ORGANOTIN CHEMISTRY FOR SYNTHESIS APPLICATIONS

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Abstract - A variety of synthetically useful organotin reactions have been investigated. Tin hydrides, under free radical conditions, selectively cause the reductive ring-opening of cyclopropylketones, vinylcyclopropanes and cyclopropylcarbinyl halides. With alkyl-substituted cyclopropyl groups the direction of the ring-opening depends on the configuration of the substrate, the nature of the substituent and on reagent concentrations.
Different functional groups can be transfered from tin to organic substrates. For instance, allyltins directly undergo substitution reactions with alkyl halides and add to aldehydes or ketones. Specially designed model compounds have been synthesized in order to investigate the stereochemical aspects of the tin-allyl reactions. The direct reactions of vinyltins with acyl and alkyl halides have also been explored. Since electrophilic cleavages of tin-aromatic bonds can be used to selectively introduce substituents into the ring, preliminary stannylation of aromatic halides has been investigated with emphasis on its regioselectivity.
Finally an efficient route to dialkoxymethyltin derivatives has been discovered. Upon transmetallation, these compounds are transformed into lithium analogs which can be used as nucleophilic masked carbonyl groups.

INTRODUCTION

In the recent years there has been an increasing interest in organotin compounds as reagents or intermediates for organic synthesis (1). The main reasons for this attraction reside in two elements :
- Firstly, the general knowledge of the synthesis and the reactivity of organotin compounds has markedly increased in the last twenty five years. A number of organotin reagents are now commercially available or easily prepared in high yields, often from reasonably cheap industrial starting materials.
- Secondly and perhaps more importantly, some of the world's most active and famous groups in organic synthesis have begun to use organotin reagents with success and have found exciting new applications. In a few months they have gained more publicity for organotin compounds than had been obtained from the many years of work by specialized organometallic chemists !
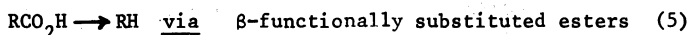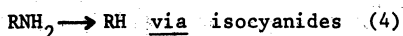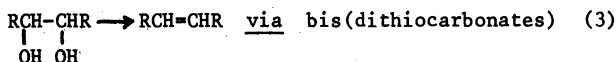
We wish to present here some results which have been recently obtained by the organotin group at Bordeaux. Several examples of direct applications of organotin compounds for specific transformations will be shown. In addition, we will present some experiments which were undertaken in order to give a better understanding of synthetically interesting organotin reactions. Whenever possible, our results will be compared with related studies from other research groups. Two topics will be presented :
- tin hydride reductions involving cyclopropylcarbinyl-allylcarbinyl radical rearrangements.
- transfer of functional groups by cleavage of tin-carbon bonds.

TIN HYDRIDE REDUCTIONS INVOLVING CYCLOPROPYLCARBINYL-ALLYLCARBINYL RADICAL REARRAN-
GEMENTS

The reduction of organic halides to hydrocarbons still constitutes the most popular use of organotin hydrides but a number of new applications have appeared recently. Amongst these are a set of new reduction processes discovered by D.H.R. Barton and his coworkers and largely used in the synthesis of natural products :

ROH $\longrightarrow$ RH via thio derivatives such as dithiocarbonates(2)

$$\underset{\underset{OH}{|}}{R\overset{}{C}H}-\underset{\underset{OH}{|}}{\overset{}{C}HR} \longrightarrow RCH=CHR \quad \underline{via} \quad bis(dithiocarbonates) \quad (3)$$

$$RNH_2 \longrightarrow RH \quad \underline{via} \quad isocyanides \quad (4)$$

$$RCO_2H \longrightarrow RH \quad \underline{via} \quad \beta\text{-functionally substituted esters} \quad (5)$$

Also of importance are the desulfonylations and the deoxygenations of allylic substrates, obtained by Y. Ueno. Both reactions occur through allyltin intermediates :
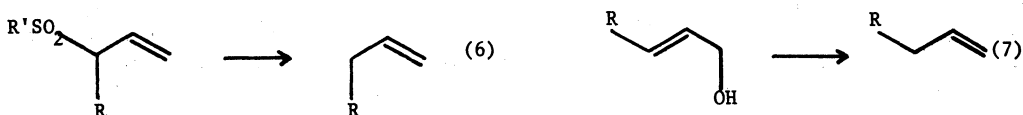
It is interesting to note that all these reactions involve radical processes with hydrogen abstraction from tin hydride after fragmentation of an initially formed free radical. In these reactions, as in any radical rearrangement, the concentration of the reagent is an important factor in determining the final products. For instance, in the case of alkyl halide reductions :

$$R_3Sn\cdot \quad + \quad R'X \longrightarrow R_3SnX \quad + \quad R'\cdot$$
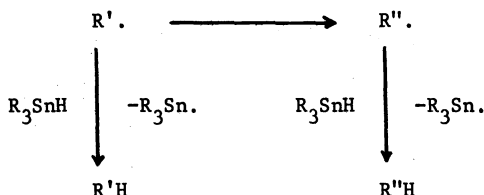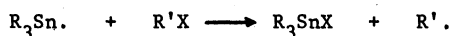
With a high concentration of tin hydride the initially formed radical is rapidly trapped, yielding R'H. On the other hand a low concentration will allow time for rearrangement or fragmentation and large amounts of R"H are obtained.

We have studied in detail the rearrangement of the cyclopropylcarbinyl radical to the allylcarbinyl radical :


Initially we met this rearrangement in the tin hydride reduction of cyclopropylketones. Whereas the reaction in methanol gave only the corresponding cyclopropylcarbinol (nucleophilic addition followed by methanolysis of the organotin adduct), under free radical conditions (U.V. irradiation or azobisisobutyronitrile, AIBN, as initiator) the ring opened ketone was the only reduction product (8) :
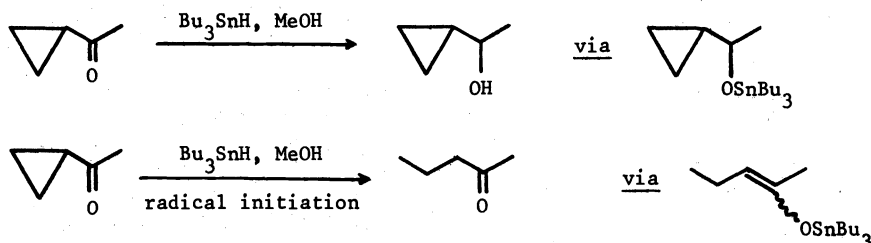

The course of the reaction involves the sequence : (i) addition of the tin radical, (ii) fast and complete ring opening, (iii) formation of an organotin enolate and (iV) methanolysis (9) :
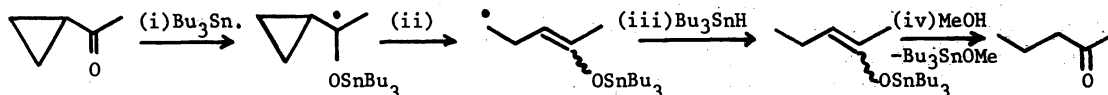
The success of this reduction prompted us to investigate related cases such as vinylcyclo-propanes. It was possible to perform selective reduction of the cyclopropane ring through radical hydrostannation, followed by electrophilic cleavage of the allyltin adduct (10) :
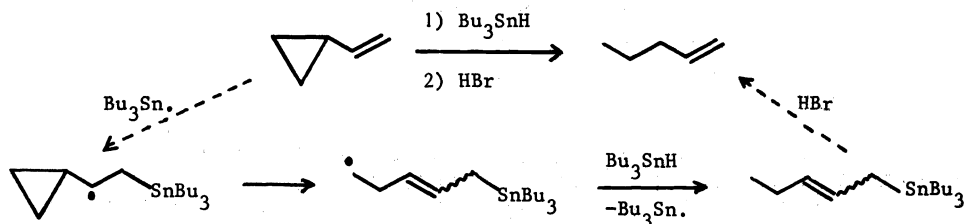
The yields of the overall reduction process were found to strongly depend on the substitu-tion at the double bond, which controls the efficiency of the initial organotin radical addition :

