PART I : CHEMICAL AND SPECTROSCOPIC INVESTIGATIONS OF TRIALKYLSILYL AND TRIALKYLSTANNYL METALLOIDS. PART II : THE SYNTHESIS OF POTENTIAL INHIBITORS OF SQUALENE SYNTHETASE

by

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Part I: Chemical and Spectroscopic Investigations of Trialkylsilyl and Trialkylstannyl Metalloids.

Part II: The synthesis of Potential Inhibitors and Squalene Synthetase.

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ABSTRACT

Low-temperature, heteronuclear (^{1}H, ^{7}Li, ^{13}C, ^{29}Si and ^{119}Sn) NMR spectroscopy was used to study the constitution of trialkylsilyl [$(R_3Si)_nCuLi_{n-1}\cdot LiX$] and trialkylstannyl [$(R_3Sn)_nCuLi_{n-1}\cdot LiX$; R = alkyl, n=1, 2 or 3 and X = CN or Br] cuprates derived from CuCN and CuBr•Me_2S. These studies revealed that in composition, the metallocuprates are similar to alkylcyanocuprates ($R_nCuLi_{n-1}\cdot LiCN$) in that the sequential addition of R_3SiLi, R_3SnLi or RLi to CuCN yields $RCu(CN)Li$ and $R_2Cu(CN)Li_2$. Further addition of R_3MLi (M = Si or Sn, R = alkyl) leads to the formation of *hitherto* unknown $(R_3M)_3CuLi_2$. In the case of alkylcyanocuprates addition of RLi beyond a RLi:CuCN ratio of 2:1 yields no new species but gives solutions with hydrogen abstracting ability attributable to RLi. The formation of mixed cuprates $R_3M(Me)_nCuLi_n\cdot LiCN$ (M = Si or Sn, n = 1 or 2) was also studied by low-temperature NMR spectroscopy. These studies revealed that like mixed alkylcyanocuprates, ligands on copper readily exchanged in these metallocuprates.

The ability of methyl as a ligand to tenaciously bind to copper resulted in the exclusive transfer of R_3Si and R_3Sn ligands in additions to α,β-unsaturated enones and 1-alkynes.

Low-temperature heteronuclear (^{2}H, ^{11}B, ^{29}Si and ^{119}Sn) NMR spectroscopy was also employed to study the cuprous salt catalyzed addition of bimetallic [($Me_3SnAlEt_2$, $Me_3SiAlEt_2$, $(Me_3Sn\text{-}9\text{-}BBN\cdot OMe)^-Li^+$ and $(Me_3Si\text{-}9\text{-}BBN\cdot OMe)^-Li^+$; BBN = 9-borabicyclo[2.2.1]nonane)] reagents to 1-alkynes. This study suggested that metallometallations involve initial silyl- or stannylcupration followed by transmetallation of a vinyl-copper bond by the electrophilic metal partner generated *in situ*. Hence, metallometallations could be conducted either by addition of "R_3SiCu" or

"R_3SnCu" to 1-alkynes followed by addition of Et_2AlCl or Br-9-BBN, or by preformation of $(R_3Sn\text{-}9\text{-}BBN{\bullet}OMe)^-Li^+$ or $(R_3Si\text{-}9\text{-}BBN{\bullet}OMe)^-Li^+$ and $R_3SnAlEt_2$ or $R_3SiAlEt_2$ followed by addition of 1-alkynes and catalytic amounts of cuprous salts.

The 1,2-dimetallic adducts produced by metallometallation of 1-alkynes contain well differentiated 1,2-dianion equivalents capable of forming new carbon-carbon bonds. This chemistry yielded mild and efficient methods for the synthesis of stereo- and regio-defined trisubstituted olefins.

Also described in this thesis are the total syntheses of some sulfonium ion analogues of carbocationic intermediates presumed to be involved in the dimerization of farnesyl pyrophosphate to squalene by squalene synthetase. These sulfonium ions are presumptive inhibitors of this enzyme.

TO AMIT

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I will be failing in my duty if I conclude this acknowledgement without referring to the courteous behaviour and cooperation of the NMR committee at the University of British Columbia, especially Dr. S.O. Chan and Mrs. M. Austria for recording the ^{1}H, ^{7}Li, ^{13}C and ^{119}Sn NMR spectra .

Sunaina Sharma

July 21st 1989.

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LIST OF ABBREVIATIONS

9-BBN	9-Borabicyclo[3.3.1]nonane
CH_2Cl_2	Dichloromethane
CTAB	Cetyltetramethylammonium bromide
DIBALH	Diisobutylaluminum hydride
$(Siam)_2BH$	Disiamylborane
DMF	N,N-Dimethylformamide
DMS	Dimethylsulfide
DMSO	Dimethylsulfoxide
HMPA	Hexamethylphosphoramide
LAH	Lithium aluminum hydride
LDA	Lithium diisopropylamide
MEMCl	2-Methoxyethoxymethyl chloride
Michler's ketone	4,4'-Bis(dimethylamino)benzophenone
NaH	Sodium hydride
TMEDA	N,N,N',N'-Tetramethylethylenediamine
TMS	Tetramethylsilane
p-TsCl	*p*-Toluenesulfonyl chloride

PART I: CHEMICAL AND SPECTROSCOPIC INVESTIGATIONS OF TRIALKYLSILYL AND TRIALKYLSTANNYL METALLOIDS

CHEMICAL AND SPECTROSCOPIC INVESTIGATIONS OF ORGANOCUPRATES

Introduction

Advances in the development of organometallic reagents have often been accelerated by an improved understanding of the species and mechanisms involved in reactions of these reagents.[1] Nowhere is this more apparent than in the organic chemistry of copper which has emerged as the most heralded among the transition metals in organic synthesis. The pivotal role played by copper-complexes containing transferable ligands is attested to by the frequent reviews[2] which strive to keep organic chemists abreast of the rapidly expanding methodological advances and applications of copper-based reagents.

The *ate* complexes of copper developed in the years since Gilman's initial report[3] of the formation of Me_2CuLi (**1**, Gilman's reagent) are as varied as their chemistry. Reactivity of these reagents can be changed by altering several parameters: the ratio of CuX (X = Br or I) to R-M (being either stoichiometric or catalytic in CuX);[2,4] the gegenion involved (usually M = MgX or Li and more recently Na and Zn);[5] the presence of additives such as sulfides, phosphines or Lewis acids that solubilize, stabilize or activate;[2,6] and lastly, the choice of solvent (almost always ethereal).[2]

In addition to these "lower order" (LO) cuprates of the general formula "R_2CuLi" (**2**), "higher order" (HO) reagents, "R_3CuLi_2" (**3**), i.e., R_2CuLi + RLi, and "$R_2Cu(CN)Li_2$" (**4**), i.e., 2RLi + CuCN, have begun to vie for share of the attention afforded to cuprates. Higher order species are differentiated from lower order reagents on

the basis of formal charge associated with the copper containing center: hence, the latter are monoanionic, while the former are Cu(I) dianions (Figure 1).[7]

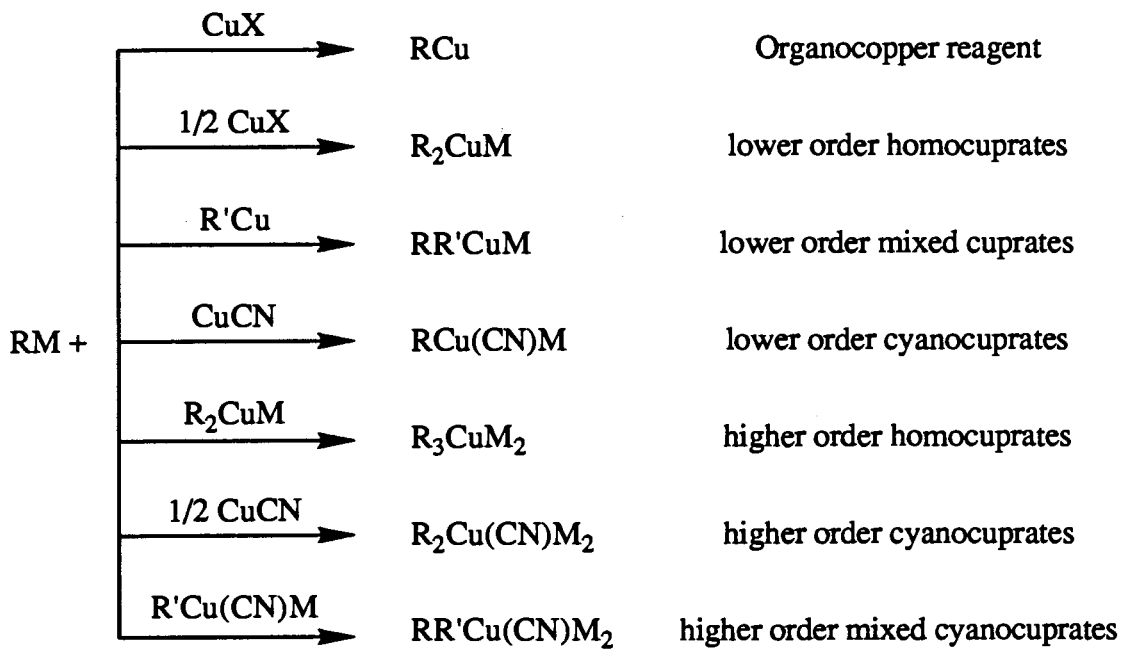


Figure 1

ALKYLCUPRATES DERIVED FROM CUPROUS HALIDES

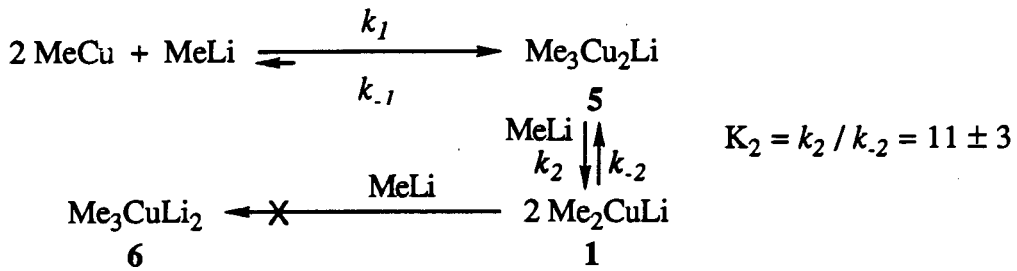
Although organocuprates are by far the most popular organotransition metal-containing reagents for structural elaborations, very little is actually known about the species involved. Until the recent spectroscopic studies by Lipshutz, *et al.*[7] on Cu(I) halide derived alkylcuprates, utilization of "R2CuLi" (**2**) in reality implied nothing more than a stoichiometric representation of the precursors from which it had been prepared. A detailed examination of the ^{1}H and ^{7}Li NMR of solutions containing a 1:1 ratio of MeLi

and MeCu (halide free) led this group to conclude that in THF these reagents existed as an equilibrium mixture of free MeLi, Me_3Cu_2Li (**5**) and Me_2CuLi (**1**).[7]

Thus, the combination of MeLi (0.5 equivalent) with LiI-free MeCu (1.0 equivalent, as a slurry in THF), afforded a single ^7Li signal (Figure 2a) attributed to Me_3Cu_2Li (**5**) implying that any equilibrium of the type shown in Scheme 1 must heavily favour **5** (i.e., $k_1 >> k_{-1}$).[7,8] As a result, and in the absence of other processes, combination of equimolar quantities of MeLi and MeCu would be expected to lead to either the formation of 0.5 equivalents of Me_3Cu_2Li and 0.5 equivalents of MeLi or 1.0 equivalent of Me_2CuLi (**1**). The ^7Li NMR spectrum for the 1:1 combination of MeLi:MeCu at -70°C (Figure 2c) showed two resonances of unequal intensity.[7] This required both MeLi and Me_3Cu_2Li (**5**) as well as a third species, Me_2CuLi (**1**) to be present. A single chemical shift (-0.38 ppm) for both **5** and **1** was rationalized by postulating rapid equilibration between these species leading to an averaging of signals, a phenomenon well precedented for other organometallics (e.g., MeLi/Me_2Zn, MeLi/Me_2Mg).[7,9]

Introduction of a further equivalent of MeLi to a final MeLi to MeCu ratio of 2:1 did not result in the formation of Me_3CuLi_2 (**6**).[7,8] Rather the proportion of free MeLi increased. Since no new species was observed it was postulated that the relative concentrations of **5** and **1** shifted toward the latter (Figure 2d).[7]

These studies suggested the equilibria shown in Scheme 1.



Scheme 1

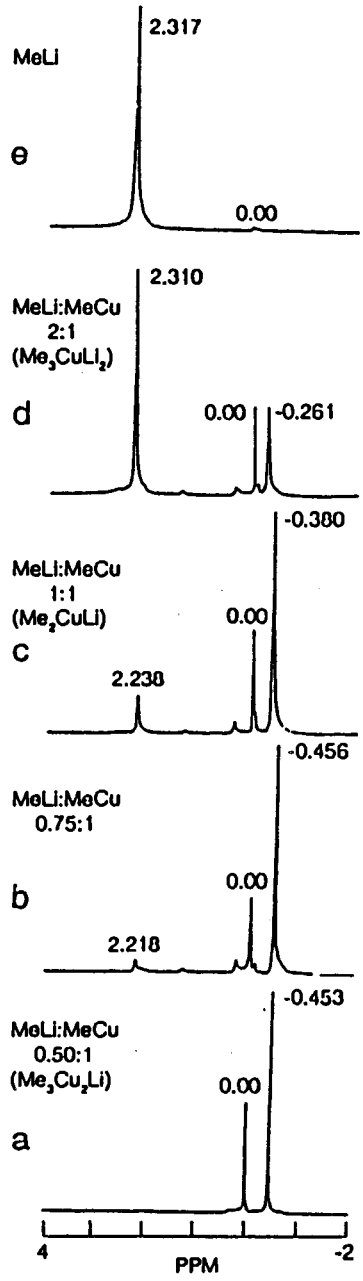


Figure 2. ^{7}Li NMR spectra for solutions containing different ratios of MeLi and MeCu (prepared from CuI) in THF/Et_2O at -70°C (a) MeLi:MeCu, 0.5:1 (b) MeLi:MeCu, 0.75:1 (c) MeLi:MeCu, 1:1 (d) MeLi:MeCu, 2:1, (e) MeLi.

Solutions containing MeLi and MeCu (with LiI) in THF/Et_2O in a molar ratio of 1:1 exhibited only one ^7Li signal which was attributed to a halide-containing Me_2CuLi, **1**.[7] However, a *very* fast equilibration of two or more cuprate species cannot be entirely ruled out.

In Et_2O, $Me_5Cu_3Li_2$ (**7**, derived from the combination of 1.66 equivalents of MeLi and 1.0 equiv. CuI), was the major species in solution.[10] Addition of 0.34 equivalent of MeLi (which increases the ratio of MeLi to MeCu to 2:1) converted the aggregate $Me_5Cu_3Li_2$ (**7**) to a different form of "Me_2CuLi" (**1**) since no equilibrium as postulated in THF/Et_2O was observed.[7] More remarkable was the observation that "Me_2CuLi" prepared initially in Et_2O (without LiI) to which THF was added, was spectroscopically different (Figure 3) than that formed initially in the same final Et_2O/THF ratio (compare Figure 2c with Figure 3b).[7]

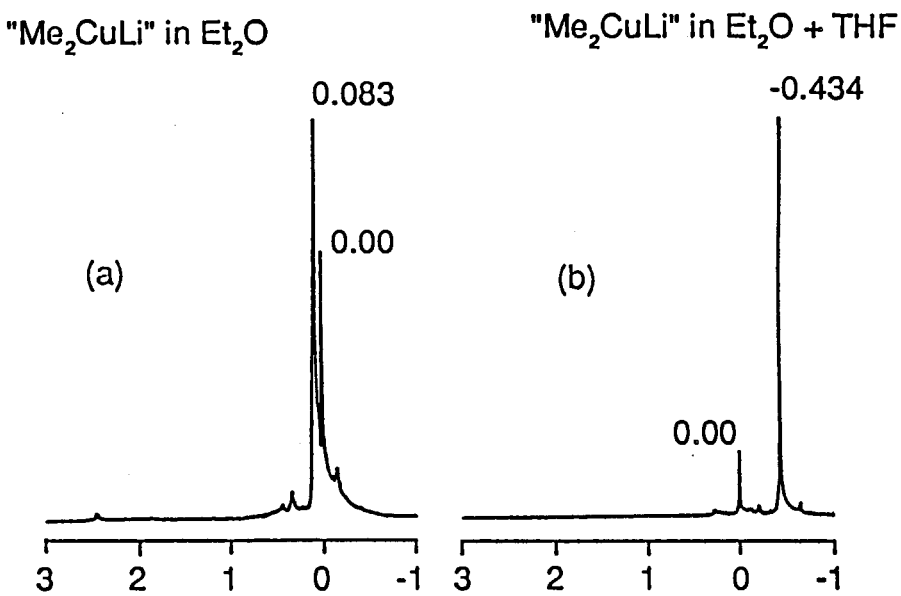


Figure 3. ^7Li NMR (a) "Me_2CuLi" in Et_2O at -70°C (b) "Me_2CuLi" initially prepared in Et_2O to which THF was added; the spectra were recorded at -70°C.

Existence of free MeLi in the solutions of cuprates in THF/Et_2O was supported by chemical reactivity studies. Side-by-side reactions were conducted on cyclohexanone (**8**, Scheme 2) and methyl benzoate (**9**, Scheme 3), each being treated with MeLi, "Me_2CuLi" with LiI and "Me_2CuLi" without LiI. As expected, "Me_2CuLi" with LiI

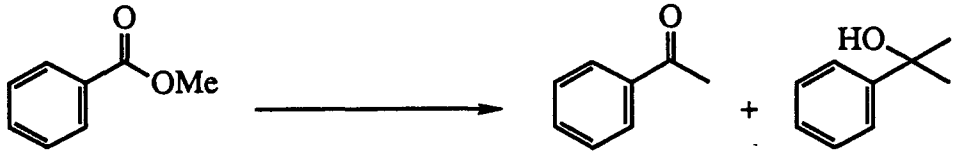
Scheme 2. Addition reaction of "Me_2CuLi" reagents to cyclohexanone, **8**.

8

MeLi	76%
Me_2CuLi + LiI in THF / Et_2O	0%
Me_2CuLi (no LiI) in THF / Et_2O	18%

did not react with either electrophile under these reaction conditions. The absence of LiI, however, led to substantial amounts of products attributable to 1,2-addition of MeLi.[7]

Scheme 3. Addition reactions of "Me_2CuLi" reagents to methyl benzoate, **9**.

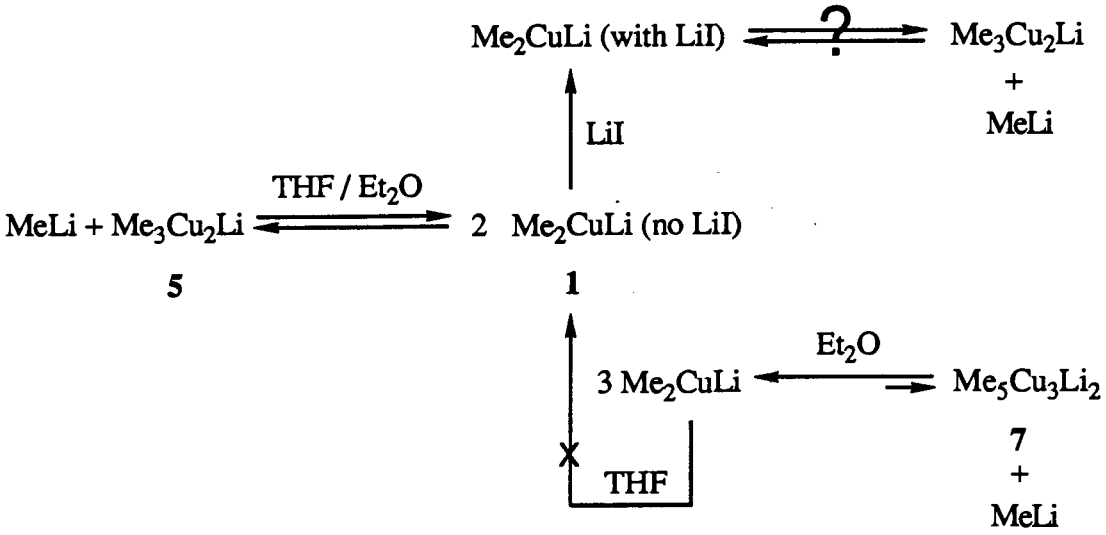


9

MeLi	15%	9%
Me_2CuLi (no LiI) in THF / Et_2O	10%	8%
Me_2CuLi (no LiI) in Et_2O	4%	1%

In support of the ^{7}Li NMR results, treatment of methyl benzoate with "Me_2CuLi" (LiI-free) in Et_2O gave negligible 1,2-addition product while "Me_2CuLi" (no LiI) in THF/Et_2O yielded 8% of the 1,2-adduct (Scheme 3).[7]

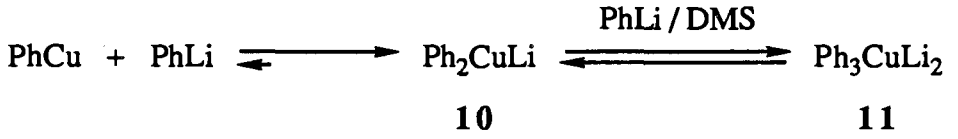
In conclusion, it is clear that several forms of "Me_2CuLi" exist (*vide supra*), the relationships among these are summarized in Scheme 4. The presence of added lithium salts and solvent may effect the nature of lower order cuprates and can be the determining factors in the outcome of the reactions. It is also apparent that in ethereal solvents (e.g., Et_2O or THF), R_3CuLi_2 (**3**) produced using copper halides, is in reality a mixture of lower order cuprate "R_2CuLi" (**2**) and free organolithium. Such preparations exhibit reactions characteristic of free RLi.



Scheme 4

The reagent having the stoichiometry Ph_2CuLi-PhLi appeared to be more reactive than Ph_2CuLi (**10**) in metal-halogen exchange reactions and coupling with aryl bromides. This led House *et al.* to propose the existence of Ph_3CuLi_2 (**11**).[11]

However, this reagent has not been confirmed spectroscopically in THF. In THF, ratios of PhLi to PhCu in excess of 1:1 contain free PhLi rather than forming **11** (Scheme 5), whereas in dimethyl sulfide (DMS), **11** is an identifiable species which exists as a halide-free higher order copper species.[12]



Scheme 5

In DMS, Ph_2CuLi (in the presence of LiI) exists as *two* different complexes that can be studied by NMR below -80°C.[12] The two sets of signals are attributed to Ph_2CuLi (**10**) in equilibium with LiI containing species, $Ph_2CuLi{\cdot}LiI$ (**12**).[12]

At -100°C in DMS, the ^{13}C NMR spectrum (Figure 4a) of Ph_2Cu^6Li, prepared from CuI and two equivalents of Ph^6Li consisted of eight lines: four major (δ161.9, *ipso*; 143.0, *ortho*; 128.5, *meta*; 127.4, *para*) and four minor (163.1, 143.6, 128.1, 127.0 ppm) due to two different Ph groups.[12] These were assigned to $Ph_2CuLi{\cdot}LiI$ (**12**) and Ph_2CuLi (**10**) respectively. Substitution of CuBr for CuI gave halide-free Ph_2CuLi (**10**) owing to the precipitation of LiBr from DMS. The four peaks in the ^{13}C spectrum of this reagent were at precisely the same positions as the peaks of the minor Ph_2CuLi species derived from CuI (Figure 4a, inset, only shown for the *ipso* carbon).[12]

The ^6Li NMR spectra of Ph_2CuLi prepared from CuI and CuBr (Figure 5a) were in harmony with the ^{13}C NMR results. The ^6Li spectrum of the reagent prepared

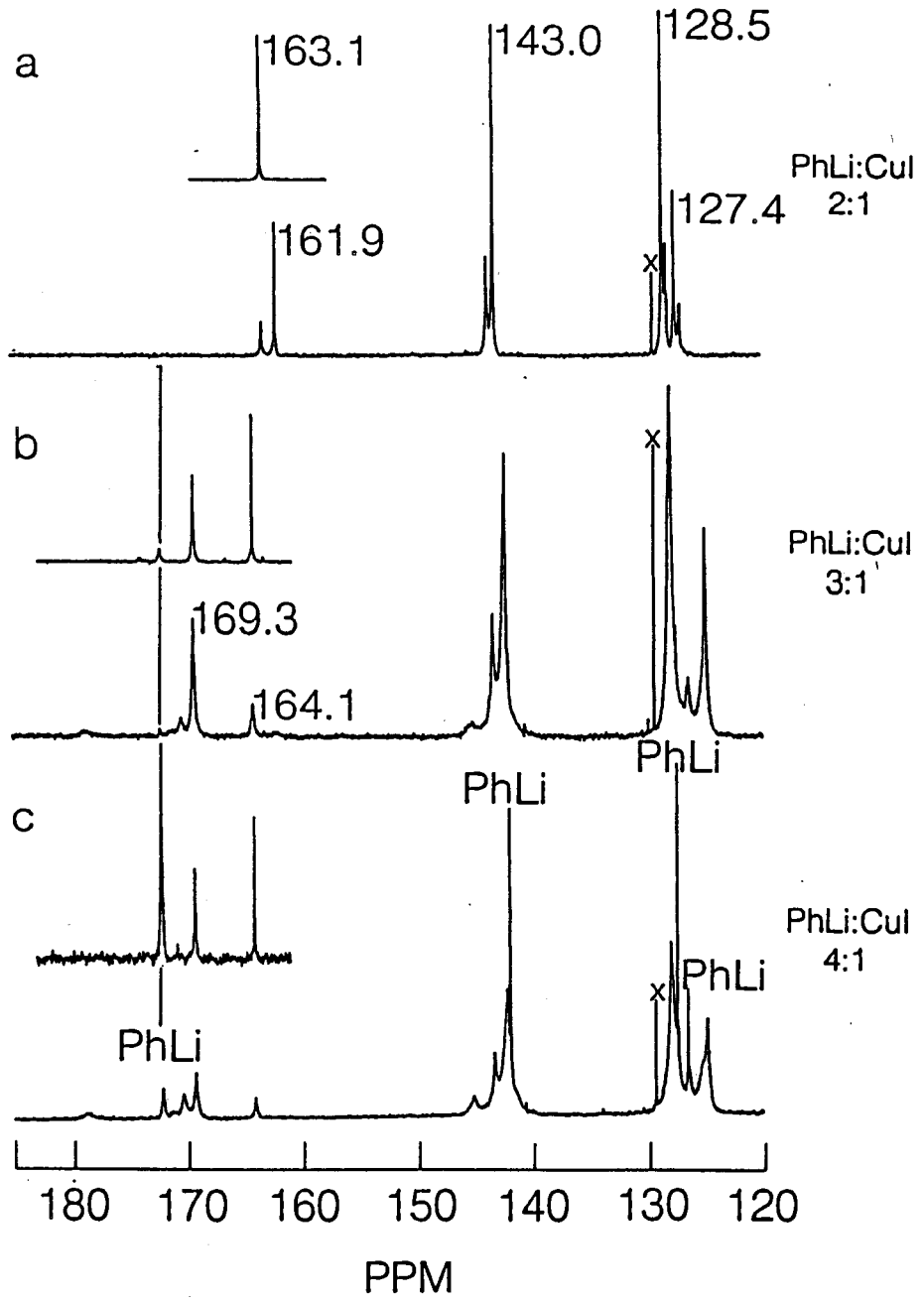


Figure 4. ^{13}C NMR spectra for solutions containing different ratios of PhLi and PhCu (prepared from CuI) in DMS at -100°C (a) PhLi:PhCu, 1:1 (b) PhLi:PhCu, 2:1 (c) PhLi:PhCu, 3:1; insets are for reagents prepared from CuBr.

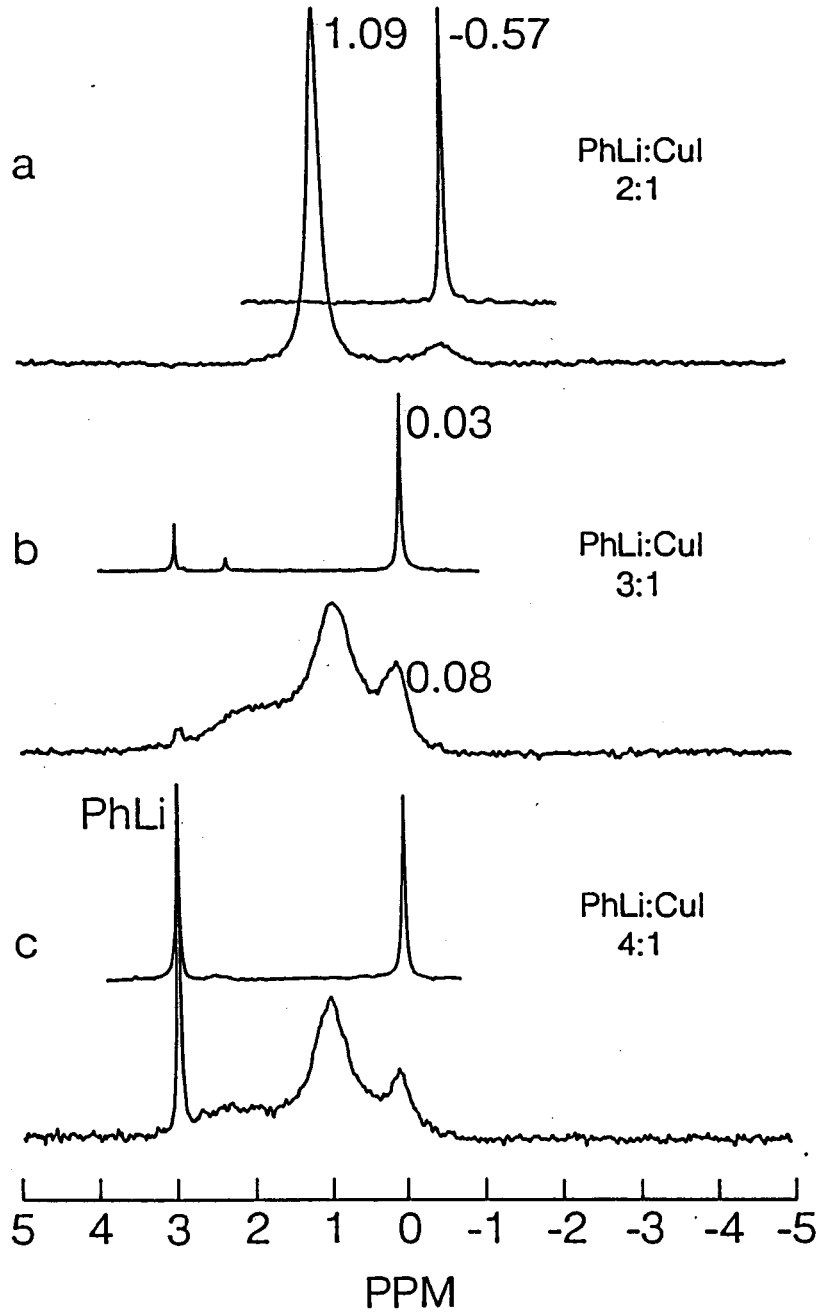


Figure 5. ^{6}Li NMR spectra for solutions containing different ratios of PhLi and PhCu (prepared from CuI) in DMS at -100°C (a) PhLi:PhCu, 1:1 (b) PhLi:PhCu, 2:1 (c) PhLi:PhCu, 3:1; insets are for reagents prepared from CuBr.

