6-1990

The synthesis of allylic organotin compounds for the enantioselective formation of homoallylic alcohols

Jean-Claude David Abed
Union College - Schenectady, NY

The Synthesis of Allylic Organotin Compounds for the Enantioselective Formation of Homoallylic Alcohols

By

Jean-Claude David Abed

****

Submitted in partial fulfillment
of the requirements for
Honors in the Department of Chemistry

UNION COLLEGE

June, 1990

Abstract

Allylic tins when reacted with aldehydes are known to be diastereoselective for the resulting homoallylic alcohols. It is believed that a diastereomeric transition state can be created if the allylic tin contains a chiral ligand. Enantiomerically enriched α-pinene was chosen for the chiral ligand and brominated by an electrophilic addition of HBr to form enantiomerically enriched endo-2-bromobornane. This was then reacted with various alkyltin anions prepared from the chlorides, R_3SnCl (R=Ph, Bu, & Me). Of the alkyltin chlorides chosen Me_3SnCl produced the desired product in the best yield; the others were either very slow in reacting or unreactive. The final step was the addition of an allylic group to the organotin compound. Crotyl and cinnamyl were the allylic groups chosen. Model compounds were prepared to investigate attaching crotyl and cinnamyl to tin. The cinnamyl group was chosen since it is known to go by way of a cyclic transition state, when attached to an organometallic compound and reacted with an aldehyde. In forming cinnamyldimethylisobornyltin, the chiral allylic tin, a rearrangement of the double bond on the cinnamyl group occurred and the product was a mixture of two isomers. Because of this and the very low yield, the final reaction with the aldehyde was not carried out.

I would like to acknowledge and thank Professor McGahey for his instruction and friendship, which has enabled me to complete this project, as well as helping me decide my future.

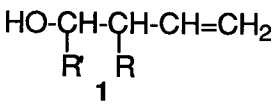
Table of Contents

Table of Figures

Introduction:

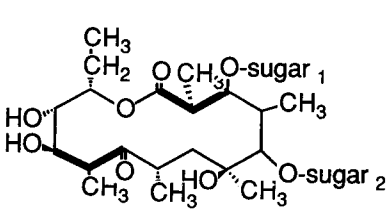
The goal of this project was to determine if it would be possible to synthesize enantiomerically pure homoallylic alcohols by using organotin compounds containing a chiral ligand.

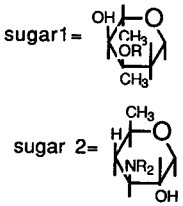
Homoallylic alcohols with the following basic structure:



1

are important pharmaceutically because they are the "building blocks" for the synthesis of macrocyclic antibiotics, especially when R= CH_3. An example of an antibiotic is erythromycin[1].



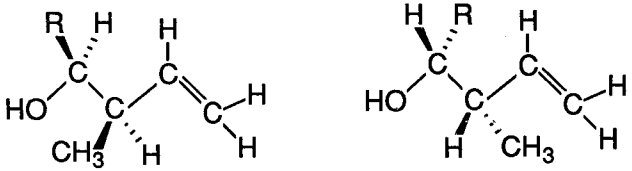


The dark lines represent the units derived from the homoallylic alcohols.

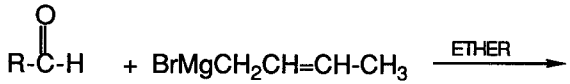
The enantiomeric purity is very important to drug companies, since one enantiomer may have different and/or harmful biochemical effects on the human body. So in synthesizing an antibiotic, complete stereochemical control is desired, in order to be able to produce a synthetic

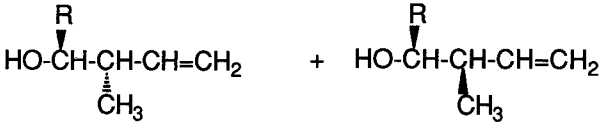
antibiotic with the exact stereochemical makeup as that of the natural counterpart.

A pair of enantiomers are two compounds that are mirror images of each other, as well as being nonsuperimposable. A simple example is your hands. The following is an example of a homoallylic alcohol and its enantiomer.



A traditional synthesis of homoallylic alcohols was by way of Grignard reactions:





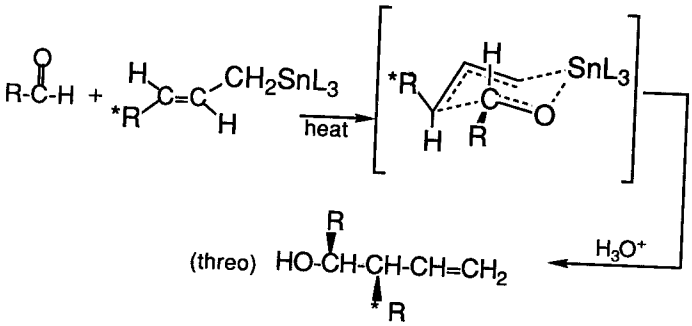
Erythro
(and its enantiomer)

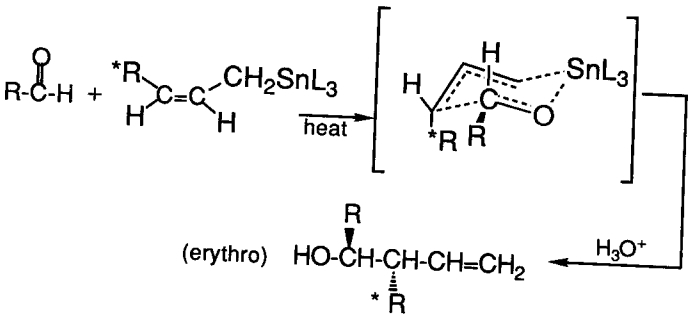
Threo
(and its enantiomer)

However, as shown, this procedure gives a mixture of the diastereomers, which are stereo-isomers but not enantiomers.

So this procedure was inadequate, and a better procedure had to be found.

Another approach was the use of certain organometallic reagents, such as allylic organotins, in reactions with aldehydes[2]. This is known to be diastereoselective, in that the *trans* alkene will give a racemic mixture of the *threo* diastereomer, and the *cis* alkene a racemic mixture of the *erythro* diastereomer.

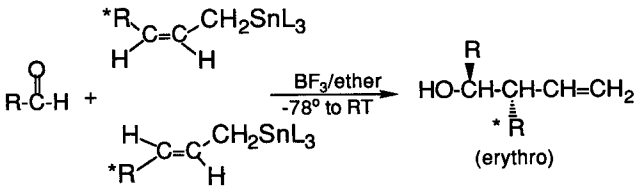




The above addition reaction proceeds through a cyclic, chair-like transition state. This transition state is the reason that one of the diastereomers is exclusively favored over the other.

Yet there are a few problems with this approach. First the pure alkene isomers are not readily obtainable, and secondly the end product is still a mixture of the two enantiomers.

The first problem was later solved by Dr. Y. Yamamoto and his coworkers[3]. They discovered that the acid-catalyzed addition of allylic organotins to aldehydes occurred readily even at low temperatures to give only the *erythro* homoallylic alcohol from either *cis* or *trans* alkenes.



Unlike the non acid-catalyzed addition reaction this is presumed to follow through an acyclic transition state.

Proposal:

Given that it is possible to select a particular diastereomer in the addition reaction, can a approach be found to further

select for a single enantiomer?

Each enantiomer has the same energy of activation, so they form at the same rates. In order to form one enantiomer in excess of the other, their respective transition states would have to be of different energies, or diastereomeric. It is our feeling that we might be able to create diastereomeric transition state by adding a chiral ligand to the tin atom.

Ideally the chiral ligand should be available in pure form and cheap. Many terpene-derived groups meet these requirements. a-Pinene and its Bornane derivative was chosen for our work.

The project was carried out in three parts. The first part was concerned with the synthesis of the chiral ligand, to be later attached to the alkyltin compound. Once the chiral ligand was synthesized and purified, optical rotation values were determined, and it was further characterized by NMR, IR, GC and melting point.

The second part was then the attachment of the chiral ligand to various alkyltin compounds. Of the alkyltin compounds used trimethyltin chloride gave the best yield. This was also characterized.

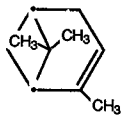
Finally, in the third part either a cinnamyl or crotyl group was added to the previously synthesized alkyltin compound. This product was then characterized so that it could be used to react with aldehydes in an attempt to form enantiomerically pure homoallylic alcohols.

Theory and Results

Part 1: The Synthesis of a Chiral Ligand

Theory:

α-Pinene was chosen as the starting material for the chiral ligand because of its two chiral centers, denoted by dots in the diagram.

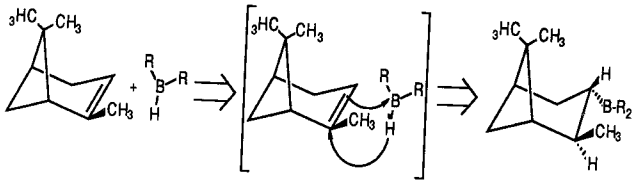


α-pinene

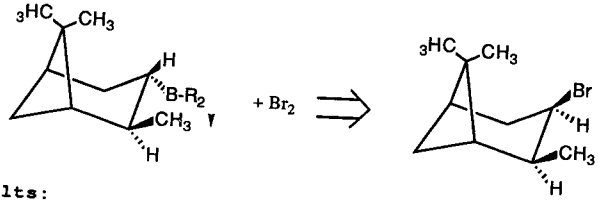
To attach this compound to our allylic tin compound an alkyl bromide was required. Two products were possible, one with the bromine on the more substituted carbon, and the other with the bromine on the less substituted carbon. At first, the product with the bromine on the less substituted carbon of the double bond was desired. This meant adding hydrogen bromide in an anti-Markovnikov manner. To do so, a hydroboration reaction followed by bromination was attempted since this is known to give the expected results.

The mechanism for this class of reactions is as follows. In using BH_3 or BHR_2 the interactions taking place are between the H, the B, and the p-electrons of the double bond . (The bulkiness of the R groups merely acts to increase the regioselectivity) In borane the hydrogen is more electronegative then boron. As a result, it acts as a hydride ion and bonds to the more substituted double bond carbon. Both the hydrogen and boron add simultaneously in a

carbon. Both the hydrogen and boron add simultaneously in a *syn* fashion from underneath the pinene to give a *trans* product.



Once this is achieved it is reacted with Br_2 in the presence of a base. A backside electrophilic attack at boron by bromine gives the bromination of the less substituted double bond carbon with an inversion of configuration.



Results:

i. <u>The Preparation of 3-Bromopinane:</u>

Reaction 1:

In this reaction 9-borabicyclo[3.3.1]nonane (9-BBN) was used since it is known to give even higher yields of the less substituted product then normally expected with other boranes. This is true because of the bulkiness of the bicyclo[3.3.1]nonane group. The added steric hindrance

more favored.

An NMR and IR spectrum (figure 1 & 2) were taken of α-pinene to use as references.

The α-pinene was reacted with 9-BBN in THF and the solvent removed. NMR and IR spectra were taken of the resulting product, Alpine-Borane, to determine if all of the α-pinene had reacted.

IR (figure 3)

3210 cm^{-1}	large & broad	-OH or -BH
1705 cm^{-1}	medium	C=O
1650 cm^{-1}	no peak	C=C

The peaks at 3210 cm^{-1} and 1705 cm^{-1} would tend to indicate that the expected product was not present. However the peaks could also be resulting from -BH stretching. In light of this 3.48 g of the product was brominated. Aqueous sodium hydroxide was added at completion of the reaction to destroy any remaining Br_2. The resulting product was finally isolated by passing it through silica gel.

IR (figure 4)

3400 cm^{-1}	narrowed	-OH or -BH
1725 cm^{-1}	medium	C=O
1650 cm^{-1}	no peak	C=C
680 cm^{-1}	medium	C-Br

There still are two peaks at 3400 cm^{-1} (although narrowed) and 1725 cm^{-1}. However, there was also a peak corresponding

Figure 1: HNMR of α-Pinene

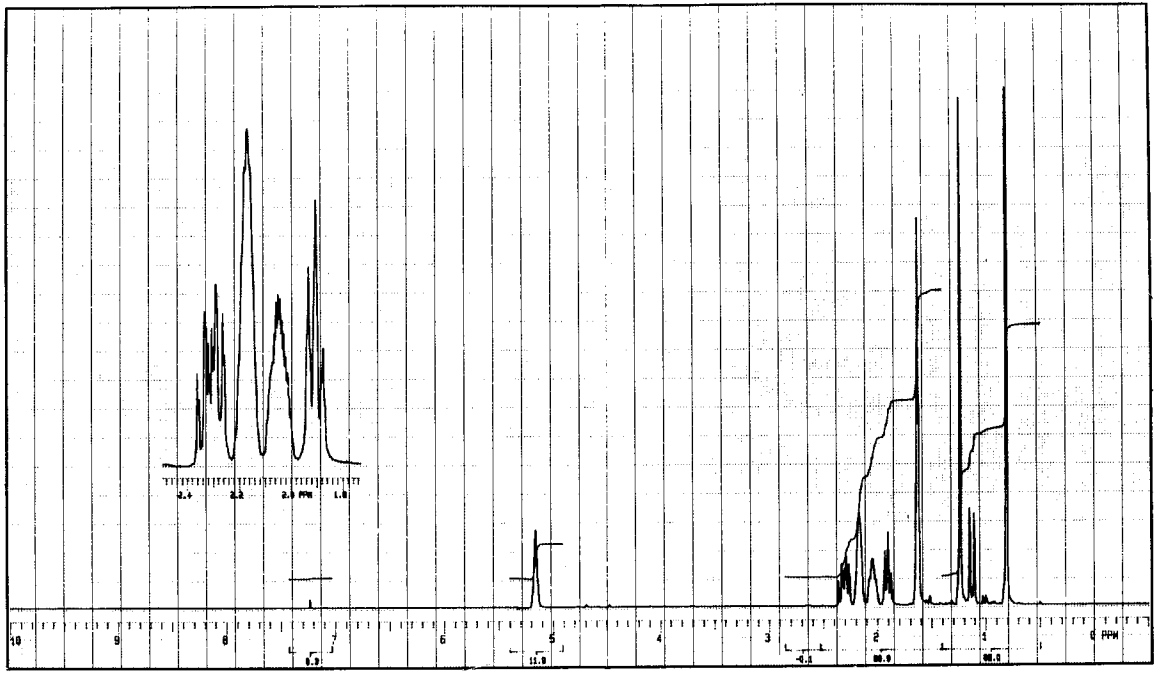

PART NO. 997339
CHART & SERIES
2.4
2.2
2.0 PPM
1.8
10
9
8
7
6
5
4
3
2
1
0 PPM
SAMPLE
A-PINENE
ADED

Figure 2: IR of α-Pinene

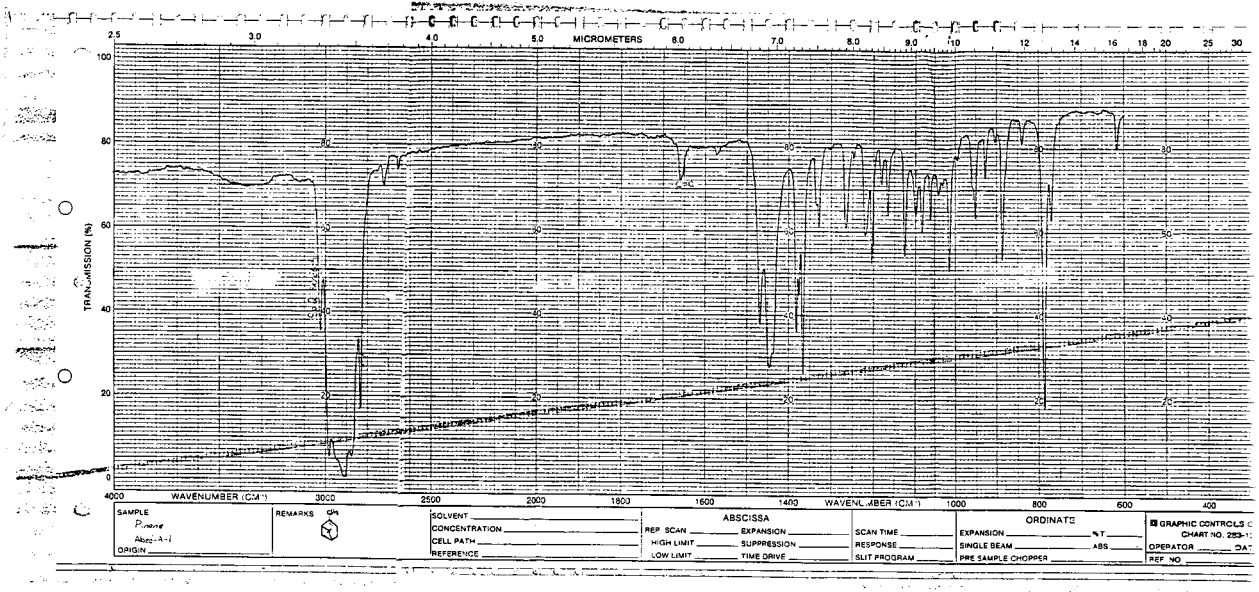

2.5
3.0
4.0
5.0
MICROMETERS
6.0
7.0
8.0
9.0
10
12
14
16
18
20
25
30
100
80
60
40
20
0
TRANSMISSION (%)
4000
WAVENUMBER (CM⁻¹)
3000
2500
2000
1800
1600
1400
WAVENUMBER (CM⁻¹)
1000
800
600
400
SAMPLE
Pinene
Abbe-A-1
ORIGIN
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP. SCAN
EXPANSION
HIGH LIMIT
SUPPRESSION
LOW LIMIT
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
%T
SINGLE BEAM
ABS
PRE SAMPLE CHOPPER
GRAPHIC CONTROLS
CHART NO. 283-1
OPERATOR
DA
REF. NO.

Figure 3: IR of Alpine-Borane (crude)

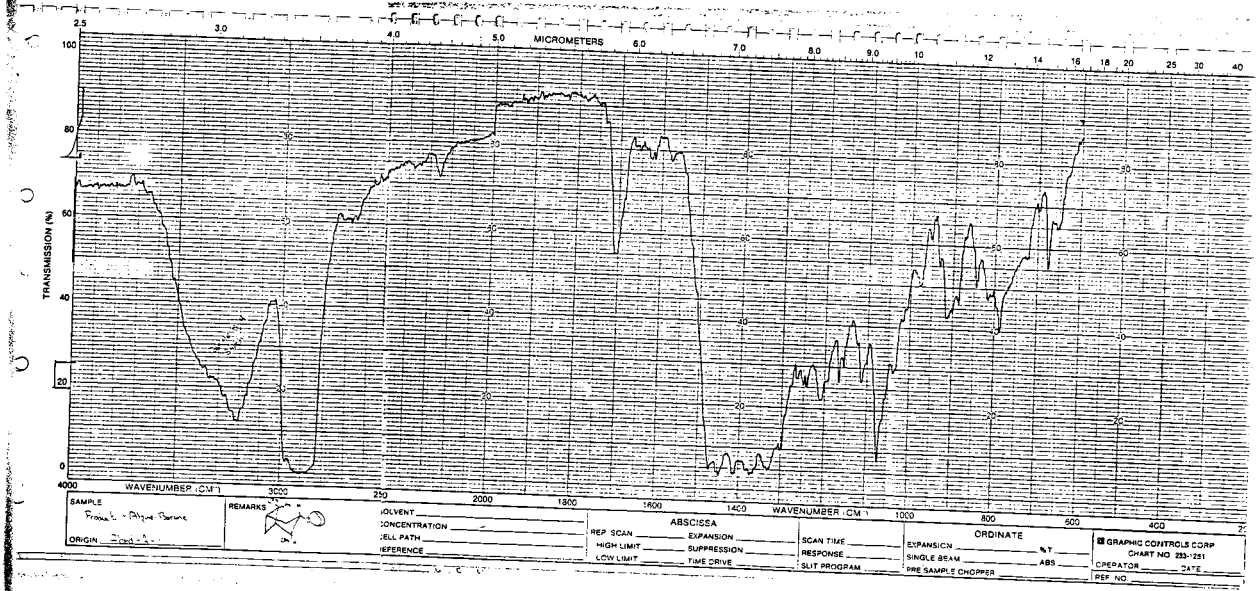
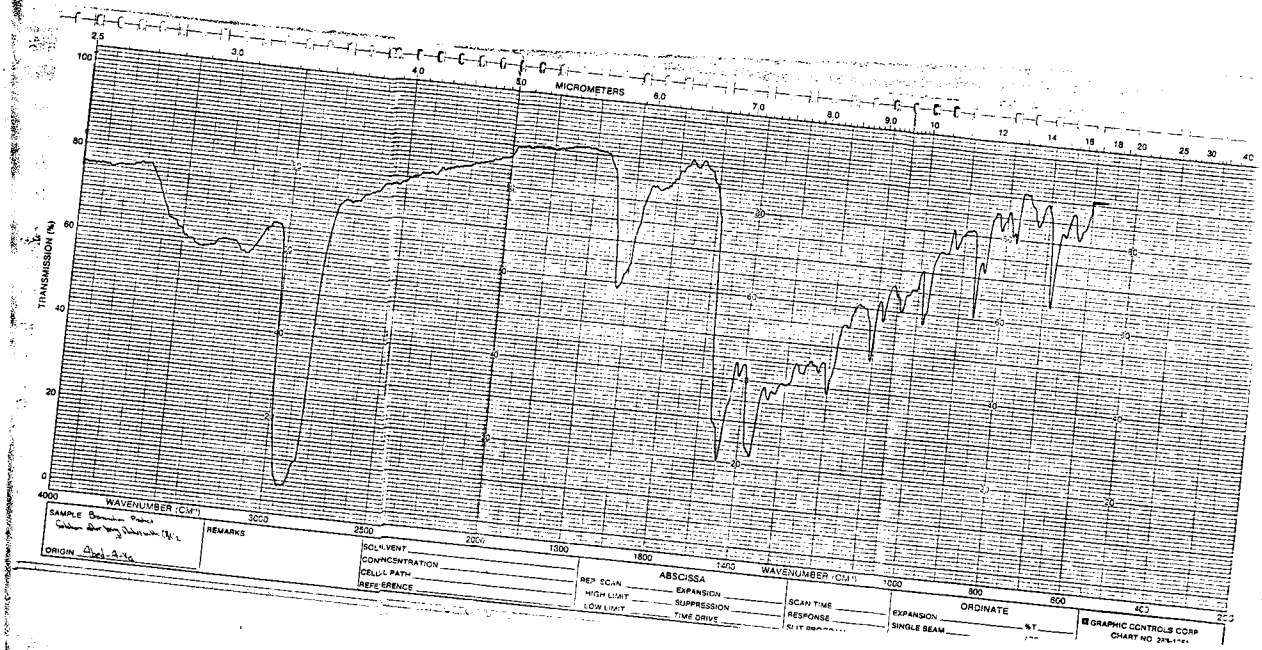
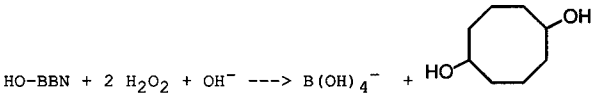

2.5
3.0
4.0
5.0
MICROMETERS
6.0
7.0
8.0
9.0
10
12
14
16
18
20
25
30
40
100
80
60
40
20
0
TRANSMISSION (%)
4000
WAVENUMBER (CM-1)
3000
2500
2000
1800
1600
1400
WAVENUMBER (CM-1)
1000
800
600
400
SAMPLE
Product + Polyol Blend
ORIGIN
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP SCAN
HIGH LIMIT
LOW LIMIT
EXPANSION
SUPPRESSION
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
%T
SINGLE BEAM
ABS
PRE SAMPLE CHOPPER
GRAPHIC CONTROLS CORP
CHART NO 253-1251
OPERATOR
DATE
REF NO

Figure 4: IR of Alpine-borane Brominated product (after chromatography)


MICROMETERS
2.5
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
12
14
16
18
20
25
30
40
TRANSMISSION (%)
100
80
60
40
20
0
WAVENUMBER (CM-1)
4000
3500
3000
2500
2000
1500
1800
1600
1400
1200
1000
900
800
700
600
400
200
SAMPLE
ORIGIN
REMARKS
SOLVENT
CONNCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP. SCAN
HIGH LIMIT
LOW LIMIT
EXPANSION
SUPPRESSION
TIME DRIVE
SCAN TIME
RESPONSE
ORDINATE
EXPANSION
SINGLE BEAM
%T
GRAPHIC CONTROLS CORP

to a C-Br stretch which would tend to indicate that there may also be some expected product.