yields $\geq$ 80% $\sim$ 50%   none
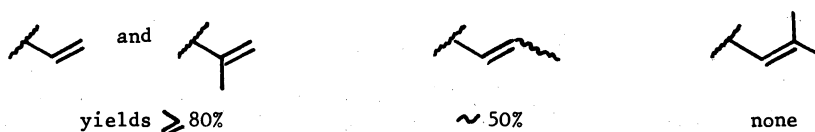
A new situation was reached when ring substituted compounds were used : an interesting regioselective ring-opening was observed with 2-substituted derivatives (11). For instance *trans*-2-methylcyclopropylketone reacted with an equimolar amount of tributyltin hydride, without solvent, and gave essentially the branched opened ketone. On the other hand *cis*-2-methylcyclopropylketone gave mainly the linear ketone :

	90%	10%
cis	90%	10%
trans	25%	75%
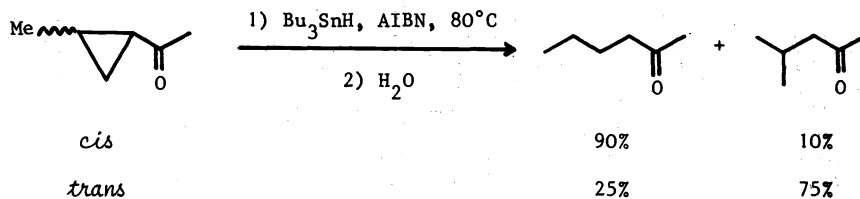
Similar results were obtained from 2-ethyl or 2-t-butyl substituted cyclopropylketones (12). If the regioselectivity of the ring opening of the *cis*-substituted ketones can be easily rationalized by the consideration of stereoelectronic effects of conformational origin (11, 13) it is striking that in the *trans* series the less substituted and less stable radical, was produced in the major amount :

rather than
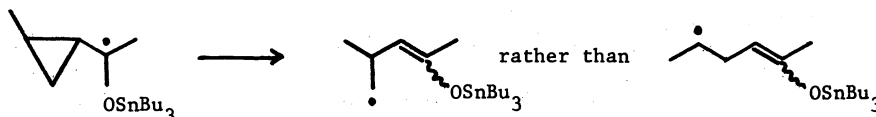
This behavior can be considered as general since similar data were obtained in related systems, again without solvent and using either 1:1 or 2:1 stoichiometries :

Bu$_3$SnH (1:1) , 25°C, U.V.   (14)

66%   34%

1) Bu$_3$SnH (2:1), 60°C, U.V.
2) HBr   (15)

53%   47%
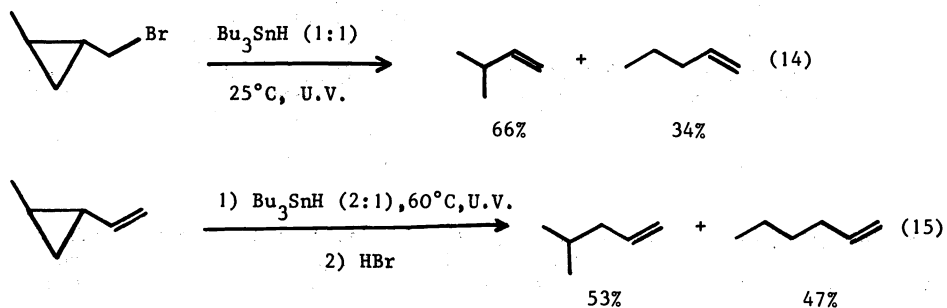
However it was found that in each case the ratio branched to linear compounds, which is related to the regioselectivity of the opening of the cyclopropylcarbinyl radical, depended on the concentration of tin hydride (14-16) :

iBu
1) Bu$_3$SnH, 80°C, AIBN
2) H$_2$O
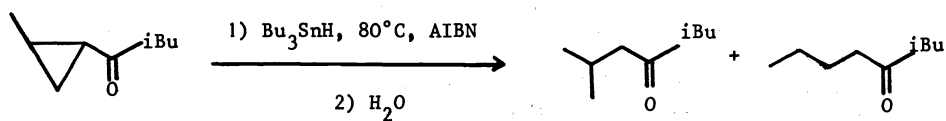
[Bu$_3$SnH] in benzene : 0.2 M   24%   76%
                         1.0 M   58%   42%

1) Bu$_3$SnH, 60°C, U.V.
2) HBr
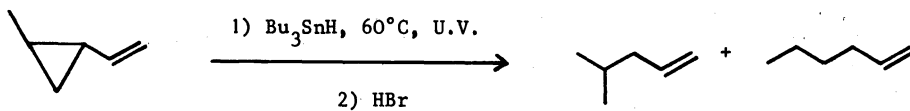
[Bu$_3$SnH] in hexane : 0.2 M   28%   72%
                        1.5 M   52%   48%

Br
Bu$_3$SnH, 45°C, AIBN
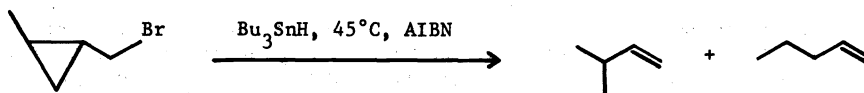
[Bu$_3$SnH] in benzene : 0.02 M   8%   92%
                         0.2 M   26%   74%

In all the cases studied (reduction of cyclopropylketones, vinylcyclopropanes or cyclopropyl-carbinyl halides), the ring-opened radicals which are first formed are the primary, less stable ones. Depending on the concentration of the organometallic reagent, situations close to kinetic or thermodynamic control can be reached. When the concentration of the organotin is high, primary radicals are rapidly trapped. When the tin hydride concentration is low the radicals escape capture for long enough to approach equilibration by reversible ring-closing and ring-opening through the cyclopropylcarbinyl radical :

primary radical

(less stable)

Bu$_3$SnH

secondary radical

(more stable)

Bu$_3$SnH
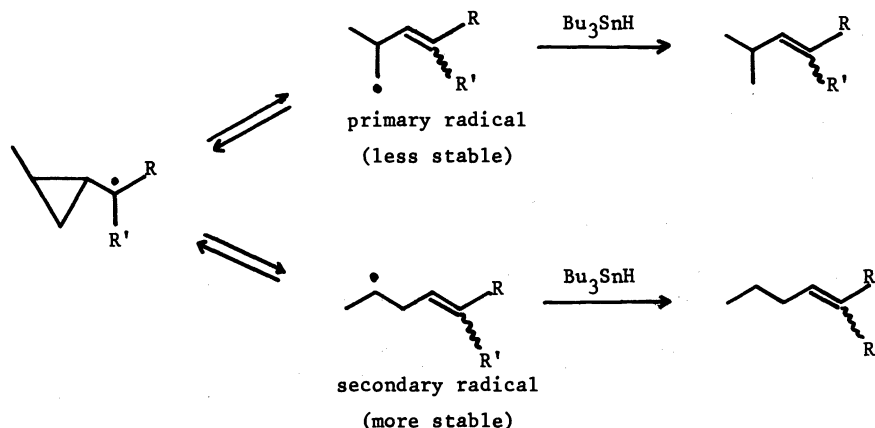
As a direct application of this situation we have performed the tin hydride reduction of stoichiometric amount of 4-bromo-3-methyl-1-butene under different experimental conditions (14) :

+ Bu$_3$SnH $\xrightarrow[\text{AIBN}]{45°C}$ +

|		
neat	90%	10%
0.2 M/C$_6$H$_6$	41%	59%
0.02M/C$_6$H$_6$	14%	86%
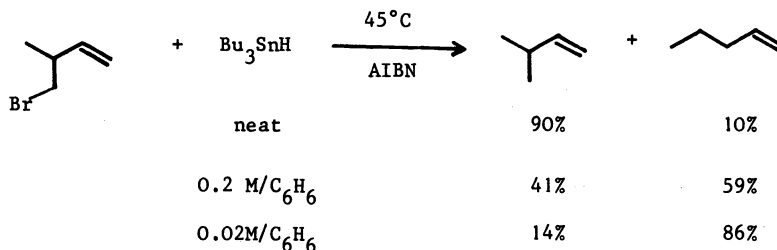
Thus the reduction of the acyclic bromide may follow completely different courses depending on the dilution of the hydrogen transfer reagent.

