I HETEROCYCLES OF BIVALENT AND QUADRIVALENT TIN II THE REDUCTION OF ALDEHYDES AND KETONES WITH ORGANOTIN HYDRIDES

OSCAR FRANCIS BEUMEL JR.

Follow this and additional works at: https://scholars.unh.edu/dissertation

Recommended Citation
https://scholars.unh.edu/dissertation/767

This Dissertation is brought to you for free and open access by the Student Scholarship at University of New Hampshire Scholars' Repository. It has been accepted for inclusion in Doctoral Dissertations by an authorized administrator of University of New Hampshire Scholars' Repository. For more information, please contact nicole.hentz@unh.edu.
I HETEROCYCLES OF BIVALENT AND QUADRIVALENT TIN II
THE REDUCTION OF ALDEHYDES AND KETONES WITH
ORGANOTIN HYDRIDES

Keywords
Chemistry, Organic

This dissertation is available at University of New Hampshire Scholars' Repository: https://scholars.unh.edu/dissertation/767
BEUMEL, Jr., Oscar Francis. I. HETERO-CYCLES OF BIVAulenT AND QUADRIVALENT TIN. II. THE REDUCTION OF ALDEHYDES AND KETONES WITH ORGANOTIN HYDRIDES.

University of New Hampshire, Ph.D., 1960
Chemistry, organic

University Microfilms, Inc., Ann Arbor, Michigan
I. HETEROCYCLES OF BIVALENT AND QUADRIVALENT TIN

II. THE REDUCTION OF ALDEHYDES AND KETONES WITH ORGANOTIN HYDRIDES

BY

OSCAR FRANCIS BEUMEL, JR.

B.S., University of Notre Dame, 1952

A THESIS
Submitted to the University of New Hampshire
In Partial Fulfillment of
The Requirements for the Degree of
Doctor of Philosophy

Graduate School
Department of Chemistry
June, 1960
This thesis has been examined and approved.

J. A. Smith

Date: May 23, 1960

Paul R. Jones

Date: May 23, 1960
ACKNOWLEDGEMENT

This research project was carried out in the Department of Chemistry of the University of New Hampshire under the supervision of Dr. Henry G. Kuivila.

I wish to express my sincere thanks to Dr. Kuivila for the unlimited assistance offered at all times. I would also like to thank the other members of the Chemistry Department for the cooperation and aid offered me.

This research was supported by the Office of Ordinance Research, U. S. Army.
TABLE OF CONTENTS

LIST OF TABLES

LIST OF ILLUSTRATIONS

Part I

I. INTRODUCTION ........................................... 2

II. RESULTS AND DISCUSSION ............................... 6

III. EXPERIMENTAL ........................................ 17

1. o-Bromobenzyl Bromide ................................. 17
2. p,p' -Dibromobibenzyl ................................ 17
3. 5,5-Diphenyl-10,11-dihydrodibenzo(b,f)stanniepin 18
4. 5,5-Dichloro-10,11-dihydrodibenzo(b,f)stanniepin 19
5. 5,5-Dimethyl-10,11-dihydrodibenzo(b,f)stanniepin 21
6. Cleavage of 5,5-Diphenyl-10,11-dihydrodibenzo(b,f)stanniepin with Bromine .......................... 21
7. 10,11-Dihydrodibenzo(b,f)stannoepin .................. 22
8. 5,5-Dichloro-10,11-dihydrodibenzo(b,f)stanniepin 24
9. 5-Thio-10,11-dihydrodibenzo(b,f)stanniepin ...... 24
10. 5-Oxo-10,11-dihydrodibenzo(b,f)stanniepin .... 25

IV. SUMMARY ................................................. 26

BIBLIOGRAPHY ................................................. 27

Part II

I. INTRODUCTION ........................................... 32

II. RESULTS AND DISCUSSION ................................ 34

1. General .................................................. 35
2. Reduction of Saturated Aldehydes ...................... 44
3. Reduction of Unsaturated Aldehydes ................... 44
4. Reduction of Saturated Ketones ....................... 46
5. Reduction of Unsaturated Ketones .................... 47
6. Reduction of Nitrocarbonyls ............................ 49
7. Stereochemistry of Reduction of Simple Cyclic Ketones .............................................. 49
8. Reduction of Ketosteroids: Structure of Products 58
9. Reduction of Ketosteroids: Stereochemistry of Products .............................................. 70
III. EXPERIMENTAL ........................................ 75

1. Preparation of Organotin Hydrides ............. 76
   a. Triphenyltin Hydride ...................... 76
   b. Tributyltin Hydride ....................... 77
   c. Diphenyltin Dihydride .................... 78
   d. Dibutyltin Dihydride ..................... 78
   e. Phenyltin Trihydride...................... 79
   f. Butyltin Trihydride ....................... 80
2. Reductions with Organotin Hydrides .............. 81
   a. Triphenyltin Hydride Reductions .......... 81
   b. Tributyltin Hydride Reductions .......... 83
   c. Diphenyltin Dihydride Reductions .......... 83
   d. Dibutyltin Dihydride Reductions .......... 92
   e. Phenyltin Trihydride Reductions .......... 98
   f. Butyltin Trihydride Reductions .......... 99
   g. Reduction of Ketosteroids ............... 102

IV. SUMMARY ............................................. 110

BIBLIOGRAPHY ........................................... 111

BIOGRAPHICAL DATA ................................. 113
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Number</th>
<th>Table Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Reduction of Aldehydes and Ketones with Diphenyltin Dihydride and Di-n-butyltin Dihydride</td>
<td>48</td>
</tr>
<tr>
<td>2.</td>
<td>Stereochemistry of Reduction of Cyclohexanones by Organotin Hydrides, Complex Metal Hydrides, and Aluminum Isopropoxide</td>
<td>52</td>
</tr>
<tr>
<td>3.</td>
<td>Reduction of Ketosteroids with Diphenyltin Dihydride</td>
<td>69</td>
</tr>
</tbody>
</table>
# LIST OF ILLUSTRATIONS

<table>
<thead>
<tr>
<th>Number</th>
<th>Illustration</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Heterocycle flow sheet</td>
<td>15</td>
</tr>
<tr>
<td>2.</td>
<td>Infrared absorption spectra of 5,5-Diphenyl-10, 11-dihydrodibenzo(b,f)stanniepin and 5,5-Di-methyl-10,11-dihydrodibenzo(b,f)stanniepin</td>
<td>28</td>
</tr>
<tr>
<td>3.</td>
<td>Infrared absorption spectra of 10,11-Dihydro-dibenzo(b,f)-stanniepin and 5,5-Dichloro-10, 11-dihydrodibenzo(b,f)stanniepin.</td>
<td>29</td>
</tr>
<tr>
<td>4.</td>
<td>Infrared absorption spectra of 5-Thio-10,11-dihydrodibenzo(b,f)stanniepin and 5-Oxo-10,11-dihydrodibenzo(b,f)stanniepin.</td>
<td>30</td>
</tr>
</tbody>
</table>
PART I

HETEROCYCLES OF BIVALENT AND QUADRIVALENT TIN
INTRODUCTION

Although the literature of organometallic compounds of group IV-A is quite extensive, that dealing with the heterocycles of these elements is limited. The early history of these heterocycles describes compounds of quite similar structure. In 1915 Bygden$^1$ prepared the first silicon heterocycles by treating pentamethylene dimagnesium bromide with silicon tetrachloride, dimethyldichlorosilane and diethyldichlorosilane.

\[
\text{BrMg(CH}_2)_5\text{MgBr} + \text{SiCl}_4 \rightarrow \text{Cl} \quad \text{(1)}
\]

\[
+ (\text{CH}_3)_2\text{SiCl}_2 \rightarrow \text{CH}_2 \quad \text{(2)}
\]

\[
+ (\text{Et})_2\text{SiCl}_2 \rightarrow \text{Et} \quad \text{(3)}
\]

Except for silicon, whose chemistry has recently been greatly expanded, these three reactions describe the complete reported chemistry of group IV-A heterocycles.
series was selected for study for several reasons. First, Letsinger and Skoog had recently published a paper in which the preparation of a seven membered heterocycle of boron had been described; the starting material which they had used was readily available and might easily be used to prepare some tin heterocycles.

\[
\begin{align*}
\text{Li} & \quad \text{CH}_2\text{-CH}_2 & \quad \text{Li} \\
\text{B} & \quad \text{(BuO)}_2\text{B} & \quad \text{P} \\
\text{Bu} & \quad \text{O} \\
\end{align*}
\]

Second, no tin heterocycles with rings of this size had been prepared. Third, it seemed reasonable to expect that both quadrivalent and bivalent tin could be introduced into the ring if the tin were attached to the two aromatic rings since it has been shown that diphenyltin dihydride decomposes with hydrogen evolution to form diphenyltin. 10

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{Sn} & \quad \text{Sn} \\
\end{align*}
\]

It was supposed that the analogous reaction could be affected with the dibenzocycloheptadiene system.
The analogous reaction for dialkyltin dihydrides has not been reported.
RESULTS AND DISCUSSION

The first attempts at ring closure followed the pattern used in previous syntheses of group IV-a heterocycles. α-Bromotoluene was photobrominated to form α-bromobenzyl bromide.

\[
\text{CH}_3\text{Br} + \text{Br}_2 \xrightarrow{H_\text{v}} \text{CH}_2\text{Br} + \text{HBr}
\]

A half-mole of phenyllithium was added to the α-bromobenzyl bromide to effect a halogen-metal interconversion, and coupling took place to form α,α'-dibromobibenzyl.

\[
\text{CH}_2\text{Br} \quad \text{Li} \quad \rightarrow \quad \text{CH}_2\text{Li} \quad \text{Br} + \text{Br}
\]

Two moles of butyllithium was added to this to effect another halogen-metal interconversion and form α,α'-dilithiobibenzyl.
This lithium reagent was allowed to react with diphenyltin dichloride under varying conditions. The product obtained was always a colorless, amorphous, polymeric mass which was infusible, and insoluble in all solvents tried. These included ethanol, acetone, ether, benzene and ethyl acetate. Present also in yields of 1-3% was the monomeric, cyclic product 5,5-diphenyl-10,11-dihydridobenzo(b,f)stanniepin.*

* Since both bicovalent and quadricovalent tin heterocycles are described in this paper, the nomenclature used must distinguish between these two kinds of tin. We have chosen to indicate this distinction with the classical -ic and -ous suffixes. A stanniepin will contain quadrivalent tin in the ring, and a stannoepin will contain bivalent tin in the ring.
Chromatography of the mother liquors on alumina failed to show the presence of more monomer. After repeated recrystallizations, the product melted 136-137° if the last solvent used was ligroin (60-90°) and 146-147° if the last solvent used was 95% ethanol. The lower melting form could be converted to the higher melting form by heating at its melting point for a few minutes.

It was then decided to attempt a ring closure of the $o,o'$-dilithiobibenzyl with dimethyltin dichloride. Again, a polymeric mass was obtained but it was separated into a series of fractions, none pure, melting from room temperature to above 250°. This work was abandoned since the yield of monomer, if present, was necessarily small.
This approach was obviously unsatisfactory since polymer formation seemed to be the main reaction. It was therefore necessary to devise an approach where polymerization could be minimized, such as infinite dilution techniques, or one where polymerization would prove to be less of a disadvantage. Because of the chemical behavior of organic groups attached to a tin atom, the second method was chosen.

One mole of o,o'-dilithiobibenzyl was allowed to react with a half-mole of stannic chloride. The expected products of this reaction would be a spiro compound or polymeric products in which the chlorine atoms on the tin are replaced by the o-phenyl groups of the bibenzyl.
This mixture was isolated but not purified and heated with another half-mole of stannic chloride.

Now it is known that if tetraphenyltin is heated with varying amounts of stannic chloride, or the two even allowed to stand together for a sufficient length of time at room temperature, triphenyltin chloride, diphenyltin dichloride, and phenyltin trichloride can be isolated. In the present case it seemed reasonable to suppose that

\[
\text{Ph}_4\text{Sn} + \text{SnCl}_4 \rightarrow \text{Ph}_3\text{SnCl} + \text{Ph}_2\text{SnCl}_2 + \text{PhSnCl}_3
\]

5,5-dichloro-10,11-dihydrodibenzo(b,f)stanniepin would be the lowest boiling of any of the possible products of the reaction since it would have by far the lowest molecular weight. This appears to be borne out by the fact that 35% yields of the dichloro compound (m.p. 106-107°) were obtained when the reaction mixture was heated above the boiling point of the monomer and the distillate collected over a period of
several hours. The observations that the molecular weight and analysis of this compound agree with those of the proposed structure are taken as evidence that it, and each of the other compounds described below is cyclic, rather than polymeric.

The diphenyl compound whose synthesis was first attempted was now quite readily prepared by allowing the dichloride to react with phenyllithium. The yield was 83%. Thus, the over-all yield of this compound from $o$-$o'$-dibromobibenzyl is improved to 29% from less than 3%.

\[
\begin{align*}
\text{PhLi} & \quad \text{Sn} & \quad \text{Ph} \\
\text{Cl} & \quad \text{Cl} & \quad + 2 \text{LiCl}
\end{align*}
\]

The dimethyl compound whose synthesis was previously attempted by direct cyclization was also easily prepared by allowing the dichloride to react with methyl magnesium bromide. The yield was 73%. It proved to be a liquid at room temperature. This product was cleaved by adding bromine
in carbon tetrachloride. An 85% yield of 2,2'-dibromobibenzy1 was obtained. The other expected product, dimethyltin dibromide was not isolated.

The dichloride was then allowed to react with alcoholic sodium hydroxide, whereupon a quantitative yield of the polymeric oxide was obtained. This is an insoluble, infusible, colorless solid as are the other known diorgano-tin oxides.

The bivalent tin heterocycle 10,11-dihydrodibenzob (b,f)stannoepin (IX) was prepared using a reaction sequence developed in these laboratories by Albert K. Sawyer. The dichloride was treated with an excess of lithium aluminum hydride and apparently formed the dihydride (X) (as diphenyltin
dichloride produces the dihydride under similar conditions.)
This dihydride decomposed upon standing at room temperature when the ether solution was poured into methanol. Hydrogen was evolved slowly and the analytically pure bivalent heterocycle precipitated out of solution in 70-90% yields. The color of the material varied from colorless to bright yellow. The first material to form was generally colorless and melted in the neighborhood of 60°. As precipitation continued, the material became more and more yellow with higher melting points until the last material obtained usually melted above 160°. The colorless material is very soluble in normal organic solvents with the exception of the alcohols. As the color deepens the solubility lessens until the brighter yellow fractions are quite insoluble. Apparently, color and melting point are indications of an increasing degree of polymerization of the product obtained. Diphenyltin is known to exist in several modifications which differ in molecular weight, solubility, color and crystalline form,
\[ \text{C}_{14}\text{H}_{12}\text{Sn} \rightarrow (\text{C}_{14}\text{H}_{12}\text{Sn})_x \]

as well as reactivity.

Chlorine gas was bubbled through a solution of the bivalent tin compound in a methylene chloride solution and produced a nearly quantitative yield of the dichloride. This lends support to its structure. It was also allowed

\[ \begin{array}{c}
\text{Sn} \\
\text{Sn}
\end{array} + \text{Cl}_2 \rightarrow \begin{array}{c}
\text{Sn} \\
\text{Cl} \\
\text{Cl}
\end{array} \]

to react with sulfur in toluene to form the sulfide, in 85% yield. After repeated attempts at purification the sample could not be made analytically pure, however.

\[ \begin{array}{c}
\text{Sn} \\
\text{Sn}
\end{array} + \text{S}_8 \rightarrow \begin{array}{c}
\text{Sn} \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \\
\cdot \cdot \cdot \"]

All of the above reactions are summarized on the flow sheet.
Having prepared these derivatives of the dibenzo-
stanniepin and dibenzostannoepin series a simpler system
was sought which would allow varying the ring size and
placing functional groups in the ring.