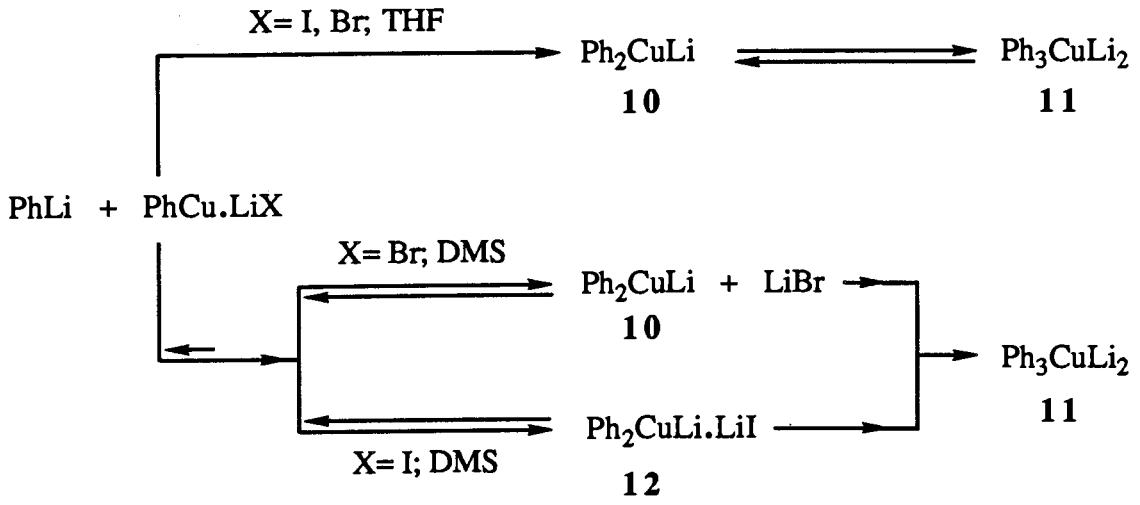
from PhLi (2.0 equivalents) and CuI consisted of two peaks; the major one at δ 1.09 was assigned to the LiI-complexed copper species (**12**) while the minor one (δ -0.57) was attributed to the halide-free complex (**10**). The ^{6}Li NMR spectrum of CuBr derived Ph_2CuLi (minus LiBr) showed a singlet at -0.57 ppm (Figure 5a, inset).[12]

The ^{13}C NMR spectrum of Ph_3CuLi_2, prepared from 3.0 equivalents of PhLi and either CuI or CuBr, contained seven major peaks (δ 169.3, 164.1, 143.2, 142.2, 128.0, 126.4, 124.9, Figure 4b), neither of which corresponded to free PhLi, Ph_2CuLi (**10**) or Ph_2CuLi·LiI (**12**). The two sets of signals coalesced to one set of four lines at ~ -80°C and were concentration dependent. The possibility of a slow exchange between Ph_3CuLi_2·LiI and Ph_3CuLi_2 was ruled out because the same set of signals was obtained in halide-free preparations (compare Figure 4b with 4b inset).[12] These two sets of signals were attributed to different aggregation states of Ph_3CuLi_2 (**11**). The ^{6}Li NMR spectrum of **11** consisted of a broad multi-humped peak spanning the region assigned to LiI (2.3 ppm) and halide-free Ph_3CuLi_2 (~0.08 ppm, Figure 5b). Ph_3CuLi_2 derived from CuBr exhibited a major singlet at 0.03 ppm (Figure 5b, inset).[12] The presence of a signal for LiI at 2.3 ppm in the latter spectrum indicates that exchange between lithium containing cuprates and free LiI is slow on the NMR time scale.[7,9] Alternatively, the signals at δ 2.3 and 0.9 ppm may correspond to different aggregation states of **11** which is also suggested by the ^{13}C NMR (*vide supra*). Fast interaggregate exchange would explain the broad signals at -100°C.

While no free PhLi is detectable by NMR spectroscopic techniques in the solutions of Ph_3CuLi_2 prepared from CuI (Figure 4b) substantial amounts of PhLi are detected both in the ^{13}C (Figure 4c) and ^{6}Li (Figure 5c) spectra of Ph_3CuLi_2 (**11**) + PhLi.

It appears that "Ph_2CuLi", like "Me_2CuLi", is a more complex species than its straightforward preparation indicates. In DMS, "Ph_2CuLi" prepared with CuI consists

primarily (>70%) of the LiI-associated copper species, $Ph_2CuLi{\cdot}LiI$ (**12**), while CuBr derived phenylcuprates in DMS are free of LiBr due to precipitation of this salt in this solvent (Scheme 6).[12] Futhermore in DMS, Ph_3CuLi_2 (**11**) is an identifiable higher order reagent and not a mixture of PhLi and Ph_2CuLi as is the case in THF.



Scheme 6

Structural determinations by spectroscopic techniques and a heightened demand for ligand efficiency have led to the development of mixed cuprates wherein the alkyl residues exhibit significantly different transferabilities. Thus, use of non-transferable or *residual*, (R_rLi) ligands permits full utilization of potentially valuable *transferable*, (R_tLi) ligands. Such mixed cuprates R_tR_rCuLi (**13**) are generally prepared *via* prior formation of R_rCu (**14**) to which the organolithium R_tLi possessing the ligand of interest is added (Scheme 7).

$$R_tLi + CuX \longrightarrow \underset{\mathbf{14}}{R_tCu} + LiX \xrightarrow{R_tLi} \underset{\mathbf{13}}{R_tR_tCuLi}$$

Scheme 7

The most popular types of non-transferable ligands are the 1-alkynyl residues. Cuprates possesing these ligands include pentynylcopper, $C_3H_7C{\equiv}C\text{-}Cu$ (**15a**),[13a] *t*-butyl-ethynylcopper, *t*-$C_4H_9C{\equiv}C\text{-}Cu$ (**15b**),[13a] (3-methyl-3-methoxybutynyl)-copper, $CH_3OC(CH_3)_2C{\equiv}C\text{-}Cu$ (**15c**),[13b] trimethylsilylethynylcopper, $(CH_3)_3SiC{\equiv}C\text{-}Cu$ (**15d**),[13c] and 3-(dimethylamino)-propynylcopper, $(CH_3)_2NCH_2C{\equiv}C\text{-}Cu$ (**15e**).[13d] Each has its advantages and disadvantages with regard to selectivity of transfer, solubility, and cost effectiveness. Other mixed cuprates which provide alternatives to homocuprates include heteroatom containing ligands e.g., *t*-C_4H_9O,[14a,b] and thienyl[14c,d] groups. Heterocuprates formed from lithium diphenylphosphide, $(C_6H_5)_2PLi$, and lithium dicyclohexylamide, $(C_6H_{11})_2NLi$, are also being used due to their increased thermal stability.[15] The most recent and widely accepted non-transferable ligand is nitrile.[16] This ligand, isoelectronic with acetylides, is the only member of this class of ligands which does not require manipulation of an air sensitive copper-containing precursor prior to addition of R_tLi (Equation 1).

$$R_tLi + R_tCu \longrightarrow \underset{\mathbf{13}}{R_tR_tCuLi}$$

$R_t = CN$

Equation 1

These alkylcyanocuprates not only deliver exclusively the R_t moiety in substitution and addition reactions attributed to cuprates, but also exhibit higher selectivity compared with dialkylcuprates derived from cuprous halides (i.e., Me_2CuLi,

selectivity compared with dialkylcuprates derived from cuprous halides (i.e., Me_2CuLi, **1**) in these reactions.[2] This higher selectivity has been recently attributed to the stabilizing π–accepting nitrile ligand.[16]

ALKYLCUPRATES DERIVED FROM CUPROUS CYANIDE

When organocuprates were derived from MeLi and CuCN in THF, no equilibrium among MeCu(CN)Li (**16**), $Me_2Cu(CN)Li_2$ (**17**) and free MeLi (Scheme 8) was evident.[17] Thus, when equimolar amounts of MeLi and CuCN were mixed in THF at -20°C a ^1H signal attributed to **16** was observed (Figure 6a). Introduction of a further equivalent of MeLi to solutions containing MeCu(CN)Li (**16**) produced a signal assigned to **17** (Figure 6d). Addition of MeLi to solutions of $Me_2Cu(CN)Li_2$ (**17**) resulted in formation of no new species but gave solutions exhibiting signals attributable to both free MeLi and $Me_2Cu(CN)Li_2$ (Figure 6e).[17]

The ^{13}C NMR spectra of the various ratios of MeLi to CuCN are in agreement with the ^1H spectral data.[17b] Thus, these spectra were consistent with the sequential formation of MeCu(CN)Li (**16**, 1:1, Figure 7b) and $Me_2Cu(CN)Li_2$ (**17**, 2:1, Figure 7c). Addition of a further equivalent of MeLi to **17** resulted in the formation of no new species (Figure 7d). Addition of CuCN to **17** regenerated **16** (Figure 7e) suggesting that the species derived from MeLi and CuCN (analogous to lower order cuprates, *vide supra*) are also in a dynamic equilibrium.[17b]

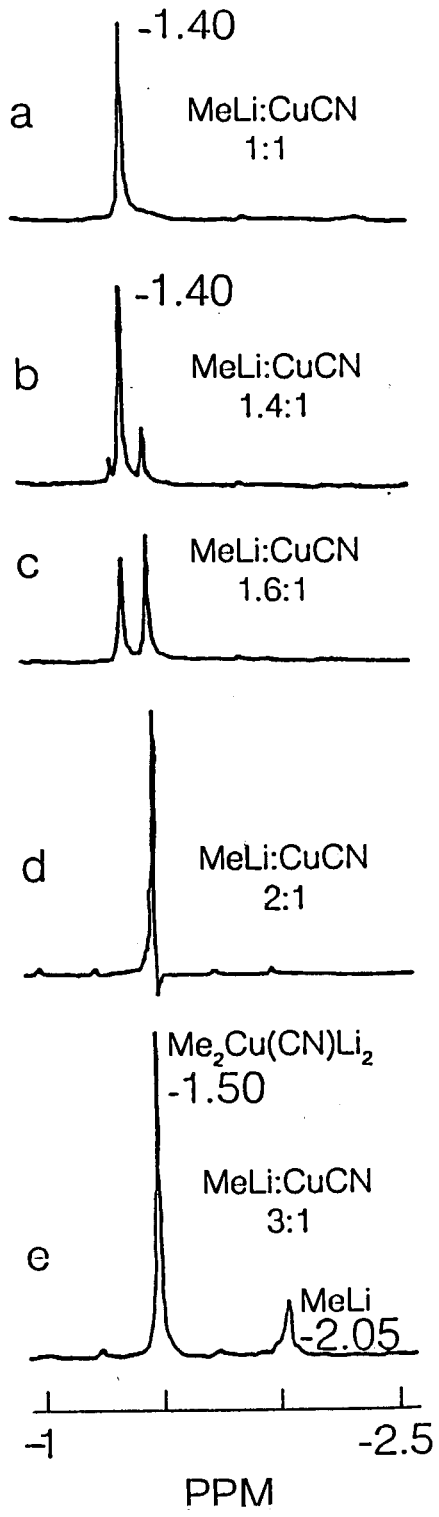


Figure 6. ^{1}H NMR spectra for solutions containing different ratios of MeLi and CuCN in THF/Et_2O at -20°C (a) MeLi:CuCN, 1:1 (b) MeLi:CuCN, <1.5:1 (c) MeLi:CuCN, >1.5:1 (d) MeLi:CuCN, 2:1, (e) MeLi:CuCN, 3:1.

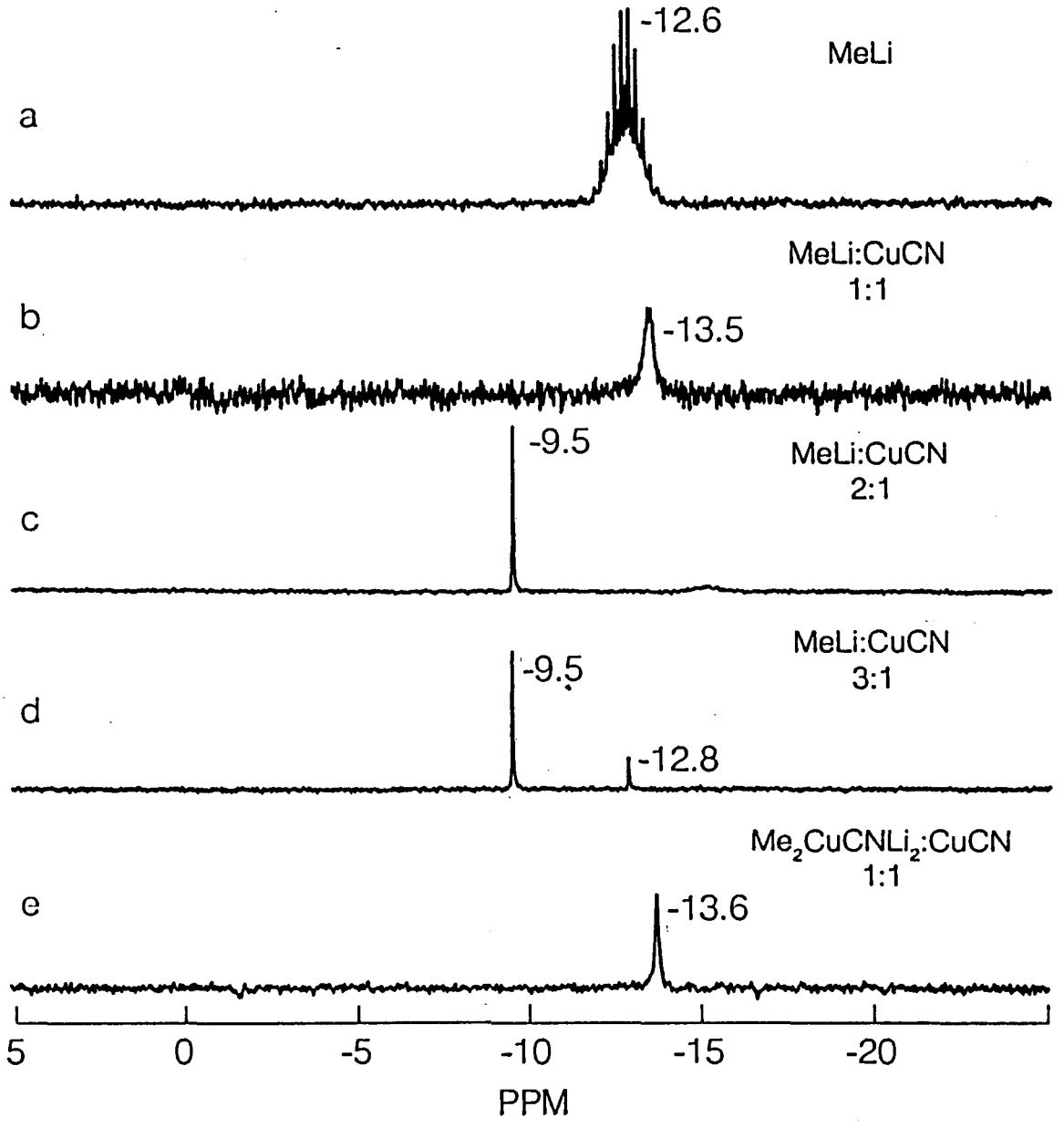
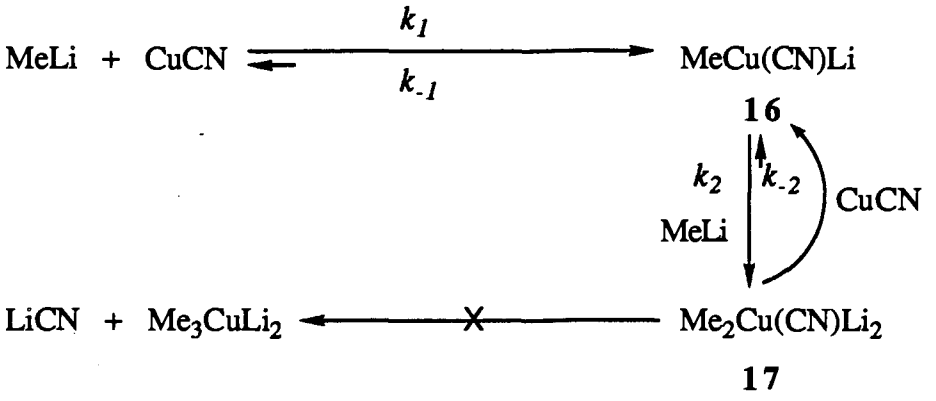


Figure 7. ^{13}C NMR spectra for solutions containing different ratios of MeLi and CuCN in THF/Et_2O at -70°C (a) MeLi (b) MeLi:CuCN, 1:1 (c) MeLi:CuCN, 2:1 (d) MeLi:CuCN, 3:1 (e) $Me_2Cu(CN)Li_2$ + CuCN.



Scheme 8

The ability of ligands on copper to exchange as well as the formation of mixed higher order cuprates of the general formula RR'Cu(CN)Li2 (**18**) were also studied by ^{1}H NMR spectroscopy.[17a] These studies indicated that stoichiometry represented by Me(*n*-Bu)Cu(CN)Li2 (**19**) could be obtained by sequential addition of MeLi and *n*-BuLi to CuCN (Figure 8c) or by mixture (Figure 8d) of Me2Cu(CN)Li2 (**17**, Figure 8a) with *n*-Bu2Cu(CN)Li2 (**20**, Figure 8b). Most significant was the occurrence of two methyl signals in the ^{1}H spectrum of **19** neither of which corresponded to **17**.[17a]

Thus, the ^{1}H NMR spectrum of the preformed reagent (CuCN + MeLi + *n*-BuLi) recorded at -27°C had two peaks (δ -1.53 and -1.56) of similar chemical shift in addition to a doublet of triplets centered at δ -0.38 suggesting two different kinds of methyl and methylene groups (Figure 8c). That the singlets at -1.53 and -1.56 ppm were due to two different methyl groups was further substantiated by ^{13}C{^{1}H} NMR spectroscopy which revealed two distinct singlets at -10.99 and -11.10 ppm (Figure 9).[17a] This spectroscopic observation, taken together with the assumption that Cu(I) species are tetrahedral,[18] implied that **19** (and hence most likely **18** and **4**) cannot be monomeric unless they are square planar.[17a]

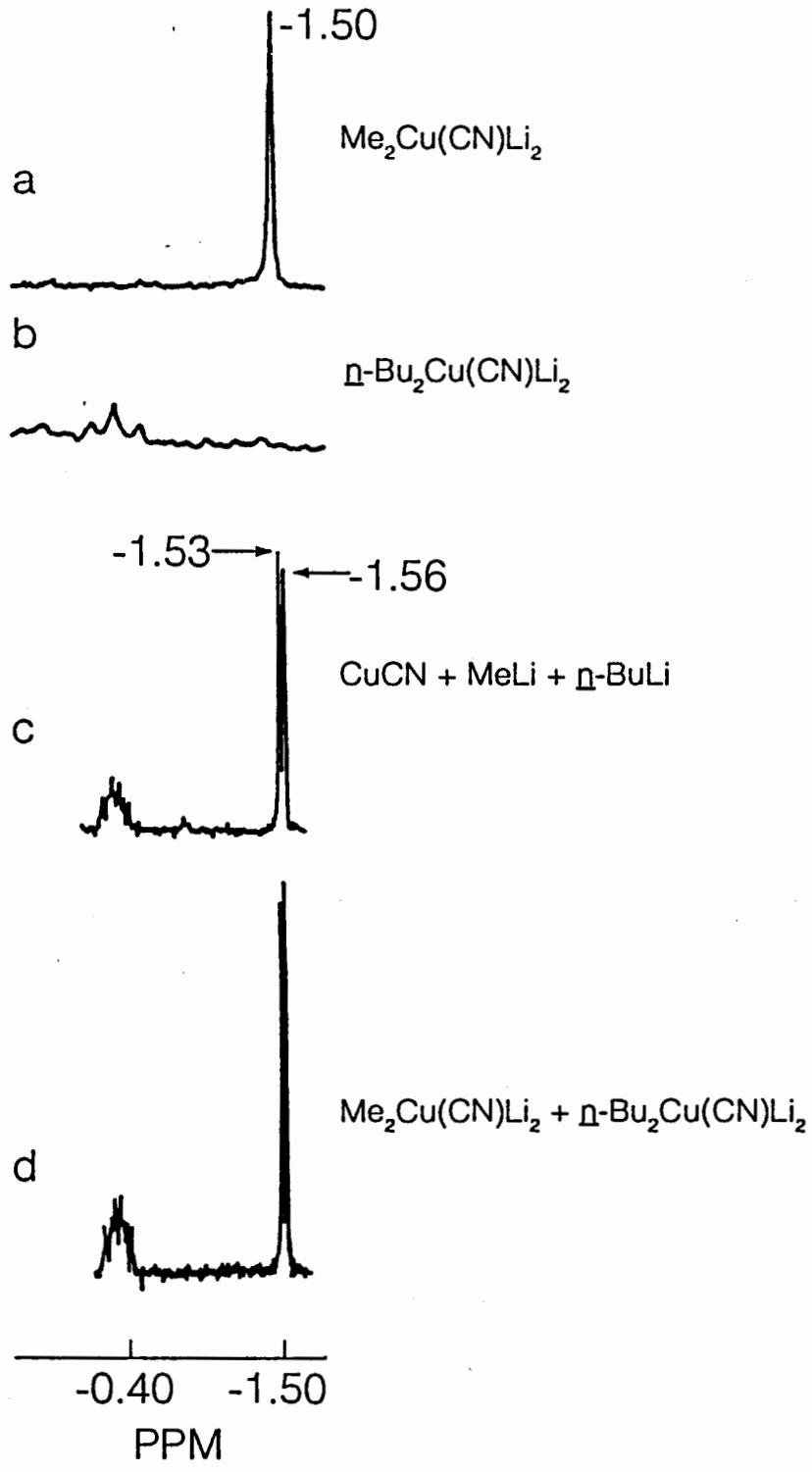


Figure 8. ^{1}H NMR spectra of (a) $Me_2Cu(CN)Li_2$ (b) *n*-$Bu_2Cu(CN)Li_2$ (c) CuCN + MeLi + *n*-BuLi (d) $Me_2Cu(CN)Li_2$ + *n*-$Bu_2Cu(CN)Li_2$; the spectra were recorded in THF/Et_2O at -27°C.

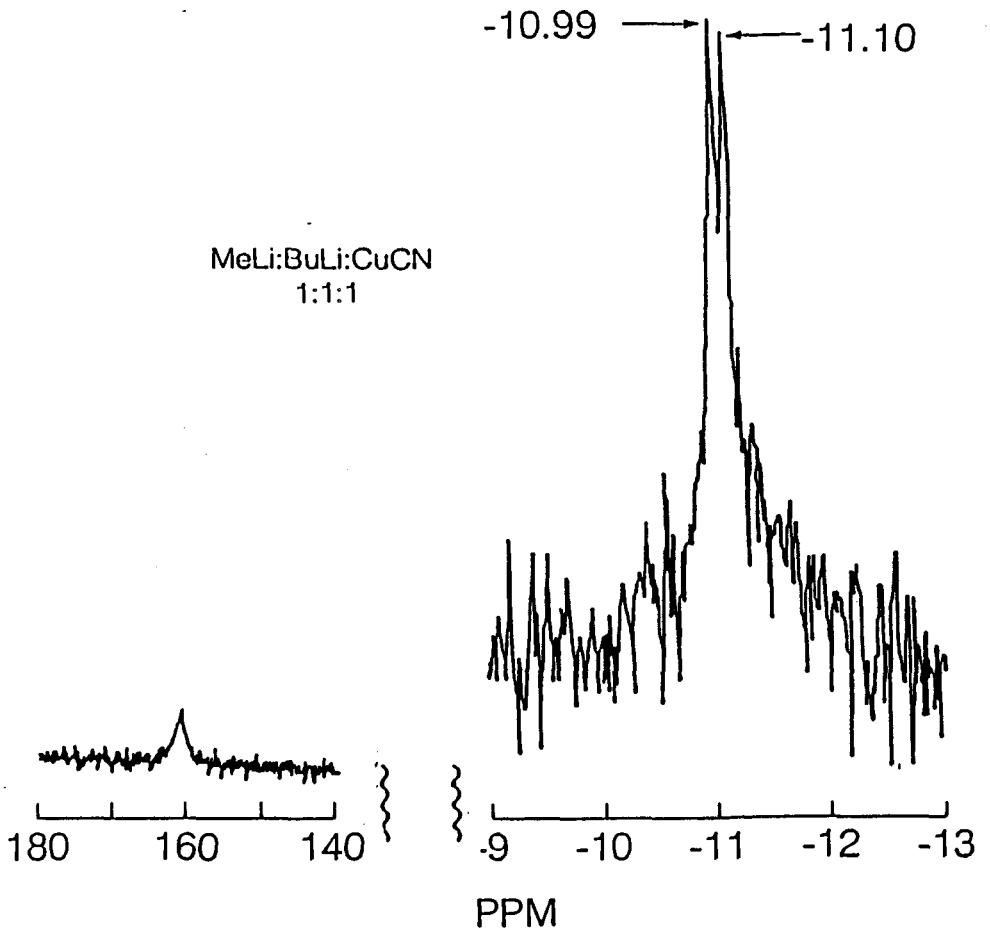


Figure 9. ^{13}C NMR spectrum of Me(*n*-Bu)Cu(CN)Li2 recorded in THF/Et2O at -27°C.

It seems clear that copper halides do not react in THF with more than two equivalents of an organolithium reagent to form stoichiometric cuprates beyond a traditional copper(I) monoanionic species (i.e., $[(R_2Cu^I)^-]Li^+$, rather than $(R_3Cu^I)^{2-}2Li^+$) while the existence of CuCN derived higher order cuprates is far more common.[17] It is likely that the cyanide ligand permits the accumulation of negative charge on copper in these complexes to formally produce copper(I) dianions (i.e., $[\{R_2Cu^I(CN)\}^{2-}]2M^+$). The unusual stability[19] of these reagents is attributed to the dπ back-bonding between the nitrile ligand and copper as illustrated in Figure 10.

COMPLEXES OF π-ACCEPTOR LIGANDS

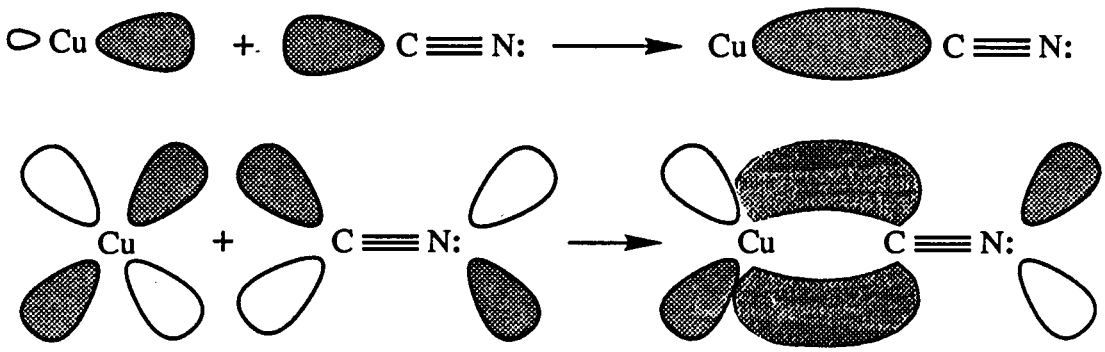


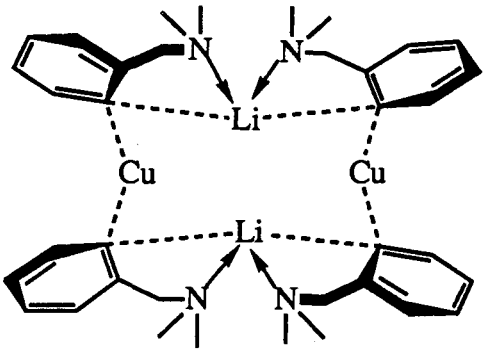
Figure 10

SOLID STATE/X-RAY ANALYSES

The sensitivity of most lithio organocuprates to moisture and oxidation as well as their thermal instability has seriously hampered efforts to form crystalline materials suitable for X-ray analysis. Although successful preparations of mononuclear species $[(R_2Cu^I)^-]M^+$ are rare, several neutral clusters have been reported.[20] Most of these contain bridging aryl groups including $[Cu_2Li_2][(C_6H_4CH_2NMe_2)_4]$[21] (**21**) and $[(Et_2O)_2][Li_2Cu_2(p\text{-Tol})_4]$[22] (**22**, Figure 11).

Perhaps the species most relevant to synthetic use of lower order cuprates is **21**, an example of a lithium cuprate containing Li and Cu in a 1:1 ratio as a part of the central core.[21] As shown in Figure 11, this molecule has a planar tetranuclear structure in which each aryl group asymmetrically bridges a copper lithium pair. The *ortho*-N,N-dimethyl-

aminomethyl residues in **21** serve as well-positioned intramolecular solvent that satisfy the preference of lithium for tetracoordination and do not effect the basic structural



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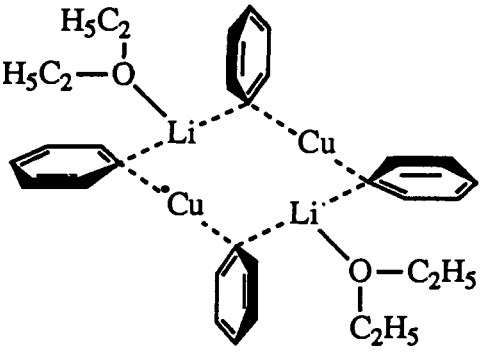

22

Figure 11

features of the cuprate. This interpretation was supported by the similar tetranuclear structure observed for **22** in which one Et_2O molecule coordinates to each Li atom (Figure 11).[22] Solution NMR spectroscopic studies (observation of $^1J^7$Li-^{13}C) of both **21** and **22** also point to a dimeric array involving bridging ligands to Cu and Li.[23a,b] This feature is apparently intrinsic to other group 11 metal-lithium clusters (e.g., $Ar_4M_2Li_2$, M = Ag, Au).[23c-d]

These dimeric solid structures support the data on solution species of Me_2CuLi (**1**) and Me_3Cu_2Li (**5**) which are in turn based on solution X-ray scattering and molecular weight measurements.[8] The observation of scalar coupling between ^{7}Li-^{13}C in **21** and **22** imply σ type interactions between ligands on copper and lithium.

Furthermore, a comparison of the solution ^{1}H NMR spectrum of **23** (δ 0.15, Me on Cu)[24] with that of Me_2CuLi (**1**, δ -1.2), leads to the conclusion that a large upfield

shift for protons on carbon attached to copper in **1** may be due to direct interactions between Me^- and Li^+, since no such interactions are possible in the lithium-free dialkyl-cuprate (**23**, Figure 12, Structure as determined by X-ray analysis of $[Cu(PMe_3)_4)]^+[CuMe_2]^-$.

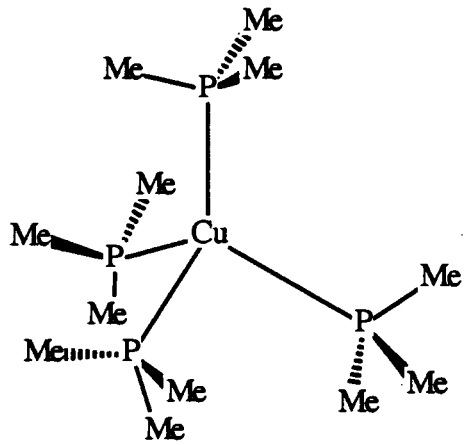

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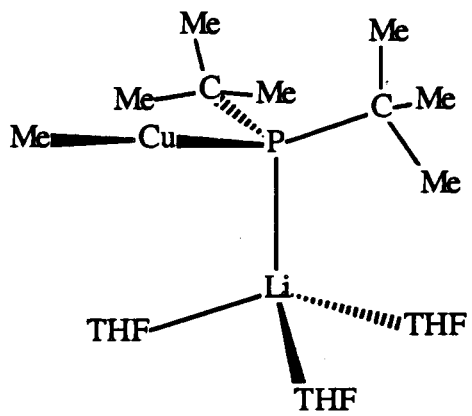
Figure 12

Recently, this has been challenged by Whangbo on the basis of extended Hückel calculations for dimeric Me_2CuLi, which predict preferential ligand bonding to copper rather than lithium.[25]

Placement of bulky groups on copper or sequestering of lithium by 12-crown-4 ether has led to the characterization of the monomeric complexes

$[Li(THF)_4][Cu(C(SiMe_3)_3)_2]$[26a] and $[Li(12\text{-crown-}4)_2][CuMe_2]$[26b] respectively. A novel heteroligand containing species $MeCuP(t\text{-}Bu)_2Li$ (**24**, Figure 13) is also monomeric.[26c] As observed for alkyl- and aryl-substituted homocuprates R_2CuLi, the copper atom of **24** exhibits a linear geometry and the Cu-C distance in **24** [1.940(6) Å] compares favorably with that found in $(CuMe_2)^-$[1.935(8) Å].[20a] However, an unusual feature of this complex is a strong association of the lithium cation with the phosphorus atom[26d] [Li-P = 2.54(1) Å]. As a result, four-coordinate lithium relies on three molecules of THF as ligands, and hence **24** is more accurately described as $[RCuP(t\text{-}Bu)_2\{Li(THF)_3\}]$.[26c]



24

Figure 13

The first structural characterization of a higher order organocuprate has recently been realized by Power *et al.*[26e] This compound was crystallized from a mixture of 3.0 equivalents of PhLi and $CuBr{\cdot}Me_2S$.[12] The structure can be represented as a combination of $(CuPh_2)^-$ and $(CuPh_3)^{2-}$ linked by three bridging Li^+ ions (Figure14) i.e., $[Li_3Cu_2Ph_5(SMe_2)_4]$. The copper centers are trigonal (119.1°) and the

i.e., $[Li_3Cu_2Ph_5(SMe_2)_4]$. The copper centers are trigonal (119.1°) and the average Cu-C bond length is 1.925 for the $(Ph_2Cu)^-$ ion and 2.02 Å for $(Ph_3Cu)^{2-}$ moiety, which is a little longer owing to the higher coordination number of the copper center. Two different types of distorted tetrahedral coordination of the lithium centers are also apparent. Li(1) is coordinated by two DMS and two bridging phenyl groups, whereas both Li(2) and Li(3) are coordinated to one thioether and three phenyl rings. This structure bears little resemblance to the previously reported clusters[20] $Li_n^+[Cu(5-n)Ph6]^-$ which are based solely on the association of three $(Ph_2Cu)^-$ moieties with bridging Li^+ or Cu^+ ions. The ^{13}C NMR spectrum of this molecule showed peaks similar to those attributed by Bertz[12] to Ph_3CuLi_2 and Ph_2CuLi.