Now the question which remains is the following : why do *trans*-2-alkyl cyclopropylcarbinyl radicals tend to open, under conditions close to kinetic control, to give the less stable allylcarbinyl radical ? Note also that more rigorous kinetic control is obtained at low temperature and highly regioselective rearrangements were observed by e.s.r. in favor of the primary alkyl radical (12,14,15,16,17,18). We have suggested that an explanation might be based on the differential interaction of the substituent on the ring with the orbitals of the two bonds which can undergo cleavage (15). Thus if the cyclopropyl ring is regarded as a system of localized σ-bonds, a nucleophilic radical would be expected to interact mainly with the σ* rather than the σ-orbitals of the bonds C1-C2 or C1-C3. If the substituent releases electrons (as do alkyl groups) this would break the degeneracy of the σ* orbitals in the way which is presented on the left side of the figure below. Thus, the radical centre would interact principally with the σ* orbital of the C1-C3 bond, leading to the formation of the primary alkyl radical, as is observed.

σ^{*}_{1-2}

LUMO

σ^{*}_{1-3}

σ^{*}_{1-3}

LUMO

σ^{*}_{1-2}

SOMO
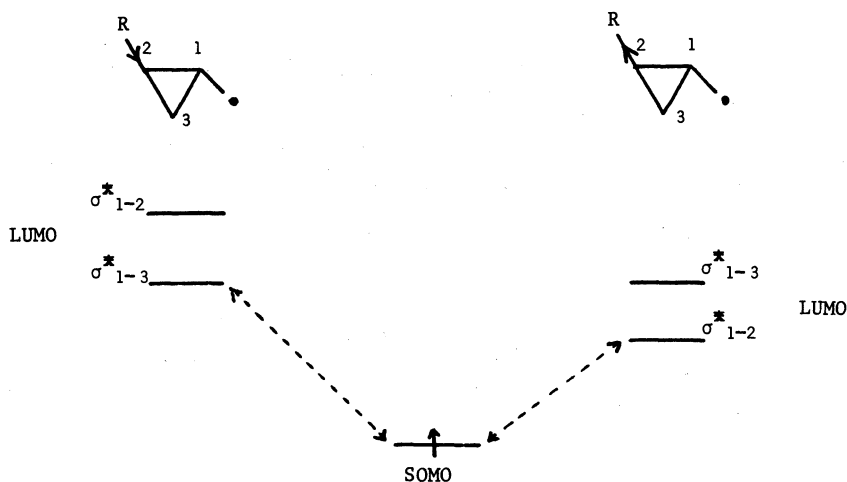
It is worth mentioning that a very similar interpretation has been independently proposed by P.S. Mariano (19) and a related one by A.L.J. Beckwith (20).

If this explanation is correct, it could be predicted that an electron withdrawing group in the cyclopropane would have the inverse effect, promoting cleavage of the C1-C2 bond (as shown on the right side of the figure). We have indeed observed such a cleavage with a trifluoromethyl substituent, under experimental conditions favoring kinetic control (21) :

1) Me$_3$SnH, neat

U.V., 25°C

2) HBr

80%   20%
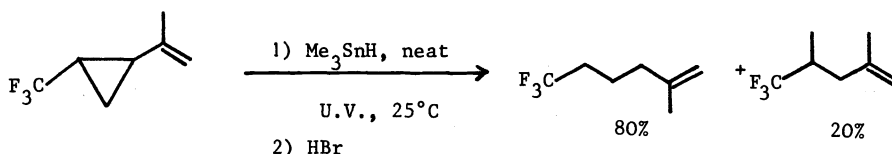
The same kind of regioselectivity was also observed, at lower temperatures, by e.s.r. monitoring of the ring opening of related *trans*-2-trifluoromethyl substituted cyclopropylcarbinyl radicals (21).

A further question may have preparative interest : Is it possible to prevent the ring opening process ? Although theoretically the largest possible tin hydride concentration should be used, there are obvious upper limits which cannot be passed (i.e. neat reagents). In addition, the ring opening processes are very fast because of the release of energy strain. Under special conditions, we partly succeeded in limiting the rearrangement during the radical hydrostannation of cyclopropylketones. For instance with tin hydride in excess, without solvent, and under U.V. irradiation at -65°C, cyclopropylmethylketone gave approximately a 1:1 ratio of methylpropylketone to cyclopropylmethylcarbinol, but at the expense of the overall yield which was under 10% (9). We have quite recently obtained very promising results using the technique of high pressure chemistry. For instance, 2-chlorobicyclo[4.1.0] heptane was reduced by an equimolar amount of tributyltin hydride, without solvent and under 10 kbars pressure (overall yield $\simeq$ 65%) (22). The composition of the mixture was strikingly different from that obtained from the reaction performed under usual conditions (23) :

Bu$_3$SnH

Cl

+   +

55°C, 48 h, 10 kbars   86%   4%   10%

3°C, 4 h
U.V. irradiation (23)   1%   2%   97%
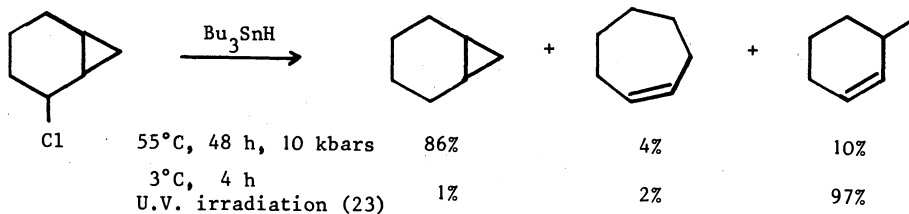
The high pressure technique might well be of considerable value for other synthetic applications involving organotin hydrides.
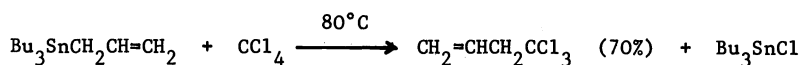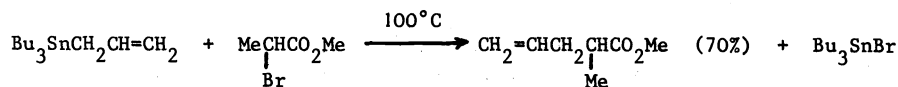
TRANSFER OF FUNCTIONAL GROUPS BY CLEAVAGE OF TIN-CARBON BONDS
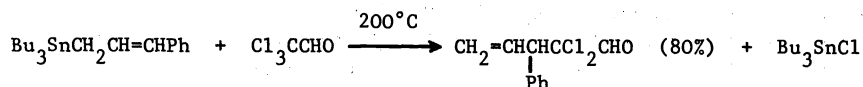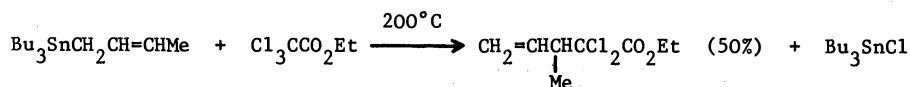
Direct cleavage of the tin-allyl bond

