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INVESTIGATION OF NEW ROUTES TO THE STEREOSPECIFIC SYNTHESIS OF 1,4-DIENES USING ORGANOCOPPER REAGENTS

by

Michael W. Hutzinger

B.Sc., University of Guelph, 1985

M.Sc., Simon Fraser University, 1987

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Examining Committee
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Dr. A.C. Oehlschlager, Senior Supervisor

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December 9, 1991
(date)

ABSTRACT

Stereospecific synthesis of 1,4 dienes has been achieved *via* palladium-catalyzed cross-coupling of 3(*E*)-tri-*n*-butylstannyl allylic substrates with *E* or *Z* vinyl organometallic reagents. Replacement of the trialkyltin moiety with hydrogen under mild acidic conditions affords the unisomerized *Z,E*- or *Z,Z*-1,4 diene. This strategy has been applied to the synthesis of the insect pheromones containing *Z,Z*- [dodeca-3,6-diene-1-ol (**48**), (9*Z*,12*Z*)-tetradeca-9,12-dienyl acetate (**58b**)] and *Z,E*-1,4-diene [(4*E*,7*Z*)-trideca-4,7-dienyl acetate (**106**)] fragments.

^{13}C and ^{2}H NMR investigations of addition of stannylcuprates to 1-alkynes provide compelling evidence for the formation of vinyl adducts. These intermediates are thermodynamically preferred over starting materials. This process is reversible and is more facile for the lower order reagent, *n*-$Bu_3SnCu(CN)Li$ (**64**) than the higher order (*n*-$Bu_3Sn)_2Cu(CN)Li_2$ (**65**) species. These reagents exhibit opposite regioselectivity in their addition to 1-alkynes which is attributed to the differences in steric demand between monomeric (**65**) and more bulky (**64**) species.

Reaction of homo higher order alkylcuprates, $R_2Cu(CN)Li_2$,with hexaalkyldistannanes, $(R_3Sn)_2$, represents a new, convenient route to the preparation of mixed higher order trialkylstannyl(alkyl)cyanocuprates, $R_3Sn(R)Cu(CN)Li_2$. These reagents react with a variety of organic substrates without the formation of excessive quantities of tin byproducts.

Regioselective formation of 2-stannyl and 1-stannyl alkenes has been achieved in stannylcupration of 1-alkynes by incorporating electron donating and withdrawing ligands, respectively, into the mixed stannylcuprate reagent. It

is postulated that the acetylenic moiety initially coordinates to copper to form a π-complex with copper. Polarization of the triple bond in this complex is dependent on the nature of the cuprate ligands and governs the regioselectivity in these reactions.

Several new alkynylcuprate-based species have been identified using ^{13}C NMR and IR spectroscopic techniques. These studies indicate that $(R\text{-}C{\equiv}C)_2CuLi{\cdot}LiI$ and $(R\text{-}C{\equiv}C)_3CuLi_2{\cdot}LiI$ are formed as distinct species in the reaction of CuI with two and three equivalents of lithium acetylide, respectively. Formation of dimeric species, $Me_3Sn(R\text{-}C{\equiv}C)CuLi{\cdot}LiI$ and $Me_3Sn(R\text{-}C{\equiv}C)_2Cu_2Li{\cdot}LiI$, is proposed in solutions comprised of a 1:1:1 mixture of Me_3SnLi, $R\text{-}C{\equiv}CLi$ and CuI. Addition of one equivalent of either $R\text{-}C{\equiv}CLi$ or Me_3SnLi to this solution gives rise to the mixed higher order reagent $Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$.

DEDICATION

To my parents

ACKNOWLEDGMENTS

I wish to thank my senior supervisor, Dr. Cam Oehlschlager, for introducing me to the field of organocuprate chemistry and for the opportunity to make contributions to this exciting area of research. I am particularly grateful for having been given the freedom and encouragement to pursue my own research ideas. The responsibility of managing my own projects has acquainted me with the processes involved in research - from the formulation of ideas to the publishing of results.

I would also like to thank fellow graduate student, Robert D. Singer, with whom I collaborated on several exciting projects. The many stimulating hours working together as a team was not only enjoyable but extremely productive. The pride and satisfaction derived from our accomplishments is not easily forgotten.

I am also indebted to post doctoral fellow, Dr. S. Mohan Singh, whose untiring assistance and expert guidance helped overcome even the most challenging of hurdles.

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Abbreviations

AIBN	2,2'-azobisisobutyronitrile
9-BBN	9-borabicyclo[3.3.1]nonyl
n-Bu_4NF	tetrabutylammonium fluoride
CI	chemical ionization (MS)
cp	cyclopentadienyl (C_5H_5)
d	doublet (NMR)
δ	chemical shift in ppm downfield from TMS (NMR)
DIBAH	diisobutylaluminum hydride
DIGLYME	bis(2-methoxyethyl) ether
DIPA	diisopropylamine
DMAP	dimethylaminopyridine
DMF	dimethylformamide
DMS	dimethyl sulphide
E	electrophile
EI	electron impact (MS)
EtOAc	ethyl acetate
g	grams
GC	gas chromatography
HMPA	hexamethylphosphoramide
H.O.	higher order
HRMS	high resolution mass spectroscopy
ISTD	internal standard
LDA	lithium diisopropylamide

L.O.	lower order
m	medium (IR); multiplet (NMR)
mm Hg	millimeters of mercury (pressure)
mmol	millimoles
MS	mass spectroscopy
m/z	mass to charge ratio (MS)
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance
NR	no reaction
NT	non-transferable
Nuc	nucleophile
Ph	phenyl
ppm	parts per million (NMR)
q	quartet (NMR)
quint	quintet (NMR)
s	strong (IR); singlet (NMR)
sext	sextet (NMR)
t	triplet (NMR)
2-Th	2-thienyl
THF	tetrahydrofuran
THP	tetrahydropyranyl
TLC	thin layer chromatography
TMS	tetramethylsilane
w	weak (IR)

CHAPTER I

Introduction

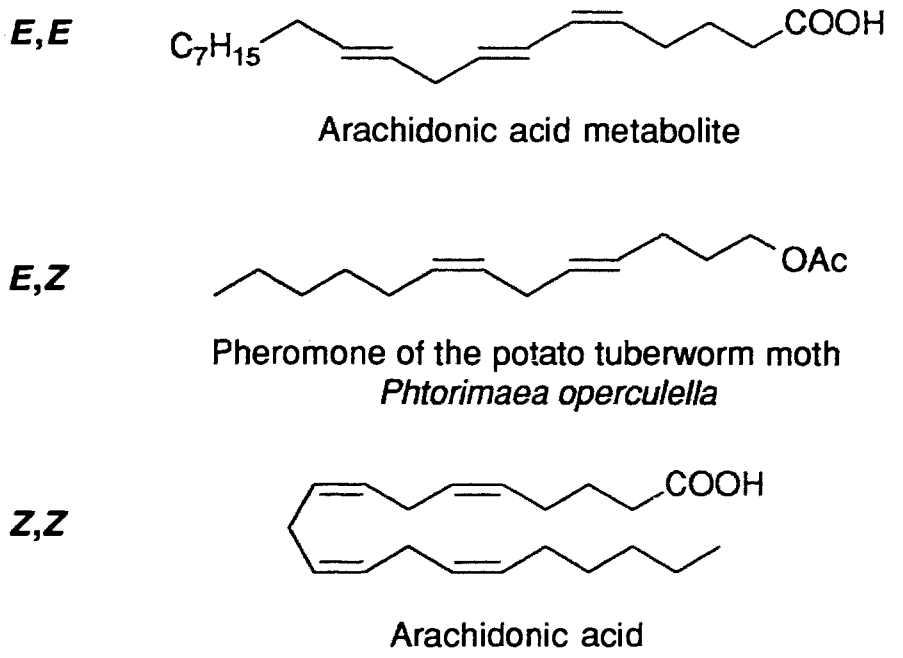
It has been estimated that the agricultural industry loses billions of dollars annually as a result of insect damage to crops. Today's pest management programs rely heavily on insecticides as a means of controlling insect populations. However, extensive spraying of these chemicals is not only expensive but raises important health and environmental questions. Therefore, the integration of pheromones into existing pest management programs is emerging as a promising alternative to existing technology.[1] Pheromone traps for example, provide a means of monitoring insect populations and allow the degree of infestation of an affected area to be determined. Spraying of insecticides that coincides with the onset of infestation is more efficient and less expensive than prophylactically timed applications. Alternatively, random dispersion of pheromones in infested areas causes communication disruption among insects and can prevent rapid increase in population size. Strategies of this nature have been successfully adopted by agricultural and other resource based industries in North America in combating insect damage to crops.

Bombykol or (10*E*,12*Z*)-hexadeca-10,12-dien-1-ol was the first pheromone to be isolated and was obtained from the silk worm moth *Bombyx mori*. Since this landmark achievement by Butenandt *et al.* in 1961,[2] a vast array of pheromones have been isolated and the chemical synthesis for many of them reported. The majority of these compounds contain one or more *E* or *Z* double bonds and it is the strict maintenance of double bond geometry which often poses the greatest difficulty in their preparation. The increasing demand

for pheromones of high isomeric purity has spurred development of improved syntheses of these biologically active molecules.[3]

In connection with ongoing projects dealing with the isolation, characterization and synthesis of insect pheromones in our laboratory, new methods have been investigated which would allow stereospecific assembly of disubstituted double bonds in a 1,4 fashion. 1,4-Dienes are structural units commonly found in a multitude of biologically active molecules and exist in all possible (*E,E*; *E,Z*; *Z,Z*) double bond combinations (Figure A.1).

Figure A.1 Examples of *E,E*- *E,Z*- and *Z,Z*-1,4-Dienes in Biologically Active Molecules.

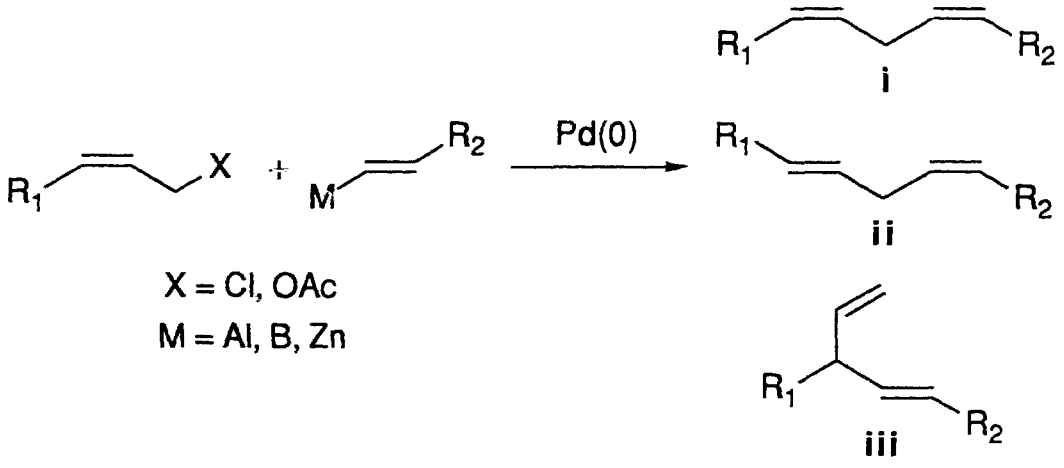


Stereospecific assembly of 1,4-diunsaturated aliphatic compounds has been investigated extensively. The most successful and commonly used methods can be broadly divided into three categories: (a) Stereospecific reduction of 1,4-diynes by catalytic hydrogenation[4a] or reduction with sodium in liquid ammonia.[4b] Propargylic alcohols, as part of 1,4-enyne

liquid ammonia.[4b] Propargylic alcohols, as part of 1,4-enyne systems, can be selectively reduced.[4c] (b) Stereospecific coupling of carbonyl compounds with ylides in Wittig and related reactions[5] and (c) Stereospecific carbon-carbon bond forming reactions employing organometallic reagents.[6]

Palladium-catalyzed cross-coupling of allylic substrates with vinyl organometallic reagents has been investigated as a new route to the stereospecific synthesis of 1,4-dienes.[7] While cross-coupling of γ,γ-*di*substituted allylic compounds generally proceeds with a high degree of stereo- and regioselectivity, similar reactions with γ-*mono*substituted analogues give rise to mixtures of isomers. (**i**,**ii** and **iii**, Scheme A.1).

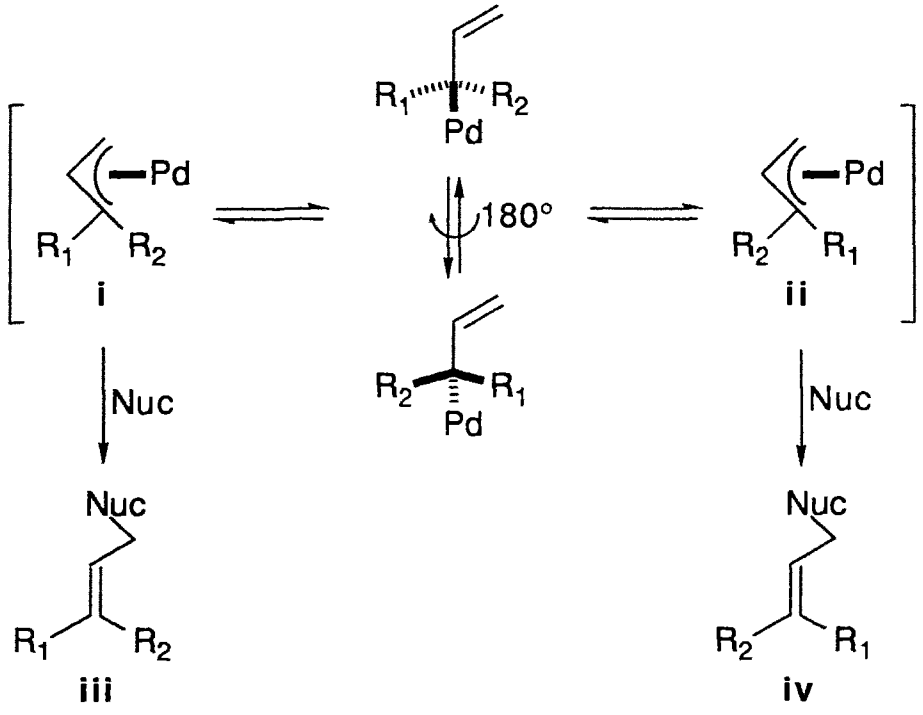
Scheme A.1 Palladium-Catalyzed Cross-Coupling of γ-Monosubstituted Allylic Substrates with Vinyl Organometallic Reagents.



Superior selectivity in palladium-catalyzed reactions involving γ,γ-disubstituted allylic compounds is likely due to steric effects in the resultant π–allylpalladium complex. In the currently accepted mechanism of isomerization, π-allylpalladium species are postulated to exist in equilibrium with σ-bonded counterparts. Rotation about the C_2 - C_3 bond in the σ-bonded complex

followed by formation of a π-allylpalladium intermediate results in isomerization of the allylic double bond.[8] Presumably, greater steric repulsion at C_3 disfavours formation of a σ-bonded palladium-C_3 intermediate, essential for *E* to *Z* interconversion (i.e. between species **i** and **ii**, Scheme A.2).

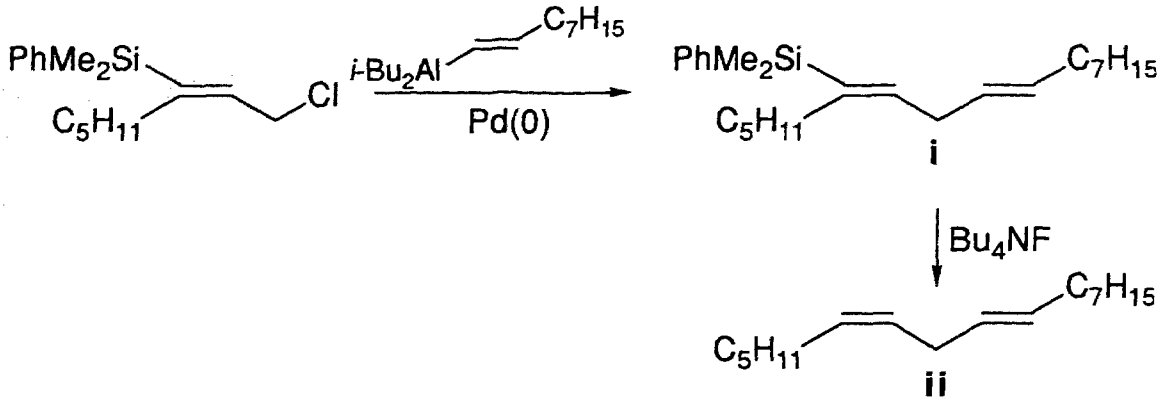
Scheme A.2 Double Bond Isomerization in π-Allylpalladium Complexes.



Recently, a new cross-coupling strategy was developed which showed promise as a highly stereoselective route to the synthesis of molecules containing the 1,4-diene fragment.[9] It was demonstrated that isomerzation processes in palladium-catalyzed cross-coupling reactions of allylic substrates with *E* vinyl organometallic reagents could effectively be eliminated by substitution of the γ-hydrogen in the allylic coupling partner with a $PhMe_2Si$ group. The stereochemical integrity of the double bonds is maintained throughout the coupling sequence yielding a 1,4-diene containing a vinyl

$PhMe_2Si$ functionality (**i**, Scheme A.3). Stereospecific replacement of the trialkylsilyl moiety by hydrogen afforded the desired *Z,E*-1,4-diene (**ii**, Scheme A.3) in good yield.

Scheme A.3 γ-Substitution in Allylic Substrates with a $PhMe_2Si$ Group as a Strategy to the Stereospecific Synthesis of 1,4-Dienes.



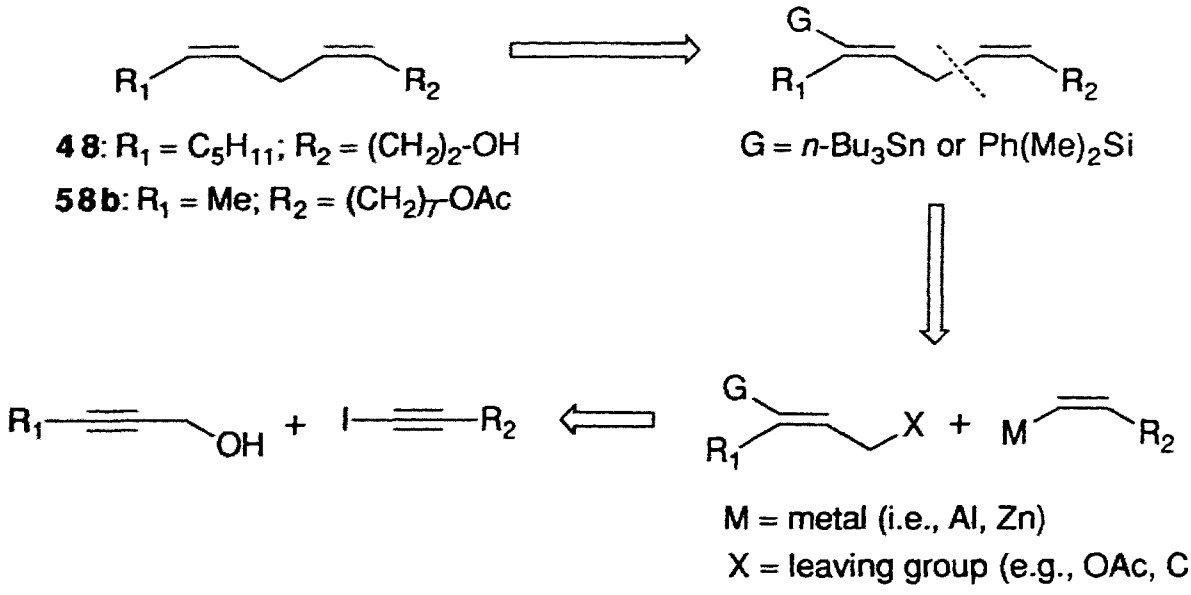
An additional advantage of this method lies in the mildness of the reaction conditions which are tolerated by the presence of a variety of functional groups. This feature has important synthetic implications in that assembly of 1,4-dienes could in principle be accomplished as a final step from precursors already containing the requisite, unprotected functionalities. Thus, extensive functional group manipulation in the coupled product could be avoided. Based on this rationale and in light of the remarkable stereochemical control achieved in preliminary studies, it appeared that this approach was ideally suited for the synthesis of pheromones containing 1,4-dienes and warranted further investigation.

I.1 Objective.

Early successes achieved in cross-coupling reactions outlined above prompted the investigation of this approach as a useful method for the synthesis of bioactive molecules containing 1,4-dienes. Initial efforts were targeted at conditions establishing yet milder reaction conditions without sacrificing stereospecificity. With this in mind, γ substituents other than $PhMe_2Si$ in the allylic substrate were investigated. It was hoped that in addition to safeguarding against isomerization these could be more easily removed in the coupled product. Preparation of suitable allylic substrates and *Z* vinyl organometallic reagents was explored. This coupling strategy was also applied to the synthesis of insect pheromones containing *Z,Z*-1,4-diene fragments.

The potentially attractive retrosynthetic analysis of the termite trail marker pheromone[10] (**48**) and the sex pheromone inhibitor of the Indian meal moth[11] (**58b**) is shown in Scheme I.1. Disconnection of the indicated strategic bond of the dienic system leads to allylic and a vinyl synthons. Coupling of these fragments represents the crucial step in this synthesis. Positioning of a bulky trialkylsilyl or stannyl group at the γ carbon of the allylic coupling partner was expected to prevent double bond isomerization in the π-allylpalladium complex, thus ensuring stereospecific coupling. Vinyl organometallic reagents can be related to the corresponding acetylenic iodides and the allylic fragments traced to propargylic substrates. Both acetylenic starting materials are readily prepared by known chemistry.

Scheme I.1 Retrosynthetic Analysis of the Termite Trail Marker Pheromone (**48**) and the Sex Pheromone Inhibitor of the Indian Meal Moth (**58b**).

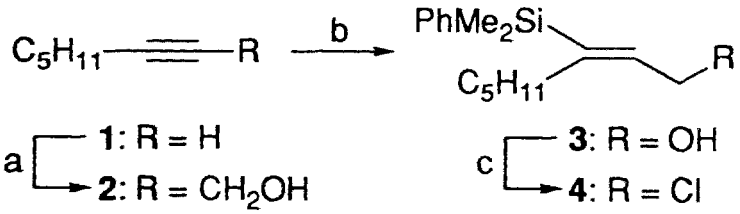


I.2 Preparation of γ-Trialkylsilyl and γ-Trialkylstannyl-2(*E*)-Allylic Substrates.

Preparation of γ-$PhMe_2Si$ substituted allylic chloride, **4**, was readily accomplished following a literature procedure and served as a model for subsequent syntheses of γ-substituted allylic substrates (Scheme I.2).[12] Propargylic alcohol, **2**, was used as the starting material in all cases and was readily prepared by treatment of the acetylide anion of 1-heptyne with paraformaldehyde.[13] Stereospecific incorporation of $PhMe_2Si$ into the allylic backbone was accomplished by silylzincation of propargylic alcohol, **2**, and yielded allylic alcohol, **3**, uncontaminated with isomers. Treatment of **3** with PPh_3, CCl_4/CH_3CN gave allylic chloride **4** in high yield.[14] It was observed that acetonitrile dramatically enhanced the rate of conversion in the latter reaction, reducing the completion time for this reaction from 5-8 hours to just 45 minutes.

The presence of the polar co-solvent presumably lowers the energy of an ionic transition state.

Scheme I.2 Synthesis of γ-$PhMe_2Si$ Substituted Allylic Substrates.



(a) *n*-BuLi, THF, -78 °C/30 min, $(CH_2O)_n$ (1.3 equiv), -78 °C → r.t. over 12hr, 85 %; (b) $PhMe_2SiZnEt_2Li$ (3 equiv), CuCN (2 %), THF, -78 °C → r.t. over 12 hr, 83 %; (c) PPh_3, CCl_4/CH_3CN (1:1), r.t./45 min, 81 %.

In earlier investigations it was established that the method of choice for replacing $PhMe_2Si$ with a hydrogen atom in the coupled product was to heat the 1,4-diene in DMF in the presence of *n*-Bu_4NF.[15] In search of a more mild desilylation procedure it was rationalized that nucleophilic attack of fluoride ion might be facilitated by reducing the steric crowding around silicon. Incorporation of a γ-Me_3Si moiety into the allylic backbone was initially attempted by treating propargylic alcohol, **2**, with $(Me_3Si)_2Zn$. However, none of the desired product was formed under these reaction conditions. The reaction mixture consisted primarily of unconsumed starting material and the Me_3Si ether of propargylic alcohol, **2**, which was identified by GC/MS. This material was not stable to silica and decomposed to starting material when subjected to flash chromatography. Although the formation of the silyl ether was not further investigated, it was noted that the amount of this product formed varied with the amount of CuCN catalyst used. This observation points to the possible involvement of a mixed trimethylsilylalkoxycuprate species giving rise to the silyl ether in a reductive

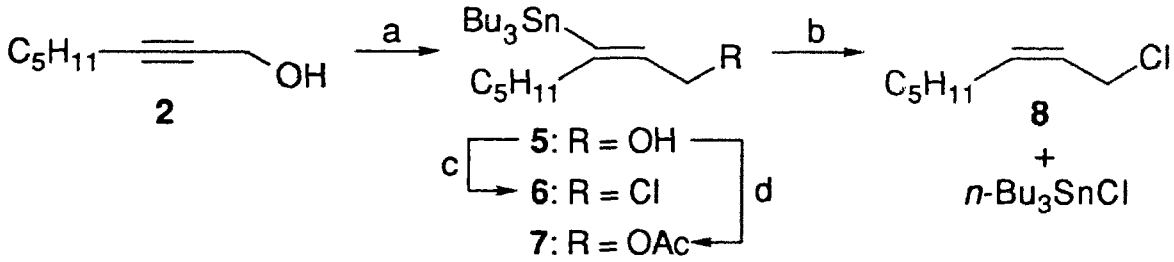
elimination process. A similar observation has been made for $(n\text{-}Bu_3Sn)_2Cu(CN)Li_2$ that gradually decomposes to form $(n\text{-}Bu_3Sn)_2$ among other byproducts.[16] A second attempt at preparation of the vinyl trimethylsilane was made by using a similar reagent employed in the synthesis of allylic alcohol, **3**. Silylzincation of propargylic alcohol, **2**, with $Me_3SiZnEt_2Li$, however, resulted in the formation of unidentified low boiling compounds as the only products.

In light of the inherent difficulty at synthesis of the trimethylsilylated compound, attention was next focused on the incorporation of a trialkystannyl group. Although stannylzincation of terminal alkynes was known,[17] addition to propargylic systems had not previously been reported. It was reasoned that since delivery of a silyl group in silylzincation of propargylic alcohols was stereospecific,[12b,c] this result could be duplicated for a trialkyl tin group in a related *stannyl*zincation reaction. Indeed, stannylzincation of propargylic alcohol, **2**, with $(n\text{-}Bu_3Sn)_2Zn$ yielded allylic alcohol, **5**, without formation of isomers (Scheme I.3). Conversion of **5** to allylic acetate, **7**, was accomplished without complication by treatment of the allylic alcohol with pyridine/acetic anhydride.

Synthesis of allylic chloride, **6**, was not as straightforward as the preparation of the dimethyl(phenyl)silyl analogue, **4**. Under usual reaction conditions (PPh_3, CCl_4/CH_3CN) allylic alcohol **5** was not converted to **6** but yielded instead destannylated allylic chloride, **8**, and $n\text{-}Bu_3SnCl$ (Scheme I.3). It was speculated that under these reaction conditions nucleophilic attack of chloride ion on tin generates a vinyl anion that is then immediately quenched by H^+ to give the *Z* allylic isomer. Therefore, it was reasoned that elimination of the proton source from this reaction would allow conversion of allylic alcohol, **5**, to

the corresponding chloride, **6**, leaving the trialkylstannyl moiety intact. Water, introduced as the result of using "wet" solvents, was a likely proton source and could be easily eliminated by ensuring anhydrous conditions. Another possibility was that the relatively acidic hydroxyl proton of the propargylic alcohol was responsible for quenching the presumptive vinyl anion intermediate. In this scenario synthesis of **6** *via* this route would be thwarted by the presence of the quenching agent (OH) contained within the substrate.

Scheme I.3 Synthesis of γ-*n*-Bu_3Sn Substituted Allylic Substrates.

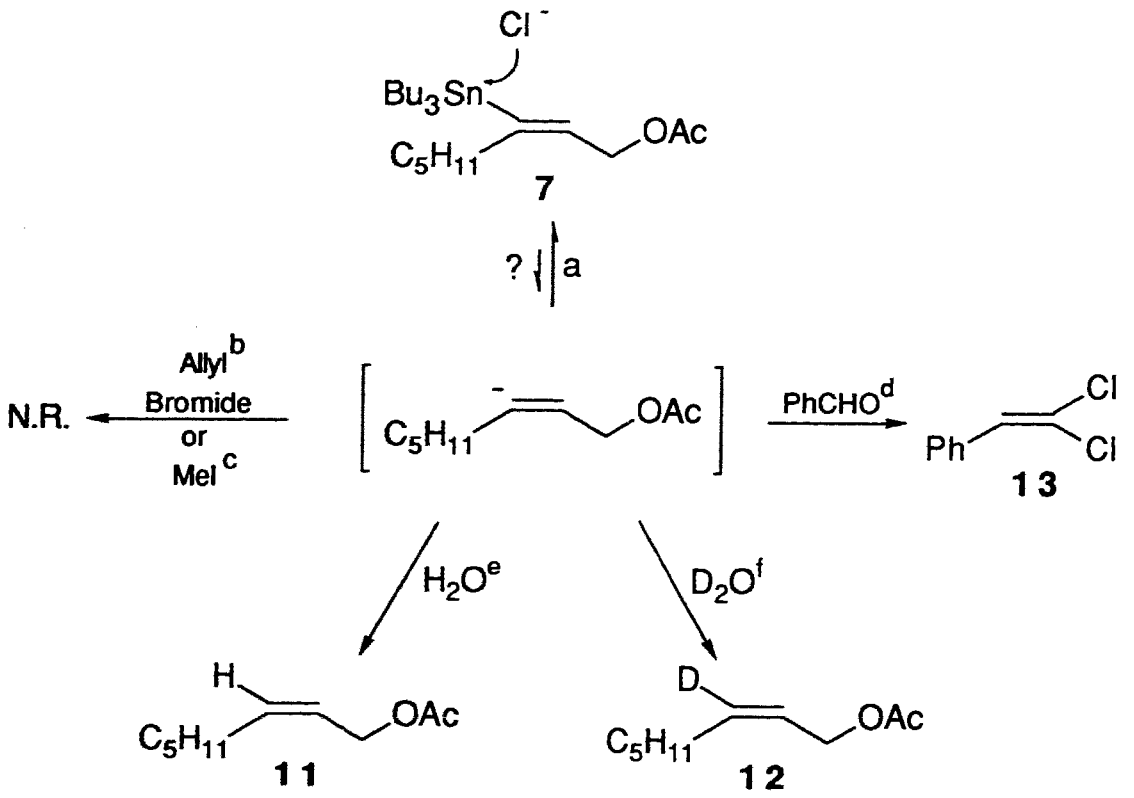


(a) $(n\text{-}Bu_3Sn)_2Zn$ (2.3 equiv), CuCN (10 %), THF, -30 °C → r.t. over 12 hr, 41 %; (b) PPh_3, CCl_4/CH_3CN (1:1), r.t./45 min, 90 %; (c) PPh_3, CCl_4/CH_3CN (1:1, *anhydrous*), r.t./1 hr, 95 %; (d) Pyridine, acetic anhydride, r.t./45 min, 91 %.

The origin of H^+ was established by D_2O/H_2O quenching experiments. When allylic acetate, **7**, was stirred in a solution of PPh_3, CCl_4/CD_3CN under anhydrous conditions and subsequently quenched with water, allylic acetate, **11**, was obtained. In a similar experiment, deuterated acetonitrile was replaced by anhydrous CH_3CN and the reaction quenched with D_2O to afford deuterated allylic acetate, **12**, (Scheme I.4). These results clearly indicated that, in the case of allylic acetate **7**, the vinyl proton was derived from water. These experiments did not rule out the possible involvement of the free hydroxyl group of a propargylic alcohol in destannylation.

In a final experiment, propargylic alcohol, **2**, was stirred in an anhydrous solution of PPh_3, CCl_4/CH_3CN and solvent removed *in vacuo* prior to work-up. Under these reaction conditions allylic chloride, **6**, was obtained in excellent yield (Scheme I.3). The fact that H^+, generated in the reaction of the allylic alcohol with the phosphonium salt, does not contribute substantially to destannylation is conceivably due to rapid consumption by the basic Cl_3C^- anion to yield chloroform. This process likely functions as an acid sink, ensuring low concentrations of HCl.

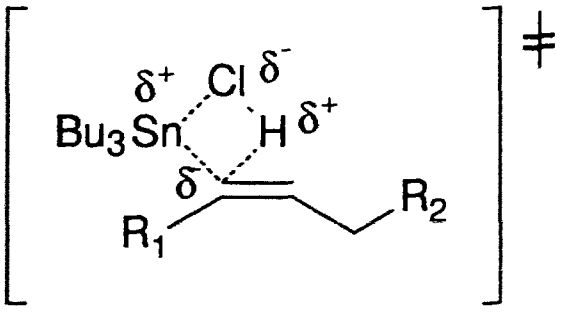
Scheme I.4 Electrophilic Capture of the Presumptive Vinyl Anion Intermediate.



(a) PPh_3, CCl_4/CH_3CN (1:1, *anhydrous*), r.t./15 min; (b) Allyl bromide (2.1 equiv), r.t./12 hr; (c) MeI (2 equiv); (d) PhCHO (2.2 equiv), r.t./1 hr; (e) H_2O (excess), 95 %; (f) D_2O (excess), 80 %; N.R. = no reaction, starting material not consumed.

To provide evidence for the formation of the postulated intermediate, attempts were made to trap the vinyl anion with electrophiles other than H^+ (Scheme I.4). No products were formed when allylic acetate, **7**, was stirred in the presence of allyl bromide or iodomethane under usual (anhydrous) chlorination conditions. Addition of benzaldehyde yielded the Wittig product, **13**, that was also formed in the absence and hence, independently of **7**. Destannylation under nucleophilic (KX/18-crown-6) or radical (AIBN) reaction conditions were also unsuccessful.

Figure I.1 Possible Cyclic Transition State in Reactions of Vinylstannanes with Acid.

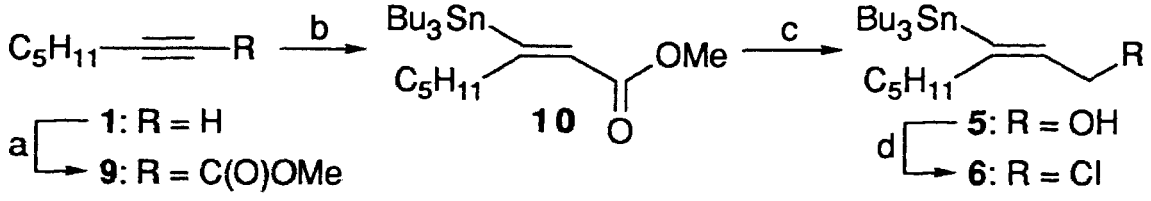


In spite of failed attempts to prove the intermediacy of a vinyl anion, evidence favouring the formation of this species could be deduced by analysis of reaction products. The double bond geometry of the allylic products formed in this reaction is exclusively *Z*. Since involvement of a cationic or radical intermediate would be expected to result in the formation of *E* and *Z* product mixtures, destannylation *via* these alternative intermediates is highly improbable. Furthermore, generation of a vinyl cation is inconsistent with the observed formation of *n*-Bu_3SnCl since in this scenario, protonation of the tri-*n*-butyl tin moiety would yield *n*-Bu_3SnH. These observations point to the

involvement of a vinyl anion in destannylation reactions investigated, although formation of a solvated species in solution is less likely. Perhaps build-up of negative charge at the vinyl carbon occurs in a cyclic transition state in which bond-forming and bond-breaking occurs simultaneously (Figure I.1).

Although the method developed for the synthesis of γ-*n*-Bu_3Sn substituted allylic substrates was adequate for the production of small quantities, it was less suited for large scale reactions in which removal of tin and triphenylphosphine byproducts became a formidable task. It was found that use of PPh_3 could be circumvented in the synthesis of allylic chloride, **6**, by treating allylic alcohol, **5**, with *N*-chlorosuccinimide/DMS (Scheme I.5).[18] This route was high yielding and more importantly, left the tri-*n*-butyl tin group untouched. A second improvement to the overall synthesis was the discovery that allylic alcohol, **5**, could be produced by reducing ester, **10**, with DIBAH. Preparation of **10** was readily accomplished following a literature procedure[19] in which far less tin byproducts were formed than in the earlier method. As a result, work-up and purification were greatly facilitated.

Scheme I.5 Alternative Synthesis of Allylic Chloride **6**.

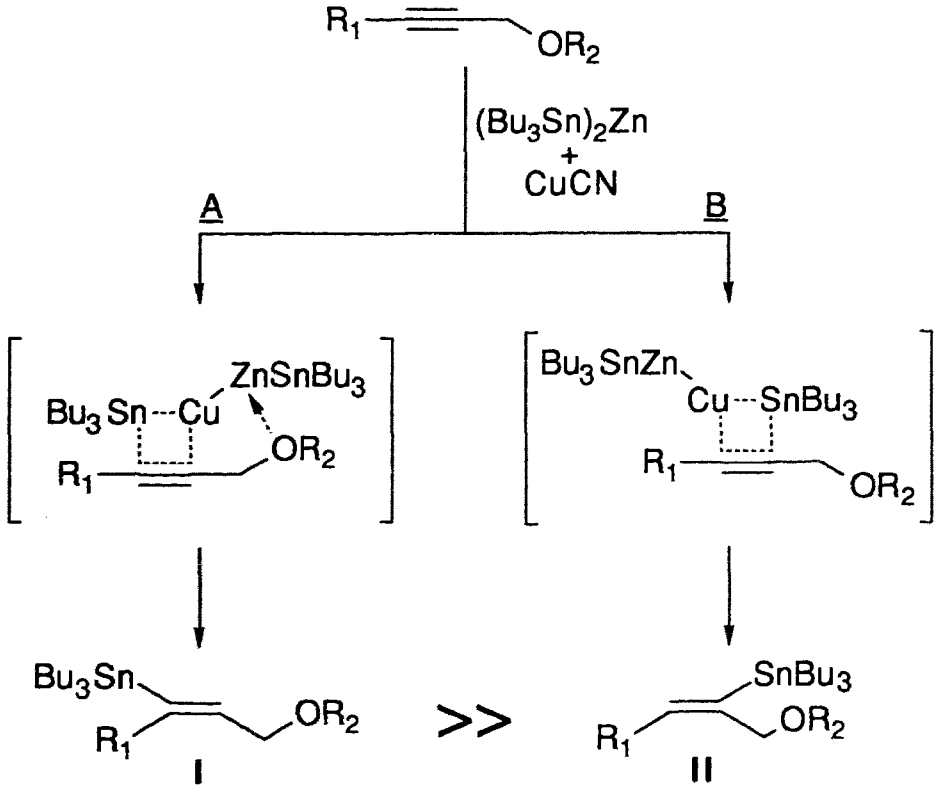


(a) *n*-BuLi, THF, -78 °C/30 min, methyl chloroformate, -78 °C → r.t. over 15 min, 97 %; (b) *n*-Bu_3SnLi (1.3 equiv), CuBr·DMS (1.3 equiv), THF, -78 °C/30 min, **9**, -78 °C/1 hr, MeOH (excess), -78 °C → r.t. over 12 hr, 91 %; (c) DIBAH (2.4 equiv), THF, -78 °C/1 hr, 93 %; (d) *N*-Chlorosuccinimide (1.2 equiv), DMS (1.4 equiv), CH_2Cl_2, 0 °C/10 min, **5**, 0 °C/1 hr, 84 %.

I.3 Investigation of Stannylzincation of Propargylic Substrates.

The remarkable stereoselectivity observed in the stannylzincation of propargylic alcohol, **2**, prompted further investigation of this reaction. It was felt that oxygen played a key role in determining the mode of addition of the stannylzinc reagent to the triple bond. In the envisioned process, coordination of an oxygen lone pair to zinc causes alignment of the mixed stannylzinc cuprate along the axis of the carbon-carbon triple bond so that delivery of tin occurs at the distal acetylenic carbon (Scheme I.6). While syn addition with the opposite regiochemistry is also possible, the latter is presumably energetically less favorable due to the absence of a stabilizing oxygen-zinc interaction.

Scheme I.6 Anchimeric Assistance of Oxygen in Stannylzincation of Propargylic Substrates.



Based on this reasoning, stannylzincation of other propargylic substrates was expected to exhibit a similar trend in which γ substitution predominated over β substitution. This prediction was borne out in the CuCN catalyzed addition of $(n\text{-}Bu_3Sn)_2Zn$ to THP and $t\text{-}BuMe_2Si$ protected propargylic alcohols, **14** and **15** (Table I.1, entries 2 and 3). With the exception of **14**, in which

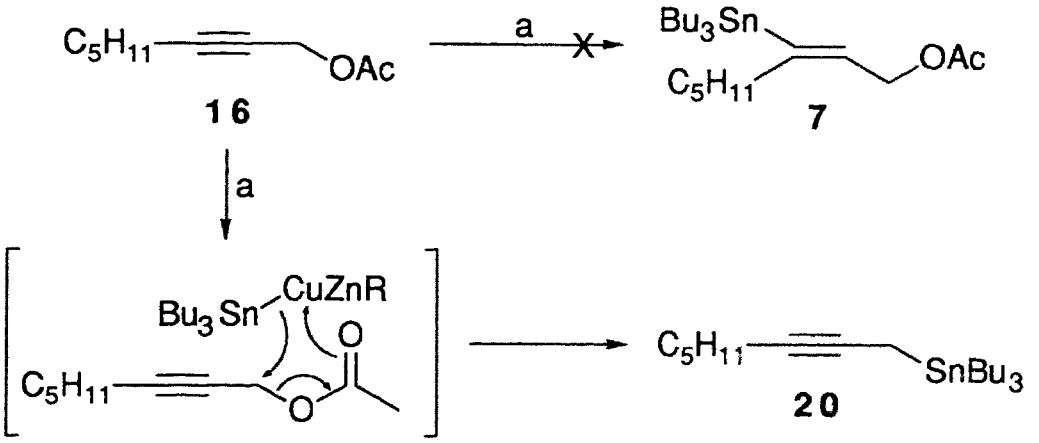
Table I.1 Stannylzincation of Propargylic Substrates.[a]

Entry	Substrate R (#)	Yield %[b] (#)
1	H (**2**)	41 (**5**)
2	THP (**14**)	32 (**18**)
3	$Si(t\text{-}Bu)Me_2$ (**15**)	36 (**19**)

(a) Reaction conditions: $(n\text{-}Bu_3Sn)_2Zn$ (2 equiv), CuCN (10 %), THF, -30 °C → r.t. over 12 hr; (b) Isolated yields.

approximately 3 % of the β-n-Bu_3Sn isomer was formed, addition of tin under these reaction conditions was stereo- and regiospecific for the propargylic substrates investigated. Stannylzincation of propargylic acetate, **16**, was opposite to this trend. Instead of the forming allylic acetate, **7**, **16** was converted to alkyne, **20**, in this reaction. Displacement of acetate by tin is apparently more rapid than addition to the triple bond and is conceivably facilitated by polarization of the carbonyl oxygen in a cyclic transition state (Scheme I.7).

Scheme I.7 Stannylzincation of Propargylic Acetate **16**.



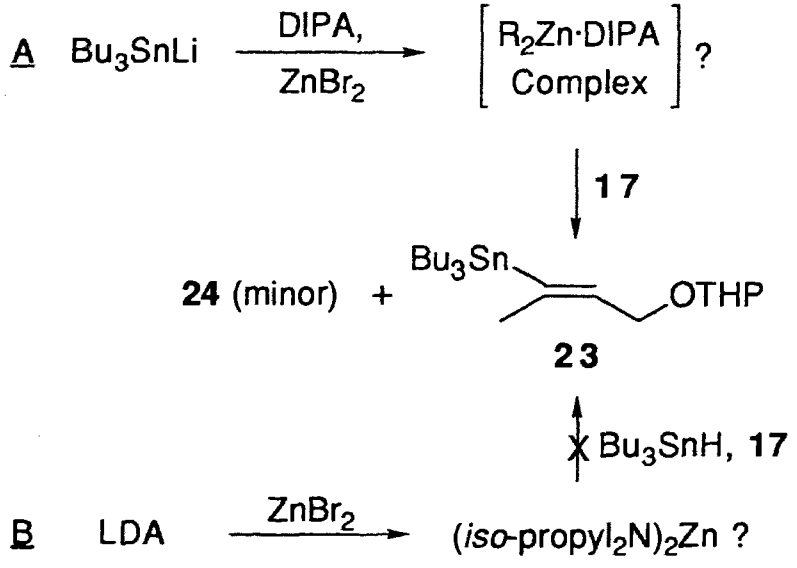
(a) $(n\text{-}Bu_3Sn)_2Zn$ (2 equiv), CuCN (10 %), THF, -30 °C → r.t. over 12 hr, 65 %.

As mentioned earlier, one of the main drawbacks of these reactions is the formation of tin byproducts that are unavoidably generated in the preparation of $(n\text{-}Bu_3Sn)_2Zn$ (**21a**). Cleavage of $(n\text{-}Bu_3Sn)_2$ with *n*-BuLi as a means of producing $n\text{-}Bu_3SnLi$[20] also generates one equivalent of $n\text{-}Bu_4Sn$ which is not only wasteful but often complicates product isolation and purification. In search of a more efficient route, alternative preparations of stannylzinc reagents were explored.

Deprotonation of $n\text{-}Bu_3SnH$ with lithium diisopropylamide is an effective means of generating $n\text{-}Bu_3SnLi$ without formation of $n\text{-}Bu_4Sn$.[21] This method has been previously adopted for the preparation of $(n\text{-}Bu_3Sn)_2Zn$ and its synthetic utility demonstrated in stannylzincation of alkynes.[17b] Initial trials with this reagent in reactions with propargylic alcohol, **2**, were unsuccessful. It was determined that incomplete reaction of lithium diisopropylamide (LDA) with $n\text{-}Bu_3SnH$ was responsible for initial failures. In separate stannylzincations where LDA was allowed to react with $ZnBr_2$ *prior* to addition of $n\text{-}Bu_3SnH$ no products

were formed and only starting material was recovered (Scheme I.8). Presumably, LDA is consumed by $ZnBr_2$ to yield $(i\text{-propyl}_2N)_2Zn$ which is not likely to be sufficiently basic to deprotonate $n\text{-Bu}_3SnH$.

Scheme I.8 Effect of Diisopropylamine (DIPA) and Lithium Diisopropylamide (LDA) on Stannylzincation of Alkyne **17**.

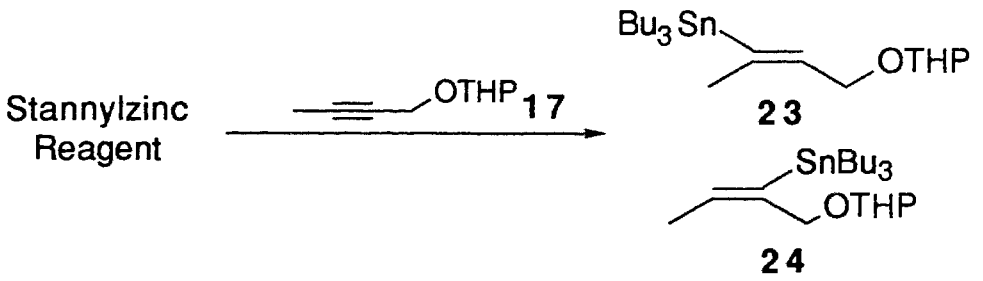


(A) $n\text{-Bu}_3SnLi$ (3 equiv, prepared from $(n\text{-Bu}_3Sn)_2$), DIPA (3 equiv), THF, -30 °C/5 min, $ZnBr_2$ (1.5 equiv), 0 °C/30 min, **17**, CuCN (10 %), -30 °C → r.t. over 5 hr, **23** and **24** (93:7), 73 %; (B) LDA (3 equiv), $ZnBr_2$ (1.5 equiv), THF, 0 °C/30 min, $n\text{-Bu}_3SnH$ (3 equiv), 0 °C/30 min, **17**, CuCN (10 %), -30 °C → r.t. over 5 hr, 70 % **17** recovered, no products detected (by GC).

As anticipated, careful preparation of $(n\text{-Bu}_3Sn)_2Zn$ (**21b**) in which excess LDA was avoided, provided a reactive stannylzincation reagent. Thus, addition of propargylic substrate, **17**, to a solution of **21a** in the presence of CuCN catalyst afforded vinyl stannanes, **23** and **24**, in good yield, accompanied by markedly reduced amounts of tin byproducts (Table I.2, entry 2). Further reduction of tin byproducts was thought possible by decreasing the

number of equivalents of tin per stannylzinc reagent from two to one. Preparation of *n*-$Bu_3SnZnEt_2Li$ reagents (**22a** and **22b**) was inspired by reports that the related $PhMe_2SiZnEt_2Li$ reagent was reactive toward both internal and terminal alkynes.[12a,b] Surprisingly, stannylzincation of **17** with either **22a** or **22b** did not yield **23** or **24** and left the starting material unconsumed (Table I.2, entries 3 and 4).

Table I.2 Variation of Reagent in Stannylzincation of Alkyne **17**.[a]



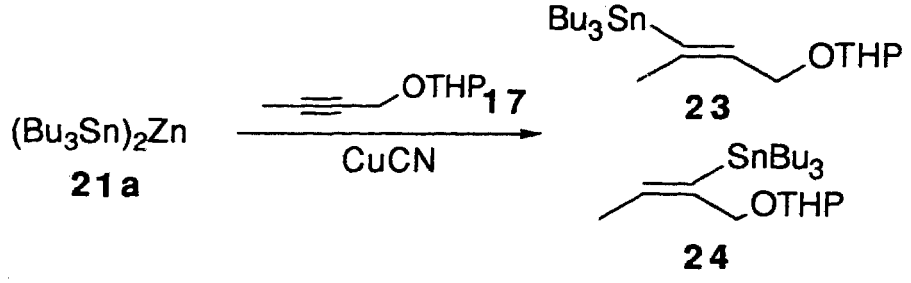
Entry	Reagent (#)	**23** : **24**[b]	Yield %[c]
1	(*n*-$Bu_3Sn)_2Zn$ (**21a**)[d]	98 : 2	76 (39)[f]
2	(*n*-$Bu_3Sn)_2Zn$ (**21b**)[e]	96 : 4	73
3	*n*-$Bu_3SnZnEt_2Li$ (**22a**)[d]	/	78[g]
4	*n*-$Bu_3SnZnEt_2Li$ (**22b**)[e]	/	70[g]

(a) Reaction conditions: stannylzinc reagent (1.5 equiv), **17**, THF, -30 °C → r.t. over 5 hr; (b) Ratios determined by GC; (c) Isolated yields; (d) Prepared from (*n*-$Bu_3Sn)_2$; (e) Prepared from *n*-Bu_3SnH; (f) -30 °C → r.t. over 12 hr; (g) Recovered **17**. **23** and **24** not detected (by GC).

It was noted that prolonged reaction times in stannylzincation of propargylic substrates resulted in diminished product yields (e.g. Table I.2, entry 1). A possible explanation for this observation is that the vinyl adduct formed

initially is converted to a vinyl distannane in a CuCN mediated process. Although the formation of such a byproduct was not investigated for this particular case, bis(tri-*n*-butylstannyl) alkenes have been isolated in related stannylcupration reactions.[22] Alternatively, decomposition of the stannylzinc reagent in a reversible, CuCN catalyzed addition process might cause gradual consumption of products as the reagent is removed from the equilibrium. It was therefore rationalized that the extent of side reactions could be minimized by employing less CuCN catalyst.

Table I.3 Effect of CuCN on Stannylzincation of Alkyne **17**.[a]



Entry	equiv[b] CuCN	23 : 24[c]	Yield %[d]
1	0	92 : 8	26
2	0.1	96 : 4	76
3	0.5	26 : 74	23
4	1.0	31 : 69	21

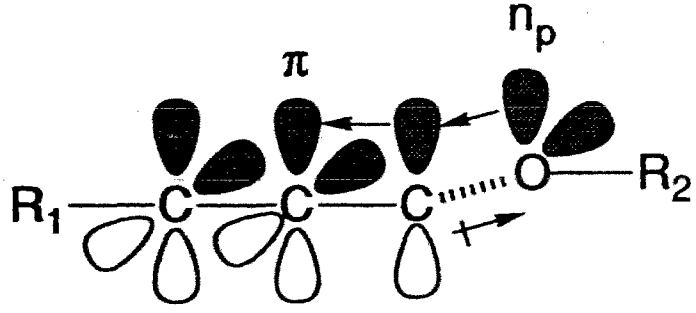
(a) Reaction conditions: **21a** (1.5 equiv), **17**, CuCN, THF, -30 °C → r.t. over 5 hr; (b) Based on **21a**; (c) GC Ratios; (d) Isolated yields.

Stannylzincation experiments in which the amount of CuCN was varied indicated that the presence of one half of an equivalent or more of CuCN had

detrimental effects on reaction yields. More interestingly, at higher proportions of CuCN, a change in the distribution of product isomers was observed in which **24** was favoured over **23** (Table I.3, entries 3 and 4). These solutions had a characteristic red colour, reminiscent of solutions of lower order stannylcuprates, suggesting that a new reagent was formed under these conditions. Addition of reagents devoid of zinc, to propargylic substrates might be expected to be less stereoselective due to the absence of a directing interaction between reagent and the propargylic oxygen (see above). Such species could account for the predominance of **24** over **23** at elevated concentrations of CuCN in stannylcupration of **17**.

Unexpectedly, stannylzinc reagent, **21a**, was found to add to **17** in the absence of CuCN. To rule out the possibility that addition was due to residual CuCN or some other catalyst from a previous reaction, this experiment was repeated with use of a new flask and stirbar. Again, formation of products was observed, albeit in low yield (Table I.3, entry 1). In contrast, stannylzincation of aliphatic internal or terminal acetylenes does not proceed without catalyst. Perhaps proximity of oxygen to the acetylenic moiety in propargylic substrates

Figure I.2 Triple Bond Polarization by Resonance or Induction in Propargylic Substrates.

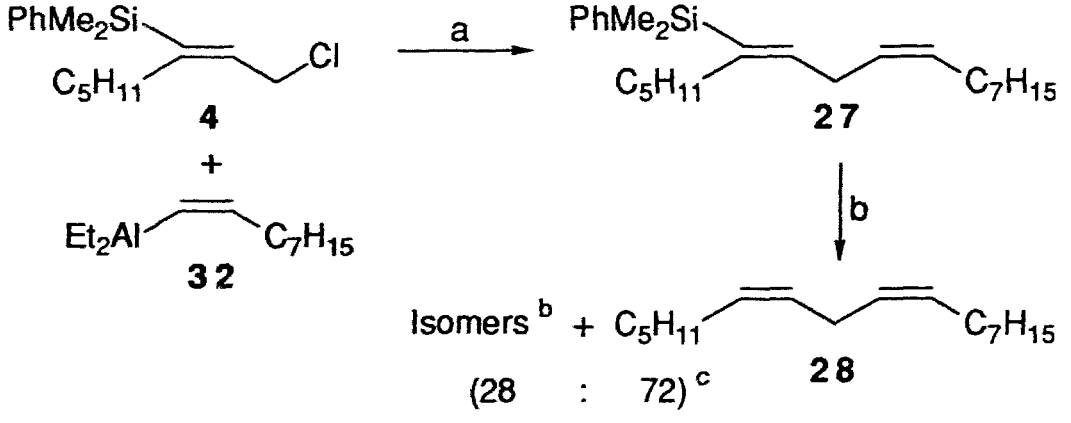


causes sufficient polarization of the triple bond to enable the addition of stannylzinc reagent to proceed uncatalyzed. This type of activation could occur inductively, or by resonance interaction in which the lone pair of electrons on oxygen (*np*) interact with a π orbital of the acetylene group (Figure I.2).

I.4 Model Syntheses of *Z,Z*-1,4-Dienes.

To determine optimum cross-coupling conditions, reactions of a variety of allylic and vinyl organometallic reagents were investigated. It had previously been shown[9] that allylic chloride, **4**, could be coupled with 1(*E*)-noneneyldiisobutylalane in the presence of palladium catalyst at room temperature (Scheme A.3). The analogous reaction of **4** with 1(*Z*)-noneneyldiethylalane,however, required more forcing conditions and afforded

Scheme I.9 Trial Synthesis of (6*Z*,9*Z*)-Heptadeca-6,9-diene (**28**).

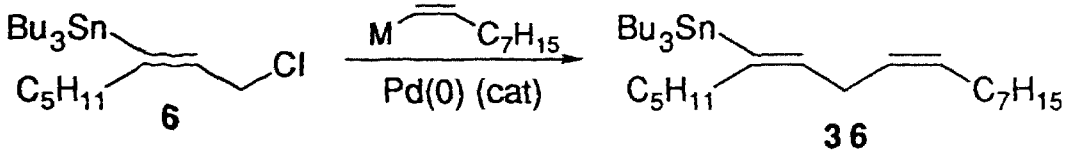


(a) $Pd(PPh_3)_4$ (10 %), THF, 60 °C/2 hr; (b) *n*-Bu_4NF (excess), DMF, 60 °C/1.5 hr; (c) Determined by GC/MS; (d) GC ratio.