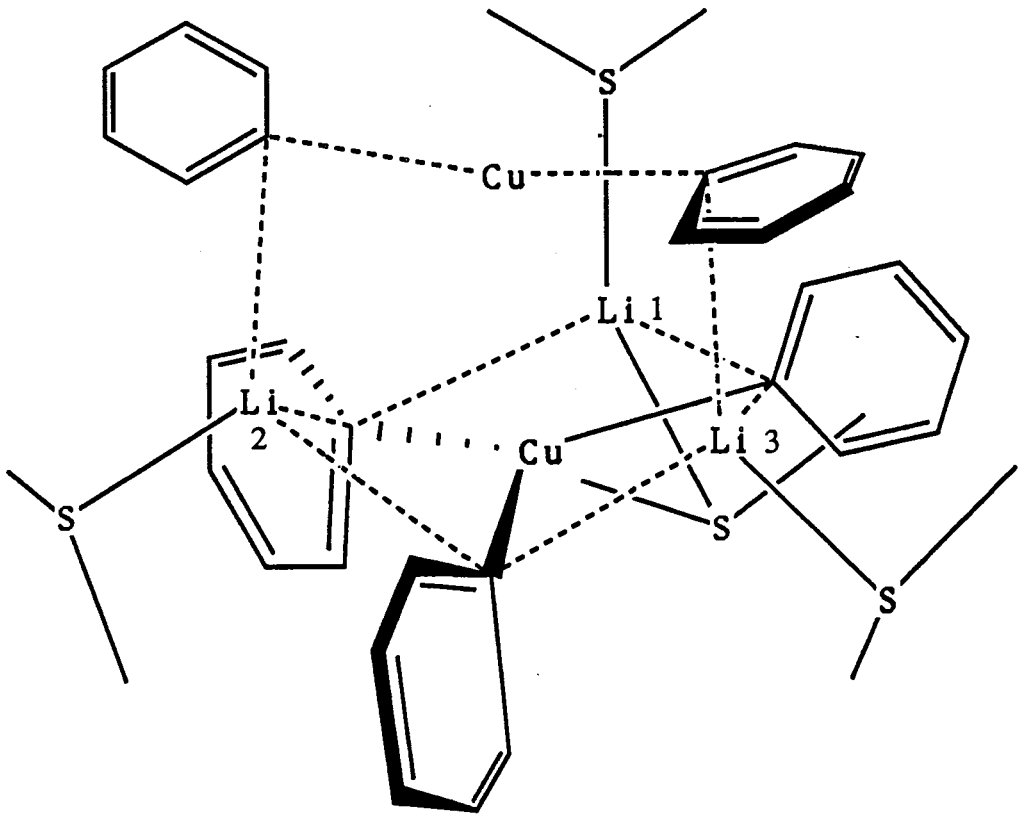


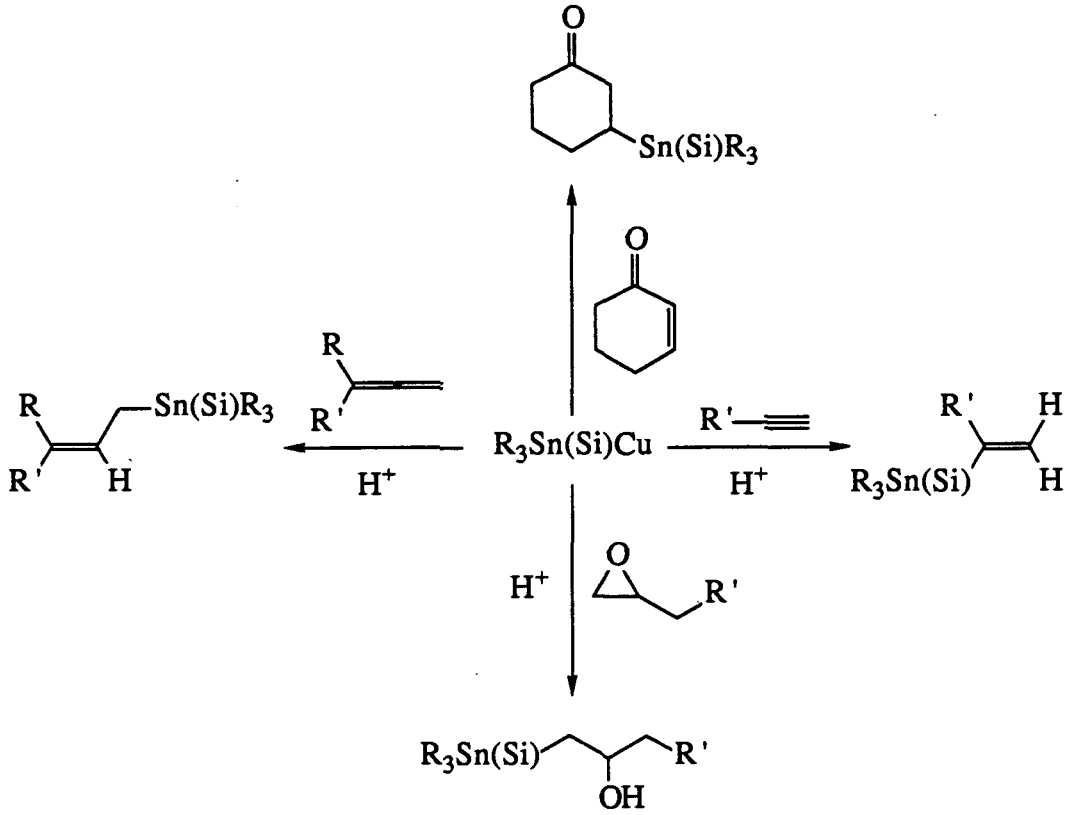
Figure 14

In the final analysis, organocopper reagents tend to be oligomeric whereas lower order cuprates can be either dimeric or monomeric depending upon the nature and steric bulk of the ligands. The *only* higher order cuprate examined by X-ray analysis is monomeric and in agreement with earlier cryoscopic measurements made by Ashby[8] on Me_3CuLi_2 (**6**).

CHEMICAL AND SPECTROSCOPIC INVESTIGATIONS OF TRIALKYLSILYL- AND TRIALKYLSTANNYLCUPRATES

Introduction

Recently, silylcopper, $[(R_3Si)_nCuLi_{n-1}\cdot LiX]$[27] and stannylcopper $[(R_3Sn)_nCuLi_{n-1}\cdot LiX$; R = alkyl, n = 1 or 2][28] reagents have begun to receive a significant share of the attention afforded to alkylcuprates by synthetic organic chemists. An appreciation of their considerable synthetic utility can quickly be gained from inspection of the numerous reactions (shown below) that these reagents effect. The range of substitution reactions encompasses primary alkyl and acyl centers.[28,29] Displacements following S_N2' pathways occur in propargylic and allylic systems.



Additions to unconjugated acetylenes,[30] allenes[31] and Michael acceptors[32] such as enones, enoates or ynoates comprise a second major reaction type. As initially with alkylcuprates, the structures of these silyl- and stannylcopper reagents proposed to date have been based solely on the stoichiometry of the solutions generated to achieve the desired chemistry.

Research proposal

It is proposed to spectroscopically study the solution phenomenon associated with the formation of silyl [$(R_3Si)_nCuLi_{n-1}\cdot LiX$] and stannyl [$(R_3Sn)_nCuLi_{n-1}\cdot LiX$] cuprates and their reactions with metal salts. It is anticipated that information gained from such studies will not only shed light on the nature of these useful synthetic reagents but also provide insights into the differences between silyl- and stannylcuprates derived from CuCN and CuX (where X = Br or I). The effect of added halide salts (i.e., LiBr *vs.* LiI) on the composition of the metallocuprates will also be examined.

It is also proposed to spectroscopically study the formation of mixed metallocuprates $(R_3Si)_n(R)CuLi_n\cdot LiCN$ and $(R_3Sn)_n(R)CuLi_n\cdot LiCN$ derived from CuCN. These reagents were of interest because of the possibility that they would selectively transfer their metallo anions in preference to their alkyl anions in reactions with organic substrates.

TRIALKYLSILYLCUPRATES DERIVED FROM CUPROUS CYANIDE

Low-temperature ^{29}Si, ^{13}C, ^{1}H and ^{7}Li NMR spectroscopy was employed to probe the composition of solutions generated by mixing dimethylphenylsilyllithium

($PhMe_2SiLi$, **25**) with CuCN. Species likely to be formed in these experiments are lower order (**26** and **27**) and higher order (**28** and **29**) silylcuprates, respectively.[7]

Lower Order Silylcuprates	**26** $(PhMe_2Si)Cu(CN)Li$
	27 $(PhMe_2Si)_2CuLi$
Higher Order Silylcuprates	**28** $(PhMe_2Si)_2Cu(CN)Li_2$
	29 $(PhMe_2Si)_3CuLi_2$

Silicon-29 NMR studies

Dimethylphenylsilyllithium (**25**) in THF was prepared by reaction of $PhMe_2SiCl$[33a] (**30**) or $(PhMe_2Si)_2$[33b] (**31**) and lithium metal. Preparations were conducted at -5°C in THF and both sources of $PhMe_2SiLi$ (**25**) gave ^{29}Si signals at -28.5 ppm (Figure 15a). Solutions of silylcuprates[27b] were generated by addition of **25** (prepared from **30** and Li metal) to THF solutions of copper cyanide at -50°C. When the ratio of $PhMe_2SiLi$ (**25**) to CuCN was 1:1 a major singlet at -25.5 ppm was observed in the ^{29}Si spectrum (Figure 15b) which is attributed to $PhMe_2SiCu(CN)Li$ (**26**). Supporting evidence for this formulation comes from infrared analysis of these solutions which shows a bound nitrile (ν_{CN}= 2111 cm^{-1})[17,34] but no free LiCN or CuCN.[35]

As the ratio of $PhMe_2SiLi$ (**25**) to CuCN was raised from 1:1 to 2:1 (>0.5 but <1.0 equivalent), a new peak at -24.7 ppm in the ^{29}Si spectrum increased in intensity at the expense of the signal at -25.5 ppm (Figure 15c). When the ratio of $PhMe_2SiLi$ to CuCN reached 2:1, the major signal was that at -24.4 ppm and a minor signal at -18.8 ppm was visible (Figure 15d). The signal at -24.4 ppm is assigned to $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) and not $(PhMe_2Si)_2CuLi$ (**27**) again based on the absence

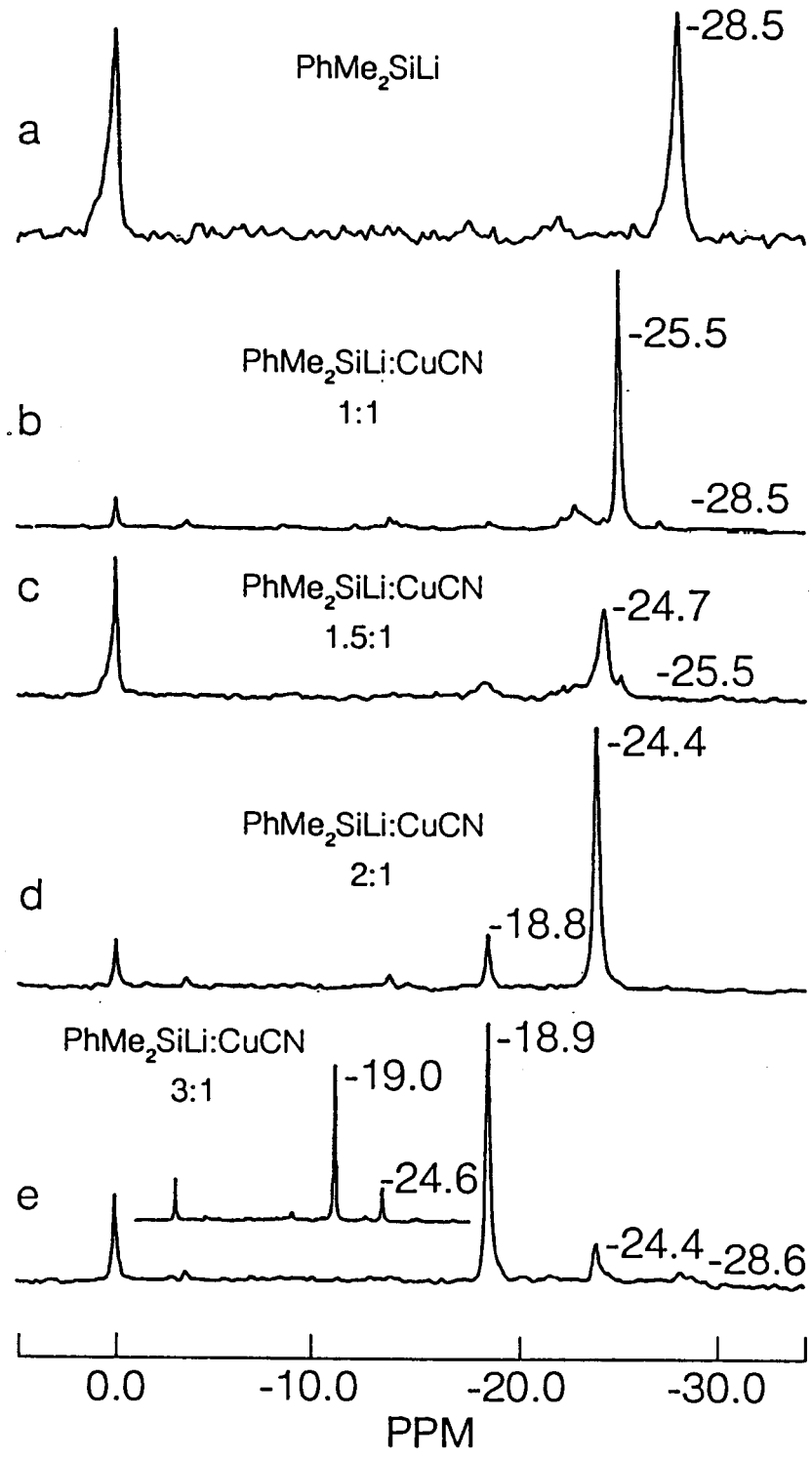


Figure 15. ^{29}Si NMR spectra for $PhMe_2SiLi$:CuCN in various ratios in THF at -50°C (a) $PhMe_2SiLi$ (b) $PhMe_2SiLi$:CuCN, 1:1 (c) $PhMe_2SiLi$:CuCN, 1.5:1 (d) $PhMe_2SiLi$:CuCN, 2:1 (e) $PhMe_2SiLi$:CuCN, 3:1 (inset 15e) $PhMe_2SiLi$:CuBr, 3:1.

of free cyanide in the solution as judged by infrared (ν_{CN}= 2123 cm^{-1}) and ^{13}C chemical shifts (163 ppm, *vide infra*). Alternative species possessing stoichiometries of $PhMe_2SiLi$ to Cu(I) other than 2:1 or disproportionation of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) would generate either free **25** or free CuCN neither of which is observed by ^{29}Si NMR (δ -28.5) or IR (ν_{CN}= 2148 cm^{-1}).[34b]

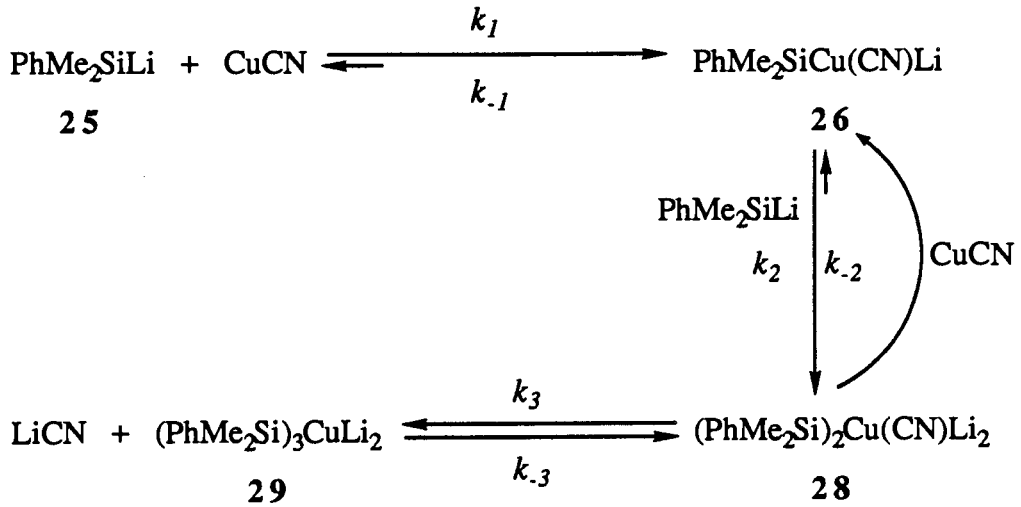
Addition of another equivalent of $PhMe_2SiLi$ (**25**) to the above sample (Figure 15d) would be expected to generate free $PhMe_2SiLi$ (δ -28.5) by analogy with CuCN based alkylcuprates. Contrary to these expectations, only a minor signal attributable to **25** was observed in this experiment (Figure 15e). Instead, in solutions containing $PhMe_2SiLi$ (**25**) and CuCN in a 3:1 ratio, a major signal at -18.9 ppm as well as a small signal assigned to $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**, -24.4 ppm) were observed. The appearance of signals for both **28** and **25** in the ^{29}Si spectrum of this solution indicates that chemical exchange between these three species is slow on the NMR time scale.

An attractive formulation for the species exhibiting a ^{29}Si signal at -18.9 ppm is $(PhMe_2Si)_3CuLi_2$ (**29**). This composition is supported by the infrared spectrum of this solution which exhibited a major absorption for free LiCN (ν_{CN} = 2085 cm^{-1}).[35] The formation of a species in which three $PhMe_2Si$ groups are directly associated with the copper center requires a cyanide to be displaced.

That the formation of $PhMe_2SiCu(CN)Li$ (**26**), and $(PhMe_2Si)_3CuLi_2$ (**29**) are reversible was shown by addition of 0.5 equivalent of CuCN to the solution whose ^{29}Si NMR spectrum is shown in Figure 15e. This results in the regeneration of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**, Figure 15d). Further introduction of CuCN to this solution results in the regeneration of the spectrum shown in Figure 15b.

Solutions prepared using 3:1 molar ratios of $PhMe_2SiLi$:CuBr·Me_2S exhibited a ^{29}Si spectra with signals at -19.0 ppm and -24.6 ppm (Figure 15e inset), but again no free $PhMe_2SiLi$ (**25**). These signals are very close to those assigned to **29** and **28**

respectively. The dynamic equilibria in which the species exhibiting signals at -25.5, -24.4 and -18.9 ppm are participating is represented in Scheme 9.



$K_3 = k_3 / k_{-3} = 34$

Scheme 9

The relative intensities of the ^{29}Si signals attributed to contributing species in solutions whose spectra are shown in Figure 15 allow estimation of the positions of the equilibria shown in Scheme 9. The equilibrium (k_1/k_{-1}) between **25**, CuCN and PhMe2SiCu(CN)Li (**26**) lies significantly on the side of **26** (i.e., $k_1 >> k_{-1}$). Likewise, in solutions containing PhMe2SiLi (**25**) and CuCN in a 2:1 ratio (PhMe2Si)2Cu(CN)Li2 (**28**) is favored ($k_2 >> k_{-2}$) to the spectroscopic exclusion of PhMe2SiCu(CN)Li (**26**). In solutions comprised ot PhMe2SiLi:CuCN in the molar ratio 3:1, (PhMe2Si)3CuLi2 (**29**) predominates over (PhMe2Si)2Cu(CN)Li2 by ~4:1. This leads to the calculation of an equilibrium constant K3. The value of K3 and the error reported were calculated by averaging three determinations.[36]

It is interesting that the ^{29}Si chemical shift change observed when lower order silylcyanocuprates are converted to higher order silylcyanocuprates is opposite to what would be expected from simple arguments based on electronegativity. Addition of electron-rich $PhMe_2SiLi$ (**25**) to $PhMe_2SiCu(CN)Li$ (**26**) should increase the electron density at a coordinating copper and hence at both silicons in the higher order species. The ^{29}Si resonance in the latter would therefore be expected to be upfield of that in the lower order reagents, not downfield as found. This anomolous pattern of shielding for nuclei like carbon[37] and silicon[38] compared to ^{1}H has been explained by semiempirical calculations of p-orbital "imbalance"and its contribution to the paramagnetic term of nuclear shielding.[37b] The observation that the ^{29}Si signals of higher order silylcyanocuprates are downfield to those of lower order silylcyanocuprates has a parallel in ^{13}C NMR spectroscopy. Deshielding of the carbonyl carbon of transition metal carbonyls increases with increased metal-to-carbonyl π back-donation. This is evidenced by an inverse linear relationship between metal-carbonyl IR stretching constants and ^{13}C chemical shifts of such carbonyls.[39] Increased metal-to-carbonyl π back-donation has been attributed to a decrease in the magnitude of the separation between the ground state and the lowest lying excited states of these molecules.[39] The observation that the ^{29}Si chemical shifts change in the same manner as the ^{13}C chemical shifts of metal-bonded carbonyls, suggests that there is a significant π bonding in both the M-CO and the Cu-Si bonds.

Carbon-13 NMR Studies

The chemical shifts of the ^{13}C resonances for the silylcuprates and their precursors are shown in Table I. Specific peak assignments were made with the aid of proton decoupled as well as proton coupled spectra. The major trends apparent in Table I

are that the formation of silylanions from neutral silyl derivatives caused both the *ipso* and methyl carbons to be strongly deshielded and the *para* carbons to be shielded with the maximum effect observed in the case of $PhMe_2SiLi$. This effect is expected by extension of the Cu-Si π bonding arguments advanced above to Si-C bonds. Such π bonding would be predicted to be more significant for $Si\text{-}C_{sp2}$ than for $Si\text{-}C_{sp3}$. As expected the *ipso* carbons of $PhMe_2SiLi$ experience larger deshielding than the methyl carbons compared to $PhMe_2SiCl$.[40]

Similar reasoning can be used to explain the chemical shift changes observed for the ^{13}C resonance of the *ipso* carbon upon the addition of electron releasing ligand ($PhMe_2SiLi$) to $PhMe_2SiCu(CN)Li$. Thus, as one progresses in the series $PhMe_2SiCu(CN)Li \rightarrow (PhMe_2Si)_2Cu(CN)Li_2 \rightarrow (PhMe_2Si)_3CuLi_2 \rightarrow PhMe_2SiLi$ the *ipso* carbon is progressively deshielded (152.0 → 158.6 → 164.3 → 166.3 ppm, Figure 16).

Table I. ^{13}C Chemical shifts of silyl metals and related species in THF. All the spectra except for $PhMe_2SiCl$ were recorded at -70°C and are referenced to THF.

	Ipso	Ortho	Meta	Para	Me
25 $PhMe_2SiLi$	166.3	133.5	126.6	122.7	7.6
29 $(PhMe_2Si)_3CuLi_2$	164.3	134.5	126.0	122.8	8.1
28 $(PhMe_2Si)_2Cu(CN)Li_2$	158.7	134.7	126.8	124.9	5.4
26 $PhMe_2SiCu(CN)Li$	152.0	136.5	128.5	126.0	6.6
30 $PhMe_2SiCl$	136.3	133.1	130.3	128.1	2.0

The aforementioned solutions of silylcuprates[27b] were generated by addition of $PhMe_2SiLi$ (prepared from $PhMe_2SiCl$ and Li metal,[33] Figure 16a) to THF solutions of CuCN·2LiCl at -50°C. The ^{13}C NMR spectrum of $PhMe_2SiCu(CN)Li$ (**26**) at -70°C, exhibits a complex pattern consisting of a combination of sharp and broad signals in the methyl as well as the phenyl region (Figure 16b). The sharp peaks are assigned to $(PhMe_2Si)_2$ which is formed as a result of decomposition of **26**. The broad peaks in the ^{13}C NMR spectrum of **26** can be attributed to either slow equilibration between species of different silicon to copper stoichiometry or different aggregation states of **26**.

The possibility that signal broadening observed in the ^{13}C NMR of **26** was due to slow equilibration of species possessing different silicon to copper ratios was ruled out by parallel on solutions in which the silicon to copper ratios was systematically varied from 1:1 to 4:1. These solutions exhibited clearly observable and differentiable ^{1}H, ^{13}C and ^{29}Si chemical shifts (*vide supra*).

Alternatively, the ^{13}C line broadening observed in the spectrum of **26** could be attributed to slow exchange between LiCl associated and LiCl-free forms of this cuprate was also considered. The ^{13}C NMR spectrum of **26** which were generated free of LiCl was identical to the one which contained this salt (compare Figure 16b with Figure 17b). Thus, this origin of line broadening is also ruled out.

It is also possible that the line broadening in the ^{13}C NMR spectrum of **26** is due to slow exchange between $PhMe_2SiCu(CN)Li$ and "$PhMe_2SiCu$". Solutions of

$$PhMe_2SiLi + CuCN \longrightarrow\!\!\!\!\!\!\times \quad \text{"}PhMe_2SiCu\text{"} + LiCN$$

Scheme 10

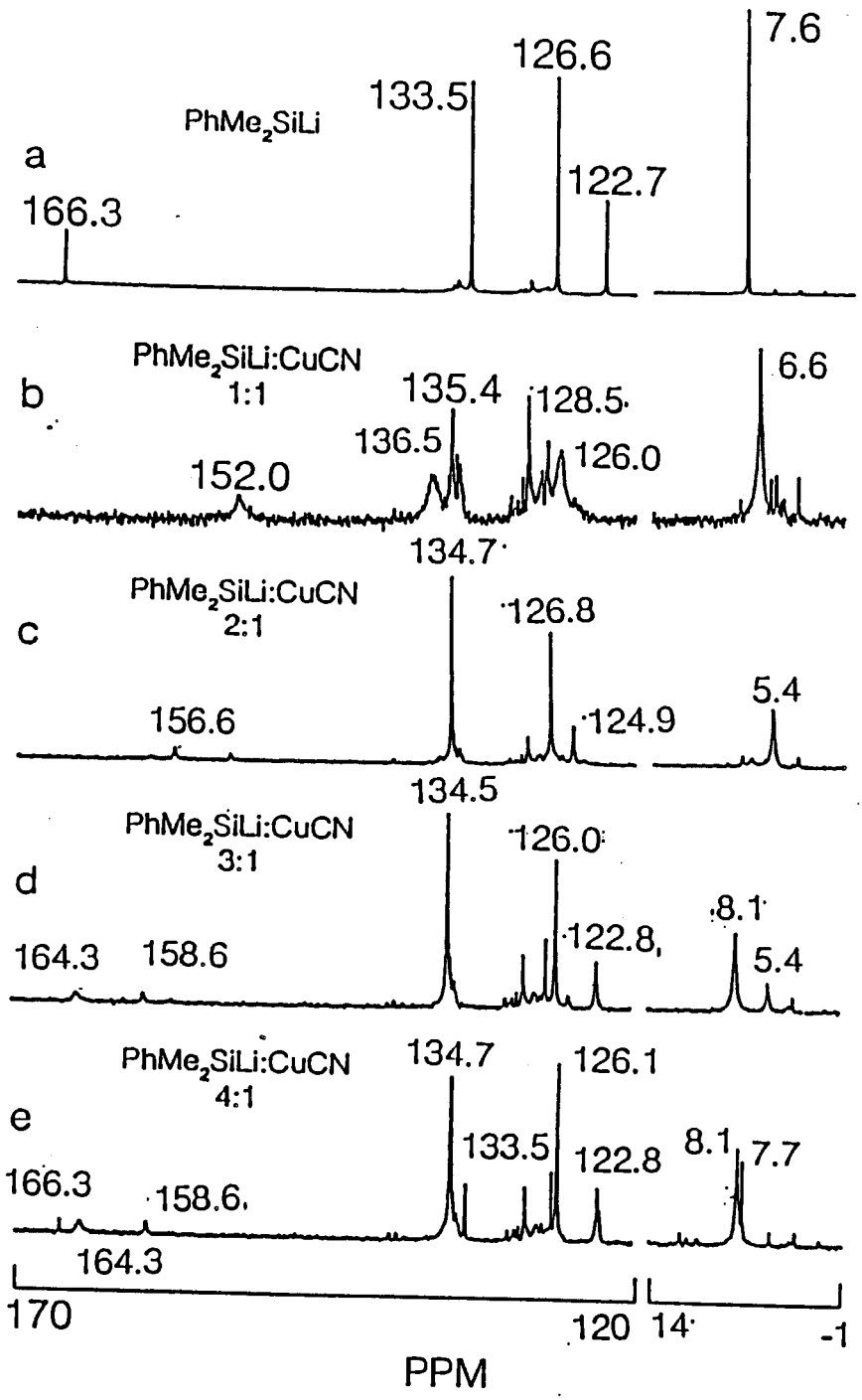


Figure 16. ^{13}C NMR spectra for $PhMe_2SiLi$:CuCN in various ratios in THF at -70°C (a) $PhMe_2SiLi$ (b) $PhMe_2SiLi$:CuCN, 1:1 (c) $PhMe_2SiLi$:CuCN, 2:1 (d) $PhMe_2SiLi$:CuCN, 3:1 (e) $PhMe_2SiLi$:CuCN, 4:1; all solutions contain LiCl.

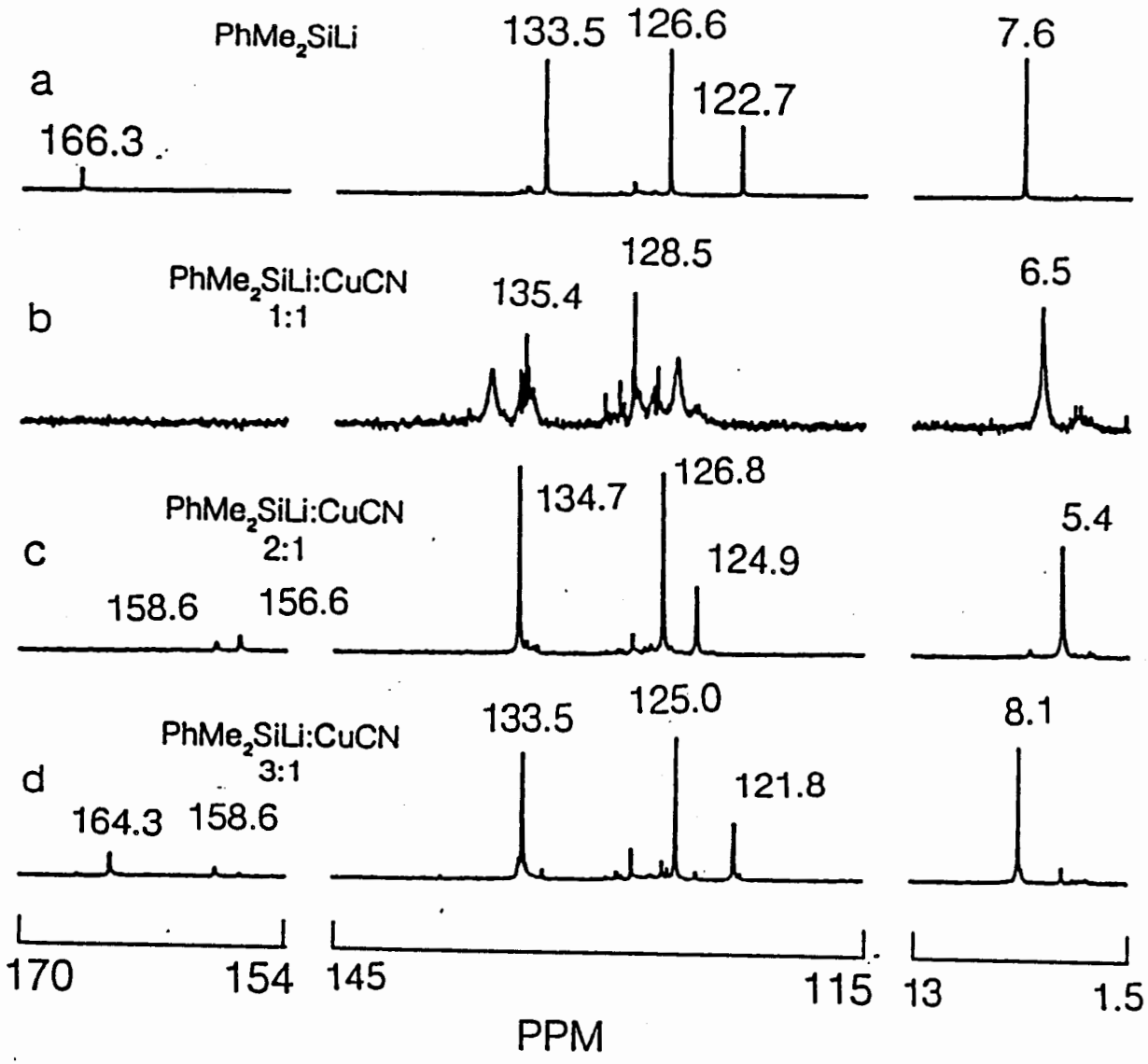


Figure 17. ^{13}C NMR spectra for PhMe2SiLi:CuCN in various ratios in THF at -70°C (a) PhMe2SiLi (b) PhMe2SiLi:CuCN, 1:1 (c) PhMe2SiLi:CuCN, 2:1 (d) PhMe2SiLi:CuCN, 3:1; the solutions are free of LiCl.

