and
-78°C, again without a discernible pattern). What seemed to
be a random array of yields, varying from 40% each of cis-
and trans-enone up to 70% cis- and 5% trans-enone was obtained.
The higher yields of cis-enones in some reactions could not be
reproduced in spite of many efforts.

After much frustration it was decided that this reaction
was not sufficiently reproducible to make it of value syntheti-
cally.

5. Mechanism

There are at least three possible mechanisms that can be
written for the aluminum chloride promoted reactions: (1) the
formation of a vinylalane by transmetallation with aluminum
chloride, followed by acylation (Eq. 56); (2) direct electro-
philic substitution at the carbon-mercury bond (Eq. 57); and

$$R \!\!\!\!\diagdown \!\!\!\!\! C \!\!=\!\! C \!\!\!\! \diagup \!\!\!\! H + AlCl_3 \xrightarrow[-HgCl_2]{} R \!\!\!\!\diagdown \!\!\!\!\! C \!\!=\!\! C \!\!\!\! \diagup \!\!\!\! H \xrightarrow[\substack{RCCl \\ -AlCl_3}]{\overset{\overset{O}{\|}}{}} R \!\!\!\!\diagdown \!\!\!\!\! C \!\!=\!\! C \!\!\!\! \diagup \!\!\!\! H \quad (56)$$

$$R \!\!\!\!\diagdown \!\!\!\!\! C \!\!=\!\! C \!\!\!\! \diagup \!\!\!\! H + R' \overset{\overset{O}{\|}}{C}Cl \cdot AlCl_3 \xrightarrow[\text{substitution}]{\text{direct}} R \!\!\!\!\diagdown \!\!\!\!\! C \!\!=\!\! C \!\!\!\! \diagup \!\!\!\! H \quad (57)$$

(3) addition of the acid chloride-aluminum chloride complex to the carbon-carbon double bond followed by elimination of mercuric chloride to form the α,β-unsaturated ketone (Eq. 58).

$$\text{(58)}$$
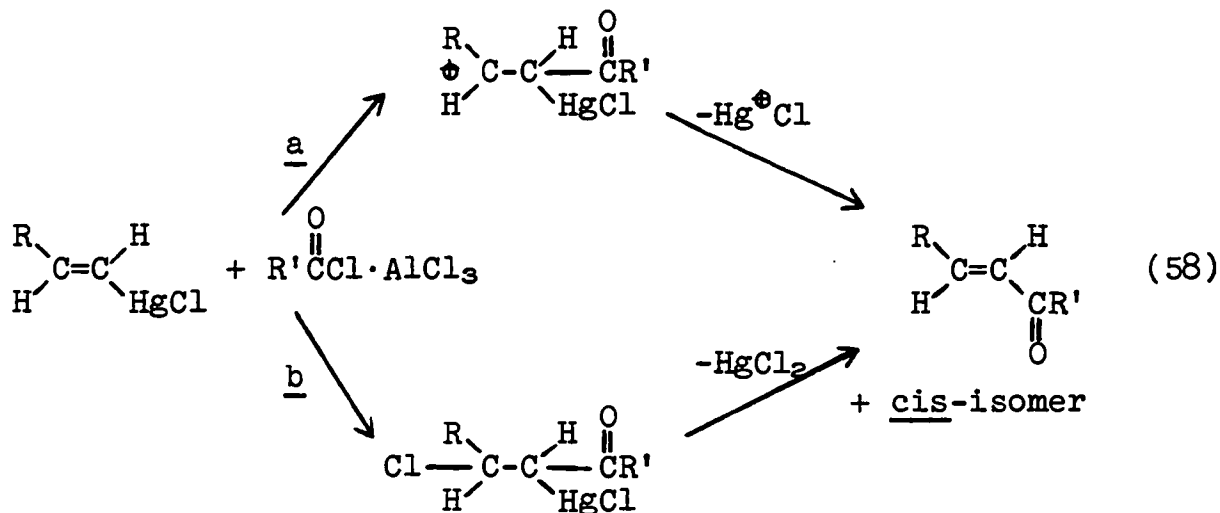
In order to investigate the first possible mechanism, two exchange reactions were investigated. Aluminum chloride was reacted with either <u>trans</u>-1-decenylmercuric chloride or stilbenylmercuric chloride in methylene chloride, and the reaction was quenched with 10% sodium hydroxide. If exchange occurred the vinylalane formed would be expected to react with water to form a hydrocarbon. If no exchange occurred no hydro-

carbon would be observed. A basic quench was used to prevent the generation of acid from hydrolysis of the unreacted aluminum chloride which could then cleave the carbon-mercury bond. Quenching the stilbenylmercuric chloride-aluminum chloride mixture after five minutes led to a 14% yield of cis- and trans-stilbenes. The reaction of trans-1-decenylmercuric chloride and aluminum chloride resulted in a 7% yield of 1-decene when quenched after five minutes. Quenching after three hours did not increase the yield of hydrocarbon in either reaction. Trans-1-decenylmercuric chloride was chosen for the ease of analyzing the resultant hydrocarbon, while stilbenyl-mercuric chloride was chosen because stilbene was seen in its reaction with butyryl chloride (see Table VII). From these results it appears that stilbene may have arisen from acid cleavage of the starting mercurial. In conclusion, it appears that the first mechanism (vinylmercurial exchange with aluminum chloride) can be ruled out since exchange does not occur quickly enough to account for a near quantitative yield of ketone in less than five minutes.

The second and third mechanisms must both be considered seriously. Direct electrophilic cleavage would result in complete retention of stereochemistry since the reaction would occur at the carbon-mercury bond and would not affect the

arrangement of atoms around the carbon-carbon double bond. A large portion of the reaction could be occurring by this route since the reaction is highly stereospecific. However, the presence of small quantities of cis-α,β-unsaturated ketone suggests that at least some of the product might arise from an addition-elimination mechanism. Another possibility is that the cis-isomer arises from Lewis acid isomerization of the trans-enone. Isomerization of the enones will be discussed later in this section.

Three reactions tend to support the addition-elimination mechanism: (1) the reaction of 3,3-dimethylbutyryl chloride with vinylmercuric chloride which gives 5,5-dimethyl-1-hexen-3-one and 1-chloro-5,5-dimethyl-3-hexanone (Eq. 54); (2) the reaction of benzoyl chloride with E-4,4-dimethyl-2-chloro-mercuri-2-pentene which gives E-1-phenyl-2,4,4-trimethyl-2-penten-1-one (2) and 4,5-dihydro-2-phenyl-3,4,5,5-tetramethyl-furan (3) (Eq. 55); and (3) the titanium tetrachloride promoted reactions, which result in a high percentage of inverted enones. Each of these will be discussed in turn.

In the reaction of vinylmercuric chloride with 3,3-di-methylbutyryl chloride, the formation of the β-chloroketone could arise from either route shown in Equation 58 (Scheme 7).

Scheme 7
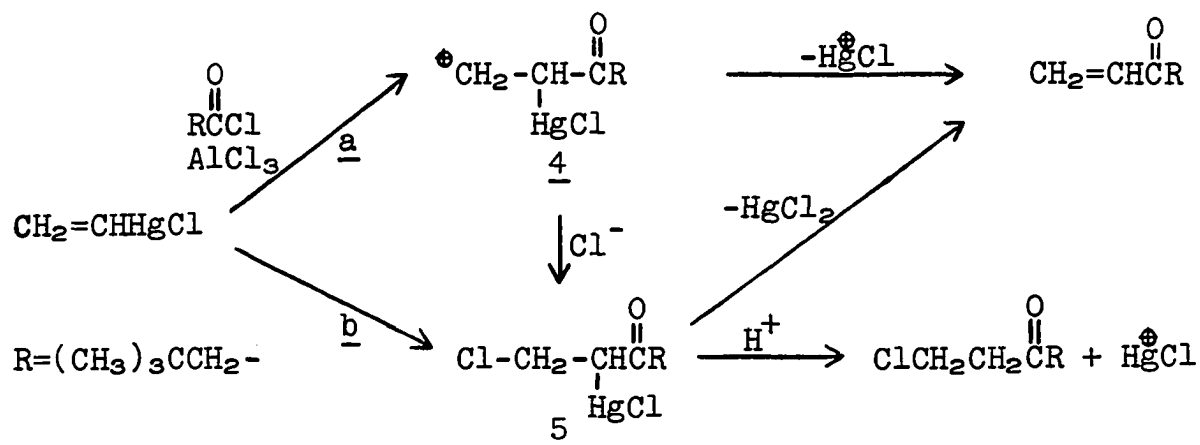
The β-chloromercurial (5) is probably an intermediate in the

reaction. Carbonium ion 4, or a mercurinium ion (6), may be
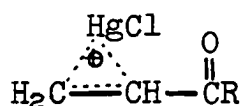

6

an intermediate or merely a transition state on the way to 5.

The unsaturated ketone can arise from either 4 by elimination

of a chloromercuri ion or 5 by elimination of mercuric

chloride. The β-chloroketone probably comes from 5 by acid

cleavage of the carbon-mercury bond. α-Chloromercuriketones,

such as 5 have been reported to be especially vulnerable to

acid cleavage (61, 78). The acid could arise from either

aluminum chloride as an impurity or an aqueous work up.

Studies on the reaction of benzoyl chloride and E-4,4-

dimethyl-2-chloromercuri-2-pentene (Eq. 55) indicate that the

dihydrofuran (3) arises directly from starting materials by rearrangement of an intermediate carbonium ion (Scheme 8).

Scheme 8

3
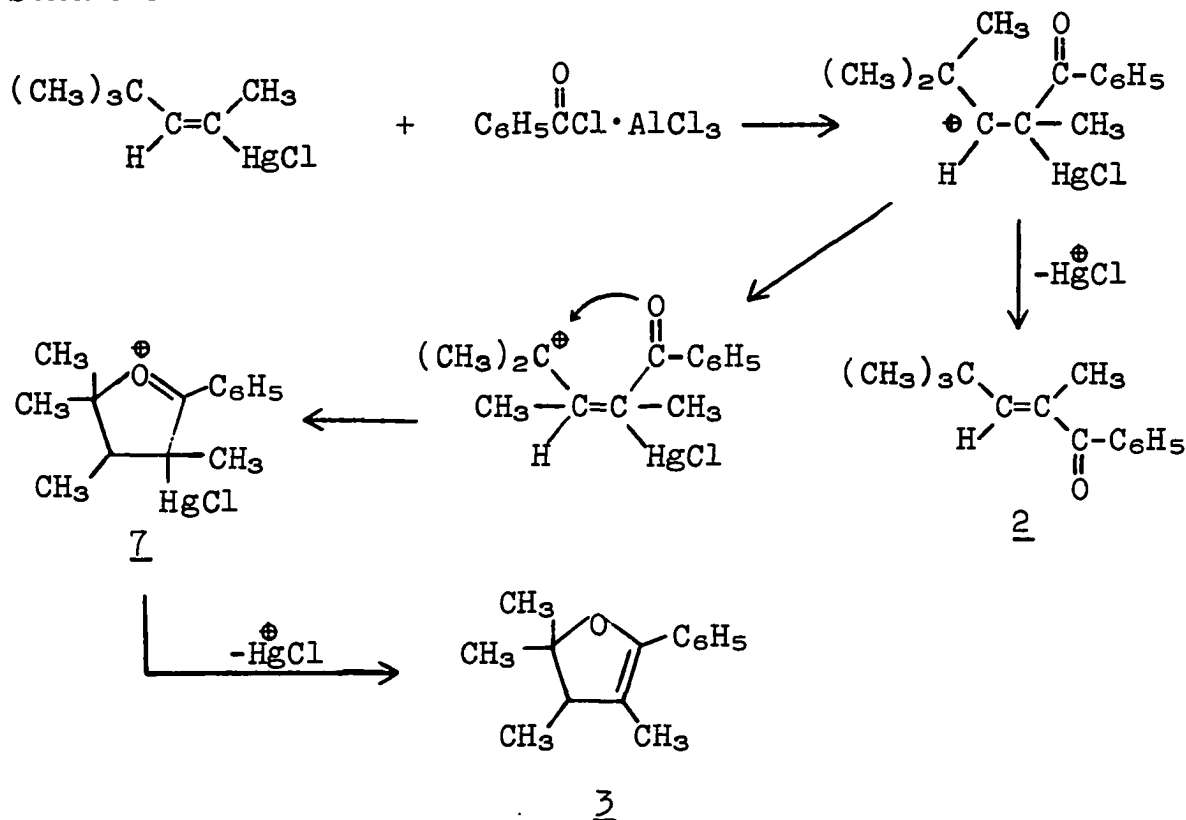
Sampling the reaction after short reaction times showed that both enone 2 and dihydrofuran 3 were present in the reaction shortly after mixing, but that enone 2 reached a maximum yield of 31% in one hour and then decreased to 20% while the yield of dihydrofuran 3 continued to rise until reaching 45% after six hours. Dihydrofuran 3 is stable under the reaction conditions. Stirring 3 with aluminum chloride does not result in rearrangement. Stirring enone 2 with equimolar amounts of aluminum chloride and mercuric chloride did not result in

any rearrangement. However, excess aluminum chloride caused complete rearrangement to 2-methyl-3-t-butyl-1-indanone (8) (Scheme 9). Small amounts of indanone 8 were also observed

Scheme 9
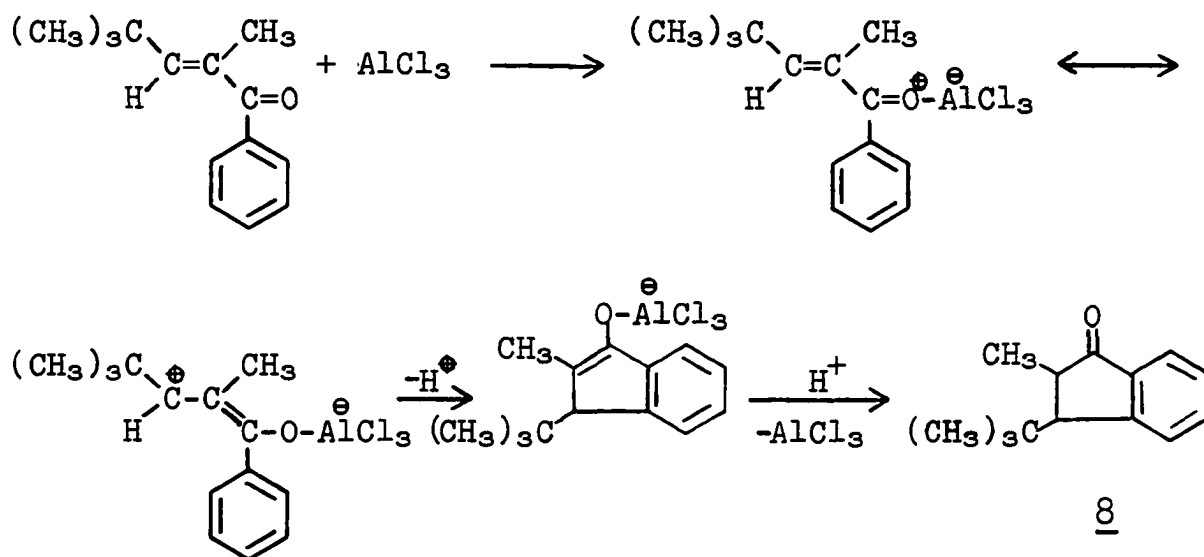
in the reaction of benzoyl chloride and E-4,4-dimethyl-2-chloromercuri-2-pentene. The structures of the rearrangement products 3 and 8 were assigned on the basis of spectral data.

Since both enone 2 and dihydrofuran 3 arise directly as the reaction progresses, it appears that this reaction at least occurs by an addition-elimination mechanism.

Literature precedent exists for much of the chemistry observed in this system. Pines and Douglas (79) observed that 4'-fluoro-2-methylacrylophenone cyclized to 2-methyl-5-fluoro-1-indanone (Eq. 59) under the influence of aluminum

$$(59)$$
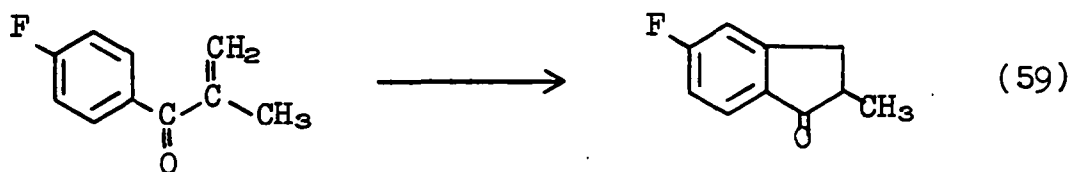
chloride or sulfuric acid. A cyclic oxonium ion (Eq. 60) was

$$(60)$$
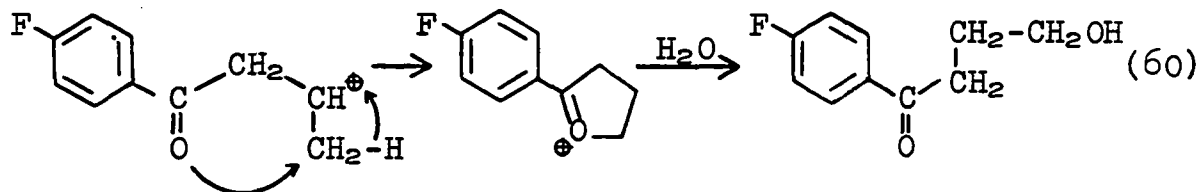
also observed by ^{13}C nmr in their studies. This shows the plausibility of intermediate 7, which would be expected to lose $^{\oplus}HgCl$ and form the dihydrofuran 3.