27 in 73 % yield upon heating the reaction mixture for two hours at 60 °C. Presumably, the *Z* geometry of the vinyl organometallic reagent increases steric

crowding due to closer proximity of the alkyl side chain to the reacting centre. Although stereospecific assembly of a 1,4-diene could be achieved by this method, subsequent desilylation of **27** afforded a mixture of isomers in addition to the desired 1,4-diene, **28** (Scheme I.9). In light of this difficulty, attention was focused on cross-coupling reactions of allylic substrates in which the γ-silane was substituted by a trialkyltin moiety. It was hoped that replacement of tin with hydrogen in the coupled product could be achieved under more mild reaction conditions, leaving the geometry of the double bonds intact.

Table I.4 Palladium-Catalyzed Cross-Coupling of Allylic Chloride **6** with *Z* Vinyl Organometallic Reagents.



Entry	Reagent M (#)	Reaction Conditions	Yield %[a]
1	Li (**31**)	A	46
2	Et_2Al (**32**)	B	42
3	MeOBBNLi (**33**)	C	5
4	BrZn (**34**)	D	80[b]
5	Cp_2ClZr (**35**)	C	4

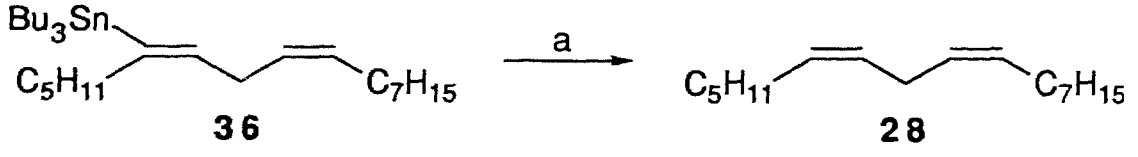
Reactions conducted in THF/ether (1:1): A = -30 °C/30 min, -30 → r.t. over 15 min; B = 50 °C/2 hr; C = 60 °C/3 hr; D = r.t./30 min; (a) GC yield; (b) 16 % of another isomer also formed.

Treatment of *Z* vinyl alane, **32**, with allylic chloride, **6**, in the presence of a catalytic amount of $Pd(PPh_3)_4$ afforded 1,4-diene, **36**, stereospecifically, in

moderate yield (Table I.4, entry 2). As in the case of the related reaction involving allylic chloride, **4**, this process required heating for several hours. Cross-coupling of **6** with vinyl boron and vinyl zirconium reagents **33** and **35** were less successful, as evidenced in low product yield (Table I.4, entries 3 and 5). Poor yields in these reactions are likely due to the bulky bicyclic and cyclopentadienyl metal ligands that hinder the coupling process. Heating these reactions to higher temperatures did not improve yields suggesting that decomposition of the organometallic reagent occurred under these conditions.

The highest yield was obtained with vinyl zinc reagent, **34**, affording **36** in 80 % yield (Table I.4, entry 4). Unfortunately, formation of **36** was accompanied by 16 % of another isomer, rendering this process unsuitable in synthetic applications requiring stringent control of stereochemistry. Quite unexpectedly, cross-coupling of **6** with 1(*Z*)-nonenyllithium (**31**) furnished **36** in respectable 46 % yield (Table I.4, entry 1). This result was somewhat surprising, since palladium-catalyzed cross-coupling of allylic substrates with vinyllithium

Scheme I.10 Destannylation of (6*E*,9*Z*)-6-Tri-*n*-butylstannylheptadeca-6,9-diene (**36**).



36 **28**

(a) *p*-Toluenesulfonic acid (excess), THF, r.t./30 min, 90 % (by GC).

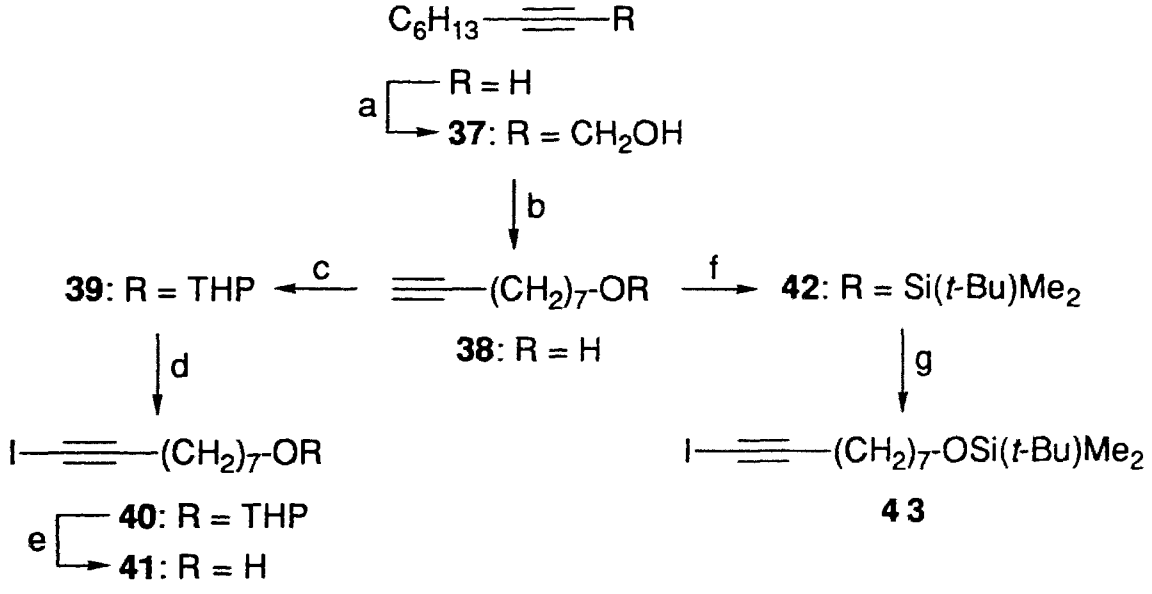
reagents had not been previously reported. Later experiments revealed that palladium was actually not required in this reaction, suggesting that coupling in this case proceeds *via* S_N2 displacement of chloride by vinyllithium. As was

hoped, conditions were found that enabled stereospecific replacement of the trialkyltin moiety by hydrogen in the coupled product. Thus, treatment of diene, **36**, with an excess of *p*-toluenesulfonic acid in THF gave the unisomerized diene, **28**, in excellent yield (Scheme I.10).

I.5 Preparation of *Z* Vinyl Organometallic Synthons.

Conversion of 1-iodo-1-alkynes to the corresponding 1-iodo-1(*Z*)-alkenes was a key step in the synthesis of *Z*,*Z*-1,4-dienes. Hydroboration (BH_3·DMS) of alkynyl iodides containing simple alkyl side chains was an effective means of stereospecifically preparing *Z* vinyl iodides. However, since hydrolysis of the vinyl borane in the final step required refluxing propionic acid,

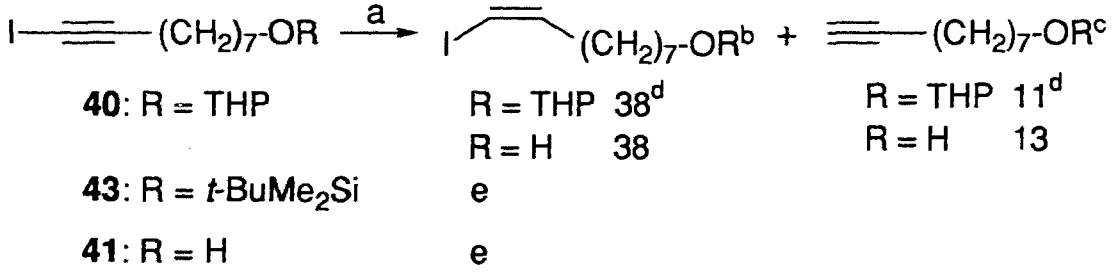
Scheme I.11 Synthesis of Alkynyl Iodides Containing ω-OR Functionalities.



(a) *n*-BuLi, THF, -78 °C 30 min, $(CH_2O)_n$ (1.3 equiv), -78 °C → r.t. over 12 hr, 89 %; (b) Li (6.5 equiv), diaminopropane, r.t./5 hr, *t*-BuOK (4 equiv), r.t./30 min, **37**, r.t./2 hr, 91 %; (c) Dihydropyran (2 equiv), *p*-toluenesulfonic acid cat., CH_2Cl_2, r.t./45 min, 94 %; (d) *n*-BuLi, THF, -78 °C/30 min, I_2, -78 °C, 87 %; (e) *p*-Toluenesulfonic acid cat., MeOH, r.t./30 min, 78 %; (f) *t*-$BuMe_2SiCl$ (1.1 equiv), Et_3N (excess), DMAP cat., CH_2Cl_2, r.t./3 hr, 88 %; (g) As in d, 89 %.

it was recognized that acid-sensitive groups contained in pheromone synthons might not withstand these conditions. In light of this possibility, alkynyl iodides containing various ω-OR functionalities were prepared (Scheme I.11) and their stability under hydroboration conditions investigated (Scheme I.12). As anticipated, hydroboration of alkynyl iodide, **40**, resulted in partial hydrolysis of the THP protected alcohol. In addition, a mixture of 1-alkynes was formed, presumably arising from the trans elimination of boron and iodide in the vinyl

Scheme I.12 Trial Syntheses of *Z* Vinyl Iodides Containing ω-OR Functionalities.

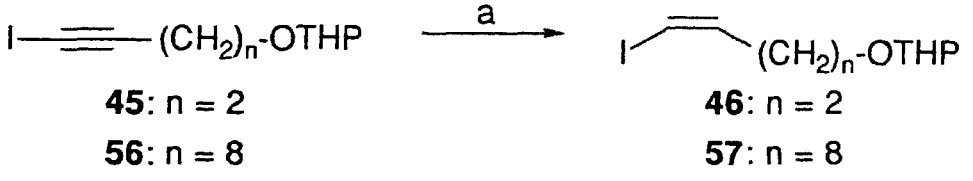


(a) BH_3·DMS (0.3 equiv), diglyme, 0 °C/1 hr then r.t./2 hr, propionic acid, reflux/3 hr; (b) Identified by GC/MS; (c) Identified by coinjection with authentic samples; (d) GC ratios, yields not determined; (e) Starting materials consumed to form unidentified, low boiling compounds.

borane adduct. Repetition of this experiment with alkynyl iodide, **43**, containing a *t*-$BuMe_2Si$ protected alcohol was not successful and yielded unidentified decomposition products. Since both protecting groups investigated did not withstand conditions of vinyl borane hydrolysis, hydroboration of the unprotected alcohol was examined. Although starting material was consumed, none of the desired *Z* vinyl iodide was formed. Instead, the starting alkyne was converted to a mixture of low boiling compounds.

In search of more mild reaction conditions that tolerated the presence alcohol protecting groups and did not lead to product decomposition, preparation of *Z* vinyl iodides was attempted by using disiamylborane.[23,24] Indeed, hydroboration of alkynyl iodides, **45** and **56**, with $(siam)_2BH$, followed by treatment with glacial acetic acid at room temperature furnished the corresponding *Z* vinyl iodides, **46** and **57**, in respectable yield (Scheme I.13).

Scheme I.13 Syntheses of *Z* Vinyl Iodides **46** and **57**.



45: n = 2
56: n = 8

46: n = 2
57: n = 8

(a) 2-methyl-2-butene, BH_3·DMS, neat, 0 °C/2 hr, **45** or **56**, THF, r.t./2 hr, glacial acetic acid, r.t./2 hr, **46**: 56 %, **57**: 67 %.

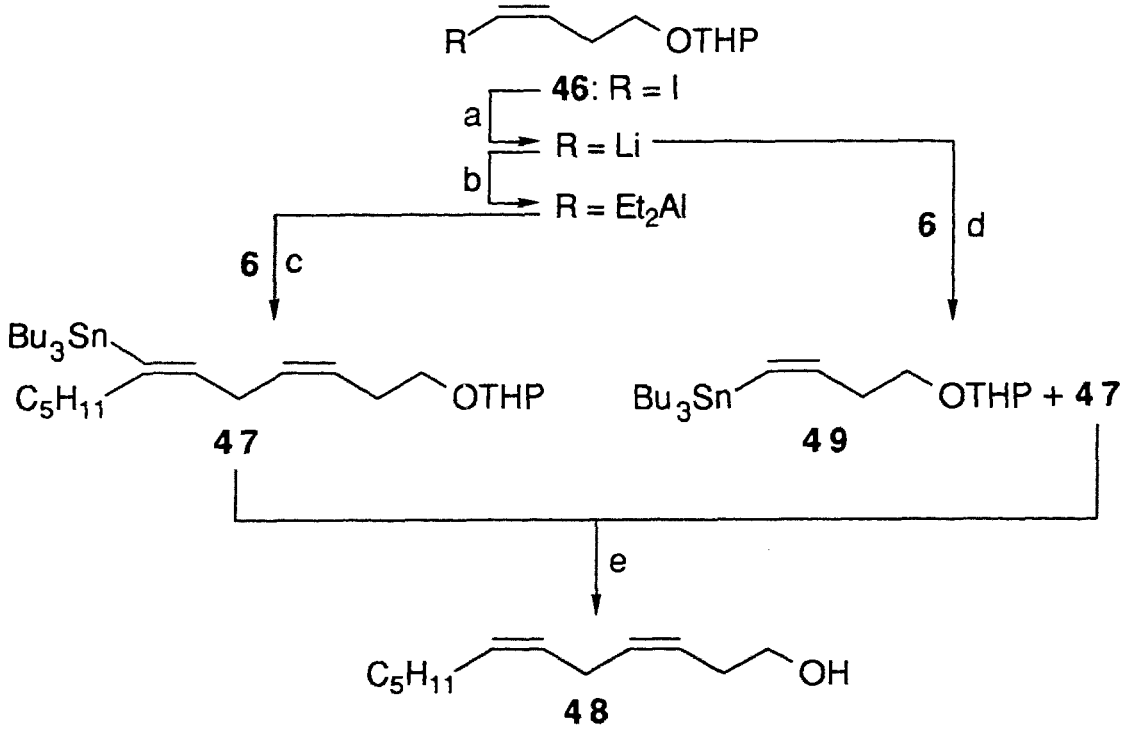
I.6 Synthesis of the Termite Trail Marker Pheromone (48) and the Sex Pheromone Inhibitor of the Indian Meal Moth (58b).

With both allylic and vinyl coupling partners at hand, synthesis of pheromones, **48** and **58a**, was attempted according to the cross-coupling strategy outlined above. Based on preliminary studies, lithium and aluminum based vinyl organometallic species seemed the reagents of choice in cross-coupling reactions with allylic chlorides (Table I.4). Reaction of the vinyllithium reagent derived from vinyl iodide, **46**, with allylic chloride, **6**, in the presence of $Pd(PPh_3)_4$ (10 %) afforded diene, **47**, in 38 % yield (Scheme I.14).

However, in addition to **47**, a significant amount of *Z* vinyl stannane, **49**, was also formed, undoubtedly the result of nucleophilic attack of the vinyl anion

on the tri-*n*-butyltin moiety of **6**. In contrast, none of **49** was detected in cross-coupling of **6** with the less reactive vinyl aluminum reagent and gave rise to **47**

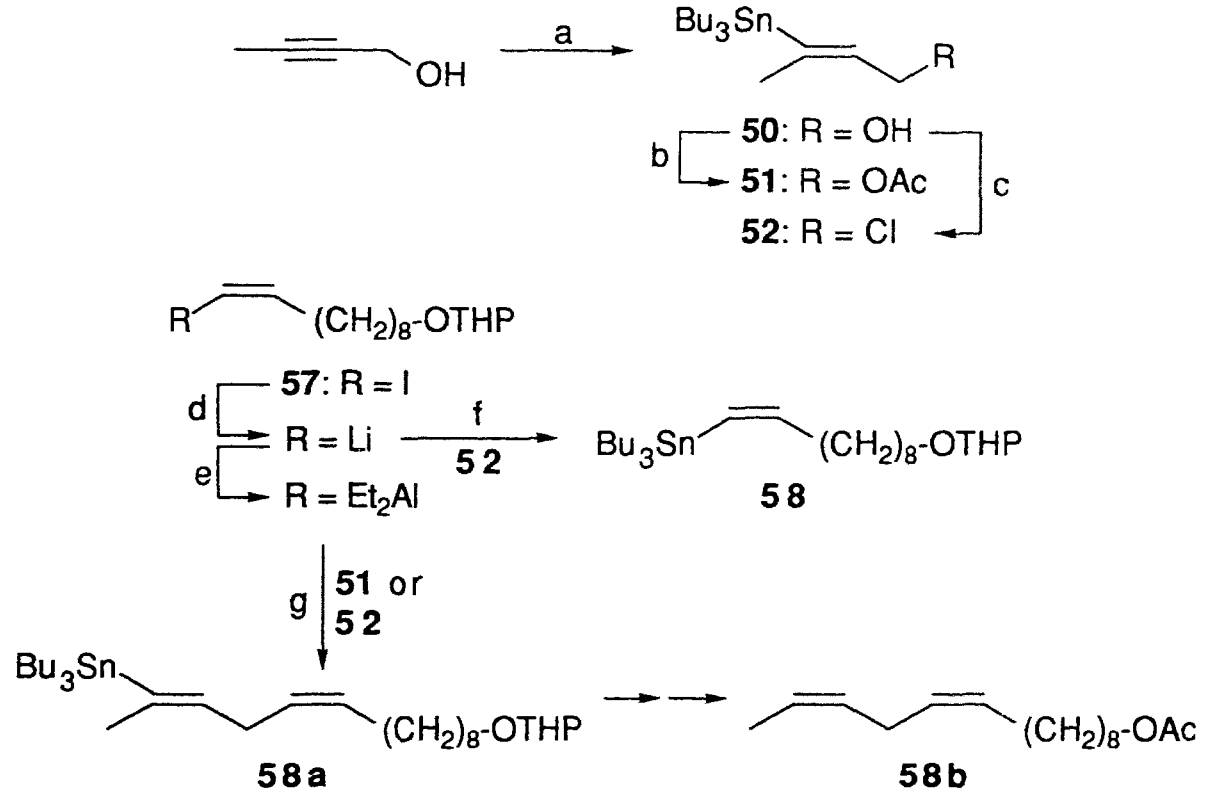
Scheme I.14 Synthesis of the Termite Trail Marker Pheromone, (3*Z*,6*Z*)-Dodeca-3,6-dien-1-ol (**48**).



(a) *t*-BuLi (2 equiv), ether, -70 °C/30 min, -30 °C/30 min; (b) Et_2AlCl, THF/ether (1:1), -30 °C/15 min; (c) **6**, $Pd(PPh_3)_4$ (10 %), THF/ether (1:1), 50 °C/2 hr, 51 %; (d) **6**, $Pd(PPh_3)_4$ (10 %), THF/ether (1:1), -30 °C/ 30 min, -30 °C → r.t. over 30 min, 38 %; (e) *p*-Toluenesulfonic acid (excess), THF/MeOH (1:1), r.t./30 min, 77 %.

in higher (51 %) yield. Tri-*n*-butyltin and THP groups were readily removed in a single step by stirring **47** in an acidified (*p*-toluenesulfonic acid) solution of THF/MeOH (1:1), affording pheromone, **48**, in 77 % yield. The *Z* double bond geometry was ascertained by ^1H decoupling experiments which revealed the proton coupling constants for both double bonds to be 10.5 Hz. This value is characteristic for proton coupling in *Z* double bonds.[25]

Scheme I.15 Synthesis of the Sex Pheromone Inhibitor, (9*Z*,12*Z*)-Tetradeca-9,12-dienyl Acetate (**58b**).



(a) (n-$Bu_3Sn)_2Zn$ (2 equiv), THF, -30 °C → r.t. over 12 hr, 47 %; (b) Pyridine, acetic anhydride, r.t./45 min, 94 %; (c) *N*-Chlorosuccinimide (1.2 equiv), DMS (1.4 equiv), CH_2Cl_2, 0 °C/10 min, **57**, 0 °C/1 hr, 85 %; (d) *t*-BuLi (2 equiv), ether, -70 °C/30 min, -30 °C/30 min; (e) Et_2AlCl, THF/ether (1:1), -30 °C/15 min; (f) **52**, $Pd(PPh_3)_4$ (10 %), THF/ether, -30 °C/30 min, -30 °C → r.t. over 30 min, 91 %; (g) **52** (or **51**), $Pd(PPh_3)_4$ (10 %), THF, 50 °C/2 hr.

Preparations of allylic (**51**, **52**) and vinyl (**57**) synthons for the synthesis of pheromone, **58b**, was carried out in an analogous fashion described for substrates required in the assembly of pheromone, **48**. Reaction of the vinyllithium reagent derived from vinyl iodide, **57**, with allylic chloride, **52**, afforded a major product, initially thought to be diene, **58a**, but later identified as the *Z* vinyl stannane, **58** (Scheme I.15). This result was surprising, since in

the related reaction leading to diene, **47**, (Scheme I.14), *both* **47** and *Z* vinyl stannane were formed. Apparently, nucleophilic attack on tin is greatly favoured over displacement of chloride in reaction with allylic chloride, **52**. Presumably, the methyl group in **52** poses less of an obstacle for an incoming vinyl anion than the bulkier alkyl residue in **6**. As observed previously, formation of the *Z* vinyl stannane byproduct could be avoided completely by conversion of the vinyllithium reagent to the corresponding aluminum species. Cross-coupling of the vinylalane with allylic substrates, **51** or **52**, yielded a single crude product whose ^{1}H NMR was consistent with the structure represented by **58a**. It is presumed that transfomation of **58a** to **58b** can be accomplished in a similar fashion described for the preparation of **48**, followed by acetylation of the alcohol in pyridine/acetic anhydride (see also preparation of **106**, Chapter III).

I.7 **Summary and Conclusion.**

Stereospecific synthesis of *Z,Z*-1,4-dienes has been achieved in the palladium-catalyzed cross-coupling of allylic substrates with vinyl organometallic reagents. Key to this synthesis was the development of methods that enabled regiospecific incorporation of a tri-*n*-butylstannyl group into the γ position of the allylic cross-coupling partner. The steric bulk of this moiety ensures the stereochemical integrity of the allylic double bond throughout the coupling sequence and is easily replaced by hydrogen in the coupled product.

Cross-coupling of allylic substrates with a variety of *Z* vinyl organometallic reagents has been examined. The reactivity of vinyl synthons appears to depend on the steric bulk of the ligands of the associated metal/metalloid fragment, Li > Zn > Al > B ~ Zr, lithium being the most and boron and zirconium the least reactive. Vinyl aluminum species proved to be the reagents of choice in cross-coupling reactions with allylic substrates, providing coupled product in respectable yield and in > 95 % stereoselectivity. This strategy has been applied to the synthesis of insect pheromones, **48** and **58b**, containing *Z,Z*-1,4-diene fragments.

CHAPTER II

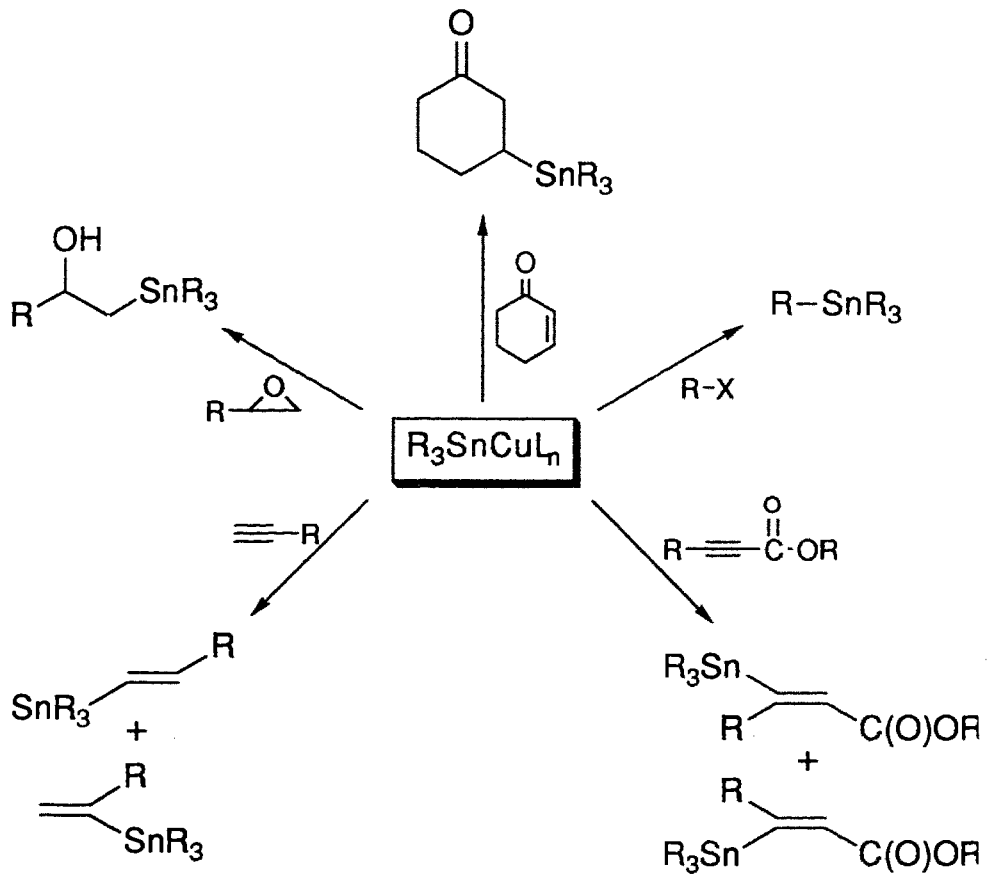
Introduction

Since the preparation of PhCu first by Reich[26a] and later by Gilman and Straley[26b] more than half a century ago, organocuprates have evolved to become some of the most important and widely used reagents in organic synthesis.[27] Chemical and spectroscopic investigations of these reagents have led to the development of organocuprates with compositions as diverse as their synthetic applications. A turning point in the development of organocopper chemistry was the discovery that carbon ligands of conventional reagents could be replaced by silicon and tin to afford cuprates that deliver these metallic anions. The synthetic utility of trialkylsilyl copper reagents was demonstrated by Fleming *et al.* in reactions with enones and acetylenes that afforded stable β-silyl carbonyl and vinyl silyl compounds, respectively.[28] Piers *et al.* showed that reaction of phenylthicopper (I) with trimethyltin anion yielded trialkylstannylcuprates that, in turn, reacted with enones[29] and ynoates[30] to give the corresponding β-trimethylstannyl enones and β-trimethylstannyl α,β-unsaturated esters (Scheme B.1)

More important, however, was the discovery that the trimethylstannyl moiety was much more amenable to functional group manipulation than the trialkylsilyl group and could easily be reacted with a variety of electrophiles. The ability to elaborate a trimethyl tin group provided a new route to the synthesis of otherwise inaccessible compounds, thereby greatly extending the scope of organocuprate methodology.[29,30] Since this landmark achievement, many new stannylcuprate species have been developed and their reactions with

substrates such as epoxides[29f,g], alkyl halides[29e,f] and 1-alkynes[29e-g,31] reported (Scheme B.1)

Scheme B.1 Stannylcupration of Organic Substrates

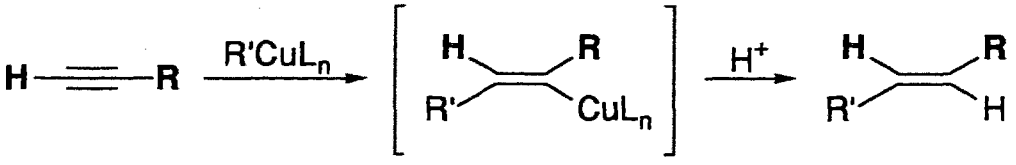


In contrast to the vast body of information available for alkyl[32] and arylcuprates,[33] reaction mechanisms involving stannylcuprates are poorly understood[29h,30a,b,d-f,31k,m] and information regarding the nature and composition of the reactive species scant.[29g,31l] Investigations of stannylcupration reactions seem to indicate that these reagents behave similarly to the alkylcuprate analogues. For example, it has been suggested[29h] that stannylcupration of α,β-unsaturated ketones proceeds *via* a copper(I)-olefin π-complex, also postulated to be involved in the parallel carbocupration

reaction.[34] Recent ^{13}C NMR investigations of the Michael addition of Me_2CuLi to alkynoates[35] has provided evidence for formation of a copper allenolate intermediate, long suspected to be responsible for double bond isomerization in these and related stannylcupration reactions.[30g]

Addition of organocuprates to alkynes proceeds *via* syn addition of the organic and copper moieties across the triple bond. The stereochemistry of this reaction has been inferred from observations that alkynyl substituents are cis to each other in the resulting vinyl products (Scheme B.2).[36] Direct evidence for the formation of the presumptive vinyl copper intermediates is not available. Based on similar stereospecificity obtained in stannylcupration of 1-alkynes, the intermediacy of a vinyl tin-copper adduct has also been assumed in these reactions.[31]

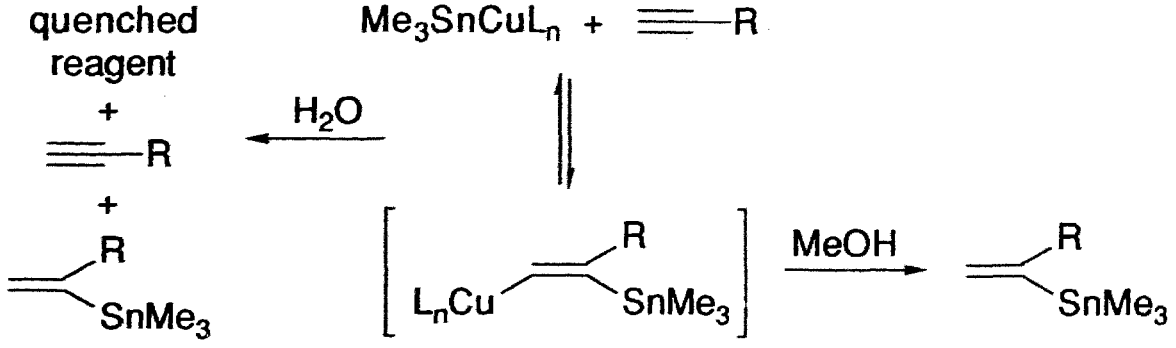
Scheme B.2 Syn Addition of Organocuprates to 1-Alkynes.



It has been recently reported that yields in stannylcupration of 1-alkynes could be increased dramatically by addition of methanol to reaction mixtures at low temperature.[31j] Based on these results the existence of an alkyne-adduct equilibrium was postulated in which vinyl adducts were only marginally favoured over starting materials. It was rationalized that poor yields obtained when reactions were quenched with aqueous solutions reflected an unfavourable alkyne-adduct equilibrium in which starting material was only partially consumed. It was further argued that unlike water, addition of methanol

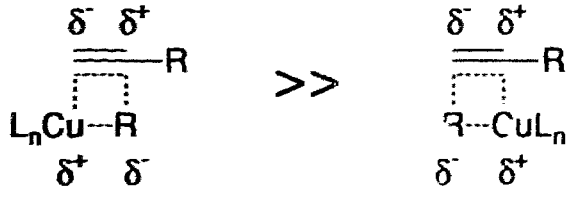
to these solutions did not destroy the stannylcuprate reagent.[30b,e] It was concluded that the higher yields obtained with methanol were due to selective quenching of the vinyl adducts, causing continuous reestablishment of the equilibrium until all starting material was consumed (Scheme B.3).

Scheme B.3 H_2O versus Methanol as Quenching Agents in Stannylcupration of 1-Alkynes.



Of the two possible regioisomeric products formed in stannylcupration of 1-alkynes, 2-trialkylstannyl alkenes are generally preferred over the 1-trialkylstannyl isomer. This trend has been ascribed to electronic factors governing the mode of addition. It has been hypothesized that the orientation of the organocuprate reagent with respect to the triple bond is dictated by the

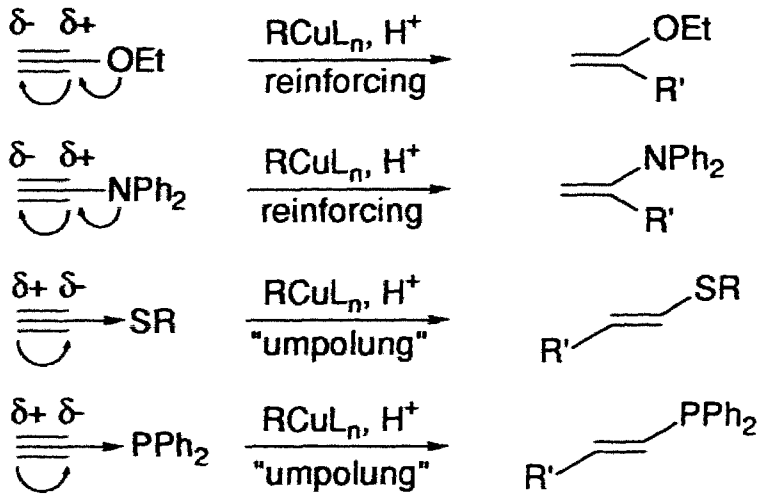
Figure B.1 Electronic Factors Governing the Mode of Addition in Carbocupration of 1-Alkynes.



direction of bond polarization of the reactants causing alignment of oppositely charged atoms in a four membered transition state (Figure B.1) Molecular orbital calculations have shown that for propyne the π electron density is greater at C_1 than at C_2.[37]

In support of this theory it has been shown that electron withdrawing groups adjacent to the acetylenic moiety cause "umpolung" of the triple bond and give rise to products with opposite regiochemistry.[38] Thus, carbocupration

Scheme B.4 Carbocupration of Heterosubstituted Acetylenes.

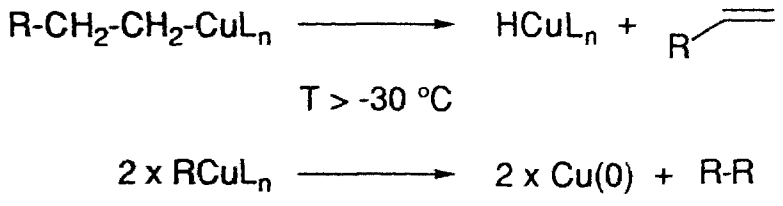


of heterosubstituted acetylenes containing sulphide and phosphide groups yielded the corresponding vinyl products alkylated at C_1. In contrast, electron donating OR and NR_2 groups reinforced the "normal" mode of addition to the triple bond and yielded alkenes alkylated at the internal vinyl carbon (Scheme B.4). It should be noted that isomer ratios are less predictable in stannylcupration reactions and vary considerably depending on experimental conditions. The extent to which factors such as stannylcuprate reagent,

temperature, solvent and quenching agent influence the regiochemical outcome of these reactions has not been determined. Since these criteria are not known, regioselective syntheses rely largely on empirical methods and efforts aimed at controlling regiochemical biases are subject to trial and error.

In spite of the indisputable synthetic advantages of organocuprates it was recognized in early studies that these reagents suffered shortcomings of thermal instability and poor solubility. House *et al.* have elucidated various decomposition pathways, among the most important are copper hydride elimination and oxidation leading to coupling of the organic residues (Scheme B.5).[39]

Scheme B.5 Thermal Decomposition of Organocuprates.



In an attempt to circumvent these side reactions, organocuprates (R_2CuLi) were prepared wherein one of the alkyl groups was replaced by a stabilizing ligand. Indeed, greater stability has been reported for these so-called mixed cuprates (R(X)CuLi) containing nitrile[40], acetylide[39b,41] and 2-thienyl[41d,42] ligands. Some success has also been achieved with heterocuprates incorporating alkoxides, phenoxides, mercaptides, amides and phosphides.[43]

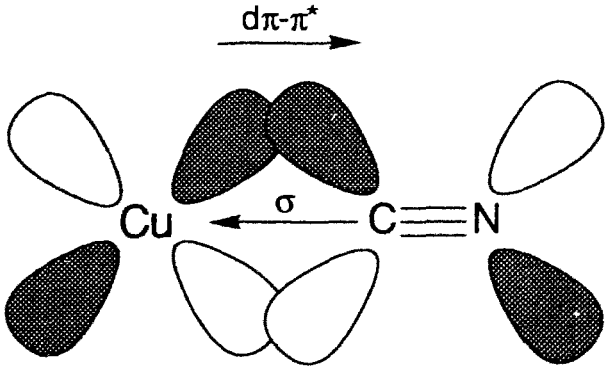
These advances were quintessential to the development of stannylcuprate reagents that are notoriously unstable in the absence of

stabilizing ligands. Phenylthio, 2-thienyl and acetylide ligands have shown to provide enhanced stability to stannylcuprate reagents and in doing so have extended their synthetic utility.[30b] Thus, the greater thermal stability of these mixed reagents has increased the scope of stannylcupration reactions tremendously by enabling reactions with substrates requiring elevated temperatures. In this regard, perhaps one of the most significant achievements has been the development by Lipshutz *et al.* of so-called higher order cuprates.[44] These species, which are formally copper(I) dianions $\{[R_2Cu(CN)]^{2-}\ 2M^+\}$, exhibit remarkable thermal stability, particularly in conjunction with other stabilizing ligands (e.g. 2-thienyl(*n*-Bu_3Sn)$Cu(CN)Li_2$).[29f,30f] As indicated by the general formula, these reagents are typically derived from CuCN and are conveniently prepared by combining CuCN with two equivalents of anion in ethereal solvents. Homo higher order trialkylstannylcyanocuprates, $(R_3Sn)_2Cu(CN)Li_2$, for instance, have been used in a wide variety of synthetic transformations and are clearly superior to the lower order reagents.

Although higher order stannylcuprates have gained increasing popularity, information on the composition of these novel reagents has lagged behind developments on the synthetic front. Evidence for the existence of higher order cuprates in which three ligands are bonded to copper has, nevertheless, been obtained for phenylcuprates.[33a] ^{13}C NMR studies of solutions of Ph_2CuLi + PhLi in dimethyl sulfide revealed the formation of a new and distinct species, presumed to be Ph_3CuLi_2. Similarly, free MeLi could not be detected in solutions of $Me_2Cu(CN)Li_2$ suggesting that this higher order cuprate is thermodynamically preferred over the lower order (MeCu(CN)Li) species.[45] In contrast, spectroscopic investigations have shown that Me_3CuLi_2 is not formed,[46a] or at least not as cleanly,[46b] in solutions containing Gilman's

reagent, Me_2CuLi, and MeLi. Based on these observations it has been conjectured that accommodation of a third ligand on copper is dependent upon the complex's ability to delocalize additional negative charge. It has been postulated[47] that charge build-up is permitted in phenyl and cyanocuprates due to stabilizing $d\pi$-π^* backbonding interactions between the d^{10} copper atom and associated π acceptor ligands (Figure B.2).[48] In light of these arguments it is not difficult to imagine that higher order stannylcuprates owe their unique reactivity and stability to the formation of similar dianionic species, distinct from their lower order counterparts.

Figure B.2 Stabilizing $d\pi$-π^* Backbonding Interactions in Higher Order Cyanocuprate Complexes.



II.1 **Objective.**[a]

Investigation of stannylcupration of 1-alkynes was inspired by the demonstrated synthetic utility of the resulting vinylstannanes[31b-g,50] and in particular, the potential application of these compounds to the preparation of 1,4-dienes. A goal of this project was to improve the efficiency and the regioselectivity of these reactions. Since little was known about the mechanism of stannylcupration of 1-alkynes,[29h,30a,d-f,31j-m] efforts were focused on gaining a better understanding of the processes involved. Insight into the reaction mechanism and the nature of the reactive stannylcuprate species would allow rational design of more efficient reagents and development of improved reaction conditions. The questions that were addressed are summarized below:

- Does stannylcupration of 1-alkynes proceed via vinyl cuprate intermediates?

- To what extent, if at all, are these reactions reversible?

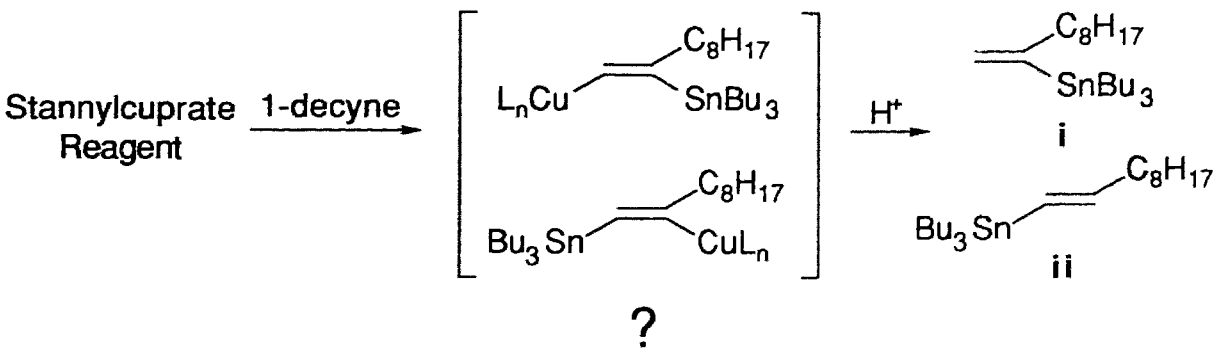
- What governs the regioselectivity? Can it be controlled by appropriate choice of reagents and reaction conditions?

(a) Experiments in sections II.2 and II.3 conducted jointly with Robert D. Singer.[49]

II.2 ^{2}H and ^{13}C NMR Investigations of Stannylcupration of 1-Alkynes.[49]

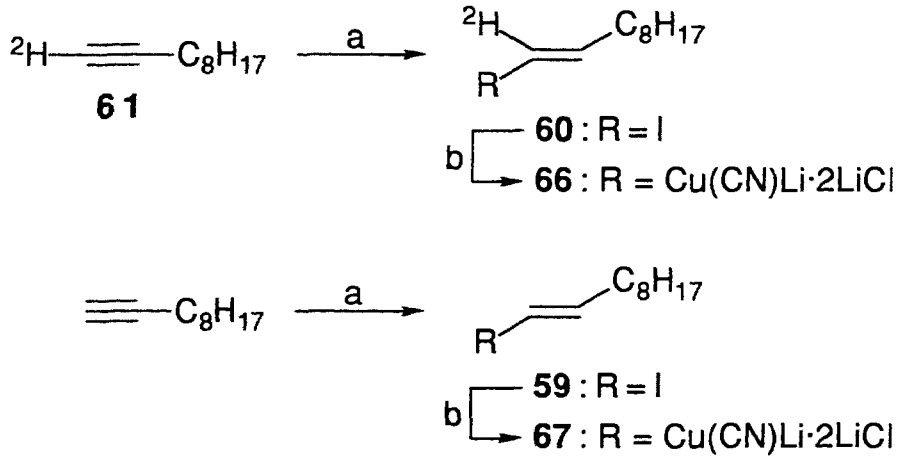
To probe the existence of a stannylcuprate intermediate in stannylcupration of 1-alkynes, solutions of reagents *n*-$Bu_3SnCu(CN)Li{\cdot}2LiCl$ (**64**) and $(n\text{-}Bu_3Sn)_2Cu(CN)Li_2$ (**65**) containing 1-decyne were monitored by ^{13}C NMR spectroscopy over a temperature range of -78 °C to 0 °C. Warming above -30 °C resulted in the gradual disappearance of the sp carbon signals of 1-decyne (84.9, 70.3 ppm) and concomitant emergence of new downfield signals at 150.1, 129.5 ppm (**64**) and 200.3, 170.8, 159.0, 129.7 ppm (**65**), respectively. The chemical shifts of these signals were distinguishable from those of 1-decyne and the vinylstannane hydrolysis products (156.1, 151.2, 127.7, and 126.1 ppm) (**i** and **ii**, Scheme II.1). Since the chemical shifts of the signals observed in the initial reaction of stannylcuprate and 1-decyne were characteristic of sp^2 carbons, formation of a vinyl cuprate adduct was suspected.

Scheme II.1 Possible Formation of Vinyl Cuprate Intermediates in Stannylcupration of 1-Alkynes.



To confirm this possibility, a related vinyl cuprate species, **67**, was prepared by lithiation/cupration of vinyl iodide, **59** (Scheme II.2). The ^{13}C NMR spectrum of this species exhibited signals (195.6 and 159.0 ppm) that appeared in the same region as those observed in the reaction of stannylcuprates and 1-decyne. Other signals due to unreacted **59** and and alkene impurities were also present.[51]

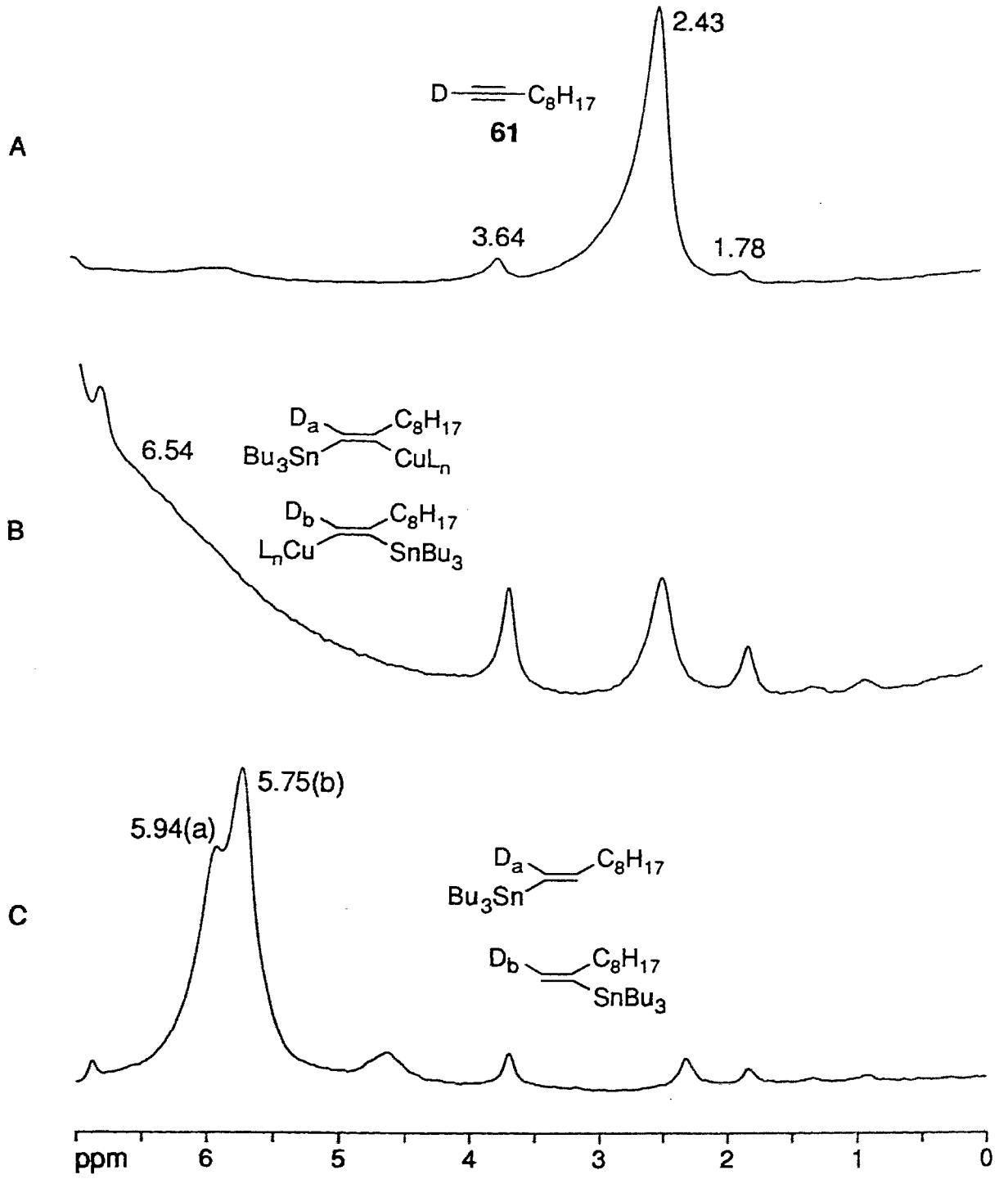
Scheme II.2 Preparation of Vinyl Cuprates **66** and **67**.



(a) DIBAH, hexanes, 50 °C/2.5 hr, I_2, THF, -40 °C, 57 % (from **61**), 55 % (from 1-decyne); (b) *n*-BuLi, THF, -30 °C/30 min, CuCN·2LiCl, -30 °C/30 min.

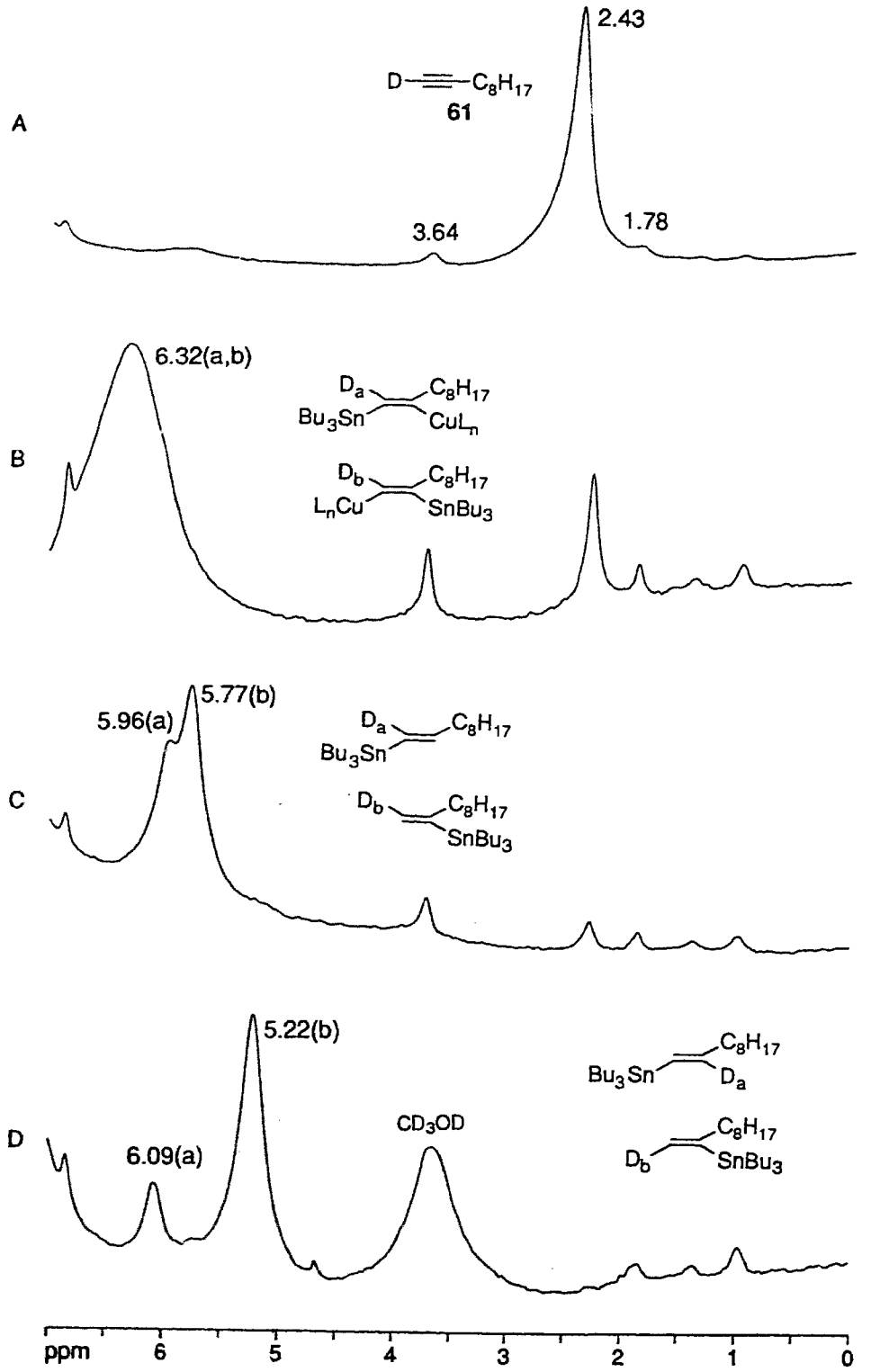
Corroborating evidence for the formation of vinyl cuprate intermediates was gained by monitoring the reactions of deuterated alkyne, **61**, with stannylcuprates, **64** and **65**, by ^2H NMR spectroscopy. In both solutions onset of addition to the triple bond was observed above -30 °C, evidenced by the disappearance of the sharp alkynyl ^2H signal at 2.43 ppm and formation of very broad signals centered at 6.54 and 6.32 ppm, respectively (spectrum B, Figures II.1 and II.2). The fact that only a single signal was observed instead of two (one

Figure II.1 ^{2}H NMR Spectra of Addition of *n*-$Bu_3SnCu(CN)Li{\cdot}2LiCl$ (**64**) to [1-^{2}H]-1-Decyne (**61**).[a]



(a) Spectra recorded at -35 °C; (A) **64** + **61** + MeOH, THF, -78 °C; (B) **64** + **61**, THF, -30 °C→0 °C; (C) **64** + **61**, THF, -30 °C → 0 °C → -35 °C, MeOH.

Figure II.2 ^2H NMR Spectra of Addition of $(n\text{-}Bu_3Sn)_2Cu(CN)Li_2$ (**65**) to [1-^2H]-1-Decyne (**61**) and 1-Decyne.[a]



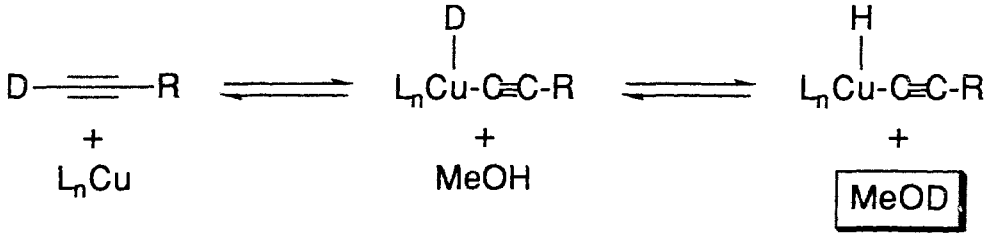
(a) Spectra recorded at -35 °C; (A) **65** + **61** + MeOH, THF, -78 °C; (B) **65** + **61**, THF, -30 °C→0 °C; (C) **65** + **61**, THF, -30 °C → 0 °C → -35 °C, MeOH; (D) **65** + 1-decyne, THF, -30 °C → 0 °C, CD_3OD.

for each vinyl cuprate regioisomer) is attributed to quadrupolar broadening due to ^{63}Cu, ^{65}Cu and ^{2}H nuclei. Presumably, quadrupolar coupling to copper causes already overlapping deuterium signals to merge into a single broad peak. Hydrolysis of these solutions with methanol resulted in the disappearance of the broad signal and the formation of two new upfield peaks at 5.94, 5.75 ppm and 5.96, 5.77 ppm, respectively, attributed to the corresponding vinylstannanes (spectrum C, Figures II.1 and II.2).

Additional support for the formation of the putative vinyl cuprate intermediates was obtained from ^{2}H NMR analysis of the related vinyl cuprate species, **66**, (Scheme II.2). The ^{2}H NMR spectrum of this solution exhibited a well defined signal at 5.72 ppm, which is comparable to the chemical shifts observed for the presumptive deuterated vinyl cuprate intermediates. A comparatively narrow peak was observed in this case and can explained by stereospecific formation of **66**, giving rise to a single isomeric species. The ^{2}H NMR spectrum of a quenched (CD_3OD) solution of stannylcuprate, **65**, and 1-decyne, exhibited two new signals at 6.09 and 5.22 ppm attributed to the formation of vinylstannanes in which deuterium is *cis* to the tri-*n*-butylstannyl moiety (spectrum D, Figure II.2). This set of isomers differs from products obtained in stannylcupration of alkyne, **61**, in which deuterium is cis to the alkyl group (spectrum C, Figure II.2). The ^{2}H NMR spectra of solutions stannylcuprate reagent, **64** or **65**, alkyne, **61**, and methanol also exhibited a new signal at 3.64 ppm. Based on the similar chemical shift of CD_3OD, this new peak is attributed to the formation of CH_3OD, possibly *via* C-D activation of the alkynyl deuterium followed by hydrogen-deuterium exchange (Scheme II.3). The fact that spectra C and D (Figure II.2) do not share common vinyl deuterium signals indicates that *E* to *Z* interconversion is negligible under these reaction

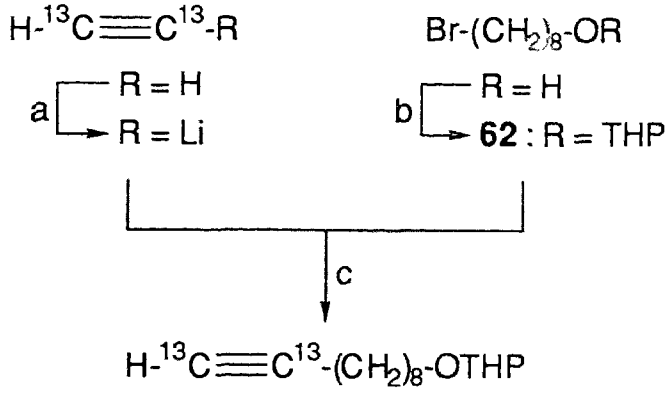
conditions. These observations lend credence to the notion that addition of stannylcuprate reagents to triple bonds occurs in a syn fashion to yield stereodefined vinyl adducts.