$PhMe_2SiLi$ (**25**) and $CuBr{\bullet}Me_2S$ which are expected to form "$PhMe_2SiCu$" exhibited different ^{29}Si chemical shifts than solutions of **26** (*vide infra*). This observation coupled with the absence of free LiCN as indicated by IR analysis further rules out the possibility of "$PhMe_2SiCu$" in these solutions (Scheme 10).

The last possibility considered was that the ^{13}C signal broadening was due to slow exchange between different aggregation states of **26** in THF. This phenomena has precedent in the alkylcuprates. The latter were found to exhibit broad ^{13}C and ^{1}H NMR signals in ethereal solvents but sharp signals in strongly coordinating solvents such as N,N,N',N'-tetramethylethylenediamine (TMEDA).[23] The observation that addition of a coordinating solvent like hexamethylphosphoramide (HMPA) results in

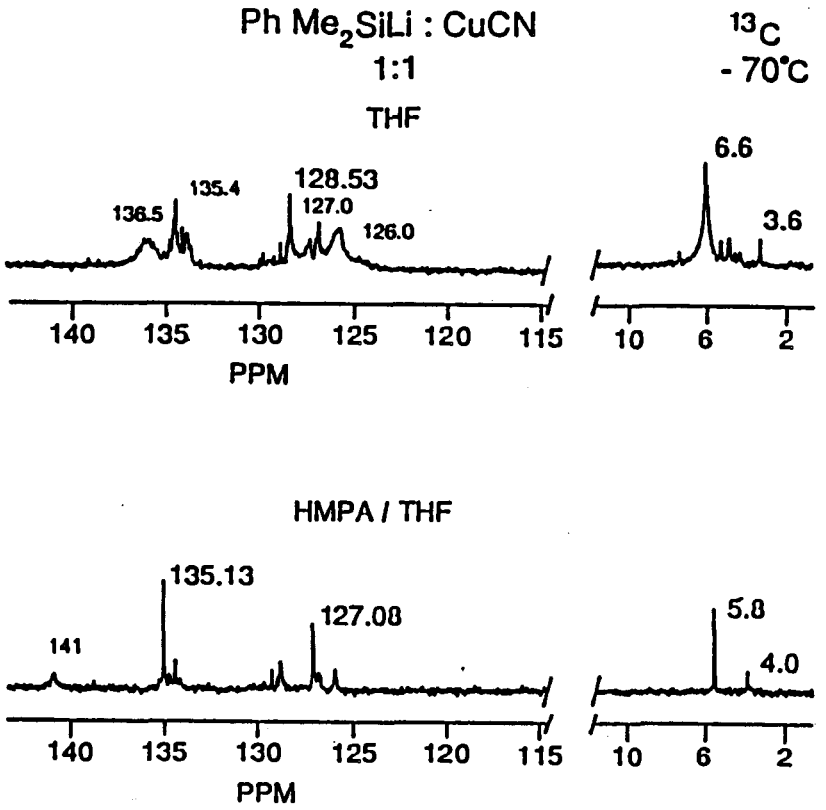


Figure 18. ^{13}C NMR spectra of $PhMe_2SiCu(CN)Li$ in (a) THF (b) THF/HMPA, 1:1.

considerable sharpening of the ^{13}C NMR signals (Figure 18) of **26** is consistent with the existence of this reagent in a less aggregated state in HMPA compared to ethereal solvents.

Warming solutions of **26** to -20°C resulted in the rapid formation of $(PhMe_2Si)_2$ due to decomposition of this reagent at and above this temperature. When ^{13}C NMR spectra of **26** were recorded at this temperature no alteration in the ^{13}C line shapes of this cuprate were observed suggesting the rate processes giving rise to the broadening were too slow. Spectra below -70°C could not be obtained due to appreciable precipitation of the reagent at this temperature. This precluded determination of exchange rates for species involved in ^{13}C signal broadening.

The ^{13}C NMR spectrum of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) consists of six sharp lines: four in the phenyl region (δ 158.6, *ipso*; 134.7, *ortho*; 126.8, *meta*; 124.9, *para*), one due to the nitrile carbon (156.6 ppm) and a methyl signal at 5.4 ppm (Figure 16c). As observed earlier, substituting $PhMe_2SiLi$, free of LiCl, for LiCl-containing $PhMe_2SiLi$, did not change the ^{13}C NMR chemical shifts (compare Figures 16c and 17c) implying that the presence or absence of halide has no noticeable effect on the solution composition of higher order silylcyanocuprates. The presence of a single species in the ^{13}C NMR spectrum is in agreement with the ^{29}Si spectrum (*vide supra*) which showed a single peak for this reagent (Figure 15d). A single species is similarly indicated by the ^{7}Li NMR spectrum (*vide infra*) of **28** which exhibits a sharp singlet at -0.96 ppm.

In agreement with the ^{29}Si NMR analysis, the ^{13}C NMR spectrum of $(PhMe_2Si)_3CuLi_2$ showed signals corresponding to both **28** and **29** in a ~4:1 ratio (Figure 16d). Halide free $(PhMe_2Si)_3CuLi_2$ prepared from **25** gives rise to the same principal lines, but they are sharper (Figure 17d). The ^{7}Li spectrum of **29** shows a broad hump centering at δ -0.74. This is attributed to slow intermolecular exchange of lithium

among various lithium containing species.[7,9,12] Similar signal broadening is observed in both ^{13}C and ^{7}Li NMR spectra of Ph_3CuLi_2 in DMS even at -100°C (*vide supra*).[12]

Introduction of a further equivalent of **25** did not result in the formation of any new species but rather showed signals corresponding to free $PhMe_2SiLi$ (Figure 16e).

As pointed out earlier, sequential addition of $PhMe_2SiLi$ to highly aggregated **26** in THF results in formation of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) and $(PhMe_2Si)_3CuLi_2$ (**29**) which are apparently less aggregated as judged from their sharp NMR signals. Whether **28** is monomeric or dimeric is not clear. If it is monomeric there is the possibility that the complexes could be solvated according to the equilibrium in Equation 2. With

$$CuL_2L' \text{ (solvent)} \rightleftharpoons CuL_2L' + \text{solvent}$$

$L = PhMe_2Si$
$L' = CN$

Equation 2

coordinated solvent the likely geometries about Cu^+ are tetrahedral or square planar. In the uncoordinated form a trigonal array around Cu^+ is likely. Of further interest is the location of the two lithium ions in the copper cluster. The placement of two lithium ions in a tetrahedral array could convey an element of asymmetry to the complex and yet no such asymmetry was noted in the present studies.

A dimeric species could either be cyclic or acyclic. The cyclic arrangement must contend with planarity requirements of two nitrile ligands. An acyclic dimer containing nitrile should permit further associations *via* this ligand. The difficulty in formulating structures of dimeric cyanocuprates is reflected in the fact that no structures have been proposed to date for the alkylcyanocuprates.

Hydrogen-1 NMR Studies

The ease with which we were able to study the higher order silylcuprates derived from CuCN, by ^{29}Si and ^{13}C NMR spectroscopic techniques, encouraged us to study the formation of these species using ^{1}H and ^{7}Li NMR spectroscopy. The ^{1}H nuclear magnetic resonance spectra were recorded at -85°C at 300 MHz in the region between 1.0 ppm and -2.0 ppm with the specific goal of observing the resonances due to the methyl hydrogens (since the chemical shifts of the aromatic protons were too close to be of any significance). Solutions of $PhMe_2SiLi$ (**25**) exhibited a singlet at 0.10 ppm (Figure 19a) whereas solutions containing **25**:CuCN in a 1:1 ratio showed a broad signal at 0.22 ppm which we attribute to aggregated $PhMe_2SiCu(CN)Li$ (**26**, Figure 19b). As the ratio of $PhMe_2SiLi$ (**25**) to CuCN was increased from 1:1 to 2:1, a new signal at 0.02 ppm became visible (Figure 19c). When the ratio was precisely 2:1, the major signal observed was at 0.02 ppm; this signal was assigned to $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**, Figure 19d). Solutions containing **25**:CuCN in 2:1 molar ratio to which one or more equivalent of $PhMe_2SiLi$ had been added revealed only one major ^{1}H signal with a chemical shift close to that assigned to **28** (Figure 19e). We assume from the ^{29}Si and ^{13}C NMR studies (*vide supra*) that the chemical shifts of the methyl hydrogens attached to silicon for the presumed species **28** and $(PhMe_2Si)_3CuLi_2$ (**29**) are very similar.

Lithium-7 NMR Studies

Dimethylphenylsilyllithium (**25**, free of LiCl), was prepared from $(PhMe_2Si)_2$ (**31**) and lithium metal.[33] Initial ^{7}Li NMR studies were conducted at -70°C on THF suspensions composed of equimolar amounts of $PhMe_2SiLi$ (**25**, δ 0.29, Figure 20a) and CuCN. These solutions exhibited a major ^{7}Li signal[41b] at -0.25 ppm which was

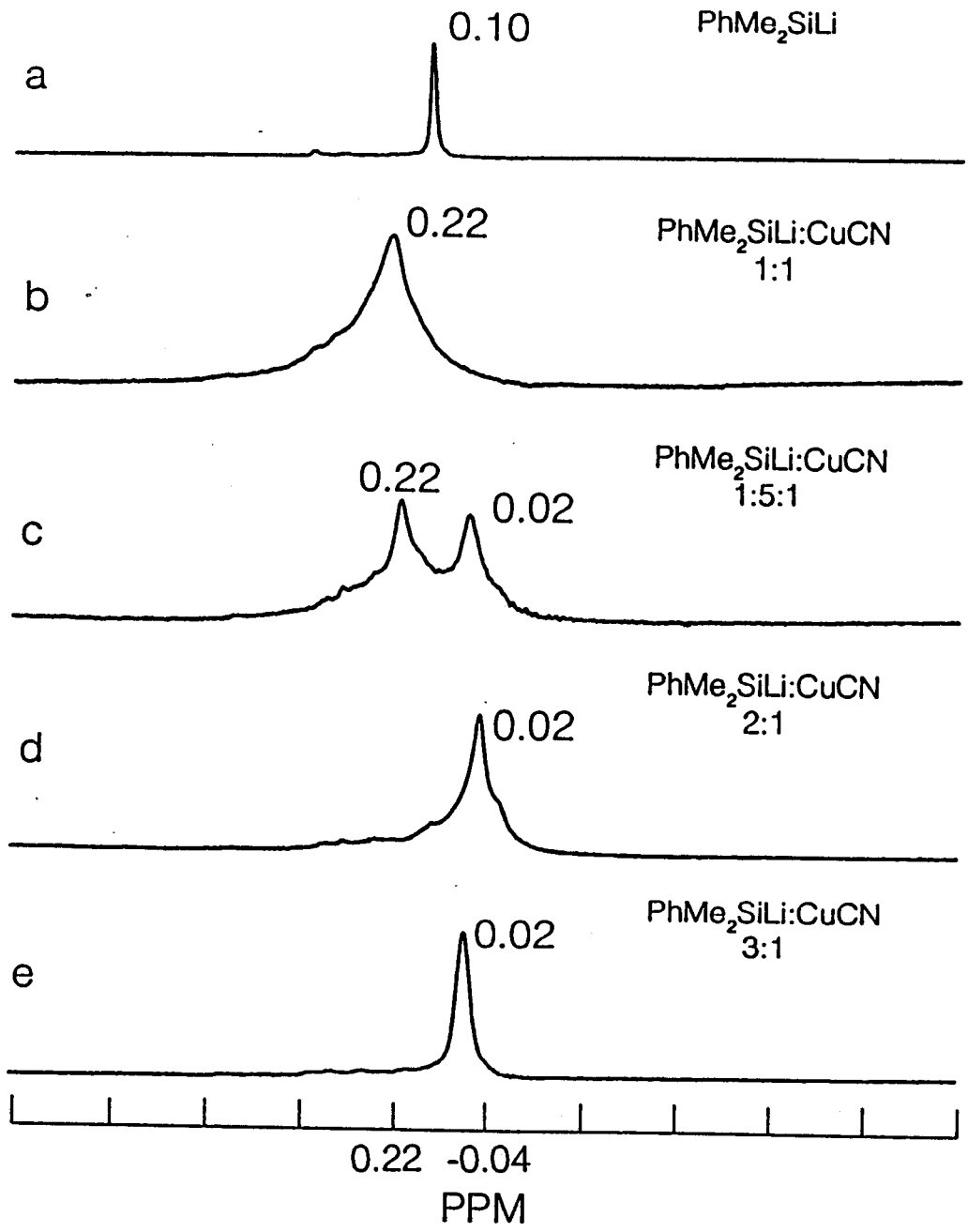


Figure 19. ^{1}H NMR spectra for PhMe2SiLi:CuCN in various ratios in THF at -85°C (a) PhMe2SiLi (b) PhMe2SiLi:CuCN, 1:1 (c) PhMe2SiLi:CuCN, 1.5:1 (d) PhMe2SiLi:CuCN, 2:1 (e) PhMe2SiLi:CuCN, 3:1; all solutions contain LiCl.

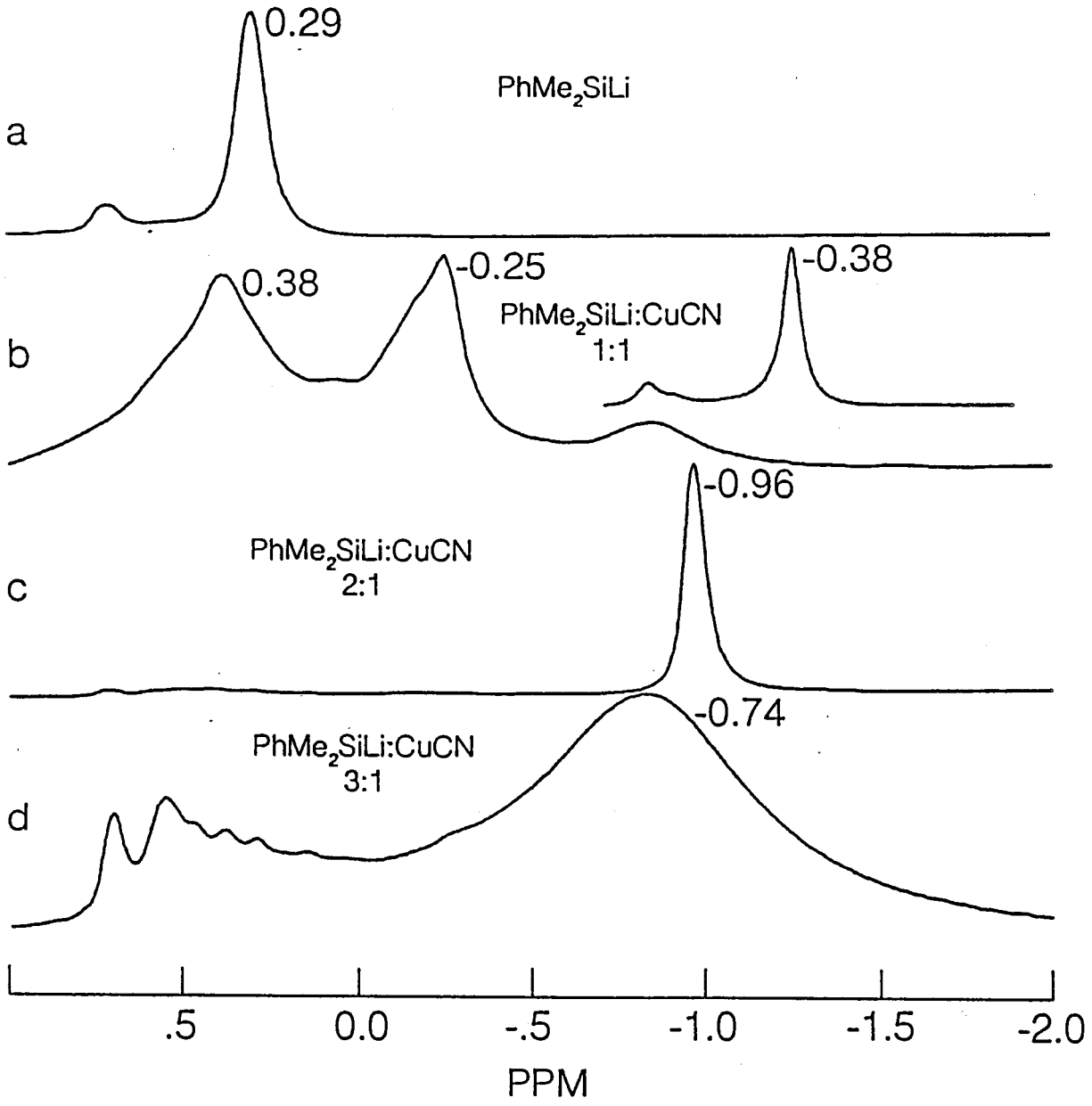


Figure 20. ^{7}Li NMR spectra for PhMe2SiLi:CuCN in various ratios in THF at -70°C (a) PhMe2SiLi (halide free) (b) PhMe2SiLi:CuCN, 1:1 (c) PhMe2SiLi:CuCN, 2:1 (d) PhMe2SiLi:CuCN, 3:1; insets are for reagents with LiCl.

assigned to $PhMe_2SiCu(CN)Li$ (**26**) along with a peak in the region for **25** (δ 0.38, Figure 20b) and a weak broad peak at -0.84 ppm. As expected, in the absence of LiCl the reaction mixture was heterogeneous due to the decreased solublity of CuCN. Addition of LiCl resulted in the disappearance of the signal due to $PhMe_2SiLi$ (**25**) and in the appearance of a single peak at -0.38 ppm (Figure 20b, inset). These observations indicate that in the absence of LiCl, exchange between **25** and **26** is slow on the NMR time scale whereas, in the presence of LiCl exchange of ^7Li between various species is rapid.[7,9] In agreement with these interpretations, a positive Gilman test[42] was obtained for the LiCl-free preparations of **26** and a negative test after LiCl was added. Sequential addition of one equivalent of LiCl-free $PhMe_2SiLi$ (**25**) to $PhMe_2SiCu(CN)Li$ (**26**) resulted in the appearance of a singlet at -0.96 ppm which we attribute to $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**, Figure 20c). The presence of a single peak in the ^7Li spectrum of **28** is in harmony with the ^{29}Si, ^{13}C and ^1H NMR studies (*vide supra*) indicating a symmetrical environment around Li^+ in the copper species.[43] The presence of rapidly exchanging species cannot be entirely ruled out.

Further introduction of halide-free **25** led to a broad signal centered at δ -0.74 (Figure 20d). This was assigned to $(PhMe_2Si)_3CuLi_2$ (**29**). The broad nature of this signal suggests averaging due to rapid chemical exchange between **28**, **29** and free LiCN.[7,9,12]

The observation of averaged signals in the cases of ^1H and ^7Li spectra but not in the case of ^{29}Si is a function of the frequency of the measurements and the chemical shift differences in Hz of the exchanging species.[44] Thus for ^{29}Si, the chemical shift differences for **26**, **28** and **29** are at least 1.0 ppm and the measurement is carried out at 79.5 MHz. If the equilibration between the species is faster than 79 Hz, an averaging of signals will be observed in the ^{29}Si spectrum. For ^1H assuming a separation of the methyl ^1H signals of **26**, **28** and **29** of ~0.1 ppm and a measurement frequency of 300

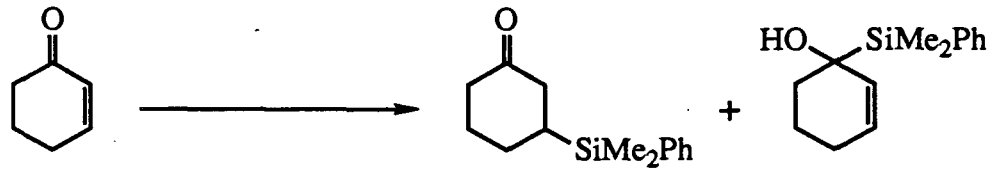
MHz the averaged signals observed require exchange to be faster than 30 Hz. Thus, at -50°C the species equilibrate at a rate of 30 to 79 Hz.

Some uncertainty in the measurement of equilibria from ^{29}Si signal intensities comes from the negative gyromagnetic ratio[36b] of ^{29}Si. Under the conditions of broad-band ^{1}H decoupling the ^{29}Si resonance will suffer a negative nuclear Overhauser effect if the ^{29}Si nucleus is in close proximity (<3 Å) to a ^{1}H nucleus. To surpress the negative nOe of ^{29}Si the decoupler was turned on during the acquisition and off during the relaxation delay. Another source of uncertainty in calculations of equilibrium constants could arise from the differential T_1's of the equilibrating species. Since the proposed species are equilibrating with a rate constant between 30 and 79 Hz which is ~10x faster than the acquisition time (0.2 s, *vide infra*) for ^{29}Si NMR experiments, the effective T_1's of the equilibrating species would be equivalent under these conditions.

Chemical tests

Perhaps the single most intriguing question which arises from ^{29}Si NMR studies relates to the composition of solutions attributed to **29**. If **29** does not have the postulated structure but rather is composed of free **25** in rapid equilibrium with silylcyanocuprates containing a Si:Cu ratio of <3:1, then the *free* $PhMe_2SiLi$ would be expected to compete in reactions with the silylcyanocuprates. To test this, side-by-side reactions were conducted on two substrates, cyclohex-2-en-1-one (**32**) and 1-octyne (**35a**), each was treated with **25**, **26**, **28**, **29** and **29** + **25**. It was found that solutions of both **28** and **29** deliver a $PhMe_2Si$ group exclusively *via* 1,4-addition to cyclohex-2-en-1-one (**32**).[32] Solutions composed of **29**, **25** and CuCN (molar ratio 1:1:0.1) also added to **32** in a 1,4-manner. These results show that "$PhMe_2SiCu$" reagents behave in

Scheme 11. Addition reaction of "$PhMe_2SiCu$" reagents to cyclohex-2-en-1-one, **32**.



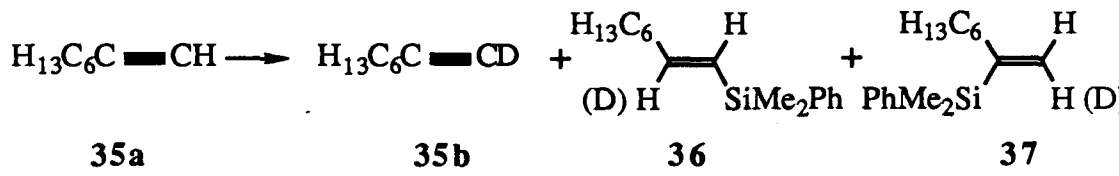
32 **33** **34**

25	$PhMe_2SiLi$	-	62%
26	$PhMe_2SiCu(CN)Li$	58%	
28	$(PhMe_2Si)_2Cu(CN)Li_2$	65%	
29	$(PhMe_2Si)_3CuLi_2$	70%	
	$(PhMe_2Si)_3CuLi_2$ + **25**	67%	

a fashion analogous to alkyl cuprates[45] in delivery of their anionic ligands in a 1,4-fashion even when copper is present only in catalytic concentrations. Thus 1,4-addition of silylanions bound to copper must be faster than 1,2-addition of the unbound species to give **34**. The observation that solutions of **29** + **25** gave **33** in high regioisomeric purity suggest that under catalytic conditions the *extra* PhMe2SiLi serves to rapidly convert any lower order cuprate formed as a result of silyl transfer back to a higher order cuprate.

Next we studied the addition of silylcuprates **25**, **26**, **28** and **29** to 1-octyne (**35a**). In agreement with existing reports,[30] we found that **26** added to **35a** to yield a mixture of **36** and **37** in a 3:2 ratio, whereas addition reactions of (PhMe2Si)2Cu(CN)Li2 (**28**) and (PhMe2Si)3CuLi2 (**29**) gave **36** in ~90% isolated yields. Under similar conditions PhMe2SiLi (**25**) abstracted the acetylenic hydrogen of

Scheme 12. Silylcupration of 1-alkynes.



35a **35b** **36** **37**

	% Composition			
	35b	**36**	**37**	%yield
$PhMe_2SiLi$	100	-	-	72
$PhMe_2SiCu(CN)Li$	-	60	40	62
$PhMe_2SiCu(CN)Li$/HMPA	-	>98	<2	86
$(PhMe_2Si)_2Cu(CN)Li_2$	-	>98	<2	92
$(PhMe_2Si)_3CuLi_2$	-	>98	<2	90

35a after ^2H_2O quench to give **35b** as judged by GC-MS (70% incorporation of ^2H in 1-octyne). No addition products were observed (capillary g.c. analysis). In support of ^{13}C NMR results, treatment of 1-octyne (**35a**) with PhMe2SiCu(CN)Li (**26**) in THF/HMPA (1:1) gave exclusively **36** in >85% yield. That *free* PhMe2SiLi is not present in the solutions of silylcuprates was confirmed by the absence of incorporation of ^2H in the vinyl products when quenched with ^2H_2O.

Gilman Tests

Support for our interpretation of the ^{29}Si, ^{13}C, ^7Li and ^1H NMR data and the propensity of solutions of **25** and CuCN studied (1:1 → 4:1) to undergo 1,4-addition to **32** and regiospecific additions to **35a** was obtained from Gilman tests on THF solutions

containing $PhMe_2SiLi$ (**25**) and CuCN.[42] As originally reported by Gilman, addition of a solution containing 4,4'-Bis(dimethylamino)benzophenone (Michler's ketone) to an organocuprate at room temperature followed by quenching with H_2O and then introduction of I_2/HOAc gives an intense greenish-blue coloration if RLi is present. A

Table II. Gilman test on CuCN-derived silylcuprates

	Reagents	Results
25	$PhMe_2SiLi$	Positive
26	$PhMe_2SiCu(CN)Li$	negative
28	$(PhMe_2Si)_2Cu(CN)Li_2$	negative
29	$(PhMe_2Si)_3CuLi_2$	negative
	$(PhMe_2Si)_3CuLi_2$ + **25**	positive

positive Gilman test was obtained for **25** in THF while a negative test was obtained for all solutions of $PhMe_2SiLi$ containing CuCN including those where these reagents are present in a 3:1 ratio. A slight green coloration was observed for solutions containing a 4:1 ratio of $PhMe_2SiLi$:CuCN indicating the presence of small amounts of $PhMe_2SiLi$ (**25**, Table II).

Conclusion

Comparison of the present silylcyanocuprate system with that of the methylcyanocuprate system studied by Lipshutz *et al.*[17] reveals several interesting

features. In both of these systems, when the ratio of RLi (R = $PhMe_2Si$ or Me) to CuCN is unity, a nitrile containing monoanionic cuprate is formed. In neither system does this species appear to be in equilibrium with other species or free RLi. As the proportion of anion is increased from an RLi:Cu ratio of 1:1 to 2:1 a new species, containing a bound nitrile, is formed in both cases. In the case of $Me_2Cu(CN)Li_2$ (**17**) association of alkyl residues with copper beyond this stoichiometry does not occur and further addition of MeLi gives solutions containing free MeLi. In the case of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) addition of further silyllithium gives solutions which contain negligible amounts of $PhMe_2SiLi$ and whose ^{29}Si, ^{13}C and ^{1}H spectra support the association of three silyl residues with the copper accompanied by displacement of the cyanide ligand. Chemical studies on two different substrate types, as well as Gilman tests for the presence of free RLi, are fully consistent with the spectroscopic data.

TRIALKYLSILYLCUPRATES DERIVED FROM CUPROUS HALIDES

In the previous section it has been demonstrated that higher order silylcuprates, $(R_3Si)_2Cu(CN)Li_2$ (**28**) retain the CN moiety. This lack of metal-metal exchange between copper and lithium (i.e., $R_3SiLi + CuCN \nrightarrow$ "R_3SiCu" + LiCN) was attributed to the likelihood of dπ backbonding between the copper and nitrile ligand.[19] More remarkable was the observation that the addition of three equivalents of $PhMe_2SiLi$ (**25**) to CuCN resulted in the unprecedented formation of $(PhMe_2Si)_3CuLi_2$ (**29**) rather than $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) and free $PhMe_2SiLi$ (Scheme 9) as was the case for alkylcuprates derived from CuCN (Scheme 8).[17] This unusual stability of **29** was attributed to significant π bonding between Cu and Si (*vide supra*). Whether such an equilibrium exists in the case of copper halide derived silylcuprates, however, remained to be elucidated and this was next undertaken.

Silicon-29, Carbon-13 and Lithium-7 NMR studies

Low-temperature ^{29}Si, ^{13}C and ^{7}Li nuclear magnetic resonance spectroscopy was employed to probe the composition of solutions generated by mixing $PhMe_2SiLi$ (**25**) with CuX (X = Br or I). Species likely to be formed in these experiments are silylcopper reagent (**38**), halide-free (**27**) and halide associated (**39**) lower and higher order silylcuprates (**29**), respectively.[7]

Silylcopper reagent	**38** $PhMe_2SiCu$
Lower Order Silylcuprates	**27** $(PhMe_2Si)_2CuLi$
	39 $(PhMe_2Si)_2CuLi{\cdot}LiX$
Higher Order Silylcuprates	**29** $(PhMe_2Si)_3CuLi_2$

Reaction of $PhMe_2SiCl$ (**30**) with lithium metal in THF gave LiCl-containing solutions of **25**.[33] Preparations were conducted at -5°C in THF and **25** gave a ^{29}Si signal at -28.5 ppm (Figure 21a). Solutions of silylcuprates (**27**) were generated by addition of THF solutions of **25** to $CuBr{\cdot}Me_2S$ at -50°C. The combination of equimolar amounts of **25** and $CuBr{\cdot}Me_2S$ yielded a suspension in which most of the ^{29}Si signal was lost (Figure 21b) presumably because the solid contained most of the silicon containing species. The resulting ^{29}Si spectrum contained several signals between -10 and -25 ppm which were attributed to polymeric "$PhMe_2SiCu$" (**38**). In agreement with the observations made with ^{29}Si NMR, most ^{13}C signal in the corresponding ^{13}C NMR spectrum was also lost in solutions containing equimolar amounts of **25** (Figure 22a) and $CuBr{\cdot}Me_2S$. The signals that were visible were due to $(PhMe_2Si)_2$ (**31**, Figure 22b, identity of **31** was confirmed by recording the ^{13}C NMR of the solution containing both **31** and **38**) formed as a result of thermal decomposition of **38**.