The bromination reaction was again tried with 3.48 g Alpine-borane. At the completion of the bromination reaction the product was washed with NaOH as before but also with 2.89 mL (30%) H_2O_2, and with 5.4 mL NaOH(3M) in order to remove any remaining borane by oxidizing it.



IR (figure 5)

3420 cm^{-1}	narrowed	-OH or -BH
1730 cm^{-1}	medium & sharp	C=O
1650 cm^{-1}	no peak	C=C
660 cm^{-1}	no peak	C-Br

Again the peaks at 3420 cm^{-1} and 1730 cm^{-1} remained, and in addition, the C-Br stretch peak was no longer present. Therefore, this procedure was no longer continued.

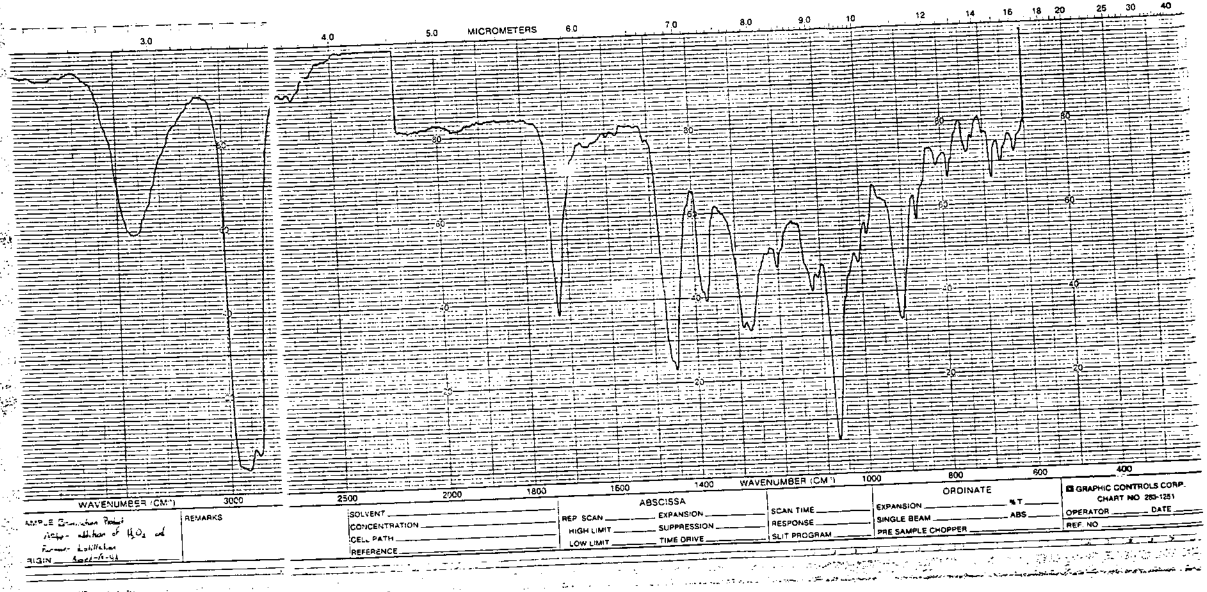
Reaction 2:

In this reaction BH_3•THF (1M) was used and added to α-pinene in a 1 to 2 mol ratio, respectively.

$$2\,\alpha\text{-pinene} + BH_3\text{•THF} \longrightarrow Ipc_2BH$$

Then CH_3OH was added in same mole ratio as the BH_3•THF to methanolyze the dialkylborane.

Figure 5: Brominated product of Alpine-Borane



MICROMETERS
WAVENUMBER (CM⁻¹)
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP SCAN
HIGH LIMIT
LOW LIMIT
EXPANSION
SUPPRESSION
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
SINGLE BEAM
PRE SAMPLE CHOPPER
%T
ABS
GRAPHIC CONTROLS CORP.
CHART NO 283-1251
OPERATOR
DATE
REF. NO

$$Ipc_2BH + CH_3OH \longrightarrow Ipc_2BOCH_3 + H_2$$

An excess of Br_2 was added, in anticipation of a backside electrophilic attack at the boron, resulting in the expected product with an inversion of configuration.

$$Ipc_2BOCH_3 + 2Br_2 + 3\ CH_3O^- \longrightarrow 2\ IpcBr + B(OCH_3)_4 + 2Br^-$$

At the completion of the bromination, additional $NaOCH_3$ was added to destroy any remaining Br_2. The product was then washed and isolated by evaporating the solvent under vacuum.

IR (figure 6)

3380 cm^{-1}	large & broad	-OH
1710 cm^{-1}	medium	C=O
1650 cm^{-1}	no peak	C=C
660 cm^{-1}	no peak	C-Br

HNMR (figure 7)

4.05 ppm	quintet	H on carbinol carbon
4.35 ppm	multiplet	H on C-Br carbon

As with the reaction with HBBN the product seemed to be predominantly a mixture of the oxidized α-pinene, (=pinanol), with some presence of the brominated pinane. In light of this, the synthesis of the less substituted brominated product was abandoned.

Figure 6: Brominated product of Alpine-Borane (trial 2)

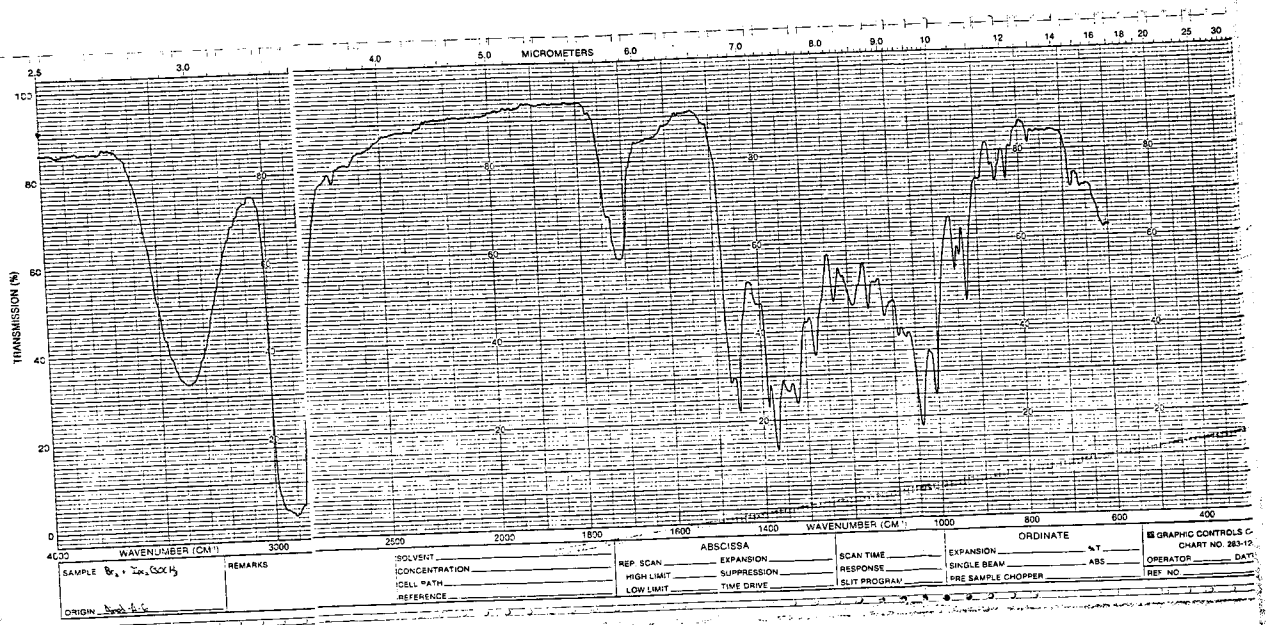

MICROMETERS
2.5
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
12
14
16
18
20
25
30
TRANSMISSION (%)
100
80
60
40
20
0
WAVENUMBER (CM⁻¹)
4000
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
SAMPLE Br₂ + Zn(OCH₃)₂
ORIGIN Sadtler Lab
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP. SCAN
EXPANSION
HIGH LIMIT
SUPPRESSION
LOW LIMIT
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
%T
SINGLE BEAM
ABS
PRE SAMPLE CHOPPER
GRAPHIC CONTROLS C
CHART NO. 283-12
OPERATOR
DATE
REF. NO.

Figure 7: HNMR of crude 3-Bromopinane

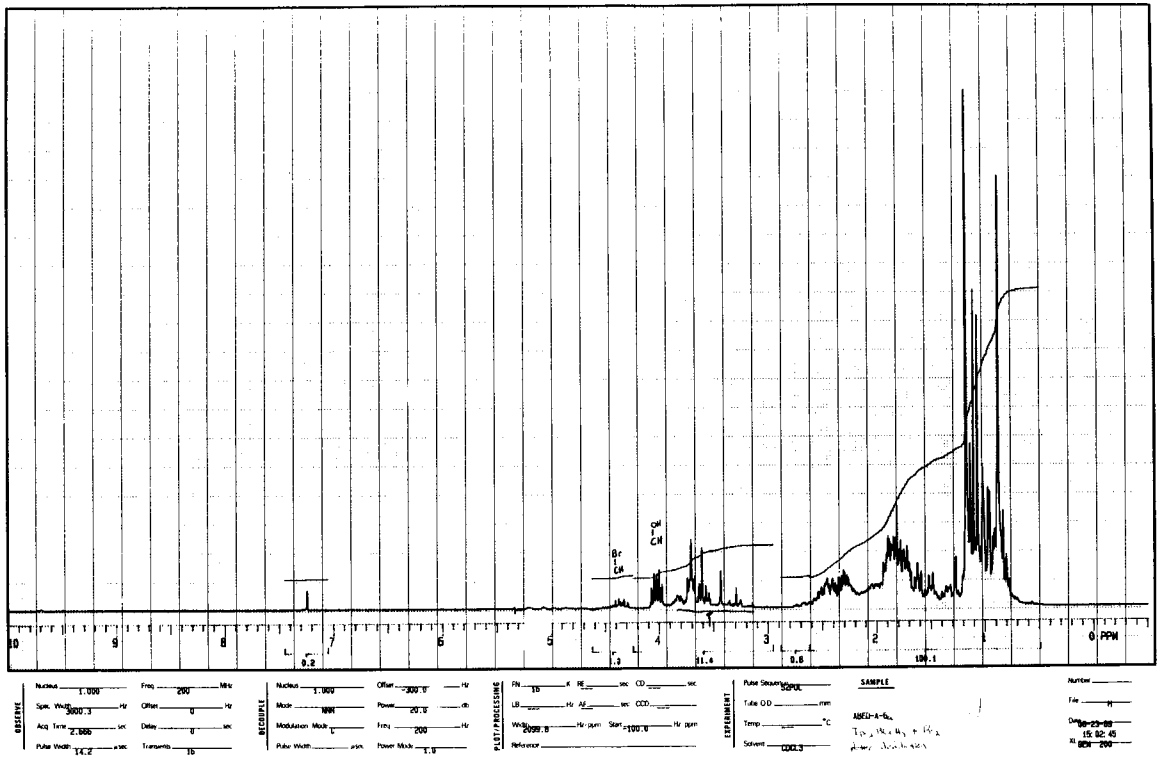


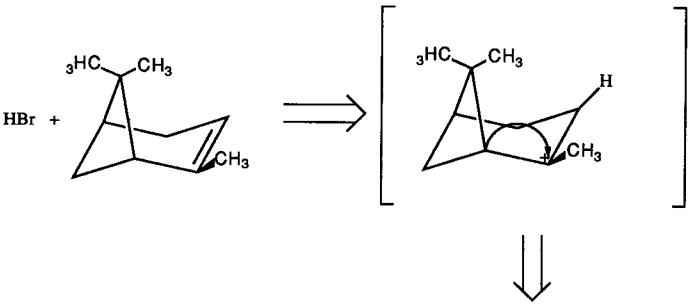
CHART XL SERIES
PART NO. 997259
10
9
8
7
6
5
4
3
2
1
0 PPM
Br
CH
OH
CH
OBSERVE
Nucleus 1.000
Freq 200 MHz
Spec. Width 3000.3 Hz
Offset 0 Hz
Acq. Time 2.666 sec
Delay 0 sec
Pulse Width 14.2 usec
Transmtr 16
DECOUPLE
Nucleus 1.000
Offset -200.0 Hz
Mode NNN
Power 20.0 db
Modulation Mode L
Freq 200 Hz
Pulse Width usec
Power Mode 1.0
PLOT/PROCESSING
FN 16
RE sec
CD sec
LB Hz
AF sec
CCD
Width 2099.8 Hz ppm
Start -100.0 Hz ppm
Reference
EXPERIMENT
Pulse Sequence SGPUL
Tube OD mm
Temp °C
Solvent CDCl3
SAMPLE
Number
File H
Date 06-23-98
15:32:45
XL BCM 200

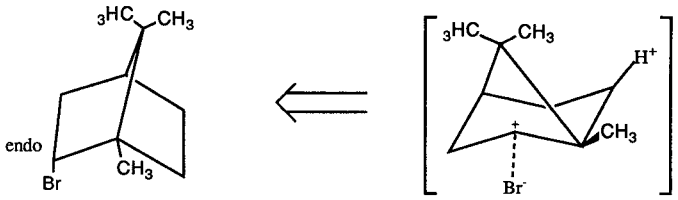
ii. The Preparation of Bornyl bromide:

Theory:

This was carried out by an electrophilic addition of HBr to α-pinene. In this reaction the H of the hydrogen halide, which has a partial positive charge due to the highly polar H-X bond, was added to the pi bond of the alkene at the less substituted carbon, forming an intermediate carbocation. The carbocation then quickly reacted with the negative halide ion yielding the alkyl halide.

However, α-pinene is a bicyclic system with a very strained four membered ring. As a result, before the reaction with the halide ion takes place a rearrangement occurs to relieve the ring strain. The halide ion then reacts with the newly formed carbocation where the ring was originally.





Results:

Reaction 1:

Once α-pinene was reacted with HBr the solution was neutralized with saturated aqueous $NaHCO_3$. The product was vacuum distilled, and two crops were obtained by recrystallizing the distillate from methanol. The white solid was characterized by IR and NMR, melting point, optical rotation, and gas chromatography (figure 10).

Percent Yield of purified product reaction 1 = 45.4%

Melting point
crop 1: 92-95 °C
crop 2: 92°C

Optical Rotation from 'Beilstein'
for α-pinene $[\alpha]_D$= -21 at 20 °C
for 2-bromobornane $[\alpha]_D$= -31.5 at 21°C

Optical Purity
for α-pinene = 88.9%

Optical Rotation
[solvent = $CHCl_3$ & l=1dM]
crop 1: $[\alpha]_D$= -28.1 (at 26°C)
crop 2: $[\alpha]_D$= -27.9 (at 27°C)

IR (figure 8)

3300 cm^{-1}	no peak	-OH
1640 cm^{-1}	small	C=C
650 cm^{-1}	large	C-Br

HNMR (figure 9)

4.3 ppm	multiplet	hydrogen attached to brominated carbon
0.85 ppm	two singlets	methyls on bornyl group
0.93 ppm	singlet	bridgehead methyl

In the IR a sharp peak at 650 cm^{-1} would indicate the stretching vibration of the C-Br bond, and the lack of any OH stretching peaks would indicate that no alcohol formed. However, there was a small peak at 1640 cm^{-1} which would indicate C=C stretching. This was most likely due to some unreacted α-pinene. The HNMR spectrum showed a complex coupling pattern at 4.3 ppm which would also confirm the presence of the brominated product. Finally, the gas chromatogram showed the presence of three peaks, two of which were the 2-bromobornane, and its isomer, fenchyl bromide, the other was α-pinene (as determined by retention time analysis with known sample α-pinene). With these results it can be concluded that the more substituted product was in fact synthesized.

Reaction 2:

Again as above the product was isolated and

Figure 8: IR of Bornyl bromide

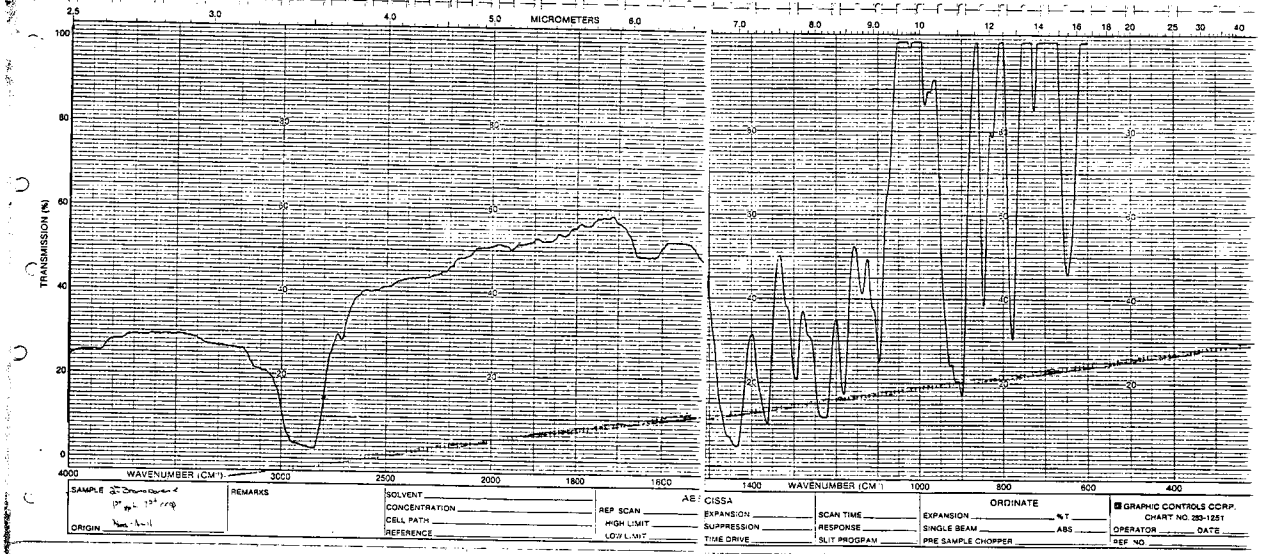
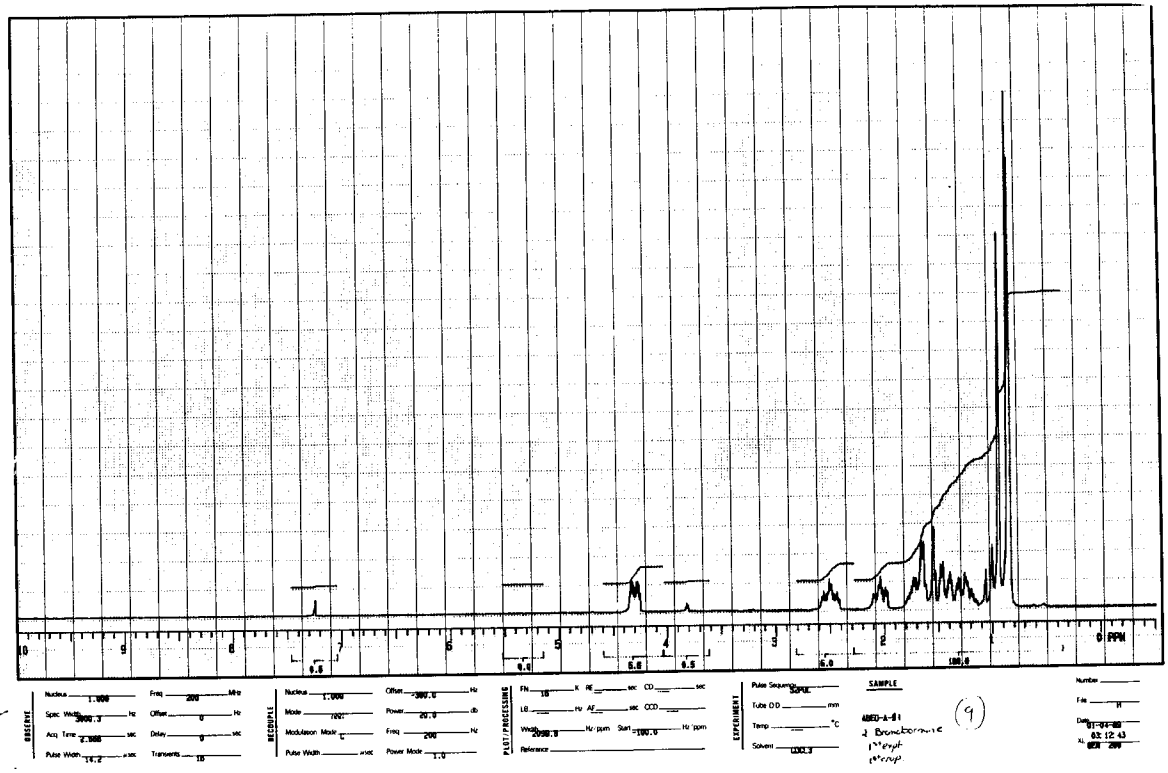

2.5
3.0
4.0
5.0
MICROMETERS
6.0
7.0
8.0
9.0
10
12
14
16
18
20
25
30
40
100
80
60
40
20
0
TRANSMISSION (%)
4000
WAVENUMBER (CM⁻¹)
3000
2500
2000
1800
1600
1400
WAVENUMBER (CM⁻¹)
1000
800
600
400
SAMPLE
ORIGIN
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
REP SCAN
HIGH LIMIT
LOW LIMIT
AE: CISSA
EXPANSION
SUPPRESSION
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
%T
SINGLE BEAM
ABS
PRE SAMPLE CHOPPER
GRAPHIC CONTROLS CORP.
CHART NO. 283-1251
OPERATOR
DATE
REF NO

Figure 9: HNMR of Bornyl bromide


PART NO. 997250
CHART N SERIES
10
9
8
7
6
5
4
3
2
1
0 PPM
RESERVE
Nucleus 1.000
Spec Width 2000.3 Hz
Acq Time 2.995 sec
Pulse Width 14.2 μsec
Freq MHz
Offset 0 Hz
Delay 0 sec
Transients 16
DECOUPLE
Nucleus 1.000
Mode NOE
Modulation Mode C
Pulse Width μsec
Offset -300.0 Hz
Power 40.0 db
Freq 200 Hz
Power Mode 1.0
PLOT/PROCESSING
FN 16 K
LB Hz
Width 2000.0 Hz/ppm
Reference
RE sec
AF sec
Start -100.0 Hz/ppm
CD sec
CCD
EXPERIMENT
Pulse Sequence SINGLE
Tube OD mm
Temp °C
Solvent CDCl3
SAMPLE
ABED-A-81
2 Bromobenzoic
1st expt
1st exp
(9)
Number
File H
Date 01-04-88
XL 08:12:43
BCH 200

characterized.

