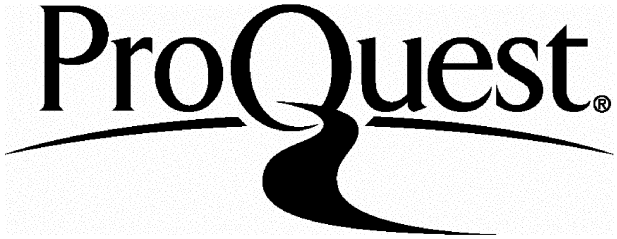
Preparation, Properties and Reactions of Organotin Hydrides

by

Daniel Kwasi Osei-Kissi

A thesis presented to the University of London in partial fulfilment of the requirements for the degree of Doctor of Philosophy

Department of Chemistry
University College London
November 1992



Dedicated with love to my Parents
and my beloved Anna

"He that is void of wisdom despiseth
his neighbour: but a man of
understanding, holdeth his peace"

Proverbs 11:12

Father, Mother
Provide me with pen and slate
I want to learn.
Land is gone
Cattle and sheep are not there
Not there any more
What's left?
Learning, learning.

Siriana's Song, in The River Between

Ngugi Wa Thiong'o

The true seeker of truth never loses hope.
The true seeker of real justice never tires.
A farmer does not stop planting seeds just
because of the failure of one crop. Success is
born of trying and trying again. Truth must seek
justice. Justice must seek the truth. When justice
triumphs, truth will reign on earth.

Matigari, in 'Matigari'

Ngugi Wa Thiong'o

"The quality of mercy is not strained,
It droppeth as a gentle rain from heaven
Upon the place beneath: it is twice blessed
It blesseth him that gives and him that takes....."

Portia, in The Merchant of Venice

William Shakespeare

Acknowledgements

I would like to give my most sincere thanks to my supervisor, Professor A G Davies FRS, for his advice, encouragement and friendship throughout this work.

My thanks also to the Science and Engineering Research Council and the International Tin Research Institute for granting a CASE award and in particular to my industrial supervisor, Dr P J Smith.

I would also like to thank Dang, Cai and Kai, all members of the Davies group, for their friendship and support during the desperate hours of this thesis.

I am grateful to the technical staff for their help and advice, expecially Jill Maxwell, Steve Corker and Alan Stones for their excellent support services.

Finally, I would like to thank my parents for their love and encouragement throughout my life and to my beloved wife, Anna, for putting up with the long hours of work during the past three years. It is to them that I dedicate this thesis.

ABSTRACT

Trialkyltin hydrides, particularly tributyltin hydride are familiar reagents with an established place in organic synthesis, but little work has been carried out on the properties and applications of other tin hydrides.

This thesis reports a study of the reaction of tributyl and triphenyltin hydrides with a variety of alkynes at, or above, 80°C in the presence of a radical initiator to give the corresponding vinyltin compounds. The characteristic NMR spectra are used to define the regio- and stereo- selectivity of the reactants.

A series of dibutyltin hydrides, Bu_2SnXH, have been prepared by disproportionation between Bu_2SnH_2 and Bu_2SnX_2, where X = Cl, $OCOCH_3$, $OCOCF_2Cl$, $OCOC_6H_5$. At room temperature these compounds Bu_2SnXH evolve hydrogen with formation of the corresponding distannanes $XBu_2SnSnBu_2X$ and the mechanism of these reactions has been shown to be a radical chain process, involving, we believe, homolytic substitution of a tin radical at a tin centre with the displacement of a hydrogen atom.

These hydrides, Bu_2SnXH, are then shown to bring about hydrostannation and hydrostannolysis reactions at or below room temperature in the absence of an initiator. It is suggested that the spontaneous homolytic decomposition initiates the familiar radical reactions with the substrates.

The regio- and stereo- selectivities of the reactions are deduced from the NMR spectra and compared with those of the corresponding trialkyltin hydrides. These reactions, which occur readily under very mild conditions, have some potential applications in organic synthesis.

ABBREVIATIONS

NMR	Nuclear Magnetic Resonace
ESR	Electron Spin Resonance
AIBN	Azobis (isobutyronitrile)
UV	Ultraviolet
IR	Infra red
MHz	Mega Hertz
mol dm^{-3}	Moles per cubic decimetre
mmol	Millimoles
M.S.	Mass Spectrum

CONTENTS **Page**

1 INTRODUCTION: ORGANOTIN HYDRIDES

1.1 PREPARATION

The organotin hydrides first became readily available in 1947 when Schlesinger and his colleagues showed that the recently prepared lithium aluminium hydride would reduce methyltin chlorides in diethyl ether to the corresponding hydrides (equation 1.1.a).[1]

$$4\ Me_nSnCl_{4-n} + 4\text{-}n\ LiAlH_4 \longrightarrow 4\ Me_nSnH_{4-n} + 4\text{-}n\ LiAlCl_4 \quad (1.1.a)$$

This general method is still the one which is used most widely.[2] The solvents which have been employed, apart from diethyl ether, include dibutyl ether, diethoxyethyl ether, and tetrahydrofuran, and, apart from the chlorides, organotin bromides, iodides, alkoxides and oxides can be used.[3] The products are usually isolated by distillation and yields are in the range of 80-90%.

A variety of other metal hydrides react in the same way. Diethyl- or diisobutyl-aluminium hydride react under solvent-free conditions,[4] and give good yields of hydrides, but are not popular because of the difficulty of handling the reagents. Diborane is also effective,[4] but has not been widely used. A very convenient and cheap laboratory preparation involves the use of poly(methylhydrosiloxane),[5] which is a by-product from the manufacture of silicone precursors. The organotin oxide is heated in the polysiloxane, which is an involatile oil and the hydride can be distilled off. For example, tributyltin hydride can be prepared from bis(tributyltin) oxide by this process in 90% yield (equation 1.1.b).

$$-(MeSiH\text{-}O)_n- + (Bu_3Sn)_2O \longrightarrow -(MeSi\text{-}O_{1.5})_n- + Bu_3SnH \quad (1.1.b)$$

Dibutyltin oxide can be reduced by this technique if it is first rendered soluble by heating it with butanol to give $Bu_4Sn_2(OBu)_20$.[6]

A further reagent which is particularly relevant to the work described in this thesis is sodium borohydride. Birnbaum and Javora[7] showed that it had no reaction with chlorides in diethyl ether or THF, but if the reaction was carried out in monoglyme or diglyme, reduction was instantaneous and the corresponding hydride could be isolated by distillation. Thus in diglyme, Me_2SnCl_2 reacted to give 96% Me_2SnH_2 and in monoglyme, Bu_2SnCl_2 gave 56% of Bu_2SnH_2.

When the organotin hydrides are used in organic synthesis they present the difficulty of separating and disposing of the organotin by-product (often the halide) and to avoid this, a number of attempts have been made to prepare and use polymer-bound organotin hydrides. For example Neumann has reported the hydrostannation of vinylated polystyrene with Bu_2SnHCl, then the reduction of the SnCl group with Bu_2AlH. The product contained 1.5 mmol of SnH per gramme of resin.[8]

The above methods can be used for preparing mono-, di- and tri-hydrides, though only the first two are commonly used in organic synthesis. The dialkyltin halide hydrides R_2SnXH (X = Cl, Br or I), however have some special properties in organic synthesis and are of particular concern in this thesis. They have been prepared by the disproportionation between the corresponding dialkyltin dihydrides and dialkyltin dihalides and the reaction is usually rapid and essentially complete. For example, by monitoring the integration of the ^1H NMR signals for the Sn-H groups, dibutyltin dihydride and dibutyltin dichloride have been reported to react rapidly in the absence of a solvent to give a mixture containing 93% of the chloride hydride and only 7% of the reactants (equation 1.1.c).[9,10,11,12]

$$\underset{7\%}{Bu_2SnH_2} + Bu_2SnCl_2 \rightleftharpoons \underset{93\%}{2Bu_2SnClH} \qquad (1.1.c)$$

On attempted distillation at reduced pressure, the equilibrium was reversed and dibutyltin dihydride was collected as the most volatile component.

Other compounds R_2SnXH which have been prepared by similar exchange reactions include the acetate hydride $Bu_2Sn(OCOMe)H$[9] and the alkoxide hydrides $Bu_2Sn(OMe)H$ and $Bu_2Sn(OCH_2\text{-}CH{=}CH_2)H$,[10,13] as well as the chloride hydrides $BuSnClH_2$ and $BuSnCl_2H$.[10]

1.2 REACTIONS OF ORGANOTIN HYDRIDES

During the past 25 years, organotin hydrides have developed into important reagents in organic synthesis.[14,15,16,17] The initial uses involved the reduction of organic halides and the addition to alkenes, but a wide variety of further processes have since been developed. Most of the reactions involve homolytic chain reactions, which are usually initiated with AIBN or photolytically, and many variants have been introduced which involve transformations (particularly ring closing or ring opening) of the intermediate radicals. The rates of many of the elementary processes, which are involved have been measured, or can be estimated from data on related processes, and make it possible to design new reactions with some confidence.

The reactions involving halides, alkenes and alkynes are now considered in more detail.

1.2.1 Reduction of Alkyl Halides

This reaction was discovered by van der Kerk in 1957,[2] and shown to be a radical chain reaction by Kuivila in 1962.[18,19,20] The individual steps in the chain are as follows (Scheme 1) :

$$R_3SnH \xrightarrow{R_i} R_3Sn^{\cdot} \qquad (1)$$

$$R_3Sn^{\cdot} + R'X \xrightarrow{k_{p2}} R_3SnX + R'^{\cdot} \qquad (2)$$

$$R'^{\cdot} + R_3SnH \xrightarrow{k_{p3}} R'H + R_3Sn^{\cdot} \qquad (3)$$

$$2\,R_3Sn^{\cdot} \xrightarrow{2k_{t4}} \text{PRODUCTS} \qquad (4)$$

$$R_3Sn^{\cdot} + R^{\cdot} \longrightarrow \text{PRODUCTS} \qquad (5)$$

$$2\,R^{\cdot} \xrightarrow{2k_{t6}} \text{PRODUCTS} \qquad (6)$$

Scheme 1

With alkyl bromides and iodides, reaction (3) is rate-determining and termination is by reaction (6). The usual steady state treatment of the kinetics then gives the following rate equation (equation 1.2.1.a).

$$-d[R'X]/dt = k_{p3}[R_3SnH](R_i/2k_{t6})^{1/2} \qquad (1.2.1.a)$$

With alkyl chlorides, the propagation reactions (2) and (3) have similar rates, but by a suitable adjustment of concentrations, reaction (2) can be caused to be rate determining and termination is then by reaction (4). Under these conditions, the rate equation becomes (equation 1.2.1.b):

$$-d[R'X]/dt = k_{p2}[R'X](R_i/2k_{t4})^{1/2} \qquad (1.2.1.b)$$

Absolute values for the rate constants for the elementary steps were first determined by the rotating sector method,[21] then later refined (increased by a factor of about 2) by the method of laser flash photolysis, the concentration of the intermediate radicals being monitored by time-resolved UV spectroscopy.[22] A large number of relative rate constants have been further obtained by competition experiments. All these values up to 1989 are recorded in Landolt-Börnstein.[23] A selection of the absolute values are as follows:

TABLE. 1. Absolute values of rate constants (dm^3 mol^{-1} s^{-1} at 300 K)

$$R^{\cdot} + Bu_3SnH \longrightarrow RH + Bu_3Sn^{\cdot}$$

R	Me	Et	Bu	i-Pr	c-C_6H_{11}	t-Bu
10^{-6} k_{p3}	10	2.0	2.3	1.3	2.4	1.8

$$2\ R_3Sn^{\cdot} \longrightarrow \text{PRODUCTS}$$

$R_3Sn^{\cdot}$	$Bu_3Sn^{\cdot}$	$Bu_2\dot{S}nH$	$Bu_2\dot{S}nCl$
$10^{-9}k_6$	1.4	1.6	3.6

$$R_3Sn^{\cdot} + \text{t-BuCl} \longrightarrow R_3SnCl + \text{t-Bu}^{\cdot}$$

$R_3Sn^{\cdot}$	$Bu_3Sn^{\cdot}$	$Bu_2Sn^{\cdot}H$	$Bu_2Sn^{\cdot}Cl$
k_6	1.6×10^4	4.7×10^3	3.9×10^3

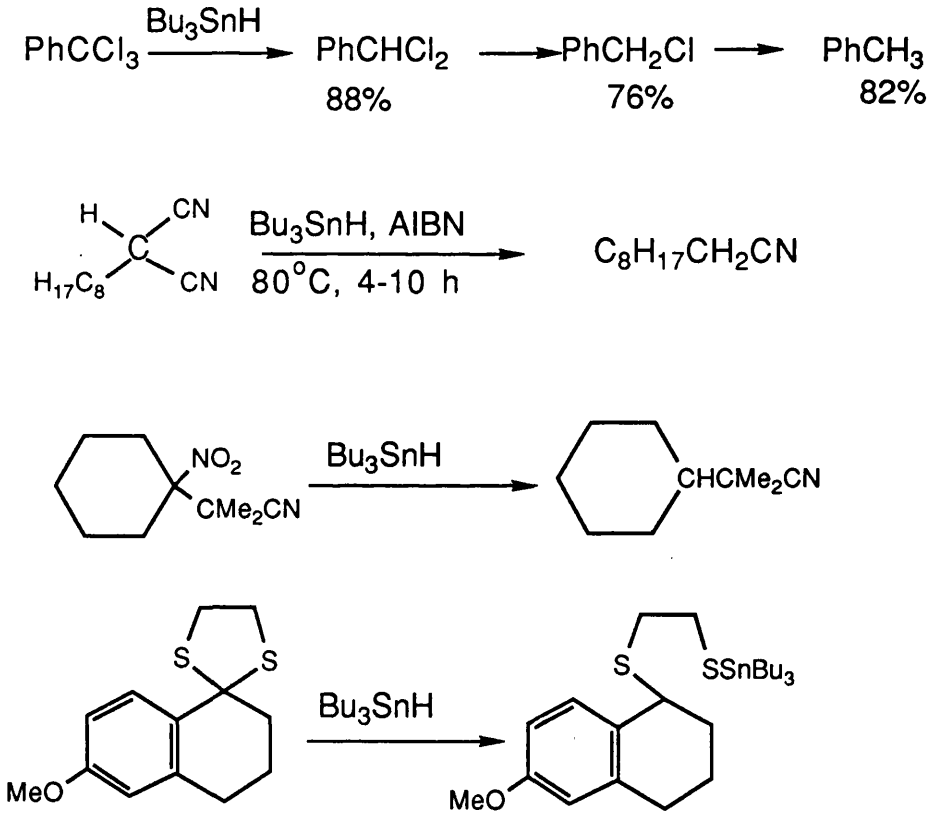
From these data and the many relative rate constants which have been determined, the following generalisations can be drawn.

(1) All alkyl radicals, primary, secondary and tertiary, react with tributyltin hydride at approximately the same rate of 2×10^6 dm^3 mol^{-1} s^{-1} .

(2) The rates of self reaction of the organotin radicals $Bu_3Sn\cdot$, $Bu_2HSn\cdot$ and $Bu_2ClSn\cdot$ (and indeed of most small radicals) is close to the diffusion controlled limit of 2×10^9 dm^3 mol^{-1} s^{-1} .

(3) The reactivity of different halides RX follows the sequence I > Br > Cl > F.

Other groups that can be removed by hydrostannolysis include CN, NO_2, and RS as illustrated in Scheme 2.

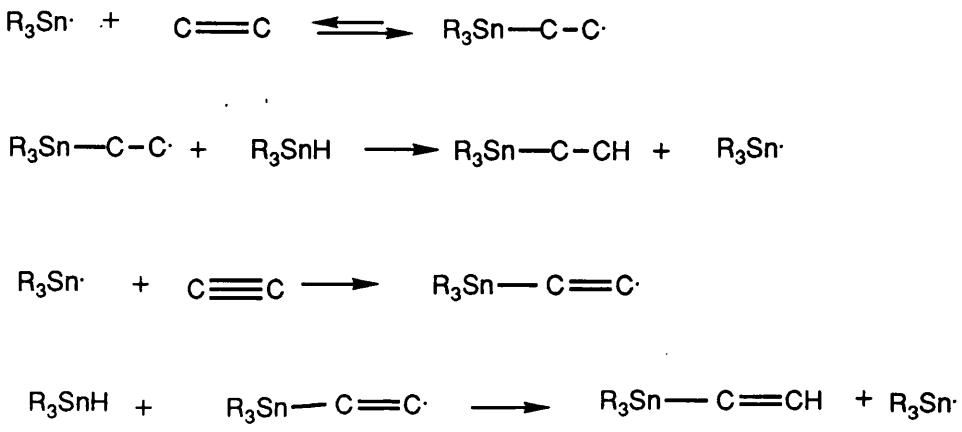


Scheme 2

These hydrostannolysis reactions like those involving alkyl halides, all apparently involve similar radical chain mechanisms. The generation of the alkyl radical often serves as the first of a series of inter- or intra-molecular radical transformations, and this application of organotin hydrides in organic synthesis provides the major area of development of organotin chemistry.

1.2.2 Addition to Alkenes and Alkynes

The propagation steps of the addition to alkenes and alkynes are:



Scheme 3

No rate data appear to be available for the addition of stannyl radicals to alkenes or alkynes, but many studies have been made of the regioselectivity and the stereoselectivity of the reactions.

1.3 HYDROSTANNATION

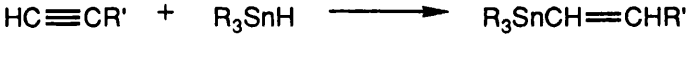
The term hydrostannation was coined in the early 1960's by Kuivila in an analogy with similar designations such as hydroboration, hydrosilation and hydroformylation.[24] It refers to the addition of a tin-hydrogen bond across an unsaturated compound (Scheme 3).

Although several organotin hydrides are readily available and give facile hydrostannation, by far the most common is tributyltin hydride (Bu_3SnH) and to some extent triphenyltin hydride. Hydrostannation is now not only confined to alkenes and alkynes, but it has been extended to include carbonyls, cyanides, isocyanates and thioisocyanates.[25, 26] We are here principally concerned with the hydrostannation of alkynes.

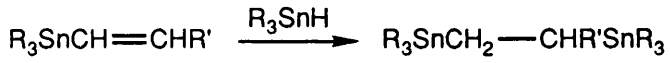
1.3.1 Hydrostannation of Alkynes

Triorganotin hydrides react much more quickly with alkynes than with alkenes, for example, tri-n-propyltin hydride reacts with 1-hexyne and propargyl alcohol without a catalyst but fails to react with 1-octene.[26a]

These reactions have become the major source of vinyltin compounds. Addition can yield both mono- and di-adducts (equation 1.3.1.a).



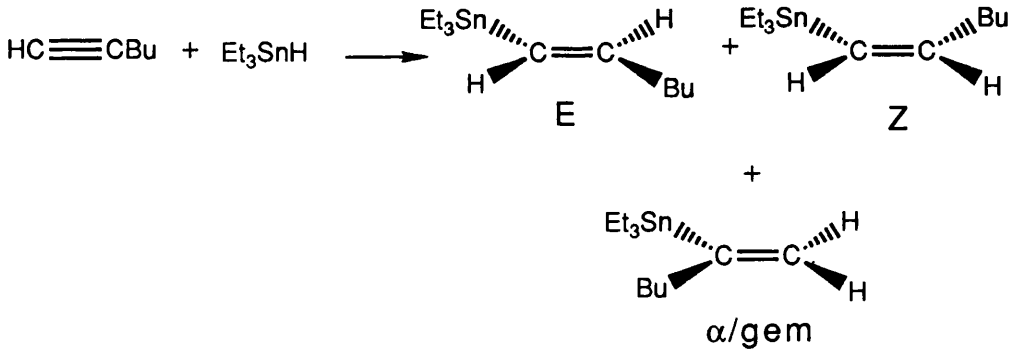
$$HC{\equiv}CR' + R_3SnH \longrightarrow R_3SnCH{=}CHR'$$



$$R_3SnCH{=}CHR' \xrightarrow{R_3SnH} R_3SnCH_2{-}CHR'SnR_3$$

(1.3.1.a)

The mono adduct is usually a mixture of Z and E isomers, an example of this being the addition of triethyltin hydride to 1-hexyne to give the E and Z isomers and a small amount of gem isomer.[27] If the reaction is prolonged by several hours the amount of E isomer increases (Scheme 4).

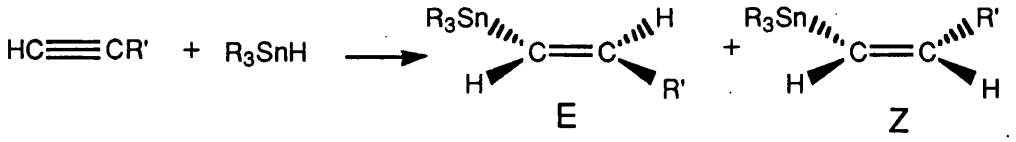


Scheme 4

These reactions have been shown to proceed by a free radical chain mechanism, similar to that of alkene additions.

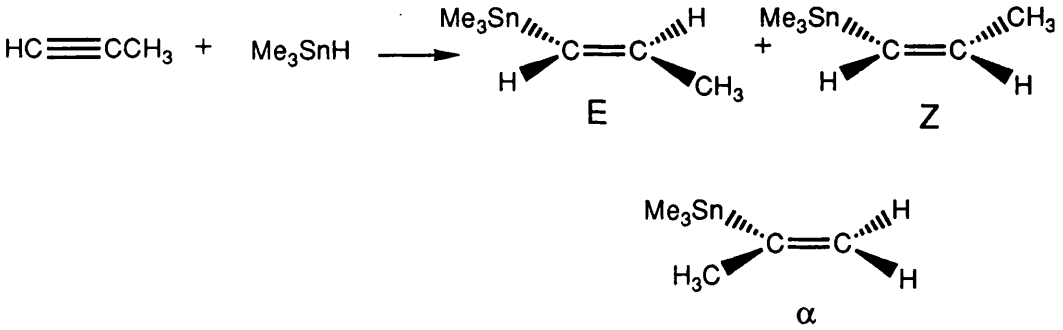
Extensive work on the mechanism of addition has been conducted by Leusink et al.,[28,29,30,31] who studied the products of the hydrostannation of various alkynes with a variety of triorganotin hydrides. They conclude that addition to mono-substituted alkynes

results in the formation of Z-adducts and that any E-adduct arises from the primarily formed Z-adduct. (Scheme 5)



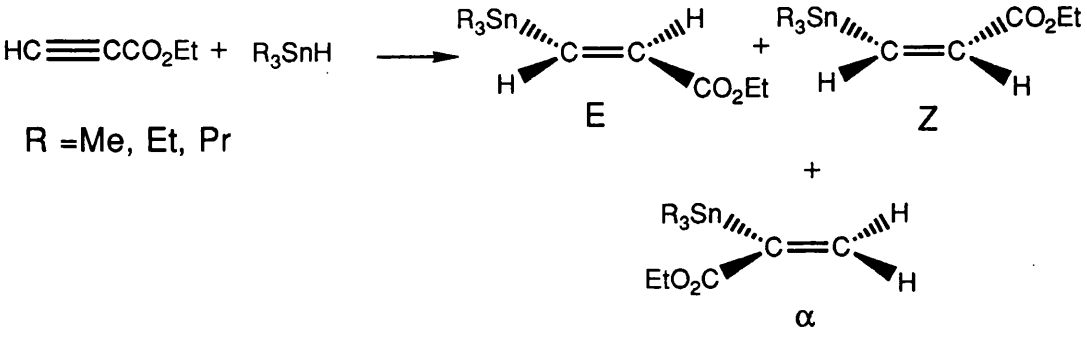
Scheme 5

Seyferth and Vaughan[32], however found that addition of trimethyltin hydride to propyne yielded not just Z and E adducts, but also a few percent of the non-terminal α-adduct (Scheme 6).



Scheme 6

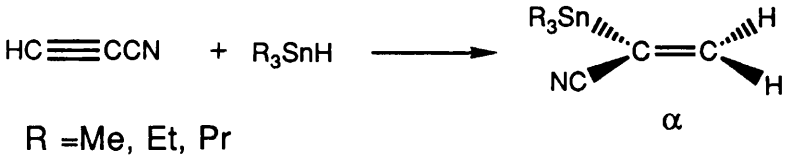
Similar results were obtained with 1-pentyne and 1-heptyne. Investigations by Leusink into reactions of ethyl propiolate gave a considerable amount of other products[33] in addition to the terminal adducts expected (Scheme 7).



Scheme 7

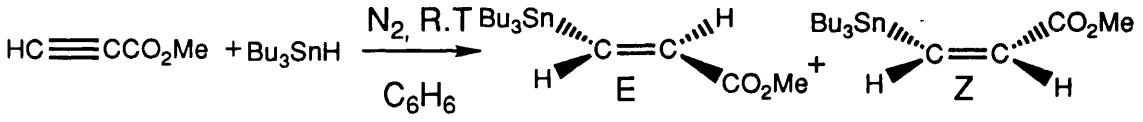
Their work demonstrates the following:

(i) Addition to monosubstituted acetylenes containing a strongly electron-withdrawing substituent (COOR or CN) gives mainly the α-adduct (Scheme 8).



Scheme 8

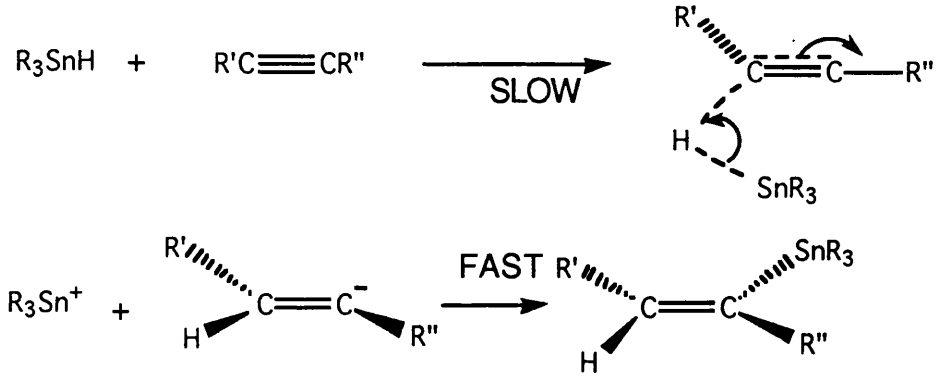
However, work conducted recently by Sweeney et al.[34] gave different results. They found no evidence of the α-adduct when reacting tributyltin hydride with methyl propiolate (Scheme 9).



Scheme 9

It may well be that conducting the reaction at room temperature does affect the nature of the product.

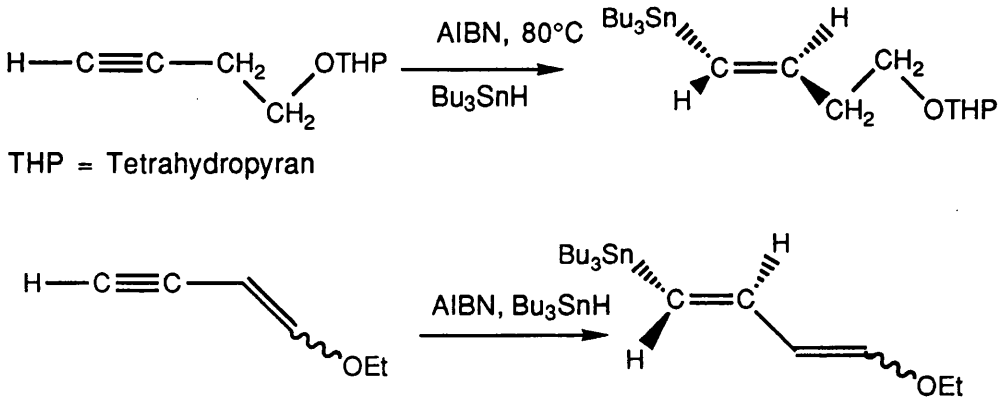
By following the reaction and studying the effects of radical initiators and scavengers on the formation of products, Leusink concluded that the formation of the α-adduct proceeds by an ionic mechanism as its formation was not affected by radical initiators or scavengers.[33]



Scheme 10

(ii) Addition to monosubstituted acetylenes with weakly electron-releasing (C_4H_9, OR etc) and weakly electron withdrawing (CH_2OH, C_6H_5) substituents gave mainly the E and Z (β-adducts) with only small amounts of the α-adducts, and several groups have found that no α-adducts are obtained (Scheme 11).[35,36,37]

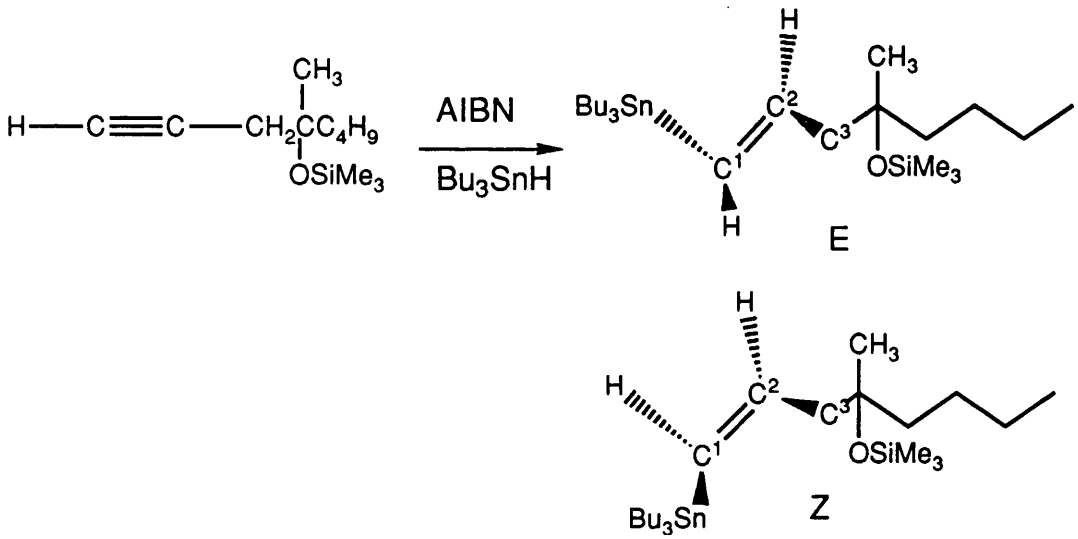
This particular field has received considerable attention as it provides vinyltin intermediates for synthetic organic chemists.



Scheme 11

In an investigation into organometallic reagents useful for synthesis of prostaglandins and prostaglandin intermediates, Chen et al. reported that 1-alkynes react with tributyltin hydride to give the Z and E addition products,[38] although the Z was obtained only in small amounts or not at all.

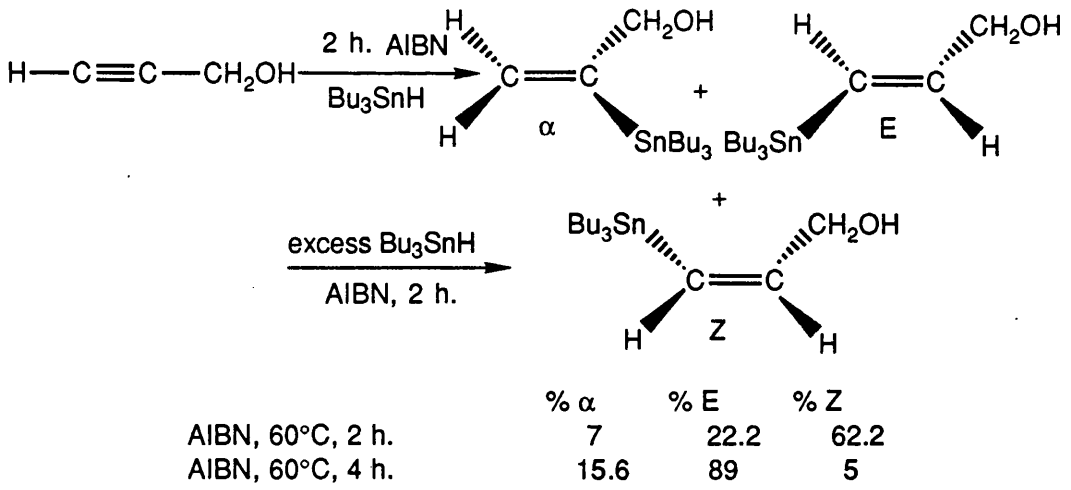
The Z-adduct as reported by Leusink and others,[33,39,40] presumably isomerises to the E-adduct.



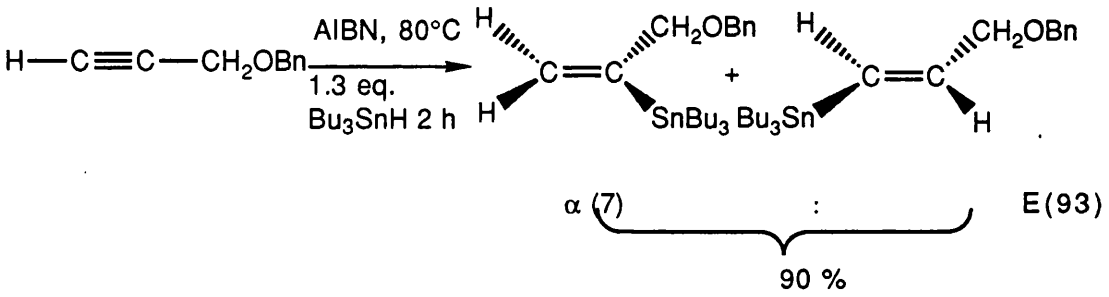
Scheme 12

This was confirmed by the reaction of tributyltin hydride with 4-methyl-(4-trimethylsilyloxy)-octyne (Scheme 12). After 2 hours at 135°C, the reaction yields a 10:1 ratio of Z and E-isomer and the ratio remains unchanged even after an additional 2 hours of heating and further addition of AIBN. However, upon the addition of 0.4 equivalents of Bu_3SnH and AIBN and on further heating the Z/E ratio was 2:3, and further addition of AIBN and Bu_3SnH results in a Z/E ratio of 1:9.

Similar observations were made by Jung et al.[40] for the reaction of propargyl alcohol with tributyltin hydride; they also observed the formation of the α-adduct (Scheme 13).

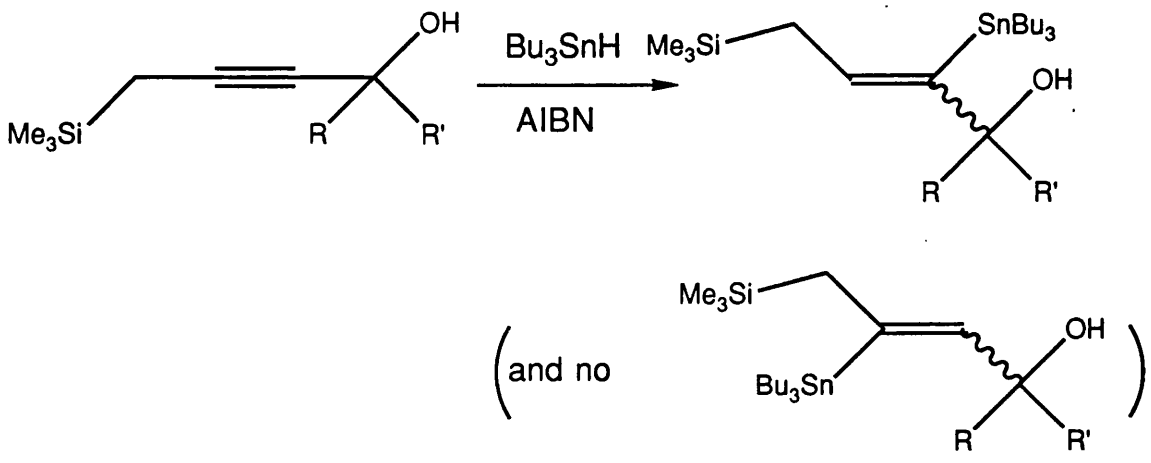


	% α	% E	% Z
AIBN, 60°C, 2 h.	7	22.2	62.2
AIBN, 60°C, 4 h.	15.6	89	5



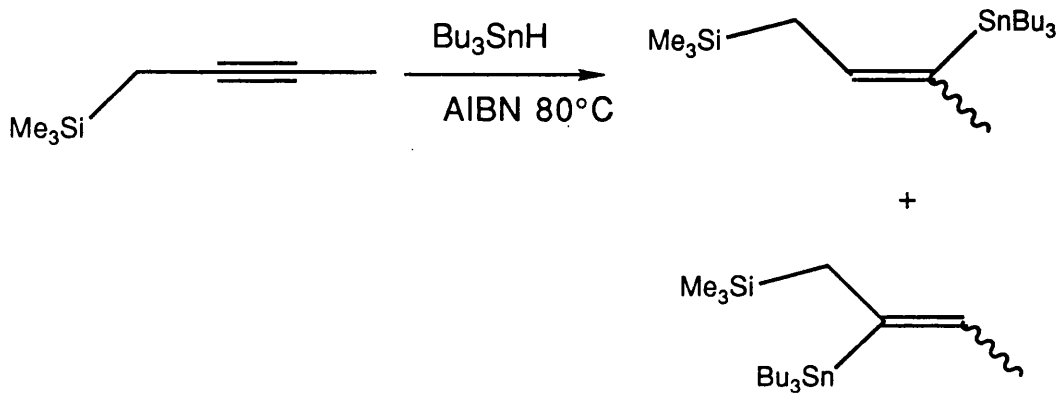
Scheme 13

Extensive work by Taddei[39] on the stereo- and regio-chemistry of hydrostannation of substituted propargyl alcohols gave an understanding of the composition of the products and the possible mechanism involved in the isomerisation of the Z to E-adduct.



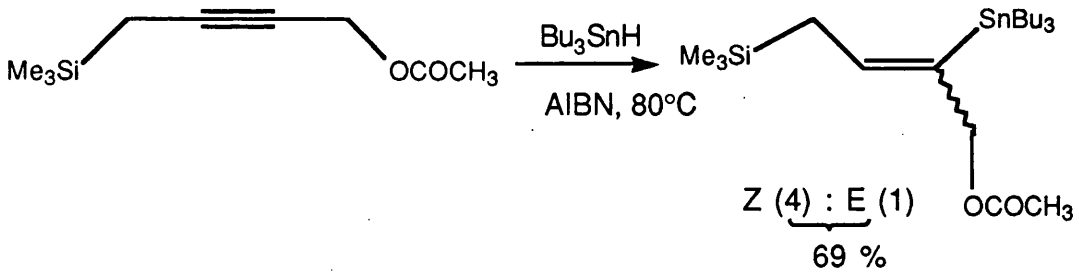
Scheme 14

They found that the regio-isomer always obtained had the tin moiety near the OR group (Scheme 14), and they concluded that this was due to the presence of the oxygen on the carbon directly bonded to the triple bond. Absence of the OR group resulted in the formation of two regio-isomers with predominance of the product with the stannyl group at the least hindered position i.e. adjacent to the Me_3SiCH_2 group (Scheme 15).



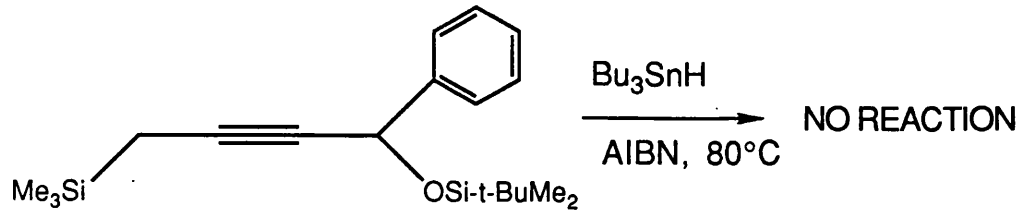
Scheme 15

They found that protecting the OH group did not affect the regiochemistry (Scheme 16).



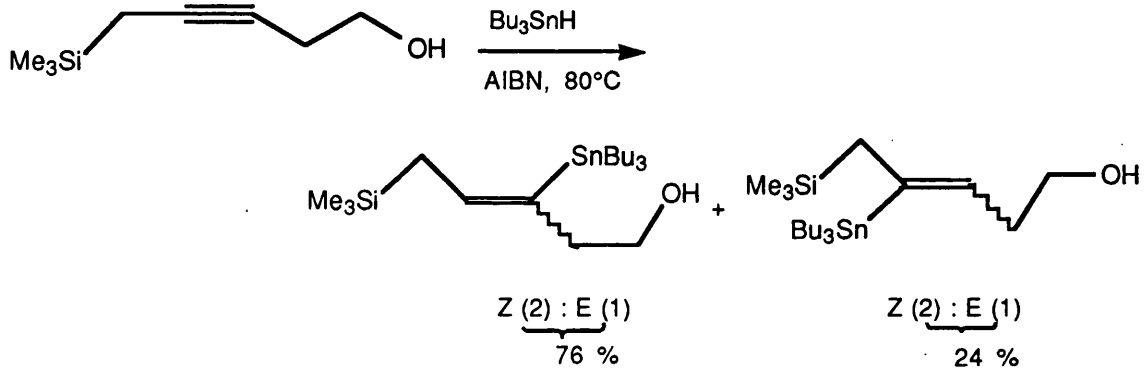
Scheme 16

No reaction occurs when the triple bond is sterically hindered in the region of the oxgen (Scheme 17).



Scheme 17

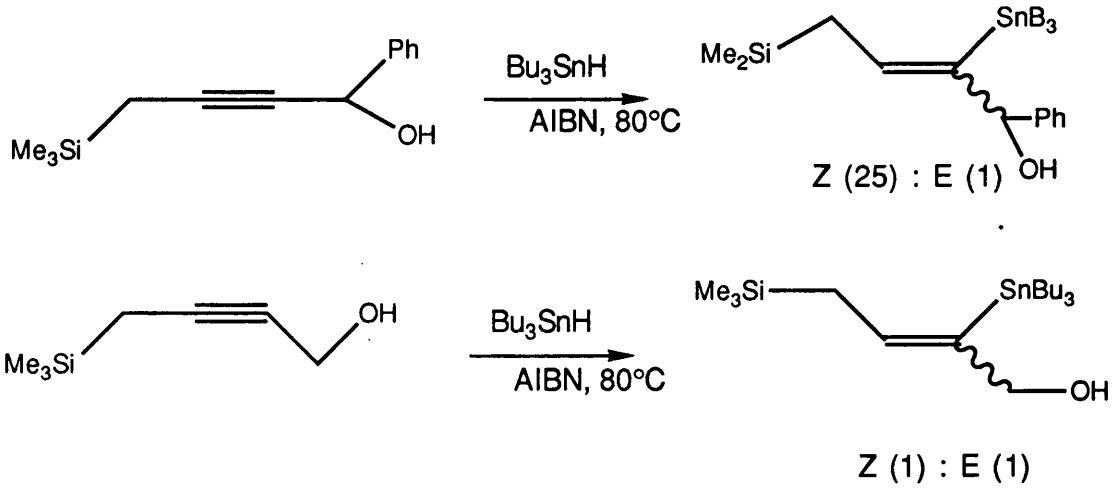
When a CH_2 group was interposed between the triple bond and the CH_2OH group, the reaction showed a low regioselectivity (Scheme 18).



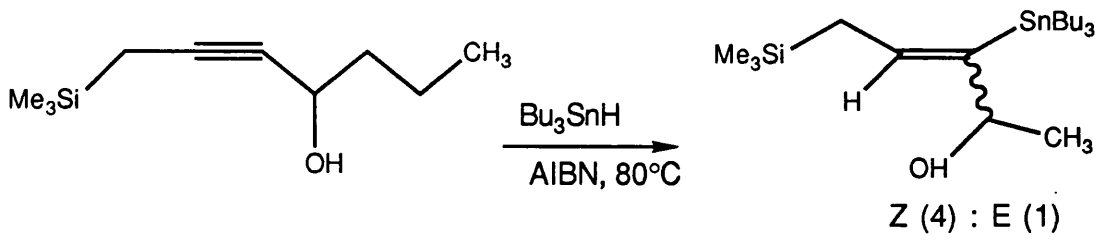
Scheme 18

1.3.1.1 Stereochemistry

The stereochemistry about the double bond in the products is dependent on the nature of the substituents as well as the reaction conditions. Bulky R groups gave an increase in the Z/E ratio (Schemes 19 and 20).