Scheme II.3 Formation of MeOD in Stannylcupration of [1-^{2}H]-1-Decyne (**61**).



Encouraged by results obtained in ^{2}H NMR experiments, it was decided to repeat earlier ^{13}C NMR investigations but with ^{13}C enriched alkyne. Preparation of alkyne, **63**, labelled at C_1 and C_2 with ^{13}C was readily accomplished treating the monoacetylide of ^{13}C enriched acetylene with alkyl bromide, **62** (Scheme II.4). Incorporation of an OTHP group facilitated isolation and purification. The ^{13}C NMR spectrum of the reaction of stannylcuprate, **65**, with alkyne, **63**, revealed that the starting alkyne is consumed and four new downfield doublets appear. More significant, however, is the observation that two of these signals display ^{117}Sn and ^{119}Sn satellites, indicating that tin is bonded directly to carbon (spectrum B, Figure II.3). This observation in addition to the fact that the other two signals do not exhibit one bond tin coupling provides compelling evidence for the formation of two regioisomeric vinyl adducts containing a vinyl carbon-tin and, presumably, a vinyl carbon-copper bond. The signals centered at δ 170.8 (d, $^1J_{C\text{-}C}$ = 40.1 Hz) and 159.0 (d, $^1J_{C\text{-}C}$ = 40.1 Hz; $^1J^{119}_{Sn\text{-}C}$ = 560.9 Hz; $^1J^{117}_{Sn\text{-}C}$ = 544.2 Hz) are attributed to the major

Scheme II.4 Synthesis of (1,2-^{13}C)-10-Tetrahydropyranyloxy-1-decyne (**63**).[a]



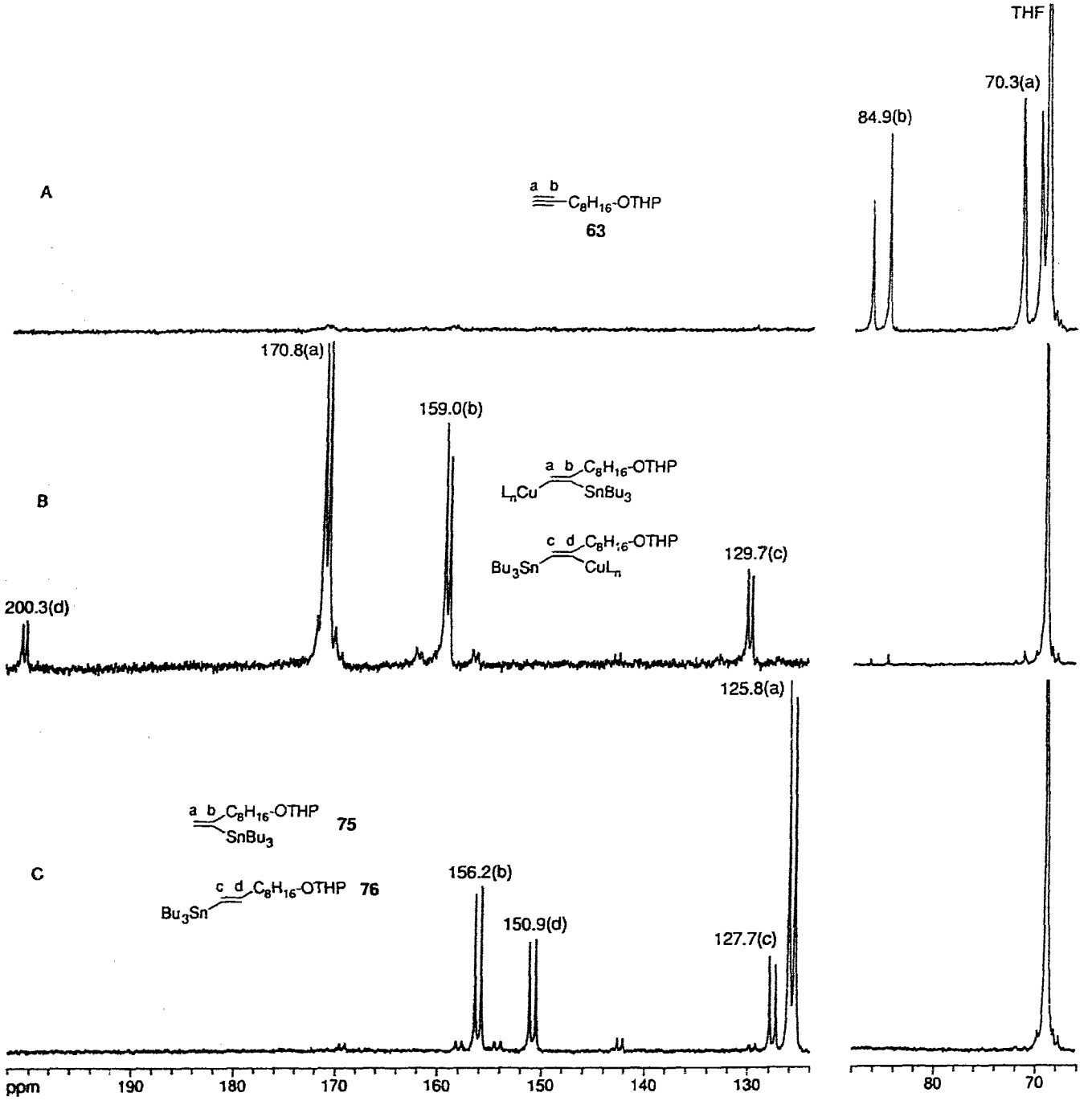
63

(a) *n*-BuLi, THF, -78 °C/30 min; (b) Dihydropyran (2 equiv), CH_2Cl_2, r.t./45 min, 86 %; (c) **62**, THF/HMPA (5:1), -78 °C → r.t. over 12 hr, 76 %.

isomer and those at δ 200.3 (d, $^1J_{C\text{-}C}$ = 50.3 Hz) and 129.7 (d, $^1J_{C\text{-}C}$ = 50.3 Hz, $^1J^{119}_{Sn\text{-}C}$ = 473.4 Hz, $^1J^{117}_{Sn\text{-}C}$ = 435.6 Hz) to the minor one.[52] Addition of methanol to this solution resulted in the immediate formation of two new sets of doublets centered at 156.2, 125.8 ppm and 150.9,127.7 ppm assigned to vinylstannanes, **68** and **69**, respectively (spectrum C, Figure II.3). The most dramatic upfield shift was observed for carbon signals at 200.3 and 170.3 ppm. Such a shift is consistent with the hydrolysis of a vinyl carbon-copper bond in which the strongly deshielding metal is replaced by hydrogen. On the other hand, chemical shift differences between carbon atoms attached to tin in quenched and unquenched solutions are comparatively small, suggesting that formation of the vinyl carbon-tin bond is essentially complete in the stannylcuprate adduct.

While vinylstannanes were formed immediately upon quenching solutions of stannylcuprates, **64** or **65**, and alkynes with methanol above -30 °C, no products were detected when methanol was added to these

Figure II.3 ^{13}C NMR Spectra of Addition of (n-$Bu_3Sn)_2Cu(CN)Li_2$ (**65**) to [1,2-^{13}C]-10-Tetrahydropyranyloxy-1-decyne (**63**).[a]

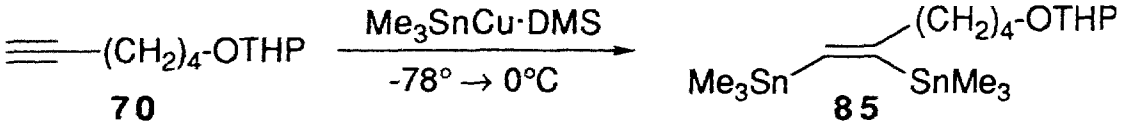


(a) Spectra recorded at -20 °C; (A) **65** + **63** + MeOH, THF, -78 °C, spectrum recorded at -35 °C; (B) **65** + **63**, THF, -30 °C→0 °C; (C) **65** + **63**, THF, -30 °C → 0 °C → -20 °C, MeOH.

solutions maintained between -78 °C and -35 °C (spectrum A, Figures II.1, II.2 and II.3). Solutions in which stannylcuprates had already reacted with the alkyne (T > -30 °C) could, however, be readily hydrolyzed to products at temperatures *below* -30 °C. When the temperature of solutions containing stannylcuprate, unreacted alkyne and methanol were raised above -30 °C, the only signals observed were due to products. These observations are in agreement with a two-step process in which vinyl cuprate intermediates are initially formed in a slow step and then are rapidly hydrolyzed to vinylstannane products.

It is interesting to note that starting alkynes were almost completely consumed by the stannylcuprate reagents chosen for investigation, suggesting a strong thermodynamic preference for formation of vinyl adducts. This observation is in contrast with arguments advanced by Piers *et al.* regarding equilibria in these reactions.[31j] Poor yields obtained in stannylcupration of 1-alkynes were attributed to alkyne-adduct equilibria in which vinylcopper intermediates were only marginally favoured. In light of the observations detailed above, it was reasoned that Piers' results might alternatively be explained by sluggish formation of vinyl adducts under the reaction conditions employed (-78 °C). To distinguish between these possibilities, stannylcupration of alkyne, **70**, was repeated following Piers' procedure with the exception that the solution was allowed to warm to 0 °C prior to quenching with aqueous ammonium chloride. However, the major product formed in this reaction was distannane, **85**, and therefore no definite conclusions could be drawn from this experiment (Scheme II.5). The fact that the alkyne was largely consumed does, however, support the view that vinyl adducts are thermodynamically preferred over starting materials.

Scheme II.5 Stannylcupration of 1-Alkyne **70**



70 **85**

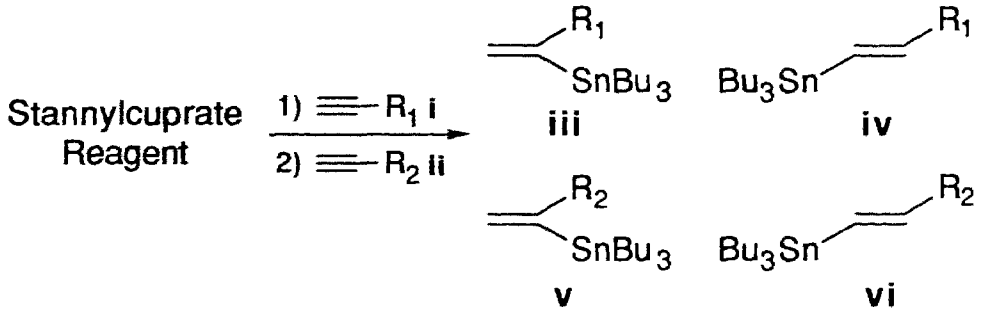
It is likely that the apparent discrepancies between the present spectroscopic studies and Piers' obsevations are due to the fact that stannylcuprates employed in these investigations were not the same. Examination of stannylcupration of 1-alkynes using CuBr·DMS derived tin-copper reagents by NMR spectroscopy would help clarify this question. It should also be mentioned that the rates of these bimolecular reactions are likely concentration dependent. Solutions of stannylcuprates used in spectroscopic studies were 10 -20 times more dilute (ca. 0.05 M) than those employed in chemical investigations and might explain differences in reactivity between stannylcuprate reagents. Establishing the kinetics of these reactions would be useful in gaining further insight into the intermediates and the mechanisms of these processes and would allow optimization of reaction conditions. This information could be readily obtained by measuring the rate of adduct formation (in stannylcupration of 1-alkynes) using NMR spectroscopy.

II.3 Crossover Experiments.[49]

Having provided strong evidence for the formation of vinyl cuprate intermediates in stannylcupration of 1-alkynes, the existence of an alkyne-adduct equilibrium (Scheme B.3) was examined next. Although ^{2}H and ^{13}C NMR experiments indicated a strong thermodynamic preference for adduct formation, the possibility of an alkyne-adduct equilibrium could not be ruled out

a priori. It was reasoned that evidence for this process might be gained by intercepting recombination of starting materials with a structurally similar alkyne. In this scenario, the continuously regenerated stannylcuprate reagent would react indiscriminately with either of the alkynes in solution to form the corresponding adducts which, upon hydrolysis, would yield products derived from both substrates.

Table II.1 Crossover Experiments with (n-Bu_3Sn)Cu(CN)Li·2LiCl (**64**) and (n-Bu_3Sn)$_2$Cu(CN)Li_2 (**65**).



Entry	Reagent	Reaction Conditions	Substrates i : ii (%)[a]	Products iii : iv : v : vi (%)[b]
1	**64**[c]	A	48 : 52 (68)	27:24:26:23 (58)
2		B	26 : 74 (69)	61:28:9:2 (60)
3	**65**[d]	A[e]	23 : 77 (57)	10:85:1:4 (81)
4		C	39 : 61 (53)	31:27:17:25 (82)

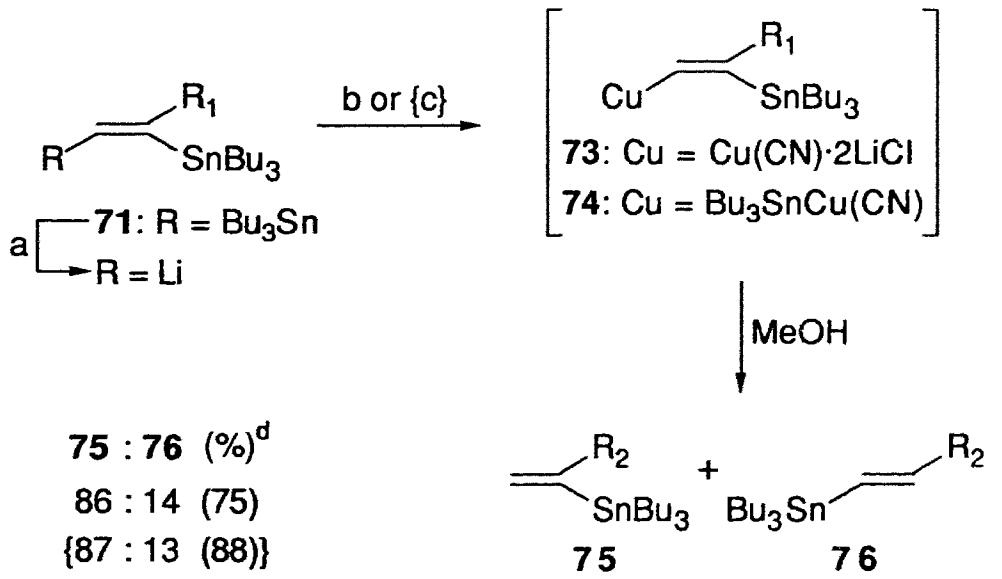
Reactions conducted in THF: (A) **i** (1 equiv), 0 °C/1.5 hr then **ii** (1 equiv), 0 °C/1.5 hr, $NH_4Cl_{(aq)}$; (B) **i** (1 equiv), 0 °C/1.5 hr then **ii** (1 equiv), -78 °C/1.5 hr, $NH_4Cl_{(aq)}$; (C) **i** (2 equiv), 0 °C/1.5 hr then **ii** (2 equiv), r.t./12 hr, MeOH; (a) Percent recovery. Based on sum of starting materials; (b) Isolated yields. Based on available n-Bu_3Sn; (c) **i** = **55**, R_1 = $(CH_2)_8$-OTHP, **ii** = **39**, R_2 = $(CH_2)_7$-OTHP; (d) **i** = **55**, R_1 = $(CH_2)_8$-OTHP, **ii** = **70**, R_2 = $(CH_2)_4$-OTHP; (e) 2 equiv of **i** and **ii**.

Addition of alkyne, **ii**, to a solution of adducts formed in the reaction of stannylcuprate, **64**, and alkyne, **i**, gave, after work up, a 27.24:26:23 mixture of products **iii**, **iv**, **v** and **vi** in 58 % yield. In addition, 68 % of starting alkynes, **ii** and **i**, (48:52) were recovered (Table II.1, entry 1). These results clearly demonstrate the reversibility of this reaction. Not surprisingly, it was noted that this process was temperature dependent. In a crossover experiment similar to the one described above, a solution of stannylcuprate, **64**, and alkyne, **i**, was cooled to -78 °C, then alkyne, **ii**, added. Rapid quenching of this mixture yielded only 11 % of crossover product (Table II.1, entry 2). These observations are consistent with evidence obtained from NMR studies that adduct formation is negligible at temperatures below -35 °C. The fact that some (11 %) crossover product was formed is possibly due to brief warming during the quenching procedure. It should, however, be pointed out that these reactions were conducted at highly dilute concentrations (ca. 0.05 M). Since stannylcupration of 1-alkynes is a bimolecular process, low concentrations of reactants is likely to be the main reason for sluggish reactions under these conditions.

Reversible processes in reactions involving stannylcuprate **65** were found to be less facile. Addition of alkyne, **ii**,[53] to a solution of stannylcuprate, **65**, and alkyne, **i**, under the conditions employed in crossover studies of stannylcuprate, **64**, afforded a 10:85:1:4 (as determined by GC) mixture of products **iii**, **iv**, **v** and **vi** in 81 % yield. The small extent of crossover was also reflected by the amount of unreacted alkyne, **ii**, that made up 77 % of total starting materials recovered (Table II.1, entry 3). Contrary to crossover experiments involving **64**, formation of crossover products in solutions of **65** required prolonged reaction times at higher temperature (Table II.1, entry 4).

To unequivocally establish that stannylcupration of 1-alkynes is reversible under these conditions, vinyl adducts generated in these reactions were prepared by alternative routes and subjected to usual crossover reaction conditions. Preparation of vinyl adducts, **73** and **74**, was accomplished by treating distannane, **71**, with *n*-BuLi followed by reaction with CuCN·2LiCl or *n*-$Bu_3SnCu(CN)Li$. Quenching solutions of these species, maintained at temperatures below -30 °C, afforded a mixture of vinylstannanes, **75** and **76**, in which the former predominated (> 85 %) (Scheme II.6).

Scheme II.6 Preparation and Proton Capture of Vinyl Cuprate Intermediates **73** and **74**.

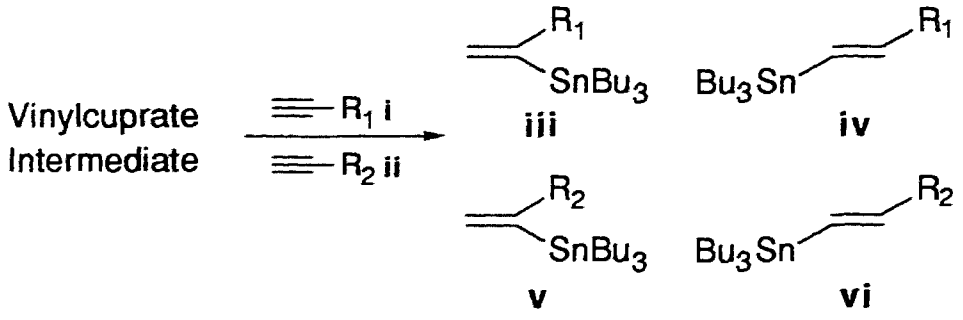


Reactions conducted in THF: (a) *n*-BuLi, -78 °C → -30 °C over 1 hr; (b) CuCN·2LiCl, -30 °C/1 hr; (c) *n*-$Bu_3SnCu(CN)Li$ (**72**), -30 °C/1 hr; (d) Isolated yields. Based on distannane **71**; $R_1 = (CH_2)_8$-OTHP.

Formation of approximately 15 % of **76** is unlikely to be the result of isomerization in either adduct, **73** or **74**, since this process has been

demonstrated to be exceedingly slow at these temperatures (see above). Rather, formation of **76** likely has its origin in the initial reaction of **71** with *n*-BuLi in which a certain amount of the sterically more congested internal tri-*n*-butyl tin moiety reacts to form the corresponding vinyl anion. Stirring a solution of alkyne, **70**, and vinyl cuprate, **73**, at 0 °C for 1.5 hours gave, after

Table II.2 Crossover Experiments with Vinyl Cuprate Intermediates **73** and **74**.



Entry	Vinyl Cuprate	Reaction Conditions	Substrates i : ii (%)[a]	Products iii : iv : v : vi (%)[b]
1	**73**[c]	A	47 : 53 (65)	33:19:27:21 (59)
2	**74**[d]	B	40 : 60 (53)	38:24:14:24 (93)

Reactions conducted in THF: (A) **ii** (1 equiv), 0 °C/1.5 hr, $NH_4Cl_{(aq)}$; (B) **i** (1 equiv), r.t./30 min then **ii** (2 equiv), r.t./12 hr, MeOH; (a) Percent recovery. Based on sum of starting materials; (b) Isolated yields. Based on available *n*-Bu_3Sn; (c) **i** = **55**, R_1 = $(CH_2)_8$-OTHP, **ii** = **39**, R_2 = $(CH_2)_7$-OTHP; (d) **i** = **55**, R_1 = $(CH_2)_8$-OTHP, **ii** = **70**, R_2 = $(CH_2)_4$-OTHP.

work-up and purification, a 33:19:27:21 mixture of products **iii**, **iv**, **v** and **vi** in 59 % yield. Alkynes, **i** and **ii**, (47:53) were recovered in 65 % yield from this reaction (Table II.2, entry 1). Similar results were obtained in the reaction of vinyl cuprate, **74**, and alkyne, **ii**, after stirring at room temperature for 12 hours

(Table II.2, entry 2). These results closely parallel those obtained earlier in related crossover experiments (Table II.1, entries 1 and 4) and together provide strong evidence for the reversible formation of vinyl adducts in stannylcupration of 1-alkynes.

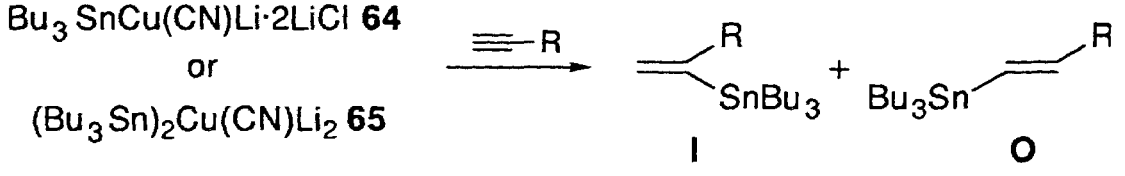
II.4 Chemical Investigations of Stannylcupration of 1-Alkynes.

It was recognized that higher efficiency and better control of regioselectivity in stannylcupration of 1-alkynes would greatly enhance the synthetic utility of these reactions. Since factors governing the yield and regiochemical outcome of these reactions were poorly understood, the effects of reagent, temperature and solvent were examined in a systematic study. As anticipated, rapid quenching of solutions of stannylcuprates, **64** or **65**, and alkyne, **70**, maintained at -78 °C, yielded largely unreacted starting material and very little products (Table II.3, entries 1 and 5). These observations are in agreement with sluggish formation of vinyl adducts at low temperatures (see above). Addition of methanol to these solutions at -78 °C followed by warming to room temperature gave vinylstannanes in good yields. Under these conditions the 2-stannyl alkene predominated (ca. 90 %) over the 1-stannyl isomer (Table II.3, entries 2 and 6).

Based on the rationale described above for preferential alkylation at the internal alkynyl carbon in carbocupration of 1-alkynes, it seemed logical that similar electronic factors were also prevalent in related stannylcupration reactions. According to this postulate, bond formation between copper and C_1, and tin and C_2 might be expected to occur selectively, owing to mutual attraction of oppositely polarized atoms (Figure II.4). It was therefore rationalized that the presence of methanol in these solutions permitted proton

capture of the kinetic adduct, giving rise to a predominance of the 2-trialkylstannyl isomer.

Table II.3 Variation of Reagent and Temperature in Stannylcupration of 1-Alkynes **55** and **70**.



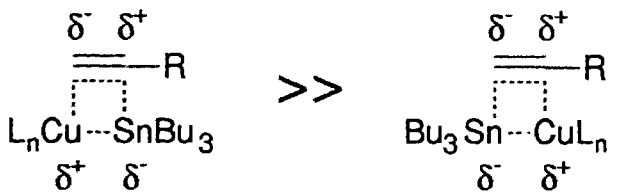
Entry	Reagent	Reaction Conditions	I : O	Yield %[a]
1	**64**	A	90 : 10	5 (81)[b]
2		B	89 : 11	61
3		C	61 : 39	62
4		D	54 : 46	66
5	**65**	A	33 : 67	8 (78)[b]
6		B	91 : 9	85
7		C	15 : 85	90
8		E	56 : 44	80

Reactions conducted in THF: (A) **70**, -78 °C/1 hr, $NH_4Cl_{(aq)}$; (B) **55**, MeOH, -78 °C → 0 °C over 12 hr; (C) **70**, -30 °C → 0 °C over 1 hr, MeOH; (D) **55**, -30 °C, 0 °C/12 hr; (E) **70**, -30 °C, r.t./12 hr; (a) Isolated yields; (b) Recovered **70**.

Stirring solutions for extended periods at elevated temperatures yielded nearly equimolar amounts of product isomers, suggesting that isomerization had occurred (Table II.3, entries 4 and 8). Isomerization in adducts derived from stannylcuprate, **64**, is particularly facile as evidenced by a marked decrease in

regioselectivity when solutions were stirred between -30 °C and 0 °C for a relatively short period (Table II.3, entry 3). It was noted that yields and regioselectivity varied in reactions of the lower order stannylcuprate, **64**, with 1-alkynes and is thought to be a consequence of the heterogeneous nature of these solutions (compare Table II.3, entry 3 and Table II.5, entry 1).

Figure II.4 Electronic Factors Governing the Mode of Addition in Stannylcupration of 1-Alkynes.

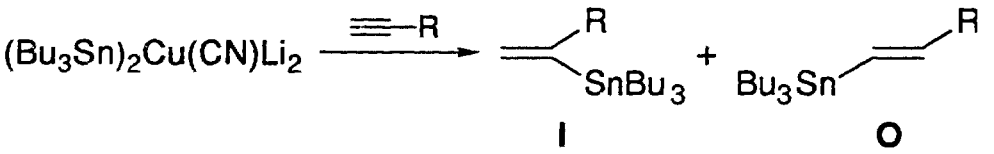


Quenching a solution of stannylcuprate, **65**, and alkyne, **70**, at 0 °C yielded a mixture of products enriched (85 %) in the 1-stannyl alkene (Table II.3, entry 7). This result deviated from the trend observed in these reactions in which formation of 2-stannyl alkenes was favoured. A plausible explanation for this observation was that rapid isomerization prior to hydrolysis yielded the thermodynamically favoured 1-stannyl isomer. This possibility, however, was discounted by later experiments which revealed that approximately equal amounts of both isomers were formed upon stirring solutions of **65** and 1-alkynes at room temperature for extended reaction times (Table II.3, entry 8). Since these conflicting results could not be readily explained by kinetic or thermodynamic arguments, an alternative rationale was considered. Spectroscopic and mechanistic investigations of alkyl and arylcuprates have shown these organocuprates to exist in solution as equilibrium mixtures of various species.[32,33] It was therefore speculated that addition of methanol to

solutions containing stannylcuprate, **65**, and 1-alkyne might result in the formation of a different cuprate species that yielded 2-stannyl alkenes selectively.

The influence of methanol as a co-solvent on the regiochemical outcome in stannylcupration of 1-alkynes prompted further investigation of solvent effects

Table II.4 Variation of Solvent and Temperature in Stannylcupration of 1- Alkynes.



I **O**

Entry	Solvent	Reaction Conditions	I : O	Yield %[a]
1	DMF	A	90 : 10	86
2		B	70 : 30	85
3	DMS	A	91 : 9	81
4		B	54 : 46	83
5	DIGLYME	A	83 : 17	86
6		B	79 : 21	78
7	THF	A[b]	91 : 9	85
8		B	15 : 85	90
9	HMPA	C	26 : 74	54

(A) **70**, MeOH, -50 °C → r.t. over 12 hr; (B) **70**, -30 °C → 0 °C over 1 hr, MeOH; (C) **70**, -10 °C → 0 °C over 1 hr, MeOH; (a) Isolated yields; R = $(CH_2)_4$-OTHP; (b) Alkyne **55** added at -78 °C, R = $(CH_2)_8$-OTHP.

on these reactions. Studies were limited to polar solvents since stannylcuprate, **65**, was found to be insoluble in apolar liquids. Addition of methanol to cooled (-78 °C) solutions of **65** and alkyne, **70**, in DMF, DMS, DIGLYME and THF gave predominantly 2-stannyl alkenes upon warming to 0 °C (Table II.4, entries 1,3,5 and 7). Formation of the 2-stannyl isomer was also favoured when MeOH was added after solutions (DMF, DMS and DIGLYME) were warmed to 0 °C, suggesting that under these conditions formation of 2-stannyl alkenes is kinetically preferred (Table II.4, entries 2,4 and 6). In contrast, addition of MeOH at 0 °C to similar reactions conducted in THF and HMPA yielded a mixture of vinylstannanes in which the 1-stannyl isomer predominated (Table II.4, entries 8 and 9). These results demonstrate that regioselective formation of 1-stannyl or 2-stannyl alkenes can be achieved by variation of solvent in stannylcupration of 1-alkynes. These observations also suggest that solvents affect the regiochemical outcome of these reactions by altering the nature of the stannylcuprate reagent.

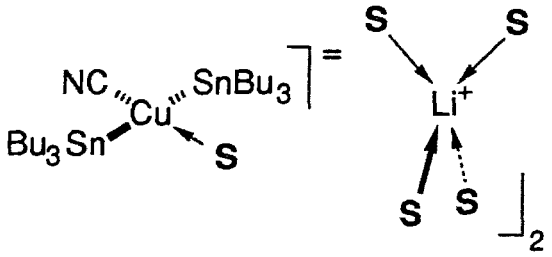
Figure II.5 Steric Factors Governing the Mode of Addition in Stannylcupration of 1-Alkynes.

For species in which Bu_3Sn is bulkier than CuL_n

Preferential formation of 1-stannyl alkenes in stannylcupration of 1-alkynes points to the possible involvement of steric factors that oppose and are greater than electronic effects. Stannylcuprates containing a copper moiety that is sterically less demanding than the bulky tri-*n*-butyl tin group might be

expected to yield adducts in which steric interactions between tri-*n*-butyl tin and the acetylenic side chain are minimized (Figure II.5). Formation of such monomeric species might be favoured in the presence of strong coordinating solvents such as THF and HMPA (Figure II.6).

Figure II.6 Solvation of Monomeric Stannylcuprate Species.

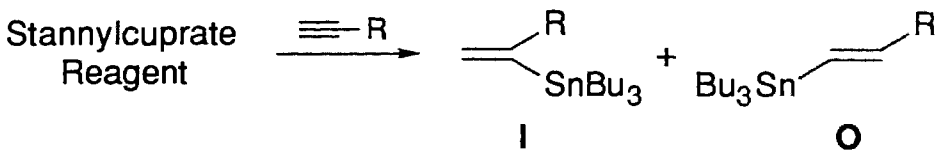


S = Solvent

Based on the above it appeared that the composition of stannylcuprate species was a decisive factor in determining the regiochemical outcome in stannylcupration of 1-alkynes. In an attempt to provide further chemical evidence for this hypothesis, reactions were conducted in solutions comprised of different tin:copper ratios. Solutions containing a 1:1 mixture of tri-*n*-butyl tin anion and CuCN were red and heterogeneous in appearance and afforded mainly 2-stannyl alkene. The relatively poor yield obtained in this reaction is presumably due to formation of insoluble and less reactive aggregates at the expense of the active reagent (Table II.5, entry 1). Interestingly, addition of one half of an equivalent of tin anion to this mixture caused the slurry to become homogeneous. Although no significant change in regioselectivity was noted, the product yield was appreciably higher. Apparently, reaction of added tin anion with the insoluble material generates a solution consisting of soluble stannylcuprate species, thereby increasing the "availability" of reagent in these

solutions (Table II.5, entry 2). At ratios of tin anion to CuCN of two and above, formation of primarily 1-stannyl alkene was observed (Table II.5, entries 3 and 4). It was reasoned that the regioselectivity might be improved by forcing the

Table II.5 Variation of Sn : Cu Ratios in Stannylcupration of 1-Alkyne **70**.[a]



Entry	Bu_3SnLi : CuCN	Appearance of Solution	I : O	Yield %[b]
1	1 : 1	Red, Heterogeneous	75 : 25	56[c]
2	1.5 : 1	Orange, Homogeneous	84 : 16	79
3	2 : 1	Yellow, Homogeneous	15 : 85	90
4	8 : 1	Yellow, Homogeneous	19 : 81	67

(a) Reaction conditions: **70**, THF, -30 °C → 0 °C over 1hr, MeOH; (b) Isolated yields; R = $(CH_2)_4$-OTHP; (c) R = $(CH_2)_8$-OTHP

equilibrium toward the reagent responsible for formation of this isomer. However, solutions containing still higher ratios of tin anion to CuCN did not provide enhanced regioselectivity and gave lower product yields.

II.5 Spectroscopic Investigations of Solutions of $Me_3SnCu(CN)Li$ (100) and $(Me_3Sn)_2Cu(CN)Li_2$ (81).

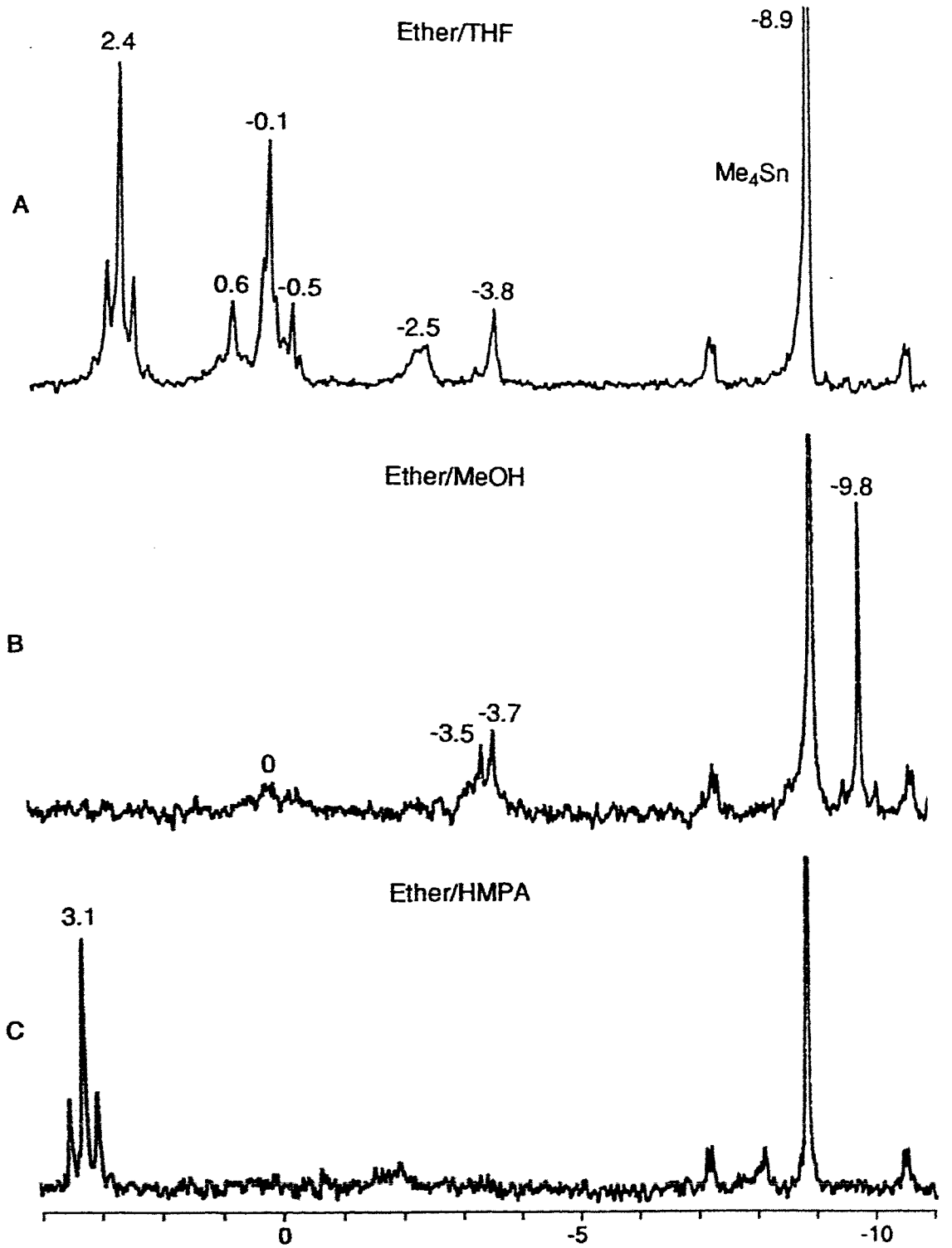
Supporting evidence for the solvent dependent formation of different stannylcuprate species was gained from ^{13}C NMR studies of $(Me_3Sn)_2Cu(CN)Li_2$ (**81**) in various solvents. The ^{13}C NMR spectrum of a solution of **81** in diethyl ether/THF exhibited a number of complex signals

centered at 2.4, 0.6, -0.1, -0.5, -2.5 and -3.8 ppm presumably due to several different stannylcuprate species. The spectrum also displayed a sharp signal at -8.9 ppm assigned to Me_4Sn, generated as a byproduct in this reaction (Figure II.7, spectrum A). In the presence of methanol the ^{13}C NMR spectrum of this solution changed dramatically and exhibited three broad signals centered at 0, -3.5 and -3.7 ppm in addition to a sharp peak at -9.8 ppm (Figure III.7, spectrum B). In contrast to the above solutions, the ^{13}C NMR spectrum of a solution of **81** in ether/HMPA was comparatively simple and displayed a single multiplet (tin-carbon coupling) centered at 3.1 ppm (Figure II.7, spectrum C). These experiments clearly indicate that solvents profoundly effect the solution composition of stannylcuprate species.

Having investigated solutions of stannylcuprate, **81**, in various solvents, the composition of higher order and lower order reagents in the *same* solvent was examined. The composition of stannylcuprates, **81** and **100**, has been previously investigated by ^{13}C NMR spectroscopy.[31l] The ^{13}C NMR spectra of these cuprates in THF exhibited different Me_3Sn signals, suggesting that higher order and lower order reagents were composed of different species. Corroborating evidence for these findings comes from IR and ^{13}C NMR investigations of the nitrile moiety in higher order and lower order cyanocuprates.

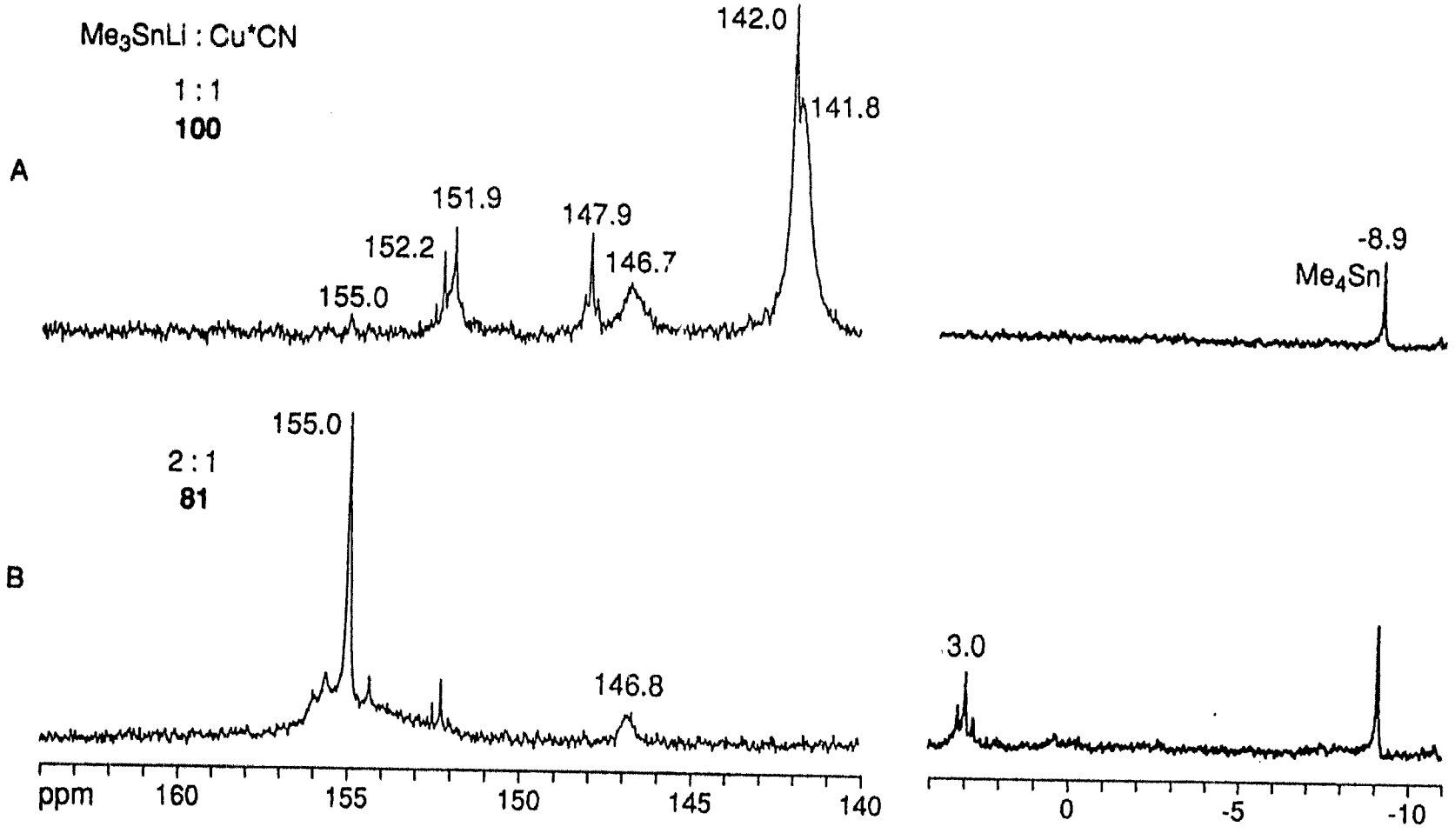
To circumvent extended ^{13}C NMR acquisition times typically required for unambiguous assignment of nitrile signals, reagents were prepared using ^{13}C enriched CuCN.[80] The difference in solution composition of stannylcuprates, **81** and **100**, immediately becomes apparent upon comparison of their ^{13}C NMR spectra (Figure II.8). The ^{13}C NMR spectrum of a solution (THF/HMPA) of

Figure II.7 ^{13}C NMR Spectra of Solutions of $(Me_3Sn)_2Cu(CN)Li_2$ (**81**) in Various Solvents.[a]



(a) Spectra recorded at -30 °C; (A) 0.3 M Ether/THF (1:4); (B) 0.2 M Ether/MeOH (3:2); (C) 0.2 M Ether/HMPA (3:2).

Figure II.8 ^{13}C NMR Spectra of Solutions of $(Me_3Sn)Cu(^*CN)Li$ (**100**) and $(Me_3Sn)_2Cu(^*CN)Li_2$ (**81**).[a]



(a) Spectra recorded at 0 °C. CuCN carbon > 99 % 13 C enriched; (A) 0.13 M THF/HMPA/ Ether (5:2:1; (B) 0.1 M THF/HMPA/Ether (6:2:2).

stannylcuprate, **81**, exhibited a strong signal at 155.0 ppm and a symmetrical multiplet centered at 3.0 ppm. The simplicity of this spectrum suggests the presence of a dominant stannylcuprate species in this solution. The ^{13}C NMR spectrum of **100**, on the other hand, was more complex and contained six major nitrile signals between 153 and 140 ppm. No distinct Me_3Sn peaks were observed which is likely due to signal averaging of equilibrating species. Further evidence for the different composition of solutions of **81** and **100** was gained from IR investigations. While the IR spectrum of a solution of **100** displayed a strong nitrile absorption at 2126 cm^{-1}, that of **81** exhibited a strong band at 2103 cm^{-1}. Several other less intense bands were also observed in the former spectrum which, together with ^{13}C NMR data, suggests that solutions of **81** are more complex than those containing **100**.

II.6 Summary and Conclusion.

^{13}C and ^{2}H NMR investigations of stannylcupration of 1-alkynes provide compelling evidence for the formation of vinyl adducts in these reactions. Monitoring these solutions from -78 °C to 0 °C revealed that onset of addition occurs at approximately -30 °C. It was further demonstrated that intermediates formed are thermodynamically preferred over starting materials. In a series of crossover experiments it was shown that addition of stannylcuprates to 1-alkynes is reversible and that these processes are more facile for *n*-$Bu_3SnCu(CN)Li$ (**64**) than (*n*-$Bu_3Sn)_2Cu(CN)Li_2$ (**65**). These observations can be explained by the relative stabilities of vinyl adducts formed from **64** and **65**. Equilibration between the less stable adduct derived from **64** and starting materials is likely to be energetically less demanding than the analogous process involving **65**. The fact that intermediates derived from lower order stannylcuprates, such as **64**, are more prone to thermal decomposition than their higher order counterparts, lends credence to this postulate.

Systematic variation of reagent, solvent, temperature and reaction time in stannylcupration of 1-alkynes led to the discovery that the regiochemical outcome in these reactions can be controlled by judicious choice of reaction conditions. Based on these studies it is proposed that variable regioselectivity in stannylcupration of 1-alkynes is due to formation of different stannylcuprate species in these solutions.

A protocol has been developed for stannylcupration of 1-alkynes resulting in the selective formation of 1-stannyl alkenes. It is thought that formation of a monomeric stannylcuprate reagent is critical to the regiochemical outcome of these reactions. In the envisioned process, steric repulsion between

the alkynyl side chain and the bulky tri-*n*-butyl tin moiety of the cuprate reagent is believed to guide addition of the tri-*n*-butyl tin group toward the terminal acetylenic carbon.

^{13}C NMR and IR spectroscopic investigations of solutions of **81** and **100** indicate that while solutions of the former reagent are comprised of a single dominant species, solutions of the latter variety are much more complex. These analyses are in agreement with previous studies[31l] that stannylcuprates of the type $(R_3Sn)_2Cu(CN)Li_2$ and $R_3SnCu(CN)Li$ are indeed different reagents.

CHAPTER III

III.1 Objective.

A serious drawback of homo higher order stannylcuprates, $(R_3Sn)_2Cu(CN)Li_2$, is the requirement of two equivalents of trialkyltin per reagent which is not only wasteful but also leads to excessive formation of tin byproducts that often complicate isolation and purification. A main goal of this project was to develop more efficient reagents and reaction conditions in which formation of undesirable tin byproducts was minimized, ideally without sacrifice in yield. In earlier work on alkylcuprates it had been demonstrated that alkyl ligands of such reagents, R_2CuLi, could be replaced by non-transferable groups (X) to afford mixed reagents, R(X)CuLi, that selectively delivered the alkyl moiety in reactions with organic substrates.[39b-43] Earlier work in this laboratory showed that this strategy could be extended to the preparation of mixed higher order stannylcuprates, $R_3Sn(X)Cu(CN)Li_2$, by substitution of a trialkyltin group in homo higher order reagents with an alkyl ligand.[31l] One goal of this study was to develop more efficient methods to prepare these mixed reagents.

A second objective of this project was to explore the effect of various non-transferable ligands of mixed stannylcuprate reagents on the regiochemistry in reactions with 1-alkynes. Development of new methods that improved regioselectivity in favour of formation of (*E*)-1-trialkylstannyl alkenes were investigated.

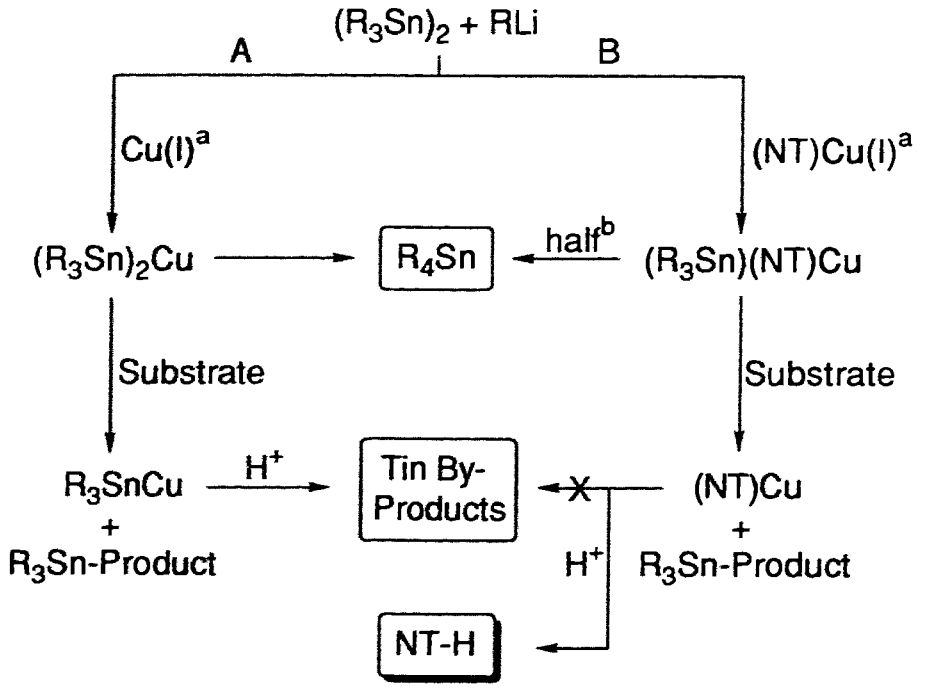
III.2 Investigations of Mixed H.O. Trialkylstannyl(alkyl)-cyanocuprates: $R_3Sn(R)Cu(CN)Li_2$.

During the evolution of trialkylstannylcuprate chemistry one aspect that has remained invariant has been their method of preparation. These cuprates have historically been synthesized by combination of trialkylstannyllithium reagents with cuprous salts.[29-31] In spite of the synthetic utility of this methodology, these reactions are beset with difficulties of product purification due to the formation tin byproducts. Trialkylstannyl anions are traditionally generated by cleavage of a hexaalkyldistannane with an alkyllithium giving rise to one equivalent of tetraalkyl tin in addition to R_3SnLi.[20] Alternatively, trialkylstannyl anions can be prepared by reaction of a trialkylstannyl hydride with LDA which avoids *in situ* generation of R_4Sn.[21] An additional complication stems from unconsumed trialkylstannyl anions (i.e., in $(R_3Sn)_2Cu(CN)Li_2$) that are converted to tin byproducts upon work-up. Unless the desired product contains a polar functional group, removal of tin impurities by column chromatography is virtually impossible.

A remedy to this type of problem was first reported by Fleming and Newton who found that the mixed cuprate, $PhMe_2Si(Me)Cu(CN)Li_2$, reacted with organic substrates by exclusive donation of the trialkylsilyl moiety. Substitution of a trialkyl silyl group in $(PhMe_2Si)_2Cu(CN)Li_2$ with a non-transferable methyl group served a dual purpose in that one equivalent of R_3SiLi was conserved and formation of disilane was reduced.[54] Lipshutz *et al.* has recently shown that a similar strategy can be applied in stannylcupration reactions using the related *n*-Bu_3Sn(*n*-Bu)$Cu(CN)L_2$ reagent.[55] It was demonstrated that this reagent selectively transferred a tri-*n*-butylstannyl group to organic substrates, leaving the hydrocarbon bonded to copper. The obvious

advantage of using such mixed cuprates is that the remaining alkyl ligand is eventually converted into an easily removable, volatile hydrocarbon (Scheme III.1).

Scheme III.1 General Strategy of Reducing Tin Byproducts in Stannylcupration Reactions using Non-Transferable (NT) Ligands.



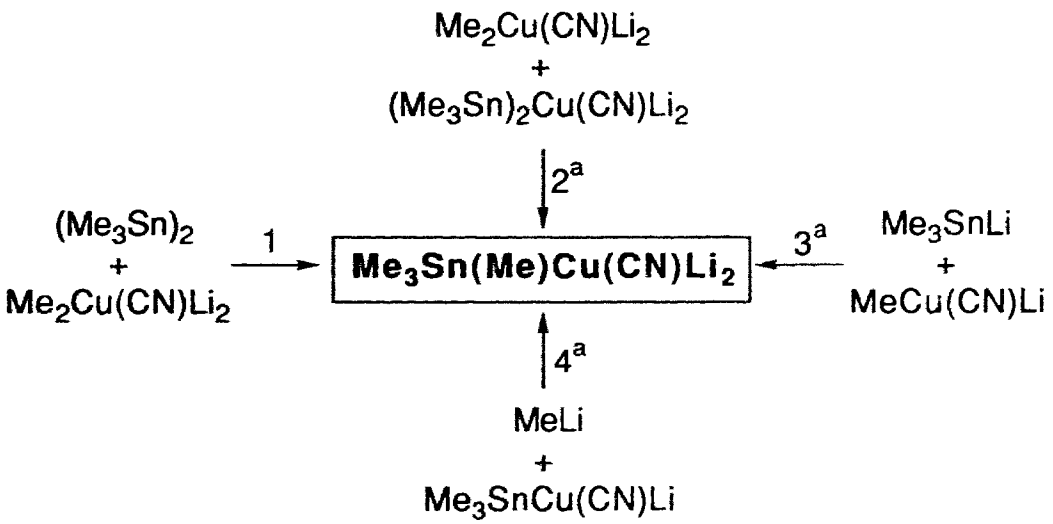
(a) Lithium cations and ligands associated with Cu omitted; (b) 1 equiv of R_4Sn per cuprate reagent produced in path B compared to 2 equiv in path A.

Since the reported method of preparation of *n*-Bu_3Sn(*n*-Bu)Cu(CN)Li_2 proceeds from reaction of *n*-$Bu_2Cu(CN)Li_2$ with two equivalents of *n*-Bu_3SnH, generating one equivalent of *n*-Bu_4Sn, this approach provides only a partial solution to the complications of product isolation. In principle, this problem could be circumvented by use of $Me_3Sn(Me)Cu(CN)Li_2$ (**86**) since in this scenario the low boiling Me_4Sn byproduct is easily removed by distillation. While it was recognized that **86** would provide definite advantages over previous cuprate

reagents, its preparation by the strategy outlined above did not seem practical due to the toxicity and volatility of trimethyltin hydride.[56]

It had been previously reported[31l] that solutions containing Me_3SnLi, MeLi and CuCN in a 1:1:1 ratio gave rise to the stannylcuprate reagent, **86**. Moreover, it was demonstrated by spectroscopic means that this mixed reagent could be prepared by any order of combination of the various starting materials (Scheme III.2, paths 2-4).[31l,57]. Based on the observation that cleavage of the tin-hydrogen bond in *n*-Bu_3SnH could be effected by *n*-$Bu_2Cu(CN)Li_2$, it was conjectured that methyl anions as part of a cuprate complex might also be sufficiently nucleophilic to cleave bis(trimethyltin). This process would generate stannylcuprate, **86**, in addition to Me_4Sn and provide a new and convenient route to the preparation of mixed trialkystannyl(alkyl)cyanocuprates (Scheme III.2, path 1).

Scheme III.2 Generation of $Me_3Sn(Me)Cu(CN)Li_2$ (**86**) *via* Different Routes.

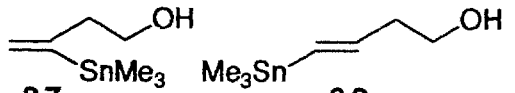
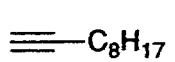
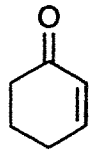
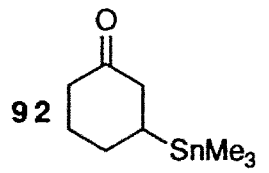
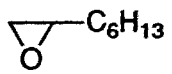
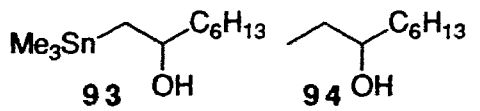
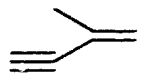
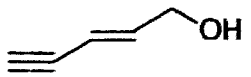
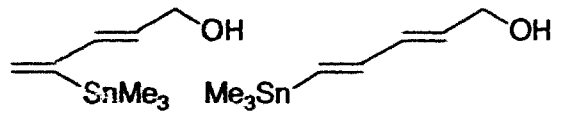
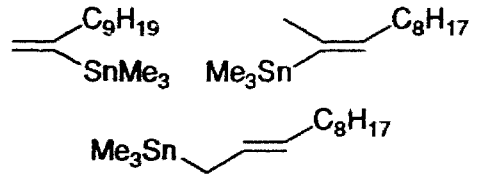


(a) Sharma, S. see references 31l and 57.