Percent Yield of purified product crop 2 = 60.0%

Melting point

crop 1: 93-94 °C
crop 2: 92.5-93.5 °C
crop 3: 94-95 °C

Optical Rotation

crop 1: $[\alpha]_D$= -28.0 (at 26°C)
crop 2: $[\alpha]_D$= -27.1 (at 26°C)
crop 3: $[\alpha]_D$= -26.7 (at 27°C)

Both the IR's, NMR's, and the GC's were all the same or very similar to the previous two crops from experiment 1.

Figure 10: G.C. of Bornyl bromide

expt. 1
Creq. 1

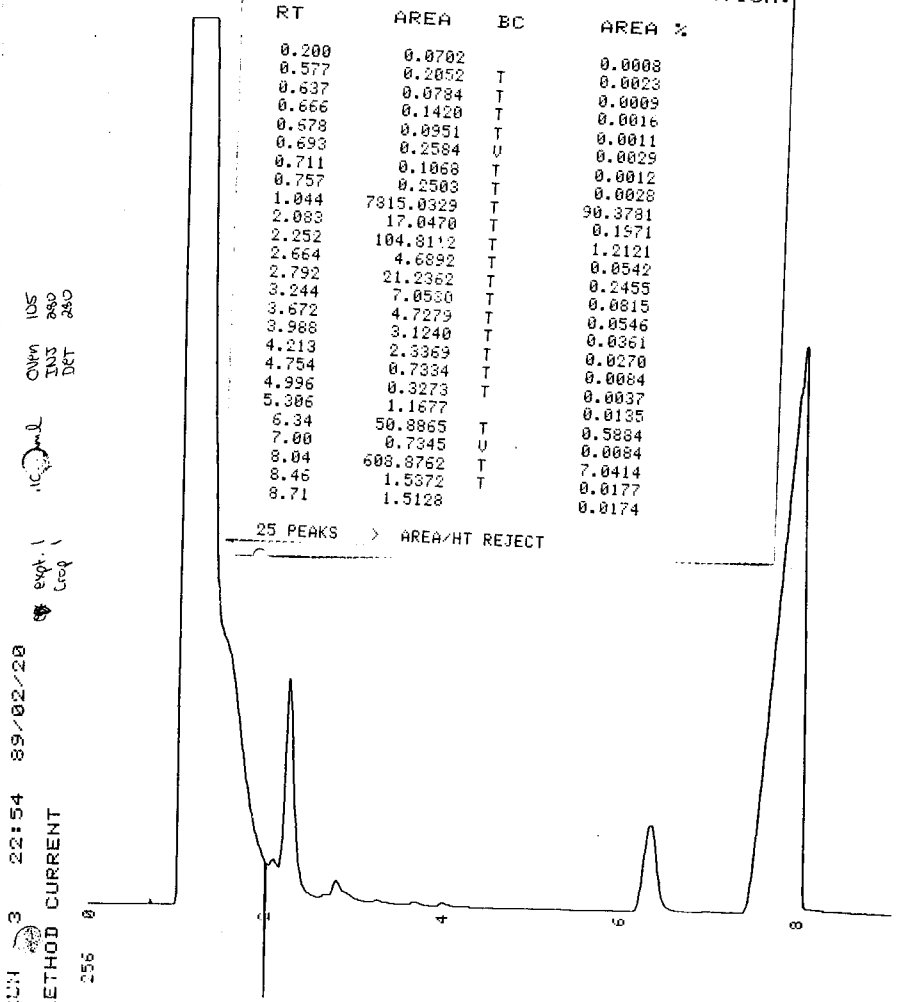
RUN 3 22:54 89/02/20

METHOD CURRENT

CALCULATION:

RT	AREA	BC	AREA %
0.200	0.0702		0.0008
0.577	0.2052	T	0.0023
0.637	0.0784	T	0.0009
0.666	0.1420	T	0.0016
0.678	0.0951	T	0.0011
0.693	0.2584	V	0.0029
0.711	0.1068	T	0.0012
0.757	0.2503	T	0.0028
1.044	7815.0329	T	90.3781
2.083	17.0470	T	0.1971
2.252	104.8112	T	1.2121
2.664	4.6892	T	0.0542
2.792	21.2362	T	0.2455
3.244	7.0530	T	0.0815
3.672	4.7279	T	0.0546
3.988	3.1240	T	0.0361
4.213	2.3369	T	0.0270
4.754	0.7334	T	0.0084
4.996	0.3273	T	0.0037
5.306	1.1677		0.0135
6.34	50.8865	T	0.5884
7.00	0.7345	V	0.0084
8.04	608.8762	T	7.0414
8.46	1.5372	T	0.0177
8.71	1.5128		0.0174

25 PEAKS > AREA/HT REJECT

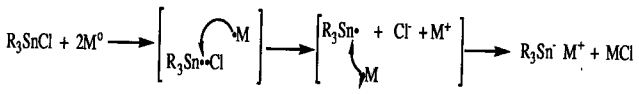


Part2: The Attachment of the Chiral Ligand to the Organotin Compound.

Theory:

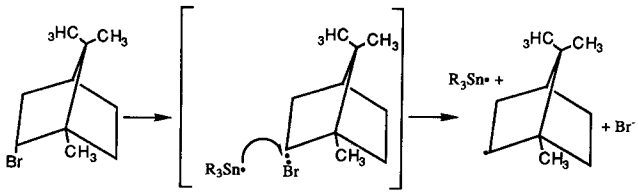
In this reaction the mechanism was a single electron transfer, (SET). For this to occur a good electron-donating nucleophile and a good electron accepting carbon-halogen bond were needed.

The nucleophile used was the organotin anion R_3Sn^-, where R=(Ph, Bu, or Me), synthesized by the following reaction which proceeds by a SET mechanism:



where M= Li or Na

The anion formed was reacted with the bornyl bromide. This proceeded by a SET mechanism to give predominantly the *exo* isomer. The *exo* form of the compound is favored because there is less steric hindrance when the stannyl radical $R_3Sn\bullet$ comes in from the side as opposed as from the bottom. In addition, the observed reactivity of the anion is as follows: Me_3Sn^- > Bu_3Sn^- > Ph_3Sn^- (least reactive). The phenyl rings and the large alkyl groups tend to delocalize the negative charge making it a more stable reactant.



At this stage there exists two free radicals; three different reactions can occur.

1. $R_3Sn\bullet + R^{*}\bullet$ --------> $R_3Sn\text{-}R^{*}$ (fast)

2. $2\ R_3Sn\bullet$ --------> $R_3Sn\text{-}SnR_3$ (slow)

3. $2\ R^{*}\bullet$ --------> $R^{*}\text{-}R^{*}$ (slow)

The first is faster then the last two because of the existence of a solvent cage which reduces the ability of the free radicals to move around. So the organo tin compound with the chiral ligand should be present in a reasonable yield.

Results:

i.<u>The Reaction of Triphenyltin anion with endo-2-bromobornane</u>

Even though it is known that Ph_3Sn^{-} is less reactive than Me_3Sn^{-}, it was tried first, since the phenyls are

easily replaced, and their peaks on a NMR would be separated from those of the bornyl peaks. The problem would be in overcoming the expected decrease in reactivity due to the stabilizing effects of the phenyl rings on the anion. Three reactions were used to produce the anion: two used sodium and the third used lithium.

Reaction 1:

In this reaction Na was used as the metal (M in first diagram) in synthesizing the anion. To do this liquid NH_3 had to be used as a solvent. The endpoint was indicated by a blood red color. After the completion of the reaction between the anion and 2-bromobornane, H_2O_2 was added. This was done in an attempt to convert any existing $Ph_3Sn\text{-}SnPh_3$, produced from the coupling of the anion, as well as any remaining anion, to Ph_3SnOH.

$$Ph_3Sn\text{-}SnPh_3 + H_2O_2 \text{ ----> } 2\ Ph_3SnOH$$

$$Ph_3Sn^- + H_2O_2 \text{ ----> } Ph_3SnH + H_2O \text{ ----> } Ph_3SnOH + H_2\ (g)$$

An IR was taken of the organic phase after being washed with H_2O and the solvent remove under vacuum.

IR (figure 11)

3400 cm^{-1}	small & broad	-OH
3050 cm^{-1}	medium	sp^2 CH stretch on Ph
1380 cm^{-1}	medium	CH_3's on 2-bromobornane
725 & 695 cm^{-1}	strong & sharp	out of phase CH bend on Ph

As shown above there was evidence of the expected product along with some possible Ph_3SnOH or H_2O, from incomplete drying, evident by the OH stretch at 3400 cm^{-1}.

The product was then further isolated by chromatography, and a NMR spectrum was taken.

NMR (figure 12)

7.55 ppm	multiplet	H's on Ph
7.35 ppm	multiplet	"
4.20 ppm	multiplet	H on C-Br carbon of 2-bromobornane
0.8 ppm	2 singlets	2 CH_3's
0.9 ppm	singlet	CH_3 at bridgehead

The NMR spectrum clearly showed the existence of the expected product as well as the presence of some 2-bromobornane (4.2 ppm). However due to the lack of any substantial yield the reaction had to be repeated.

Reaction 2:

Again sodium was used in producing the anion, but after the reaction with 2-bromobornane the resulting product was not washed with H_2O_2 (30%). Instead it was merely washed with H_2O and rotovapped to give a semi-solid product. Further purification of the product was attempted by column chromatography. However, this was unsuccessful and yielded a very small amount of product with a similar NMR spectrum as

Figure 11: IR of crude Triphenylisobornyltin

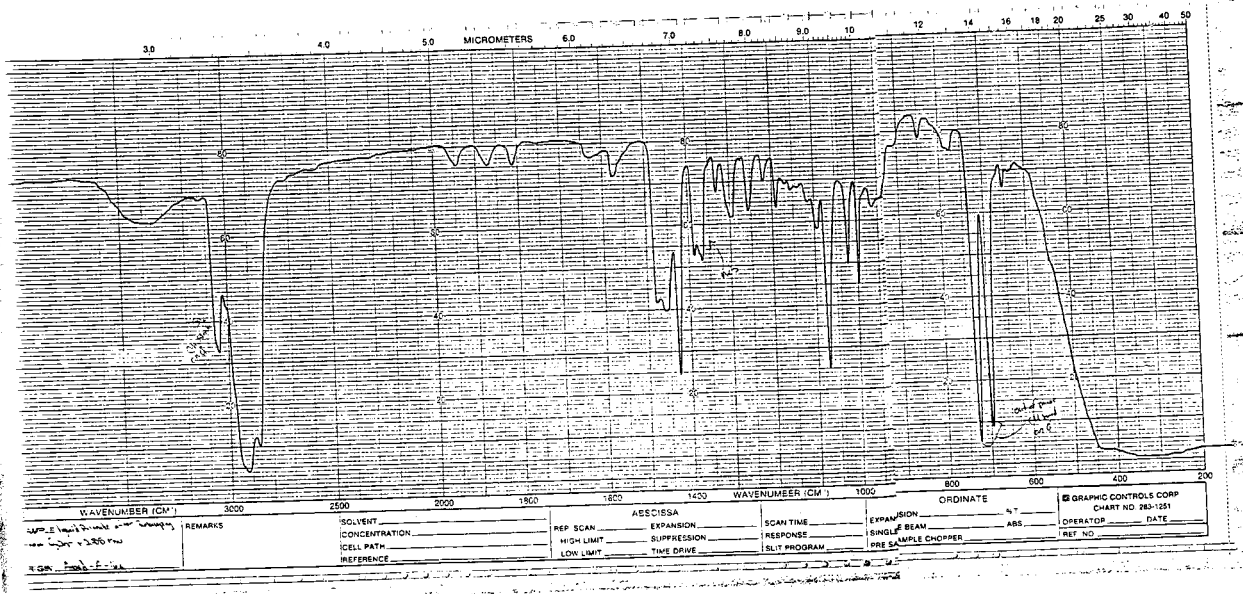
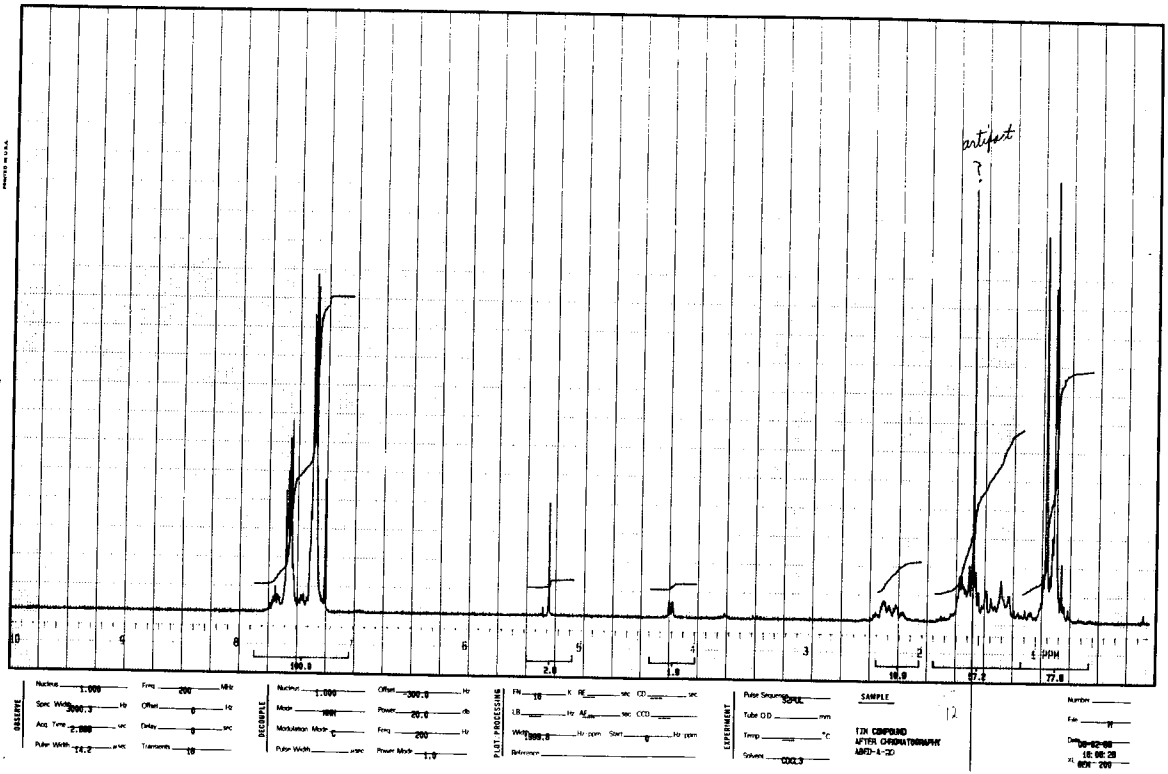

3.0
4.0
5.0
MICROMETERS
6.0
7.0
8.0
9.0
10
12
14
16
18
20
25
30
40
50
WAVENUMBER (CM⁻¹)
3000
2500
2000
1800
1600
1400
WAVENUMBER (CM⁻¹)
1000
800
600
400
200
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP SCAN
HIGH LIMIT
LOW LIMIT
EXPANSION
SUPPRESSION
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
SINGLE BEAM
ABS
SAMPLE CHOPPER
PRE SAMPLE
GRAPHIC CONTROLS CORP
CHART NO. 283-1251
OPERATOR
DATE
REF. NO.

Figure 12: HNMR of Triphenylisobornyltin (after column chromatography, trial 1)


artifact
?
10
9
8
7
6
5
4
3
2
1
PPM
100.0
2.0
1.0
10.0
87.2
77.8
CHART XL SERIES
PART NO. 917150
OBSERVE
DECOUPLE
PLOT PROCESSING
EXPERIMENT
SAMPLE
TJK COMPOUND
AFTER CHROMATOGRAPHY
ABFD-4-2D

the first reaction.

Reaction 3:

This time the anion was formed by using lithium, in THF, instead of sodium due to it being more reactive. Once the anion was formed it was reacted with 2-bromobornane. The resulting crude product was washed with H_2O, but in addition to the previous procedure, the crude product was added to petroleum ether and heated to boiling. Upon cooling it was filtered in an attempt to remove any remaining 2-bromobornane which is not very soluble in petroleum ether.

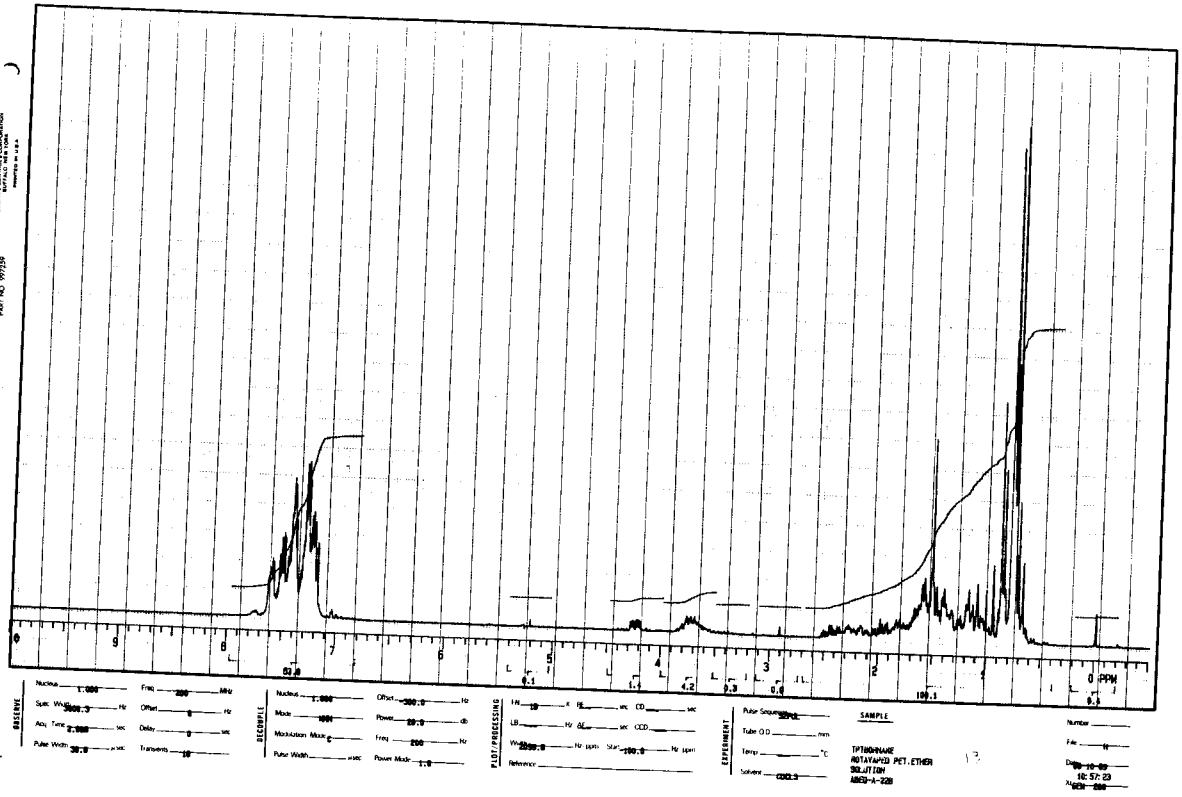
	NMR (figure 13)	
7.2-7.6 ppm	complex splitting	aromatic H's
4.25 ppm	multiplet	H on C-Br of 2-bromobornane
0.8 ppm	2 singlets	2 CH_3's
0.9 ppm	singlet	CH_3 at bridgehead

Again the product was impure, and the yield was extremely low.

ii. The Reaction of Dibutylphenyltin anion with 2-bromobornane

Dibutylphenyltin anion was used in hope that the substitution of two butyl groups for phenyl groups would increase the reactivity of the anion. The anion was formed by using lithium, in THF, and reacted with 2-bromobornane. The crude product was washed with H_2O and rotovapped. A TLC was taken of the product and referenced with a sample of pure 2-bromobornane and dibutylphenyltinbromide. This showed the

Figure 13: HNMR of crude Triphenylisobornyltin (trial 3)


PART NO. 997250
CHART XL SERIES
0 PPM

product to have many impurities including the two reference samples.

HNMR

7.2-7.6 ppm	complex splitting	aromatic H's
4.25 ppm	multiplet	H on C-Br of 2-bromobornane
0.7-0.9 ppm	complex	CH_3's on bornyl & Butyls

Although the peaks a 7.2-7.6 indicate that the product contains aromatics, the complexity of the peaks in the region of 0.7-0.9 ppm makes it difficult to analyze the spectrum. For this reason and the lack of product this reaction was abandoned.

iii. The Reaction of Tributyltin anion with 2-bromobornane

In theory the butyl groups shouldn't be able to stabilize the negative charge of the anion to any reasonable degree, and with the loss of the phenyl groups the stabilization of the anion should be at a minimum. Methyl groups would be even better then the butyl groups but the cost of the tributyltinchloride is much less. However, the chemical shifts of the protons on the butyl groups are in the same region of the protons on the bornane group, making it slightly more difficult to determine a correct ratio for the two groups.

Reaction 1:

In the reaction small amounts of the reactants were used to determine if the reaction would give a good yield of the product. The anion was produced by using lithium, in THF,

and reacted with 2-bromobornane. Once the crude product was isolated after washing, an IR and NMR spectra revealed the presence of the expected product.

Reaction 2:

The same procedure was followed with larger amounts of reactants. The crude product was washed and the solvent distilled off. However the mixture started to decompose during the distillation. The recovered crude product was added to acetone and $KMnO_4$ (3.52 g, 0.022 mols), in an attempt to oxidize any remaining hexabutylditin as was done with the H_2O_2. The crude product was then washed again, and a mass was taken.

To further purify the crude product it was vacuum distilled with four fractions being collected:

fraction	pressure (mm Hg)	Temp (^oC)
1	0.1	84-94
2	0.1	95-100
3	0.1	100-105
4	0.1	106-108

The IR's and NMR's of each fraction were identical.