Scheme 19

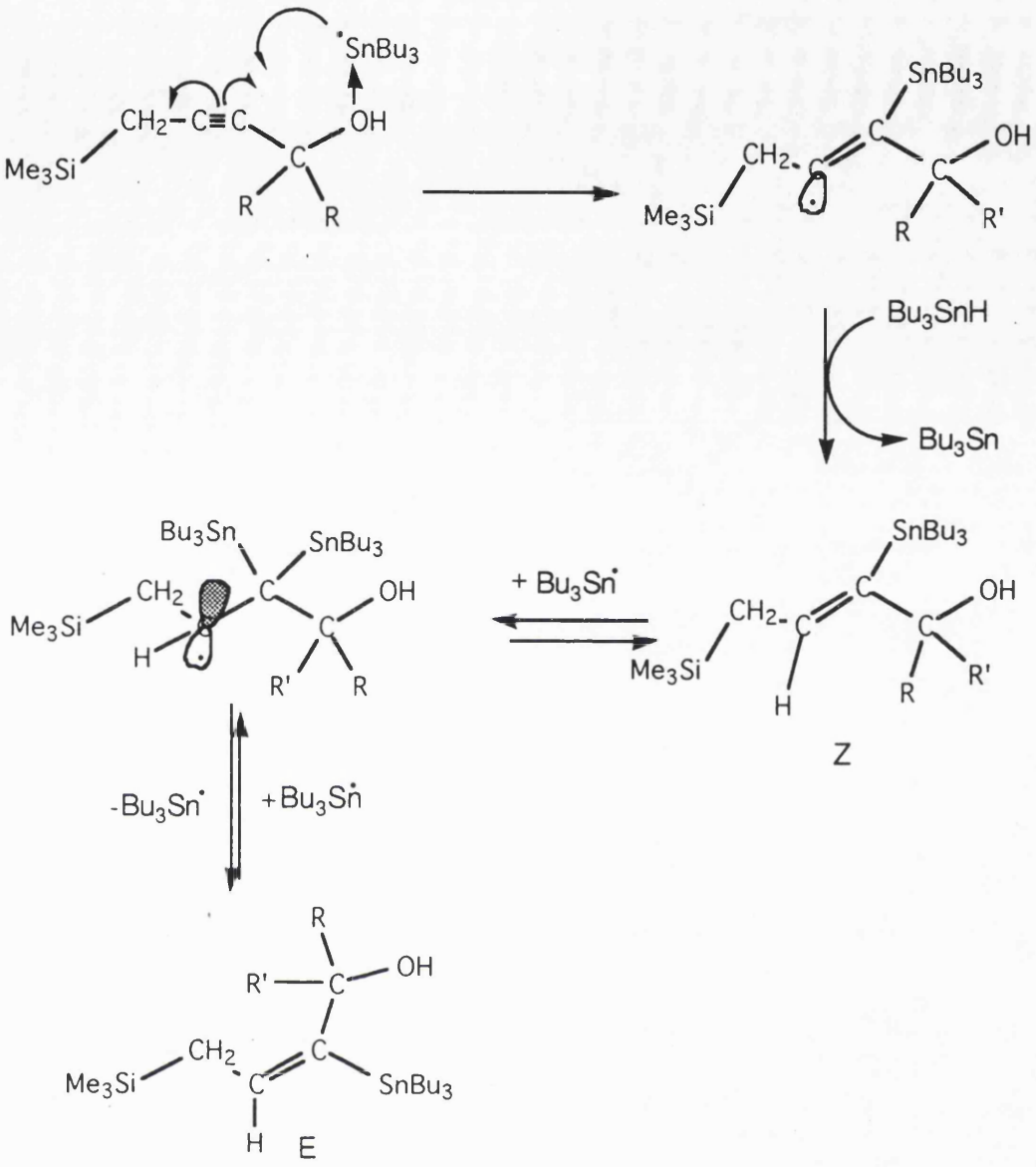


Z (4) : E (1)

Scheme 20

Taddei et al.[39] conclude that the final outcome of the reaction involves several factors, such as the reaction time, temperature, and the amount of Bu_3SnH used. Longer reaction times often result in a lower Z:E ratio (1:1) whilst performing the reaction at 60°C results in a high Z:E ratio (12:1), and decreasing the amount of Bu_3SnH also gave a higher Z:E ratio.

From these observations the following mechanism (Scheme 21) was proposed for the reaction. The $Bu_3Sn\cdot$ radical co-ordinates to the oxygen and then forms a C-Sn bond. Abstraction of H· gives the kinetically controlled Z-isomer, which then undergoes radical equilibration at high temperatures to give the E-isomer.

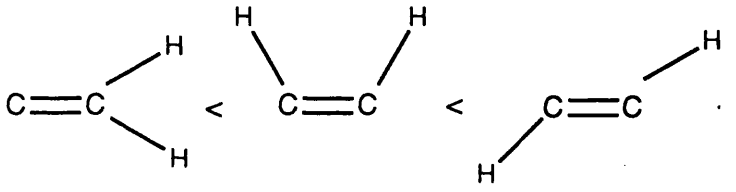

SnBu3
CH2–C≡C
OH
Me3Si
R
R
SnBu3
CH2
OH
Me3Si
R
R'
Bu3SnH
Bu3Sn
Bu3Sn
SnBu3
CH2
OH
Me3Si
H
R'
R
+ Bu3Sn
SnBu3
CH2
OH
Me3Si
H
R
R'
Z
-Bu3Sn
+Bu3Sn
R
R'
OH
CH2
Me3Si
SnBu3
H
E

Scheme 21

1.3.1.2 ^{1}H NMR Spectroscopy

The characterisation of vinylstannanes has always been through proton nmr spectroscopy. The chemical shifts of the olefinic protons are not diagnostic for the Z, E and α–isomers, but the H-H and Sn-H coupling constants are. The ground-breaking work by Leusink[33] has established a range of coupling constants for the α, Z and E isomers.

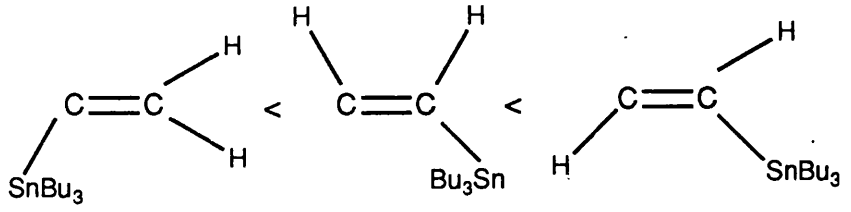
The initial characterisation can be achieved by comparing the H-H coupling constants to those of simple vinyl compounds, in which J_H (Hz) increases in the following order (Figure 1).[41]



FULL RANGE (Hz)	0 - 3.5	0 - 12	12 - 18
TYPICAL RANGE (Hz)	2	7 - 10	14 - 16

Figure 1

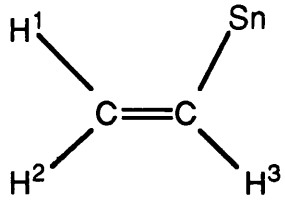
The literature provides the following ranges of J_H (Hz) specifically for vinyltin compounds (Figure 2).[33,40,42]



J_H (Hz)	0 -2.7	7.6- 13.6	14.5 - 20.4

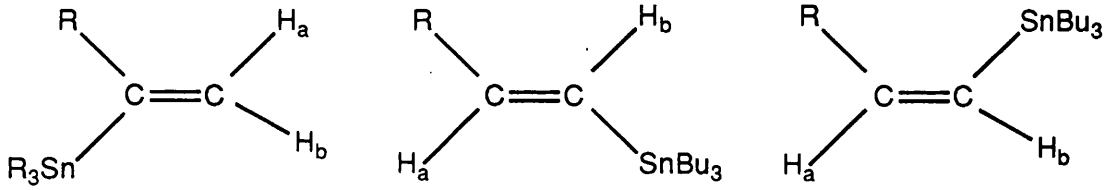
Figure 2

Values of the Sn-H coupling constant are more useful. Moore and Happe[43] reported the values for tetravinyltin given in Figure 3 which compare favourably with those given by Leusink and by Ensley for tributyl(vinyl)tin compounds (Figure 4).[33,42]



J_{Sn-H1}	J_{Sn-H2}	J_{Sn-H3}
90.6 Hz	183.1 Hz	98.3 Hz

Figure 3



J_{Sn-Ha} (Hz)	92-102	64 - 88	111 - 176
J_{Sn-Hb} (Hz)	88-97	73 - 90	54 - 92

Figure 4

1.3.2 Hydrostannation of Alkenes

A convenient way of synthesising organotin compounds is through the hydrostannation of alkenes.[43] Trialkyltin hydrides do not react readily with simple alkenes such as 1-octene but triphenyltin hydride reacts to give 72% yield of the adduct.[44] If the reaction is initiated with benzoyl peroxide or UV irraditation, tetraphenyltin is obtained instead of triphenyl-1-octyltin.

Dialkylchlorotin hydrides have also been reported to be more reactive than trialkyltin hydrides and give the adduct with 1-octene at 20 - 45°C in 75% yield.[44,45]

Introduction of an electron-withdrawing group and the use of AIBN as free radical catalyst have resulted in successful addition to alkenes as shown in Equation 1.3.2.a.

$$(C_2H_5)_3SnH + CH_2{=}CHX \xrightarrow{AIBN} (C_2H_5)_3SnCH_2CH_2X$$

where X = CH_2OH, CO_2CH_3, CN (1.3.2.a)

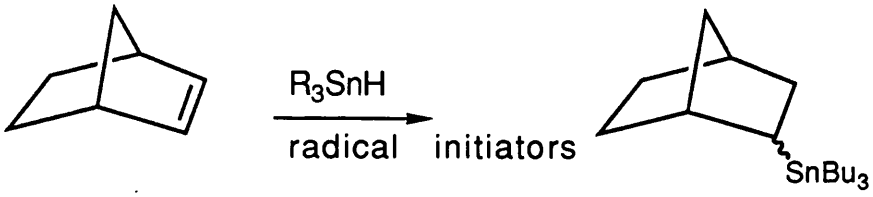
The main hydrostannation product is usually a terminal adduct, however, some reactions have been known to give a small amount of the non-terminal product as well; the hydrostannation of trimethylstannyl-substituted alkenes gives 1,2- and 1,1-distannyl alkenes as shown in Equation 1.3.2.b.[43]

$$Me_3SnH + Me_3SnCR{=}CH_2 \xrightarrow{AIBN} (Me_3Sn)_2CRCH_3 + Me_3SnCHRCH_2SnMe_3$$

where R = H, t-Bu, Ph, Me_3Si, Me_3Sn.

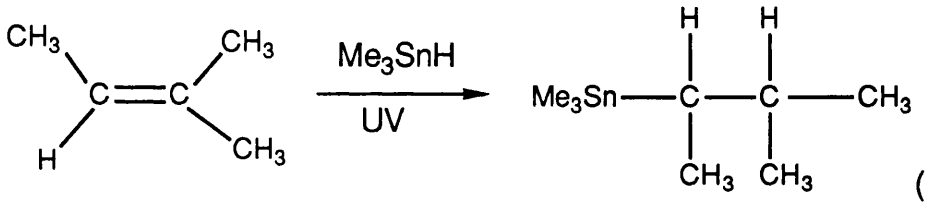
(1.3.2.b)

The major product is as expected, the 1,2-distannyl alkane, but where R = H or R = Me_3Sn, 40% of the 1:1-isomer $(Me_3Sn)_2CRCH_3$ is obtained. The tin moiety then adds at the least sterically hindered carbon.[43,46] Hydrostannation of norbornene (equation 1.3.2.c) with triorganotin hydride confirms this observation by giving a mixture of the endo- and exo-2-triorganostannyl norbornene at 45°C - 70°C; at low temperatures the attack of the organotin radical occurs preferentially at the less hindered exo face, and with Me_3SnH or Bu_3SnH, only the exo adduct is obtained.[47]



R = Me, Bu, Ph (1.3.2.c)

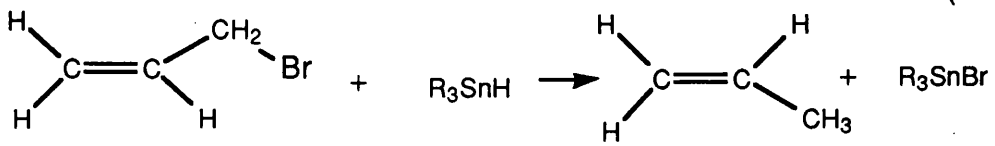
Most of the early examples of hydrostannation involved terminal alkenes unless the double bond was activated by electron attracting groups, but in recent years hydrostannation of simple internal alkenes with Me_3SnH has been shown to occur under UV irradiation (equation 1.3.2.d).[48]



(1.3.2.d)

The presence of functional groups however can sometimes interfere with the hydrostannation reactions. Thus allyl bromides[48] and cis and trans-bromostilbene undergo reduction to the corresponding alkenes rather than hydrostannation, whilst triphenyltin hydride reduces the carbonyl groups of methyl vinyl ketone and phenyl vinyl ketone (equation 1.3.2.e and f).[49,50]

(1.3.2.e)



R = Me, Ph

(1.3.2.f)

1.3.2.1 Mechanism

The catalysis by radical initiators such as AIBN[51,52] and ultraviolet irradiation[51,53,54] and retardation by radical inhibitors such galvinoxyl[52] are evidence for the free radical chain mechanism which is given in Section 3.

This can account for the direction of the addition of organotin hydrides to terminal alkenes: the organotin radical adds to the terminal carbon because the resulting secondary alkyl radical is more stable than a primary alkyl radical. The intermediate carbon- and tin-centred radicals have been identified by ESR spectroscopy.[43] If the substituent on the unsaturated carbon can stabilise the intermediate alkyl radical, the reaction can proceed without a catalyst, but acceleration or retardation is possible with AIBN or phenol respectively.

1.4 REFERENCES

1. Finholt, A.F., Bond, A.C., Wilzbach, K.E. and Schlesinger, H.J., J. Am. Chem. Soc., **69**, 2692 (1947).

2. van der Kerk, G., Noltes, J.G., and Luijten, L.G.A., J. Appl Chem., **7**, 366 (1957).

3. Neumann, W.P., 'The Organic Chemistry of Tin', The Wiley, London, 1970, p282.

4. Neumann, W.P. and Niermann, H., Annalen, **653**, 164 (1963).

5. Hayashi, K., Iyoda, J., and Shiihara, I., J. Organomet. Chem. **10**, 81 (1967).

6. Knocke, R. and Neumann, W. P., Annalen, 1486 (1974).

7. Birnbaum, E. R. and Javora, P. H., J. Organomet. Chem. **9**, 379 (1967).

8. Gerlach, M., Jordens, F., Kuhn, H., Neumann, W. P., and Petersenn, M., J Org. Chem., **56**, 5971 (1991).

9. Sawyer, A. K. and Kuivila, H. G., Chem. Ind. London, 260 (1961).

10. Sawyer, A. K. and Brown, J. E., J Organmet. Chem., **5**, 438 (1966).

11. Sawyer, A. K., Brown, J. E. and Hanson, E. L., J Organomet Chem., **3**, 464 (1968).

12. Sawyer, A. K., May, G. S. and Schofield, R. E., J. Organomet. Chem., **14**, 213 (1968).

13. Massol, M., Barrau, J., Satge, J.and Bouyssieres, J. Organomet, Chem., **80**, 47 (1974).

14. Mathiasch, B., Inorg. Nucl. Chem. Lett., **13**, 13 (1977).

15. Neumann, W. P. and Pedain, J., Tetrahedron Lett., 2461 (1964).

16. Currant, D. P., Synthesis, 417 (1988).

17. Neumann, W. P., Synthesis, 665 (1987).

18. Kuivila, H. G., Menapace, L. W. and Warner, C. R., J. Am. Chem. Soc., **84**, 3584 (1962).

19. Manapace, L. W., and Kuivila, H. G., J. Am. Chem. Soc., **86**, 3047 (1964).

20. Kuivila. H. G., Acc. Chem. Res., **1**, 299 (1968).

21. Carlsson, D. J.and Ingold, K. H., J. Am. Chem. Soc., **90**, 1055 (1968).

22. Chatgilialoglu, C., Ingold, K. H. and Scaiano, J. C., J. Am. Chem. Soc., **103**, 7739 (1981).

23 Landolt-BörnStein, Numerical Data and Functional Relationships in Science and Technology Vol. 13 Part C Spruger, Berlin, 1983.

24. Kuvilia, H. G., Adv. Organomet. Chem.,**1**, 47 (1964)

25. Noltes, J. G. and Janssen, M. J., J. Organomet. Chem., **1**, 346 (1964).

26. Neumann, W. P. and Heymann, E., Ann. Chem., **11**, 693 (1965).

27. Leusink, A. J., Budding, H. A. and Marsman, J. W., Organomet. Chem., **9**, 285 (1967).

28. Leusink, A. J., and Budding, H. A., J. Organomet. Chem., **11**, 533 (1968).

29. Leusink, A. J., Budding, H. A. and Drenth, W., J. Organomet. Chem. **9**, 295 (1967).

30. Leusink, A. J., Budding, H. A. and Drenth, W., J. Organomet. Chem. **11**, 541 (1968).

31. Leusink, A. J., Budding, H. A. and Drenth, W., J. Organomet. Chem. **13**, 155 (1968).

32. Seyferth, D. and Vaughan, L. G., J. Organomet. Chem. **1**, 138 (1963).

33. Leusink, A. J., Hydrostannation, Schotanus and Jens, Utrecht, (1966).

34. Bew, S. P. and Sweeney, J. B., Synlett, 109 (1990).

35. Stork. G., Mook, R., Biller, S. A. and Rychonsky, S. D., J. Am. Chem. Soc. **105**, 3741 (1983).

36. Ladlow, M. and Pattenden, G., Tetrahedron Lett. **25**, 4317 (1984).

37. Ueno, Y., Khare, R. K. and Okawara, M., J. Chem. Soc. Perkin 1., 2637 (1983).

38. Chen, S. M. L., Schaub, R. E., and Grudzinskas, C. V., J. Org. Chem., **43** (1978).

39. Nativi. C. and Taddei, M., J. Org. Chem., **53**, 820 (1988).

40. Jung, M. E. and Light, L. A., Tetrahedron Lett. **23**, **(88),** 3851 (1982).

41. Williams, D. H. and Fleming, I., "Spectroscopic Methods in Organic Chemistry"; McGraw-Hill (UK) Limited.

42. Ensley, H. E., Buescher, R. K., Lee, K., J. Org. Chem., **47**, 404(1982).

43. Moore, D. W. and Happe, A., J. Chem. Phys., **39**, 1518 (1983).

44. Wilkinson, G., Stone, F. G. A. and Abel, E. W., Comprehensive Organometallic Chemistry, Pergamon Press, Oxford, **Vol. 2,** 1982, p 519.

45. Fuchs, R. and Gilman, H., J. Org. Chem. **22**, 1009 (1957).

46. Neumann, W. P. and Pedain, J., Tetrahedron Let., 2461 (1964).

47. Mitchell, T. N., Reimann, W. and Nettlebeck, C., Organometallics,**4**, 1044 (1985).

48. Rahm, A., Grimeau, J., Petraud, M. and Barbe, B., J. Organomet. Chem., 232, 297 (1985).

49. Drago, R. S., Physical Methods in Inorganic Chemistry, Reinhold, New York, 1964, p 48.

50. Noltes, J. G. and van der Kerk, G. J. M., Chem. Ind. (London) 294 (1959).

51. van der Kerk, G. J. M. and Noltes, J. G., J. Appl. Chem., **9**, 106 (1959).

52. Del Franco, G. J., Resnick, and Dillar, C. R., J. Organomet. Chem., **4**, 57 (1965).

53. Neumann, W. P. and Sommer, R., Annalen. **675**, 10 (1964).

54. Barnetson, C., Clark, H. C. and Kwon, J. T., Chem. Ind. (London), 458 (1964).

55. Clark, H. C., Farnival, S. G. and Kwon, J. T., Can. J. Chem., **41**, 2889 (1963).

56. Clark, H. C.and Kwon, J. T., Can. J. Chem., **42**, 1288 (1964).

PURPOSE OF THIS WORK

The vast majority of synthetic organic reactions involving a tin hydride have made use of tributyltin hydride, which has a low toxicity and is cheap and commercially available. In general, synthetic organic chemists have not been prepared to modify the tin hydride used and thus to improve on its performance. However, there are indications in the literature, particularly from work by Neumann, Kuivila and Sawyer, that other readily available hydrides, particularly, the dialkyltin halide hydrides and dialkyltin carboxylate hydride, R_2SnXH, might have special properties which may be exploited in synthesis.

We have been interested in the hydrostannation of 17α-ethynylestradiol as a route to radioactive iodides which are used in cancer treatment. From this starting point we have examined in this thesis the reaction of tributyltin hydride and triphenyltin hydride with a number of alkynes and related molecules. We then describe a study of the properties of the dibutyltin halide hydrides and carboxylate hydrides, and their behaviour as reagents for hydrostannation and hydrostannolysis, and compare their properties with those of the more familiar tributyltin and triphenyltin hydrides.

2 PREPARATIONS AND PROPERTIES OF ORGANOTIN HYDRIDES

2.1 RESULTS

2.1.1 Tributyltin and Triphenyltin Hydrides

Tributyltin hydride (Aldrich Chemical Company) was characterised by NMR spectroscopy as follows

δ_H 4.78 ($^1J^{117}_{Sn}$ 1537.5 Hz, $^1J^{119}_{Sn}$ 1609.0 Hz);

δ_C 9.38 ($^1J^{117}_{Sn}$ 324.5 Hz, $^1J^{119}_{Sn}$ 339.4 Hz; C-α); 13.79 (C-δ);

27.24 ($^3J_{Sn}$ 52.0 Hz; C-γ); 29.10 ($^2J_{Sn}$ 20.3 Hz; C-β).

ν_{max} (neat liquid) 1812 cm^{-1} (Sn-H)

Triphenyltin hydride (Aldrich Chemical Company) was characterised as follows:

δ_H 6.88 ($^1J^{117}_{Sn}$ 1850 Hz, $^1J^{119}_{Sn}$ 1936 Hz).

δ_C 142.20 ($^1J^{117}_{Sn}$ 518.9 Hz, $^1J^{119}_{Sn}$ 543.3 Hz; C ipso) 136.81 ($^2J_{Sn}$ 37.1 Hz; C ortho), 128.38 ($^3J_{Sn}$ 50.5 Hz; C meta); 128.3 (C para),

ν_{max} (neat liquid) 1843 cm^{-1} (Sn-H)

Both these hydrides can be stored under argon for long periods with negligible decomposition, but, upon exposure to air they are oxidized to the organotin oxide and hydroxide (equations 2.1.1.a and b)

$$2\ Bu_3SnH + O_2 \longrightarrow H_2O + [Bu_3Sn]_2O \quad (2.1.1.a)$$

$$2\ Ph_3SnH + 0_2 \longrightarrow 2\ Ph_3SnOH \quad (2.1.1.b)$$

Tributyltin hydride is much more stable than triphenyltin hydride, which deposits the hydroxide within ca. 1 day if it has not been completely deaerated.

2.1.2 Dibutyltin Dihydride

Dibutyltin dihydride was prepared by three different methods:

(a) Following Hayashi's procedure,[1] dibutyltin oxide was heated in poly(methylhydrosiloxane) at 100°C. The hydride was isolated by distillation at 43-51°C/0.05 mmHg, in 50-60% yield leaving an insoluble yellow residue (equation 2.1.2.a).

$$Bu_2SnO + (MeSiH\text{-}O)_n \longrightarrow Bu_2SnH_2 + (MeSi\text{-}O_{1.5})_n \quad (2.1.2.a)$$

(b) Secondly, using Neumann's modification,[2] dibutyltin oxide was heated with butanol under reflux, until it was converted to the soluble tetrabutyl-dibutoxydistannoxane. The addition of poly(methylsiloxane) with subsequent distillation then gave the dihydride (50-60% yield) (equation 2.1.2.b).

$$(Bu_2SnOBu)_2O + (MeSiH\text{-}O)_n \longrightarrow Bu_2SnH_2 + BuOH + (MeSi\text{-}O_{1.5})_n \quad (2.1.2.b)$$

(c) The best method was to treat dibutyltin dichloride with lithium aluminium hydride in over 50% excess as described by van der Kerk[3]. Subsequent ether extraction and distillation gives the required dihydride in quantitative yield (2.1.2.c).

$$2\ Bu_2SnCl_2 + LiAlH_4 \longrightarrow 2\ Bu_2SnH_2 + LiAlCl_4 \quad (2.1.2.c)$$

The dibutyltin dihydride could be kept refrigerated under argon for several weeks before it started to precipitate an insoluble white solid which presumably is dibutyltin oxide formed by adventitious air oxidation. The characteristics of the dibutyltin dihydride were as follows:

δ_H 4.58 (2H, m, $^1J^{117}_{Sn}$ 1542.8 Hz; $^1J^{119}_{Sn}$ 1614.7 Hz; SnH_2).

δ_C 7.11 ($^1J^{117}_{Sn}$ 357.9 Hz, $^1J^{119}_{Sn}$ 374.5 Hz; C-α); 13.90 (C-δ); 27.16 ($^3J_{Sn}$ 64.7; C-γ); 30.61 ($^2J_{Sn}$ 23.7 Hz; C-β).

ν_{max}(neat liquid) 1835 cm^{-1} (Sn-H).

2.1.3 Dibutyltin Chloride Hydride

Dibutyltin chloride hydride was first prepared accidentally when attempting to prepare dibutyltin dihydride by Birnbaum and Javora's method.[4] Dibuyltin dichloride in 1,2-dimethoxyethane (glyme, $MeOCH_2CH_2OMe$) was added dropwise to a 5 fold excess of sodium borohydride in the same solvent at -15°C. The solution was then allowed to warm to room temperature and the solvent was removed at 12 mmHg at 0°C. The ^1H NMR spectrum of the product showed the signal for the SnH proton at δ 7.42 characteristic of the chloride hydride and not δ 4.58 as expected for the dihydride. This was obtained in yields of 60-70%. The product was then isolated by distillation, b.p 35-40°C/0.03 mmHg. The characteristics of the dibutyltin chloride hydride are as follows:

δ_H (C_6D_6) 7.42 (1H, s, $^1J^{117}_{Sn}$ 1875.8 Hz, $^1J^{119}_{Sn}$ 1963.0 Hz; SnHCl).

δ_C 13.65 (C-γ); 17.00 ($^1J^{117}_{Sn}$ 379.7 Hz, $^1J^{119}_{Sn}$ 397.4 Hz; C-α); 27.65 ($^3J_{Sn}$ 63.37 Hz; C-γ); 28.20 ($^2J_{Sn}$ 40.24 Hz; C-β).

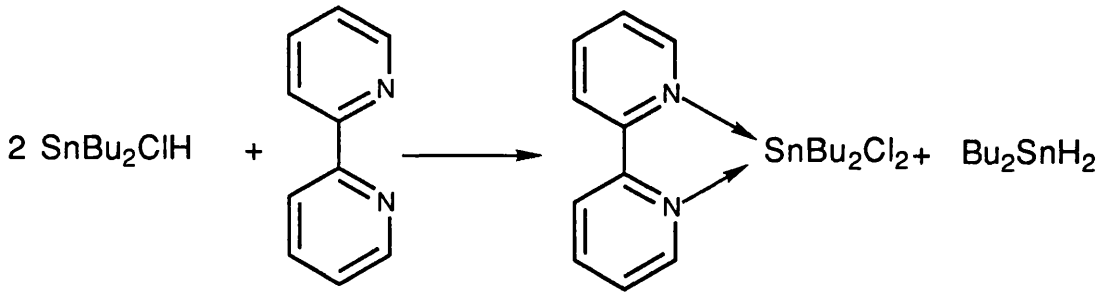
ν_{max} (ethanol) 1853 cm^{-1} (Sn-H)

The second and more convenient method of preparing the chloride hydride is by a disproportionation reaction between the dihydride and the chloride (equation 2.1.3.a):[5,6,7,8]

$$Bu_2SnH_2 + Bu_2SnCl_2 \rightleftharpoons 2\ Bu_2SnHCl \qquad (2.1.3.a)$$

When the components were mixed in equimolar amounts in ethanol, benzene or toluene, the proton NMR spectrum showed that an equilibrium mixture containing about 97% of the chloride hydride and 3% of the reactants was formed in 90 minutes at room temperature. Small amounts of 2,6-di-t-butyl-4-methylphenol had no effect on the rate of reaction, confirming that it does not follow a free radical chain mechanism.

When an equimolar amount of 2,2-bipyridyl was added to the mixture, the ^1H NMR spectrum showed that the reaction had been reversed, the peak at δ 7.42 had disappeared and that at δ 4.58 had increased in intensity. Removal of the solvent left a white crystalline solid which was identified as 2,2-bipyridyl dibutyltin dichloride by m.p (180 - 182°C) and proton and carbon-13 NMR spectroscopy.



(2.1.3.b)

In an analogy with the decomposition of triorganotin hydrides reported by Neumann,[9] we treated the dibutyltin chloride hydride, in d_6-benzene, with pyridine and observed the evolution of hydrogen, which ceased on addition of 2,6 -di-t-butyl-4-methyphenol. Similarily the evolution of hydrogen ceases if 2-methyl-3-butyn-2-ol.was added instead of the phenol.

Proton NMR spectroscopy of the mixture showed that hydrostannation had occurred giving the Z vinyl adduct. The alkyne appears to be acting as a radical trap for the $Bu_2Sn{\cdot}Cl$ radical generated by the pyridine.

The chloride hydride could not be stored over long periods and thus had to be freshly made for each reaction. In a few hours at room temperature it precipitated an insoluble white solid which presumably was dibutyltin oxide, whilst in $CDCl_3$ solution it deposited what appears to be metallic tin on the walls of the NMR tube. Neumann and Pedain[9] have reported that phenyltin trihydride decomposes at 60°C to give metallic tin, hydrogen and hydrocarbon. At no time during the decomposition processes did we observe the evolution of hydrogen.

In the presence of oxygen, Bu_2SnHCl reacts to form a white crystalline solid, which was readily soluble in most organic solvents. This was identified by its m.p (111°C - 114°C) and $\delta^{119}Sn$ NMR spectrum (δ -100 and δ -150) to be tetrabutyldichlorodistannoxane (equation 2.1.3.c).

$$2\ Bu_2SnHCl + O_2 \longrightarrow (ClBu_2SnOSnBu_2Cl)_2 + H_2O \qquad (2.1.3.c)$$

The equilibration reaction between Bu_2SnCl_2 and Bu_2SnH_2 to Bu_2SnHCl was confirmed by observing the disappearance (and hence the appearance of Bu_2SnHCl) of Bu_2SnH_2 against time, by ^1H NMR spectroscopy.

A graph of the standardised integrals of Bu_2SnH_2 and Bu_2SnHCl against time shows that for every mole of Bu_2SnH_2 used up a mole of Bu_2SnHCl is formed, (Figure1).

$Bu_2Sn(OCOCH_3)H$

δ_H 7.6 (1H, s, SnH)

δ_C 13.71 (C-δ); 18.75 ($^1J^{117}_{Sn}$ 415.9 Hz, $^1J^{119}_{Sn}$ 435.2 Hz; C-α); 26.82 ($^3J_{Sn}$ 78.9 Hz; C-γ); 27.85 ($^2J_{Sn}$ 24.8 Hz; C-β)

$Bu_2Sn(OCOCF_2Cl)H$

δ_H 8.45 (1H, s, SnH)

δ_C 13.42 (C-δ), 19.12 ($^1J^{117}_{Sn}$ 472.1 Hz, $^1J^{119}_{Sn}$ 494.1 Hz; C-α); 26.54 ($^3J_{Sn}$ 84.1 Hz; C-γ); 27.64 ($^2J_{Sn}$ 29.3 Hz; C-β);

$Bu_2Sn(OCOPh)H$

δ_H 7.38 (1H, s, $^1J^{117}_{Sn}$ 1940.9 Hz, $^1J^{119}_{Sn}$ 1985.8 Hz, SnH)

δ_C 13.54 (C-δ); 25.485 ($^1J^{117}_{Sn}$ 523.7 Hz, $^1J^{119}_{Sn}$ 548.1 Hz; C-α); 26.30 ($^3J_{Sn}$ 79.2 Hz; C-γ); 27.83 ($^2J_{Sn}$ 31.6 Hz; C-β).

2.1.4.1 Decomposition of Dibutyltin Carboxylate Hydrides

When dibutyltin dihydride and dibutyltin diacetate were mixed in toluene in an NMR tube at 25°C, a stream of hydrogen bubbles could be seen rising through the solution. A similar reaction was observed for the difluorochloroacetate, and for the benzoate. In each case, the organotin product was isolated and identified as the corresponding tetrabutyldicarboxylatodistannanes by m.p, ^1H, ^{13}C and ^{119}Sn NMR spectroscopy and by elemental analysis. The reaction is therefore that shown (equation 2.1.4.1), as reported by Kuivila for the acetate.[10]

$$2\ Bu_2Sn(OCOR)H \longrightarrow [Bu_2Sn(OCOR)]_2 + H_2 \qquad (2.1.4.1)$$

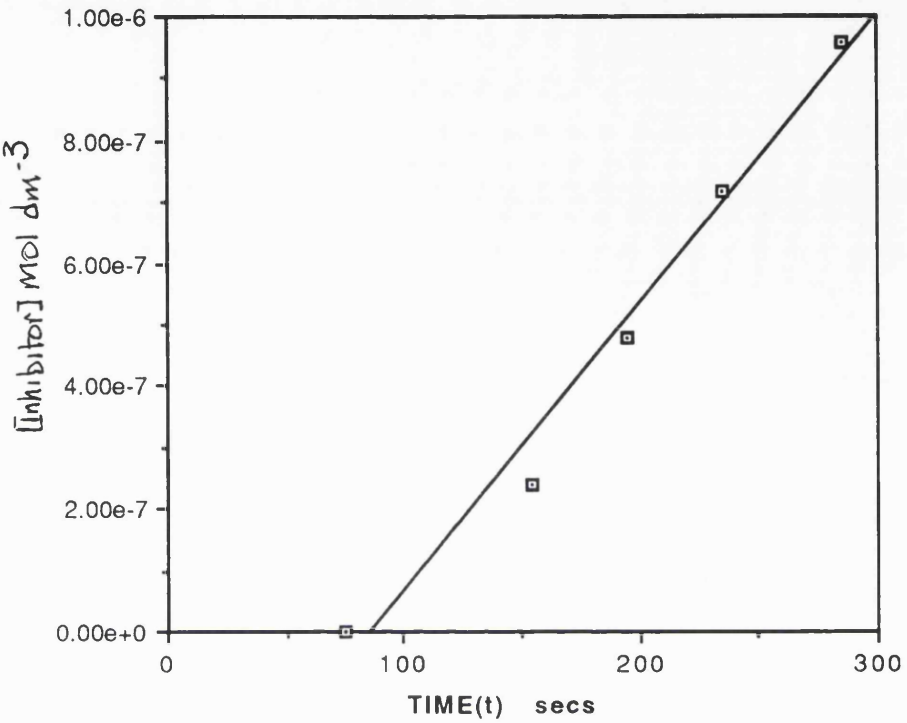
If a small amount of 2,6-di-t-butyl-4-methylphenol was added and the tube was shaken, the evolution of hydrogen ceased, but it resumed after a few minutes.

Similar kinetic experiments were carried out at room temperature with solutions of dihydride and diacetate in toluene containing varying amounts of the phenolic inhibitor. The time for the appearance of the first bubbles of hydrogen was noted.

The results for the acetate hydride ([hydride] = 2 [Bu_2SnH_2] + BuSn(OAc)H]) are shown in Table 1 and Figures 2, 3 and 4.

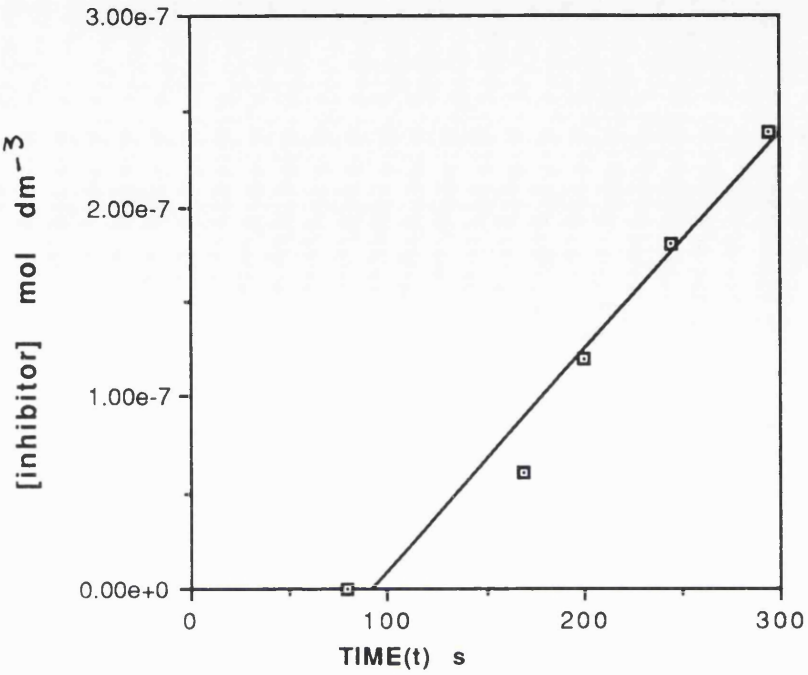
Table 1. Showing the induction period for the evolution of hydrogen at specific concentrations of acetate hydride when the reaction is inhibited by increasing amounts of 2,6-di-t-butyl-4-methylphenol.

[$Bu_2Sn(OCOR)H$] Mol dm^{-3} R = CH_3	[inhibitor] Mol dm^{-3} x10^{-7}	Mole % of inhibitor	Time(t) s
4.80 x 10^{-6}	2.39	2.5	155
	4.79	5.0	195
	7.18	7.5	235
	9.58	10.0	285
	0	0	75
2.40 x10^{-6}	0.60	2.5	170
	1.20	5.0	200
	1.80	7.5	245
	2.40	10.0	295
	0	0	80
9.58 x10^{-6}	2.39	2.5	145
	4.79	5.0	185
	7.19	7.5	230
	9.58	10.0	280
	0	0	65



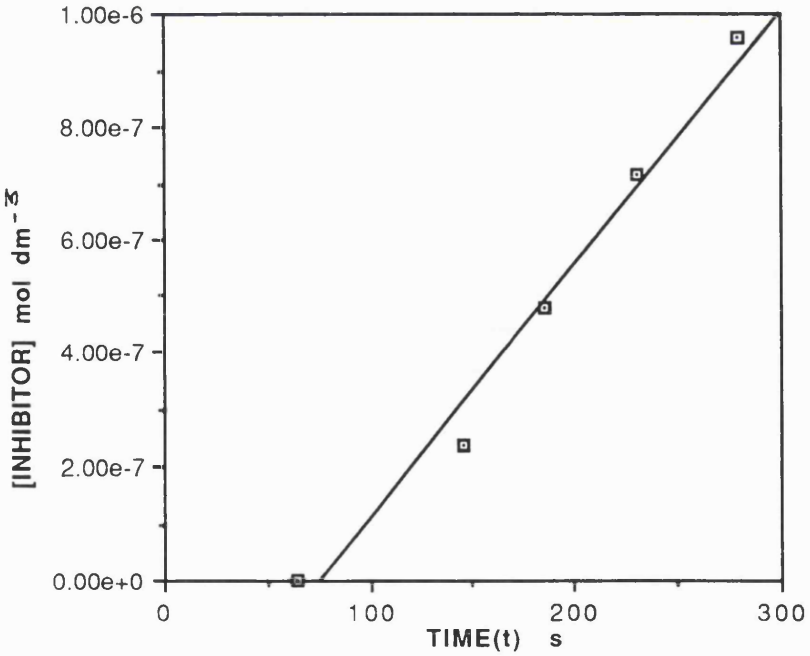
Graph of [inhibitor] (mol dm^{-3}) vs time (t) s at 4.8 x 10^{-6} mol dm^{-3} of hydride

Figure 2



Graph of [inhibitor] (mol dm^{-3}) vs time (t) s at 2.4 x 10^{-6} mol dm^{-3} of hydride

Figure 3



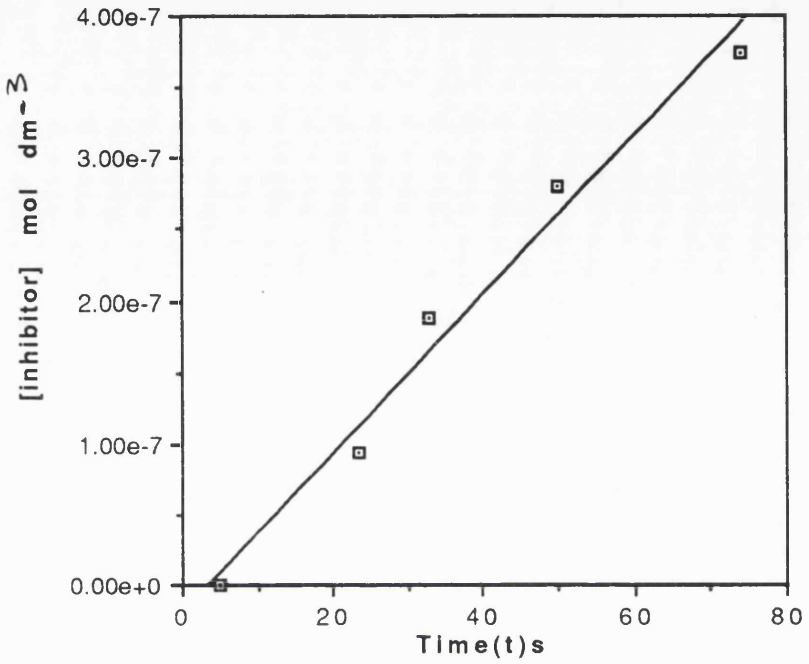
Graph of [inhibitor] (mol dm^{-3}) vs time (t) at 9.58 x 10^{-6} mol dm^{-3} of hydride

Figure 4

Similarly the results for the difluorochloroacetate hydride are shown in Table 2, and Figures 5, 6 and 7,

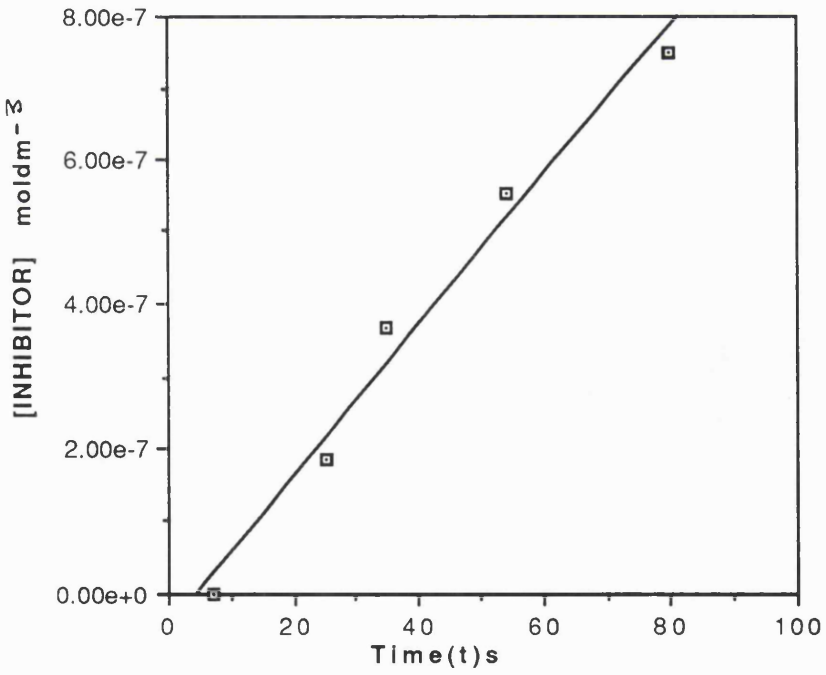
Table 2 Showing the induction period for the evolution of hydrogen at concentrations of difluorochloroacetate hydride when the reaction is inhibited by increasing amounts of 2,6-di-t-butyl-4-methylphenol.

$[Bu_2Sn(OCOCF_2Cl)H]$ mol dm^{-3}	[inhibitor] Mol $dm^{-3} \times 10^{-7}$	mole % of inhibitor	Time(t) s
3.74×10^{-6}	0.94	2.5	25
	1.87	5.0	35
	2.81	7.5	50
	3.74	10.0	72
	0	0	5
7.48×10^{-6}	1.84	2.5	25
	3.68	5.0	35
	5.53	7.5	54
	7.48	10.0	80
	0	0	7
0.15×10^{-6}	3.74	2.5	28
	7.49	5.0	40
	0.11	7.5	60
	0.15	10.0	87
	0	0	5



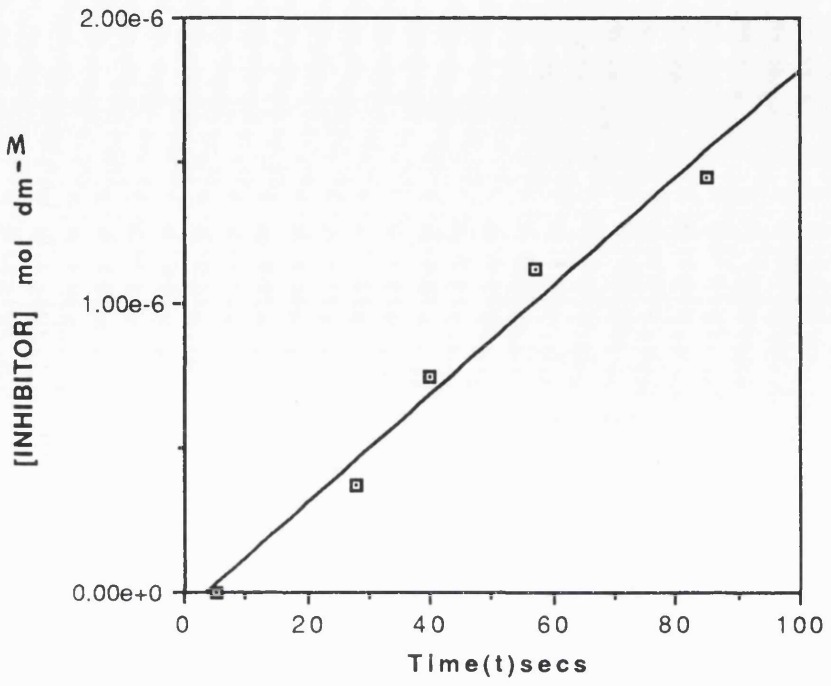
Graph of [inhibitor] mol dm^{-3} vs time (t) at 3.74 x 10^{-6} mol dm^{-3} of hydride

Figure 5



Graph of [inhibitor] mol dm^{-3} vs time (t) at 7.48 x 10^{-6} mol dm^{-3} of hydride

Figure 6



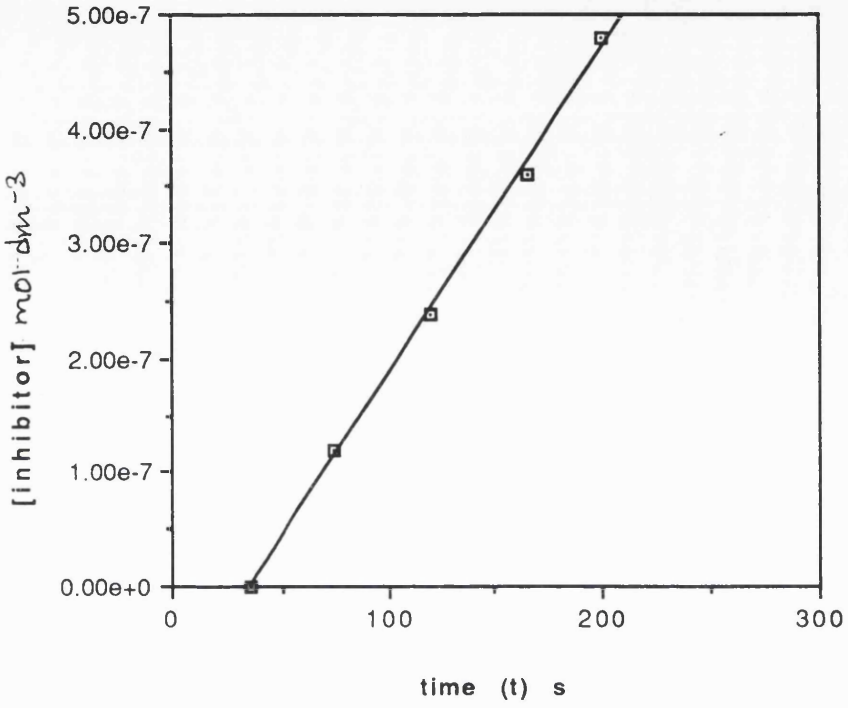
Graph of [inhibitor] mol dm^{-3} vs time (t) at 0.1500 x 10^{-6} mol dm^{-3} of hydride

Figure 7

Finally the results for the benzoate hydride are shown in Table 3, and Figures 8, 9 and 10.