The combination of **25** and $CuBr{\cdot}Me_2S$ in a 1.5:1 molar ratio gave a nearly homogeneous solution exhibiting a ^{29}Si signal at -24.4 ppm attributed to $(PhMe_2Si)_2CuLi$ (**27**, Figure 21c). The assignment of this signal to **27** was facilitated by the observation that at a 2:1 ratio of **25** to $CuBr{\cdot}Me_2S$ the signal at -24.4 ppm remained intense while a minor signal at -18.9 ppm appeared (Figure 21d). A signal at -24.4 ppm has previously been observed for $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) produced by the reaction of two equivalents of **25** and CuCN. That $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) and $(PhMe_2Si)_2CuLi$ (**27**) are, however, different species was confirmed by ^{13}C NMR spectral analysis which revealed different chemical shifts for the silyl methyl and phenyl signals in these two species (compare Figure 22c with Figure 22d). The ^{13}C NMR spectrum of $(PhMe_2Si)_2CuLi$ (**27**) consists of four resonances in the phenyl region (δ 162.0, *ipso*; 134.7, *ortho*; 126.3, *meta*; 124.9, *para*) one due to DMS (17.8 ppm) and a methyl signal at 6.04 ppm (Figure 22c) whereas $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) exhibited

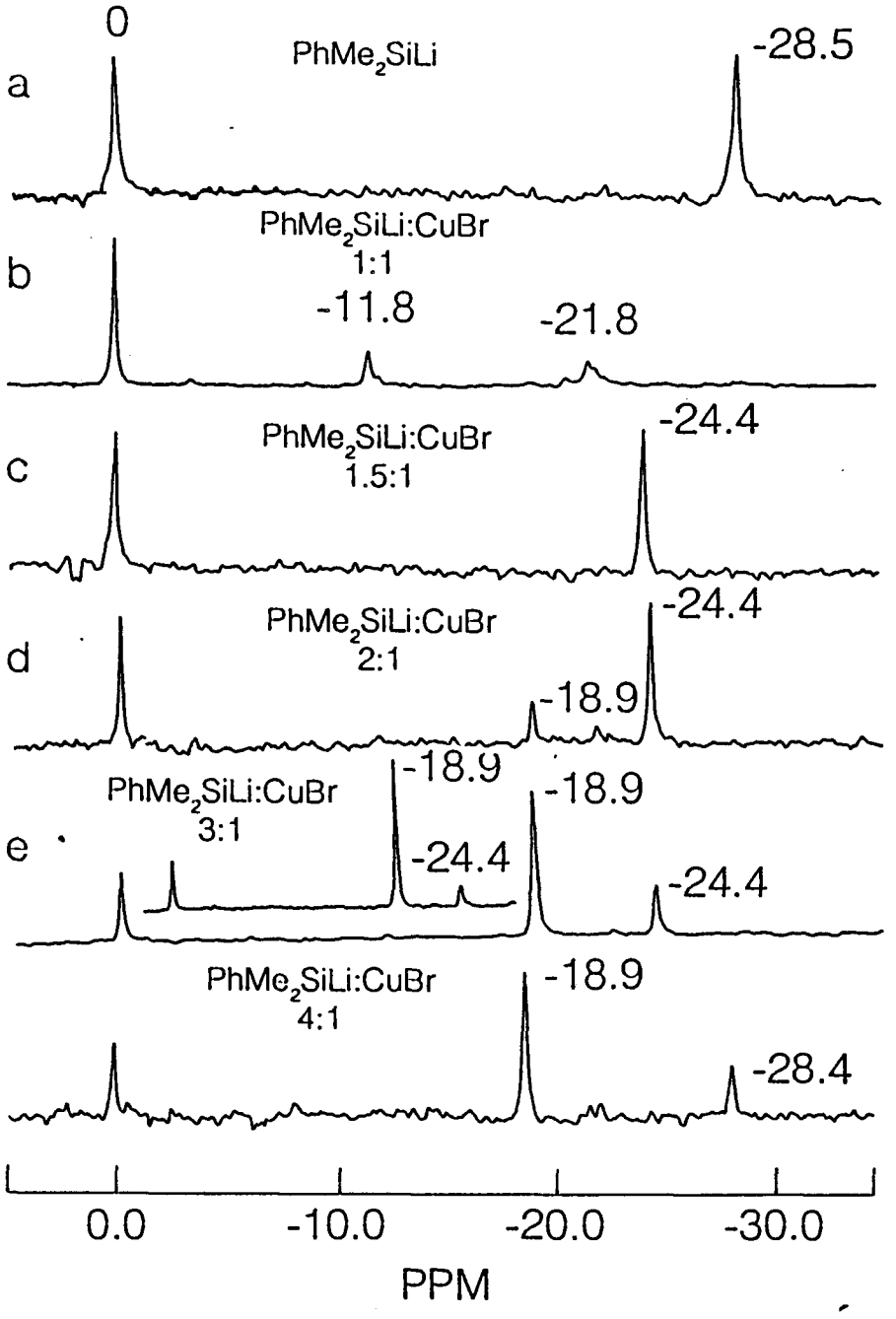


Figure 21. ^{29}Si NMR spectra for PhMe2SiLi and CuBr in various ratios in THF at -50°C (a) PhMe2SiLi (b) PhMe2SiLi:CuBr, 1:1 (c) PhMe2SiLi:CuBr, 1.5:1 (d) PhMe2SiLi:CuBr, 2:1 (e) PhMe2SiLi:CuBr, 3:1 (inset 21e) PhMe2SiLi:CuCN, 3:1 (f) PhMe2SiLi:CuBr, 4:1.

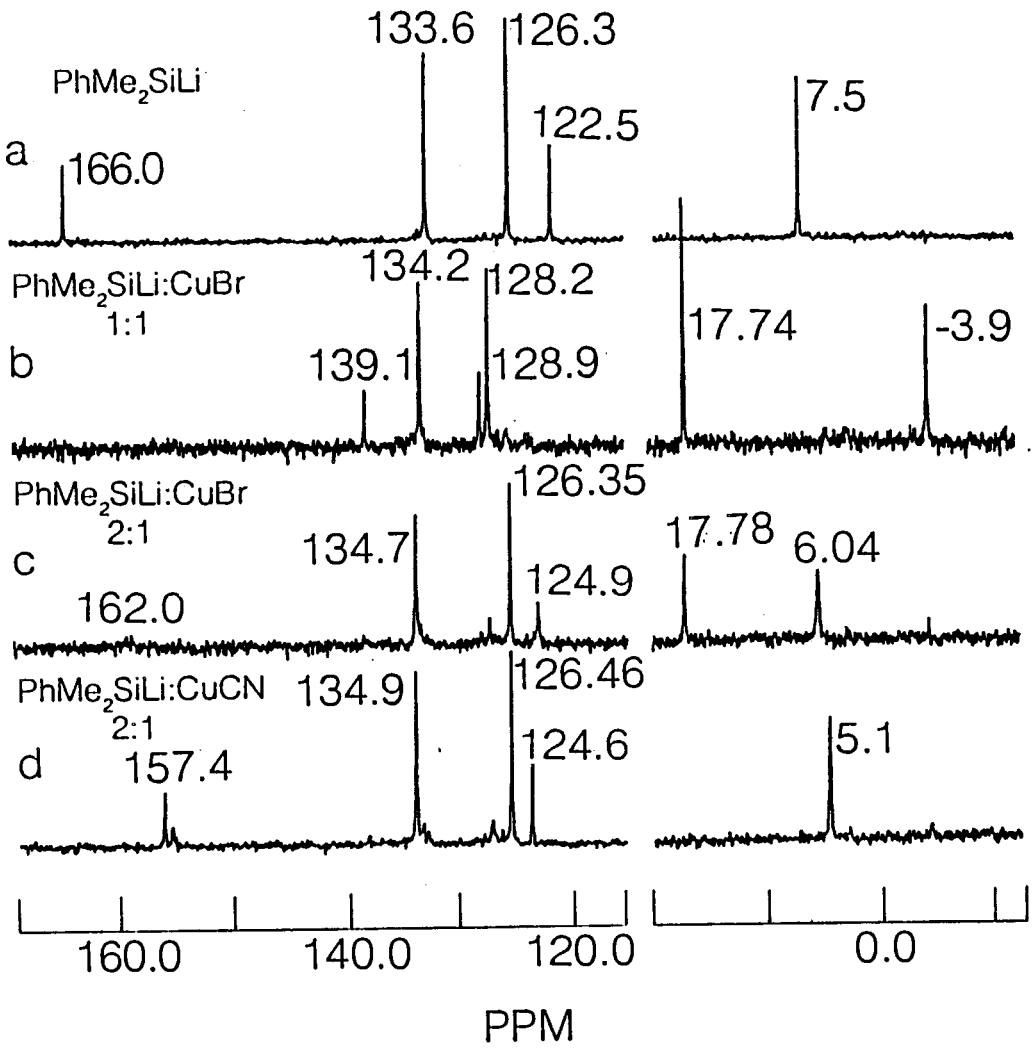


Figure 22. ^{13}C NMR spectra in THF at -20°C (a) $PhMe_2SiLi$ (b) $PhMe_2SiLi$:CuBr, 1:1 (c) $PhMe_2SiLi$:CuBr, 2:1 (d) $PhMe_2SiLi$:CuCN, 2:1.

resonances at 157.4, *ipso*; 134.9, *ortho*; 126.5, *meta*; 124.6, *para*; a nitrile carbon at 156.7 and a methyl signal at 5.1 ppm (Figure 22d). As previously reported, evidence for the formulation of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) came from the infrared analysis of this solution which shows a bound nitrile (ν_{CN} = 2123 cm^{-1}) but no free LiCN.[34] The coincidence of the ^{29}Si chemical shifts of **28** and **27** is attributed to the accidental chemical degeneracy of the resonances and suggests a similar electronic environment around silicon in **28** and **27**.

Solutions containing $PhMe_2SiLi$ (**25**) and $CuBr{\cdot}Me_2S$ in a 3:1 ratio exhibited a significant ^{29}Si NMR signal at -18.9 ppm as well as a small signal assigned to $(PhMe_2Si)_2CuLi$ (**27**, -24.4 ppm, Figure 21e). An attractive formulation for the species exhibiting a ^{29}Si signal at -18.9 ppm is $(PhMe_2Si)_3CuLi_2$ (**29**). The chemical shift of this species is identical to that previously observed for $(PhMe_2Si)_3CuLi_2$ (prepared from three equivalents of $PhMe_2SiLi$ and CuCN, Figure 21e inset). Secondly, the ^{13}C NMR spectra at -70°C of the two solutions exhibited identical chemical shifts for silyl bound methyl and phenyl signals (δ 164.3, *ipso*; 134.5, *ortho*; 126.0, *meta*; 122.8, *para* and a methyl signal at 8.1 ppm).

That the conversions of "$PhMe_2SiCu$" (**38**) to $(PhMe_2Si)_2CuLi$ (**27**) and **27** to $(PhMe_2Si)_3CuLi_2$ (**29**) are reversible was shown by addition of 0.5 equivalent of $CuBr{\cdot}Me_2S$ to **29** whose ^{29}Si NMR spectrum is shown in Figure 21e. This resulted in the regeneration of $(PhMe_2Si)_2CuLi$ (**27**, Figure 23a). Further introduction of one equivalent $CuBr{\cdot}Me_2S$ to **27** resulted in the regeneration of "$PhMe_2SiCu$" (**38**, Figure 23b).

While no free $PhMe_2SiLi$ was detectable in solutions containing **25** and $CuBr{\cdot}Me_2S$ in a 3:1 ratio, a substantial amount of $PhMe_2SiLi$ appeared in the spectrum of solutions where this ratio was 4:1 (Figure 21f). This interpretation was reinforced by a positive Gilman test[42] for $PhMe_2SiLi$ (**25**) in THF and a negative test for all solutions

of **25** containing CuBr·Me2S including those where these reagents were present in a 3:1 ratio. A slight green coloration was observed for PhMe2SiLi:CuBr·Me2S in 4:1 molar ratio indicating small quantities of free PhMe2SiLi (**25**).

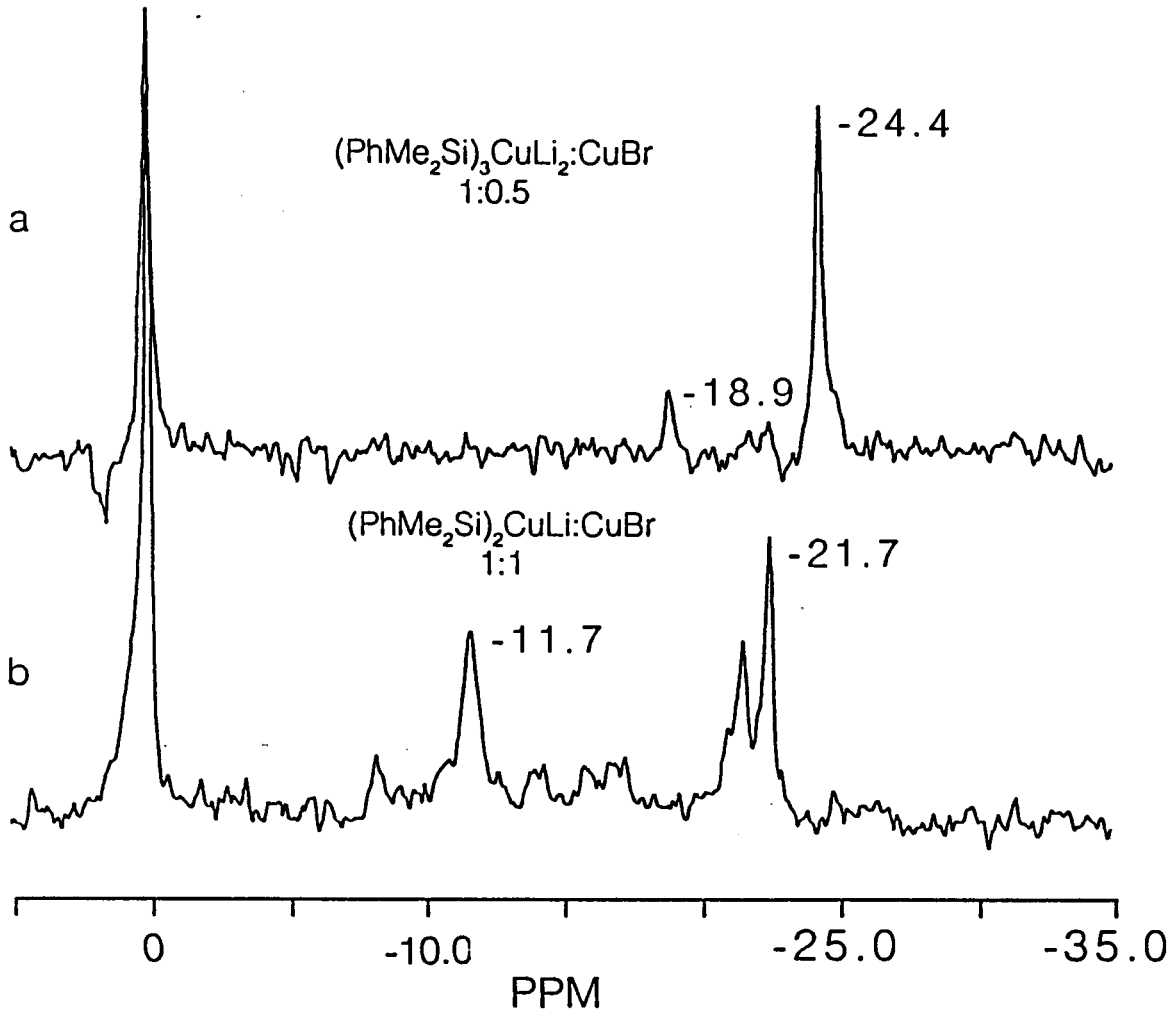
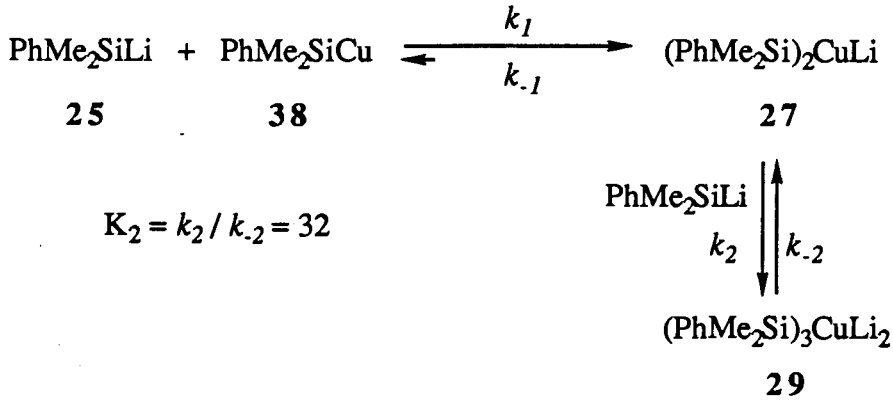


Figure 23. ^{29}Si NMR spectra in THF at -50°C (a) (PhMe2Si)3CuLi2 + CuBr, 1:0.5 (b) (PhMe2Si)2CuLi + CuBr, 1:1.

The relative intensities of the ^{29}Si signals attributed to contributing species in solutions whose spectra are shown in Figure 21 allow estimation of the positions of the equilibria shown in Scheme 13.



Scheme 13

The equilibrium between PhMe2SiLi (**25**), "PhMe2SiCu" (**38**) and (PhMe2Si)2CuLi (**27**) lies significantly on the side of **27** (i.e., $k_1 >> k_{-1}$). In solutions comprised of PhMe2SiLi:CuBr·Me2S, (3:1) (PhMe2Si)3CuLi2 (**29**) predominates over (PhMe2Si)2CuLi by ~4:1. This allows calculation of the equilibrium constant (K_2) for the process. The value of K_2 and the error reported were calculated as outlined earlier by averaging three determinations.[36]

The ease with which we were able to differentiate between the higher order silylcuprates derived from CuCN and the lower order reagents prepared from CuBr·Me2S by ^{13}C NMR spectroscopy encouraged us to undertake a study of the complexation of LiX with these reagents. Specifically, solutions containing (PhMe2Si)2CuLi (**27**) were prepared from CuBr·Me2S or CuI in DMS or THF. The ^{13}C NMR spectra were recorded in the region between 0 and 10.0 ppm with the goal of observing the resonances due to the methyl carbons.

At -85°C in DMS, the ^{13}C NMR spectrum of (PhMe2Si)2CuLi (**27**), prepared from CuBr·Me2S and two equivalents of PhMe2SiLi (**25**, prepared from (PhMe2Si)2 and Li metal)[33] consisted of a singlet at 4.2 ppm (in the 0 to 10.0 ppm region, Figure

24a). This was attributed to halide-free $(PhMe_2Si)_2CuLi$ (**27**) due to the precipitation of LiBr from DMS. Substitution of CuI for $CuBr{\cdot}Me_2S$ gave a solution that exhibited two signals in the ^{13}C NMR spectrum: one major (δ 4.9) and a minor one at 4.2 ppm (Figure 24b). These were assigned to the methyl carbons of LiI-containing silylcuprate $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**), and LiI-free silylcuprate $(PhMe_2Si)_2CuLi$ (**27**), respectively. The assignment of the signal at 4.2 ppm to LiI-free silylcuprate **27** was facilitated by the observation that the resonance of the methyl in the ^{13}C NMR spectrum of this reagent was precisely at the same position as the methyl resonance of LiBr-free silylcuprate $(PhMe_2Si)_2CuLi$.

The ^{7}Li NMR spectra of $(PhMe_2Si)_2CuLi$ prepared from CuI and CuBr were in harmony with the ^{13}C NMR results. At -70°C in DMS, the ^{7}Li spectrum of the reagent prepared from $PhMe_2SiLi$ and $CuBr{\cdot}Me_2S$ (without LiBr) showed a single resonance at 0.43 ppm, which is assigned to the LiBr-free silylcuprate $(PhMe_2Si)_2CuLi$ (**27**). Under the same conditions the ^{7}Li NMR spectrum of $(PhMe_2Si)_2CuLi$ derived from CuI consisted of two signals; the major one at δ 0.77 was assigned to $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**) while the minor one (δ 0.48) was attributed to the halide-free complex, **27**.

The ^{13}C NMR spectrum of $(PhMe_2Si)_3CuLi_2$ (**29**) prepared by the addition of LiCl-free **25** to LiBr-free $(PhMe_2Si)_2CuLi$ (**27**) exhibited signals corresponding to $(PhMe_2Si)_2CuLi$ (**27**, δ 4.2) and higher order species **29** (δ 5.4, Figure 24c). Similarly, $(PhMe_2Si)_3CuLi_2$ (**29**) prepared from CuI exhibited two major methyl resonances at 4.9 ppm and 5.4 ppm which were attributed to $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**) and $(PhMe_2Si)_3CuLi_2$ (**29**), respectively, along with a minor peak at δ 4.2 ppm which was assigned earlier to halide-free $(PhMe_2Si)_2CuLi$ (**27**, Figure 24d).

In agreement with the above results, the ^{7}Li NMR spectrum at -70°C of $CuBr{\cdot}Me_2S$ derived $(PhMe_2Si)_3CuLi_2$ in DMS exhibited signals at 0.45 and 0.21 ppm attributable to **27** and **29** respectively, while $(PhMe_2Si)_3CuLi_2$ prepared from CuI

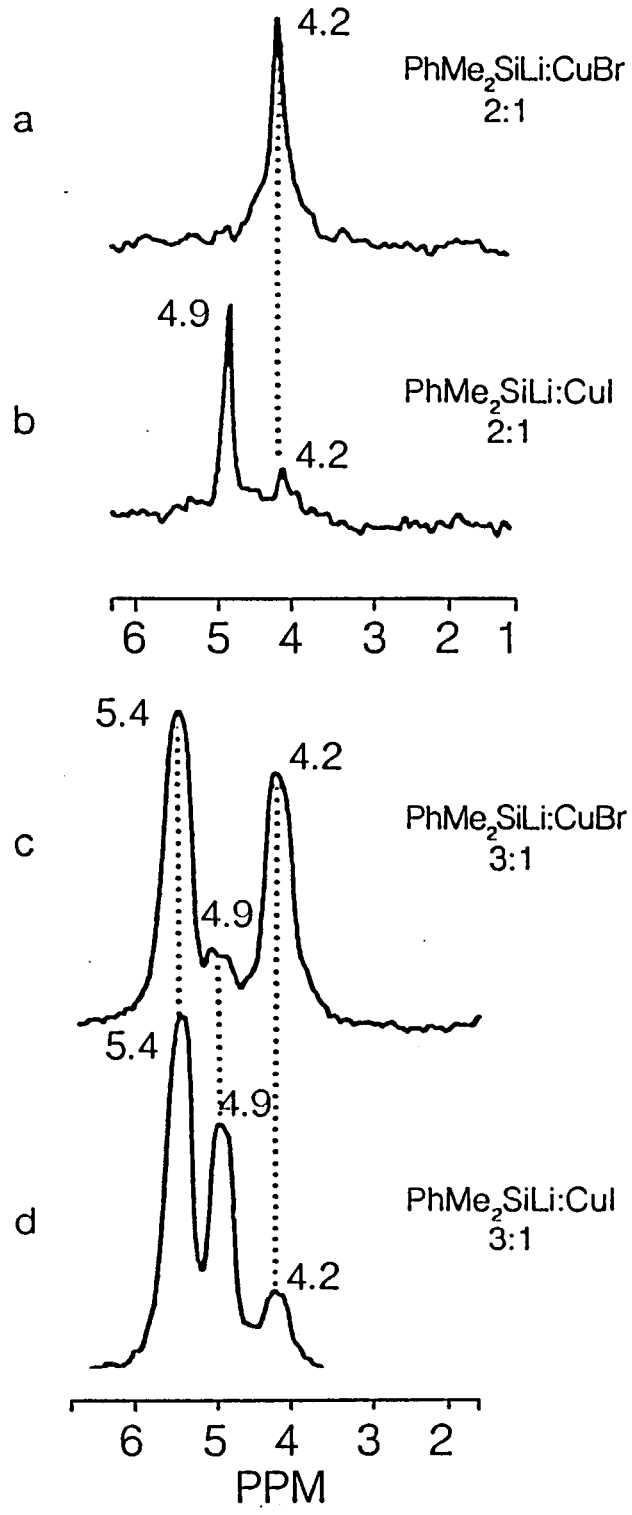
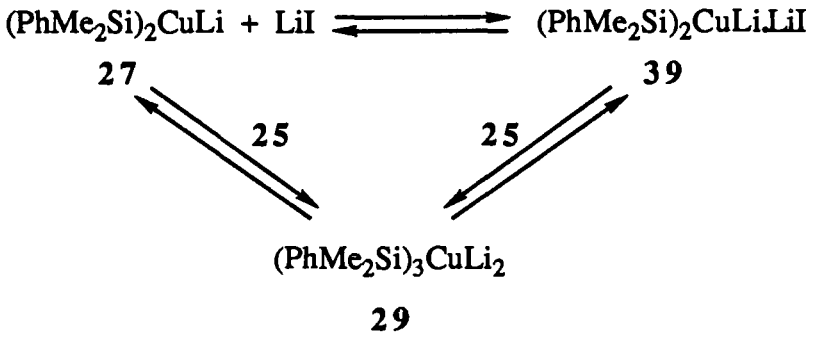


Figure 24. ^{13}C NMR spectra in DMS at -85°C (a) PhMe2SiLi:CuBr, 2:1 (b) PhMe2SiLi:CuI, 2:1 (c) PhMe2SiLi:CuBr, 3:1 (d) PhMe2SiLi:CuI, 3:1.

consisted of a broad multiplet spanning the region assigned to LiI-containing lower order species (0.76 ppm) and a halide-free $(PhMe_2Si)_3CuLi_2$ (**29**) species (~0.40 ppm). The presence of broad signals in these spectra indicates that the rate of exchange between the various lithium containing species is near the NMR time scale, an observation in agreement with literature precedents.[7,9,12]

As in the case of preparations of $(PhMe_2Si)_3CuLi_2$ from $CuBr{\cdot}Me_2S$ in THF, no free $PhMe_2SiLi$ was detectable in the solutions of this reagent prepared from CuI in DMS until the ratio of silyl anion to CuI exceeds 3:1.

In DMS, $(PhMe_2Si)_2CuLi{\cdot}LiX$ (**39**) and $(PhMe_2Si)_2CuLi$ (**27**) are in dynamic equilibria with $(PhMe_2Si)_3CuLi_2$ (**29**) as represented in Scheme 14. The reversibility of interconversion between $(PhMe_2Si)_2CuLi$ (**27**) and $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**) was established by the observation that the silyl methyl signals in these species coalesced to a single peak as the temperature is increased from -85°C to 0°C, and upon cooling to -85°C, the same-two signal pattern reappears.



Scheme 14

That LiBr is also associated with trialkylsilylcuprates in THF was evident from ^{13}C NMR of $(PhMe_2Si)_2CuLi$ (**27**, prepared from two equivalents of LiCl-free $PhMe_2SiLi$[33] and $CuBr{\cdot}Me_2S$ at -85°C). The ^{13}C NMR spectrum

(Figure 25a) showed two methyl signals, the major one at 4.9 ppm and a minor one at 4.2 ppm which are identical to the methyl resonances assigned to $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**) and $(PhMe_2Si)_2CuLi$ (**27**) respectively in DMS (Figure 25b).

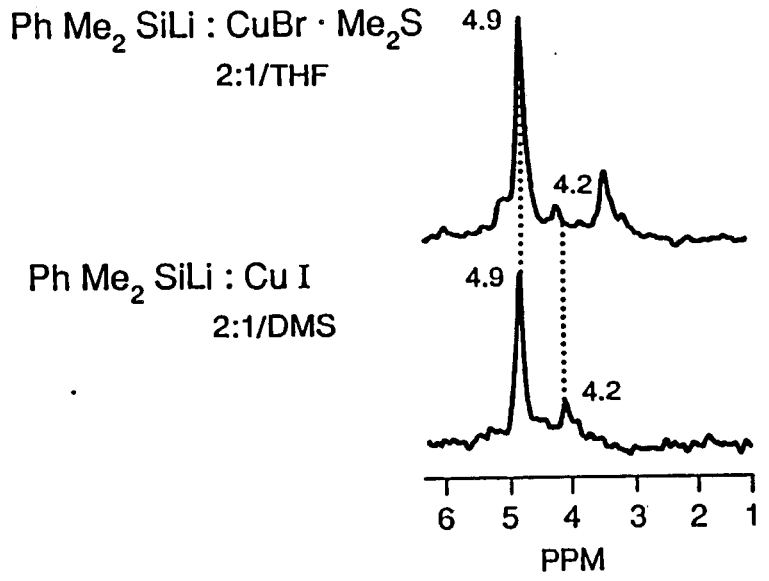
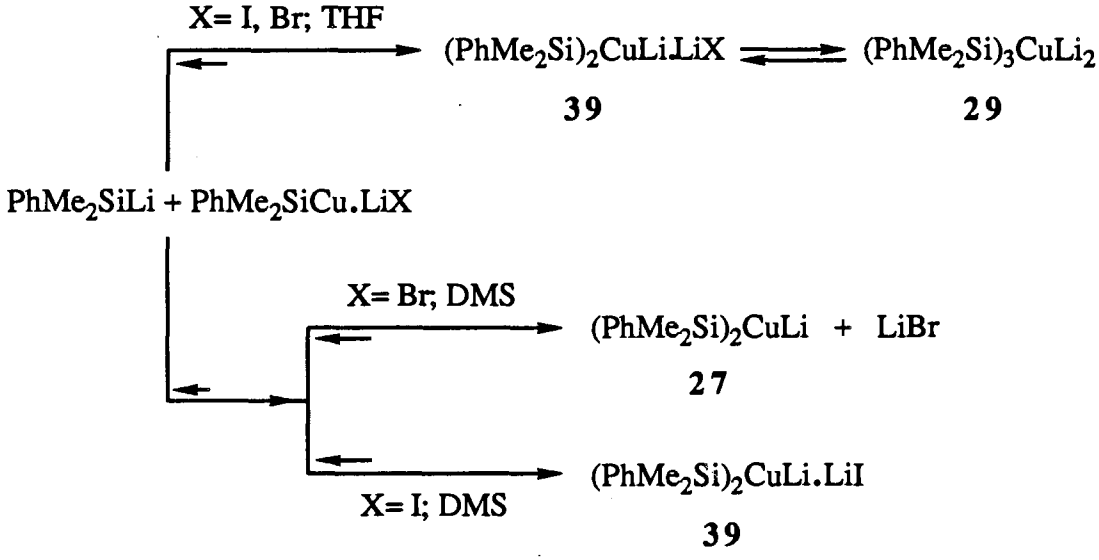


Figure 25. ^{13}C NMR spectra of (a) $PhMe_2SiLi$:CuBr, 2:1 in THF (b) $PhMe_2SiLi$:CuI, 2:1 in DMS; the spectra were run at -85°C.

It appears that the lower order silylcuprate $(PhMe_2Si)_2CuLi$ (**27**) is a more complex species than its straightforward preparation indicates. In DMS, when it is prepared with CuI, this reagent consists mostly of the LiI-associated copper species, $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**), but when it is derived from $CuBr{\cdot}Me_2S$, it is free of LiBr. In THF, when CuI or $CuBr{\cdot}Me_2S$ is used in the preparation, this reagent exists

primarily as LiX-associated copper species and should be represented as $(PhMe_2Si)_2CuLi{\cdot}LiX$ (Scheme 15).



Scheme 15

One would expect the degree of association of LiX (X = Br or I) with lower order silylcuprates to vary with the nature of the silyl substitution. We suspect the trends discovered in this investigation namely that LiX association is high in solvents such as THF in which LiX salts are soluble to be of general applicability.

It has recently been pointed out by Bertz[12] that THF and DMS are complimentary solvents with regard to copper halide based organocuprates. These reactions commence with copper halides and alkyllithiums and produce lithium halide which may be associated with the organocuprate formed. LiI (the solubility of LiI in DMS is ~10 mg/mL at 25°C) and LiBr (the solubility of LiBr in DMS is ~0.3 mg/mL at 25°C) are relatively insoluble in DMS but both LiI and LiBr are soluble in THF

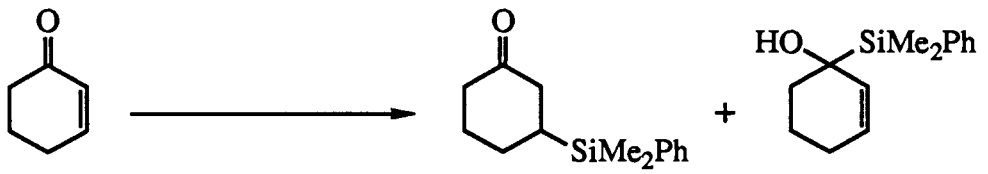
(solubility of LiI and LiBr in THF is >130 mg/mL at 25°C).[12] Therefore, in the latter solvent LiI and LiBr association with cuprates is at least feasible.

The proposed formation of $(PhMe_2Si)_2CuLi{\cdot}LiX$ in THF provides an explanation for the observation that **27** exhibits a ^{29}Si NMR resonance with a chemical shift (Figure 21d) similar to that assigned to $(PhMe_2Si)_2Cu(CN)Li_2$, **28** (Figure 15d). Thus, if the former existed primarily complexed with LiBr the only structural difference between **28** and **27** is the substitution of a CN by a Br.

Chemical tests

As observed earlier for silylcuprates derived from CuCN, it was found that solutions of both **27** and **29** deliver a $PhMe_2Si$ group exclusively *via* 1,4-addition to cyclohex-2-en-1-one (**32**, Scheme 16). Solutions composed of **29**, **25** and CuX in a

Scheme 16. Addition of "$PhMe_2SiCu$" reagents to cyclohex-2-en-1-one, **32**.



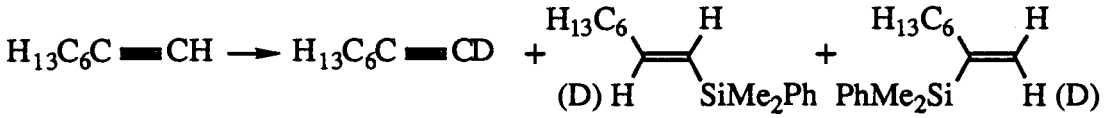
32 **33** **34**

25	$PhMe_2SiLi$	-	62%
27	$(PhMe_2Si)_2CuLi$	66%	
29	$(PhMe_2Si)_3CuLi_2$	70%	
	$(PhMe_2Si)_3CuLi_2$ + **25**	70%	

1:1:0.1 molar ratio also added to **32** in a 1,4-manner.[32,45] Similar observations have been made before in the catalytic cuprate chemistry.

Next the addition of silylcuprates **27**, **29** and **39** to 1-octyne (**35a**) was studied. In agreement with ^{13}C NMR results, it was found that $(PhMe_2Si)_2CuLi$ (**27**, prepared from CuBr) in DMS added to **35a** to yield a mixture of **36** and **37** in a 1:1 ratio, whereas addition reactions of $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**) and $(PhMe_2Si)_3CuLi_2$ (**29**)

Scheme 17. Silylcupration of 1-alkynes.



35a **35b** **36** **37**

		% Composition			
		35b	**36**	**37**	%yield
25	$PhMe_2SiLi$	100	-	-	72
27	$(PhMe_2Si)_2CuLi$	-	50	50	69
39	$(PhMe_2Si)_2CuLi.LiI$	-	>98	<2	86
29	$(PhMe_2Si)_3CuLi_2$	-	>98	<2	90

gave exclusively **36** in ~90% isolated yields (Scheme 17). As previously reported, under similar conditions $PhMe_2SiLi$ (**25**) abstracts the acetylenic hydrogen of **35a** to give **35b** as judged by GC-MS (70% incorporation of ^2H in 1-octyne using ^2H_2O); no addition products were observed (capillary g.c. analysis).