IR (figure 14)

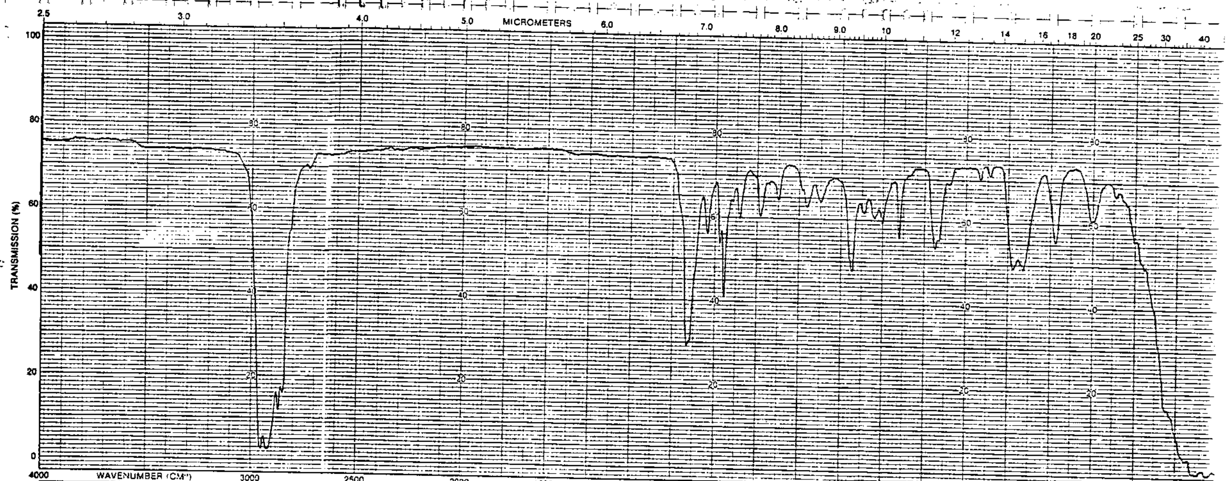
1370 cm^{-1}	sharp	CH_3's on 2-bromobornane
590 cm^{-1}	small	Sn-C bond

NMR (figure 15)

0.85 ppm	multiplet

Again it is difficult to differentiate the peaks in the region of 0.8-1.0 ppm, but the IR indicated that the sample contains the bornyl group, from the CH_3 stretch, as well as

Figure 14: IR of Tributylisobornyltin
(trial 1)



SAMPLE Bu_3Sn-330 Abd-2-38b After final distillation

ORIGIN Fraction 2

REMARKS

SOLVENT ______
CONCENTRATION ______
CELL PATH ______
REFERENCE ______

ABSCISSA
REP. SCAN ______ EXPANSION ______
HIGH LIMIT ______ SUPPRESSION ______
LOW LIMIT ______ TIME DRIVE ______

SCAN TIME ______
RESPONSE ______
SLIT PROGRAM ______

ORDINATE
EXPANSION ______ %T ______
SINGLE BEAM ______ ABS ______
PRE SAMPLE CHOPPER ______

GRAPHIC CONTROLS CORP
CHART NO. 283-1251
OPERATOR ______ DATE ______
REF. NO. ______

Figure 15: HNMR of Tributylisobornyltin

(trial 1)

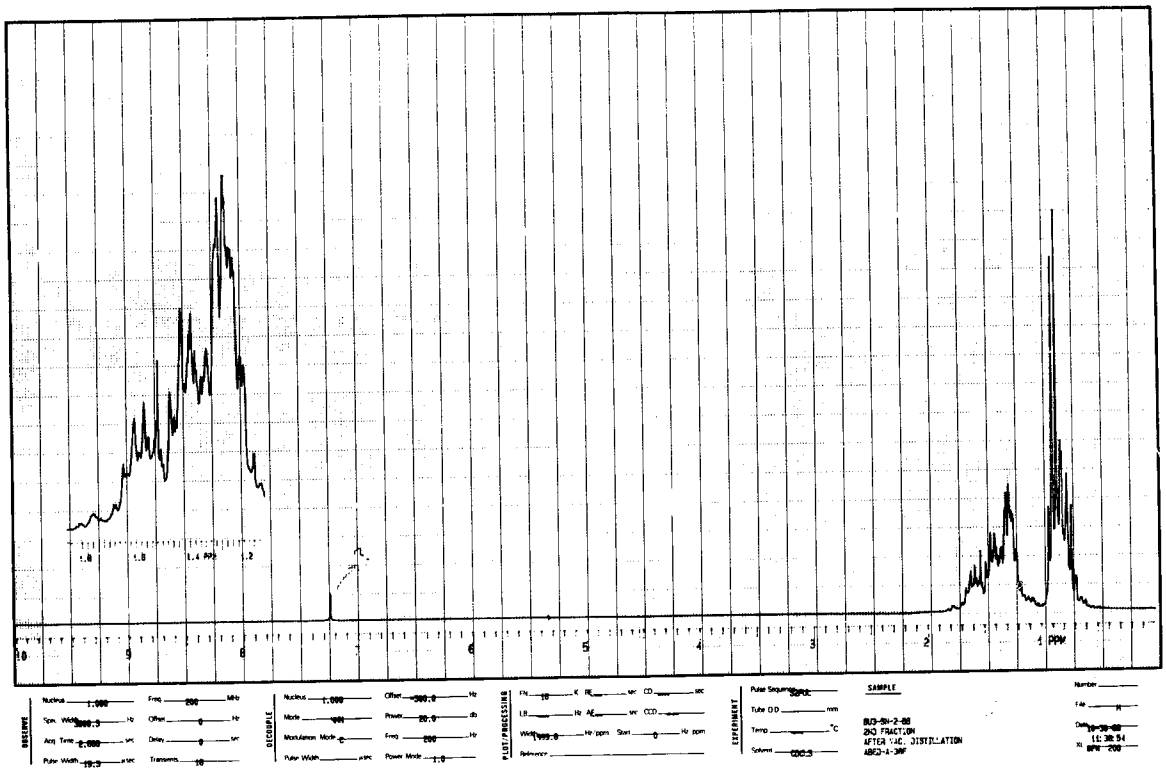


CHART XL SERIES
PART NO. 997259
1.8
1.6
1.4 PPM
1.2
10
9
8
7
6
5
4
3
2
1 PPM
OBSERVE
Nucleus 1.000
Spec. Width 3000.0 Hz
Acq Time 2.000 sec
Pulse Width 19.0 usec
Freq 200 MHz
Offset 0 Hz
Delay 0 sec
Transients 16
DECOUPLE
Nucleus 1.000
Mode wbi
Modulation Mode C
Pulse Width usec
Offset -500.0 Hz
Power 20.0 db
Freq 200 Hz
Power Mode 1.0
PLOT/PROCESSING
FN 16 K RE sec CD sec
LB Hz AE sec CCD sec
Width 1999.9 Hz ppm Start 0 Hz ppm
Reference
EXPERIMENT
Pulse Sequence sgnoe
Tube OD mm
Temp °C
Solvent CDCl3
SAMPLE
BU3-SH-2-88
2ND FRACTION
AFTER VAC. DISTILLATION
ABE2-A-30F
Number
File
Date 10-20-88
11:38:54
XL 6PM -200

a C-Sn bond.

Reaction 3:

Again the reaction was stepped up and a crude product was washed as before. However, in addition it was washed with saturated KF (45 mL). The KF replaces a chlorine, of the R_3SnCl, with a fluorine. The fluorines on the alkyltin then bridge between tin atoms to form an insoluble polymer which precipitates out of solution.

An attempt was then made at further purifying the crude by high vacuum distillation with a fractionating column and was unsuccessful. So a high vacuum simple distillation was done. Carbon NMR as well as proton NMR spectra were taken of the distillate.

HNMR (figure 16)

complex splitting pattern in the region of 0.8 - 1.7

CNMR (figure 17)

8.87 ppm	CH_2 of butyl group attached to Sn
9.49 ppm	CH_2 of butyl group one away from Sn
10.11 ppm	CH_3 of butyl group
10.41 ppm	CH_2 of butyl group attached to CH_3
13.87 ppm	CH_3 on bornyl group

iv. The Reaction of Trimethyltin anion with 2-bromobornane

In the last attempt Me_3SnCl was used. This compound has been shown to react with 2-bromobornane to produce trimethylisobornyltin in good yield, by Dr. H. Kuivila. The

Figure 16: HNMR of Tributylisobornyltin
(trial 2)

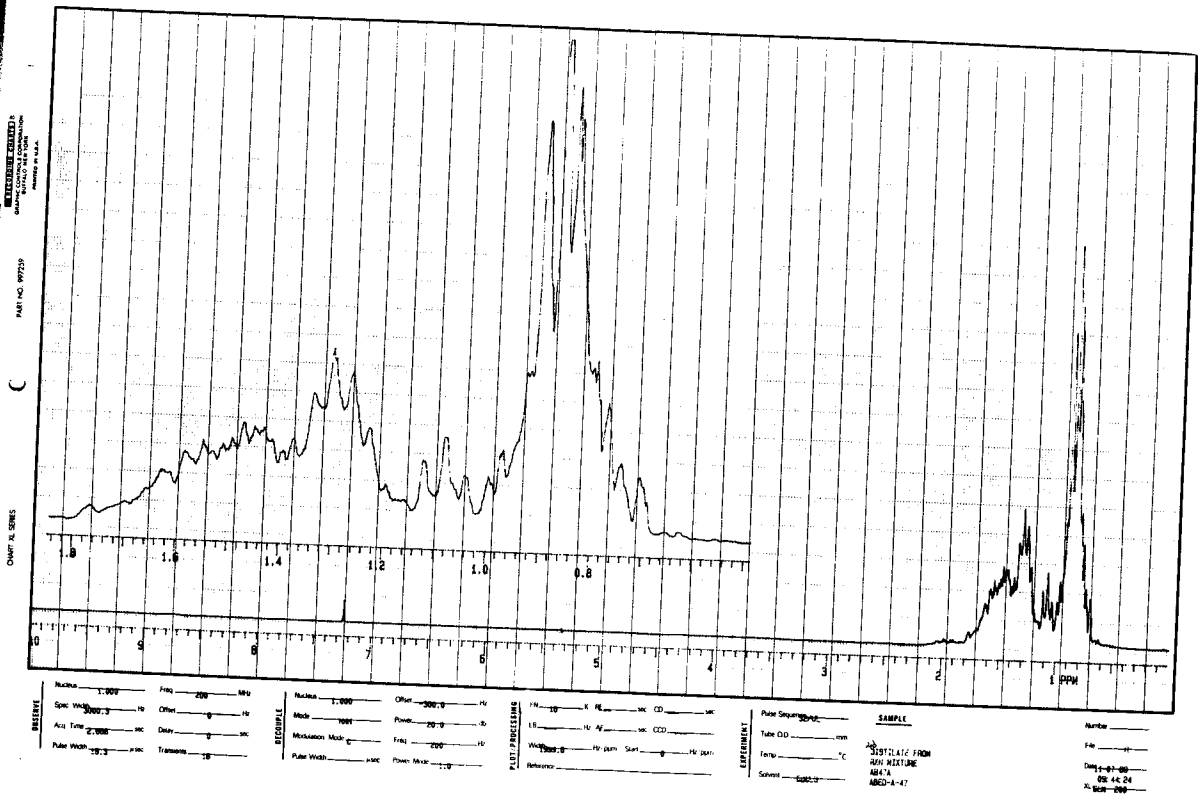
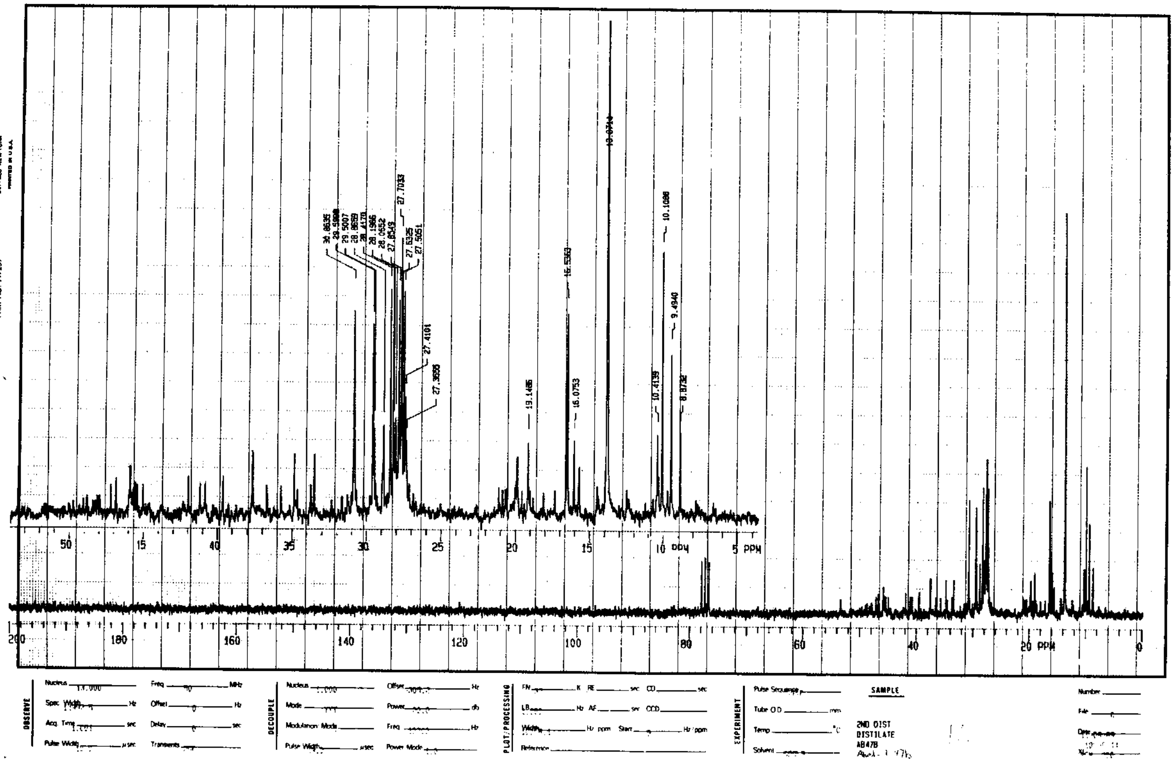

1.8
1.6
1.4
1.2
1.0
0.8
10
9
8
7
6
5
4
3
2
1 PPM
PART NO. 997539
CHART XL SERIES
RESERVE
Nucleus 1.000
Spec Width 3000.3 Hz
Acq Time 2.000 sec
Pulse Width 19.3 µsec
Freq 200 MHz
Offset 0 Hz
Delay 0 sec
Transients 16
DECOUPLE
Nucleus 1.000
Mode noe
Modulation Mode C
Pulse Width µsec
Offset -300.0 Hz
Power 20.0 db
Freq 200 Hz
Power Mode 1.0
PLOT PROCESSING
FN 10 K
LB Hz
WW Hz ppm
Reference
RE sec
AF sec
Start 0 Hz ppm
CD sec
CCD
EXPERIMENT
Pulse Sequence
Tube O.D. mm
Temp °C
Solvent
SAMPLE
DISTILLATE FROM
RAW MIXTURE
AB4"A
ABCD-A-47
Number
File
Date 1-01-80
09:44:24
XL SCR 200

Figure 17: CNMR of Tributylisobornyltin
(trial 2)



procedure used to synthesis trimethylisobornyltin in Dr. Kuivila's paper was followed.

Reaction 1:

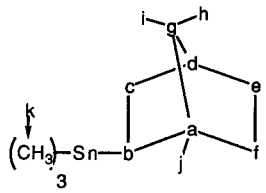
Once the crude product was washed by H_2O, by the same steps used in washing the Bu_3Sn2BB, (tributylisobornyltin), it was purified by high vacuum distillation. The distillate was then characterized by NMR and IR.

Pressure	temp.(°C)	fraction
0.2	54-60	1

mass of fraction 1: 5.18 g

HNMR (figure 18)

0.07 ppm	singlet	Methyl H on tin
0.85 ppm	2 singlets	Methyl on bornane



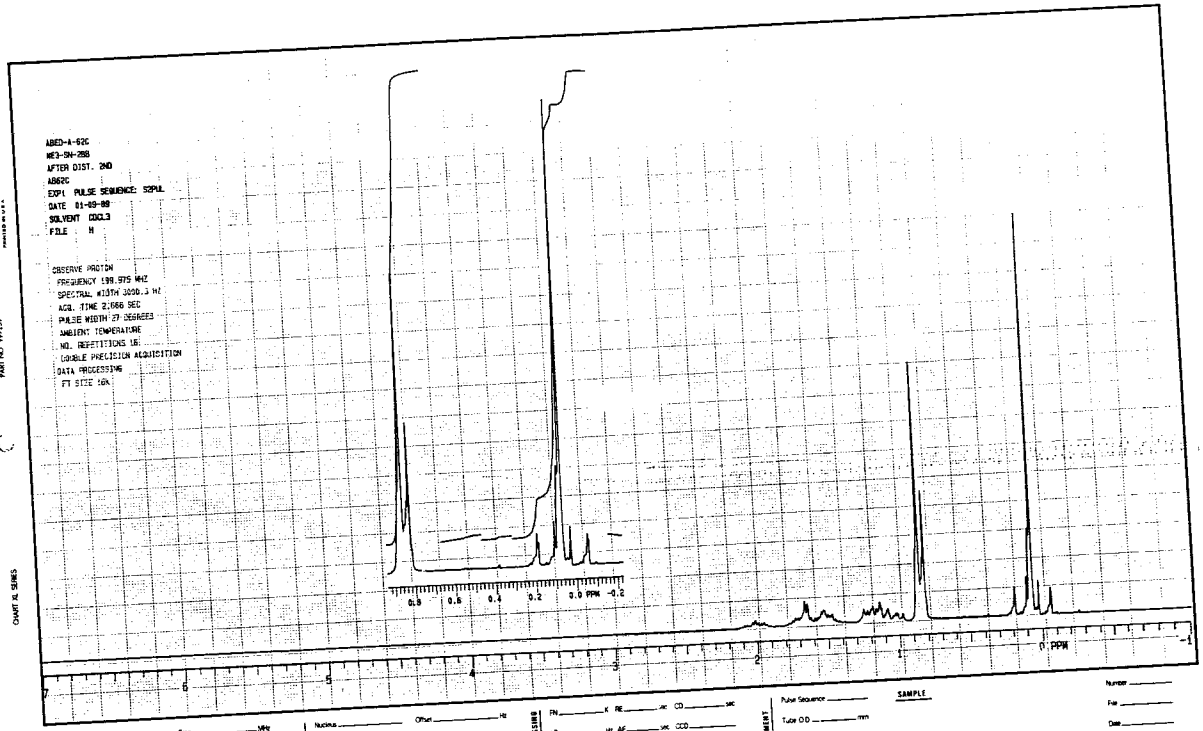
CNMR (in ppm figure 19)

-9.24 = k	35.27 = b	
16.42 = i(or h)	37.07 = f	
19.08 = h(or i)	45.96 = d	
19.78 = j	48.10 = g	
28.71 = e	49.52 = a	
33.15 = c		

values from Dr. Kuivila's work[4]

a = 49.1	g = 48.1
b = 35.2	h = 19.0 (or i)
c = 33.1	i = 16.3 (or h)
d = 45.9	j = 19.7
e = 28.6	k = -9.2
f = 37.0	

Figure 18: HNMR of Trimethylisobornyltin


ABED-A-62C
ME3-SN-258
AFTER DIST. 2ND
AB62C
EXP: PULSE SEQUENCE: S2PUL
DATE 01-09-89
SOLVENT CDCL3
FILE H
OBSERVE PROTON
FREQUENCY 199.975 MHZ
SPECTRAL WIDTH 3000.3 HZ
ACQ. TIME 2.066 SEC
PULSE WIDTH 27.3586ES
AMBIENT TEMPERATURE
NO. REPETITIONS 16
DOUBLE PRECISION ACQUISITION
DATA PROCESSING
FT SIZE 16K
0.8 0.6 0.4 0.2 0.0 PPM -0.2
0 PPM
OBSERVE
DECOUPLE
PULS/PROCESSING
EXPERIMENT
SAMPLE

equilibrated, crotyl chloride (9.78 g, 0.108 mols) dissolved in 20 mL of THF was added to the addition funnel. The crotyl chloride solution was then added dropwise over a period of 20 minutes to the reaction mixture. At the completion of the addition of the crotyl chloride solution, the reaction was allowed to proceed for an additional 30 minutes. Then the slush bath was allowed to come to room temperature, and the reaction continued for 24 hours more.

At the completion of the reaction 70 mL of $NH_4Cl_{(aq)}$ was added dropwise to the reaction mixture and stirred magnetically. Two phases were present with solid matter in the bottom phase. The mixture was filtered by gravity to remove the solid matter. The filtrate again had two liquid phases so they were separated with a separatory funnel, and the organic phase was dried with $MgSO_4$, filtered, and the solvent removed (rotovap).

A vacuum distillation was attempted but most of the crude product was lost. Both CNMR and HNMR spectra were taken.

Synthesis of Crotyltrimethyltin expt. 2:

The same set up and procedure was followed for the formation of the anion as in the first trial, using Me_3SnCl (21.45 g, 0.108 mols), Li (4.08 g, 0.588 mols), and THF (150 mL). Crotyl chloride, (9.88 g, 0.109 mols) was again added as in the previous trial over a period of 15 minutes. It was reacted at -36°C for an additional 30 minutes. Then after the mixture equilibrated at room temperature it was

reacted for another 3 hours.

At this time 200 mL of $NH_4Cl_{(aq)}$ was added dropwise to the stirred mixture. The mixture had two phases with solid matter present in the lower phase, and so was filtered by gravity. The filtrate again had two phases which were separated with a separatory funnel. The H_2O phase was washed three times with 50 mL of ether, and the organic phases were combined, dried with $MgSO_4$, and filtered into a 500-mL round-bottom flask. The ether was then removed by simple distillation. The crude product was then distilled with a fractionating column at reduced pressure. Three fractions were collected, and CNMR spectra were taken of fractions two and three (figures 25 & 26).

Synthesis of Cinnamyltrimethyltin :

A 250-mL round-bottom flask was flame dried and placed in a glove bag under an Argon atmosphere. Me_3SnCl (9.94 g, 0.050 mols) and THF (75 mL), dried by distillation from sodium under argon, were added and stirred magnetically. Over a period of 20 minutes, Li metal (2.01 g, 0.290 mols) was added in small pieces and reacted over a 24 hour period.

The dark green-black mixture was then filtered through glass wool into another flame dried 500-mL round-bottom flask. This was then removed from the bag and equipped with a self equalizing addition funnel. A N_2 inlet/bubbler was added to the addition funnel. Next the round-bottom flask was immersed in a xylene/$N_{2(l)}$ slush bath, at approximately $-36^{o}C$. Cinnamyl chloride (7.96 g, 0.052 mols) was dissolved

with 20 mL of THF and added to the addition funnel. The cinnamyl chloride solution was then added dropwise, over a period of 20 minutes to the reaction mixture.