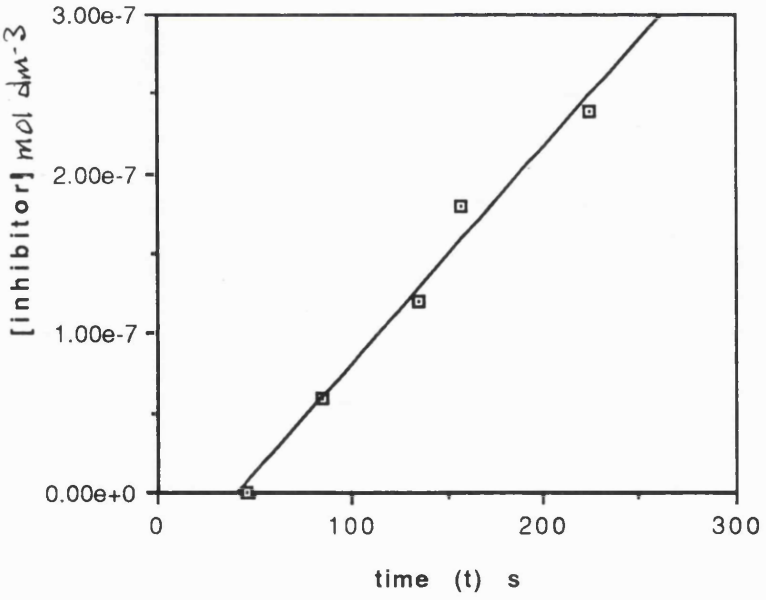
Table 3. Showing the induction period for the evolution of hydrogen at concentrations of benzoate hydride when the reaction is inhibited by increasing amounts of 2,6-di-t-butyl-4-methylphenol.

[BuSn(OCOPh)H] mol dm^{-3}	[inhibitor] Mol mol dm^{-3}	Mole % of inhibitor	Time(t) s
4.79×10^{-6}	1.20	2.5	75
	2.40	5.0	120
	3.60	7.5	165
	4.80	10.0	200
	0	0	35
2.40×10^{-6}	5.99	2.5	85
	1.20	5.0	136
	1.79	7.5	158
	2.40	10.0	225
	0	0	45
9.58×10^{-6}	2.40	2.5	60
	4.79	5.0	115
	7.19	7.5	145
	9.58	10.0	190
	0	0	30



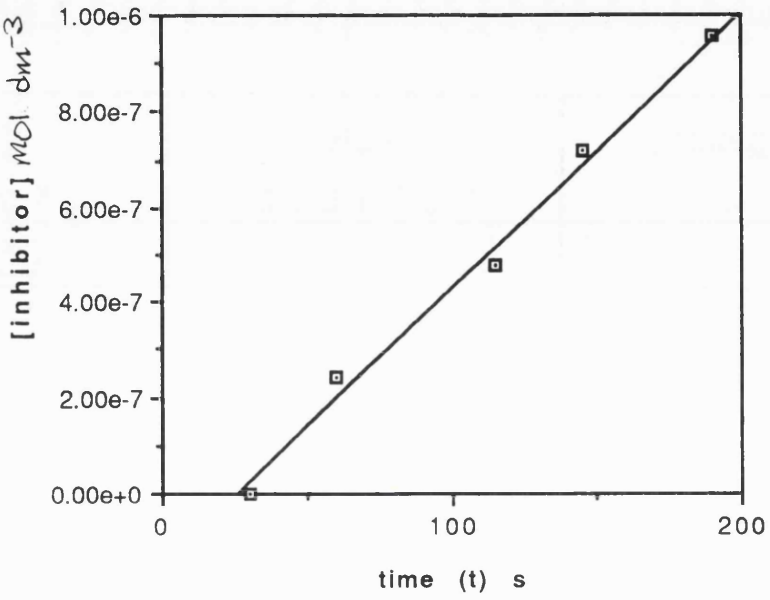
Graph of [inhibitor] (mol dm^{-3}) vs time (t) s at (4.79 x 10^{-6}mol dm^{-3} of hydride

Figure 8



Graph of [inhibitor] (mol dm^{-3}) vs time (t) s at 2. 40 x 10^{-6} mol dm^{-3} of hydride

Figure 9



Graph of [inhibitor] (mol dm^{-3}) vs time (t) s at 9.58 x 10^{-6} mol dm^{-3} of hydride

Figure 10

It will be seen from the graphs that the induction period for hydrogen evolution is roughly proportional to the amount of inhibitor present, if allowance is made for the blank reaction, which may represent the period it takes for the solution to become saturated with hydrogen.

The rate of the formation of radicals which are trapped by the inhibitor is then given by [inhibitor] / induction period. Values for the rate and for the initial hydride concentration, $\{[R_2SnH_2]+[R_2SnX_2]\}$ are given in Table 4, which also shows the value of the Rate/[hydride concentration].

Table 4. Dependence of initiation rate on hydride concentration.

[SnH] Mol dm $^{-3}$	Rate Mol dm $^{-3}$ s $^{-1}$	Rate/[SnH] s $^{-1}$
$Bu_2Sn(OCOMe)H$		
4.79 x 10 $^{-6}$	4.69 x 10 $^{-9}$	9.80 x 10 $^{-4}$
2.39 x 10 $^{-6}$	1.15 x 10 $^{-9}$	4.80 x 10 $^{-4}$
9.59 x 10 $^{-6}$	4.57 x 10 $^{-9}$	4.77 x 10 $^{-4}$
$Bu_2Sn(OCOCF_2Cl)H$		
3.74 x 10^{-6}	5.57 x 10 $^{-9}$	1.50 x 10 $^{-3}$
7.48 x 10 $^{-6}$	1.04 x 10 $^{-8}$	1.39 x 10 $^{-3}$
0.15 x 10 $^{-6}$	1.89 x 10 $^{-8}$	1.26 x 10 $^{-3}$
$Bu_2Sn(OCOPh)H$		
4.79 x 10 $^{-6}$	2.91 x 10 $^{-9}$	6.00 x 10 $^{-4}$
2.40 x 10 $^{-6}$	1.37 x 10 $^{-9}$	5.72 x 10 $^{-4}$
9.58 x 10 $^{-6}$	5.87 x 10 $^{-9}$	6.12 x 10 $^{-4}$

2.2. DISCUSSION

2.2.1 Dibutyltin Chloride Hydride

Birnbaum and Javora[4] reported that they obtained dibutyltin dihydride by the reduction of dibutyltin dichloride in glyme with sodium borohydride, whereas, under the same conditions we obtained only partial reduction to dibutyltin chloride hydride. This difference is surprising and not easy to account for. The purity of our reactants seems above suspicion, but the solvent is notoriously difficult to

purify and it is possible that the presence of some hydroxylic impurity in their solvent or ours may be responsible for the difference.

The reaction presumably involves nucleophilic attack of the borohydride anion at the tin centre. This would be expected to take place more readily with the dichloride than with the chloride hydride, so that the first step of the reaction should occur more rapidly than the second. As the reaction proceeds, however, the BH_4- anion becomes converted into the anions BH_nCl_{4-n}-, and it is difficult to analyse the mechanism in detail.

Whatever the cause of this discrepancy, we were able to exploit it in generating Bu_2SnClH <u>in situ</u> for carrying out hydrostannations as discussed below.

The disproportionation reaction between dibutyltin dihydride and dibutyltin dichloride, as expected, shows no signs of a free radical mechanism. The redistribution of ligands between tin compounds is very familiar, though the conditions under which it occurs depend on the nature of the ligands. Thus the Kocheshkov disproportionation (equation 2.2.1.a) between tetrabutyltin and tin tetrachloride is carried out at 200°C,[11,12,13,14] but the reaction between tetra-allyltin and tin tetrachloride (equation 2.2.1.b) occurs at room temperature,[15,16] and dibutyltin dichloride and dibutyltin diacetate react immediately on mixing (equation 2.2.1.c).[17a, b]

$$Bu_4Sn + SnCl_4 \rightleftharpoons 2\ Bu_2SnCl_2 \qquad (2.2.1.a)$$

$$(CH_2{=}CH{-}CH_2)_4Sn + SnCl_4 \rightleftharpoons 2\ (CH_2{=}CH{-}CH_2)_2SnCl_2 \qquad (2.2.1.b)$$

$$Bu_2SnCl_2 + Bu_2Sn(OAc)_2 \rightleftharpoons 2\ Bu_2Sn(OAc)Cl \qquad (2.2.1.c)$$

The dihydride/dichloride disproportionation may be regarded as a further member of this group of reactions. The ready reversibility of the process is shown by the reaction of bipyridyl to give the complex with dibutyltin dichloride. A similar reaction is known for example, with the acetate chloride.

It is significant, however, that we were able to distill the chloride hydride at 35-40°C/0.03 mmHg, whereas Neumann and Pedain[9] reported that distillation provided the dihydride as the most volatile component of the equilibration. The nature of the product which is obtained will depend on the rate of the equilibration versus the rate of distillation. The former will depend on the temperature (and hence pressure) and probably on the presence of impurities (eg other tin halides as Lewis acids) and the latter will depend on the temperature (and hence pressure), and the dimensions and design of the apparatus. We must assume that under our conditions the chloride hydride distilled over at a rate faster than that at which reversion of the chloride hydride to the dihydride could occur.

The reaction of the chloride hydride with aerobic oxygen probably involves a radical chain mechanism with the following propagation steps (2.2.1.d and e):

$$Bu_2\dot{S}nCl + O_2 \longrightarrow Bu_2Sn(Cl)OO\cdot \qquad (2.2.1.d)$$

$$Bu_2Sn(Cl)O\dot{O} + Bu_2SnHCl \longrightarrow Bu_2Sn(Cl)OOH + Bu_2\dot{S}nCl \qquad (2.2.1.e)$$

The hydroperoxide then oxidises the hydride to give the hydroxide chloride, which dehydrates. The ready oxidation of the chloride hydride is therefore not surprising in view of its reactivity in other free

radical processes (e.g. hydrostannation and hydrostannolysis) as discussed in this thesis.

The instability of the chloride hydride even in the absence of air again is not surprising, but the mechanism is less apparent. We suggested above that the reduction of tin halides by sodium borohydride (or lithium aluminium hydride) was a polar process, but tin halides and related compounds can also be reduced with tin hydrides to give tin-tin bonds (equation 2.2.1.f).

$$2\ Bu_3SnH + (Bu_3Sn)_2O \longrightarrow 2\ Bu_3SnSnBu_3 + H_2O \quad (2.2.1.f)$$

In the tin halide hydride we have both a reducing $(SnH)^{\cdot}$ and a reducible (SnCl) group, and self-reduction would be expected to take place to give the distannanes. The first steps of the reaction would be (2.2.1.g):

$$2\ Bu_2SnHCl \longrightarrow ClBu_2SnSnBu_2H + HCl \quad (2.2.1.g)$$

But in view of the ready disproportionation of H and Cl ligands about the tin, compounds such as $ClBu_2SnSnBu_2Cl$ and $HBu_2SnSnBu_2H$ might be formed. Complete reduction would then give the oligomeric stannylene $(Bu_2Sn)_n$. It might be assumed that this self reduction, like the reductions with $NaBH_4$ or $LiAlH_4$ is a polar process.

It will be noted that the byproduct of the self reduction is HCl which might be expected to react with the parent hydride chloride to give dibutyltin dichloride and more H_2.

There is an established method of forming Sn - Sn bonds in which a tin hydride is treated with an amine and hydrogen is evolved (equations 2.2.1.h and i).[9]

$$6\ Ph_2SnH_2 \xrightarrow{C_5H_5N} (Ph_2Sn)_6 + 6H_2 \qquad (2.2.1.h)$$

$$2\ Et_3SnSnEt_2SnEt_2H \xrightarrow{R_3N} Et_3Sn(SnEt_2)_4SnEt_3 + H_2 \qquad (2.2.1.i)$$

Dibutyltin chloride hydride reacts under these conditions to give H_2 and $ClBu_2SnSnBu_2Cl$, and in this thesis we present evidence which shows that this is a free radical chain process.

2.2.2 CARBOXYLATE HYDRIDES

The first significant difference between the chloride hydrides and the carboxylate hydrides is that the ^1H NMR spectra show that equilibration in the latter lies much further over to the side of the dihydride and the dicarboxylate (equation 2.2.2.a).

$$Bu_2SnH_2 + Bu_2Sn(OCOR)_2 \rightleftharpoons 2\ BuSn_2(OCOR)H \qquad (2.2.2.a)$$

This may be a consequence of the fact that the carboxylate groups can act as bidentate ligands, and in solution the dicarboxylates have an octahedral 6-co-ordinate monomeric structure (Figure 10) which confers stability.

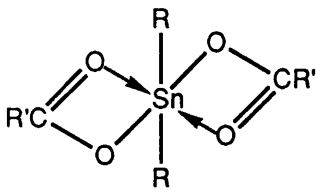


Figure 10

In the carboxylate hydride the tin would be a weaker Lewis acid, and any such stabilising co-ordination would be less significant. This would tend to displace the equilibrium to the side of the dicarboxylate and the dihydride.

The second obvious point is that the carboxylate hydrides are less stable than the chloride hydrides, in that the evolution of hydrogen occurs spontaneously with the former compounds but has to be induced with an amine with the halide hydride. This spontaneous decomposition to give hydrogen and the dicarboxylatodistannane is a remarkable reaction (equation 2.2.2.b): we are not aware of any similar reaction of metal hydrides for which mechanistic investigations have been carried out.

$$2\,Bu_2Sn(OCOR)H \longrightarrow H_2 + RCO_2Bu_2SnSnBu_2OCOR \qquad (2.2.2.b)$$

The fact that the addition of a phenolic inhibitor delays the onset of the evolution of hydrogen establishes that it is a free radical reaction and that the function [inhibitor concentration]/ induction period gives a measure of the rate of formation of radicals at a particular tin hydride concentration. The equilibrium between the dihydride and hydride carboxylate (equation 2.2.2.a), which will vary with the nature of the carboxylate, complicates the issue but in Table 4 we have given the value for the total SnH concentration, i.e $2[Bu_2SnH_2] + [Bu_2Sn(OCOR)H]$. The results in the table shows that the rate of radical formation is greater for the difluorochloroacetate than for the acetate or benzoate. The last column in the Table appears to suggest that this rate is essentially independent of the total hydride concentration over the range of concentration of our experiments.

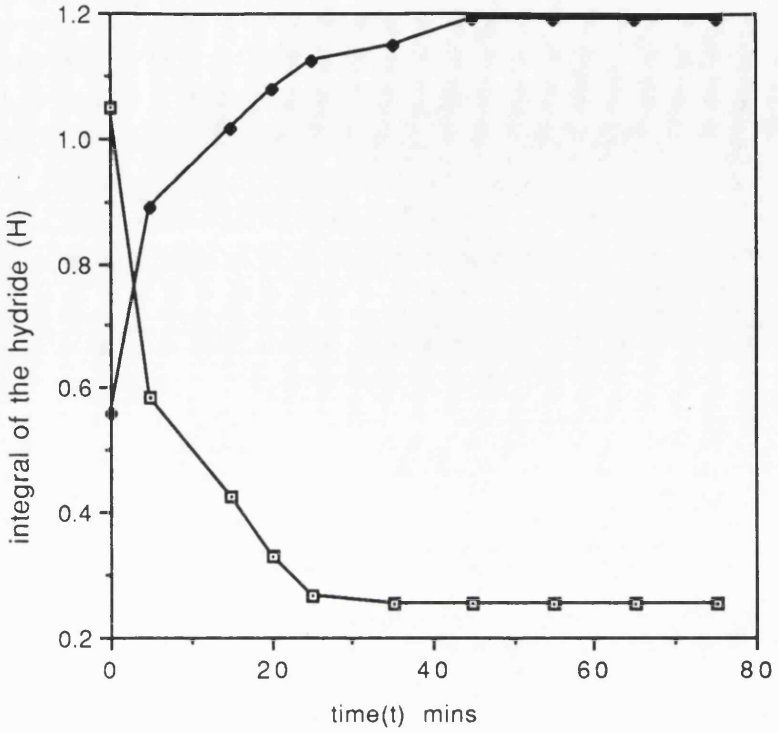


Figure 1. showing the formation of Bu_2SnHCl (-▪-▪-) from Bu_2SnH_2 (-□-□-) and Bu_2SnCl_2 (0.0225 mmol) at 25°C

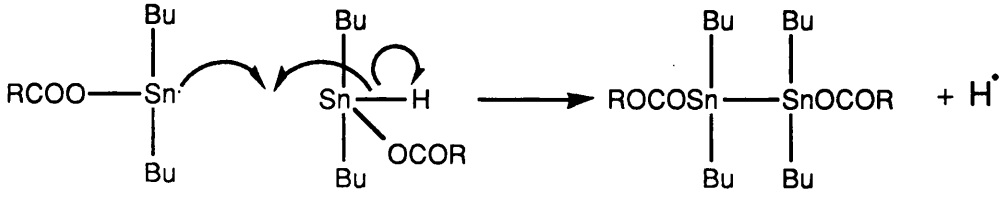
2.1.4 Dibutyltin Carboxylate Hydrides

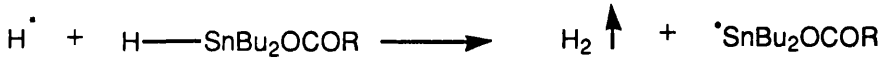
Dibutyltin carboxylate hydrides were prepared by the disproportionation reaction between the dihydride and the appropriate dicarboxylate (equation 2.1.4). [5,6,7,8]

$$Bu_2SnH_2 + Bu_2Sn(OCOR)_2 \rightleftharpoons 2\ Bu_2Sn(OCOR)H \qquad (2.1.4)$$

The reactions where R = CH_3, CF_2Cl, or C_6H_5 appear to have reached equilibrium before the NMR spectrum could be scanned. They showed the presence of a small amount of the hydride carboxylates with the following characteristics. The SnH signal was too small for the values of J_{Sn-H} to be recorded.

How can we account for the radical chain reaction in which 2 SnH ---> Sn-Sn + H-H ? The only reasonable model appears to be that in which a tin radical attacks a tin centre to displace a hydrogen atom. This hydrogen atom then abstracts hydrogen from a second hydride molecule to give dihydrogen.





Scheme 1

The abstraction of hydrogen by hydrogen is readily accepted, but we are not aware of any previous suggestion of a process in which a metal radical brings about an S_H2 reaction at the same metal to displace a hydrogen atom. Sn-Sn And Sn-H bond strengths are not known in these particular compounds, but values for related compounds suggest that the reaction would be near thermal neutrality.[20]

The evolution of hydrogen would be delayed by a phenolic inhibitor which would scavenge the tin radical (equation 2.2.2.c):

$$R_2SnOCOR + ArOH \longrightarrow R_2Sn(OCOR)H + ArO\cdot \qquad (2.2.2.c)$$

No hydrogen would be evolved until all the inhibitor was removed. The induction period would therefore be proportional to the inhibitor concentration as we observed.

If this pair of propagation steps are accepted we have yet to account for the formation of the tin radical at room temperature, i.e the initiation process. Again, there seems little useful precedent in the literature, but we suggest that homolysis may be induced by an electron transfer reaction. Any one or two of the components Bu_2SnH_2, $Bu_2Sn(OCOR)_2$, and $Bu_2Sn(OCOR)H$ may be involved, but from the likely ionisation energies and electron affinities, electron transfer from the dihydride to the diacetate seems most likely (equation 2.2.2.d).

$$Bu_2SnH_2 + Bu_2Sn(OCOR)_2 \rightleftharpoons Bu_2\dot{S}nH_2^{+} + Bu_2Sn(OCOR)_2^{\bullet -} \quad (2.2.2..d)$$

The diacetate radical anion would then be expected to dissociate into the acetate anion and the dibutylacetoxytin radical (equation 2.2.2.e).

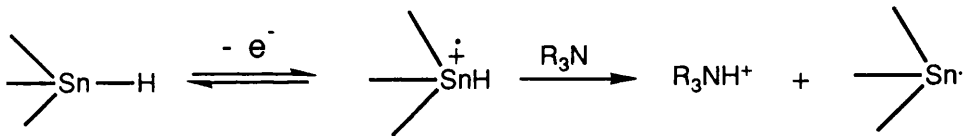
$$Bu_2S\dot{n}(OCOR)_2 \longrightarrow Bu_2S\dot{n}(OCOR) + RCO_2^- \quad (2.2.2.e)$$

This radical would then be trapped by the phenolic inhibitor (equation 2.2.2.c) until all the inhibitor was consumed. The tin radical would then proceed to attack the tin centre in the hydride (Scheme 1) with the formation of the Sn-Sn bond, and the evolution of hydrogen.

We feel that it would be a mistake to try to interpret our crude kinetic data in more detail as the acetoxy and hydride groups are probably transferred rapidly between the various possible tin centres, and we do not know the position of the various equilibria which are possible. The increase of reactivity with the increase in the strength of the acid RCO_2H might result from the greater electron affinity of the carboxylate in the single electron transfer (SET) step (equation 2.2.2.d)

or the more ready dissociation of the radical anion (equation 2.2.2.e), or from the position of the various equilibria (equation 2.2.2.a), which may be obtained.

In the light of this model, we can reassess the behaviour of the dibutyltin chloride hydride and the alkyltin hydrides which give hydrogen only when an amine is added. We suggest that the amine may facilitate the electron transfer either in its own right or as an amine complex with the tin hydride or may assist in loss of a proton from a tin hydride radical cation, preventing reversal of the SET step.



Scheme 2

2.3 CONCLUSION

We conclude that the spontaneous evolution of hydrogen by the hydride carboxylates and the induced evolution of hydrogen by the chloride hydride are both free radical reactions. The proposed mechanism where by a tin radical attacks at a tin centre to displace a hydrogen atom is highly unusual and has not been reported before, but this is the only mechanism that we know of that would lead to hydrogen evolution and the formation of distannanes, which we have identified by melting point and NMR spectroscopy.

2.4 EXPERIMENTAL

Dibutyltin dihydride, (Bu_2SnH_2), was prepared by procedures in the literature, whilst dibutyltin diacetate ($Bu_2Sn(OAc)_2$) was obtained courtesy of Dr P. G. Smith of the International Tin Research Institute.

2.4.1 Preparation of Dibutyltin Chloride Hydride (Bu_2SnHCl)

This was first obtained by Birnbaum and Javora's[4] method where Bu_2SnCl_2 (0.574 g, 1.89 mmol), in 2-dimethoxyethane (glyme) (10 cm^3) was added dropwise to $NaBH_4$ (0.38 g, 9.73 mmol) in glyme (30 cm^3) over 30 minutes at -10 to 15°C under an inert atmosphere. After the addition, the mixture was allowed to warm up to room temperature, and the solvent was removed in vacuo at 0°C.

The resultant solid was washed with diethyl ether (3 x 25cm^3) which was evaporated to give a colourless liquid which was distilled at 35 - 40°C/0.03 mmHg.

Yield, 0.45 g, (70%)

δ_H (C_6D_6, 400 MHz); 0.85-1.96 (18H, m, 2 x C_4H_9); 7.42 (1H, s, $^1J^{117}_{Sn}$ 1875.8 Hz, $^1J^{119}_{Sn}$ 1963.0 Hz; SnHCl).

δ_C (C_6D_6, 100.58 MHz); 13.65 (C-δ); 17.00 ($^1J^{117}_{Sn}$ 379.7 Hz, $^1J^{119}_{Sn}$ 397.4 Hz; C-α); 27.65 ($^3J^{117/119}_{Sn}$ 63.32 Hz; C-γ); 28.20 ($^2J^{117/119}_{Sn}$ 40.24 Hz; C-β).

ν max (ethanol) 185.3 cm^{-1} (Sn-H)

Bu_2SnHCl Was also prepared by Sawyer and Kuivila's method[5] of mixing equimolar amounts of Bu_2SnCl_2 and Bu_2SnH_2 in ethanol or toluene, in an disproportionation reaction that gives 97% of Bu_2SnHCl.

2.4.2 Preparation of 2,2-Bipyridyldibutyltin Dichloride

A 1:1 mole reaction of Bu_2SnCl_2 (80 mg, 0.26 mmol) with Bu_2SnH_2 (88 mg) was followed by proton NMR spectroscopy in C_6D_6 when the production of Bu_2SnHCl could be observed at δ 7.42. To this mixture was added 2,2-bipyridyl, (60 mg, 0.20 mmol) when the Bu_2SnHCl peak at δ 7.42 disappeared and was replaced by a peak at δ 4.58 corresponding to Bu_2SnH_2.

The solvent was removed and the residue was recrystallised from ethanol to give white needle shaped crystals.

Yield, 0.123 g, (90%), M.p 180 - 182°C (Lit.[17a] 180°C).

Found: C, 47.21; H, 5.80; Cl, 15.40; N, 5.96.

Calc For: $C_{18}H_{26}N_2Cl_2Sn$; C, 47.00; H, 5.70; Cl, 15.41; N, 6.09%

δ_H ($CDCl_3$); 0.56 - 1.87 (18H, m, 2 x C_4H_9); 4.58 (2H, s, Bu_2SnH_2); 7.25 - 8.73 (8H, m, Aromatic).

δ_C ($CDCl_3$); 7.89 (C-δ); 26.32 ($^1J^{117}_{Sn}$ 378.9 $^1J^{119}_{Sn}$ 396.6 Hz; C -α); 27.56 ($^3J^{117/119}_{Sn}$ 50.6 Hz; C-γ); 28.05 ($^2J^{117/119}_{Sn}$ 80.34 Hz; C-β); 126 - 148.56 (Aromatics).

2.4.3 Preparation of Dibutyltin Dibenzoate and Dibutyltin Bis(difluorochlorodiacetate)

Dibutyltin dibenzoate was obtained by refluxing benzoic anhyride (15.72 g, 0.106 mol), and Bu_2SnO (12.60 g, 0.051 Mol) in toluene until

the Bu_2SnO had dissolved. The solvent was then removed in vacuo and the resultant solid recrystallised from ethyl acetate.

Yield 49.4 g, (98.5%) M.p 67 - 69°C (Lit[17a] 65 -67°C)

Found: C, 55.75; H, 5.85

Calc For: $C_{22}H_{28}O_4Sn$: C, 55.61; H, 5.94%

δ_H ($CDCl_3$); 0.85 (18H, m, 2 x C_4H_9); 7.50-7.70 (10H, m, Aromatic).

δ_C ($CDCl_3$); 13.58 (C-δ); 25.53 (C-α); 26.43 (C-γ); 26.89 (C-β); 129.20; 130.88; 132.58; 177.61 (C=0).

Dibutyltin bis(difluorochloroacetate), was obtained in a similar reaction between dibutyltin oxide (8 g, 0.032 mol) and difluorochloro acetic acid (8.81 g, 0.068 mol). The resultant solid was recrystallised from diethyl ether-ethanol (4:6 v/v).

Yield, 32.5 g, (98%) M.p 101- 103°C

Found: C, 29.6; H, 3.75; Cl, 14.45

Required for: $C_{12}H_{18}O_4SnF_4Cl_2$: C, 29.30; H, 3.69; Cl, 14.42%

δ_H ($CDCl_3$); 0.98-1.94 (18H, m, 2 x C_4H_9).

δ_C ($CDCl_3$); 13.34 (C-δ); 26.32 (C-γ and C-β); 27.59 ($^1J^{117/119}Sn$ 484.7 Hz; C-α); 117.62 ($^1J_{C-F}$ 603.5 Hz; CF_2); 165.36 ($^2J_{C-F}$ 66.5 Hz; C=O).

2.4.4 Kinetic studies of the decomposition of Dibutyitin Carboxylate Hydrides $Bu_2Sn(OCOR)H$ R = CF_2Cl, Ph ,CH_3

$(Bu_2SnOCOR)_2$ was obtained during the decomposition of $Bu_2SnH(OCOR)$.

$Bu_2Sn(OCOR)_2$ and Bu_2SnH_2 were mixed in equimolar amounts in an NMR tube, and the time taken for hydrogen to evolve was noted. The evolution of hydrogen was then inhibited by a known concentration of 2,6-di-t-butyl-4-methyl phenol and the time taken for the resumption of hydrogen evolution was again noted. This was repeated for three different concentrations of the hydride carboxylates and inhibited with varying amounts of phenolic inhibitor.

The product of the decomposition was obtained by removal of the solvent in vacuo and flash column chromatography with n-hexane-ethyl acetate (6:4 v/v).

(i) $Bu_2SnH(OCOCH_3)$

$Bu_2SnH(OCOCH_3)$ (4.80×10^{-6}, 2.40×10^{-6}, 0.58×10^{-6} mol dm^{-3}) was inhibited by 2,6-di-t-butyl-4-methylphenol (2.5, 5.0, 7.5, 10.0%). The tetrabutyldiacetatodistannane was obtained as an oil.

Yield 0.67g, 1.42g, 95%

$\delta^{119}Sn$ -220

(ii) $Bu_2SnH(OCOCF_2Cl)$

$Bu_2SnH(OCOCF_2Cl)$ (3.74×10^{-6}, 7.48×10^{-6}, 0.15×10^{-6} mol dm^{-3}) was inhibited by 2,6-di-t-butyl-4-methyl phenol (2.5, 5, 7.5, 10%). The distannane was obtained as a solid which was recrystallised from ethanol.

Yield 0.69g, 2.9mg, 85-90%, M.p 78 - 80°C

δ^{119}_{Sn}-173.13

(iii) $Bu_2SnH(OCOPh)$

$Bu_2SnH(OCOPh)$ (4.80×10^{-6}, 2.40×10^{-6}, 9.58×10^{-6} mol dm^{-3}) was inhibited by 2,6-di-t-butyl-4-methyl phenol (2.5, 5.0, 7.5, 10%). The distannane was obtained as a white crystalline solid which was recrystallised from ethanol.

Yield 85%, M.p 33-34°C (Lit[19]. 31.5 - 32.5°C)

δ^{119}_{Sn} - 180

2.5 REFERENCES

1. Hayashi, K., Iyoda J. and Shiihara, I, J. Organomet. Chem., **10**, 81 (1967)

2. Knocke, R. and Neumann, W.P., Annalen, 1486 (1977)

3. Van der Kerk, G. J. H., Noltes, J. G. and Luijten, L. G. A., J. Appl. Chem., **7**, 366 (1957)

4. Birnbaum, E. R. and Javora, P. H., J Organomet. Chem., **9**, 379 (1961)

5. Sawyer, A. K. and Kuivila, H. G., Chem. Ind. (London), 260 (1961)

6. Sawyer, A. K. and Brown, J. E., J Organomet. Chem, **5**, 438 (1966)

7. Sawyer, A. K. and Brown, J. E., and Hanson, E. L., J. Organomet. Chem., **3**, 464 (1965)

8. Sawyer, A. K., May, G. S. and Schofield, R. E., J Organomet. Chem., **14**, 213 (1968)

9. Neumann, W. P. and Pedain, J., Tetrahedron Lett., 2461 (1964)

10. Sawyer, A. K. and Kuivila, H. G., J. Am. Chem. Soc., **82**,5958

(1960)

11. Kocheskov, K. A., Chem. Ber., **62**, 996 (1929)

12. Kocheskov, K. A., Chem. Ber., **66**, 1661 (1933)

13. Kocheskov, K. A. and Nad, M. M., Chem. Ber., **67**, 717 (1934)

14. Kocheskov, K. A., Nad, M. M. and Alexandrov, A. P., Chem. Ber., **67**, 1348 (1934)

15. Rosenberg, S. D. and Gibbons, A. J., J. Am. Chem. Soc., **79**, 2138 (1957)

16. Seyferth, D. and Stone, F. G. A., J. Am. Chem. Soc., **79**, 515 (1957)

17a Alleston, D. L. and Davies, A.G., J. Chem. Soc. 2050 .(1962)

17b Davies, A. G. and Harrison, P.G., J Chem Soc., C, 298 (1967)

18. Sawyer, A. K. and Kuivila, H. G., J. Am. Chem. Soc., **85**, 1010 (1963)

19. Kuivila, H. G. and Sawyer, A. K., J. Am. Chem. Soc., **82**, 5958 (1960).

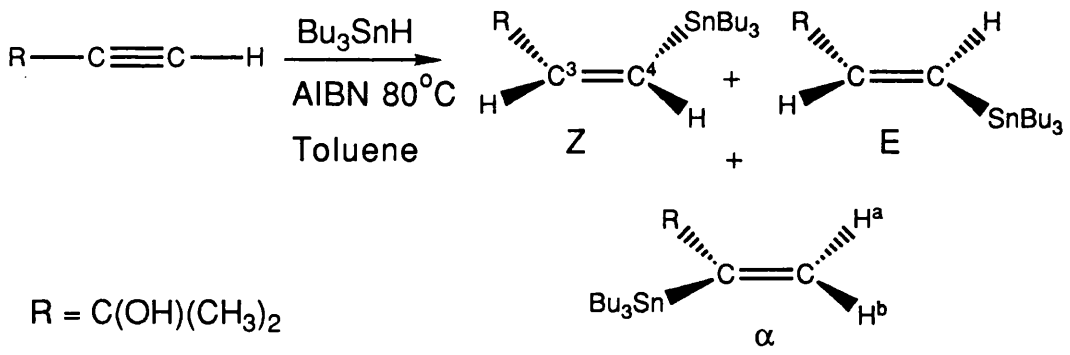
20. The Hand Book of Chemistry and Physics Ed. West, C.R. The Chemical and Rubber Publishing Company.

3.0. Reactions of Tributyltin Hydride

3.1 RESULTS

As already mentioned, the reaction of 17α-ethynylestradiol[1] with tributyltin hydride yields a mixture of Z and E vinyltin isomers. In order to study the profile of the reaction and the isomer composition, a model compound, 2-methyl-3-butyn-2-ol, was studied to see if pure Z and E isomers could be obtained.

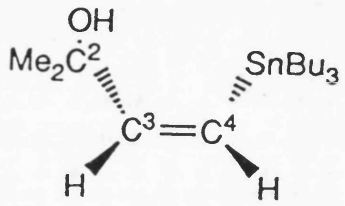
3.1.1 2-Methyl-3-butyn-2-ol



Scheme 3.1.1

The reaction of 2-methyl-3-butyn-2-ol with tributyltin hydride in the presence of AIBN in toluene at 80°C was carried out over a two hour period. The reaction was followed by tlc and the pure products were isolated by distillation at 84°- 86°C /0.05 mmHg in yields of 75 - 80%.

The products were then separated by hplc and identified as the Z and E isomers (Scheme 3.1.1) by proton NMR spectroscopy, which shows characteristic patterns in the olefinic region. Previous work on the addition of organotin hydrides to alkynes,[2,3,4] which is discussed in the introduction, has shown that the Z, E and α–alkene



Z -isomer

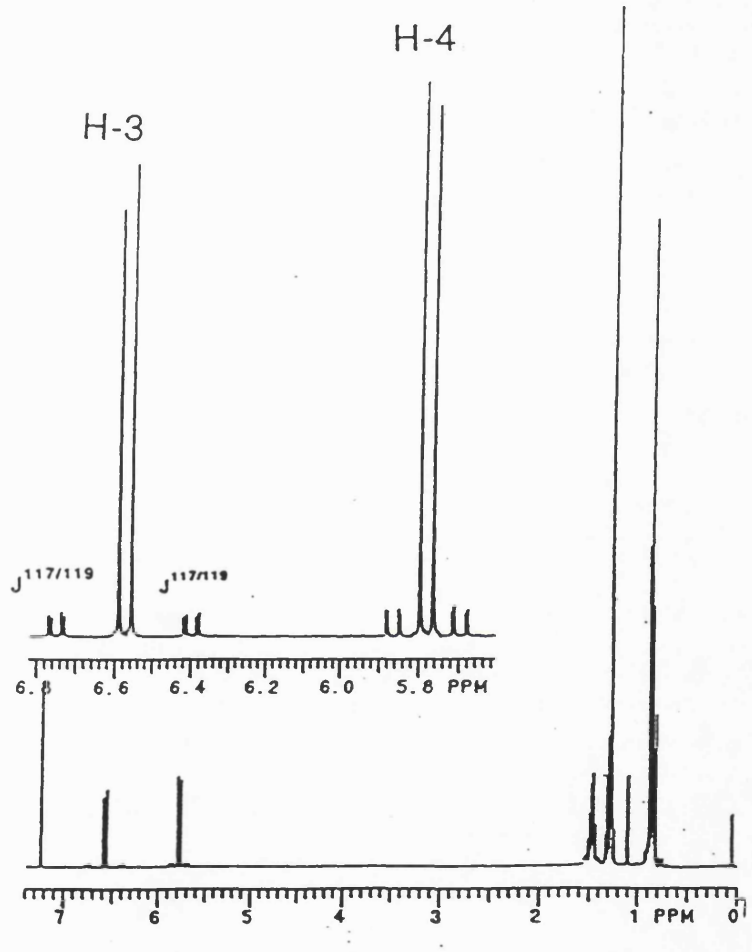


Figure 1 400 MHz ^{1}H NMR spectrum of (Z)- 4-tributylstannyl- 2-methyl-3-buten-2-ol, showing (inset) the olefinic region.

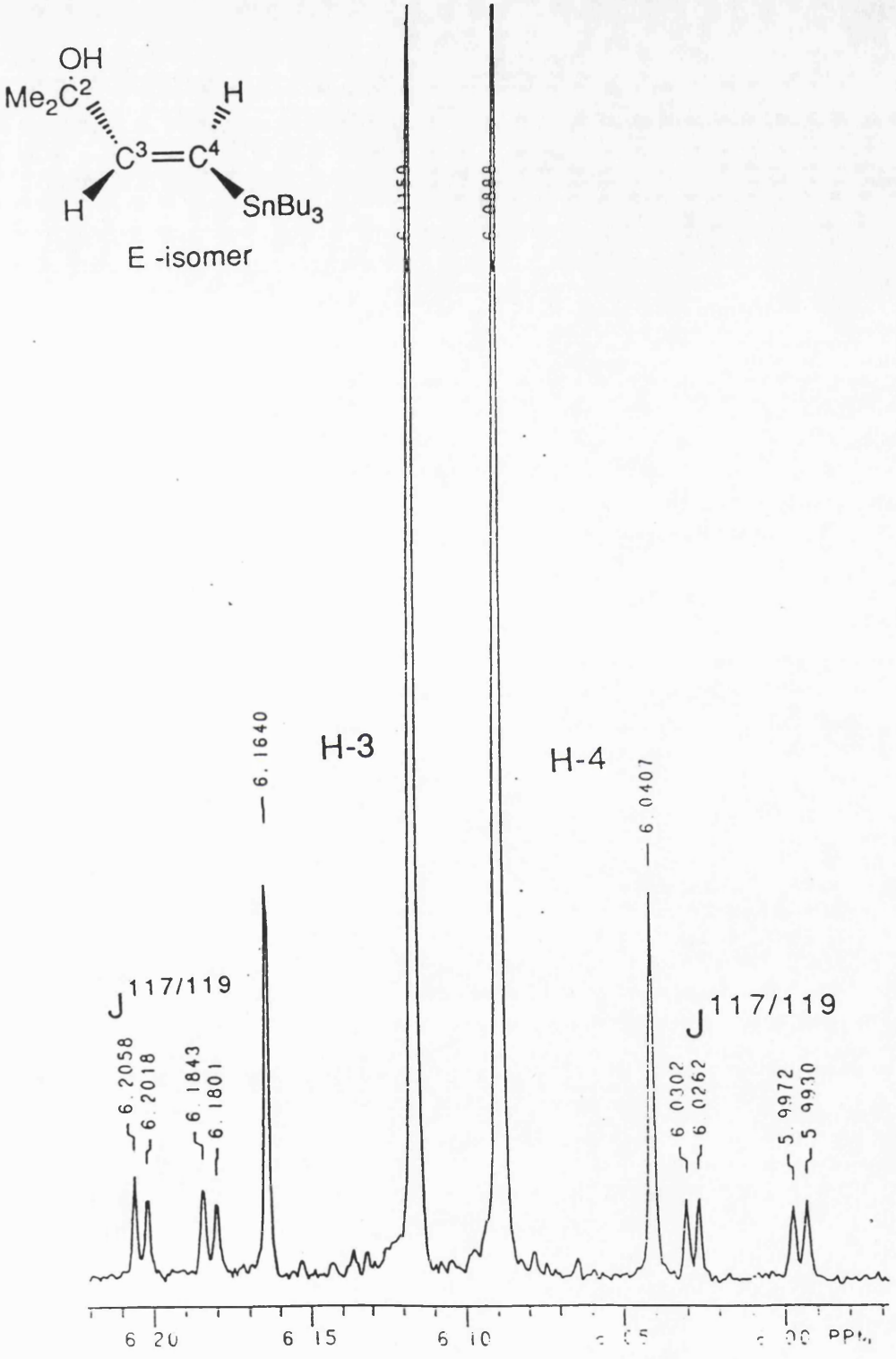


Figure 2 Partial 400 MHz ^{1}H NMR spectrum of (E) -4-tributylstanny-2-methyl-3-buten -2-ol, showing $^{117/119}Sn$ coupling to the olefinic region.

adducts have characteristic coupling constants for the olefinic protons. These range from 12 - 13 Hz, 137 - 114 Hz and 65 - 68 Hz for $^{3}J_{H-H}$, $^{3}J_{Sn-H}$ and $^{2}J_{Sn-H}$ in the Z-isomer, and from 18 - 19 Hz, 73 - 78 Hz and 63 - 68 Hz for $^{3}J_{H-H}$, $^{2}J_{Sn-H}$ and $^{3}J_{Sn-H}$ in the E-isomer. The α-isomer shows $^{2}J_{H-H}$ 0 - 3 Hz and $^{3}J_{Sn-H}$ 67 - 164 Hz.

The proton NMR spectrum (Figure 1) of the Z-isomer which was isolated shows two doublets at:

δ_H 6.58 (1H, d, $^{3}J_H$ 13.4 Hz, $^{3}J^{117}_{Sn}$ 136.6 Hz, $^{3}J^{119}_{Sn}$ 143.1 Hz; H-3);
5.75 (1H, d, $^{3}J_H$ 13.4 Hz, $^{2}J^{117}_{Sn}$ 65.5 Hz, $^{2}J^{119}_{Sn}$ 68.6 Hz; H-4).

These coupling constants fall close to the range for Z isomers as given above in the introduction and as obtained by Ensley.[2]

The carbon-13 NMR spectrum of this compound showed peaks at:

δ_C 72.44 ($^{3}J_{Sn}$ 57.4 Hz; C-2); 124.90 ($^{1}J^{117}_{Sn}$ 393.2 Hz, $^{1}J^{119}_{Sn}$ 411.3 Hz, C-3); 152.80 (C-4).

The proton NMR spectrum of the E-isomer (Figure 2) showed peaks centred at:

δ_H 6.07 (1H, d, $^{3}J_H$ 19.2 Hz, $^{2}J^{117}_{Sn}$ 75.2 Hz, $^{2}J^{119}_{Sn}$ 78.5 Hz; H-4);
6.14 (1H, d, $^{3}J_H$ 19.2 Hz, $^{3}J^{117}_{Sn}$ 68.6 Hz; $^{3}J^{117}_{Sn}$ 71.8 Hz; H-3).

The carbon-13 NMR spectrum of the E isomer shows peaks which can be assigned as follows:

δ_C 122.44 ($^{1}J^{117}_{Sn}$ 358.2 Hz, $^{1}J^{119}_{Sn}$ 377.9 Hz; C-4); 155.56 (C-3).

The ^{13}C spectrum was interpreted by comparison with those of other vinyltin compounds such as tetravinyltin.[5]

A further experiment was carried out in which the progress of the reaction of 2-methyl-3-butyn-2-ol with tributyltin hydride in the presence of AIBN was followed by proton NMR spectroscopy in a sealed NMR tube. The significant signals to observe were at δ 2.2-2.5 for the acetylenic proton and δ 5.8-6.8 for the olefinic protons.

At 25°, 35° and 50°C no reaction was observed, whilst at 75°C we observed that the acetylenic proton signal reduced in intensity and the Z-isomer was formed and had started to convert into the E-isomer; after five minutes the Z/E ratio was 4:1. After 10 minutes the Z/E ratio was 2:1 with further reduction of the acetylenic peak. After 20 minutes the Z/E ratio was 3:2 and eventually reached a steady 1:1 ratio after 35 - 40 minutes, when the acetylenic proton had been lost.