The titanium tetrachloride reaction probably proceeds by an addition-elimination reaction as well. Either a trans-addition--trans-elimination or cis-addition--cis-elimination sequence would be expected to result in an inversion about the carbon-carbon double bond. Casey, et al., (40) proposed such a trans-addition, trans-elimination sequence to explain the formation of a trans-vinylbromide from the bromination of a cis-alkenylmercuric bromide (Eq. 19 and Scheme 3). A similar scheme may be invoked to explain the inversion of stereochemistry here (Scheme 10). The difference between the reaction of aluminum chloride and titanium tetrachloride may be in the nature of the complex formed with the acid chloride or in the formation of different intermediates in the two reactions. In an effort to determine if a difference

Scheme 10

$$R-CH=CH-HgCl + R'CCl \cdot TiCl_4 \longrightarrow \text{[intermediate]} \longrightarrow$$

$$\xrightarrow{-HgCl_2}$$
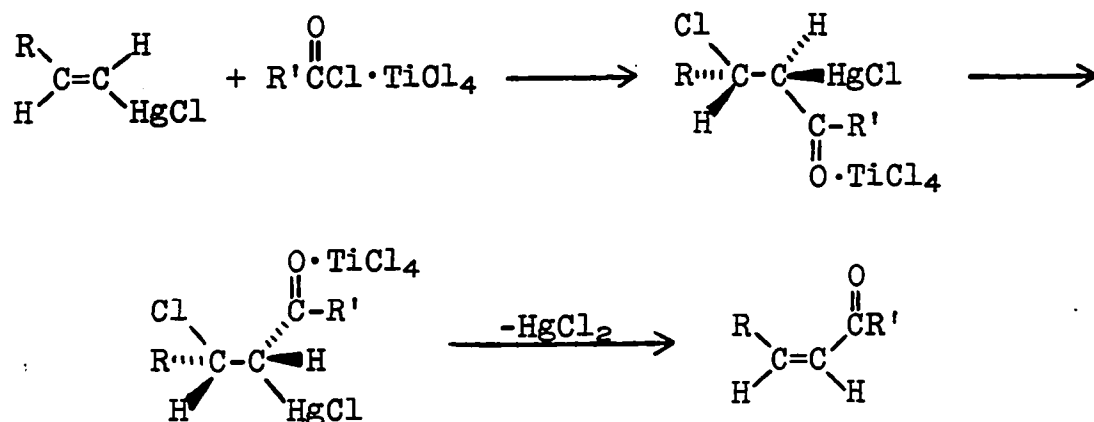
in the Lewis acid complex was responsible for the difference in the course of these reactions, ir studies on the $TiCl_4$-acetyl chloride and $AlCl_3$-acetyl chloride complexes were carried out. D. Cook (80) reported that if acetyl chloride is complexed through the oxygen (9) the C=O stretch would be

$$CH_3C(=O^{\oplus}-\overset{\ominus}{Al}Cl_3)Cl \qquad CH_3C^{\oplus}\equiv O \quad \overset{\ominus}{Al}Cl_4$$
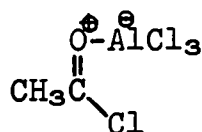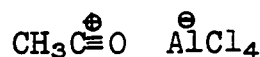
9   10

lowered from 1808 cm^{-1} to 1637 cm^{-1} while formation of the acylium ion (10) would raise the absorption to 2307 and 2203 cm^{-1}. Cook found all three absorptions in a neat mixture of acetyl chloride and aluminum chloride, while in chloroform only the 1637 cm^{-1} absorption was seen. Equal amounts of aluminum chloride and acetyl chloride in di-chloromethane showed two absorptions, 1805 cm^{-1} and 1640 cm^{-1}, with little decrease in the strength of the 1805 cm^{-1} band.

Likewise, equimolar amounts of $TiCl_4$ and acetyl chloride showed both the 1805 cm^{-1} and 1630 cm^{-1} bands. The slight difference in frequencies for the complexes may indicate slightly tighter complexing for $TiCl_4$ than for $AlCl_3$. The intensity of the 1805 cm^{-1} band decreased by ~10% on standing for two hours indicating a relatively small degree of complexation. Similar results were seen for aluminum chloride.

It may well be that in the aluminum chloride reaction path a of Equation 58 may be preferred, while in the $TiCl_4$ reaction a trans-addition according to path b may be the route of choice. At higher temperatures path a may begin to predominate resulting in the formation of trans-enones. On the other hand, aluminum chloride may prefer the direct substitution route (Eq. 57).

The final point of discussion concerns the stability of the products formed under the reaction conditions. Stirring trans-3-octen-2-one with one equivalent of aluminum chloride in dichloromethane, or with equimolar amounts of aluminum chloride and mercuric chloride, showed that 91% of the trans-enone was still present in the reaction mixture after 8 hours. After 27 hours the yield of ketone was still 86%. No cis-enone was seen in either case.

The isomerization of cis-enones was studied on cis-5-decen-4-one. Stirring the cis-enone with aluminum chloride

at room temperature resulted in a 91%:5% cis:trans mixture after five minutes and a 43%:22% mixture of enones after 24 hours. An equimolar mixture of aluminum chloride and mercuric chloride resulted in a 95%:5% cis-trans mixture after five minutes and a 5%:35% mixture after 24 hours. The titanium tetrachloride isomerization was studied in the same manner. After five minutes no trans-enone was seen and 88% of the cis-enone remained. After 24 hours only traces of either enone were observed. After five minutes with equimolar amounts of titanium tetrachloride and mercuric chloride 3% trans-enone was observed while 84% of the cis-enone remained. After 24 hours 2% of each enone was observed.

Based on the evidence obtained it appears the Lewis acid promoted acylation of vinylmercuric chlorides proceeds by way of an addition-elimination reaction. While the evidence is not conclusive, all of the side reactions discussed, as well as the formation of small amounts of cis-enone observed in most reactions, may be explained by this mechanism. However, none of the data available precludes a direct substitution reaction as being the major route with small amounts of addition-elimination accounting for the traces of the less stable cis-enones.
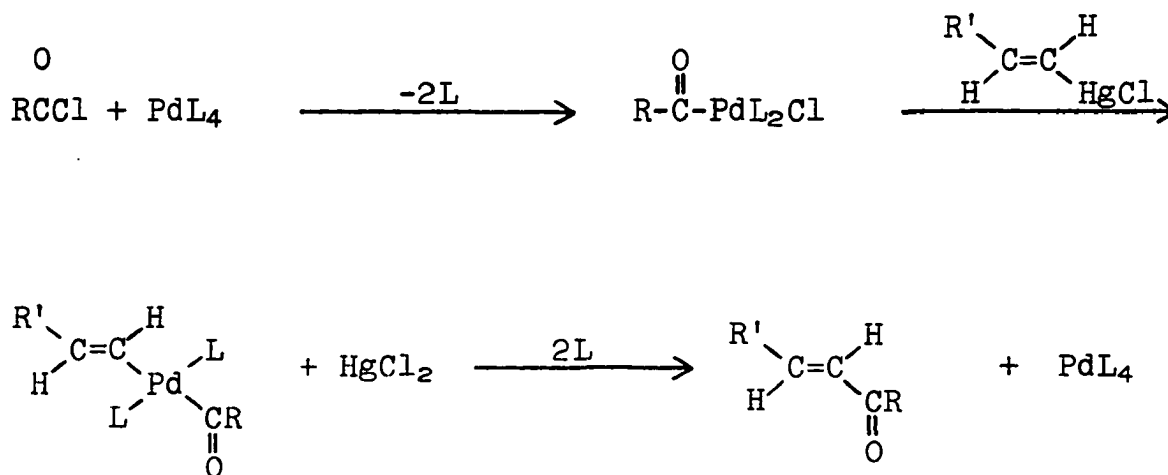
The titanium tetrachloride reaction most likely proceeds via trans-addition--trans-elimination or cis-addition--cis-elimination both of which would result in inversion of stereochemistry around the carbon-carbon double bond. However,

experimental evidence, which could either prove or disprove this proposal is lacking.

Enone isomerization probably does not account for the small amounts of cis-enone observed with aluminum chloride or the substantial yields of cis-enone with titanium tetrachloride.

The transition metal catalyzed reaction is envisioned as involving an initial oxidative addition between $Pd(PPh_3)_4$ and the acid chloride. Exchange of the vinyl group on mercury for the chlorine on palladium followed by reductive elimination would then result in the formation of the α,β-unsaturated ketone (Scheme 11). The oxidative addition of acid

Scheme 11

$$RCCl + PdL_4 \xrightarrow{-2L} R\text{-}\overset{O}{\underset{}{C}}\text{-}PdL_2Cl \xrightarrow{\underset{H}{\overset{R'}{\diagdown}}C=C\overset{H}{\underset{HgCl}{\diagup}}}$$

$$\underset{H}{\overset{R'}{\diagdown}}C=C\overset{H}{\underset{}{\diagup}}\underset{L}{\overset{}{\underset{CR}{\overset{\diagup L}{\underset{\parallel}{Pd}}}}} + HgCl_2 \xrightarrow{2L} \underset{H}{\overset{R'}{\diagdown}}C=C\overset{H}{\underset{CR}{\diagup}}\underset{\parallel}{\underset{O}{}} + PdL_4$$

chlorides to $Pd(PPh_3)_4$ to give acyl palladium complexes has been previously reported (81) and transmetallations between

vinylmercurials and palladium(II) species have also been proposed (43-46). The reductive elimination of transition metal complexes contain acyl and alkyl groups to give ketones has been proposed as well (82, 83) making this proposed mechanism quite reasonable.

C. Conclusion

This chapter has discussed the development of a convenient synthesis of α,β-unsaturated ketones from vinylmercuric chlorides and acid chlorides which proceeds in excellent yield and high stereospecificity under mild conditions. An interesting reaction in the presence of titanium tetrachloride was observed and discussed. Finally, mechanistic possibilities were presented.

D. Experimental Section

1. Reagents

All chemicals were used directly as obtained commercially unless otherwise noted. HMPA was distilled from lithium aluminum hydride (LAH) under vacuum. Dichloromethane was shaken with concentrated sulfuric acid, washed with water and saturated sodium chloride, dried over calcium chloride and distilled. Ether and THF were distilled from LAH.

The vinylmercuric chlorides used have all been described previously and were prepared using methods described in Chapter II.

$(Ph_3P)_2Rh(CO)Cl$ (Alfa Inorganics-Ventron), $[ClRh(CO)_2]_2$ (PCR), aluminum chloride (Fisher Scientific), and aluminum bromide (Fisher Scientific) were all used directly as obtained commercially. Wilkinson's catalyst, $(Ph_3P)_3RhCl$, was prepared according to published procedures (84).

All GLC yields are corrected by the use of appropriate hydrocarbon internal standards and calculated correction factors.

2. The reaction of trans-styrylmercuric chloride with acetyl chloride

The following procedure for the reaction of styryl-mercuric chloride with acetyl chloride is representative. Styrylmercuric chloride (1.0 mmol), acetyl chloride (1.0 mmol), and an internal hydrocarbon standard were dissolved in DMF (10 ml) under nitrogen. Aluminum bromide (1.0 mmol) was then added and the reaction stirred for 24 hours at 25°C. A solid formed in the reaction and the liquid was decanted into 3M sodium thiosulfate and ether was added. The ether was then analyzed by GLC (10' DC-550 at 200°C).

Distyrylmercury (0.5 mmol) was used in some reactions in the place of styrylmercuric chloride (1.0 mmol). When water immiscible solvents were used for the reaction, samples were

taken and quenched with water before GLC analysis.

The GLC correction factor was calculated using a commercial sample of trans-4-phenyl-3-buten-2-one. The product was verified by comparison with the commercial authentic sample.

3. The reaction of trans-1-hexenylmercuric chloride and acetyl chloride

An authentic sample of trans-3-octen-2-one was prepared by the following route (85). 1-Hexene (12.5 ml, 100 mmol) was was dissolved in a mixture of acetic acid (5.6 ml) and trifluoroacetic anhydride (14.0 ml) and stirred at room temperature for 20 min., then 40°C for 1.5 hr. and finally at room temperature overnight. The product was distilled under aspirator vacuum and then GLC prepped. ^{1}H NMR (CCl$_4$) δ0.92 (3H, not resolved, -CH$_3$), 1.40 (4H, m, -CH$_2$CH$_2$-), 2.18 (3H, s, $\overset{O}{\overset{\|}{C}}CH_3$), 2.2 (2H, m, CH$_2$-CH=), 5.95 (1H, d, J=17 Hz, $\overset{O}{\overset{\|}{C}}$-CH=), and 6.80 (1H, d of t, J=17 and 7 Hz, $\overset{O}{\overset{\|}{C}}$CH=CH-); ir (max) (thin film) 2970, 2950, 2860, 1675, 1630, 1460, 1430, 1360, 1255, 1180, 980, 930, and 735 cm^{-1}; m/e 126.1042 ± .0006 (calcd for C$_8$H$_{14}$O, 126.1045). Further samples of trans-3-octen-2-one were prepared by the procedure developed in this chapter.

The following procedure is representative for the model studies in this section. Tetradecane, trans-1-hexenylmercuric chloride (1.0 mmol), and acetyl chloride (1.0 mmol) were dissolved in dichloromethane (10 ml). Aluminum bromide (1.0

mmol) was added and the reaction stirred at room temperature under nitrogen. Samples (0.5 ml) were taken, added to water, and then analyzed by GLC.

When temperatures other than room temperature were desired, the vinylmercurial and acid chloride were added and cooled down to the desired temperature in the appropriate temperature bath before the Lewis acid was added. Samples were taken as above. Addition of the vinylmercurial to a solution of Lewis acid and acid chloride also results in a satisfactory reaction.

In studying the effect of various Lewis acids, all variables were kept constant except reaction time and the Lewis acid. The solvents were investigated at room temperature for the time periods listed in table III. Likewise, the effects of temperature, Table IV, and reaction time, Table V, were studied holding all other variables constant.

The transition metal catalyzed reactions were studied as with the Lewis acid reactions. The transition metal complex (0.1 mmol) was added to a solution of the vinylmercuric chloride and acid chloride in the appropriate solvent, and analyzed directly by GLC. The ether and dichloromethane reactions were quenched with water. The THF reactions were quenched with saturated ammonium chloride and the HMPA reactions were quenched by adding water and ether and then analyzing the ether layer, or by analyzing without quenching.

The side products in the transition metal reactions were identified as follows: In THF, the product from reaction of acetyl chloride with the solvent, 4-acetoxy-1-chlorobutane, had a GLC retention time (10% DC-550, 10', 150°C) very similar to that for trans-3-octen-2-one and was determined to be different by coinjecting ketone and the reaction mixture and observing two peaks. The side product was confirmed to have come from THF by stirring the rhodium catalyst, THF, and acetyl chloride in the absence of vinylmercurial and observing a product of identical retention time by co-injection with the above reaction mixture. 1-Acetoxy-4-chlorobutane: ^{1}H NMR (CCl$_4$) δ1.8 (4H, m, -CH$_2$-CH$_2$-), 2.02 (3H, s, -$\overset{O}{\overset{\|}{C}}CH_3$), 3.6 (2H, m, -CH$_2$Cl), 4.1 (2H, m, CH$_2O\overset{O}{\overset{\|}{C}}CH_3$); ir (max) (thin film) 2960, 1740, 1450, 1240, 1045, 950, 880, 750, and 720 cm^{-1}.

The structure of the symmetrical 1,3-diene from the reaction of trans-1-hexenylmercuric chloride and the rhodium catalyst in the presence of acetyl chloride (Eq. 5) was confirmed by spectral data (see Chapter V) and GLC comparison with an authentic sample of diene prepared by Larock's palladium chloride procedure (43).