Indeed, reaction of $Me_2Cu(CN)Li_2$ with $(Me_3Sn)_2$ in THF yielded a species, presumed to be **86**, that incorporated Me_3Sn into a variety of organic substrates. This mixed reagent reacted with 1-decyne to afford the vinylstannanes, **89** and **90**, and yielded predominantly the 2-stannyl isomer (Table III.1, entry 2). Separation of these non-polar vinylstannanes from tin byproducts was accomplished by distillation under reduced pressure. Stannylcupration of homopropargyl alcohol yielded the regioisomeric allylic alcohols **87** and **88** in good yield (Table III.1, entry 1). Ratios of product isomers, however, were less predictable and varied considerably from one experiment to the other for no apparent reason. Nevertheless, reaction conditions were eventually found that consistently gave predominantly 1-stannyl alkene. Addition of **86** to vinyl acetylenes[58] yielded conjugated dienes of varying isomeric distribution; reaction with monosubstituted allenes[59] afforded vinyl and allylic stannanes in near equimolar amounts (Table III.1, entries 5-7). Delivery of the trimethyltin group to the α,β-unsaturated moiety of cyclohexenone was found to occur exclusively in a 1,4 sense and gave the cyclic ketone, **92**, stannylated at the 3 position (Table III.1, entry 3). This result was not unexpected, since reactions of organocuprates with enones generally occur *via* this mode of addition.[27,29]

Treatment of a terminal epoxide with **86** resulted in ring opening from the least congested side to yield the stannylated secondary alcohol, **93**. A poor (44 %) yield was obtained which was somewhat surprising since reactions of this type generally give high yields.[60] To verify this unusual result the experiment was repeated and again, **93** was formed in low yield (Table III.1, entry 4). This time, careful analysis of the reaction mixture revealed that in addition to **93**, secondary alcohol, **94**, was formed in a significant amount. This material

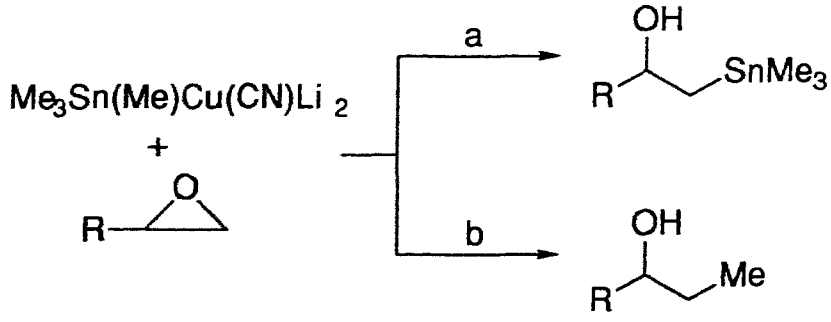
Table III.1 Addition of $Me_3Sn(Me)Cu(CN)Li_2$ (**86**) to Various Substrates.

Entry	Substrate	Products	Ratio[a]	Yield %[b]
1		 **87** **88**	3:97	77[c,d]
2		 **89** **90**	84:16	67[e]
3		 **92**		70[f]
4		 **93** **94**		38,30[g] (**93**,**94**)
5			25:75	69[h]
6			73:27	79[h]
7	CH_2=C=CH-C_8H_{17}		31:30:39	73[i]

(a) Product isomers characterized by ^1H NMR and MS. Ratios determined by GC; (b) Isolated yields; (c) Ratios and yields vary with reaction conditions; (d) THF, -78 °C → 0 °C over several hr; (e) THF, -30 °C → r.t. over 12 hr; (f) THF, -78 °C/30 min; (g) THF, -78 °C → r.t. over several hr; (h) Aksela, R. see ref. 58; (i) Singh, S. M. see ref. 59.

presumably escaped detection in earlier experiments due to its relatively low boiling point. Thus, low yields of **93** can be explained by a competing process in which the methyl group of the mixed reagent is transferred to the substrate (Scheme III.3, path b). Formation of appreciable quantities of alkylated product

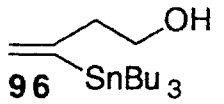
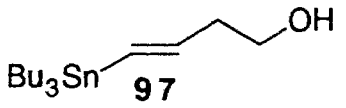
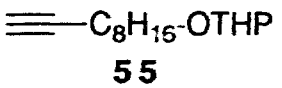
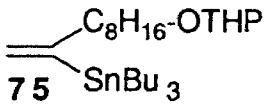
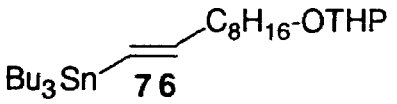
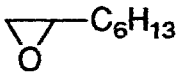
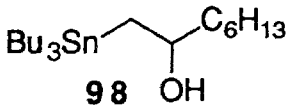
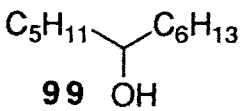
Scheme III.3 Non-selective Ligand Transfer in Reactions of $Me_3Sn(Me)Cu(CN)Li_2$ with Epoxides.



in this case is possibly due to favourable interactions between the "hard" alkyl group and the "hard" epoxide carbon.

Preparation of the mixed cuprate *n*-Bu_3Sn(*n*-Bu)$Cu(CN)Li_2$ (**95**) was accomplished following the same procedure described for the preparation of **86** and exemplified the generality of this method. Reaction of homopropargyl alcohol with **95** gave rise to vinylstannanes, **96** and **97**, in a 4:96 ratio (Table III.2, entry 1). Stannylcupration of 1-alkyne, **48**, afforded regioisomers, **75** and **76**, in approximately a 1:1 ratio (Table III.2, entry 2). This result contrasts with predominant formation of 2-stannyl alkene in stannylcupration of 1-decyne with **86** (Table III.1, entry 2). A possible explanation for the differences in regioselectivity between these related reactions is due to greater steric bulk of the tri-*n*-butyltin moiety, forcing addition of *n*-Bu_3Sn more toward the sterically

Table III.2 Addition of *n*-Bu_3Sn(*n*-Bu)Cu(CN)Li_2 (**95**) to Various Substrates.

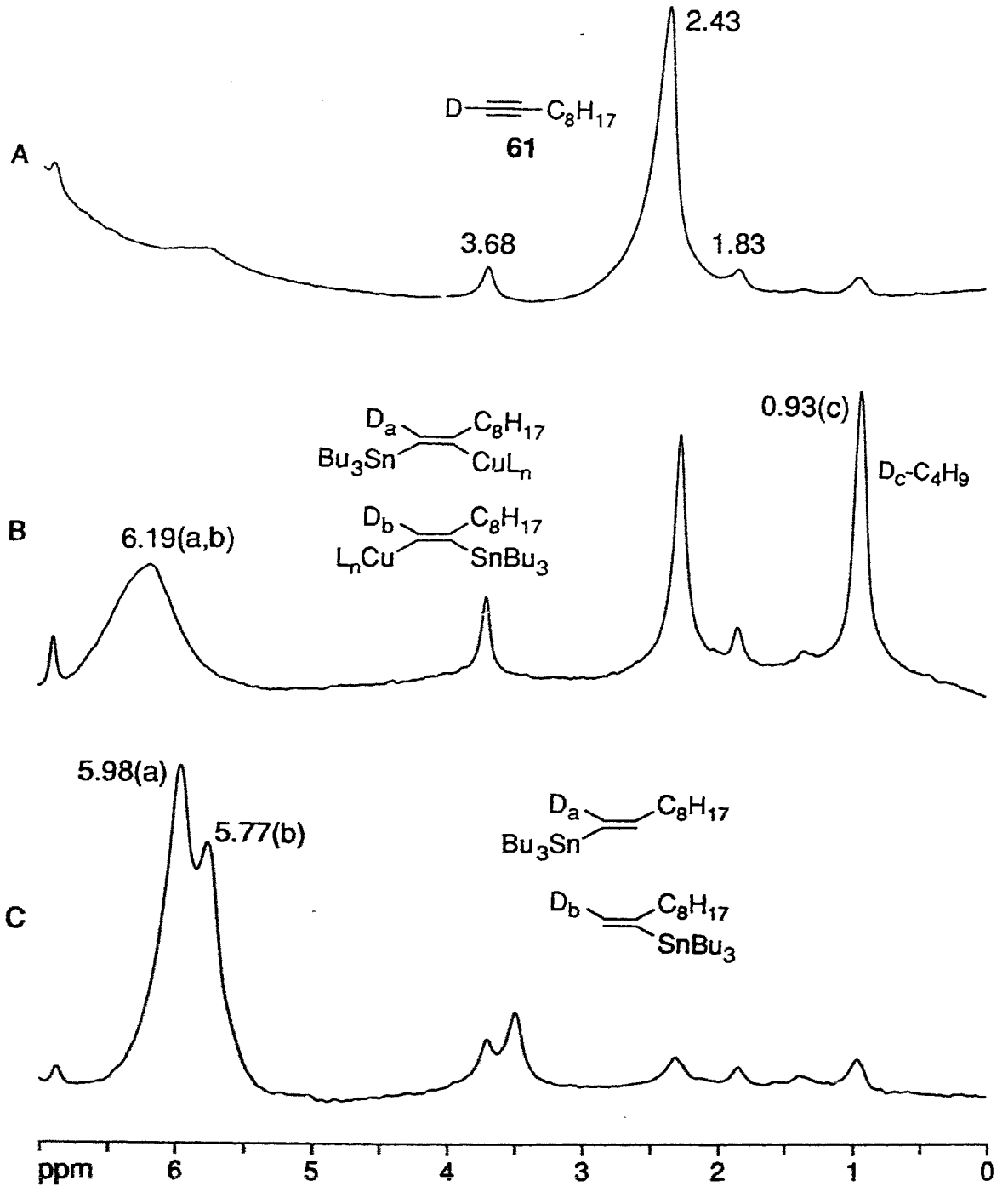
Entry	Substrate	Products	Ratio[a]	Yield %[b]
1		 **96**	4	84[c]
		 **97**	96	
2	 **55**	 **75**	55	57[d]
		 **76**	45	
3		 **98**		31[e]
		 **99**		29

(a) Product isomers characterized by ^1H NMR and MS. Ratios determined by GC; (b) Isolated yields; Reaction conditions: (c) THF, -78 °C → 0 °C over 1 hr; (d) THF, -30 °C → 0°C over 1 hr; (e) THF, -78 °C → r.t. over 12 hr.

least congested terminal carbon. Non-selective transfer of cuprate ligands in reactions of the mixed reagent, **86**, with epoxides was also observed for **95**. Treatment of a terminal epoxide with **95** gave rise to the corresponding stannylated and alkylated products, **98** and **99**, respectively (Table III.2, entry 3).

^2H NMR investigations of stannylcupration of deuterated alkyne, **61**, with **95** revealed[49] that these reactions closely parallel those involving lower order

Figure III.1 ^2H NMR Spectra of Addition of *n*-Bu_3Sn(*n*-Bu)Cu(CN)Li_2 (**95**) to [1-^2H]-1-Decyne (**61**).[a]



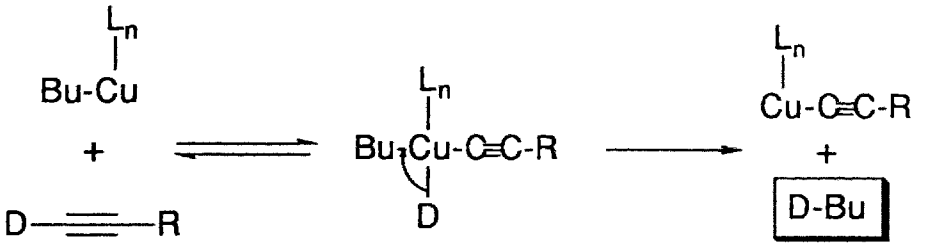
(a) Spectra recorded at -35 °C; (A) **95** + **61** + MeOH, THF, -78 °C; (B) **95** + **61**, THF, -35 °C→0 °C; (C) **95** + **61**, THF, -35 °C → 0 °C, MeOH.

(**64**) and higher order (**65**) reagents (see Chapter II). As in previous studies, no products were formed in solutions containing **95**, **61** and methanol, maintained at -78 °C (Figure III.1, spectrum A). Warming a mixture of the mixed reagent and **61** to 0 °C resulted in the disappearance of the peak at 2.43 ppm attributed to alkyne, **61**, and the emergence of a broad signal centered at 6.19 ppm (Figure III.1, spectrum B). It was assumed that this signal was comprised of two overlapping peaks of two regioisomeric adducts as observed in earlier experiments (Figures II.1 and II.2, spectrum 3). Addition of methanol to this solution at 0 °C caused the broad signal at 6.19 ppm to give way to two new, partially overlapping peaks at 5.98 and 5.77 ppm. The appearance of two distinct signals upon hydrolysis of this solution supports the formation of two regioisomeric adducts as postulated above.

It was noted that in addition to the broad signal ascribed to the vinyl adducts, the ^2H NMR spectrum of this solution also exhibited a prominent peak at 0.93 ppm which increased in intensity over time. *In situ* formation of a deuterated stannane such as *n*-Bu_3Sn^2H was initially considered to give rise to this signal but later seemed doubtful since the corresponding signal for Me_3Sn^2H appears at 3.0 ppm.[16] A more plausible explanation was derived from an earlier report that alkyl copper ligands cleaved the tin-hydrogen bond in reactions with *n*-Bu_3SnH.[55] This suggested that the butyl ligand of mixed reagent, **95**, might also be sufficiently basic to abstract the acetylenic deuterium to yield [1-^2H]-butane. Indeed, the identity of this compound was ascertained by head-space analysis of the reaction solution by mass spectroscopy. An alternative mechanism by which [1-^2H]-butane might be formed in this reaction involves initial activation of the alkynyl deuterium to form a copper deuteride

species followed by reductive elimination of butyl and deuteride ligands (Scheme III.4).

Scheme III.4 Formation of [1-^{2}H]-Butane *via* Oxidative Addition - Reductive Elimination Pathway.

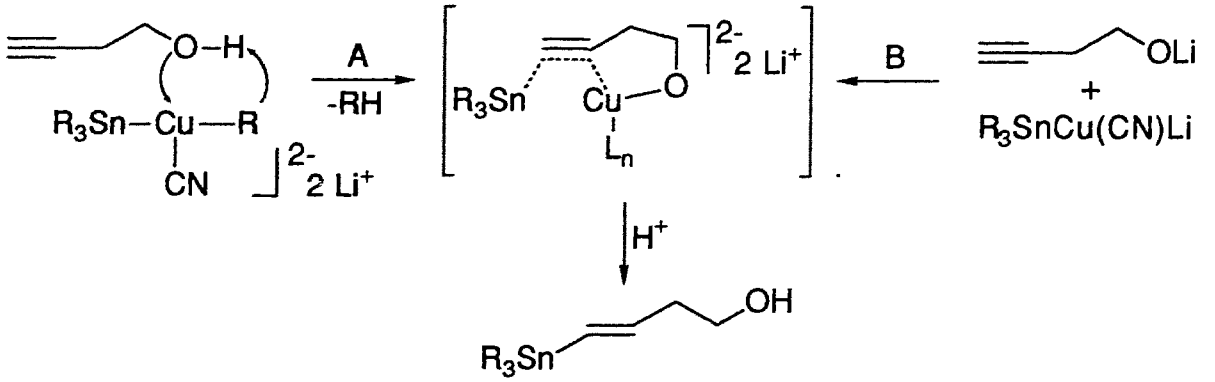


This mechanism appears more credible than the former process since formation of [1-^{2}H]-butane was also observed in the presence of excess MeOH. In an acid-base reaction, the butyl anion would be expected to react with MeOH (more acidic) before abstracting an alkynyl hydrogen. Regardless of the method of formation, generation of [1-^{2}H]-butane might help explain lower yields obtained in stannylcupration of 1-alkynes employing mixed reagents, **86** and **95**, compared to similar reactions involving the homo higher order reagent, **65** (compare yields in Table II.3, entries 5-8 with those in Tables III.1 and III.2, entry 2). Presumably, alkynyl anions generated *in situ* replace the protonated butyl ligands to form new cuprate species. Therefore, consumption of substrate *via* this competing process would occur at the expense of product formation.

Another trend observed in reactions of mixed stannylcuprate reagents with 1-alkynes was a notable preference for formation of 1-stannyl alkenes in reactions with substrates containing hydroxyl groups (Tables III.1 and III.2, entry 1). In earlier investigations of stannylzincation of propargylic substrates the oxygen moiety was considered to play a critical role in determining the

regiochemical outcome of these reactions. It was suggested that oxygen-metal coordination was a key interaction governing the orientation of the stannylcuprate reagent to the triple bond, guiding addition of the stannyl moiety to the distal acetylenic carbon. Based on these results it was reasoned that a similar process might also be responsible for the regioselectivity in stannylcupration of hydroxy acetylenes. In the envisioned process the hydroxyl group is deprotonated by the alkyl ligand of the mixed stannylcuprate reagent to form the corresponding lithium alkoxide and an inert hydrocarbon. Subsequent formation of an alkoxycuprate complex would guide addition of tin toward the terminal acetylenic carbon (Scheme III.5, path A).

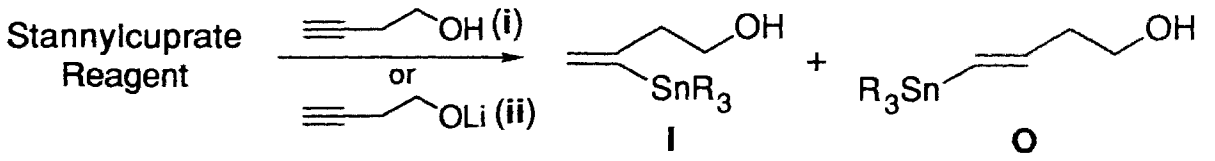
Scheme III.5 Formation of an Alkoxycuprate Intermediate in Stannylcupration of Homopropargyl alcohol.



To test this hypothesis, generation of the alkoxycuprate complex was attempted by an alternative route. It was argued that predominant formation of the 1-stannyl alkene regioisomer in reactions of independently prepared lithium alkoxide and lower order cuprates, $R_3SnCu(CN)Li$, would support the critical participation of oxygen in this process (Scheme III.5, path B). Preferential formation of (*E*)-1-trialkylstannyl alkenes was in fact observed in

stannylcupration of lithium 3-butyn-1-oxide with trimethyl- and tri-*n*-butyltin derived lower order reagents, **72** and **100** (Table III.3, entries 3 and 6).

Table III.3 Stannylcupration of 3-Butyn-1-ol and Lithium 3-Butyn-1-oxide.[a]



Entry	Reagent	Substrate	I : O	Yield %[b]
1	*n*-Bu_3Sn(*n*-Bu)Cu(CN)Li_2 (**95**)	i	4 : 96	84
2	*n*-$Bu_3SnCu(CN)Li$ (**72**)	i	69 : 31	78
3		ii	25 : 75	73
4	$Me_3Sn(Me)Cu(CN)Li_2$ (**86**)	i	3 : 97	77
5	$Me_3SnCu(CN)Li$ (**100**)	i	81 : 19	74
6		ii	35 : 65	69

(a) Reaction conditions: substrate, THF, -78 °C → 0 °C over 1 hr; (b) Isolated yields.

Corroborating evidence for the involvement of the proposed intermediate was gained from stannylcupration of the *protonated* substrate under otherwise identical reaction conditions. Thus, treatment of 3-butyn-1-ol with lower order reagents, **72** and **100**, resulted in the formation mainly 2-stannyl alkene (Table III.3, entries 2 and 5). The fact that opposite regioselectivity can be obtained by conversion of a hydroxyl group to its anion underscores the importance of

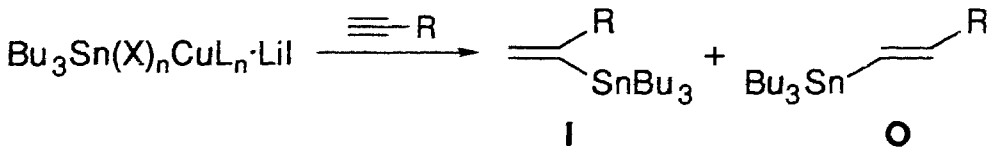
oxygen-copper coordination in determining the regiochemical outcome of these reactions. It should be pointed out that regiochemical bias in favour of the 1-stannyl alkene isomer was not as pronounced in stannylcupration of the alkoxide compared to addition of mixed higher order reagents to the alcohol (compare entries 3 and 6 with 1 and 4, Table III.3). Formation of the alkoxycuprate species is likely to be facile in homogeneous solutions of mixed higher order cuprates and precede addition to the triple bond. On the other hand, generation of this intermediate might be expected to be more sluggish in heterogeneous suspensions of lower order stannylcuprates. In this case, competing reactions of "uncomplexed" cuprate reagent could contribute to the formation of the 2-stannyl alkene.

III.3 Investigations of CuI and CuCN Derived Mixed H.O. and L.O. Tri-*n*-butylstannylcuprates: $R_3Sn(X)_nCuLi_n$ and $R_3Sn(X)Cu(CN)Li_2$.

In light of difficulties (proton abstraction and non-selective ligand transfer) encountered in reactions employing mixed trialkylstannyl(alkyl)cuprate reagents, efforts were directed toward the preparation of mixed stannylcuprates incorporating hetero atoms as the non-transferred ligands. Since preparation of mixed alkylcuprates containing alkoxide, amide, phosphide and acetylide ligands had been reported,[41,43] it was surmised that this strategy could be extended to the synthesis of related trialkylstannyl(hetero)cuprates. A series of such reagents, composed of tri-*n*-butyltin in combination with one or two non-transferable ligands were prepared and their reactivity examined in addition reactions to 1-alkynes.

Preparation of mixed tri-*n*-butylstannylcuprates was readily accomplished by first treating the cuprous salt (CuI) in THF with the anion of the desired ligand followed by *n*-Bu_3SnLi. The order of addition was found to be critical. Addition of *n*-Bu_3SnLi to CuCN gave rise to *n*-$Bu_3SnCu(CN)Li$ that reacted sluggishly with added ligands (Ph_2P, MeO), often requiring elevated temperatures (>0 °C) at which decomposition became significant. Similarly, reaction of *n*-Bu_3SnLi with CuI yielded stannylcuprate species that were thermally unstable, decomposing within minutes at temperatures as low as -78 °C. With the exception of mixed reagents containing selenide ligands, it can be stated that reactions of mixed stannylcuprates with 1-alkynes generally gave low yields (Tables III.4 and III.5). It can be speculated that the poor yields obtained in reactions involving mixed reagents containing alkoxide, amide and phosphide ligands are due to thermal decomposition of these relatively unstable species. In support of this hypothesis, it was found that yields in reactions of the corresponding mixed *cyano*cuprates were generally higher (compare Table III.4, entries 3-6 with Table III.5, entries 2-5). This rationale does not, however, hold for reactions of mixed higher order amide, selenide and acetylide species since these reagents exhibited excellent thermal stability. A possible explanation for low product yields in these reactions might be an unfavourable alkyne-adduct equilibrium in which a substantial amount of starting material is left unconsumed. The observation that vinyl adducts are thermodynamically preferred in revesible reactions with (*n*-$Bu_3Sn)_2Cu(CN)Li_2$ (**65**) (Chapter II) does not preclude the presence of less favourable equilibria in reactions involving these mixed stannylcuprate reagents.

Table III.4 Stannylcupration of 1-Alkynes with CuI Derived Mixed L.O. and H.O. Tri-*n*-butylstannylcuprates.[a]



I O

Entry	Xn	I : O	Yield %[b]
1	MeO	69 : 31	39
2	$(MeO)_2$	89 : 11	26
3	Et_2N	50 : 50	24
4	$(Et_2N)_2$	>99 : 1	36[c]
5	Ph_2P	17 : 83	17
6	$(Ph_2P)_2$	10 : 90	36
7	*n*-BuSe	81:19	70
8	$(n\text{-BuSe})_2$	29 : 71	48
9	(R'-C≡C)	65 : 35	77[d]
10	$(R'\text{-C}\equiv C)_2$	2:98 (4:96)	33 (71)[d]
11	(Ph-C≡C)	65 : 35	21
12	$(Ph\text{-C}\equiv C)_2$	3:97 (3:97)	24 (79)[d]

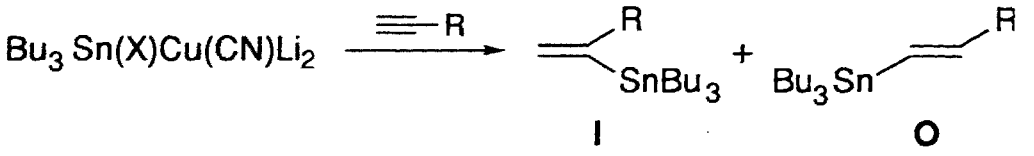
(a) Reaction conditions: 1-Alkyne, THF, -30 °C → 0 °C over 1 hr, MeOH; (b) Isolated yields; R = $(CH_2)_4$-OTHP; (c) R = $(CH_2)_8$-OTHP; (d) 2 equiv of stannylcuprate reagent; R' = C_8H_{17}.

Perhaps most surprising was the observation that the regiochemical outcome in stannylcupration of 1-alkynes was profoundly affected by variation of the non-transferable ligand of the mixed reagent. Moreover, preferential formation of 2-stannyl and 1-stannyl alkenes did not follow the trend observed

in previous investigations using *n*-$Bu_3SnCu(CN)Li$ (**64**) and $(n\text{-}Bu_3Sn)_2Cu(CN)Li_2$ (**65**) reagents (Chapter II). The earlier studies suggested that the regiochemical biases in stannylcupration of 1-alkynes were primarily due to steric factors. It was rationalized that higher order species were sterically less demanding than their bulkier lower order counterparts and therefore gave predominantly 1-stannyl alkenes. In violation of this hypothesis, reactions of several mixed higher order species showed a preference for the 2-stannyl alkene (Table III.4, entries 2 and 4; Table III.5, entries 1,2 and 4) and conversely, lower order reagents containing amide or phosphide ligands were either non-selective or afforded mainly the 1-stannyl isomer (Table III.4, entries 3 and 5). These results clearly indicated that factors other than steric ones control the regioselectivity in reactions of mixed stannylcuprates.

Examination of mixed higher order reagents that exhibited preference for formation of 2-stannyl alkenes in reactions with 1-alkynes (see above) revealed these species to contain electron donating selenide, alkoxide and amide ligands. Electron donation is likely to be particularly effective in cuprate species comprised of amide and alkoxide ligands as a result of overlap between filled *np* and copper dπ orbitals. In contrast, reactions of mixed higher order stannylcuprates containing π-acidic ligands yielded predominantly 1-stannyl alkenes (Table III.4, entries 6, 8, 10 and 12; Table III.5, entries 3, 5 and 6). Phosphorus and selenium contain vacant dπ orbitals and can therefore accept electrons in dπ-dπ backbonding interactions.[61] Likewise, electron density can be delocalized into the π^* antibonding orbital of the acetylide ligand. These rationales suggest that electronic effects play an important role in detemining the regiochemical outcome of these reactions.

Table III.5 Stannylcupration of 1-Alkynes with CuCN Derived Mixed H.O. Tri-*n*-butylstannylcuprates.[a]



I O

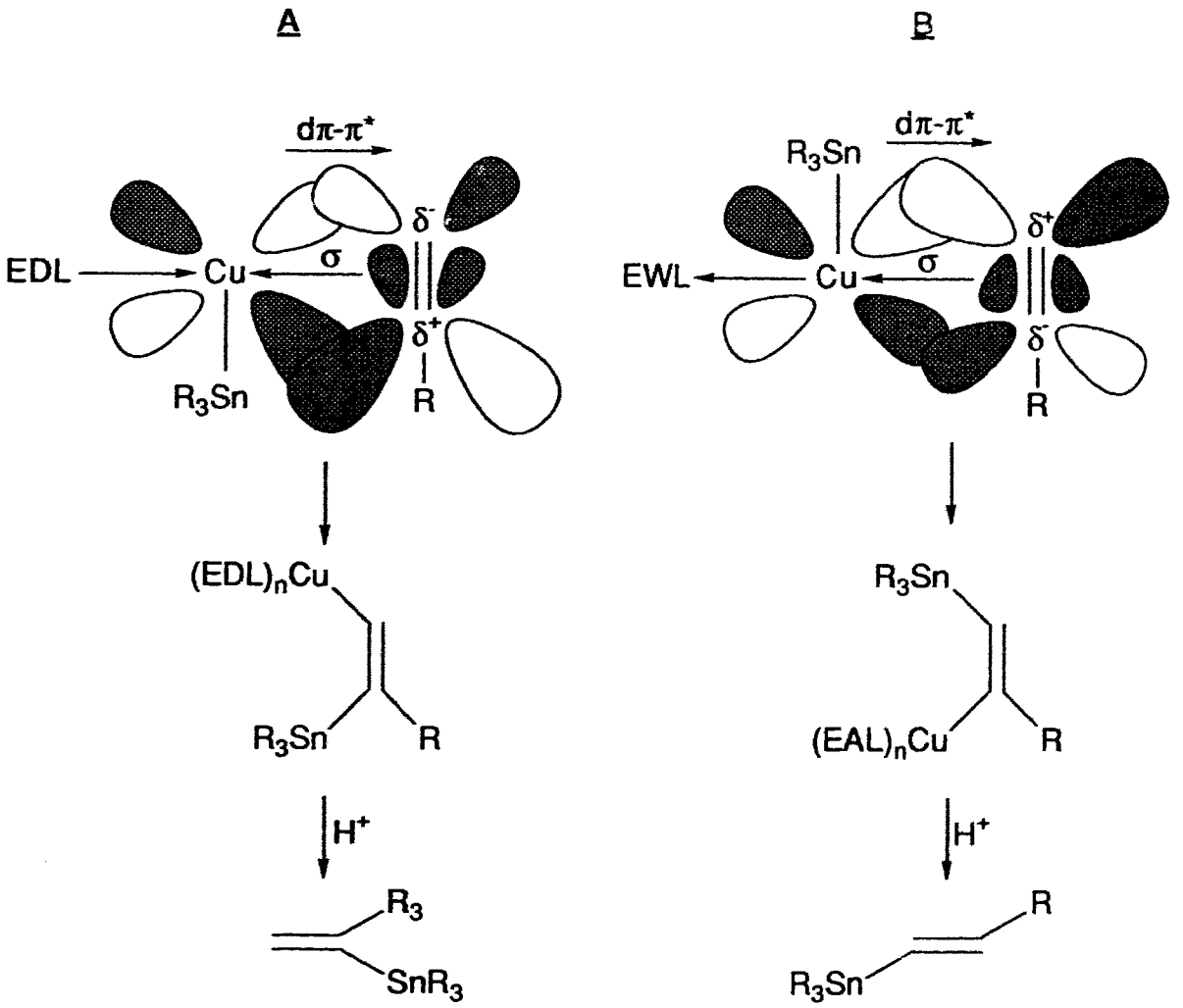
Entry	X	I : O	Yield %[b]
1	MeO	55 : 45	25
2	Et_2N	58 : 42	53[c]
3	Ph_2P	13 : 87	52[c]
4	*n*-BuSe	71 : 29	74
5	(R'-C≡C)	14 : 86	68[d]
6	(Ph-≡)	9 : 91	62[d]

(a) Reaction conditions: 1-Alkyne, THF, -30 °C → 0 °C over 1 hr, MeOH; (b) Isolated yields; R = $(CH_2)_4$-OTHP; (c) R = $(CH_2)_8$-OTHP; (d) 2 equiv of stannylcuprate reagent; R = C_8H_{16}.

In a study of carbocupration of heterosubstituted acetylenes it was demonstrated that addition to triple bonds of reversed polarity yielded products of opposite regiochemistry (Scheme B.4).[38] In view of this, it was hypothesized that polarization of the alkyne moiety could also occur in a copper-alkyne π complex that preceded formation of the vinyl cuprate adduct. It was conjectured that the direction of triple bond polarization was influenced by the nature of the appended ligands. In mixed stannylcuprate reagents containing electron donating ligands, accumulation of negative charge on the copper atom is likely reduced by increased back-bonding from a filled dπ copper orbital to an empty

alkyne π * orbital. The resulting net increase in electron density at the acetylenic moiety accentuates the charge distribution

Scheme III.6 Effect of Electron Donating and Electron Withdrawing Ligands on Triple Bond Polarization in Copper-Alkyne Complexes.



EDL = electron donating ligand; EWL = electron withdrawing ligand.

between C_1 (δ^-) and C_2 (δ^+) acetylenic termini. Consequently, addition of these mixed reagents to 1-alkynes leads to formation of predominantly 2-stannyl alkenes (Scheme III.6, path A). Conversely, it can be argued that π-acidic ligands associated with copper cause reverse polarization of the triple bond by

shifting electron density from the alkyne toward the copper moiety.[62] In this case, delivery of tin (δ^-) to the terminal acetylenic carbon (δ^+) is preferred, yielding mainly 1-stannyl alkenes (Scheme III.6, path B).

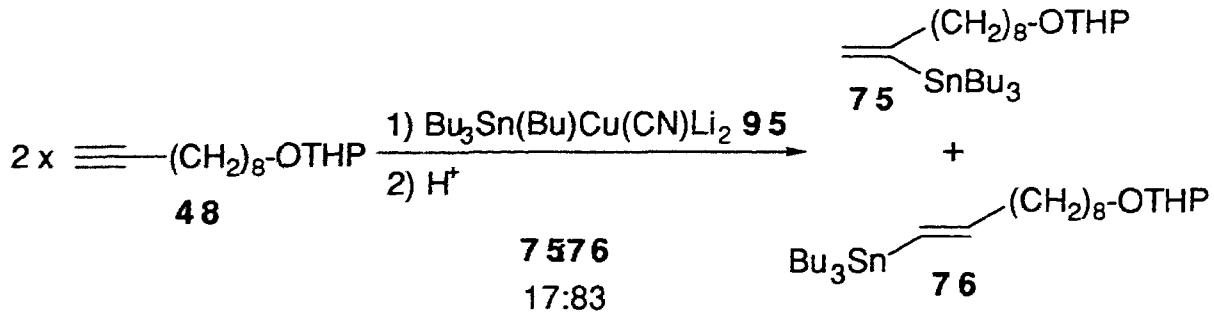
It is interesting to note that the effect of cuprate ligands on the regioselectivity in these reactions appears to be additive. For example, while addition of *n*-$Bu_3Sn(Et_2N)CuLi\cdot LiI$ to 1-alkyne, **70**, yielded an equimolar mixture of regioisomers, the analogous reaction employing *n*-$Bu_3Sn(Et_2N)_2CuLi_2\cdot LiI$, incorporating a *second* equivalent of Et_2NLi, afforded the 2-stannyl alkene almost exclusively (compare entries 3 and 4, Table III.4). Similar reinforcing effects were observed for alkoxide and phosphide containing reagents (compare entries 1 and 2, 5 and 6, Table III.4). A high degree of regioselectivity was also achieved with mixed reagents that combined the electron accepting capabilities of two different (nitrile + acetylide and nitrile + phosphide) ligands (Table III.5, entries 3,5 and 6). Not surprisingly, reactions involving mixed reagents comprised of both electron donating (alkoxide or amide) and electron accepting (nitrile) ligands were less regioselective (Table III.5, entries 1 and 2).

Reactions of lower order and higher order mixed tri-*n*-butylstannylselenenyl- and alkynylcuprates did not follow this trend and yielded products of opposite regiochemistry (compare entries 7 and 8, 9 and 10, 11 and 12, Table III.4). Stannylcupration of 1-alkyne, **70**, with *n*-Bu_3Sn(*n*-BuSe)$CuLi\cdot LiI$ afforded a mixture of vinylstannanes composed of 81 % of the 2-stannyl alkene. In contrast, the analogous reaction with *n*-$Bu_3Sn(n\text{-BuSe})_2CuLi_2\cdot LiI$ gave rise to a 29:71 product ratio in favour of the 1-stannyl isomer. Such dramatic differences in regioselectivity were also observed in reactions of lower order and higher order tri-*n*-butylstannylcyanocuprates, **64** and **65**, (Table II.3,

entries 3 and 7). Presumably, similar steric effects govern the regiochemical outcome in reactions of tri-*n*-butylstannylselenenylcuprates with 1-alkynes. Addition of a mixed stannylcuprate reagent containing both nitrile and selenide ligands to 1-alkyne, **70**, yielded predominantly 2-stannyl alkene (Table III.5, entry 4). This result seemed anomalous since formation of the 1-stannyl alkene isomer was preferred in reactions of mixed reagents that combined nitrile and other π-acidic ligands. Although selenium contains an empty dπ orbital available for back-bonding, it apparently does not function as an effective acceptor ligand in these cuprate complexes.

During the course of a comparative study on the efficiency of $(n\text{-Bu}_3\text{Sn})_2\text{Cu(CN)Li}_2$ and $n\text{-Bu}_3\text{Sn}(n\text{-Bu})\text{Cu(CN)Li}_2$ reagents in the addition to 1-alkynes, it was noted that reactions involving the latter species were generally lower yielding. ^{2}H NMR investigations of addition of $n\text{-Bu}_3\text{Sn}(n\text{-Bu})\text{Cu(CN)Li}_2$ (**95**) to 1-alkyne, **61**, suggested that abstraction of the acetylenic hydrogen by a butyl anion might account for the diminished product yields observed in reactions employing these mixed reagents. A logical remedy to this problem was to conduct these reactions in the presence of two equivalents of alkyne, thus ensuring adequate supply of substrate. As predicted, addition of two equivalents of 1-alkyne, **48**, to a solution of mixed reagent, **95**, afforded vinylstannanes, **75** and **76**, in 80 % yield after work-up and purification. Quite unexpectedly, however, was the observation that the 1-stannyl alkene, **76**, was formed in approximately 83 % isomeric purity (Scheme III.7). This result contrasted starkly with preponderance of 2-stannyl alkenes generally observed in stannylcupration reactions.

Scheme III.7 Addition of *n*-Bu_3Sn(*n*-Bu)Cu(CN)Li_2 to 1-Alkyne **48**

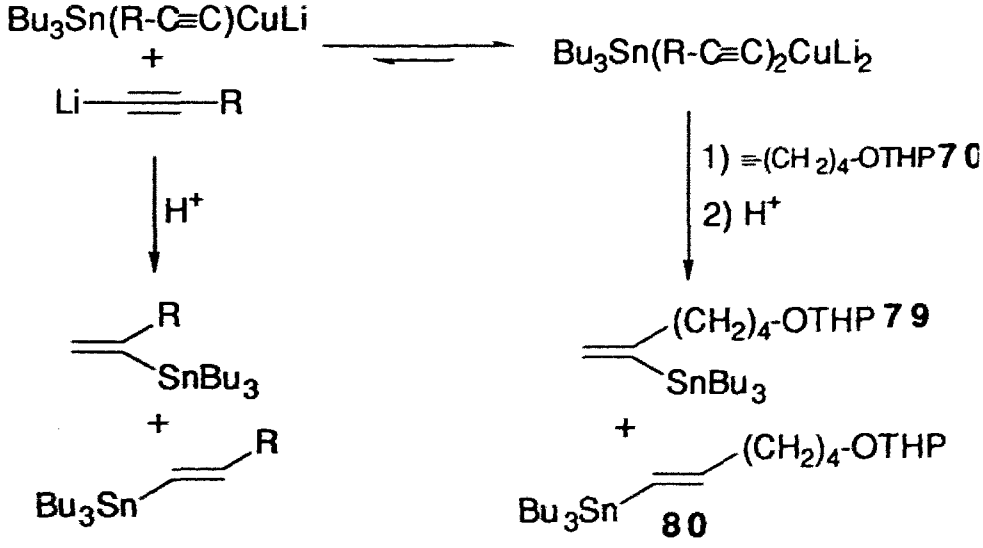


It was speculated that the altered regioselectivity in this reaction might be due to *in situ* formation of a mixed trialkylstannylalkynylcuprate species. It was recognized that such reagents were potentially useful in regioselective syntheses of (*E*)-1-trialkylstannyl alkenes and were therefore examined more closely. It was found that these hypothetical reagents, prepared *directly* from alkynyl anions, reacted with 1-alkynes to yield predominantly 1-stannyl alkenes. The fact that similar results were obtained by this alternative method of reagent preparation provided further evidence for the formation of a mixed species containing an acetylide ligand.

Stannylcupration of 1-alkyne, **70**, with lower order reagents composed of a 1:1:1 mixture of copper, tin and acetylide were moderately selective, giving rise to a 30 % excess of 2-stannyl alkene (Table III.4, entries 9 and 11). Mixed higher order tri-*n*-butylstannylalkynylcuprates containing two acetylide ligands exhibited remarkable thermal stability and could be stirred a room temperature in THF solution for extended periods without signs of decomposition. This was not entirely surprising, since it is known that cuprous acetylides (CuC≡C-R), much like CuCN, are thermally stable and resist oxidation to Cu(II) species.[63] Since acetylide is isoelectronic with nitrile, it presumably confers stability on

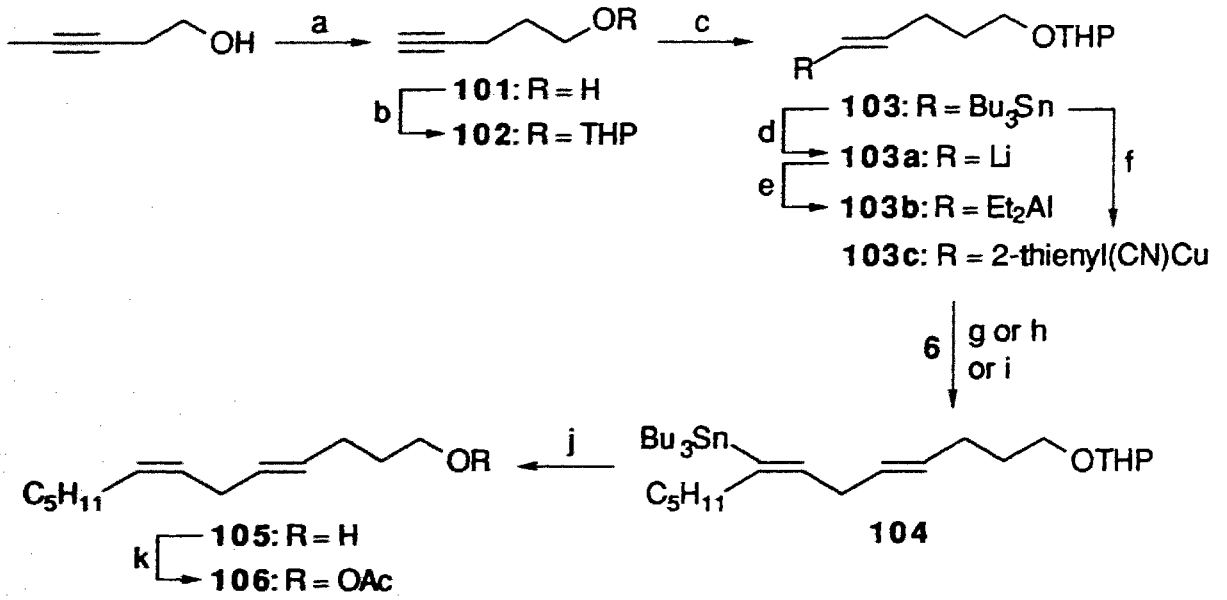
these complexes through similar metal-ligand ($d\pi$-π^*) backbonding interactions (see Chapter II). Stannylcupration of 1-alkynes with these reagents afforded 1-stannyl alkenes in unprecedented (>95 %) selectivity (Table III.4, entries 10 and 12). Unfortunately, to obtain respectable yields, more than one equivalent of reagent per substrate was required. It was noted that in addition to the desired products, vinylstannanes derived from acetylide ligands were also obtained. Based on this observation it was concluded that consumption of stannylcuprate reagent in a competing reaction with acetylide ligand was at least partially responsible for diminished product yields (Scheme III.8). This result was interesting since it implicated the existence of an equilibrium between acetylene reactant and stannylcuprate species. Indeed, spectroscopic investigations of these solutions provided evidence in favour of such processes (see below).

Scheme III.8 Competing Reaction in Addition of *n*-$Bu_3Sn(R\text{-}C{\equiv}C)_2CuLi_2$ to 1-Alkyne **70**.



The remarkable regioselectivity observed in stannylcupration of 1-alkynes with n-$Bu_3Sn(R\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$ allowed application of this method to the stereoselective synthesis of a pheromone containing a "skipped" *E,Z*-1,4-

Scheme III.9 Synthesis of the Leafminer Moth Sex Attractant, (4*E*,7*Z*)-Trideca-4,7-dienyl Acetate (**106**).



(a) Li (6.5 equiv), diaminopropane, r.t./5 hr, *t*-BuOK (4 equiv), r.t./30 min, 3-pentyn-1-ol, r.t/2 hr, 78 %; (b) Dihydropyran (2 equiv), CH_2Cl_2, r.t./45 min, 94 %; (c) n-$Bu_3Sn(Ph\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$ (2 equiv), THF, -30 °C → 0 °C over 1 hr, MeOH, 53 %; (d) *t*-BuLi (2 equiv), ether, -70 °C/30 min, -30 °C/30 min; (e) Et_2AlCl, THF/ether (1:1), -30 °C/15 min; (f) Lithium 2-thienylcyanocuprate, MeLi, THF, -10 °C/10 min, **103**, 0 °C/1.5 hr; (g) **6**, $Pd(PPh_3)_4$ (10 %), THF/ether, -30 °C/30 min, -30 → r.t. over 30 min, 21 % + **103**; (h) **6**, $Pd(PPh_3)_4$ (10 %), THF/ether, 50 °C/2 hr, 73 %; (i) **6**, -78 → r.t. over 12 hr, 55 %; (j) *p*-Toluenesulfonic acid (excess), MeOH/THF (1:1), r.t./30 min, 75 %; (k) Pyridine, acetic anhydride, r.t./45 min, 56 %.

diene. Synthesis of the leafminer moth sex attractant, (4*E*,7*Z*)-trideca-4,7-dienyl acetate[64] (**106**) is shown in Scheme III.9. Preparation of the requisite vinylstannane **103** was accomplished in 78 % yield by treatment of alkyne,

102, with *n*-$Bu_3Sn(Ph\text{-}C{\equiv}C)_2CuLi_2$·LiI. To reduce the amount of tin byproducts *n*-Bu_3SnLi was generated in the reaction of *n*-Bu_3SnH and LDA.[21] This method avoided formation of *n*-Bu_4Sn,[20] thereby facilitating work-up and purification. Transmetallation of **103** to a vinyllithium species was readily achieved by treatment of the vinylstannane with *n*-BuLi at -30 °C. Reaction of vinyllithium reagent, **103a**, with allylic chloride, **6**, in the presence of $Pd(PPh_3)_4$ (10 %) afforded diene, **104**, in 21 % yield. In addition, a substantial amount of vinylstannane, **103**, was formed. Nucleophilic attack of the vinyllithium reagent on the tri-*n*-butyltin moiety of the allylic substrate, giving rise to **103** in this case, has been observed in earlier syntheses of pheromones, **48** and **58b** (Chapter I). As noted previously, this side reaction could be avoided by conversion of the vinyllithium reagent to the corresponding vinyl aluminum species. Thus, palladium-catalyzed cross-coupling of vinylalane, **103b**, with **6** afforded diene, **104**, in 77 % isolated yield and in >95 % isomeric purity.

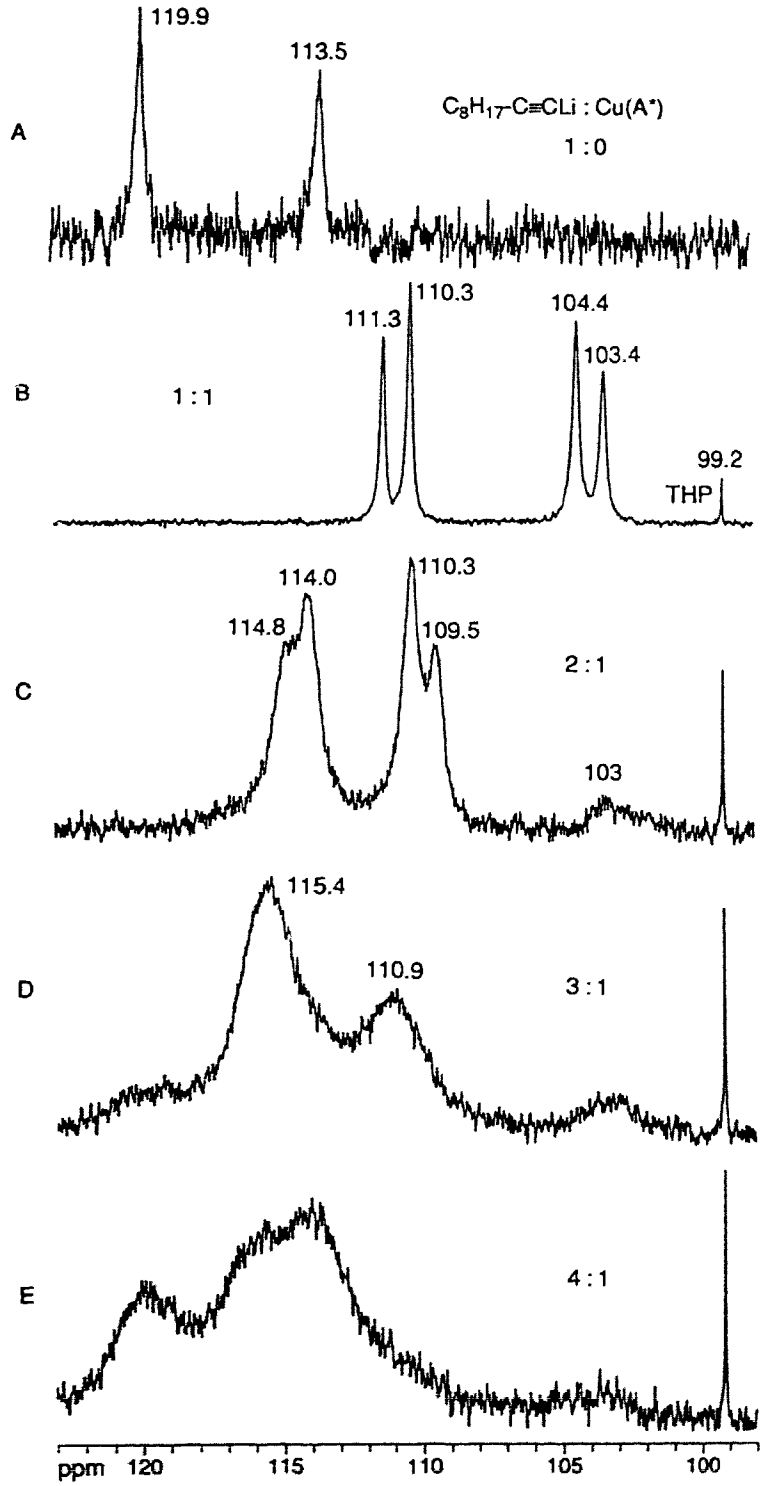
It had been reported that vinyl cuprates reacted efficiently with enones,[65] secondary halides and epoxides,[60] affording products of vinyl substitution. It was therefore speculated that vinyl cuprates might also undergo coupling with allylic substrates to afford 1,4-dienes without the requirement of a palladium catalyst. Indeed, *in situ* formation of cuprate, **103c**, by treatment of vinylstannane, **103**, with $Me(2\text{-}Th)Cu(CN)Li_2$,[65] followed by addition of allylic chloride, **6**, gave **104** in moderate yield. This procedure, however, was less stereoselective than palladium-catalyzed cross-coupling reactions, giving rise to approximately 10 % of isomers. Removal of *n*-Bu_3Sn and THP groups was accomplished in a single step by stirring **104** in a solution of MeOH and THF containing excess *p*-toluenesulfonic acid. Finally, acetylation of alcohol, **105**, under standard conditions afforded the desired pheromone, **106**. The ^1H NMR

spectrum of this compound exhibited proton resonances for two different double bonds. ^{1}H decoupling experiments revealed the presence of a trans coupling of 16 Hz.[25] Although the compexity of the second vinyl resonance did not allow measurement of a coupling constant, its width (12.5 Hz) suggested the presence of a *Z* double bond.[25]

III.4 Spectroscopic Investigations of Solutions of $(Me_3SnLi)_m$: $(R\text{-}C{\equiv}CLi)_n$: CuI.

Incorporation of the ^{13}C labelled alkyne, **63**, into copper complexes allowed ready examination of these species by ^{13}C NMR spectroscopy. The fact that the acetylide moiety can be detected by IR spectroscopy also permitted investigation of solutions by this technique. Addition of one equivalent of decynyllithium to a suspension of **63** derived R-C≡CCu·LiI in THF yielded a clear solution whose ^{13}C NMR spectrum exhibited two sharp doublets at 111.3, 110.3 and 104.4, 103.4 ppm, attributed to the acetylide carbons of $(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$ (Figure III.2, spectrum B). Two absorption bands were detected in the IR spectrum which is likely due to a symmetric and an antisymmetric stretch of two acetylide ligands bonded to copper (Table III.6, entry 3). The ^{13}C NMR spectrum of a solution comprised of three equivalents of R-C≡CLi per CuI displayed two broadened doublets that appeared downfield (114.8, 114.0 and 110.2, 109.5 ppm) from those in solutions of $(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$. A smaller, broad signal at 103 ppm, likely due to a small amount of the latter species, was also observed. The IR spectrum of this solution displayed a new absorption at 2059 cm^{-1} which, together with ^{13}C NMR data, pointed to the formation of a new species, presumed to be $(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ (Table III.6, entry 4).

Figure III.2 ^{13}C NMR Spectra of Solutions of $(C_8H_{17}\text{-}C{\equiv}CLi)_n$: $Cu(^*C{\equiv}C^*\text{-}C_8H_{16}\text{-}OTHP)$.[a]



(a) Solutions in THF. Spectra recorded at 0 °C. Acetylene carbons > 99 % ^{13}C enriched; (A) 1 M; (B) 0.1 M; (C) 0.09 M; (D) 0.08 M; (E) 0.08 M; $A^* = {}^*C{\equiv}C^*\text{-}C_8H_{16}\text{-}OTHP$.

Table III.6 IR ν(C≡C) Bands of Solutions of $(C_8H_{17}\text{-}C{\equiv}CLi)_n$: CuI.[a]

Entry	R-C≡CLi : CuI	cm^{-1} (rel. intensity)
1	R-≡-Li	2052
2	1 : 1	b
3	2 : 1	2087(s), 2023(w)
4	3 : 1	2059
5	4 : 1	2054[c]
6	5 : 1	2053[c]

(a) Spectra recorded at 0 °C. Solutions 0.1 M (based on Cu) in THF; (b) Film (nujol), absorbance not detected; (c) Has shoulder on high frequency side; R = C_8H_{17}.

Subsequent additions of R-C≡CLi to this solution caused a further downfield shift of the doublets and resulted in extensive broadening of these signals (Figure III.2, spectra C-E). It was interesting to note that in the downfield progression of these peaks, changes in chemical shift were not the same for both pairs of doublets. Comparison of ^{13}C NMR spectra B and C of solutions of $(R\text{-}C{\equiv}C)_2CuLi{\cdot}LiI$ (Δ 6 ppm) and $(R\text{-}C{\equiv}C)_3CuLi_2{\cdot}LiI$ (Δ 3.5 ppm) provides a dramatic example of this phenomenon. Based on these chemical shift differences, the upfield signals were assigned to the terminal acetylenic carbon, since C_1 is likely to be affected by changes in the environment to a greater extent than C_2. It should also be mentioned that in the presence of excess R-C≡CLi, distinct signals for this species were not detected in the ^{13}C NMR spectrum which suggests that "free" lithium acetylide is in rapid equilibrium with alkynylcuprates, giving rise to an averaged spectrum. These observations are

consistent with rapid exchange between R-C≡CLi, $(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$ and $(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ species, described by equilibrium b shown below:

$$ACu + ALi \xrightarrow{a} A_2CuLi$$

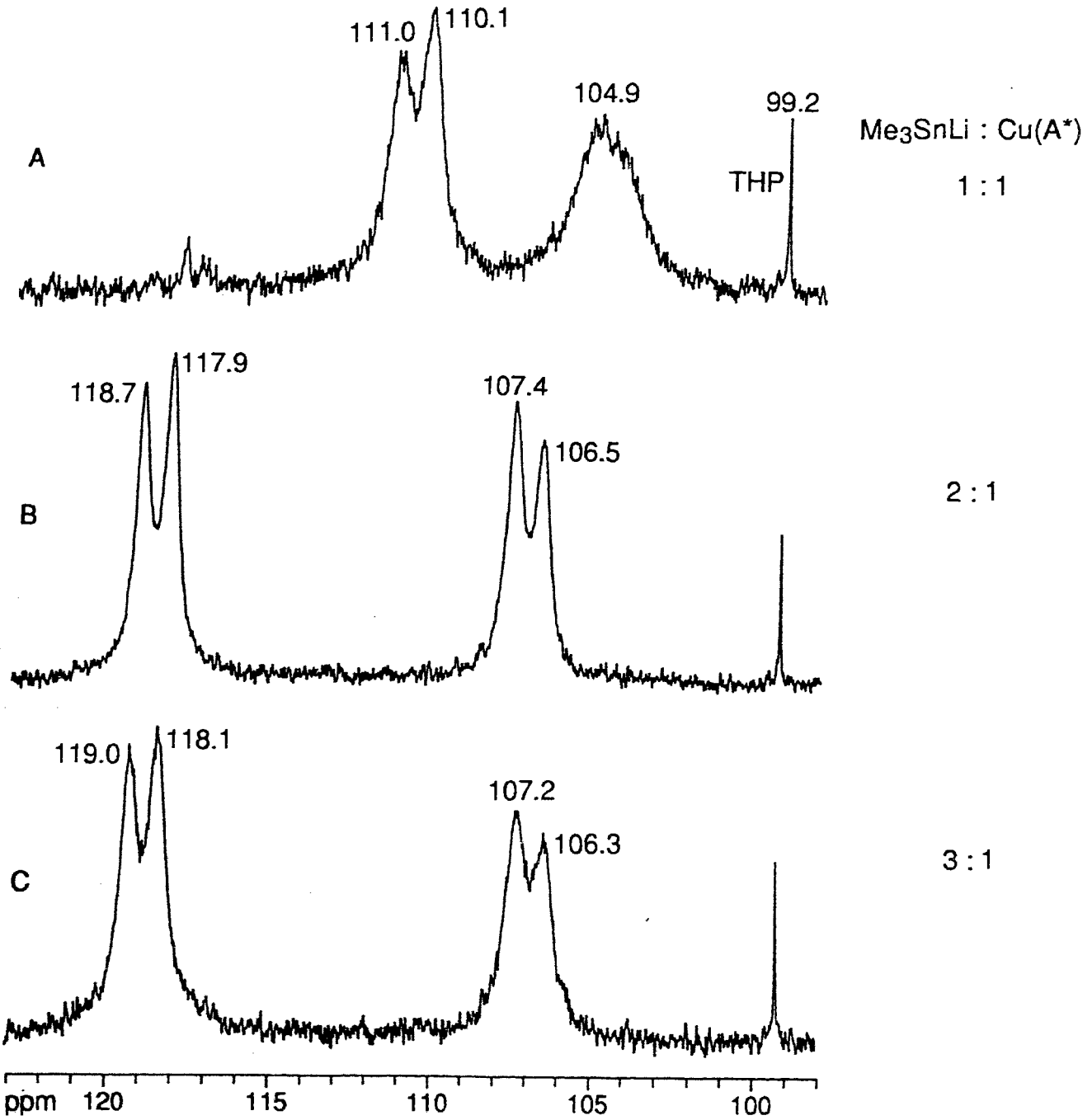
$$A_2CuLi + ALi \underset{}{\overset{b}{\rightleftharpoons}} A_3CuLi_2$$

A = R-C≡C ; LiI omitted for sake of clarity

The IR spectra of solutions composed of 4:1 and 5:1 ratios of R-C≡CLi and CuI displayed wide absorption bands at 2054 and 2053 cm^{-1}, respectively (Table III.6, entries 5 and 6). The absence of distinct absorbances for $(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ (2059 cm^{-1}) and R-C≡CLi (2052 cm^{-1}) is likely due to poor resolution of these bands which differ only by 7 cm^{-1}.