Allyltin compounds show a very high reactivity and have been involved in a number of allyl transfer reactions. One of the first reactions to be studied was the substitution by organic halides :

$$R_3SnC-C=C \quad + \quad R'X \longrightarrow C=C-C-R' \quad + \quad R_3SnX$$
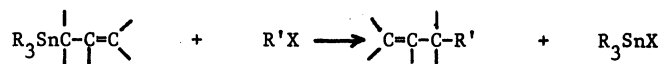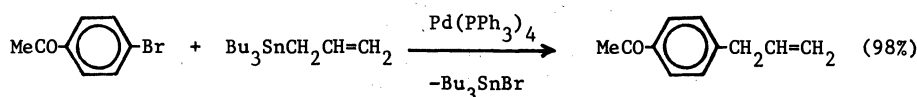
The substitutions are free radical reactions (24) and we found that it is possible to react functionally substituted compounds which would not have survived in more conventional organometallic reactions (Grignard or lithium reagents, for instance) :

$$Bu_3SnCH_2CH=CH_2 \quad + \quad MeCHCO_2Me \xrightarrow{100°C} CH_2=CHCH_2CHCO_2Me \quad (70\%) \quad + \quad Bu_3SnBr$$
$$\underset{Br}{} \qquad \qquad \underset{Me}{}$$

$$Bu_3SnCH_2CH=CH_2 \quad + \quad CCl_4 \xrightarrow{80°C} CH_2=CHCH_2CCl_3 \quad (70\%) \quad + \quad Bu_3SnCl$$

Substituted allyltin reagents were found to react with complete allylic rearrangements :

$$Bu_3SnCH_2CH=CHMe \quad + \quad Cl_3CCO_2Et \xrightarrow{200°C} CH_2=CHCHCCl_2CO_2Et \quad (50\%) \quad + \quad Bu_3SnCl$$
$$\underset{Me}{}$$

$$Bu_3SnCH_2CH=CHPh \quad + \quad Cl_3CCHO \xrightarrow{200°C} CH_2=CHCHCCl_2CHO \quad (80\%) \quad + \quad Bu_3SnCl$$
$$\underset{Ph}{}$$

Less reactive substrates do not react simply on heating but do in the presence of transition metal catalysts, e.g., with aromatic halides (25)

$$MeCO-\langle\bigcirc\rangle-Br \quad + \quad Bu_3SnCH_2CH=CH_2 \xrightarrow[-Bu_3SnBr]{Pd(PPh_3)_4} MeCO-\langle\bigcirc\rangle-CH_2CH=CH_2 \quad (98\%)$$

and with acyl chlorides (26) :

$$EtCOCl \quad + \quad Bu_3SnCH_2CH=CHMe \xrightarrow[-Bu_3SnCl]{(PPh_3)_3RhCl} EtCOCH_2CH=CHMe \quad (64\%)$$
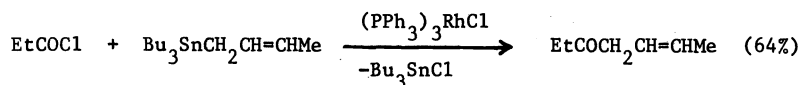
Note here that no allylic rearrangement has occured. Recently palladium catalysts have been used also with success for cross coupling reactions between allylstannanes and allyl acetates (27) or allyl bromides (28), which occur with allyltin rearrangements :

X = Br, OAc
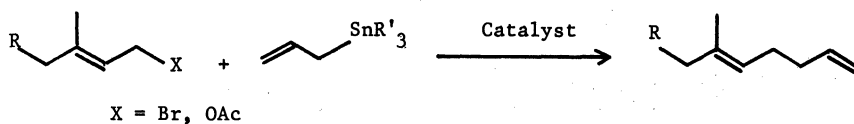
Another interesting use of allyltin compounds is the addition to aldehydes or ketones which eventually yields homoallylic alcohols (29) :

$$R_3Sn-\overset{|}{\underset{|}{C}}-\overset{|}{C}=C\overset{\diagup}{\diagdown} \quad + \quad \overset{\diagdown}{\diagup}C=O \longrightarrow \overset{\diagdown}{\diagup}C=C-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-OSnR_3 \xrightarrow{\text{protolysis}} \overset{\diagdown}{\diagup}C=C-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-OH$$

At moderate temperatures allyltrialkyltin compounds give reasonable yields with aldehydes and activated carbonyl derivatives,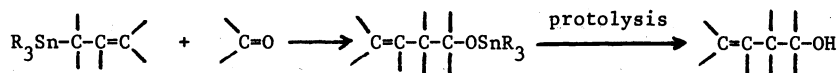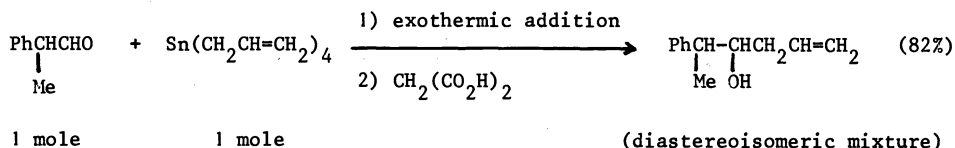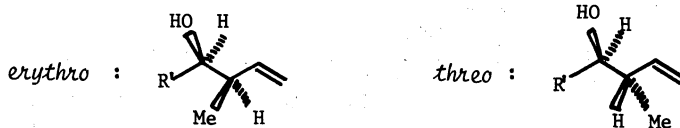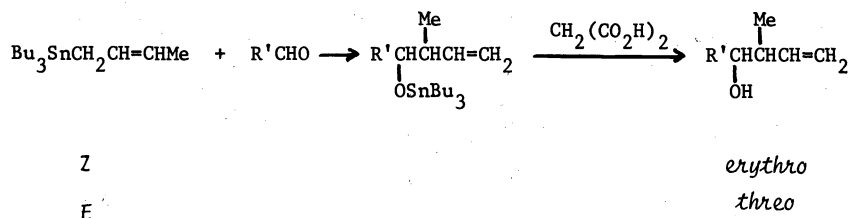 but catalysts have been proposed (30). The efficiency of boron trifluoride is to be underlined since it also catalyses the 1,4 addition to α-enones and the allylation of quinones (31).

It has also been shown that allyl-tin halides, such as dibutylallyltin chloride or triallyl-tin chloride, are more reactive, without a catalyst, than for instance allyltributyltin : additions were performed exothermically with aldehydes and at room or moderate temperatures with non-activated ketones (32). We have found that a similar reactivity is shown by tetra-allyltin (33). For instance, whereas allyltributyltin gave addition to hydratropic aldehyde at 200°C with moderate yield, tetraallyltin reacted exothermically :

$$\underset{\underset{\text{Me}}{|}}{\text{PhCHCHO}} \quad + \quad Sn(CH_2CH=CH_2)_4 \xrightarrow[\text{2) } CH_2(CO_2H)_2]{\text{1) exothermic addition}} \underset{\underset{\text{Me OH}}{| \ |}}{\text{PhCH--CHCH}_2CH=CH_2} \quad (82\%)$$

1 mole   1 mole   (diastereoisomeric mixture)
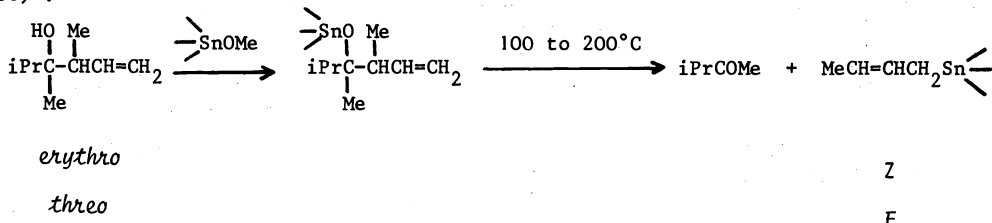
Several allyl groups on tin can react, e.g. : 4 moles aldehyde with 1 mole organotin reagent gave 50% yields of isolated homoallylic alcohols.