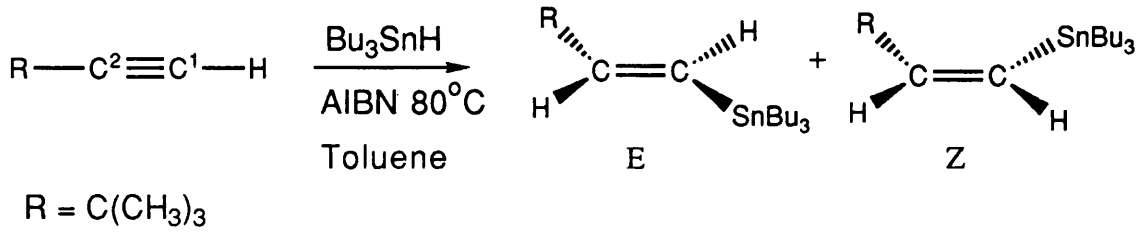
HPLC of the sample showed that three rather than two isomers were present. Two of these were identified as the E and Z isomers by the values of J_{H-H} and J_{Sn-H}. The third isomer which was present in ca. 20% of the total adducts showed two doublets centred at:

δ_H 5.12 (1H, s, ^3J_H 1.5 Hz, $^3J_{Sn}$ 67.7 Hz; H-4^B) and at δ 5.70 (1H, s, ^3J_H1.5 Hz, $^3J_{Sn}$ 164.6 Hz; H-4^A). This small amount might go undetected by NMR spectroscopy

These values suggest that there are two close-coupled protons, one <u>cis</u> to the tin and the other <u>trans</u> to the tin. From this, and from comparisons with values obtained by Leusink,[3] for other α-adducts we conclude that this is the α-isomer (Scheme 3.1.1), where the tin is attached to C-3.

3.1.2 3,3-Dimethyl-1-butyne

To investigate the influence of the hydroxyl group on the reaction we decided to study the reaction of the above compound for comparison.



Scheme 3.1.2

3,3-Dimethyl-1-butyne reacted with tributyltin hydride at 80°C in toluene with AIBN as radical initiator to give a 100% yield of E-1-tributylstannyl-3,3-dimethyl-1-butene (Scheme 3.1.2), which was purified by distillation at 140°C/0.08 mmHg.

The proton NMR spectrum of the product showed characteristic olefinic protons at:

δ_H 5.75 (1H, d, ^3J_H 19.4 Hz, $^2J^{117}_{Sn}$ 67.4 Hz, $^2J^{119}_{Sn}$ 70.5 Hz; H-1);
5.71 (1H, d, ^3J_H 19.4 Hz, $^3J^{117}_{Sn}$ 75.6 Hz, $^3J^{119}_{Sn}$ 79.2 Hz; H-2).

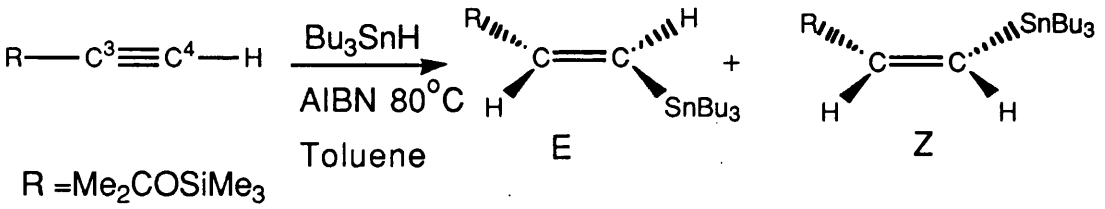
The carbon-13 NMR spectrum of the E-isomer similarly showed the expected vinyl carbons with associated values of J_{Sn-C} as follows:

δ_C 119.64 (J^{117}_{Sn} 397.8 Hz, J^{119}_{Sn} 404.30 Hz; C-1); 35.93 ($^3J_{Sn}$ 55.1 Hz; C-2); 159.95 (C-2).

The formation of the Z and E-isomers with time was monitored by NMR spectroscopy. We observed that now the formation of the E-isomer was immediate with only 33% Z-isomer being present, and after 40 minutes of reaction only the E-isomer was present. This confirms that the Z-adduct, in this instance, isomerizes to the E-adduct faster than does (Z)-4-tributylstannyl-2-methyl-3-buten-2-ol, presumably because there is no oxygen atom present to form a stabilizing tin-oxygen linkage.

3.1.3 2-Methyl-2-(trimethylsilyloxy)-3-butyne

Silylation of the oxygen at the C-2 position would be expected to reduce the Lewis basicity of the oxygen and thus the extent of Sn<-O association which might affect the isomeric ratio of the products.



Scheme 3.1.3

The reaction was carried out as previously and the proton NMR spectrum, after the first hour of reaction, showed that the E and Z isomers were present in a ratio of 2:1, but after three hours of reaction there was 100% of the E isomer. This was then purified by column chromatography. Proton NMR spectroscopy showed characteristic signals at:

δ_H 6.09 (1H, d, ^3J_H 19.4 Hz, $^3J^{117}$ 77.5 Hz, $^3J^{119}_{Sn}$ 81.1 Hz; H-3);
5.95 (1H, d, ^3J_H 19.4 Hz, $^2J^{117}_{Sn}$ 70.1 Hz, $^2J^{119}_{Sn}$ 73.4 Hz; H-4).

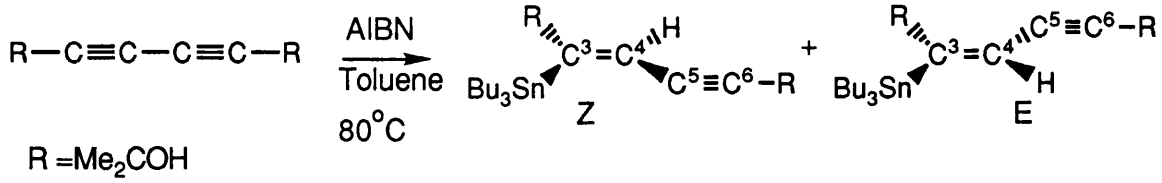
The proton NMR spectrum of the Z-isomer showed signals at:
δ 5.86 (1H, d, ^3J_H 13.4 Hz); 6.91 (1H, d, ^3J_H 13.4 Hz);

The amount of the Z-isomer which was available was too small for J_{Sn-H} to be observed clearly.

The $^3J_{H-H}$, $^3J_{Sn-H}$ and $^2J_{Sn-H}$ values obtained compare favourably with the range of values obtained for E and Z-isomers by ourselves and other workers.[2, 3]

3.1.4 2,7-Dimethyl-3,5-octadiyne-2,7-diol

17α-Tributylstannylvinylestradiol reacts with radioactive iodine to give the iodovinyl adducts, which are then used in the radio-imaging of certain lymphatic cancers. It was hoped that a diyne at the 17α position would increase the potential for radio-imaging at the cancer site by perhaps forming a bis-adduct with Bu_3SnH, and thus the reaction of 2,7-dimethyl-3,5-octadiyne-2,7-diol was studied with this end (Scheme 3.1.4).



Scheme 3.1.4

Hydrostannation of the diacetylene was a facile reaction giving a yield of crude product of 84%. Flash column chromatography eluting with ethyl acetate-hexane (35% EtOAc), was used to purify the product(s). It was noted that the amount of AIBN used in this reaction was very important; higher concentrations of AIBN gave low

yields of adducts, and gave a substantial amount of an insoluble yellow compound which is probably a polymer of the diyne. After several attempts, the ratio of AIBN was reduced to 0.1 mol equivalent with respect to the tin hydride. This gave only a little of the yellow compound (0.14%). It was also noted that the products seemed to be unstable on silica and appeared to break down to starting materials during HPLC.

Proton NMR spectroscopy of the crude product showed three singlets in the olefinic region . The first is centred at:
δ_H 6.30 (1H, s, $^3J^{117}_{Sn}$ 112.0 Hz, $^3J^{119}_{Sn}$ 117.2 Hz; H-4); and refers to the product of trans-addition, i.e the Z-isomer (Scheme 3.1.4). The next singlet at:
δ_H 5.90 (1H, s, J_{Sn} 39.9 Hz); refers to the cis addition product, i.e the E-isomer (Scheme 3.1.4). The fact that the intensities of these signals are in a 2:1 ratio suggests that they relate to two separate products.

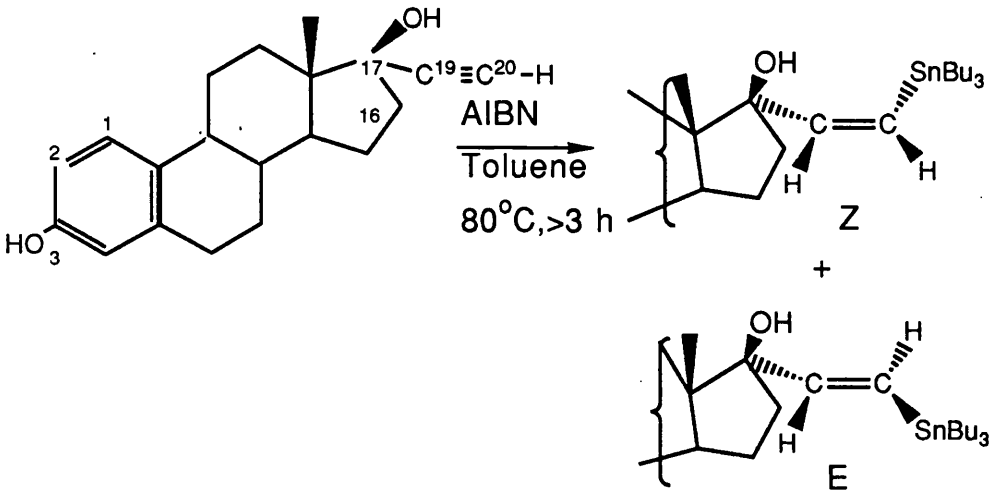
The third peak was centred at:
δ_H 5.69 (1H, s, J^{117}_{Sn} 45.8 Hz, J^{119}_{Sn} 47.9 Hz).

This seems to point to an E-isomer by virtue of the small tin-proton coupling constants. There is no evidence for a di-addition compound.

A similar reaction using only 0.01 mol equivalents of AIBN gave one product in 80-90% yield. The olefinic region of the proton NMR spectrum showed a singlet peak at:
δ_H 6.28 (1H, s, $^3J^{117}_{Sn}$ 112.0 Hz, $^3J^{119}_{Sn}$ 117.2 Hz; H-4).

This showed that the Z-isomer had been obtained in good yield by limiting the amount of AIBN.

3.1.5 17α-Ethynylestradiol



Scheme 3.1.5

17α-Ethynylestradiol was treated with tributyltin hydride and AIBN at 80°C. After 1 hour, tlc showed the presence of the reactant and of a new component, which was isolated in 50-60% yield by flash column chromatography.

Proton NMR spectroscopy of the product showed the characteristic olefinic protons at:

δ_H 5.84 (1H, d, ^3J_H 13.2 Hz, $^2J^{117}_{Sn}$ 69.8 Hz, $^2J^{119}_{Sn}$ 73.2 Hz; H-20);
6.75 (1H, d, ^3J 13.2 Hz, $^3J^{117}_{Sn}$ 138.6 Hz, $^3J^{119}_{Sn}$ 145.2 Hz; H-19).

The coupling constants identified the product as the Z-isomer (Scheme 3.1.5), as found by other workers.[1, 5]

On the other hand when the reaction was left for more than three hours, the only isomer detected was the E-isomer. This agrees with the basic premise of previous work that the Z-isomer, as the kinetically favoured product, is always formed first, but subsequently isomerises to the E-isomer, the thermodynamically favoured product.

The proton NMR spectrum of the E-isomer (Scheme 3.1.5) showed the familiar pattern for E-compounds of previous compounds at:

δ_H 5.95 (1H, d, J_H 19.3 Hz, $^3J^{117}_{Sn}$ 69.1 Hz, $^3J^{119}_{Sn}$ 72.3 Hz; H-19);
6.13 (1H, d, ^3J_H 19.3 Hz, $^2J^{117}_{Sn}$ 64.9 Hz, $^2J^{119}_{Sn}$ 67.4 Hz; H-20).

These coupling constants enable us to assign the structures confidently as they agreed with those obtained by various groups.[1,5]

The ^{13}C NMR spectrum showed characteristic olefinic carbons at:

δ_C 85.38 ($^3J_{Sn}$ 54.8 Hz; C-17); 122.3 (C-20); 170.77 (C-19).

We were unable to observe coupling to the olefinic carbons, due perhaps to overlap by the many signals relating to the steriod structure.

3.2 DISCUSSION

In order to understand the reported behaviour of tributyltin hydride with 17α-ethynylestradiol,[1] 2-methyl-3-butyn-2-ol was used as a model compound. NMR studies of the reaction of this acetylene with tributyltin hydride in the presence of AIBN showed that the Z-isomer was formed initially, but it then isomerises to the E-isomer.

Table1 Ratio of Z, E and α vinyltin adducts obtained under the same reaction conditions at 80°C

Bu_3SnH, AIBN 80°C, Toluene	OH $Me_2C-C\equiv CH$				OSiMe$_3$ $Me_2C-C\equiv CH$				CH_3 $Me_2C-C\equiv CH$				OH, C≡CH			
	Z	E	α	%	Z	E	α	%	Z	E	α	%	Z	E	α	%
1 h	80	20	-		33	66	-		33	66	-		80	20	-	
> 3 h	38	38	24		-	100	-		-	100	-		20	80	-	
$\delta^{119}Sn$	-63	-40	-		+33	+18	-									

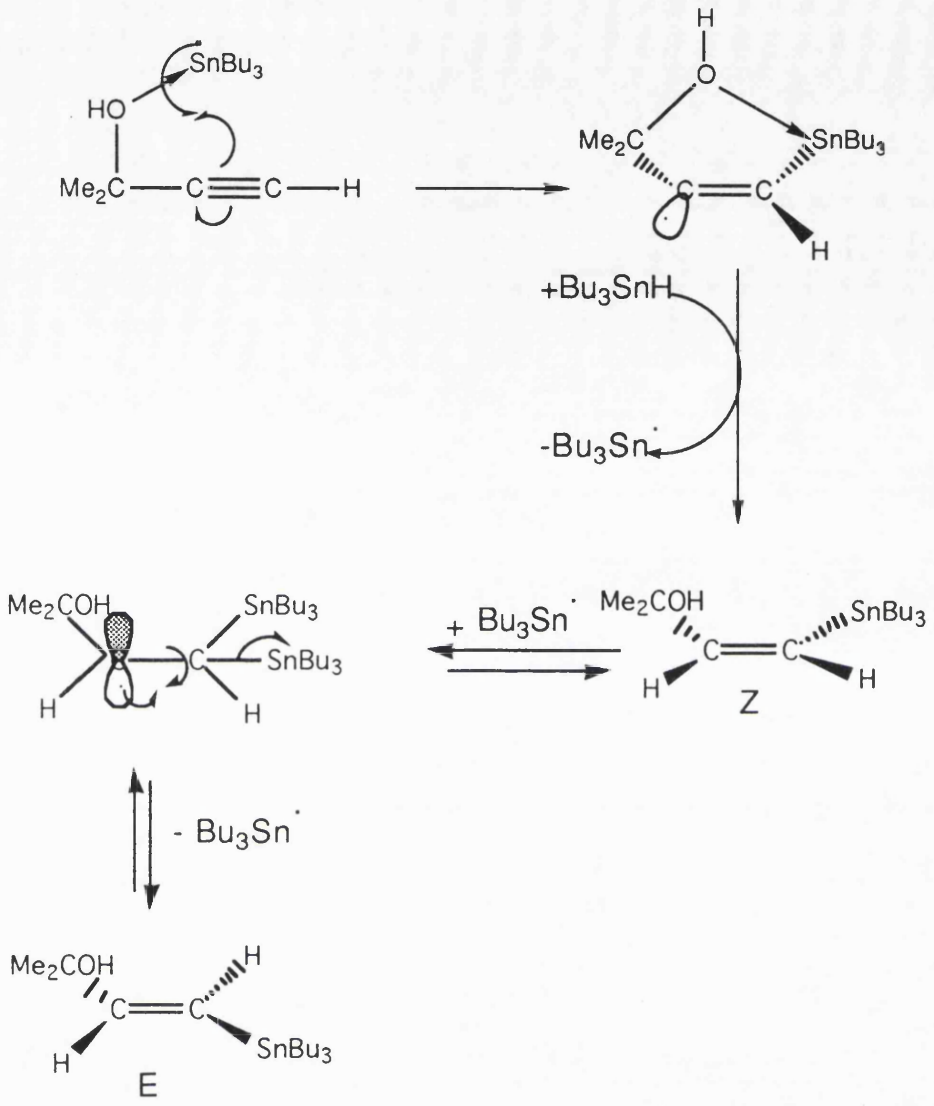
Table 1 Shows the percentage of Z, E and α–adducts obtained under the reaction conditions stated. The Z isomer was obtained as the major product in the initial 1/2 hour to an hour with 2-methyl-3-butyn-2-ol and 17α–ethynylestradiol; after three hours the former compound yields an equal amount of Z and E-isomers plus a smaller amount (24% after 2 hours) of an α isomer, whilst the latter gives a 4 :1 ratio of E and Z-isomers.

The reaction with 3,3-dimethylbut-1-yne and 2-methyl-2-(trimethylsilyloxy)-3-butyne both gave a 2:1 ratio of E and Z-isomers after an hour and 100% E isomer after three hours or more. The $\delta^{119}Sn$ NMR spectra of some of these isomers suggested that the tin moiety was in a different environment for the hydroxyl and the silyloxy compounds. This however did not suggest five co-ordinate tin formation. Literature values of δ_{Sn} for five co-ordinate tin are usually >δ -100[6] depending on the ligands on the tin. Whatever the case, the presence of the oxygen seems to influence the final isomeric ratio.

Investigations by Taddei[7] suggest that although the Z-isomer formed as the kinetically favoured isomer, it is stereochemically unstable under the free-radical conditions. We have observed along with Taddei that the Z-isomer could be isomerised to give a 1:1 mixture of Z/E-isomers at about 100°C or greater with an excess of tributyltin hydride and AIBN.

Our results suggest that a link exists between the presence of the OH on the C-2 carbon and the nature of the products obtained, confirming the extensive work by Taddei[7a,7b] and Ensley[2] which was detailed in Chapter 1.

The free-radical mechanism for this reaction as proposed by Taddei[7] seems to bear out the results we obtained. He suggests that the tributyltin radical associates itself with the oxygen on the adjacent carbon, in our case the C-2 carbon. This then directs the attack at the acetylene carbon exclusively in the Z position, followed by attack of the tin hydride at the vacant <u>trans</u> position to give the kinetically favoured Z-isomer (Scheme 3.2.a). Further attack by another tributyltin radical results in a species with two tins on the same carbon. Free rotation about the C-C bond and loss of a tributyltin radical then results in an E-isomer being formed.

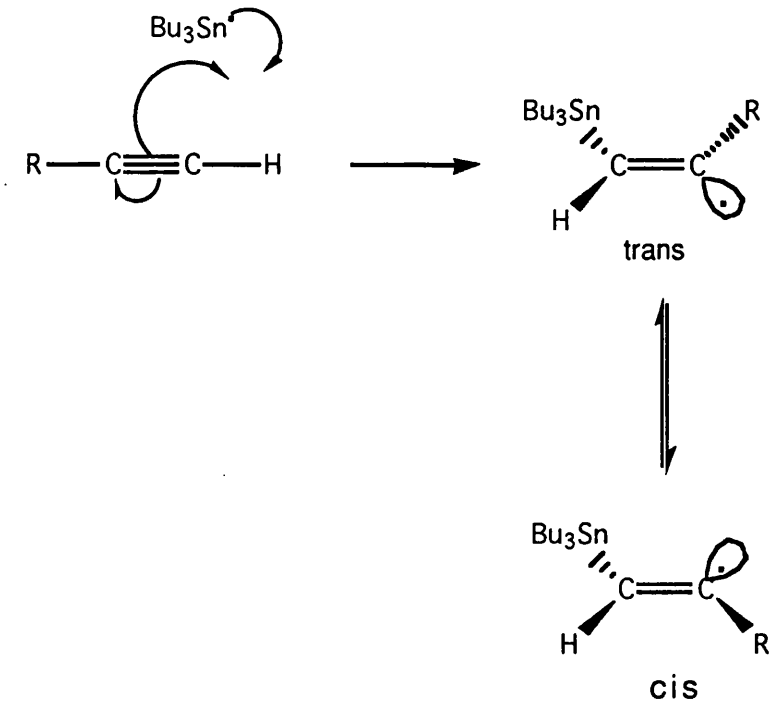


Scheme 3.2.a

By observing the reaction in a NMR tube we noted the isomerisation of the Z-isomer to the E-isomer, to give a 1:1 mixture. Could the extra stability associated with O->Sn association be preventing total isomerisation to the E-product? If this were the case then the Z-isomer would be 5-co-ordinate and this would be confirmed by the ^{119}Sn NMR spectrum of the (Z)-4-tributylstannyl-3-buten-2-ol (Table 1.). However the value of $\delta - 63$, is low for five co-ordinate tin.[6]

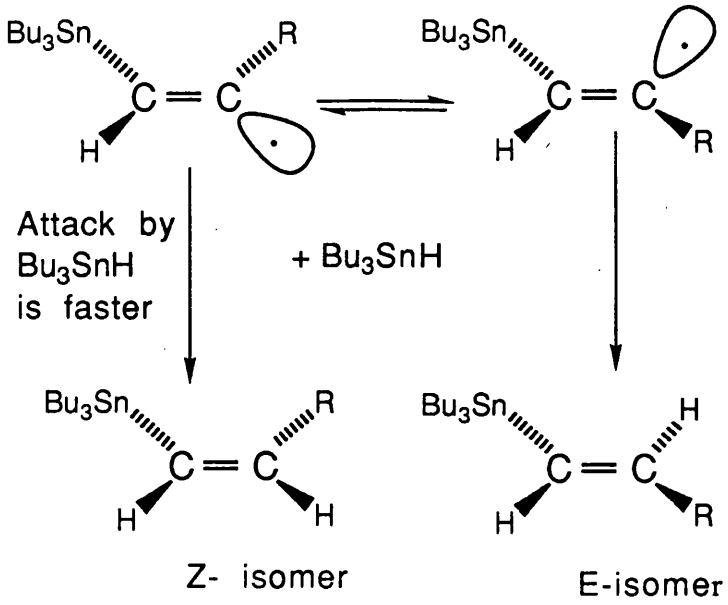
In an attempt to examine further the role of the oxygen we decided to silylate the OH with trimethylsilyl imidazole to give the 2-methyl-3-butyn-2-trimethylsilyl ether. The empty d orbitals of the silicon atom will attract the lone pairs of the oxygen making them less available for association with the tin atom. Thus hydrostannylation of the vinyl ether should result in more E-isomer than Z. This is in fact what was observed with only 33% of Z-isomer being obtained after an hour and none after 2 hours of reaction.

Further reaction with 3,3-dimethyl-1-butyne, (which possesses no C-2 oxygen), results in a 1:10 ratio of Z and E isomers. Thus it would appear that the presence of the oxygen at the C-2 carbon does influence the outcome of the reaction. However, if this was the sole deciding factor, then we would expect no Z-isomer at all in the reaction with 3,3-dimethyl-1-butyne, but we have an initial formation of Z, albeit in small amounts, suggesting that the Z is formed regardless of the nature of the groups adjacent to the acetylenic carbon. It is highly probable that steric factors are also involved, resulting in formation of the thermodynamically favoured E-adduct. To fully explain why we obtain Z and E-isomers in the reaction of tributyltin radical to alkynes we need to look at the work conducted by Kupchik et al.[8] Their work establishes that an addition of trialkytin radicals to any alkyne gives cis and trans vinyl radicals in equilibrium.



Scheme 3.2.b

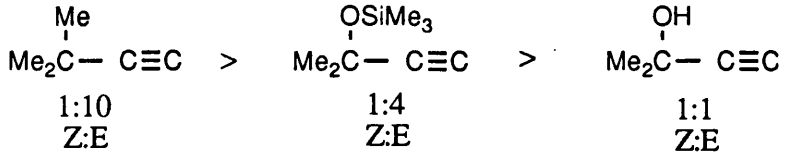
The rate constant for this type of isomerisation has been shown by ESR spectroscopy to be ca. 10^9 s^{-1}.[9].The kinetically controlled products then result from the different rate of attack by Bu_3SnH: the trans radical reacts faster because steric hindrance is less, giving more Z-product. However, in the adducts, the E is probably less sterically crowded and is structurally more stable. Equilibriation then gives more E as the thermodynamically controlled product.



Scheme 3.2.c

This model fits our results. The fact that sometimes we could not observe the Z isomer free of E-isomer, does suggest that the trans and cis tributylstannylvinyl radicals exist in equilibrium. We could then observe the conversion of the Z into the E-isomer. The exception seems to be the 4-tributylstannyl-2-methyl-3-buten-2-ol where the two isomers were obtained in 1:1 ratio, presumably because of extra stability afforded the Z-isomer by the O->Sn association. The difference between the ^{119}Sn NMR chemical shift for the E-isomer (δ –40) and of the Z-isomer (δ -63) is smaller than that which might be expected for 4- and 5-co-ordinate tin, but is in the right direction.

Our results therefore suggest the following order for the rate of isomerisation of the Z ---> E adducts for the various alkynes used (Scheme 3.2.d).

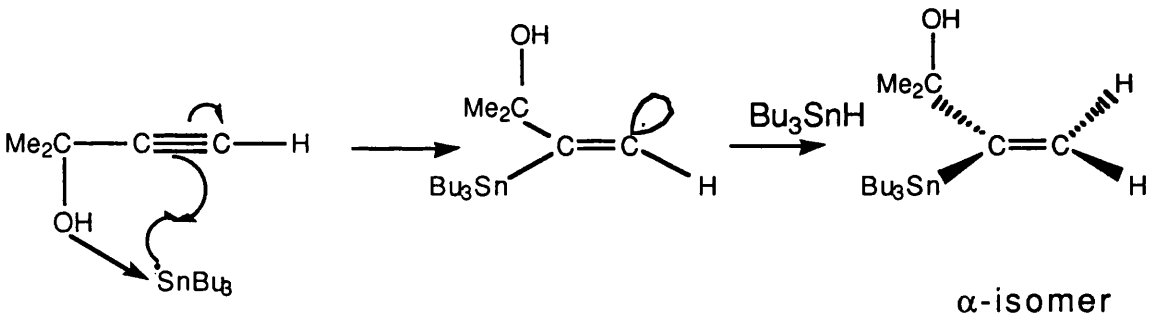


Ratio of products formed at 80°C with AIBN
for 3 hours in toluene

Scheme 3.2.d

Hydrostannation of the alkynes by using trialkyltin hydrides is thus a complex free radical process in which the products which are observed may result from kinetic or thermodynamic control: the Z-isomer is dominant if the products are under kinetic control, whilst the E-isomer is favoured if the products are under thermodynamic control.

This model does not explain the formation of the α–isomer which was only observed during reaction with 2-methyl-3-butyn-2-ol. Its formation can be rationalised as follows:



Scheme 3.2.e

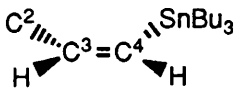
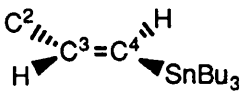
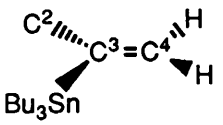
It is assumed that tributyltin radical associates with the oxygen and is steered into the C-3 carbon giving a vinyl radical (Scheme 3.2.e), which then abstracts hydrogen from the hydride.

The general course of the reaction is now well established. Our results agree with those of Taddei,[7] and Ensley[2] and to some extent those of Leusink,[3] however, we find that the formation of the α-isomer is also a free radical process and not as suggested by Leusink[3a,b,c,d] an ionic reaction which is promoted by the presence of strong electron withdrawing groups.

The proton and carbon-13 NMR spectra which we have obtained, of the vinyltin adducts confirm and extend the data which can be used for characterising the Z, E and α -adducts. Table 2 shows the extended range of H-H and Sn-H coupling constants which we have identified in the ^1H NMR spectra.

These coupling constants clearly differentiate the Z, E and α isomers and provide the basis for the identification of these adducts. The trend of Sn-H coupling generally follows that of the more familiar H-H coupling in the sequence: ^3J trans > ^3J cis > ^3J gem .[10]

Table 2 Range of H - H and Sn - H coupling constants (Hz) for Z, E and α vinyltin adducts.

	 Z	 E	 α
$^{3}J_{H-H}$ (cis)	13.2 -13.3	-	-
$^{3}J_{H-H}$ (trans)	-	19.2 - 19.4	-
$^{3}J_{H-H}$ (gem)	-	-	0 - 1.5
$^{2}J_{Sn-H}$	65.5 - 73.2	64.6 - 73.4	-
$^{3}J_{Sn-H}$	112.0 - 145.2	72.3 - 81.1	-
$^{3}J_{Sn-H}$ (trans)	-	-	164.6
$^{3}J_{Sn-H}$ (cis)	-	-	67.7

Sn-^{13}C Coupling constants for vinyltin adducts have been discussed in the literature[11,12,13] and support what we have observed. The $^{2}J_{Sn-C3}$ (Figure 3) coupling tends to be immeasurably small, $^{3}J_{Sn-C2}$ ranges from 40 - 50 Hz, whilst $^{1}J_{Sn-C\alpha}$ is smaller than $^{1}J_{Sn-C4}$.

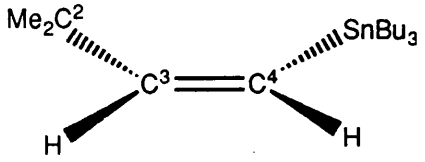


Figure 3

3.3 EXPERIMENTAL

Tributyltin hydride, 2-methyl-3-butyn-2-ol, 3,3-dimethyl-1-butyne and 17α-ethynylestradiol were all commercial grade materials obtained from the Aldrich Chemical Company, and 2-methyl-2-(trimethylsilyloxy)-3-butyne was obtained by the silylation of the alcohol with trimethylsilyl imidazole according to Chen et al[4].

All NMR spectra were recorded on a Varian VXR-400 spectrometer (400 MHz) on solutions in $CDCl_3$ or d_6-benzene (C_6D_6) and the chemical shifts (δ) were measured in patrs per million (p.p.m) The following abbreviations are used in signal assignments; s (singlet), d (doublet), t (triplet), m (multiplet) and dd (doublet of doublets). ^{13}C and ^{119}Sn NMR spectra were recorded at 100.58 MHz and 74.6 MHz respectively on the Varian VXR-400 spectrometer. Commercially available Merck Kieselgel 60 F_{254} plates was used for analytical thin layer chromatography (t.l.c.). They were visualised with ultra violet light or iodine. Column chromatography were performed using Merck flash silica gel (200-400 mesh) stationary phase and hplc was performed on a 5μm silica gel column with ethyl acetate-n-hexane as the mobile phase. All reactions were carried out under inert conditions using dry argon or nitrogen. All glassware for the reactions were dried in an oven at 130°C for at least 24 hours. Temperatures below 0°C were obtained by cooling acetone with solid carbon dioxide (Cardice).

General Method for Hydrostannation with Bu_3SnH

Toluene ($25cm^3$) was heated up to 80°C in a thermostated oil bath and the alkyne was added. When the temperature was steady at 80°C, tributyltin hydride (Bu_3SnH) and AIBN were added. The mixture was then heated under an inert atmosphere for 3 hours, after which the toluene was removed in vacuo. The resulting colourless oil was

distilled in vacuo and the isomers separated by flash column chromatography using n-hexane-ethylacetate (6.5 : 3.5 v/v) as eluent, or by hplc.

3.3.1. Preparation of E/Z-4-tributylstannyl-2-methyl-3-buten-2-ol

This was synthesised as an oil, giving a 4:1 ratio of Z- and E-isomers, using the above method and the following mole ratio of reactants:

Bu_3SnH (1.7 g, 5.8 mmol, 1.57 ml), 2-methyl-3-butyn-2-ol (1.34 g, 15.95 mmol, 1.55 ml) and AIBN (27 mg, 0.164 mmol).

Yield 4.57 g, 78%; B.p. 84 - 86°C (0.03 mmHg), [Lit[2]. 90 - 94°C (0.1 mmHg)];

IR (neat) 3330 (OH, st), 1620 (C=C, st) cm^{-1}.

δ_H ($CDCl_3$);1.00 - 0.80 (9 H, m; CH_3); 1.75 - 1.25 (25H, m);

Z-isomer

Found: C, 54.35; H, 9.62.

Calc. for: $C_{17}H_{36}OSn$; C, 54.43; H, 9.67%

δ_H 5.75 (1H, d, ^3J_H 13.4 Hz, $^3J^{117}_{Sn}$ 136.6 Hz, $^3J^{119}_{Sn}$ 143.1 Hz; H-3);
6.58 (1H, d, ^3J_H 13.4 Hz, $^2J^{117}_{Sn}$ 65.5 Hz, $^2J^{119}_{Sn}$ 68.6 Hz; H-4).

δ_C ($CDCl_3$), 9.45 ($^1J^{117}_{Sn}$ 306.0 Hz, $^1J^{119}_{Sn}$ 343.5 Hz; Cα); 13.76 (Cδ); 27.27 ($^3J_{Sn}$ 53.4 Hz; C-γ); 29.09 ($^2J_{Sn}$ 20.4 Hz; C-β); 29.49 (C-1); 72.44 ($^3J_{Sn}$ 57.40 Hz; C-2); 124.90 ($^1J^{117}_{Sn}$ 393.2 Hz, $^1J^{119}_{Sn}$ 411.3 Hz; C-3); 152.0 (C-4).

δ^{119}_{Sn} -60.83

E-isomer

δ_H 6.07 (1H, d, ^3J_H 19.2 Hz, $^2J^{117}_{Sn}$ 75.2 Hz, $^2J^{119}_{Sn}$ 78.5 Hz; H-4); 6.14 (1H, d, ^3J 19.2 Hz, $^3J^{117}_{Sn}$ 68.6 Hz, $^3J^{119}_{Sn}$ 71.8 Hz; H-3).

δ_C 9.45 ($^1J^{117}_{Sn}$ 328.3 Hz, J^{119}_{Sn} 343.6 Hz; C-α); 13.75 (C-δ); 27.27 ($^3J^{117/119}_{Sn}$ 53.4 Hz; C-γ); 29.09 ($^2J^{117/119}_{Sn}$ 20.4 Hz; C-β); 29.48 (C-1); 72.49 ($^3J_{Sn}$ 57.4 Hz; C-2); 122.44 ($^1J^{117}_{Sn}$ 358.2 Hz; $^1J^{119}_{Sn}$ 377.9 Hz; C-4) 155.56 (C-3).

δ^{119}_{Sn} -40.56

3.3.2. Preparation of (E)-4-Tributylstannyl-2,2-dimethyl-4-butene

Again this compound was synthesised as an oil by the general method using the following mole ratio of reactants.

Bu_3SnH (1.77 g, 6.09 mmol); 3,3-dimethyl-1-butyne (0.4 g, 6.09 mmol) and AIBN (0.61 mmol).

Yield: 2.04 g, (90%) B.p. 94 - 97°C/0.08 mmHg.

Found: C, 57.41; H, 10.66.

Calc. for: $C_{18}H_{38}Sn$: C, 57.93, H, 10.26%

IR. (neat) 1618 (C=C)cm^{-1}

δ_H ($CDCl_3$); 0.8 - 1.83 (36 H, m), 5.75 (1H, d, ^3J_H 19.4 Hz, $^2J^{117}_{Sn}$ 67.4 Hz, $^2J^{119}_{Sn}$ 70.6 Hz; H-4); 5.70 (1H, d, ^3J_H 19.4 Hz,$^3J^{117}_{Sn}$ 75.6 Hz, $^3J^{119}_{Sn}$ 79.2 Hz; H-3).

δ_C ($CDCl_3$), 9.37 ($^1J^{117}_{Sn}$ 376.0 Hz, $^1J^{119}_{Sn}$ 393.5 Hz; C-α); 13.74 (C-δ);

29.60 ($^2J^{117/119}Sn$ 20.5 Hz; C-β); 27.20 ($^2J^{117/119}Sn$ 32.6 Hz; C -γ); 119.64 ($^1J^{117}Sn$ 396.3 Hz, $^1J^{119}Sn$ 404.3 Hz; C-4); 35.93 ($^3J^{117/119}Sn$ 55.1 Hz; C-2); 159.95 (C-3).

3.3.3 Preparation of (E)-4-tributylstannyl-2-methyl-2 -(trimethylsilyloxy)-4-butene

Again the reaction was carried out as detailed above, and the product obtained as an oil, with the following mole ratio of reactants:

Bu_3SnH (0.46 g, 1.59 mmol) AIBN (0.159 mmol) and 2-methyl-2-(trimethylsilyloxy)-3-butyne (0.1 g; 1.59 mmol)

Yield: 0.263 g (100%)

Found: C, 53.65; H, 9.91

Required for:. for $C_{20}H_{44}OSiSn$, C, 53.70; H, 9.91%

δ_H ($CDCl_3$); 0.03 (9H, s, Si-$(CH_3)_3$); 0.8 - 1.91 (33H, m,); 6.09 (1H, d, ^3J_H 19.4 Hz, $^3J^{117}Sn$ 77.5 Hz, $^3J^{119}Sn$ 81.1 Hz; H-3); 5.95 (1H, d, ^3J_H 19.4 Hz,$^2J^{117}Sn$ 70.1, $^2J^{119}Sn$ 73.4 Hz; H-4).

δ_C ($CDCl_3$); 2.34 (Si-CH_3), 9.26 ($^1J^{117}Sn$ 334.5 Hz, $^1J^{119}Sn$ 350.0 Hz; C -α);13.85 (C-δ); 27.26 ($^3J^{117/119}Sn$ 55.6 Hz; C-γ); 29.09($^2J^{117/119}Sn$ 23.7 Hz; C-β); 30.00 (C-1); 75.30 ($^2J^{117/119}Sn$ 50.6 Hz;); 122.40 ($^1J^{117}Sn$ 338.1 Hz; $^1J^{119}Sn$ 353.8 Hz; C-4); 157.83 (C-3).

$\delta^{119}Sn$ +33

3.3.4. Preparation of (Z)-4-tributylstannyl-4 -octene,2,7-dimethyl-5-octyne-2,7-diol

The reaction was carried out by the same procedure as above in the following mole ratios. The product was obtained as a solid and recrystallised from ethanol:

Bu_3SnH (0.876 g, 3.0 mol), diyne (0.5 g, 3.00 mmol) and AIBN (0.003 mmoles).

Yield, 1.17 g, 85%; M.p. 135 - 140°C

Found: C 56.90, H, 9.01;

Calc. for: $C_{22}H_{42}OSn$: C, 57.79, H, 9.29%

δ_H ($CDCl_3$) 0.88 - 1.55 (40H, m); 1.83 (2H, s, 2xOH); 6.28 (1H, s, $^3J^{117}_{Sn}$111.9 Hz, $^3J^{119}_{Sn}$ 117.08 Hz; H-3).

δ_C ($CDCl_3$) 11.70 ($^1J^{117}_{Sn}$ 326.6 Hz; C-α); 29.19 ($^3J^{117/119}_{Sn}$ 19.0 Hz; C -γ); 30.08 (C-1); 31.31 (C-8); 65.57 (C-7); 75.47 ($J^{117/119}$ 20.1 Hz; C-2); 82.18 (C-5); 95.59 (C-6); 115.05 (C-3); 170.6 (C-4).

3.3.5. Preparation of Z/E-17α-[2-(tributylstannyl) vinyi]estradiol

The reaction was carried out as above and the product was obtained as a solid and recrystallised from ethanol

17α-Ethynylestradiol (0.25 g, 0.843 mmol), Bu_3SnH (0.245 g, 0.843 mmol), AIBN (0.08 mmol).

Z

Yield, 0.27 g, (55%) M.p 140-141°C

Found : C, 66.03; H, 8.60,

Required for: $C_{20}H_{52}O_2Sn$: C 66.08, H, 8.02%

δ_H ($CDCl_3$) 0.7 - 2.4 (45H, m, steroid and Bu_3Sn - envelope); 2.65 - 2.75 (2H, m, C-6 methylene); 5.84 (1H, d, ^3J_H 13.2 Hz, $^2J^{117}_{Sn}$ 69.8 Hz, $^2J^{119}$ 73.2 Hz; H-20); 6.75 (1H, d, ^3J 13.2 Hz; $^3J^{117}_{Sn}$ 138.6 Hz, $^3J^{119}_{Sn}$ 145.2 Hz; H-19) 6.7 - 7.2 (3H, m, aromatic protons).

δ_C ($CDCl_3$) 9.89 ($^1J^{117/119}_{Sn}$ 382.2 Hz; C-α); 13.89 (C-δ); 27.65 ($^3J^{117/119}_{Sn}$ 86.70 Hz; C-17); 29.58 ($^2J^{117/119}_{Sn}$ 23.5 Hz); 14 - 49 (steroid envelope); 85.38 ($^3J^{117/119}_{Sn}$ 54.8 Hz; C-17); 122.30 (C -20); 170.77 (C-19); 119.06; 124.18; 126.09; 139.00; 148.00; 152.08 (aryl).

3.4 REFERENCES

1. Davies, A. G., Symes, E. K., Bishop, P. B. and Coulson, D. E., Biochem. Pharmacol., **44**, 741 (1992).

2. Ensley, H. E., Buescher, R. K. and Lee, K., J. Org. Chem., **47**, 404 (1982).

3a. Leusink, A. J., Hydrostannation, Schotanus and Jens, Utrecht (1966).

3b. Corey, E. J. and Wollenberg, R. H., J. Org. Chem., **40**, 2265 (1975).

3c. Corey, E. J., Ulruh, P. and Fitzpatrick, J. M., J. Am. Chem. Soc., **98,** 222 (1976).

3d. Leusink, A. J. and Budding, H. A., J. Organomet. Chem., **9,** 285 (1967).

4. Chen, S-M. L., Sohaub, R. E. and Gradzinkas, C. V., J. Org. Chem., **43**, 3450 (1978).

5. Hofmeister, H., Laurent, H., Schulze, P. E. and Weichert. R., Tetrahedron, **42**, 3575 (1986).

6. Pretrosyan, V. S., 'Progress in NMR Spectroscopy', **11**, 115 (1977).

7.a Nativi, C. and Taddei, M., J. Org. Chem., **53**, 820 (1988)

7.b Leusink, A. J., Budding, H. A. and Dreuth, W., J. Organomet. Chem., **11**, 541 (1968).

8. Kupchik, E. J. in Organotin Compounds, Ed. Sawyer, A. K., Chap. 2, Dekker, M. New York 1972.

9. Landolt-Börnstein, Numerical Data and Functional Relationships in Science and Technology, Vol. 13. Part C, Springer, Berlin, 1983.

10. Moore, D. W. and Happe, J. A., J. Phys. Chem. **65**, 224 (1961).

11. Lunazzi, E. and Taddei, M., Spectrochem. Acta, **25A**, 611 (1969).

12. Kuivila, H. G., Considine, J. L., Mymott, R. J. and Sarma, R. H., J. Organomet. Chem. **55**, C11 (1978).

13. Cawley, S. and Danyluk, S. S., Can. J. Chem., **46**, 2373 (1968).

14. Mitchell, T. N. and Kummetat, C., J. Organomet. Chem., **157**, 275 (1978).

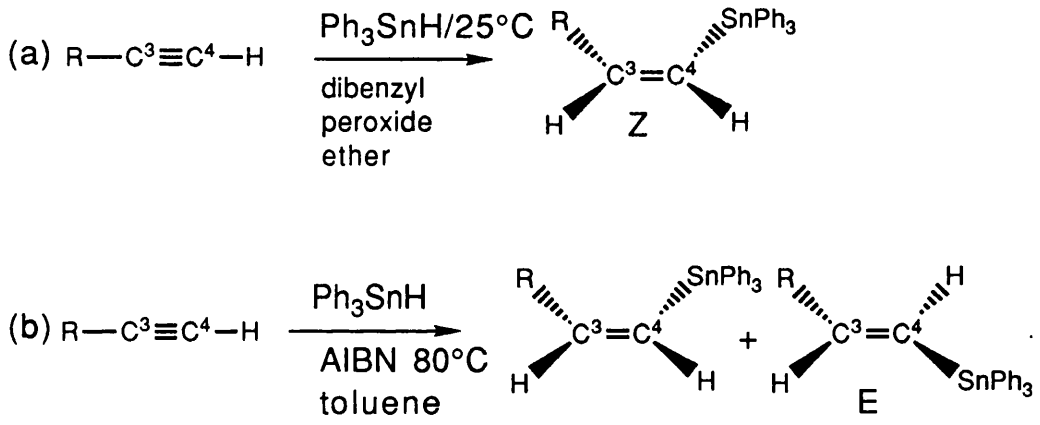
15. Jung, M. E. and Light, L. A., Tetrahedron, Lett. **23**, 3851 (1982).

4.0 Reaction of Triphenyltin Hydride

4.1 RESULTS

Triphenyltin hydride (Ph_3SnH) reacts with 17α-ethynyl-4-estren-17-ol[1] at room temperature to give only the (Z)-vinyltin adduct, thus we were interested in its behaviour with 17α-ethynyl-estradiol and to this end we looked at the reaction of Ph_3SnH with our model compounds as we had previously done with Bu_3SnH.

4.1.1 2-Methyl-3-butyn-2-ol



Scheme 4.1.1

The first reaction at 25°C (Scheme 4.1.1.a) gave a good yield (90%) of a white crystalline solid which was identified as the pure Z-adduct by its proton and ^{13}C NMR spectra:

δ_H 6.17 (1H, d, ^3J 12.4 Hz, $^2J^{117}_{Sn}$ 90.3 Hz, $^2J^{119}_{Sn}$ 94.5 Hz; H-4);
6.86 (1H, d, ^3J 12.4 Hz, $^3J^{117}_{Sn}$ 175.5 Hz, $^3J^{119}_{Sn}$ 183.7 Hz; H-3).