4. The synthesis of α,β-unsaturated ketones

The following synthesis of trans-3-octen-2-one is representative. To a thoroughly dried round bottom flask equipped with a septum inlet and flushed with nitrogen was added di-

chloromethane (100 ml), aluminum chloride (1.33 g, 10 mmol),
and acetyl chloride (0.80 ml, 10 mmol). After stirring
briefly, trans-1-hexenylmercuric chloride (3.1 g, 10 mmol)
was added while backflushing with nitrogen, and the reaction
was stirred for five minutes. A white solid (presumably
mercuric chloride) precipitated almost immediately. The
reaction mixture is then poured into water and the layers
separated. The aqueous layer was extracted with dichloro-
methane. The organic layer was then washed with 5% sodium bi-
carbonate, 3M sodium thiosulfate, and water. The combined
aqueous washes were re-extracted with dichloromethane, and the
combined organic layers dried over anhydrous sodium sulfate.
Removal of solvent yielded 1.22 g (97%) of essentially pure
trans-3-octen-2-one as a colorless oil. GLC analysis showed
5% or less of the undesired cis isomer. Spectral properties
were identical to those reported earlier in this experimental
discussion.

The following compounds were prepared in like manner.
Trans-5,5-dimethyl-3-hexen-2-one: ^{1}H NMR (CCl$_4$) δ1.10 (9H, s,
C(CH$_3$)$_3$), 2.15 (3H, s, $\overset{O}{\overset{\|}{C}}CH_3$), 5.90 (1H, d, J=16 Hz, -$\overset{O}{\overset{\|}{C}}$CH=),
6.70 (1H, d, J=16 Hz, -$\overset{O}{\overset{\|}{C}}$CH=CH-); ir (max) (thin film) 3030,
2950, 2860, 1680, 1620, 1365, 1290, 1250, and 980 cm^{-1}; m/e
126.1044 ± .0006 (calcd for C$_8$H$_{14}$O, 126.1045). E-3,5,5-tri-
methyl-3-hexen-2-one: ^{1}H NMR (CCl$_4$) δ1.20 (9H, s, C(CH$_3$)$_3$),
1.83 (3H, d, J=1.5 Hz, =C-CH$_3$), 2.20 (3H, s, $\overset{O}{\overset{\|}{C}}CH_3$), 6.50 (1H,
q, J=1.5 Hz, -CH=); ir (max) (thin film) 2960, 2860, 1680,

1640, 1470, 1370, 1250, 1200, and 1030 cm^{-1}; $\underline{m}/\underline{e}$ 140.1201 ±

.0007 (calcd for $C_9H_{16}O$, 140.1201). $\underline{Trans}$-1-cyclohexyl-1-

hexen-3-one: ^{1}H NMR (CCl$_4$) δ0.9 (3H, t, $\underline{J}$=6 Hz, CH$_2$C$\underline{H}_3$),

1-2 (13 H, m, ⬡ and -C$\underline{H}_2$-CH$_3$), 2.3 (2H, t, $\underline{J}$=7 Hz, $\overset{O}{\overset{\|}{C}}CH_2$),

5.90 (1H, d, $\underline{J}$=16 Hz, -$\overset{O}{\overset{\|}{C}}C\underline{H}$=CH-), and 6.65 (1 H, d of d, $\underline{J}$=

16 Hz and 6 Hz, -$\overset{O}{\overset{\|}{C}}$CH=C$\underline{H}$-); ir (max) (thin film) 2920, 2840,

1670, 1620, 1448, 1365, 1190, and 978 cm^{-1}; $\underline{m}/\underline{e}$ 180.1512 ±

.0009 (calcd for $C_{12}H_{20}O$, 180.1514). $\underline{E}$-1,1-dichloro-3-ethyl-

3-hexen-2-one: ^{1}H NMR (CCl$_4$) δ1.1 (6 H, overlapping triplets,

$\underline{J}$=7 Hz, CH$_3$'s), 2-2.6 (4 H, overlapping CH$_2$'s, $\underline{J}$=7 Hz), 5.5

(1 H, t, $\underline{J}$=7 Hz, -CH=C), and 6.0 (1 H, s, $\overset{O}{\overset{\|}{C}}$CHCl$_2$); ir (max)

(thin film) 2950, 2920, 2860, 1660-1640, 1460, 1375, 1310,

1250, 1210, 1140, 1080, 990, 790, 760, and 735 cm^{-1}; sample

decomposed before mass spectra could be obtained. $\underline{E}$-1,2-Di-

phenyl-1-hexen-3-one: ^{1}H NMR (CCl$_4$) δ0.90 (3H, t, $\underline{J}$=7 Hz,

-CH$_3$), 1.65 (2 H, sextet, $\underline{J}$=7 Hz, -C$\underline{H}_2$CH$_2$$\overset{O}{\overset{\|}{C}}$-), 2.50 (2 H, t,

$\underline{J}$=7 Hz, -$\overset{O}{\overset{\|}{C}}CH_2$-) 7-7.7 (11 H, m, $\underset{|}{C_6H_5CH=CC_6H_5}$); ir (max) (thin

film) 3060, 3030, 1685, 1615, 1595, 1495, 1450, 1200, 1135,

1070, 765, and 700 cm^{-1}; $\underline{m}/\underline{e}$ 250.1359 ± .0013 (calcd for

$C_{18}H_{18}O$, 250.1358). 12-Carbomethoxy-3-dodecen-2-one: ^{1}H NMR

δ1.3 (12H, br s, CH$_2$'s), 2.1 (3 H, s, $\overset{O}{\overset{\|}{C}}CH_3$), 2.2 (4 H, m

$\underset{|}{\overset{H}{=}}$C-C$\underline{H}_2$ and CH$_2$$\overset{O}{\overset{\|}{C}}OCH_3$), 3.55 (3 H, s, -$\overset{O}{\overset{\|}{C}}OCH_3$), 5.95 (1 H, d, $\underline{J}$=

16 Hz, -$\overset{O}{\overset{\|}{C}}C\underline{H}$=), 6.7 (1 H, d of t, $\underline{J}$=16 and 7 Hz, $\overset{O}{\overset{\|}{C}}$CH=C$\underline{H}$-);

there is evidence in the nmr of the cis isomer being present

as well, but the peaks are poorly resolved; ir (max) (KBr)

2980, 2920, 2850, 1745, 1680, 1600, 1470, 1440, 1385, 1340,

1320, 1280, 1245, 1205, 1175, 1000, 980, 880, 720, and 690

cm^{-1}; m/e 240.1721 ± .0008 (calcd for $C_{14}H_{24}O_3$, 240.1726).

Trans-2-methyl-4-tridecen-3-one: ^1H NMR (CCl$_4$) δ1.00 (3H, t,

J=7 Hz, -CH$_2$CH$_3$), 1.05 (6 H, d, J=7 Hz, CH(CH$_3$)$_2$), 1.3 (12 H,

broad s, -CH$_2$-), 2.2 (2 H, m, CH$_2$-CH=), 2.7 (1 H, septet, J=

7 Hz, CH(CH$_3$)$_2$), 6.0 (1 H, d, J=16 Hz, $\overset{O}{\overset{\|}{C}}$CH=), 6.75 (1 H, d

of t, J= 16 and 7 Hz, $\overset{O}{\overset{\|}{C}}$CH=CH-); m/e 210.1989 ± 2.7 ppm (calcd

for $C_{14}H_{26}O$, 210.1984). Trans, trans-2,5-nonadien-4-one: ^1H

NMR (CCl$_4$) δ1.00 (3 H, t, J=7 Hz, CH$_3$), 1.5 (2 H, sextet,

J=7 Hz, CH$_2$CH$_2$CH$_3$), 1.94 (3 H, d, J=7 Hz, =CHCH$_3$), 2.20 (2 H,

t, J=7 Hz, =CH-CH$_2$-), 6.15 (2 H, d, J~16 Hz, $\overset{O}{\overset{\|}{C}}$CH='s), 6.80

(2 H, d of t, J=16 and 7 Hz, $\overset{O}{\overset{\|}{C}}$CH=CH-'s); ir (max) (thin film)

3040, 3020, 2950, 2940, 2860, 1665, 1640-1620, 1440, 1380,

1335, 1300, 1200, 1150, 1080, 1040 and 980 cm^{-1}; m/e 138.1040

± 3.6 ppm (calcd for $C_9H_{14}O$, 138.1045). Trans-1-phenyl-2-

hepten-1-one: ^1H NMR (CCl$_4$) δ1.00 (3 H, t, J=7 Hz, -CH$_3$), 1.5

(4 H, m, -CH$_2$CH$_2$-), 2.3 (2 H, m, =CHCH$_2$-), 6.85 (2 H, m,

vinyl), 7.4 (3 H, m, $\overset{O}{\overset{\|}{C}}$-⟨O⟩-H), 7.85 (2 H, m, $\overset{O}{\overset{\|}{C}}$-⟨O⟩); ir

(max) (thin film) 3060, 2960, 2930, 2870, 1670, 1620, 1600,

1580, 1450, 1390, 1280, 1220, 1180, 1000, 980, 920, 880, 860,

and 790 cm^{-1}; sample identical with a sample prepared from

condensing the lithium enolate of acetophenone (lithium di-

isopropylamide, THF, -78°C) with valeraldehyde followed by

dehydration (62).

5. The reaction with titanium tetrachloride

This reaction was investigated in the same manner as were the Lewis acid reactions previously discussed. Two cis-enones were isolated and characterized, cis-3-octen-2-one and cis-5-decen-4-one. The correction factor used for cis-3-dodecene-2-one was measured from a sample of the trans-isomer. Cis- and trans-3-octen-2-one agree within $\pm 2\%$ for their correction factors, so that errors introduced by the use of the trans isomer are minimal.

Spectral data on the compounds not previously given follows. Cis-3-octen-2-one: ^{1}H NMR (CCl$_4$) δ0.9 (3 H, t, J=7 Hz, CH$_2$CH$_3$), 1.4 (2 H, sextet, J=8 Hz, CH$_2$CH$_3$), 2.1 (5 H, m with s superimposed, -CCH$_3$ and =CHCH$_2$CH$_2$-), 3.0 (2 H, t, J= 4 Hz, =CH-CH$_2$), and 5.5 (2 H, m, -CH=CH-); ir (max) (thin film) 2940, 2910, 2860, 1715, 1680, 1365, 1160, and 965 cm^{-1}; m/e 126.1047 ± .0006 (calcd for C$_8$H$_{14}$O, 126.1045). Cis-5-decen-4-one: ^{1}H NMR (CCl$_4$) δ0.90 (6 H, t, J=7 Hz, -CH$_3$'s), 1.2-2.1 (6 H, m, 3-CH$_2$'s), 2.35 (2 H, t, J=7 Hz, -CCH$_2$-), 3.0 (2 H, m, -CH$_2$-C=), 5.5 (2 H, m, -CH=CH); m/e 154.1354 ± 2.7 ppm (calcd for C$_{10}$H$_{18}$O 154.1358). Trans-5-decen-4-one: ^{1}H NMR (CCl$_4$) δ0.90 (6 H, t, J=7 Hz, -CH$_3$'s), 1.4 (6 H, m, -CH$_2$-), 2.3 (2 H, m, =CHCH$_2$), 2.4 (2 H, t, J=7 Hz, CCH$_2$); 6.1 (1 H, d, J=16 Hz, CCH=), 6.8 (1 H, d of t, J=16 and 7 Hz, -CCH=CH-); m/e 154.1357 ± .6 ppm, (calcd for C$_{10}$H$_{18}$O, 154.1358).

6. Mechanism

The exchange reactions of stilbenylmercuric chloride and trans-1-decenylmercuric chloride with aluminum chloride were studied as follows: the mercurial (1.0 mmol) and an appropriate internal hydrocarbon standard were dissolved in dichloromethane (10 ml). Aluminum chloride (1.0 mmol) was added and the reaction mixture stirred at room temperature. A sample was taken after five minutes and quenched by pouring into 10% sodium hydroxide. Samples were analyzed by GLC. Correction factors were calculated from authentic samples of 1-decene and stilbene.

The isomerization of trans-3-octen-2-one by aluminum chloride was studied as follows. Trans-3-octen-2-one (0.216 mmol) and an internal standard were dissolved in dichloromethane (2.3 ml). Aluminum chloride (0.271 mmol) was added and the mixture stirred at room temperature. Samples were taken at 0.5, 1, 4, 8 and 27 hours and quenched with water before GLC analysis. Other isomerizations were studied in like manner. When mercuric chloride was used, it was added in approximately equimolar amounts.

The studies on the reaction of $\underline{E}$-4,4-dimethyl-2-chloromercuri-2-pentene with benzoyl chloride were carried out in the same manner as the reactions of trans-1-hexenylmercuric chloride with acetyl chloride. $\underline{E}$-1-phenyl-2,4,4-trimethyl-2-penten-1-one: ^{1}H NMR (CCl$_4$) δ1.3 (9 H, s, -C(CH$_3$)$_3$), 2.1 (3 H, d, $\underline{J}$=1 Hz, =C-CH$_3$), 6.15 (1 H, q, $\underline{J}$=1 Hz, $\overset{O}{\overset{\|}{C}}$-C=CH-), and