A further point of interest in the allyltin additions to the carbonyl group concerns the stereochemistry of the adducts obtained from aldehydes and substituted organometallic reagents. A few years ago we showed that Z or E crotyltributyltin reacted stereospecifically (34), for example with chloral Cl_3CCHO (10 h at 20°C) or benzaldehyde and p-Cl-C_6H_4CHO (16 h at 200°C) :

$$Bu_3SnCH_2CH=CHMe \quad + \quad R'CHO \longrightarrow \underset{\underset{OSnBu_3}{|}}{R'\overset{\overset{\overset{Me}{|}}{}}{CH}CHCH=CH_2} \xrightarrow{CH_2(CO_2H)_2} \underset{\underset{OH}{|}}{R'\overset{\overset{\overset{Me}{|}}{}}{CH}CHCH=CH_2}$$

Z $erythro$

E $threo$

$erythro$: $threo$:

However chloral at 100°C gave essentially the $threo$ isomer (∼90%) irrespective of the configuration of the tin reagent : at 100°C a rapid $Z \longrightarrow E$ isomerization occured, possibly promoted by the higher Lewis acidity of the substrate (at higher temperature, 200°C, the already mentioned substitution occured in 70% yield). These results have found recent confirmation in a study of the stereospecific thermal reversibility of allylstannation (35,36) :

$$\underset{\underset{\text{Me}}{|}}{\overset{\overset{\text{HO Me}}{| \ |}}{iPrC}-CHCH=CH_2} \xrightarrow{-SnOMe} \underset{\underset{\text{Me}}{|}}{\overset{\overset{\text{SnO Me}}{| \ |}}{iPrC}-CHCH=CH_2} \xrightarrow{\text{100 to 200°C}} iPrCOMe \quad + \quad MeCH=CHCH_2Sn\overset{\diagup}{\diagdown}$$

$erythro$ Z

$threo$ E

It is however striking that the boron trifluoride-catalyzed additions of crotyltins to aldehydes have been described as *erythro*-selective regardless of the geometry of the crotyl unit (37) :

$$Bu_3SnCH_2CH=CHMe + R'CHO \xrightarrow[\substack{-78°C \text{ to } 0°C \\ 2) H_2O}]{1) BF_3, CH_2Cl_2}$$

E or Z
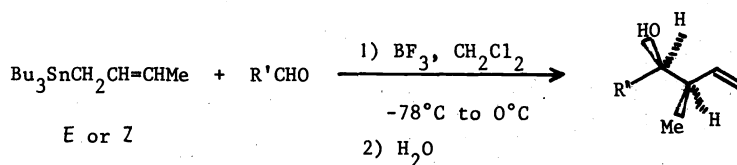
These new results clearly have preparative and mechanistic interest.

In an effort to learn more about the cleavage of the allyl-tin bond we synthesized diastereoisomeric allyltins. Such materials would allow us to determine whether the substitutions occur in a *supra* or *antara* way by reference to a substituent playing the role of a stereochemical probe :
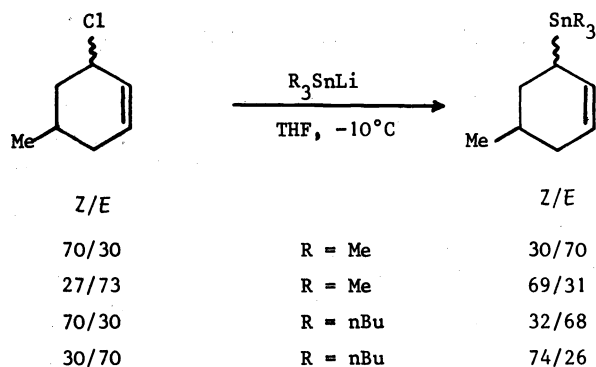
supra-substitution

antara-substitution
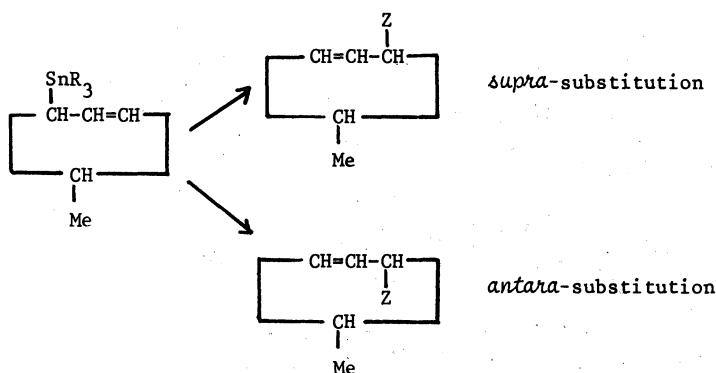
The first approach involved the hydrostannation of a vinylcyclopropane (38) :
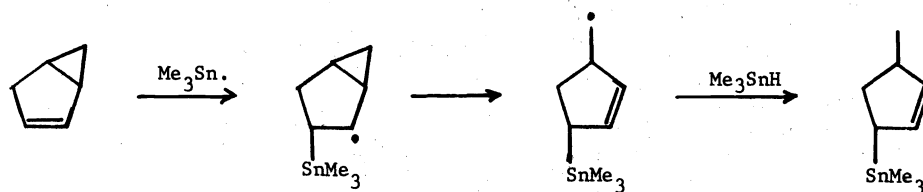
The reaction gave unfortunately a mixture of four isomers, due to the reversible addition of the stannyl radical to the initially formed allyltin :

(49%)

Z + E

(51%)

Z + E
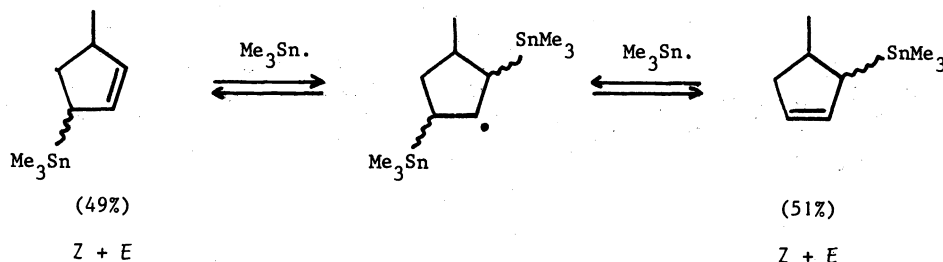
Attempts to remain under kinetic control failed and since the isomer separation was tedious, we decided to investigate instead the stannylation of Z- and E-5-methyl-2-cyclohexenyl chlorides. Within the limits of the experimental error, the reaction occured with complete inversion of configuration (39) :

| Z/E		Z/E
70/30	R = Me	30/70
27/73	R = Me	69/31
70/30	R = nBu	32/68
30/70	R = nBu	74/26