Van der Kerk and coworkers recently reported the
addition of organotin hydrides to aliphatic double bonds.
It was thought that the addition of an organotin dihydride
to two molecules of a substance with both a double bond
and some functional group would provide a molecule that
\[
\text{Ph}_2\text{SnH}_2 + 2 \text{CH}_2=\text{CH-C-CH}_3 \rightarrow \text{Ph}_2\text{Sn} (\text{CH}_2-\text{CH}_2-\text{C-CH}_3)_2
\]
could be cyclized by conventional means. By varying the
chain lengths a whole series of compounds with varying
ring sizes could be formed.

Methyl vinyl ketone was allowed to react with
diphenyltin dihydride. However, instead of obtaining the
addition product, diphenyltin was observed to precipitate
out of solution but there was no evolution of gas which
should accompany decomposition of the hydride. An infrared
spectrum showed that the ketone had been reduced to an
\[
\text{Ph}_2\text{SnH}_2 + \text{CH}_2=\text{CH-C-CH}_3 \rightarrow \text{Ph}_2\text{Sn} + \text{CH}_2=\text{CH-CH-CH}_3
\]
alcohol. Since this reduction appeared to be of more
general interest than the heterocycle synthesis it was
decided to discontinue work with tin heterocycles for the
present time and to study the reduction of carbonyls with
organotin hydrides.
EXPERIMENTAL

Tin analyses were carried out by the method of Gilman and Rosenberg.\textsuperscript{12} Other analyses were performed by The Galbraith Laboratories, Knoxville, Tennessee. Melting points are uncorrected.

**o-Bromobenzyl Bromide** was prepared according to the method of Letsinger and Skoog\textsuperscript{8} with modifications as indicated.

Bromine (172 ml., 3.55 moles) was added dropwise over a three-hour period to 547 g. (3.55 moles) of \(\text{o-bromotoluene}\) illuminated by a 150 watt incandescent lamp. The mixture was stirred throughout the addition period and for one additional hour. Distillation yielded 617 g. (74\%) of \(\text{o-bromobenzyl bromide}\); b.p. 127-133° (15 mm.) (Letsinger and Skoog used a mercury arc lamp for irradiation and obtained a 59\% yield of bromide.)

**o,o'-Dibromobenzyl** was prepared according to the method of Letsinger and Skoog.\textsuperscript{8}

Phenyllithium (890 ml. of a 1.06 N ether solution) was added slowly to a solution of 492 g. (1.97 moles) of \(\text{o-bromobenzyl bromide}\) in 500 ml. of ether. During the addition of the phenyllithium the ether refluxed spontaneously. The next day the pale yellow solution was hydrolyzed with 300 ml. of water, the resulting layers were separated, and the ether layer was washed, dried and distilled. The bromo compound distilled at 193-200° at 5 mm. and solidified
on cooling. After recrystallization from 125 ml. of ethanol it melted at 83°; weight 191 g. (60% yield). The reported melting point is 84.5°. 9

5,5-Diphenyl-10,11-dihydrodibenzo(b,f)stanniepin. A. To 200 ml. of 0.345 M butyllithium in ether, cooled in an ice-water bath, was added 78 g. (0.031 mole) of \( \text{\textsubscript{2}} \text{,2}' \)-dibromobibenzyl in 100 ml. of ether over a period of about one hour. (A nitrogen atmosphere was maintained throughout the reaction.) The ice-bath was then removed and the mixture was stirred for 1.5 hours, and 11.6 g. (0.039 mole) of diphenyltin dichloride dissolved in 100 ml. of ether was then added dropwise over 0.5 hour. After stirring for an hour at room temperature, the reaction mixture was heated under reflux for two hours and then allowed to stand overnight.

The white solid present in the reaction mixture was removed by filtration and digested with boiling water to remove the lithium salts. There remained 3 g. of a colorless, insoluble, and infusible solid, which was apparently polymeric. This material was discarded. The ethereal filtrate was concentrated by passing a stream of air over it. A precipitate gradually appeared as concentration progressed. When the liquid volume reached 10 ml., 4.4 g. of this material had been obtained. This solid was recrystallized repeatedly from ethanol and ligroin. If ethanol was the last solvent used the product had m.p. 146-147°. When this was recrystallized from ligroin it
melted at 136-137°. When this lower melting product was
heated above its melting point for a few minutes it resolid-
ified and then melted at 146-147°. The yield of pure
product amounted to 1-3%.

Anal. Calcd. for C_{26}H_{22}Sn: C, 68.91; H, 4.91;
Sn, 26.19. Found: C, 68.48, H, 5.03; Sn, 25.90.

B. 5,5-Dichloro-10,11-dihydrodibenzo(b,f)stannie-
pin (1 g., 0.0027 mole) was dissolved in 25 ml. of ether
and added dropwise to 0.0068 mole of phenyllithium in 25 ml.
of ether. The reaction mixture was heated under reflux for
two hours, then hydrolyzed with 30 ml. of water. The ether
layer was evaporated to dryness and taken up in 10 ml. of
60-90° ligroin, treated with decolorizing charcoal, filtered
and cooled. The yield was 0.94 g. (82.5%) of crystals,
m.p. 145-146°, undepressed upon admixture with those
described above. Furthermore, the two samples showed
identical infrared spectra.

5,5-Dichloro-10,11-dihydrodibenzo(b,f)stanniepin.

2,2'-Dibromobibenzyl (25.2 g., 0.074 mole) dissolved in 200
ml. of diethyl ether was added dropwise to 0.50 mole of
butyllithium in 200 ml. of ether cooled in an ice-bath.
After the addition was complete, the flask was heated under
reflux for an hour. It was then cooled in an ice-bath, and
9.6 g. (0.037 mole) of anhydrous stannic chloride in 10 ml.
of benzene was added dropwise. Again the solution was
heated under reflux for two hours. After cooling, the solution was hydrolyzed with distilled water. The ether layer was dried over calcium chloride and then evaporated until nothing could be removed at steam-bath temperature and aspirator vacuum.

Stannic chloride (9.6 g., 0.037 mole) was again added, the mixture heated on a steam-bath for a half-hour, and then placed in a bath at 150° for three hours. (Both larger and smaller amounts of stannic chloride were added at this point, but the best yield was obtained when a mole per mole ratio was used. An attempt was also made to add all the stannic chloride in the first step. The yield dropped off sharply if this or other modifications were made to the method used.) The contents of the flask were then distilled under vacuum. The fraction boiling from 175-190° (0.4 mm.) was collected. In actual operation, the pot temperature was raised to about 225-250° and maintained there for several hours. As the monomer formed in the equilibrium mixture of polymeric material it distilled and was collected. It was only in this way that a satisfactory yield could be obtained, since essentially all the material was initially polymeric. The distillate was a pale yellow and crystallized in the receiver. It was washed with 5 ml. of petroleum ether (40-60°) which removed the color. It was then dried and dissolved in 50 ml. of ether and filtered through a bed of decolorizing charcoal. The product was recrystallized by allowing the ether to evaporate
at room temperature to near dryness. After two recrystal-
lizations 9.8 g. (35.7%) of crystalline solid was obtained,
m.p. 106-106.5°.

Anal. Calcd. for C_{14}H_{12}Sn: C, 45.46; H, 3.27;
Cl, 19.17; Sn, 32.09; molecular weight, 369.9. Found:
C, 45.39; H, 3.39; Cl, 19.1; Sn, 31.39; molecular weight,
380 (isopiestic in CH_{2}Cl_{2}).

5,5-Dimethyl-10,11-dihydrodibenzo(b,f)stanniepin.
Methylmagnesium bromide was prepared from 0.786 g, (0.0324
mole) of magnesium in 200 ml. of ether. To this was added
a solution of 3 g. (0.0081 mole) of 5,5-dichloro-10,11-
dihydrodibenzo(b,f)stanniepin in 50 ml. of dry ether. The
mixture was stirred at room temperature for two hours. It
was then hydrolyzed with 50 ml. of 1% hydrochloric acid
solution, the two layers were separated and the ether layer
was dried over magnesium sulphate. The mixture was filtered
and the ether distilled off on a steam-bath, leaving a
colorless oily residue. The oil obtained was distilled
under vacuum and the fraction boiling 130-135° (0.2 mm.)
n^2_{D} 1.6130, was collected. The yield was 73%, 1.95 g.

Anal. Calcd. for C_{16}H_{18}Sn: C, 58.36; H, 5.47;
Sn, 36.08. Found: C, 58.26; H, 5.51; Sn, 35.63.

Cleavage of 5,5-Dimethyl-10,11-dihydrodibenzo(b,f)
stanniepin with Bromine. 5,5-Dimethyl-10,11-dihydrodibenzo
(b,f)stanniepin (1.016 g., 0.00309 mole) was dissolved in
10 ml. of \( \text{CCl}_4 \). Bromine (0.989 g., 0.00618 mole) dissolved in 10 ml. of \( \text{CCl}_4 \) was added dropwise. The solution was decolorized immediately.

Removal of the solvent left a colorless crystalline residue which was dissolved in 25 ml. of ether and extracted with four 10 ml. portions of distilled water. The ether layer was treated with decolorizing charcoal and filtered. The filtrate was evaporated and 0.978 g. (93% yield) of \( \text{o, o'} \)-dibromobibenzyl, m.p. 77-81°, was obtained. Recrystallization from 60-90° ligroin gave 0.79 g. (75%) of product melting 81-83°. Mixture melting point with an authentic sample gave no depression.

**10,11-Dihydrodibenzo(b,f)stannoepin.** Finely divided lithium aluminum hydride (0.394 g., 0.01 mole, 100% excess), was suspended in 20 ml. of dry ether and cooled in an ice-bath. Then solid 5,5-dichloro-10,11-dihydrodibenzo(b,f)-stanniepin (3.70 g., 0.01 mole), was added in five approximately equal portions at 5 minute intervals. After the addition was complete the mixture was stirred for a half-hour.

A mixture of 1 ml. of methanol and 1 ml. of ether was added dropwise very slowly, followed by the addition of 10 ml. of distilled water. (It is important that this hydrolysis be done slowly so that the temperature does not rise to room temperature. Any warming will cause excessive polymerization of the product as revealed by a yellow color and low solubility.)
The mixture was stirred for an additional 10 minutes. The ether layer was washed three times with 10 ml. portions of ice-cold water, and then filtered into 50 ml. of methanol and allowed to stand at room temperature in the dark, under nitrogen.

After standing for from one to three hours a precipitate began to form and gas began to evolve. At first the precipitate was a sticky white semi-solid and later, a pale yellow solid. It was collected in several fractions and dried in vacuum desiccator. All fractions turned solid and the fractions which precipitated first were more soluble in organic solvents than the later, light yellow fractions. The yield was 2.69 g. or 90%.

Melting points were taken of one typical series of products. The following results were obtained; the temperatures listed are the lowest temperatures which would give complete melting on immersion in a pre-heated bath.

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Weight g.</th>
<th>M.p., °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.222</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>0.717</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>0.344</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>0.104</td>
<td>86</td>
</tr>
<tr>
<td>5</td>
<td>0.230</td>
<td>160</td>
</tr>
</tbody>
</table>

Anal. Calcd. for C_{14}H_{12}Sn: C, 56.26; H, 4.02; Sn, 39.72. Found: C, 56.39; H, 4.12; Sn, 39.50.
**5,5-Dichloro-10,11-dihydrodibenzo(b,f)stanniepin.** 10,11-Dihydrodibenzo(b,f)stannoepin (2.2 g., 0.0074 mole) was dissolved in 15 ml. of methylene chloride. Chlorine gas was bubbled in slowly until the white precipitate which formed at first completely disappeared. Ligroin (60-90°, 5 ml.) was added and the methylene chloride was allowed to evaporate; yield 2.2 g. (81%), m.p. 106-107°. Mixture melting point with a sample made by the previously described method gave no depression.

**5-Thio-10,11-dihydrodibenzo(b,f)stanniepin.** Flowers of sulfur (0.18 g., 0.057 mole), was placed in 50 ml. of toluene and heated under reflux until the sulfur dissolved. The solution was filtered and 1.5 g. (0.0445 mole) of 10,11-dihydrodibenzo(b,f)stannoepin was added as a finely divided solid. The flask was stoppered tightly and allowed to stand overnight.

The following day there was colorless crystals and a small amount of brown powdery material in the reaction mixture. It was then evaporated to dryness and the sulfide recrystallized repeatedly from methylene chloride; yield 1.15 g. (69%), m.p. 274-275°.

**Anal.** Calcd. for C_{14}H_{12}SSn: C, 50.81; H, 3.63; S, 9.69; Sn, 35.86. Found: Preparation 1: C, 48.80; H, 3.99; S, 9.02. Preparation 2: C, 48.58, 48.45; H, 3.74, 3.65; S, 9.60; Sn, 34.13, 34.12.
5-Oxo-10,11-dihydrodibenzo(b,f)stanniepin.  5,5-Dichloro-10,11-dihydrodibenzo(b,f)stanniepin (1.5 g., 0.0405 mole) was dissolved in 10 ml. of 1,4-dioxane and 0.0648 g. (0.0162 mole) of NaOH dissolved in 10 ml. of 50% ethanol-water mixture was added. A precipitate formed immediately. The mixture was placed on a steam-bath for an hour. It was then filtered and washed repeatedly with distilled water. The solid was then dried and digested in boiling water for an hour. Again it was filtered and washed, then dried overnight in a drying pistol: yield 1.1 g. (86.5%).

Anal. Calcd. for C_{14}H_{12}OSn:  C, 53.41; H, 3.81; Sn, 37.70. Found:  C, 53.35; H, 3.88; Sn, 37.66.

Infrared spectra were obtained using KBr pellets containing 1% of the sample with the exception of the dimethyl derivative which was run as a smear.
SUMMARY

The preparation of heterocycles of tin with structures I and II are described. Compound II is the first known heterocycle of divalent tin. The cyclic structures are assigned on the basis of elemental analysis, molecular weight and cleavage by bromine to produce \( o,o' \)-dibromo-bibenzyl.
BIBLIOGRAPHY

1. A. Bygden, Ber., 48,1236(1915).
    K. A. Kocheskov, M. M. Nad and A. P. Alexandrov, ibid.,
    64,628(1931).
5,5-Diphenyl-10,11-dihydrodibenz[b,f]stanniepin

5,5-Dimethyl-10,11-dihydrodibenz[b,f]stanniepin
10,11-Dihydrodibenzo(b,f)stannoeepin

5,5-Dichloro-10,11-dihydrodibenzo(b,f)stannoeepin
5-Thio-10,11-dihydrodibenzo(b,f)stanniepin

5-Oxo-10,11-dihydrodibenzo(b,f)stanniepin
PART II

THE REDUCTION OF ALDEHYDES AND KETONES WITH ORGANOTIN HYDRIDES
INTRODUCTION

The discovery that diphenyltin dihydride reduced methyl vinyl ketone to methyl vinyl carbinol rather than adding across the double bond seemed quite interesting. It was felt that it was worthy of further study at this time. The fact that diphenyltin dihydride was a reducing agent was, although interesting, not too surprising. The real surprise lay in the formation of diphenyltin as the other product in the reduction reaction.

When any of the complex metal hydrides is allowed to react with a ketone, a hydrogen is added to the carbonyl carbon and the metal is added at the oxygen. Hydrolysis of this alkoxide adds the second hydrogen to the alcohol. In the case of diphenyltin dihydride, both hydrogens come from

$$\text{R-C-R} + \text{MH} \longrightarrow \text{R-CH-R}$$

$$\text{R-CH-R} + \text{H}_2\text{O} \longrightarrow \text{R-CH-R} + \text{HOM}$$

the reducing agent which halves the reducing power of the hydride but makes the hydrolysis step unnecessary. It is

$$\text{Ph}_2\text{SnH}_2 + \text{R-C-R} \longrightarrow \text{Ph}_2\text{Sn} + \text{R-CH-R}$$

therefore possible to carry out the reduction and isolation under anhydrous conditions.