The ^{13}C NMR spectrum of a solution containing a 1:1 mixture of Me_3SnLi and $Cu^*C{\equiv}C^*\text{-}(CH_2)_8\text{-}OTHP$ showed doublets at 111.0 and 110.1 ppm and a broad signal at 104.9 ppm (Figure III.3, spectrum A). The broad upfield signal is presumably due to a "collapsed" doublet of C_1 (see above) indicating rapid ligand exchange between various species. IR analysis of this mixture revealed the presence of two distinct absorption bands at 2087 and 2023 cm^{-1} (Table III.7, entry 1). It was noted that ^{13}C NMR and IR spectra of this solution closely resembled those of $(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$. A likely explanation for this is the formation of $Me_3Sn(R\text{-}C{\equiv}C)CuLi\cdot LiI$ and $Me_3Sn(R\text{-}C{\equiv}C)_2Cu_2Li\cdot LiI$[66] species in the former solution (Scheme III.10, equilibrium a). Examination of the proposed dimeric[66,67] structures for these cuprate species reveals the presence of a common structural unit, (R-C≡C)CuLi, that could account for the spectral similarities observed for solutions of $(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$ and $Me_3Sn(R\text{-}C{\equiv}C)CuLi\cdot LiI$ (Figure III.4). Formation of $(Me_3Sn)_2(R\text{-}C{\equiv}C)Cu_2Li\cdot LiI$ is less likely

Figure III.3 ^{13}C NMR Spectra of Solutions of Me_3SnLi : $(C_8H_{17}\text{-}C{\equiv}CLi)_n$: $Cu(^*C{\equiv}C^*\text{-}C_8H_{16}\text{-}OTHP)$.[a]



(a) Spectra recorded at 0 °C. Acetylene carbons > 99 % ^{13}C enriched; (A) 0.1 M THF/Ether (9:1); (B) 0.09 M THF/Ether (10:1); (C) 0.08 M THF/Ether (11:1); (D) 0.08 M THF/Ether (12:1); A* = $^*C{\equiv}C^*\text{-}C_8H_{16}\text{-}OTHP$.

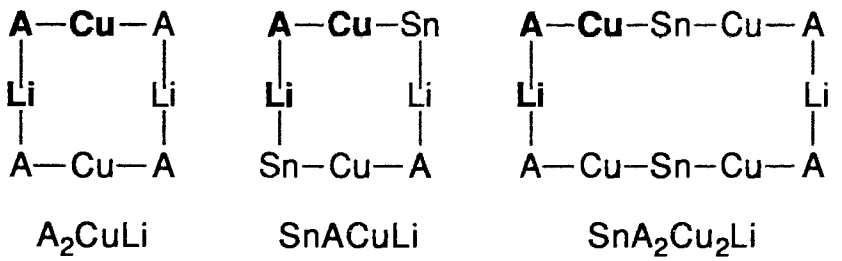
Table III.7 IR ν(C≡C) Bands of Solutions of $Me_3SnLi : (C_8H_{17}\text{-}C{\equiv}CLi)_n : CuI$.[a]

Entry	$Me_3SnLi : R\text{-}C{\equiv}CLi : CuI$	cm^{-1} (rel. intensity)
1	1 : 1 : 1	2087(s), 2023(w)
2	1 : 2 : 1	2063
3	1 : 3 : 1	2063(w)[b], 2053(s)

(a) Spectra recorded at 0 °C. Solutions 0.1 M (based on Cu) in THF/Ether (9:1); (b) Weak shoulder; R = C_8H_{17}.

due to the absence of an IR absorbance for R-C≡CLi (2052 cm^{-1}) in this solution (Scheme III.9, equilibrium b).

Figure III.4 Possible Structures for $(R\text{-}C{\equiv}C)_2CuLi$, $Me_3Sn(R\text{-}C{\equiv}C)CuLi$ and $Me_3Sn(R\text{-}C{\equiv}C)_2Cu_2Li$ Species.

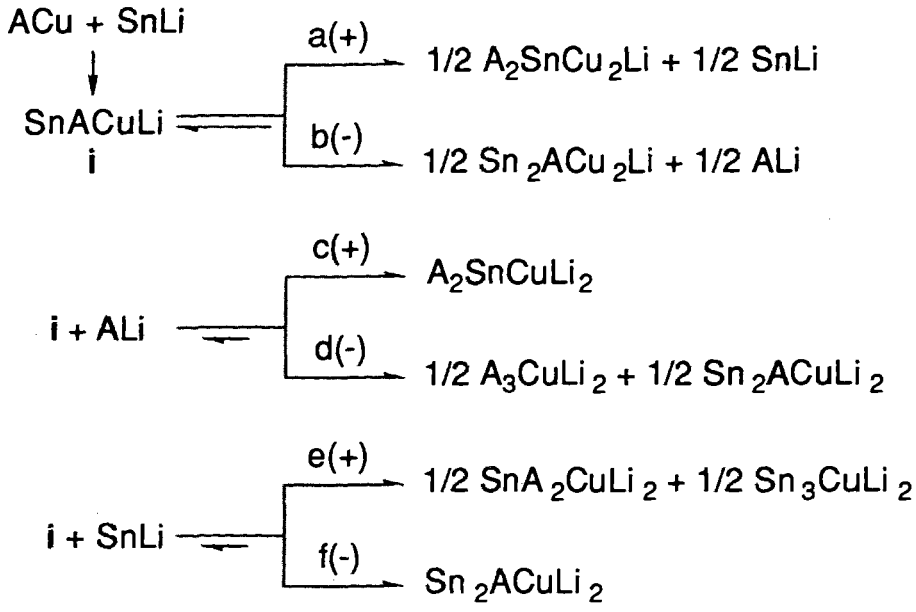


A = R-C≡C; Sn = Me_3Sn; Common structural unit, ACuLi, highlighted in bold.

Addition of one equivalent of R-C≡CLi to the mixed reagent, $Me_3Sn(R\text{-}C{\equiv}C)CuLi{\cdot}LiI$, gave rise to a new species, evidenced by new alkynyl signals observed in the ^{13}C NMR spectrum (Figure III.3, spectrum B) as well as a new IR band at 2063 cm^{-1} (Table III.7, entry 2). It was recognized that in principle, formation of two different mixed higher order species,

$Me_3Sn(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$ and $(Me_3Sn)_2(R\text{-}C{\equiv}C)CuLi_2\cdot LiI$ was possible (Scheme III.10, equilibria c and d). However, since $(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ was not detected in this solution, formation of $(Me_3Sn)_2(R\text{-}C{\equiv}C)CuLi_2\cdot LiI$ seemed less probable. Further addition of R-C≡CLi caused substantial broadening and a downfield shift of alkynyl signals in the ^{13}C NMR spectrum as observed in solutions of

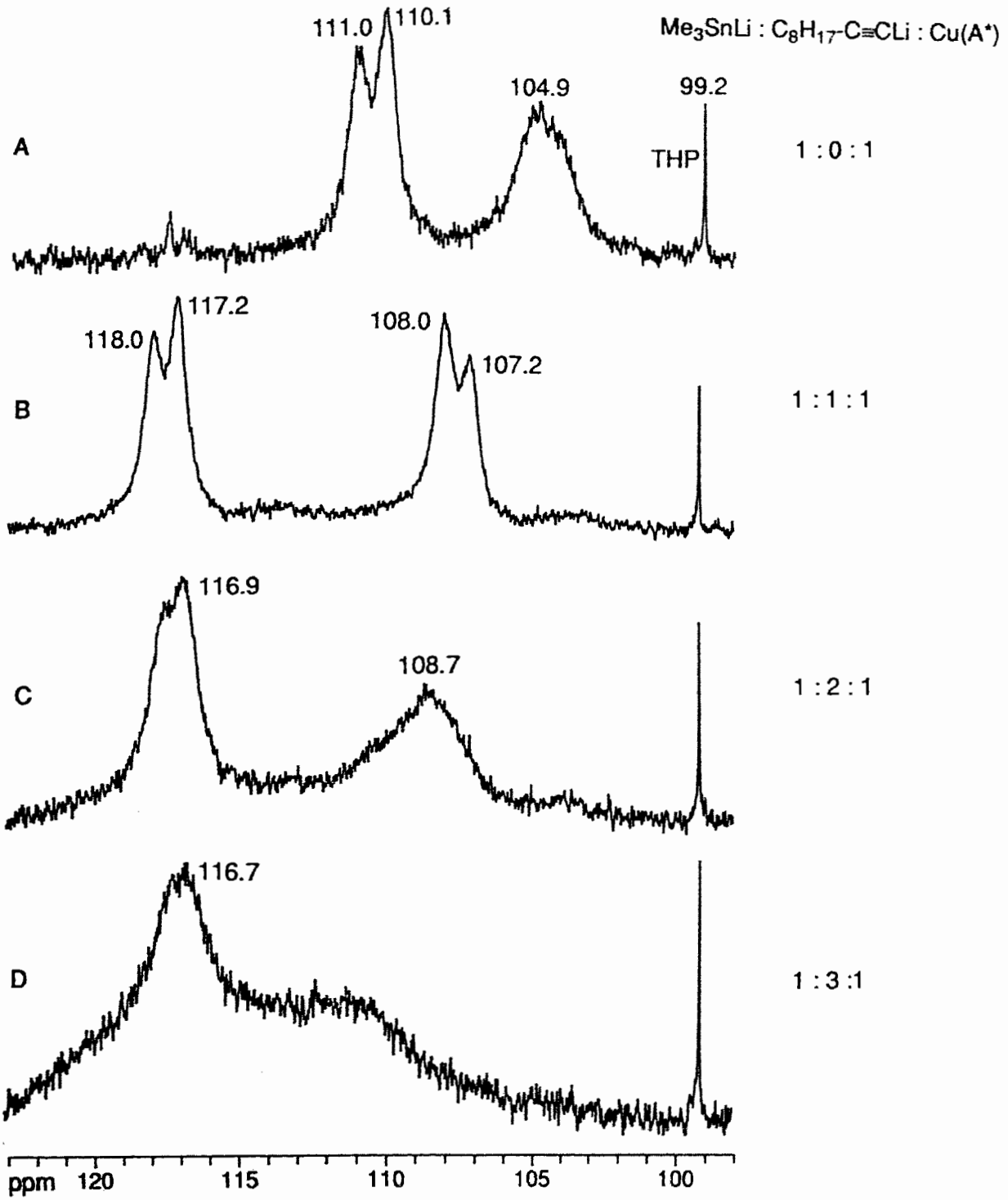
Scheme III.10 Possible Equilibria in Solutions of Mixed Trialkystannylalkynylcuprates.



A = R-C≡C ; Sn = R_3Sn; (+) = likely; (-) = not likely; LiI omitted for sake of clarity.

$(R\text{-}C{\equiv}C)_nCuLi_{n-1}\cdot LiI$ (Figure III.3, spectra C and D). In the presence of excess R-C≡CLi (four equivalents) alkynyl peaks merged to a broad signal spanning a range of more than 20 ppm (!) This observation is interpreted to be due to rapid equilibration between R-C≡CLi, $Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$ and possibly $Me_3Sn(R\text{-}C{\equiv}C)CuLi\cdot LiI$ and $Me_3Sn(R\text{-}C{\equiv}C)_2Cu_2Li\cdot LiI$ species. Supporting evidence for such exchange was obtained from IR analysis of a solution comprised of a 1:3:1 mixture of Me_3SnLi, R-C≡CLi and CuI that displayed

Figure III.5 ^{13}C NMR Spectra of Solutions of $(Me_3SnLi)_n$: $Cu(^*C{\equiv}C^*\text{-}C_8H_{16}\text{-}OTHP)$.[a]



(a) Spectra recorded at 0 °C. Acetylene carbons > 99 % ^{13}C enriched; (A) 0.1 M THF/Ether (9:1); (B) 0.08 M THF/Ether (10:2); (C) 0.07 M THF/Ether (11:3); A* = $^*C{\equiv}C^*\text{-}C_8H_{16}\text{-}OTHP$.

Table III.8 IR ν(C≡C) Bands of Solutions of $(Me_3SnLi)_n$: C_8H_{17}-C≡CLi : CuI.[a]

Entry	Me_3SnLi : R-C≡C-Li :CuI	cm^{-1} (rel. intensity)
1	1 : 1 : 1	2087(s), 2023(w)[b]
2	2 : 1 : 1	2086(w), 2064(s)[c] 2023(w)[b]
3	3 : 1 : 1	2087(w), 2064(s)[d]

(a) Spectra recorded at 0 °C. Solutions 0.1 M (based on Cu) in THF/Ether; Solvent ratios: (b) 9:1; (c) 10:2; (d) 11:3; R = C_8H_{16}.

absorbances (2063 and 2053 cm^{-1}), characteristic of the former two species (Table III.7, entry 3). These observations lend credence to the argument made earlier, that low yields in stannylcupration of 1-alkynes employing $Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$ is due to consumption of reagent by "free" acetylide ligand.

The ^{13}C NMR spectrum of a solution of a 2:1:1 mixture of Me_3SnLi, R-C≡CLi and CuI was almost identical to that of a solution comprised of these components in a 1:2:1 ratio (compare spectra B, Figure III.3 and III.5). Both spectra exhibited two pairs of alkynyl signals centered at 118 and 107 ppm. The commonality of a prominent absorption band at 2063(4) in the IR spectra of these solutions is further evidence that the same species, presumed to be $Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$, is generated in both solutions (compare entries 2, Table III.7 and III.8). Further addition of Me_3SnLi to the former solution did not bring about a significant change in the ^{13}C NMR or IR spectra, indicating that

new species were not formed in the presence of excess tin anion (Figure III.5, spectrum C).

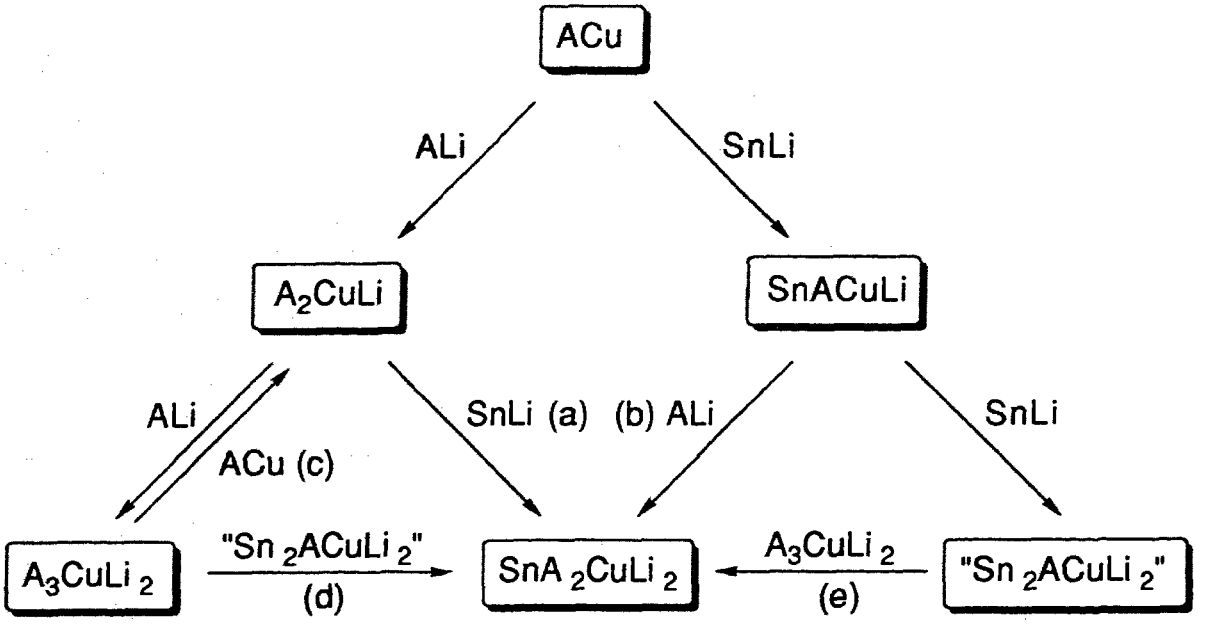
Table III.9 Spectral Data for CuI Derived Alkynylcuprates.

Species	^{13}C NMR[a] (C≡C) ppm	IR (C≡C) cm^{-1}
R-C≡CLi	120, 114	2052
$(R\text{-}C{\equiv}C)_2CuLi\cdot LiI$	111, 104	2087, 2023
$(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$	114, 110	2059
$Me_3Sn(R\text{-}C{\equiv}C)CuLi\cdot LiI$	111, 105	2087, 2023
$Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2$	118, 107[b]	2063

(a) Values are for centre of doublets; (b) Average of 2 values.

Corroborating evidence for preferential formation of $Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$ in solutions of mixed trialkylstannylalkynylcuprates was obtained from IR investigations of reactions of "$(Me_3Sn)_2(R\text{-}C{\equiv}C)CuLi_2\cdot LiI$" and $(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$. It was found that, regardless of the order of addition, combined solutions of these species gave identical IR spectra (Scheme III.11, paths d and e). The same IR spectra were obtained for solutions of $(Me_3Sn)(R\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$, prepared by two alternate routes (Scheme III.11, paths a and b). Addition of $(R\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ to a slurry of $(R\text{-}C{\equiv}C)Cu\cdot LiI$ afforded a homogeneous solution whose IR spectrum was consistent with the formation of $(R\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$ (Scheme III.11, path c). These experiments clearly demonstrate the ease with which disproportionation between cuprate species occurs in these solutions.

Scheme III.11 Disproportionation between Alkynylcuprate Species.[a]



(a) 0.1 M THF solutions (based on Cu); A = C_8H_{17}-C≡C; Sn = Me_3Sn; LiI omitted for sake of clarity.

III.5 **Summary and Conclusion.**

Reaction of homo higher order alkylcuprates, $R_2Cu(CN)Li_2$, with hexaalkyldistannanes, $(R_3Sn)_2$, represents a new, convenient route to the preparation of mixed higher order trialkylstannyl(alkyl)cyanocuprates, $R_3Sn(R)Cu(CN)Li_2$. These reagents react with a variety of organic substrates without the formation of excessive quantities of tin byproducts, that often complicate isolation and purification. Removal of low boiling tin impurities generated in reactions of $(Me_3Sn)MeCu(CN)Li_2$ is readily accomplished under high vacuum at ambient temperature.

With the exception of epoxides, transfer of the trialkyltin moiety occurs selectively in reactions with organic substrates. The alkyl moiety of these reagents is, however, sufficiently basic to abstract both acetylenic and hydroxyl hydrogens. Diminished yields in reactions of these reagents with 1-alkynes is attributed to this side reaction. Formation of an alkoxycuprate intermediate in stannylcupration of hydroxy acetylenes is believed to be a key interaction dictating the regioselective formation of 1-stannyl alkenes in these reactions.

Regioselective formation of 2-stannyl and 1-stannyl alkene isomers has been achieved in stannylcupration of 1-alkynes by incorporating electron donating and withdrawing ligands, respectively, into the mixed stannylcuprate reagent. It is postulated that the acetylenic moiety initially coordinates to copper to form a π-complex. Polarization of the triple bond in this complex is dependent on the nature of the cuprate ligands and governs the regioselectivity in these reactions. The synthetic utility of the mixed n-$Bu_3Sn(R\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$ reagent has been demonstrated in the highly regioselective (>95 %) conversion of a 1-alkyne to the corresponding (*E*) vinylstannane as a key step in the

stereospecific synthesis of the leafminer moth sex attractant, (4*E*,7*Z*)-trideca-4,7-dienyl acetate (**106**).

Several new alkynylcuprate-based reagents have been identified by using ^{13}C NMR and IR spectroscopic techniques. These studies indicate that $(R\text{-}C{\equiv}C)_2CuLi{\cdot}LiI$ and $(R\text{-}C{\equiv}C)_3CuLi_2{\cdot}LiI$ are formed as distinct species in the reaction of CuI with two and three equivalents of lithium acetylide, respectively. Formation of dimeric species, $Me_3Sn(R\text{-}C{\equiv}C)CuLi{\cdot}LiI$ and $Me_3Sn(R\text{-}C{\equiv}C)_2Cu_2Li{\cdot}LiI$, is proposed in solutions comprised of a 1:1:1 mixture of Me_3SnLi, R-C≡CLi and CuI. Addition of one equivalent of either R-C≡CLi or Me_3SnLi to this solution gives rise to the mixed higher order reagent, $Me_3Sn(R\text{-}C{\equiv}C)_2CuLi_2{\cdot}LiI$. Disproportionation between alkynylcuprates is extremely facile, allowing ready interconversion between higher order and lower order species by addition of appropriate reagents.

EXPERIMENTAL

GENERAL

Solvents. Solvents were purchased from Aldrich, Fisher or Malincrodt chemical companies and used directly without further purification. Anhydrous conditions: THF and diethyl ether were freshly distilled over potassium benzophenone-ketyl. CH_2Cl_2 was freshly distilled from CaH_2. Diglyme was purchased as an anhydrous liquid. Dried DMF (distilled from CaH_2) was distilled at room temperature under reduced pressure prior to use. DMSO, benzene, hexanes and Et_3N were distilled from CaH_2 and stored over 4 A molecular sieves under a positive pressure of argon. HMPA and CH_3CN were distilled from CaH_2 and stored, under argon, in bottles equipped with a three-way valve assembly. MeOH was distilled from $Mg(OMe)_2$ and stored over 4 A sieves. DMS was purchased as an anhydrous liquid and stored at -20 °C over 4 A sieves. CD_3CN was purchased as an anhydrous liquid in sealed ampules. The ampules were opened under nitrogen, fitted with rubber septa and CD_3CN transferred via cannula.

Reagents. Chemicals obtained commercially were of reagent grade quality and used directly without further purification unless indicated. Acetylenes were purchased from Farchan Laboratories Inc., distilled and stored at room temperature under positive pressure of argon. Diisopropylamine was distilled from CaH_2 and stored at room temperature under argon. Liquid reagents synthesized in the laboratory were stored at -20 °C in rubber septum capped vials under positive pressure of argon. *n*-Bu_3SnH was stored at -20 °C, under argon, in a brown bottle containing several crystals of *o*-benzoquinone as

a stabilizer. MeLi and *n*-BuLi were stored at -20 °C under argon and titrated periodically according to a literature procedure.[68] Air and moisture sensitive solids were stored in an evacuated desiccator containing $CaSO_4$ as a drying agent. $ZnCl_2$ was dried from the melt under reduced pressure. The cooled, glassy substance was ground with a mortar and pestle under an atmosphere on nitrogen. $ZnBr_2$ was dried by refluxing in SO_2Cl_2 for 2 hr followed by solvent removal under reduced pressure. *N*-chlorosuccinimide was recrystallized from acetic acid. CuCN was dried under high vacuum at 40 °C for 12 hr. CuI was purified according to a literature procedure and stored in a brown tinted vial under argon.[69] $Pd(PPh_3)_4$ was purchased from Aldrich chemical company.

Manipulation of air and moisture sensitive reagents. Glassware, syringes, stainless steel needles and cannulae were dried in an oven at 150 °C for a minimum or 1 hr and then cooled by flushing with argon prior to use. Syringe plungers were coated with sufficient mineral oil to provide a gas tight seal with their respective barrels. Spatulas and other miscellaneous tools were flame dried directly prior to use and cooled under an atmosphere of nitrogen. Measurement and delivery of air and moisture sensitive liquids was accomplished with dry syringes. Solvents or solutions were transferred from one flask to another under anhydrous conditions *via* dry cannulae. Air and moisture sensitive solids were weighed in a glove bag under an atmosphere of nitrogen and stored in sealed vials prior to use. Solid samples were added to solutions from well inside the neck of the reaction vessel under a countercurrent of argon.

Reactions demanding strict anhydrous conditions were carried out under slight positive pressure of argon in dry reaction vessels fitted with a rubber stopper. Argon was supplied to each flask *via* Teflon and Tygon tubing. An 18

gauge needle, secured to the terminus of each argon line was pierced through the rubber septum and provided a gas-tight connection with the argon source. Pressure and flow of argon into the flask were monitored and controlled by means of a U-tube shaped mineral oil bubbler.

Purification. Purification by flash chromatography was performed according to a literature procedure with SiO_2 (230-400 mesh) as the stationary phase.[70]

Aluminum backed TLC plates were treated (after development) with an acidic solution of $Ce(SO_4)_2$ (1 %) and molybdic acid (1.4 %) followed by charring on a hot plate in order to make the separated compounds visible.

Preparative TLC plates were prepared by coating glass plates with an aqueous slurry of SiO_2 powder. The apparatus used in this procedure allowed the stationary phase to be applied at a thickness of 0.5 or 0.75 mm. The plates were air dried and activated by storing them at 150 °C overnight. Silver nitrate impregnated plates were prepared by admixing $AgNO_3$ (20 % by weight of silica) to the SiO_2 slurry. 1,4-dienes purified by preparative TLC were visualized by spraying developed plates with a solution of rhodamine 6 G (1 % in acetone). These compounds appeared as bright fluorescent bands under UV light.

Air and moisture sensitive liquids were distilled under argon by using a vacuum-jacketed distillation apparatus fitted with a short Vigreux column. Liquids with boiling points greater than 100 °C were distilled under reduced pressure. Reported boiling points are uncorrected.

Analyses. Gas Chromatographic analyses were performed on Hewlett Packard 5880A and 5890 chromatographs equipped with DB-1 capillary columns (15 m, id: 0.25 mm, film: 0.25 μm) and F. I. D. detectors. Injection ports

and detectors were operated at 260 °C and 275 °C, respectively. Helium was used as the carrier gas. GC analytical data was recorded on a Hewlett Packard Model 3392A integrator.

GC yields were determined by using hexadecane as an internal standard and calculated according to the formula: $g_1 = A_1/A_2 \times RRF \times g_2$ (g_1 = grams of product; g_2 = grams of ISTD.; A_1 = area under product (g_1) peak ; A_2 = area under ISTD. (g_2) peak; RRF = relative response factor, Rf_1/Rf_2). Rf (g_x/A_x) values were determined for solutions containing a known mixture of g_1 and g_2. An average value for solutions of varying concentration was used. Calculations and analyses were performed on the same gas chromatograph under identical operating conditions.

Mass spectral analyses were performed on a Hewlett Packard 5985B GC/MS equipped with a DB-1 capillary column (30 m, id: 0.32 mm film: 0.25 μm) and a quadrupole mass analyzer. Ionization by electron impact (EI) was typically carried out at 70 eV. Isobutane was used for chemical ionization (CI). High boiling liquids were analyzed by direct insertion probe. The ion source was operated at 200 °C. Data reported refer to the mass (m/e) and, in parentheses, the relative abundance of ion fragments.

^1H, $^{13}C\{^1H\}$ and ^2H Nuclear magnetic resonance data were obtained on a Bruker AMX-400 spectrometer equipped with a BT 1000 temperature control unit at an operating frequency of 400.13, 100.62 and 61.43 MHz, respectively. Unless specified, spectra were recorded at 298 °K in $CDCl_3$. ^1H chemical shifts are reported relative to TMS (δ 0 ppm). ^2H chemical shifts are referenced to C_6D_6 (δ 7.40 ppm). ^{13}C $\{^1H\}$ chemical shifts are referenced to: δ 77.0 ppm ($CDCl_3$ solutions), δ 128.0 ppm (C_6D_6 solutions) and δ 68.6 ppm (THF solutions). Unless specified, tin-proton coupling constants are reported as the average of ^{119}Sn and ^{117}Sn values.

Infra red spectra were recorded on Perkin-Elmer Model 599 B (calibrated to polystyrene) and Perkin-Elmer Model 1605 FT-IR spectrophotometers. Vapour phase IR spectra were obtained on a Bruker GC/FT/IR Model IFS85 spectrometer. FT-IR data reported for liquids are of neat films between NaCl discs. Routine IR spectra were obtained at ambient temperature with a resolution of 4 cm^{-1}.

Densities of liquids are reported as averages of three weight determinations of 1 mL samples. The volume was measured by using a 1 mL syringe fitted with a 20 gauge needle.

Elemental analyses were performed by Mr. M. K. Yang of the microanalytical laboratory at Simon Fraser University using a Carlo Erba Model-1106 Elemental Analyzer.

CHAPTER I

I.1 Preparation of γ-Trialkylsilyl- and γ-Trialkylstannyl-2(*E*)-Allylic Substrates.

I.1.1 *$PhMe_2Si$ Substituent.*

2-Octyn-1-ol (2). This compound was prepared according to a literature procedure.[13] To a two-necked round-bottom flask containing a cooled (-78° C) solution of 1-heptyne (20 g, 0.21 mol) in THF (200 mL), was added a slight excess of *n*-BuLi (84 mL, 0.21 mol). After 30 min, paraformaldehyde (6.3 g, 0.21 mol) was added to the faint green solution as a solid, in one portion. The resultant suspension was warmed to room temperature over a period of ca. 12 hr during which time a homogeneous, colourless solution formed. The mixture was poured into an ice-water slurry (100 mL) and this mixture subsequently

extracted with diethyl ether (3 x 50 mL). The combined organic fractions were dried over $MgSO_4$ and the solvent removed under reduced pressure. The remaining yellow oil was distilled under reduced pressure to afford **2** (22.5 g, 86 %): bp: 51 °C/0.25 mmHg (lit.[71] 91 °C/12 mmHg). The authenticity of **2** was verified by coinjection (GC) with an independently prepared and previously characterized sample.[9]

3-Dimethyl(phenyl)silyl-2(*E*)-octen-1-ol (3). This compound was prepared according to a literature procedure[12] from propargylic alcohol, **2**, (1.70 g, 10 mmol) in THF (10 mL). The solution was quenched at room temperature by slow addition of a saturated aqueous solution of NH_4Cl (50 mL) and then sufficient HCl (2 M) added to dissolve zinc and aluminum hydroxides. Extractive work-up with diethyl ether (3 x 50 mL) yielded, after concentration, a crude oil which was flash chromatographed (SiO_2, 10 % EtOAc in hexanes) to afford pure **3** (2.18 g, 83 %) as a colourless liquid. The authenticity of **3** was verified by coinjection (GC) with an independently prepared and previously characterized sample.[9]

1-Chloro-3-dimethyl(phenyl)silyl-2(*E*)-octene (4). This compound was prepared according to a literature procedure[14] from allylic alcohol, **3**, (2.0 g, 7.6 mmol). After stirring the solution at room temperature for 45 min, the reaction mixture was extracted with hexanes (3 x 50 mL) and the combined organic fractions concentrated under reduced pressure. The remaining oil was flash chromatographed (SiO_2, 100 % hexanes) to afford **4** (1.73 g, 81 %) as a colourless liquid. The authenticity of **4** was verified by coinjection (GC) with an independently prepared and previously characterized sample.[9]

I.1.2 *Me_3Si Substituent (attempted).*

[a] To a solution of Me_3SiLi[72] (10 mmol) in HMPA (10 mL) was added at -10 °C $ZnBr_2$ (1.13 g, 5 mmol) giving rise to a pale yellow, homogeneous solution within 30 min. Propargylic alcohol, **2**, (0.5 g, 4 mmol) was added followed by CuCN (0.02 g, 0.2 mmol) and the solution stirred at room temperature for several hours. GC/MS analysis of the crude mixture revealed that the starting alcohol, **2**, had been consumed to form a major reaction component that exhibited a mass fragmentation pattern consistent with the Me_3Si ether of **2**: (M^+ 198), 183(-Me), 153(- 3xMe), 127(- C_5H_{11}), 75(= $HOSiMe_3$), 74(= $OSiMe_3$). This material proved to be unstable to silica and purification of the crude extract by flash chromatography (SiO_2, 5 % EtOAc in hexanes) resulted in conversion to starting alcohol, **2**.

[b] To a solution of $ZnEt_2$ (1.02 mL, 10 mmol) in diethyl ether (5 mL) was transferred a solution of Me_3SiLi (10 mmol) [prepared by reacting $(Me_3Si)_2$ with MeLi][72] in HMPA (5 mL) at 0 °C. Propargylic alcohol, **2**, (0.5 g, 4 mmol) was added to the yellow, homogeneous solution after 30 min followed by CuCN (0.02 g, 0.22 mmol). Stirring was continued at room temperature for several hours during which time the solution became progressively darker to eventually form a heterogeneous, black mixture. GC analysis of a quenched aliquot withdrawn from the reaction mixture showed that starting material had been consumed to form (unidentified) low boiling compounds.

I.1.3 *n-Bu_3Sn Substituent.*

3-Tri-*n*-butylstannyl-2(*E*)-octen-1-ol (5). To a solution of

stannylzinc reagent, **21a**, (17.8 mmol) in THF (50 mL) was added a solution of propargylic alcohol, **2**, (1.0 g, 7.9 mmol) in THF (2 mL) at -30 °C followed by addition of CuCN (0.15 g, 1.7 mmol). Addition of CuCN caused the solution to briefly turn red, then return to its original amber colour after approximately 30 sec. The solution was warmed to room temperature overnight. Standard work-up and purification yielded **5** (1.35 g, 41 %) as a colourless oil: IR (neat) 3330(s), 2954(s), 2853(s), 2360(w), 1464(s), 1418(w), 1376(m), 1340(w), 1292(w), 1060(m), 1004(s) cm^{-1}; ^1H NMR δ 5.37 (1 H, tt, J = 6 Hz; 1.2 Hz; $^3J^{119}_{Sn-H}$ = 70 Hz; $^3J^{117}_{Sn-H}$ = 67 Hz, $Bu_3SnRC{=}CHR$), 4.23 (2 H, d, J = 2 Hz), 2.26 (2 H, t, J = 7 Hz; $^3J_{Sn-H}$ = 56 Hz, CH_2OH), 1.52-1.44 (6 H, m, $R_3Sn(RCH_2)C{=}CHR$), 1.35-1.28 (12 H, m, CH_2), 0.96-0.86 (18 H, m, CH_2, CH_3); mass spectrum (EI) 361(M^+ -Bu, 100), 359(72), 357(43), 305(75), 303(57), 301(35), 249(95), 247(68), 245(41), 179(42), 177(60), 175(39), 137(78), 135(59), 133(38), 121(39), 119(31); Anal. Calcd. for $C_{20}H_{42}OSn$: C, 57.55; H, 10.07. Found: C, 57.26; H, 10.10.

1-Chloro-3-tri-*n*-butylstannyl-2(*E*)-octene (6). To an oven dried flask was added, under an atmosphere of argon, PPh_3 (0.7 g, 4 mmol) and the flask subsequently fitted with a rubber serum stopper. Anhydrous CCl_4 (3 mL) was then injected, followed by transfer of a solution of allylic alcohol, **5**, (0.9 g, 2 mmol) in anhydrous CH_3CN (3 mL). After stirring at room temperature for 1 hr the solution was concentrated under reduced pressure and the resultant yellow paste suspended in diethyl ether (2 mL). This mixture was subjected to flash chromatography (SiO_2, hexanes) to give **6** containing allylic chloride, **8**, as a minor impurity (6 % by GC). The latter was removed from the mixture under high vacuum overnight to yield **6** (0.89 g, 95 %) as a colourless liquid: d = 1.072; ^1H NMR (C_6D_6) δ 5.92 (1 H, tt, J = 7 Hz; 1.1 Hz; $^3J^{119}_{Sn-H}$ = 66 Hz; $^3J^{117}_{Sn-H}$ = 64

Hz, $Bu_3SnRC{=}CHR$), 3.94 (2 H, d, J = 7 Hz, CH_2Cl), 2.31 (2 H, dt, J = 7 Hz; 1.1 Hz; $^3J_{Sn\text{-}H}$ = 57 Hz, $R_3Sn(RCH_2)C{=}CHR$), 1.72-1.52 (6 H, m, CH_2), 1.46-1.35 (8 H, m, CH_2), 1.34-1.21 (4 H, m, CH_2), 1.10-0.92 (18 H, m, CH_2, CH_3); mass spectrum (EI) 381(22), 379(M^+ -Bu, 54), 377(44), 375(20), 343(14), 341(12), 325(19), 323(44), 321(31), 319(17), 291(14), 289(13), 273(17), 271(36), 269(100), 267(99), 265(58), 215(13), 213(27), 211(27), 209(13), 179(24), 177(47), 175(33), 173(19), 157(19), 155(35), 153(28), 151(17), 121(21), 119(15), 117(11), 67(19), 57(23); Anal. Calcd. for $C_{20}H_{41}ClSn$: C, 55.05; H, 9.40. Found: C, 54.88; H, 9.22.

3-Tri-*n*-butylstannyl-2(*E*)-octenyl acetate (**7**). To a solution of allylic alcohol, **5**, (1.0 g, 2.4 mmol) in acetic anhydride (5 mL) was added pyridine (ca. 2 mL) and the solution stirred at room temperature for 45 min. The solution was concentrated under high vacuum and then subjected to flash chromatography (SiO_2, 5 % EtOAc in hexanes) where compound **7** (1.10 g, 91 %) was obtained as a colourless oil: IR (neat) 2960(s), 2940(s), 2890(s), 2870(s), 1470(m), 1380(m), 1080(w), 1030(m), 970(w) cm^{-1}; ^1H NMR δ 5.62 (1 H, tt, J = 6.5 Hz; 1.5 Hz; $^3J^{119}_{Sn\text{-}H}$ = 68 Hz; $^3J^{117}_{Sn\text{-}H}$ = 65 Hz, $Bu_3SnRC{=}CHR$), 4.64 (2 H, d, J = 6.5 Hz, CH_2OAc), 2.29 (2 H, t, J = 7.5 Hz; $^3J_{Sn\text{-}H}$ = 57 Hz, $R_3Sn(RCH_2)C{=}CHR$), 2.08 (3 H, s, $C(O)CH_3$), 1.53-1.45 (6 H, m, CH_2), 1.36-1.27 (12 H, m, CH_2), 0.98-0.88 (18 H, m, CH_2, CH_3); mass spectrum (EI) 403(M^+ -Bu, 8), 401(7), 399(4), 293(100), 291(79), 289(48), 233(24), 231(17), 229(10), 179(74), 177(77), 175(50), 121(21), 119(17), 117(11), 67(14), 57(15), 43(38); Anal. Calcd. for $C_{22}H_{44}O_2Sn$: C, 57.52; H, 9.59. Found: C, 57.56; H, 9.89.

Methyl 2-octynoate (**9**). To a solution of 1-heptyne (8.73 mL, 65 mmol) in THF (100 mL) was added at -78 °C *n*-BuLi (26 mL, 2.5 M, 65 mmol)

followed after 30 min by methyl chloroformate (5.0 mL, 65 mmol). The solution was warmed to room temperature, quenched with brine (10 mL) and diluted with diethyl ether (50 mL). The mixture was washed with brine (3 x 50 mL) and the pooled aqueous layers back-extracted with hexanes (10 mL). Concentration of the organic fractions yielded after distillation **9** (9.76 g, 97 %) as a colourless liquid: bp: 37 °C/0.01 mmHg; IR (neat) 2956(s), 2863(s), 2238(s), 1718(s), 1459(m), 1435(s), 1254(s), 1077(s) cm^{-1}; ^1H NMR δ 3.75 (3 H, s, OCH_3), 2.32 (2 H, t, J = 7.1 Hz, $CH_2C{\equiv}CR$, 1.62-1.53 (2 H, m, CH_2), 1.42-1.26 (4 H, m, CH_2), 0.89 (3 H, t, J = 7.1 Hz, CH_2, CH_3); mass spectrum (EI) 139(M^+ -Me, 7), 123(46), 95(91), 93(39), 81(28), 79(81), 69(28), 67(74), 66(100), 59(37), 55(76), 53(50); Anal. Calcd. for $C_9H_{14}O_2$: C, 70.13; H, 9.09. Found: C, 69.99; H, 9.05.

Methyl 3-tri-*n*-butylstannyl-2(*E*)-octenoate (10). This compound was prepared following a literature procedure.[30b] To a solution of *n*-Bu_3SnLi[21] (70 mmol) in THF (200 mL) was added at -78 °C CuBr·DMS (14.4 g, 70 mmol). The solution turned black immediately; the solution was stirred at -78 °C for 30 min. A solution of alkynynoate, **9**, (8.3 g, 54 mmol) in THF (10 mL) was then added to the mixture. After 1 hr anhydrous MeOH (excess) was introduced and the solution warmed to room temperature overnight. The mixture was subsequently poured into brine (300 mL) and extracted with diethyl ether (3 x 50 mL). Concentration of the combined organic layers under reduced pressure yielded a crude liquid which was purified by flash chromatography (SiO_2, 3 % EtOAc in hexanes) to afford **10** (28.4 g, 91 %) as a colourless liquid: IR (neat) 2956(s), 2854(s), 1721(s), 1592(m), 1464(m), 1432(w), 1377(w), 1351(m), 1254(w), 1191(s), 1167(s), 1128(w), 1073(w), 1040(w) cm^{-1}; ^1H NMR (C_6D_6) δ 6.36 (1 H, t, J = 1.2 Hz; $^3J^{119}_{Sn\text{-}H}$ = 67 Hz; $^3J^{117}_{Sn\text{-}H}$ = 65 Hz, $Bu_3SnRC{=}CHR$), 3.46 (3 H, s, OCH_3), 3.27 (2 H, dt, J = 7 Hz; 1.2 Hz; $^3J_{Sn\text{-}H}$ = 59 Hz,

$R_3Sn(RCH_2)C=CHR)$, 1.70-1.55 (8 H, m, CH_2), 1.53-1.33 (10 H, m, CH_2), 1.12-0.92 (18 H, m, CH_2, CH_3); mass spectrum (EI) 389(M^+ -Bu, 100), 387(70), 385(43), 333(51), 331(36), 329(22), 277(43), 275(37), 273(25), 179(20), 177(27), 175(18), 151(32), 149(27), 147(15); Anal. Calcd. for $C_{21}H_{42}O_2Sn$: C, 56.50; H, 9.42. Found: C, 56.88; H, 9.27.

Alternative preparation of 5. To a solution of alkenoate, **10**, (7.72 g, 17.4 mmol) in THF (150 mL) was added dropwise, at -78 °C, neat diisobutylaluminum hydride (7.5 mL, 42 mmol) and the solution stirred for 1 hr. The solution was warmed to -30 °C and carefully quenched (exothermic !) after 1 hr by dropwise addition of MeOH. The mixture was diluted at room temperature with brine (200 mL), acidified (2 M HCl) and extracted with diethyl ether (3 x 50 mL). The combined organic extracts were concentrated and the resultant crude oil purified by flash chromatography (SiO_2, 10 % EtOAc in hexanes) to afford **5** (6.71 g, 93 %) as a colourless oil.

Alternative preparation of 6. This compound was prepared by reacting allylic alcohol **5** (6.71 g, 16.1 mmol) with *N*-chlorosuccinimide (0.23 g, 1.7 mmol) and DMS (0.15 mL, 2 mmol) in CH_2Cl_2 (5 mL) at 0 °C for 1 hr according to a literature procedure.[18] Work-up and purification by flash chromatography (SiO_2, hexanes) yielded **6** (5.9 g, 84 %).

I.1.4 *Attempted Syntheses of Allylic Chloride 6.*

[a] To a solution of allylic alcohol, **5**, (0.20 g, 0.48 mmol) in CCl_4 (2 mL) was added at room temperature PPh_3 (0.25 g, 0.95 mmol). Wet CH_3CN (2 mL) was added to the mixture after the PPh_3 had completely dissolved (several min). After 45 min the solution was concentrated under reduced pressure to

approximately 1 mL and the resulting slurry purified by flash chromatography (SiO_2, hexanes) to yield 1-chloro-2(*Z*)-octene, **8**, (0.06 g, 90 %) as a colourless liquid. The authenticity of this compound was verified by coinjection (GC) with an independently prepared and previously characterized sample.[9]

[b] To a solution of allylic alcohol, **5**, (0.20 g, 0.48 mmol) in dry benzene (5 mL) was added at room temperature, under argon, $SOCl_2$ (0.05 mL, 0.7 mmol). Gas chromatographic analysis of a quenched (H_2O) sample taken from the mixture after 2 min revealed the major product to be 1-chloro-2(*Z*)-octene.

[c] To a solution of allylic alcohol, **5**, (0.20 g, 0.48 mmol) in freshly distilled THF (5 mL) was added at room temperature anhydrous $ZnCl_2$ (0.07 g, 0.5 mmol) followed by PPh_3 (0.40 g, 1.5 mmol). After the solids had dissolved (ca. 10 min) diethyl azodicarboxylate (0.24 mL, 1.5 mmol) was added slowly *via* syringe and the solutions stirred for 24 hr at room temperature.[73] Gas chromatographic analysis of aliquots taken from the solution at regular intervals revealed that **6** had not formed. GC integration revealed that the ratio of **5** to dodecane (ISTD) remained constant throughout the reaction indicating that the starting material was not consumed.

I.2 Investigation of the Destannylation of 3-Tri-*n*-butylstannyl Allylic Substrates.

I.2.1 *Attempted Destannylation.*

[a] To a solution of allylic acetate, **7**, (0.50 g, 1 mmol) in THF (10 mL) was added either KCl (0.08 g, 1 mmol), KBr (0.13 g, 1 mmol) or KI (0.18 g, 1 mmol) followed by 18-crown-6 (0.29 g, 1 mmol). Transformation of **7** to the

destannylated product, **11**, was not detected even after refluxing for 4 hr.

[b] To a solution of allylic acetate, **7**, (0.50 g, 1 mmol) in CCl_4 (5 mL) CH_3CN (5 mL) was added AIBN (0.50 g, 2.6 mmol). The mixture was stirred at 50 °C overnight in an oil bath with simultaneous irradiation with a 100 W light bulb. Comparison of GC integration values indicated that the composition of the mixture remained unchanged i.e., none of the destannylated material, **11**, was detected.

I.2.2 *Electrophilic Capture of the Presumptive Vinyl Anion Intermediate.*

[a] With H_2O: 2(*Z*)-Octenyl acetate (11). An anhydrous solution of allylic acetate, **7**, (0.10 g, 0.22 mmol), PPh_3 (0.12 g, 0.46 mmol), CD_3CN (2 mL), CCl_4 (2 mL) [prepared as described in the synthesis of allylic chloride, **6**] was stirred at room temperature for 1 hr followed by addition of H_2O (excess). Extraction with diethyl ether (3 x 10 mL), concentration and purification of the crude liquid by flash chromatography (SiO_2, 15 % EtOAc in hexanes) yielded **11** (0.035 g, 95 %) as a colourless liquid. ^1H NMR and MS data for the isolated material were identical to those of an authentic sample.[9]

[b] With ^2H_2O: [3-^{2}H]-2(*Z*)-octenyl acetate (12). An anhydrous solution of allylic acetate, **7**, (0.1 g, 0.22 mmol), PPh_3 (0.12 g, 0.46 mmol), CH_3CN (2 mL), CCl_4 (2 mL) was stirred at room temperature for 1 hr followed by addition of ^2H_2O (excess). Work-up and purification as in [a] yielded **12** (0.03 g, 80 %) as a colourless liquid: ^1H NMR δ 5.61-5.44 (1 H, m, ^{2}HRC=C*H*R), 4.62 (2 H, d, J = 7 Hz, CH_2OAc), 2.13-2.06 (2 H, t, J = 7 Hz, ^{2}H(RCH_2)C=CHR), 2.06 (3 H, s, C(O)CH_3), 1.42-1.22 (6 H, m, CH_2), 0.90 (3 H, t, J = 7 Hz, CH_3); mass spectrum (EI) 171(M^+, <1), 142(3), 129(32), 128(12), 96(17), 82(62), 69(38),

68(49), 55(47), 43(100).

[c] With MeI: To an anhydrous solution of allylic acetate, **7**, (0.50 g, 1.1 mmol), PPh_3 (0.50 g, 1.9 mmol), CH_3CN (5 mL), CCl_4 (5 mL) was added at room temperature MeI (1.3 mL, 2.1 mmol). The mixture was stirred at room temperature for 12 hr and the reaction monitored by GC analysis of aliquots removed at regular intervals. Starting material was not consumed and no new GC peaks attributable to coupled product were detected.

[d] With allyl bromide: To an anhydrous solution [b] was added allyl bromide (0.04 mL, 46 mmol) and the mixture stirred at room temperature for 12 hr. GC analysis of aliquots removed at regular intervals revealed that starting material was not consumed. No new GC peaks attributable to coupled product were detected.

[e] With benzaldehyde: 1,1-dichloro-2-phenylethene (13). To anhydrous solution [b] was added benzaldehyde (0.5 mL, 49 mmol) at room temperature and the mixture stirred for 1 hr. Work-up and purification yielded **13** as a colourless liquid: ^{1}H NMR δ 7.57-7.50 (2 H, m, Ar), 7.42-7.35 (3 H, m, Ar), 6.87 (1 H, s, Ph*H*C=CCl_2); mass spectrum (EI): 176(10), 174(67), 172(M^+, 100), 139(21), 137(65), 112(19), 102(19), 102(96), 101(54), 75(29), 68(9), 51(27).

I.3 Preparation of Propargylic Substrates.

1-Tetrahydropyranyloxy-2-octyne (14). This compound was prepared following a literature procedure.[74] To a cooled solution (0 °C) of alcohol, **2**, (1.0 g, 7.9 mmol) in CH_2Cl_2 (5 mL) was added an excess of 3,4-dihydro-2*H*-pyran (1 mL) followed by several crystals (ca. 2 mg) of *p*-

toluenesulfonic acid. After 10 min the flask was removed from the ice bath and stirring continued for 1 hr at room temperature. Solvent and unreacted 3,4-dihydro-*2H*-pyran were removed under reduced pressure and the remaining oil purified by flash chromatography (SiO_2, 5 % EtOAc in hexanes) to yield **14** (1.32 g, 80 %) as a colourless oil: IR (neat) 2936(s), 2860(s), 2237(w), 1455(m), 1344(m), 1201(m), 1118(m), 1024(m) cm^{-1}; ^1H NMR δ 4.80 (1 H, t, *J* = 3.5 Hz, C*H* (THP)), 4.28 (1 H, dt, *J* = 14 Hz; 2.5 Hz, CH*H*OTHP), 4.18 (1 H, dt, *J* = 14 Hz; 2.5 Hz, CH*H*OTHP), 3.88-3.82 (1 H, m, CH*H* (THP)), 3.55-3.48 (1 H, m, CH*H* (THP)), 2.18 (2 H, tt, *J* = 7 Hz; 2.5 Hz, $CH_2C{\equiv}CR$), 1.90-1.70 (2 H, m, CH_2), 1.67-1.47 (6 H, m, CH_2), 1.40-1.25 (4 H, m, CH_2), 0.88 (3 H, t, *J* = 7 Hz, CH_2, CH_3); mass spectrum (CI) 211($(M+1)^+$, 100), 109(17); Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.47. Found: C, 74.50; H, 10.70.

1-(*tert*-Butyldimethylsiloxy)-2-octyn-1-ol (15). To a solution of alcohol, **2**, (1.0 g, 7.9 mmol) in anhydrous CH_2Cl_2 (50 mL) was added *t*-$BuMe_2SiCl$ (1.3 g, 8.6 mmol) and the slurry stirred at room temperature until a clear solution was obtained. The solution was cooled to 0 °C and an excess of dry Et_3N (ca. 3 mL) added followed by several crystals (ca. 5 mg) of 4-dimethylaminopyridine. The reaction vessel was removed from the cooling bath and the solution stirred for 3 hr at room temperature. The mixture was diluted with diethyl ether (100 mL), washed with brine (50 mL) and the organic layer dried over $MgSO_4$. Concentration under reduced pressure yielded crude **15** (> 90 % pure). Removal of minor contaminants was achieved by flash chromatography (SiO_2, 15 % EtOAc in hexanes) to yield **15** (1.80 g, 94 %) as a colourless liquid: IR (neat) 2956(s), 2930(s), 2858(s), 2234(w), 1471(m), 1462(m), 1368(m), 1253(m), 1081(s) cm^{-1}; ^1H NMR δ 4.30 (2 H, t, *J* = 2 Hz, CH_2OSi*t*-$BuMe_2$), 2.19 (2 H, tt, *J* = 7 Hz; 2 Hz, CH_2), 1.49 (2 H, quint, *J* = 7 Hz,

CH_2), 1.40-1.25 (4 H, m, CH_2), 0.93-0.83 (12 H, m, CH_2, CH_3), 0.12 (6 H, s, $Si(CH_3)_2$); mass spectrum (CI) 241((M+1)$^+$, 100), 183(28), 145(12), 109(49); Anal. Calcd. for $C_{14}H_{28}OSi$: C, 70.00; H, 11.67. Found: C, 69.78; H, 11.45.

2-Octynyl acetate (16). To a solution of alcohol, **2**, (1.00 g, 7.94 mmol) in acetic anhydride (3 mL) was added pyridine (ca. 2 mL) and this mixture stirred at room temperature for 45 min. Concentration under high vacuum yielded a crude liquid which was purified by flash chromatography (SiO_2, 15 % EtOAc in hexanes) to afford **16** (0.71 g, 53 %) as a colourless liquid: IR (neat) 2934(s), 2861(s), 2238(w), 1749(s), 1456(m), 1436(m), 1378(m), 1359(m), 1223(s), 966(m) cm^{-1}; ^{1}H NMR δ 4.67 (2 H, t, J = 2.5 Hz, CH_2OAc), 2.20 (2 H, tt, J = 7 Hz; 2.5 Hz, $RCH_2C{\equiv}CR$), 2.10 (3 H, s, $C(O)CH_3$), 1.35 (2 H, quint, J = 7 Hz, CH_2), 1.25 (4 H, m, CH_2), 0.83 (3 H, t, J = 7 Hz, CH_3); mass spectrum (CI) 169((M+1)$^+$, 100), 127(83), 109(92); Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.43; H, 9.52. Found: C, 71.36; H, 9.74.

1-Tetrahydropyranyloxy-2-butyne (17). This compound was prepared according to the procedure outlined for the synthesis of alkyne **14**, starting with 2-butyn-1-ol (3.0 g, 43 mmol). Work-up and purification by distillation yielded **17** (4.97 g, 75 %) as a colourless oil: d = 0.966; bp: 55 °C/0.25 mmHg; IR (neat) 2942(s), 2869(s), 2222(w), 1722(w), 1442(m), 1346(m), 1132(m), 1117(m), 1026(s) cm^{-1}; ^{1}H NMR δ 4.80 (1 H, t, J = 3 Hz, CH (THP), 4.28 (1 H, dq, J = 15.5 Hz; 2.5 Hz, $CHHOTHP$), 4.16 (1 H, dq, J = 15.5 Hz; 2.5 Hz, $CHHOTHP$), 3.88-3.79 (2 H, m, CH_2 (THP)), 1.85 (3 H, t, J = 2.5 Hz, CH_3), 1.83-1.48 (6 H, m, CH_2 (THP)); mass spectrum (EI) 153(M$^+$ -H, 3), 111(25), 101(79), 85(100), 84(18), 83(26), 71(12), 69(10), 67(25), 57(15), 56(13), 55(30), 53(53), 43(19), 41(19), mass spectrum (CI) 155(M+1)$^+$; Anal. Calcd. for $C_9H_{14}O_2$: C, 70.13; H, 9.09. Found: C, 70.28; H, 8.81.

Alternative preparation of 17. To a solution of 3-tetrahydropyranyloxy-1-propyne (10.0 g, 71.4 mmol) in THF (200 mL) at -78 °C was added *n*-BuLi (29 mL, 73 mmol) over a period of 10 min. After 30 min at -78 °C, MeI (4.6 mL, 74 mmol) was added and the solution stirred at -30 °C for 30 min before adding anhydrous HMPA (ca. 100 mL). The mixture was warmed slowly to room temperature and then allowed to stand overnight; it was then diluted with brine (50 mL) and hexanes (100 mL). The solution was washed with brine (3 x 100 mL), the aqueous layers back-extracted with hexanes and the combined organic fractions dried ($MgSO_4$) and concentrated under reduced pressure. Distillation of the crude pale green oil yielded **17** (10.74 g, 98 %) as a colourless liquid.

I.4 Stannylzincation of Alkynes.