Conclusion

Comparison of the present silylcuprate system with that of the methylcuprate[7,8] system reveals several similarities. When the ratio of RLi (R = $PhMe_2Si$ or Me) to CuX (X = I or Br) in THF is 2:1, a new species, $R_2CuLi{\cdot}LiX$, is formed in both cases. In the case of LO Me_2CuLi, association of alkyl residues with copper beyond this stoichiometry does not occur and further addition of MeLi beyond this point gives solutions containing free MeLi (Scheme 1).[7]

In the case of $(PhMe_2Si)_2CuLi{\cdot}LiX$, addition of further silyllithium gives solutions which contain negligible amounts of free silyl anions and whose ^{29}Si NMR spectra support the association of three silyl residues with the copper. In THF the novel species $(PhMe_2Si)_3CuLi_2$ is formed regardless of which copper(I) salt is employed.

In DMS, $(PhMe_2Si)_2CuLi$ (derived from CuI) exists as an equilibrium mixture of halide-containing $(PhMe_2Si)_2CuLi{\cdot}LiI$ (**39**) and halide-free $(PhMe_2Si)_2CuLi$ (**27**) species. In contrast, lower order silylcuprates derived from CuBr are primarily devoid of LiBr because of the insolubility of this salt in this solvent. This behaviour is analogous to that of phenylcuprates.[12]

MIXED TRIALKYLSILYL AND HOMO- AND MIXED TRIALKYL-STANNYLCUPRATES DERIVED FROM CUPROUS CYANIDE

Silyl- and stannylcopper reagents are invaluable reagents for the construction of carbon-silicon and carbon-tin bonds respectively. In general, reactions of these reagents occur under relatively mild conditions and tolerate polar functional groups. Indeed, one has many literature examples from which to decide upon reaction parameters.[27,28] Most commonly sought are lithium-based cuprates, $(R_3M)_nCuLi_{n-1}\cdot LiX$ (M = Si or Sn, n = 1 or 2, X = Br or CN; **40**) prepared stoichiometerically from cuprous salts and 1 to 2 equivalents of R_3MLi.[27,28] While homotrialkylsilyl- and stannylcuprates serve admirably as donors of R_3M anions, problems attend the use of these reagents in that not all the metal anions bound to copper are transferred in these processes. Consequently, R_3MH, $R_3M\text{-}MR_3$ and R_3MOH are produced in workup which complicate product isolation.[27,28]

The possibility arises that mixed systems $R_3Si(R')CuLi\cdot LiX$ (**41**) or $R_3Sn(R')CuLi\cdot LiX$ (**42**) would present opportunities for preferential R_3M anion transfer and thereby increase ligand efficiency of these reagents. The ability of methyl to serve as an efficient non-transferrable ligand in highly mixed organoalkylcuprates[17] led us to determine the composition of mixed silyl- and stannylcuprates derived from CuCN with methyl serving as the second or third anionic ligand.

It was anticipated that information gained from such studies would not only shed light into the nature of these cuprates but also provide insights into the selectivity of ligand transfer. It was envisioned that these studies would help in understanding the mechanism of catalytic addition reactions of these cuprates and define alternate strategies for conducting such reactions.

Silicon-29 and Carbon-13 NMR Studies on Mixed TrialkylsilylCuprates

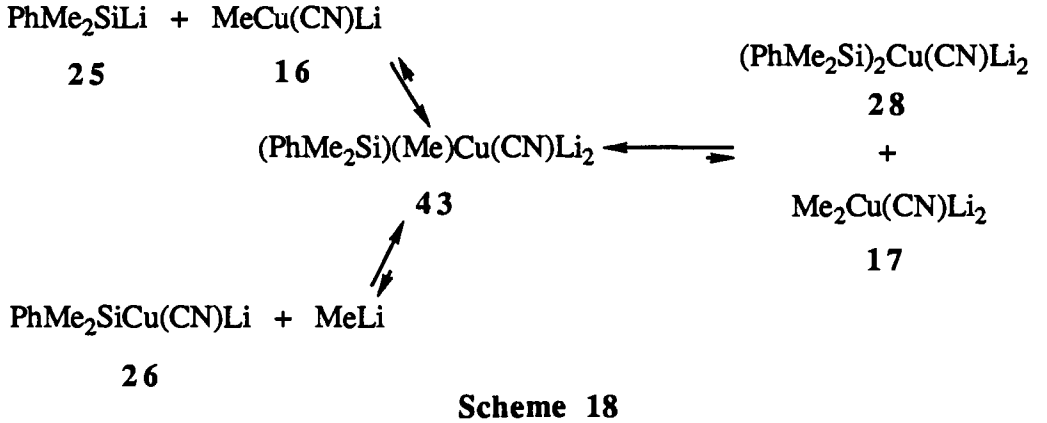
Low-temperature ^{29}Si and ^{13}C NMR spectroscopy was employed to probe the composition of solutions generated by mixing dimethylphenylsilyllithium (**25**) with equimolar solutions of MeLi and CuCN. Species likely to be formed in these experiments are higher order mixed silylcuprates $PhMe_2Si(Me)Cu(CN)Li_2$ (**43**), $(PhMe_2Si)_2(Me)CuLi_2$ (**44**) and $PhMe_2Si(Me)_2CuLi_2$ (**45**).

Results and Discussion

Dimethylphenylsilyllithium (**25**) in THF was prepared by reaction of $PhMe_2SiCl$ (**30**) and lithium metal and therefore contained LiCl.[33] Solutions of this reagent at -5°C gave a ^{29}Si NMR signal at –28.5 ppm (Figure 26a). Solutions of mixed silylcuprates (**43**) were generated by addition of THF solutions of **25** to equimolar THF solutions of MeLi and CuCN at -70°C. The combination of one equivalent of **25** and $MeCu(CN)Li$[17] (**16**) yielded a solution that afforded a single ^{29}Si signal at -20.6 ppm (Figure 26d) attributable to $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**) implying that any equilibrium of the type shown in Scheme 18 must lie heavily toward **43** (i.e., $k_1 >> k_{-1}$). To probe the generality of ligand mobility, solutions containing copper to methyl anion to silyl anion ratio of 1:1:1 were generated by adding MeLi to preformed $PhMe_2SiCu(CN)Li$ (**26**, Figure 26b). These solutions gave the same spectral results as obtained earlier from the combination of $MeCu(CN)Li$ and $PhMe_2SiLi$.

To establish that **43** could be produced by mutual alkyl and silyl anion exchange. equivalent amounts of $Me_2Cu(CN)Li_2$ (**17**) and $(PhMe_2Si)_2Cu(CN)Li_2$, (**28**, Figure 26c) were prepared separately and then combined *via* a cannula at -70°C. The ^{29}Si NMR spectrum, taken at -70°C, of the reagent formed in this experiment (Figure 26e) was

identical to the one obtained previously (Figure 26d) from the mixture of $PhMe_2SiLi$ (**25**) and MeCu(CN)Li (**16**). As anticipated, the spectra from all three reagent combinations, i.e., MeCu(CN)Li-$PhMe_2SiLi$, $PhMe_2SiCu(CN)Li$-MeLi and $Me_2Cu(CN)Li_2$ - $(PhMe_2Si)_2Cu(CN)Li_2$ indicated the same species (**43**) had been formed (Scheme 18).



Scheme 18

The ^{13}C NMR spectrum (Figure 27d) of $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**) at -70°C, prepared from a THF solution of MeCu(CN)Li (**16**) and $PhMe_2SiLi$ (Figure 27b),[33] consisted of seven lines: four in the phenyl region (δ 158.5, *ipso*; 134.9, *ortho*; 126.7, *meta*; 124.8, *para*), one nitrile (δ 159.4) and two different methyl groups. The upfield signals were assigned to a methyl bound to silicon (6.0 ppm) and a methyl bound to copper (-5.0 ppm), respectively, in $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**). These results indicated the presence of a single species, **43**, and support the interpretation of the ^{29}Si NMR spectra (Figure 26d and 26e) given above.

The ^{13}C NMR spectra of solutions resulting from the admixture of $Me_2Cu(CN)Li_2$ (**17**) and $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**, Figure 27e) did not show signals characteristic of the individual reagents (Figure 27a and Figure 27c respectively). Rather

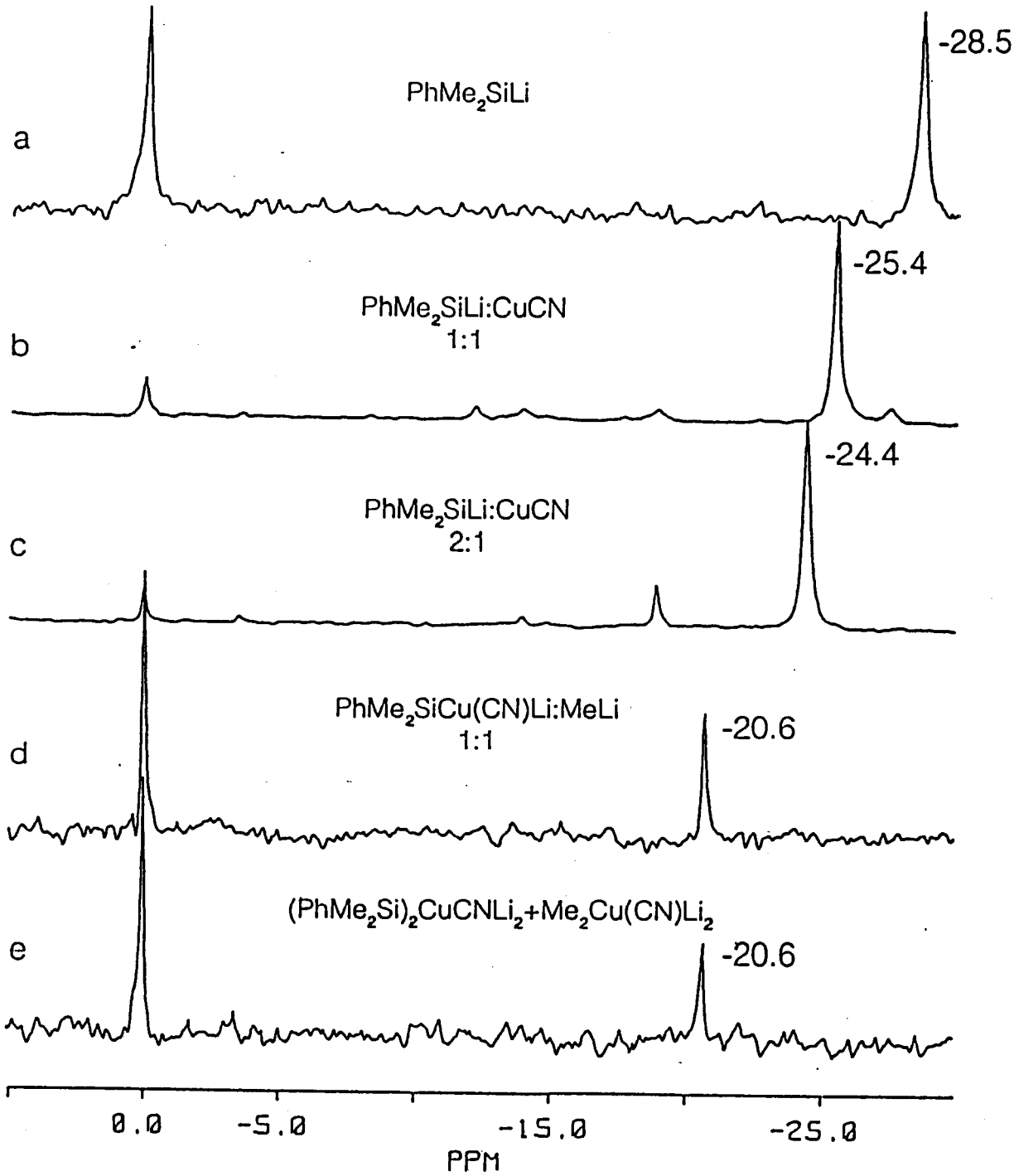


Figure 26. ^{29}Si NMR spectra of (a) $PhMe_2SiLi$ (b) $PhMe_2SiCu(CN)Li$ (c) $(PhMe_2Si)_2Cu(CN)Li_2$ (d) $PhMe_2SiCu(CN)Li$ + MeLi (e) $(PhMe_2Si)_2Cu(CN)Li_2$ + $Me_2Cu(CN)Li_2$; spectra were run at -50°C.

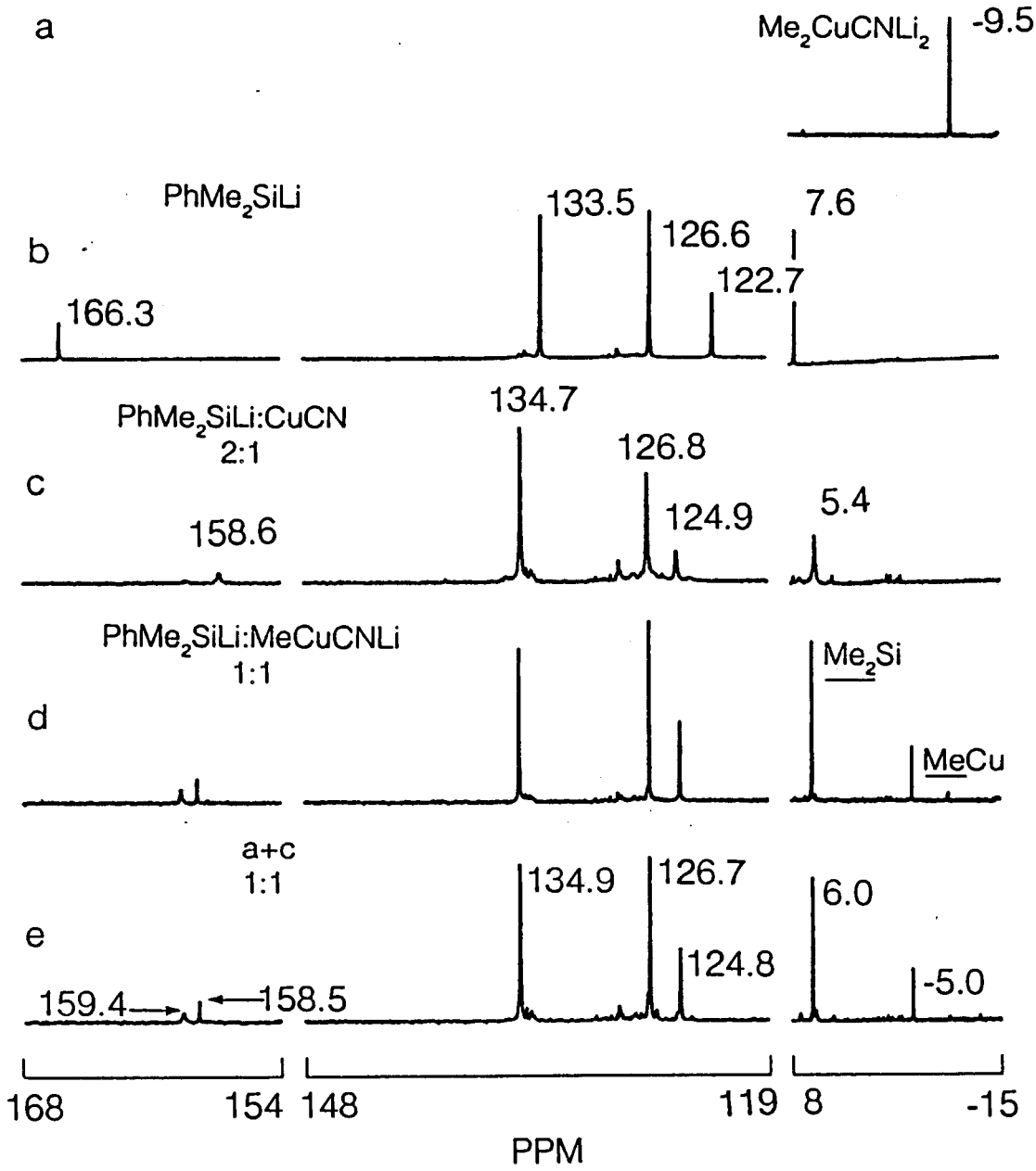
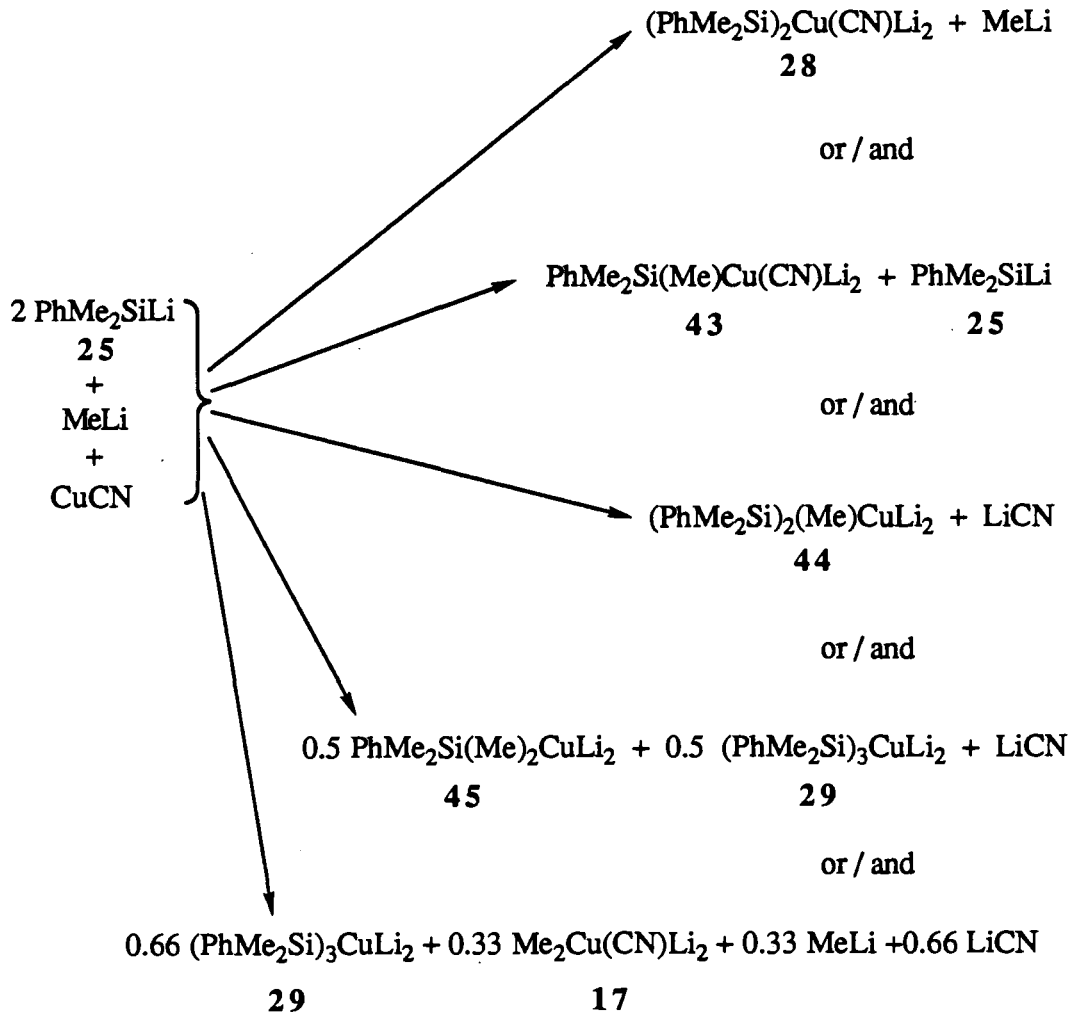


Figure 27. ^{13}C NMR spectra of (a) $Me_2Cu(CN)Li_2$ (b) $PhMe_2SiLi$ (c) $(PhMe_2Si)_2Cu(CN)Li_2$ (d) $PhMe_2SiLi$ + $MeCu(CN)Li$ (e) $(PhMe_2Si)_2Cu(CN)Li_2$ + $Me_2Cu(CN)Li_2$; spectra were run at -70°C.

these solutions gave the same ^{13}C NMR signals as obtained previously from the combination of $PhMe_2SiLi$ (**25**) and $MeCu(CN)Li$ (**16**, Figure 27d).

Thus, mixed-alkyl silylcuprates as well as silylcuprates and alkylcuprates, irrespective of the mode of preparation, revert to the same species, **43**, when the ratio of silyl anion to alkyl anion to cuprous ion is 1:1:1 (Scheme 18).

The ^{13}C NMR spectra of solutions containing two equivalents of silyl anion to



Scheme 19

one equivalent each of methyl anion and cuprous ion was next examined. Solutions generated by addition of two equivalents of $PhMe_2SiLi$ (**25**) to solutions containing one equivalent each of MeLi and CuCN would be expected to lead to the formation of an equivalent each of $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**) and $PhMe_2SiLi$ (**25**), or an equivalent each of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) and MeLi, or $(PhMe_2Si)_2(Me)CuLi_2$ (**44**) and LiCN, or an equivalent each of $(PhMe_2Si)(Me)_2CuLi_2$ (**45**), $(PhMe_2Si)_3CuLi_2$ (**29**) and LiCN, depending on whether this mixed system exhibits behaviour similar to alkyl[17] or homosilylcuprates (Scheme 19).

The ^{13}C NMR spectrum for the 2:1 combination of $PhMe_2SiLi$ (**25**) and MeCu(CN)Li (**16**) at -85°C is shown in Figure 28b. Identical spectra were obtained when equivalent molar amounts of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) and MeLi were mixed at -85°C. These spectra exhibited three resonances of unequal intensity in the methyl region (δ -5.3, -3.7 and 6.0) as well as several signals in the phenyl region (124.7, 126.6, 127.7, 128.6, 134.0, 134.5, 134.9) indicating the presence of more than one species. Signals at 6.0 ppm and -5.3 ppm are very close to those previously assigned to **43** (Figure 28a), but the absence of signals corresponding to $PhMe_2SiLi$ (**25**) rules out the presence of **43**. Futhermore, the absence of signals corresponding to MeLi (-14 ppm) eliminates $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) as a major species and supports our earlier observation that the silylcuprates exhibit significant tendencies to exist as higher order cuprates, i.e., $(R_3Si)_3CuLi_2$.

Warming these solutions to -70°C led to more complex spectra (Figure 28a) that exhibited five peaks in the methyl region (8.1 ppm, 5.9 ppm, 5.5 ppm, -3.8 ppm and -5.3 ppm).

The composition of the species in solutions comprised of $PhMe_2SiLi$ (**25**), MeLi and CuCN (2:1:1) was deduced from the absence of $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**), $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**), $Me_2Cu(CN)Li_2$ (**17**) and MeLi. The expected species is

$(PhMe_2Si)_2(Me)CuLi_2$ (**44**). Thus, the signal at -3.7 ppm was assigned to methyl bound to copper in $(PhMe_2Si)_2(\underline{Me})CuLi_2$ (**44**) while the signal at 5.9 ppm was assigned to the silyl bound methyls in this species. The signals at 8.1 ppm and 164.3 ppm correspond to the methyl and *ipso* carbon, respectively, in $(PhMe_2Si)_3CuLi_2$ (**29**). Observation of $(PhMe_2Si)_3CuLi_2$ (**29**) requires species such as

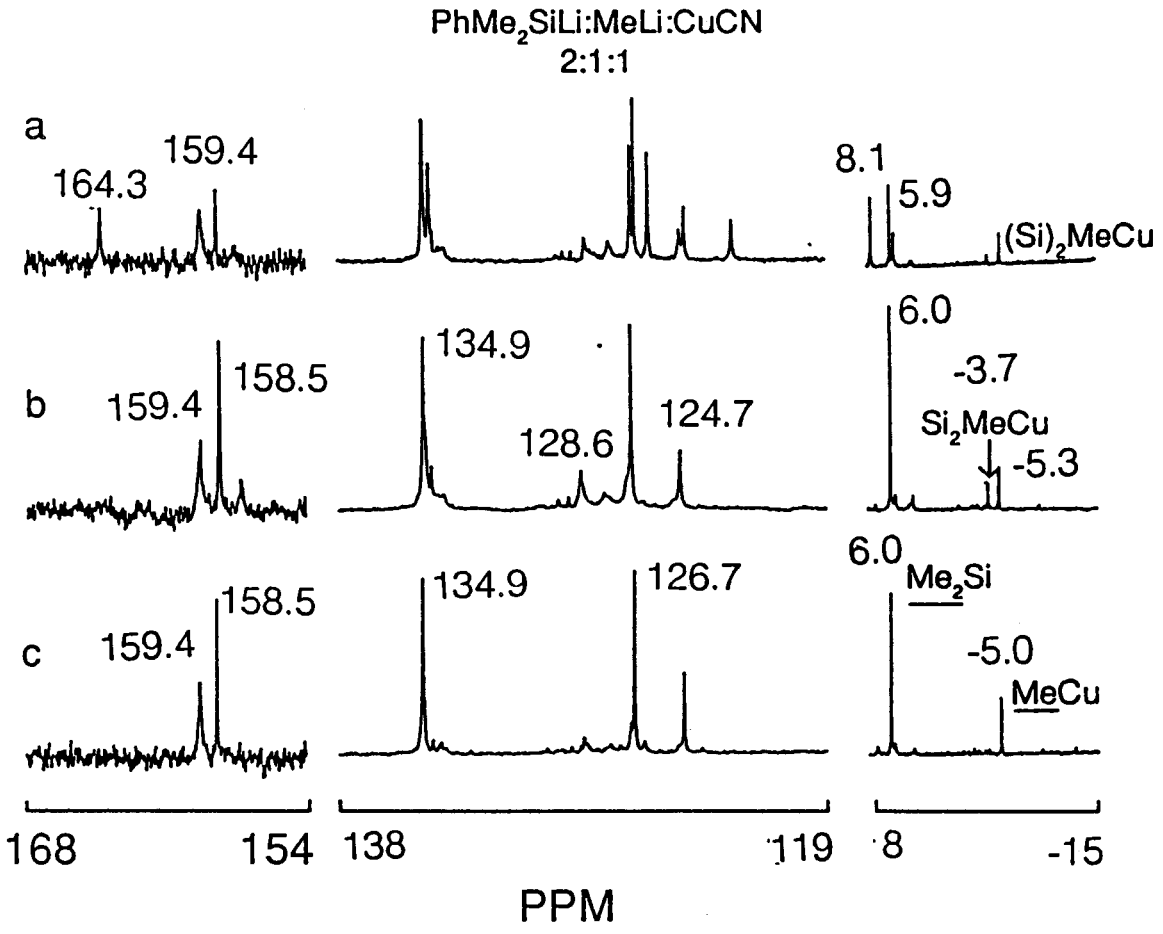
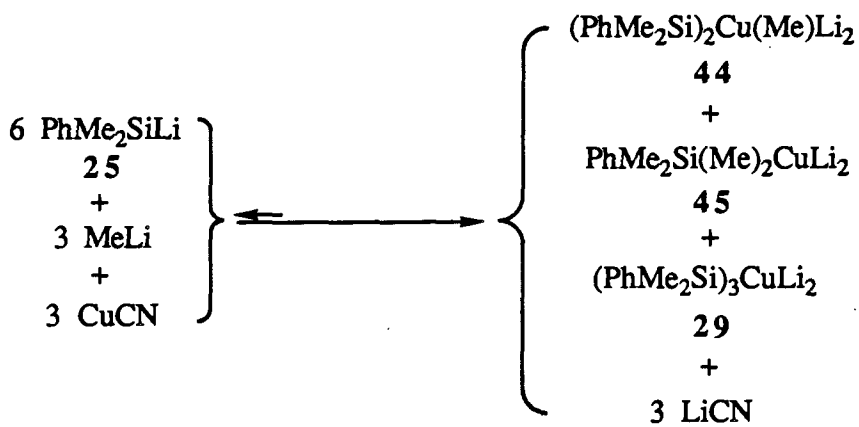


Figure 28. ^{13}C NMR spectra of (a) 2 $PhMe_2SiLi$ + MeLi + CuCN at -70°C (b) 2 $PhMe_2SiLi$ + MeLi + CuCN at -85°C (c) $PhMe_2Si(Me)Cu(CN)Li_2$ at -70°C.

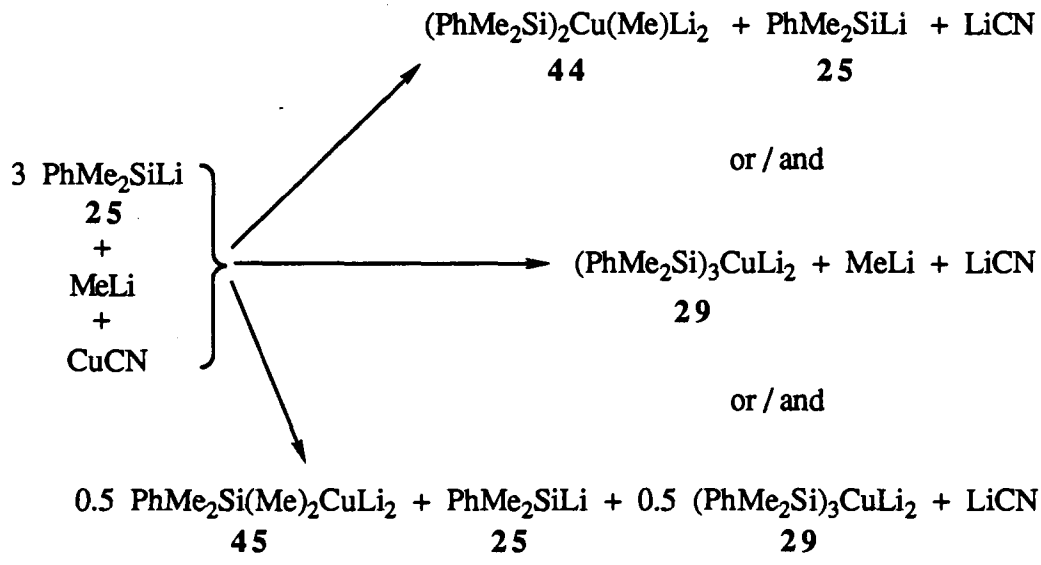
$(PhMe_2Si)(Me)_2CuLi_2$ (**45**) with two alkyl residues per copper atom to maintain methyl anion/copper cation balance. Thus, the peak at -5.3 ppm was assigned to the two copper bound methyls of $PhMe_2Si(\underline{Me})_2CuLi_2$ (**45**) and the signal at 5.5 ppm is attributed to the silyl bound methyls in this species. In agreement with this assignment the signal at -3.7 ppm assigned to **44** decreases in intensity with respect to that at -5.3 ppm assigned to **45**, as the solution is warmed, and produces signals due to **29**.

According to this analysis, the mixed silyl-alkyl-cyanocuprates wherein the silyl anion to alkyl anion to copper cation ratio is 2:1:1 exist in the dynamic equilibria shown in Scheme 20. The equilibria are similar to those observed earlier in the case of homosilylcyanocuprates.



Scheme 20

Addition of three equivalents of $PhMe_2SiLi$ (**25**) to a combination of one equivalent each of MeLi and CuCN could result in the formation of one or all of the possible combinations of silylcuprates shown below in Scheme 21.

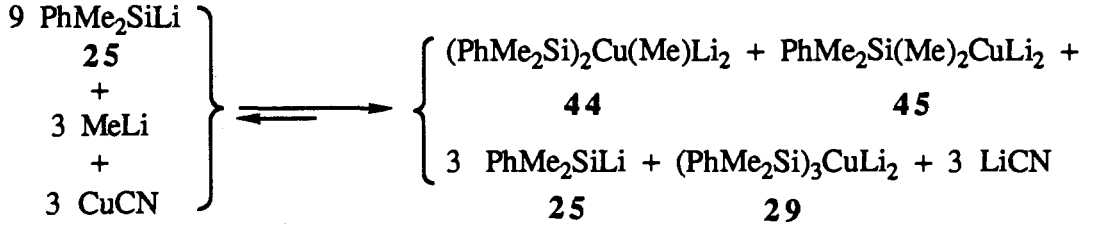


Scheme 21

The ^{13}C NMR spectrum of the solution generated from the addition of 3.0 equivalents of **25** to one equivalent of MeLi and one equivalent of CuCN at -85°C showed similar features to the ones generated from the combination of 2.0 equivalents of dimethylphenylsilyllithium to one equivalent of methyllithium and one equivalent of copper cyanide. The signal originally present for MeLi (-14 ppm) was replaced by signals characteristic of the mixed cuprates obtained previously for the 2:1:1 case, i.e., (PhMe2Si)2(Me)CuLi2 (**44**), (PhMe2Si)(Me)2CuLi2 (**45**) and (PhMe2Si)3CuLi2 (**29**). Similar results were obtained by addition of MeLi to preformed (PhMe2Si)3CuLi2 (**29**) at -85°C. This experiment shows that for this ratio of silyl anion to cuprous ion, PhMe2SiLi (**25**) is liberated by methyllithium.