δ_C 73.16 ($^2J_{Sn}$ 31.0 Hz; C-2); 121.13 ($^1J^{117}_{Sn}$ 553.4 Hz, $^1J^{119}_{Sn}$ 579.0 Hz; C-4); 155.54 (C-3).

δ_{Sn} -156

When the reaction was carried out in toluene with AIBN as initiator, at 80°C, the proton NMR spectrum showed that a 1:2 mixture of the E- and Z-isomers was formed in 80% yield; these compounds could not be separated by flash column chromatography.

In the proton NMR spectrum the E-isomer (Scheme 4.1.1.b) showed in the olefinic region 2 doublets:

δ_H 6.45 (1H, d, ^3J_H 19.9 Hz, $^2J^{117}_{Sn}$ 77.1 Hz, $^2J^{119}_{Sn}$ 80.7 Hz; H-4);
6.36 (1H, d, ^3J_H 19.9 Hz,$^3J^{117}_{Sn}$ 84.3 Hz, $^3J^{119}_{Sn}$ of 88.2 Hz; H -3).

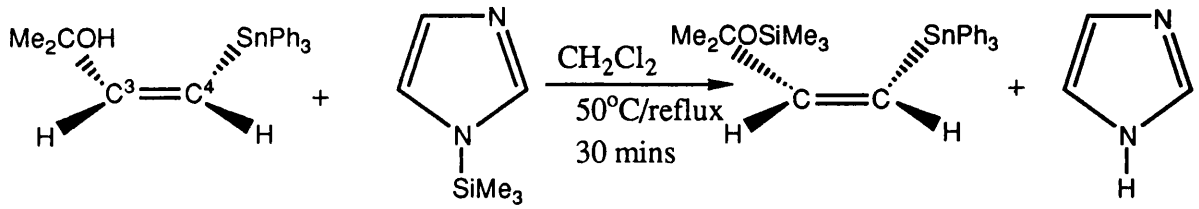
δ_C 72.78 ($^3J_{Sn}$ 30.1 Hz; C-1), 119.06 ($^1J^{117}_{Sn}$ 499.7 Hz, $^1J^{119}_{Sn}$ 522.9 Hz; C-2); 154.76 (C-3);

δ_{Sn} -135.

The large values of $^3J_{H-H}$ (trans) or $^3J_{Sn-H}$ (trans), and the small values of $^3J_{H-H}$ (cis) or $^3J_{Sn-H}$ (cis) identify the Z- and E-isomers respectively.[2,3,4]

4.1.2 Silylation of (Z)-4-Triphenylstannyl-2-methyl-3-buten-2-ol

Silylation of (Z)-4-triphenylstannyl-2-methyl-3-buten-2-ol (Scheme 4.1.2.a)[5] should enable us to determine whether the tin is five co-ordinate. The d orbitals of the silicon attract the lone pair of electrons on the oxygen thus making them less available for a O->Sn association. The high-field ^{119}Sn chemical shift for the alcohol, at -156,[6,7,8] suggests that the tin is five co-ordinate. Silylation should result in a downfield shift for the tin atom.



Scheme 4.1.2.a

The silylation was followed by tlc, and the resultant orange crystalline solid (m.p 80 - 85°C) was purified by recrystallisation from ethanol. The proton NMR spectrum showed olefinic protons at:

δ_H 5.83 (1H, d, ^3J_H 13.3 Hz, $^2J^{117}Sn$ 76.5 Hz, $^2J^{119}Sn$ 80.1 Hz; H-4);
6.85 (1H, d, ^3J_H 13.3 Hz, $^3J^{117}Sn$ 177.4 Hz, $^3J^{119}Sn$ 185.7 Hz; H-3).

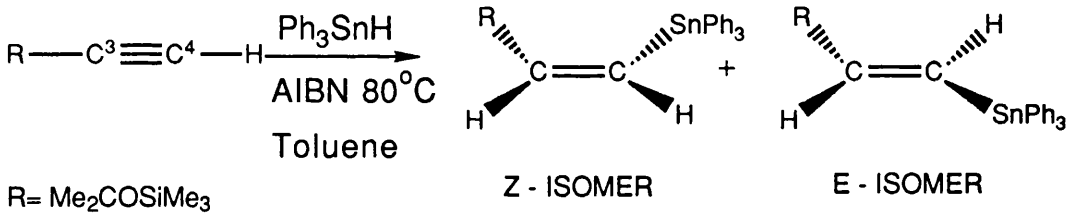
Compared to the OH compound, the H-4 proton had shifted upfield in the silyl ether compound by 0.34 ppm. The value of J_{H-H} was now 13.3 Hz compared with 12.4 Hz for the OH equivalent and J_{Sn-H} had decreased by 18-20 Hz.

The situation with the H-3 proton is less clear cut; J_{H-H} is now 13.3 Hz, but the peak was still observed at δ 6.8 and there was no change in J_{Sn-H}. The ^{13}C NMR spectrum showed that only two

signals were affected, that at δ 76.00 ($^3J_{Sn-C}$ 30.2 Hz; C-2) (a downfield shift of 2.84 ppm), and that at δ 117.36 (C-4) (a downfield shift of 3.77 ppm).

The ^{119}Sn NMR spectrum showed a sharp singlet at δ +33; this downfield shift of 189 ppm in going from 4.1.1.a to 4.1.2.a established that the tin is five co-ordinate in the former compound, and four co-ordinate in the latter.[6,7,8]

What then would be the nature of the products if 2-methyl-3-butyn-2-trimethylsilylether reacted with triphenyltin hydride in the presence of AIBN at 80°C for 3 hours?



Scheme 4.1.2.b

After initial column chromatography the proton NMR spectrum showed that there was a 1:1 mixture of E and Z isomers in a yield of 75 - 80%. Upon separation of the E and the Z isomers it was observed that the silyl group had been cleaved off but this did not affect the Z/E ratio.

As with the above Z-adduct, the structure was again determined by the proton and the ^{13}C NMR spectra as the E-isomer. Proton NMR spectroscopy showed two doublets:

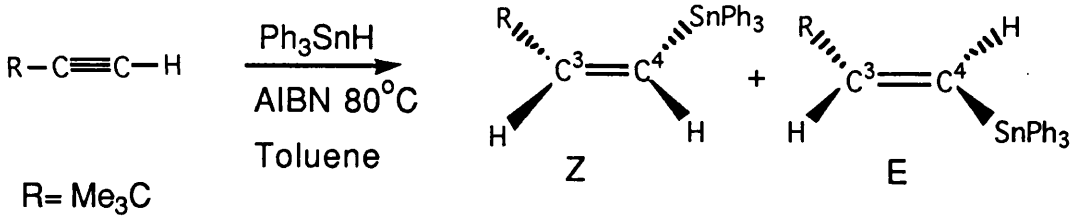
δ_H 6.43 (1H, d, ^3J_H 18.9 Hz, $^3J^{117}_{Sn}$ 86.4 Hz, $^3J^{119}_{Sn}$ 90.4 Hz; H-3);

6.38 (1H, d, ^3J_H 18.8 Hz, $^2J^{117}_{Sn}$ 82.2 Hz, $^2J^{119}_{Sn}$ 86.0 Hz; H-4).

$\delta^{13}C$ 72.78 ($^3J^{117/119}$ 29.8); 119.06 ($^1J^{117}_{Sn}$ 495.6 Hz, $^1J^{119}_{Sn}$

518.9 Hz; C-4); 159.10 (C-3).

4.1.3 3,3-Dimethyl-1-butyne



Scheme 4.1.3

The products from this reaction were isolated by flash column chromatography, which allowed the separation of two isomers, which were identified by proton and ^{13}C NMR spectroscopy. The first isomer showed characteristic olefinic peaks at:

δ_H 6.30 (1H, d, ^3J_H 19.0 Hz, $^3J^{117}_{Sn}$ 83.6 Hz, $^3J^{119}_{Sn}$ 87.5 Hz; H-3); 6.09 (1H, 3, ^3J_H 19.1 Hz, $^2J^{117}_{Sn}$ 95.7 Hz, $^2J^{119}_{Sn}$ 100.00 Hz; H -4).

The J_{H-H} value indicates an E-isomer whilst the J_{Sn-H} values point to protons gem and cis to the tin moiety respectively.[2,3,4,9]

The second isomer showed peaks centred at:

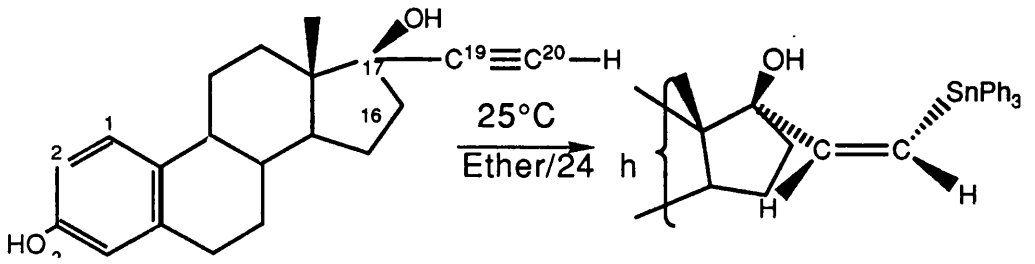
δ_H 6.93 (1H, d, ^3J_H 13.5 Hz, $^3J^{117}_{Sn}$ 185.4 Hz, $^3J^{119}_{Sn}$ 194.0 Hz; H -3); 5.91 (1H, d, ^4J_H 13.5, $^2J^{117}_{Sn}$ 76.9, $^2J^{117}_{Sn}$ 80.0 Hz; H-4).

The values of J_{H-H} and J_{Sn-H} are characteristic of geminal and trans coupling constants respectively, identifying the compound as the Z-isomer.

The ^{13}C NMR spectrum showed signals at:

δ_C 72.44 ($^3J_{Sn}$ 57.4 Hz; C-2), 122.44 ($^1J^{117}_{Sn}$ 516.2, $^1J^{119}$ 540.20; C-3); 163.94; (C-3).

4.1.4 17α-Ethynylestradiol



Scheme 4.1.4

17α-Ethynylestradiol reacts with triphenyltin hydride at room temperature in the presence of dibenzyl peroxide in ether over 24 hours.[1] The Z-isomer was obtained exclusively, and was isolated in 65% yield.

As with previous products this was identified by proton and ^{13}C NMR spectroscopy which showed characteristic patterns in the olefinic region at:

δ_H 6.18 (1H, d, ^3J_H 12.0 Hz, $^2J^{117}_{Sn}$ 91.2 Hz, $^2J^{119}_{Sn}$ 95.4 Hz; H-20); 6.86 (1H, d, ^3J_H 12.0 Hz, $^3J^{117}_{Sn}$ 203.6 Hz, $^3J^{119}_{Sn}$ 213.1 Hz; H -19).

δ_C 85.89 ($^3J_{Sn}$ 29.4 Hz; C-17); 126.58 (C-20); 155.86 (C-19).

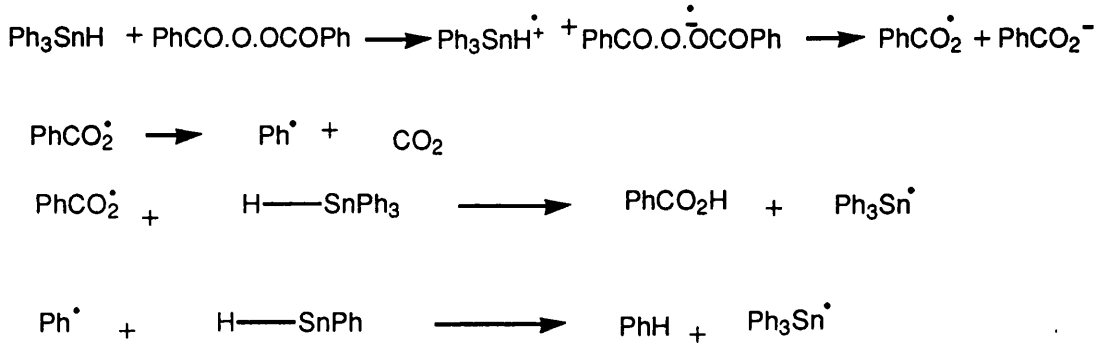
These H-H and Sn-H coupling constants compare favourably with those reported for the tributyltin analogue earlier and those

reported by Gielen et al.[1] for the adduct of 17α-ethynyl-4-estren-17-ol and confirm that the compound is the Z-isomer.

4.2. DISCUSSION

Triphenyltin hydride reacts readily with acetylenic bonds, such as in phenylacetylene[10] to give triphenyl-β-styryltin or 1-phenyl-1,2-bis(triphenylstannyl)ethane depending on the mole ratio of the reagents. It also reacts with propargyl alcohol[10] and the methyl ester of propiolic acid to give (3-hydroxy-l-propenyl)triphenyltin and 1-methoxycarbonyl-1,2-bis(triphenylstannyl)ethane respectively.[10] Gielen et al.[1] have also reported its reaction with 17α-ethynyl-4-estren-17-ol at room temperature to give the Z-triphenyltin adduct exclusively. It was thus expedient to study its reaction with our model compound, 2-methyl-3-butyn-2-ol, in comparison with tributyltin hydride.

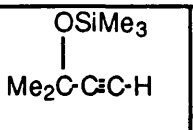
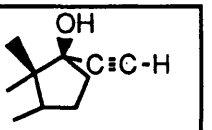
These reactions were facile and could be performed at room temperature with dibenzoyl peroxide as the radical initiator, or at >80°C with AIBN as radical initiator. The triphenyltin hydride presumably reacts with dibenzoyl peroxide to give the required tin radical in the following process: (Scheme 4.2)



Scheme 4.2

4.2.1 Regioselectivity

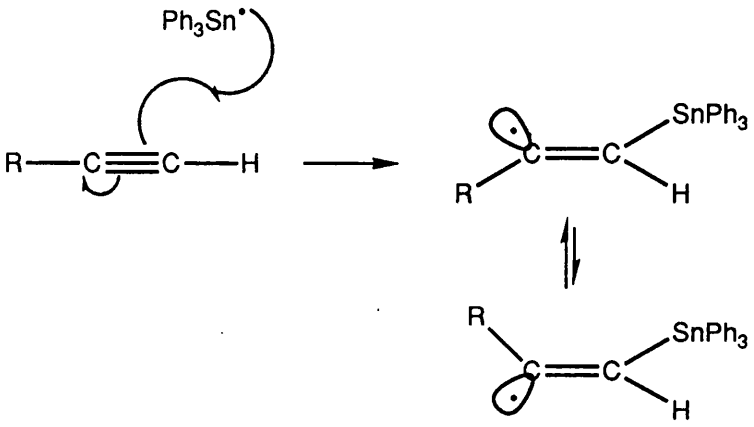
Table 4.2.1 Showing isomeric ratio of products under the same reaction conditions

Reaction conditions	$Me_3C-C\equiv C-H$	$Me_2(OH)C\cdot C\equiv C\cdot H$		
	% Z, E, α	Z, E, α	Z, E, α	Z, E, α
1 h	33 66 0	80 20 0	33 66 0	-
3 h	10 90 0	66 33 0	33 66 0	-
RT, 24 h BPO	-	100 0 0	-	100 0 0
$\delta^{119}Sn$	-	-156 -135 -	+33 - -	-

The reaction of triphenyltin hydride with these alkynes is highly regioselective, in that only attack at the β carbon was observed, presumably because attack at the α-carbon is highly hindered by the bulky nature of the phenyl groups.

4.2.2 Stereochemistry

Attack at the β-carbon results in the formation of two stereoisomers as already discussed extensively in the analogous reactions of Bu_3SnH (Chapter 3).



Scheme 4.2.2

From Table 4.2.1 we observe that the ratio of Z and E isomers varies with the group on C-2 and the reaction conditions. This supports what we found with the Bu_3SnH reactions; that if an OH group was attached to the C-2 position, more Z-isomer was obtained, but where the OH was silylated or replaced with a methyl group, more of the E-isomer was obtained.

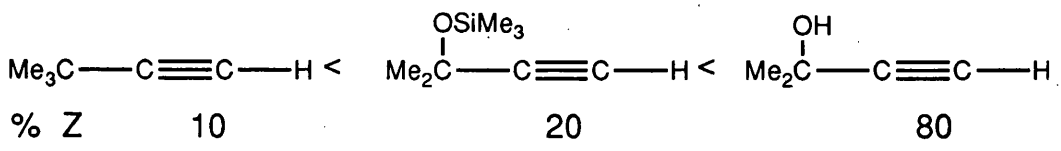


Figure 3

This confirms our assertion in the analogous Bu_3SnH reactions, that the dominance of the Z-isomer is dependent on the availability of the C-2 oxygen to form an Sn<--O association. The triphenyltin moiety is a better Lewis acid than the Bu_3Sn moiety and thus has a greater potential to form an intramolecular association between the tin and oxygen and hence stabilize the Z-isomer.

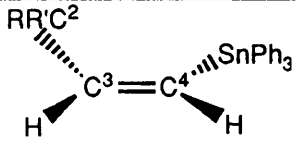
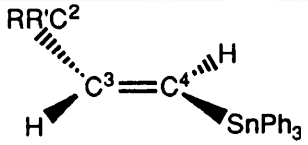
Increasing the time of the reaction also affects the isomeric ratio of products. We have already discussed extensively in the analogous reactions with Bu_3SnH how the Z-isomer isomerizes to the E-isomer[4] if the reaction is heated at 80°C or greater for more than 3 hours. These same observations are made here, regardless of the nature of the group at the C-2 position. Table 4.2.1 shows that after 1 hour of reaction, 66% of the E-isomer is obtained with 3,3-dimethyl-1-butyne and 2-methyl-2-(trimethylsilyloxy)-3-butyne. Only 20% of the E-isomer is obtained with the OH compound at the same stage, however, after 3 hours of heating the amount of E-isomers increases to 90%, 66% and 33% respectively. These findings support those for the analogous Bu_3SnH reactions, except with the hydroxyl (OH) compound where only a 2:1 ratio of Z and E isomers was obtained for the Ph_3SnH reaction, compared to a 1:1 ratio in the Bu_3SnH reaction. This is another indication of Sn <-- 0 association, which stabilizes the Z-isomer and reduces the extent of isomerization to the E-adduct.

The reaction at room temperature is a special case and suggests that under special conditions pure Z-isomers can be obtained. It also confirms that formation of the E-isomer has a slightly higher energy of activation than the Z-isomer (see later).

4.2.3 NMR Analysis and Evidence for Intramolecular Co-ordination

As reported in the section dealing with Bu_3SnH reactions (Section 3), the structures of the various isomers formed were determined by analysis of the NMR coupling constants of the olefinic protons.[2,3,4] Table 4.2.3 summarises the range of H-H and Sn-H coupling constants which we have observed.

Table 4.2.3 Range of H-H and Sn-H coupling constants (Hz) for the E and Z isomers

R = Me R^1 = $OSiMe_3$ or OH or Me		
^3J_H (cis)	12.4 - 13.3	-
^3J_H (trans)	-	18.8 - 19.9
$^2J_{Sn}$ (gem)	90.3 - 94.5	78.1 - 80.7
$^3J_{Sn}$ (trans)	173.9 - 194.0	-
$^3J_{Sn}$ (cis)		84 - 88.2

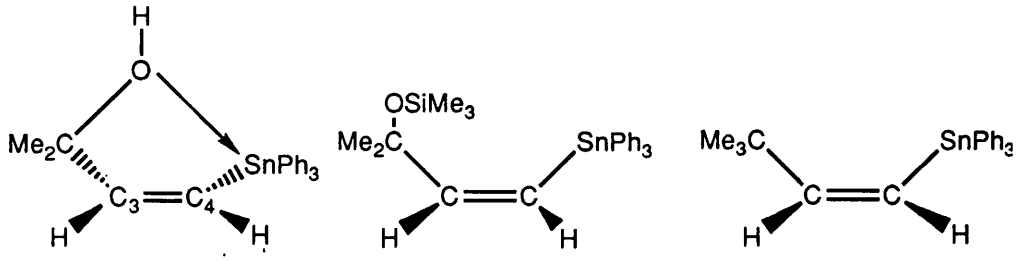
These data support those in Table 2 for the analogous Bu_3SnH adducts, in that:

$$^3J_H \text{ (cis)} < {}^3J_H \text{ (trans)}$$

as would be expected for cis and trans protons. A similar trend is also apparent for the Sn-H coupling constants.

$$J_{Sn\text{-}H} \text{ (trans)} > J_{Sn\text{-}H} \text{ (gem)}$$

The size of ^3J_H for the Z-isomers varies with the extent of the Sn <— O association.



J_H(Hz)	12 - 12.4	13.3	13.5
δ_{Sn}	-156	+33	-

Figure 4

Although these differences in J are small they tend to support the view that intramolecular association between the tin and oxygen results in a reduction in the H-H coupling constant. This effect has been documented by Gielen et al.[1], when reacting triphenyltin hydride with 17-α-ethynyl-4-estrene-17-ol. On reacting the resultant Z-17-[2-(triphenylstannyl)vinyl]-4-estren-17-ol with iodine the Z-17-[(diphenyliodostannyl)vinyl]-4-estren-17-ol obtained shows a change in ^3J_H from 13 to 11 Hz. The iodine is more electronegative than a phenyl group and encourages intramolecular association.

Further evidence of Sn <— 0 association was obtained from the ^{119}Sn NMR spectra where values of δ -156 and +33 for the OH and the silyloxy compound respectively indicate a tin atom in a different environment. The shift of δ -156 is reasonable for a five co-ordinate compound.[6,7,8]

As with the tributylstannylvinyl adducts obtained in the previous chapter, the ^{13}C NMR spectra of these triphenylstannylvinyl adducts cannot generally be used to identify the Z and E isomers. However, the same observations made in the previous chapter clearly apply here. We note that $^1J_{Sn\text{-}C4}$ tends to be greater than

$^{1}J_{Sn\text{-}Cortho}$, and $^{3}J_{Sn\text{-}C2}$ is much larger than $^{2}J_{Sn\text{-}C3}$. These observations been reported previously by Kuivila and other workers.[11,12,13]

4.3 CONCLUSION:

Reactions of Tributyl- and Triphenyl-tin Hydrides

We have established that the reaction of R_3SnH (where R = Ph or Bu), with alkynes gives initially the Z-adducts which then isomerise to the E adducts. The process can be rationalised by activation energy diagram below (Figure 5). The organotin radical attacks the alkyne to give cis and trans vinyltin radicals in equilibrium, but attack by R_3SnH at the trans radical is faster because it is less sterically hindered, resulting in a lower activation energy for the formation of the Z-isomer, hence the Z-isomer is the product of kinetic control. The cis vinyltin radical is more hindered to attack by R_3SnH, thus formation of the E-adduct has a higher activation energy, but this isomer is less sterically crowded, and thus more stable than the Z-adduct hence it is the major product of thermodynamic control.

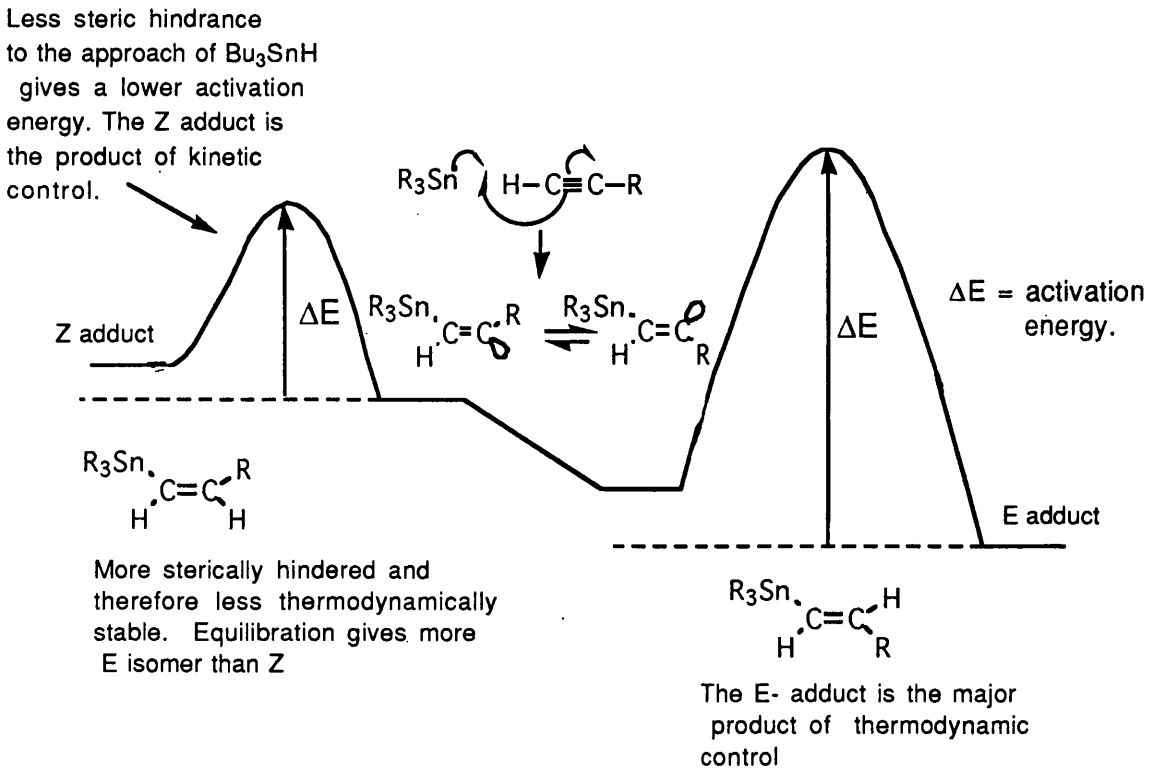


Figure 5

The Z-isomer is stabilised by the formation of Sn —> O association to give five co-ordinate tin as evidenced by the high δ ^{119}Sn NMR chemical shift. The Sn —> O association is weaker in Bu_3Sn adducts than in the Ph_3Sn adducts.

The α-adduct was only obtained when the OH group was present and then only with Bu_3SnH and not with Ph_3SnH. We suspect that co-ordination of the HO to the tin radical steers it to attack the α-carbon. An equivalent reaction is not observed with Ph_3SnH because it is too bulky and thus sterically hindered for attack to occur at the α-carbon. Further evidence of this appears when we discuss the Bu_2SnHCl additions.

4.4 EXPERIMENTAL

Two methods were used in the following experiments; the first involved AIBN initiation at 80°C as discussed previously, and the second involved benzoyl peroxide (0.772 mmol) initiation at 25°C[1] in ether and the reaction being stirred for 24 h. This gave the Z adduct exclusively in 90% yield

4.4.1 Preparation of (Z)-4-triphenylstannyl-2-methyl -3-buten-2-ol

A mixture of 2-methyl-3-butyn-2-ol (0.65 g, 7.72 mmol). Ph_3SnH (2.71 g, 7.72 mmol) and AIBN (0.772 mmol) in toluene (25 cm^3) was heated at 80°C for 3 hours. The product was obtained as a solid and was recrystallised from ethanol. The Z- and E-isomers were obtained in a 2:1 ratio

Yield, 2.86 g, 85%; M. p. 98 - 105°C

Found: C, 63.50; H, 5.45,

Calc. for $C_{23}H_{24}OSn$; C 63.49; H, 5.56%

M.S. m/z: 434; 358; 340; 197

Z-isomer

δ_H ($CDCl_3$); 1.23 (6H, s, $2CH_3$), 6.17 (1H, d, ^3J_H 12.4 Hz, $^2J^{117}_{Sn}$ 90.3 Hz, $^2J^{119}_{Sn}$ 94.5 Hz; H-4); 6.18 (1H, d, ^3J 12.4 Hz, $^3J^{117}_{Sn}$ 175.5 Hz, $^3J^{119}_{Sn}$ 183.7 Hz; H-3).

δ_C ($CDCl_3$); 30.34 (C-1); 128.36 ($^3J^{117/119}_{Sn}$ 50.5 Hz; C-meta); 138.81 ($^2J^{117/119}_{Sn}$ 37.1 Hz; C-ortho); 142.18 ($^1J^{117}_{Sn}$ 519.3 Hz;$^1J^{119}_{Sn}$ 543.4 Hz; C-ipso); 128.26 (C-para). 73.16 ($^3J^{117/119}_{Sn}$ 31.0 Hz; C-2); 121.13 (J^{117}_{Sn} 553.4 Hz; J^{119}_{Sn}539.0 Hz; C-4); 155.54 (C-3).

$\delta^{119}Sn$ ($CDCl_3$) -156

E-isomer

δ_H 6.45 (1H, d, ^3J_H 19.9 Hz, $^3J^{117}Sn$ 77.1 Hz, $^3J^{119}Sn$ 80.7 Hz; H-4); 6.30 (1H, d, ^3J_H 19.9 Hz, $^2J^{117}Sn$ 84.3 Hz, $^2J^{119}Sn$ 88.2 Hz; H-3).

δ_C 72.78 ($^3J_{Sn}$ 30.1 Hz; C-2); 119.06 ($J^{117}Sn$ 499.7 Hz, $J^{119}Sn$ 522.9 Hz; C-4); 154.76 (C-3).

$\delta^{119}Sn$ -135.

4.4.2 Silylation of (Z)-4-triphenylstannyl-2-methyl-3-buten-2-ol

(Z)-4-Triphenylstannyl-2-methyl-3-buten-2-ol (0.16 g, 0.36 mmoles) was refluxed in dichloromethane (40 cm^3) with 1-(trimethylsilyl)imidazole under nitrogen for 30 minutes. The solvent was removed in vacuo and the resulting orange crystals purified by flash column chromatography using ethyl acetate (40%) and hexane as the eluant.

The orange crystals were recrystallised from absolute alcohol.

Yield, 170 mg, (94%). M.p. 80 - 85°C.

Found: C, 61.40, H, 6.45,

Required for: $C_{26}H_{32}OSnSi$; C, 61.43; H, 6.54%

δ_H ($CDCl_3$); 0.080 (9H, s, $Si(CH_3)_3$); 1.44 (6H, s, $2CH_3$); 5.83 (1H, d, ^3J_H13.3 Hz, $^2J^{117}Sn$ 76.5 Hz, $^2J^{119}Sn$ 80.1 Hz; H-4); 6.85 (1H, d, ^3J_H13.3 Hz, $^3J^{117}Sn$ 177.4 Hz, $^3J^{119}Sn$ 185.7

Hz; H-3); 7.30 - 7.60 (15H, m, aromatic).

δ_C 2.77 ($SiCH_3$); 30.63 (C-1); 76.00 ($^3J^{117/119}Sn$ 30.2 Hz; C-2); 117.36 ($J^{117}Sn$ 539.18 Hz, $J^{119}Sn$ 564.61 Hz; C-4); 128.10 ($^3J^{117/119}Sn$ 43.7 Hz; C-meta); 128.34 (C-para); 136.98 ($^2J^{117/119}Sn$ 37.0 Hz; C-ortho); 142.14 ($J^{117}Sn$ 515.8 Hz; $J^{119}Sn$ 540.3 Hz; C-ipso).

4.4.3 Preparation of (Z/E)-4-triphenylstannyl-2-methyl-2-(trimethylsilyloxy)-3-butene

The 2-methyl-2-(trimethylsilyloxy)-3-butyne (0.25 g, 1.156 mmol), Ph_3SnH (0.41 g, 1.156 mmol) and AIBN (0.1156 mmol), in toluene was heated at 80°C for 2 hours.

This reaction gave the E and Z isomer in 1:1 ratio.

E - isomer

Yield, 60 mg, (73%) M.p. 90°C - 105°C.

δ_H ($CDCl_3$) 1.34 (6H, s, $2CH_3$), 1.56 (1H, s, OH); 6.43 (1H, d, ^3J_H 18.9 Hz, $^3J^{117}Sn$ 86.4 Hz, $^3J^{119}Sn$ 90.4 Hz; H-3); 6.38 (1H, d, ^3J_H 18.38 Hz, $^3J^{117}Sn$ 82.2 Hz, $^2J^{119}Sn$ 86.0 Hz; H-4).

δ_C 29.45 (C-1); 72.77 ($^3J^{117/119}Sn$ 29.4 Hz; C-2); 119.1 ($J^{117}Sn$ 497.3 Hz, $J^{119}Sn$ 503.5 Hz; C-4); 128.54 ($^3J^{117/119}Sn$ 51.1 Hz; C-meta); 129.03 ($^4J^{117/119}Sn$ 11.1 Hz; C-para); 137.01($^2J^{117/119}Sn$ 36.8 Hz; C-ortho); 138.13 ($J^{117}Sn$ 501.6 Hz, $J^{119}Sn$ 524.9 Hz; C-ipso).

4.4.4 Preparation of (Z/E)-triphenylstannyl-2,2 -dimethyl-4-butene

The reaction was carried out at 80°C, with 3,3-dimethyl-1-butyne (0.25 g, 3.043 mmol), Ph_3SnH (1.07 g, 3.04 mmol) AIBN (0.304 mmol) in toluene for 3 hours and separated by flash column chromatography using ethyl acetate (35%)/hexane.

This gave a 1:10 mixture of Z- and E-isomers.

Yield, 1.05 g, (80%) b.p 100 - 103°C/0.03 mmHg

Found: C, 66.35; H, 6.01

Required for: $C_{24}H_{26}Sn$: C, 66.35; H, 6.05%.

E-isomer

δ_H ($CDCl_3$) 0.97 (9H, s, $3CH_3$); 6.30 (1H, d, ^3J_H 19.0 Hz, $^3J^{117}_{Sn}$ 83.6 Hz, $^3J^{119}_{Sn}$ 87.5 Hz; H-3); 6.09 (1H, d, ^3J_H 19.1 Hz, $^2J^{117}_{Sn}$ 95.7 Hz, $^2J^{119}_{Sn}$ 100.0 Hz; H-4); 7.37 - 7.56 (15H, m, aromatics).

δ_C 30.56 (C-2); 29.13 (CH_3), 122.44 ($^1J^{117}_{Sn}$ 516.2 Hz, $^1J^{119}_{Sn}$ 540.2 Hz; C-4); 128.5 ($^1J^{117/119}_{Sn}$ 50.1 Hz; C-meta); 128.91 ($^4J^{117/119}_{Sn}$ 10.9 Hz; C-para); 137.10 ($^2J^{117/119}_{Sn}$ 36.5 Hz; C -ortho); 168.68 (C-3).

Z-isomer

δ_H 0.97 (9H, s, $3CH_3$), 6.93 (1H, d, ^3J_H 13.5 Hz, $^3J^{117}_{Sn}$ 183.4 Hz, $^3J^{119}_{Sn}$ 194.0 Hz; H-3); 5.91 (1H, d, ^4J_H 13.5, $^2J^{117}_{Sn}$ 76.9 Hz $^2J^{119}_{Sn}$ 80.0 Hz; H-4).

4.4.5 Preparation of (Z)-17α[2- (triphenylstannyl vinyl)]estradiol

The above compound was synthesised at 25°C in ether using the following mole ratio of reactants;

Ethynylestradiol (151 mg, 0.51 mmol), Ph_3SnH (0.1776 g, 0.51 mmol) BPO (40 mg, 0.165 mmol).

The resultant vinyl adduct was purified by flash column chromatography using ethyl acetate (35%) hexane as eluant and recrystallised from absolute ethanol.

Yield: 327 mg, (60%) M.p. 146 - 148°C.

Found: C, 71.25; H, 5.85%

Required for: $C_{39}H_{39}O_2Sn$: C, 71.14; H, 5.97%

δ_H ($CDCl_3$,) 0.85 - 2.45 (19H, m, steroid envelope); 6.18 (1H, d, ^3J_H 12.0 Hz, $^2J^{117}_{Sn}$ 91.2 Hz, $^2J^{119}_{Sn}$ 95.4 Hz; H-20); 6.86 (1H, d, ^3J_H 12.0 Hz, $^2J^{117}_{Sn}$ 203.6 Hz; $^3J^{119}_{Sn}$ 213.1 Hz; H-19).

δ_C 85.89 ($^3J_{Sn}$ 29.4 Hz; C-17), 126.58 (C-20); 155.86 (C-19).

4.5 REFERENCES

1. Pan, H., Willem, R., Meunier-Piret, J. and Gielen, M., Organometallics, **9**, 2199 (1990).

2. Ensley, H. E., Buescher, R. R. and Lee, K., J. Org. Chem., **47**, 404 (1982).

3. Leusink, A. J., 'Hydrostannation', Schotanus and Jens, Utrecht (1966).

4. Chen, S-M. L., Schaub, R. E. and Gradzinkas, C. V., J. Org. Chem., **43**, 3450 (1978).

5. Skotnicki, J. S., Schaub, R. E., Bernady, K. F., Siuta, G. J., Poletto, J. F., Weiss, M. J. and Dezoy, F., J. Med. Chem., **20**, 1551 (1977).

6. Holecek, J., Nadvornik, M., Handlir, K. and Lycka, A., J. Organomet. Chem. **241** 177 (1983)

7. Holecek, J., Nadvornik, M., Handlir, K. and Lycka, A., J. Organomet. Chem., **275** 43 (1984)

8. Otera, J., J. Organomet. Chem. **221,** 57 (1981)

9. Brouwer, H. and Stothers, J. B. Can. J. Chem., **50**, 1361 (1972).

10. van der Kerk, G. J. M. and Noltes, J. G., J. Appl. Chem., **9**, 107

(1959).

11. Seebach, D., and Meyer, N., Chem. Ber. **113**, 1290 (1980).

12. Kuivila, H. G., Considine, J. L., Nyrott, R. J. and Sarma, R. H., J. Organomet. Chem. **55**, C11 (1973).

13. Jung, M. E. and Light, L. A., J. Org. Chem., **23**, 3851 (1982).

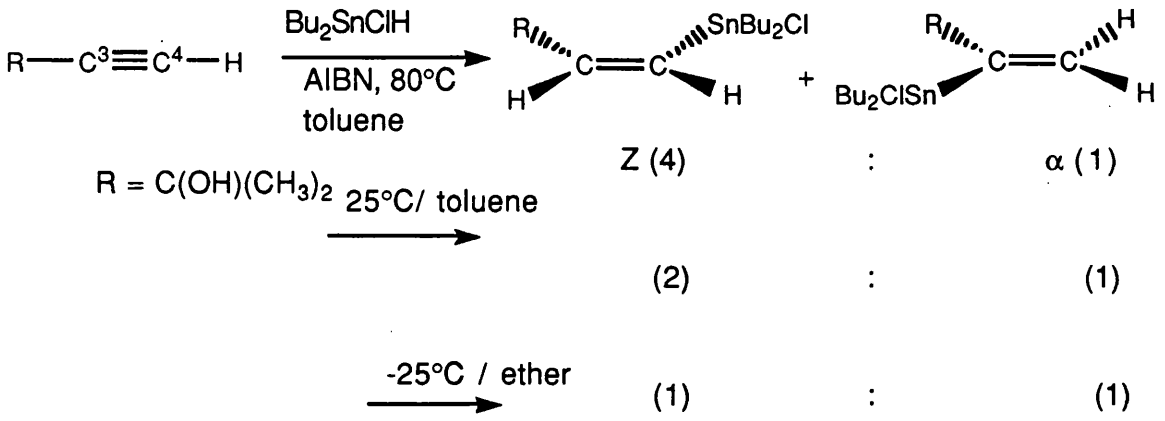
5.0 Reactions of Dibutyltin Chloride Hydride

5.1 RESULTS

Tributyl- and triphenyl-tin hydrides are both useful hydrostannating agents used extensively in synthetic organic chemistry.[1,2] The reaction of Bu_3SnH with alkynes is not stereospecific giving the Z-, E- and α-adducts depending on the alkyne, the temperature and the duration of the reaction; our results with 2-methyl-3-butyn-2-ol provide a typical example. The reaction of triphenyltin hydride with this alkynol can be made stereospecific if it is carried out at room temperature with dibenzoyl peroxide as radical initiator, when only the Z-isomer is obtained. This is presumably due to intramolecular association between the Sn moiety and the C-2 oxygen.

We have developed dibutyltin chloride hydride as an alternative to Bu_3SnH, because its tin atom is more electropositive and this should encourage intramolecular association between the tin moiety and the C-2 oxygen, leading presumably to increased stereoselectivity. To this end Bu_2SnHCl was reacted with the following alkynes.

5.1.1 2-Methyl-3-butyn-2-ol



Scheme 5.1.1.a

The reaction of dibutyltin chloride hydride with 2-methyl-3-butyn-2-ol was carried out at 80°C in toluene with AIBN initiator. Tlc showed that the reaction was complete in about 3 hours and the adduct was isolated by flash column chromatography as a colourless oil in yields of 60-70% (Scheme 5.1.1.a).

Proton NMR spectroscopy showed that two products were present in a ratio of 4:1. The principal isomer showed the presence of two olefinic doublets with H-H and Sn-H couplings which, on the basis of the data given for the equivalent tributyltin hydride adduct, identifies this as the Z-isomer.[3,4]

δ_H 6.08 (1H, d, ^3J_H 11.7 Hz, $^2J^{117}_{Sn}$ 92.8 Hz, $^2J^{119}_{Sn}$ 97.2 Hz; H-4);
6.32 (1H, d, ^3J_H 11.7 Hz, $^3J^{117}_{Sn}$ 204.0 Hz, $^3J^{119}_{Sn}$ 212.2 Hz; H-3).

δ_C 30.04 (C-1); 75.59 ($^3J_{Sn}$ 39.0 Hz, C-2); 128.91 (J^{117}_{Sn} 561.5 Hz; J^{119}_{Sn} 586.7 Hz; C-4) 150.51 (C-3).

It will be noted that, as with the Bu_3SnH adducts, no ^2J couplings could be observed to the C-3 olefinic carbon.

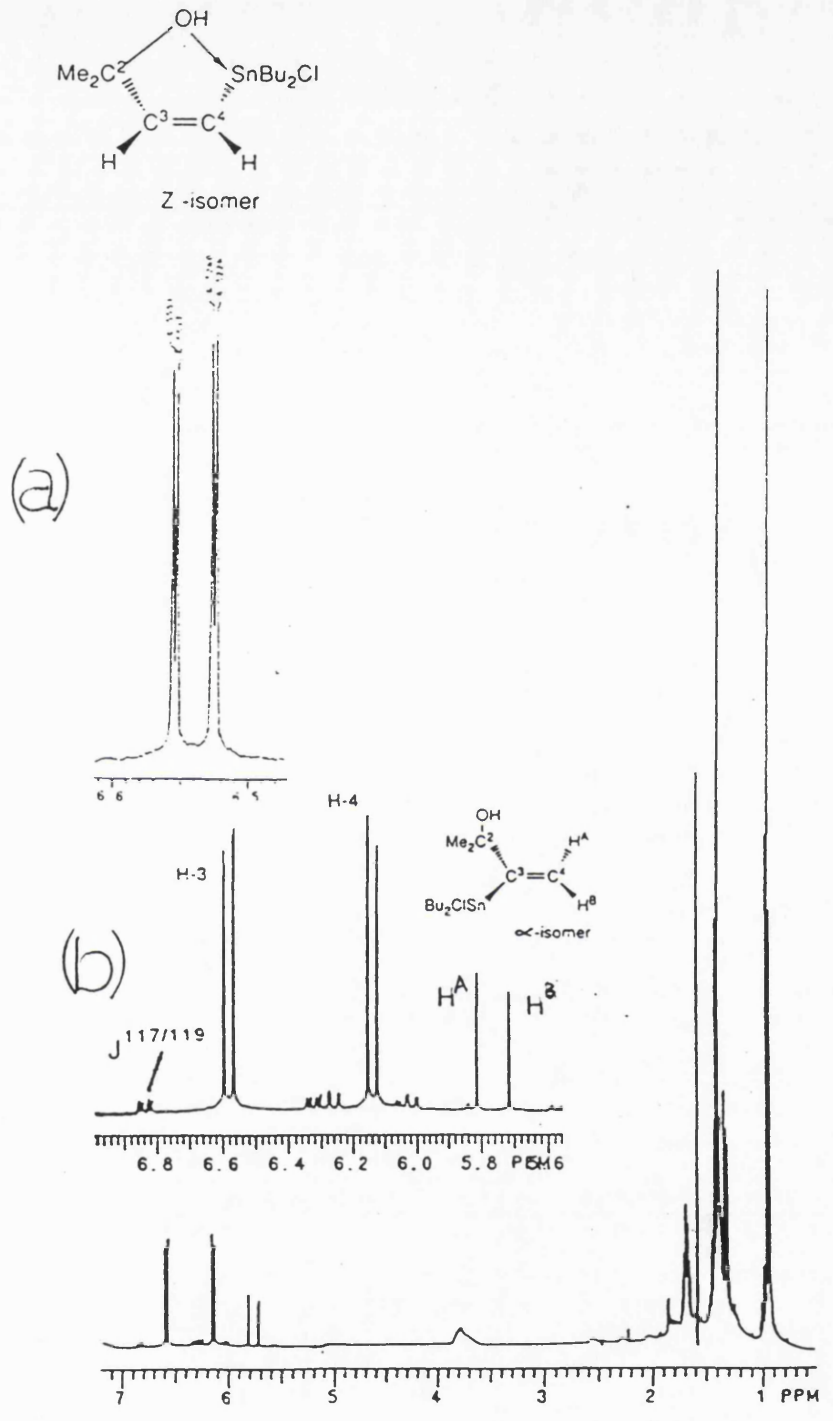


Figure 1 400 MHz ^{1}H NMR spectra of a mixture of (Z)-4- dibutylchloro-stannyl-2-methyl-3-buten -2-ol and 3-dibutylchloro-stannyl-2-methyl-3-buten -2-ol, showing, inset (a) ^{4}J(HO~CH) coupling in the Z-isomer and (b) $^{117/119}Sn$ coupling in the Z- and α -isomer.