$NH_4Cl_{(aq)}$ (70 mL, saturated aqueous solution) was added dropwise and the mixture was stirred magnetically, then filtered by gravity to remove the solid matter in the lower phase. The two liquid phases were then separated, and the H_2O phase was washed three times with ether. The resulting organic phases and the previous organic phase were all combined, dried with $MgSO_4$, and filtered into a 500-mL round-bottom flask. The solvents were then distilled off. The crude product was vacuum distilled, and three fractions were collected. Both CNMR and HNMR spectra were taken of fractions two and three (figures 29 & 30).

Synthesis of Cinnamyltrimyrtanyltin :

A 100-mL round-bottom flask was flame dried and placed in a glove bag under an Argon atmosphere. Myr_3SnBr, trimyrtanyltinbromide (2.22 g, 0.00343 mols) and THF (10 mL), dried by distillation from sodium under argon, were added and stirred magnetically. Over a period of 20 minutes, Li metal (0.97 g, 0.140 mols) was added in the form of sand and reacted over a 24 hr. period.

The black mixture was then filtered through glass wool into another flame dried 100-mL round-bottom flask. This was then removed from the bag, and it was equipped with a self-equalizing addition funnel. A N_2 inlet/bubbler was added to the addition funnel. Next, the round-bottom was immersed in

a xylene/$N_{2(l)}$ slush bath, at approximately $-36^{o}C$. The addition funnel was removed and replaced by a serum cap. Cinnamyl chloride (0.52 g, 0.00341 mols) was added via syringe. Again the reaction proceeded at $-36^{o}C$ for 30 minutes, at which time the bath was allowed to warm to room-temperature and the mixture reacted over night. $NH_4Cl_{(aq)}$ (5 mL) was added to the dark black-red mixture and stirred magnetically. The resulting two phases were filtered to remove the solid matter in the lower phase and separated. The H_2O phase was washed with 10 mL of ether. The two organic phases were combined and washed three times with 7 mL of H_2O. $KF_{(aq)}$ (1.5 mL) was added to the organic phase and stirred magnetically for 10 minutes. This was then separated, and the organic phase was dried with $MgSO_4$, filtered, and the solvent removed (rotovap). Both HNMR & CNMR spectra were taken of the crude product.

In an effort to purify the crude product, 20 mL of petroleum ether was added along with 0.5 g of activated charcoal, refluxed, and stirred magnetically for 15 minutes. The mixture was filtered, solvent evaporated, and a HNMR spectrum obtained.

Synthesis of Cinnamyldimethylisobornyltin :

A 250-mL round-bottom flask was flame dried and placed in a glove bag under an Argon atmosphere. Bromodimethylisobornyltin, (12.51 g, 0.0342 mols) and THF (70 mL), dried by distillation from sodium under argon, were added and stirred magnetically. Over a period of 10 minutes,

Li metal (1.44 g, 0.207 mols) was added in the form of sand and reacted over a 24 hr period.

The black mixture was then filtered through glass wool into another flame-dried 100-mL round-bottom flask. This was then removed from the bag and was equipped with a self equalizing addition funnel. A N_2 inlet/bubbler was added to the addition funnel. Next the round-bottom was immersed in a xylene/$N_{2(l)}$ slush bath. Cinnamyl chloride, (5.42 g, 0.0355 mols) was added through the addition funnel. Again the reaction proceeded at -36°C for 30 minutes, at which time the bath was allowed to warm to room-temperature and the mixture reacted over night.

$NH_4Cl_{(aq)}$ (50 mL) was used to neutralize any remaining anion. The mixture, containing two phases, was then filtered, and the solid washed with 80 mL of ether. The filtrate was separated, and the organic phase was washed three times with 50 mL of H_2O. The organic phase was then dried with $MgSO_4$, filtered, and the solvent removed. A HNMR spectrum was taken of the crude product.

Petroleum ether (20 mL) was added to the crude product and refluxed until all of it dissolved. The solution was then cooled in an attempt to crystallize the product. However, since the product was either low melting or very soluble the solid product was not recovered.

It was vacuum distilled using a simple distillation. Four fractions were recovered and HNMR and CNMR spectra were taken of each (figures 33 & 34).

Conclusion:

α–Pinene was chosen as the starting material for the chiral ligand, since it rotated the plane of polarized light, and itself had an excess of one enantiomer. The α–Pinene was brominated by an electrophilic addition of HBr, and the product, 2-bromobornane, was comprised of largely the endo-isomer as well as being optically active itself.

2-Bromobornane was first reacted with triphenyltin chloride. However, the phenyl rings acted to stabilize the anion in making the coupling reaction very slow and unreactive. So finally trimethyltin chloride was used, and the organotin compound with a chiral ligand was synthesized.

The next step was the addition of the allylic group. Two groups were chosen, cinnamyl and crotyl. Model reactions were first used in order to become familiar with the procedure as well as determining which group would be most effective for our compound. When the cinnamyl group was used with trimyrtanyltin bromide it gave a mixture of two isomers, where the double bond on the cinnamyl group rearranges. Yet when trimethyltin chloride was used no rearranged product was formed. The crotyl group also formed only the unrearranged product, but since the cinnamyl is known to go by a cyclic transition state when attached to a organometallic compound and reacted with an aldehyde, it was chosen.

Before the cinnamyl group was added to the organotin compound, the organotin compound was first brominated, by way of an aliphatic electrophilic substitution. The cinnamyl

group was then added by a S_n2 reaction using the anion prepared from the tin bromide.

As expected the product was a mixture of the two isomers, as shown by the HNMR spectra However, this should not interfere with the reaction with the aldehyde. The problem is that there will be two homoallylic alcohols each being isomers of each other.

It may be possible that in using the crotyl group instead of the cinnamyl group one does not get the rearranged product. However, when this is reacted with the aldehyde it is known to go by an acyclic transition state, and a cyclic transition state is desired since it allows for more stereochemical control.

In theory the organotin should react with an aldehyde in the presence of a Lewis acid to form a homoallylic alcohol, however we were unable to persue this. Yet if the reaction is able to create a diastereomeric transition state, and so becoming enantioselective, it will allow chemists to not only synthesize antibiotics, but to synthesize them in one pure enantiomeric form as in nature.

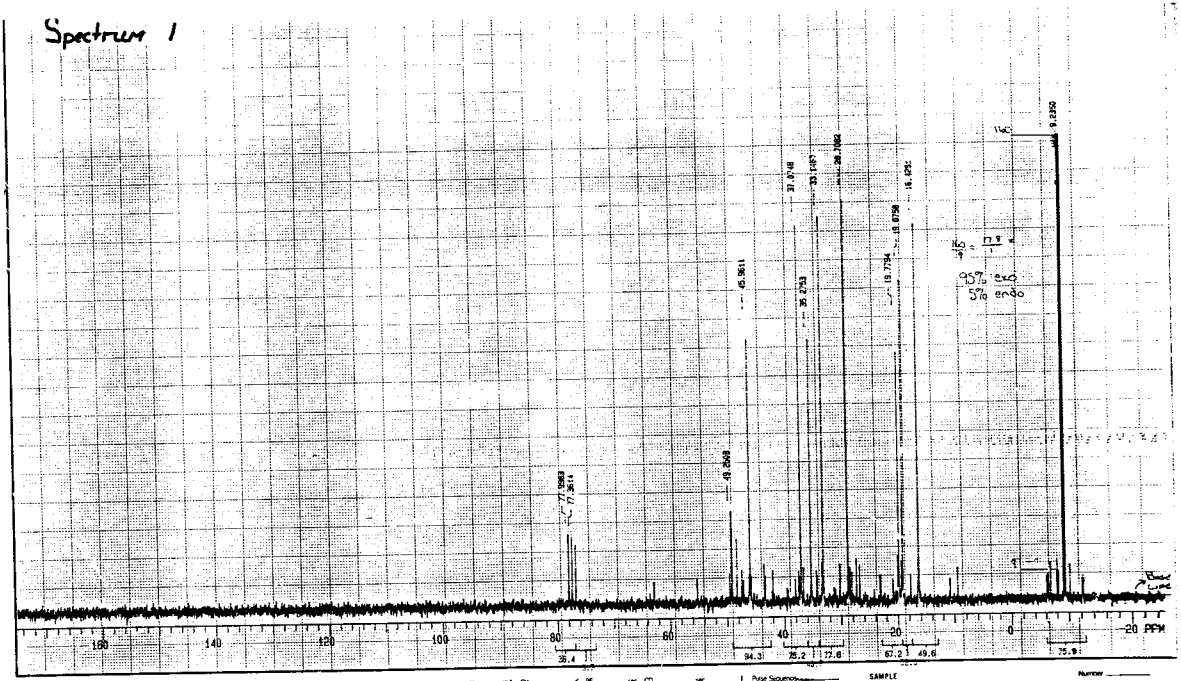
Bibliography

1. The Merck Index, 9th edition, Merck & CO., INC. Rahaway, N.J, 486
2. Yoshinori Yamamoto, *J. Am. Chem. Soc* **1980,** *102,* 7107
3. Ibid.
4. Ramesh Krishananmurti and Henery G. Kuivila, *J. of Org. Chem.* **1986,** *51,* 4947
5. Matarasso-Tchiroukhine and P. Cadiot, *J. Organometallic Chem.* **1976,** *121,* 155
6. Herbert C. Brown, Clinton F. Lane and Norman R. De Lue, *Tetrahedron* **1988,** *10,* 2773
7. Herbert C. Brown and Clinton F. Lane, *Tetrahedron* **1988,** *10,* 2763
8. Ramesh Krishananmurti and Henery G. Kuivila, *J. of Org. Chem.* **1986,** *51,* 4947

PREVIOUS DOCUMENTS IN POOR ORIGINAL CONDITION

Figure 19: CNMR of Trimethylisobornyltin

Spectrum 1



GE/OMEGA SERIES 5
PART NO. 997259
CHART XL SERIES

OBSERVE: Nucleus 13.000 | Freq 50 MHz | Spec Width 1998.5 Hz | Offset 0 Hz | Acq Time 1.001 sec | Delay 0 sec | Pulse Width 3.0 µsec | Transients 250

DECOUPLE: Nucleus 1.000 | Offset 200.2 Hz | Mode | Power 20.0 db | Modulation Mode G | Freq 10200 Hz | Pulse Width 28.0 µsec | Power Mode 1.0

PLOT/PROCESSING: FN 32 | RE sec | CD sec | LB 1.000 Hz | AF sec | DCD | Width 10050.1 Hz/ppm | Start -1257.4 Hz/ppm | Reference

EXPERIMENT: Pulse Sequence SGPU | Tube O.D. mm | Temp °C | Solvent CDCl3

SAMPLE
ABED-I-57
MES- 398
AFTER DISTILLATION
FRACTION 1

Number
File ABED
Date 27-02-98
94:21:38
XL- BDF 250

	IR (figure 20)	
1750 cm^{-1}	medium	C=O
1490 & 1470 cm^{-1}	medium	CH_3's
760 cm^{-1}	strong	Sn-O
520 cm^{-1}	strong	Sn-C

In looking at the NMR (especially the carbon) all of the major peaks identified matched well with the peak values given in Dr. Kuivila's paper. This indicated that that compound present was in fact the desired product. However the IR data showed distinctly the presence of a C=O and Sn-O. Which would in turn mean the possible presence of hexamethylditinoxide produced by oxidation of the tin anion of hexamethylditin.

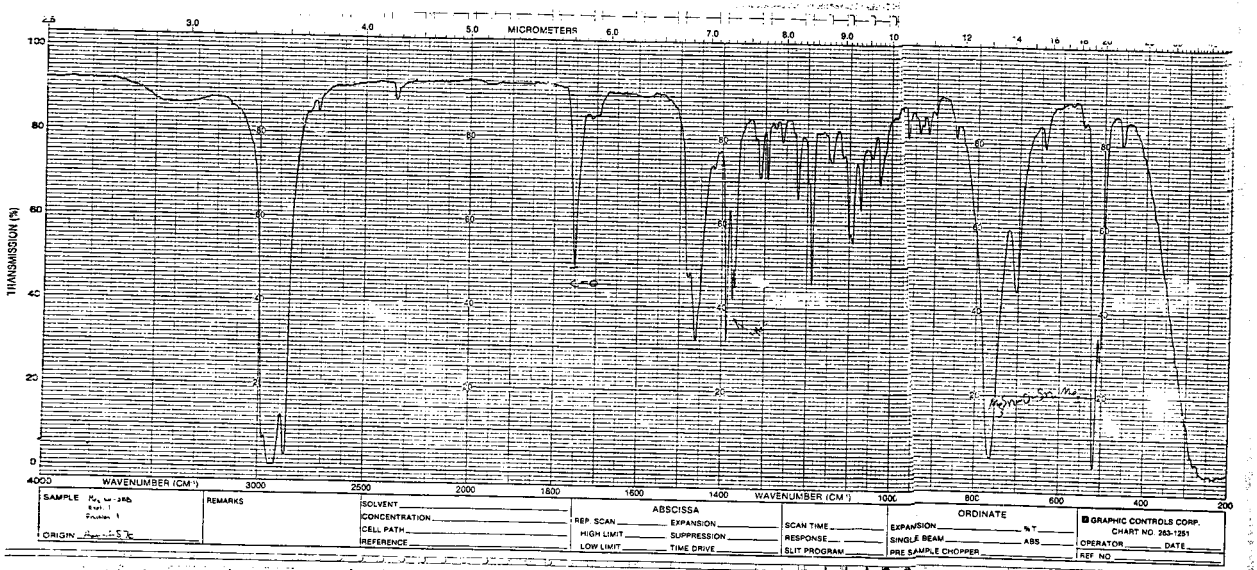
The distillate was then washed with H_2SO_4 (60mL, 15 %) twice. An IR spectrum of this showed the continuing presence of the suspected Sn-O bond but the C=O peak had nearly disappeared.

Reaction 2:

The same procedure was followed as before, but in addition the crude product was reacted with H_2O_2 (30 %) to remove any hexamethyltin. Once all the solvents were removed and the crude product was isolated it was fractionally distilled under vacuum, and three fractions were collected. The mass of each fraction was recorded and IR's and NMR's were taken.

(Temp 1 is the temperature at the column inlet and Temp 2 is the temperature at the stillhead after the fractionating column)

Figure 20: IR of Trimethylisobornyltin


MICROMETERS
TRANSMISSION (%)
WAVENUMBER (CM⁻¹)
WAVENUMBER (CM⁻¹)
SAMPLE
REMARKS
SOLVENT
CONCENTRATION
CELL PATH
REFERENCE
ABSCISSA
REP. SCAN
HIGH LIMIT
LOW LIMIT
EXPANSION
SUPPRESSION
TIME DRIVE
SCAN TIME
RESPONSE
SLIT PROGRAM
ORDINATE
EXPANSION
SINGLE BEAM
PRE SAMPLE CHOPPER
%T
ABS
GRAPHIC CONTROLS CORP.
CHART NO. 263-1251
OPERATOR
DATE
REF NO
ORIGIN

Pressure	temp1 (°C)	temp2 (°C)	fraction
0.2	65-68	55-58	1
0.2	69-70	58-55	2
0.2	72-75	55-54	3

mass of fraction 1: 5.23 g
mass of fraction 2: 10.78 g
mass of fraction 3: 0.30 g

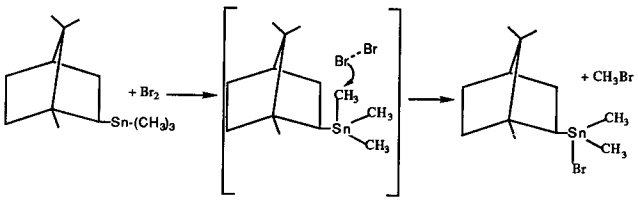
The IR's of the three fractions were similar and also contained a strong Sn-O peak. The CNMR as before had peak values that matched those given by Dr.Kuivila.

Part 3: The Addition of an allylic group to the previously synthesized organotin compound

i. The Bromination of Trimethylisobornyltin:

Theory:

The mechanism involved in this reaction is an aliphatic electrophilic substitution. The bromine acts as the electrophile and forms C-Br and Sn-Br bonds as the tin-methyl bond is breaking.



The result is a substitution of one bromine for one methyl. To ensure this, a slight deficiency of bromine was employed.

Results:

The crude Bromodimethylisobornyltin was isolated by removal of the solvent. A TLC was taken of the yellow-white solid which showed a relatively pure product. It was recrystallized from methanol. The white crystals were isolated, dried, and characterized.

mass of crop 1: 11.13 g
mass of crop 2: 2.69 g

(the following results are for crop 1)
Melting pt. 80-83 °C

Optical rotation
[solvent = $CHCl_3$, l= 1dM]

crop 1: $[\alpha]_D$= -19.5 (at 27.8 °C)

HNMR (figure 21)

0.73 ppm	singlet	Methyls on tin
0.85 ppm	two singlets	Methyls on 2-bromobornane
0.92 ppm	singlet	bridgehead methyl

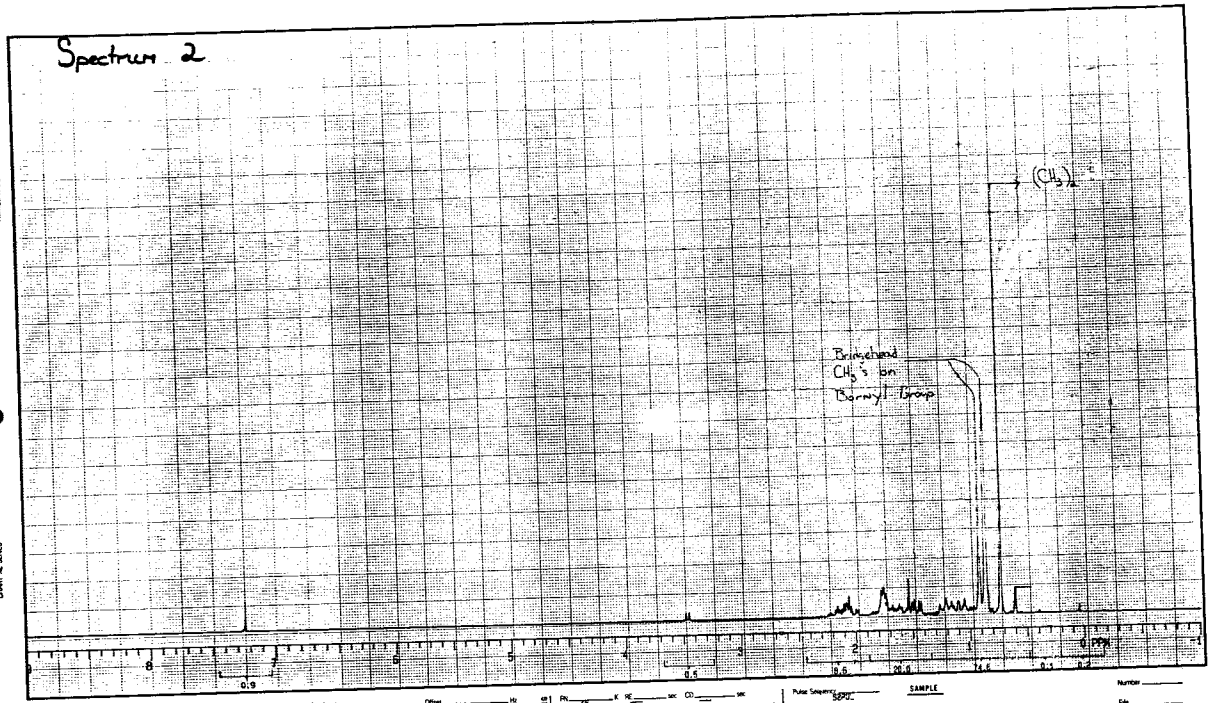
CNMR (figure 22)

similar to that of the Me_3-Sn-Bornyl,(Pg. 20) except for carbon b which is at 44.26 ppm in the brominated product. the Me peaks anr also diastereotopic.

The NMR spectra tend to indicate the the product is in fact our desired product. Due to the fact that it was recrystallized also tells us that it is probably quite pure as well.

Figure 21: HNMR of Bromodimethylisobornyltin

Spectrum 2.



OBSERVE: Nucleus 1.000 | Sync Width 3000.0 Hz | Acq. Time 2.000 sec | Pulse Width 19.3 usec | Freq. 200 MHz | Offset 0 Hz | Delay 0 sec | Transients 16

DECOUPLE: Nucleus 1.000 | Mode NNI | Modulation Mode C | Pulse Width usec | Offset -300.0 Hz | Power 20.0 db | Freq. 200 Hz | Power Mode 1.0

PLOT/PROCESSING: PR 10 K | RF sec | CD sec | LB Hz | AF sec | CCD | Width 2000.0 Hz ppm | Start -200.0 Hz ppm | Reference

EXPERIMENT: Pulse Sequence s2pul | Tube O.D. mm | Temp °c | Solvent CDCL3

SAMPLE: CHIP 1 | BARE2-91-29B | ABD-A-79A | AB79A

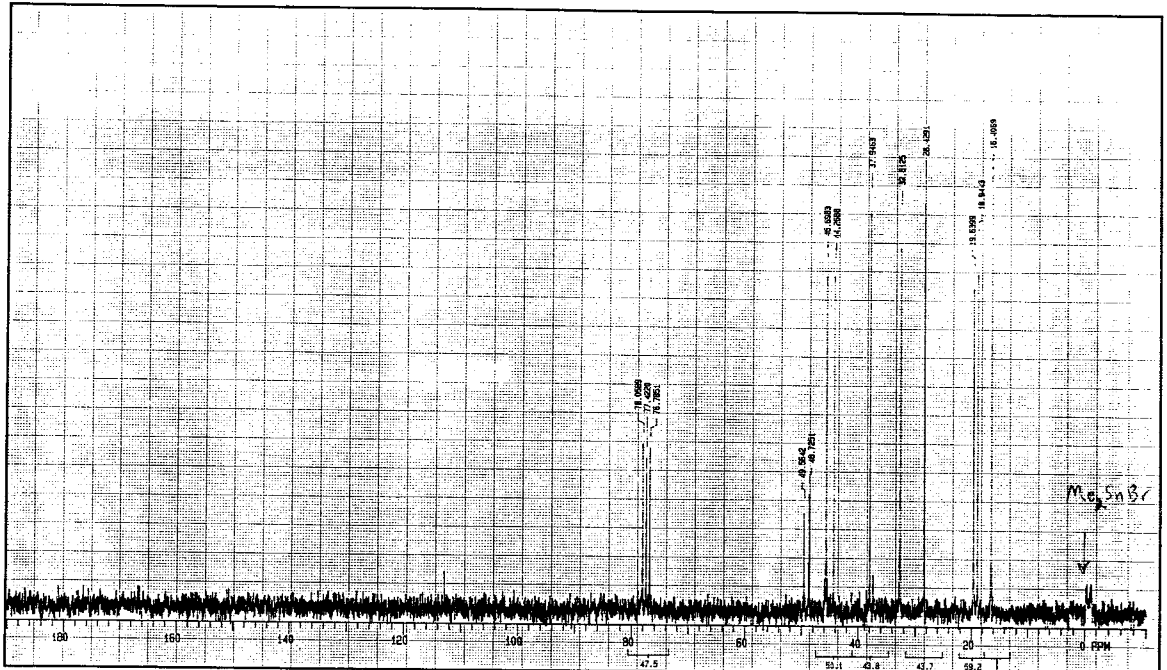
Number | File AB79A | Date 02-21-89 | XL 12:51:02 | BEH 200

DIGITAL CONVERSION & CURVE FITTING SUPPLIED BY NICOLET PRINTED IN U.S.A.