After a number of aldehydes and ketones were reduced with diphenyltin dihydride and it appeared that it was a fairly general reducing agent, dibutyltin dihydride,
butyltin trihydride, tributyltin hydride, phenyltin trihydride and triphenyltin hydride were prepared and attempts were made to use them as reducing agents.

The mechanism of the reduction is unknown, except that it is not the same as that for the usual complex metal hydrides. This left open the possibility that if the attacking species was the organotin hydride molecule, then the great bulk of the tin atom might play an important role in the stereochemistry of the reductions with these hydrides. Also, if the large tin atom has an effect, might not the progression from butyltin trihydride to triphenyltin hydride not also have an effect upon the composition of the product? If this were true then not only a new method of reduction has been found, but many stereochemically different compositions of products of the reduction might be obtainable by varying the organic groups attached to the tin.

First, several reductions were studied to see just what aldehydes and ketones could and could not be reduced. Then the stereochemistry of several reductions with various organic groups attached to the tin were studied. Lastly, the selectivity of the reducing agent was investigated by attempting to reduce polyketones stepwise. Five steroids were reduced in this phase of the research.
RESULTS AND DISCUSSION
GENERAL

In studying the reductions with organotin hydrides it was decided to use the mono-, di-, and trihydrides of an aliphatic and an aromatic tin compound. The representative organic groups chosen were the n-butyl and phenyl groups. The following hydrides were prepared by reducing the corresponding organotin chlorides with lithium aluminum hydride, a method which has been described previously.\(^1,2\)

\[
\begin{align*}
4R_3SnCl + LiAlH_4 & \longrightarrow 4R_3SnH + LiCl + AlCl_3 \\
2R_2SnCl_2 + LiAlH_4 & \longrightarrow 2R_2SnH_2 + LiCl + AlCl_3 \\
4RSnCl_3 + 3LiAlH_4 & \longrightarrow 4RSnH_3 + 3LiCl + 3AlCl_3
\end{align*}
\]

The triorganotin hydrides are clear, colorless viscous liquids which are thermally stable at room temperature and decompose slowly around 125°. They must be protected from the atmosphere since they react with oxygen to form a white amorphous oxide.

\[
2R_3SnH + O_2 \longrightarrow 2R_3SnOH \longrightarrow R_3Sn-O-SnR_3 + H_2O
\]

Van der Kerk\(^3\) and coworkers have shown that they add readily across the double bond in an olefin to form a saturated tin compound.

\[
R_3SnH + CH_2=CH-R \longrightarrow R_3Sn-CH_2-CH_2-R
\]

They have also shown that they are capable of reducing an aromatic halide to the hydrocarbon.\(^3\)
In these laboratories, Dr. Kuivila has shown that they react with aliphatic halides forming the hydrocarbon. This particular reaction is highly exothermic.

\[
\text{R}_3\text{SnH} + \text{PhBr} \rightarrow \text{R}_3\text{SnBr} + \text{Ph-H}
\]

It has been found in the course of these studies that the triorganotin hydrides react with carbonyl compounds to form alcohols and hexaorganoditins.\(^4\) The reaction is slow and requires heating near 100° for the triphenyl and 140° for the tributyltin hydride to reduce benzaldehyde in a reasonable length of time. At these temperatures, the reductions are complete in several days. In the presence of both a double bond and a carbonyl group the triorganotin hydrides will sometimes add across the double bond and sometimes reduce the carbonyl to the corresponding unsaturated alcohol.\(^2\)

A competing reaction is the thermal decomposition of the hydrides which gives the same tin products as the reduction reaction. The decomposition is slow at the reaction temperature, but so is the reduction, so it is necessary that

\[
2\text{R}_3\text{SnH} \rightarrow \text{R}_3\text{SnSnR}_3 + \text{H}_2
\]

an excess of hydride be present in order to assure complete reduction of the carbonyl.
The triorganotin hydrides are good organic solvents. While using them as reducing agents they were obtained pure by distillation and then mixed with the carbonyl to be reduced. A homogeneous solution was obtained in every instance.

The hexaphenylditin produced from the reductions with triphenyltin hydride crystallized as it formed in the course of the reaction. It was used as a qualitative guide as to the extent of decomposition of the hydride. Since it melts at 232°, it was necessary only to distill out the alcohol produced by the reduction. It is only slightly soluble in most organic solvents. It can be recrystallized from acetone or chloroform.

The hexabutylditin produced from the reductions with tributyltin hydride was a high boiling liquid. The alcohols were distilled from the mixture. When distillation of the hexabutylditin was attempted, tetrabutyltin and tin were obtained.

\[ 2 \text{Bu}_3\text{SnSnBu}_3 \rightarrow 3 \text{Bu}_4\text{Sn} + \text{Sn} \]

The diorganotin dihydrides are clear, colorless, mobile liquids. Dibutyltin dihydride is relatively stable at room temperature. It can be stored indefinitely at room temperature in sealed ampoules or it can be stored in a tightly stoppered flask that has been flushed with nitrogen. Shelf life is prolonged if it is kept in a refrigerator. It is readily distilled under vacuum (below 10 mm. of pressure),
but decomposes very rapidly if heated near 125°.

Diphenyltin dihydride is unstable at room temperature and can be prepared and handled only near 0°. It can be prepared by reducing the dichloride with lithium aluminum hydride while being cooled in an ice-water bath. Any attempt to distil the product even under high vacuum leads to the formation of the yellow solid, diphenyltin. The hydride can be isolated by evaporating down an ether solution of the hydride under vacuum at -78°, which yields a colorless solid. Slight warming produces the familiar colorless liquid. On warming to near room temperature, the liquid begins to decompose. For our purposes, the ether solution obtained from the reduction of the chloride proved to be quite satisfactory. Yields were obtained between 95-100% and no purification was necessary.

The competing side reactions noted with the triorganotin hydrides are present here also, but with different emphasis. Where the triorganotin hydrides oxidized slowly in air, dibutyltin dihydride reacted fairly rapidly and diphenyltin dihydride reacted very rapidly to form the white, amorphous, polymeric oxide, which precipitated out of solution.

\[ \text{R}_2\text{SnH}_2 + \text{O}_2 \rightarrow (\text{Sn-O})_x + \text{H}_2\text{O} \]

It is of the utmost importance to keep air from contact with these hydrides.
Addition of the hydrides across the double bond of a compound, on the other hand, was greatly diminished. Reduction of methyl vinyl ketone with dibutyltin dihydride, for instance, gave a sixty percent yield of the unsaturated alcohol. This held true for all of the unsaturated carbonyls tested. With diphenyltin dihydride, no addition across a double bond was noted. If it took place at all, it was a rather unimportant side reaction. Diphenyltin dihydride is therefore the best choice when reducing unsaturated carbonyls.

It has been found in these laboratories that diphenyltin exists in many forms differing mainly on the degree of polymerization. There are varying shades of color from white through yellow and orange to deep red. A colorless, crystalline form has been found as well. One white form is of low molecular weight (apparently a cyclic pentamer or hexamer) and is fairly soluble in most organic solvents with the notable exception of alcohols, mainly methanol, and amines. The yellow through orange forms are rather insoluble in most organic solvents.

In the course of the reductions of carbonyls with diphenyltin dihydride, the white form of diphenyltin was produced. This is the form that is fairly soluble in ether. If the solution was filtered after standing for several hours, some diphenyltin was removed, but on further standing it continued to precipitate as polymerization continued. If a distillation of the alcohol from the reduction was attempted, the heat would speed this precipitation and
bumping would occur. It was therefore necessary to remove nearly all the diphenyltin before attempting a distillation. Standing for several weeks would cause the white form to turn yellow and its solubility decrease to nearly zero. This was not practical. Evaporating the mixture to near dryness, then redissolving it in methanol was effective due to the relative insolubility of the diphenyltin in methanol. After standing in methanol for an hour nearly all the diphenyltin had precipitated. Adding several drops of diethyl amine caused an immediate change in color and a heavy precipitate to form. This was very effective also. The amine also quickly decomposes any remaining hydride. As a last resort, the flask could be opened to the atmosphere and any diphenyltin in solution would quickly oxidize to the oxide. In practice, the use of methanol or diethyl amine after the reduction was complete proved to be the most useful methods.

Dibutyltin, which is the residue formed in the reduction reactions involving dibutyltin dihydride, is a viscous, lemon-yellow oil which is converted to a glass on cooling. It is soluble in most organic solvents with the exception of alcohols and in solution it is fairly reactive toward atmospheric oxygen. Out of solution it seems to form a protective film which protects the bulk of the material from oxidation. It is difficult to obtain an analytically pure sample of dibutyltin since it oxidizes so readily, but on the other hand it is very slow to form the polymeric oxide. It apparently forms some intermediate oxide which is
fairly stable. Several samples of dibutyltin were allowed
to stand for several months with cork stoppers sealing their
containers. Although the seal was not tight there was no
change in appearance. If methanol was added to these samples,
however, a colorless crystalline substance appeared which
melted 113–116° if air dried, with the melting point gradu-
ally falling to 80° or less if the sample was vacuum dried or
if it was heated near the melting point. Infrared showed
only bands that could be expected for dibutyltin with the
exception of a large hydroxy band. It was assumed at first
that this hydroxy band was due to a methanol complex being
formed. Recrystallization from acetone and acetonitrile gave
the same product, however. Although the tin analysis was
nearly a percent low, the carbon and hydrogen analysis were
very close to those for dibutyltin dihydroxide.

The organotin trihydrides were clear, colorless,
fluid liquids which were unstable at room temperature.
Phenyltin trihydride could be distilled at 39°/6 mm. with
some decomposition occurring during the distillation. At
room temperature it noticeably discolored in an hour and on
prolonged standing turned to a red solid with a tin-mirror
on the glass ampoule. It reacted quickly at first with
ketones, but after several days at room temperature a sample
contained both hydride and ketone as shown by infrared
analysis. Heating removed the hydride band, but the ketone
band remained. Using a 10% excess of the hydride, approxi-
mately 60% of a cyclohexanone sample was converted to
cyclohexanol when all the hydride was gone.

Butyltin trihydride was more stable than the phenyltin trihydride and could be distilled at atmospheric pressure with some decomposition occurring. Distilling at reduced pressure greatly increased the yield but extreme care had to be taken in removing the ether solvent from the hydride since the volatile hydride was easily distilled off with the ether. The pure, vacuum distilled product was stable at 0° and discolored slightly only after several hours at room temperature. It, too, decomposed to form hydrogen and a deep red solid. The solid did not decompose to form the tin mirror mentioned with the phenyltin trihydride, however.

The red \((\text{BuSn})_x\) mentioned above has not been reported in the literature. It can be prepared either by the thermal decomposition of butyltin trihydride or by using the hydride as a reducing agent. The samples that were obtained were a mixture of these two products, if they differ, since a large excess of butyltin trihydride was used in all the reactions.

The \((\text{BuSn})_x\), as well as the butyltin trihydride, was extremely reactive toward atmospheric oxygen. The reaction mixture was very carefully shielded with nitrogen during the course of the reaction and isolation of the alcohol. The alcohols were vacuum distilled and the vacuum broken with prepurified nitrogen. At this time the residue was a deep-red, heavy paste which was easily dissolved in chloroform or removed with a spatula. It was placed in a vacuum desiccator under nitrogen and dried at room temperature and
0.3 mm. for one day. A hard, red-orange solid resulted. It decolorized bromine and iodine solutions and reduced silver ions to metallic silver.

This dry solid, if finely divided heated up rapidly in air and gave off a foul smelling smoke. An old sample, thrown into a waste basket, started a fire. Even a momentary loss of the nitrogen atmosphere caused sufficient oxidation to prevent a satisfactory analysis.

The dried polymer was not very soluble in organic solvents and appeared to be a mixture of polymers. Some of it dissolved readily and some seemed virtually insoluble. Attempts to determine a molecular weight were abandoned since it was impossible to dissolve a sample completely.
REDUCTION OF SATURATED ALDEHYDES

In studying the reduction of carbonyl compounds it was decided first to determine which hydrides might be useful for this purpose by trying to reduce probably the most easily reducible carbonyl functional group, an aldehyde. Benzaldehyde was allowed to react with diphenyltin dihydride, triphenyltin hydride and tributyltin hydride.

Diphenyltin dihydride reacted vigorously and exothermally with benzaldehyde to give a 62% yield of benzyl alcohol. Triphenyltin hydride gave an 85.5% yield but only after heating the reaction mixture on a steam bath for fifteen hours. Tributyltin hydride, on the other hand, required 140° for fifteen hours to give an 86% yield of benzyl alcohol. This one example seems to indicate a scale of reactivity of these hydrides which carries through all other reactions.

REDUCTION OF UNSATURATED ALDEHYDES

The question now arises as to the competition between the reduction of the carbonyl group and the addition of the hydride across a carbon-carbon double bond. Several aldehydes with double bonds in the molecule were used for this purpose. Since it has been shown how difficult it was to reduce even benzaldehyde with the triorganotin hydrides and since van der Kerk has found it so easy to add them across double bonds, no attempt was made to use these hydrides as reducing agents with unsaturated aldehydes, however since
this work was completed it has been shown that methyl vinyl ketone could be reduced to methyl vinyl carbinol with triphenyltin hydride.\textsuperscript{23}

Crotonaldehyde (CH\textsubscript{3}CH=CHCH\textsubscript{2}O) was allowed to react with diphenyltin dihydride and dibutyltin dihydride. Both reactions were vigorous and exothermic. A yield of 59\% of crotyl alcohol was obtained from the diphenyltin dihydride reduction and a yield of 45.5\% was obtained from the dibutyltin dihydride reduction. The generally low yield with both hydrides was probably due to the impurity of the starting material but the difference in the yields was thought to be due to the addition of dibutyltin dihydride to the double bond of some of the crotonaldehyde or the alcohol.

Freshly distilled cinnamaldehyde was allowed to react with diphenyltin dihydride and dibutyltin dihydride. A 75\% yield of the unsaturated alcohol was obtained from the diphenyltin dihydride reduction. A 50\% yield of the unsaturated alcohol was obtained when dibutyltin dihydride was used.
REDUCTION OF SATURATED KETONES

Cyclohexanone, benzophenone and camphor were allowed to react with some of the organotin hydrides. Varying degrees of success were achieved.

Cyclohexanone reacted vigorously and exothermally with diphenyltin dihydride to give an 82% yield of cyclohexanol. Phenyltin trihydride even when in 27% excess, after standing for five days at room temperature gave only a weak hydroxyl absorption band in the infrared. Triphenyltin hydride and the ketone were heated on a steam bath for two days until all of the hydride had decomposed, yet only about half the ketone was reduced. Tributyltin hydride and cyclohexanone were heated at 140° for five days with only a trace of reduction occurring. Only the dihydrides appear to be stable enough, yet reactive enough to give a good yield of alcohol from a ketone without using a large excess of hydride.

Benzophenone reacted with diphenyltin dihydride to give a 59% yield of benzhydrol while dibutyltin dihydride gave a yield of 85%. d,l-Camphor gave only about 50% reduction with both diphenyltin dihydride and dibutyltin dihydride when the hydrides were used in 10% excess. In the latter case the reaction mixture was refluxed in isopropyl ether for 15 hours.
REDUCTION OF UNSATURATED KETONES

The reduction of methyl vinyl ketone with diphenyltin dihydride was the first experiment conducted. Several other unsaturated ketones were then tried to see if the reaction was general. Although methyl vinyl ketone reacted with diphenyltin dihydride to give a 59% yield of methyl vinyl carbinol, the reduction with dibutyltin dihydride gave yields ranging between 12 1/2% and 31% of the unsaturated alcohol. The addition side reaction apparently plays an important role in this case.