From the corresponding tosylates we found that substitution by tributylstannyllithium gave essentially inversion of configuration, but trimethylstannyllithium, for unclear reasons, was much less specific. Control experiments with a deuterated substrate showed indeed that in this particular case we were not dealing with a clean S_N2-like substitution :
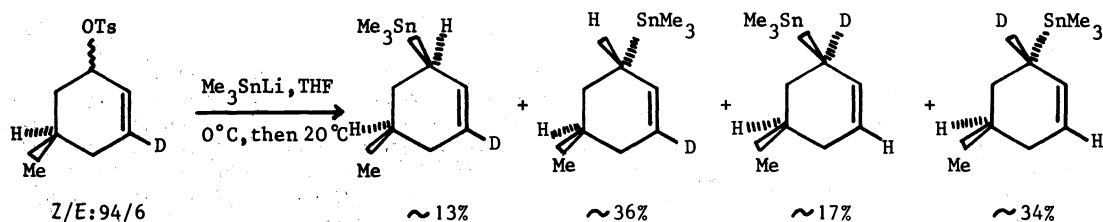
The qualitative and quantitative analysis of this complex mixture was made from a single ^{119}Sn NMR spectrum using chemical shifts values and $^nJ(SnD)$ coupling constants (40).

Using the cyclohexenyltin model compounds, we have already started to investigate the stereochemistry of allyltin reactions (41). While the electrophilic cleavage with chlorine could not be studied at this time (intervention of isomerizations of the substrates or the products promoted respectively by the organotin halide or the electrophile), it has been possible to obtain data for a recently published reaction with peracids (42). Among the two mechanisms which had been proposed by the authors, a direct substitution through a cyclic transition state, can be now ruled out by the data which show a preference for *antara*-substitution (41) :

Z/E		Z/E
63/37		34/66
22/78		56/44
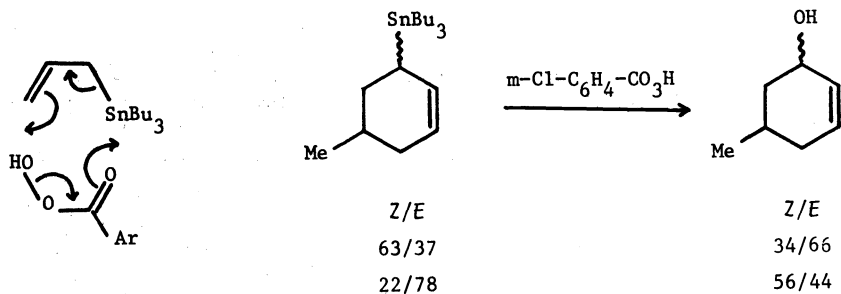
The stereochemical study of other kinds of allyltin substitutions is presently underway.

Direct cleavage of the tin-vinyl bond
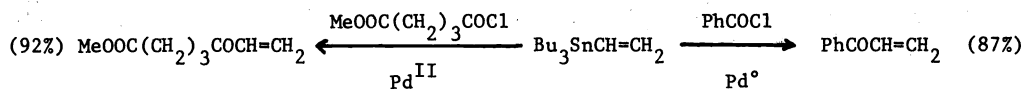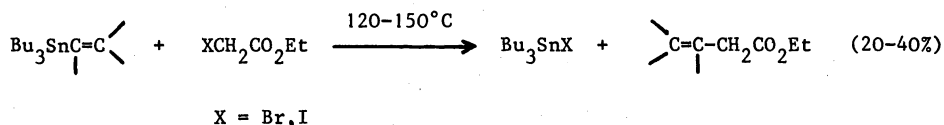It was of interest to test the ability of vinyltins to transfer the unsaturated moiety to organic substrates. While acyl chlorides did not react directly, we found that the use of Lewis acids like aluminium chloride in stoichiometric amounts led to α-enones with moderate yields of isolated products (43). For instance :

$$Bu_3SnCH=CHMe \xrightarrow[AlCl_3, -10°C]{MeCOCl, CH_2Cl_2} MeCOCH=CHMe \quad (65\%)$$

64% Z + 36% E   E

$$Bu_3SnCH=CMe_2 \xrightarrow[AlCl_3, -10°C]{PhCOCl, CH_2Cl_2} PhCOCH=CMe_2 \quad (58\%)$$

$$Bu_3SnCH=CHPh \xrightarrow[AlCl_3, -10°C]{MeCOCl, CH_2Cl_2} MeCOCH=CHPh \quad (49\%)$$

86% E + 14% Z   E
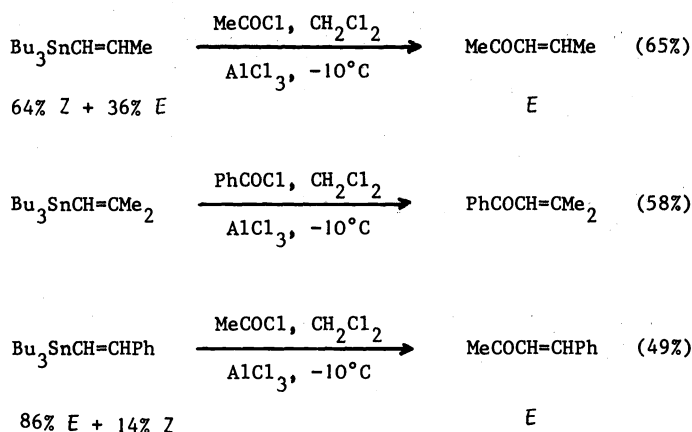
Under the same conditions, acyl anhydrides reacted similarly (43). It has been shown, almost at the same time, that palladium derivatives are very efficient catalysts for vinyl transfers to acyl chlorides (44) :

$$(92\%)\ MeOOC(CH_2)_3COCH=CH_2 \xleftarrow[Pd^{II}]{MeOOC(CH_2)_3COCl} Bu_3SnCH=CH_2 \xrightarrow[Pd°]{PhCOCl} PhCOCH=CH_2 \quad (87\%)$$

It is noteworthy that these catalysts also allow alkyl transfers from alkyl-tin bonds usually much less reactive than vinyl-tin bonds. Our attempts to transfer vinyl groups to organic halides, without catalysts, have met so far with limited success (43) :

$$Bu_3SnC=C\diagup\diagdown + XCH_2CO_2Et \xrightarrow{120-150°C} Bu_3SnX + \diagdown C=C-CH_2CO_2Et \quad (20-40\%)$$

X = Br,I

However nitroolefins can be obtained with high efficiency through the reaction of vinyltins with tetranitromethane (45).

Direct cleavage of the tin-aromatic bond
Aromatic organotins are cleaved regiospecifically by various electrophilic reagents (1) :

$$\Sigma\!\!-\!\!\bigcirc\!\!-SnR_3 \xrightarrow{E^+} \Sigma\!\!-\!\!\bigcirc\!\!-E$$
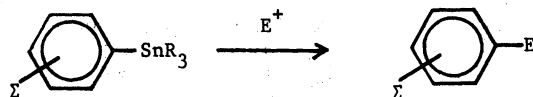
In this way the organotin substituent acts as a template for the introduction of the electrophile at a selected position. It is evident that the usefulness of organotin compounds as intermediates depends on how easy it is to get the initial tin substituent into the right place. An efficient method for the synthesis of the tin-aromatic carbon bond is the reaction of organostannylanions with aryl halides (46).For instance H.G. Kuivila reported the successful metallation (60 to 80% yields) of a series of functionally substituted bromobenzenes which could not have been carried out using the more conventional Grignard route (47) :