7.5 (5 H, m, C$_6$H$_5$); ^{13}C NMR (CDCl$_3$) 13.4 ppm (=C-C$\underline{H}$$_3$), 30.1 (-C(C$\underline{H}$$_3$)$_3$], 33.7 [-$\underline{C}$(CH$_3$)$_3$], 127.9 and 129.4 (-⟨O⟩-), 131.3 (-⟨O⟩-), 134.8 ($\underline{C}$$\underline{C}$=C), 138.6 ($\underline{C}$-⟨O⟩), 154.6 (-$\underline{C}$C=$\underline{C}$-), and 200.1 ($\underline{C}$); ir (max) (thin film) 3060, 3030, 2960, 2870, 1650, 1600, 1580, 1470, 1450, 1370, 1315, 1300, 1290, 1210, 1040, 965, 875, and 710 cm^{-1}. 4,5-Dihydro-2-phenyl-3,4,5,5-tetra-methylfuran: ^{1}H NMR (CCl$_4$) δ1.05 (3 H, d, $\underline{J}$=6Hz, $\underline{C}$H-C$\underline{H}$$_3$), 1.28 and 1.38 (3 H each, s, (C$\underline{H}$$_3$)$_2$C) 1.85 (3 H, s, =C-C$\underline{H}$$_3$), 2.57 (1 H, q, $\underline{J}$=6 Hz, -C$\underline{H}$-), 7.2-7.5 (5 H, m, C$_6$H$_5$), see Fig. 1; ^{13}C NMR (CDCl$_3$) 11.4 ppm (-CH-$\underline{C}$H$_3$), 13.8 (=C$\underline{C}$H$_3$), 22.1 and 28.6 (($\underline{C}$H$_3$)$_2$C), 51.7 (-$\underline{C}$H-CH$_3$), 83.8 ((CH$_3$)$_2$$\underline{C}$-), 109.9 (=$\underline{C}$-Ph), 127.0 and 128.0 (-⟨O⟩), 127.3 (-⟨O⟩-), 132.7 (-⟨O⟩), 145.9 ( ), see Fig. 1; ir (max) (thin film) 3080, 3060, 3020, 2985, 2920, 2860, 1670, 1600, 1500, 1450, 1380, 1365, 1260, 1100, 1070, 990, 860, 770, and 690 cm^{-1} (Fig. 1); m/e 202 (parent, 51%), 200 (19%), 187 (66%), 185 (16%), 129 (22%), 121 (17%), 105 (base peak, 100%), 97 (19%), and 77 (36%). 2-Methyl-3-$\underline{t}$-butyl-1-indanone: ^{1}H NMR (CCl$_4$) δ1.00 (9 H, s, -C(CH$_3$)$_3$), 1.23 (3 H, d, $\underline{J}$=7 Hz, -CH-C$\underline{H}$$_3$), 2.50 (1 H, d of q, $\underline{J}$=2 and 7 Hz, -C$\underline{H}$-CH$_3$), 2.72 (1 H, d, $\underline{J}$=2 Hz, -C$\underline{H}$-$\underline{C}$H-), 7.2-7.8 (4 H, m, ⟨O⟩) (Fig. 2); ir (thin film)(max) 3070, 2960, 2870, 1725, 1610, 1460, 1395, 1365, 1325, 1290, 1270, 1230, 1210, 1150, 1085, 960, 930, 920, 790, and 745 cm^{-1} (Fig. 2); m/e 202 (parent) (2%), 187 (3%), 174 (2%), 158 (3%), 145 (100%, P-$\underline{t}$-butyl), 131 (27%), 116 (15%) 104 (6%), 57 (17%, $\underline{t}$-butyl).
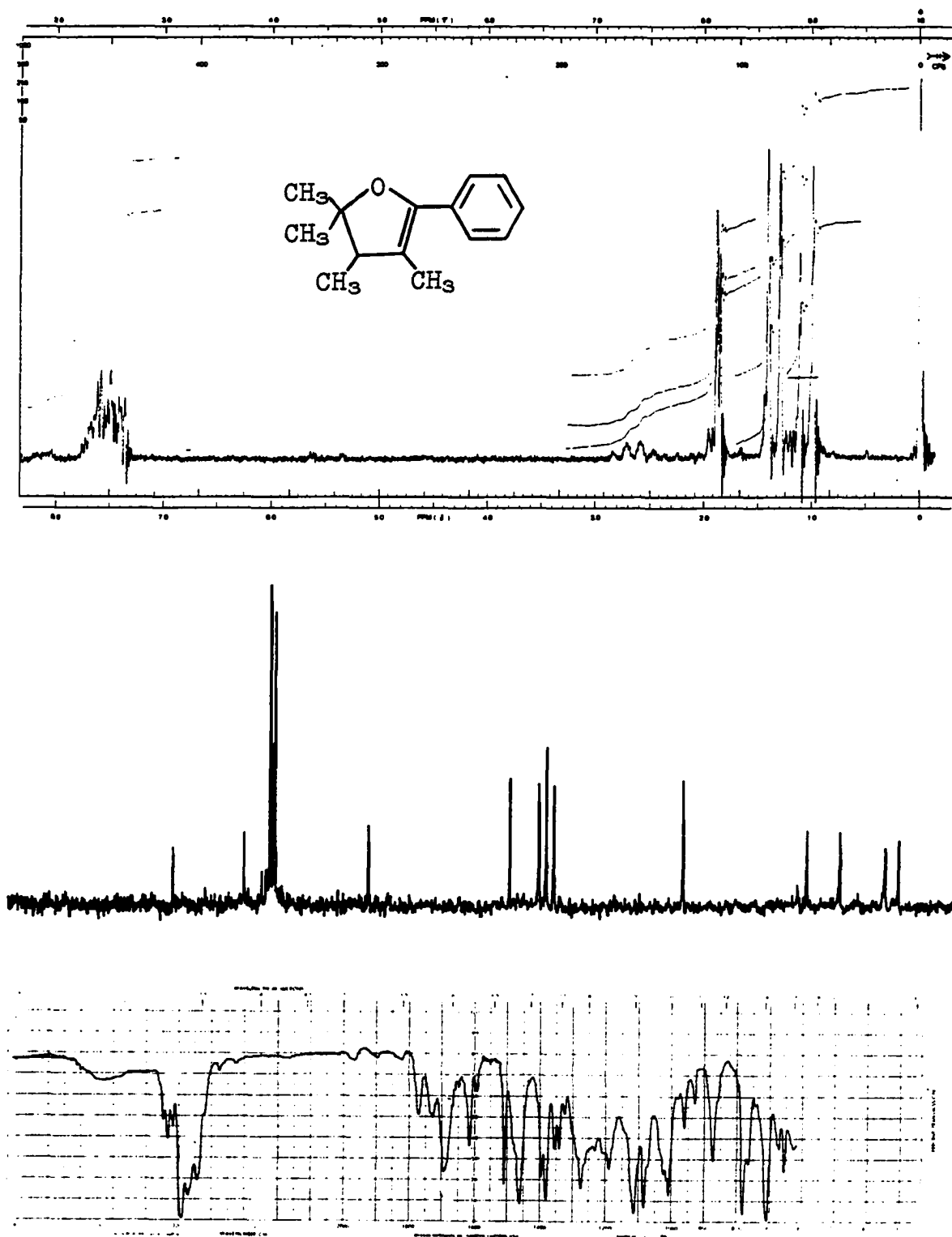
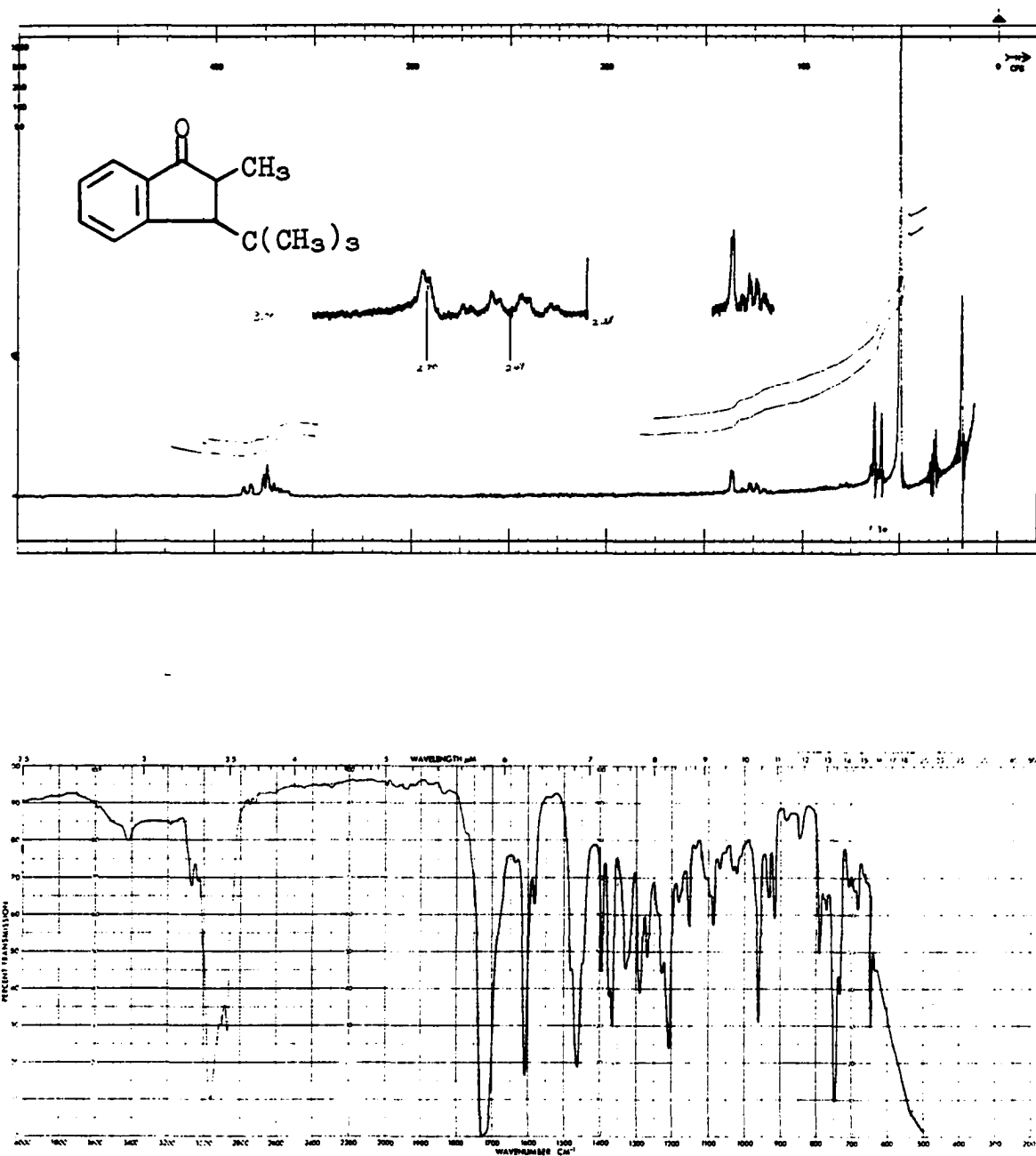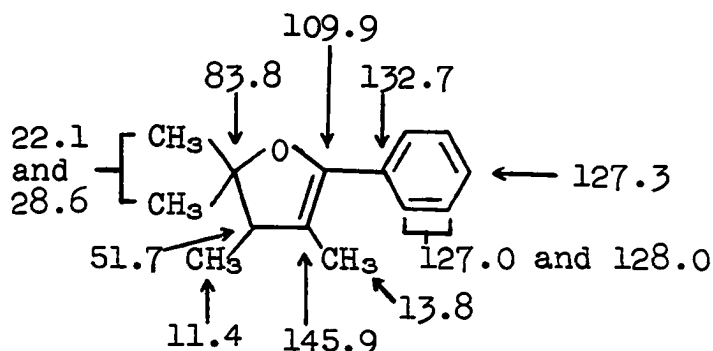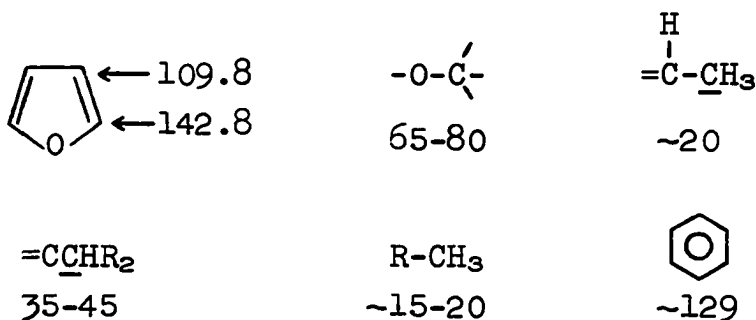Figure 1. ¹H NMR (top), ¹³C NMR (middle), and infrared (bottom) spectra of 4,5-dihydro-2-phenyl-3,4,5,5-tetramethylfuran (3).

Figure 2. ^{1}H NMR (top) and infrared (bottom) spectra of 3-t-butyl-2-methyl-1-indanone (8).

The ^{13}C NMR assignments for dihydrofuran $\underline{3}$ are as follows:

22.1 and 28.6 ─[CH₃ / CH₃]

83.8

109.9

132.7

127.3

51.7 CH₃   CH₃   127.0 and 128.0

11.4   145.9   13.8

The bases for these assignments are taken from **The Chemist's Companion** (86) and are listed below. All ^{13}C shifts are relative to TMS defined as 0.00. Since vinyl and aromatic

←109.8
←142.8

$-O-\overset{/}{\underset{\diagdown}{C}}-$

65-80

$\overset{H}{\underset{|}{=C}}-\underline{C}H_3$

~20

$=C\underline{C}HR_2$

35-45

$R-\underline{C}H_3$

~15-20

~129

carbons are very similar in chemical shift, the shifts in furan and dihydrofuran $\underline{3}$ are expected to be similar. The additive effect of the oxygen and carbon-carbon double bond explain the downfield shift of carbon number 4 of the dihydrofuran ring. The remaining chemical shifts are similar to those in the reference tables of **The Chemist's Companion.**

Several unsuccessful attempts were made to obtain chemical confirmation of dihydrofuran $\underline{3}$, all without success.

Reduction under one atmosphere of hydrogen over Wilkinson's catalyst in benzene for two days resulted in recovery of the intact dihydrofuran (NMR analysis). Palladium on charcoal in ethyl acetate at one atmosphere, likewise resulted in recovery of dihydrofuran. Increasing the pressure to 40 psi in a Parr hydrogenator resulted in recovery of an oil, probably picked up from the hydrogenation apparatus. Attempts to cleave the ring to a δ-hydroxy ketone with p-toluene-sulfonic acid in aqueous acetone (~40% H_2O) again resulted only in recovery of starting material. Switching to concentrated hydrochloric acid in acetone resulted in recovery of products resulting from the self-condensation of acetone which masked the presence of any products from the dihydro-furan. No further attempts at chemical confirmation were attempted.

Isomerization studies in this system were carried out in the same manner as the isomerization of enones already discussed.

In the reaction of 3,3-dimethylbutyryl chloride with vinylmercuric chloride, 5,5-dimethyl-1-hexen-3-one was identified by its ^1H NMR spectrum: δ1.0 (9 H, s, C(CH$_3$)$_3$), 2.4 (2 H, s, -CH$_2$Ö-), 5.65 (1 H, d of d, J=4 and 8 Hz, -ÖCH=), 6.15 (2 H, m, -ÖCH=CH$_2$). Further characterization was not carried out. 1-Chloro-5,5-dimethyl-3-hexanone was characterized fully: ^1H NMR (CCl$_4$) δ1.0 (9 H, s, -C(CH$_3$)$_3$), 2.25 (2 H, s, -ĊCH$_2$Ö-), 2.75 (2 H, t, J=7 Hz, -ÖCH$_2$CH$_2$Cl),

3.6 (2 H, t, $\underline{J}$=7 Hz); ir (max) (thin film) 2940, 1710, 1360, 1180, and 830 cm^{-1}; $\underline{m}/\underline{e}$ 162.0812 ± .0008 (calcd for $C_8H_{15}OCl$, 162.0812).

V. THE SYNTHESIS OF SYMMETRICAL 1,3-DIENES

A. Introduction

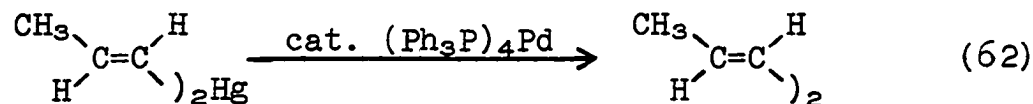Conjugated dienes are important for their use in the Diels-Alder reaction as well as in their own right (87). New methods for their synthesis have recently been reported utilizing organoaluminum (88), -boron (88b, 89), -copper (90), -lithium (90, 91, 92), -magnesium (93), -nickel (94), and -silver (91b, 92) reagents. Larock (43) recently published a synthesis of symmetrical 1,3-dienes from vinylmercuric chlorides which required stoichiometric amounts of palladium chloride and lithium chloride in hexamethylphosphoramide (HMPA) solvent and produced the diene in high yield (Eq. 61). The

$$2 \underset{H}{\overset{R}{\diagdown}} C=C \underset{HgCl}{\overset{H}{\diagup}} + PdCl_2 \xrightarrow[\text{HMPA}]{\text{LiCl}} \underset{H}{\overset{R}{\diagdown}} C=C \underset{)_2}{\overset{H}{\diagup}} + Pd^0 + 2HgCl_2 \qquad (61)$$
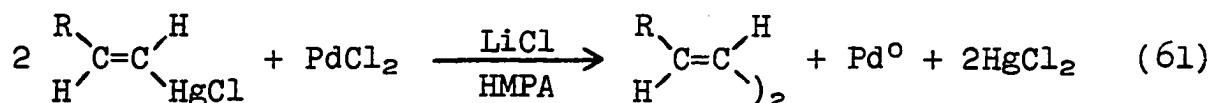
reaction suffered three major drawbacks. First, it required stoichiometric amounts of expensive palladium chloride. Second, in order to get high isomeric purity it was necessary to run the reaction at temperatures close to the freezing point of HMPA. Third, there have recently appeared reports that HMPA may be carcinogenic. At the same time, Vedejs and Weeks (95a) reported the dimerization of cis- and trans-dipropenylmercury using catalytic quantities of tetrakis(triphenylphosphine)palladium (Eq. 62). The catalytic nature of

$$\underset{\substack{\text{H}}}{\overset{\substack{\text{CH}_3}}{\diagdown}}C=C\underset{\substack{)_2\text{Hg}}}{\overset{\substack{\text{H}}}{\diagup}} \xrightarrow{\text{cat. (Ph}_3\text{P)}_4\text{Pd}} \underset{\substack{\text{H}}}{\overset{\substack{\text{CH}_3}}{\diagdown}}C=C\underset{\substack{)_2}}{\overset{\substack{\text{H}}}{\diagup}} \qquad (62)$$

this reaction is offset by the use of the liquid divinyl-
mercurials which are harder to purify than the solid vinyl-
mercuric chlorides. Also, divinylmercury compounds are more
volatile and therefore presumably more toxic. A 4-8% loss of
stereochemistry was also observed.

I have developed a synthesis of dienes and polyenes
which overcomes the drawbacks encountered in both of these
procedures and results in the synthesis of dienes and polyenes
in high yield and high isomeric purity.

B. Results and Discussion

1. Synthesis of dienes and polyenes

During the course of our studies on the synthesis of
α,β-unsaturated ketones (Chapter IV) we used a number of
transition metal catalysts in various solvents. In most
solvents, small quantities of symmetrical 1,3-dienes were seen
as side products. In HMPA and THF the diene was seen as the
only product of the reaction derived from the mercurial. We
therefore investigated the effect of 10% quantities (calcu-
lated on the basis of mercurial) of various rhodium catalysts
on trans-1-hexenylmercuric chloride in HMPA at room temper-
ature (Eq. 63). The results are summarized in Table VIII.

Table VIII. Rhodium Catalyzed Dimerization of Trans-1-hexenylmercuric Chloride[a]

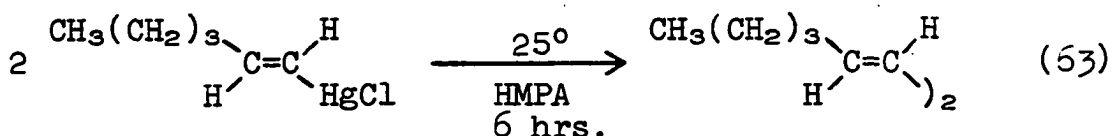| Rhodium Complex	Diene Yield(%)[b]
$ClRh(P\emptyset_3)_3$	28
$ClRh(CO)(P\emptyset_3)_2$	74
$[ClRh(CH_2=CH_2)_2]_2$	70
$[ClRh(COD)]_2$[c]	81
$[ClRh(CO)_2]_2$	87
$[ClRh(CO)_2]_2/LiCl$[d]	95
$RhCl_3 \cdot nH_2O$[e]	61
$RhCl_3 \cdot nH_2O$[e]$/LiCl$[d]	94

[a]All reactions were run with 10% "rhodium" per vinylmercurial (5% for dimeric rhodium complexes) for 6 hr. at room temperature in HMPA under a nitrogen atmosphere.