I.4.1 *Of Propargylic Substrates.*

General Procedure. Substrates were added to the stannylzinc reagent, **21a**, in THF (20 mL) at -30 °C followed by CuCN (0.18 g, 0.20 mmol, 10 %). Solutions were warmed slowly to room temperature and allowed to stand overnight. Reaction mixtures were diluted with brine (100 mL), extracted with hexanes (3 x 50 mL) and the organic layers combined, dried ($MgSO_4$) and concentrated under reduced pressure. The crude products were purified by flash chromatography.

1-Tetrahydropyranyloxy-3-tri-*n*-butylstannyl-2(*E*)-octene (18). Reaction of alkyne, **14**, (0.20 g, 0.95 mmol) yielded **18** (0.15 g, 32 %) as a colourless oil after work-up and purification by flash chromatography (SiO_2, 5 %

EtOAc in hexanes): IR (neat) 2956(s), 2922(s), 1463(m), 1376(m), 1117(m), 1077(m), 1024(s) cm^{-1}; ^1H NMR δ 5.90 (1 H, t, J = 6 Hz; $^3J_{Sn-H}$ = 70 Hz, $(R_3Sn)RC{=}CHR$), 4.63 (1 H, t, J = 4 Hz, CH (THP), 4.26 (1 H, dd, J = 12.5 Hz, 5.5 Hz, $CHHOTHP$)), 4.17 (1 H, dd, J = 12.5 Hz; 7 Hz, $CHHOTHP$)), 3.93-3.86 (1 H, m, CHH (THP)), 3.54-3.48 (1 H, m, CHH (THP)), 2.35-2.15 (2 H, m, $(R_3Sn)RCH_2C{=}CHR$), 1.91-1.80 (1 H, m, CHH (THP)), 1.77-1.68 (1 H, m, CHH (THP)), 1.63-1.42 (10 H, m, CH_2), 1.35-1.22 (12 H, m, CH_2), 0.93-0.83 (18 H, m, CH_2, CH_3); Anal. Calcd. for $C_{25}H_{50}O_2Sn$: C, 59.88; H, 9.98. Found: C, 59.61; H, 9.69.

1-(*tert*-Butyldimethylsiloxy)-3-tri-*n*-butylstannyl-2(*E*)-octen-1-ol (19). Reaction of alkyne, **15**, (0.25 g, 1.0 mmol) yielded **19** (0.2 g, 36 %) as a colourless oil after work-up and purification by flash chromatography (SiO_2, hexanes): IR (neat) 2956(s), 2926(s), 2855(s), 1464(m), 1253(m), 1096(m), 1072(m) cm^{-1}; ^1H NMR δ 5.62 (1 H, tt, J = 5.5 Hz; 1.5 Hz; $^3J^{119}_{Sn-H}$ = 72 Hz; $^3J^{117}_{Sn-H}$ = 70 Hz, $(Bu_3SnRC{=}CHR)$), 4.30-4.25 (2 H, m, CH_2OSi*t*-$BuMe_2$), 2.10 (2 H, t, J = 7 Hz; $^3J_{Sn-H}$ = 58 Hz, $(R_3Sn)RCH_2C{=}CHR$)), 1.52-1.43 (6 H, m, CH_2), 1.35-1.24 (12 H, m, CH_2), 0.92-0.83 (27 H, m, CH_2, CH_3), 0.10 (6 H, s, $Si(CH_3)_2$); mass spectrum (CI) 475(M^+ -Bu, 14), 473(12), 471(5), 291(100), 289(76), 287(24), 133(29); Anal. Calcd. for $C_{26}H_{56}OSiSn$: C, 58.75; H, 10.55. Found: C, 58.60; H, 10.25.

1-Tri-*n*-butylstannyl-2-octyne (20). Reaction of propargylic acetate, **16**, (0.45 g, 2.6 mmol) yielded **20** (0.68 g, 65 %) as a colourless oil after work-up and purification by flash chromatography (SiO_2, hexanes): IR (neat) 2940(s), 2910(s), 2840(s), 2200(w), 1453(m), 1370(m), 1150(m), 1068(m) cm^{-1}; ^1H NMR δ 2.13 (2 H, tt, J = 4 Hz; 2.5 Hz, $CH_2C{\equiv}CCH_2SnBu_3$), 1.61-1.40 (10 H, m, CH_2), 1.39-1.24 (10 H, m, CH_2), 1.05-0.85 (18 H, m, CH_2, CH_3); ^{13}C NMR δ 80.0

(C≡C), 77.9 (C≡C), 31.6, 31.2, 29.3, 29.0, 27.3($^1J_{Sn-C}$ = 53.5 Hz), 22.3, 19.1, 14.0, 13.6, 9.8($^1J_{Sn-C}$ = 312.4 Hz); mass spectrum (EI) 343(M^+ -Bu, 12), 341(10), 339(5), 291(55), 289(42), 287(21), 235(68), 233(57), 231(36), 177(100), 175(66), 173(23), 121(40), 119(34), 117(19), 95(28), 83(25), 71(33), 70(29), 69(26), 67(31), 57(45), 55(41); Anal. Calcd. for $C_{20}H_{40}Sn$: C, 60.14; H, 10.02. Found: C, 60.34; H, 10.20.

I.4.2 *Stannylzincation of Alkyne **17** with Various Reagents.*

General Procedure. To solutions of stannylzinc reagents **21a-22b** (2 mmol) were sequentially added alkyne, **17**, (0.21 mL, 1.3 mmol) in THF (2 mL) and CuCN (0.018 g, 0.20 mmol). The solutions were warmed to room temperature over 5 hr and quenched by careful addition of a saturated NH_4Cl solution. The mixtures were diluted with brine (100 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and the resulting liquids purified by flash chromatography (SiO_2, 5 % EtOAc in hexanes).

Preparation of (n-$Bu_3Sn)_2Zn$ (21a) derived from (n-$Bu_3Sn)_2$. To a solution of n-Bu_3SnLi (4.0 mmol) [prepared by treatment of (n-$Bu_3Sn)_2$ with n-BuLi at -30 °C for 1 hr][20] in THF (20 mL) at -30 °C was added anhydrous $ZnBr_2$ (0.45 g, 2.0 mmol) or $ZnCl_2$ (0.27 g, 2.0 mmol). The yellow suspension was subsequently warmed to 0 °C and stirred until all the solid zinc halide had reacted to form an amber solution (ca. 30 min).

Preparation of n-$Bu_3SnZnEt_2Li$ (21b) derived from (n-$Bu_3Sn)_2$. To a solution of n-Bu_3SnLi[20] (2.0 mmol) in THF (20 mL) at -30 °C was added $ZnEt_2$ (0.20 mL, 2.0 mmol) as a neat liquid. The mixture was stirred

at 0 °C for 30 min to give desired yellow solution

Preparation of (n-$Bu_3Sn)_2Zn$ (22a) derived from n-Bu_3SnH. A THF (20 mL) solution of this reagent was prepared in a similar manner to **21a** with the exception that n-Bu_3SnLi (4.0 mmol) was generated by deprotonation of n-Bu_3SnH with lithium diisopropylamide.[21] The tin anion prepared in this fashion reacted with $ZnBr_2$ (0.45 g, 2.0 mmol) or $ZnCl_2$ (0.27 g, 2.0 mmol) to give an amber coloured solution after stirring at 0 °C for 30 min.

Preparation of n-$Bu_3SnZnEt_2Li$ (22b) derived from n-Bu_3SnH. To a cooled (-30 °C) solution of n-Bu_3SnLi[21] (2 mmol) in THF (20 mL) was added neat $ZnEt_2$ (0.20 mL, 2.0 mmol). The mixture was stirred at 0 °C for 30 min to give the desired yellow solution.

[a] Reaction of alkyne, **17**, with stannylzinc reagent, **21a**, yielded **23** and **24** (98:2, 0.44 g, 76 %) as a colourless liquid after work-up and purification. Prolonged reaction times resulted in lower yields (r.t./12hr, 0.23 g, 39 %).

[b] Reaction of alkyne, **17**, with stannylzinc reagent, **21b**, yielded **23** and **24** (94:6, 0.42 g, 73 %) after work-up and purification.

[c] Reaction of alkyne, **17**, with stannylzinc reagent, **22a**, yielded no detectable amount of **23** (by GC). Alkyne **17** was recovered (0.16 g, 78 %) after work-up and purification.

[d] Reaction of alkyne, **17**, (2.0 g, 1.3 mmol) with stannylzinc reagent, **22b**, also yielded no detectable amount of **23** (by GC). Alkyne, **17**, was recovered (0.14 g, 70 %) after work-up and purification.

4-Tetrahydropyranyloxy-2-tri-*n*-butylstannyl-2(*E*)-butene (23). IR (neat) 2955(s), 2923(s), 2871(s), 2851(s), 1464(m), 1116(m), 1078(m), 1025(m) cm^{-1}; ^1H NMR δ 5.70 (1 H, m, $^3J_{Sn-H}$ = 70 Hz, $Bu_3SnRC{=}CHR$), 4.65-4.60 (1 H, m, C*H* (THP)), 4.33-4.25 (1 H, m, CH*H*OTHP), 4.22-4.15 (1 H, m, CH*H*OTHP), 3.95-3.87 (1 H, m, CH*H* (THP)), 3.55-3.48 (1 H, m, CH*H* (THP)), 1.95-1.80 (4 H, m, CH_2 (THP)), 1.78-1.68 (1 H, m, CH*H* (THP)), 1.63-1.44 (10 H, m, CH_2, CH_3), 1.28 (6 H, sext, *J* = 7 Hz, CH_2), 0.97-0.80 (15 H, m, CH_2, CH_3); mass spectrum (EI) 389(M^+ -Bu, 44), 387(32), 385(19), 305(66), 303(47), 301(28), 287(15), 285(10), 179(17), 177(31), 175(23), 173(13), 121(12), 85(100); Anal. Calcd. for $C_{21}H_{42}O_2Sn$: C, 56.50; H, 9.42. Found: C, 56.67; H, 8.93.

4-Tetrahydropyranyloxy-3-tri-*n*-butylstannyl-2(*E*)-butene (24). An analytically pure sample was prepared by purification of a mixture of **23** and **24** by flash chromatography (SiO_2, 2 % EtOAc in hexanes): IR (neat) 2954(s), 2925(s), 2871(s), 2851(s), 1456(m), 1128(m), 1078(m), 1025(m) cm^{-1}; ^1H NMR δ 5.64 (1 H, qt, *J* = 6.6 Hz; 2.5 Hz; $^3J^{119}_{Sn-H}$ = 71 Hz; $^3J^{117}_{Sn-H}$ = 69 Hz, $RHC{=}CRSnBu_3$), 4.66 (1 H, t, *J* = 3 Hz, C*H* (THP)), 4.55 (1 H, dq, *J* = 12 Hz; 1 Hz, CH*H*OTHP), 4.05 (1 H, dq, *J* = 12 Hz; 1 Hz, CH*H*OTHP), 3.90-3.79 (1 H, m, CH*H* (THP)), 3.55-3.46 (1 H, m, CH*H* (THP)), 1.91-1.79 (1 H, m, CH*H* (THP)), 1.67 (3 H, d, *J* = 6.6 Hz, CH_3), 1.66-1.58 (1 H, m, CH*H* (THP)), 1.56-1.42 (10 H, m, CH_2), 1.30 (6 H, sext, *J* = 7 Hz, CH_2), 0.91-0.84 (15 H, m, CH_2, CH_3); mass spectrum (EI) 389(M^+ -Bu, 71), 387(48), 385(31), 335(58), 333(50), 331(26), 251(100), 249(81), 247(49), 235(30), 233(28), 231(17), 179(70), 177(90), 175(59), 137(56), 135(42), 133(28), 121(35), 119(25), 117(15); Anal. Calcd. for $C_{21}H_{42}O_2Sn$: C, 56.50; H, 9.42. Found: C, 56.43; H, 9.25.

I.4.3 *Effect of Diisopropylamine and Lithium Diisopropylamide on Stannylzincation of Alkyne* ***17.***

[a] To a solution of *n*-Bu_3SnLi[20] (4 mmol) in THF (20 mL) at -30 °C was added diisopropylamine (0.56 mL, 4 mmol) followed by $ZnBr_2$ (0.45 g, 2 mmol) and the suspension stirred at 0 °C for 30 min. The yellow solution was cooled to -30 °C, alkyne, **17**, (0.21 mL, 1.3 mmol) was added followed by CuCN (0.018 g, 0.2 mmol) and the mixture warmed to room temperature over 5 hr. Work-up and purification in the usual manner yielded **23** and **24** (93:7 (by GC), 0.42 g, 73 %).

[b] To a solution of LDA (4 mmol) in THF (20 mL) at -30 °C was added $ZnBr_2$ (0.45 g, 2 mmol) and the suspension stirred at 0 °C for 30 min. To the colourless solution was then added *n*-Bu_3SnH (1.1 mL, 4 mmol) and the mixture stirred for 30 min. The mixture was cooled to -30 °C, alkyne, **17**, (0.21 mL, 1.3 mmol) added and the solution warmed with stirring to room temperature over 5 hr. Work-up and purification in the usual manner yielded **17** (0.14 g, 70 % recovered). Stannanes, **23** and **24**, were not detected by GC analysis.

I.4.4 *Effect of CuCN on Stannylzincation of Alkyne* ***17.***

General Procedure. The following experiments were conducted in a manner identical to that described for the stannylzincation of alkyne, **17**, (1.3 mmol) with stannylzinc reagent, **21a**, (2 mmol). Varying amounts of CuCN were added to these solutions which were then warmed to room temperature over 5 hr and subsequently quenched with MeOH. Work-up and purification was carried out as described above for stannylzincation reactions. Ratios of product isomers were determined by GC analysis.

[a] When no CuCN was added to the solution, work-up and purification yielded **23** and **24** (92:8, 0.15 g, 26 %).

[b] When 0.1 equiv. of CuCN (0.018 g, 0.2 mmol) was added to the solution, work-up and purification yielded **23** and **24** (98:2, 0.44 g, 76 %).

[c] When 0.5 equiv. of CuCN (0.09 g, 1 mmol) was added to the mixture, a burgundy solution was obtained immediately. Work-up and purification yielded **23** and **24** (26:74, 0.13 g, 23 %).

[d] When 1 equiv. of CuCN (0.18 g, 2 mmol) was added to the mixture a red solution as in [c] was formed. Work-up and purification yielded **23** and **24** (31:69, 0.12 g, 21 %).

I.5 **Model Syntheses of *Z,Z*-1,4-Dienes.**

1-Iodo-1-nonyne (25). To a solution of 1-nonyne (3.0 g, 24 mmol) in THF (50 mL) was added at -78 °C *n*-BuLi (10 mL, 2.5 M, 4.5 mmol). After 30 min a solution of I_2 (7.6 g, 60 mmol) in THF (ca. 10 mL) was slowly added until a red colour persisted for 10 min. The mixture was warmed to room temperature and diluted with brine (100 mL) and a saturated solution of $Na_2S_2O_8$ (10 mL). The solution was extracted with hexanes (3 x 50 mL) and the combined organic layers dried ($MgSO_4$) and concentrated to give a green oil. Purification by distillation afforded **25** (5.6 g, 93 %) as a faint pink liquid: bp: 56 °C/0.3 mmHg. The authenticity of **25** was verified by coinjection (GC) with an independently prepared and previously characterized sample.[9]

1-Iodo-1(*Z*)-nonene (26). To a solution of alkynyl iodide, **25**, (9.6 g, 38 mmol) in anhydrous diglyme (50 mL) at 0 °C was added BH_3·DMS (1.4 mL, 10-10.2 M, ca. 14 mmol). Stirring was continued for 1 hr at 0 °C and then at room temperature for 2 hr during which time the solution turned deep red. Propionic acid (3 mL, 40 mmol) was added and the mixture refluxed for 3 hr, cooled to room temperature and subsequently poured into an ice-water solution of NaOH (2 M, 200 mL). The quenched mixture was diluted with hexanes (100 mL) and washed with brine (3 x 50 mL). Back-extraction of the aqueous layers with hexanes (10 mL) followed by concentration of the combined organic fractions under reduced pressure yielded a crude orange liquid. Purification by distillation afforded **26** (4.70 g, 49 %) as a faint pink liquid: bp: 65 °C/0.3 mmHg; IR (vapour) 2964(m), 3080(s), 2868(m), 1607(w), 1464(w), 1288(m), cm^{-1}; ^1H NMR δ 6.02-6.13 (2 H, m, I*H*C=C*H*R), 2.18-2.08 (2 H, m, IHC=CHCH_2), 1.48-1.38 (2 H, m, CH_2), 1.38-1.20 (8 H, m, CH_2), 1.90 (3 H, t, J = 7 Hz, CH_3); mass spectrum (EI) 252(M^+, 3), 167(10), 154(13), 83(53), 70(14), 69(100), 67(10), 57(17), 56(13), 55(50), 53(10), 43(35), 41(39); Anal. Calcd. for $C_9H_{17}I$: C, 42.86; H, 6.75. Found: C, 43.14; H, 6.58.

1.5.1 *Cross-Coupling of Allylic Chloride **4** with 1(Z)-Nonenyldiisobutylalane.*

(6*E*,9*Z*)-6-Dimethyl(phenyl)silylheptadeca-6,9-diene (27). To a solution of vinylalane, **32**, (1.1 mmol) in diethyl ether (2 mL)/THF (2 mL) at -30 °C was added allylic chloride, **4**, (0.174 g, 1 mmol) and $Pd(PPh_3)_4$ (0.1 g, 0.1 mmol) and the yellow solution heated to 60 °C for 2 hr. The solution was diluted with aqueous NH_4Cl (100 mL) and this mixture extracted with hexanes (2 x 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The resulting crude oil was purified by

preparative TLC (SiO_2-$AgNO_3$ (20 %), hexanes) to yield **27** (0.22 g, 73 %) as a colourless oil: ^{1}H NMR δ 7.55-7.43 (2 H, m, Ar), 7.38-7.28 (3 H, m, Ar), 5.77 (1 H, t, *J* = 7Hz, $PhMe_2SiRC{=}CHR$), 5.45-5.32 (2 H, m, $RHC{=}CHR$), 2.85 (2 H, t, *J* = 6.5 Hz, $C{=}CCH_2C{=}C$), 2.13-2.00 (4 H, m, $C{=}CRCH_2$), 1.34-1.06 (16 H, m, CH_2), 0.83 (3 H, t, *J* = 7 Hz, CH_3), 0.76 (3 H, t, *J* = 7 Hz, CH_3), 0.28-0.25 (6 H, m, $Si(CH_3)_2$); ^{13}C NMR δ 139.4, 134.0, 130.5, 128.7, 127.7, 127.6, 32.2, 31.9, 29.9, 29.7, 29.3, 29.2, 27.3, 27.1, 22.7, 22.4, 14.1, 14.0, -2.6; mass spectrum (EI) 370(M^+, <1), 234(4), 152(1), 137(5), 136(14), 135(100), 123(1), 122(2), 121(11), 119(2), 109(2), 107(4), 105(3), 91(2), 81(2), 79(2), 59(4), 43(7); Anal. Calcd. for $C_{25}H_{42}Si$: C, 81.08; H, 11.35. Found: C, 80.97; H, 11.48.

(6*Z*,9*Z*)-Heptadeca-6,9-diene (28) [impure]. To a solution of diene, **27**, (0.19 g, 0.5 mmol) in DMF (5 mL) was added *n*-Bu_4NF (1.0 mL, 1.0 M, 1.0 mmol) and the mixture heated to 60 °C. Desilylation was monitored by GC and was complete after 1.5 hr to form diene, **28**, and other products that gave closely eluting peaks to that of **28** (GC) in an overall ratio of 72:28, respectively. The latter compounds were identified by GC/MS to have the same molecular weight as **28** and therefore are presumed to be isomers of **28**.

I.5.2 *Cross-Coupling of Allylic Chloride **6** with Z Vinyl Organometallic Reagents.*

B-methoxy-9-BBN (29). This compound was prepared according to a literature procedure.[75] Addition of anhydrous MeOH (2 mL, 32 mmol) to a THF solution of 9-BBN (40 mL, 0.5 M/THF, 20 mmol) afforded **29** (2.8 g, 92 %) as a colourless liquid after distillation: bp: 36 °C, 0.2 mmHg.

1(*Z*)-Nonenyl-9-BBN (30). This compound was prepared according to a literature procedure.[76] Treatment of the *Z* vinylboronate with $BF_3 \cdot Et_2O$ in the final step yielded a slurry which was passed through a sintered glass filter under argon to give a clear, pale green solution. Solvent was removed under reduced pressure and the remaining olive green oil distilled to afford **30** as a colourless liquid: bp: 60 °C/0.025 mmHg; ^{1}H NMR δ 6.43 (1 H, dt, *J* = 13.5 Hz; 7.5 Hz, $R_2BHC{=}CHR$), 6.13 (1 H, dt, *J* = 13.5 Hz; 1 Hz, $R_2BHC{=}CHR$), 2.31 (2 H, ddt, *J* = 7.5 Hz, 1 Hz, $R_2BHC{=}CHCH_2$), 1.98-1.67 (12 H, m, CH_2), 1.50-1.16 (12 H, m, CH, CH_2), 0.86 (3 H, t, *J* = 7 Hz, CH_3).

[a] Cross-Coupling with 1(*Z*)-Nonenyllithium (31). To a solution of vinyl iodide, **26**, (0.13 g, 0.5 mmol) in diethyl ether (2 mL) at -70 °C was added *t*-BuLi (0.59 mL, 1.7 M, 1 mmol). A white precipitate was formed within seconds; the solution was stirred at -70 °C for 30 min and then at -30 °C for an additional 30 min. The mixture was diluted with THF (2 mL) which caused the precipitate to dissolve. Allylic chloride, **6**, (0.2 mL, 0.5 mmol) was added followed by hexadecane (ISTD, 0.2 mL) and $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol). The solution was stirred at -30 °C for 30 min and then warmed to room temperature over 15 min. Gas chromatographic analysis of a quenched aliquot revealed that diene, **36**, had formed in 46 % yield.

[b] Cross-Coupling with 1(*Z*)-Nonenyldiisobutylalane (32). To a solution of vinyllithium, **31**, (0.5 mmol) in diethyl ether (2 mL)/THF (2mL) at -30 °C was added Et_2AlCl (0.06 mL, 0.5 mmol) giving rise to a white suspension (LiCl) within seconds. After 15 min allylic chloride, **6**, (0.2 mL, 0.5 mmol) was added followed by hexadecane (ISTD, 0.2 mL) and $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol) and the mixture heated to 50 °C for 2 hr. Gas chromatographic analysis of a quenched aliquot revealed that diene, **36**, had formed in 42 % yield.

[c] Cross-Coupling with 1(*Z*)-Nonenyl-B-methoxy-9-BBN (33). To a solution of **31** (1.5 mmol) in THF (5 mL) was added at -30 °C a solution of **29** (0.23 g, 1.5 mmol) in THF (1 mL). After 5 min NaOMe (0.25 g, 5 mmol) was added followed by allylic chloride, **6**, (0.2 mL, 0.5 mmol), hexadecane (ISTD, 0.2 mL) and $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol). The solution was heated to 60 °C for 3 hr. Gas chromatographic analysis of a quenched aliquot revealed that diene, **36**, had formed in 5 % yield. Similar results were obtained starting with vinylborane, **30**, (0.123 g, 0.5 mmol).

[d] Cross-Coupling with 1(*Z*)-Nonenylzinc bromide (34). To a solution of vinyllithium, **31**, (0.5 mmol) in diethyl ether (2 mL)/THF (2 mL) at -30 °C was added $ZnBr_2$ (0.113 g, 0.5 mmol). The suspension was stirred at 0 °C for 15 min during which time the precipitate dissolved. Allylic chloride, **6**, (0.2 mL, 0.5 mmol) was then added followed by hexadecane (ISTD, 0.2 mL) and $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol) and the solution stirred at room temperature for 30 min. Gas chromatographic analysis of a quenched aliquot revealed that diene, **36**, was formed in 80 % yield. In addition, a compound presumed to be an isomer of **36** (close GC retention time) was formed in 16 %.

[e] Cross-Coupling with 1(*Z*)-Nonenylcyclopentadienyl zirconocene chloride (35). To a solution of vinyllithium, **31**, (0.5 mmol) in diethyl ether (2 mL)/THF (2 mL) at -30 °C was added Cp_2ZrCl_2 (0.15 g, 0.5 mmol). The suspension was stirred at 0 °C for 15 min to yield a faint yellow solution. Allylic chloride, **6**, (0.2 g, 0.5 mmol) was added followed by hexadecane (ISTD, 0.2 mL) and $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol). The mixture was heated to 60 °C for 3 hr. Gas chromatographic analysis of a quenched aliquot revealed that diene, **36**, was formed in 4 % yield.

(6*E*,9*Z*)-6-Tri-*n*-butylstannylheptadeca-6,9-diene (36). An

analytically pure sample was obtained by flash chromatography (SiO_2, hexanes): ^1H NMR δ 5.48 (1 H, t, J = 7 Hz; $^3J^{119}_{Sn-H}$ = 105 Hz; $^3J^{117}_{Sn-H}$ = 92 Hz, $Bu_3SnRC{=}CHR$), 5.45-5.33 (2 H, m, $RHC{=}CHR$), 2.80 (2 H, t, J = 5 Hz, $C{=}CHCH_2HC{=}C$), 2.26-2.18 (2 H, m, $^3J_{Sn-H}$ = 60 Hz, $R_3Sn(RCH_2)C{=}CHR$), 1.98 (6 H, q, J = 7 Hz, CH_2), 1.52-1.22 (22 H, m, CH_2), 0,92-0.80 (21 H, m, CH_2, CH_3); mass spectrum (EI): 469(M^+ -Bu, 100), 467(74), 465(43), 413(40), 411(29), 409(18), 357(39), 355(32), 353(25), 235(16), 233(15), 231(9), 179(53), 177(80), 175(51), 123(10), 121(40), 119(30).

(6*Z*,9*Z*)-Heptadeca-6,9-diene (28). To a solution of diene, **36**, (0.06 g, 0.1 mmol) and hexadecane (ISTD, 0.059 g) in THF (5 mL) at room temperature were added several crystals of *p*-toluenesulfonic acid and the solution stirred for 30 min. Gas chromatographic analysis of an aliquot withdrawn after this time showed that destannylation was complete and that **28** had formed (90 %). An analytically pure sample was obtained by preparative TLC (SiO_2-$AgNO_3$ (20 %), hexanes): ^1H NMR δ 5.43-5.28 (4 H, m, $RHC{=}CHR$), 2.78 (2 H, t, J = 6.5 Hz, $C{=}CHCH_2HC{=}C$), 2.05 (4 H, q, J = 7 Hz, $C{=}CHCH_2$), 1.41-1.20 (18 H, m, CH_2), 0.94-0.84 (6 H, m, CH_3); ^{13}C NMR δ 130.21 (=C), 127.98 (=C), 31.86, 31.53, 29.35, 29.28, 29.21, 27.24, 27.21, 25.64, 22.65, 22.56, 14.06; mass spectrum (EI) 236(M^+, 4), 138(2), 110(9), 96(15), 95(18), 81(39), 79(24), 67(69), 55(47), 54(39), 43(45), 41(100); Anal. Calcd. for $C_{17}H_{32}$: C, 86.44; H, 13.56. Found: C, 86.15; H, 13.41.

I.6 Trial Syntheses of 1-Iodo-1(*Z*)-alkene Substrates.

2-Nonyn-1-ol (37). This compound was prepared as described for the synthesis of propargylic alcohol, **2**, starting with 1-octyne (15.72 g, 142.7 mmol).

Work-up and purification by distillation yielded **37** (17.83 g, 89 %) as a colourless oil: bp: 61 °C/1.5 mmHg; IR (neat) 3310(s), 2934(s), 2858(s), 1462(m), 1434(m), 1378(m), 1332(m), 1055(m) cm^{-1}; ^1H NMR δ 4.25 (2 H, dt, J = 7 Hz; 2.5 Hz, CH_2OH), 2.21 (2 H, tt, J = 7 Hz; 2.5 Hz, $CH_2C{\equiv}CR$), 1.63 (1 H, t, J = 7 Hz, OH), 1.52 (2 H, quint, J = 7 Hz, CH_2), 1.43-1.22 (6 H, m, CH_2), 0.89 (3 H, t, J = 7 Hz, CH_3); mass spectrum (CI) 141($(M+1)^+$, 6), 139(25), 123(100), 113(54), 111(52); Anal. Calcd. for $C_9H_{16}O$: C, 77.14; H, 11.43. Found: C, 76.88; H, 11.21.

8-Nonyn-1-ol (38). This compound was prepared according to a literature procedure[77] starting with alcohol, **37**, (10.0 g, 90.1 mmol). Work-up and purification by distillation yielded **38** (9.10 g, 91 %) as a colourless oil: bp: 58 °C/1 mmHg; IR (neat) 3300(s), 2931(s), 2857(s), 2117(w), 1708(w), 1464(m), 1433(m), 1057(m), cm^{-1}; ^1H NMR δ 3.65 (2 H, t, J = 7 Hz, CH_2OH), 2.85 (2 H, td, J = 7 Hz; 2.5 Hz, $HC{\equiv}CCH_2$), 1.95 (1 H, t, J = 2.5 Hz, $HC{\equiv}CR$, 1.62-1.25 (10 H, m, CH_2, CH_3); mass spectrum (CI) 141(M^{+1}, 8), 137(2), 123(100), 121(4), 111(3); Anal. Calcd. for $C_9H_{16}O$: C, 77.14; H, 11.43. Found: C, 76.95; H, 11.42.

9-Tetrahydropyranyloxy-1-nonyne (39). This compound was prepared as described for the synthesis of alkyne, **14**, starting with alcohol, **38**, (8.0 g, 57 mmol). Work-up and purification yielded **39** (12.0 g, 94 %) as a colourless oil: IR (neat) 3310(m), 2937(s), 2858(s), 1465(m), 1441(m), 1352(m), 1137(m), 1120(m), 1078(m), 1035(m) cm^{-1}; ^1H NMR δ 4.58-4.52 (1 H, m, C*H* (THP), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.73 (1 H, dt J = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, J = 9.5 Hz: 7 Hz, CH*H*OTHP), 2.20 (2 H, dt, J = 7 Hz; 2.5 Hz, $HC{\equiv}CCH_2$), 1.93 (1 H, t, J = 2.5 Hz, *H*C≡CR), 1.88-1.75 (1 H, m, CH*H* (THP)), 1.75-1.65 (1 H, m, CH*H* (THP)), 1.63-1.45 (8 H, m, CH_2), 1.45-1.25 (6 H, m, CH_2, CH_3); mass spectrum (CI)

225((M+1)$^+$, 100), 141(8), 123(21); (EI) 223(M$^+$ -H, 5), 101(35), 85(100), 81(32), 79(18), 67(23), 55(21); Anal. Calcd. for $C_{14}H_{24}O_2$: C, 75.00; H, 10.71. Found: C, 75.05; H, 11.01.

1-Iodo-9-tetrahydropyranyloxy-1-nonyne (40). This compound was prepared as described for the synthesis of alkynyl iodide, **25**, starting with a solution of alkyne, **39**, (12.0 g, 53.6 mmol) in THF (50 mL). Work-up and purification by flash chromatography (SiO_2, 5 % EtOAc in hexanes) yielded **40** (18.8 g, 87 %) as a colourless oil: IR (neat) 2940(s), 2852(s), 2186(w), 1453(m), 1351(m), 1200(m), 1136(m), 1119(m), 1077(m), 1028(m), 988(m) cm^{-1}; ^{1}H NMR δ 4.57 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.73 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.47 (1 H, m, CH*H* (THP)), 3.38 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.35 (2 H, t, *J* = 7 Hz, IC≡CCH_2), 1.86-1.75 (1 H, m, CH*H* (THP)), 1.75-1.65 (1 H, m, CH*H* (THP)), 1.65-1.45 (8 H, m, CH_2) 1.42-1.20 (6 H, m, CH_2); mass spectrum (CI) 351((M+1)$^+$, 36), 267(7), 249(7), 223(14), 205(7), 169(6), 139(35), 121(100); Anal. Calcd. for $C_{14}H_{23}O_2I$: C, 48.01; H, 6.62. Found: C, 48.27; H, 6.56.

9-Iodo-8-nonyn-1-ol (41). A solution of alkynyl iodide, **40**, (1.0 g, 2.9 mmol) in MeOH (10 mL) was stirred at room temperature in the presence of a catalytic amount of *p*-toluenesulfonic acid (ca. 2 mg). The solution was concentrated after 30 min under reduced pressure and the residue flash chromatographed (SiO_2, 15 % EtOAc in hexanes) to give pure **41** (0.59 g, 78 %) as a colourless oil: IR (neat) 3386(s), 2972(s), 2934(s), 2858(s), 1652(m), 1456(m), 1380(m), 1327(m), 1087(m), 1048(m) cm^{-1}; ^{1}H NMR δ 3.63 (2 H, t, *J* = 6.5 Hz, CH_2OH), 2.36 (2 H, t, *J* = 7 Hz, IC≡CCH_2), 1.62-1.47 (4 H, m, CH_2), 1.43-1.27 (6 H, m, CH_2); mass spectrum (CI) 267((M+1)$^+$, <1), 249(2), 221(2), 207(3), 196(2), 195(2), 180(3), 139(18), 121(100); Anal. Calcd. for $C_9H_{15}OI$: C, 40.62;

H, 5.68. Found: C, 41.22; H, 5.97.

1-(*tert*-Butyldimethylsiloxy)-8-nonyn-1-ol (42). This compound was prepared as described for the synthesis of alkyne, **15**, starting with alcohol **38** (2.0 g, 14 mmol). Work-up and purification yielded **42** (3.64 g, 88 %) as a colourless oil: IR (neat) 3314(m), 2934(s), 2857(s), 2120(w), 1472(m), 1463(m), 1388(w), 1361(w), 1255(m), 1102(m) cm^{-1}; ^1H NMR δ 3.60 (2 H, t, J = 6.5 Hz, CH_2OSi*t*-$BuMe_2$), 2.18 (2 H, dt, J = 7 Hz; 3 Hz, $HC{\equiv}CCH_2$), 1.93 (1 H, t, J = 3 Hz), 1.57-1.46 (4 H, m, $HC{\equiv}CR$), 1.45-1.27 (6 H, m, CH_2), 0.89 (9 H, s, CH_3), 0.25 (6 H, s, $Si(CH_3)_2$); mass spectrum (CI) 255($(M+1)^+$, 100), 197(29), 179(4), 165(2), 145(2), 133(13), 123(23); Anal. Calcd. for $C_{15}H_{30}OSi$: C, 70.86; H, 11.81. Found: C, 70.79; H, 11.72.

1-(*tert*-Butyldimethylsiloxy)-9-iodo-8-nonyn-1-ol (43). This compound was prepared as described for the synthesis of alkynyl iodide, **25**, starting with alkyne, **42**, (3.0 g, 12 mmol). Work-up and purification yielded **43** (4.3 g, 89 %) as a colourless oil: IR (neat) 2931(s), 2857(s), 1462(m), 1388(w), 1360(w), 1255(m), 1102(m), 1005(w) cm^{-1}; ^1H NMR δ 3.75 (2 H, t, J = 7 Hz, CH_2OSi*t*-$BuMe_2$), 2.35 (2 H, t, J = 7 Hz, $HC{\equiv}CCH_2$), 1.55-1.45 (4 H, m, CH_2), 1.42-1.23 (6 H, m, CH_2), 0.88 (9 H, s, CH_3), 0.04 (6 H, s, $Si(CH_3)_2$); mass spectrum (CI) 381($(M+1)^+$, 100); Anal. Calcd. for $C_{15}H_{29}OSiI$: C, 47.36; H, 7.68. Found: C, 47.58; H, 7.60.

I.6.1 *Attempted syntheses of 1-Iodo-1(Z)-alkenes.*

Transformations of the following 1-iodo-1-alkynes to the corresponding vinyl iodides were attempted under conditions (0.3 equiv. BH_3·DMS/2 hr; propionic acid/reflux 4 hr) described for the preparation of vinyl iodide, **26**.

[a] Reaction of alkynyl iodide, **40**, (1.0 g, 2.8 mmol) under these conditions gave a 1:1 mixture of 9-tetrahydropyranyloxy-1-nonene and presumably the *Z* isomer of 1-iodo-9-tetrahydropyranyloxy-1-nonene (identified by GC/MS). In addition, approximately 10 % each of alkynes, **39** and **40**, was obtained.

[b] Treatment of alkynyl iodide, **41**, (0.35 g, 1.3 mmol) with BH_3·DMS (0.09 mL, 0.9 mmol = 2 x 0.3 equiv.) resulted in the consumption of starting material and formation of low boiling compounds.

[c] Alkynyl iodide, **43**, (0.50 g, 1.3 mmol) was consumed under these conditions. Gas chromatographic analysis of the worked up mixture revealed a complex mixture of low boiling compounds.

I.7 Synthesis of the Termite Trail Marker Pheromone, (3*Z*,6*Z*)-Dodeca-3,6-dien-1-ol (48).

4-Tetrahydropyranyloxy-1-butyne (44). This compound was prepared as described for the synthesis of alkyne, **14**, starting with 3-butyn-1-ol (5.0 g, 71.4 mmol). Work-up and purification yielded **44** (9.5 g, 92 %) as a colourless liquid: d = 0.973; IR (neat) 3292(s), 2942(s), 2874(s), 2121(w), 1441(m), 1353(m), 1260(m), 1201(m), 1123(m), 1071(m), 1034(m) cm^{-1}; ^1H NMR δ 4.62-4.59 (1 H, m, C*H* (THP)), 3.90-3.75 (2 H, m, CH_2OTHP), 3.59-3.44 (2 H, m, CH_2 (THP)), 2.48 (2 H, dt, *J* = 7 Hz; 2.5 Hz, HC≡CCH_2), 1.96 (1 H, t, *J* = 2.5 Hz, *H*C≡CR), 1.87-1.63 (2 H, m, CH_2 (THP)), 1.62-1.43 (4 H, m, CH_2 (THP)); mass spectrum (EI) 153(M^+ -H, 13), 125(7), 115(9), 101(7), 99(12), 96(9), 85(100), 83(8), 79(7), 67(12), 53(9); Anal. Calcd. for $C_9H_{14}O_2$: C, 70.13; H, 9.09. Found: C, 70.18; H, 9.24.

1-Iodo-4-tetrahydropyranyloxy-1-butyne (45). This compound was prepared as described for the synthesis of alkynyl iodide, **25**, starting with alkyne, **44** (5.0 mL, 32 mmol). Work-up and purification yielded **45** (8.2 g, 92 %) as a colourless oil: d = 1.543; IR (neat) 2939(s), 2872(s), 2189(w), 1440(m), 1352(m), 1201(m), 1121(m), 1070(m), 1032(m) cm^{-1}; ^1H NMR δ 4.62-4.59 (1 H, m, C*H* (THP)), 3.90-3.75 (2 H, m, CH_2OTHP), 3.59-3.46 (2 H, m, CH_2 (THP)), 2.66 (2 H, t, *J* = 7 Hz, IC≡CCH_2), 1.88-1.38 (6 H, m, CH_2 (THP)); mass spectrum (EI) 279(M^+ -H, < 1), 225(9), 224(21), 179(30), 178(50), 115(13), 85(100), 67(12), 52(10); Anal. Calcd. for $C_9H_{13}O_2I$: C, 38.57; H, 4.64. Found: C, 38.68; H, 4.67.

1-Iodo-4-tetrahydropyranyloxy-1(*Z*)-butene (46). To a round bottom flask containing disiamylborane (5 mmol) [prepared by adding BH_3·DMS (0.47 mL, 5 mmol) to 2-methyl-2-butene (1.1 mL, 10 mmol) at 0 °C/2 hr][23,24] was added THF (4 mL) followed by alkynyl iodide, **45**, (0.91 mL, 5.0 mmol) and the homogeneous solution stirred at room temperature for 2 hr. The mixture was then treated with glacial acetic acid (1 mL) and poured into a solution of NaOH (2 M, 50 mL) after 2 hr. The solution was extracted with hexanes (3 x 10 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. The resulting crude oil was purified by flash chromatography (SiO_2, 5 % EtOAc in hexanes) to afford **46** (0.80 g, 56 %) as a colourless liquid: IR (neat) 3067(w), 2940(s), 2869(s), 1610(w), 1440(m), 1352(m), 1284(m), 1258(m), 1201(m), 1135(m), 1080(m), 1033(m) cm^{-1}; ^1H NMR δ 6.33-6.26 (2 H, m, I*H*C=C*H*R), 4.63-4.58 (1 H, m, C*H* (THP)), 3.89-3.76 (2 H, m, CH_2OTHP), 3.54-3.45 (2 H, m, CH_2 (THP)), 2.51-2.39 (2 H, m, C=CHCH_2), 1.88-1.77 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.63-1.43 (4 H, m, CH_2 (THP)); mass spectrum (EI) 281(M^+ -H, < 1), 198(100), 183(61),

182(24), 181(90), 180(80), 168(78), 167(40), 127(28), 115(12), 85(76), 84(16), 71(21); Anal. Calcd. for $C_9H_{15}O_2I$: C, 38.30; H, 5.32. Found: C, 38.61; H, 5.36.

(6*E*,9*Z*)-12-Tetrahydopyranyloxy-6-tri-*n*-butylstannyldodeca-6,9-diene (47).

[a] To a solution of vinyl iodide, **46**, (0.28 g, 1 mmol) in diethyl ether (2 mL) was added at -70 °C *t*-BuLi (1.18 mL, 1 mmol) resulting in the immediate formation of a white suspension. The solution was stirred at -70 °C for 30 min and then at -30 °C for an additional 30 min. The slurry was diluted with THF (2 mL) and gave rise to a clear solution. Allylic chloride, **6**, (0.4 mL, 1 mmol) and $Pd(PPh_3)_4$ (0.1 g, 0.1 mmol) were added successively, the mixture stirred at -30 °C for 30 min and the warmed to room temperature over 30 min. The yellow solution was quenched with aqueous NH_4Cl (100 mL) and extracted with hexanes (3 x 10 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated under reduced pressure. The resulting crude oil was purified by flash chromatography (SiO_2, 3 % EtOAc in hexanes) to afford **47** (0.21 g, 38 %) as a faint yellow oil.

[b] To a solution of the vinyl anion (1 mmol) prepared as described in [a] was added at -30 °C Et_2AlCl (0.13 mL, 1 mmol) which resulted in the formation of a white precipitate (LiCl) within several minutes. After 15 min allylic chloride, **6**, (0.4 mL, 1 mmol) was added followed by $Pd(PPh_3)_4$ (0.1 g, 0.1 mmol) and the mixture warmed to 50 °C for 2 hr. The mixture was worked-up and purified as described in [a] to afford **47** in >95 % isomeric purity (0.28 g, 51 %) as a faint yellow oil: IR (neat) 3011(w), 2955(s), 2922(s), 2871(s), 2853(s), 1600(w), 1464(m), 1377(w), 1352(w), 1138(m), 1121(m), 1073(m), 1034(m) cm^{-1}; ^1H NMR δ 5.49-5.37 (3 H, m, $^3J_{Sn-H}$ = 70 Hz), 4.63-4.58 (1 H, m, C*H* (THP)), 3.92-

3.83 (1 H, m, CH*H* (THP)), 3.75 (1 H, dt, J = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.54-3.47 (1 H, m, CH*H* (THP)), 3.42 (1 H, dt, J = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.89 (2 H, dt, J = 6.5 Hz, C=CHCH_2HC=C), 2.38 (2 H, q, J = 6.7 Hz, C=CHCH_2), 2.24 (2 H, t, J = 7 Hz; $^3J_{Sn\text{-}H}$ = 60 Hz, C=CSnBu$_3$CH_2), 1.88-1.78 (1 H, m, CH_2), 1.75-1.67 (1 H, m, CH_2), 1.63-1.38 (10 H, m, CH_2), 1.34-1.23 (12 H, m, CH_2), 0.94-0.81 (18 H, m, CH_2, CH_3); ^{13}C NMR δ 144.7 (=C), 138.0 (=C), 130.4 (=C), 125.7 (=C), 98.8, 67.1, 62.2, 33.2, 31.9, 30.8, 30.0, 29.1, 28.1, 27.4, 27.0, 25.5, 22.6, 19.6, 14.0, 13.6, 9.7; mass spectrum (EI) 499(M^+ -Bu, 42), 497(33), 495(7), 415(37), 413(30), 411(16), 235(5), 233(5), 179(12), 177(17), 175(12), 121(14), 119(10), 85(100), 67(30), 57(36); Anal. Calcd. for $C_{29}H_{56}O_2Sn$: C, 62.59; H, 10.07. Found: C, 62.87; H, 10.11.

(3*Z*,6*Z*)-Dodeca-3,6-dien-1-ol (48). To a solution of diene, **47**, (0.2 g, 0.36 mmol) in THF/MeOH (1:1, 4 mL) was added at room temperature an excess of *p*-toluenesulfonic acid (ca. 0.1 g). The mixture was stirred at room temperature for for 30 min and then concentrated to ca.1 mL under slightly reduced pressure (product is volatile). The suspension was flash chromatographed (SiO_2, 15 % EtOAc in hexanes) and yielded **48** (0.50 g, 77 %) as a colourless liquid: IR (neat) 3328(s), 3011(w), 2957(s), 2927(s) 2872(s), 1654(w), 1458(m), 1048(m) cm^{-1}; ^{1}H NMR δ 5.58-5.49 (1 H, m, R*H*C$_4$=C$_3$HR), 5.44-5.28 (3 H, m, RHC$_4$=C$_3$*H*R, R*H*C$_7$=C$_6$*H*R), 3.65 (2 H, t, J = 6.5 Hz, CH_2OH), 2.82 (2 H, t, J = 7 Hz, C=CHCH_2HC=C), 2.36 (2 H, q, J = 7 Hz, CH_2), 2.05 (2 H, q, J = 7 Hz, CH_2), 1.50 (1 H, s, O*H*), 1.40-1.22(6 H, m, CH_2), 0.88 (3 H, t, J = 7 Hz, CH_3); ^{13}C NMR δ 131.5 (=C), 130.6 (=C), 127.4 (=C), 125.3 (=C), 62.3 (CH_2OH), 31.5, 30.9, 29.3, 27.2, 25.8, 22.5, 14.0; mass spectrum (EI) 182(M^+, 1), 135(5), 121(11), 107(15), 93(45), 91(26), 81(46), 79(100), 77(26), 67(65), 55(30); Anal. Calcd. for $C_{12}H_{22}O$: C, 79.05; H, 12.16. Found: C, 78.77; H, 12.02.

4-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*Z*)-butene (49). An authentic sample was prepared by reaction of a diethyl ether/THF solution (1:1, 4 mL) of the vinyl anion derived from **46** (0.94 mmol) [prepared as described in the synthesis of **47**] with *n*-Bu_3SnCl (0.33 mL, 1.2 mmol) at -50 °C. The solution was stirred at room temperature for 15 min during which time a white precipitate was formed. The mixture was diluted with brine (100 mL), extracted with hexanes (3 x 10 mL) and the combined organic fractions dried ($MgSO_4$) and concentrated under reduced pressure. The crude liquid was purified by flash chromatography (SiO_2, 5 % EtOAc in hexanes) to afford **49** (0.29 g, 93 %) as a colourless liquid: IR (neat) 2956(s), 2923(s), 2870(s), 2853(s), 1600(m), 1464(m), 1456(m), 1137(m), 1121(m), 1080(m), 1033(m) cm^{-1}; ^1H NMR δ 6.53 (1 H, dt, J = 12.5 Hz; 7 Hz; $^3J^{119}_{Sn-H}$ = 141 Hz; $^3J^{117}_{Sn-H}$ = 135 Hz, $R_3SnHC{=}CHR$), 5.91 (1 H, d, J = 12.5 Hz; $^3J^{119}_{Sn-H}$ = 71 Hz; $^3J^{117}_{Sn-H}$ = 69 Hz, $R_3SnHC{=}CHR$), 4.63-4.52 (1 H, m, C*H* (THP)), 3.91-3.82 (1 H, m, CH*H* (THP)), 3.76 (1 H, dt, J = 9.6 Hz; 7 Hz, CH*H*OTHP), 3.55-3.46 (1 H, m, CH*H* (THP)), 3.42 (1 H, dt, J = 9.6 Hz; 7 Hz, CH*H*OTHP), 1.89-1.78 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.63-1.44 (10 H, m, CH_2), 1.30 (6 H, sext, J = 7.3 Hz, CH_2), 1.10-0.82 (15 H, m, CH_2, CH_3); mass spectrum (EI) 389(M^+ -Bu, 7), 387(5), 385(3), 305(100), 303(72), 301(42), 121(10), 119(7), 85(37), 57(12), 55(12); Anal. Calcd. for $C_{21}H_{42}O_2Sn$: C, 56.50; H, 9.42. Found: C, 56.73; H, 9.46.

I.8 Synthesis of the Sex Pheromone Inhibitor, (9*Z*,12*Z*)-Tetradeca-9,12-dienyl Acetate (58b).

3-Tri-*n*-butylstannyl-2(*E*)-buten-1-ol (50). This compound was prepared as described for the synthesis of allylic alcohol, **5**, starting with

2-butyn-1-ol (1.8 mL, 24 mmol). Work-up and purification by flash chromatography (SiO_2, 5 % EtOAc in hexanes) yielded **50** (3.89 g, 47 %) as a colourless oil: IR (neat) 3300(s), 2956(s), 2925(s), 2871(s), 2853(s), 1464(m), 1367(m), 1340(w), 1292(w), 1059(m), 1004(m) cm^{-1}; ^1H NMR (C_6D_6) δ 5.96-5.91 (1 H, m, $^3J_{Sn-H}$ = 69 Hz, $R_3SnMeC{=}CHR$), 4.15 (2 H, d, J = 5.5 Hz, CH_2OH), 1.89-1.87 (3 H, m, $^3J_{Sn-H}$ = 46 Hz, CH_3), 1.73-1.53 (6 H, m, CH_2), 1.47-1.36 (6 H, m, CH_2), 1.11-0.90 (15 H, m, CH_2, CH_3); mass spectrum (EI) 305(M^+ -Bu, 76), 303(66), 301(46), 249(63), 247(57), 245(44), 193(82), 191(71), 189(60), 179(45), 177(58), 175(39), 137(100), 135(83), 133(57), 121(91), 119(71), 118(51), 117(42), 71(26), 57(96); Anal. Calcd. for $C_{16}H_{34}OSn$: C, 53.04; H, 9.39. Found: C, 53.33; H, 9.35.

3-Tri-*n*-butylstannyl-2(*E*)-butenyl acetate (51). To a solution of alcohol, **50**, (2.0 g, 5.5 mmol) in acetic anhydride (5 mL) at room temperature was added pyridine (2 mL). After 45 min the mixture was diluted with diethyl ether and washed with brine (3 x 50 mL). The pooled aqueous layers were back-extracted with hexanes (10 mL) and the combined organic fractions concentrated under reduced pressure. The residual crude oil was purified by flash chromatography (SIO_2, 5 %, in hexanes) to afford **51** (2.1 g, 94 %) as a colourless liquid: IR (neat) 2955(s), 2871(s), 1744(s), 1464(s), 1376(s), 1229(s), 1071(m), 1024(m) cm^{-1}; ^1H NMR δ: 5.66 (1 H, m, $^3J_{Sn-H}$ = 65 Hz, $R_3SnMeC{=}CHR$), 4.68 (2 H, d, J = 6 Hz, CH_2OAc), 2.06 (3 H, s, $C(O)CH_3$), 1.90 (3 H, t, $^3J_{Sn-H}$ = 45 Hz, $R_3SnCH_3C{=}C$), 1.50-1.44 (6 H, m, CH_2), 1.39-1.26 (6 H, m, CH_2), 0.97-0.85 (15 H, m, CH_2, CH_3); Anal. Calcd. for $C_{18}H_{36}O_2Sn$: C, 53.47; H, 8.91. Found: C, 53.30; H, 8.80.

1-Chloro-3-tri-*n*-butylstannyl-2(*E*)-butene (52). This compound was prepared according to a literature procedure starting with alcohol, **50**, (6.28

g, 17.4 mmol).[18] Work-up and purification by flash chromatography (SiO_2, hexanes) yielded **52** (5.5 g, 85 %) as a colourless liquid: d = 1.152; ^{1}H NMR (C_6D_6) δ 5.91 (1 H, tq, J = 7 Hz; 2 Hz; $^3J_{Sn-H}$ = 64 Hz, $R_3SnMeC{=}CHR$), 3.90 (2 H, d, J = 7 Hz, CH_2Cl), 1.82 (3 H, d, J = 2 Hz; $^3J_{Sn-H}$ = 45 Hz, $R_3SnCH_3C{=}C$), 1.67-1.47 (6 H, m, CH_2), 1.43-1.33 (6 H, m, CH_2), 1.05-0.87 (15 H, m, CH_2, CH_3); mass spectrum (EI) 325(M^+ -Bu, 34), 323(95), 321(69), 319(31), 271(23), 269(55), 267(100), 265(72), 263(32), 235(17), 233(15), 213(33), 211(55), 209(41), 177(26), 175(18); Anal. Calcd. for $C_{16}H_{33}ClSn$: C, 50.53; H, 8.68. Found: C, 50.80; H, 8.83.

2-Decyn-1-ol (53). This compound was prepared as described for propargylic alcohol, **2**, starting with 1-nonyne (18.6 g, 150 mmol). Purification by distillation yielded **53** (20.8 g, 90 %) as a colourless liquid: bp 69 °C / 1.8 mmHg; IR (neat) 3312(s), 2930(s), 2858(s), 1462(m), 1434(m), 1055(m) cm^{-1}; ^{1}H NMR δ 4.25 (2 H, dt, J = 7 Hz; 2 Hz, CH_2OH), 2.20 (2 H, tt, J = 7 Hz; 2 Hz, $CH_2C{\equiv}C$), 1.67 (1 H, t, J = 7 Hz, CH_2), 1.50 (2 H, quint, J = 7 Hz, CH_2), 1.41-1.25 (8 H, m, CH_2), 0.88 (3 H, t, J = 7 Hz, CH_2, CH_3); mass spectrum (EI) 154(M^+, <1), 123(26), 121(23), 111(37), 107(34), 93(80), 83(69), 81(100), 79(85), 70(73), 69(53), 67(95), 55(79).

9-Decyn-1-ol (54). This compound was prepared according to a literature procedure[77] starting with propargylic alcohol, **53**, (20.0 g, 130 mmol). Purification of the crude oil by flash chromatography (SiO_2, 10 % EtOAc in hexanes) yielded **54** (17.8 g, 89 %) as a colourless oil: IR (neat) 3306(s), 2920(s), 2856(s), 2117(w), 1464(m), 1432(m), 1057(m) cm^{-1}; ^{1}H NMR δ 3.62 (2 H, t, J = 7 Hz, CH_2OH), 2.17 (2 H, dt, J = 7 Hz; 3 Hz, $CH_2C{\equiv}C$), 1.93 (1 H, t, J = 3 Hz, $HC{\equiv}C$), 1.64-1.46 (4 H, m, CH_2), 1.43-1.22 (8 H, m, CH_2, CH_3); mass spectrum (EI) 153(M^+ -H, <1), 135(<1), 121(9), 107(18), 95(46), 93(62), 81(70),

79(100), 67(69), 55(46); Anal. Calcd. for $C_{10}H_{18}O$: C, 77.92; H, 11.69. Found: C, 77.61; H, 11.87.

10-Tetrahydropyranyloxy-1-decyne (55). This compound was prepared as described for the synthesis of alkyne, **14**, starting with alcohol, **54**, (5.0 g, 33 mmol). Work-up and purification yielded **55** (7.0 g, 91 %) as a colourless liquid: d = 0.916; IR (neat) 3310(s), 2930(s), 2855(s), 2118(w), 1465(m), 1441(m), 1352(m), 1200(m), 1136(s), 1120(s), 1078(s), 1032(s) cm^{-1}; ^1H NMR δ 4.58-4.55 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.17 (2 H, dt, *J* = 7 Hz; 2.6 Hz, CH_2C≡C), 1.93 (1 H, t, *J* = 2.6 Hz, *H*C≡C), 1.89-1.78 (1 H, m, CH*H* (THP)), 1.75-1.67 (1 H, m, CH*H* (THP)), 1.63-1.47 (8 H, m, CH_2), 1.43-1.26 (8 H, m, CH_2, CH_3); mass spectrum (EI) 238(M^+, 2), 237(10), 101(34), 95(12), 85(100), 81(15), 67(13), 55(10); Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 10.92. Found: C, 75.30; H, 11.19.

1-Iodo-10-tetrahydropyranyloxy-1-decyne (56). This compound was prepared as described for the synthesis of alkynyl iodide, **25**, starting with alkyne, **55**, (3.0 g, 13 mmol). Work-up and purification by flash chromatography (SiO_2, 5 % EtOAc in hexanes) yielded **56** (4.33 g, 94 %) as a colourless oil: d = 1.290; IR (neat) 2937(s), 2853(s), 2186(w), 1453(m), 1352(m), 1200(m), 1136(m), 1119(m), 1077(m), 1028(m) cm^{-1}; ^1H NMR δ 4.59-4.54 (1 H, m, C*H* (THP)), 3.90-3.82 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, *J* = 9.6 Hz; 6.9 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 6.7 Hz, CH*H*OTHP), 2.34 (2 H, t, *J* = 7 Hz, CH_2C≡C), 1.87-1.77 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.62-1.45 (8 H, m, CH_2), 1.41-1.24 (8 H, m, CH_2, CH_3); mass spectrum (EI) 363(M^+ -H, < 1), 165(8), 101(24), 93(11),

85(100), 81(9), 80(9), 79(13), 67(14), 56(10), 55(15); Anal. Calcd. for $C_{15}H_{25}O_2I$: C, 49.45; H, 6.89. Found: C, 49.61; H, 6.87.