PART NO. 997239

DART XL SERIES

Figure 22: CNMR of Bromodimethylisobornyltin



OBSERVE
Nucleus 13.000
Spec. Width 992.5 Hz
Acq. Time .001 sec
Pulse Width 10.0 µsec
Freq. 30 MHz
Offset 0 Hz
Delay 0 sec
Transients 256

DECOUPLE
Nucleus 1.000
Mode YYY
Modulation Mode 3
Pulse Width 29.0 µsec
Offset 303.2 Hz
Power 20.0 db
Freq. 10200 Hz
Power Mode 1.0

PLOT/PROCESSING
FN 32 K
RE ___ sec
CD ___ sec
LB 1.000 Hz
AF ___ sec
CCD ___
Width 10058.1 Hz/ppm
Start 302.9 Hz/ppm
Reference ___

EXPERIMENT
Pulse Sequence S2PUL
Tube O.D. ___ mm
Temp ___ °C
Solvent CDCL3

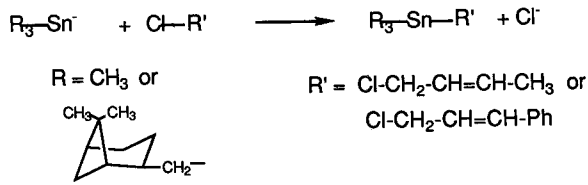
SAMPLE
CROP t
BRME2-SN-298
ABED-A-708
AB70C

Number ___
File A3^00
Date 02-22-89
14:10:51
XL-BSM-299

The Addition of an Allylic Group to the Dimethylisobornyltin compound:

Theory:

The mechanism of this reaction is a simple S_N2 displacement, with the tin anion acting as the nucleophile by displacing the chlorine on the crotyl or cinnamyl group.



Before our sample of bromodimethylisobornyltin was used we chose to use two model compounds, namely trimethyltin chloride, (Me_3SnCl), and trimyrtanyltinbromide, (Myr_3SnBr). The Me_3SnCl was chosen to since it was readily available and Myr_3SnBr since it would model a bulky compound.

HNMR and CNMR spectra were taken of the crotyl chloride used as a reactant used in the following reactions. (figures 23 & 24)

Results:

ii. Synthesis of Crotyltrimethyltin :

Reaction 1:

The following reaction procedure and work-up is is taken from the work of Dr. Cadiot and his coworkers[5]. Anion

Figure 23: HNMR of Crotyl chloride

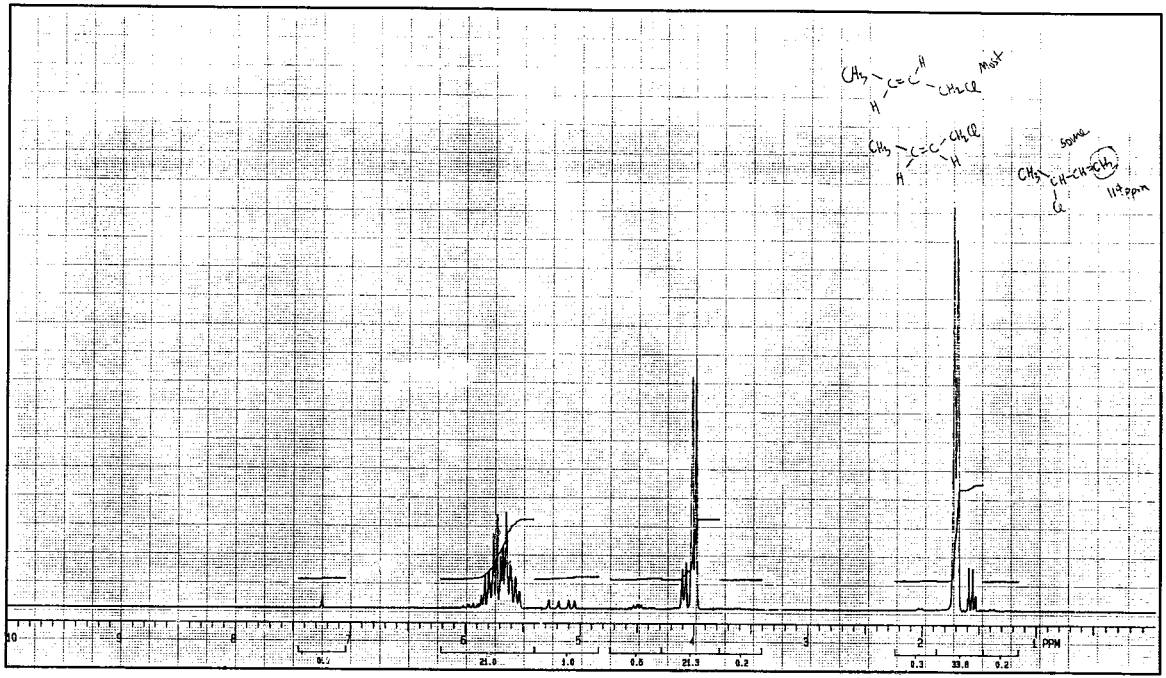
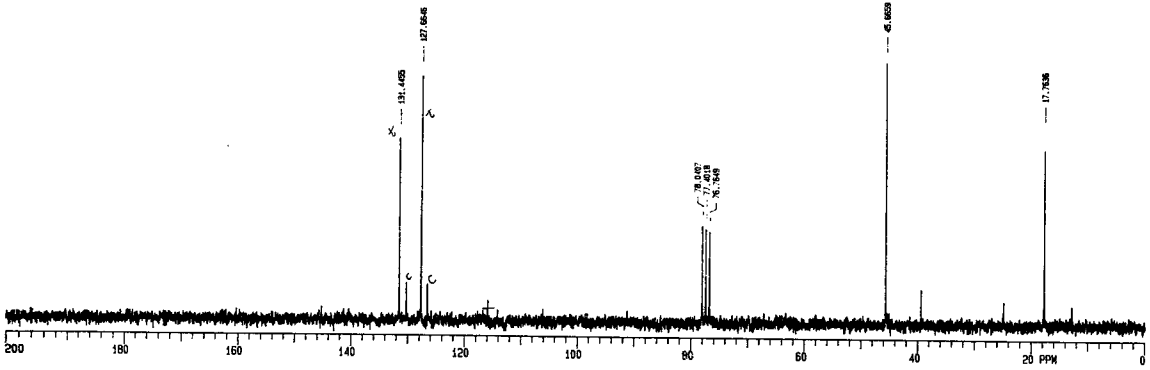


Figure 24: CNMR of Crotyl chloride



13.000	50	1.000	-305.2	32	—	—	S2PUL	
14992.5	0	YYY	20.0	1.000	—	—		C
1.001	0	S	10200	10058.1		0	—	02-27-89
10.0	256	28.0	1.0				CDCL3	15:38:21

ASC-A-75B
AG758

SGN: 200

prepared as before in THF with Lithium metal. At the completion of the reaction, the mixture was washed with $NH_4Cl_{(aq)}$ in order to neutralize any remaining anion. The crude product was isolated by removing the solvent (rotovap), and further purified by vacuum distillation. However, problems arose and most of the product was lost in the process, except for a very small amount which was used to get a HNMR spectra.

HNMR (figure 25)

0.05 ppm	singlet	Methyls on tin
5.1-5.6 ppm	complex	double bond CH's on Crotyl group

The singlet at 0.05 ppm indicating the methyls on the tin, and the double bond protons at 5.1-5.6 ppm would support the formation of our desired product.

Reaction 2:

Again the same procedure was used to wash and isolate the crude product as in the previous trial. The crude product was also fractionally distilled at reduced pressure, and three fractions were collected. A CNMR spectra of fraction three was taken.

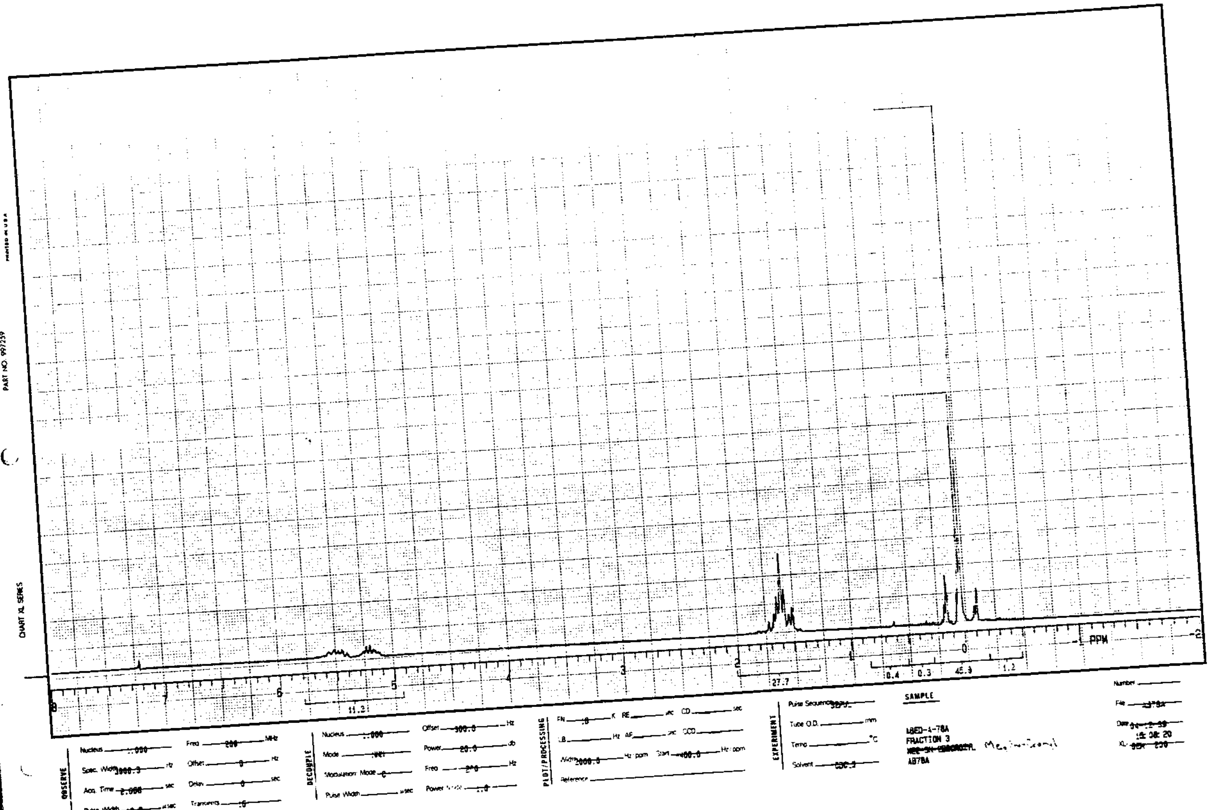
Pressure	temp.(^{o}C)	fraction
67 mmHg	57-62	1
68 mmHg	79-80	2
68 mmHg	80-81	3

mass of fraction 1: .09 g
mass of fraction 2: 4.10 g
mass of fraction 3: 3.96 g

CNMR (figure 26)

-10.28 ppm	singlet	Methyls on tin of each isomer
-9.87 ppm	"	
118.88 ppm	singlet	Double bond CH attached

Figure 25: HNMR of Crotyltrimethyltin



PPM
27.7
0.4
0.3
45.9
1.2
11.2
SAMPLE
ABED-4-78A
FRACTION 3
AB78A
OBSERVE
DECOUPLE
PLOT/PROCESSING
EXPERIMENT
Pulse Sequence
Tube O.D. mm
Temp °C
Solvent
Number
File
Date
CHART XL SERIES
PART NO. 997259

120.84 ppm	"	to end CH_3
129.14 ppm	singlet	Double bond CH attached
129.90 ppm	"	to CH_2

From this we can determine the percentage of *cis-trans* by simply taking the ratio of the three peaks, A, B, and C in the spectrum. In doing so it appears that the product is 74 % *trans* and 26 % *cis*.

ii. Synthesis of Cinnamyltrimethyltin :

Both a HNMR and CNMR, (figure 27 & 28), were taken of the cinnamyl chloride in order have spectra of the pure compound.

The CH_3Sn^- anion wasprepared as before in THF with Lithium metal. The crude product was neutralized with $NH_4Cl_{(aq)}$ washed, and the solvent removed as in the previous experiment. The product was then vacuum distilled, and three fractions were collected , with a HNMR and CNMR taken of the second fraction.

CNMR (figure 29)

-10.28 ppm	singlet	Methyls on tin
46.0 ppm	singlet	CH_2 on cinnamyl chloride

peaks assigned an A in spectra belong to unreacted cinnamyl chloride

HNMR (figure 30)

0.40 ppm	singlet	Methyls on tin
2.2 ppm	doublet	protons on C attached to Sn
6.4-6.9 ppm	complex	protons on both double bond C's
7.5-7.7 ppm	complex	protons on phenyl
4.4 ppm	doublet	protons on CH_2 of cinnamyl chloride

Both spectra clearly show the presence of cinnamyl chloride

Figure 26: CNMR of Crotyltrimethyltin

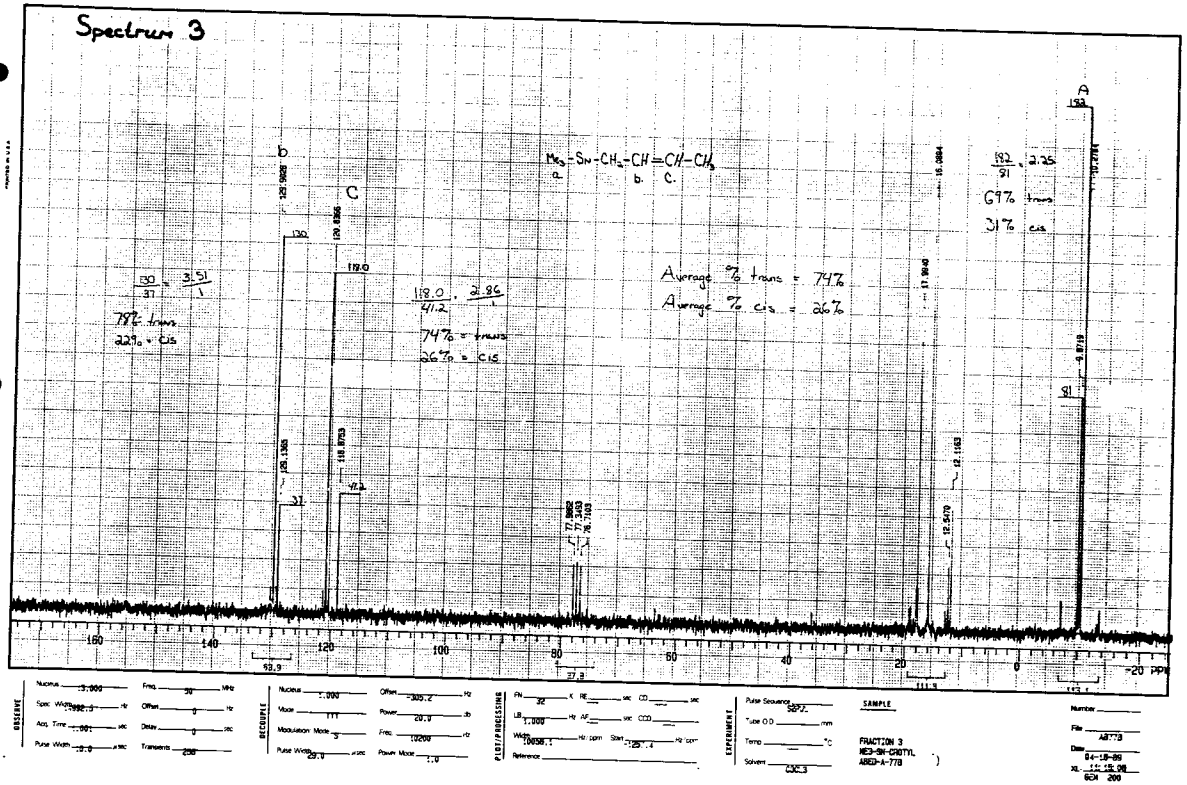
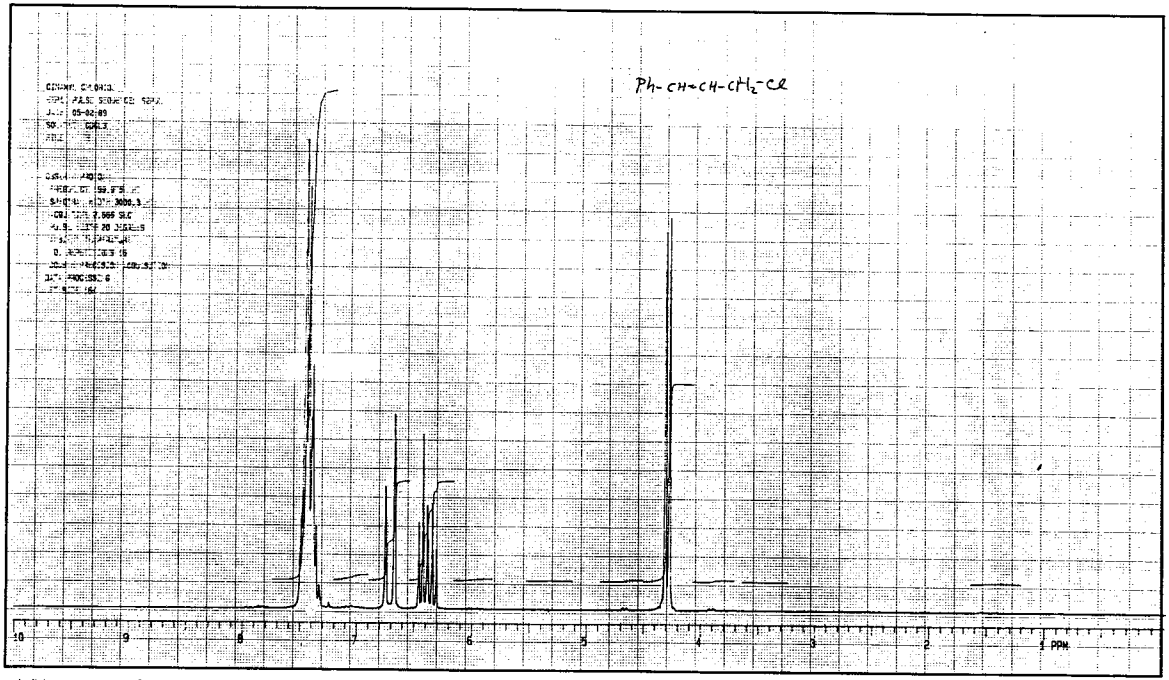

Spectrum 3
b
C
A
$Me_3Si-O-CH_2-CH=CH-CH_3$
p. b. c.
130 / 37 = 3.51 / 1
78% trans
22% = cis
118.0 / 41.2 = 2.86 / 1
74% = trans
26% = cis
Average % trans = 74%
Average % cis = 26%
192 / 91 = 2.35
69% trans
31% cis
130
119.0
37
91
160
140
120
100
80
60
40
20
0
-20 PPM

Figure 27: HNMR of Cinnamyl chloride



OBSERVE: Nucleus ____ Freq ____ MHz; Spec. Width ____ Hz Offset ____ Hz; Acq. Time ____ sec Delay ____ sec; Pulse Width ____ µsec Transients ____

DECOUPLE: Nucleus ____ Offset ____ Hz; Mode ____ Power ____ db; Modulation Mode ____ Freq ____ Hz; Pulse Width ____ µsec Power Mode ____

PLOT/PROCESSING: PW ____ K PE ____ sec CD ____ sec; LB ____ Hz AF ____ sec CCD ____; Width ____ Hz ppm Start ____ Hz ppm; Reference ____

EXPERIMENT: Pulse Sequence ____; Tube O.D. ____ mm; Temp ____ °C; Solvent ____

SAMPLE

Number ____; File ____; Date ____; ID ____

CHART 3L SERIES PART NO. 997239 VARIAN CONTROL DATA CORPORATION PRINTED IN U.S.A.