[b]All yields were determined by GLC analysis using an internal standard.

[c]COD=1,5-cyclooctadiene.

[d]Two equivalents of lithium chloride were employed.

[e]n is approximately 2.3.

$$2 \quad \underset{H}{\overset{CH_3(CH_2)_3}{>}}C=C\underset{HgCl}{\overset{H}{<}} \quad \xrightarrow[\substack{HMPA \\ 6 \text{ hrs.}}]{25^\circ} \quad \underset{H}{\overset{CH_3(CH_2)_3}{>}}C=C\underset{)_2}{\overset{H}{<}} \qquad (53)$$

All of the rhodium catalysts studied proved to be catalytic. In general, the trans, trans-diene was obtained in greater than 98% stereospecificity and the use of lower reaction temperatures was found not to be necessary. Lithium chloride (2 mmol per mmol of mercurial) was found to improve the yield of diene. It was subsequently found that allowing the reaction to proceed for 24 hours resulted in higher yields. Both $[ClRh(CO)_2]_2$ and $RhCl_3 \cdot nH_2O$ in the presence of lithium chloride were found to be quite effective in catalyzing the reaction. We then studied the effect of lower concentrations of these two complexes and found that $[ClRh(CO)_2]_2$ was the better catalyst for the reaction (Table IX). This catalyst was found to be effective even at the 0.01% level under either air or nitrogen. We chose 1% of this rhodium catalyst as the best quantity for our studies for the sake of ease of handling. We then studied the effect of using ether or tetrahydrofuran (THF). THF was found to generally be as effective as HMPA, with ether being only marginally less effective.

We then undertook to investigate the scope of the reaction using a number of vinylmercuric chlorides. The results are summarized in Table X. Trans-monosubstituted mercurials give excellent yields. However, internal

Table IX. Comparison of Rhodium Catalyst Activity

$$2 \quad \begin{array}{c} CH_3(CH_2)_3 \\ \\ H \end{array} C=C \begin{array}{c} H \\ \\ HgCl \end{array} \longrightarrow \begin{array}{c} CH_3(CH_2)_3 \\ \\ H \end{array} C=C \begin{array}{c} H \\ \\ )_2 \end{array}$$

Rhodium Catalyst	Solvent	Concentration(%)[a]	Yield(%)[b]
$RhCl_3 \cdot nH_2O$[c]/LiCl	HMPA	10	100
		1	85
$[ClRh(CO)_2]_2$/LiCl		10	98
		1	100
		.01	90
			95[d]
	Et_2O	1	90
	THF	1	78[e]
		1	99

[a]Percent "rhodium" per vinylmercurial.
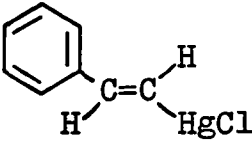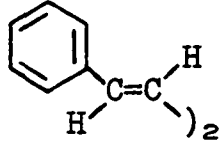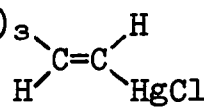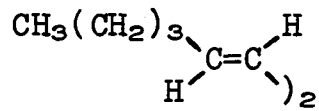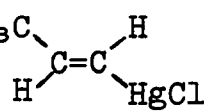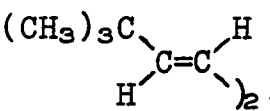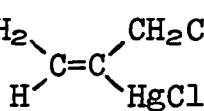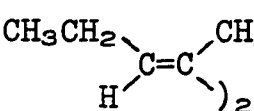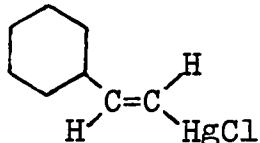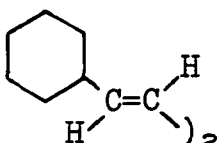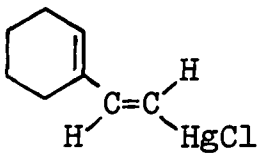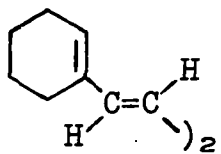
[b]Analysis by GLC using an internal standard.

[c]n is approximately 2.3.

[d]Reaction run in the presence of air (all others are under nitrogen).

[e]No lithium chloride used.

Table **X**. Synthesis of Dienes and Polyenes

Vinylmercurial	Catalyst[a]	Solvent	Diene	Yield (%)[b]
	RhCl$_3$·nH$_2$O [ClRh(CO)$_2$]$_2$	HMPA THF		65 100 84
	RhCl$_3$·nH$_2$O [ClRh(CO)$_2$]$_2$	HMPA THF		85 100 99
	RhCl$_3$·nH$_2$O [ClRh(CO)$_2$]$_2$	HMPA THF		98 100(88) 100
	RhCl$_3$·nH$_2$O [ClRh(CO)$_2$]$_2$	HMPA		24[c] 35[c]
		HMPA THF		(90) (97)
		HMPA		(92)

[a] 1% "Rhodium" per vinylmercurial.

[b] GLC analysis (isolated yield).

[c] Reactions run at 75°C.

mercurials do not react as readily and in this case Larock's palladium chloride procedure is better. Of special interest is the last entry in Table X. Our synthesis provides a mild, convenient dimerization of mercurials derived from enynes thus giving good yields of polyenes (Eq. 64).

$$\text{(structure)} -C\equiv CH \longrightarrow \text{(structure)} \overset{H}{\underset{H}{C}} = C \overset{H}{\underset{HgCl}{}} \longrightarrow \text{(structure)} \overset{H}{\underset{H}{C}} = C \overset{H}{\underset{}{}} \Big)_2 \qquad (64)$$
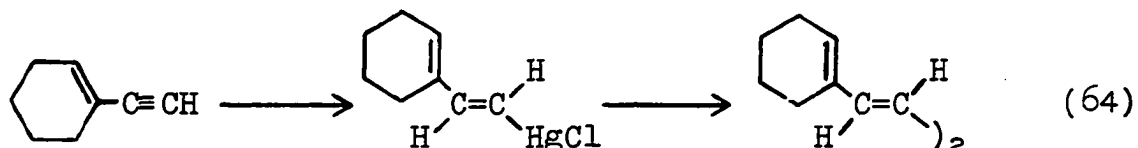
Three other vinylmercuric chlorides were tried with little or no success. E-3-acetoxy-2-chloromercuri-2-butene did not dimerize successfully. Whereas the successful dimerizations all had gray residues develop during the course of the reaction, this reaction remained clear, indicating that no reaction occurred. Considering the difficulty of dimerizing simple internal mercurials this result is not surprising. Trans-β-chlorovinylmercuric chloride likewise showed no gray color and no diene products were isolated. The reaction was also tried at 80°C, again with no success. Trans-5-cyano-1-pentenylmercuric chloride showed some indications of dimerizing, but a satisfactory yield of pure diene was never obtained. NMR spectra of product mixtures showed the expected pattern of vinyl hydrogen absorption corresponding to that observed for other 1,3-dienes, but there were also substantial aliphatic resonances observed which were not to be expected from the desired product. The product appeared to be a mixture of solid and liquid materials and was not successfully

separated by GLC or other techniques. The yield of diene appeared to be rather low in any case, so the reaction was not pursued further.

2. Attempted dimerization of n-hexylmercuric chloride

In an attempt to extend the synthesis of dienes to the dimerization of alkylmercuric chlorides, n-hexylmercuric chloride (1 mmol) was stirred with two equivalents of lithium chloride and 1% "rhodium" in the form of $[ClRh(CO)_2]_2$. After 24 hours in HMPA under nitrogen, no dodecane was seen by GLC analysis. Heating to 180°C for a second 24 hours, followed by GLC analysis, was again found to be ineffective in producing dodecane. This result is consistent with Larock's earlier observation with palladium chloride (43). While we can not absolutely rule out the possibility of a reaction occurring, it looks highly unlikely that conditions can be found to successfully dimerize alkylmercurials.

3. Mechanism

While analogies to other transition metal reactions, expecially those of nickel, palladium, and rhodium can be cited, we have little direct evidence on which to base a mechanism. The mechanism probably involves first, the transfer of an alkenyl group to rhodium, generating mercuric chloride and an alkenylrhodium(I) species; second, oxidative addition of a second mercurial molecule to generate a rhodium-

(III) species; and finally, reductive elimination of two alkenyl groups to regenerate a rhodium(I) species and the diene, along with metallic mercury (Scheme 12). The many

Scheme 12

$$RHgCl + RhCl \longrightarrow Rh-R + HgCl_2$$

$$Rh-R + RHgCl \longrightarrow R_2RhHgCl$$

$$R_2RhHgCl \longrightarrow R-R + RhCl + Hg$$

reported exchange reactions of organomercurials with palladium salts suggest that rhodium should also undergo such reactions. The large number of oxidative addition reactions of rhodium(I) species, including the reported rhodium(I) oxidative addition of organomercurials across the carbon-mercury bond (95b) lend credence to the second step of the proposed mechanism. In line with Larock's report of the palladium promoted synthesis of dienes (43), one might expect the rhodium(III) species to reductively eliminate the dimeric product. Metallic mercury is in fact observed during the course of the reaction. While it might be expected that mercuric chloride and metallic mercury would disproportionate to mercurous chloride, we observed that mercurous chloride dissolved in HMPA readily precipitated metallic mercury.

Since a rhodium(III) species is an intermediate in the proposed mechanism, we suspected that rhodium(III) chloride would be catalytic and indeed it was. Initial transmetallation

to form a dialkenylrhodium(III) species directly, followed by reductive elimination of the diene to give a rhodium(I) chloride, probably solvated by HMPA, should produce a rhodium-(I) species (Scheme 13) which would serve as a catalyst as outlined in Scheme 12.

Scheme 13

$$2 \text{ RHgCl} + \text{RhCl}_3 \longrightarrow \text{R}_2\text{RhCl} + \text{HgCl}_2$$

$$\text{R}_2\text{RhCl} \longrightarrow \text{R-R} + \text{RhCl}$$

C. Experimental Section

1. Reagents

All chemicals were used directly as obtained commercially unless otherwise indicated. HMPA was distilled from lithium aluminum hydride (LAH) under vacuum. Pentane was stirred over fuming sulfuric acid, washed with water and stored over anhydrous sodium sulfate after distillation. Ether and THF were distilled from LAH.

The vinylmercurials used have all been described previously and were prepared using methods discussed in Chapter II.

$[\text{ClRh(CO)}_2]_2$ (PCR), $[(\text{CH}_2=\text{CH}_2)_2\text{RhCl}]_2$ (Strem), (1,5-COD RhCl)$_2$ (ROC/RIC), $(\text{Ph}_3\text{P})_2\text{Rh(CO)Cl}$ (Alfa Inorganics-Ventron), and $\text{RhCl}_3 \cdot n\text{H}_2\text{O}$ (Matthey Bishop) were used directly as obtained. Wilkinson's catalyst, $(\text{Ph}_3\text{P})_3\text{RhCl}$, was prepared according to published procedures (84).

All GLC yields are corrected by the use of appropriate hydrocarbon internal standards.

2. Rhodium catalyzed dimerization of trans-1-hexenylmercuric chloride.

The catalytic activity of a variety of different rhodium catalysts was examined using the following standard procedure for the dimerization of trans-1-hexenylmercuric chloride. The catalyst (0.10 mmol of monomeric, and 0.05 mmol of dimeric rhodium catalysts), tetradecane (internal standard, approx. 5 mmol) and lithium chloride (2.0 mmol) where appropriate were dissolved in HMPA (5 ml) in a 25 ml round bottom flask which had been previously flushed with nitrogen. The trans-1-hexenylmercuric chloride (1.00 mmol) was added and the reaction stirred for 6 hr. at room temperature. Ether (5 ml) was then added and the mixture analyzed on a 10' 10% DC-550 GLC column. The results are included in Table VIII.

3. Comparison of rhodium catalyst activity.

The appropriate amount of $RhCl_3 \cdot nH_2O$ (n≈2.3) (0.1 or .01 mmol) or $[ClRh(CO)_2]_2$ (0.05, .005 or .00005 mmol), lithium chloride (2 mmol), and tetradecane were dissolved in 5 ml of the appropriate solvent. Trans-1-hexenylmercuric chloride (1 mmol) was added and the reaction stirred for 24 hr. at room temperature. The yields in HMPA were determined by GLC as described above. The ether and THF reactions were analyzed

by GLC after adding water or saturated ammonium chloride solution respectively. 0.01% [ClRh(CO)$_2$]$_2$ was achieved by adding 0.025 ml of a solution containing 4.0 mg of catalyst in 5.0 ml HMPA. The results are summarized in Table IX.

4. Synthesis of dienes and polyenes

The following procedure for the synthesis of trans, trans-2,2,7,7-tetramethylocta-3,5-diene is representative. [ClRh(CO)$_2$]$_2$ (0.05 mmol) and lithium chloride (20 mmol) were placed in a 250 ml round bottom flask equipped with a septum inlet and gas inlet tube which has been flushed with nitrogen. HMPA (50 ml) and then trans-3,3-dimethyl-1-butenylmercuric chloride (10.0 mmol) were added and the reaction stirred for 24 hr. at room temperature. The reaction mixture was poured into water and pentane added. A gray suspension formed and was filtered off. The gray residue was washed with pentane. The pentane layer was separated and the water layer re-extracted with pentane. The combined pentane extracts were washed with water, dried over anhydrous sodium sulfate, and the pentane removed under vacuum. A white solid (0.73 g, 88%, crude mp 74-77°C, mp 77-78°C (EtOH), lit.(43) mp 78-79°C) was obtained. ^{1}H NMR (CCl$_4$) δ1.00 (18H, s, CH$_3$) and 5.6 (4H, m, vinyl).

The following new compounds were prepared in a similar manner. Trans, trans-1,4-di(1-cyclohexenyl)buta-1,3-diene:

yellowish solid, mp 100-104°C (pentane); ^{1}H NMR (CCl$_4$) δ1.50 (8H, m, aliphatic), 2.10 (8H, m, allyl), 5.56 (2H, m, cyclohexenyl vinyl), 5.97 (4H, s, vinyl); ir (max) (KBr) 3020, 2940, 2920, 1625, 1440, 1345, 1130, 1070, 980, 920, and 850 cm^{-1}; m/e 214.1723 (calcd for C$_{16}$H$_{22}$, 214.1722). Trans, trans-1,4-dicyclohexylbuta-1,3-diene: low melting solid (~20-25°C), ^{1}H NMR (CCl$_4$) δ0.8-2.3 (22H, m, cyclohexyl), and 5.1-6.1 (4H, m, vinyl); ir(max)(nujol) 3015, 1455, 1355, 990, 965, 895, and 845 cm^{-1}; m/e 218.2040 (calcd for C$_{16}$H$_{26}$, 218.2035).

The THF preparative reaction was worked up by adding saturated ammonium chloride, separating the layers, and washing the aqueous layer with hexane. The combined organic layers were then washed with saturated ammonium chloride, 3M sodium thiosulfate, and saturated sodium chloride, dried over anhydrous sodium sulfate, and the solvent removed.

All GLC yields were determined on reactions run on one-tenth the above scale following GLC analysis procedures identical to those outlined above. Internal standard correlation factors were determined using authentic diene samples (43).

VI. THE SYNTHESIS OF BIARYLS

A. Introduction

Biaryls are usually prepared from aryl iodides by heating
with copper metal according to the Ullmann reaction (96).
Zerovalent nickel reagents (97) have been used, and aromatic
Grignard (98) or lithium (98e-g, 99) reagents have been
treated with salts of thallium, uranium, or the first group
transition metals.

As we were completing our work Kretchmer and Glowinski
(100) reported a synthesis of biaryls using arylmercuric
chlorides or acetates, catalytic amounts of palladium chloride
and excess metallic copper in refluxing pyridine for from five
to twenty-two hours. Their reactions works well for most
arylmercuric salts, with the exception of those containing
hydroxy or carboxylic acid functionality or those suffering
from steric hindrance. The reaction apparently requires a
basic solvent, pyridine, and moderately high temperatures,
115°C. The reaction succeeds with amines and amides, but
fails with acids and phenols.

The Ullmann reaction also requires high temperatures,
often in excess of 200°C, and is unable to dimerize aryl-
halides containing active hydrogens (such as primary or
secondary amines, primary amides, alcohols, or acids).