$$\text{(}\Sigma = \text{p-CN, o-, m- and p-COMe, etc...)}$$
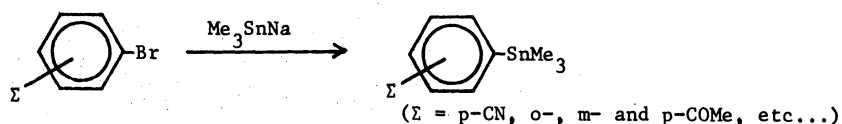
We have recently made efforts to study the regiochemistry of this metallation using available reagents like tributylstannyllithium and cheaper aromatic compounds like chlorides. We found first that t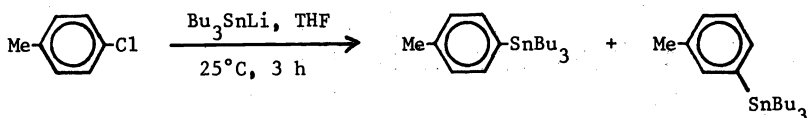ributylstannyllithium in THF (prepared from hexabutylditin and lithium) or in HMPA (prepared from hexabutylditin and butyllithium), reacted with bromides in high yields with a complete regioselectivity : e.g. o-, m- and p-bromotoluene gave respectively only o-, m- and p-tributylstannyltoluene (48). In these cases the substitution occurs mainly through an initial halogen-metal exchange. In striking contrast we found tributylstannyllithium in THF reacting less readily with chlorides to give essentially non-regioselective substitution (48). The following results are illustrative :

ortho	ortho (35%) + meta (65%)
meta	ortho (15%) + meta (57%) + para (28%)
para	meta (25%) + para (75%)
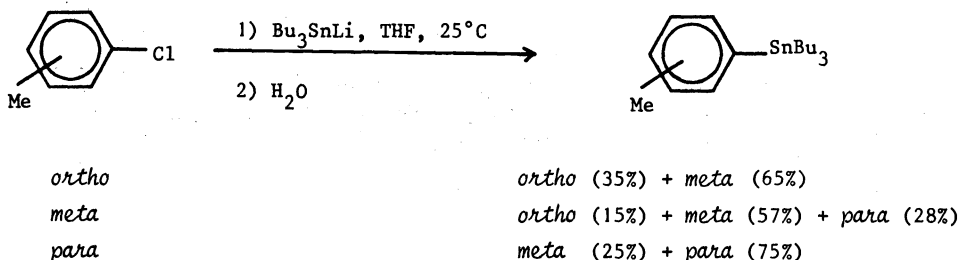
These data which are indicative of arynic processes (induced by catalytic amounts of butyl-lithium present in the organometallic reagent), show clearly that aromatic chlorides should be avoided if a given electrophile is to be introduced at a precise position :
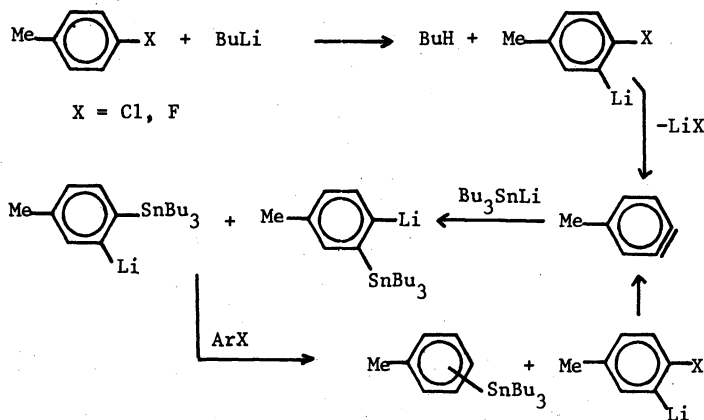
In the course of the mechanistic study of the metallation we found also that cine-substitution is not the exclusive process for chlorides (or for fluorides). Indeed some factors modify the relative amounts of p- and m-tolyl-tributyltin obtained from tributylstannyl-lithium and p-chlorotoluene in THF. Amongst these is the presence of lithium metal, which is present in solution or in suspension in amounts dependent on the "age" of the reagent, and the exposure to light. There is in fact a competition between the arynic process and a regioselective route which is most likely a free radical pathway following a single electron transfer from the stannylanion. With an excess of a "young" reagent (incorporating unreacted lithium) and in the light, the rate of the regioselective substitution was increased but stayed somewhat lower than for bromides (46,48) :

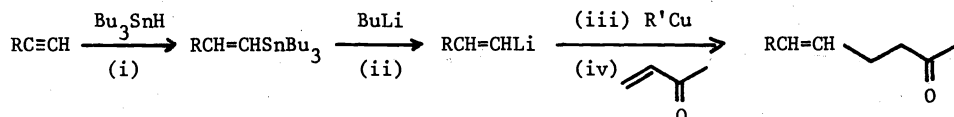$$\text{Me}-\!\langle\bigcirc\rangle\!-\text{Cl} \xrightarrow[\text{25°C, 3 h}]{\text{Bu}_3\text{SnLi, THF}} \text{Me}-\!\langle\bigcirc\rangle\!-\text{SnBu}_3 \quad + \quad \text{Me}-\!\langle\bigcirc\rangle\!-\text{SnBu}_3$$

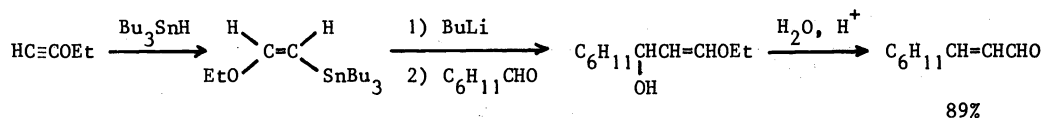| reagent's "age" :	24 h	daylight	92	8
		dark	88	12
	96 h	daylight	80	20
		dark	58	42

Tin-carbon bond cleavage via transmetallation

A very interesting route to lithium reagents was found by D.Seyferth 20 years or so ago, by an exchange reaction initially reported to give vinyl- or allyllithiums (49) :
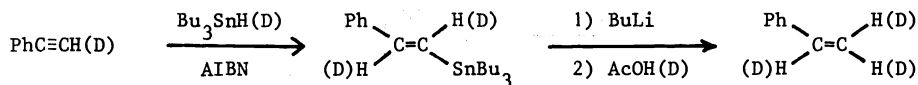
$$\underset{/}{\overset{\backslash}{-}}\text{Sn}-\text{C}\underset{\backslash}{\overset{/}{-}} \quad + \quad \text{RLi} \quad\longrightarrow\quad \underset{/}{\overset{\backslash}{-}}\text{Sn}-\text{R} \quad + \quad \underset{/}{\overset{\backslash}{-}}\text{C}-\text{Li}$$
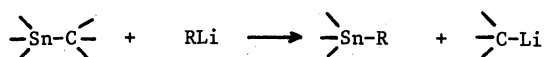
The synthetic use of this transmetallation process became more apparent later when E.J. Corey used a sequence corresponding to a nucleophilic vinylation ; namely (i) hydrostannation of substituted alkynes, (ii) exchange with butyllithium, (iii) transformation to cuprates and (iv) conjugated addition to α-enones (50).