Chalcone and mesityl oxide both reacted readily with diphenyltin dihydride. The former gave a 75% yield of phenyl vinyl carbinol and the latter a 60% yield of 4-methyl-3-pentene-2-ol.

Benzoquinone gave a vigorous reaction with diphenyltin dihydride to give an 86% yield of hydroquinone and with dibutyltin dihydride to give a 66% yield. It was therefore somewhat surprising when anthraquinone did not react under the same conditions, but seemed instead to catalyze the decomposition of the diphenyltin dihydride.
### Table I

Reduction of Aldehydes and Ketones with Diphenyltin Dihydride and Di-\(n\)-butyltin Dihydride

<table>
<thead>
<tr>
<th>Carbonyl compound</th>
<th>(\text{Ph}_2\text{SnH}_2)</th>
<th>(\text{n-Bu}_2\text{SnH}_2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclohexanone</td>
<td>82</td>
<td>--</td>
</tr>
<tr>
<td>benzophenone</td>
<td>59</td>
<td>85</td>
</tr>
<tr>
<td>2-methylcyclohexanone</td>
<td>83</td>
<td>94</td>
</tr>
<tr>
<td>4-methylcyclohexanone</td>
<td>82.5</td>
<td>76.5</td>
</tr>
<tr>
<td>4-t-butylcyclohexanone</td>
<td>85.5</td>
<td>93.5</td>
</tr>
<tr>
<td>(\text{l-}\text{menthone})</td>
<td>81.5</td>
<td>81.5</td>
</tr>
<tr>
<td>(\text{d-}\text{carvone})</td>
<td>83.5</td>
<td>70.5</td>
</tr>
<tr>
<td>(\text{dl-}\text{camphor})</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>benzaldehyde</td>
<td>62</td>
<td>--</td>
</tr>
<tr>
<td>methyl vinyl ketone</td>
<td>59</td>
<td>31, 12.5</td>
</tr>
<tr>
<td>cinnamaldehyde</td>
<td>75</td>
<td>50</td>
</tr>
<tr>
<td>crotonaldehyde</td>
<td>59</td>
<td>43.5</td>
</tr>
<tr>
<td>mesityl oxide</td>
<td>60</td>
<td>--</td>
</tr>
<tr>
<td>chalcone</td>
<td>75</td>
<td>--</td>
</tr>
<tr>
<td>benzoquinone</td>
<td>59</td>
<td>66</td>
</tr>
<tr>
<td>anthraquinone</td>
<td>c</td>
<td>--</td>
</tr>
<tr>
<td>benzil</td>
<td>87.5</td>
<td>93</td>
</tr>
<tr>
<td>acetone</td>
<td>c</td>
<td>--</td>
</tr>
<tr>
<td>dimethyldihydroresorcinol</td>
<td>c</td>
<td>--</td>
</tr>
<tr>
<td>2-acetylcyclohexanone</td>
<td>c</td>
<td>--</td>
</tr>
</tbody>
</table>

\(^a\)Partial reduction along with considerable hydride decomposition.

\(^b\)About 50\% reduction upon refluxing in di-isopropyl ether for 15 hours.

\(^c\)Only decomposition of the hydride appeared to occur.
REDUCTION OF NITROCARBONYLS

Diphenyltin dihydride was allowed to react with m-nitrobenzaldehyde, p-nitrobenzaldehyde and m-nitroacetophenone. In all three cases it was the nitro group that was reduced. A 62.5% yield was obtained from m-amino-benzaldehyde. The other two nitro compounds gave low yields of amines that were difficult to isolate from the colored oils. The most significant things learned from these reactions is that nitro groups are more easily reduced than aldehyde and ketone groups, as might be expected, and that it is impractical to reduce nitro groups with diphenyltin dihydride since the amines produced decompose the hydride.

STEREOCHEMISTRY OF REDUCTION OF SIMPLE CYCLIC KETONES

Several substituted cyclic ketones were allowed to react with one or more organotin hydrides in order to study the steric requirements of the tin hydride molecules. Nothing was known of the mechanism of these reductions so it was difficult to anticipate the stereochemistry of the products obtained. There are several factors to be considered. First, since there is apparently no complex formed in the sense that lithium aluminum hydride and sodium borohydride form complexes that must be hydrolyzed
in order to complete the reduction, then it is at least theoretically possible that the reduction is initiated by transfer of hydride ion. If this is the case, we would expect the steric requirements of the attacking species to be small and uniform for all the organotin hydrides. Only the rates should be affected since the organic groups would influence the availability of these hydride ions. Secondly, if the attack is by the organotin hydride molecule we should have relatively large steric requirements which would be dependent upon two other considerations. If the requirements of the tin atom are large with respect to the organic groups attached by virtue of their greater distance from the tin-hydrogen bond, then changing the organic groups will not noticeably affect the composition of the product. On the other hand, if the bulk of the organic groups attached to the tin is important, then the composition of the products from reductions with butyltin trihydride should be considerably different from the composition of the products from reductions with triphenyltin hydride. It is therefore possible to get a small amount of insight into the mechanism of the reduction by running only a few selected reductions.
The ketones selected for these experiments were 4-t-buty1cyclohexanone, 4-methylcyclohexanone, carvone and menthone. These were selected because something is known about their conformations and because of the ease and accuracy of determining the stereochemistry of the products. The cis, trans ratio of 4-t-buty1cyclohexanol and 4-methylcyclohexanol can be determined by infrared spectra,\textsuperscript{17} and it can be determined for carvone and menthone by comparing optical activity.

In the case of 4-t-buty1cyclohexanol, there are two possible conformations. In the one conformation the t-butyl group is in an axial arrangement (I) while in the other, the t-butyl group is in an equatorial arrangement (II). It is not difficult to predict that II would be predominant, if not sole conformation present since it would require an undue expenditure of energy to place the bulky alkyl group in the less favorable axial position.\textsuperscript{24}

Menthone has nearly the same cis, trans ratio as the 4-t-buty1cyclohexanone. In this instance, instead of having one t-butyl group in an equatorial position, it has both an isopropyl and a methyl group in an equatorial arrangement (III).
Table 2

Stereochemistry of Reduction of Cyclohexanones by Organotin Hydrides, Complex Metal Hydrides, and Aluminum Isopropoxide

<table>
<thead>
<tr>
<th>reducing agent</th>
<th>% trans-alcohol obtained in the reduction of 4-t-butyl cyclohexanone</th>
<th>4-methyl-cyclohexanone</th>
<th>(%I) from carvone</th>
<th>(%II) from menthone</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-BuSnH₃</td>
<td>92</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n-Bu₂SnH₂</td>
<td>88</td>
<td>75</td>
<td>94.7</td>
<td>59.5</td>
</tr>
<tr>
<td>Ph₂SnH₂</td>
<td>87</td>
<td>76</td>
<td>97.1</td>
<td>48</td>
</tr>
<tr>
<td>Ph₃SnH</td>
<td>87</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LiAlH₄</td>
<td>91-93&lt;sup&gt;a&lt;/sup&gt;</td>
<td>79-81&lt;sup&gt;a&lt;/sup&gt;</td>
<td>94</td>
<td>71&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>NaBH₄</td>
<td></td>
<td>75</td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>Al(OPr-i)₃</td>
<td>77-81&lt;sup&gt;a&lt;/sup&gt;</td>
<td>67</td>
<td>58&lt;sup&gt;c&lt;/sup&gt;</td>
<td>30</td>
</tr>
<tr>
<td>Equilibrium</td>
<td>77-81&lt;sup&gt;a&lt;/sup&gt;</td>
<td>69-71&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The energy to convert both of these to an axial arrangement (IV) would be prohibitive.

With 4-methylcyclohexanol the situation is different. Even though the equatorial methyl (V) would be favored energetically, the differences between (V) and (VI) are necessarily small and a mixture of the two is present with (V) predominating.\textsuperscript{24}

![Chemical structures](https://example.com/structures.png)

Carvone has the added problem of a double bond in the ring which makes the conventional axial and equatorial forms less meaningful. It can still have the isopropenyl group in a pseudo-axial (VII) and pseudo-equatorial (VIII) arrangement, however, with the equatorial arrangement the more stable.

The results obtained from the reductions with the various organotin hydrides are summarized in table 2. It can be seen that in each case, where comparison can be made, the products closely resemble the products obtained from the sodium borohydride reduction of the ketone. This can be discussed in terms of the principles suggested by
It has been shown that 4-\textit{t}-butylcyclohexanone would have almost exclusively the conformation (II). Due to the remote position of the \textit{t}-butyl group with respect to the carbonyl it would not affect the approach of the hydride from either the axial or equatorial position. This would mean that an axial attacking species would have to cope only with the \(\beta\)-axial hydrogens. If the attacking group is small, these hydrogens will have little effect and the amount of "steric approach control" will be negligible. The attacking group can come in either axially or equatorially. Since the axial approach is preferred and there is little hindrance to that approach, most of the attack by hydrogen, will be axial. The thing that will mainly determine the structure of the products will be "product development control". This means that once the hydride-ketone complex forms, the factor that will determine the conformation of the product will be the energetics of the formation of the products from this complex. Since an axial approach is favored, and, since the equatorial hydroxide is thermodynamically more stable, you would expect the more stable trans-alcohol (IX) to form almost exclusively if the attacking species is small. If the attacking species is large it would be hindered by the \(\beta\)-axial hydrogens and cause equatorial attack to occur to a
limited extent. This would cause a hydrogen to be placed on the carbonyl carbon in the equatorial arrangement and the hydroxyl to be placed axially (X).

We can see from table 2 that there is little difference in the stereochemistry of the reduction products from any of the tin hydrides. Yet, what little trend there may be lies in the direction that would be predicted from an attack by molecular organotin hydride. The products appear to be almost completely "product development controlled", which would mean a great predominance of equatorial hydroxy formed. The larger the attacking group the more axial hydroxy would be expected since the $\beta$-axial hydrogens would force more equatorial attack and "steric approach control" would begin to compete.

Menthone is found almost exclusively with the two alkyls in the equatorial conformation. This leaves the molecule open for attack from either the equatorial or axial positions if the attacking species is small. Because of the ortho-isopropyl group, however, any bulk on the part of the hydride would cause an equatorial attack to be more competitive. In the case of lithium aluminum hydride, it can be seen that an axial approach forming an equatorial hydroxy (menthol) is the preferred reaction. The attacking group is small and product development control is the predominant factor. Diphenyltin dihydride on the other hand is larger and steric approach control enters the picture causing the more equatorial approach with the resulting formation of the
axial hydroxy compound, neomenthol.

4-Methylcyclohexanone poses a different problem from the two we have just seen. The two possible conformations (V) and (VI) are identical as far as the steric hindrance at the ω-carbon is concerned. The alkyl group is too far away to have much effect. Also, since the alkyl group is methyl, the energy differences between the two structures is not very great (only 2.36 kcal./mole), so a significant amount of the less stable conformation will be present.

There is little hindrance in the ω-position for a small hydride like lithium aluminum hydride, so most of the attack will be axial with the formation of equatorial hydrate. For the molecules in conformation (V) this will mean mostly trans cyclohexanol will be formed. For the molecules in conformation (VI) the product will be mostly cis. Since (V) predominates, the isolated product is mostly trans.

A larger hydride, like an organotin hydride would encounter greater steric hindrance and steric approach control would become important. This would mean that more cis would be formed from (V) and more trans would be formed from (VI). Since (V) predominates, this would mean an overall increase in cis produced.

Carvone has a rigid, distorted structure which offers very little hindrance to axial attack since there is only one ω-axial hydrogen and, due to the shape of the ring, this hydrogen is less hindering than in the saturated cyclohexanones. This would lead to almost pure product development control and would account for the high yield of trans product.
From what has just been said it seems that the attacking group must contain the bulky organotin group.
REDUCTION OF KETOSTEROIDS: STRUCTURE OF PRODUCTS

Up to now it has been shown that the organotin hydrides are suitable reagents for reducing aldehydes and ketones. It has also been shown that they will reduce polyketones such as quinone and benzil. Further investigation showed that under the usual conditions, diphenyltin dihydride would not reduce 2-acetylcyclohexanone. This hydride would also not reduce dimethyldihydroresorcinol. In fact, this last ketone seemed to catalyze the decomposition of the hydride.

This and other information available led to one conclusion. Although the organotin hydrides are generally good reducing agents they are somewhat selective and this selectivity could probably be shown most interestingly by allowing them to react with polyketones where the environment of the two ketones differ either sterically or electronically or both. It was decided that a series of keto-steroids might help to show this selectivity.

The first steroid used for this study was pregnenolone (XI). It is a simple, monoketosteroid which would show readily whether reduction would be possible. The course of the reaction could be followed by infrared spectra simply by determining the increased presence of the hydroxyl absorption band near 3500 cm\(^{-1}\) and the disappearance of the carbonyl absorption band near 1700 cm\(^{-1}\).
The organotin hydride selected as the reducing agent for all of these reactions was diphenyltin dihydride. The reasons for the selection were twofold. First, it could be made quickly in quantitative yield and need not be isolated. Second, it had given no evidence of addition to carbon-carbon double bonds, which would be present in the ketosteroids selected for this study.

The reaction was run in the usual manner and the mixture was allowed to stand overnight. Infrared analysis showed the complete absence of carbonyl bands and an increase in intensity of the hydroxyl absorption. The reaction mixture was acetylated and chromatographed. The expected 3,20-diol, diacetate (XII) was isolated in 60% yield.

With this piece of encouragement, the first test of selectivity was begun. The steroid used was progesterone (XIII), which has keto groups in the 3- and 20-positions. At a glance the problem seems to be a simple competition between a cyclic ketone and an acyclic ketone. There is apparently a lot more to it than that.
The similarity in selectivity of the organotin hydrides to that of sodium borohydride was brought out in the study of the stereochemistry of reduction of simple cyclic ketones, above. It might therefore be assumed that the products of the organotin hydride reductions of the steroids would be similar, though not necessarily identical to those obtained when sodium borohydride was used.

It has been found\textsuperscript{6,7} that sodium borohydride reduces the 3-ketones in preference to 11-, 12-, 17- or 20-ketones unless a double bond is present between the 4- and 5-carbons. In this case, a 20-keto group is reduced in preference to a 3-keto group.

Progesterone (XIII) has a $\Delta^4$ (4-5 double bond), 3-keto structure, therefore sodium borohydride gives the 20-reduced product. It is only by blocking the 20-keto group that it has recently been possible to obtain the 3-ol with the 20-keto present.\textsuperscript{8,9} It was therefore very interesting to find that the diphenyltin dihydride reduction of progesterone led to a 91% yield of the crude 20-ketone product (XIV) and a 14% yield of the crude 3-keto (XV) product.
This is an important improvement over the other methods used to produce the 3-ol. In both of the other methods the 20-keto group must first be blocked with some other reagent to prevent its reduction. Although the blocking reaction is usually satisfactory, some losses are encountered. The new compound must then be reduced. This causes additional losses. A further loss is encountered when the 20-keto group is reformed by removing the blocking group. The present, one-step method not only gives a better yield than the overall yield of the three different reactions, it also saves a lot of time since it involves only one step.
It would be well to mention at this time how it was possible to differentiate between the 3-keto and 20-keto absorption bands in the infrared. In all of the di- and tri-ketones used in this study the 3-keto group is always in conjugation with a double bond. This $\Delta^4$-3-keto carbonyl absorbs between 1668-1660 cm.$^{-1}$. The 11- and 20-keto groups under observation on the various steroids absorb between 1707 and 1695 cm.$^{-1}$ since there is no conjugated unsaturation. It is therefore relatively easy to run an infrared spectrum on the isolated product to see which carbonyl has been eliminated in each case. This does not give a solution to the problem of stereochemistry at the point of reduction but it does make it easy to determine which carbonyl has been reduced.