I have developed a synthesis of biaryls which overcomes
most of these drawbacks and results in biaryls in excellent
yield and high purity.
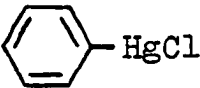
B. Results and Discussion
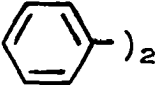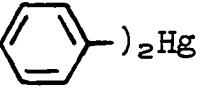
1. Synthesis of biaryls

Our success with the dimerization of vinylmercuric chlorides prompted us to study the rhodium catalyzed dimerization of arylmercuric chlorides. As our starting point we used the conditions worked out for the synthesis of symmetrical 1,3-dienes, i.e. 1 mmol of phenylmercuric chloride, 2 mmol of lithium chloride and 1% "rhodium" in 5 ml of hexamethylphosphoramide (HMPA) at room temperature. We also studied the effects of various other solvents on the reaction. The results of this study are summarized in Table XI.

It was immediately obvious that arylmercuric chlorides are less reactive than vinylmercuric chlorides towards dimerization. 1% "Rhodium" seems to be the optimum concentration of catalyst with either more or less catalyst resulting in lower yields. Higher temperatures were also necessary, with 80°C being adequate for good yields. The higher polarity solvents worked best, with HMPA being significantly better than any of the others tried.

The scope of this reaction has been investigated on a variety of arylmercuric chlorides (Table XII). In general the yields are comparable with those obtained by other routes. However, the reaction conditions are much milder than those required for the Ullmann reaction and somewhat milder than those used by Kretchmer. The Ullmann reaction is unsuccessful with aromatic amines, amides, phenols (ethers are formed) and

Table XI. [ClRh(CO)$_2$]$_2$ Catalyzed Dimerization of Aryl-
mercurials[a]

Arylmercuric Chloride[b]	Biaryl	Solvent	Catalyst Concentration(%)[c]	Temp (°C)	Yield (%)[d]
⬡–HgCl	⬡–)$_2$	THF	1	66	15[e]
			1		55
		MeOH	1	65	24
		CH$_3$CN	1	82	65
		HMPA	1	25	25
			0.5		61
			1		81
			2		67
			1	125	78
⬡–)$_2$Hg			1	25	36
			1	80	66

[a]All reactions were run for 24 hr in HMPA under nitrogen
atmosphere.
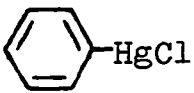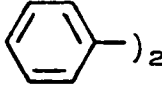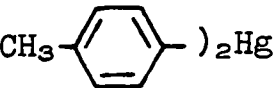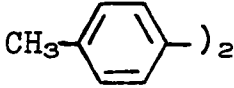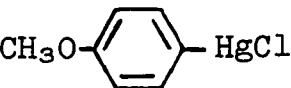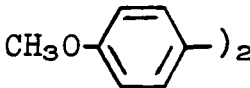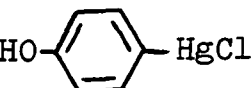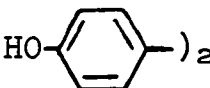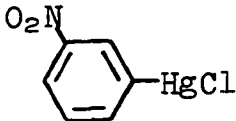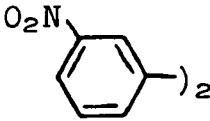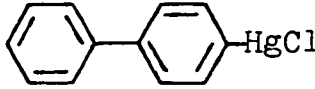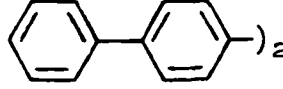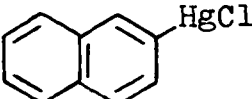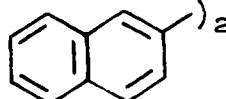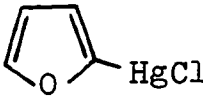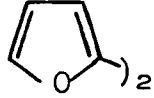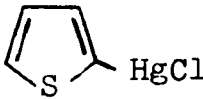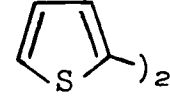
[b]One mmol phenylmercuric chloride or 0.5 mmol of diphenyl-
mercury.

[c]Percent "rhodium" per vinylmercurial.

[d]GLC analysis using an internal standard.

[e]No LiCl present. All others used 2mmol LiCl/mmol mercurial.

Table XII.   Synthesis of Biaryls

Arylmercuric Chloride	Biaryl	Isolated Yield(%)	mp(°C) (lit mp)	Ref.
		84	62-65.5 (70.5)	101
		92	120-121.5 (121-122)	102
		88	177-178 (175)	103
		88	277-278.5 (272)	104
		53	202-202.5 (200)	105
		40	312-313 (320)	106
		94	185-186 (187-8)	107
		70	oil	108
		96	32-33 (32.5)	109

acids. Kretchmer's procedure works with amines and amides but not acids or phenols. Our reaction works only poorly with amines, if at all, but somewhat better with phenols. Mercurials containing carboxylic acid functionality were not examined since it is reported that HMPA reacts with acids under conditions similar to ours (110).

Two arylmercuric chloride dimerizations were attempted without success. Mesitylenemercuric chloride yielded only a small quantity of impure material which was determined to be the starting mercurial. 4-Aminophenylmercuric chloride yielded a small quantity of impure material which could not be crystallized and was not identified. In any event the yield would have been less than 20%.

2. Mechanism

The mechanism for the formation of biaryls is envisioned to be the same as that proposed for the synthesis of dienes and polyenes (see the mechanistic discussion in Chapter V). Briefly, it involves transmetallation to form an arylrhodium(I) compound; oxidative addition of another arylmercuric chloride to this species to form a diarylrhodium(III) mercuric chloride complex and elimination of the biaryl and metallic mercury (Scheme 12, Chapter V). Metallic mercury is again observed in this reaction. Rhodium(III) catalysts were not tried in this reaction in view of their lower catalytic activity as observed in the synthesis of 1,3-dienes.

C. Experimental Section

1. Reagents

All chemicals were used directly as obtained commercially unless otherwise indicated. HMPA was distilled from lithium aluminum hydride (LAH) under vacuum and THF was distilled from LAH at atmospheric pressure.

Phenylmercuric chloride (Aldrich), diphenylmercury (Eastman), di-p-tolylmercury (Eastman), and 4-chloromercuriphenol (Eastman) were used directly as obtained. 4-Methoxyphenylmercuric chloride (111), 4-aminophenylmercuric chloride (112, 113), 3-nitrophenylmercuric chloride (114), 2-chloromercurinaphthalene (115), mesitylenemercuric chloride (13a), 2-chloromercurifuran (10), 2-chloromercurithiophene (69a, 116) and 4-chloromercuribiphenyl (13a) were all prepared using literature procedures.

[ClRh(CO)$_2$]$_2$ was obtained from PCR and used directly.

All GLC yields are corrected by the use of appropriate internal standards.

2. [ClRh(CO)$_2$]$_2$ catalyzed dimerization of arylmercurials

The effect of catalytic amounts of [ClRh(CO)$_2$]$_2$ on the dimerization of phenylmercuric chloride and diphenylmercury was examined as follows. The appropriate quantity of [ClRh(CO)$_2$]$_2$ (.01, .005 and .0025 mmol), lithium chloride (2.0 mmol) and octadecane were dissolved in the appropriate

solvent (5 ml) in a 25 ml roundbottom flask equipped with a rubber septum. After adding phenylmercuric chloride (1.0 mmol) or diphenylmercury (0.50 mmol) the reaction was stirred for 24 hr. at room temperature or in a preheated oil bath. The HMPA reaction was poured into water and ether added. The ether layer was analyzed by GLC on a 10' 10% DC-550 column. The THF reactions were analyzed as described previously and the methanol and acetonitrile reactions were analyzed directly.

3. Synthesis of biaryls.

The following procedure for the synthesis of 4,4'-bi-anisole is representative. $[ClRh(CO)_2]_2$ (0.05 mmol) and lithium chloride (20 mmol) were dissolved in HMPA (20 ml) in a 250 ml roundbottom flask equipped with a gas inlet tube and a sidearm fitted with a rubber septum. After adding 4-methoxy-phenylmercuric chloride (10 mmol) the reaction was stirred in a preheated oil bath at 80°C for 24 hr. A puddle of metallic mercury was observed. The reaction mixture was then poured onto ice and benzene added. After separating the layers, the water was re-extracted with benzene. The combined organic layers were washed with water, 10% HCl, 3M sodium thiosulfate, water and saturated sodium chloride, and dried over anhydrous magnesium sulfate. Removal of the solvent under vacuum provided 0.94 g of white solid (88%): mp 174.5-175.5°C before recrystallization, mp 177-178°C (hexane) (lit. (103) mp 175°C).

The following biaryls were prepared in a similar manner. Biphenyl: 84% yield; crude mp 62-65.5°C (lit. (101) mp 70.5°C). 4,4'-Bitolyl: (from di-p-tolylmercury) 92%, mp 118-120°C, 120-121.5°C (hexane) (lit. (102) mp 121-122°C). Bifuran: 70% reddish oil (108); H^1 NMR (CCl_4) δ6.15 (2H, dd, $\underline{J}$=1Hz and 3Hz, 4 and 4'), 6.35 (2H, d, $\underline{J}$=3Hz, 3 and 3'), and 7.10 (2H, d, $\underline{J}$=1Hz, 5 and 5') (nmr assignments based on those of reference 108). 3,3'-Dinitrobiphenyl: 53%, mp 200.5-201°C, mp 202-202.5 (benzene) (lit. (105) mp 200°C). 2,2'-Binaphthyl: 94%, mp 184.5-185°C, mp 185-186°C (benzene-hexane) (lit. (107) mp 187-188°C). Bithiophene: 96%, greenish oil which solidifies on standing, mp 30-32°C, mp 32-33°C (hexane) (lit. (109) mp 32.5°C). Quaterphenyl: 40%, mp 307-310°C, mp 312-313°C (benzene) (lit. (106) mp 320°C). 4,4'-Dihydroxybiphenyl: 88%, mp 267-271°C, mp 277-278.5°C (ether-hexane) (lit. (104) mp 272°C).

The following biaryls required the indicated modifications in their work-up. 3,3'-Dinitrobiphenyl: a suspension occurred on adding benzene, so the resulting mixture was filtered and the solid washed with a large volume of benzene. The aqueous and organic layers were then worked up according to the standard procedure. Quaterphenyl: the reaction was carried out at 120°C and worked up by pouring the reaction mixture onto ice, filtering and collecting the crude solid, washing with water, and then dissolving in a large volume of boiling benzene and filtering hot. The benzene was removed under

vacuum and a white solid collected. 4,4'-Dihydroxybiphenyl:
ether was used for the work-up and sodium thiosulfate was
omitted during the work-up. Extra water washes were required
to remove HMPA.

VII. THE SYNTHESIS OF 1,4-DIENES

A. Introduction

1,4-Dienes are common in biologically occurring fatty acids such as arachadonic acid, the biological precursor to the prostaglandins and other polyunsaturated fatty acids. Several methods for the synthesis of 1,4-dienes utilizing organometallic reagents have appeared recently. Lynd and Zweifel (117) have reacted vinylalanes, generated from acetylenes and diisobutylaluminum hydride with allylic halides (Eq. 65) in the presence of cuprous chloride to get 1,4-

$$\underset{H}{\overset{R}{>}} C=C \underset{AlR_2''}{\overset{R'}{<}} + CH_2=CH-CH_2Br \xrightarrow[\text{hexane}]{CuCl} \underset{H}{\overset{R}{>}} C=C \underset{CH_2-CH=CH_2}{\overset{R'}{<}} \quad (65)$$
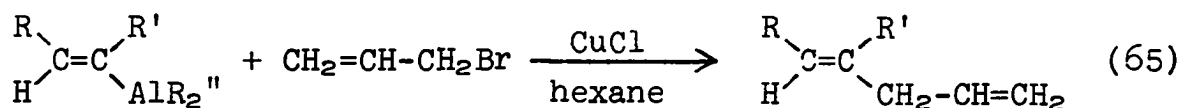
dienes. Similarly Yamamoto et al. (118) has treated divinyl-chloroboranes, obtained from acetylenes and chloroborane, with allylic halides and methyl copper to prepare 1,4-dienes (Eq. 66). In a very similar reaction Normant et al. (119) has

$$\underset{H}{\overset{R}{>}} C=C \underset{)_2BCl}{\overset{R'}{<}} + CH_2=CH-CH_2Cl \xrightarrow[\text{Et}_2O]{CH_3Cu} \underset{H}{\overset{R}{>}} C=C \underset{CH_2-CH=CH_2}{\overset{R'}{<}} \quad (66)$$
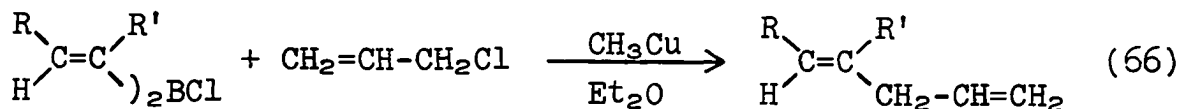
treated vinylcopper reagents, also derived from acetylenes, with allylbromide to obtain 1,4-dienes (Eq. 67). Henrick and

$$\underset{C_2H_5}{\overset{C_4H_9}{>}} C=C \underset{Cu}{\overset{H}{<}} + CH_2=CHCH_2Br \xrightarrow[\text{HMPA}]{} \underset{C_2H_5}{\overset{C_4H_9}{>}} C=C \underset{CH_2-CH=CH_2}{\overset{H}{<}} \quad (67)$$
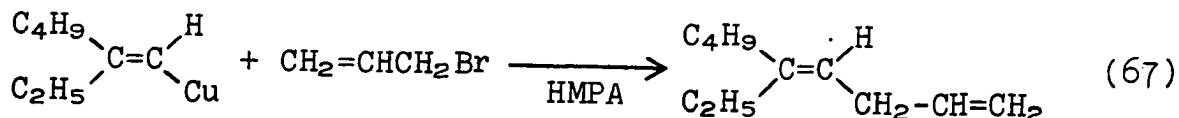
Siddall extended this reaction to functionally substituted cuprates (120) (Eq. 68). Using a different approach Corey and

$$\underset{C_2H_5}{\overset{CH_3}{\diagdown}}C=C\underset{Cu}{\overset{CO_2CH_3}{\diagup}} + CH_2=CHCH_2Br \xrightarrow{THF} \underset{C_2H_5}{\overset{CH_3}{\diagdown}}C=C\underset{CH_2CH=CH_2}{\overset{CO_2CH_3}{\diagup}} \qquad (68)$$

Semmelhack (121) treated vinylbromide with π-methallylnickel bromide and obtained the corresponding 1,4-diene (Eq. 69).

$$CH_3-C\underset{CH_2}{\overset{CH_2}{\diagdown}} \quad NiBr/_2 + CH_2=CHBr \longrightarrow CH_2=CH-CH_2\overset{CH_3}{\underset{|}{C}}=CH_2 \qquad (69)$$
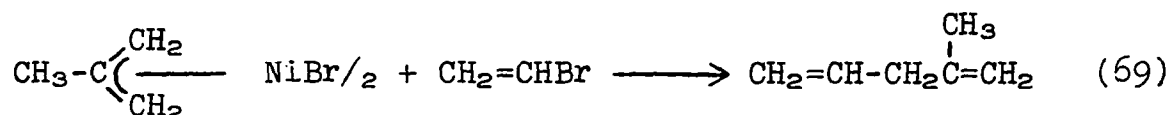
I have developed a synthesis of 1,4-dienes from vinyl-mercuric chlorides and allylic chlorides which utilizes palladium chloride to generate 1,4-dienes in moderate to excellent yield.

B. Results and Discussion

1. Electrophilic approaches

After the success with the synthesis of α,β-unsaturated ketones by electrophilic cleavage of vinylmercurials, I examined the Lewis acid catalyzed reaction of allyl chloride and <u>trans</u>-1-hexenylmercuric chloride (Eq. 70). The

$$\underset{H}{\overset{\underline{n}-C_4H_9}{\diagdown}}C=C\underset{HgCl}{\overset{H}{\diagup}} + CH_2=CH-CH_2Cl \xrightarrow[CH_2Cl_2]{AlCl_3n} \underset{H}{\overset{C_4H_9}{\diagdown}}C=C\underset{CH_2-CH=CH_2}{\overset{H}{\diagup}} \qquad (70)$$
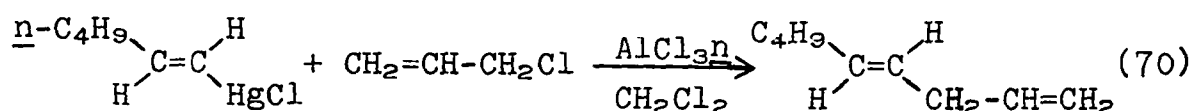
reaction of the mercurial and one equivalent each of aluminum chloride and allyl chloride at room temperature in dichloromethane resulted in precipitation of mercuric chloride, but no 1,4-diene was observed by gas chromatographic analysis. Reducing the amount of aluminum chloride to 0.1 equivalent showed the precipitation of mercuric chloride, but still no 1,4-diene was observed. Lowering the temperature to $0^\circ C$ and $-78^\circ C$ with one equivalent of aluminum chloride did not improve the situation. One equivalent of titanium tetrachloride or ferric chloride at $0^\circ C$ likewise produced no diene products. Treatment with aluminum powder, as with the reaction of styrylmercuric chloride and acetyl chloride, did not result in the formation of 1,4-diene even though metallic mercury was observed in the reaction vessel. Hashimoto et al. (122) observed that allyl acetate reacted with alkylalanes in an alkylation reaction, therefore we treated the vinylmercurial with allyl acetate and aluminum powder at room temperature but, as before no 1,4-diene was observed.