The second isomer showed in the ^1H NMR spectrum two singlets at:

δ_H 5.72 (1H, s, $^3J^{117}_{Sn}$ 97.5 Hz, $^3J^{119}_{Sn}$ 102.0 Hz; H-4^B); 5.81 (1H, s, $^3J^{117}_{Sn}$ 192.9 Hz, $^3J^{119}_{Sn}$ 201.8 Hz; H-4^A).

On the basis of the data obtained for the Bu_3SnH adduct, this would not be acceptable for the E-adduct which should show proton - proton coupling of ca. 19.0 Hz. The values of the tin coupling constants suggest that there is one proton olefinically cis and one trans to the tin, but none geminal, ie that this is the alpha adduct as shown in the scheme above. The peak at δ 5.72 with the smaller value of J_{Sn} is due to the proton cis to the tin and the other at δ 6.32 to the proton trans to the tin.

The ^{13}C NMR spectrum showed olefinic signals at δ 122.0 and 166.0. We assigned these to the C-4 and C-3 carbons respectively, on the basis of the data obtained for the first isomer. The significance of the formation of this α-adduct is discussed later.

Previous work by Bouyssieres et al.[5a,5b] implies that the addition of the chloride hydride will occur at room temperature without induced initiation. The reaction was repeated at room temperature with no initiator and was complete in 2 - 3 hours and gave the Z- and α-isomers now in a 2:1 ratio.

The proton resonance spectrum of the Z-isomer (Figure 1) was better resolved than previously and now showed a further smaller doublet splitting of 1.4 Hz on H-3. No such coupling was seen for H-4. When D_20 was added to the sample, this doublet coupling was lost at the same spectrum resolution (Figure 2). We conclude that it

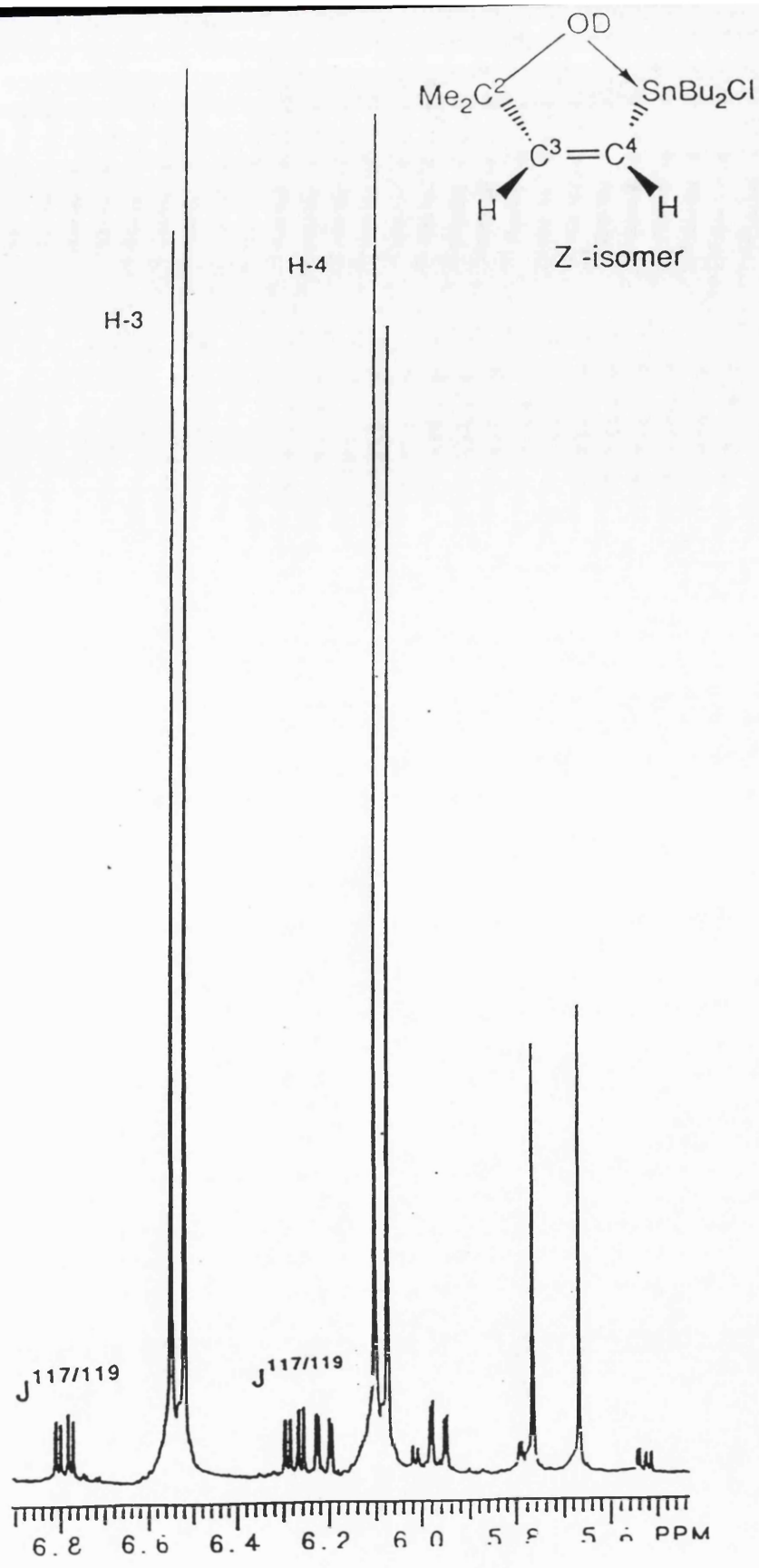


Figure 2 Partial 400 MHz ^{1}H NMR spectrum of a mixture of (Z)-4-dibutyl-chlorostannyl-2-methyl-3-buten -2-ol and 3-dibutylchlorostannyl-2-methyl-3-buten -2-ol after D_2O addition. The ^{4}J (HO~CH) coupling in the Z - isomer has completely disappeared.

represents coupling by an exchangeable proton, ie that of the OH group. This will be discussed in more detail later on.

As this reaction was taking place at room temperature with no induced initiation, it appeared that it might not be a radical chain process. However, when 2,6-di-t-butyl-4-methylphenol was added after 20 minutes to a reaction which was being monitored by ^1H NMR spectroscopy, the reaction immediately stopped and no formation of either the Z or α isomers took place during 2 hours. Both isomers are therefore produced in a free radical chain reaction. The formation of the α-isomer has been discussed previously with acetylenes carrying electron withdrawing groups,[6] but these reactions were thought to be polar rather than free radical processes.

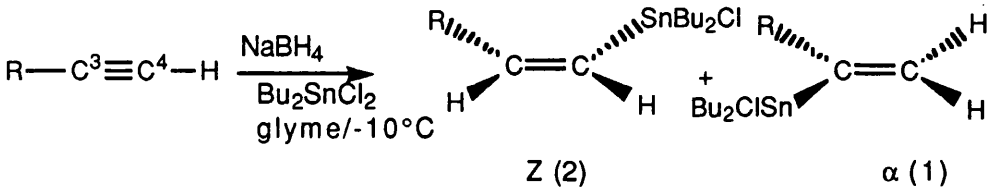
As the reactions could be carried out at room temperature it was simple to monitor the formation and reaction of the chloride hydride by ^1H NMR spectroscopy. When the dichloride and dihydride (δ_H 4.58) were mixed (C_6D_6), a signal for the chlorohydride at δ 7.42 could immediately be detected, and the intensity of the signal increased for 75 minutes as the reaction progressed.

If the acetylene was then added, the olefinic signals for the adducts were immediately apparent. After 1.5 - 2 hours the addition reaction was virtually complete and showed the presence of the Z and α adducts in a ratio of 2:1.

In the previous section we saw that sodium borohydride will reduce dibutyltin dichloride in glyme to the hydride chloride at -10°C and here we have shown that the hydride chloride will add to acetylene without an added initiator, at room temperature.

These two reactions can be combined into a one-pot synthetic method for the hydrostannation of alkynes (Scheme 5.1.1.b), to give

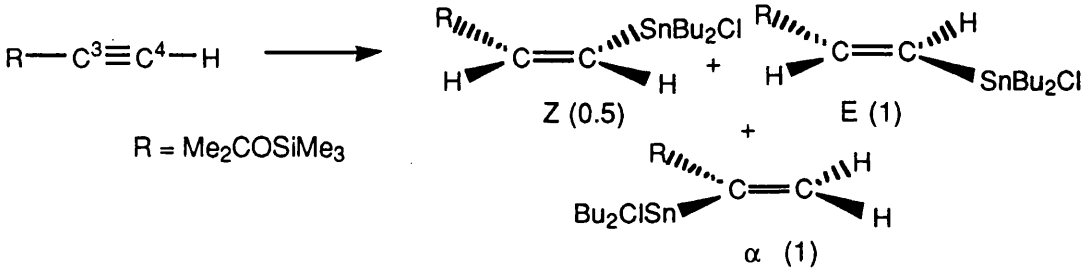
the α and Z-isomers in a yield of 70-75%. This method has the advantage that it eliminates the preparation of Bu_2SnH_2 and the workup involves a simple ether extraction to remove the vinyl adducts.



Scheme 5.1.1.b

5.1.2 2-Methyl-3-butyne-2-(trimethylsilyl)ether

As in the previous reaction, (Scheme 5.1.1.a) the OH group appeared to be reacting with the Bu_2SnCl group, affecting the orientation of the addition, the relative stabilities of the adducts, and the NMR spectrum,[7] we studied the reaction of the silyl ether under similar conditions. The silyloxy group would be expected to be a weaker ligand for the Bu_2SnCl group and any differences between the behaviour of the silyloxy compound and the OH compound should be informative.



Scheme 5.1.2

The reaction of the chloride hydride with the acetylene occurs readily at room temperature without an external initiator and the products were isolated by flash column chromatography, giving a colourless liquid in a 65 - 70% yield. ^1H and ^{13}C NMR spectroscopy

showed signals in the olefinic region corresponding to the Z-, E- and α–isomers (Scheme 5.1.2), in a ratio of 0.5:1:0.5. The spectroscopic characteristics were as followed:

Z-isomer

δ_H 5.98 (1H, d, ^3J_H 12.2 Hz, $^2J^{117}Sn$ 74.8 Hz, $^2J^{119}Sn$ 78.4 Hz; H-4); 6.49 (1H, d,^3J_H 12.2 Hz, $^3J^{117}Sn$ 194.0 Hz, $^3J^{119}Sn$ 203.0 Hz; H-3).

δ_C 76.86 ($^2J_{Sn}$ 28.4 Hz; C-2); 126.06 ($J^{117}Sn$ 533.0 Hz, $J^{119}Sn$ 558.0 Hz; C-4); 152.38 (C-3);

E-isomer

δ_H 6.11 (1H, d, ^3J_H 18.9 Hz, $^2J^{117}Sn$ 75.9 Hz, $^2J^{119}Sn$ 79.5 Hz; H-4); 6.27 (1H, d, ^3J_H 18.9 Hz, $^3J^{117}Sn$ 95.4 Hz, $^3J^{119}Sn$ 99.8 Hz; H-3).

δ_C 76.85 ($^3J_{Sn}$ 28.4 Hz; C-2); 122.86 ($^1J^{117}Sn$ 534.0 Hz, $^1J^{119}Sn$ 562.0 Hz; C-4), 150.8 (C-3).

On the basis of the results obtained with the adduct of Bu_3SnH, this can confidently be identified as the E-isomer.[8]

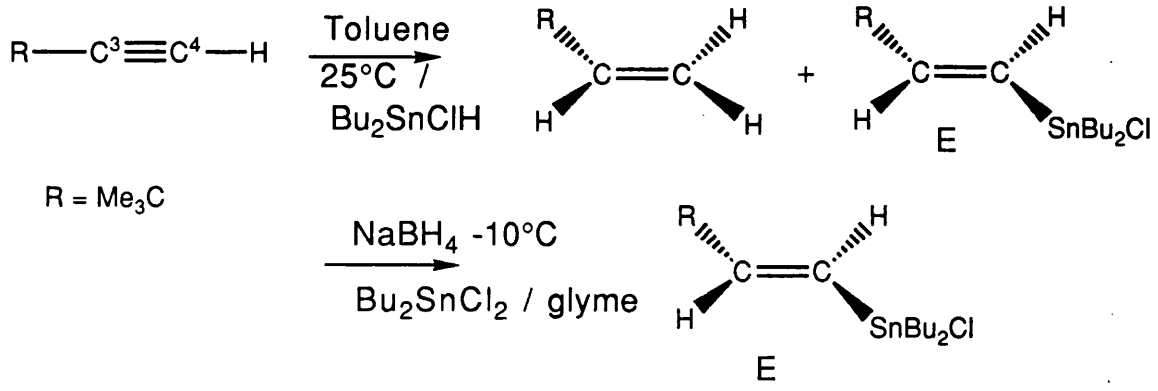
α-Isomer

δ_H 5.65 (1H, s, $^3J^{117}Sn$ 98.2 Hz, $^3J^{119}Sn$ 102.8; H-4_A); 5.71 (1H, s, $^3J^{117}Sn$ 192.9 Hz, $^3J^{119}Sn$ 201.8; H-4_B).

δ_C 121.71 ($^2J_{Sn}$ 16.1 Hz; C-4); 167.70 ($^1J^{117}Sn$ 538.2 Hz, $^1J^{119}Sn$ 563.Hz; C-3), 81.79 ($^2J_{Sn}$ 28.4 Hz; C-2)

5.1.3 3,3-Dimethylbut-1-yne

The behaviour of this hydrocarbon alkyne should highlight the ligating behaviour of the oxygen substituent in the two previous alkynes.



Scheme 5.1.3

The addition of the chloride hydride occurred at room temperature, with no added initiator (Scheme 5.1.3). The principal product was the E-adduct which showed the following NMR spectrum.

δ_H 5.89 (1H, d, ^3J_H 19.2 Hz, $^3J^{117}_{Sn}$ 113.5 Hz, $^3J^{119}_{Sn}$ 118.6 Hz; H -3); 6.18 (1H, d, ^3J_H 19.2 Hz, $^2J^{117}_{Sn}$ 90.2 Hz, $^2J^{119}_{Sn}$ 94.6 Hz; H -4).

δ_C 120.63 ($^1J^{117}_{Sn}$ 447.4 Hz, $^1J^{119}_{Sn}$ 467.7 Hz; C-4); 162.34 (C-3).

The proton NMR spectrum of the crude material showed a second product in ca. 10% yield with olefinic signals, but no detectable tin satellites. The olefinic region showed three doublets

of doublets and we identified the compound as 3,3-dimethylbut-1-ene.

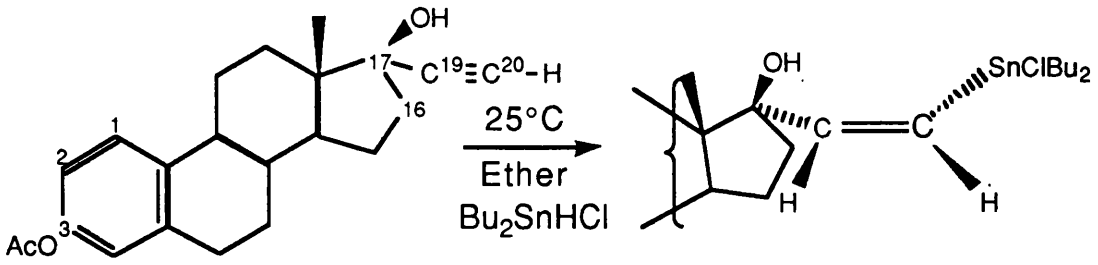
δ_H 5.80 (1H, dd, ^3J 17.5 Hz, ^3J 10.6 Hz; H-3), 4.70 (1H, dd, ^3J 10.6 Hz, ^2J_H 1.5 Hz; H-4); 4.85 (1H, dd, ^3J 17.5 Hz, ^2J 1.5 Hz; H-4_A).

Values in the literature are:[9]

δ_H 5.85 (1H, dd, ^3J 18.0 Hz, ^3J 10.6 Hz; H-3).4.90 (1H, dd, ^3J 10.6 Hz, ^2J_H 1.5 Hz; H-4); 4.85 (1H, dd, ^3J_H 18.0 Hz, ^2J_H 1.5 Hz; H-4_A);

We were not able to isolate this product because of its low boiling point. The same reaction was carried out at -10 to -15°C by generating the chloride hydride <u>in situ</u> in 1,2-dimethoxyethane from dibutyltin dichloride and sodium borohydride.[10] The proton NMR spectrum showed that the E-isomer was formed exclusively.

5.1.4 17α-Ethynylestradiol-3-acetate



Scheme 5.1.4

No reaction occurred between 17α-ethynylestradiol and dibutyltin chloride hydride at room temperature, but after the phenolic OH group was acetylated, hydrostannation took place over 2.5 hours. The product was isolated by flash column chromatography,

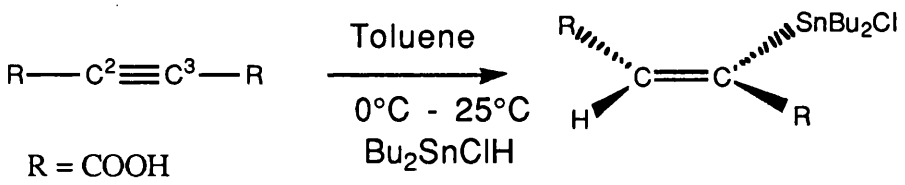
giving the Z-adduct in 60-65% yield, and no E- or α-adduct was detected (Scheme 5.1.4). The NMR spectra in the olefinic region showed the following characteristic signals:

δ_H 6.73 (1H, d, ^4J_H 1.4 Hz, ^3J_H 12.1 Hz, $^3J^{117}_{Sn}$ 201.5 Hz, $^3J^{119}_{Sn}$ 206.1 Hz; H-19); 6.17 (1H, d, ^3J_H 12.0 Hz; $^2J^{117}_{Sn}$ 92.2 Hz, $^2J^{119}_{Sn}$ 96.5 Hz; H-20).

δ_C 88.06 ($^3J_{Sn}$ 25.6 Hz; C-17); 128.91 (C-20); 154.00 (C-19).

5.1.5 Acetylene Dicarboxylic Acid.

Tributyltin hydride is known to react with the above compound at room temperature to give exclusively the Z-isomer of the bis-tributyltin ester of 2-tributylstannyl fumaric acid.[11]



Scheme 5.1.5

The addition of dibutyltin chloride hydride to acetylene dicarboxylic acid was carried out at 0°C and at 25°C (Scheme 5.1.5). Flash column chromatography gave the adduct as a white crystalline solid in 60-70% yield with the following NMR characteristics.

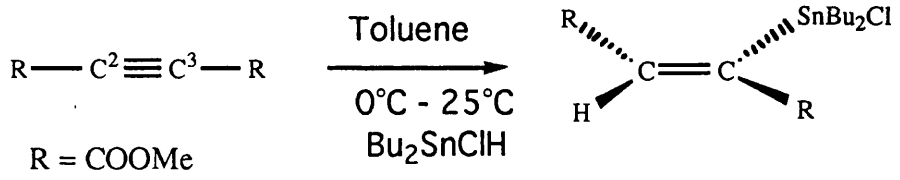
δ_H 6.68 (1H, s, $^3J^{117}_{Sn}$ 156.2 Hz, $^3J^{119}_{Sn}$ 163.5 Hz; H-2).

δ_C 168.64 (J_{Sn} 355.0 Hz; C-3); 130.63 (C-2); 170.52 ($^2J_{Sn}$ 24.9 Hz; C -1); 172.15 ($^3J_{Sn}$12.5 Hz; C-4).

These coupling constants are similar to those of other Z-isomers obtained by ourselves and other workers. Under our conditions the reaction gave the diacid rather than the ditin ester

5.1.6 Dimethyl Acetylenedicarboxylate

Similarly tributyltin hydride reacts with dimethyl acetylene carboxylate to give the Z- and E-adducts in 20:1 ratio at 0°C.[11,12]



Scheme 5.1.6

Again the reaction with Bu_2SnClH was carried out at 0°C and 25°C and the Z-isomer was isolated in 70-75% yield (Scheme 5.1.6) by flash column chromatography, and showed the following NMR characteristics:

δ_H 6.79 (1H, s, $^3J^{117}_{Sn}$ 117.6 Hz, $^3J^{119}_{Sn}$ 123.0 Hz; H-2).

δ_C 52.40 ($^5J_{Sn}$ 178.8 Hz; OCH_3); 60.30 ($^4J_{Sn}$ 180.5 Hz; OCH_3);129.44 (C-2); 169.05 ($^1J^{117}_{Sn}$ 327.5 Hz, $^1J^{119}_{Sn}$ 342.9 Hz; C-3); 170.21 ($^4J_{sn}$ 31.2 Hz; C-1); 172.56 ($^2J_{Sn}$ 14.0 Hz; C-4).

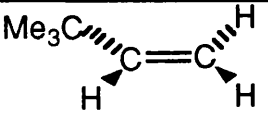
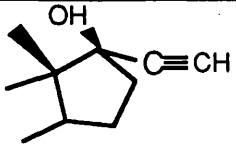
We confirmed this to be the Z-isomer by comparing the coupling constants obtained here with those of our previous Z-isomers and those of other workers.[12]

5.2. DISCUSSION

Hydrostannation of alkynes with dibutyltin chloride hydride has been shown to occur over a wide temperature range (-25°C to 80°C). We have shown that the reaction is a free radical chain process by inhibiting it with 2,6-di-t-butyl-4-methylphenol.

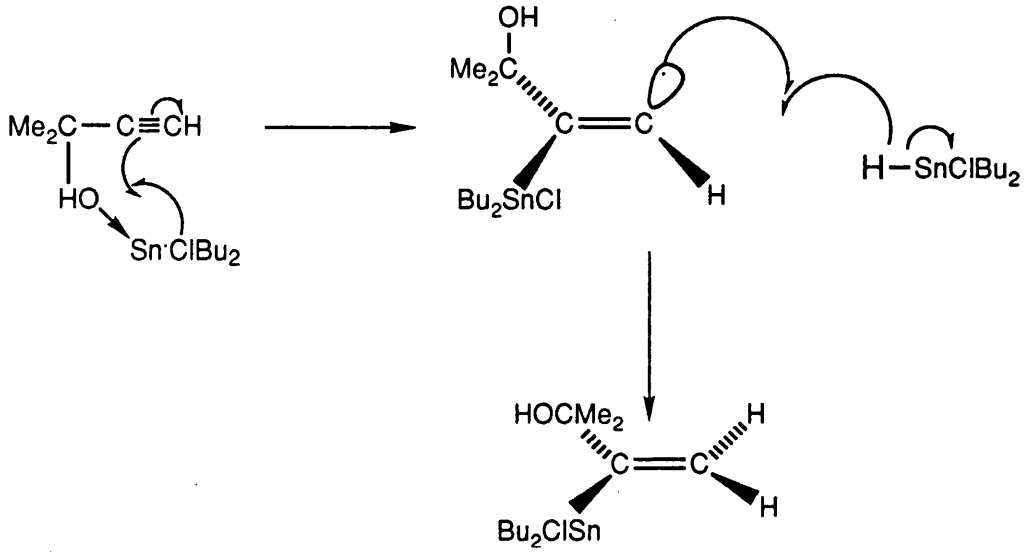
Table 1 below shows the yields of regio and stereo-isomers obtained.

Table 1 Dependence of regio- and stereo-selectivity on reaction conditions.

REACTION CONDITIONS	% Z - ISOMER	% E - ISOMER	% α - ISOMER
$Me_2C(OH)-C\equiv CH$			
80°C/AIBN	80	0	20
25°C	66	0	33
0°C	50	0	50
$Me_2C(OSiMe_3)-C\equiv CH$			
25°C	20	40	40
$Me_2C(CH_3)-C\equiv CH$			
25°C	0	90	 10
			
25°C	100	0	0

5.2.1 Regioselectivity

Hydrostannation of the triple bond involves initial Bu_2SnCl radical attack. In 3,3-dimethyl-1-butyne, this is wholly at the terminal carbon at 20°C, but in 2-methyl-3-butyn-2-ol, 33% of the reaction occurs at the non-terminal carbon to give the α-adduct (Table 1). This suggests that the Sn radical is being steered onto the α-carbon by association with the OH group.



Scheme 5.2.1.a

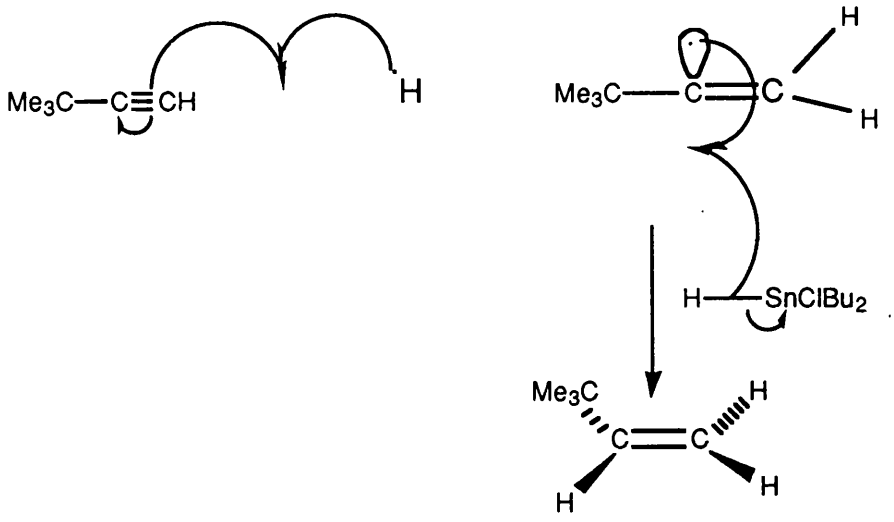
The yield of the α-adduct seems to increase with a decrease in the temperature, suggesting that the reaction has a low activation energy. The Me_3Si0 group would be a weaker ligand for the radical and less effective in directing its approach, so we would expect a smaller proportion of α–adduct. However, this is not the case, and 40% of the reaction goes to form the α-adduct. The reason for this is not clear and we do not have sufficient independent evidence for the ligation of a tin radical. Although many organotin radicals have been observed by ESR spectroscopy in fluid conditions, non-polar

solvents[12, 14] have always been used and there appears to be no ESR evidence for interaction with a hydroxylic solvent.

No α-adduct was observed on reaction with 17α-ethynylestradiol-3-acetate, due presumably to steric hindrance by the large and rigid ring system.

The detection of the formation of 3,3-dimethyl-1-butene from 3,3-dimethyl-1-butyne is very interesting (Scheme 5.2.1.b). As far as we can determine this is the first example of a tin hydride adding the equivalent of H-H rather than of H-Sn. In our discussion of the decomposition of the chloride hydride and carboxylate hydrides to give H_2 and the distannane we were led to conclude that the process involved homolytic attack of a tin radical at a tin centre to displace a hydrogen atom. This hydrogen atom then went on to abstract hydrogen from the Sn-H bond to give H_2.

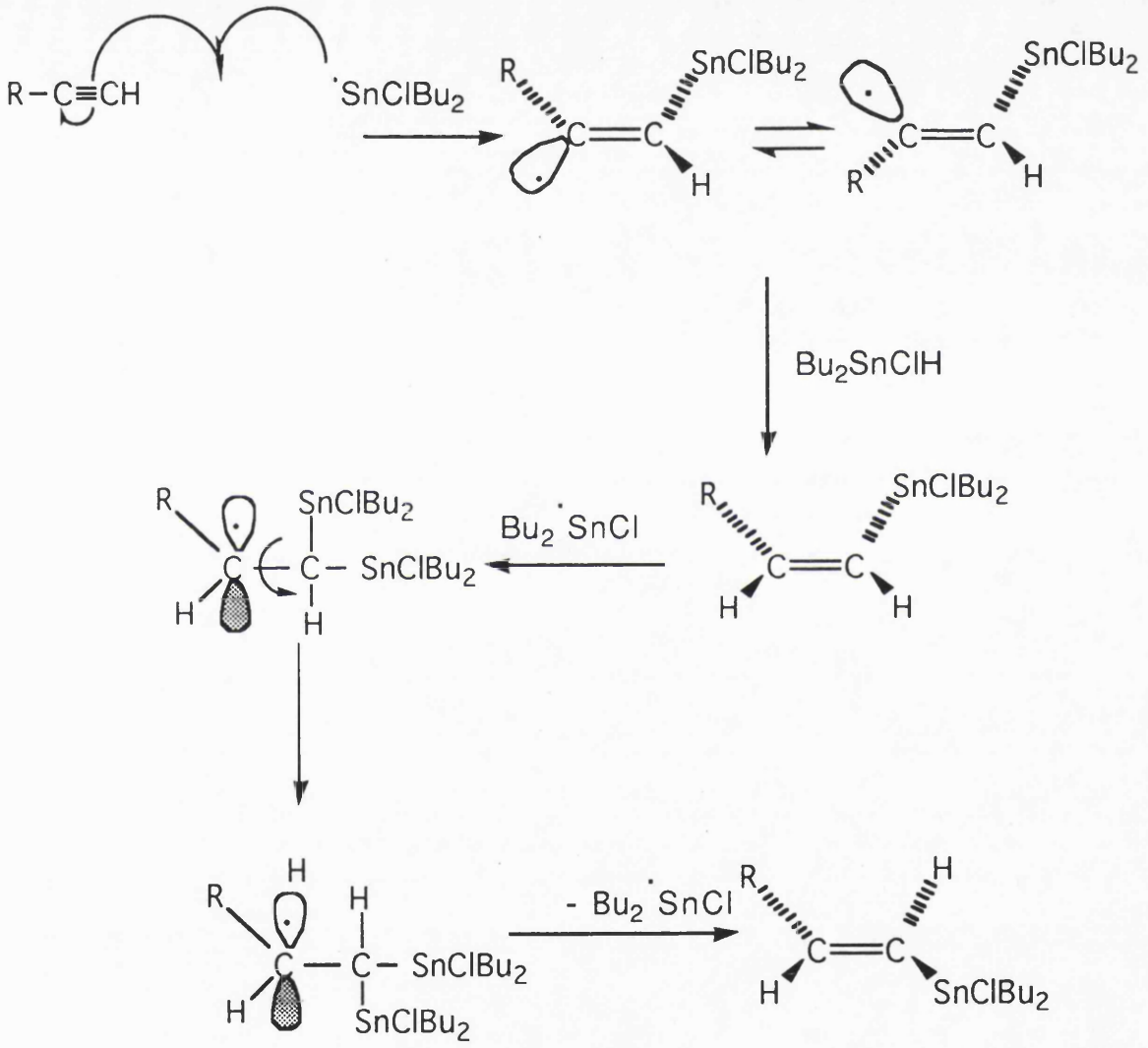
We suggest that the alkyne traps the hydrogen atom and gives an H_2 adduct by the following reactions:



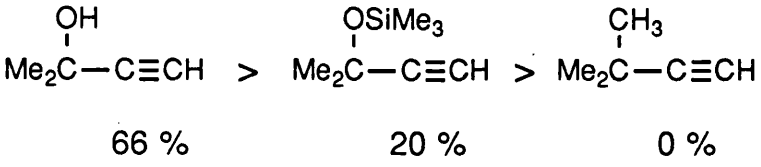
Scheme 5.2.1.b

5.2.2 Stereochemistry

It appears that with Bu_2SnClH as with Bu_3SnH the initial addition occurs to give the Z adduct, for steric reasons. Further attack of Bu_2SnClH can lead to isomerisation to form the E-adduct.



Scheme 5.2.2.a



Dependence of the formation of the Z-isomer on the extent of ligation between the C-2 oxygen and Bu_2SnCl.

Figure 4

Figure 4 shows how, under the same conditions (of 25°C), the yield of the Z-isomer decreases depending on the structure of the alkyne. This could be the result of O-->Sn co-ordination which would be greatest in the OH compound (Figure 5) and absent in 3,3-dimethyl-1-butyne.

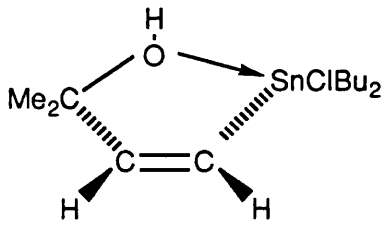
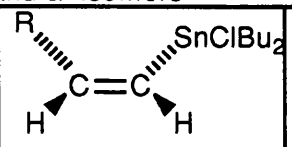
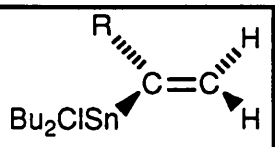
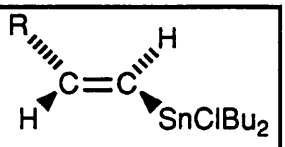


Figure 5

5.2.2.1 NMR Spectroscopic Analysis

Table 2 Range of H-H and Sn-H coupling constants (Hz) for the Z-, E- and α–isomers

			
$^3J_{H-H}$	11.7 - 12.2	----------	19.2
$^2J_{Sn-H}$ (gem)	74.0 - 96.0	----------	90.0 - 94.0
$^3J_{Sn-H}$ (trans)	194.0- 212.0	192.0 - 201.0	
$^3J_{Sn-H}$ (cis)	----------	98.0 - 102.0	113.0 - 118.0
$^4J_{H-OH}$	1.4		

The above tabulation gives the range for H-H, Sn-H and H-OH coupling constants, which enables us to assign the structures of the isomers. As with the Bu_3SnH and Ph_3SnH adducts, the following relationship is evident.

$$^3J_H\ (\underline{trans}) > {}^3J_H\ (\underline{cis}) > {}^2J_H\ (\underline{gem})$$

19.6 11.7-12.2 0 Hz

A similar relationship exists for J_{Sn-H}.

$$^3J_{Sn-H}\ (\underline{trans}) > {}^3J_{Sn-H}\ (\underline{cis}) > {}^2J_{Sn-H}\ (\underline{gem})$$

192 - 212 98 - 118 74 - 96 Hz

These observations are generally true for vinyl proton couplings and vinyl proton metal couplings, and Moore and Happe[15]

have found that in tetravinyltin the gem and cis tin-proton coupling are nearly equal.

As we showed in the reactions of tributyl- and triphenyl-tin hydrides, the coupling constants and chemical shifts in the ^{13}C NMR spectrum of the with Bu_3SnH adducts are not indicative of Z, E or α isomers, but they are similar to those obtained by other workers.[16,17,18]

5.2.2.2 NMR Spectroscopic Evidence for Intramolecular Co-ordination

Intramolecular association in the Z and perhaps the α–isomer might be looked for in the value of the tin chemical shift, which should be more upfield with increasing ligation (Figure 6).[19, 20, 21]

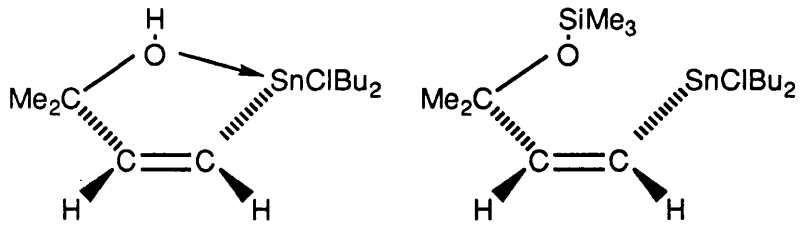


Figure 6

Some further evidence for OH co-ordination, may come from the ^1H NMR spectrum, where a coupling constant of 1.4 Hz is shown between the OH proton, and the α-CH group. This could result from the O-H bond being held in an W–conformation (Figure 7) with respect to the olefinic C-H bond, which would be inducive to coupling. In the absence of co-ordination in the Bu_3SnH adduct, free rotation about the bonds would result in a variety of orientations between these groups and an immeasurably small coupling would result.

There also appears to be a relationship between the value ^3J_H in the OH compound and the possibility of Sn<—0 association. Where the prospect of Sn<—0 association is greatest ^3J_H is 11.6 Hz, as in (Z)-4-dibutylchlorostannyl-2-methyl-2-butene-2-ol, however, on reducing the likelihood of ligation as in (Z)-4-dibutylchlorostannyl-2-methyl-2(trimethylsilyloxy)-3-butene ^3J_H increases to 12.3 Hz.

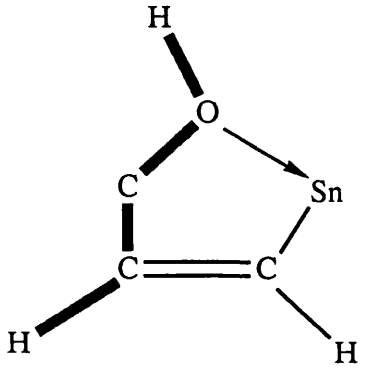


Figure 7

5.2.2.3 17α-Ethynylestradiol-3-acetate

This compound is interesting in the context of hydrostannation, because it provides a route to derivatives labelled with radioactive iodine which are potentially useful in cancer treatment,[20] because it is related to 2-methyl-3-butyn-2-ol which we have already studied, and because Gielen had reported the determination by single crystal X-ray diffraction of the structure of the adduct formed with triphenyltin hydride at room temperature with benzoyl peroxide.[22]

Whereas dibutyltin chloride hydride reacted in the presence of 2-methyl-3-butyn-2-ol to form both the Z- and the α-adduct, the rigid, bulky, ring system in the estradiol sterically prevents the formation of the α-adduct.

Gielen's X-ray structure showed that the tin atom in the adduct was intramolecularly co-ordinated by the OH group. We do not have

any ^{119}Sn NMR spectrum of our equivalent adduct because not enough material was available, which might have given evidence for Sn<—O association, but the fact that we observe $^{4}J_{H\text{-}OH}$ 1.4 Hz does suggest some type of Sn<—O association.

5.3 CONCLUSION

We have successfully hydrostannated alkynes with Bu_2SnClH at room temperatures and below zero without the use of radical initiators such AIBN, and improved the basic reaction by generating the hydride chloride in situ, by the reduction of Bu_2SnCl_2 with $NaBH_4$.

In contrast hydrostannation with Bu_3SnH and Ph_3SnH only gives substantial yields of products when the hydrides are initiated by AIBN or benzoyl peroxide, however even these hydrides can react at low temperatures if a source of radicals is made available, as is the case when triethylborane (Et_3B) is used to initiate the hydrostannation of alkynes with Bu_3SnH and Ph_3SnH at -78°C. The Et_3B is able to induce radical formation at low temperatures by reaction with oxygen.[24]

We believe that the enhanced reactivity of Bu_2SnClH is due to its ability to autogenerate radicals at low temperatures by an electron transfer process as detailed in Section 2.

5.4 EXPERIMENTAL

Dibutyltin chloride hydride was generated from dibutyltin dichloride and dibutyltin dihydride by the disproportionation method. Dibutyltin dichloride was obtained from the Aldrich Chemical Company whilst dibutyltin dihydride was obtained by van der Kerk's method.[3]

5.4.1 Preparation of (Z)-4-dibutylchlorostannyl-2-methyl-3-buten-2-ol and 3-dibutylchlorostannyl-2-methyl-3-buten-2-ol.

The above compounds were obtained by three different methods, firstly at 80°C using AIBN as a radical initiator, secondly conducting the reaction between -25°C and 25°C without radical initiator and finally by the in situ generation of Bu_2SnHCl from $NaBH_4$ and Bu_2SnCl_2.

Method 1.

2-Methyl-3-butyn-2-ol (0.18 g, 2.245 mmol) in toluene (20 cm^3) was added dropwise over 10 minutes to a solution of Bu_2SnCl_2 (0.082 g, 2.245 mmol) and Bu_2SnH_2 (0.56 g, 2.215 mmol) in toluene with AIBN (0.2245 mmol). The reaction mixture was heated at 80°C for 3 hours and followed by tlc with n-hexane-ethyl acetate (6:4 v/v) as eluent.

The solvent was removed in vacuo and the resultant oil was purified by column chromatography using n-hexane-ethyl acetate as eluent.

The proton NMR spectrum of the product showed that the Z- and α– isomers were obtained in a 4:1 ratio:

Yield 0.506g, (96%)

Method 2.

Bu_2SnCl_2 (0.452g, 1.486 mmol) in monoglyme (10 ml) was added dropwise to solution of $NaBH_4$ (0.2896 g, 7.65 mmol) in glyme (40 cm^3) at -10°C to -15°C. To this solution was added 2-methyl-3-butyn-2-ol (0.25 g, 2.97 mmol). The reaction mixture was stirred at -15°C for 30 minutes and then slowly warmed to room temperature.

The solvent was removed in vacuo at 0°C and the product extracted by washing with diethyl ether (3 x 50 cm^3).

Removal of the ether left a colourless oil, proton NMR spectrum of which showed that the Z and α isomers had been obtained in a 2:1 ratio.

Method 3.

Using the same mole ratio of reactants as in Method 1 without AIBN, the reaction was repeated at -25°C to give a 1:1 ratio of Z- and α–isomers and at 25°C to give a 2:1 ratio of Z- and α–isomers. The Z- and α–isomers were separated by flash column chromatography using n-hexane-ethyl acetate (6.5 - 3.5 v/v).

Yield, 0.588 g, (98%)

δ_H ($CDCl_3$) 0.8 - 1.63 (24 H, m, 2 x C_4H_9 and 2 x CH_3)

Z-isomer

Found: C, 44.10; H, 7.85, Cl,10.30,

Required for: $C_{13}H_{27}OSnCl$; C, 44.17; H, 7.70; Cl, 10.03%

δ_H 6.08 (1H, d, ^3J_H 11.6 Hz, $^2J^{117}_{Sn}$ 92.8 Hz, $^2J^{119}_{Sn}$ 97.2 Hz; H-4);

6.32 (1H, d, ^3J_H 11.7, $^3J^{117}_{Sn}$ 204.0 Hz; $^3J^{119}_{Sn}$ 212.2 Hz; H

-3).

δ_C ($CDCl_3$); 13.65 (Cδ); 21.59 ($^1J^{117}_{Sn}$ 456.3 Hz, $^1J^{119}_{Sn}$ 477.5 Hz; C-α); 30.04 (C-1); 75.59 ($^3J^{117/119}_{Sn}$ 39.0 Hz; C-2); 128.91 ($^1J^{117}_{Sn}$ 561.5 Hz, $^1J^{119}_{Sn}$ 586.7 Hz; C-4); 150.51 (C-3).

α-Isomer

δ_H 5.72 (1H, s, $^3J^{117}_{Sn}$ 97.5 Hz, $^3J^{119}_{Sn}$ 102.0 Hz; H-4^A); 5.81 (1H, s, $^3J^{117}_{Sn}$ 192.9 Hz, $^3J^{119}_{Sn}$ 201.7 Hz; H-4^B).

δ_C 80.03 ($^1J^{117}_{Sn}$ 450.7 Hz, $^1J^{119}_{Sn}$ 480.0 Hz; C-α); 26.19 ($^3J^{117/119}_{Sn}$ 76.4 Hz; C-γ), 27.82 ($J^{2\ 117/119}_{Sn}$ 30.36 Hz; C-β); 70.07 ($^3J^{117/119}_{Sn}$ 39.6 Hz; C-2); 122.06 (C-4); 164.78 (C-3).

5.4.2 (Z)/(E)-4-(dibutylchlorostannyl)-2-(trimethyl silyloxy)-2-methyl-3-butene and 3-(dibutyl chlorostannyl)-2-(trimethylsilyloxy)-2-methyl-2 -butene.

The above products were obtained by Method 3 using 2-methyl-2-(trimethylsilyloxy)-3-butyne. (0.500g, 3.20 mmol) Bu_2SnCl_2 (0.486 g, 1.60 mmol) and Bu_2SnH_2 (0.358, 1.60 mmol), and separated by flash column chromatography using n-hexane-ethyl acetate (6:4 v/v).
Yield 0.954 g, (70%)

Z-isomer

δ_H 5.95 (1H, d, ^3J_H 12.2 Hz, $^2J^{117}_{Sn}$ 74.8 Hz, $^2J^{119}_{Sn}$ 78.4 Hz; H -4); 6.49 (1H, d, ^3J_H 12.2 Hz, $^3J^{117}_{Sn}$ 194.0 Hz, $^3J^{119}_{Sn}$ 203.0 Hz; H-3).

δ_C ($CDCl_3$) 2.59 (Si-C); 13.64 (C-δ); 19.96 ($^1J^{117}_{Sn}$ 396.8 Hz, $^1J^{119}_{Sn}$ 415.0 Hz; C-α); 26.65 ($^3J^{117/119}_{Sn}$ 74.68; C-γ); 27.95 ($^2J^{117/119}_{Sn}$ 30.0 Hz; C-β); 30.76 (C-1); 76.86 ($^3J^{117/119}_{Sn}$ 28.4 Hz; C-2); 126.06 ($^1J^{117}_{Sn}$ 561.0 Hz; $^1J^{119}_{Sn}$ 588.0 Hz; C -4); 152.38 (C-3).

E-isomer

δ_H 6.11 (1H, d, ^3J_H 18.9 Hz, $^2J^{117}_{Sn}$ 75.9 Hz, $^2J^{119}_{Sn}$ 79.5 Hz; H-4); 6.27 (1H, d, ^3J_H 18.9 Hz, $^3J^{117}_{Sn}$ 95.4 Hz, $^3J^{119}_{Sn}$ 99.8 Hz; H-3).

δ_C 76.86 ($^3J^{117/119}$ 28.4 Hz; C-2); 122.86 ($^1J^{117}$ 534.0 Hz, $^2J^{119}$ 562.0 Hz; C-4); 150.8 (C-3).

α-isomer

Found: C, 46.10; H, 8.47; Cl, 8.14

Required for: $C_{16}H_{35}OSiSnCl$, C, 45.15; H, 8.28; Cl 8.33%

δ_H 5.65 (1H, s, $^2J^{117}_{Sn}$ 98.2 Hz, $^3J^{119}_{Sn}$ 102.9 Hz; H-4^A); 5.71 (1H, s, $^3J^{117}_{Sn}$ 192.9 Hz, $^3J^{119}_{Sn}$ 201.8 Hz; H-4^B).