Figure 28: CNMR of Cinnamyl chloride

CHART R SERIES
PART NO 997750
EXPERIMENT
SAMPLE
PULSE
DETECTOR
PULSE/PROCESSING
DISPLAY

Figure 29: CNMR of cinnamyltrimethyltin

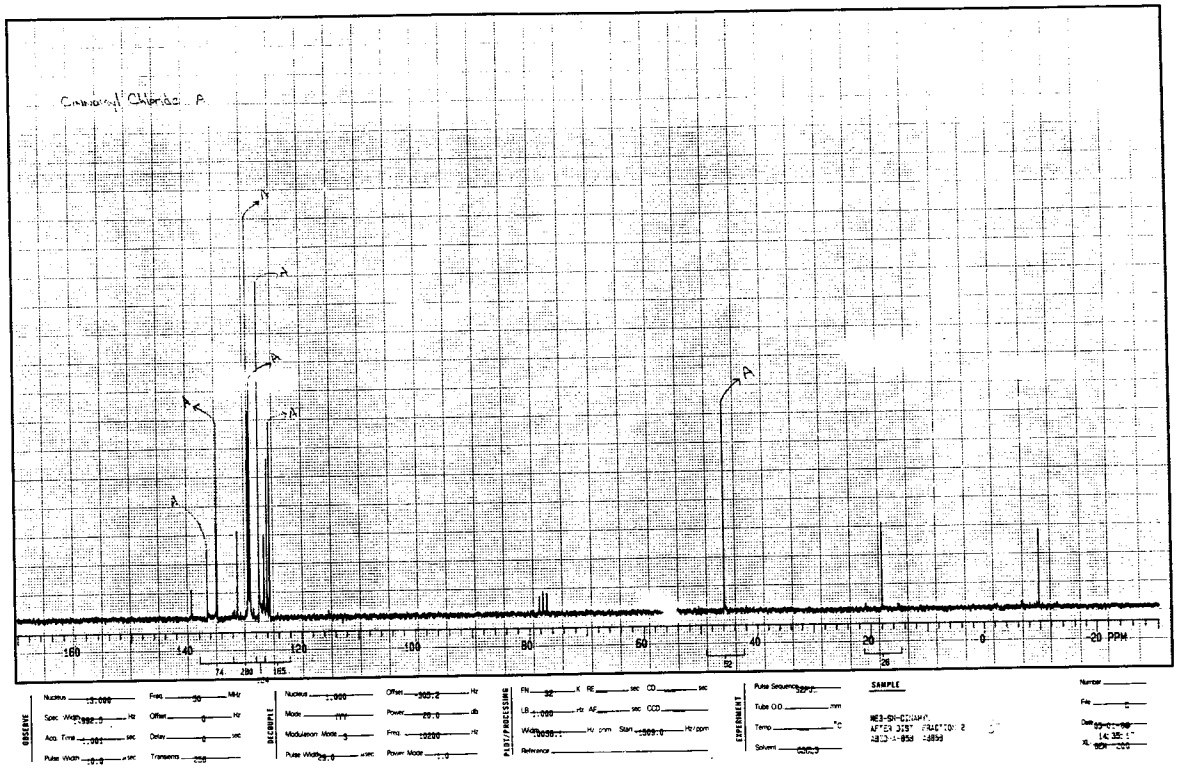
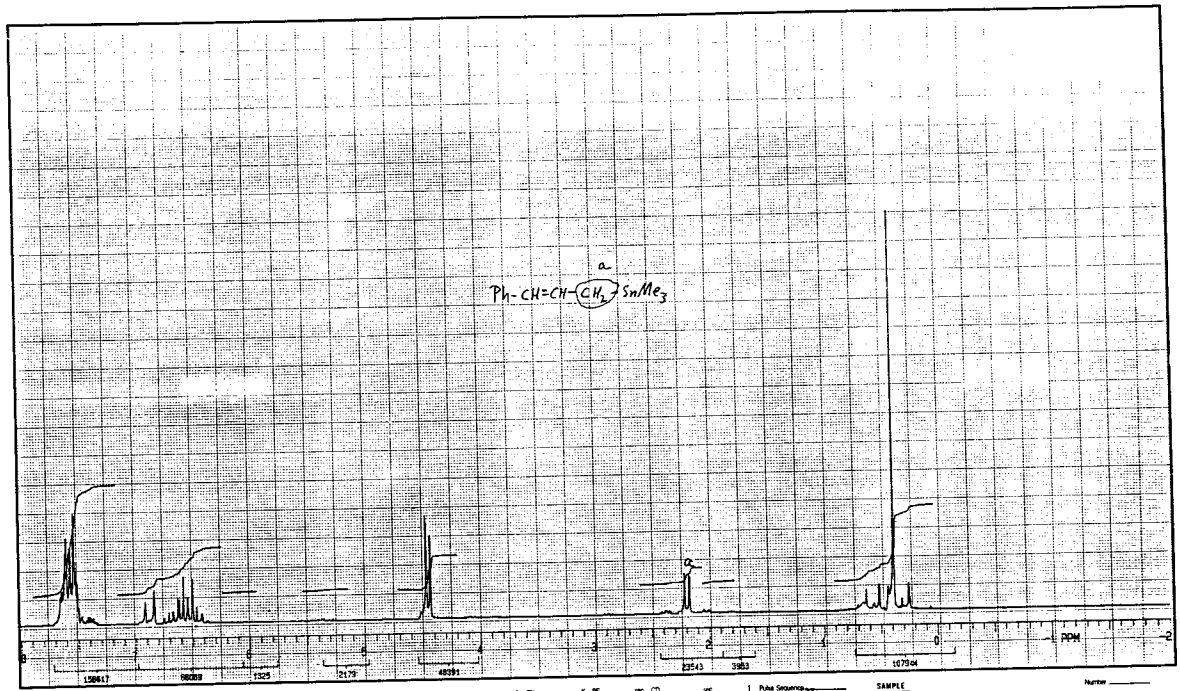

Chemical Chemical P
-20 PPM
OBSERVE
DECOUPLE
PLOT/PROCESSING
EXPERIMENT
SAMPLE
AFTER DIST FRACTION 2

Figure 30: HNMR of Cinnamyltrimethyltin


a
Ph-CH=CH-CH2-SnMe3
a
PPM
150617
88089
7325
2179
48391
23543
3983
107904

indicating that the reaction did not go to completion. Yet it also shows the existence of our desired product.

ii. Synthesis of Cinnamyltrimyrtanyltin :

The anion was prepared as before in THF with Lithium metal. Again the crude product was neutralized with $NH_4Cl_{(aq)}$ washed with H_2O, and the solvent removed as in the previous experiment. In an attempt to purify the crude product it redissolved in petroleum ether and 0.5 g of activated charcoal was added. This was done in an effort to remove any colored impurities, since they would tend to adsorb on the charcoal.

HNMR (figure 31)

0.85 ppm	2 singlets	Methyls on Myrtanyl
7.5-7.7 ppm	complex(weak)	protons on phenyl

CNMR (figure 32)

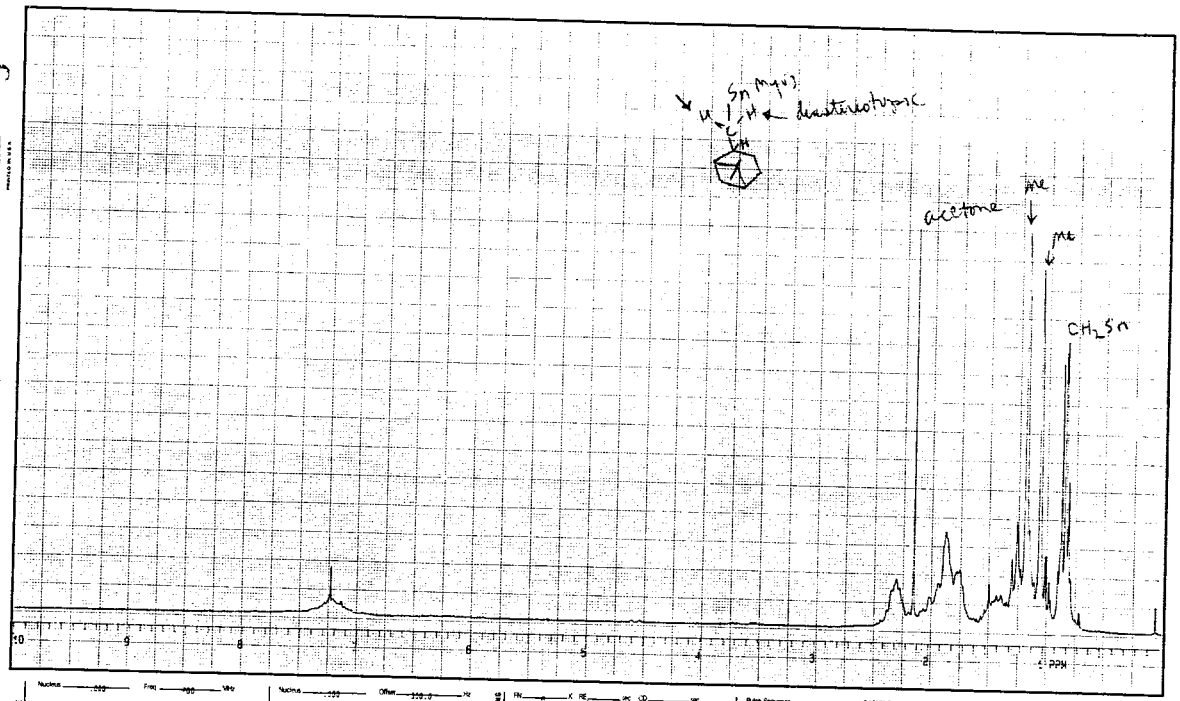
23-50 ppm	singlets	C's on the myrtanyl
126-129 ppm	complex(weak)	C's on phenyl

The signals from the cinnamyl group are weak because there are three myrtanyl groups which overwhelm it. As a result it is difficult to determine if there is any rearranged product.

iii. Synthesis of Cinnamyldimethylisobornyltin :

The anion was prepared as before in THF with Lithium metal. After reaction with cinnamyl chloride any remaining anion was neutralized with $NH_4Cl_{(aq)}$, and the crude product was washed with H_2O. After the solvent was removed, a recrystallization was attempted with petroleum

Figure 31: HNMR of Cinnamyltrimyrtanyltin



OBSERVE
Nucleus 200
Spec. Width 1000.3 Hz
Acq. Time 4.096 sec
Pulse Width 3.3 μsec
Freq 200 MHz
Offset 0 Hz
Delay 0 sec
Transients 5

DECOUPLE
Nucleus 200
Mode
Modulation Mode
Pulse Width μsec
Offset 350.2 Hz
Power 70.0 dB
Freq 200 Hz
Power Mode

PLOT/PROCESSING
FN 0 K
LB Hz
Width 999.8 Hz/ppm
Reference
RE sec
AF sec
Start 1 Hz/ppm
CD sec
CCD sec

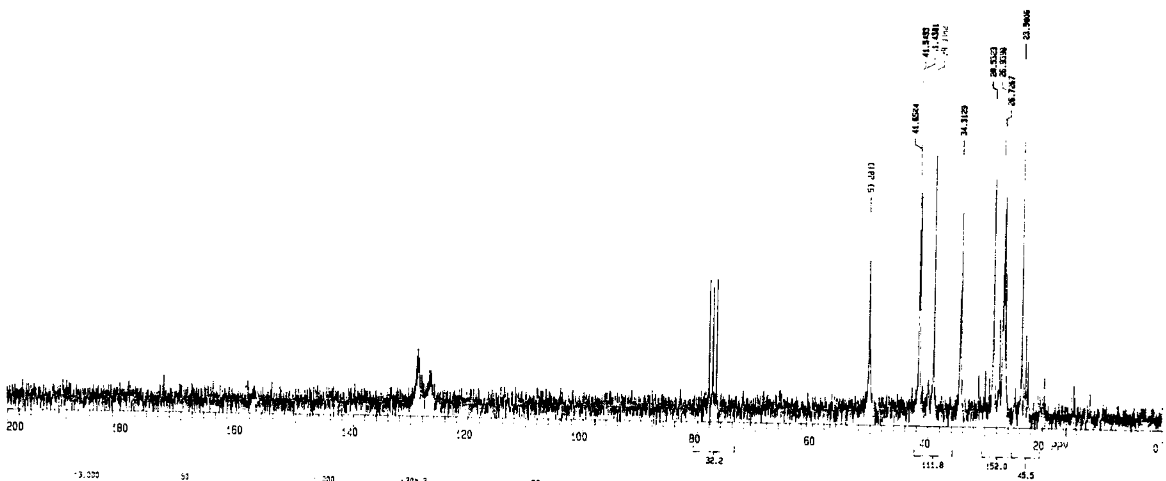
EXPERIMENT
Pulse Sequence
Tube OD mm
Temp °C
Solvent

SAMPLE
Compound — $Sn-(Mgr)_3$
AFTER CHARCOAL
ABED-A-98

Number
File
Date 28-09-89
XL 9 00

PART NO. W7259
CHART XL SERIES

Figure 32: CNMR of Cinnamyltrimyrtanyltin



Myr3-Sn-Cinnamyl
[redacted]
After Charcoal

ether as the solvent. Although a solid was crystallized attempts to recover it failed, since it was very low melting. The crude product was then vacuum distilled using a simple distillation apparatus.

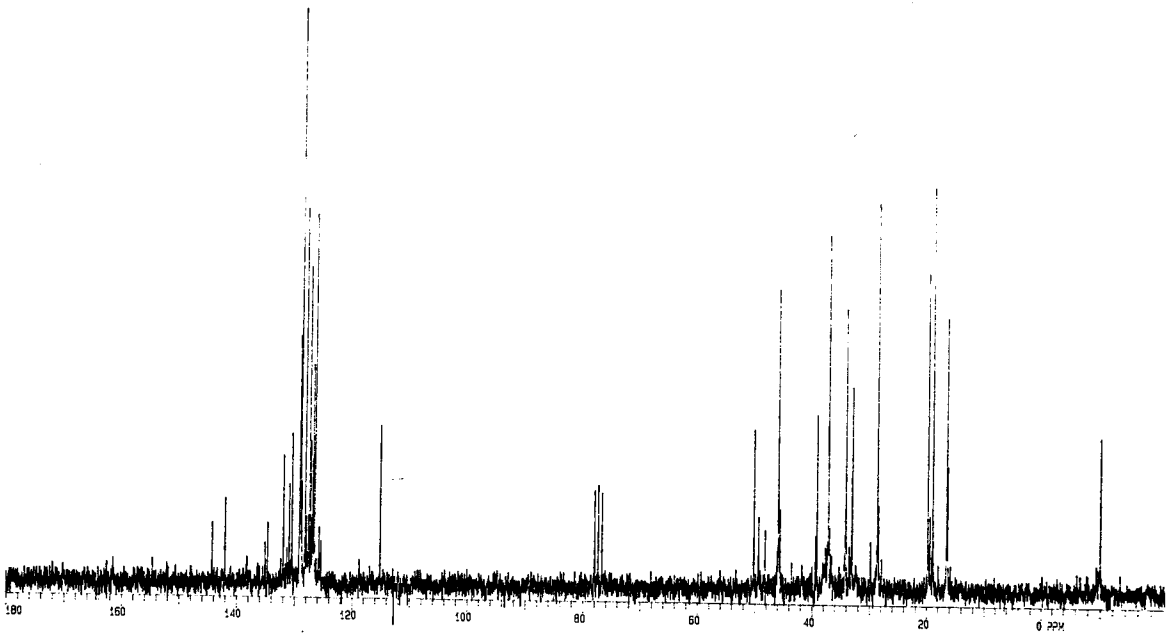
Pressure	temp.(^{o}C)	fraction
0.3 mmHg	62-75	1
0.3 mmHg	79-115	2
0.2 mmHg	122-127	3
0.2 mmHg	127-137	4
0.2 mmHg	137-145	5
0.2 mmHg	145-150	6

CNMR (figure 33)

-10.28 ppm	singlet	Methyls on tin
115.2 ppm	singlet	$=CH_2$ in rearranged product
124-132 ppm	many singlets	C's on phenyl
142 & 144 ppm	two singlets	Double bond CH's on cinnamyl group

The spectra indicates the distinct presence of the rearranged product, 115.2 ppm, as well as the desired product. Since the carbon for the 115.2 ppm peak is not equivalent to the carbon of the 142 ppm peak the ratio's can not be compared to get an idea of the amounts of each.

Figure 33: CNMR of Cinnamyldimethylisobornyltin


180
160
140
120
100
80
60
40
20
0 PPM

HNMR (figure 34)

0.24 ppm	two singlets	Methyls on tin
2.2 ppm	doublet	protons on C attached to Sn
5.05 ppm	doublet	$=CH_2$ on rearranged cinnamyl group
6.4-6.9 ppm	complex	protons on both double bond C's
7.5-7.7 ppm	complex	protons on phenyl

Both NMR's show the distinct presence of the rearranged product of the cinnamyl group:

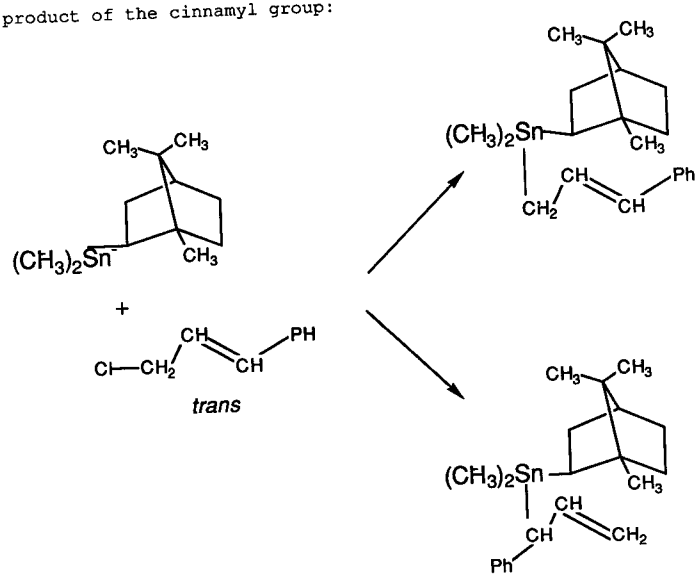
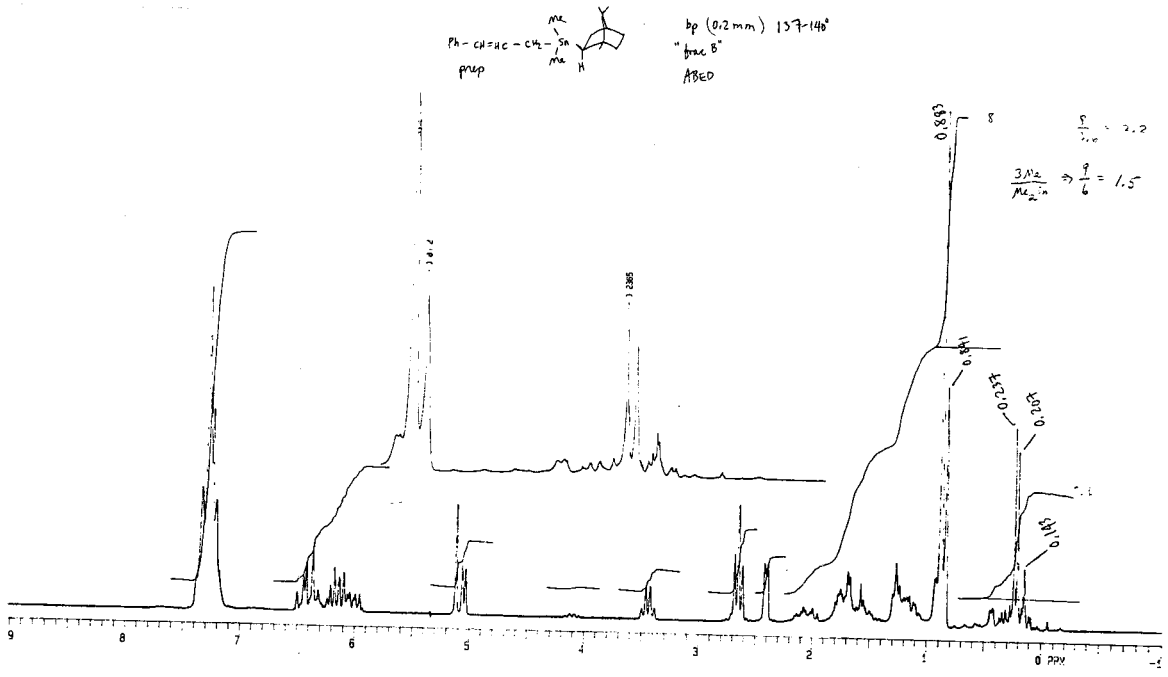


Figure 34: HNMR of Cinnamyldimethylisobornyltin


Ph – CH=HC – CH2 – Sn
Me
Me
H
prep
bp (0.2 mm) 137-140°
"trace B"
ABED
0.893
0.841
0.257
0.209
0.145
3.012
2.865
9
8
7
6
5
4
3
2
1
0 ppm

EXPERIMENTAL

Part 1: The Synthesis of a Chiral Ligand

Synthesis of Alpine-Borane [6]:

α-Pinene, 1.60 g (0.0117 mol, [α]=-42.0) ,25 mL of THF, and a magnetic stirrer were added to a dry 100-mL, three necked, round-bottom flask. A reflux condenser equipped with a $N_{2(g)}$ inlet and bubbler was attached to the middle neck. The remaining two necks were closed with either a glass stopper or serum cap. H-BBN (25mL, 1.0M, 0.0125 mol in THF) was then added over a period of 5 minutes *via* a syringe. The reaction was allowed to reflux for 18.66 hrs.

The reaction mixture was then rotovapped to remove all of the THF, and both IR and NMR spectra, figures 1 and 2, were obtained from the crude product.

Attempted Bromination of Alpine-Borane in Methylene Chloride [7]:

A dry 50-mL round-bottom flask was placed in an ice bath and covered with aluminum foil in order to exclude light. Methylene chloride(4 mL) and 1.75 g (0.00678 mol) of alpine-borane were stirred magnetically. Then 0.23 mL (0.0045 mol) of bromine was added dropwise.

After 30 min the ice bath was removed and the reaction was continued for 1 hour at room temperature before 3 mL NaOH(conc.) was added to destroy any remaining Br_2. The organic phase was separated and dried with K_2CO_3 to remove any water, and the methylene chloride was then removed by simple distillation.

An infrared spectrum was taken of the olive-green product, which revealed the presence of a C=O peak, as well as the semblance of an OH peak. The product was then dissolved in 10 mL of petroleum ether and passed through a column packed with silica gel. The yellow-brown extrudate was then rotovapped to remove the petroleum ether, and both IR and HNMR spectra were taken of the residue.

Again the IR spectrum showed the presence of a C=O peak, although slightly diminished, and a somewhat narrowed peak at 3200 cm^{-1}.

Attempted Bromination of Alpine-Borane in Methylene Chloride (expt. II):

The same procedure was followed as before except for the doubling of the amounts of alpine-borane, methylene chloride, NaOH, and the addition of 0.75 mL of Br_2.

After the crude product was separated and dried, the methylene chloride was distilled off, and an IR was taken of the brown crude product. Again there was a broadened peak from 1720-1610 cm^{-1} and an OH peak.

The crude product was then passed through a column packed with silica gel using petroleum ether, diethyl ether, and dichloromethane as solvents in the before mentioned order. Three fractions were collected and an IR spectrum was taken for each one.

Each IR showed varying degrees of the two peaks in question, so the solvents were removed and the fractions were added together. In an attempt to remove any residual

borane the crude product was added to 4 mL of THF and treated with 5.4 mL of NaOH and 2.98 mL of (30%)H_2O_2.

The two phases were separated and the water phase was washed twice with 3 mL of THF. The resulting organic phase was mixed with the previous organic phase. This was then washed with 4 mL of brine, separated, and dried with K_2CO_3.

The solvent was then rotovapped off and a final IR was taken. The spectrum still showed the presence of the two peaks in question, and so this procedure was abandoned.

Attempted synthesis of 3-bromo-2,7,7-trimethyl bicyclo[3.1.1] heptane by way of BH_3:

A dry three-necked 100-mL round-bottom flask was equipped with a N_2 gas inlet and bubbler, an addition funnel, and a serum cap. A magnetic stirrer, α-pinene (2.14 mL, 0.018 mols), and 1 mL of THF were added and allowed to stir. The BH_3•THF(10 mL, 1M) was added by syringe over a period of 20 minutes. After 5 minutes 1 mL of methanol was added and the reaction stirred.

Another new dry three-necked 100-mL round-bottom flask was fitted with an addition funnel, a glass cap, and a thermometer adapter. The Ipc_2BOCH_3(diisopinocampheyl-methoxyborane) from the previous step was added to the flask and stirred. Sodium methoxide (1.90 g, 32.2 mmol) freshly prepared from methanol and sodium was added to the addition funnel. In another funnel bromine (1 mL, 19.5 mmols) was added slowly simultaneously with the $NaOCH_3$. After all of

each reactant was added, an additional 12 mL of $NaOCH_3$ solution was added to the orange solution to destroy any remaining Br_2.

The resulting colorless liquid and white solid were washed with 3x10 mL of petroleum ether. The organic phases from the washings were then mixed together, washed with 20 mL of H_2O, and separated. Finally 11 mL of brine was used to wash the organic phase, which was separated and dried with $MgSO_4$. This was filtered by gravity, and the petroleum ether was rotovapped off.