Since progesterone (XIII) was reduced mainly in the 3-position, it seemed reasonable to assume that any additional crowding that could be caused in the 20-position would force the reaction to go more completely at C-3. The next steroid studied was Reichstein's compound S acetate (XVI). The A, B, and C rings are the same as for progesterone but additional crowding is present around the 20-carbon.

Reichstein's compound S acetate was allowed to react with one mole of diphenyltin dihydride and 13% of the starting material was recovered, a 36.8% yield of product reduced in the 20-position only (XVII) was isolated and a 31% yield of 3,20-diol (XVIII) was obtained. No product was isolated in which only the 3-carbonyl was reduced.
In this case the diphenyltin dihydride followed the rule of 20-reduction first if there is a 4-5 double bond. It is apparent from this reaction that the added bulk had little influence on the point of attack. In fact, it seemed to work just the opposite. It is more likely that the effect was not steric but electronic.

Two moles of diphenyltin dihydride were then allowed to react with the compound S acetate and 8.7% of the starting material was recovered, a yield of 37.9% of the 20-ol (XVIII) was obtained and a 53.3% yield of 3,20-diol (XVIII) was isolated.
It is interesting to note that each mole of hydride added was less efficiently used than the one before it. Based on material isolated, about 86% of the first mole of hydride used actually reduced a keto group. When two moles of hydride were used, the overall reduction amounted to 73% of the hydride added. This means that the second mole was very inefficiently used.

The preceding steroid showed that small structural changes can cause large, unpredictable changes in the selectivity of the reduction. The next compound to be studied therefore had a small, subtle change, distant from both points of attack to see if this could cause a noticeable effect in selectivity.

Hydrocortisone acetate (XIX) was allowed to react with one mole of diphenyltin dihydride and a 63% yield of 20-ol (XX) was obtained plus a 14% yield of 3, 20-diol (XXI). This compound, therefore, gave the same selectivity as compound S acetate and follows the general rules for sodium borohydride reduction.
Two moles of diphenyltin dihydride were then added and a 63% yield of 3, 20-diol (XXI) was obtained plus a 24% yield of 20-ol (XX). Again, a great drop in efficiency was experienced (from 91% to 75%) when two moles of hydride were used.

One further, less subtle, change was then studied. Cortisone acetate (XXII) was the steroid used. The physical change involves replacing the 11-hydroxy group with an 11-keto group. This effects the molecule in a number of ways, however. The first and most obvious of these is the fact that there are now three carbonyl groups present, any of
which could theoretically be reduced. The rules for sodium borohydride reduction tell us however that the 11-keto should be the hardest of the three to reduce. This is easy to see when one remembers that the two angular methyl groups (numbers 18 and 19) are actually very close to the 11-position and tend to block any attack there. The mere presence of another carbonyl would affect the electron density around the carbons in the immediate area but the 3- and 20-positions are so far away it is unlikely that they would be much affected. Last, but very important, is the fact that the shape of the whole molecule is affected since the 11-carbon had previously been tetracovalent with a tetrahedral arrangement of the atoms around it. With the 11-keto group present it is in a planar, tricovalent configuration which would distort the shape of the whole molecule. Which of these is most important or whether there are other influencing factors is not known but the experimental facts tell us that there is an important difference.

Cortisone acetate (XXII) reacted with one mole of diphenyltin dihydride to give a 50% yield of 3-ol and a 25% yield of 3, 20-diol. This is in agreement with the results obtained from the progesterone reduction but it contradicts the rules for sodium borohydride reduction and is opposite to the results obtained in the Reichstein's compound S acetate and hydrocortisone acetate reductions.
Two moles of diphenyltin dihydride reacted with cortisone acetate to give a 46.3% yield of 3-ol (XXIII) and a 37.5% yield of doubly reduced product (XXIV). Three moles of diphenyltin dihydride reacted with cortisone acetate to give a yield of 26.3% of 3-ol (XXIII) and a 62.2% yield of doubly reduced (XXIV) product.

From these steroid reductions which are summarized in Table 3, several things were learned. The first is that diphenyltin dihydride does not follow the simple rules of selectivity that sodium borohydride does. The reasons for
its preference for the C-3 carbonyl in the case of progesterone and cortisone acetate are not known but are likely to be discovered if more work was done on other ketosteroids. A second thing learned is that if more than one keto group is to be reduced with diphenyltin dihydride, a large excess of hydride must be used.
Table 3

REDUCTION OF KETOSTEROIDS WITH DIPHENYL Tin DIHYDRIDE

<table>
<thead>
<tr>
<th>Hydroxyl Produced</th>
<th>Moles of Hydride</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

Pregnenolone

| 20β               |    |   | 79% |

Progesterone

| 20β          | 14 | 0  |
| 3β           | 90 | 0  |
| 3β,20β       | 0  | 72 |

Reichstein's S Acetate

| Starting material | 13 | 8.7 |
| 20β              | 20 | 0   |
| 3β,20α           | 4.2| 7.1 |
| 3β,20β           | 26.8| 46.2|
| 20α              | 16.8| 37.9|

Hydrocortisone Acetate

| 3β,20β           | 14 | 63 |
| 20β              | 63 | 24 |

Cortisone Acetate

| 3β               | 27.8| 22.7| 6.7 |
| 3β,20β           | 25  | 37.5| 52.5|
| 3α               | 22.3| 23.6| 19.7|
| 3α,20β           | trace| trace| 12 |
REDUCTION OF KETOSTEROIDS: STEREOCHEMISTRY OF PRODUCTS

The use of infrared spectra alone was sufficient to determine which keto group was reduced in the course of the reduction of the various ketosteroids. It would be desirable to know, as well, the stereochemistry of the reduction at each carbon. This is a much more difficult task. The problems are manifold. In some cases the products obtained from the organotin hydride reductions have not been reported in the literature. In others, where they have been reported, the data available is incomplete. Most important, the products obtained from these reductions were seldom completely pure and some samples, where special mention will be made, were apparently rather impure. The recent papers by J. H. Brewster were consulted but due to the problems mentioned above the identity of some of the products are still questionable.

Pregnenolone.- This steroid has only one keto group which is in the 20-position. The problem was to determine whether the 20-ol or the 20-ol was formed. Melting point, and optical rotation showed the one product to be the 3,20-diol. It might therefore be assumed that the other product obtained was 20-ol. Infrared and melting point showed, however, that it was 3,20-diol 3-monoacetate. The sample was not pure, and it is likely that there was some 20-ol present as an impurity. There could not have been much 20-ol formed however, unless it
was preferentially lost in isolation of the sample.

**Progesterone.**- It has been shown that this diketone can be singly reduced in both the 3- and 20-positions. Sodium borohydride normally gives the 20β-ol with a small amount of 20α-ol and by blocking the 20-position it was possible to get the 3β-ol. Diphenyltin dihydride gave a mixture of 3β- and 20β-ol with a predominance of the 3β-ol. If any 3α- or 20α-ols were formed the amount was small and they were present only as impurities. Melting points, infrared spectra and optical rotations were in fair agreement with literature reports. When two moles of hydride were used, one somewhat impure product was obtained in 72% yield and it appeared to be mainly the 3β,20β-diol, which would certainly be expected from a further reduction of the two singly reduced products.

**Reichstein's S Acetate.**- Since diphenyltin dihydride reduced the carbonyls in this steroid in the same order as did other reducing agents reported, the problem of identifying the products was somewhat simplified. Four products were isolated. Two of them were reduced in the 20-position only and two were reduced in both the 3- and 20-positions. Unfortunately, only one of the products was pure enough to give a melting point. The other three were oils at steam-bath temperature and cooled to hard glasses at room temperature. Fraction (a) proved to have an infrared spectrum identical to that recorded for Δ⁴-preg-
nene-17α,20β,21-triol-3-one 20,21-diacetate. The other product reduced only in the 20-position, fraction (d), had to be the 20α-isomer by elimination. There was also optical rotation data that helped to confirm this assignment. The 20α-isomer had a \([\alpha]_D^{25} +35^\circ\) (chloroform) according to the literature and fraction (d) had a \([\alpha]_D^{25} +30^\circ\) (c=2 in chloroform). The assignments for the two doubly reduced products was a little more difficult since no literature values were available but it was felt an assignment was justified on the basis of yields of the various products. If fraction (b) was assigned the structure \(\Delta^4\)-pregnene-3β,17α,20α,21-tetrol-3,20,21-triacetate and fraction (c) was assigned the structure \(\Delta^4\)-pregnene-3β,17α,20β,21-tetrol-3,20,21-triacetate then when 1 mole of hydride was used the total 20β-reduction obtained amounted to 46.8% and the total 20α-reduction obtained amounted to 21%. With 2 moles of hydride the total 20β-reduction obtained equaled 46.2% and the total 20α obtained equaled 45%. It would therefore seem that when 1 mole of hydride was used fraction (d) was not completely removed from the column. Since it was the last to be removed and the yield was barely over 80%, this could easily be the case. Also, when 2 moles of hydride were used the 20β-product was converted to 3β,20β-ol and the 20α-product was converted to 3β,20α-ol. If the shortage in fraction (d) with 1 mole was allowed for, the summation was nearly precise. If any other assignments were given it
would be impossible to explain the presence of the products. Some \(3\alpha\)-product was probably present in the direduced products but it was not possible to isolate any of the material.

**Hydrocortisone Acetate.**- Only two fractions were obtained from this reduction. One was reduced in the 20-position and the other in both the 3- and 20-positions, as shown by infrared. Unfortunately, both of these fractions were impure. It was impossible to get either of these to crystallize. Since there has been a predominance of \(\beta\)-products from the reductions of the other steroids it was assumed that the singly reduced product was mainly \(\Delta^4\)-pregnene-11\(\beta\),17\(\alpha\),20\(\beta\),21-tetrol-3-one 20,21-diacetate with 20\(\alpha\)-ol contaminating it. The doubly reduced product was assumed to be mainly \(\Delta^4\)-pregnene-3\(\beta\),11\(\beta\),17\(\alpha\),20\(\beta\),21-pentol 3,20,21-triacetate for the same reason.

**Cortisone Acetate.**- When cortisone acetate was reduced with diphenyltin dihydride the order of reduction of the three keto groups was changed. It was therefore impossible to check any of the products obtained with data from the literature. It was still possible to draw certain conclusions, however, and to give tentative assignments of configuration. By glancing at the yield of the different fractions when reduced with 1, 2 and 3 moles of hydride it was easy to see a direct connection between fractions (a) and (b) and fractions (c) and (d) (see table 3). If
allowances were made for the differences in yield and normal experimental error it could be seen that the singly reduced fraction (a) was converted to the doubly reduced fraction (b) and that the singly reduced fraction (c) was converted to the doubly reduced fraction (d) as additional hydride was used. Again, in the other reductions discussed the $\beta$-forms of the alcohols have predominated (sometimes only slightly), but sufficiently to say that the most plentiful pair of products was probably the one where $\beta$-form is present. This means that the tentative assignments of structure would be fraction (a) $\Delta^4$-pregnene-3$\beta$,17$\alpha$,21-triol-11,20-dione 3,21-diacetate, fraction (b) $\Delta^4$-pregnene-3$\beta$,11$\alpha$,20$\beta$,21-tetrol-11-one 3,20,21-triacetate, fraction (c) $\Delta^4$-pregnene-3$\alpha$,17$\alpha$,21-triol-11,20-dione 3,21-diacetate, and fraction (d) $\Delta^4$-pregnene-3$\alpha$,17$\alpha$,20$\beta$,21-tetrol-11-one 3,20,21-triacetate. It is significant that although the last three fractions appear to be fairly clean chromatographic separations, fraction (a) appears to be a definite mixture and contain several impurities in significant amount. The melting point 208-215° recorded in the experimental is for the main constituent in this mixture.
EXPERIMENTAL
PREPARATION OF ORGANOTIN HYDRIDES

Organotin hydrides were first prepared by reducing organotin chlorides with lithium aluminum hydride by Finholt et. al.\(^2\) This method has been used by several other workers with van der Kerk et. al.\(^1,3\) preparing a large number of them.

The method used in the following preparations was similar to that used by van der Kerk except for time, temperature and hydrolysis. In all of his hydride preparations, he adds quinol, water, and sodium potassium tartrate in the process of hydrolyzing the sample and removing precipitated alumina. The use of ice-water only in the hydrolysis is not only simpler and time-saving, it avoids a number of product losing steps.

**Triphenyltin Hydride.**—Triphenyltin chloride, 38.5 g. (0.1 mole) and lithium aluminum hydride 1.56 g. (0.04 mole) were mixed in the solid state in a 500 ml., 3-neck flask fitted with a nitrogen inlet tube, a dropping funnel and a stirrer. The flask was placed in an ice-bath and 150 ml. of anhydrous ether was added. In fifteen minutes the ice-bath was removed and the mixture stirred at room temperature for three hours. The mixture was slowly hydrolyzed with 100 ml. of ice-water and the two layers separated. The ether layer was washed with two 100 ml. portions of water and dried over anhydrous magnesium sulphate. The ether was stripped off and the hydride flash-distilled by placing the distilling
flask in a bath preheated to 200°. The fraction boiling 162-168°/0.5 mm. was collected. Yield 27-29 g. (77-83%).

Van der Kerk obtained yields of from 49-70% with an average of 61%. In this case the difference in yields was probably due mainly to distillation technique. It was found by Van der Kerk that a portion of the hydride always decomposed at the start of the distillation. In this work it was found that by immersing the hydride in a pre-heated bath this decomposition could be minimized and a yield of approximately 80% was obtained consistently.

**Tributyltin Hydride.**- Into a 500 ml. flask immersed in an ice-bath and fitted with a stirrer, dropping funnel and a nitrogen inlet tube was transferred 2.85 g. (0.075 mole) of lithium aluminum hydride, followed by 75 ml. of anhydrous ether. Tributyltin chloride, 65 g. (0.20 mole) in 100 ml. of ether was added dropwise over a period of fifteen minutes. An additional 25 ml. of anhydrous ether was used to wash out the dropping funnel and added to the reaction mixture. The ice-bath was then removed and the mixture allowed to stir at room temperature for a half-hour. It was then hydrolyzed with 100 ml. of ice-water and the ether layer separated and washed with two 100 ml. portions of water. The solvent was stripped off and the fraction boiling 68-74°/0.3 mm. was collected. Yield 50.5 g. (87%).
Van der Kerk obtained a yield of 74% for this hydride. The simpler procedure and lower boiling point due to increased vacuum minimized decomposition and probably accounts for the difference in yield.

**Diphenyltin Dihydride.**—Into a 500 ml. flask immersed in an ice-bath and fitted with a stirrer, dropping funnel and a nitrogen inlet tube was transferred 3.94 g. (0.100 mole) of lithium aluminum hydride, followed by 50 ml. of anhydrous ether. Diphenyltin dichloride, 51.6 g. (0.150 mole) in 100 ml. of ether was added dropwise over a period of fifteen minutes. Stirring was continued for half an hour after the addition. The mixture was hydrolyzed with 10 ml. of ice-water and then washed three times with 100 ml. portions of ice-water. The ether layer was separated and used without further treatment. Yield: 95-100%. (Determined by adding acid to a sample and measuring H₂ evolved.)

It was found, as Van der Kerk reports that diphenyltin dihydride cannot be distilled. This hydride was therefore used in solution and this was found to be quite satisfactory.