Thus, solutions generated by combination of PhMe2SiLi, MeLi and CuCN in the ratios of 2:1:1 and 3:1:1 contain **44**, **45** and **29** except that in the latter the proportion of PhMe2SiLi is increased in accordance with the equilibria shown in Scheme 22. In

support of this analysis, the ^{29}Si NMR spectrum of solutions generated from admixture of 3.0 equivalents of $PhMe_2SiLi$ (**25**) and one equivalent each of MeLi and CuCN showed appreciable amounts of free $PhMe_2SiLi$ (**25**, -28.5 ppm).



Scheme 22

Tin-119, Carbon-13 and Hydrogen-1 NMR Studies on Homotrialkylstannylcuprates

Prior to examination of the composition of mixed triakylstannylcuprates $R_3Sn(R')CuLi{\cdot}LiX$ (**42**), the composition of homotrialkylstannylcuprates was studied. Low-temperature ^1H NMR spectroscopic studies were initially conducted on $(Me_3Sn)_nCuLi_{n-1}{\cdot}LiCN$ (n = 1, 2 or 3) in the region between 1.0 ppm and -2.0 ppm with the specific goal of observing the resonances due to the various methyl groups.

Reaction of $(Me_3Sn)_2$ (**46**) and methyllithium at -45°C in THF gave a solution containing equimolar amounts of Me_4Sn (δ 0) and Me_3SnLi (**47**).[46a,b] These preparations gave a broad ^1H signal at -0.35 ppm (Figure 30a)[46c,d] and, as previously reported, no $^1J(^{119}Sn\text{-}^1H)$ coupling was observed. The ^{119}Sn NMR[47] spectrum of solutions resulting from the reaction of hexamethylditin (**46**, Figure 31a) with MeLi revealed a signal for Me_3SnLi (**47**, Figure 31b) at -187.9 ppm. The high field position

of this signal (*the highest of any trimethyltin derivative yet reported*) has been attributed to the presence of the negative charge on the tin [i.e., $(Me_3Sn)^-$].[48] The $^{13}C\{^1H\}$ NMR spectrum of solutions of Me_3SnLi (**47**, Figure 32a) in THF exhibited a broad signal at -3.7 ppm. Contrary to what might be expected of this solution, no ^{13}C-^{119}Sn coupling was observed for this species in THF. At least two mechanisms can account for this lack of Sn-C coupling. First, rapid exchange of methyl groups between Me_3SnLi and $(Me_3Sn)_2$ would destroy the correlation between the ^{13}C and ^{119}Sn spin states and therefore no coupling would be seen. Second, association of THF molecules to give $[Me_3Sn(THF)_x]^-$ solvated anions would lower the symmetry of the anion and quadrupolar relaxation effects would average out the coupling. At present we cannot distinguish these two possibilities, although the lack of coupling even at -85°C, where methyl exchange rates are apt to be slow, suggests that solvation of the anion is a more likely explanation. This explanation is consistent with the observation that the ^1H and ^{13}C NMR chemical shifts of this reagent are concentration dependent.

Solutions of stannylcuprates[28] were generated by addition of copper(I) cyanide to THF solutions of Me_3SnLi (**47**) at -78°C. Combination of equimolar ratios of **47** and CuCN resulted in a nearly homogeneous solution, which showed several ^1H NMR signals in the range -0.1 to -0.3 ppm with major signals centered near -0.18 ppm (Figure 30b). The major signal at -0.18 ppm is assigned to polymeric $Me_3SnCu(CN)Li$ (**48**). Supporting evidence for this formulation comes from infrared analysis of these solutions which show a major absorption due to bound nitrile at 2111 cm^{-1} accompanied by a less intense absorption at 2082 cm^{-1} due to free LiCN.[34] The presence of the latter requires Me_3SnLi (**47**) be present. However, the ^{13}C NMR (*vide infra*) failed to reveal this component. We attribute the presence of free LiCN as detected by infrared spectroscopy as being due to thermal decomposition of $Me_3SnCu(CN)Li$ (**48**) during the infrared analysis.[34c]

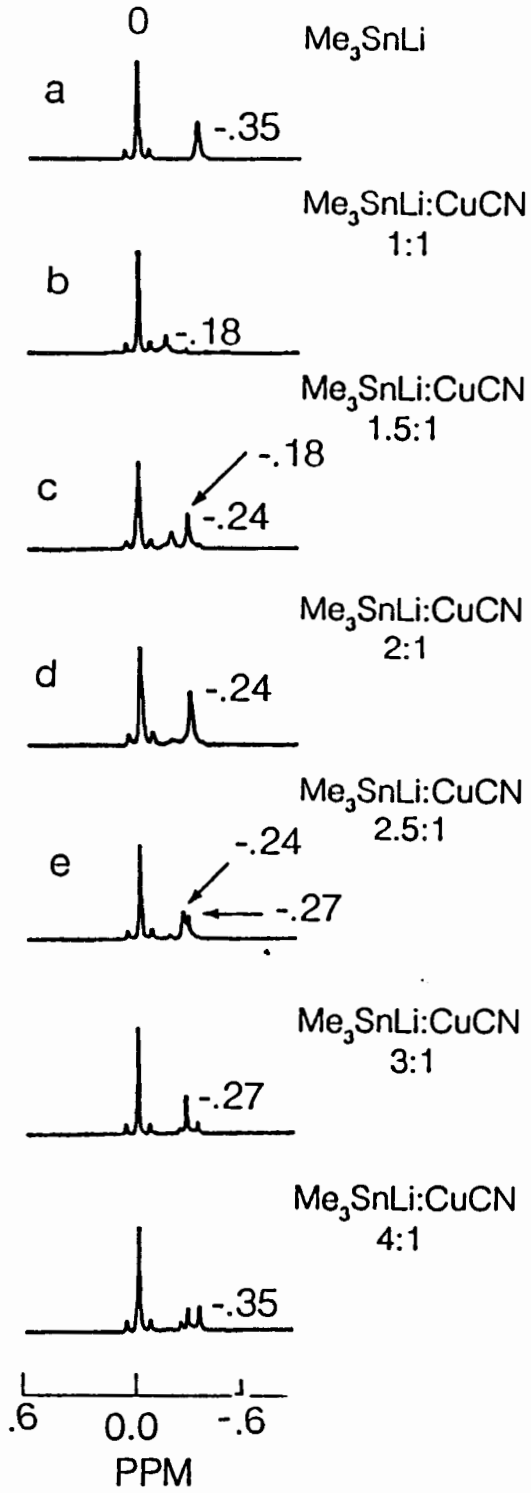


Figure 29. ^{1}H NMR spectra of (a) Me3SnLi (b) 1.0 Me3SnLi + CuCN (c) 1.5 Me3SnLi + CuCN (d) 2.0 Me3SnLi + CuCN (e) 2.5 Me3SnLi + CuCN (f) 3.0 Me3SnLi + CuCN (g) 4.0 Me3SnLi + CuCN; the spectra were run at -70°C.

The 1:1 combination of Me_3SnLi and CuCN yielded a slurry exhibiting a multitude of ^{119}Sn signals in the region of -140 to -160 ppm accompanied by a minor signal at -109 ppm due to Me_6Sn_2 (**46**, Figure 31c). The former were assigned to polymeric $Me_3SnCu(CN)Li$ (**48**) based on the observations made earlier on $PhMe_2SiCu(CN)Li$ (*vide supra*). The ^1H NMR spectrum of this solution exhibited several broad signals centered around -0.18 ppm supporting the view that this reagent is polymeric.

The solution of "Me_3SnCu" (**49**) prepared from Me_3SnLi (**47**) and $CuBr{\cdot}Me_2S$ exhibited several ^{119}Sn signals centered around -179 ppm (Figure 31d) suggesting it is also polymeric. In agreement with this interpretation most of the intensity of ^{13}C and ^1H NMR signals was lost in solutions containing equimolar amounts of **47** and $CuBr{\cdot}Me_2S$. The signals that were visible were due to $(Me_3Sn)_2$ (**46**). Lower order cuprates containing one equivalent of RLi to each cuprous ion equivalent such as $PhMe_2SiCu(CN)Li$, "$PhMe_2SiCu$" and CH_3Cu[2,3] are also polymeric. Appearance of signals for Me_6Sn_2 (**46**) in the ^{119}Sn NMR spectrum but not in the ^1H or ^{13}C spectra (*vide infra*) is attributed to the decomposition of $Me_3SnCu(CN)Li$ (**48**) during the longer time required to acquire the ^{119}Sn spectrum.

The ^{13}C NMR spectrum of **48** exhibited a broad triplet at -4.5 ppm (Figure 32b). The possibility that the multiplicity of this signal is due to ^2J (^6Li-^{13}C) coupling (^6Li and ^{13}C coupling has been observed in Me_2CuLi,[24] **1**) is ruled out because the observed satellites (total intensity of 16.5%) are more intense than calculated (7.42% of ^6Li) and the coupling is significantly larger than expected.[41] The satellites of this signal are attributed to $^1J(^{119}Sn$-$^{13}C)$ coupling (Figure 32b) in agreement with natural abundance of ^{119}Sn (natural abundance of ^{119}Sn is 8.5% and that of ^{117}Sn is 7.6% ; since the ratio of $J^{117}Sn$-$C/J^{119}Sn$-C = 1.046, individual satellite peaks due to each of these isotopes cannot usually be resolved for Me_3SnM species[47a]). The very low

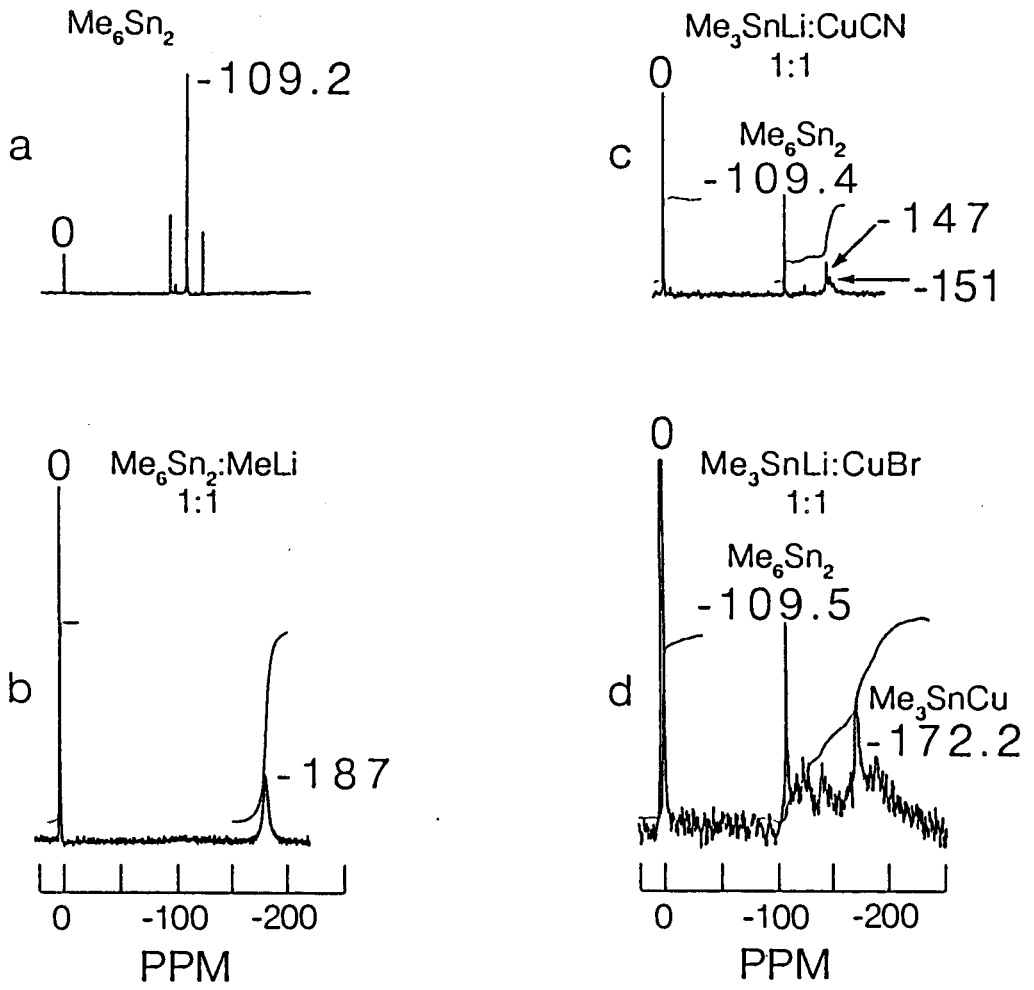


Figure 30. ^{119}Sn NMR spectra of (a) Me3SnSnMe3 (b) Me3SnLi (c) 1.0 Me3SnLi + CuCN (d) 1.0 Me3SnLi + CuBr; the spectra were run at -70°C.

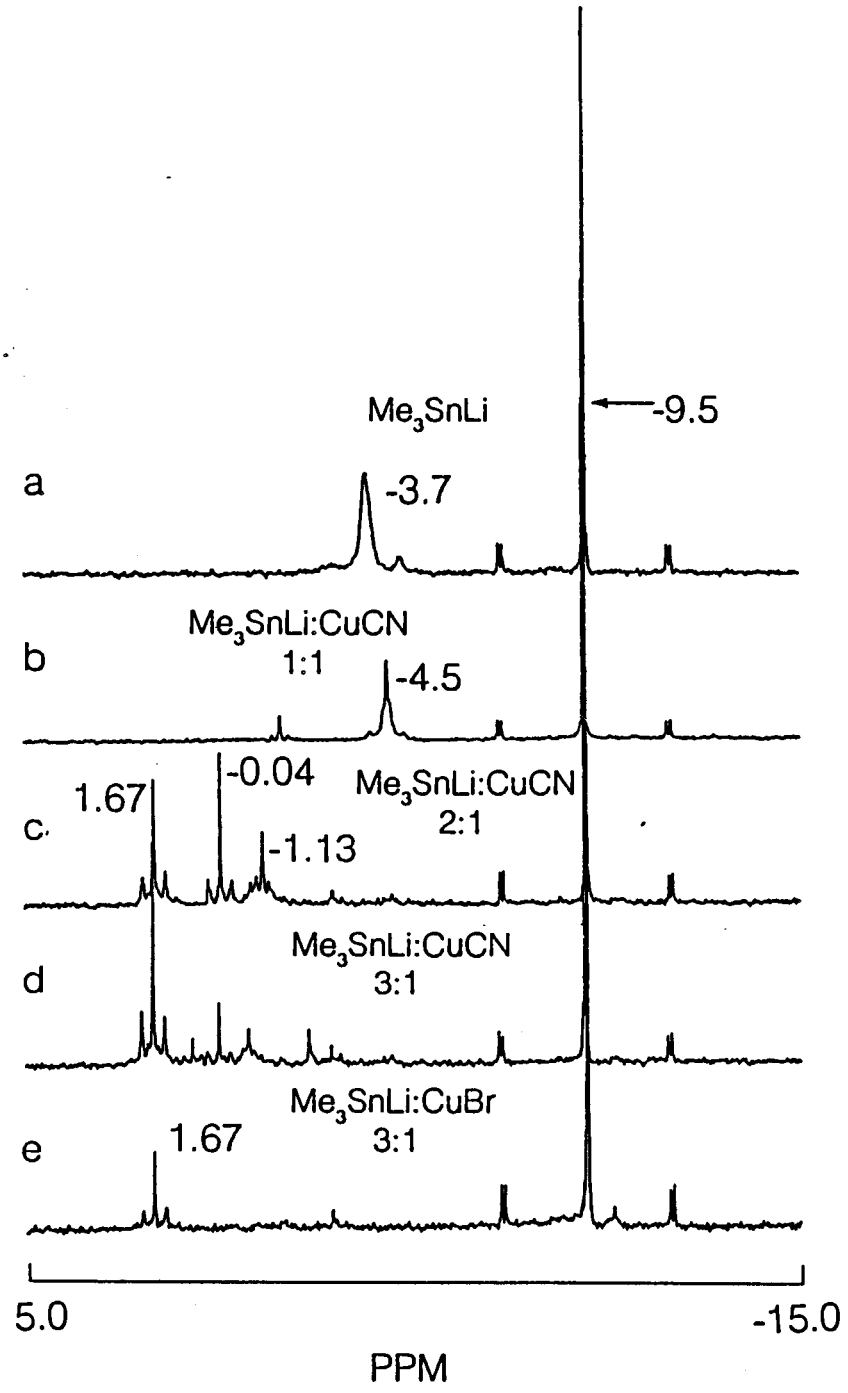
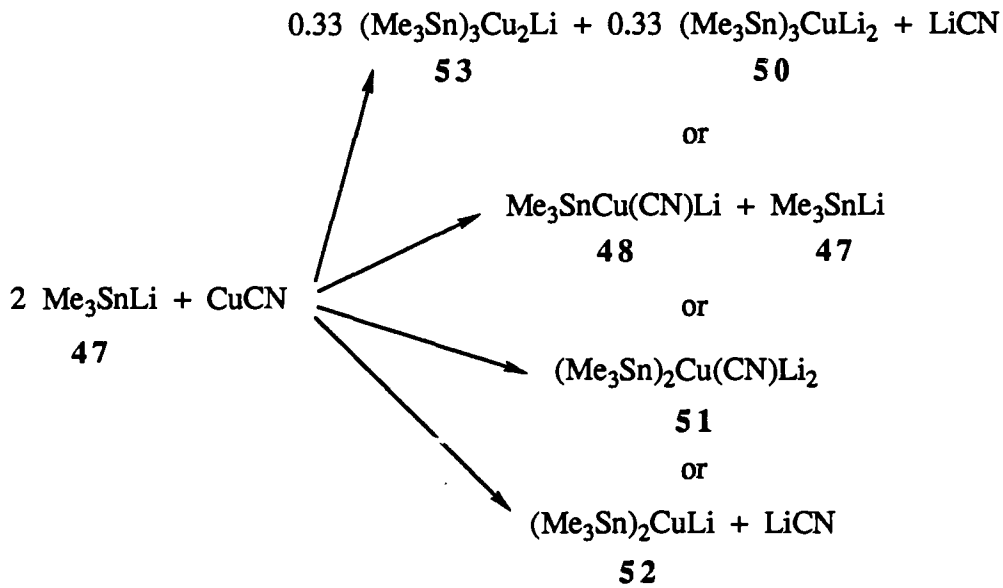


Figure 31. ^{13}C NMR spectra of (a) Me3SnLi (b) 1.0 Me3SnLi + CuCN (c) 2.0 Me3SnLi + CuCN (d) 3.0 Me3SnLi + CuCN (e) 3.0 Me3SnLi + CuBr; the spectra were run at -70°C.

coupling constant of $J = 63$ Hz is indicative of a trimethyltin group bonded to a weakly electron-attracting moiety as in the case of Me_3SnLi [$^1J(^{119}Sn\text{-}^{13}C) = 120$ Hz)].[46c,d,47a,49a]

As the ratio of Me_3SnLi (**47**) to CuCN was increased from 1:1 to 2:1, a new peak at -0.24 ppm in the ^1H spectrum appeared and increased in intensity at the expense of the signal at -0.18 ppm (Figure 30c). When the ratio of Me_3SnLi (**47**) to CuCN reached 2:1, minor signals due to $Me_3SnCu(CN)Li$ (**48**, δ -0.18) and $(Me_3Sn)_3CuLi_2$ (**50**, δ -0.27, *vide infra*) and a major signal at -0.24 ppm (Figure 30d) appeared. The latter signal is attributed to a species containing Me_3Sn/Cu ratios between 1:1 and 3:1.

It is significant that both the ^1H and ^{13}C (*vide infra*) NMR spectra revealed the absence of **47** in these solutions. This limits consideration of the composition of the stannylcuprates possessing Me_3Sn/Cu ratios between 1:1 and 3:1 to $(Me_3Sn)_3CuLi_2$ (**50**), $(Me_3Sn)_2Cu(CN)Li_2$ (**51**), $(Me_3Sn)_2CuLi$ (**52**) and $(Me_3Sn)_3Cu_2Li$ (**53**, Scheme 23).



Scheme 23

The ^{13}C NMR spectra of solutions prepared from 2.0 equivalents of Me_3SnLi (**47**) and one equivalent of CuCN contained three signals (δ 1.67, -0.04 and -1.13, Figure 32c). Each signal is accompanied by a set of satellites attributed to coupling of the two tin nuclides of spin 1/2 to carbon. The observation of spin coupling allows the establishment of Cu-Sn stoichiometry in solution[47a] based on the relative intensities. Thus, the signal centered at 1.67 ppm exhibited ^{119}Sn-^{13}C coupling of 44.3 Hz and satellites of 45% intensity indicating ^{13}C coupling to three tin atoms, while that at -0.04 ppm was accompanied by satellites revealing a ^{119}Sn-^{13}C coupling of 46.8 Hz to two tin atoms (26%) and the signal at -1.13 ppm exhibited ^{119}Sn-^{13}C couplings of 46.8 and 23.8 Hz due to two different tin atoms in the ratio of 3:2.

The signal at 1.67 ppm is assigned to $(Me_3Sn)_3CuLi_2$ (**50**) based on the observation that this signal grows at the expense of the signals at -0.04 ppm and -1.13 ppm as the Sn/Cu ratio is increased from 2:1 to 3:1 and beyond (Figure 32c, 32d and 32e). The presence of signals corresponding to **50** requires the presence of species containing a 1.5:1 ratio of Me_3Sn/Cu to maintain the copper-tin balance in these solutions. The ^{13}C NMR spectrum of a solution generated by admixture of 1.5 equivalents of Me_3SnLi (**47**) with one equivalent of $CuBr{\cdot}Me_2S$ exhibits a broad peak at -1.13 ppm. Hence, $(Me_3Sn)_3Cu_2Li$ (**53**) is assigned to the latter signal. The ^{13}C NMR spectrum of a solution generated from the combination of two equivalents of Me_3SnLi (**47**) and one equivalent of $CuBr{\cdot}Me_2S$ exhibits a broad signal at -1.35 ppm assigned to $(Me_3Sn)_2CuLi$ (**52**). This signal is absent in solutions generated from a 2:1 combination of Me_3SnLi and CuCN. Thus, the stannylcuprates eliminated from consideration as the species giving rise to the signals centered at -0.04 ppm are $Me_3SnCu(CN)Li$ (**48**), $(Me_3Sn)_2CuLi$ (**52**) and $(Me_3Sn)_3Cu_2Li$ (**53**). This signal is therefore attributed to $(Me_3Sn)_2Cu(CN)Li_2$ (**51**).

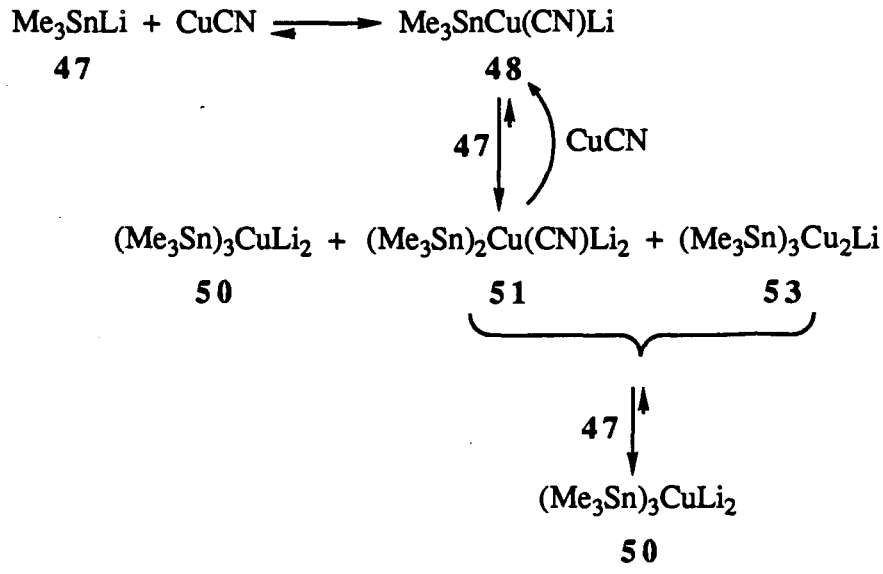
This interpretation is in agreement with the ^{1}H NMR analysis of these solutions which revealed a major signal at -0.24 ppm at a Sn/Cu ratio of 2:1 and that the intensity of ^{119}Sn-^{13}C satellites surrounding the ^{13}C NMR signal for this reagent (*vide supra*) corresponded to the presence of two tins.

Sequential addition of Me_3SnLi (**47**) to the above solution (< 0.5 equivalent) resulted in the appearance of a new signal at -0.27 ppm in the ^{1}H NMR spectrum (Figure 30e). When the ratio of **47** to CuCN was precisely 3:1, the major ^{1}H signal observable was at -0.27 ppm accompanied by a minor signal due to $(Me_3Sn)_2Cu(CN)Li_2$ (**51**, Figure 30f). The peak at -0.27 ppm was attributed to $(Me_3Sn)_3CuLi_2$ (**50**) by analogy with our earlier observations on the trialkylsilylcuprates.

In support of our interpretation of the ^{1}H NMR spectral data, the ^{13}C NMR spectrum of this solution showed a major signal at 1.67 ppm along with a minor signal assigned to **51** and **53** (Figure 32d). Moreover, solutions of Me_3SnLi:CuBr·Me_2S (3:1) exhibited ^{13}C NMR spectra with a signal at 1.67 ppm (Figure 32e).

While no appreciable amounts of Me_3SnLi (**47**) were detectable by ^{1}H NMR spectroscopy in solutions containing 3.0 equivalents of Me_3SnLi to one equivalent of CuCN, substantial amounts of Me_3SnLi were detected by ^{1}H NMR analysis (Figure 30g) in solutions containing more than 3.0 equivalents of **47** to each equivalent of CuCN.

That the formation of $Me_3SnCu(CN)Li$ (**48**) and $(Me_3Sn)_3CuLi_2$ (**50**) are reversible was shown by addition of 0.5 equivalent of CuCN to the solution whose ^{1}H NMR spectrum is shown in Figure 30f. This results in the regeneration of the spectrum shown in Figure 30d. Further introduction of CuCN (1.0 equivalent) to this solution results in the regeneration of the spectrum shown in Figure 30b. Thus, the species exhibiting signals at -4.5 ppm, -1.13 ppm, -0.04 ppm and 1.67 ppm are in dynamic equilibria as represented by Scheme 24.



Scheme 24

The chemical shift change observed when lower order stannylcyanocuprates are converted to higher order stannylcyanocuprates is opposite to what would be expected from simple arguments based on electronegativity. Coordination of an electron-rich Me3SnLi (**47**) to the copper centre in Me3SnCu(CN)Li (**48**) should increase the electron density at copper and hence at both tins in the resultant HO species. The ^{119}Sn resonance in the HO species would therefore be expected to be upfield of that in the LO reagents, not downfield as found. An anomolous pattern of shielding was also observed for ^{29}Si in trialkylsilylcyanocuprates (**46**) and presumably has its origin in the p-orbital "imbalance" and its contribution to the paramagnetic term of nuclear shielding.[37b]

The observed $^{1}J(^{119}Sn\text{-}^{13}C$ coupling decreases as one proceeds from LO to HO stannylcuprates i.e., $^{1}J(^{119}Sn\text{-}^{13}C$, 63 Hz) of Me3SnCu(CN)Li (**48**, δ -4.5) > $^{1}J(^{119}Sn\text{-}^{13}C$, 46.8 Hz) of (Me3Sn)2Cu(CN)Li2 (**51**, δ -0.04) > $^{1}J(^{119}Sn\text{-}^{13}C$, 44.3 Hz) of (Me3Sn)3CuLi2 (**50**, δ 1.67). The small $^{119}Sn\text{-}^{13}C$ coupling observed in HO

stannylcuprates as compared to LO stannylcuprates is consistent with a greater electron density on the tin atom in the former.[46d,48] According to this rationale a greater negative charge on the tin atom would lead to a greater *s*-character in the orbital containing the lone pair bound to copper.[46d] An increase in the fractional *s*-character of the bond should lead to a decrease in *s*-character of the remaining tin-carbon bonds and result in a lower ^{119}Sn-^{13}C coupling as observed.[46d,47a]

A final point of interest is the observation that the intensities of the ^{119}Sn-^{13}C satellites surrounding the ^{13}C NMR signals at 1.67 ppm, -0.04 ppm and -1.13 ppm (attributed to $(Me_3Sn)_3CuLi_2$ (**50**); $(Me_3Sn)_2Cu(CN)Li_2$ (**51**); and $(Me_3Sn)_3Cu_2Li$, (**53**); respectively) with respect to the central signal are greater than the 15:85 ratio expected for ^{13}C coupling to a single ^{119}Sn nucleus. We have observed the same phenomenon for stannylmetalloids such as $Me_3SnAlEt_2$ (**54**) and $[(Me_3Sn\text{-}9\text{-}BBN{\bullet}OMe)^-]Li^+$ (**55**). The small coupling constants of **54** [$^1J(^{119}Sn$-^{13}C, 40 Hz] and **55** [$^1J(^{119}Sn$-^{13}C, 56 Hz] are very close to those observed for the stannylcuprates mentioned above.

54 **55**

A priori one would ascribe the increased satellite intensities to a rapid exchange of alkyl residues between tins. At least in the case of stannylcuprates we have demonstrated that such exchange does not occur between Bu_3Sn and Me_3Sn groups associated with cuprous ion. Thus, one equivalent of CuCN was added to one equivalent

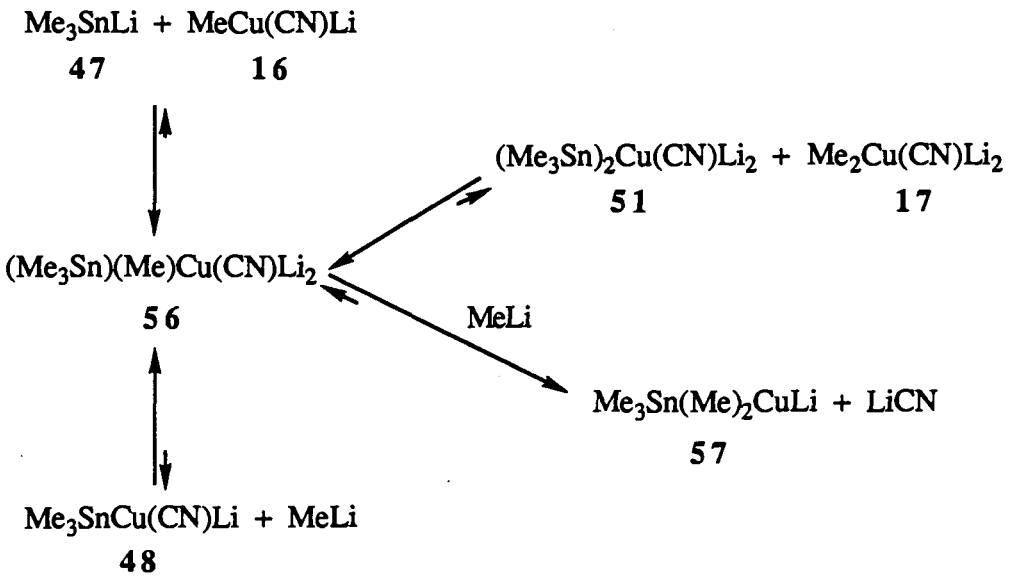
each of Bu_3SnLi and Me_3SnLi at -70°C and the reaction quenched with NH_4Cl after two hours at -50°C. Analysis by GC-MS revealed no Bu_2MeSn or $BuMe_2Sn$ moieties. Although this experiment rules out the exchange between methyl and a butyl group on tin in HO stannylcuprates, it does not unequivocally rule out methyl-methyl exchange in these cuprates. Crossover experiments using cuprates generated from $(CH_3)_3SnLi$ and $(CD_3)_3SnLi$ should be carried out to observe the formation of $(CD_3)_n(CH_3)_{3-n}Sn$ species in the reaction mixtures.

An alternative possibility is that the enhanced satellite intensity is due to the equivalency of $^1J(^{119}Sn\text{-}^{13}C)$ and $^3J(^{119}Sn\text{-}^{13}C)$ in these complexes. For alkyl tin compounds where the $^{119}Sn\text{-}^{13}C$ coupling is through a carbon frame, $^1J > {}^3J > {}^2J > {}^4J$ and all these can be appreciable.[50a] Thus, the equivalency of ^1J and ^3J in the present system is not entirely unreasonable.

Tin-119, Carbon-13 and Hydrogen-1 NMR studies on Mixed Trialkylstannylcuprates

We next focused on mixed reagent $(Me_3Sn)(Me)Cu(CN)Li_2$ (**56**). Earlier spectroscopic studies on the silylcuprates (*vide supra*) indicated that $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**) can be produced either by the sequential addition of MeLi and $PhMe_2SiLi$ (**25**) to CuCN or upon admixture of $Me_2Cu(CN)Li_2$ (**17**) with $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**). If $(Me_3Sn)(Me)Cu(CN)Li_2$ (**56**) is produced in similar experiments with stannyl anions one should obtain two high field signals corresponding to two methyl groups, one bound to copper and the other to tin. On the other hand the various equilibria exhibited by the higher order homo-trimethylstannylcuprate (**51**, *vide supra*) could result in the formation of species having more than one tin.