1-Iodo-10-tetrahydropyranyloxy-1(*Z*)-decene (57). This compound was prepared as described for the synthesis of vinyl iodide, **46**, starting with alkynyl iodide, **56**, (1.4 mL, 5.0 mmol). Work-up and purification yielded **57** (1.67 g, 64 %) as a colourless liquid: IR (neat) 3067(w), 2930(s), 2854(s), 1610(w), 1464(m), 1352(m), 1283(m), 1200(m), 1136(m), 1120(m), 1078(m), 1032(m) cm^{-1}; ^1H NMR δ 6.19-6.12 (2 H, m, I*H*C=C*H*R), 4.59-4.54 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.73 (1 H, m, CH*H* (THP)), 3.58-3.46 (1 H, m, CH*H*OTHP), 3.38 (1 H, dt, *J* = 9.5 Hz; 6.7 Hz, CH*H*OTHP), 2.16-2.08 (2 H, m, C=CHCH_2), 1.90-1.77 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.63-1.47 (6 H, m, CH_2), 1.46-1.26 (10 H, m, CH_2, CH_3); mass spectrum (EI) 366(M^+, < 1), 365(3), 239(13), 180(100), 167(51), 154(10), 137(12), 95(36), 85(50), 84(14), 83(10), 81(38), 69(12), 67(23), 55(21).

10-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*Z*)-decene (58). This compound was isolated as the main product in the coupling reaction of allylic chloride, **52**, (0.33 mL, 1 mmol) and the *Z* vinyllithium reagent (1 mmol) derived from **57** under conditions described in the preparation of diene, **47**, method [a]. Work-up and purification yielded **58** (0.48 g, 91 %) as a colourless oil: IR (neat) 2955(s), 2924(s), 2870(s), 2853(s), 15948(w), 1464(m), 1376(w), 1352(w), 1136(m), 1121(m), 1079(m), 1034(m) cm^{-1}; ^1H NMR δ 6.50 (1 H, dt, *J* = 12 Hz; 7 Hz; $^3J_{Sn-H}$ = 142 Hz), 5.76 (1 H, dt, *J* = 12 Hz; 1 Hz; $^1J_{Sn-H}$ = 73 Hz), 4.59-4.54 (1 H, m, C*H* (THP)), 3.91-3.82 (1 H, m, CH*H* (THP)), 3.73 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.38 (1 H, dt, *J* = 9.5 Hz; 6.5 Hz, CH*H*OTHP), 2.0 (2 H, q, *J* = 7 Hz, C=CHCH_2), 1.88-1.78 (1 H, m, CH*H* (THP)), 1.63-1.43 (20 H, m, CH_2), 1.40-1.22 (15 H, m, CH_2, CH_3); mass

spectrum (EI) 473(4), 471(3), 443(4), 441(3), 389(40), 387(30), 385(18), 179(7), 1779), 175(7), 121(10), 119(8), 85(100), 67(21); Anal. Calcd. for $C_{27}H_{54}O_2Sn$: C, 61.13; H, 10.19. Found: C, 61.38; H, 10.25.

CHAPTER II

II.1 ^2H and ^{13}C NMR Investigations of Stannylcupration of 1-Alkynes.

1-Iodo-1(*E*)-decene (59). To a solution of 1-decyne (0.72 mL, 4.0 mmol) in anhydrous hexanes (20 mL) was added at room temperature DIBAH (4.0 mL, 1 M, 4.0 mmol).[78] The solution was heated to 50 °C for 2.5 hr, cooled to room temperature and the bulk of solvent removed under reduced pressure. The remaining white slurry was dissolved in pre-cooled (-40 °C) THF (20 mL) and a solution of I_2 (1.1 g, 4.3 mmol) in THF (5 mL) added. The red mixture was warmed to room temperature, diluted with a solution of NaCl/$Na_2S_2O_8$, acidified with HCl (2 M) and extracted with hexanes (2 x 20 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated under reduced pressure to afford a crude red oil which, after Kugelrohr distillation, yielded **59** (0.60 g, 57 %) as a faint pink liquid: bp: 56 °C/1 mmHg; ^1H NMR δ 6.51 (1 H, dt, *J* = 14 Hz; 7 Hz, IHC=C*H*R), 5.96 (1 H, dt, *J* = 14 Hz; 1.5 Hz, I*H*C=CHR), 2.04 (2 H, dq, *J* = 7 Hz; 1.5 Hz, C=CHCH_2), 1.44-1.34 (2 H, m, CH_2), 1.34-1.18 (10 H, bs, CH_2), 0.88 (3 H, t, *J* = 7 Hz, CH_3); mass spectrum (EI) 266(M^+, 55), 176(53), 154(21), 127(10), 97(38), 83(100), 69(71), 67(25), 57(46), 55(95).

[1-^2H]-1-Iodo-1(*E*)-decene (60). This compound was prepared as described for the synthesis of vinyl iodide, **59**, starting with alkyne, **61**, (0.72 mL, 4.0 mmol). Work-up and purification by Kugelrohr distillation yielded **60**

(0.60 g, 55 %): bp: 54 °C/1 mmHg; ^{1}H NMR δ 6.47 (1 H, tt, *J* = 7 Hz; 2 Hz, ^{1}²HC=C*H*R), 2.04 (2 H, q, *J* = 7 Hz, C=CHC*H*$_2$), 1.44-1.34 (2 H, m, C*H*$_2$), 1.34-1.18 (10 H, bs, C*H*$_2$), 0.88 (3 H, t, *J* = 7 Hz, C*H*$_3$); mass spectrum (EI) 267(M$^+$, 86), 168(74), 155(30), 127(15), 98(34), 97(19), 84(86), 83(52), 70962), 69(54), 55(100).

[1-^{2}H]-1-Decyne (61). To a solution of 1-decyne (3.0 g, 22 mmol) in THF (20 mL) at -78 °C was added *n*-BuLi (8.7 mL, 2.5 M, 22 mmol) The solution was warmed to 0 °C after 1 hr, quenched with D_2O and diluted with brine (20 mL). The mixture was extracted with hexanes and the combined organic layers dried ($MgSO_4$) and concentrated under reduced pressure. The remaining crude liquid was subjected to flash chromatography (SiO_2, hexanes) to give **61** (2.5 g, 84 %) as a colourless liquid: IR (neat) 3314(w), 2925(s), 2856(s), 2597(s), 1465(m) cm^{-1}; ^{1}H NMR δ 2.18 (2 H, t, *J* = 7 Hz, C≡CC*H*$_2$), 1.52 (2 H, quint, *J* = 7 Hz, C*H*$_2$), 1.43-1.33 (2 H, m, C*H*$_2$), 1.28 (8 H, bs, C*H*$_2$), 0.88 (3 H, t, *J* = 7 Hz, C*H*$_3$); mass spectrum (EI) 110(M$^+$ -C_2H_5, 9), 96(37), 83(26), 82(100), 81(34), 80(22), 69(26),68(52), 67(52), 57(23), 56(21), 55(55), 54(18).

1-Bromo-8-tetrahydropyranyloxyoctane (62). This compound was prepared by treating 8-bromo-1-octanol (3.0 g, 14 mmol) with 3,4-dihydro-2*H*-pyran according to the procedure outlined for the synthesis of alkyne, **14**. Work-up and purification yielded **62** (3.6 g, 86 %) as a colourless oil: d = 1.160; IR (neat) 2935(s), 2856(s), 1454(w), 1440(w), 1352(w), 1200(w), 1135(m), 1120(w), 1078(m), 1034(m), 987(w) cm^{-1}; ^{1}H NMR δ 4.88-4.45 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.42-3.34(3 H, m, CH*H*OTHP, C*H*$_2$Br), 1.75-1.67 (1 H, m, CH*H* (THP)), 1.63-1.48 (6 H, m, C*H*$_2$), 1.46-1.28 (8 H, m, C*H*$_2$); mass spectrum (EI) 293(5), 291(5), 221(1), 219(1), 164(1), 162(1),

150(2), 148(2), 137(2), 135(2), 101(9), 85(100), 69(23), 56(16); Anal. Calcd. for $C_{13}H_{25}O_2Br$: C, 53.24; H, 8.53. Found: C, 52.89; H, 8.45.

[1,2-^{13}C]-10-Tetrahydropyranyloxy-1-decyne (63). A solution of [1,2-^{13}C]-ethyne was prepared by transferring the gas from an ampule (0.10 L, 4.1 mmol) *via* cannula to a cooled flask containing THF (20 mL, -78° C). The tip of the cannula was submerged into the rapidly stirred solvent and the gas injected slowly over 10 min. To the solution was then added at -78° C *n*-BuLi[79] (1.64 mL, 2.5 M, 4.1 mmol) followed after 30 min by a solution of alkyl bromide, **62**, (1.2 g, 4.1 mmol) in THF (2 mL) and HMPA (5 mL). The mixture was slowly warmed to room temperature and allowed to stand overnight, extracted with brine (3 x 100 mL) and the pooled aqueous fractions back-extracted with diethyl ether (2 x 50 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated under reduced pressure to yield a crude oil consisting of an inseparable mixture of **63** and unreacted **62**. Final purification was accomplished by conversion of **62** to its corresponding phosphonium salt (PBu_3/acetone, reflux/4 hr) which was easily removed by flash chromatography (SiO_2, 5 % EtOAc in hexanes) to yield **63** (0.98 g, 76 %) as a colourless oil: IR (neat) 3298(m), 2937(s), 2856(s), 2044(w), 1465(m), 1464(m), 1441(m), 1352(m), 1201(m), 1136(s), 1120(s), 1078(s), 1032(s) cm^{-1}; ^{1}H NMR δ 4.59-4.54 (1 H, m, C*H* (THP)), 3.90-3.82 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.45 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.19-2.12 (2 H, m, C≡CCH_2), 1.92 (1 H, dt, *J* = 298 Hz; 2.5 Hz, *H*C≡C), 1.87-1.77 (1 H, m), 1.74-1.46 (9 H, m, CH_2), 1.43-1.26 (8 H, m, CH_2); ^{13}C NMR δ 98.84, 84.73 (d, J_{C-C} = 170.1 Hz, HC≡*C*R), 68.07, 67.96 (d, J_{C-C} = 170.1 Hz, H*C*≡CR), 67.62, 30.79, 29.72, 29.30, 29.01, 28.74, 28.40, 26.18, 25.52, 19.69; mass spectrum (EI): 240(M^+, <1), 239(6), 115(3), 101(38), 97(12),

85(100), 83(18), 81(10), 69(8), 67(10), 57(6), 56(12), 55(12); Anal. Calcd. for $^{13}C_2C_{13}H_{56}O_2$: C, 75.00; H, 10.83. Found: C, 75.34; H, 10.90.

***n*-Bu_3SnCu(CN)Li·2LiCl (64)** [0.15 M THF]. To a solution of *n*-Bu_3SnLi[20] (3.05 mmol) in THF (15 mL) at -30 °C was added a solution of CuCN (0.273 g, 3.05 mmol) and LiCl (0.256 g, 6.10 mmol) in THF (3 mL + 2 mL rinse). An orange solution formed immediately turning burgundy red after 1 hr. C_6D_6 (0.05 mL, 0.56 mmol) was added for ^2H NMR experiments.

(*n*-$Bu_3Sn)_2$Cu(CN)Li_2 (65) [0.15 M THF]. To a solution of *n*-Bu_3SnLi[20] (6.1 mmol) in THF (20 mL) was added at -30 °C CuCN (0.27 g, 3.05 mmol). The suspension that formed turned yellow immediately and became homogeneous after 30 min. Stirring was continued for an additional 30 min. C_6D_6 (0.05 mL, 0.56 mmol) was added for ^2H NMR experiments.

II.1.1 *^2H NMR Studies.*

Sample Preparation. To a dry 10 mm NMR tube immersed in a -78 °C bath and fitted with a septum was transferred a 3 mL aliquot (0.46 mmol) of stannylcuprate solutions. Reagents (alkynes and MeOH) were subsequently added as neat liquids by allowing them to flow down the inside wall of the cooled NMR tube. NMR samples were then vortexed briefly at room temperature to ensure solution homogeneity. Spectra were recorded at -35 °C.

1. Addition of *n*-Bu_3SnCu(CN)Li·2LiCl (64) to [1-^2H]-1-Decyne (61).

[a] To an NMR tube containing stannylcuprate, **64**, (3 mL, 0.46 mmol) at -78 °C was added alkyne, **61**, (0.8 mL, 0.44 mmol) followed by MeOH (0.02 mL,

0.49 mmol) and the ^2H NMR spectrum recorded within 15 min.

[b] To an NMR tube containing stannylcuprate, **64**, (3 mL, 0.46 mmol) at -30 °C was added alkyne, **61**, (0.8 mL, 0.44 mmol). The solution was allowed to stand at 0 °C for 15 min prior to ^2H NMR analysis.

[c] To NMR tube 1 [b] was added at -35 °C MeOH (0.02 mL, 0.49 mmol) and the ^2H NMR spectrum recorded within 15 min.

2. Addition of (*n*-$Bu_3Sn)_2Cu(CN)Li_2$ (65) to [1-^2H]-1-Decyne (61) and 1-Decyne.

[a] The same procedure was followed as described in 1 [a].

[b] The same procedure was followed as described in 1 [b].

[c] The same procedure was followed as described in 1 [c].

[d] To an NMR tube containing stannylcuprate, **65**, (3 mL, 0.46 mmol) at -30 °C was added 1-decyne (0.8 mL, 0.44 mmol). The solution was warmed to 0 °C over 15 min followed by addition of CD_3OD (0.02 mL, 0.49 mmol). The ^2H NMR spectrum recorded within 15 min.

3. [1-^2H]-1(*E*)-1-Decenylcyanocuprate (66).

To a solution of vinyl iodide, **60**, (0.2 g, 0.75 mmol) in THF (5 mL) at -30 °C was added *n*-BuLi (0.3 mL, 2.5 M, 0.75 mmol) and the solution stirred for 30 min. Transfer of the vinyl anion at -30 °C to a solution of CuCN (0.067 g, 0.75 mmol) and LiCl (0.063 g, 1.5 mmol) in THF (5 mL) resulted in the immediate formation of a deep violet solution. The mixture was stirred at -30 °C for 1 hr prior to ^2H NMR analysis.

II.1.2 *^{13}C NMR Studies.*

Sample Preparation. ^{13}C NMR samples were prepared in a manner analogous to the procedure described for ^{2}H NMR experiments.

1. Addition of *n*-$Bu_3SnCu(CN)Li{\cdot}2LiCl$ (64) to 1-Decyne.

[a] To an NMR tube containing stannylcuprate, **64**, (3 mL, 0.46 mmol) at -30 °C was added 1-decyne (0.08 mL, 0.44 mmol). The solution was allowed to stand at 0 °C for 15 min prior to ^{13}C NMR analysis.

[b] To NMR tube 1 [a] at -35 °C was added MeOH (0.02 mL, 0.49 mmol) and the ^{13}C NMR spectrum recorded within 15 min.

2. 1(*E*)-1-Decenylcyanocuprate (67). This compound was prepared in an analogous fashion described for vinyl cuprate, **66**, from vinyl iodide, **59**, (0.2 g, 0.75 mmol).

3. Addition of (n-$Bu_3Sn)_2Cu(CN)Li_2$ (65) to [1,2-^{13}C]-10-Tetrahydropyranyloxy-1-decyne (63).

[a] To an NMR tube containing stannylcuprate, **65**, (3 mL, 0.46 mmol) at -78 °C was added alkyne, **63**, (0.11 mL, 0.44 mmol) followed by MeOH (0.02 mL, 0.49 mmol). The ^{13}C NMR spectrum was recorded within 15 min.

[b] To an NMR tube containing stannylcuprate, **65**, (3 mL, 0.46 mmol) at -30 °C was added alkyne, **63**, (0.11 mL, 0.44 mmol). The solution was warmed to 0 °C over 15 min prior to ^{13}C NMR analysis (at -20 °C).

[c] To an NMR tube containing the sample in experiment 3 [b] at -20 °C was added MeOH (ca. 0.1 mL). The ^{13}C NMR spectrum was recorded at that

temperature after approximately 15 min.

[1,2-^{13}C]-10-Tetrahyropyranyloxy-2-tri-*n*-butylstannyl-1-decene (68). Quenched solutions from experiments 3 [a-c] were pooled, extracted with hexanes and the concentrated organic fractions purified by flash chromatography (SiO_2, 5 % EtOAc in hexanes). IR and ^{1}H NMR analysis revealed a 76:24 mixture of **68** and **69**: IR (neat) 3017(w), 2923(s), 2862(s), 1545(w), 1464(m), 1200(m), 1136(m), 1120(m), 1079(m), 1034(m), 988(m); ^{1}H NMR (relative number of hydrogens): δ 5.64 (1 H, d, $J_{C\text{-}H}$ = 151 Hz, $H_{trans}H_{cis}C$=CRSnBu$_3$), 4.93 (1 H, d, $J_{C\text{-}H}$ = 151 Hz, $H_{trans}H_{cis}C$=CRSnBu$_3$), 4.59-4.54 (m, C*H* (THP)), 3.91-3.83 (m, CH*H* (THP)), 3.72 (dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (m, CH*H* (THP)), 3.37 (dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.22 (2 H, t, *J* = 7 Hz, C=CHCH_2), 1.88-1.77 (m, CH*H* (THP)), 1.75-1.66 (m, CH*H* (THP)), 1.63-1.42 (m, CH_2), 1.39-1.23 (m, CH_2), 0.91-0.84 (m, CH_2, CH_3); ^{13}C NMR (THF): δ 156.2 (C$_2$, d, $J_{C\text{-}C}$ = 60.4 Hz; $^1J^{119}_{Sn\text{-}C}$ = 381.5 Hz; $^1J^{117}_{Sn\text{-}C}$ = 365.5 Hz, H_2C=*C*RSnBu$_3$), 125.8 (C$_1$, d, $J_{C\text{-}C}$ = 60.4 Hz, H_2C=CRSnBu$_3$); mass spectrum (EI): 475(M$^+$ -Bu, 68), 473(49), 471(32), 446(6), 417(19), 391(48), 389(39), 387(19), 333(5), 179(8), 177(14), 175(12), 137(5), 135(5), 133(5), 121(13), 119(8), 85(100), 67(13), 55(25).

[1,2-^{13}C]-10-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*E*)-decene (69). This compound was isolated as described above as a 76:24 mixture of **68** and **69** : IR (neat): see **68**; ^{1}H NMR (relative number of hydrogens): δ 6.16-5.98 (1 H, m, R$_3$Sn*H*C=CHR), 5.79-5.61 (1 H, m, R$_3$SnHC=C*H*R); 4.59-4.54 (m, C*H* (THP)), 3.91-3.83 (m, CH*H* (THP)), 3.72 (dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (m, CH*H* (THP)), 3.37 (dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.10 (m, C=CHCH_2), 1.88-1.77 (m, CH*H* (THP)), 1.75-1.66 (m, CH*H* (THP)), 1.63-1.42 (m, CH_2), 1.39-1.23 (m, CH_2), 0.91-0.84 (m, CH_2, CH_3);

^{13}C NMR (THF): δ 150.9 (d, J_{C-C} = 60.4 Hz, $R_3SnHC{=}CHR$), 127.7 (d, J_{C-C} = 60.4 Hz; $^1J^{119}_{Sn-C}$ = 404.0 Hz; $^1J^{117}_{Sn-C}$ = 386.6 Hz, $R_3SnHC{=}CHR$); mass spectrum (EI): 475(M^+ -Bu, 19), 473(15), 446(35), 391(35), 389(29), 387(25), 235(4), 233(5), 179(8), 177(13), 175(12), 135(9), 133(9), 121(15), 119(13), 85(100), 69(27), 67(22), 57(37), 55(67).

II.2 Crossover Experiments with CuCN Derived Reagents.

6-Tetrahydropyranyloxy-1-hexyne (70). This compound was prepared as described for the synthesis of alkyne, **14**, starting with 5-hexyn-1-ol (5.0 g, 51 mmol). Work-up and purification yielded **70** (8.1 g, 87 %) as a colourless oil: IR (neat) 3295(s), 2942(s), 2869(s), 2117(w), 1453(m), 1440(m), 1352(m), 1200(m), 1137(m), 1120(m), 1076(s), 1024(s), 1022(s) cm^{-1}; ^1H NMR δ 4.59-4.55 (1 H, m, C*H* (THP)), 3.88-3.81 (1 H, m, CH*H* (THP)), 3.75 (1 H, dt, *J* = 9.5 Hz; 6.5 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.40 (1 H, dt, *J* = 9.5 Hz; 6.5 Hz, CH*H*OTHP), 2.22 (2 H, dt, *J* = 7 Hz; 2.5 Hz, $CH_2C{\equiv}C$), 1.94 (1 H, t, *J* = 2.5 Hz, *H*C≡C), 1.86-1.76 (1 H, m, CH*H* (THP)), 1.75-1.67 (1 H, m, CH*H* (THP)), 1.75-1.46 (9 H, m, CH_2); mass spectrum (EI) 182(M^+, <1), 181(<1), 154(<1), 140(<1), 126(2), 101(15), 85(100), 81(21), 79(30), 67(19), 57(10), 56(31), 55(17); Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.53; H, 9.89. Found: C, 72.30; H, 9.96.

10-Tetrahydropyranyloxy-1,2-bis(tri-*n*-butylstannyl)-1(*Z*)-decene (71). To a solution of $(n\text{-}Bu_3Sn)_2Cu(CN)Li_2$ (**65**) (3.8 mmol) in THF (20 mL) was added alkyne, **48**, (1.0 mL, 3.8 mmol) at -30° C. After stirring the reaction mixture at 0° C for 1 hr the solution was cooled to -50° C and $n\text{-}Bu_3SnCl$ (1.36 mL, 5 mmol) added. The temperature was maintained at -50°

C for 30 min and then raised to room temperature for 15 min before quenching with brine (100 mL). The mixture was extracted with diethyl ether (3 x 50 mL) and the combined organic fractions dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the crude oil by flash chromatography (SiO_2, 5 % EtOAc in hexanes) afforded **71** (2.6 g, 81 %) as a colourless oil: IR (neat) 2923(s), 2870(s), 2863(s), 1542(w), 1463(m), 1376(m), 1200(m), 1164(m), 1120(m), 1078(m), 1034(m); ^{1}H NMR δ 6.55 (1 H, s, $^3J^{119}_{Sn\text{-}H}$ = 192 Hz; $^2J^{119}_{Sn\text{-}H}$ = 78 Hz; $^3J^{117}_{Sn\text{-}H}$ = 183 Hz; $^2J^{117}_{Sn\text{-}H}$ = 75 Hz, $R_3SnHC{=}C$), 4.60-4.55 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.27 (2 H, t, *J* = 7 Hz; $^3J_{Sn\text{-}H}$ = 43 Hz, $C{=}CSnBu_3CH_2$), 1.88-1.77 (1 H, m, CH*H* (THP)), 1.75-1.67 (1 H, m, CH*H* (THP)), 1.53-1.40 (20 H, m, CH_2), 1.40-1.30 (20 H, m, CH_2), 0.97-0.78 (30 H, m, CH_2, CH_3) mass spectrum (EI) 758-761(M^+ -Bu, <1), 672-681(1), 519-526(1), 469-477(31), 441-445(2), 413-417(5), 393(16), 391(15), 390(18), 389(100), 388(34), 387(76), 386(31), 385(45), 291(12), 289(10), 235(15), 233(13), 179(28), 177(33), 175(22), 121(16); Anal. Calcd. for $C_{39}H_{81}O_2Sn_2$: C, 57.14; H, 9.89. Found: C, 57.30; H, 9.76.

II.2.1 *Crossover Experiments with Tri-n-butylstannylcuprates.*

Product yields are based on available tri-*n*-butyltin. Percent recovery is based on the sum of starting materials.

1. With *n*-$Bu_3SnCu(CN)Li{\cdot}2LiCl$ (64).

[a] To stannylcuprate, **64**, (1 mmol) in THF (20 mL) at -30 °C was added one equivalent of alkyne, **48**, (0.24 g, 1.0 mmoL) and the solution warmed with

stirring to 0 °C. After 1.5 hr one equivalent of a second alkyne, **38**, (0.23 g, 1.0 mmol) was added and stirring continued for an additional 1.5 hr. The black solution was subsequently poured into a saturated solution of NH_4Cl (100 mL), extracted with diethyl ether (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to give a crude oil. Purification by flash chromatography (SiO_2, 5 % EtOAc in hexanes) yielded starting alkynes, **48** and **38**, (48:52, 0.31 g, 68 % recovered) and products **75**, **76**, **77** and **78** (27:24:26:23, 0.30 g, 58 %).

[b] A solution of stannylcuprate, **64**, (1 mmol) and alkyne, **48**, (0.24 g, 1.0 mmoL) (prepared as in 1 [a]) was stirred at room temperature for 1.5 hr, cooled to -78 °C and one one equivalent of alkyne, **38**, (0.23 g, 1.0 mmol) in THF (2 mL) added slowly. The mixture was quenched after stirring for 1.5 hr at -78 °C by pouring the contents of the flask into a rapidly stirred solution of NH_4Cl (200 mL). Work-up and purification yielded starting alkynes, **48** and **38**, (26:74; 0.31 g, 69 % recovered) and products **75**, **76**, **77** and **78** (61:28:9:2; 0.32 g, 60 %).

2. With (n-$Bu_3Sn)_2Cu(CN)Li_2$ (65).

[a] To stannylcuprate, **65**, (0.5 mmol) in THF (10 mL) at 0 °C were added two equivalents of alkyne, **48**, (0.26 mL, 1.0 mmol). After 1.5 hr, two equivalents of a second alkyne, **70**, (0.19 mL, 1.0 mmol) were added and the solution stirred for an additional 1.5 hr. Addition of MeOH to the yellow solution followed by work-up and purification yielded starting alkynes, **48** and **70**, (23:77, 0.22 g, 57 % recovered) and products **75**, **76**, **79** and **80** (10:85:1:4, 0.42 g, 81 %).

[b] A crossover experiment was carried out as described in 2 [a] with the exception that the solution was stirred at room temperature for 12 hr following

addition of the second alkyne. Work-up and purification yielded starting alkynes, **48** and **70**, (39:61, 0.21 g, 53 % recovered) and products **75**, **76**, **79** and **80** (31:27:17:25, 0.41 g, 82 %).

II.2.2 *Crossover Experiments with Vinyl Cuprate Intermediates.*

Product yields are based on available tri-*n*-butyltin. Percent recovery is based on the sum of starting materials.

***n*-$Bu_3SnCu(CN)Li$ (72)** The following procedure is representative: To a solution of *n*-Bu_3SnLi[20] (3.05 mmol) in THF (20 mL) at -30 °C was added CuCN (0.273 g, 3.05 mmol). The initial yellow suspension was stirred at -10 °C for 1 hr and eventually yielded a red slurry.

1. 10-Tetrahydropyranyloxy-2-tri-*n*-butylstannyl-1(*Z*)-decenyl cyanocuprate (73).

[a] To distannane, **71**, (0.49 g, 0.6 mmol) in THF (5 mL) at -78 °C was added *n*-BuLi (0.26 mL, 2.5 M, 0.6 mmol) and the solution warmed to -30 °C over 1 hr. The mixture was transferred to a cooled (-30 °C) solution of CuCN (0.054 g, 0.6 mmol) and LiCl (0.05 g, 1.2 mmol) in THF (5 mL) and stirred for 1 hr during which time a red solution formed. The mixture was quenched with MeOH, diluted with brine (100 mL) and extracted with hexanes (3 x 50 mL). The combined organic exctracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 5% EtOAc in hexanes) to yield products, **75** and **76** (86:14, 0.24 g, 75 %). A trace amount of alkyne, **48**, was formed (< 1 % by GC).

[b] To a solution of vinyl cuprate, **73**, (0.5 mmol) was added at -30 °C a solution of alkyne, **38**, (0.112 g, 0.5 mmol) in THF (2 mL). The solution was stirred at 0 °C for 1.5 hr and the black mixture quenched with a saturated solution of NH_4Cl. Work-up and purification yielded starting alkynes, **48** and **38**, (47:53, 0.15 g, 65 % recovered) and products **75**, **76**, **77** and **78** (33:19:27:21, 0.15 g, 59 %).

2. 10-Tetrahydropyranyloxy-2-tri-*n*-butylstannyl-1(*Z*)-decenyl tri-*n*-butylstannylcyanocuprate (74).

[a] To distannane, **71**, (0.41g, 0.5 mmol) in THF (5 mL) at -78 °C was added *n*-BuLi (0.2 mL, 2.5 M, 0.5 mmol) and the solution warmed to -30 °C over 1 hr. The mixture was transferred to a cooled (-30 °C) solution of stannylcuprate, **72**, (0.5 mmol) in THF (5 mL) and the solution stirred for 1.5 hr at 0 °C. The yellow solution was quenched with MeOH, worked-up and purification as described in experiment 1[a] yielded products, **75** and **76** (87:13, 0.23 g, 88 %). A trace amount of alkyne, **48**, was formed (< 1 % by GC).

[b] To an unquenched solution of vinyl cuprate, **74**, prepared as described in 2 [a] at -30 °C, was added one equivalent of alkyne, **48**, (0.13 mL, 0.5 mmol), the mixture warmed to room temperature and two equivalents of alkyne, **70**, (0.19 mL, 1 mmol) added after 30 min. The solution was stirred at room temperature for 12 hr and then quenched with MeOH. Work-up and purification in the usual manner yielded starting alkynes, **48** and **70**, (40:60, 0.21 g, 53 % recovered) and products **75**, **76**, **79** and **80** (38:24:14:24, 0.47 g, 93 %).

10-Tetrahyropyranyloxy-2-tri-*n*-butylstannyl-1-decene (75). The following data was obtained for a 95:5 mixture of **75** and **76**: IR (neat)

3031(w), 2926(s), 2853(s), 1596(w), 1463(m), 1200(m), 1136(s), 1121(m), 1079(m), 1034(m), 911(m) cm^{-1}; ^1H NMR δ 5.65 (1 H, dt, J = 2.9 Hz; 1.4 Hz; $^3J_{Sn-H}$ = 140 Hz, $H_{trans}H_{cis}C$=CRSnBu$_3$), 5.08 (1 H, d, J = 2.9 Hz; $^3J_{Sn-H}$ = 65 Hz, $H_{trans}H_{cis}C$=CRSnBu$_3$), 4.59-4.55 (1 H, m, C*H* (THP), 3.90-3.83 (1 H, m, CH_2 (THP)), 3.72 (1 H, dt, J = 9.5 Hz; 7 Hz, CH_2OTHP), 3.53-3.46 (1 H, m, CH_2 (THP)), 3.37 (1 H, dt, J = 9.5 Hz; 7 Hz, CH_2OTHP), 2.22 (2 H, t, J = 7 Hz, C=CSnBu$_3$CH_2), 1.87-1.78 (1 H, m, CH_2 (THP)), 1.75-1.66 (1 H, m, CH_2 (THP)), 1.63-1.43 (14 H, m, CH_2), 1.39-1.24 (14 H, m, CH_2), 0.91-0.76 (15 H, m, CH_2, CH_3); mass spectrum (EI): 473(M^+ -Bu, 7), 471(5), 469(3), 389(100), 387(76), 385(44), 179(25), 177(33), 175(22), 137(13), 135(13), 121(23), 119(17).

10-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*E*)-decene (76). The following data was obtained for a 10:90 mixture of **75** and **76**: IR (neat) 2922(s), 2853(s), 1598(w), 1464(m), 1200(m), 1136(m), 1121(m), 1079(m), 1034(m), 989(m) cm^{-1}; ^1H NMR δ 5.94 (1 H, dt, J = 19 Hz; 6 Hz, R$_3$Sn*H*C=CHR), 5.84 (1 H, d, J = 19 Hz, R$_3$SnHC=C*H*R), 4.95-4.55 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, J = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, J = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.11 (2 H, q, J = 7 Hz, C=CHCH_2), 1.87-1.78 (1 H, m, CH*H* (THP)), 1.75-1.67 (1 H, m, CH*H* (THP)), 1.63-1.43 (14 H, m, CH_2), 1.43-1.25 (14 H, m, CH_2), 0.92-0.76 (15 H, m, CH_2, CH_3); mass spectrum (EI) 473(M^+ -Bu, 5), 471(3), 469(2), 389(76), 387(54), 385(34), 307(100), 305(86), 303(45), 179(74), 177(72), 175(49), 137(56), 135(45), 133(31), 121(52).

10-Tetrahyropyranyloxy-2-tri-*n*-butylstannyl-1-nonene (77). An authentic sample was prepared as follows: To a solution of stannylcuprate, **65**, (1 mmol) in THF (10 mL) at -78 °C was added 1-alkyne, **38**, (0.24 mL, 1 mmol) followed by anhydrous methanol (excess). The solution was warmed to 0 °C

over several hours and the black mixture worked-up and purified as usual to yield **77** and **78** as a colourless liquid (89:11, 0.428 g, 83 %): IR (neat) 3031(w), 2924(s), 2854(s), 1598(w), 1464(m), 1200(m), 1136(m), 1120(m), 1078(m), 1035(m), 911(m) cm^{-1}; ^1H NMR δ 5.67-5.62 (1 H, m, $^3J_{Sn-H}$ = 139 Hz, $H_{trans}H_{cis}C=CHSnBu_3$), 5.08 (1 H, d, J = 2 Hz; $^3J_{Sn-H}$ = 63 Hz, $H_{trans}H_{cis}C=CHSnBu_3$), 4.59-4.55 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, J = 9.5 Hz; 6.9 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.38 (1 H, dt, J = 9.4 Hz; 7.2 Hz, CH*H*OTHP), 2.22 (2 H, t, J = 6.9 Hz; $^3J_{Sn-H}$ = 47 Hz, $C=CSnBu_3CH_2$), 1.88-1.77 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.64-1.42 (12 H, m, CH_2), 1.39-1.22 (14 H, m, CH_2), 0.91-0.84 (15 H, m, CH_2, CH_3); mass spectrum (EI) 459(M^+ -Bu, 3), 457(3), 375(56), 373(48), 371(25), 179(15), 177(23), 175(17), 121(18), 119(12), 117(7), 85(100), 67(19), 57(15), 56(13), 55(19); Anal. Calcd. for $C_{26}H_{52}O_2Sn$: C, 60.47; H, 10.08. Found: C, 60.59; H, 10.20.

10-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*E*)-nonene (78). The following data was obtained for a 89:11 mixture of **77** and **78**: IR (neat) see **77**; ^1H NMR (relative number of hydrogens) δ 5.94 (1 H, dt, J = 19 Hz; 7 Hz, $R_3SnHC=CHR$), 5.84 (1 H, d, J = 19 Hz, $R_3SnHC=CHR$), 4.59-4.55 (m, C*H* (THP)), 3.90-3.83 (m, CH*H* (THP)), 3.72 (dt, J = 9.5 Hz; 6.9 Hz, CH*H*OTHP), 3.53-3.46 (m, CH*H* (THP)), 3.38 (dt, J = 9.4 Hz; 7.2 Hz, CH*H*OTHP), 2.11 (2 H, q, J = 7 Hz, $C=CHCH_2$), 1.88-1.77 (m, CH*H* (THP)), 1.75-1.66 (m, CH*H* (THP)), 1.64-1.42 (m, CH_2), 1.39-1.22 (m, CH_2), 0.91-0.84 (m, CH_2, CH_3); mass spectrum (EI) 459(M^+ -Bu, 6), 457(4), 375(43), 373(37), 371(21), 179(12), 177(19), 175(16), 121(18), 119(13), 117(9), 67(23), 57(18), 56(16), 55(31).

6-Tetrahyropyranyloxy-2-tri-*n*-butylstannyl-1-hexene (79). The following data was obtained for a 91:9 mixture of **79** and **80**: IR (neat) 3031(w),

2026(s), 2853(s), 1598(w), 1464(m), 1456(m), 1200(m), 1136(m), 1120(m), 1077(m), 1034(m), 1021(m), 910(m) cm^{-1}; ^1H NMR δ 5.68-5.65 (1 H, m, $^3J_{Sn-H}$ = 140 Hz, $H_{trans}H_{cis}C=CRSnBu_3$), 5.11-5.08 (1 H, m, $^3J_{Sn-H}$ = 65 Hz, $H_{trans}H_{cis}C=CRSnBu_3$), 4.61-4.57 (1 H, m, C*H* (THP)), 3.90-3.82 (1 H, m, CH*H* (THP)), 3.71 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.51-3.45 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.26 (2 H, t, *J* = 7 Hz, $C=CSnBu_3CH_2$) 1.87-1.78 (1 H, m, CH_2 (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.63-1.38 (12 H, m, CH_2), 1.36-1.24 (8 H, m , CH_2), 0.91-0.84 (15 H, m, CH_2, CH_3); ^{13}C NMR δ 155.37 ($H_2C=CRSnBu_3$), 124.85 ($H_2C=CRSnBu_3$), 98.71, 67.36, 62.13, 41.14, 30.76, 29.41, 29.22, 29.13, 27.38, 26.27, 25.54, 19.56, 13.66, 9.58, 9.40; mass spectrum (EI) 417(M^+ -Bu, 2), 415(2), 333(100), 331(73), 329(44), 179(17), 177(24), 175(17), 137(11), 135(9), 121(14), 119(1), 85(51); Anal. Calcd. for $C_{23}H_{46}O_2Sn$: C, 58.35; H, 9.73. Found: C, 58.21; H, 9.66.

6-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*E*)-hexene (80). The following data was obtained for a 2:98 mixture of **79** and **80**: IR (neat) 2922(s), 2853(s), 1598(w), 1464(m), 1465(m), 1200(m), 1137(m), 1120(m), 1077(m), 989(m) cm^{-1}; ^1H NMR δ 5.95 (1 H, dt, *J* = 19 Hz; 6 Hz, $R_3SnHC=CHR$), 5.86 (1 H, d, *J* = 19 Hz, $R_3SnHC=CHR$), 4.59-4.55 (1 H, m, C*H* (THP)), 3.90-3.83 (1 H, m, CH*H* (THP)), 3.72 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.38 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.15 (2 H, q, *J* = 7 Hz, $C=CHCH_2$), 1.87-1.78 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.65-1.37 (12 H, m, CH_2), 1.35-1.24 (8 H, m, CH_2), 0.92-0.76 (15 H, m, CH_2, CH_3); ^{13}C NMR δ 149.34 ($R_3SnHC=CHR$), 127.43 ($R_3SnHC=CHR$), 99.82, 67.48, 62.29, 37.63, 30.78, 29.41, 29.22, 29.12, 27.26, 27.00, 25.58, 25.53, 19.67, 13.70, 9.57, 9.40; mass spectrum (EI) 417(M^+ -Bu, 100), 515(71),

413(42), 333(48), 331(36), 277(18), 275(15), 235(16), 233(15), 203(14), 201(12), 179(47), 177(59), 175(43), 137(30), 135(24), 121(26), 119(19), 85(52); Anal. Calcd. for $C_{23}H_{46}O_2Sn$: C, 58.35; H, 9.73. Found: C, 57.96; H, 9.53.

II.3 Chemical Investigations of Stannylcupration of 1-Alkynes.

II.3.1 *Variation of Reagent and Temperature.*

General Procedure. Alkynes, **48** or **70**, were added to solutions of stannylcuprates, **64** and **65**, in THF (10 mL) under reaction conditions described below. Purification of products and starting materials was achieved by flash chromatography (SiO_2, 5 % EtOAc in hexanes) after standard work-up.

[a] Alkyne, **70**, (0.10 mL, 0.5 mmol) was added at -78 °C to solutions of stannylcuprates, **64** and **65**, (0.5 mmol). The mixtures were quenched after 1.5 hr by pouring them into well-stirred solutions of NH_4Cl. Yield from **64**: **70** (0.074 g, 81 % recovered), **79**:**80** (90:10, 0.012 g, 5 %); from **65**: **70** (0.071 g, 78 % recovered), **79**:**80** (33:67, 0.019 g, 8 %).

[b] Alkyne, **48**, (0.13 mL, 0.5 mmol) was added at -78 °C to solutions of stannylcuprates, **64** and **65**, (0.5 mmol) followed by MeOH (2 mL, 49 mmol). Solutions were allowed to warm to 0 °C over 12 hr; they turned red to black at approximately -30 ° C. Yield from **64**: **75**:**76** (89:11, 0.16 g, 61 %); from **65**: **75**:**76** (91:9, 0.23 g, 85 %).

[c] To solutions of stannylcuprates, **64**, (1 mmol) and, **65**, (0.5 mmol) at -30 °C was added 0.19 mL (1 mmol) and 0.1 mL (0.5 mmol) of alkyne, **70**, respectively. The mixtures were warmed to 0 °C over 1 hr and quenched with MeOH. Yield from **64**: **79**:**80** (61:39, 0.30 g, 62 %); from **65**: **79**:**80** (15:85. 0.21

g, 90 %).

[d] Alkynes, **48**, (0.13 mL, 0.5 mmol) and, **70**, (0.1 mL, 0.5 mmol) were added at -30 °C to solutions of stannylcuprates, **64** and **65**, (0.5 mmol), respectively. The solution containing **64** was stirred at 0 °C for 12 hr and the solution containing **65** was stirred at room temperature over 12 hr before quenching with MeOH. The yield from **64**: **75**:**76** (54:46, 0.18 g, 66 %); from **65**: **79**:**80** (56:44, 0.19 g, 80 %).

II.3.2 *Variation of Solvent and Temperature.*

General Procedure. Solutions of stannylcuprate, **65**, (1 mmol) in THF (10 mL) were diluted with a solvent (10 mL) and THF removed under high vacuum. Alkyne, **70**, (0.19 mL, 1 mmol) was added to the yellow solutions under the described reaction conditions. Purification was accomplished by flash chromatography (SiO_2, 5 % EtOAc in hexanes) after work-up.

1. Stannylcupration in Dimethylformamide.

[a] Alkyne, **70**, and MeOH (1 mL) at -50 °C were added sequentially and the solution warmed to room temperature overnight. The black suspension was diluted with brine (200 mL) and extracted with diethyl ether (3 x 50 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure and the resultant crude oil purified to yield **79** and **80** (90:10, 0.41 g, 86 %).

[b] Alkyne, **70**, at -30 °C was added, the solution warmed to 0 °C over 1 hr and then quenched with MeOH. Work-up and purification yielded **79** and **80** (70:30, 0.40 g, 85 %).

2. Stannylcupration in Bis(2-methoxyethyl) ether.

[a] The same procedure was followed as described in 1 [a]. Work-up and purification of the black suspension yielded **79** and **80** (87:17, 0.41 g, 86 %).

[b] The same procedure was followed as described in 1 [b]. Work-up and purification yielded **79** and **80** (79:21, 0.37 g, 78 %).

3. Stannylcupration in Hexamethylphosphoramide.

[a] Alkyne, **70**, at -10 °C was added to a slurry and the mixture warmed to 0 °C over 1 hr. The pale yellow solution was quenched with MeOH and the resulting black suspension worked-up and purified to yield **79** and **80** (26:74, 0.26 g, 54 %).

4. Stannylcupration in Dimethyl Sulfide. Solvent was removed from a solution of stannylcuprate at 0 °C in THF under high vacuum and the resulting yellow paste dissolved in DMS to give a yellow solution.

[a] The same procedure was follwed as described in 1 [a]. Work-up and purification of the black suspension yielded **79** and **80** (91:9, 0.38 g, 81 %).

[b] The same procedure was followed as described in 1 [b]. Work-up and purification yielded **79** and **80** (54:46, 0.39 g, 83 %).

II.3.3 *Variation of Sn : Cu Ratios in Stannylcupration of 1-Alkyne **70**.*

General Procedure. Solutions of stannylcuprates in THF (10 mL) were prepared as descibed below. Preparation of *n*-Bu_3SnLi stock solution is described in section III.1. Purification of products and starting materials was

achieved by flash chromatography (SiO_2, 5 % EtOAc in hexanes) after standard work-up.

[a] [1:1]. To a solution of stannylcuprate, **72**, (0.5 mmol) in THF (10 mL) at -30 °C was added alkyne, **48**, (0.13 mL, 0.5 mmol). The mixture was warmed to 0 °C and quenched with MeOH. Yield: **75**:**76** (75:25, 0.15 g, 56 %).

[b] [1.5:1]. To a suspension of CuCN (0.045 g, 0.5 mmol) in THF (8.5 mL) at -30 °C was added *n*-Bu_3SnLi (1.5 mL, 0.5 M, 0.75 mmol) giving rise to an orange solution within 30 min. Alkyne, **70**, (0.1 mL, 0.5 mmol) was added, the mixture warmed to 0 °C over 1 hr and quenched with MeOH. Yield: **79**:**80** (84:16, 0.19 g, 79 %).

[c] [2:1]. See experiment II.3.1 [c].

[d] [8:1]. To a suspension of CuCN (0.045 g, 0.5 mmol) in THF (2 mL) at -30 °C was added *n*-Bu_3SnLi (8.0 mL, 0.50 M, 4.0 mmol) giving rise to a yellow solution within several minutes. Alkyne, **70**, (0.1 mL, 0.5 mmol) was added after 30 min, the mixture warmed to 0 °C over 1 hr and quenched with MeOH. Yield: **79**:**80** (19:81, 0.16 g, 67 %).

II.4 Spectroscopic Investigations of Solutions of $Me_3SnCu(CN)Li$ (100) and $(Me_3Sn)_2Cu(CN)Li_2$ (81).

II.4.1 *^{13}C NMR Studies of Solutions of $(Me_3Sn)_2Cu(CN)Li_2$ (81) in various Solvents.*

Sample Preparation. Solutions were analyzed by transferring an aliquot (ca. 0.3 mL) *via* cannula, under argon, to cooled (-30 °C) 5 mm NMR

tubes fitted with a rubber stopper. Cannulae were coated on the outside with a thin film of mineral oil in order to facilitate penetration and withdrawal through the rubber septum. The solutions were stirred at -30 °C for 30 min prior to ^{13}C NMR analysis. ^{13}C NMR spectra were recorded at -30 °C.

1. Ether/THF (1:4, 0.3 M). To a solution of $(Me_3Sn)_2$ (2 g, 6.1 mmol) in THF (16 mL) at -40 °C was added MeLi (4.36 mL, 1.4 M, 6.1 mmol) and stirring continued between -40 °C and -30 °C for one hour. The solution was then transferred to a separate flask containing CuCN (0.27 g, 3 mmol) (no solvent) at -30 °C. A red suspension that was formed initially dissolved to a yellow solution after several minutes.

2. Ether/MeOH (3:2, 0.2 M). To a solution of $(Me_3Sn)_2$ (0.42 mL, 2 mmol) in diethyl ether (1 mL) at -30 °C was added MeLi (2.1 mL, 0.93 M, 2 mmol). After 1 hr CuCN (0.09 g, 1 mmol) was added and stirring continued for 1 hr. The yellow solution was cooled to -40 °C and anhydrous MeOH (2 mL) added. An immediate colour change from yellow to red was noted.

3. Ether/HMPA (3:2, 0.2 M). This solution was prepared as described in 2 with the exception that HMPA (2 mL) was added to the solution instead of MeOH. Addition of HMPA caused the solution to turn amber.

II.4.2 *^{13}C NMR Studies of Solutions of $Me_3SnCu(^{13}CN)Li$ (**100**) and $(Me_3Sn)_2Cu(^{13}CN)Li_2$ (**81**).*

Sample Preparation. Solutions were prepared as described in section II.4.1. ^{13}C NMR spectra were recorded at 0 °C.

Preparation of $Cu^{13}CN$ (82). Prepared according to a literature procedure[80] from $K^{13}CN/H_2O$ (2.00 g, 30.7 mmol)/6 mL; $CuSO_4/H_2O$ (8.00 g, 32.0 mmol)/25 mL and $NaSO_4/H_2O$ (1.7 g, 16.3 mmol)/6 mL. $Cu^{13}CN$ was obtained as a fine, tan coloured powder (2.29 g, 82 %).

Preparation of Me_3SnLi stock solution [0.5 M THF/Ether]. The following procedure is representative: To a test tube containing a magnetic stirbar were added exactly 8.0 mL of THF and the bottom of the meniscus marked by etching the side of the glass. The calibrated test tube/stirbar assembly was oven dried, fitted with a rubber stopper and cooled under a stream of argon. The test tube was charged with THF (2 mL) and then $(Me_3Sn)_2$ (0.84 mL, 4.0 mmol) added. MeLi (4.26 mL, 0.94 M, 4.0 mmol) was added at -40 °C and the solution subsequently diluted (THF) to the 8.0 mL mark. The light green solution was stirred for 1hr between -40 °C and -30 °C.

$Me_3SnCu(^{13}CN)Li$ (100) (0.13 M THF/HMPA/Ether). To a suspension of $Cu^{13}CN$ (0.09 g, 1 mmol) in THF (4 mL) at -10 °C was added Me_3SnLi (2 mL, 0.5 M THF/Ether, 1 mmol). This gave rise to a red slurry within 30 min. HMPA (2 mL) was added causing the mixture to become homogeneous.

$(Me_3Sn)_2Cu(^{13}CN)Li_2$ (81) (0.1 M THF/HMPA/Ether). To a solution of **100** (above) at -10 °C was added Me_3SnLi (2 mL, 0.5 M THF/Ether, 1 mmol) to give rise to a yellow solution.

II.4.3 *Infrared Studies of Solutions of $Me_3SnCu(CN)Li$ (**100**) and $(Me_3Sn)_2Cu(CN)Li_2$ (**81**).*

Sample Preparation and Analyses. Infrared spectra of solutions were recorded on a Perkin-Elmer Model 1605 FT-IR spectrometer at 0 °C by using an infrared cell (pathlength = 1 mm) fitted with CaF_2 windows. The temperature of solutions was controlled by a CO_2/acetone bath inside a "cold finger" which formed an integral part of the IR cell assembly. A pair of inlet and outlet canulae enabled transfer of solutions from the cooled reaction flask (ca. -20 °C) to a receiver flask *via* the IR cell under an inert atmosphere. Typically, the IR cell was washed with anhydrous solvent for approximately 1 min and then the solution introduced until it could be seen dripping into the receiver flask. The temperature was allowed to equilibrate for 1 min before acquiring the spectrum. This cycle was repeated for each experiment. The absorption spectrum of each solvent system was recorded independently and electronically subtracted from IR spectra of samples. Unless indicated otherwise, 64 scans were taken for each run at a resolution of 4 cm^{-1}.

$Me_3SnCu(CN)Li$ (100) (0.1 M THF/HMPA/Ether). This solution was prepared by adding Me_3SnLi (2 mL, 0.5 M THF/Ether, 1 mmol) to a suspension of CuCN (0.09 g, 1 mmol) in THF (6 mL). HMPA (2 mL) was added after 30 min and caused a slight darkening of the solution.

$(Me_3Sn)_2Cu(CN)Li_2$ (81) (0.1 M THF/HMPA/Ether). This solution was prepared by adding Me_3SnLi (4 mL, 0.5 M THF/Ether, 2 mmol) to a suspension of CuCN (0.09 g, 1 mmol) in THF (4 mL). HMPA (2 mL) was added after 30 min and caused a slight darkening of the solution.

6-Tetrahyropyranyloxy-2-trimethylstannyl-1-hexene (83). The following data was obtained for a 98:2 mixture of **83** and **84**: IR (neat) 3033(w), 2938(s), 2870(s), 1597(w), 1454(m), 1440(m), 1352(m), 1200(m), 1136(m), 1119(m), 1078(m), 1035(m), 911(m) cm^{-1}; ^1H NMR δ 5.64 (1 H, dt, J = 2.8 Hz; 1.4 Hz; $^3J_{Sn-H}$ = 154 Hz, $H_{trans}H_{cis}C$=CRSnMe_3), 5.14 (1 H, dt, J = 2.8 Hz; 1.6 Hz; $^3J_{Sn-H}$ = 72 Hz, $H_{trans}H_{cis}C$=CRSnMe_3), 4.60-4.55 (1 H, m, C*H* (THP)), 3.90-3.82 (1 H, m, CH_2 (THP)), 3.73 (1 H, dt, J = 9.6 Hz; 6.6 Hz, CH_2OTHP), 3.53-3.46 (1 H, m, CH_2 (THP)), 3.37 (1 H, dt, J = 9.6 Hz; 6.5 Hz, CH_2OTHP), 2.30 (2 H, t, J = 7.5 Hz; $^3J_{Sn-H}$ = 52 Hz, C=CSnMe_3CH_2), 1.87-1.77 (1 H, m, CH_2 (THP)), 1.74-1.66 (1 H, m, CH_2 (THP)), 1.63-1.40 (8 H, m, CH_2), 0.12 (9 H, s, $^2J_{Sn-H}$ = 53 Hz, Sn(CH_3)$_3$); mass spectrum (EI) 333(M^+ -Me, 8), 331(6), 329(3), 249(100), 247(73), 245(44), 231(10), 229(8), 165(40), 163(29), 161(16), 151(9), 150(8), 149(9), 135(17), 133(13), 85(64), 67(13); Anal. Calcd. for $C_{14}H_{28}O_2Sn$: C, 48.45; H, 8.13. Found: C, 48.90; H, 8.27.

6-Tetrahydropyranyloxy-1-trimethylstannyl-1(*E*)-hexene (84). The following data was obtained for a 14:86 mixture of **83** and **84**: IR (neat) 2938(s), 2869(s), 1600(m), 1453(m), 1440(m), 1352(m), 1201(m), 1136(m), 1120(m), 1077(m), 1035(m), 989(m) cm^{-1}; ^1H NMR δ 5.98-5.93 (2 H, m, $^3J_{Sn-H}$ = 85 Hz, Me_3Sn*H*C=C*H*R), 4.60-4.54 (1 H, m, C*H* (THP)), 3.91-3.82 (1 H, m, CH*H* (THP)), 3.74 (1 H, dt, J = 9.6 Hz; 6.5 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.39 (1 H, dt, J = 9.6 Hz; 6.5 Hz, CH*H*OTHP), 2.19-2.21 (2 H, m, C=CSnMe_3CH_2), 1.88-1.78 (1 H, m, CH*H* (THP)), 1.75-1.66 (1 H, m, CH*H* (THP)), 1.64-1.43 (8 H, m, CH_2), 0.09 (9 H, s, $^2J_{Sn-H}$ = 53 Hz, Sn(CH_3)$_3$); mass spectrum (Ei) 333(M^+ -Me, 100), 331(71), 329(3), 249(66), 247(46), 245(28), 231(17), 229(13), 167(12), 165(24), 163(16), 151(14), 149(12); Anal. Calcd. for $C_{14}H_{28}O_2Sn$: C, 48.45; H, 8.13. Found: C, 48.48; H, 8.10.

6-Tetrahydropyranyloxy-1,2-bis(trimethylstannyl)-1(*Z*)-hexene (85). IR (neat) 2938(s), 2869(s), 1548(w), 1453(m), 1440(m), 1352(m), 1200(m), 1186(m), 1137(m), 1120(m), 1077(m), 1034(m), 1022(m) cm^{-1}; ^1H NMR δ 6.61 (1 H, t, *J* = 1.2 Hz; $^3J_{Sn-H}$ = 197 Hz; $^2J_{Sn-H}$ = 87 Hz, Me_3SnHC=CSnMe_3R), 4.60-4.50 (1 H, m, C*H* (THP)), 3.90-3.82 (1 H, m, CH*H* (THP)), 3.37 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 3.53-3.46 (1 H, m, CH*H* (THP)), 3.57 (1 H, dt, *J* = 9.5 Hz; 7 Hz, CH*H*OTHP), 2.36 (2 H, dt, *J* = 7 Hz; 1.2 Hz, C=CSn$Me_3C$$H_2$), 1.89-1.78 (1 H, m, CH*H* (THP)), 1.75-1.67 (1 H, m, CH*H* (THP)), 1.62-1.48 (6 H, m, CH_2), 1.47-1.38 (2 H, m, CH_2), 0.16 (9 H, s, $^3J_{Sn-H}$ = 52 Hz, Sn(CH_3)$_3$), 0.15 (9 H, s, J_{Sn-H} = 52 Hz, Sn(CH_3)$_3$); ^{13}C NMR δ 168.8 (Me_3SnHC=*C*SnMe_3R), 143.0 (Me_3SnHC=CSnMe_3R), 98.8, 67.4, 62.2, 47.3, 30.8, 29.2, 26.4, 25.5, 19.6, -7.5, -7.7; mass spectrum (EI) 347(M^+ -SnMe_3, <1), 315(2), 313(2), 311(2), 263(9), 261(8), 259(4), 249(4), 247(10), 245(8), 243(4), 231(3), 229(2), 135(20), 133(16), 85(96); Anal. Calcd. for $C_{17}H_{36}O_2Sn_2$: C, 40.0; H, 7.06. Found: C, 40.57; H, 6.77.

CHAPTER III

III.1 Chemical Investigations of CuCN and CuI Derived Mixed Higher Order and Lower Order Trialkylstannylcuprates.

Preparation cf *n*-Bu_3SnLi stock solution [0.5 M THF]. This solution was prepared by treating a solution of (*n*-$Bu_3Sn)_2$ (2.53 mL, 5.0 mmol) in THF (4 mL) with *n*-BuLi (2 mL, 2.5 M, 5 mmol) following the same procedure as described for the preparation of Me_3SnLi stock solution[20] (see Chapter II). The mixture was diluted with THF to a final volume 10 mL.