δ_C 81.79 ($^3J^{117/119}_{Sn}$ 28.4 Hz; C-2); 121.71 ($^2J^{117/119}_{Sn}$ 16.1 Hz; C-4); 167.70 ($^1J^{117}_{Sn}$ 538.2 Hz; $^1J^{119}_{Sn}$ 563.4 Hz; C-3).

δ^{119}_{Sn}; +33.

5.4.3 Preparation of (E)-4-dibutylchlorostannyl-2,2-dimethyl-3-butene

This compound was obtained by Methods 1 and 2 with the following mol ratio of reactants:

By Method 1.

Bu_2SnCl_2 (0.93 g, 3.043 mmol), Bu_2SnH_2 (0.68 g, 3.043 mmol) and 3,3-dimethyl-1-butyne (0.5 g, 6.086 mmol). The proton NMR spectrum of the crude product showed that there were two products, the E-stannylvinyl adduct and 3,3-dimethyl-1-butene in a 9:1 ratio. After column chromatography the latter compound was not observed. The E-adduct was obtained as an oil.

Yield, 1.48 g, (70%).

By Method 2.

3,3-Dimethyl-1-butyne (0.25 g, 3.043 mmol), Bu_2SnCl_2 (0.925 g, 3.043 mmol), $NaBH_4$ (0.593 g, 15.67 mmol), glyme (30 cm^3).

After ether extraction, the pure E-isomer was obtained as the only adduct.

Yield, 0.89 g, (84%).

E-isomer

Found: C, 47.80, H, 8.35, Cl, 9.95,

Required for: $C_{14}H_{29}SnCl$; C, 47.71; H, 8.30; Cl, 9.93.

δ_H ($CDCl_3$); 0.9 - 1.95 (27 H, m, 2 x C_4H_9); 5.89 (1H, d, ^3J_H 19.2 Hz, $^3J^{117}_{Sn}$ 113.5 Hz, $^3J^{119}_{Sn}$ 118.6 Hz; H-3); 6.18 (1H, d, ^3J_H 19.2, $^2J^{117}_{Sn}$ 90.2 Hz, $^2J^{119}_{Sn}$ 94.6 Hz; H-4).

δ_C 13.58 (C-δ); 17.52 ($^1J^{117}_{Sn}$ 364.5 Hz, $^1J^{119}_{Sn}$ 381.5 Hz; C-α); 26.67 ($^3J^{117/119}_{Sn}$ 66.4 Hz; C-γ); 17.69 ($^2J^{117/119}_{Sn}$ 24.1 Hz; C-β); 29.46 (C-1); 120.63 ($^1J^{117}_{Sn}$ 447.4 Hz, $^1J^{119}_{Sn}$ 467.7 Hz; C-4); 162.34 (C-3).

5.4.4 Preparation of 17α-2-(dibutylchlorostannylvinyl)] estradiol-3-acetate

The above compound was only obtained by Method 3 where 17α-ethynylestradiol-3-acetate (0.043 g, 0.12 mmol) Bu_2SnCl_2 (0.039 g, 0.128 mmol) and Bu_2SnH_2 (0.028 g, 0.127 mmol) were reacted together under inert conditions at room temperature.

The reaction was followed by tlc with n-hexane-ethyl acetate (6:4 v/v) as eluent. When the reaction was complete the solvent was removed in vacuo and the residue was chromatographed on a silica gel column with n-hexane-ethylacetate as eluent to give the (Z)-isomer exclusively, which was then recrystallised from acetone.

Yield: 62 mg, (80%). M.p 192 - 196°C

Found: C, 59.10; H, 7.51; Cl; 5.85

Required for: $C_{30}H_{45}O_3SnCl$: C, 59.18; H, 7.46; Cl, 5.83.

δ_H ($CDCl_3$); 0.98-2.30 (36H, m, steroid envelope, 2 x C_4H_9); 2.81 (3H, t, OCH_3), 4.60 (1H, s, OH); 6.73 (1H, d, ^4J_H 1.4 Hz, ^3J_H 12.1 Hz, $^3J^{117}_{Sn}$ 201.5 Hz, $^3J^{119}_{Sn}$ 206.1 Hz; H-19); 6.17 (1H, d, ^3J_H 12.0 Hz, $^2J^{117}_{Sn}$

92.2 Hz, $^2J^{119}_{Sn}$ 96.5 Hz; H-4).

δ_C 13.68 (C-δ); 14.05, 20.64 ($^1J^{117}_{Sn}$ 449.8 Hz, $^1J^{119}_{Sn}$ 470.3 Hz; C-α); 21.03, 23.32; 24.05; 24.26; 24.20; 27.32 ($^3J^{117/119}_{Sn}$ 29.0 Hz; C-γ); 28.11 ($^2J^{117/119}_{Sn}$ 27.8 Hz; C-β); 28.98; 32.38; 38.26; 39.86; 42.98; 46.51; 46.87; 88.06 ($^3J^{117/119}_{Sn}$ 23.4 Hz; C-17); 112.34; 114.50; 124.03; 128.91 (C-20); 132.16; 138.06; 144.67; 154.00 (C-19); 170.38.

5.4.5 Preparation of (Z)-2-(dibutylchlorostannyl)-2 -butene-2,3-dicarboxylic acid

The above compound was prepared according to Method 3 with acetylene dicarboxylic acid (0.2 g, 1.75 mmol), Bu_2SnH_2 (0.195 g, 0.88 mmol) and Bu_2SnCl_2 (0.266 g, 0.876 mmol) in ether. Evaporation of the solvent left a yellow viscous oil, which solidified after 4 hours refrigeration. The solid was purified by flash column chromatography with n-hexane-ethylacetate (65:35 v/v) as eluent, and then recrystallised from dimethylformamide.

Yield, 0.47 g, (70%), M.p >285°C

Found: C, 37.65; H 5.55, Cl, 9.25

Required for: $C_{12}H_{21}O_4SnCl$; C, 37.59; H, 5.52; Cl, 9.25.

δ_H ($CDCl_3$): 0.85 - 1.70 (18H, m, 2 x C_4H_9); 6.68 (1H, s, $^3J^{117}_{Sn}$ 156.2 Hz, $^3J^{119}_{Sn}$ 163.5 Hz; H-2).

δ_C 13.51(C-δ); 19.24 ($^1J^{117}_{Sn}$ 516.2 Hz, $^1J^{119}_{Sn}$ 540.2 Hz; C-α); 26.45 ($^3J^{117}_{Sn}$ 88.0 Hz, $^3J^{119}_{Sn}$ 92.1 Hz; C-γ); 27.59 ($^2J^{117/119}_{Sn}$ 32.4 Hz; C-β); 168.74 ($^1J^{117}_{Sn}$ 359.8 Hz, $^1J^{119}_{Sn}$ 376.5 Hz; C-3); 133.56 (C-2)170.52 ($^2J^{117/119}_{Sn}$ 24.9; C-4); 172.15 ($^3J_{Sn}$ 12.5 Hz; C-1).

5.4.6 Preparation of dimethyl (Z)-3-dibutylchloro stannyl-2-butene-2,3-dicarboxylate

The above compound was synthesised by Method 3 with dimethyl acetylene dicarboxylate (0.5 g, 0.43 ml, 3.52 mmol), Bu_2SnCl_2 (0.53 g, 1.74 mmol) and Bu_2SnH_2 (0.34, 1.75 mmol).

The reaction was followed by tlc with n-hexane-ethyl acetate (7.5 : 2.5 v/v) as eluent and when complete the solvent was evaporated and the viscous oil was column chromatographed on silica gel with n-hexane-ethyl acetate (6:3 v/v) as eluent.

Yield, 0.138 g, (80%)

Found: C, 40.50; H, 6.05; Cl, 8.41

Required for: $C_{14}H_{25}O_4SnCl$: C, 40.86, H, 6.12; Cl, 8.62%.

M.S. m/z; 418 ; 376 (M-Cl).

δ_H ($CDCl_3$); 0.85-1.68 (18H, m, 2 x C_4H_9); 3.85 (6H, d, 2x CH_3); 6.79 (1H, s, $^3J^{117}_{Sn}$ 117.6 Hz, $^3J^{119}_{Sn}$ 123.0 Hz; H-2).

δ_C ($CDCl_3$); 13.51 (C-δ); 19.56 ($^1J^{117}_{Sn}$ 516.3 Hz, $^1J^{119}_{Sn}$ 540.2 Hz; C-α); 26.25 ($^3J^{117/119}_{Sn}$ 95.6 Hz; C-γ); 27.60 ($^2J^{117/119}_{Sn}$ 32.4 Hz; C-β); 60.30 ($^3J^{117/119}_{Sn}$ 180.5 Hz; OCH_3); 129.44 (C-2); 169.05 ($^1J^{117}$ 327.5 Hz, $^1J^{119}_{Sn}$ 342.9 Hz; C-3); 170.21

($^{2}J^{117/119}_{Sn}$ 31.2 Hz; C=0); 172.56

($^{3}J^{117/119}_{Sn}$ 14.0 Hz; C=0).

5.5 REFERENCES

1. van der Kerk and G. J. M., Noltes, J. G., J. Appl. Chem., **9**, 107, (1959).

2. Neumann, W. P., Synthesis 664 (1987).

3. Ensley, H. E., Buescher, R. R. and Lee, K., J. Org. Chem., **47**, 404 (1982).

4. Leusink, A. J., 'Hydrostannation' Schotanus and Jens Utrecht (1966).

5. Massol, M., Barrau, J., Satge, J. and Bouyssieres, B., J. Organomet. Chem., **80**, 47 (1974).

6. Leusink, A. J., Budding, H. A. and Krenth, W., J. Organomet. Chem., **9**, 295 (1967).

7. Nativi, C. and Taddei, J. J., Org. Chem. **53**, 820 (1988).

8. Brouwer, H. and Stothers, J. B., Can. J. Chem, **50**, 1361 (1972).

9. The Aldrich library of NMR spectra **Vol.1** Ed. Pouchert, C. J. 'The Aldrich Chemical Company'

10. Birnbaum, E. R. and Javora, P. H., J. Organomet. Chem. **9**, 319 (1967).

11. Bew, P. S. and Sweeney, J. B., Synlett, **2**, 109 (1991).

12. Leusink, A. J., Marsmann, J. W., Budding, H. A., Noltes, J. G. and van der Kerk, G. J. M., Rec. Trav, Chem., **84**, 567 (1965).

13. Lehnig, M. and Doreu, K., J. Organomet. Chem., **210**, 3310 (1981).

14. Davies, A. G., 'Chemistry of Tin' Ed. Harrison P. G., Blackie, Glasgow, (1980).

15. Moore, D. W. and Happe, J. A., J. Phys. Chem., **65**, 224 (1961).

16. Kuivila, H. G., Considine, J. L., Mynott, R. J. and Sarma, R. H., J. Organomet. Chem. **55,** C11 (1973).

17. Mitchell, T. N. and Kummetat, C., J. Organomet. Chem. **157**, 255 (1978).

18. Jung, M. E. and Light, L. A., Tetrahedron, Lett., **23**, 3851 (1982).

19. Holecek, J., Nadvornik, M., Handlir, K. and Lycka, A., J. Organomet. Chem. **241** 177 (1983)

20 Holecek, J., Nadvornik, M., Handlir, K. and Lycka, A., J. Organomet. Chem., **275** 43 (1984)

21 Otera, J., J. Organomet. Chem. **221,** 57 (1981)

22. Pan, H., Willem, R., Meunier-Piret, J. and Gielen, M. Organometallics **9,** 2199 (1990).

23. van der Kerk, G. Noltes, J. G. and Luijten, L. G. A., J. Appl. Chem., **7**, 366 (1957).

24. Nozaki, K., Oshima, K. and Utimoto, K., Tetrahedron, **45**, 923 (1989)

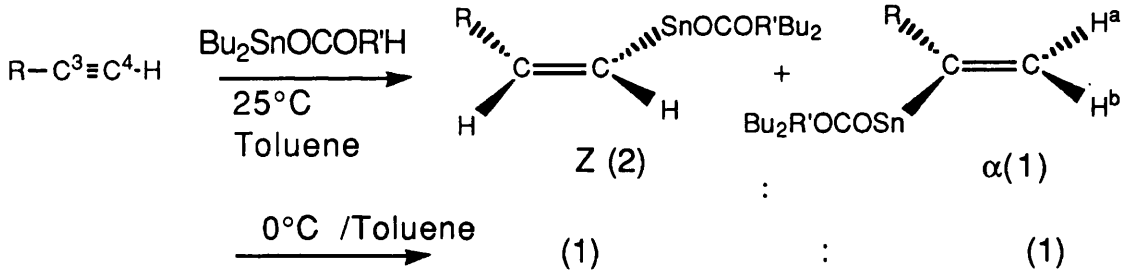
6.0 Reactions of Dibutyltin Carboxylate Hydrides

6.1 RESULTS

6.1.1 Dibutyltin acetate hydride

We have studied the following hydrostannation reactions of dibutyltin acetate hydride at room temperature without the use of a catalyst, in contrast with the conditions required for similar reactions with Bu_3SnH (80°C, AIBN) and Ph_3SnH (25°C, dibenzoyl peroxide).

6.1.1.1 2-Methyi-3-butyn-2-ol



R = $C(OH)(CH_3)_2$
R' = CH_3

Scheme 6.1.1.1

The above reaction (Scheme 6.1.1.1)was carried out at room temperature and at 0°C for 1.5 - 2 hours and the adducts were isolated by flash column chromatography in yields of 50 - 60%

Proton and ^{13}C NMR spectroscopy showed the presence of the Z and α-adducts in a ratio of 2:1 for the reaction at 25°C and 1:1 at 0°C. The characteristic signals in the olefinic region were as follows:

Z-isomer

δH 6.51 (1H, d, ^3J_H 11.6 Hz, $^3J^{117}Sn$ 197.9 Hz, $^3J^{119}Sn$ 207.3 Hz; H-3); 6.01 (1H, d, ^3J_H 11.6 Hz, $^2J^{117}Sn$ 93.7 Hz, $^2J^{119}Sn$ 98.0 Hz; H-4).

δC 75.31 ($^3J_{Sn}$ 27.6 Hz, C-2); 129.09 ($^1J^{117}Sn$ 561.8 Hz, $^1J^{119}Sn$ 587.8 Hz; C-4); 160.05 (C-3); 171.52 (C=0).

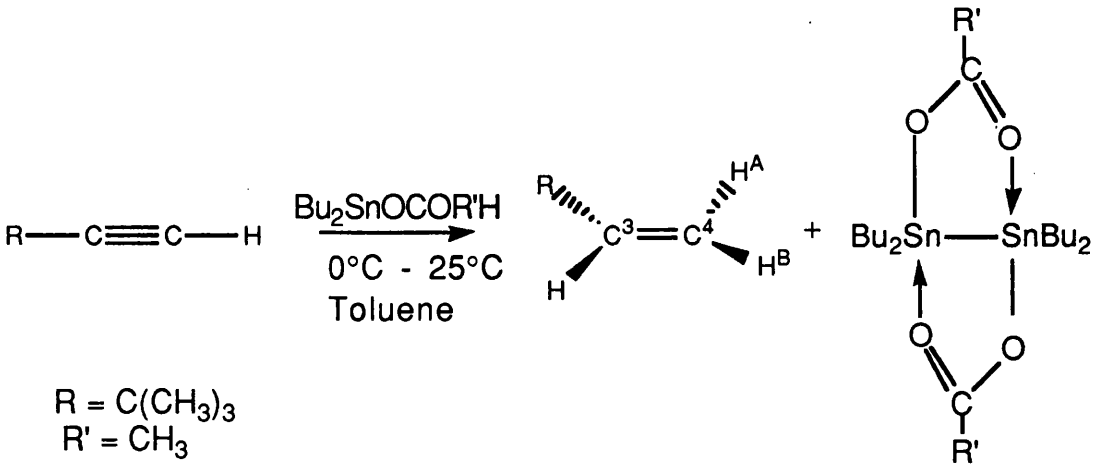
α-isomer

δH 5.45 (1H, s, $^3J^{117}Sn$ 85.1 Hz, $^3J^{119}Sn$ 89.0 Hz; H-4^A); 5.71 (1H, s, $^3J^{117}Sn$ 174.7 Hz, $^3J^{119}Sn$ 182.8 Hz; H-4^B).

δC 121.96 (C-4); 166.11 (C-3); 176.92 (C=0).

These compounds were identified as the Z and α-isomers by comparison of these coupling constant with those of our previous compounds and those in the literature.[1,2,3,4]

6.1.1.2 3,3-Dimethyl-1-butyne



Scheme 6.1.1.2

The reaction of the acetate hydride with 3,3-dimethyl-1-butyne proceeded readily at 0-25°C (Scheme 6.1.1.2), and the proton NMR spectrum of the crude product showed the following characteristic patterns:

δ_H 5.82 (1H, dd, ^3J_H 17.5 Hz, ^3J_H 10.6 Hz; H-3); 4.79 (1H, dd, ^3J_H 10.6 Hz, ^2J_H 1.5 Hz, H-4^B); 4.87 (1H, dd, ^3J_H 17.5 Hz, ^2J_H 1.5 Hz; H-4^A).

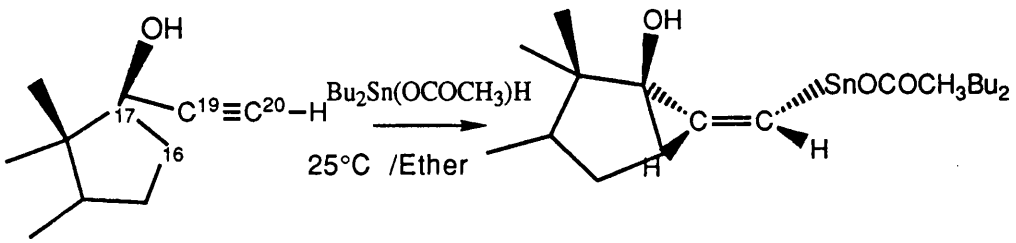
These coupling constants are characteristic of vinyl protons[5] and are similar to those of authentic t-butylethylene and of the adduct which we obtained with Bu_2SnHCl.

We attempted to separate the products by flash column chromatography but obtained only the distannane compound, presumably because of the rather low boiling point of 3,3-dimethyl-1-butene (b.p. 41°C).[6]

The proton and ^{13}C NMR spectra of the distannane showed no olefinic protons and carbons, but only the butyl and carbonyl systems. The product was a yellow oil.

The ^{119}Sn NMR spectrum of this compound had a singlet peak at δ -220 clearly indicating five co-ordinate tin.

6.1.1.3 17α-Ethynylestradiol-3-acetate



Scheme 6.1.1.3

The reaction of dibutyltin acetate hydride with 17α-ethynylestradiol-3-acetate (Scheme 6.1.1.3) was carried out at 25°C without AIBN. Tlc showed that the reaction was complete after 3 hours, and the product was isolated by flash column chromatography as a white crystalline solid in 70% yield.

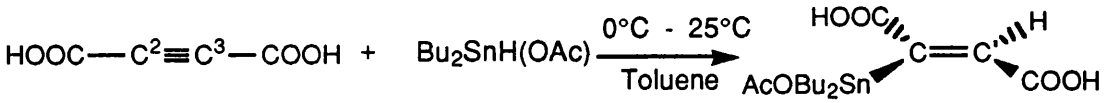
Proton and ^{13}C NMR spectroscopy showed that the Z-isomer had been obtained exclusively:

δH 6.20 (1H, d, $^{3}J_{H}$ 11.9 Hz, $^{2}J^{117}_{Sn}$ 94.6 Hz, $^{2}J^{119}_{Sn}$ 99.0 Hz; H -20); 6.74 (1H, d, $^{3}J_{H}$ 11.9 Hz, $^{3}J^{117}_{Sn}$ 191.0 Hz, $^{3}J^{119}_{Sn}$ 204.0 Hz, H -19).

δC 89.75 ($^{3}J_{Sn}$ 26.9 Hz, C-17); 128.9 (C-19); 156.80 (C-20); 180.56 (C=0)

Comparison of these data with those obtained in the analogous Bu_3SnH and Bu_2SnHCl reactions, confirmed this compound to be the Z-adduct.

6.1.1.4 Acetylenedicarboxylic acid



Scheme 6.1.1.4

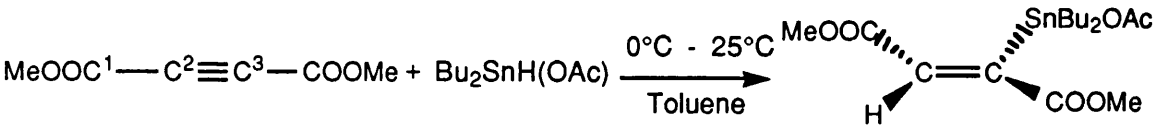
The above reaction (Scheme 6.1.1.4) was carried out readily at 0 - 25°C over a 3 hour period without AIBN. Subsequent flash column chromatography gave a 75% yield of a white crystalline solid that melted at 236°C - 238°C, and showed the following NMR characteristics:

δH 6.75 (1H, s, $^{3}J^{117}Sn$ 118.0 Hz, $^{3}J^{119}Sn$ 124.0 Hz; H-3)

δC 168.28 (^{1}JSn 356.4 Hz, ^{1}JSn 376.9 Hz; C-3); 170.54 (^{3}JSn 24.9 Hz; C-1); 172.5 (^{2}JSn 12.4 Hz; C-4); 153.63 (C-2).

Comparison of these coupling constants with those obtained for the analogous reaction of Bu_2SnHCl confirms that this is a Z-isomer.

6.1.1.5 Dimethyl acetylenedicarboxylate



Scheme 6.1.1.5

As with the previous reaction this was carried out at 0°C and 25°C and the product was isolated by flash column chromatography to give a 70-75% yield of an oil, (Scheme 6.1.1.5) with the following NMR characteristics:

δH 6.84 (1H, s, $^{3}J^{117}Sn$ 117.5 Hz, ^{3}JSn 121.6 Hz; H-3)

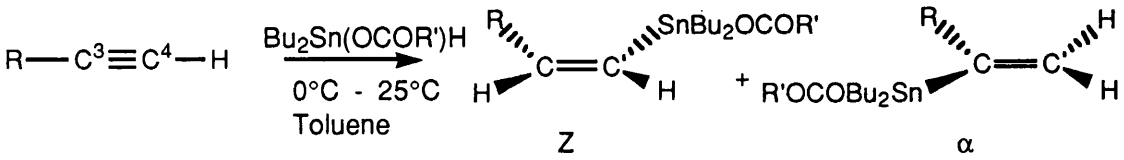
δC 153.64 (C-2); 168.70 ($J^{117}Sn$ 352.4 Hz; $J^{119}Sn$ 376.5 Hz, C-3); 171.56 (^{3}JSn 24.9 Hz; C-1) 172.51 (^{2}JSn 12.5 Hz, C-4).

Again these coupling constants are similar to those obtained in the Bu_2SnHCl adduct and confirm that we have obtained the Z-isomer.

6.1.2 Reactions of Dibutyltin Difluorochloroacetate Hydride

The following hydrostannation reaction of $Bu_2Sn(OCOCF_2Cl)H$ occur at room temperature without the use of the radical initiators.

6.1.2.1 2-Methyl-3-butyn-2-ol



R = $C(OH)(CH_3)_2$
R' = CF_2Cl

Scheme 6.1.2.1

Dibutyltin difluorochloroacetate hydride reacts readily with 2-methyl-3-butyn-2-ol at 0-25°C without AIBN (Scheme 6.1.2.1). Proton NMR spectroscopy of the reaction at 25°C showed that the Z and α isomers were obtained in a 4:1 ratio, with the characteristic olefinic signals observed at:

Z-Isomer

δ_H 6.60 (1H, d, ^3J_H 11.6 Hz, $^3J^{117}Sn$ 213.1 Hz, $^3J^{119}Sn$ 223.0 Hz; H-3); 6.15 (1H, d, ^3J_H 11.4 Hz, $^2J^{117}Sn$ 106.2 Hz, $^2J^{119}Sn$ 111.1 Hz; H-4).

δ_C 75.96 ($^3J_{Sn}$ 27.6 Hz; C-2); 118.13 (J_{C-F} 643.3 Hz; CF_2Cl); 126.19 ($^1J^{117}Sn$ 599.2 Hz, $^1J^{119}Sn$ 625.4 Hz; C-4); 151.52 (C-3); 163.15 ($^2J_{C-F}$ 63.7 Hz; C=0).

α-isomer

δH 5.51 (1H, s, $^3J^{117}Sn$ 99.8 Hz, $^3J^{119}Sn$ 104.4 Hz, H-4^B), 5.74 (1H, s, $^3J^{117}Sn$ 191.0 Hz, $^3J^{119}Sn$ 200.0 Hz; H-4^A).

δC 79.00 (C-2); 128.30 (C-3), 151.52 (C-4), 165.60 (C=0); 121.88 (CF_2Cl)

The reaction at 0°C showed the presence, after column chromatography, of three rather than two adducts, in the ratio 4 : 1 : 8. The major component was the α-adduct with the same characteristics as above. The other two components appeared to be two closely related Z-adducts with the following characterstics:

Z-isomer

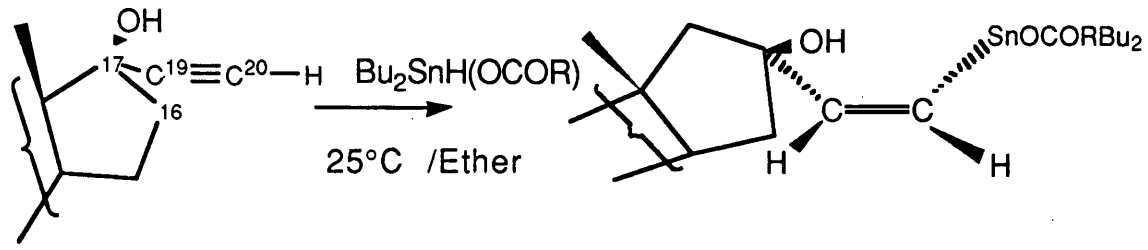
δH 6.55 (1H, d, ^3J_H 11.6 Hz, $^3J_{H\text{-}OH}$ 1.3 Hz, $^3J^{117}Sn$ 195.9 Hz, $^3J^{119}Sn$ 205.0 Hz; H-3); 6.12 (1H, d ^3J_H 11.8 Hz, $^2J^{117}Sn$ 101.0 Hz, $^2J^{119}Sn$ 106.3 Hz; H-4).

The second Z-isomer was observed at:

δH 6.51 (1H, d, ^3J_H 12.28 Hz; H-3), 5.98 (1H, d, ^3J_H 12.28 Hz; H-4).

Attempts to separate these two by flash column chromatography resulted in only the second component being isolated showing no OH coupling. It appears likely that the first of the two Z-adducts is 5-co-ordinate by intramolecular association; and the second has undergone solvolysis of the difluorochloro-acetate group to give the corresponding tin hydroxide (or oxide). Intramolecular dehydration to the cyclic oxastannole seems unlikely as this has been reported in the literature with different proton chemical shifts.[3]

6.1.2.2 17α-Ethynylestradiol-3-acetate



R = CF_2Cl

Scheme 6.1.2.2

Dibutyltin difluorochloroacetate hydride reacts readily with 17α-ethynylestradiol-3-acetate to give the Z-vinyl isomer (Scheme 6.1.2.2), in 60-65% yield. This was purified by flash column chromatography and identified by ^{13}C and proton NMR spectroscopy, which showed characteristic signals in the olefinic region at:

δH 6.17 (d, 1H, ^4J_H 1.2 Hz, ^3J_H 12.0 Hz; $^2J^{117}Sn$ 91.5 Hz, $^2J^{119}Sn$ 95.8 Hz; H-20); 6.74 (1H, d ,^3J_H 1.3 Hz, ^3J_H 12.0 Hz, $^3J^{117}Sn$ 201.8 Hz, $^3J^{119}Sn$ 211.4 Hz; H-19).

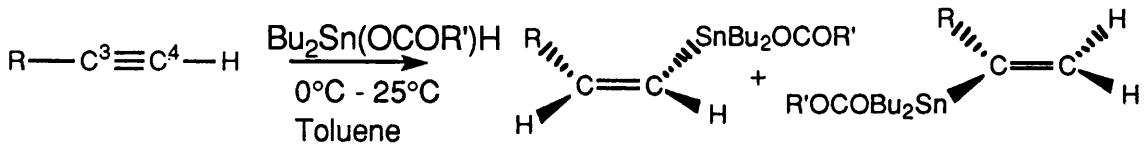
δC 89.50 (C-2), 126.88 (C-4), 152.60 (C-3).

Again this was authenticated as the Z-isomer by comparing its coupling constants with those of analogous compounds obtained by us and other workers.[7,8,9]

6.1.3 Reactions of Dibutyltin Benzoate Hydride

Similarly, as with the above hydrides, the benzoate hydride gives hydrostannation reactions at room temperature without added radical initiators.

6.1.3.1 2-Methyl-3-butyn-2-ol



Z (4) : α (1)

R = $C(OH)(CH_3)_2$
R' = Ph

Scheme 6.1.3.1

Dibutyltin benzoate hydride reacts readily with 2-methyl-3-butyn-2-ol at room temperature and at 0°C to give a 4:1 ratio of Z and a isomers (Scheme 6.1.3.1.) Proton NMR spectroscopy was used to determine the isomeric ratio and the types of isomer present.

Z-isomer

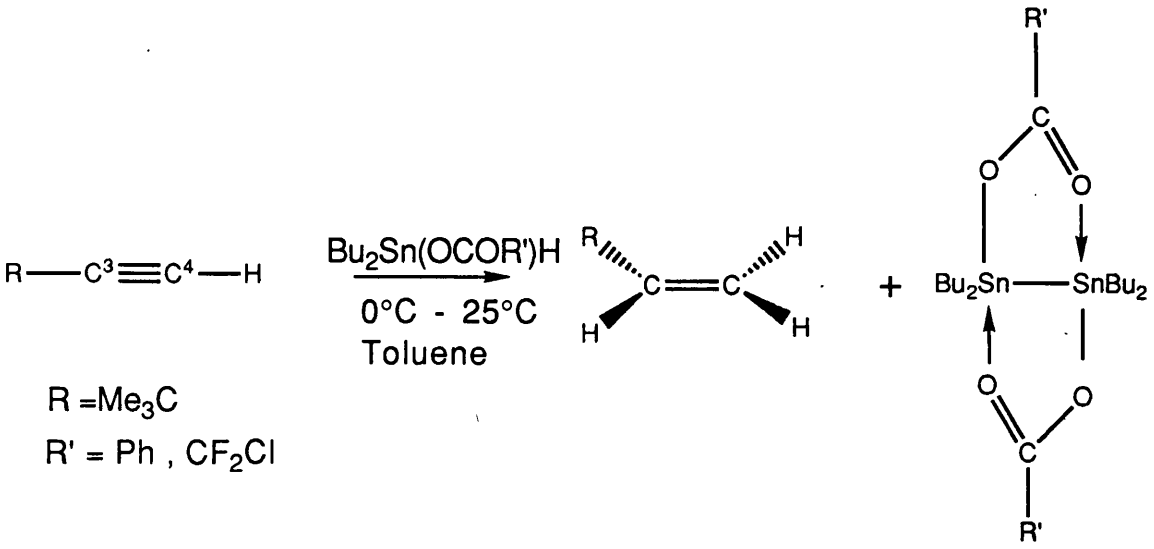
δ_H 6.62 (1H, d, ^3J_H 11.5 Hz, $^3J^{117}Sn$ 190.2 Hz, $^3J^{119}Sn$ 199.0 Hz; H-3); 6.19 (1H, d, ^3J_H 11.6 Hz, $^2J^{117}Sn$ 92.5 Hz, $^2J^{119}Sn$ 96.8 Hz; H-4).

δ_C 72.45 (C-2), 122.00 (C-4), 152.05 (C-3), 168.15 (C=0).

The Z-isomer was authenticated by comparison of the coupling constants obtained here with those from previous Z-isomers.

The α-isomer was characterised by two singlets at δ 5.5 and 5.7.in the olefinic region of the proton NMR spectrum The tin proton coupling constants were immeasurably small.

6.1.3.2 3,3-Dimethyl-1-butyne



Scheme 6.1.3.2

Dibutyltin benzoate hydride reacted readily with 3,3-dimethyl-1-butyne at 25°C and 0°C (Scheme 6.1.3.2), but the proton NMR spectrum of the crude product showed only the n-butyl and phenyl protons and no olefinic protons. The product was purified by flash column chromatography m.p. (33 - 34°C) and characterised by proton and ^{13}C NMR spectroscopy, which indicated that the phenyl and butyl protons were in a ratio of about 10:36. The product is therefore not dibutyltin dibenzoate, which has a m.p 65 - 67°C, and a phenyl: butyl proton ratio of 10:18. The ^{119}Sn NMR chemical shift of δ -181 would be similar to that of tetrabutyldistannanedibenzoate and this was confirmed by elemental analysis.

Dibutyltin difluorochloroacetate hydride reacts with 3,3-dimethyl-1-butyne to give a crystalline compound, m.p. 78- 80°C in which the proton NMR spectrum showed only the presence of the butyl groups on the tin. The ^{119}Sn chemical shift of -173.13 shows that the compound is 5-co-ordinate and elemental analysis identified it as tetrabutyldistannane bis(difluorochloroacetate). The

3,3-dimethyl-1-butene, which presumably is also formed, boils at 41°C and probably was lost during the work up.

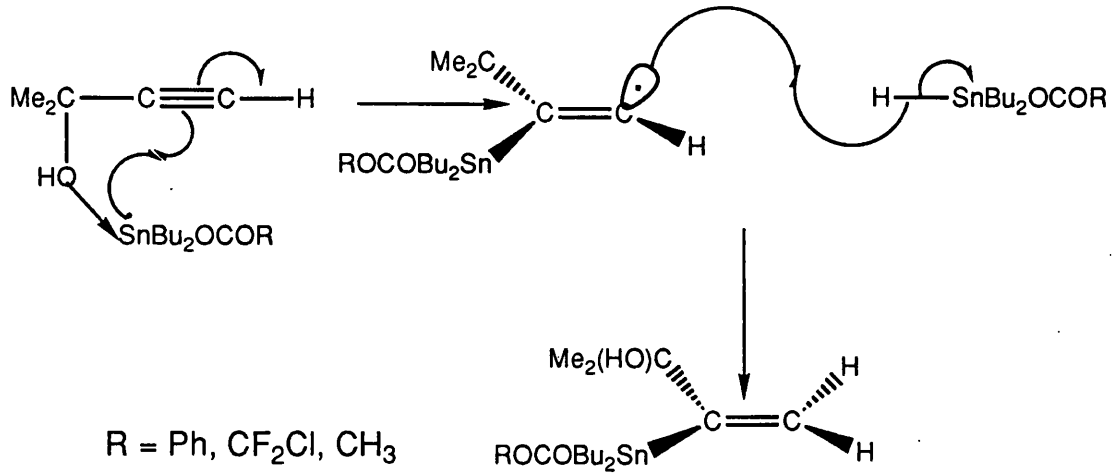
6.2 DISCUSSION

The reactions of these dibutyltin carboxylate hydrides with alkynes are facile and can be conducted from 0°C to 25°C without the use of AIBN. They are readily inhibited by 2,6-di-t-butyl-4-methylphenol and are thus free-radical chain reactions and comparable with the reactions of dibutyltin chloride hydride (Bu_2SnHCl), tributyltin hydride (Bu_3SnH) and triphenyltin hydride (Ph_3SnH). The reactions are faster than those of Bu_2SnHCl, being complete in 1 to 1.5 hours at room temperature compared to 1.5 to 2 hours for Bu_2SnHCl, and 2 - 3 hours for Bu_3SnH at 80°C with AIBN, and 24 hours for Ph_3SnH at 25°C with dibenzoyl peroxide.

6.2.1 Regiochemistry

As with the reactions of Bu_2SnHCl, hydrostannation with these carboxylate hydrides proceeds through the $Bu_2Sn(OCOR)$ radical, which attacks the alkynes at the α carbon (as illustrated in Chapter 5) and at the β carbon to give two types of adducts.

The regiochemistry is controlled by the presence of oxygen at C-2 (Scheme 6.2.1). The α-adduct is found only when an OH group is present at C-2, and we agree with Taddei's[8] supposition that coordination between the tin radical with the OH group steers the tin onto the α-atom. This effect is not important with the $Bu_3Sn\cdot$ and $Ph_3Sn\cdot$ radicals because they are weaker Lewis acids



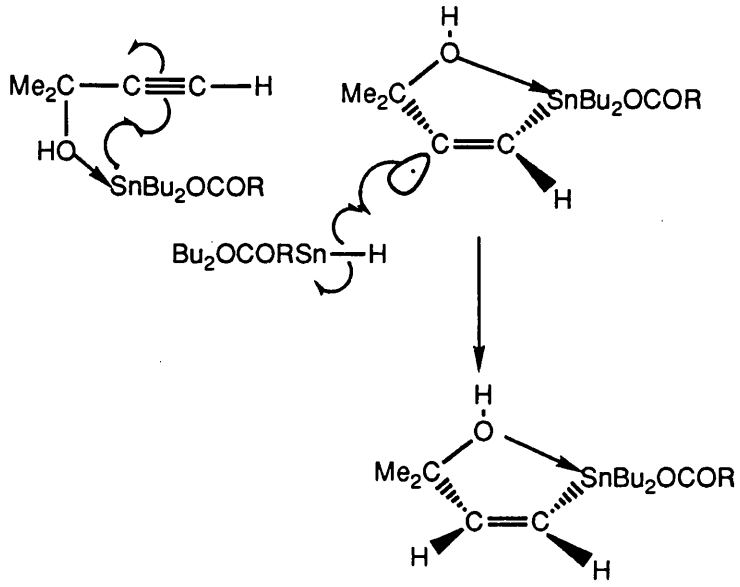
R = Ph, CF_2Cl, CH_3

Scheme 6.2.1

The α-carbon however is highly sterically hindered, and the α-adducts will be least stable with the more bulky carboxylate ligands. This may explain why lowering the temperature of the reaction results in an increase of the yield of the α-adduct only when the reagent is the acetate hydride, and not when it is the difluorochloro acetate or the benzoate hydride.

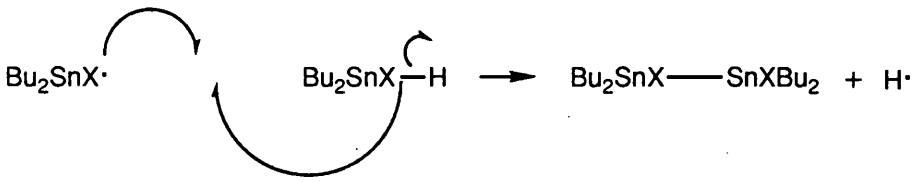
6.2.2 Stereochemistry

As we have already detailed in our previous chapters, attack at the β-carbon can result in the formation of two products, the Z and E-isomers. We, however, do not observe the formation of the E-isomer, due, presumably, to the stability afforded the Z-isomer by Sn<--0 association in, for example, Z-4-dibutylstannylcarboxylato-2-methyl-3-buten-2-ol (Scheme 6.2.2.a).



Scheme 6.2.2.a

We were surprised that, whereas the reaction of Bu_2SnClH with 3,3-dimethyl-1-butyne gave the E-adduct together with $Bu_4Sn_2Cl_2$ and 3,3-dimethyl-1-butene, the corresponding reaction of the tin carboxylate hydrides gave no tin adduct, Z or E, but only the distannanes $Bu_4Sn_2(OCOR)_2$ and presumably 3,3-dimethyl-1-butene. This appears to suggest that the reaction leading to the formation of the distannanes (Scheme 6.2.2.b)

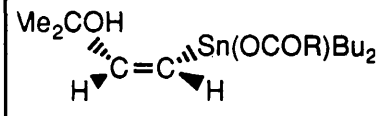
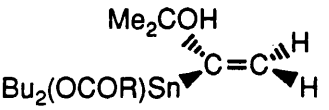


Scheme 6.2.2.b

proceeds more readily when X is carboxylate rather than when X is Cl, which is reasonable in view of the extra stability conferred on the carboxylate product by intramolecular coordination. This substitution generates the hydrogen atom which attacks the butyne to give ultimately the butene. (Scheme. 5.2.1.b)

6.2.3 NMR Spectroscopic Analysis and Evidence for Intramolecular Co-ordination

Table 1: Proton-proton and tin-proton coupling constants (Hz) for the vinyltin carboxylate adducts.

		
^3J_H	11.4 - 12.1	-
$^2J_{Sn-H}$ (gem)	94.0 - 111.0	-
$^3J_{Sn-H}$ (trans)	192.0 - 223.0	174.0 - 200.0
$^3J_{Sn-H}$ (cis)		86.0 - 104.0

The above table shows the range of H-H and Sn-H coupling constants obtained for the Z and α isomers of the dibutylcarboxylato tin compounds. As with previous compounds the actual chemical shifts of the olefinic protons are not diagnostic for Z or α-isomers, however, the J_{H-H} and the J_{Sn-H} are and it can be seen from the Table that the relationship J_H (cis) > J_H (gem), and J_{Sn-H} (trans) > J_{Sn-H} (gem) > J_{Sn-H} (cis) holds

6.3 CONCLUSION

We have succeeded in synthesising new organotin hydrides, which undergo free-radical chain reactions at room temperature or below, with alkynes to give some stereo and regio selectivity. They provide an alternative to tributyltin hydride and triphenyltin hydride as the reactions can be conducted without AIBN or dibenzoyl peroxide at temperatures which do not encourage the formation of by products. They are more reactive than other hydrides discussed in

this thesis, but are also more unstable. If an electron donating group, such as oxygen, is adjacent to the acetylenic carbon to steer the tin moiety into attacking the acetylenic bond, hydrostannation can be achieved. In the absence of such an assisting group, the alkyne undergoes hydrostannation to give an alkene. This suggests that the carboxylate hydrides may have a more general potential as reducing and hydrogenating agents

6.4 EXPERIMENTAL

6.4.1 Preparation of Z-dibutylacetatostannyl-2-methyl-3-buten-2-ol and 3-dibutylacetatostannyl-2-methyl-3-buten-2-ol

The above products were obtained in a 1:1 and 2:1 ratio by conducting the reaction at 0°C and 25°C according to Method 3 using 2-methyl-3-butyn-2-ol (0.072 g, 0.856 mmol) dibutyltin diacetate (0.15 g, 0.427 mmol) and Bu_2SnH_2 (0.13 g, 0.584 mmol) in toluene.

The products were purified by flash column chromatograpy using n-hexane-ethyl acetate (7:3 v/v) as eluent to give a yellow oil.

Yield, 0.226 g, (70%).

Z-isomer

Found: C, 47.5; H, 8.3.

Required for: $C_{15}H_{30}O_3Sn$: C, 47.72; H, 8.02%

δ_H ($CDCl_3$), 0.18 - 1.87 (24H, m, 2 x C_4H_9 +2 x CH_3); 1.89 (3H, s, b, OCH_3), 6.51 (1H, s, ^3J_H 11.6 Hz, $^3J^{117}_{Sn}$ 197.9 Hz, $^3J^{119}_{Sn}$ 207.3 Hz; H-3) 6.01 (1H, s, ^3J_H 11.6 Hz, $^2J^{117}_{Sn}$ 93.7 Hz, $^2J^{119}_{Sn}$ 98.0 Hz; H-4).

δ_C ($CDCl_3$), 13.71 (C-δ); 18.74 ($^1J^{117}_{Sn}$ 415.7 Hz, $^1J^{119}_{Sn}$ 435.2 Hz; C-α); 26.82 ($^3J^{117/119}_{Sn}$ 78.93 Hz; C-γ); 27.85 ($^2J^{117/119}_{Sn}$ 24.75 Hz; C-β); 30.74 (C-1); 60.08 (OCH_3); 75.31 ($^3J^{117/119}_{Sn}$ 27.6 Hz; C-2); 129.09 ($^2J^{117}_{Sn}$ 561.86, $^2J^{119}_{Sn}$ 587.8 Hz; C-4); 150.00 (C-3); 171.52 (C=0).

α-isomer

δ_H ($CDCl_3$), 5.45 (1H, s $^2J^{117}_{Sn}$ 86.1 Hz; $^3J^{119}_{Sn}$ 89.0 Hz; H-4^A);
5.71 (1H, s, $^3J^{117}_{Sn}$ 174.7 Hz, $^3J^{119}_{Sn}$ 182.8 Hz; H-4^B).

δ_C ($CDCl_3$), 121.96 (C-4); 166.11 (C-3); 176.92 (C=O).

6.4.2 Preparation of tetrabutyldiacetatodistannane and 3,3-dimethyl-1-butene

The following compounds were obtained by following Method 3 at 0°C and 25°C, by reacting Bu_2SnH_2 (0.208 g, 0.934 mmol) and $Bu_2Sn(OAc)_2$ (0.32 g, 0.921 mmol) with 3,3-dimethyl-1-butyne.

The proton NMR spectrum of the crude product showed we had obtained 3,3-dimethyl-1-butene which was lost after column chromatography with n-hexane-ethyl acetate (7:3 v.v).

The resultant tetrabutyldiacetatedistannane was obtained as an oil.

Yield 0.33 g, (70%)

Found: C, 49.91; H, 8.93

Required for: $C_{20}H_{42}O_4Sn$: C, 49.92; H, 8.8 %

δ_H ($CDCl_3$), 0.84 -1.63 (36 H, m; 4 x C_4H_9)

δ_C ($CDCl_3$), 13.68 (C-δ); 20.59 (C-α); 26.32 (C-γ); 27.89 (C-β);
52.56 (OCH_3); 182.23 (C=O)

δ^{119}_{Sn} ($CDCl_3$), -220

6.4 3 Preparation of (Z)-17α-(dibutylacetatostannyl vinyl) estradiol-3-acetate

The (Z)-vinyl adduct was obtained exclusively by following Method 3, with 17-ethynylestradiol (0.1, 2.96 mmol), Bu_2SnH_2 (0.32 g, 1.48 mmol) and $Bu_2Sn(OAc)_2$ (0.52 g, 1.48 mmol) in diethylether (25 cm^3)[3]. The reaction was followed by tlc with n-hexane-ethylacetate (6.5:3.5 v/v). When the reaction was complete the solvent was removed in vacuo, and the resultant solid was purified by flash column chromatography with n-hexane-ethyl acetate as the eluent. The white crystalline solid obtained was then recrystallised from acetone.