The success of Heck's reaction of phenylmercuric chloride and allylic chlorides in the presence of palladium chloride (123) suggested the possibility that palladium chloride would catalyze the reaction of vinylmercuric chlorides and allylic halides to form 1,4-dienes. It was envisioned that a vinylpalladium species would be formed which would add to the carbon-carbon double bond of the allyl chloride and then eliminate palladium chloride, forming a 1,4-diene (Eq. 71).

$$R{\diagdown}C{=}C{\diagup}^{H}_{HgCl} + PdCl_4^{-2} \longrightarrow \left[R{\diagdown}C{=}C{\diagup}^{H}_{PdCl_3} \right]^{-2} + HgCl_2$$

$$\left[R{\diagdown}C{=}C{\diagup}^{H}_{PdCl_3} \right]^{-2} + CH_2{=}CH{-}CH_2Cl \longrightarrow \left[R{\diagdown}C{=}C{\diagup}^{H}_{CH_2{-}CH{-}CH_2Cl} \right]^{-2} \longrightarrow$$

$$PdCl_3$$

(71)

$$R{\diagdown}C{=}C{\diagup}^{H}_{CH_2CH{=}CH_2} + PdCl_4^{-2}$$
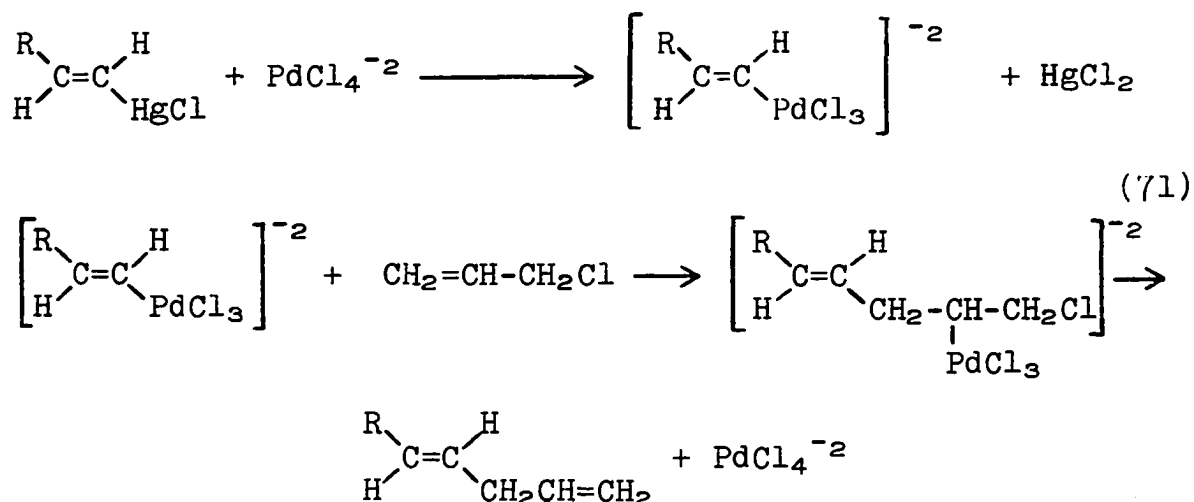
2. Initial studies

The first system chosen for study was the reaction of trans-3,3-dimethyl-1-butenylmercuric chloride and allyl chloride. The effect of solvent, lithium chloride, cupric chloride, varying amounts of palladium chloride, and the quantity of allyl chloride on the yield of 1,4-diene was studied. The results of this study are summarized in Table XIII. Tetrahydrofuran (THF) proved to be the best solvent for the reaction. As with the palladium chloride promoted synthesis of symmetrical-1,3-dienes (43), lithium chloride was seen to be essential for the reaction. Five equivalents of allyl chloride provided optimum yields of 1,4-dienes. 10% Palladium chloride worked as well as one equivalent, but 1% catalyst resulted in only a 10% yield. Added cupric chloride improved the reaction only slightly and a second product, possibly trans-1-chloro-3,3-dimethyl-1-butene, was observed. This second product was also observed in the reaction of the vinyl-

Table XIII. Stoichiometry Studies on Trans-3,3-dimethyl-1-butenylmercuric Chloride
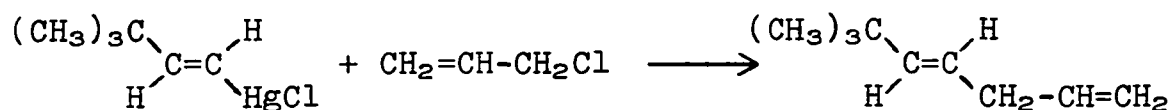
Solvent	PdCl₂	LiCl	CuCl₂	CH₂=CH-CH₂Cl	Yield of 1,4-dienes (%)[b]
THF	1	0	0	1	0
		2			46
		4			45
		2		2	78
				5	98
	0.1				96
	0.01				10
			2		37[c]
	1		0	1	48[d]
					47[e]
Et₂O					30
CH₂Cl₂					34
CH₃OH					6
CH₃CN					23
HMPA					<3[f]
C₆H₆	0.1			5	43[f]

[a] Ten ml solvent and 1 mmol mercurial starting at -78°C.

[b] GLC yield corrected by the use of an internal standard.

[c] A second product, presumed to be trans-1-chloro-3,3-dimethyl-1-butene, is observed.

[d] Start at -22°C.

[e] Start at 25°C.

[f] Start at 0°C.

mercurial, with cupric chloride, and lithium chloride in the absence of palladium chloride and allyl chloride. Starting the reaction at -22°C or 25°C appeared to have no effect on the reaction. The reaction at room temperature was observed to occur immediately upon mixing of the reagents. -78°C was chosen for further reactions in order to allow complete mixing of the reagents before reaction occurred. However, in attempting to scale up the reaction it was found that ten equivalents of allyl chloride was necessary to maintain the near quantitative yield.

Allyl bromide was found to be as effective as allyl chloride, but allyl iodide appeared to be more erratic and seems to give poorer yields of 1,4-dienes. The reaction is also not limited to halides, but gives a modest yield of 1,4-diene when using allyl acetate. The results of these studies are summarized in Table XIV.

Two other systems were then studied in detail. The reaction of trans-3,3-dimethyl-1-butenylmercuric chloride with 3-chloro-1-butene is summarized in Table XV. It should be noted that the product obtained is that of an S_N2' allylic displacement rather than direct substitution. This is discussed in more detail in the mechanistic section. Under most conditions significant yields of the symmetrical 1,3-diene, trans, trans-2,2,7,7-tetramethyl-3,5-octadiene, were observed along with the desired 1,4-diene. No conditions were found which would completely eliminate its formation. One equiv-

Table XIV. The Reaction of Trans-3,3-dimethyl-1-butenyl-
mercuric Chloride with Other Allyl Derivatives

$$(CH_3)_3C \diagdown C=C \diagup H \atop H \diagdown HgCl \quad + \quad CH_2=CH-CH_2X \quad \xrightarrow[\text{THF}]{2 \text{ LiCl}} \quad (CH_3)_3C \diagdown C=C \diagup H \atop H \diagdown CH_2-CH=CH_2$$
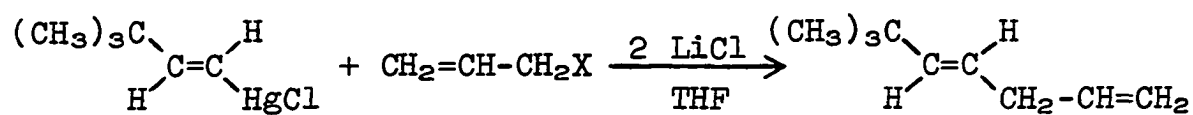
PdCl$_2$ (mmol)	CH$_2$=CH-CH$_2$X		Yield of 1,4-diene (%)[a]
	X	mmol	
1	Br	1	40-69
	I		13-50
	OAc		33
		5	65
0.1			14

[a]GLC yield corrected by the use of an internal standard.

Table XV. Reaction of Trans-3,3-dimethyl-1-butenylmercuric Chloride and 3-Chloro-1-butene.

$$(CH_3)_3C \diagdown C=C \diagup H + CH_2=CH-\underset{\underset{Cl}{|}}{CH}-CH_3 \longrightarrow (CH_3)_3C \diagdown C=C \diagup H$$
$$H \diagup \diagdown HgCl \qquad\qquad\qquad\qquad\qquad H \diagup \diagdown CH_2-CH=CH-CH_3$$
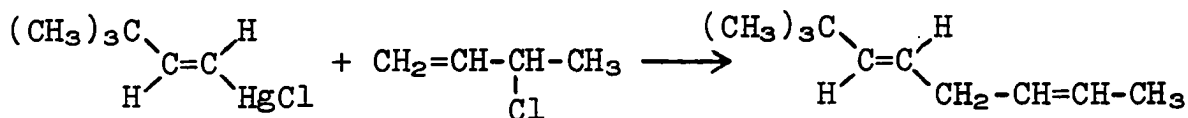
Solvent[a]	PdCl$_2$	CuCl$_2$	CH$_2$=CHCHCH$_3$ $\underset{Cl}{|}$	Yield of diene(%)	
				1,4	1,3[b]
THF	0.1	0	5	44	20
		2		52	37
		0	10	39	10
		2		40	24
	1.0	0	5	38	6
			10	49	10
		2		32	36
Et$_2$O	0.1	0		9	30
		2		51	11

[a]Ten ml; 1 mmol of vinylmercurial and 2 mmol LiCl starting at -78°C.

[b]GLC yield corrected by the use of calculated correction factors.

[c]1,3-Diene ≡ trans, trans-2,2,7,7-tetramethyl-3,5-octadiene; yield calculated on the basis of mercurial used.

alent of palladium chloride and ten equivalents of allylic chloride proved to be the optimum conditions in this system.

Trans-1-hexenylmercuric chloride also required additional study since the conditions used for trans-3,3-dimethyl-1-butenylmercuric chloride were not successful in this system. The results of this study are summarized in Table XVI. Again, one equivalent of palladium chloride and ten equivalents of allyl chloride proved to be the optimum reaction conditions. Other solvents were tried, but none were as efficient as THF. An acceptable yield was also obtained when the reaction was performed with allyl chloride as the solvent.

Mechanisms exist which would result in the generation of HCl in the reaction (see the mechanistic discussion). Therefore the effect of the added bases, magnesium oxide, potassium carbonate, and triethylamine was studied. None of the bases studied resulted in an increase in the yield of 1,4-diene. During the palladium chloride catalyzed synthesis of unsymmetrical 1,3-dienes (26) added mercuric chloride appeared to improve the yields, therefore the addition of mercuric chloride was also investigated. The yield improved to 48% when 10% palladium chloride was employed, but did not improve further when a full equivalent of palladium chloride was employed. In fact the yield of 50% was lower than in the absence of mercuric chloride.

Table XVI. Reaction of <u>Trans</u>-1-hexenylmercuric Chloride and Allyl Chloride

$$\underset{\substack{\text{n-}C_4H_9 \\ \text{H}}}{}C=C\underset{\substack{\text{H} \\ \text{HgCl}}}{} + CH_2=CH-CH_2Cl \longrightarrow \underset{\substack{\text{n-}C_4H_9 \\ \text{H}}}{}C=C\underset{\substack{\text{H} \\ CH_2-CH=CH_2}}{}$$
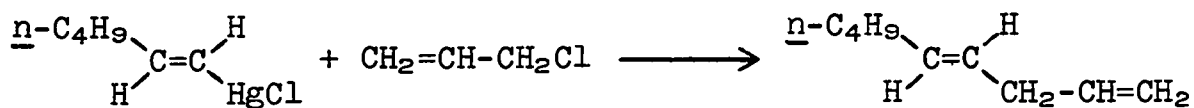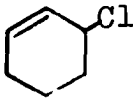
Solvent[a]	PdCl$_2$[b]	CuCl$_2$	Yield of 1,4 diene (%)[c]
C$_6$H$_6$	0.1	2	4[d]
CH$_2$Cl$_2$		0	23
		2	27
MeOH		0	16
CH$_2$=CH-CH$_2$Cl[e]			59
THF			19
		2	42
	1.0		47
		0	71
	Pd(OAc)$_2$		29

[a] Ten ml; start reaction at -78°C
[b] Mmol; with 1 mmol of mercurial and 10 mmol of allyl chloride.
[c] GLC yield corrected by the use of calculated correction factors.
[d] Start at 0°C.
[e] Five mml of allyl chloride as solvent.

3. The synthesis of 1,4-dienes

The scope of the reaction was then investigated on a series of allylic chlorides and vinylmercurials. The reactions studied fell into two categories, those that were catalytic and those that required a full equivalent of palladium chloride. The results are listed in Table XVII. Three vinylmercurials gave excellent yields with 10% palladium chloride and 10 equivalents of allyl chloride, trans-3,3-dimethyl-1-butenylmercuric chloride, trans-1-cyclohexenylethenylmercuric chloride, and E-2-chloromercuri-4,4-dimethyl-2-pentene. No other allylic chlorides resulted in as good a yield as allyl chloride itself, and all other mercurials tried required a full equivalent of palladium chloride. No trends are apparent in comparing the structure of the mercurial and the yields of 1,4-dienes. Allylic chlorides containing internal double bonds do not provide 1,4-dienes as readily as do allylic chlorides substituted at the central carbon of the allyl system. However, the reactions of methallyl chloride, 3-chloro-1-butene, and 2,3-dichloro-1-propene, all showed substantial yields of 1,3-dienes. These reactions, as well as the reaction of crotyl chloride, also showed two or three minor products by GLC analysis. In the reaction of 2,3-dichloro-1-propene, the symmetrical 1,3-diene and the desired 1,4-diene overlapped substantially upon GLC analysis on a 10' DC-550 column. The product was identified by GLC-mass spectrometric analysis (1/8" column) and high

Table XVII. Synthesis of 1,4-Dienes

Vinylmercurial	Allylic Chloride[a]	1,4-Diene	Yield (%)[b]
$(CH_3)_3C$\C=C/H ; H/C=C\$HgCl$	$CH_2=CH-CH_2Cl$	$(CH_3)_3C$\C=C/H ; H/C=C\$CH_2-CH=CH_2$	96[c]
	$\underset{CH_2=CCH_2Cl}{\overset{CH_3}{\mid}}$	$(CH_3)_3C$\C=C/H ; H/C=C\$CH_2-\underset{CH_3}{\overset{\mid}{C}}=CH_2$	45[d]
	$\underset{CH_2=C-CH_2Cl}{\overset{Cl}{\mid}}$	$(CH_3)_3C$\C=C/H ; H/C=C\$CH_2-\underset{Cl}{\overset{\mid}{C}}=CH_2$	28[d]
	$\underset{CH_2=CH-CH-CH_3}{\overset{Cl}{\mid}}$	$(CH_3)_3C$\C=C/H ; H/C=C\$CH_2CH=CHCH_3$	49[d]
$\underline{n}-C_4H_9$\C=C/H ; H/C=C\$HgCl$	$CH_2=CH-CH_2Cl$	C_4H_9\C=C/H ; H/C=C\$CH_2-CH=CH_2$	71(52)
	(cyclohexenyl chloride)	C_4H_9\C=C/H ; H/C=C\(cyclohexenyl)	39

Ph–CH=CH–HgCl (cis, H trans) CH₂=CHCH₂Cl → Ph–CH=CH–CH₂–CH=CH₂ 74(76)

C_6H_{11}–CH=CH–HgCl → C_6H_{11}–CH=CH–CH₂CH=CH₂ 73

(cyclohexenyl)–CH=CH–HgCl → (cyclohexenyl)–CH=CH–CH₂CH=CH₂ 100^c

$(CH_3)_3C$\C=C/CH_3 ... HgCl → $(CH_3)_3C$\C=C/CH_3 ... CH₂CH=CH₂   99
                                                                       98^e

$(CH_3)_3C$\C=C/H ... HgCl CH₃CH=CHCH₂Cl → $(CH_3)_3C$\C=C/H ... CH–CH=CH₂ (CH₃)   32^d

^{a}Ten equivalents of allylic chloride and 1 equivalent of palladium chloride unless otherwise indicated.
^{b}GLC yield (isolated yield).
^{c}Five equivalents of allyl chloride and 0.1 equivalents of palladium chloride.
^{d}A dimeric product is also seen, probably trans, trans-2,2,7,7-tetramethyl-3,5-octadiene.
^{e}10% Palladium chloride.

resolution mass spectrometry on the mixture of 1,4- and 1,3-
dienes obtained by preparative GLC.