**Dibutyltin Dihydride.**—Into a 500 ml. flask completely immersed in an ice-bath and fitted with a stirrer, dropping funnel and a nitrogen inlet tube was transferred 3.94 g. (0.100 mole) of lithium aluminum hydride, followed by 50 ml. of anhydrous ether. Dibutyltin
dichloride 45.6 g. (0.150 mole) in 100 ml. of ether was added dropwise over a period of fifteen minutes. The ice-bath was removed and stirring was continued for an additional hour at room temperature. The mixture was hydrolyzed slowly with 10 ml. of ice-water and then washed three times with 100 ml. portions of ice-water. The ether layer was separated and used without further treatment. Yield 95-100%. (Determined by adding acid to a sample and measuring H₂ evolved.)

Van der Kerk distilled this hydride and obtained a yield of 66%. In these reductions it was normally used in ether solution where the yields were essentially quantitative. When it was used pure, the yield was 80%.

Phenyltin Trihydride. Pheny l tin trichloride, 39 g. (0.13 mole) was dissolved in 100 ml. of ether and was added dropwise over a period of half an hour to a suspension of 4.95 g. (0.13 mole) of lithium aluminum hydride in 100 ml. of ether. The mixture was kept in an acetone and dry-ice bath during the addition. The bath was allowed to warm slowly to -20° during the three hours after the addition. The reaction flask was then placed in an ice-water bath and hydrolyzed slowly with 100 ml. of ice-water. The ether layer was then separated and a portion was analyzed for active hydrogen. A yield of 58.5%, based on active hydrogen was obtained. Distillation gave a 30% yield, b.p. 35°/2.5 mm., of phenyltin trihydride, whose analysis was not attempted because of its low stability.
Butyltin Trihydride.—Butyltin trichloride, 18.2 g. (0.1 mole) was dissolved in 100 ml. of ether and was added dropwise to a suspension of 7.6 g. (0.2 mole) of lithium aluminum hydride in 100 ml. of ether, cooled in acetone and dry-ice during the addition and for an additional half-hour. The mixture was placed in an ice-water bath for three and one-half hours and then allowed to stand at room temperature for a half-hour. The mixture was placed in an ice bath and hydrolyzed slowly with ice-water and then washed twice with 100 ml. portions of ice-water. The ether was dried over magnesium sulphate and the solvent stripped off at atmospheric pressure. The hydride was distilled under vacuum. B.p. 34°/0.5 mm. Yield: 12.5 g. (70%).

The reaction conditions and distillation pressure make a marked difference in the yields this hydride obtained. Van der Kerk ran the reaction "below 30°". In this preparation the temperature was never allowed to come near 30° until it was essentially complete. The reaction is exothermic and the hydride thermally unstable, so much lower temperatures were used throughout. In the distillation Van der Kerk used atmospheric pressure and 99-101° in contrast to the method used here where the temperature never exceeded 40°. It was found that the hydride decomposed rapidly over 70°. Van der Kerk obtained a yield of 37%. Much of the hydride probably decomposed during the distillation.
REDUCTIONS WITH ORGANOTIN HYDRIDES

All reduction products were characterized by infrared spectra and compared with authentic samples. In all operations a nitrogen atmosphere was maintained while a hydride was present.

TRIPHENYL Tin HYDRIDE REDUCTIONS

Benzaldehyde.— Triphenyltin hydride, 13.5 g. (0.038 mole) was added to 1.48 g. (0.014 mole) of freshly distilled benzaldehyde in a 15 ml. modified Claisen flask. The mixture was shaken for a few minutes until it was homogeneous. It was then heated between 90-100° over-night. As the reaction proceeded, crystalline hexaphenylditin formed in the flask. By morning the flask contained a wet, crystalline mass. Distillation directly from the reaction flask gave 1.2 g. (85% yield) of benzyl alcohol, b.p. 65°/0.8 mm. The hexaphenylditin was recrystallized from chloroform, m.p. 230-232°.

Anal. Calc. for C_{36}H_{30}Sn_{2}: Sn, 33.91%. Found: Sn, 33.76%.

4-t-Butylcyclohexanone.— Triphenyltin hydride, 21 g. (0.060 mole) was added to 2.3 g. (0.015 mole) of 4-t-butylcyclohexanone in a long test tube. The reaction was carried out as above except that as the alcohol formed, it sublimed at atmospheric pressure and collected near the top of the tube.
4-t-Butylcyclohexanol, 1.43 g. (62% yield) was collected. Infrared spectra (20 mg. of alcohol in 100 A of chloroform) showed the composition of the isomeric mixture to be 87%±2% *trans* and 13%±2% *cis*. The following data was used to determine the composition of the isomer mixture:

<table>
<thead>
<tr>
<th></th>
<th>9.90</th>
<th>10.20</th>
<th>10.51</th>
</tr>
</thead>
<tbody>
<tr>
<td>90% <em>trans</em></td>
<td>13.5</td>
<td>29.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Ph₃SnH product</td>
<td>14.5</td>
<td>29</td>
<td>13.5</td>
</tr>
<tr>
<td>85% <em>trans</em></td>
<td>15.5</td>
<td>28</td>
<td>18</td>
</tr>
</tbody>
</table>

4-Methylcyclohexanone.- Triphenyltin hydride, 27 g. (0.077 mole) was added to 2.1 g. (0.019 mole) of 4-methylcyclohexanone in a 25 ml. modified Claisen flask. The reaction was carried out as above except that the mixture was heated for two days. Distillation yielded 1.8 g. (84%) of 4-methylcyclohexanol. B.p. 56-57°/0.3 mm. Infrared spectra (50 A of the alcohol in 250 A of chloroform) showed the composition of the isomeric mixture to be 70%±2% *trans* and 30%±2% *cis*. The following data was used to determine the composition of the isomer mixture:

<table>
<thead>
<tr>
<th></th>
<th>9.94</th>
<th>10.18</th>
<th>10.57</th>
<th>10.87</th>
</tr>
</thead>
<tbody>
<tr>
<td>75% <em>trans</em></td>
<td>31</td>
<td>19</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>Ph₃SnH product</td>
<td>37</td>
<td>26</td>
<td>30</td>
<td>13</td>
</tr>
<tr>
<td>70% <em>trans</em></td>
<td>29</td>
<td>23.5</td>
<td>30</td>
<td>14.5</td>
</tr>
</tbody>
</table>
TRIBUTYLtin HYDRIDE REDUCTIONS

**Benzaldehyde.** - Tributyltin hydride, 11.1 g. (0.038 mole) was added to 1.59 g. (0.015 mole) of freshly distilled benzaldehyde in a 15 ml. modified Claisen flask. The mixture was shaken until it was homogeneous. It was then heated at 140° overnight. A clear, yellow solution containing a gray precipitate of metallic tin was present in the morning. Benzyl alcohol 1.9 g. (86% yield) was distilled from the mixture; b.p. 49-50°/0.3 mm. Further heating yielded a colorless liquid b.p. 137-145°/0.5 mm. which proved to be tetrabutyltin.

**Anal. Calc. for C_{16}H_{36}Sn: Sn, 34.19. Found: Sn, 33.63.**

DIPHENYLtin DIHYDRIDE REDUCTIONS

In all of the reactions involving diphenyltin dihydride a quantitative yield of the hydride was assumed and the concentrations of the solutions were adjusted to 1M on that assumption. Generally, a 10% excess of the hydride was used in order to compensate for the fact that the yield may not have been quantitative and to allow for any decomposition which might occur.

In general, about five minutes after the diphenyltin dihydride was added to the carbonyl, the solution became turbid and a white precipitate of diphenyltin would form.
Formation of this precipitate would continue for several hours. The diphenyltin would change color gradually on standing from white to dark yellow. After standing overnight there would be a clear solution and a heavy yellow precipitate. Addition of an amine (diethyl amine was the one used) at the end of the reaction served two purposes. It destroyed any dihydride still present (it catalyzes the decomposition of diphenyltin dihydride to diphenyltin and hydrogen) and it decreased the solubility of diphenyltin apparently by catalyzing its polymerization. The low molecular weight form is fairly soluble in most organic solvents (notable exception is methanol in which it is very insoluble), while the yellow through orange forms are rather insoluble. Diethylamine causes an almost immediate conversion of the white and yellow forms to the high molecular weight orange form. When no amine was added to the reaction mixture at the end of the reaction there was the problem of repeated filtrations being necessary. The diphenyltin would be filtered from the mixture and a distillation attempted. Heating the diphenyltin remaining in solution would cause it to polymerize and precipitate out. It would be necessary to stop the distillation and filter out the diphenyltin in order to prevent bumping. If it should be important not to use an amine, it is sufficient to allow the filtered solution to stand exposed to atmospheric oxygen for several hours, preferably with air bubbling through it, in order to convert the diphenyltin to the polymeric oxide which can readily be filtered out.
**Benzaldehyde.**— Diphenyltin dihydride solution, 50 ml., was added to 4.77 g. (0.045 mole) of freshly distilled benzaldehyde in a 125 ml. Erlenmeyer flask. The flask was fitted with a Bunsen valve so that the hydrogen formed by decomposition of excess hydride could escape. The mixture was shaken to ensure good mixing and allowed to stand at room temperature overnight. During the first five to fifteen minutes after the addition the reaction was vigorous and exothermic and it was necessary to cool the flask to prevent the ether from boiling. By the next morning most of the diphenyltin had precipitated. After the addition of 1 ml. of diethylamine the mixture was filtered and the benzyl alcohol distilled from the filtrate. Yield 3 g. (62%), b.p. 197-200°/760 mm.

**Cinnamaldehyde.**— Diphenyltin dihydride solution, 50 ml., was added to 5.95 g. (0.045 mole) of crotonaldehyde in a 125 ml. Erlenmeyer flask. The reaction was carried out as described above. Yield of cinnamyl alcohol: 4.5 g. (75%), b.p. 125-128°/7 mm.

**Crotonaldehyde.**— Diphenyltin dihydride solution, 50 ml., was added to 3.15 g. (0.045 mole) of crotonaldehyde in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield of unsaturated alcohol: 1.87 g. (59%), b.p. 117°/760 mm.
Cyclohexanone.- Diphenyltin dihydride solution, 50 ml., was added to 4.4 g. (0.045 mole) of cyclohexanone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield of cyclohexanol: 3.54 g. (82%), b.p. 155-160°/760 mm.

Benzophenone.- Diphenyltin dihydride solution, 50 ml. was added to 8.19 g. (0.045 mole) of benzophenone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. The mixture was filtered and the diphenyltin washed repeatedly with ether. The filtrate was evaporated down to yield crude benzhydrol. This was recrystallized from 60-90° ligroin to give 4.9 g. (59% yield), m.p. 67-68°.

dl-Camphor.- Diphenyltin dihydride solution, 50 ml., was added to 6.84 g. (0.045 mole) of dl-camphor in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner except that a large amount of hydrogen was evolved and an infrared spectrum showed that very little alcohol had been produced while nearly all the ketone remained.

Methyl Vinyl Ketone.- Diphenyltin dihydride solution, 50 ml., was added to 3.15 g. (0.045 mole) of methyl vinyl ketone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield of methyl vinyl carbinol: 1.8 g. (59%), b.p. 78-80°/760 mm. The allophanate
was formed; m.p. 148-149°. Lit. m.p. 151-152°.¹⁸ The yellow diphenyltin filtered from the completed reaction was analyzed for tin.

Anal. Calc. for C₁₂H₁₀Sn: Sn, 43.49. Found: Sn, 43.22.

Chalcone.- Diphenyltin dihydride solution, 50 ml., was added to 9.4 g. (0.045 mole) of chalcone dissolved in 25 ml. of ether in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner except that the unsaturated alcohol was extracted from the diphenyltin with ether and recrystallized. Yield 7.1 g. (75%), m.p. 60-61°.

Benzoquinone.- Diphenyltin dihydride solution, 50 ml., was added to 4.9 g. (0.045 mole) of benzoquinone dissolved in 50 ml. of ether, in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner except that after the hydroquinone had been extracted with ether from the diphenyltin, another 4.9 g. of benzoquinone was added to the clear solution. An immediate precipitate of quinhydrone was formed and filtered. Yield 8.5 g. (86%) quinhydrone, m.p. 168-170°.

Anthraquinone.- Diphenyltin dihydride solution, 50 ml., was added to 9.36 g. (0.045 mole) of anthraquinone in 50 ml. of ether in a 125 ml. Erlenmeyer flask. There was no apparent reaction except the decomposition of
diphenyltin dihydride, evidenced by a copious evolution of hydrogen gas.

**m-Nitrobenzaldehyde.**- Diphenyltin dihydride solution, 150 ml., was added to 7.1 g. (0.047 mole) of m-nitrobenzaldehyde dissolved in 25 ml. of ether in a 250 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield of m-aminobenzaldehyde was 3.55 g. (62%).

**p-Nitrobenzaldehyde.**- Diphenyltin dihydride solution, 150 ml., was added to 7.1 g. (0.047 mole) of p-nitrobenzaldehyde dissolved in 25 ml. of benzene in a 250 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. The product was mainly a brown oil with a small amount of material which was apparently p-aminobenzaldehyde.

**m-Nitroacetophenone.**- Diphenyltin dihydride solution, 150 ml., was added to 7.7 g. (0.047 mole) of m-nitroacetophenone dissolved in 25 ml. of ether in a 250 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. The product was mainly polymeric material (sintered at 225°).

**2-Acetylcyclohexanone.**- Diphenyltin dihydride solution, 50 ml., was added to 6.3 g. (0.045 mole) of 2-acetylcyclohexanone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Hydrogen gas was evolved freely. Infrared analysis showed that no reduction had taken place.
Dimethyldihydroresorcinol.- Diphenyltin dihydride solution, 50 ml., was added to 6.3 g. (0.045 mole) of dimethyldihydroresorcinol in 25 ml. of ether in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Hydrogen gas was evolved as the hydride decomposed. This ketone seemed to catalyze the decomposition of the hydride. Infrared analysis showed that no reduction had taken place.

Benzil.- Diphenyltin dihydride solution, 100 ml., was added to 8.4 g. (0.040 mole) of benzil in a 250 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. The diphenyltin was washed repeatedly with acetone and the hydrobenzoin obtained from evaporating the solvent was recrystallized. Yield of meso-hydrobenzoin was 7.5 g. (87.5%), m.p. 134-135°.

4-t-Butylcyclohexanone.- Diphenyltin dihydride solution, 50 ml., was added to 6.16 g. (0.040 mole) of 4-t-butylcyclohexanone in a long test tube. The reaction was carried out in the usual manner. When the reaction was complete the bottom of the test tube was heated on a steam bath. The cyclohexanol sublimed at atmospheric pressure and large, pure crystals were formed near the top of the test tube. Yield: 5.5 g. (89%). Infrared spectra (20 mg. of the alcohol in 100 A of chloroform) showed the composition of the isomer mixture to be 87%±2% trans and 13%±2% cis.
The following data was used to determine the configuration:

<table>
<thead>
<tr>
<th></th>
<th>9.90</th>
<th>10.20</th>
<th>10.51</th>
</tr>
</thead>
<tbody>
<tr>
<td>85% trans</td>
<td>15.5</td>
<td>28</td>
<td>18</td>
</tr>
<tr>
<td>Ph$_2$SnH$_2$</td>
<td>15.5</td>
<td>29</td>
<td>14.5</td>
</tr>
<tr>
<td>90% trans</td>
<td>13.5</td>
<td>29.5</td>
<td>12.5</td>
</tr>
</tbody>
</table>

4-Methylcyclohexanone. - Diphenyltin dihydride solution, 50 ml., was added to 4.48 g. (0.040 mole) of 4-methylcyclohexanone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield: 3.7 g. (82.5%), b.p. 56-57°/0.3 mm., m.p. 25-26°. Infrared spectra (50A of the alcohol in 250A of chloroform) showed the composition of the isomer mixture to be 76%+2% trans and 24% +2% cis. The following data was used to determine the configuration:

<table>
<thead>
<tr>
<th></th>
<th>9.94</th>
<th>10.18</th>
<th>10.57</th>
<th>10.87</th>
</tr>
</thead>
<tbody>
<tr>
<td>75% trans</td>
<td>31</td>
<td>19</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>Ph$_2$SnH$_2$ product</td>
<td>41.5</td>
<td>20</td>
<td>34</td>
<td>10</td>
</tr>
<tr>
<td>80% trans</td>
<td>32</td>
<td>15</td>
<td>34</td>
<td>10</td>
</tr>
</tbody>
</table>

d-Carvone. - Diphenyl dihydride solution, 50 ml. was added to 6.76 g. (0.045 mole) of d-carvone. The reaction was carried out in the usual manner. Carveol was distilled 127-128°/25 mm. Yield: 5.71 g. (83.5%). The composition of the isomer mixture was estimated by comparing the rotation of the experimental mixture with the rotation of the known d-cis [α]$_D^{25}$+22.8° and d-trans [α]$_D^{25}$+202° isomers.
$[\alpha]^{25}_D$ 29.4°±1° (c=2, chloroform), 97.1% d-cis.