Yield, 0.19 g, (70%), Mp 200 - 203°C

Found: C, 61.80; H, 7.85,

Required for: $C_{33}H_{48}O_3Sn$: C, 61.60; H; 7.52.%

δ_H ($CDCl_3$), 0.95 - 2.30 (36H, m, steroid and dibutyltin acetate) 2.80 (6H, t, 2 x OCH_3); 6.20 (1H, d, ^3J_H 11.90 Hz, $^2J^{117}_{Sn}$ 94.6 Hz, $^2J^{119}_{Sn}$ 99.0 Hz; H-20); 6.74 (1H, d, ^2J_H 11.9 Hz, $^3J^{117}_{Sn}$ 191.0 Hz, $^3J^{119}_{Sn}$ 204.0 Hz; H-19).

δ_C ($CDCl_3$), 89.75 ($^3J_{Sn}$ 26.9 Hz, C-17), 128.9 (C-19); 156.80 (C -20); 180.56 (C=O).

6.4.4 Preparation of (Z)-2-dibutylacetatostannyl-3-butene-2,3-dicarboxylic acid

The above compound was prepared by Method 3 at 0°C and 25°C in diethyl ether (25 cm^3) from the following mole ratio of reactants:

Acetylene dicarboxylic acid (0.43 g, 9.77 mmol), Bu_2SnH_2 (0.42 g, 1.88 mmol) and $Bu_2Sn(OAc)_2$ (0.66 g, 1.88 mmol).

The reaction was instantaneous and a yellow solid precipitated out. The solvent was removed in vacuo and the solid recrystallised from methanol.

Yield 1.15 g, (75%) M.p 236 - 238°C.

Found: C, 41.95; H, 5.35.

Required For: $C_{14}H_{24}OSn$, C 41.3; H, 5.95%.

δ_H ($CDCl_3$), 0.95-1.72 (18H, m, 2 x C_4H_9); 3.82 (3H, s, OCH_3); 6.75 (1H, s, $^2J^{117}_{Sn}$ 118.0 Hz, $^3J^{119}_{Sn}$ 124.0 Hz; H-3).

δ_C ($CDCl_3$); 13.84 (C-δ); 19.46 ($^1J^{117}_{Sn}$ 531.5 Hz, $^1J^{119}_{Sn}$ 556.2 Hz; C-α); 26.56 ($^3J^{117/119}_{Sn}$ 88.5 Hz, C-γ); 27.84 ($^2J^{117/119}_{Sn}$ 25.6 Hz; C-β); 52.78 (OCH_3); 168.28 ($^1J^{117}_{Sn}$ 356.4 Hz, $^1J^{119}_{Sn}$ 376.9 Hz; C-3); 153.63 (C-2); 170.54 ($^3J^{117/119}_{Sn}$ 24.9 Hz; C -1); 172.15 ($^2J^{117/119}_{Sn}$ 12.04 Hz; C-4)

6.4.5 Preparation of dimethyl (Z)-3-dibutylacetatostannyl-2-butene-2,3-dicarboxylate

The above compound was prepared from Method 3 at 0°C and 25°C in diethyl ether (25 cm^3) from dimethylacetylene dicarboxylate (0.5 g, 3.51 mmol) Bu_2SnH_2 (0.391 g, 1.76 mmol) and $Bu_2Sn(OAc)_2$ (0.62 g, 1.7 mmol). When the reaction was complete, the solvent was removed in

vacuo and the residual oil was purified by flash column chromatography with n-hexane-ethyl acetate (7:3 v/v) as eluent.

Yield, 1.10 g (70%).

Found: C: 44.41; H, 6.55.

Required For: $C_{16}H_{28}O_6Sn$; C, 44.17; H, 6.49%

δ_H ($CDCl_3$,), 0.85 - 1.50 (18H, m, 2 x C_4H_9); 0.95 - 2.00 (3H, s, b, OCH_3); 3.72 (3H, s, OCH_3); 3.85 (3H, s, OCH_3); 6.84 (1H, s, $^3J^{117}_{Sn}$ 117.5 Hz, $^3J^{119}_{Sn}$ 121.6 Hz; H-2).

δ_C ($CDCl_3$), 13.54 (C-δ); 15.67 ($^1J^{117}_{Sn}$ 452.0 Hz, $^1J^{119}_{Sn}$ 473.0 Hz; C-α); 26.81 ($^3J^{117/119}_{Sn}$ 84.5 Hz; C-γ); 28.46 ($^2J^{117/119}_{Sn}$ 25.1 Hz; C-β); 52.19 (OCH_3); 52.33 (OCH_3); 133.98 ($^2J^{117/119}_{Sn}$ 26.05 Hz; C-2); 163.91 ($^1J^{117}_{Sn}$ 278.1 Hz, $^1J^{119}_{Sn}$ 291.1 Hz; C-3); 168.23 ($^2J^{117/119}_{Sn}$ 14.4 Hz; C-4); 171.67 ($^2J^{117/119}_{Sn}$ 26.4 Hz; C-2).

6.4.6 Preparation of (Z)-4-dibutyldifluorochloroacetato stannyl-2-methyl-3-buten-2-ol and 3-dibutyl-difluorochloroacetatostannyl-2-methyl-3-buten-2-ol

2-Methyl-3-butyn-2-ol (0.8 g, 9.5 mmol) reacted with $Bu_2SnH(OCOCF_2Cl)$ (2.35 g, 4.75 mmol) and Bu_2SnH_2 (1.06 g, 4.75 mmol) in toluene (20 cm^3) by Method 3 to give, after column chromatography, the Z and α–isomers as oils in a 2:1 ratio.

Yield 0.11 g, (70%).

δ_H ($CDCl_3$), 0.85 - 1.69 (24 H, m, 2 x C_4H_9, 2 x CH_3)

Z-isomer

Found: C; 40.22; H, 6.32; Cl, 7.95.

Requires for: $C_{15}H_{27}O_3SnF_2Cl$: C, 40.26; H, 6.08; Cl, 7.92%.

δ_H 6.60 (1H, d, ^3J_H 11.6 Hz, $^3J^{117}_{Sn}$ 213.8 Hz, $^3J^{119}_{Sn}$ 223.0 Hz; H-3); 6.15 (1H, d, ^3J_H 11.4 Hz, $^2J^{117}_{Sn}$ 106.2 Hz, $^2J^{119}_{Sn}$ 111.1 Hz; H-4).

δ_C ($CDCl_3$); 13.42 (C-δ); 19.12 ($^1J^{117}_{Sn}$ 472.2 Hz, $^1J^{119}_{Sn}$ 494.2 Hz, C-α); 26.43 ($^3J^{117/119}_{Sn}$ 77.9 Hz, C-γ); 27.84 ($^2J^{117/119}_{Sn}$ 39.3 Hz; C-β); 75.96 ($^2J^{117/119}_{Sn}$ 27.6 Hz; C-2); 118.13 ($^1J_{C-F}$ 643.3 Hz; CF_2Cl); 126.19 ($^1J^{117}_{Sn}$ 599.2 Hz, $^2J^{119}_{Sn}$ 625.4 Hz; C-4); 151.52 (C-3); 163.15 ($^2J_{C-F}$ 63.7; C=0).

δ^{119}_{Sn} ($CDCl_3$) -20

α-isomer

δ_H 5.51 (1H, s, $^3J^{117}_{Sn}$ 99.7 Hz, $^3J^{119}_{Sn}$ 104.4 Hz; $H\text{-}4^B$); 5.74 (1H, s, $^3J^{117}_{Sn}$ 191.8 Hz, $^3J^{119}_{Sn}$ 200.0 Hz; $H\text{-}4^A$).

δ_C ($CDCl_3$); 13.57 (C-δ); 19.31 (C-α); 26.88 (C-γ); 27.31 (C-β); 78.61 (C-2); 118.13 (CF_2Cl); 121.17 (C-4); 128.19 (C-3); 165.8 (C=O).

6.4.7 Preparation of (Z)-17α-[2-(dibutyldifluorochloro-acetatostannylvinyl)]estradiol-3-acetate.

Pure Z-vinyl estradiol was obtained by reacting 17α-ethynylestradiol-3-acetate (50 mg, 0.147 mmol), Bu_2SnH_2 (16 mg, 0.074 mmol) and $Bu_2Sn(OCOCF_2Cl)_2$ (2.35 g, 4.78 mmol) by Method 3.

The product was purified by flash column chromatography with n-hexane-ethylacetate (7:3 v/v).

Yield 18 mg, (65%) M.p 196 - 200 °C.

Found: C; 48.7, H, 7.45, Cl, 5.75.

Required for: $C_{25}H_{45}O_5SnF_2Cl$: C, 48.61, H, 7.34; Cl, 5.74.%

δ_H ($CDCl_3$), 0.95-2.35 (39H, m, steroid envelop, 2 x C_4H_9); 2.86 (3H, t, OCH_3); 4.75 (1H, s, b, OH); 6.17 (1H, d, ^4J_H 1.2 Hz, ^3J_H 12.0 Hz, $^2J^{117}_{Sn}$ 91.5 Hz, $^2J^{119}_{Sn}$ 95.8 Hz; H-20); 6.74 (1H, d, ^4J_H 1.3 Hz, ^3J_H 12.0 Hz, $^3J^{117}_{Sn}$ 201.8 Hz, $^3J^{119}_{Sn}$ 211.4 Hz; H-19).

δ_C ($CDCl_3$), 89.5 ($^3J^{117/119}_{Sn}$ 26.5 Hz; C-17); 126.88 (C-20); 152.60 (C-19).

6.4.8 Preparation of (Z)-4-dibutylbenzoatostannyl-2-methyl-3-buten-2-ol and α-3-dibutylbenzoato stannyl-2-methyl-3-buten-2-ol.

The Z and α vinyl adduct of the benzoate hydride were obtained in a 4:1 ratio by Method 3 from 2-methyl-3-butyn-2-ol (0.25 g, 2.97 mmol), Bu_2SnH_2 (0.33 g, 1.49 mmol) and $Bu_2Sn(OCOPh)_2$ (0.71 g, 1.49 mmol). After 3 hours the products were purified by flash column

chromatography with n-hexane-ethyl acetate (7:3 v/v) solvent to give a viscous oil.

Yield, 0.13 g, (70%).

Z-isomer

Found: C; 54.65; H, 7.2;

Required for: $C_{20}H_{32}O_3Sn$; C, 54.7, H, 7.34%

δ_H ($CDCl_3$), 0.8 - 1.95 (24H, m, 2 x C_4H_9, 2 CH_3)

6.62 (1H, d, ^3J_H 11.5 Hz, $^3J^{117}_{Sn}$ 190.2 Hz, $^3J^{119}_{Sn}$ 199.0 Hz; H-3); 6.19 (1H, d, ^3J_H 11.6 Hz, $^2J^{117}_{Sn}$ 92.5 Hz, $^2J^{119}_{Sn}$ 96.8 Hz; H -4); 7.50-7.60 (5H, m, Ar-H); 8.00 (1H, b, s; OH).

δ_C ($CDCl_3$); 13.47 (C-δ); 25.49 ($^1J^{117}_{Sn}$ 522.8 Hz, $^1J^{119}_{Sn}$ 547.2 Hz; C-α); 26.61 ($^3J^{117/119}_{Sn}$ 63.2 Hz; C-γ); 27.83 ($^2J^{117/119}_{Sn}$ 29.0 Hz; C-β); 29.41 (C-1); 75.68 ($^2J^{117/119}_{Sn}$ 29.8 Hz; C-2); 124.56 ($^1J^{117}_{Sn}$ 475.1 Hz, $^1J^{119}_{Sn}$ 497.2 Hz; C-4); 124-132 (Aromatic); 152.61 (C-3); 168.08 (C=0).

α-isomer

δ_H 5.50 ($H\text{-}4^A$); 5.73 ($H\text{-}4^B$).

The value of J_{Sn} could not be obtained clearly due to the small amount of the α–adduct present.

δ_C ($CDCl_3$) 75.68 (C-2); 122.03 (C-3); 160.53 (C-4).

6.5.8 Preparation of tetrabutyldicarboxylatodistannane $(Bu_2SnOCOR)_2$ R = CF_2Cl or Ph

The distannanes were obtained by Method 3, by reacting 2,3-dimethyl-1-butyne (200 mg, 3.04 mmol) with Bu_2SnH_2 (0.34 g, 1.52 mmol) and either $Bu_2Sn(OCOCF_2Cl)_2$ (0.75 g, 1.52 mmol) or $Bu_2Sn(OCOPh)_2$, (0.72 g, 1.52 mmol). The products were purified by flash column chromatography n-hexane-ethyl acetate (50:50).

(i)Tetrabutyldi(fluorochloroacetato)distannane

Yield 0.80 g, (70%), M.p 78 - 80°C.

Found: C, 33.25, H, 4.22; Cl, 9.65.

Required For: $C_{20}H_{36}O_4Sn_2F_4Cl_2$: C, 33.14; H, 4.01; Cl, 9.78%

δ_H ($CDCl_3$) 0.85-1.65 (36H, m, 4 x C_4H_9)

δ_C 13.6 (C-δ); 19.89 ($^1J^{117/119}_{Sn}$, 568 Hz; C-α); 26.38 (C-γ); 26.50 (C-β); 119.86 ($^1J_{C-F}$ 608.5 Hz; Hz; CF_2Cl); 163.50 ($^4J_{C-F}$ 20.0 Hz; C=0).

^{119}Sn ($CDCl_3$); -173.13

(ii)Tetrabutyldibenzoatodistannane

Yield: 0.75 g, (70%) M p 33 - 34°C (Lit.[10,11]31.5 - 32.5°C)

Found: C, 50.15, H 6.4

Required For: $C_{30}H_{46}O_4Sn_2$: C, 50.89, H 6.55%

δ_H ($CDCl_3$), 0.81 - 2.00 (36H, m, 4 x C_4H_9), 7.50 - 7.70 (10H, m, Ar-H).

δ_C ($CDCl_3$), 13.56 (C-δ); 25.86 ($^1J^{117/119}Sn$ 575.3 Hz, C-α); 26.23 ($^3J^{117/119}Sn$ 46.3 Hz); 26.52 ($^2J^{117/119}Sn$ 26.0 Hz; C-β); 128.3-132.41 (C-Aromatic); 178.948 (C=0).

$\delta^{119}Sn$ ($CDCl_3$); -185

6.5 REFERENCES

1. Leusink, A. J. and Noltes, J. G., J. Organomet. Chem., **16**, 91 (1969).

2. Jung, M. E. and Light, L. A., Tetrahedron Lett. **23**, 3851 (1982).

3. Ensley, H. E., Buescher, R. R., and Lee, K., J. Org. Chem., **47**, 404 (1982).

4. Nativi, C. and Taddei, M., J. Org. Chem., **53**, 820 (1988).

5. Williams, D. H. and Fleming, I., "Spectroscopic methods in Organic Synthesis", McGraw-Hill (UK) Limited.

6. The Aldrich Library of NMR Spectra, Vol.1 Ed. Pouchert, C. J., 'The Aldrich Chemical Company'

7. Davies, A. G., Symes, E. K., Bishop, P. B. and Coulson, W. F., Biochem. Pharmacol., **44**, 741 (1992).

8. Hofmeisler, H., Laurent, H., Schulze, P. E. and Weichert, R., Tetrahedron, **42**, 3575 (1986).

9. Gielen, M., Pan, H., Willem, R. and Meuniers-Piret, J., Organometallics, **9**, 2199 (1990).

10. Kuivila, H. G. and Sawyer, A. K., J. Am. Chem. Soc., **82**, 5958 (1960).

11. Sawyer, A. K. and Kuivila, H. G., J. Org. Chem., **27**, 610 (1962).

7.0 HYDROSTANNOLYSIS

The reduction of alkyl halides (hydrostannolysis) to alkanes by tributyltin hydride (Bu_3SnH) and triphenyltin hydride (Ph_3SnH), is well known.[1,2,3,4] This section of the thesis deals with the possibility of hydrostannolysis with dibutyltin chloride hydride (Bu_2SnHCl) and dibutyltin carboxylate hydrides ($Bu_2Sn(OCOR)H$). The reactions were followed and the products identified using proton NMR spectroscopy.

Routine proton NMR spectroscopy of Bu_2SnHCl in deuterated chloroform ($CDCl_3$) showed an unexpected peak at

$$\delta_H \ 5.20 \ (2H, s, CHDCl_2),$$

as well as the expected peaks at δ 7.42 and δ 4.58, which the tin satellites confirmed were due to Bu_2SnHCl and Bu_2SnH_2. The peak at δ 5.20 was identified as being due to deuterated dichloromethane ($CHDCl_2$). The same result was observed with the carboxylate hydrides ($Bu_2(OCOR)H$).

The only source of the $CDHCl_2$ was the $CDCl_3$ solvent showing that reduction of the latter had occurred.

$$Bu_2SnHX + CDCl_3 \longrightarrow CDHCl_2 + Bu_2SnXCl \qquad (7.0)$$

We thus undertook a series of experiments that followed the hydrostannolysis of various organic halides.

7.1 RESULTS

7.1.1 Reduction of Benzyl Halides

7.1.1.1 Reduction of Benzyl Chloride

Benzyl chloride is not reduced at 25°C by Bu_3SnH, but requires initiation by ABIN at 80°C, to give toluene.[5,6] With the above hydrides (Bu_2SnHX, obtained by mixing Bu_2SnX_2 and Bu_2SnH_2 in a 1 : 1 ratio) however, the reduction takes place at 25°C without the use of

an external initiator giving 100% yield of toluene (equation 7.1.1.1), the peak at δ 5.20 (2H, s, CH_2Cl) being replaced by one at δ 2.05 (3H, s, CH_3).

$$Bu_2SnHX + PhCH_2Cl \longrightarrow PhCH_3 + Bu_2SnXCl \qquad (7.1.1.1.)$$

Where X = Cl, the reaction takes 3 - 3.5 hours, at 25°C, to be complete. We found that we could reduce the amount of Bu_2SnCl_2 used and still obtain successful reduction in the same time. This is probably because one of the products formed is Bu_2SnCl_2 and this undergoes further reduction with Bu_2SnH_2 to generate more Bu_2SnHCl.

(i) Where X = $OCOCF_2Cl$, OCOPh and $OCOCH_3$ the reaction takes 1 - 1.5, 2.5 and 3 - 4 hours respectively, for completion.

7.1.1.2 Reduction of Benzyl bromide

Reaction of alkyl bromides with Bu_3SnH occurs readily at 45°C without added radical initiators.[5,6] The equivalent reaction with Bu_2SnHX also occurs readily without radical initiators, but now at 25°C (equation 7.1.1.2).

$$Bu_2SnHX + PhCH_2Br \longrightarrow Bu_2SnBrX + PhCH_3 \qquad (7.1.1.2)$$

We observed that the peak at δ 5.00 (1H, s, CH_2Br), disappears and is replaced by a peak at δ 2.05 (3H, s, Ar-CH_3).

The reduction occurs over 1.5 hours for Bu_2SnHCl, 24 hours for the benzoate and acetate hydrides and 30 minutes for the difluorochloroacetate hydride.

7.1.1.3 Reduction of Benzyl iodide

The reaction is instantaneous with Bu_3SnH at 25°C and highly exothermic.[5,6] Similarly with Bu_2SnHX the reaction occurs at 25°C and is so exothermic that the solvent (C_6D_6) boils.

Proton NMR spectroscopy showed that the CH_2I peak at δ 4.50 had disappeared to be replaced by a peak at δ2.05 (equation 7.1.1.3):

$$C_6H_5CH_2I + Bu_2SnHX \longrightarrow C_6H_5CH_3 + Bu_2SnIX \qquad (7.1.1.3)$$

7.1.2. Reduction of Alkyl halides

7.1.2.1 Reduction of 1-Chloropentane

Having successfully reduced benzyl halides, we considered how these hydrides would behave towards aliphatic halides. The reduction of halides, such as 1-chloropentane with Bu_3SnH is reported to be slow and does not occur unless initiated by AIBN or UV irradiation.[7,8,9,10]

Similarly Bu_2SnHX reduction at room temperature did not occur even with UV irradiation and peak at δ 3.40 (2H, t, CH_2Cl) was still present.

$$Bu_2SnHX + C_5H_{11}Cl \xrightarrow{X} Bu_2SnXCl + C_5H_{12} \qquad (7.1.2.1.a)$$

Although the reaction does not occur we observed no peaks corresponding to Bu_2SnHCl at (δ 7.42) and Bu_2SnH_2 (δ 4.58). The likely explanation is that the distannane is formed although we did not observe the evolution of hydrogen.(equation 7.1.2.1.b).

$$2\ Bu_2SnHX \longrightarrow XBu_2Sn\text{—}SnBu_2X + H_2 \qquad (7.1.2.1.b)$$

7.1.2.2 Reduction of 1-Bromobutane

The reduction of alkyl bromides by Bu_3SnH is well known and occurs readily even at room temperature.[7,8,9,10] 1-Bromobutane was readily reduced at room temperature by Bu_3SnH in an exothermic reaction. However, reaction with Bu_2SnHX was not totally successful (equation 7.1.2.2).

(i) When X = Cl, the reduction occurs readily and takes 1 - 1.5 hours to complete. Proton NMR spectroscopy showed that the peak at δ 3.46 (2H, t, CH_2Br), had virtually disappeared.

$$Bu_2SnHCl + C_4H_9Br \longrightarrow Bu_2SnClBr + \underset{80\%}{C_4H_{10}} \qquad (7.1.2.2)$$

(ii) A similar reaction does not occur with the hydride carboxylates even with irradiation at 25°C. We again did not observe the peaks due to Bu_2SnH_2 or $Bu_2SnH(OCOR)$ and this suggests that the $Bu_2SnH(OCOR)$ decomposes faster than it reacts with 1-bromobutane.

7.1.2.3 Reduction of 2-Iodo-2-methylpropane

Reduction of alkyl iodides with Bu_3SnH is reported in the literature to be instantaneous at 25°C.[7,8,9,10] The reaction of Bu_2SnHX with 2-iodo-2-methylpropane is similarly instantaneous and so exothermic that the solvent (C_6D_6) boils. The purple colour of iodine disappears and the solution goes colourless.

$$(CH_3)_3CI + Bu_2SnHX \longrightarrow (CH_3)_3CH + Bu_2SnXI \qquad (7.1.2.3)$$

7.1.3 Reduction of Allyl halides

Allyl halides might be expected to react with tin hydrides by three possible routes, namely: hydrostannation; hydrostannolysis or conjugate substitution (Scheme 1).[11]

$$CH_2 = CH - CH_2X \xrightarrow{SnH} Sn\text{-}CH_2\text{-}CH_2\text{-}CH_2X$$

$$CH_2 = CH - CH_2X \xrightarrow{SnH} CH_2{=}CH\text{-}CH_3$$

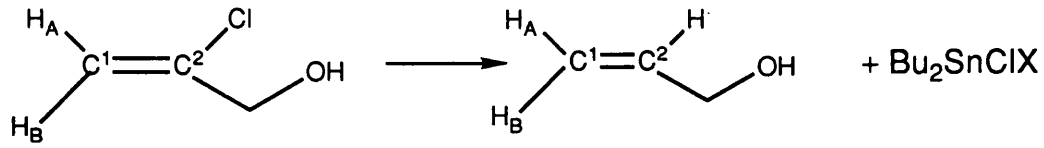
$$CH_2 = CH - CH_2X \xrightarrow{SnH} Sn\text{-}CH_2\text{-}CH{=}CH_2$$

Scheme 1

Kuivila found that with AIBN at 80°C Bu_3SnH showed that allyl bromide reacted by the hydrostannolysis route. Similarly we find that our reagents R_2SnXH similarly show the hydrostannolysis reaction, but now at room temperature.

7.1.3.1 2-Chloroallyl alcohol

2-Chloroallyl-alcohol was treated with Bu_2SnHX at room temperature with the following results (Scheme 2)



Scheme 2

(i) Where X = Cl the reduction only goes to 75% completion after 1.5 hours as evidenced by the reduction in intensity of the two singlet peaks at δ 5.20 and δ 5.40 and the appearance of peaks at

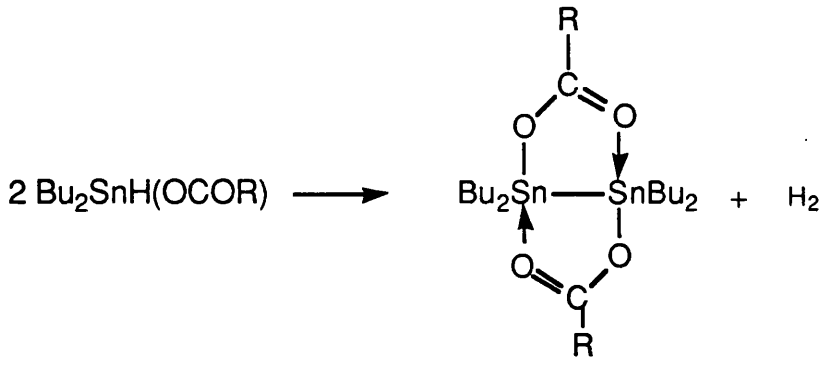
δ 5.16 (1H, dd, ^2J_H 1.3 Hz, ^3J_H 16.51 Hz; H-1^B); 5.09 (1H, dd, ^2J_H 1.3

Hz, ^3J_H 10.6 Hz; H-1^B); and δ 5.91 (1H, m; H-2).

The product was confirmed to be allyl alcohol by comparison with the spectrum of an authentic sample which showed:

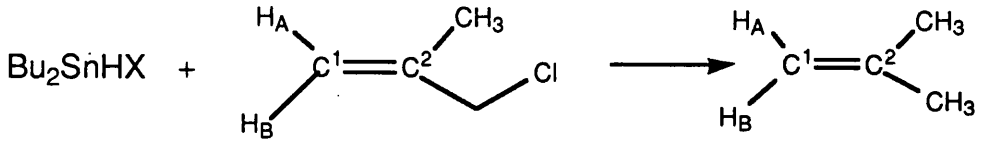
δ 5.25 (1H, dd, ^2J_H, 1.3 Hz, ^3J_H 10.5 Hz; H-1_A); 5.22 (1H, dd, ^2J_H 1.3 Hz, ^3J_H 16.40 Hz; H-1_B); 5.95 (1H, m; H-2);

(ii) When X = $OCOCF_2Cl$, OCOPh or $OCOCH_3$, the reduction was only 55%, 48% and 28% complete over a period of 30 minutes 1.5 hours and 1.5 hours respectively. Although the reductions were not 100% complete we again do not observe peaks corresponding to Bu_2SnH_2 indicating that $Bu_2SnH(OCOR)$ was formed, but decomposed rapidly before it could fully react with the 2-chloroallyl alcohol. Presumably it decomposes to form the distannane and hydrogen, although we did not observe the evolution of hydrogen (equation 7.3.1)



(7.3.1)

7.1.3.2 2-Methylallyl chloride



Scheme 3

(i) With Bu_2SnHCl

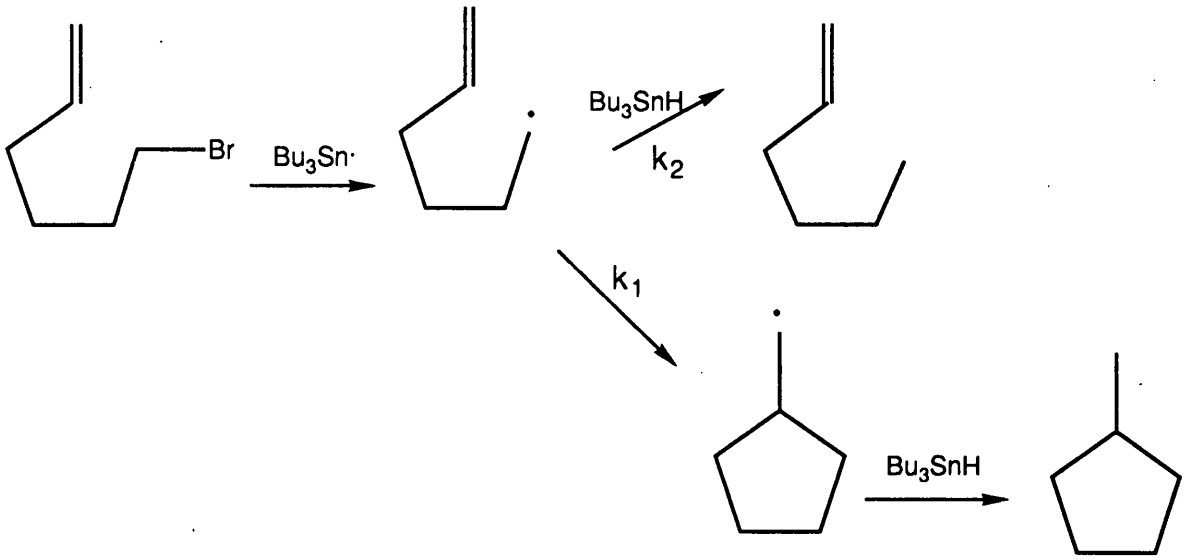
Dibutyltin chloride hydride reduces 2-methylallyl chloride completely to isobutene over 3 - 3.5 hours at 25°C without AIBN. We observed in the proton NMR spectrum that the peak at δ 4.00 (2H, s, CH_2Cl) disappears completely and this is accompanied by an increase in the intensity of the methyl peak at δ 1.73 (6H, s, $2CH_3$). The olefinic singlets at δ 4.67 and δ 4.91, are still present.

(ii) With $Bu_2SnH(OCOR)$

R = CH_3, Ph, CF_2Cl

Similarly, the carboxylate hydrides reduce 2-methylallyl chloride to isobutene (Scheme 3), although with the acetate hydride (R = CH_3), the reduction occurs over a 6 hours period and gives only 75% of isobutene. With the benzoate hydride (R = Ph), on the otherhand, reduction was complete after 2 - 2.5 hours, and the difluorochloroacetate (R = CF_2Cl) showed complete reduction after 1 - 1.5 hours.

7.1.3.3 Reduction of 6-Bromo-1-hexene



Scheme 4

The reduction of 6-bromo-1-hexene with Bu_3SnH at 80°C with AIBN has been studied extensively by Beckwith et al.[12,13] and has shown to be accompanied by intramolecular cyclisation to give the five membered ring. The formation of the five membered ring is kinetically favoured over the six membered ring (Scheme 4.).

We attempted to repeat these observations with our hydrides at room temperature without much success. Proton NMR spectroscopy of the reacting mixture showed that the CH_2Br peak at δ 3.40 was still present along with the olefinic protons at δ 5.85 and δ 5.00.

7.2 DISCUSSION

The hydrostannolysis of alkyl halides is well documented and widely used in organic synthesis, particularly where it is used to generate an alkyl radical which then takes part in a sequence of radical transfer reactions.[10] Tributyltin hydride is the most

commonly used hydride, but trimethyltin hydride and triphenyltin hydride, which have very similar properties are also sometimes used.

The hydrides Bu_2SnHX, which we studied here, provide alternative reagents with potential advantages which can be exploited by suitable choice of the electronegative substituent X. These variations are readily achieved as the compounds can be prepared by comproportionation between Bu_2SnH_2 and Bu_2SnX_2 and, at least in some cases, by partial reduction of Bu_2SnX_2 with sodium borohydride.

The enhanced reactivity of Bu_2SnHX (when X = Cl, $OCOCF_2Cl$, $OCOCH_3$, or OCOPh) is illustrated by the reduction of $CDCl_3$ to $CDHCl_2$ at room temperature without an added initiator or UV irradiation, whereas the reduction of CCl_4 and $CHCl_3$ with Bu_3SnH requires initiation or irradiation with AIBN at 80°C.[4]

$$CCl_4 \xrightarrow{Bu_3SnH} CHCl_3 \xrightarrow{Bu_3SnH} CH_2Cl_2$$

This enhanced reactivity is similar to that which we discussed in comparing the hydrostannation reactions of alkynes by Bu_3SnH and Bu_2SnHX. As we show there, the overall rate is a complex function of the rates of the initiation, propagation and termination processes, and again we ascribe the enhanced reactivity to the ability of the hydrides Bu_2SnHX to autogenerate radicals as shown by their instability at room temperature. We tentatively ascribe this homolytic decomposition to an electron-transfer process.

The rate of hydrostannolysis of the substrate RH with the reagent Bu_2SnHX depends on the nature of Y and of R in the same way as the reductions with Bu_3SnH.

$$Sn\cdot + Y—R \longrightarrow Sn—Y + R\cdot \qquad (7.4)$$

The sequence of reactivity of alkyl halides is RI > RBr > RCl > RF, reflecting the dissociation energies of the RY bonds (Table 1), and the enthalpy change in the reaction.

Table1 Dissociation energies of carbon - halogen bonds.[14]

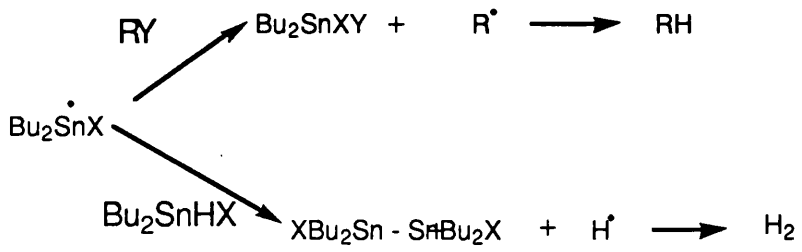
	C - I	C- Br	C - Cl	C - C	C - H	C - F
Bond Energy kJ/mol	222	290	340	357	412	445

The benzyl halides and allyl halides are more reactive than the alkyl halides, reflecting the weakening of the R-Y bonds by benzylic or allylic resonance in the fragment R (Table 2).

Table 2 Dissociation energies of benzyl-halide bonds.[14]

	X	I	Br	Cl	F	C-C	C-H
$ArCH_2X$ kJ/mol		168	214	285	-	302	357

However, some halides which we would have expected to be reduced by Bu_2SnHCl, such as 1-bromobutane, were unreactive. This may be because the substrate RY is in competition with the hydride Bu_2SnXH for reaction with the radical Bu_2SnX.(Scheme 5)



Scheme 5

No such competition is involved with the radical $Bu_3Sn\cdot$ derived from Bu_3SnH.

With the wide variety of groups that are available, it would be possible on a trial and error basis, to select the reagent Bu_2SnHX which is most appropriate for any particular hydrostannolysis or hydrostannation. Once reliable rate constants are determined for the initiation, propagation and termination reactions for the autodecomposition of the compounds R_2SnHX and data for the inhibition and addition reactions of the various radicals Bu_2SnX, it will be possible to make a much more informed choice of the tin hydride.

7.4 CONCLUSION

We believe we have established potentially useful methods for the hydrostannolysis of organic halides without the need to use AIBN at high temperatures. Reduction is facile at room temperature and high yields of products are obtained depending on the stability of the hydride used and the nature of the halide. The use of these hydrides

would be advantageous, especially where low temperatures are required for selective reduction.

Further studies are required in order to establish conditions for the reduction of other functional groups such as CN, NO_2, an OSO_2R which are readily reduced by Bu_3SnH with AIBN at 80°C or above.

7.4 EXPERIMENTAL

Hydrostannolysis with Bu_2SnHX was carried out by mixing the appropriate Bu_2SnX_2 with Bu_2SnH_2 together with the organic halide to be reduced, in an NMR tube and the reaction was followed by proton NMR spectroscopy with d_6-benzene as solvent. We did not separate any of the products as most of these were highly volatile.

7.4.1 Reductions with Bu_2SnHCl

(i) Benzyl chloride

Benzyl chloride, (0.1 mg 0.0078 mmol) was added to Bu_2SnCl_2 (0.012g, 0.0039 mmol) and Bu_2SnH_2 (8.7 mg, 0.0029 mmol) in d_6-benzene. The reaction was followed by proton NMR spectroscopy and was observed to be 100% complete after 3 hours.

(ii) Benzyl bromide

Benzyl bromide (0.15g, 0.88 mmol), Bu_2SnH_2 (0.098g, 0.44 mmol) and Bu_2SnCl_2 (0.134 g, 0.44 mmol) were mixed in an NMR tube in d_6-benzene and the reaction was again followed and observed to be 100% complete after 1.5 hours.

(iii) Benzyl iodide

A similar reaction was observed when benzyl iodide (0.15g, 0.688 mmol) Bu_2SnH_2 (0.077g, 0.344 mmol) and Bu_2SnCl_2 (0.106g, 0.344 mmol) were mixed in d_6-benzene. In this case the reaction was instantaneous and so exothermic that the solvent boiled.

7.4.2 Alkyl Halides

Similarly we attempted to reduce alkyl halides to their corresponding alkanes by reduction with Bu_2SnHCl.

(i) 1-Chloropentane

1-Chloropentane (0.05g, 0.47 mmol), Bu_2SnCl_2 (0.871g, 0.24 mol) and Bu_2SnH_2 (0.05g, 0.24 mmol) in d_6-benzene was monitored by proton NMR spectroscopy for 3 hours but reduction to pentane did not occur.

(ii) 1-Bromobutane

1-Bromobutane (0.7g, 0.73 mmol) Bu_2SnH_2 (0.083g, 0.37g mmol) and Bu_2SnCl_2 (011g, 0.37 mmol) in d_6-benzene was observed to reduce 1-bromobutane over 1-1.5 hours. The reaction however only goes to 80% completion.

(iii) 2-Iodo-2-methylpropane

The reduction of 2-iodo-2-methylpropane (0.1g, 0.54 mol) with Bu_2SnHCl (Bu_2SnCl_2, 0.08g, 0.27 mmol and Bu_2SnH_2, 0.061g, 0.27 mmol) in d_6-benzene, was instantaneous and highly exothermic.

7.4.3 Reduction of Allyl halides

(i) 2-Chloroallyl alcohol

Allyl alcohol was obtained by the reduction of 2-chloroallyl alcohol (0.15g, 1.62 mmol) by BuSnHCl (Bu_2SnH_2, 0.54g, 2.43 mmol and Bu_2SnCl_2, 0.25g, 0.81 mmol) in d_6-benzene at 25°C and again followed by proton NMR spectroscopy. The reaction was observed to be 75% complete after 1.5 hours and did not proceed any further.

(ii) 2-Methylallyl chloride

Isobutene was obtained by the reduction of 2-methylallyl chloride (0.15g, 1.11 mmol) with Bu_2SnHCl (Bu_2SnH_2; 0.49g, 2.22 mmol and Bu_2SnCl_2; 0.34g, 1.11 mmol) in d_6-benzene at 25°C. The reduction was 100% complete after 3-3.5 hours.

6-Bromo-1-hexene

The reduction of 6-bromo-hexene (0.133g, 0.82 mmol) with Bu_2SnHCl (Bu_2SnH_2; 0.188g, 0.82 mmol and Bu_2SnCl_2; 0.25g, 0.82 mmol) in d_6-benzene at 18°C was followed by proton NMR spectroscopy over 3 hours and no reaction was observed.

7.4.4 Reductions with the hydride carboxylates $Bu_2Sn(OCOR)H$ R = Ph, CF_2Cl and CH_3

As with the reductions with Bu_2SnHCl, these were carried out in an NMR tube and followed by proton NMR spectroscopy with d_6-benzene as solvent.

7.4.5 Reduction of benzyl halides to toluene

(i) Benzyl chloride

Benzyl chloride (0.15g, 1.17 mmol) was reduced to toluene by $Bu_2SnH(OCOCF_2Cl)_2$; (Bu_2SnH_2; 0.26g, 17 mmol; and $Bu_2Sn(OCOCF_2Cl)_2$; 0.58g, 1.17 mmol). The reaction was observed to be complete after 1-1.5 hours.

A similar procedure was carried out with $Bu_2SnH(OCOCH_3)$ (Bu_2SnH_2; 0.26g, 1.17 mmol and $Bu_2Sn(OCOCH_3)_2$; 0.41 g, 1.17 mmol) and the reaction was 100% complete in 3.5-4 hours.

Finally with $Bu_2SnH(OCOPh)$ (Bu_2SnH_2; 0.38g, 1.71 mmol and $Bu_2Sn(OCOPh)_2$; 0.61g, 1.71 mmol) the reaction was 100% complete in 2.5 hours.

(ii) Benzyl bromide (0.25g, 1.46 mmol)

Benzyl bromide was similarly reduced to toluene by $Bu_2SnH(OCOCF_2Cl)$ (Bu_2SnH_2; 3.2g, 1.46 mmol, $Bu_2Sn(OCOCF_2Cl)_2$, 0.71g, 1.46 mmol). The reaction was 100% complete over 30 minutes. The reduction with $Bu_2Sn(OCOPh)H$ (Bu_2SnH_2; 0.32g, 1.46 mmol, $Bu_2Sn(OCOPh)_2$; 0.70g, 1.46 mmol) was 100% complete in 24 hours. Similarly reaction with $Bu_2SnH(OCOCH_3)$ (Bu_2SnH_2; 0.32g, 1.46 mmol; $Bu_2Sn(OCOCH_3)_2$; 0.51g, 1.46 mmol) was 100% complete over 24 hours.

(iii) Benzyl iodide (0.20g, 1.17 mmol)

Benzyl iodide was also reduced to toluene with $Bu_2Sn(OCOCF_2Cl)H$ (Bu_2SnH_2; 0.26g, 1.17 mmol $Bu_2Sn(OCOCF_2Cl)_2$; 0.58g, 1.17 mmol) in an instantaneous and highly exothermic reaction. This was similarly observed with $Bu_2Sn(OCOPh)H$ (Bu_2SnH_2; 0.26g, 1.17 mmol; $Bu_2Sn(OCOPh)_2$; 0.41g, 1.17 mmol) and $Bu_2Sn(OCOCF_2Cl)H$ (Bu_2SnH_2; 0.26g, 1.17 mmol; $Bu_2Sn(OCOCH_3)_2$; 0.41g, 1.17 mmol).

7.4.6 Reduction of alkyl halides to alkanes

(i) 1-Chloropentane and 1-bromobutane (1 mole) were not reduced by the carboxylate hydrides (2 mole).

(ii) 2-Iodo-2-methyl propane (0.15 g, 0.82 mmol) was instantly reduced in a highly exothermic reaction with $Bu_2SnH(OCOCF_2Cl)$ (Bu_2SnH_2; 0.183g, 0.82 mmol, $Bu_2Sn(OCOCF_2Cl)_2$; 0.41g, 0.82 mmol), $Bu_2SnH(OCOPh)$ (Bu_2SnH_2; 0.15g, 0.82 mmol; $Bu_2Sn(OCOPh)_2$; 0.38g, 0.82 mmol), and $Bu_2SnH(OCOCH_3)$ (Bu_2SnH_2; 0.15g, 0.82 mmol; $Bu_2Sn(OCOCH_3)_2$; 0.29g, 0.82 mmol).

7.4.7 Reduction of allyl halides

(i) 2-Chloro allyl alcohol

Allyl alcohol was obtained when $Bu_2SnH(OCOCF_2Cl)$ (Bu_2SnH_2; 0.36g, 1.62 mmol; $Bu_2Sn(OCOCF_2Cl)_2$; 0.80g, 1.62 mmol) reacts with 2-chloroallyl alcohol (0.15g, 1.62 mmol). The reaction was only 86% complete after 30 minutes, but no further reaction was observed after this period.

Similarly $Bu_2SnH(OCOPh)$ (Bu_2SnH_2; 0.36g, 1.62 mmol; $Bu_2Sn(OCOPh)_2$; 0.77g, 1.62 mmol) and $Bu_2Sn(OCOCH_3)H$ (BuSnH; 0.36g, 1.62 mmol; $BuSn(OCOCH_3)$; 0.57g, 1.62 mmol) reduced 2-chloroallyl alcohol to allyl alcohol over 1.5 hours to 48% and 28% of the allyl alcohol.

(ii) 2-Methylallyl chloride

$Bu_2SnH(OCOCH_3)$ (Bu_2SnH_2, 1.62 mmol; $Bu_2Sn(OCOCH_3)_2$, 1.62 mmol) reduces 2-methylallyl chloride in 6hours to give 75% isobutene, similarily reduction with $Bu_2SnH(OCOPh)$ (Bu_2SnH_2,1.62

7.5 REFERENCES

1. Noltes, J. G. and van der Kerk, G. J. M., Chem. Ind. London, 294 1959).

2. Davies, A. G.and Smith, P. G., in Comprehensive Organometallic Chemistry, Ed Wilkinson, G., Stone, F. G. A. and Abel, E. W., Pergamon Press, Oxford, **Vol. 2**, 519 (1982).

3. Poller, R. C., The Organic Chemistry of Tin, Wiley, London, 1970.

4. Seyferth, D., Yamazaki, H. and Alleston, D. L., J. Org. Chem., 28, **703** (1963).

5. Chanon, M., Bull. Soc. Chem. Fr., **11**, 197 (1982).

6. Blackburn, E. V. and Tanner, D. D., J. Am. Chem. Soc., **102**, 2149 (1980).

7. Kuivila, H. G., Menapace, L. W. and Warner, C. R., J. Am. Chem. Soc., 84, 3584 (1962).

8. Kuivila, H. G. and Menapace, L. W., J. Org. Chem., **28**, 2165 (1963).

9. Menapace, L. W. and Kuivila, H. G., J. Am. Chem. Soc., **86**, 3047 (1964).

10. Neumann, W. P., Synthesis, 665 (1987).

11. Kuivila, H. G., Accounts Chem. Res., **1**, 299 (1968).

12. Beckwith, A. L. J., Tetrahedron, **37**, 3073 (1981).

13. Stork, G. and Kahn, M., J. Am. Chem. Soc. **107**, 500 (1985).

14. The Hand Book of Chemistry and Physics Ed. West, R.C., The Chemical Rubber Company, Cleveland, (1969)