Preparation of C_8H_{17}-C≡CLi stock solution [1.0 M THF]. The following procedure is representative: To an oven dried test tube equipped with a magnetic stirbar and calibrated to 7 mL (see above) was added THF (2 mL) followed by 1-decyne (1.27 mL, 7.0 mmol). The solution was cooled to -78 °C and *n*-BuLi (2.86 mL, 2.45 M, 7.0 mmol) added dropwise. The mixture was diluted with THF to the 7 mL mark of a calibrated reaction vessel and stirring continued at -78 °C for 30 min to afford an olive green solution.

Preparation of Ph-C≡CLi stock solution [1.0 M THF]. This solution was prepared by treating a solution of phenylacetylene (0.55 mL. 5 mmol) in THF (2 mL) with *n*-BuLi (2 mL, 2.5 M, 5 mmol) following the same procedure as described for the preparation of C_8H_{17}-C≡CLi stock solution (see above). The mixture was diluted with THF to a final volume 5 mL.

III.1.1 *Stannylcupration of Organic Substrates with $Me_3Sn(Me)Cu(CN)Li_2$ (86).*

Preparation of $(Me_3Sn)(Me)Cu(CN)Li_2$ (86). To a suspension of CuCN (0.09 g, 1 mmol) in THF (20 mL) at -30 °C was added MeLi (1.8 mL, 1 M, 2 mmol). A tan coloured solution formed within several minutes to which $(SnMe_3)_2$ (0.21 mL, 1 mmol) was added after 30 min. The yellow solution was stirred for 1 hr at -30 °C prior to addition of substrate.

3-Trimethylstannyl-3-buten-1-ol.(87). An authentic sample was prepared as follows: To a solution of $(Me_3Sn)_2Cu(CN)Li_2$ (1 mmol) in THF (20 mL) -78 °C was added 3-butyn-1-ol (0.08 mL, 1 mmol) followed by MeOH (excess). The mixture was warmed to 0 °C over several hours and subsequently worked up and purified as described for **88** to yield **87** and **88** (90:10, 0.19 g, 80 %): IR (neat) 3338(s), 3035(w), 2976(s), 2914(s), 1700(w), 1601(w),

1423(m), 1189(m), 1046(m), 989(w), 919(w) cm^{-1}; ^1H NMR δ 5.78 (1 H, dt, J = 3 Hz; 1.5Hz; $^3J_{Sn-H}$ = 147 Hz, $H_{trans}H_{cis}C$=CSnMe$_3$R), 5.33 (1 H, dt, J = 3 Hz; 1 Hz; $^3J_{Sn-H}$ = 69 Hz, $H_{trans}H_{cis}C$=CSnMe$_3$R), 3.65 (2 H, q, J = 6 Hz, CH_2OH), 2.55 (2 H, t, J = 7 Hz; $^3J^{119}_{Sn-H}$ = 56 Hz; $^3J^{117}_{Sn-H}$ = 53 Hz, C=CSnMe$_3$CH_2), 1.38 (1 H, t, J = 6 Hz, OH), 0.16 (9 H, s, $^2J_{Sn-H}$ = 51 Hz, Sn(CH_3)$_3$); mass spectrum (CI) 237(M^{+1}, 26), 235(20), 233(10), 221(51), 219(42), 217(25), 165(100), 163(68), 161(44); Anal. Calcd. for $C_7H_{16}OSn$: C, 35.74; H, 6.81. Found: C, 35.91; H, 6.57.

4-Trimethylstannylbut-3(*E*)-en-1-ol.(88). To a solution of stannylcuprate, **86**, (1 mmol) was added at -78 °C 3-butyn-1-ol (0.08 mL, 1 mmol), the mixture warmed to 0 °C over several hours and quenched with MeOH. The solution was diluted with brine (50 mL) extracted with diethyl ether (3 x 20 mL) and the combined organic layers dried ($MgSO_4$) and concentrated. The crude liquid was flash chromatographed (SiO_2, 10 % EtOAc in hexanes; silica was pretreated with a solution of Et_3N (2 %-hexanes) to afford **87** and **88** (3:97, 0.18 g, 77 %) as a colourless liquid. Stannylcupration above -30 °C resulted in the formation of isomers **87** and **88** with varied regioselectivity: IR (neat) 3334(s), 3035(w), 2967(s), 2914(s), 1708(w), 1601(m), 1422(m), 1189(m), 1046(m), 990(m), 919(m) cm^{-1}; ^1H NMR δ 6.11 (1 H, dt, J = 19 Hz; 1.5 Hz; $^2J^{119}_{Sn-H}$ = 68 Hz; $^2J^{117}_{Sn-H}$ = 64 Hz, Me$_3$SnHC=CHR), 5.93 (1 H, dt, J = 19 Hz; 6.5 Hz; $^3J^{119}_{Sn-H}$= 74 Hz; $^3J^{117}_{Sn-H}$ = 70 Hz, Me$_3$SnHC=CHR), 3.68 (2 H, q, J = 6 Hz, CH_2OH), 2.40 (2 H, dq, J = 6 Hz; 1.5 Hz, C=CHCH_2), 1.45 (1 H, t, J = 6 Hz, OH), 0.12 (9 H, s, $^2J_{Sn-H}$ = 51 Hz, Sn(CH_3)$_3$); mass spectrum (CI) 237($(M+1)^+$, 35), 235(25), 233(17), 195(5), 193(5), 165(100), 163(72), 161(46); Anal. Calcd. for $C_7H_{16}OSn$: C, 35.74; H, 6.81. Found: C, 35.47; H, 6.68.

2-Trimethylstannyl-1-decene (89). To stannylcuprate, **86**, (1 mmol) was added at -30 °C 1-decyne (0.18 mL, 1 mmol), the mixture warmed to room temperature overnight and quenched with MeOH (excess). The solution was diluted with brine (50 mL), extracted with hexanes (3 x 20 mL) and the combined organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. The crude liquid was purified by Kugelrohr distillation to yield **89** and **90** (84:16, 0.20 g, 67 %). Prolonged reaction times at room temperature resulted in the formation of increasing amounts of distannane, **91**. In a modified procedure 1-decyne (1 mmol) and MeOH (excess) were added to a solution of stannylcuprate,**86**, (2 mmol) at -78 °C and the mixture warmed to 0 °C over several hours. Work-up and purification yielded **89** and **90** (98:2, 0.26 g, 87 %): ^{1}H NMR δ 5.65 (1 H, dt, J = 3 Hz; 1.5 Hz; $^3J_{Sn-H}$ = 165 Hz, $H_{trans}H_{cis}C$=CSnMe$_3$R), 5.13 (1 H, dt, J = 3 Hz; 1 Hz; $^3J_{Sn-H}$ = 73 Hz, $H_{trans}H_{cis}C$=CSnMe$_3$R), 2.28 (2 H, t, J = 7 Hz, C=CSnMe$_3$CH_2), 1.43-1.19 (12 H, m, CH_2), 0.90 (3 H, t, J = 7 Hz, CH_3), 0.13 (9 H, s, $^2J_{Sn-H}$ = 51 Hz, Sn(CH_3)$_3$); mass spectrum (EI) 289(M$^+$ -Me, 100), 287(72), 285(45), 165(26), 163(18), 161(12), 151(27), 149(22), 147(14), 135(16), 133(13); Anal. Calcd. for $C_{13}H_{28}Sn$: C, 51.49; H, 9.24. Found: C, 51.67; H, 9.37.

1-Trimethylstannyl-1(*E*)-decene (90). The following data was obtained for a 84:16 mixture of **89** and **90**: ^{1}H NMR (relative number of protons) δ 6.45 (1 H, dt, J = 12.5 Hz; 7 Hz; $^3J_{Sn-H}$ = 154 Hz, Me$_3$SnHC=CHR), 5.77 (1 H, dt, J = 12.5 Hz; 1 Hz; $^2J_{Sn-H}$ = 82 Hz, Me$_3$SnHC=CHR), 2.02 (2 H, dq, J = 7 Hz; 1 Hz, C=CSnMe$_3$CH_2), 1.38-1.20 (m, CH_2), 0.14 (s, $^2J_{Sn-H}$ = 51 Hz, Sn(CH_3)$_3$); mass spectrum (EI) 289(M$^+$ -Me, 100), 287(79), 285(48), 165(25), 163(18), 161(12), 151(62), 149(52), 147(30), 135(36), 133(27), 131(15), 121(11), 119(9).

1,2-Bis(trimethylstannyl)-1(*Z*)-decene (91). Isolated as the main product in the stannylcupration of 1-decyne with stannylcuprate, **86**, after prolonged reaction time: ^{1}H NMR δ 6.58 (1 H, t, J = 1.5 Hz; $^3J^{119}_{Sn-H}$ = 196 Hz; $^2J^{119}_{Sn-H}$ = 87 Hz; $^3J^{117}_{Sn-H}$ = 187 Hz; $^2J^{117}_{Sn-H}$ = 83 Hz, Me_3SnHC=$CSnMe_3R$), 2.30 (2 H, dt, J = 7 Hz; 1.5 Hz, C=$CSnMe_3CH_2$), 1.35-1.20 (12 H, m, CH_2), 0.86 (3 H, t, J = 7 Hz, CH_3), 0.15 (9 H, s, $^2J_{Sn-H}$ = 51 Hz, $Sn(CH_3)_3$), 0.13 (9 H, s, $^2J_{Sn-H}$ = 51 Hz, $Sn(CH_3)_3$); mass spectrum (EI) 462-468(M^+, 1), 445-457(4), 324-334(23), 308-319(25), 303(13), 301(10), 299(6), 165(100), 163(69), 161(42), 135(10), 133(8), 121(1), 119(1).

3-Trimethylstannylcyclohexanone (92). To a solution of stannylcuprate **86** (1.1 mmol) at -78 °C was added 2-cyclohexen-1-one (0.1 mL, 1 mmol). After 30 min the mixture was warmed to room temperature, quenched with MeOH and diluted with brine (50 mL). The solution was extracted with diethyl ether (3 x 20 mL) and the combined organic layers dried ($MgSO_4$) and concentrated under reduced pressure. The remaining crude liquid was purified by flash chromatography (SiO_2, 10 % EtOAc in hexanes; silica was pretreated with a solution of Et_3N (2 %-hexanes) to afford **92** (0.18 g, 70 %) as a colourless liquid: IR (neat) 2923(s), 2859(s), 1708(s), 1444(m), 1418(m), 1341(m), 1310(m), 1225(m) cm^{-1}; ^{1}H NMR δ 2.48-2.27 (4 H, m, CH_2), 2.17-2.09 (1 H, m, CH_2), 1.97-1.88 (1 H, m, CH_2), 1.82-1.53 (3 H, m, CH_2, $CHSnMe_3$), 0.07 (9 H, s, $^2J^{119}_{Sn-H}$ = 53 Hz; $^2J^{117}_{Sn-H}$ = 52 Hz, $Sn(CH_3)_3$); mass spectrum (CI) 263($(M+1)^+$, 31), 261(25), 259(15), 247(100), 245(81), 243(48), 183(10), 181(9), 179(5), 165(33), 163(23), 161(16). HRMS Calcd. for $C_9H_{18}Sn$ (-Me): 247.014. Found: 247.0134.

1-Trimethylstannyloctan-2-ol (93). To a solution of stannylcuprate, **86**, (1.2 mmol) at -78 °C was added a solution of 1,2-epoxyoctane (0.13 g, 1

mmol) in THF (2 mL), the mixture warmed to room temperature over several hours and quenched with MeOH. Extraction with diethyl ether (3 x 20 mL) followed by drying ($MgSO_4$) and concentration of the combined organic layers gave a crude liquid which was flash chromatographed (SiO_2, 10 % EtOAc in hexanes) to afford **93** (0.13 g, 44 %) as a colourless liquid. In a second experiment, **94** was also isolated in addition to **93** (0.11 g, 38 %): IR (neat) 3362(s), 2956(s), 2926(s), 2856(s), 1466(m), 984(m) cm^{-1}; ^1H NMR δ 3.93-3.83 (1 H, m, R_2CHOH), 1.47-1.38 (2 H, m, $RCHOHCH_2$), 1.35-1.23 (8 H, m, CH_2), 1.18 (1 H, dd, J = 13 Hz; 6.5 Hz, $RCHHSnMe_3$), 1.08 (1 H, dd, J = 13 Hz; 6.5 Hz, $RCHHSnMe_3$), 0.88 (3 H, t, J = 7 Hz, CH_3), 0.09 (9 H, $^2J_{Sn-H}$ = 52 Hz, $Sn(CH_3)_3$); mass spectrum (EI) 277(M^+ -OH, 27), 275(19), 273(10), 261(24), 259(11), 257(6), 183(26), 181(21), 179(4), 165(100), 163(70), 161(42).

3-Nonanol (94). Isolated from stannylcupration of 1,2-epoxyoctane with stannylcuprate, **86**, (1.2 mmol) as a colourless liquid (0.043 g, 30 %): IR (neat) 3331(s), 2926(s), 1454(m), 1349 (m), 1136(m) 1073(m), 1012(m) cm^{-1}; ^1H NMR δ 3.52 (1 H, s, R_2CHOH), 1.57-1.2 (12 H, m, CH_2), 0.95 (3 H, t, J = 7 Hz, CH_3), 0.89 (3 H, t, J = 5 Hz, CH_3); mass spectrum (CI) 127 $(M+1)^+$, $-H_2O$).

III.1.2 *Stannylcupration of Organic Substrates with n-Bu_3Sn(n-Bu)Cu(CN)Li_2.*

Preparation of (*n*-Bu_3Sn)(*n*-Bu)Cu(CN)Li_2 (95). This reagent was prepared following the procedure described for stannylcuprate, **86**, from *n*-BuLi and $(n\text{-}Bu_3Sn)_2$ reagents.

3-Tri-*n*-butylstannyl-3-buten-1-ol (96). An authentic sample was prepared by adding 3-butyn-1-ol (0.15 mL, 2 mmol) at -78 °C to a solution of $(n\text{-}Bu_3Sn)_2Cu(CN)Li_2$ **(65)** (2 mmol) in THF (20 mL) followed by methanol

(excess) and warming this mixture to room temperature over several hours. Work-up and purification as described for **97** yielded **96** and **97** (99:1, 0.40 g, 55 %) as a colourless liquid: IR (neat) 3320(s), 3034(w), 2956(s), 2925(s), 2871(s), 2858(s), 1464(m), 1376(m), 1047(m), 917(m) cm^{-1}; ^1H NMR δ 5.81 (1 H, m, $^3J_{Sn-H}$ = 133 Hz, $H_{trans}H_{cis}C$=CSnBu$_3$R), 5.30-5.27 (1 H, m, $^3J_{Sn-H}$ = 61 Hz, $H_{trans}H_{cis}C$=CSnBu$_3$R), 3.63 (2 H, q, J = 5.9 Hz, CH_2OH), 2.52 (2 H, t, J = 6.2 Hz; $^3J^{119}_{Sn-H}$ = 47 Hz; $^3J^{117}_{Sn-H}$ = 45 Hz, C=CSnBu$_3$CH_2), 1.53-1.43 (6 H, m, CH_2), 1.31 (6 H, sext, J = 7.3 Hz, CH_2), 0.94-0.85 (15 H, m, CH_2, CH_3); mass spectrum (EI) 305(M^+ -Bu, 100), 303(72), 301(43), 249(32), 247(24), 245(13), 179(13), 177(29), 175(23), 137(55), 135(42), 133(28), 121(27), 119(20), 117(13); Anal. Calcd. for $C_{16}H_{34}OSn$: C, 53.04; H, 9.39. Found: C, 53.21; H, 9.55.

4-Tri-*n*-butylstannyl-3(*E*)-buten-1-ol (97). To a solution of stannylcuprate, **95**, (2.4 mmol) in THF (20 mL) at -78 °C was added 3-butyn-1-ol (0.15 mL, 2 mmol), the mixture warmed to 0 °C over 1 hr and quenched with MeOH. The solution was diluted with brine (100 mL), extracted with diethyl ether (3 x 20 mL) and the combined organic layers dried ($MgSO_4$) and concentrated under reduced pressure to afford a crude liquid. Purification by flash chromatography (SiO_2, EtOAc 10 % in hexanes) yielded **96** and **97** (4:96, 0.61 g, 84 %) as a colourless liquid: IR (neat) 3330(s), 2956(s), 2926(s), 2871(s), 1599(m), 1464(m), 1376(m), 1046(m), 990(m) cm^{-1}; ^1H NMR δ 6.07 (1 H, dt, J = 19 Hz; 1.5 Hz; $^2J^{119}_{Sn-H}$ = 76 Hz; $^2J^{117}_{Sn-H}$ = 72 Hz, Bu$_3$SnHC=CHR), 5.93 (1 H, dt, J = 19 Hz; 6 Hz; $^3J^{119}_{Sn-H}$ = 64 Hz; $^3J^{117}_{Sn-H}$ = 61 Hz, Bu$_3$SnHC=CHR), 3.68 (2 H, q, J = 6 Hz, CH_2OH), 2.43 (2 H, dq, J = 6 Hz; 1.5 Hz, C=CSnBu$_3$CH_2), 1.58-1.38 (6 H, m, CH_2), 1.35-1.25 (6 H, m, CH_2), 0.93-0.87 (15 H, m, CH_2, CH_3); mass spectrum (EI) 305(M^+ -Bu, 24), 303(19), 301(10), 291(100),

289(78), 287(45); Anal. Calcd. for $C_{16}H_{34}OSn$: C, 53.04; H, 9.39. Found: C, 52.99; H, 9.38.

1-Tri-*n*-butylstannyl-2-octanol (98). To a solution of stannylcuprate **95** (2.4 mmol) in THF (20 mL) at -78 °C was added a solution of 1,2-epoxyoctane (0.26 g, 2 mmol) in THF (2 mL) and the solution warmed to room temperature overnight. The mixture was quenched with MeOH, diluted with brine (100 mL) and extracted with diethyl ether (3 x 20 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated to give a crude liquid which yielded, after flash chromatography (SiO_2, 10 % EtOAc in hexanes), **98** (0.26 g, 31 %) as a colourless liquid: IR (neat) 3346(m), 2957(s), 2925(s), 2871(s), 2834(s), 1464(m), 1376(m), 1071(m), 1001(m) cm^{-1}; ^1H NMR δ 3.91-3.83 (1 H, m, R_2CHOH), 1.52-1.40 (10 H, m, CH_2), 1.38-1.23 (14 H, m, CH_2), 1.15 (1 H, dd, J = 13 Hz; 7 Hz, $RCHHSnBu_3$), 1.07 (1 H, dd, J = 13 Hz; 7 Hz, $RCHHSnBu_3$), 0.91-0.83 (28 H, m, CH_2, CH_3); mass spectrum (EI) 313(1), 291(3), 289(2), 269(100), 267(69), 265(37), 213(41), 211(37), 209(210, 177(37), 175(26), 173(15), 155(55), 153(42), 151(20), 121(20), 119(16), 117(10), 7(36); Anal. Calcd. for $C_{20}H_{44}OSn$: C, 57.29; H, 10.58. Found: C, 57.49; H, 10.79.

6-Dodecanol (99). This compound was isolated from reaction of 1,2-epoxyoctane with stannylcuprate, **95**, (2.4 mmol) as a colourless liquid (0.107 g, 29 %): IR (neat) 3332(s), 2925 (s), 1454 (m), 1378(m), 1137(m), 1073(m), 1012(m) cm^{-1}; ^1H NMR δ 3.59 (1 H, s, R_2CHOH), 1.50-1.22 (18 H, m, CH_2), 0.93-0.83 (6 H, m, CH_3); mass spectrum (EI) 185(M+, <1), 168(9), 115(37), 101(46), 97(100), 83(91), 69(17), 55(61).

Stannylcupration of 1-Alkyne (48) [1 equivalent]. To a solution of stannylcuprate **95** (1 mmol) in THF (10 mL) at -30 °C was added alkyne, **48**,

(0.26 mL, 1 mmol), the mixture warmed to 0 °C over 1 hr and quenched with MeOH. The solution was concentrated under reduced pressure and the resulting slurry suspended in hexanes (ca. 5 mL) and subjected to flash chromatography (SiO_2, 5 % EtOAc in hexanes). A colourless oil consisting of **75** and **76** (55:45, 0.30 g, 57 %) was obtained.

Stannylcupration of 1-Alkyne (48) [2 equivalents]. This reaction was carried out as described above using 1-alkyne, **48**, (0.26 mL, 1 mmol) and stannylcuprate, **95**, (0.5 mmol). Work-up and purification yieded **75** and **76** (17:83, 0.213 g, 80 % [based on available *n*-Bu_3Sn]) as a colourless oil.

III.1.3 *Stannylcupration of 3-Butyn-1-ol and Lithium 3-Butyn-1-oxide.*

[a] To a THF solution of *n*-Bu_3Sn(*n*-Bu)Cu(CN)Li_2 (**95**) (2.4 mmol) was added 3-butyn-1-ol as described in III.1.2. Work-up and purification yielded **96** and **97** (4:96, 0.61 g, 84 %).

[b] To a suspension of *n*-$Bu_3SnCu(CN)Li$ (**72**) (2.4 mmol) in THF (20 mL) at -78 °C was added 3-butyn-1-ol (0.15 mL, 2 mmol), the mixture warmed to 0 °C over 1 hr and quenched with MeOH. Work-up and purification yielded **96** and **97** (69:31, 0.56 g, 78 %).

[c] To a suspension of *n*-$Bu_3SnCu(CN)Li$ (**72**) (2.4 mmol) in THF (10 mL) at -78 °C was transferred a solution of lithium 3-butyn-1-oxide (2 mmol) in THF (10 mL) [prepared by treating a THF solution of 3-butyn-1-ol (0.15 mL, 2 mmol) with *n*-BuLi (0.8 mL, 2.5 M, 2 mmol) at -30 °C/15 min]. The mixture was warmed to 0 °C over 1 hr during which time a yellow solution was formed. Quenching with MeOH followed by work-up and purification yielded **96** and **97**

(25:75, 0.52 g, 73 %).

[d] To a THF solution of $Me_3Sn(Me)Cu(CN)Li_2$ (**86**) was added 3-butyn-1-ol as described in III.1.1. Work-up and purification yielded **87** and **88** (3:97, 0.18 g, 77 %)

[e] To a suspension of $Me_3SnCu(CN)Li$ (**100**) (1.1 mmol) in THF (20 mL) at -78 °C was added 3-butyn-1-ol (0.08 mL, 1 mmol), the mixture warmed to 0 °C over 1 hr and quenched with MeOH. Work-up and purification yielded **87** and **88** (81:19, 0.175 g, 74 %).

[f] A solution of lithium 3-butyn-1-oxide (2 mmol) in THF (10 mL) was added to a suspension of $Me_3SnCu(CN)Li$ (**100**) (2.4 mmol) in THF (10 mL) as described in [c]. Work-up and purification yielded **87** and **88** (35:65, 0.32 g, 69 %).

III.1.4 *Stannylcupration of 1-Alkynes with n-$Bu_3Sn(X)CuLi\cdot LiI$.*

General Procedure. Solutions were worked-up by addition of a saturated solution of NH_4Cl (100 mL) to reaction mixtures followed by extraction with hexanes (3 x 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The resulting crude oils were purified by flash chromatography (SiO_2, 5 % EtOAc in hexanes). Vinylstannanes were obtained as colourless liquids. Anions of MeOH,[43] Et_2NH,[43] Ph_2PH,[43] *n*-Bu_2Se[81] and R-C≡C-H[63] were prepared following literature procedures.

[a] X = MeO. To a mixture of CuI (0.19 g, 1 mmol) and MeOLi (0.038 g, 1 mmol) was added THF (8 mL) and the suspension stirred at room temperature

for 1 hr. The resulting yellow solution was cooled to -50 °C and *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added causing the mixture to turn black immediately. Alkyne,**70**, (0.19 mL, 1 mmol) was added at -30 °C, the solution warmed to 0 °C over 1 hr and quenched with MeOH. Work-up and purification yielded **79** and **80** (69:31, 0.093 g, 39 %).

[b] X = Et_2N. To a solution of Et_2NH (0.10 mL, 1 mmol) in THF (8 mL) at -30 °C was added *n*-BuLi (0.40 mL, 2.5 M, 1 mmol) and stirring continued between -30 °C and -20 °C for 45 min before adding CuI (0.19 g, 1 mmol). After 30 min the red-brown solution was cooled to -30 °C and *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added giving rise to a turbid, yellow mixture after 30 min. Alkyne, **70**, (0.19 mL, 1 mmol) was added, the solution warmed to 0 °C over 1 hr and quenched with MeOH. Work-up and purification yielded **79** and **80** (50:50, 0.057 g, 24 %).

[c] X = Ph_2P. To a solution of *n*-Bu_2PH (0.17 mL, 1 mmol) in THF (8 mL) was added at -30 °C *n*-BuLi (0.40 mL, 2.5 M, 1 mmol). The amber solution was stirred at room temperature for 10 min, cooled to -30 °C and CuI (0.19 g, 1 mmol) added giving rise to a black suspension. *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) was added followed by alkyne, **70**, (0.19 mL, 1 mmol) after 30 min (no colour change). The slurry was warmed to 0 °C over 1 hr, quenched with MeOH and diluted with NH_4Cl (100 mL). Work-up of the acidified mixture (2 M HCl) followed by purification yielded **79** and **80** (17:83, 0.081 g, 17 %).

[d] X = *n*-BuSe. To a suspension of finely granulated selenium (0.079 g, 1 mmol) in THF (8 mL) at -20 °C was added *n*-BuLi (0.40 mL, 1 mmol). The colourless solution was cooled to -30 °C and CuI (0.19 g, 1 mmol) added after 30 min. The dark brown suspension was stirred for 30 min and then *n*-Bu_3SnLi

(2 mL, 0.5 M, 1 mmol) added, followed by alkyne, **70**, (0.19 mL, 1 mmol) after an additional 30 min. Work-up of the acidified mixture (2 M HCl) followed by purification yielded : **79** and **80** (81:19, 0.17 g, 70 %).

[e] X = C_8H_{17}-C≡C. To a suspension of CuI (0.19 g, 1 mmol) in THF (3 mL) at room temperature was added C_8H_{17}-C≡CLi (1 mL, 1 M, 1 mmol). After 15 min the yellow slurry was cooled to -10 °C and *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added giving rise to a pale green solution within 10 min. After 30 min the solution was cooled to -30 °C, alkyne, **70**, (0.1 mL, 0.5 mmol) added and the mixture warmed to 0 °C over 1 hr. The solution was quenched with MeOH, worked up and purified to yield **79** and **80** (65:35, 0.18 g, 77 %).

[f] X = Ph-C≡C. To a suspension of CuI (0.10 g, 0.5 mmol) in THF (3 mL) at room temperature was added Ph-C≡CLi (0.5 mL, 1 M, 0.5 mmol). The yellow slurry was cooled to -10 °C after 30 min and *n*-Bu_3SnLi (1 mL, 0.5 M, 0.5 mmol) added giving rise to a red-brown suspension. Stirring was continued for 30 min before adding alkyne, **70**, (0.1 mL, 0.5 mmol) at -30 °C. The mixture was warmed to 0 °C over 1 hr, quenched with MeOH and worked up and purified to yield **79** and **80** (65:35, 0.056 g, 21 %).

III.1.5 *Stannylcupration of 1-Alkynes with n-$Bu_3Sn(X)_2CuLi_2$.*

[a] X = MeO. A mixture of CuI (0.19 g, 1 mmol) and MeOLi (0.78 g, 2 mmol) was stirred in THF (8 mL) for 1 hr at room temperature to give a yellow, heterogeneous solution. The mixture was cooled to -50 °C and *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added causing a gradual blackening of the solution. Alkyne, **70**, (0.19 mL, 1 mmol) was added at -30 °C, the solution warmed to 0 °C over 1 hr and quenched with MeOH. Work-up and purification afforded **79** and **80**

(89:11, 0.123 g, 26 %).

[b] X = Et_2N. To a solution of Et_2NLi (2 mmol) in THF (8 mL) at -20 °C [prepared as described above] was added CuI (0.19 g, 1 mmol) and the suspension stirred for 30 min to give a colourless solution. The mixture was cooled to -30 °C, *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added and stirring continued for 30 min (no colour change). Alkyne, **48**, (0.26 mL, 1 mmol) was added at -30 °C, causing the solution to turn yellow, and this mixture warmed to 0 °C over 1 hr. Quenching with MeOH followed by work-up and purification yielded **75** and **76** (>99:1, 0.192 g, 36 %).

[c] X = Ph_2P. To a solution of *n*-Bu_2PLi (2 mmol) in THF at -30 °C (7 mL) [prepared as described above] was added CuI (0.19 g, 1 mmol) giving rise to a black suspension. *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) was added after 30 min followed by alkyne, **70**, (0.19 mL, 1 mmol). The solution was warmed to 0 °C over 1 hr and quenched with MeOH. Work-up of the acidified mixture (2 N HCl) followed by and purification yielded **79** and **80** (10:90, 0.169 g, 36 %).

[d] X = *n*-BuSe. To a solution of *n*-BuSeLi (2 mmol) in THF (7 mL) at -30 °C [prepared as described above] was added CuI (0.19 g, 1 mmol) giving rise to a yellow solution. After 30 min *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) was added and stirring continued for 30 min (no colour change) before adding alkyne, **70**, (0.19 mL, 1 mmol). The solution was warmed to 0 °C over 1 hr and quenched with MeOH. Work-up of the acidified mixture (2 M HCl) followed by purification yielded **79** and **80** (29:71, 0.23 g, 48 %).

[e] X = C_8H_{17}-C≡C. To a suspension of CuI (0.19 g, 1 mmol) in THF (2 mL) at room temperature was added C_8H_{17}-C≡CLi (2 mL, 1 M, 2 mmol) forming a colourless solution within several minutes. The mixture was cooled to -10 °C,

n-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added and the yellow solution stirred for 15 min. Alkyne, **70**, (0.1 mL, 0.5 mmol) was added at -30 °C and the mixture warmed to 0 °C over 1 hr. The solution was quenched with MeOH, worked up and purified to yield **79** and **80** (4:96, 0.17 g, 71 %). A lower yield was obtained using only one equivalent of reagent per substrate (2:98, 0.079 g, 33 %).

[f] X = Ph-C≡C. To a suspension of CuI (0.19 g, 1 mmol) in THF (2 mL) was added Ph-C≡CLi (2 mL, 1 M, 2 mmol) and the mixture stirred at room temperature until a yellow solution was formed (ca. 30 min). The solution was cooled to -10 °C and *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added giving rise to a rust-red suspension. Alkyne, **70**, (0.1 mL, 0.5 mmol) was added at -30 °C after 30 min and the mixture warmed to 0 °C over 1 hr. Quenching with MeOH, work-up and purification yielded **79** and **80** (3:97, 0.19 g, 79 %). A lower yield was obtained when only one equivalent of reagent per substrate was used (3:97, 0.057 g, 24 %).

III.1.6 *Stannylcupration of 1-Alkyne **70** with n-$Bu_3Sn(X)Cu(CN)Li_2$.*

[a] X = MeO. A 1:1 mixture of CuCN (0.09 g, 1 mmol) and MeOLi (0.039 g, 1 mmol) in THF (8 mL) was stirred at room temperature for 1 hr to give an insoluble, green semi-liquid substance. The flask was cooled to -30 °C, *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added and the mixture stirred at room temperature for 15 min to yield a pale green solution. Alkyne, **70**, (0.19 mL, 1 mmol) was added at -30 °C and the mixture warmed to 0 °C over 1 hr. Quenching with MeOH followed by work-up and purification yielded **79** and **80** (55:45, 0.06 g, 25 %).

[b] X = Et_2N. To a solution of Et_2NLi (1 mmol) in THF (8 mL) at -10 °C [prepared as described above] was added CuCN (0.09 g, 1 mmol) yielding a white coloured suspension after 30 min. The mixture was cooled to -30 °C and *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added which caused the solution to become yellow and clear. Alkyne, **48**, (0.26 mL, 1 mmol) was added to the solution after 30 min and the mixture warmed to 0 °C over 1 hr. Quenching with MeOH followed by work-up and purification yielded **75** and **76** (58:42, 0.28 g, 53 %).

[c] X = Ph_2P. To a solution of *n*-Ph_2PLi (1 mmol) in THF (8 mL) [prepared as described above] was added at -30 °C CuCN (0.09 g, 1 mmol) giving rise to a yellow suspension after 30 min. To this mixture was added *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) followed by alkyne, **48**, (0.26 mL, 1 mmol) after 30 min. The slurry was warmed to 0 °C over 1 hr and quenched with MeOH. Work-up of the acidified mixture (2 M HCl) followed by purification afforded **75** and **76** (13:87, 0.28 g, 52 %).

[d] X = *n*-BuSe. To a solution of *n*-BuSeLi (1 mmol) in THF (8 mL) at -30 °C [prepared as described above] was added CuCN (0.09 g, 1 mmol) to give a yellow suspension after 30 min. To this mixture was added *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) giving rise to a yellow solution to which alkyne, **70**, (0.19 mL, 1 mmol) was added after 30 min. The solution was warmed to 0 °C over 1 hr and quenched with MeOH. Work-up of the acidified mixture (2 M HCl) followed by purification yielded **79** and **80** (71:29, 0.349 g, 74 %).

[e] X = C_8H_{17}-C≡C. To a suspension of CuCN (0.09 g, 1 mmol) in THF (2 mL) at room temperature was added C_8H_{17}-C≡CLi (1 mL, 1 M, 1 mmol) giving rise to a pale green solution within several minutes. The mixture was cooled to -10 °C, *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added and stirring continued

for 15 min. The yellow solution was cooled to -30 °C, alkyne, **70**, (0.1 mL, 0.5 mmol) added and the mixture warmed to 0 °C over 1 hr. The solution was quenched with MeOH, worked up and purified to yield **79** and **80** (14:86, 0.161 g, 68 %).

[f] X = Ph-C≡C. To a suspension of CuCN (0.09 g, 1 mmol) in THF (3 mL) at room temperature was added Ph-C≡CLi (1 mL, 1 M, 1 mmol). The yellow slurry was cooled to -10 °C after 30 min, *n*-Bu_3SnLi (2 mL, 0.5 M, 1 mmol) added and stirred for 30 min. The burgundy solution was cooled to -30 °C, alkyne, **70**, (0.1 mL, 0.5 mmol) added and the mixture warmed to 0 °C over 1 hr. The solution was quenched with MeOH, worked up and purified to yield **79** and **80** (9:91, 0.15 g, 62 %).

III.2 Synthesis of the Leafminer Moth Sex Attractant, (4*E*,7*Z*)-Trideca-4,7-dienyl Acetate (106).

4-pentyn-1-ol (101). This compound was prepared by analogy to the synthesis of alcohol, **38**, by using 3-pentyn-1-ol (6 mL, 65 mmol) as the starting material.[77] The crude liquid obtained after work-up was purified by distillation (19 mmHg, 70 °C) to yield **101** as a colourless liquid (4.25 g, 78 %): IR (neat) 3299(s), 2950(s), 2881(s), 2117(w), 1434(s), 1175(w), 1058(s), 944(m), 905(m) cm^{-1}; ^1H NMR δ 3.77 (2 H, t, J = 5.8 Hz, CH_2OH), 2.32 (2 H, dt, J = 7 Hz; 2.7 Hz, $HC{\equiv}CCH_2$), 1.97 (1 H, t, J = 2.7 Hz, $HC{\equiv}C$), 1.78 (2 H, quint, J = 7 Hz, CH_2); mass spectrum (EI) 84(M^+, 1), 69(7), 67(5), 56(21), 55(15), 53(16), 51(15), 50(13), 42(63), 41(100); Anal. Calcd. for C_5H_8O: C, 71.33; H, 9.51. Found: C, 70.99; H, 9.79.

5-Tetrahydropyranyloxy-1-pentyne (102). This compound was prepared in the same manner described for the synthesis of alkyne, **14**, starting with alcohol, **101** (0.75 g, 8.9 mmol). Work-up and purification yielded **102** (1.4 g, 94 %) as a colourless liquid: IR (neat) 3295(m), 2942(s), 2871(s), 2118(w), 1441(m), 1354(m), 1200(m), 1137(m), 1120(m), 1076(m), 1035(m), 934(m) cm^{-1}; ^1H NMR δ 4.61-4.58 (1 H, m, CH (THP)), 3.91-3.78 (2 H, m, CH*H* (THP), CH*H*OTHP), 3.54-3.44 (2 H, m, CH*H* (THP), CH*H*OTHP), 2.31 (2 H, dt, J = 7 Hz; 2.5 Hz, C≡CCH_2), 1.94 (1 H, t, J = 2.5 Hz, *H*C≡C), 1.86-1.76 (3 H, m, CH*H* (THP), CH_2), 1.75-1.65 (1 H, m, CH*H* (THP)), 1.62-1.46 (4 H, m, CH_2); mass spectrum (EI) 167(M^+ -H, 5), 125(6), 111(8), 101(8), 85(100), 84(16), 79(13), 67(45), 65(23), 55(23); Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.43; H, 9.52. Found: C, 71.47; H, 9.37.

5-Tetrahydropyranyloxy-1-tri-*n*-butylstannyl-1(*E*)-pentene (103). To a stirred solution of phenylacetylene (2.64 mL, 24 mmol) in THF (10 mL) at -30 °C was added *n*-BuLi. After 15 min CuI (2.29 g, 12 mmol) was added and the mixture stirred at 0 °C for 30 min. The resulting colourless solution was transferred to a solution of *n*-Bu_3SnLi (12 mmol) in THF (5 mL) [prepared in the reaction of *n*-Bu_3SnH with lithium diisopropylamide][21] at -30 °C. The yellow solution was stirred for 30 min, a THF (2 mL) solution of alkyne, **102**, (1.0 g, 6 mmol) added and the mixture warmed to 0 °C over 1 hr. The solution was quenched with methanol, diluted with brine (200 mL) and extracted with hexanes (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$), and concentrated to afford a crude oil which, after purification by flash chromatography (SiO_2, 5 % EtOAc in hexanes), yielded **103** (2.15 g, 78 %) in 96 % isomeric purity: IR (neat) 2923(s), 2870(s), 2852(s), 1599(m), 1484(m), 1376(w), 1353(w), 1136(m), 1120(m), 1077(m), 1035(m), 1022(m), 989(m) cm^{-1};

^{1}H NMR δ 5.97 (1 H, dt, *J* = 19 Hz; 5.5 Hz, $Bu_3SnHC{=}CHR$), 5.89 (1 H, d, *J* = 19 Hz, $Bu_3SnHC{=}CHR$), 4.59-4.54 (1 H, m, C*H* (THP)), 3.91-3.82 (1 H, m, CH*H* (THP)), 3.74 (1 H, dt, *J* = 9.6 Hz; 6.6 Hz, CH*H*OTHP), 3.53-3.45 (1 H, m, CH*H* (THP)), 3.39 (1 H, dt, *J* = 9.6 Hz; 6.7 Hz, CH*H*OTHP), 2.25-2.17 (2 H, m, $C{=}CHCH_2$), 1.88-1.78 (1 H, m, CH*H* (THP)), 1.75-1.65 (3 H, m, CH*H* (THP)), 1.62-1.37 (10 H, m, CH_2), 1.29 (6 H, sext, *J* = 7.6 Hz, CH_2), 0.95-0.82 (15 H, m, CH_2, CH_3); mass spectrum (EI) 403(M^+ -Bu, 13), 401(10), 399(6), 319(3), 317(3), 263(3), 261(3), 235(4), 233(4), 231(3), 207(4), 205(5) 203(4), 179(20), 177(29), 175(25), 137(18), 135(15), 133(11), 121(25), 119(20), 117(11), 85(100), 67(25), 56(47); Anal. Calcd. for $C_{22}H_{44}O_2Sn$: C, 57.39; H, 9.56. Found: C, 58.13; H, 9.32.

(6*E*,9*E*)-13-Tetrahydropyranyloxy-6-tri-*n*-butylstannyltrideca-6,9-diene (104).

[a] To a solution of vinylstannane, **103**, (0.51 g, 1.1 mmol) in THF (2 mL) at -70 °C was added *n*-BuLi (0.44 mL, 2.5 M, 1.1 mmol). The solution was stirred at -30 °C for 30 min, diluted with diethyl ether (2 mL) and then allylic chloride, **6**, (0.4 mL, 1 mmol) added followed by $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol). The mixture was stirred at -30 °C for 30 min, warmed to room temperature over 1 hr and subsequently quenched with aqueous NH_4Cl (100 mL). The solution was extracted with hexanes (3 x 10 mL) and the combined organic layers dried ($MgSO_4$) and concentrated to give a crude oil. Flash chromatography (SiO_2, 3 % EtOAc in hexanes) yielded **104** in > 99 % isomeric purity (0.12 g, 21 %) as a colourless oil.

[b] To a stirred solution of vinylstannane, **103**, (0.46 g, 1 mmol) in THF (2 mL) at -70 °C was added *n*-BuLi (0.4 mL, 1 mmol) and stirring continued at

-30 °C for 30 min. The solution was diluted with diethyl ether (2 mL) and Et_2AlCl (0.13 mL, 1 mmol) added. After 15 min allylic chloride, **6**, (0.4 mL, 1 mmol) was added to the clear solution followed by $Pd(PPh_3)_4$ (0.12 g, 0.1 mmol) and the mixture warmed to 50 °C for 2 hr. Work-up and purification as described in [a] afforded **104** in > 95 % isomeric purity (0.418 g, 73 %) as a colourless oil: IR (neat) 2955(s), 2923(s), 2853(s), 1600(w), 1464(m), 1376(w), 1352(w), 1200(w), 1138(m), 1121(m), 1078(m), 1035(m) cm^{-1}; ^1H NMR δ 5.52-5.34 (3 H, m, $Bu_3SnRC{=}C\mathit{H}CH_2\mathit{H}C{=}C\mathit{H}R$), 4.61-4.55 (1 H, m, C*H* (THP)), 3.92-3.82 (1 H, m, CH*H* (THP)), 3.73 (1 H, dt, *J* = 9.5 Hz; 6.7 Hz, CH*H*OTHP), 3.54-3.45 (1 H, m, CH*H* (THP)), 3.38 (1 H, dt, *J* = 9.6 Hz; 6.6 Hz, CH*H*OTHP), 2.84-2.76 (2 H, m, $C{=}CHC\mathit{H}_2HC{=}C$), 2.26-2.18 (2 H, m, $^3J_{Sn\text{-}H}$ = 61 Hz, $C{=}CSnBu_3C\mathit{H}_2$), 2.16-1.99 (2 H, m, $C{=}CHC\mathit{H}_2$), 1.88-1.41 (14 H, m, $C\mathit{H}_2$), 1.37-1.22 (12 H, m, $C\mathit{H}_2$), 0.95-1.21 (18 H, m, $C\mathit{H}_2$, $C\mathit{H}_3$); ^{13}C NMR δ 144.7 ($Bu_3SnR\mathit{C}{=}CHR$), 138.1 ($Bu_3SnRC{=}\mathit{C}HR$), 129.9 (=C), 129.2 (=C), 98.8, 67.0, 62.2, 33.1, 31.9, 31.6, 30.8, 30.0, 29.7, 29.2, 27.4, 25.5, 22.6, 19.6, 14.0, 13.6, 9.7; mass spectrum (EI) 513(M^+ -Bu, 23), 511(14), 509(8), 429(6), 427(5), 425(3), 319(18), 317(13), 315(7), 293(33), 291(29), 289(19), 279(30), 277(25), 275(15), 233(18), 231(12), 179(26), 177(36), 175(25), 173(11), 137(14), 135(12), 133(9), 121(22), 119(16), 117(10), 101(10), 85(100), 67(20); Anal. Calcd. for $C_{30}H_{58}O_2Sn$: C, 63.16; H, 10.17. Found: C, 63.45; H, 10.19.

[c] To a solution of lithium 2-thienylcyanocuprate (2.8 mL, 0.25 M, 0.7 mmol) in THF (5 mL) at -10 °C was added MeLi (0.5 mL, 1.4 M, 0.7 mmol) followed after 10 min by a solution of vinylstannane, **103**, (0.32 g, 0.7 mmol) in THF (2 mL). The solution was stirred at room temperature for 1.5 hr, cooled to -78 °C and then allylic chloride, **6**, (0.2 mL, 0.5 mmol) added. The solution was slowly warmed to room temperature and allowed to stand overnight. GC

analysis of the colourless oil obtained after flash chromatography revealed this material to consist of **104** and two closely eluting peaks, presumed to be isomers of **104** (10 % by GC). Combined yield: 0.16 g, 55 %.

(4*E*,7*Z*)-Trideca-4,7-dien-1-ol (105). To a solution of diene, **104**, (0.36 g, 0.61 mmol) in THF/MeOH (1:1, 5 mL) was added *p*-toluenesulfonic acid (excess) and the mixture stirred for 30 min at room temperature. The solution was concentrated to approximately 1 mL and subjected to flash chromatography (SiO_2, 10 % EtOAc in hexanes) to yield **105** (0.11 g, 89 %) as a colourless liquid: IR (neat) 3342(m) 3010(w), 2957(s), 2927(s), 2857(s), 1780(w), 1457(m), 1158(w), 1058(m), 967(m) cm^{-1}; ^1H NMR δ 5.50-5.32 (4 H, m, R*H*C=C*H*R), 3.65 (2 H, t, *J* = 6.5 Hz, CH_2OH), 2.79-2.67 (2 H, m, C=CHCH_2HC=C), 2.12-2.05 (2 H, m, C=CHCH_2), 2.02 (2 H, q, *J* = 7 Hz, C=CHCH_2), 1.63 (2 H, quint, *J* = 7.5 Hz, CH_2), 1.56 (1 H, s, O*H*), 1.39-1.21 (6 H, m, CH_2), 0.88 (3 H, *J* = 7 Hz, CH_3); ^{13}C NMR δ 131.5 (=C), 130.6 (=C), 127.4 (=C), 125.3 (=C), 62.3 (CH_2OH), 31.5, 30.9, 29.3, 27.2, 27.2, 25.8, 22.5, 14.0; mass spectrum (EI) 196(M^+, 2), 178(3), 150(2), 149(3), 135(6),121(14), 107(14), 98(14), 93(38), 81(54), 79(100), 67(59), 55(29); HRMS Calcd. for $C_{13}H_{24}O$: 196.1817. Found: 196.1822.

(4*E*,7*Z*)-Trideca-4,7-dienyl acetate (106). To a solution of diene, **105**, (0.10 g, 0.50 mmol) in pyridine (1 mL) at room temperature was added acetic anhydride (0.5 mL). After 45 min the mixture was diluted with hexanes (10 mL), washed with brine (3 x 50 mL) and the pooled aqueous layers back-extracted with hexanes (2 x 10 mL). The organic extracts were combined, concentrated and the resulting crude liquid purified by flash chromatography (SiO_2, 10 %, EtOAc in hexanes) to afford **106** (0.11 g, 86 %) as a colourless liquid: IR (neat) 3010(w), 2958(s), 2929(s), 2857(s), 1743(s), 1458(w), 1366(m),

1240(m), 1041(m), 968(m) cm^{-1}; ^1H NMR δ 5.46-5.32 (4 H, m, R*H*C=C*H*R), 4.05 (2 H, t, *J* = 7 Hz, CH_2OAc), 2.76-2.70 (2 H, m, C=CHCH_2HC=C), 2.16 (3 H, s, C(O)CH_3), 2.10-1.98 (4 H, m, C=CHCH_2), 1.68 (2 H, quint, *J* = 7 Hz, CH_2), 1.38-1.21 (6 H, m, CH_2), 0.88 (3 H, t, *J* = 7 Hz, CH_3); ^{13}C NMR δ 171.0 (*C*(O)CH_3), 130.7 (=C), 129.5 (=C), 129.0 (=C), 127.3 (=C), 63.9, 31.5, 30.3, 29.3, 28.8, 28.4, 27.1, 22.6, 22.5, 14.0; mass spectrum (EI) 238(M^+, <1), 178(20), 150(9), 135(12), 121(24), 107(20), 93(53), 79(100), 67(37), 55(14); HRMS Calcd. for $C_{15}H_{26}O_2$: 238.1932. Found: 238.1933.

III.3 Spectroscopic Investigations of Mixed Higher Order and Lower Order Trialkylstannylcuprates.

III.3.1 *^2H NMR Study of Stannylcupration of [1-^2H]-1-Decyne (**61**) with n-$Bu_3Sn(Bu)Cu(CN)Li_2$.(**95**).*

Sample Preparation. To a suspension of CuCN (0.27 g, 3 mmol) in THF (4 mL) at -30 °C was added a solution of *n*-Bu_3SnLi (14 mL, 0.21 M THF, 3 mmol) and the mixture stirred at -10 °C for 30 min. *n*-BuLi was added to the orange slurry after 30 min which resulted in the formation of a yellow solution within several minutes. Then 3 mL aliquots were transferred to 10 mm NMR tubes and mixed with reagents prior to ^2H NMR analysis (see II.1.1). The ^2H NMR spectra were recorded at -35 °C.

[a] To an NMR tube containing a solution of stannylcuprate, **95**, (3 mL, 0.46 mmol) at -78 °C was added alkyne, **61**, (0.8 mL, 0.44 mmol) followed by MeOH (0.1 mL, 2.5 mmol).

[b] To an NMR tube containing a solution of stannylcuprate, **95**, (3 mL, 0.46 mmol) at -35 °C was added alkyne, **61**, (0.8 mL, 0.44 mmol) and the mixture warmed to 0 °C over 30 min.

[c] MeOH (excess) was added at 0 °C to the NMR tube in experiment [b] (above).

III.3.2 *^{13}C NMR Study of Solutions of $(Me_3SnLi)_m$: $(C_8H_{17}\text{-}C{\equiv}CLi)_n$: $Cu(^{13}C{\equiv}C^{13}\text{-}C_8H_{16}\text{-}OTHP)$.*

Sample Preparation. These were prepared as described in II.4.1. Spectra were recorded at 0 °C.

1. $(C_8H_{17}\text{-}C{\equiv}CLi)_n$: $Cu(^{13}C{\equiv}C^{13}\text{-}C_8H_{16}\text{-}OTHP)$ [0.1-0.08 M THF].

[a] Solution n = 0. To a solution of ^{13}C labeled alkyne, **63**, (0.26 mL, 1 mmol) in THF (9 mL) at -50 °C was added *n*-BuLi (0.4 mL, 2.5 M, 1 mmol). After the mixture was stirred at -50 °C for 30 min, CuI was added and the reaction vessel warmed to 0 °C for 30 min during which time a yellow solution formed.

[b] Solutions n = 1-4. To solution 1 [a] was added at -10 °C C_8H_{17}-C≡CLi (1 mL, 1 M THF, 1 mmol). The initial pale green in colour dissipated over ca. 1 min to afford a colourless solution from which a sample was taken after 30 min for ^{13}C NMR analysis. This process was repeated three times. All solutions were colourless and appeared homogeneous.

2. (Me_3SnLi) : $(C_8H_{17}\text{-}C{\equiv}CLi)_n$: $Cu(^{13}C{\equiv}C^{13}\text{-}C_8H_{16}\text{-}OTHP)$ [0.1-0.07 M THF/ether].

[a] Solution n = 0. To a freshly prepared solution of 1 [a] (1 mmol) in

THF (7.5 mL) at -10 °C was added Me_3SnLi (2 mL, 0.5 M THF/ether, 1 mmol). The resultant burgundy solution was stirred at -10 °C for 30 min and then a sample withdrawn for ^{13}C NMR analysis.

[b] Solutions n = 1-3. To solution 2 [a] at -10 °C was added C_8H_{17}-C≡CLi (1 mL, 1 M THF, 1 mmol). The solution immediately turned bright yellow and was stirred for 30 min prior to removal of an aliquot for ^{13}C NMR analysis. Solutions of subsequent additions of C_8H_{17}-C≡CLi (1 mmol) were prepared and analyzed in the same manner.

3. $(Me_3SnLi)_n$: $(C_8H_{17}$-C≡CLi) : Cu($^{13}C≡C^{13}$-C_8H_{16}-OTHP) [0.1-0.07 M THF/ether].

Solutions n = 2-4. To a freshly prepared solution of 2 [a] at -10 °C was added a 2 mL aliquot of Me_3SnLi (0.5 M THF/ether, 1 mmol). The yellow solution was stirred for 30 min before taking a sample for ^{13}C NMR analysis. This procedure was repeated three times.

III.3.3 *Infrared Study of Solutions of $(Me_3SnLi)_m$: $(C_8H_{17}$-C≡CLi)$_n$: CuI.*

Sample Preparation. Infrared spectra of solutions were recorded at 0 °C with use of a Perkin-Elmer Model 1605 FT-IR spectrometer as described in II.4.3.

1. $(C_8H_{17}$-C≡CLi)$_n$: CuI [0.1 M THF].

[a] Solution n =1. To a suspension of CuI (0.19 g, 1.0 mmol) in THF (9 mL) at 0 °C was added C_8H_{17}-C≡CLi (1 mL, 1 M THF, 1 mmol). The mixture was warmed to room temperature and stirred for 30 min during which time a fine

yellow suspension formed. This compound is stable to water and air and was isolated as a thermally stable yellow solid.[63]

[b] Solutions n = 2-5. Prepared as described in 1 [a] starting with CuI in THF (10-n mL) followed by addition of C_8H_{17}-C≡CLi (n mL, 1 M THF, n mmol). These solutions were colourless and appeared homogeneous.

2. (Me_3SnLi) : (C_8H_{17}-C≡CLi)$_n$: CuI [0.1 M THF].

[a] Solution n = 1. To a suspension of 1 [a] (1 mmol) in THF (8 mL) at -10 °C was added Me_3SnLi (2 mL, 0.5 M THF/ether, 1 mmol). A clear solution was obtained after 30 min/-10 °C.

[b] Solutions n = 2,3. To individual flasks containing a solution of 2 [a] (1 mmol) in THF (11-n mL) at -10 °C was added C_8H_{17}-C≡CLi (n-1 mL, 1 M THF, n-1 mmol) and solutions stirred for 30 min. Solutions were yellow.

3. (Me_3SnLi)$_n$: (C_8H_{17}-C≡CLi) : CuI [0.1 M THF].

Solutions n = 2-3. Prepared in a similar manner described in 2 [a] by adding Me_3SnLi (2n mL, 0.5 M THF/ether, n mmol) to separate flasks containing a suspension of 1 [a] (1mmol) in THF (10-2n mL). Solutions were yellow.

III.3.4 *Infrared Study of Disproportionation Reactions between Solutions of (Me_3SnLi)$_m$ (C_8H_{17}-C≡CLi)$_n$ $CuLi_x$·LiI.*

Sample Preparation. Reagents were prepared as described in section III.3.3. Infrared spectra of combined solutions were recorded at 0 °C using a Perkin-Elmer Model 1605 FT-IR spectrometer as described in II.4.3.

[a] $(C_8H_{17}\text{-}C{\equiv}C)_2CuLi\cdot LiI \rightarrow Me_3Sn(C_8H_{17}\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$. To a solution of $(C_8H_{17}\text{-}C{\equiv}C)_2CuLi\cdot LiI$ (0.5 mmol) in THF (9 mL) at 0 °C was added Me_3SnLi (1 mL, 05 M THF/Ether, 0.5 mmol). The yellow solution was stirred for 30 min.

[b] $Me_3Sn(C_8H_{17}\text{-}C{\equiv}C)CuLi\cdot LiI \rightarrow Me_3Sn(C_8H_{17}\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$. To a solution comprised of a 1:1:1 mixture of Me_3SnLi, $C_8H_{17}\text{-}C{\equiv}CLi$ and CuI (0.5 mmol each) in THF (9.5 mL) at 0 °C was added $C_8H_{17}\text{-}C{\equiv}CLi$ (0.5 mL, 1 M THF, 0.5 mmol). The yellow solution was stirred for 30 min.

[c] $(C_8H_{17}\text{-}C{\equiv}C)_3CuLi_2\cdot LiI \rightarrow (C_8H_{17}\text{-}C{\equiv}C)_2CuLi\cdot LiI$. To a slurry of $(C_8H_{17}\text{-}C{\equiv}C)Cu$ (1 mmol) in THF (10 mL) at 0 °C was added a THF (10 mL) solution of $(C_8H_{17}\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ (1 mmol). The mixture was stirred for 30 min during which time a faint green solution formed.

[d] $(C_8H_{17}\text{-}C{\equiv}C)_3CuLi_2\cdot LiI \rightarrow Me_3Sn(C_8H_{17}\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$. To a solution of $(C_8H_{17}\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ (1 mmol) in THF (10 mL) was transferred a solution (THF, 10 mL) comprised of a 2:1:1 mixture of Me_3SnLi, $C_8H_{17}\text{-}C{\equiv}CLi$ and CuI, "$(Me_3Sn)_2C_8H_{17}\text{-}C{\equiv}CCuLi_2\cdot LiI$" (1 mmol). The combined reagents were stirred for 30 min at 0 °C to yield a yellow solution.

[e] $(Me_3Sn)_2(C_8H_{17}\text{-}C{\equiv}C)CuLi_2\cdot LiI \rightarrow Me_3Sn(C_8H_{17}\text{-}C{\equiv}C)_2CuLi_2\cdot LiI$. THF (10 mL) solutions of $(C_8H_{17}\text{-}C{\equiv}C)_3CuLi_2\cdot LiI$ (1 mmol) and "$(Me_3Sn)_2C_8H_{17}\text{-}C{\equiv}CCuLi_2\cdot LiI$" (1 mmol) reagents were combined as described in [b] with the exception that addition was carried out in reverse order.

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