1-Menthone.— Diphenyltin dihydride solution, 50 ml., was added to 6.95 g. (0.045 mole) of 1-menthone. The reaction was carried out in the usual manner. Yield: 5.2 g. (74.5%), b.p. 60°/0.3 mm. $[\alpha]^{25}_D$-14.0°. The composition of the isomer mixture was estimated by comparing the rotation of the experimental mixture with the rotation of the known isomers, 1-menthol $[\alpha]^{18}_D$-50.1° and d-neomenthol $[\alpha]^{17}_D$+20.7°. Reduction product is approximately 49% 1-menthol, 51% d-neomenthol.

DIBUTYL Tin DIHYDRIDE REDUCTIONS

Except where specifically stated otherwise, in all the reactions involving dibutyltin dihydride a quantitative yield of the hydride was assumed and the concentration of the solutions was adjusted to 1M on that assumption. Generally, a 10% excess of the hydride was used in order to compensate for the fact that the yield may not have been quantitative and to allow for any decomposition which might have occurred.

In general, when aldehydes were allowed to react with dibutyltin dihydride the reaction was vigorous and exothermic. With ketones it was usually gentle with a slight warming of the solution taking place. If a solvent was used the dibutyltin formed was usually soluble so there was no change in appearance except for a yellowing of the solution. If no solvent was used, two layers formed since dibutyltin is insoluble in most alcohols.
Dibutyltin.- The tin-containing reaction product from the following reactions was dibutyltin. It was difficult to obtain pure for several reasons. It oxidized readily, it was difficult to remove all the alcohol produced in the reaction and if high temperatures were used the dibutyltin disproportionated to tetrabutyltin and tin. Acetone was reduced with dibutyltin dihydride and the isopropyl alcohol produced was stripped off under vacuum. The semi-solid yellow oil that remained was analyzed for tin.

Anal. Calc. for C₈H₁₈Sn: Sn, 50.96%. Found: Sn, 48.55%. The low tin analysis was probably due to a small amount of oxidation and trapped isopropyl alcohol.

Dibutyltin Dihydroxide.- The dibutyltin from any of the reductions with dibutyltin dihydride was placed in an Erlenmeyer flask, covered with five times its volume of methanol and warmed to 45-50°. Air was bubbled through the yellow dibutyltin layer for one day. Methanol was added as it evaporated. The temperature was then raised to the boiling point of methanol and the methanol solution decanted from any remaining dibutyltin. The methanol solution was concentrated and cooled. Colorless crystals quickly appeared. After two more recrystallizations from methanol they melted at 113-116°.

Anal. Calc. for C₈H₂₀SnO₂: C, 35.99; H, 7.55; Sn, 44.47. Found: C, 35.67; H, 7.23; Sn, 43.63.
Cinnamaldehyde.— Dibutyltin dihydride solution, 50 ml., was added to 5.95 g. (0.045 mole) of freshly distilled cinnamaldehyde in a 125 ml. Erlenmeyer flask. The flask was fitted with a Bunsen valve so that any hydrogen gas formed by decomposition of excess hydride could escape. During the first five to fifteen minutes after the addition the reaction was exothermic and slight warming occurred. By the next morning the reaction was complete. The ether was stripped off and the cinnamyl alcohol vacuum distilled. Yield: 3 g. (50%), m.p. 31-32°.

Crotonaldehyde.— Dibutyltin dihydride solution, 150 ml., was added to 9.45 g. (0.135 mole) of crotonaldehyde in a 250 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. The alcohol was distilled under vacuum to ensure complete removal from the dibutyltin and redistilled at atmospheric pressure. Yield: 4.1 g. (43.5%), b.p. 117-120°/760 mm.

Benzophenone.— Dibutyltin dihydride, 1.1 g. (0.0047 mole) was added to 0.77 g. (0.0042 mole) of benzophenone in a 10 ml. Erlenmeyer flask. Gentle warming was necessary for the benzophenone to dissolve in the hydride with no solvent. The mixture was warmed between 40-60° for three hours. It was then allowed to stand overnight at room temperature. In the morning the mixture was a pale yellow semi-solid. The flask was opened to the air and the dibutyltin allowed to
oxidize to the polymeric dibutyltin oxide over a period of twelve days. The mixture was then extracted with ether and upon evaporating the ether, silky needles of benzlhydrol were formed. It was recrystallized from 60-90° ligroin. Yield: 0.66 g. (85%), m.p. 67-68°.

**dl-Camphor.**— Dibutyltin dihydride solution, 50 ml., was added to 6.8 g. (0.045 mole) of dl-camphor in a 125 ml. Erlenmeyer flask. The flask was flushed with nitrogen, stoppered and allowed to stand at room temperature overnight. After fifteen hours there was no evidence of reaction and adding a drop of the reaction mixture to concentrated hydrochloric acid caused vigorous evolution of hydrogen indicating the presence of hydride. Diisopropyl ether, 50 ml. was added as solvent and the diethyl ether distilled. The mixture was then allowed to stand at reflux for twenty-four hours. A clear, yellow solution containing a gray precipitate of metallic tin was present at this time. A sample of the reaction mixture was again given the acid test and indicated the absence of hydride. Up to this point a nitrogen atmosphere had been maintained. The solvent was stripped off and a sample was sublimed. Infrared analysis showed that approximately half the ketone had been reduced.

**Methyl Vinyl Ketone.**— Dibutyltin dihydride solution, 50 ml., was added to 3.15 g. (0.045 mole) of methyl vinyl ketone in a 125 ml. Erlenmeyer flask. The reaction was run
as it was with cinnamaldehyde. Yield of methyl vinyl carbinol: 1.0 g. (31%), b.p. 78-80°/760 mm. The reaction was repeated and a 12.5% yield of the unsaturated alcohol was isolated.

**Benzoquinone.**- Dibutyltin dihydride solution, 50 ml., was added to 2.38 g. (0.022 mole) of benzoquinone in 25 ml. of ether in a 125 ml. Erlenmeyer flask. The flask was stoppered with a Bunsen valve and the mixture was allowed to stand at room temperature. The reaction was vigorous and exothermic. Within five minutes there were crystals of quinhydrone precipitating out and in two hours all the quinhydrone had redissolved and reacted to form hydroquinone. Another 2.38 g. of benzoquinone was added in 25 ml. of ether and a heavy precipitate of quinhydrone precipitated immediately. It was filtered and washed. Yield: 3.1 g. (66%), m.p. 168-170°.

**Benzil.**- Dibutyltin dihydride solution, 100 ml., was added to 9.45 (0.045 mole) of benzil dissolved in 75 ml. of ether in a 250 ml. Erlenmeyer flask. The reaction was run in the usual manner. In the morning, crystals were present in the clear solution. Air was passed over the mixture to oxidize the dibutyltin to the oxide. A few ml. of 30% hydrogen peroxide was added to speed the process. The meso-hydrobenzoin was extracted with ether and recrystallized. Yield: 8.8 g. (93%), m.p. 134-135°.
4-t-Butylcyclohexanone. - Dibutyltin dihydride solution, 50 ml., was added to 6.94 g. (0.045 mole) of 4-t-butylcyclohexanone dissolved in 10 ml. of ether in a 125 ml. Erlenmeyer flask. The reaction was run in the usual manner. When the reaction was complete (after one day at room temperature), the solvent was stripped off and the remaining material was steam distilled. Yield: 6.55 g. (93.5%). Infrared spectra (20 mg. of alcohol in 100 A of chloroform) showed the product to be 88%±2% trans and 12%±2% cis. The following data was used to determine the composition of isomers in the mixture:

<table>
<thead>
<tr>
<th>Percentage trans</th>
<th>9.90</th>
<th>10.20</th>
<th>10.51</th>
</tr>
</thead>
<tbody>
<tr>
<td>90% trans</td>
<td>13.5</td>
<td>29.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Bu₂SnH₂ product</td>
<td>13</td>
<td>29</td>
<td>14</td>
</tr>
<tr>
<td>85% trans</td>
<td>15.5</td>
<td>28</td>
<td>18</td>
</tr>
</tbody>
</table>

4-Methylcyclohexanone. - Dibutyltin dihydride solution, 50 ml., was added to 5.05 g. (0.045 mole) of 4-methylcyclohexanone in a 125 ml. Erlenmeyer flask. The reaction was run in the usual manner. Yield: 3.9 g. (76.5%), b.p. 45°/0.4 mm. Infrared spectra (50 A of the alcohol in 250 A of chloroform) showed the product to be 75%±2% trans and 25%±2% cis. The following data was used to determine the composition of the isomer mixture:
Dibutyltin dihydride solution, 50 ml., was added to 68 g. (0.045 mole) of \textit{d}-carvone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield: 4.8 g. (70.5%), b.p. 123-125°/20 mm. The composition of the isomer mixture was estimated by comparing the rotation of the experimental mixture with the rotation of the known \textit{d}-\textit{cis} and \textit{d}-\textit{trans} isomers; \(\left[\alpha\right]_D^{\text{2}F} +34.0^\circ\pm1^\circ\) (c=2, chloroform); composition. 94.7% \textit{d}-\textit{cis}, 5.3% \textit{d}-\textit{trans}.

\textit{L}-Methone.- Dibutyltin dihydride solution, 50 ml., was added to 6.95 g. (0.045 mole) of \textit{l}-menthone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner. Yield 5.7 g. (81.5%), b.p. 60°/0.6 mm. \(\left[\alpha\right]_D^{\text{2}F} -21.31^\circ\). The composition of the mixture of diastereoisomers was estimated by comparing the rotation of the experimental mixture with the rotation of the known isomers, \textit{l}-menthol \(\left[\alpha\right]_D^{\text{2}F} -50.1^\circ\) and \textit{d}-neomenthol \(\left[\alpha\right]_D^{\text{2}F} +20.7^\circ\); composition of the mixture. 59.5% \textit{l}-methol, 40.5% \textit{d}-neomenthol.
PHENYL Tin TRIHYDRI DE REDUCTIONS

**Cyclohexanone.**—Phenyltin trihydride (0.0255 mole in 50 ml. of ether) was added to 2.94 g. (0.030 mole) of cyclohexanone in 125 ml. Erlenmeyer flask. The flask was stoppered tightly and placed in an ice-bath for one hour. Within one minute after the addition a white to pale-yellow solid began to form in the orange solution and precipitation continued slowly for several hours. The mixture was then allowed to stand at room temperature for four days. An infrared spectrum showed the reduction to be only about one-third complete with a large amount of hydride still present. Warming the mixture decomposed the hydride but did not increase the reduction appreciably. A very large excess of hydride would be necessary to cause the reduction to go to completion. It seems that the first hydrogen is very reactive as a reducing agent while the next two are not.

**4-t-Butylcyclohexanone.**—Phenyltin trihydride, (0.0255 mole in 50 ml. of ether) was added to 4.62 g. (0.030 mole) of 4-t-butylcyclohexanone dissolved in 25 ml. of ether in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner with the same results that were obtained from the cyclohexanone reaction.
1-Menthone.— Phenyltin trihydride (0.0255 mole in 50 ml. of ether) was added to 4.62 g. (0.030 mole) of 1-menthone in a 125 ml. Erlenmeyer flask. The reaction was carried out in the usual manner with the same results that were obtained from the cyclohexanone reaction.

BUTYL Tin TRIHYDRIDE REDUCTIONS

4-t-Butylcyclohexanone.— Butyltin trihydride, 4.6 g. (0.025 mole) was added to 1.54 g. (0.01 mole) of 4-t-butylcyclohexanone in a long test tube. The tube was flushed with nitrogen and attached to a mercury relief valve. The mixture was allowed to stand at room temperature for one day. At this time the reaction was incomplete so the mixture was warmed to between 40-50° and kept there for four hours. The reaction was complete. The mixture was then heated to 75° to destroy any remaining hydride. In about two hours the mixture was a red solid mass. The bottom of the test tube was heated on a steam bath at atmospheric pressure and the alcohol sublimed and collected near the top of the tube. Yield: 1.40 g. (91%). Infrared spectra (20 mg. of the alcohol in 100 Å of chloroform) showed the product to be 92%±2% trans and 8%±2% cis. The following data was used to determine the composition of the isomer mixture:
| Nature of the Tin-Containing Reaction Product From the Above Experiment. - The residue in the test tube was thrown in the waste basket and it ignited. Several reductions were run with acetone in which extreme care was taken to ensure the exclusion of oxygen so that the pure, red \((\text{BuSn})_x\) could be isolated. It proved to be a very difficult task since it was so reactive. One sample isolated gave the following analysis:  

**Anal.** Calc. for \(\text{C}_4\text{H}_9\text{Sn}\): C, 27.31, H, 5.16, Sn, 67.52.  
Found: C, 27.23, H, 5.21, Sn, 66.57.

Molecular weight determinations were attempted several times using the isopiestic method with methylene chloride as the solvent. Solids, believed to be polymeric, precipitated out before equilibrium could be reached in each case.

4-Methylcyclohexanone.- Butyltin trihydride, 8.95 g. (0.050 mole) was added to 2.8 g. (0.025 mole) of 4-methylcyclohexanone in a 15 ml. modified Claisen flask. The reagents were mixed by gentle shaking and allowed to stand at room temperature for 16 hours. It was then heated for 4 hours between 40-50° and for 4 hours between 50-60°.

<table>
<thead>
<tr>
<th>95% trans</th>
<th>10.20</th>
<th>10.51</th>
</tr>
</thead>
<tbody>
<tr>
<td>BuSnH₃</td>
<td>12.5</td>
<td>30.5</td>
</tr>
<tr>
<td>90% trans</td>
<td>13.5</td>
<td>29.5</td>
</tr>
</tbody>
</table>
Solid red material formed more rapidly. Heating to 75° for several hours was sufficient to destroy any remaining hydride. An infrared spectrum indicated hydroxy groups, no carbonyl groups or tin-hydride groups. The alcohol was distilled b.p. 55-57°/0.3 mm. Infrared spectra (50 Å of the alcohol in 250 Å of chloroform) showed the composition of the isomeric mixture to be 73%±2% **trans** and 27%±2% **cis**. The following data was used to determine the configuration:

<table>
<thead>
<tr>
<th></th>
<th>9.94</th>
<th>10.18</th>
<th>10.57</th>
<th>10.87</th>
</tr>
</thead>
<tbody>
<tr>
<td>75% <strong>trans</strong></td>
<td>31</td>
<td>19</td>
<td>34</td>
<td>11</td>
</tr>
<tr>
<td>BuSnH₃</td>
<td>30</td>
<td>24</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>70% <strong>trans</strong></td>
<td>29</td>
<td>23.5</td>
<td>30</td>
<td>14.5</td>
</tr>
</tbody>
</table>
REDUCTION OF KETOSTEROIDS

When ketosteroids were reduced with diphenyltin dihydride, the hydride was prepared in the usual manner in ether solution and analyzed for active hydrogen in a Grignard apparatus. The desired amount of this analyzed hydride solution was used.