Both an IR and NMR spectra were taken of the straw yellow product. Again as with the previous experiment a C=O and and OH peak were present in the IR The NMR also confirmed the presence of an OH peak. The sample was analyzed by capillary gas chromatography, which indicated that many different compounds were present.

The Addition of HBr to α-Pinene
Preparation of Bornylbromide [8]:

α-Pinene (22.82g, 0.167 mols) was added, with 200 mL of hexane and a stir bar, to a dry three necked 500-mL round-bottom flask immersed in an ice bath. The flask was fitted with a thermometer immersed in the solution, and a gas inlet/outlet. The tubing used was tygon™, and the outlet tube went to a large empty test tube where the exiting gas was mixed with air drawn in by aspirator. HBr was slowly bubbled through the α-Pinene at a constant rate while

maintaining the temperature below 10°C.

After 1 hr and 40 minutes the reaction was stopped, and the colorless liquid was decanted to a dry 100-mL round-bottom flask. The hexane was then rotovapped off. Hexane (50 mL) and $NaHCO_3$ (25 mL) were added and mixed. A large amount became emulsified so 45 mL of ether was added in an effort to separate the two phases. Once the phases were separated the solvent was removed by simple distillation. An IR spectrum of the crude product showed some presence of C=O and OH peaks but also a C-Br peak at 670 cm^{-1}.

A trap-to-trap distillation was then attempted, with a 500-mL round-bottom flask as the boiling pot and a 100-mL round-bottom flask as the receiving flask. The reaction pot was heated in a oil bath to 100°C and the pressure was lowered to 0.6 mm Hg. At 70-75°C a solid slurry proceeded to come over and solidify in the condenser, so the water was turned off and a Bunsen burner was used to keep the glassware hot enough to keep the distillate a liquid. A yellow brown semi-solid was collected. An IR spectrum of the solid product had no OH peak or C=O peak, but did have a nice C-Br peak again at 670 cm^{-1}.

The Addition of HBr to α-Pinene expt. 2:

The same set up as the previous experiment was used, except for different concentrations. In the experiment α-pinene (108.9 g, 0.799 mols) and 75 mL of CH_2Cl_2 were used.

After bubbling the HBr through for 5 hours and 15 minutes the reaction was stopped.

To neutralize any remaining HBr the mixture was washed with 2 X 100 mL of $NaHCO_3(aq)$. It was dried with Na_2SO_4, filtered by gravity, and rotovapped to remove the CH_2Cl_2. As before the crude product was distilled from trap to trap at a pressure of 0.5 mm Hg, and again the glassware had to be heated to prevent clogging.

After the distillation, 60 mL of methanol was added to the crude product and refluxed until the solid dissolved. This solution was transferred to a 1000-mL round-bottom flask where an additional 180 mL of methanol was added and again refluxed until one phase remained. At this point the solution was allowed to cool and crystals were formed. These were collected by filtration, and washed with 2 X 20 mL of cold methanol. A solid white product was retrieved (mass = 50.94g). The filtrate was concentrated, and a second crop weighing 28.10g was retrieved.

The two crops of the solid white product were characterized by taking IR, NMR, GC, melting point., and optical rotation measurements. The percent yield was 45.4%.

The Addition of HBr to α-Pinene expt. 3:

Again the same procedure was used as in the previous experiment, using α-pinene (109.7 g, 0.808 mols), 75mL of CH_2Cl_2, and the bubbling of HBr through the solution for 5.25 hours. For the distillation, a Hemple column was used

instead of a condenser.

Three crops of product were collected and characterized as before. A percent yield of 60.0% was attained in this experiment.

Part2: The Attachment of the Chiral Ligand to the Organotin Compound.

The Synthesis of isobornyltriphenyltin expt. 1:

A three-necked 500-mL round-bottom flask was flame dried to remove any traces of water. A mechanical stirrer was attached to the middle neck, a glass stopper placed in one side arm, and a large cold finger packed with dry ice attached to the other neck. In addition, a nitrogen inlet/bubbler was added to the top of the cold finger to keep the whole system under a nitrogen atmosphere. A stir bar along with Ph_3SnCl (19.3 g, 0.0501 mols) and hexane (15 mL) were added to the flask. With the reactants in the flask, the flask itself was encased in dry ice. Then NH_3 (100 mL) was distilled from $Na_{(s)}$ and condensed into the other reactants. Finally $Na_{(s)}$ (2.49 g, 0.0889 mols) was added, and the reaction was allowed to proceed for 1 hour at which time the NH_3 was allowed to evaporate. After all of the NH_3 was evaporated, THF (10 mL) and endo-2-bromobornane (5.40 g, 0.0249 mols) were added to the blood red mixture and allowed to react overnight.

Once the reaction was complete, H_2O_2 (7 mL, 30%) was added and stirred for several minutes(flask in an ice bath to slow the reaction). The mixture was then washed with 37 mL of H_2O and separated. The separated water phase was then washed twice with 30 mL of ether, and the organic phases were added together. They were then dried with $MgSO_4$ and filtered. The yellow-tinted filtrate was rotovapped and an IR and NMR were taken of the residue.

The purity of the product was examined by TLC on silica gel with petroleum ether developer. The results showed the product to have several impurities.

The product was then dissolved in 40 mL of pure ethanol and recrystallized. Again a TLC was taken using the same technique, but still there was no change in the purity. In a final effort to purify the product, it was passed through a column packed with 100g of Al_2O_3 and eluted with petroleum ether. Eight fractions were obtained. Each fraction was then distilled to concentrate the sample in order to take TLC's of each. An NMR was taken of both fractions 1 & 2.(figure 12)

The Synthesis of isobornyltriphenyltin expt. 2:

The same set up as the previous experiment was used with Ph_3SnCl (19.32 g, 0.0501 mols) and $Na_{(s)}$ (2.45 g, 0.0875 mols); however instead of 15 mL of hexane, 100 mL of THF was used. After the NH_3 was completely evaporated, 2-bromobornane (9.78 g, 0.0450 mols) and an additional 30 mL of THF were added and the mixture stirred for 3 hours.

At its completion, the dark brown reaction was washed with 100 mL of H_2O along with 50 mL of ether (to reduce the amount of emulsion). The water phase was then separated and washed with 3 X 75 mL of ether. The combined organic phases were washed again with 3 X 100 mL of H_2O. Finally, the

cloudy organic phase was filtered once to remove the particulate matter, and then dried with Na_2SO_4, and again filtered. The filtrate was concentrated by the evaporation of the solvents, (rotovap). An IR and NMR, (figure 16), were taken of the crude product as well as a TLC.

The crude product was then passed through a column as in the previous experiment, but difficulties arose and the procedure was aborted. The crude product was recovered as best as possible, by flushing it off the column with ethyl/acetate. However, most of the product was lost.

The Synthesis of isobornyltriphenyltin expt.3:

In this experiment, the anion was formed in a different way. First instead of $Na_{(s)}$, $Li_{(s)}$ was used, and because of the metal's reactivity with N_2 a glove bag with an Ar atmosphere had to be used. Inside the bag a flame-dried 250-mL round-bottom flask with stir bar was filled with Ph_3SnCl (10.57 g, 0.0274 mols) and THF (30 mL). To this, Li (0.69 g, 0.099 mols) cut in small pieces was slowly added and allowed to react overnight.

The reaction mixture was filtered through glass wool into a flame dried 250-mL round-bottom flask containing 10 mL of THF. Outside of the bag, a condenser with a N_2 inlet was attached. Then 2-bromobornane (5.66 g, 0.026 mols) and a stir bar were added and mixture heated to reflux.

After 24 hours, a sample of 5 mL was removed and washed with 10 mL of saturated aqueous NH_4Cl. The organic phase was

separated, and the solvent was rotovapped off. An NMR was taken to detect any desired product. As the reaction seemed successful the rest of the reaction mixture was washed with 50 mL of saturated aqueous NH_4Cl. The organic phase was separated, dried with $MgSO_4$, filtered and the solvent removed (rotovap).

In an attempt to remove any 2-bromobornane, 50 mL of petroleum ether was added to the crude product in 250-mL round-bottom flask and refluxed. The mixture was filtered upon cooling, collecting a white-gray solid. An NMR was taken of the solid and the filtrate was rotovapped. An NMR was also taken of the yellow-tan viscous crude product, (figure 13).

The Synthesis of dibutyl-phenylisobornyltin :

Before the reaction was run the $Bu_2PhSnCl$, (from Dr. L. McGahey) was distilled to purify the reactant. In a 100-mL round-bottom flask w'th a stir bar, $Bu_2PhSnCl$ (29.36 g, 0.0775 mols) were distilled at a pressure of .1 mm Hg. Four fractions of various amounts were collected in a cow fixture.

Pressure	temp.(^oC)	fraction	mass
0.1 mmHg	120-124	1	13.89 g
0.1 mmHg	125-126	2	8.88 g
0.1 mmHg	127-130	3	3.31 g
0.1 mmHg	131-138	4	4.33 g

From fraction 1, 10.38g was added to a flame dried 250-mL round-bottom flask and placed in the glove bag with an Ar atmosphere. THF (30 mL), was added and stirred. Over a

period of 15 minutes, finely cut Li (0.70 g, 0.100 mols) was added as well as an additional 40 mL of THF. This was reacted for 24 hours. The mixture was pea-green instead of black-green, so Li (0.31 g, 0.0450 mols) was again added and reacted for 24 more hours.

This time the mixture was dark black-green and it was filtered through glass wool to a 250-mL flame dried round-bottom flask. It was then removed from the glove bag, and fitted with a reflux condenser and N_2 inlet/bubbler. While stirring the mixture, 2-bromobornane (5.68 g,0.0261 mols) was added and refluxed for 24 hours.

Upon cooling, the mixture was washed with 80 mL of saturated aqueous NH_4Cl. The water phase was separated and washed with 50 mL of petroleum ether. The organic phases were combined, washed with 3 X 30 mL of H_2O, separated, dried with $MgSO_4$, filtered, and simple distilled to remove the solvent. Both an IR and NMR were taken of the resulting crude product(Pg. 28).

In addition, a TLC (developer 25% CH_2Cl_2, 75% petroleum ether), on silica gel was taken; it showed various impurities. The crude product was put under a pressure of about 1 mm Hg to remove any remaining volatiles, and another TLC, with the same solution composition, was taken. Again there were many impurities.

The Synthesis of Tributylisobornyltin:

A 250-mL round-bottom flask was flame dried and placed in a glove bag containing an atmosphere of Ar. To this, Bu_3SnCl (8.92 g, 0.0274 mols), THF (30 mL) and a magnetic stirbar were added; over a period of 20 minutes Li (0.31 g, 0.0450 mols) was added in very small pieces to the stirred solution and allowed to react for 24 hours.

After this time the dark green mixture was filtered through glass wool into another flame dried 250-mL round-bottom flask (to remove the remaining particles of Li). The flask was then taken out of the bag, and a condenser with a N_2 inlet/bubbler was attached. Endo-2-bromobornane (5.67 g, 0.0261 mols, $[\alpha]$=-28.1) was then added and mixed for 10 minutes at which time the heat was turned on, and the mixture was allowed to reflux for 20 hours.

The resulting mixture was washed with 80 mL of saturated aqueous $NH_4Cl_{(aq)}$ and separated. The water phase was then washed with 50 mL of petroleum ether and separated, with the organic phase being added to the previous organic phase. The combined organic phases were then washed with 3 X 50 mL of H_2O, dried with $MgSO_4$, filtered, and rotovapped, to remove the solvents, and put under vacuum at a pressure of 0.5 mm Hg to remove any remaining volatiles.

A TLC, IR, NMR, and the mass of the product were all taken in order to characterize the product (figure 14 & 15).

The Synthesis of Tributylisobornyltin expt. 2:

The same procedure as before was followed, using different concentrations of Bu_3SnCl (19.09 g, 0.0587 mols), Li (2.10 g, 0.303 mols), THF (40 mL), and 2-bromobornane (9.57 g, 0.044 mols). The work up, was also as before except the solvent was distilled off; however, the product began to decompose, forming a black liquid with solid particles.

To the decomposed mixture 70 mL of acetone and $KMnO_4$ (3.52 g, mols) were added and stirred for 15 minutes. This was then filtered by vacuum through a pad of celite in a Buchner funnel. The brownish filtrate was rotovapped to remove the acetone. Ether (75 mL) was added to the residue and the mixture was washed with 25 mL of H_2O three times. The separated organic phase was then washed 2 X 100 mL of brine, separated, dried with $MgSO_4$, filtered by gravity, and rotovapped.

The mass of the crude product as well as a TLC were taken. It was then distilled under a pressure of 0.1 mm Hg, and four fractions of a clear liquid were collected. Both TLC's and IR's were taken of each fraction, and NMR's were taken of fraction 1 & 2 (figures 16 & 17).

The Synthesis of Tributylisobornyltin expt. 3:

Again the same procedure for the synthesis of the product was followed, using Bu_3SnCl (81.37 g, 0.250 mols), Li (4.00 g, .576 mols), 2-bromobornane (40.75 g, 0.187 mols), and THF (90 mL). The work up of the product however

was slightly different.

The THF mixture was washed with 160 mL of saturated aqueous NH_4Cl and separated. The water phase was then washed with 100 mL of petroleum ether and this was combined with the previous organic phase. This was then washed twice with 100 mL of H_2O, and with 45 mL of saturated aqueous KF twice . Finally the resulting organic phase was dried with $MgSO_4$, filtered, and rotovapped to remove the solvents.

A TLC was taken of which showed the presence of some residual 2-bromobornane or Bu_3SnCl. The crude product was then mixed with 50 mL of diethyl ether and washed with 20 mL of saturated KF. Solid particles were present in the organic phase after separation, so it was filtered. The filtrate was then rotovapped to remove the diethyl ether. A second TLC was taken to se if any of the impurities were removed, which was negative.

At this time the crude product was dissolved in 140 mL of acetone, and solid $KMnO_4$ was added with constant stirring until a purple color remained. It was stirred for an additional 25 minutes, at which time the mixture was filtered by vacuum through a pad of celite in a Buchner funnel The filtrate was still cloudy so it was again filtered, but this time by gravity filtration through fluted filter paper. The acetone was removed by rotavapping. Ether (150 mL) was added to dissolve residue and washed with 2 X 50 mL of H_2O, followed by 3 80-mL washes of brine. The organic phase was then dried with $MgSO_4$, filtered, and rotovapped.

The mass of the crude product was recorded and it was prepared to be distilled. At first, left over 2-bromobornane distilled over at a pressure of 0.3 mm Hg, and again a Bunsen burner was needed to keep the glassware hot to prevent clogging of the system. When the halide was removed, the rest was distilled through a fractionating column at a pressure of 0.3 mm Hg.

Mixing of the remaining crops of 2-bromobornane:

In order to have sufficient amount of 2-bromobornane the crops from both experiments were mixed with 50 mL of petroleum ether and stirred for 15 minutes. The mixture was then rotovapped to remove the solvent and allowed to air dry. The optical rotation was determined by using 1.356 g of the product added to a 25-mL volumetric, with the appropriate volume of $CHCl_3$. An NMR, GC, and IR were also taken.

Optical Rotation

[solvent = $CHCl_3$ & l=1dM]

crop 1: $[\alpha]_D$= -27.4 (at 25°C)

HNMR

4.3 ppm	multiplet	hydrogen attached to brominated carbon
0.85 ppm	two singlets	methyls on bornyl group
0.93 ppm	singlet	bridgehead methyl

The Synthesis of trimethylisobornyltin :

A 500-mL round-bottom flask was flame dried and placed in a glove bag under an Argon atmosphere. Me_3SnCl (21.11g, 0.106 mols) and THF (150 mL), dried by distillation from

sodium under argon, were added and stirred magnetically. Over a period of 1.75 hours Li metal (3.78 g, 0.545 mols) was added in very small pieces, and reacted for 24 hours.

The dark green-black mixture was then filtered through glass wool into another flame dried 500-mL round-bottom flask. This was then removed from the bag and attached to a reflux condenser with a N_2 inlet/bubbler to maintain a N_2 atmosphere. At this time 2-bromobornane (17.39 g, 0.0800 mols $[\alpha]$=-28.1) was added with 12 mL of THF over a period of 15 minutes, since the reaction was exothermic, and reacted for 24 hours, at room temperature.

The mixture was then cooled to room temperature and washed with 70 mL of saturated aqueous NH_4Cl. This was an exothermic reaction and a black pasty film separated fro the two phases. The water phase was separated and washed w: 40 mL of petroleum ether. The organic phases from t two previous steps were combined and then washed with 3 X 100 mL of H_2O. Again the water phase from the previous step were combined and washed with 50 mL of petroleum ether. The newly combined organic phases were now washed with 25 mL of saturated aqueous KF twice, dried with $MgSO_4$, and filtered by gravity. The filtrate was rotovapped. The resulting clear liquid, with a slight yellow tinge, was added to 50 mL of acetone. $KMnO_4$ (4.05 g, mols) was added and stirred overnight. The purple mixture was filtered through a celite pad in a Buchner funnel by vacuum. The celite pad was then washed with 3 X 20 mL of acetone. Solid particles were present in the filtrate so the mixture was again filtered,

but this time by gravity. This was then rotovapped to remove the acetone. Once the acetone was removed 75 mL of diethyl ether was added and washed with 2 X 25 mL of H_2O. The H_2O was washed with 30 mL of diethyl ether and the organic phase was combined with the previous organic phase. This was finally washed with 30 mL of brine, separated, and dried with Na_2SO_4. The mixture was filtered by gravity and the filtrate was rotovapped to remove the solvent.

Once rotovapped, the mass of the crude product was taken and an NMR was also taken. The crude product was found to have some impurities, so it was placed into a 25 mL round-bottom flask and distilled under a pressure of 0.2 mm Hg. Four fractions of various volumes of a clear liquid were collected; they had a combined mass of 5.18g. An NMR as well as an IR were taken of each fraction. The fractions were combined, since each NMR was the same, added to 30 mL of ether and washed with 2 X 10 mL of 15% H_2SO_4. This was then dried with $MgSO_4$, filtered by gravity, and rotovapped. Again an IR was taken.

The Synthesis of trimethylisobornyltin expt. 2:

The same set-up and procedure was followed for the formation of the anion as in the first trial, using Me_3SnCl (31.64 g, 0.159 mols), Li (6.30 g, 0.908 mols), and THF(225 mL). However, the reaction of the anion with 2-bromobornane was different.

The flask containing the anion was immersed in an ice bath, and an addition funnel with a N_2 inlet was attached.

Two Page
86

The 2-bromobornane (17.26 g, 0.0794 mols) was dissolved in 15 mL of THF and added dropwise through the addition funnel, over a 15 minute period. After an additional hour of stirring, the flask was removed from the ice bath and allowed to continue to react overnight.

The flask was again placed in an ice bath, and 24 mL of 30% H_2O_2 was slowly added over 20 minutes and stirred for 40 minutes. This mixture was treated with 250 mL of H_2O and washed with 3 X 100 mL of hexane. The organic phases were combined and washed with 2 X 200 mL of 10% HCl, then 2 X 200 mL of H_2O. Finally the resulting organic phase was washed with 100 mL of $NH_4Cl_{(aq)}$, dried with $MgSO_4$, filtered by gravity, and rotovapped.

An IR, NMR, and the mass of the clear liquid crude product were taken. A vacuum distillation at a pressure of 0.2 mm Hg was done and three fractions of clear liquid were collected. The mass of each fraction was recorded and IRs, NMRs, and TLCs were also taken(figures 18, 19 & 20).

Part 3: The Addition of an Allylic Group to the Alkyltin compound

The 2-bromobornane (17.26 g, 0.0794 mols) was dissolved in 15 mL of THF and added dropwise through the addition funnel, over a 15 minute period. After an additional hour of stirring, the flask was removed from the ice bath and allowed to continue to react overnight.

The flask was again placed in an ice bath, and 24 mL of 30% H_2O_2 was slowly added over 20 minutes and stirred for 40 minutes. This mixture was treated with 250 mL of H_2O and washed with 3 X 100 mL of hexane. The organic phases were combined and washed with 2 X 200 mL of 10% HCl, then 2 X 200 mL of H_2O. Finally the resulting organic phase was washed with 100 mL of $NH_4Cl_{(aq)}$, dried with $MgSO_4$, filtered by gravity, and rotovapped.

An IR, NMR, and the mass of the clear liquid crude product were taken. A vacuum distillation at a pressure of 0.2 mm Hg was done and three fractions of clear liquid were collected. The mass of each fraction was recorded and IRs, NMRs, and TLCs were also taken(figures 18, 19 & 20).

Bromination of trimethylisobornyltin:

Me_3Sn2BB, trimethylisobornyltin, (16.01 g, 0.0532 mols) was added to a 1000-mL round-bottom flask with CCl_4 (390 mL) and CH_3OH (19 mL). A self-equalizing addition funnel charged with bromine (8.21 g, 0.0514 mols) in CCl_4 (50 mL) was connected to the flask and capped. The bromine was then slowly added over a period of 4 hrs with rapid stirring and at 0°C, then allowed to stir overnight.

The solution was rotovapped to remove the solvent, leaving a yellowish white solid. Three TLC's with chamber solutions of 100% petroleum ether, 50% petroleum ether 50% dichloromethane, and 100% dichloromethane were taken of the crude.

The product was then recrystallized in methanol (70 mL) Nice needle white crystals formed in the freezer, which were collected by vacuum filtration in a Buchner funnel, and washed with 3 X 10 mL of cold methanol. The filtrate was concentrated by distilling off some methanol and again allowed to cool in order to get a second crop. This was filtered and washed as before.

The mass of the first and second crops were recorded, and a TLC was taken of the first crop. The first crop was also characterized by an IR, HNMR, CNMR, melting point, and optical rotation measurement(Pg. 44, figures 21 & 22) .

Purification of Crotyl chloride:

The 70% *trans*-crotyl chloride (Aldrich Chemical Co.), (100 g, 1.10 moles), was added to a 250-mL round-bottom flask and equipped with a distillation system, containing a 2 ft long fractionating column, packed with small pieces of glass tubing. A 100-mL receiving flask was attached, and the solution was stirred magnetically and heated.

A large portion was collected between the temperatures of 62°C-81°C. A second portion was collected between the temperatures of 81°C-84°C. Finally a last portion, (9.78 g), was collected between the temperatures of 84°C-85°C, and it was characterized by HNMR and GC (figures 23 & 24).

Synthesis of Crotyltrimethyltin expt. 1:

A 500-mL round-bottom flask was flame dried and placed in a glove bag under an Argon atmosphere. Me_3SnCl (21.43 g, 0.108 mols) and THF (150 mL), dried by distillation from sodium under argon, were added and stirred magnetically. Over a period of 30 minutes, Li metal(4.09 g, 0.59 mols), was added in small pieces and reacted over a 24 hr.

The dark green-black mixture was then filtered through glass wool into another flame dried 500-mL round-bottom flask. This was then removed from the bag and equipped with a self-equalizing addition funnel. A N_2 inlet/bubbler, to maintain a N_2 atmosphere, was added to the addition funnel. Next the round-bottom was immersed in a xylene/$N_{2(l)}$ slush bath at approximately -36°C. Once the temperature