4. Mechanism

The mechanism of the palladium chloride promoted
reaction is suggested by the reaction of trans-3,3-dimethyl-
1-butenylmercuric chloride with 3-chloro-1-butene and by
analogy to the previously reported palladium chloride cata-
lyzed reaction of arylmercurials and allylic halides (123).
The first step must be a transmetallation reaction between
the vinylmercurial and $PdCl_4^{-2}$ to generate a vinylpalladium
species. This vinylpalladium compound then adds to the
carbon-carbon double bond to generate an alkylpalladium chlo-
ride which then eliminates $PdCl_4^{-2}$ to form the 1,4-diene
(Scheme 14). This mechanism suggests that the reaction ought

Scheme 14

$$PdCl_2 + 2\ LiCl \longrightarrow Li_2PdCl_4$$
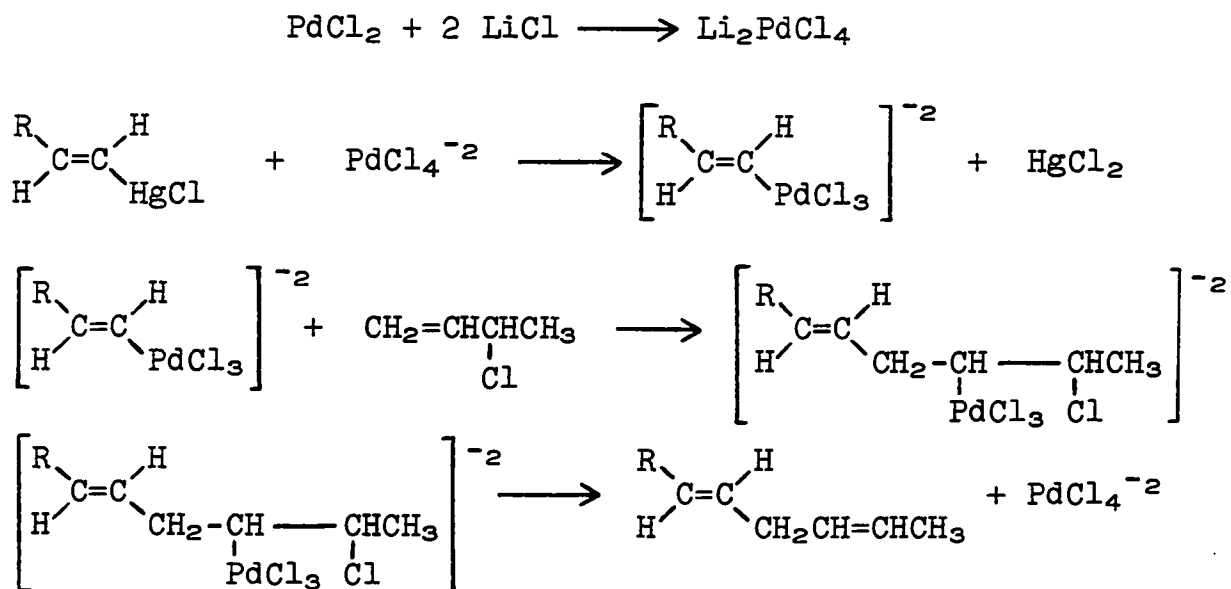
to be catalytic. One pathway for removal of palladium chloride is suggested by the major side product observed in these reactions, the symmetrical 1,3-diene. Larock (43) observed that this reaction required a stoichiometric amount of palladium chloride for optimum yields and that metallic palladium was produced in the reaction. Likewise, in many of these reactions the rust red color of palladium chloride is replaced by the black color of finely divided palladium metal as the reaction proceeds. $PdCl_4^{-2}$ is suggested as the active species due to the requirement that added lithium chloride be present in the reaction. Other methods for the removal of palladium chloride can also be envisioned. If the intermediate palladium species undergoes β-hydride elimination rather than β-chloride elimination, the resulting palladium hydride would eliminate palladium metal and generate HCl. The HCl thus produced could cause cleavage of a carbon-palladium bond in either of the organopalladium intermediates. However, added bases, such as MgO, K_2CO_3, and Et_3N, did not improve the yields in the reaction of trans-1-hexenylmercuric chloride and allyl chloride. A number of unidentified minor side products appeared in these reactions and closer examination of these side products may prove useful in determining the mechanism.

C. Experimental Section

1. Reagents

All reagents were used directly as obtained commercially unless otherwise indicated. Tetrahydrofuran and ether were distilled from lithium aluminum hydride. All allylic chlorides were distilled before use. Dichloromethane was shaken with concentrated sulfuric acid, washed with water and saturated sodium chloride, dried over calcium chloride, and distilled.

The vinylmercuric chlorides were prepared using methods described in Chapter II. Palladium chloride was supplied by Matthey Bishop.

All GLC yields are corrected by the use of appropriate hydrocarbon internal standards and calculated correction factors.

2. Electrophilic approaches

The reaction of trans-1-hexenylmercuric chloride with allyl chloride and aluminum chloride at 0°C is representative of the procedure used for these studies. A 25 ml round bottom flask was flushed with nitrogen, charged with dichloromethane (10 ml), trans-1-hexenylmercuric chloride (1.0 mmol), allyl chloride (1.0 mmol), and decane (0.26 mmol). The mixture was cooled to 0°C in an ice bath and aluminum chloride (1.0 mmol) was added. Samples were removed at 0.25, 0.5,

1, 2, 6 and 12 hours and quenched in a 1:1 mixture of saturated sodium carbonate and saturated sodium potassium tartrate. GLC analysis of the samples showed no 1,4-diene in the reaction mixture. The aluminum powder reactions were carried out as above using 4 mmol of powdered aluminum.

2. Initial studies

All GLC reactions in this section were carried out using a similar procedure. A 50 ml roundbottom flask was flushed with nitrogen, charged with 10 ml of solvent, usually THF, and cooled to -78°C in a dry ice-acetone bath. The mercurial (1 mmol), lithium chloride (2 mmol), allylic chloride (1, 2, 5, or 10 mmol) and an internal standard (0.25 or 0.50 mmol of nonane, decane, or dodecane depending on the system under study) were then added and the reaction stirred under nitrogen and allowed to warm to room temperature slowly. The reaction was quenched by the addition of saturated ammonium chloride and the THF layer analyzed by GLC (10' DC-550 or 10' SE-30 at 90°C to 150°C depending on the system and standard chosen for the reaction).

3. The synthesis of 1,4-dienes

All GLC yields were determined as discussed above. Authentic samples of trans-6,6-dimethyl-1,4-heptadiene, 3-(trans-1-hexenyl)-cyclohexene, trans-1-cyclohexyl-1,4-penta-diene, and trans-1-cyclohexenyl-1,4-pentadiene were obtained

from G. Zweifel and were used for calculating correction factors and for verification of the products obtained. Correction factors for the remaining 1,4-dienes were obtained from the products of the various reactions, which were isolated by preparative GLC.

The following procedure for the preparation of trans-1-phenyl-1,4-pentadiene is representative of the procedure used in obtaining isolated yields. A 250 ml round bottom flask equipped with a gas-inlet tube and a side arm capped with a rubber septum was flushed with nitrogen, charged with THF (100 ml) and cooled to -78°C in an acetone-dry ice bath. Styrylmercuric chloride (10 mmol), lithium chloride (20 mmol), allyl chloride (100 mmol), and palladium chloride (10 mmol) were added and the reaction stirred magnetically while allowing the cooling bath to slowly warm to room temperature over night. The reaction was quenched by adding saturated ammonium chloride. After separating the layers the ammonium chloride solution was washed with two volumes of hexanes (mixture of isomers). The organic layers were then washed twice with saturated sodium chloride, and dried over anhydrous sodium sulfate. Removal of the solvent by careful distillation yields a yellow oil. Distillation (Kugelrohr) at reduced pressure (25 mm, ~100°C) results in 1.09 g (76%) of a colorless liquid. ^{1}H NMR (CCl$_4$) δ2.9 (2 H, t, $\underline{J}$=6 Hz, =CH-C$\underline{H}_2$-CH=), 5.0 (2 H, m, =CH$_2$), 5.5-6.2 (3 H, m, remaining vinyls), 7.2 (5 H, br s, -C$_6$H$_5$), ir (thin film) (max) 3090,

3070, 3040, 3010, 2980, 2900, 2840, 1950, 1880, 1805, 1640,
1605, 1580, 1500, 1450, 1430, 1415, 1310, 1265, 1075, 1030,
995, 970, 915, 740, and 690 cm^{-1}; $\underline{m}/\underline{e}$ 144.0917 ± 15 ppm
(calcd for $C_{11}H_{12}$, 144.0939).

Trans-1,4-nonadiene was isolated in like manner (care
must be taken in distilling off the solvent since the
1,4-diene is fairly volatile): ^{1}H NMR (CCl$_4$) δ0.95 (3 H,
t, $\underline{J}$=6 Hz, -CH$_3$), 1.4 (4 H, m, -CH$_2$'s), 2.05 (2 H, m,
=CH-CH$_2$-CH$_2$-), 2.75 (2 H, m, =CH-CH$_2$-CH=), 5.0 (2 H, m,
=CH$_2$), 5.4 (2 H, m, -CH=CH-), and 5.75 (1 H, m, -CH=CH$_2$); ir
(thin film) (max) 3080, 3030, 3010, 2960, 2930, 2880, 2860,
1640, 1465, 1430, 1375, 990, 970, and 910 cm^{-1}; $\underline{m}/\underline{e}$ 124.1234±
15 ppm (calcd for C_9H_{16}, 124.1252).

The following dienes were characterized after isolation
by preparative GLC (10' DC-550). Trans-2,6,6-trimethyl-1,4-
heptadiene (GLC of the product mixture shows several side
products including trans, trans-2,2,7,7-tetramethyl-3,5-octa-
diene): ^{1}H NMR (CCl$_4$) δ1.0 (9 H, s, $\underline{t}$-butyl), 1.7 (3 H, s,
CH$_3$-C̦=), 2.7 (2 H, m, =CH-CH$_2$-), 4.7 (2 H, m, =CH$_2$), 5.4 (2 H,
m, -CH=CH-); ir (thin film) (max) 3070, 3010, 2960, 2900,
2860, 1650, 1470, 1460, 1360, 1260, 970, and 880 cm^{-1}; $\underline{m}/\underline{e}$
138.1392 ± 12 ppm (calcd for $C_{10}H_{18}$, $\underline{m}/\underline{e}$ 138.1409). Trans,
trans- and cis, trans-7,7-dimethyl-2,5-octadiene (a 1.7:1 ratio
of isomers by GLC on a 50 m SE-30 glass capillary column,
identity of the respective peaks was not established): ^{1}H NMR
(CCl$_4$) δ1.0 (9 H, s, $\underline{t}$-butyl), 1.65 (3 H, m, =CH-CH$_3$), 2.70

(2 H, m, =CH-C$\underline{H}_2$-CH=), and 5.25 (4 H, m, vinyls); ir (thin film) (max) 3030, 2960, 2900, 2870, 2830, 1475, 1460, 1390, 1360, 1270, 1200, 1080, 1020, and 970 cm^{-1}; $\underline{m}/\underline{e}$ 138.1397 ± 9 ppm (calcd for $C_{10}H_{18}$, 138.1409). Trans-4,6,6-trimethyl-1,4-heptadiene: ^{1}H NMR (CCl$_4$) δ1.1 (9 H, s, $\underline{t}$-butyl), 1.7 (3 H, d, $\underline{J}$=1 Hz, CH$_3$-$\overset{|}{C}$=), 2.6 (2 H, d of d, $\underline{J}$=1 and 6 Hz, -CH$_2$-CH=), 4.9 (1 H, br m, -CH=), 5.2 (3 H, m, -CH=CH$_2$); ir (thin film) (max) 3080, 3010, 2960, 2910, 2870, 1640, 1480, 1470, 1440, 1390, 1370, 1225, 1205, 1155, 1030, 995, 915, 850, and 815 cm^{-1}; $\underline{m}/\underline{e}$ 138.1389 ± 14 ppm (calcd for $C_{10}H_{18}$, 138.1409). Trans-2-chloro-6,6-dimethyl-1,4-heptadiene (two products were obtained which were inseparable by preparative GLC): ^{1}H NMR (CCl$_4$) (taken on the mixture obtained) δ1.0 (9 H, overlapping $\underline{t}$-butyls), 3.0 (2 H, m, -CH$_2$-), 4.7-5.9 (4 H, m, vinyls); ir (thin film on the mixture) (max) 3100, 3040, 2960, 2900, 2870, 1740, 1635, 1620, 1480, 1465, 1430, 1390, 1365, 1260, 1200, 1130, 970, 890, 880, and 690 cm^{-1}; two parent ions were seen by mass spec, $\underline{m}/\underline{e}$ 158.0846 ± 10 ppm (calcd for $C_9H_{15}Cl$, 158.0862) and $\underline{m}/\underline{e}$ 166.1697 ± 15 ppm (calcd for $C_{12}H_{22}$, 166.1722), which were verified as being derived from the prepped peak (as opposed to being an artifact from preparative GLC) by GLC/mass spec. Trans-3,6,6-trimethyl-1,4-heptadiene: the correction factor for trans-2,6,6-trimethyl-1,4-heptadiene was used in determining this yield; four products were seen by GLC, two were identified as having molecular weights indicating isomers of the desired

1,4-diene by GLC/mass spec ($\underline{m}/\underline{e}$ 138) and one as being derived from two organic groups from the mercurial, possibly the symmetrical 1,3-diene, $\underline{trans}$, $\underline{trans}$-2,2,7,7-tetramethyl-3,5-octadiene ($\underline{m}/\underline{e}$ 166 for $C_{12}H_{22}$); the products were not isolated due to the low yield and complexity of the mixture.

VIII. CONCLUSION

The ready availability of organomercurials and the ease with which they are handled inspired me to examine some possible synthetic applications of these compounds. During the course of my work I have developed convenient syntheses of α,β-unsaturated ketones, symmetrical 1,3-dienes, biaryls and 1,4-dienes.

α,β-Unsaturated ketones are prepared from acid chlorides and aluminum chloride in dichloromethane at room temperature. The reaction is complete within five minutes and excellent yields are obtained from aliphatic or unsaturated acid chlorides. Aromatic acid chlorides react more slowly requiring thirty minutes for complete reaction and the yields are lower. A number of Lewis acids and solvents were surveyed. Dichloromethane is by far the best solvent for the reaction. Only three Lewis acids showed useful activity in the reaction; aluminum chloride, aluminum bromide, and titanium tetrachloride. Aluminum bromide was significantly less stereospecific than aluminum chloride. At -78°C titanium tetrachloride caused significant yields of stereochemically inverted enones to be formed. However the reaction was not reproducible and therefore was not synthetically useful. The reaction of benzoyl chloride with E-2-chloromercuri-4,4-dimethyl-2-pentene was studied in detail and gave evidence of an addition-elimination mechanism through its major rearrange-

ment product, 4,5-dihydro-2-phenyl-3,4,5,5-tetramethylfuran. The mechanism in the case of aliphatic acid chlorides may also involve an addition-elimination process although a direct substitution mechanism has not been ruled out.

Treating vinylmercuric chlorides with 1% [ClRh(CO)$_2$]$_2$ and lithium chloride in either THF or HMPA results in the formation of symmetrical 1,3-dienes and polyenes. The rhodium catalyst is highly catalytic and gives excellent yields under mild conditions. The proposed mechanism involves formation of an intermediate divinylrhodium(III) complex which then reductively eliminates the diene and regenerates the active rhodium(I) catalyst. Rhodium(III) chloride is also catalytic, but not as effective as [ClRh(CO)$_2$]$_2$. The reaction works well for vinylmercurials derived from terminal acetylenes but only poorly with more highly substituted vinylmercurials.

Biaryls are obtained from arylmercuric chlorides by reacting them with 1% [ClRh(CO)$_2$]$_2$ and lithium chloride in HMPA at 80°C. Yields are competitive with those obtained from the Ullmann reaction and are generally around 80-90%. The reaction fails with amines, acids, and hindered mercurials, but succeeds with most other types of arylmercuric chlorides.

1,4-Dienes are prepared from allylic chlorides, palladium chloride, and lithium chloride. The yields are variable, ranging from moderate to excellent. In some systems

palladium chloride proved to be catalytic, while in the remainder a full equivalent was necessary. The reaction is of value in those systems where it works well, but does not appear to be a general high yield reaction.

These new methods increase the synthetic value of vinylmercuric chlorides and should be valuable tools for the synthetic organic chemist.

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