Fisher alumina (80-200 mesh) was used for the chromatographic separation of the steroid isomers. It was neutralized by treatment with ethyl acetate overnight followed by exhaustive washing with water and reactivating at 200° according to the method of Brooks and Norymberski. A column 2.5 cm. in diameter was packed 40 cm, deep with this alumina.

Pregnenolone.—Diphenyltin dihydride solution, 6.3 ml. (0.00174 mole), was added to 0.500 g. (0.00158 mole) of pregnenolone and dissolved in 20 ml. of dioxane. The mixture was allowed to stand at room temperature overnight. A small amount of white precipitate was present in the morning. Diethylamine, 1 ml., was added and the mixture allowed to stand for one hour to insure complete precipitation of the diphenyltin which was then removed by filtration and the solvent distilled off. This product was acetylated by adding 4 ml. of pyridine and 4 ml. of acetic anhydride and heating the mixture on a steam-bath overnight. The light-brown solution was diluted with 100 ml. of diethyl ether, hydrolyzed
with cold water, then washed repeatedly with dilute hydrochloric acid, dilute sodium carbonate solution, and distilled water. It was then dried over anhydrous magnesium sulphate and the solvent removed by distillation.

The oil from the acetylation reaction was dissolved in 25 ml. of ether and placed on a column packed with alumina. The following eluents were used: 500 ml. of ether, 200 ml. of 1% ethyl acetate in ether, 200 ml. of 5% ethyl acetate in ether, 100 ml. of 50% ethyl acetate in ether and 100 ml. of ethyl acetate. Two crystalline products were removed from the column. Fraction (a), 0.377 g., 60% yield, m.p. 125-126°, \([\alpha]_{b}^{27} -26^° (c=0.96 \text{ in ethanol})\). Literature values:\x1d 3β,20α-diol, diacetate m.p. 145-147°, 3β,20β-diol, diacetate m.p. 130-131°, \([\alpha]_{b}^{27} -23^° (c=0.96 \text{ in ethanol})\), 3β,20β-diol, 3-monoacetate m.p. 165-165.5°, \([\alpha]_{b}^{27} -61^° (c=0.42 \text{ in ethanol})\). Fraction (a) was assigned the structure \(\Delta^5\)-pregnene, 3β,20β-diol, diacetate.

Fraction (b), 0.0903 g., 19% yield, m.p. 150-160° (impure), \([\alpha]_{b}^{25} -38.1^° (c=0.42 \text{ in ethanol})\) was assigned the structure \(\Delta^5\)-pregnene, 3β,20β-diol, 3-monoacetate.

**Progesterone.**- Diphenyltin dihydride solution, 5.1 ml. (0.00174 mole), was added to 0.500 g. (0.00159 mole) of progesterone dissolved in 10 ml. of dioxane. The reaction was carried out in the usual manner. The reaction product was chromatographed without acetylation on a column packed with alumina. The following eluents (100 ml. each) were
used: 50% ethyl acetate in ether, 75% ethyl acetate in ether, ethyl acetate, 2% methanol in ether, 5% methanol in ether, and 10% methanol in ether. Two crystalline products were removed from the column. Fraction (a), 0.0772 g., 14% yield, m.p. 174-178°, \( \nu_{\text{max}} \text{CHCl}_3 \) 1662, 1620 cm\(^{-1}\) was assigned the structure \( \Delta^4 \)-pregnene, 3-one, 20\( \beta \)-ol, m.p. 173-175°, \( \nu_{\text{max}} \text{CHCl}_3 \) 1660 cm\(^{-1}\). Fraction (b), 0.4297 g., 90% yield, m.p. 151-157°, \( [\alpha]_D^{25} \) +120° (c=1.3 in chloroform), \( \nu_{\text{max}} \text{CHCl}_3 \) 1700 cm\(^{-1}\) was assigned the structure \( \Delta^4 \)-pregnene, 3\( \beta \)-ol, 20-one, m.p. 159-161°, \( [\alpha]_D^{25} \) +139° (chloroform), \( \nu_{\text{max}} \text{CHCl}_3 \) 1704 cm\(^{-1}\).

Diphenyltin dihydride solution, 12.6 ml. (0.00348 mole), was added to 0.500 g. (0.00159 mole) of progesterone in 10 ml. of dioxane. The reaction was carried out in the usual manner. A crystalline product was obtained. Recrystallization from an acetone-pentane mixture gave a solid 0.3478 g., 72% yield, m.p. 181-183°, \( [\alpha]_D^{25} \) +90.7° (c=1.3 in chloroform). This diol was assigned the structure, \( \Delta^4 \)-pregnene, 3\( \beta \),20\( \beta \)-diol. An unidentified oily mixture was also obtained which weighed 0.198 g.

**Reichstein's S Acetate.**—Diphenyltin dihydride solution, 4.0 ml. (0.00141 mole) was added to 0.500 g. (0.00128 mole) of Reichstein's S acetate dissolved in 20 ml. of dioxane. The reaction was carried out in the usual manner. The reaction product was acetylated by adding 4 ml. of pyridine and 4 ml. of acetic anhydride and heating the mixture on a steam-bath overnight. The light-brown solution
was diluted with 100 ml. of diethyl ether, hydrolyzed with cold water, then washed repeatedly with dilute hydrochloric acid, dilute sodium carbonate solution, and distilled water. It was then dried over anhydrous magnesium sulphate and the solvent removed by distillation.

The oil from the acetylation reaction was dissolved in 25 ml. of ether and placed on a column packed with activated alumina. The following eluents (100 ml. of each) were used: 25% ethyl acetate in ether, 50% ethyl acetate in ether, 75% ethyl acetate in ether, ethyl acetate, 2% methanol in ether, 5% methanol in ether and 10% methanol in ether. The fractions isolated from the column in the order in which they were eluted are: starting material 0.065 g., (13%), fraction (a) 0.1107 g., 20% yield oil, $\nu_{\text{max}} \text{CHCl}_3$ 1740, 1665 cm$^{-1}$, tentatively assigned the structure $\Delta^4$-pregnene, 17$\alpha$,20$\beta$,21-triol-3-one 20,21-diacetate, m.p. 191-193°, $[\alpha]_D^{25} +150$ (chloroform),$^8,13,14$ fraction (b) 0.0255 g., 4.2% yield, oil, $[\alpha]_D^{25} +85°$ (c=0.1 in chloroform), $\nu_{\text{max}}$ 1740 cm$^{-1}$, tentatively assigned the structure $\Delta^4$-pregnene-3$\beta$, 17$\alpha$,20$\alpha$,21-tetrol 3,20,21-triacetate, fraction (c) 0.1627 g., 26.8% yield, m.p. 167-168°, $[\alpha]_D^{25} +56°$ (c=2 in chloroform), $\nu_{\text{max}}$ 1735 cm$^{-1}$, tentatively assigned the structure $\Delta^4$-pregnene-3$\beta$,17$\alpha$,20$\beta$,21-tetrol 3,20,21-triacetate, fraction (d) 0.0929 g., 16.8% yield, oil, $[\alpha]_D^{25} +30°$ (c=2 in chloroform), $\nu_{\text{max}} \text{CHCl}_3$ 1735, 1660, 1620 cm$^{-1}$, tentatively assigned the structure $\Delta^4$-pregnene-17$\alpha$,20$\alpha$,21-triol-3-one 20,21-diacetate, m.p. 251-253°, $[\alpha]_D^{25} +35°$ (chloroform).
Diphenyltin dihydride solution, 8.0 ml. (0.00282 mole), was added to 0.500 g. (0.00128 mole) of Reichstein's 8 acetate dissolved in 20 ml. of dioxane. The reaction was carried out exactly as above except that in the acetylation step 8 ml. of pyridine and 8 ml. of acetic anhydride were used. The products isolated were identical to the ones obtained when 1 mole of hydride was used, but in different proportions. Starting material 0.0435 g., 8.7%, fraction (a) 0%, fraction (b) 0.0434 g., 7.1%, fraction (c) 0.2766 g., 46.2%, fraction (d) 0.2100 g., 37.9%.

Hydrocortisone Acetate.- Diphenyltin dihydride solution, 7.3 ml. (0.0035 mole) was added to 0.500 g. (0.0123 mole) of hydrocortisone acetate dissolved in 30 ml. of tetrahydrofuran. The reaction was carried out in the usual manner. The product was acetylated by adding 4 ml. of pyridine and 4 ml. of acetic anhydride and heating the mixture on a steam-bath overnight. After hydrolyzing the acetylated mixture in the usual way, the oil obtained was dissolved in 25 ml. of ether and placed on an alumina column. The following eluents (100 ml. each) were used: 25% ethyl acetate in ether, 50% ethyl acetate in ether, ethyl acetate, 2% methanol in ether, 5% methanol in ether, 10% methanol in ether. The fractions isolated from the column in the order in which they were eluted were: fraction (a) 0.0849 g., 14% yield, oil, $\left[\alpha\right]_{D}^{25} + 7.7^\circ$ (c=0.65 in acetone), $\nu_{\text{max}}$ CHCl$_3$ 1725 cm.$^{-1}$, tentatively assigned the structure $\Delta^4$-pregnene-3$\beta$,11$\beta$,17$\alpha$,20$\beta$, $\Delta^4$-pregnene-3$\beta$,11$\beta$,17$\alpha$,20$\beta$. 
21-pentol 3,20,21-triacetate, fraction (b) 0.3476 g., 63% yield, oil, \([\alpha]_D^{25} +29.2^\circ (c=0.85 \text{ in acetone}), \nu_{\text{max}}^\text{CHCl}_3, 1725, 1665, 1620 \text{ cm}^{-1}\), tentatively assigned the structure \(\Delta^4\)-pregnene-11\(\beta\),17\(\alpha\),20\(\beta\),21-tetrol-3-one 20,21-diacetate, 6,7,13 m.p. 225-226\(\circ\), \([\alpha]_D^{25} +169^\circ \text{ (acetone)}\).

Diphenyltin dihydride solution, 9.0 ml. (0.00270 mole), was added to 0.500 g. (0.00123 mole) of hydrocortisone acetate dissolved in 30 ml. of tetrahydrofuran. The reaction was carried out exactly as above except that 8 ml. of acetic anhydride and 8 ml. of pyridine were used in the acetylation. The products isolated were identical to the ones obtained when 1 mole of hydride was used but in different proportions. Fraction (a) 0.3802 g., 63%, fraction (b) 0.1323 g., 24%.

**Cortisone Acetate.**—Diphenyltin dihydride solution, 4.25 ml. (0.00136 mole), was added to 0.500 g. (0.00124 mole) of cortisone acetate dissolved in 20 ml. of dioxane. The reaction was carried out in the usual manner. The product was acetylated by adding 4 ml. of pyridine and 4 ml. of acetic anhydride and heating the mixture on a steam-bath overnight. After hydrolyzing the acetylated mixture in the usual way, the oil obtained was dissolved in 25 ml. of ether and placed on an alumina column. The following eluents (100 ml. of each) were used: 25% ethyl acetate in ether, 50% ethyl acetate in ether, 75% ethyl acetate in ether, ethyl acetate, 2% methanol in ether, 5% methanol in ether, 10% methanol in ether and 25% methanol in ether. The
products isolated from the column in the order in which they were eluted are: fraction (a) 0.1541 g., 27.8% yield, m.p. 208-215°, \( [\alpha]_D^{25} +33.8^\circ \) (c=1.45 in chloroform), \( \nu_{\text{max}} \text{CHCl}_3 1725, 1710 \text{ cm}^{-1} \), tentatively assigned the structure \( \Delta^4 \)-pregnene-3\( \beta \),17\( \alpha \),21-triol-11,20-dione 3,21-diacetate, fraction (b) 0.1515 g., 25% yield, m.p. 175-179°, \( [\alpha]_D^{25} +72.5^\circ \) (c=1.45 in chloroform), \( \nu_{\text{max}} \text{NUJOL} 1730, 1685 \text{ cm}^{-1} \), tentatively identified as \( \Delta^4 \)-pregnene-3\( \beta \),17\( \alpha \),20\( \beta \),21-tetrol-11-one 3,20,21-triacetate, fraction (c) 0.1353 g., 22.3% yield, oil, \( [\alpha]_D^{25} +24^\circ \) (c=1.45 in chloroform), \( \nu_{\text{max}} \text{NUJOL} 1730, 1700 \text{ cm}^{-1} \), tentatively assigned the structure \( \Delta^4 \)-pregnene-3\( \alpha \),17\( \alpha \),21-triol-11,20-dione 3,21-diacetate, fraction (d) trace, oil, \( \nu_{\text{max}} \text{NUJOL} 1735, 1700 \text{ cm}^{-1} \), tentatively assigned the structure \( \Delta^4 \)-pregnene-3\( \alpha \),17\( \alpha \),20\( \beta \),21-tetrol-11-one 3,20,21-triacetate.

Diphenyltin dihydride solution, 7.8 ml. (0.00272 mole), was added to 0.500 g. (0.00124 mole) of cortisone acetate dissolved in 20 ml. of dioxane. The reaction was carried out exactly as above except that 8 ml. of pyridine and 8 ml. of acetic anhydride were used in the acetylation. The products isolated were identical to those obtained when 1 mole of hydride was used but in different proportions. Fraction (a) 0.1255 g., 22.7%, fraction (b) 0.2273 g., 37.5%, fraction (c) 0.1434 g., 23.6%, fraction (d) trace.

Diphenyltin dihydride solution, 11.7 ml. (0.00408 mole) was added to 0.500 g. (0.00124 mole) of cortisone acetate dissolved in 20 ml. of dioxane. The reaction was carried out exactly as before except that 12 ml. of pyridine
and 12 ml. of acetic anhydride were used in the acetylation step. The products isolated were identical to those obtained when 1 mole of hydride was used, but in different proportions. Fraction (a) 0.0371 g., 6.7%, fraction (b) 0.3182 g., 52.5%, fraction (c) 0.1195 g., 19.7%, fraction (d) 0.0728 g., 12%.
SUMMARY

Six organotin hydrides were used to reduce a number of aldehydes, ketones and nitrocarbonyl compounds. The aldehydes and ketones were reduced directly to alcohols by the addition of two hydrogens without requiring an hydrolysis step. m-Nitrobenzaldehyde was reduced in good yield to m-aminobenzaldehyde while m- and p-nitroacetophenone gave a poor yield of material believed to be aminoacetophenones. In the course of the reductions the triorganotin hydrides were converted to hexaorganoditin, the diorganotin dihydrides to diorganotin and the organotin trihydrides to a polymeric organotin.

The stereochemistry of the reduction of a number of these ketones was studied and the results are reported. Very little difference in specificity was found when the number of organic groups attached to the tin was changed or when these groups were changed from aromatic to aliphatic.

Five ketosteroids, pregnenolone, progesterone, Reichstein's S acetate, hydrocortisone acetate and cortisone acetate were treated with diphenyltin dihydride. Progesterone and cortisone acetate were reduced in the 3-position first, while Reichstein's S acetate and hydrocortisone acetate were reduced in the expected 20-position first. The stereochemistry of the products was studied and it was concluded that -hydroxyl groups predominated.
BIBLIOGRAPHY


17. Doctoral Dissertation of Roland S. Ro of the University of Notre Dame, Notre Dame, Indiana.


BIOGRAPHICAL DATA

Name in Full: Oscar Francis Beumel, Jr.
Date of Birth: May 14, 1930
Place of Birth: Evansville, Indiana
Secondary education: Reitz Memorial High School for Boys, Evansville

Collegiate institutions attended Dates Degree
University of Notre Dame 9-48 to 6-52 B.S. in Chem.

Publications

Positions held
Active duty in U. S. Navy from 6-52 to 5-55.
Foote Mineral Company from 8-59 to present.