$$\text{RC}\equiv\text{CH} \xrightarrow[\text{(i)}]{\text{Bu}_3\text{SnH}} \text{RCH=CHSnBu}_3 \xrightarrow[\text{(ii)}]{\text{BuLi}} \text{RCH=CHLi} \xrightarrow[\text{(iv)}]{\text{(iii) R'Cu}} \text{RCH=CH}\diagdown\diagup\diagdown$$
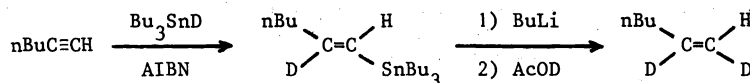
Vinyllithiums prepared by transmetallation have been very often employed (51) including for several synthesis of natural products like antibiotics (52) or prostaglandins (53). Also, suitably substituted alkynes have been used for the introduction of nucleophilic equivalents of carbonyl compounds (54). For instance :

$$\text{HC}\equiv\text{COEt} \xrightarrow{\text{Bu}_3\text{SnH}} \underset{\text{EtO}}{\overset{\text{H}}{\diagdown}}\text{C=C}\underset{\text{SnBu}_3}{\overset{\text{H}}{\diagup}} \xrightarrow[\text{2) } \text{C}_6\text{H}_{11}\text{CHO}]{\text{1) BuLi}} \text{C}_6\text{H}_{11}\underset{\text{OH}}{\overset{}{\text{CHCH=CHOEt}}} \xrightarrow{\text{H}_2\text{O, H}^+} \text{C}_6\text{H}_{11}\text{CH=CHCHO}$$

$$89\%$$

In a more modest contribution we have also used the transmetallation process for the synthesis of regioselectively and stereoselectively deuterated alkenes (55). For instance, seven mono-, di- and tri-deuterated styrenes have been selectively obtained in high purity using the following scheme in which hydrides or deuterides were employed :

$$\text{PhC}\equiv\text{CH(D)} \xrightarrow[\text{AIBN}]{\text{Bu}_3\text{SnH(D)}} \underset{\text{(D)H}}{\overset{\text{Ph}}{\diagdown}}\text{C=C}\underset{\text{SnBu}_3}{\overset{\text{H(D)}}{\diagup}} \xrightarrow[\text{2) AcOH(D)}]{\text{1) BuLi}} \underset{\text{(D)H}}{\overset{\text{Ph}}{\diagdown}}\text{C=C}\underset{\text{H(D)}}{\overset{\text{H(D)}}{\diagup}}$$

Other specifically labelled alkenes can be synthesized :

$$\text{nBuC}\equiv\text{CH} \xrightarrow[\text{AIBN}]{\text{Bu}_3\text{SnD}} \underset{\text{D}}{\overset{\text{nBu}}{\diagdown}}\text{C=C}\underset{\text{SnBu}_3}{\overset{\text{H}}{\diagup}} \xrightarrow[\text{2) AcOD}]{\text{1) BuLi}} \underset{\text{D}}{\overset{\text{nBu}}{\diagdown}}\text{C=C}\underset{\text{D}}{\overset{\text{H}}{\diagup}}$$

However we have recently found that acetic acid is able to cleave quantitatively the tin-vinyl bond, at room temperature, with essentially retention of configuration. Thus deuterated alkenes can be simply prepared without going through the transmetallation step (56).

Related transmetallation reactions have also been employed for obtaining α-heterosubstituted lithium reagents (57). For instance stannylanions may add to carbonyl groups (46) giving α-alkoxytin compounds which exchange with butyllithium :
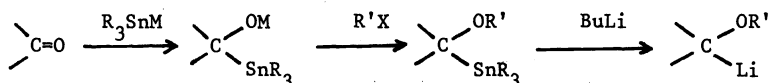

The α-alkoxy substituted lithium reagents show a remarkable configurational stability (58). Allyloxy substituted carbanions, which undergo [2,3] sigmatropic rearrangements, were also prepared by the transmetallation route (59):
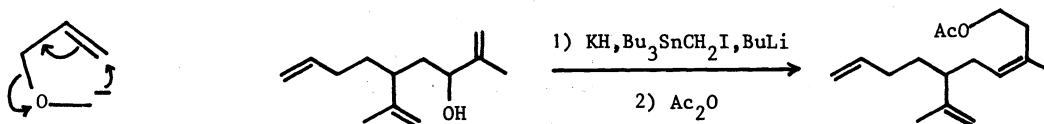


We have recently begun work on the synthesis of gem-dialkoxysubstituted organotins which would be specially interesting as masked carbonyl group reagents (60) in complement to the thio- or seleno- analogs (61). We observed the reaction of stannylanions with orthoformates according to :

$$Bu_3SnH \xrightarrow[\text{ether}]{iPrMgCl} Bu_3SnMgCl \xrightarrow{HC(OR)_3} Bu_3SnCH(OR)_2 \; + \; ROMgCl$$

$$R = Me, Et$$
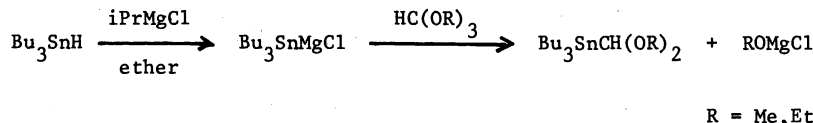
Unfortunately the yields were lower than 25% with methyl or ethyl orthoformates, but the introduction of a better leaving group, like phenoxyl, gave yields in the range of 80% of isolated organotin :

$$Bu_3SnH \longrightarrow Bu_3SnMgCl \xrightarrow{(EtO)_2CHOPh} Bu_3SnCH(OEt)_2 \; + \; PhOMgCl$$
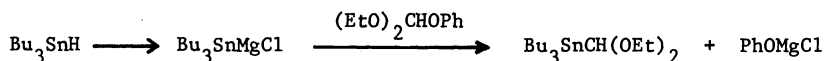
The new organotin synthon was found to quantitatively react with acetyl chloride without cleaving the tin-carbon bond :

$$Bu_3SnCH(OEt)_2 \; + \; MeCOCl \xrightarrow{20°C} Bu_3SnCHClOEt \; + \; MeCO_2Et$$
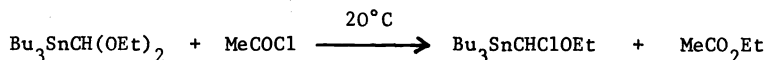
The mixed halo-alkoxy reagent is potentially of great promise, but it appears to be only moderately stable on standing. In the presence of excess cyclohexene, it gave ethoxy-norcaranes in 32% yield :
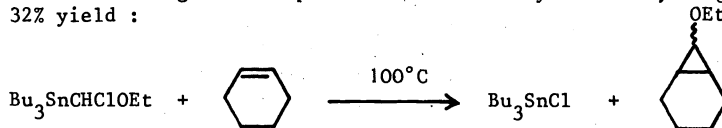

However, when freshly prepared, it can be quantitatively transformed to ethoxymethyl-tributyltin by reduction with tributyltin hydride.

We have already performed preliminary transmetallation reactions with diethoxymethyltributyl-tin. For instance, benzyl bromide gave in 78% yield an acetal which was transformed to phenyl-acetaldehyde upon mild hydrolysis :

$$Bu_3SnCH(OEt)_2 \xrightarrow[\text{2) } PhCH_2Br]{\text{1) BuLi, } -78°C} PhCH_2CH(OEt)_2 \xrightarrow{H_2O, H^+} PhCH_2CHO$$
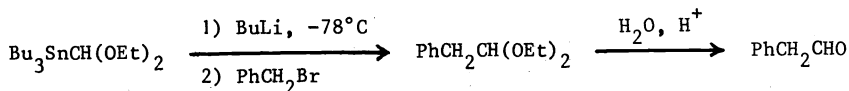
Also in the presence of cuprous iodide, conjugated addition of the lithium reagent was observed in good yield :
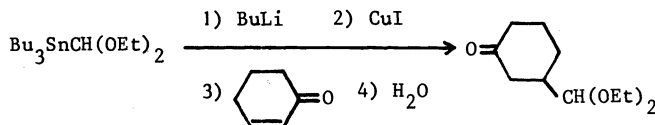
Only a few reactions of these new organotin synthons have so far been explored but it is clear that just like related reagents, they might become highly valuable in the future.

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