The ^{13}C NMR spectrum of a solution containing one equivalent each of MeLi and $Me_3SnCu(CN)Li$, **48** (Figure 33b) at -70°C is shown in Figure 33d. The combination of these reagents resulted in a simple spectrum exhibiting three signals at -2.06 ppm, -9.32 ppm and -9.5 ppm (Me_4Sn). The peaks at -2.06 ppm and -9.32 ppm were assigned to carbons of the methyls bound to tin and copper respectively, in $(Me_3Sn)(Me)Cu(CN)Li_2$ (**56**). The same spectrum (Figure 33e) was obtained when equimolar amounts of **17** (Figure 33a) were combined with **51** (Figure 33c). The intensities of the satellites of the signal at 2.06 ppm are as expected for $^1J(^{119}Sn\text{-}^{13}C$, 182.0 Hz) coupling to a single tin nucleus. No $^2J(^{119}Sn\text{-}^{13}C)$ coupling was observed between the methyl and the Me_3Sn moiety. This is attributed to a rapid intermolecular exchange between methyls on copper. Since neither $(Me_3Sn)_2Cu(CN)Li_2$ (**51**), $Me_2Cu(CN)Li_2$ (**17**), $Me_3SnCu(CN)Li$ (**48**), Me_3SnLi (**47**), $MeCu(CN)Li$ (**16**) nor MeLi are seen when the Me_3SnLi:CuCN:MeLi ratio is exactly 1:1:1, an equilibrium favouring **56** (Scheme 25), analogous to Scheme 18, must lie far to the products.



Scheme 25

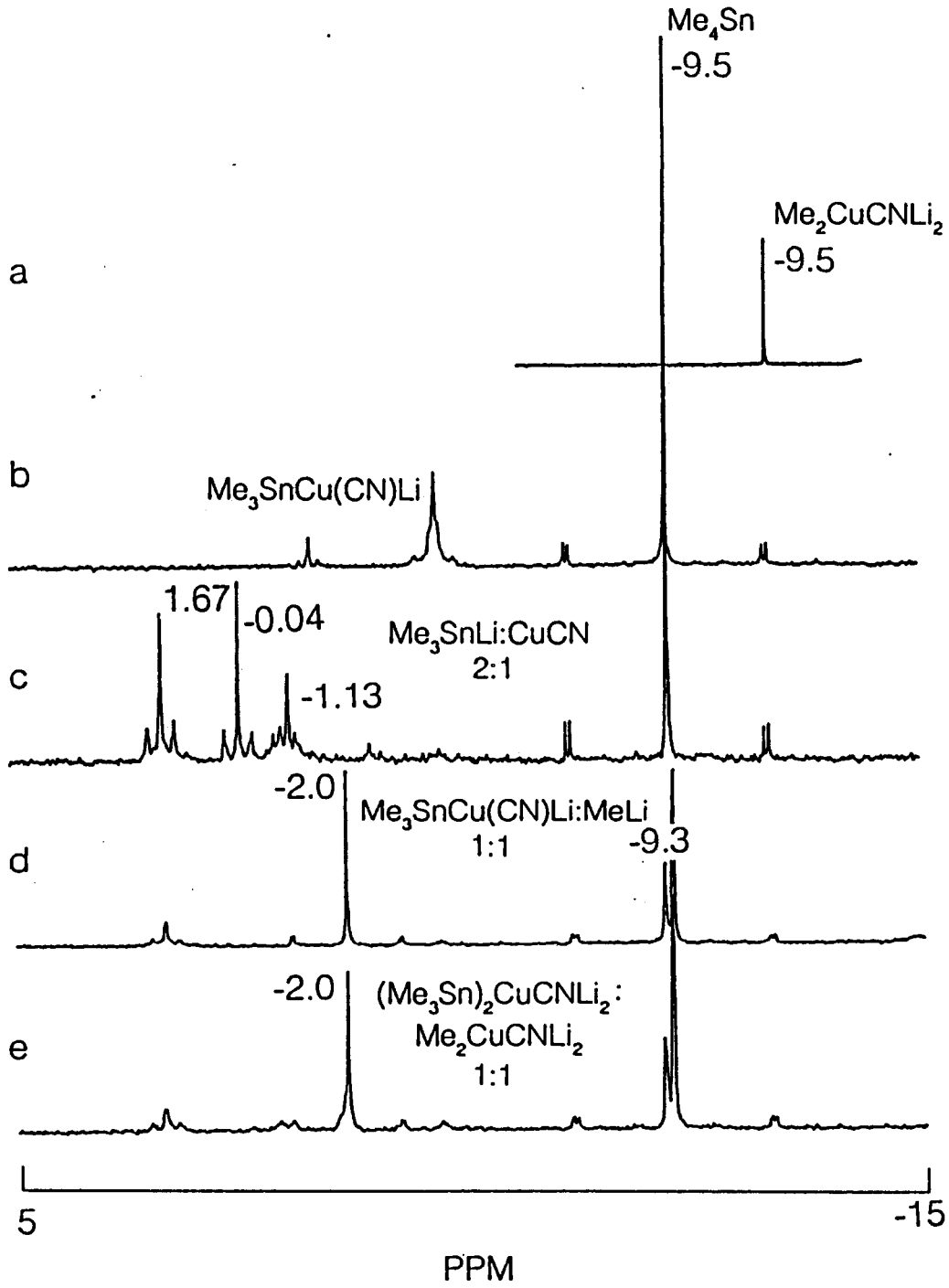


Figure 32. ^{13}C NMR spectra of (a) $Me_2Cu(CN)Li_2$ (b) 1.0 Me_3SnLi + CuCN (c) 2.0 Me_3SnLi + CuCN (d) $Me_3SnCu(CN)Li$ + MeLi (e) $(Me_3Sn)_2Cu(CN)Li_2$ + $Me_2Cu(CN)Li_2$; the spectra were run at -70°C.

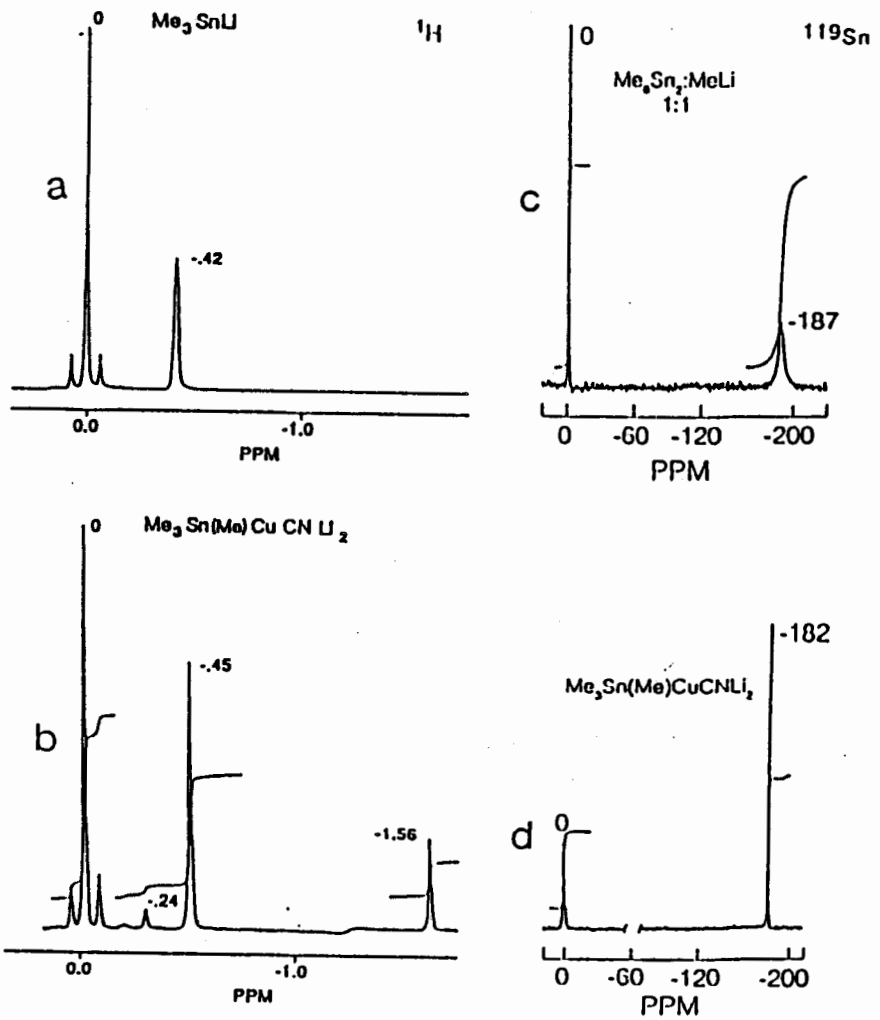


Figure 33. ^{1}H NMR spectra of (a) Me_3SnLi (b) 1.0 $(Me_3Sn)_2Cu(CN)Li_2$ + $Me_2Cu(CN)Li_2$; ^{119}Sn NMR spectra of (c) Me_3SnLi (d) Me_3SnLi + $MeCu(CN)Li$; the spectra were run at -70°C.

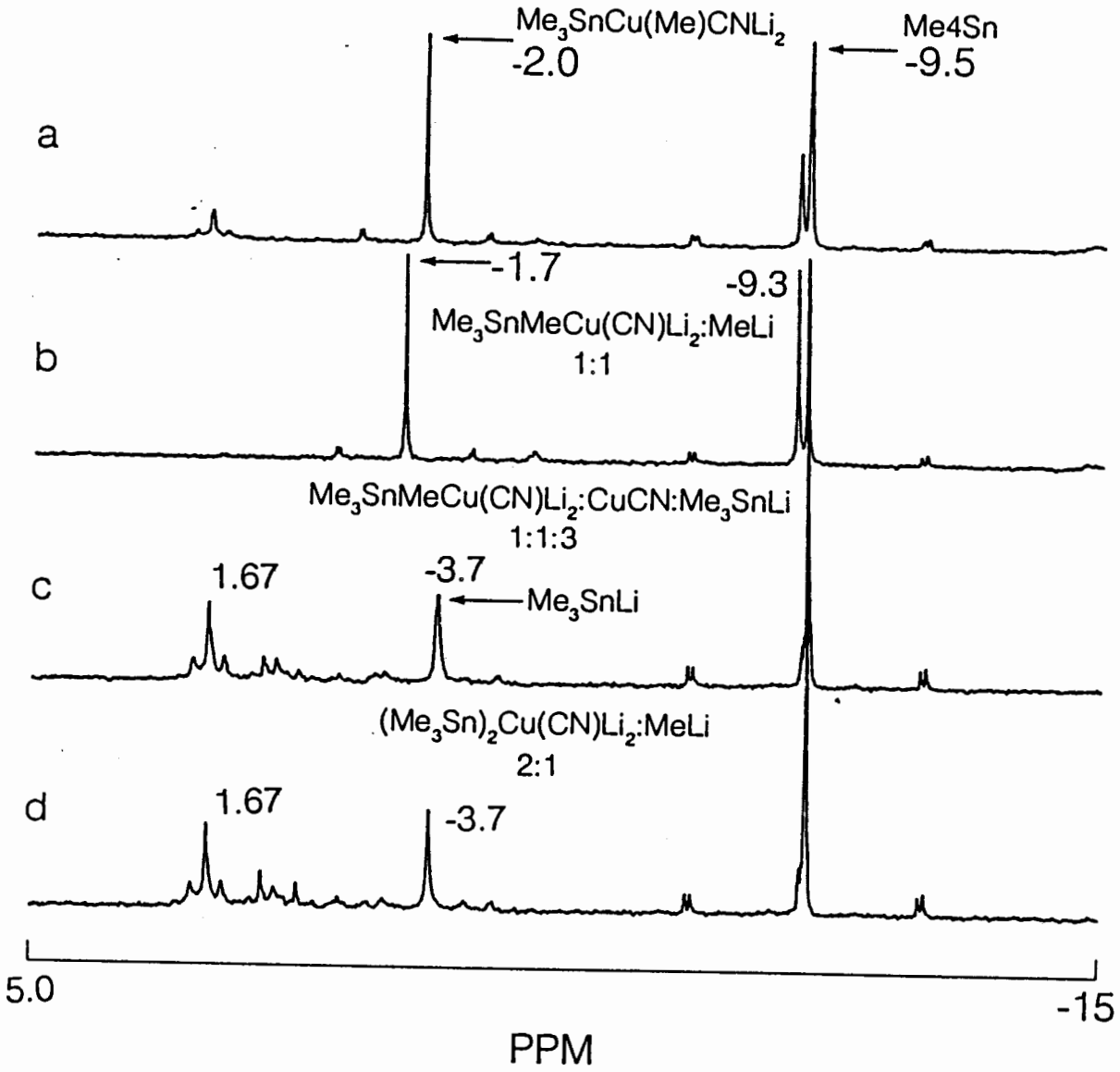


Figure 34. ^{13}C NMR spectra of (a) (Me3Sn)(Me)Cu(CN)Li2 (b) (Me3Sn)(Me)Cu(CN)Li2 + MeLi (c) (Me3Sn)3CuLi2 + (Me3Sn)(Me)Cu(CN)Li2 (d) 2.0 (Me3Sn)2Cu(CN)Li2 + MeLi; the spectra were run at -70°C.

In support of our interpretation of the ^{13}C NMR spectrum of **56**, the ^{1}H spectrum of this reagent (Figure 34b) at -70°C (prepared from equimolar amounts of $(Me_3Sn)_2Cu(CN)Li_2$ (**51**) and $Me_2Cu(CN)Li_2$ (**17**) showed two resonances in a 3:1 ratio at -0.45 (Me on tin) and -1.56 ppm (Me on copper) along with a minor peak due to **51** at -0.24 ppm. Similar results were obtained from the combination of Me_3SnLi (Figure 34a), MeLi and CuCN. The ^{119}Sn NMR spectrum (Figure 34d) of **56** showed a single peak at -182 ppm also indicating a single species.

Addition of one equivalent of MeLi to preformed $(Me_3Sn)(Me)Cu(CN)Li_2$ (**56**, Figure 35a, containing Me_4Sn, -9.5 ppm), at -70°C, yielded a solution that exhibited two ^{13}C NMR signals at -1.7 ppm $^{1}J(^{119}Sn\text{-}^{13}C$, 189 Hz) and -9.3 ppm which were attributed to $(Me_3Sn)(Me)_2CuLi_2$ (**57**, Figure 35b). This assignment was based on the increase in the intensity of the signal at -9.3 ppm when the ratio of Sn/Cu/Me was 1:1:2. No signals corresponding to other stannylcuprates were apparent in these solutions (Figure 35b). Also, no $^{2}J(^{119}Sn\text{-}^{13}C)$ was observed in this cuprate due to rapid intermolecular exchange between methyls on copper.

Addition of one equivalent of $(Me_3Sn)_3CuLi_2$ (**50**) to **56** (2:1:0.5, Sn:Cu:Me) resulted in the appearance of signals for free Me_3SnLi (**47**) as well as signals attributable to $(Me_3Sn)_3CuLi_2$ (**50**), $(Me_3Sn)_3Cu_2Li$ (**53**) and $(Me_3Sn)(Me)_2CuLi_2$, **57** (Figure 35c). Similar results were obtained when 1.0 equivalent of MeLi was added to 2.0

$$\underset{\mathbf{51}}{4\ (Me_3Sn)_2Cu(CN)Li_2} + 2\ MeLi$$

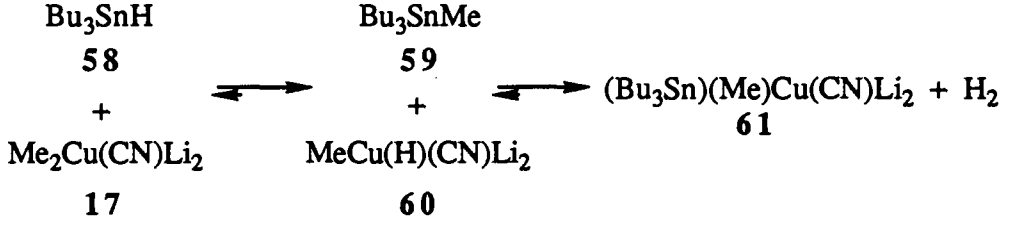
$$\Big\downarrow\Big\uparrow$$

$$\underset{\mathbf{57}}{Me_3Sn(Me)_2CuLi_2} + \underset{\mathbf{47}}{Me_3SnLi} + \underset{\mathbf{50}}{(Me_3Sn)_3CuLi_2} + \underset{\mathbf{53}}{(Me_3Sn)_3Cu_2Li} + 4\ LiCN$$

Scheme 26

equivalents of preformed $(Me_3Sn)_2Cu(CN)Li_2$ (**51**, Figure 35d). Appearance of Me_3SnLi (**47**) in the latter experiment indicates the most basic ligand, in this case methyl anion, is preferentially bound to copper in solutions deficient in methyl anion (Scheme 26).

Encouraged by the formation of $(Me_3Sn)(Me)Cu(CN)Li_2$ (**56**) we examined the low temperature ^{13}C NMR spectra of solutions generated from the mixture of one equivalent of Bu_3SnH (**58**) and $Me_2Cu(CN)Li_2$ (**17**). This combination resulted in the appearance of a single peak at -13.1 ppm (Figure 36a) corresponding to the methyl in Bu_3SnMe (**59**, Scheme 27). The stoichiometry of this reaction requires the formation of $Me(H)Cu(CN)Li_2$ (**60**) which has recently been detected by Lipshutz in 1,4-addition reaction of the hydride.[50a]



Scheme 27

Addition of a further equivalent of Bu_3SnH (**58**) to the above solution resulted in immediate release of a gas and appearance of a new signal at -9.3 ppm (Figure 36b). This signal is very close to the one observed earlier (-9.2 ppm) for methyl bound to copper in $(Me_3Sn)(\underline{Me})Cu(CN)Li_2$ (**56**). Hence, we attribute this peak to methyl bound in $(Bu_3Sn)(\underline{Me})Cu(CN)Li_2$ (**61**). The stoichiometry of the conversion of an equivalent

of Bu_3SnH (**58**) and $Me(H)Cu(CN)Li_2$ (**60**) to produce $(Bu_3Sn)(Me)Cu(CN)Li_2$ (**61**) requires the evolved gas to be hydrogen (Scheme 27).[50b]

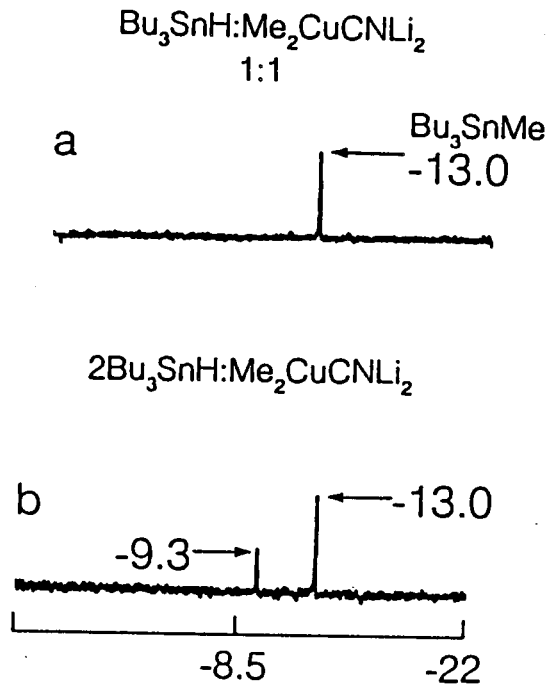


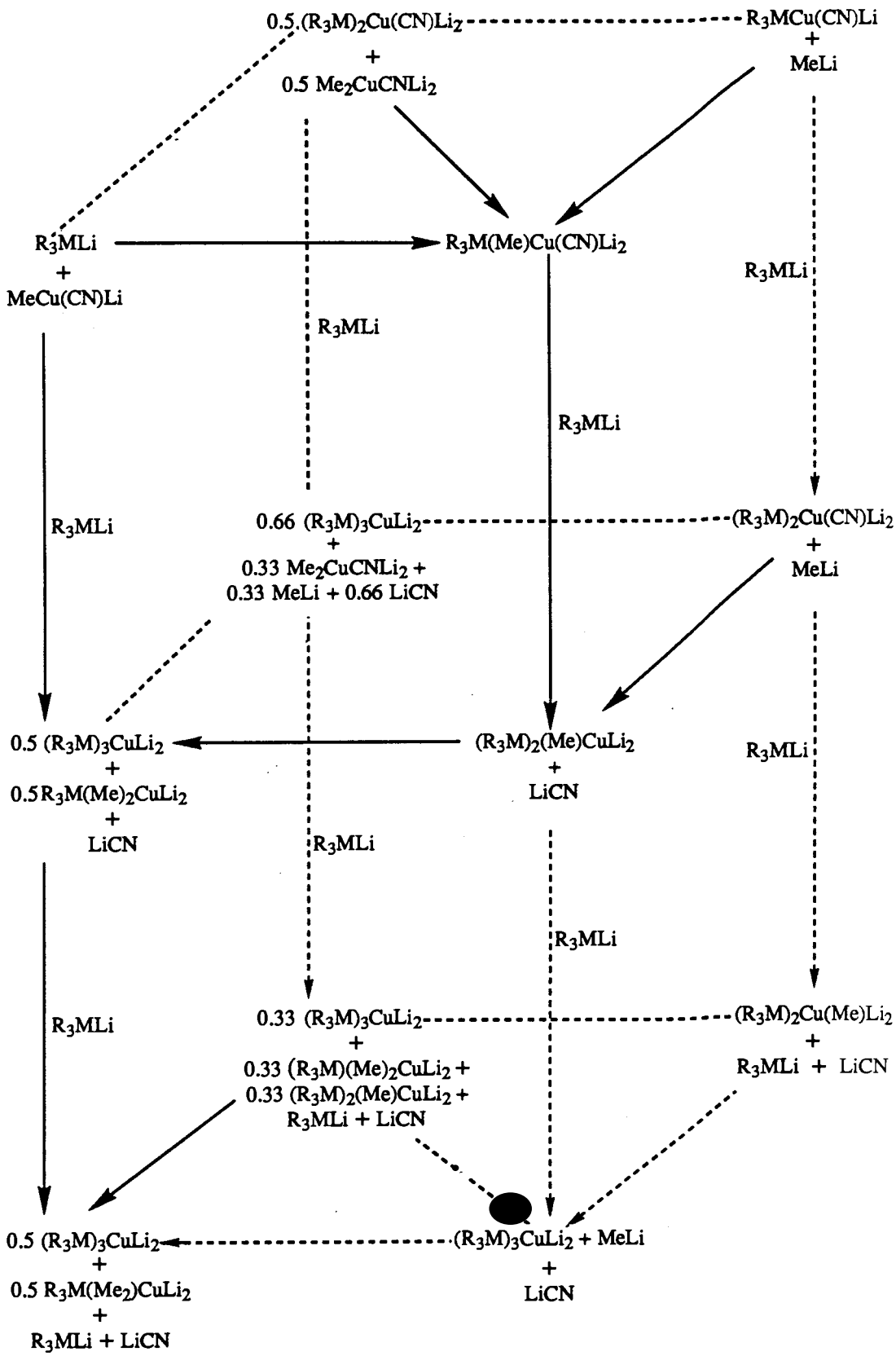
Figure 35. ^{13}C NMR spectra of (a) Bu_3SnH + $Me_2Cu(CN)Li_2$ (b) 2.0 Bu_3SnH + $Me_2Cu(CN)Li_2$; the spectra were run at -70°C.

On the basis of these NMR investigations, it is clear that ligand exchange in lower order and higher order cuprates occurs between silyl, stannyl and alkyl anions. Because of these equilibria silyl- or stannylcuprates and alkylcuprates readily form mixed

metallo-alkylcuprates. For solutions containing equimolar ratios of R_3M (M = Si or Sn) anion, methyl anion and cuprous ion, the mixed cuprate $R_3M(Me)Cu(CN)Li_2$ is the predominant species in solution (Scheme 28).

As the amount of R_3M anion is increased, a species containing two R_3M anions to each methyl and cuprous ion [$(R_3M)_2(Me)CuLi_2$] is formed. [$R_3M(Me)_2CuLi_2$] and $(R_3M)_3CuLi_2$ are also formed in these solutions. This shows that equilibria among these three species is close to unity. The observation that R_3MLi is present in solutions of higher order metallocuprates provides a pathway by which ligand exchange on cuprous ion can occur [i.e., *via* free $R_3MLi(R'Li)$].

The ability of methyl ligands to bind tenaciously to cuprous ion can be explained by the differences in basicity of MeLi ($pK_a \approx 40$), R_3MLi ($pK_a \approx 23$, M = Si or Sn) and "R_3MCu" ($pK_a \approx 15$).[28a,51] This implies that in the mixed "$R_3Si(Me)Cu$" or "$R_3Sn(Me)Cu$" reagents [i.e., $(PhMe_2Si)(Me)Cu(CN)Li_2$ (**43**); $(PhMe_2Si)_2(Me)Cu(CN)Li_2$ (**44**); $(PhMe_2Si)(Me)_2CuLi_2$ (**45**); $(Me_3Sn)(Me)Cu(CN)Li_2$ (**56**); $(Me_3Sn)(Me)_2CuLi_2$ (**57**) and $(Bu_3Sn)(Me)Cu(CN)Li_2$ (**61**)] there would be a tendency for the silyl- or the stannyl- ligands to transfer faster than methyl anions. This would result in the conservation of the more valuable silyl or stannyl residue which would, in turn, increase the efficiency of R_3M transfer reactions. Product yields would also be expected to improve because of simplification in isolation procedures since methane is the hydrolysis product whereas R_3MH and R_3MOH are the side products obtained on workup of homo-trialkylsilyl- or stannylcuprates.


0.5 $(R_3M)_2Cu(CN)Li_2$
+
0.5 $Me_2CuCNLi_2$
$R_3MCu(CN)Li$
+
MeLi
R_3MLi
+
$MeCu(CN)Li$
$R_3M(Me)Cu(CN)Li_2$
R_3MLi
R_3MLi
R_3MLi
R_3MLi
0.66 $(R_3M)_3CuLi_2$
+
0.33 $Me_2CuCNLi_2$ +
0.33 MeLi + 0.66 LiCN
$(R_3M)_2Cu(CN)Li_2$
+
MeLi
0.5 $(R_3M)_3CuLi_2$
+
0.5 $R_3M(Me)_2CuLi_2$
+
LiCN
$(R_3M)_2(Me)CuLi_2$
+
LiCN
R_3MLi
R_3MLi
R_3MLi
R_3MLi
0.33 $(R_3M)_3CuLi_2$
+
0.33 $(R_3M)(Me)_2CuLi_2$ +
0.33 $(R_3M)_2(Me)CuLi_2$ +
R_3MLi + LiCN
$(R_3M)_2Cu(Me)Li_2$
+
R_3MLi + LiCN
0.5 $(R_3M)_3CuLi_2$
+
0.5 $R_3M(Me_2)CuLi_2$
+
R_3MLi + LiCN
$(R_3M)_3CuLi_2$ + MeLi
+
LiCN

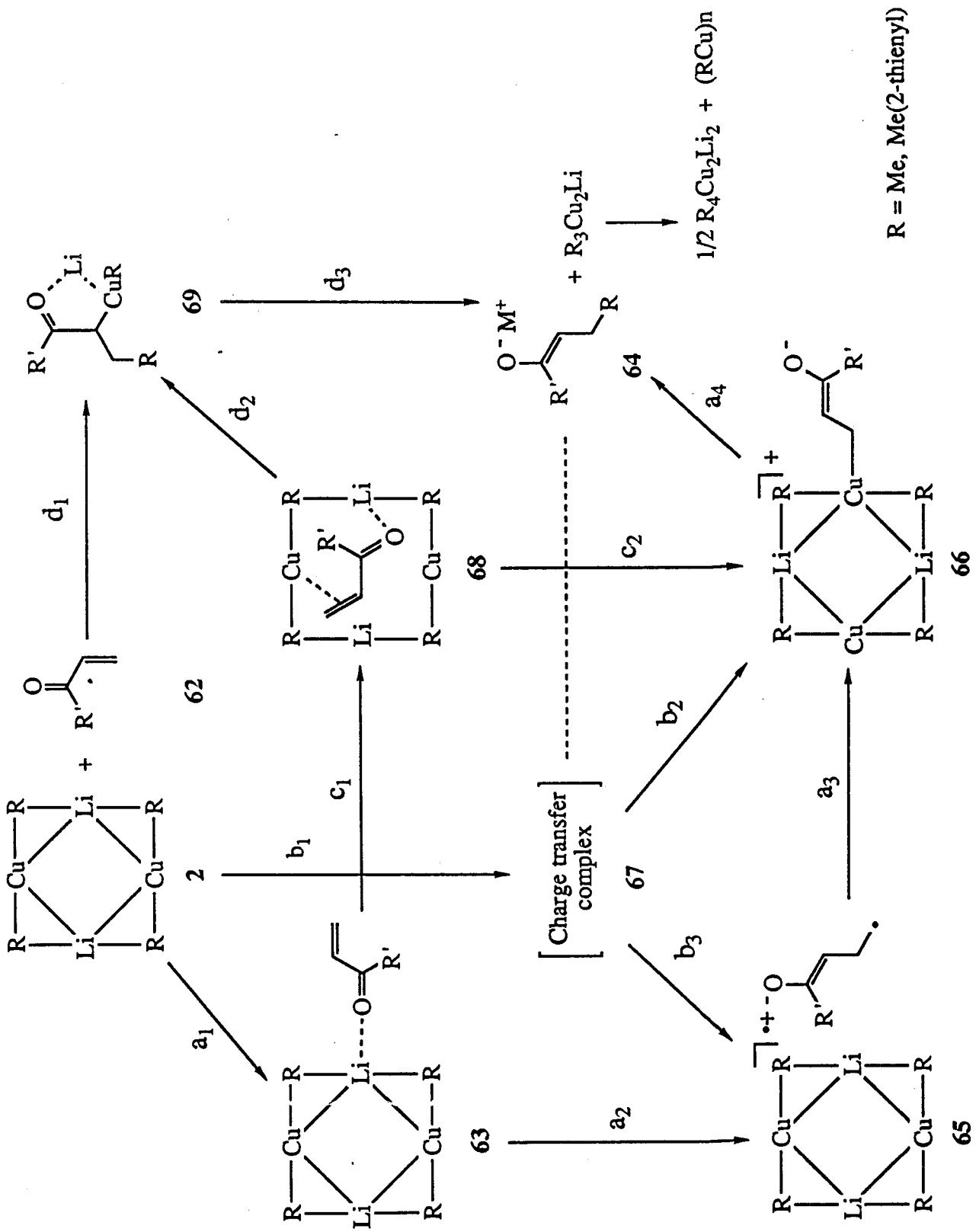
Scheme 28

Reactions of Silyl- and Stannylcuprates with α,β-unsaturated Ketones

Evidence has been obtained from our ^{13}C NMR studies (*vide supra*) that in the mixed cuprates of the general formulae $(R_3M)_n(Me)CuLi_{n-1}\cdot LiCN$ (n = 1 or 2), both Me and R_3M moieties move rapidly between parent species to preferentially yield the mixed ligand metallocuprates. It was therefore of interest to evaluate ligand transferability from these reagents to organic substrates such as α,β–enones as a step toward more efficient synthetic methodology. Futhermore the simple spectroscopic behaviour of the mixed ligand metallocuprates afforded an opportunity to study the mechanism of the reaction of these reagents with α,β-unsaturated ketones.

The facility with which cuprates bearing alkyl,[2] silyl,[32] and stannyl[32] anions introduce these groups in a Michael sense to α,β–unsaturated carbonyls compounds (**62**) makes them the reagents of choice for these transformations. Most mechanistic studies of these processes have involved Gilman reagents (i.e., R_2CuLi, **2**). While initial coordination of the substrate carbonyl with lithium (**2** + **62** → **63**) and formation of a substituted enolate (**64**) are common features, (Scheme 29) there has been considerable divergence of opinion concerning the intervening steps.

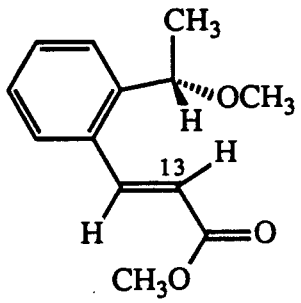
Kinetic data[52] on these Michael reactions as well as isolation of an insoluble species[53] that was convertible to a β substituted ketone (implying that the unknown species was the enolate, **64**)[53] suggest a process involving intermediates that unimolecularly rearrange to the enolate (**64**, Scheme 29). The correlation of reduction potentials of α,β-unsaturated carbonyl systems with cuprate reactivity has given rise to a proposal involving a single electron transfer mechanism.[54] Initial Lewis acid-Lewis base interaction (**63**, Scheme 29, step $\mathbf{a_1}$) encourages transfer of an electron from a dimeric cuprate to the enone to give **65** (Scheme 29, step $\mathbf{a_2}$) followed by formation of a copper-carbon bond in the species **66** (Scheme 29, step $\mathbf{a_3}$). Reductive elimination (Scheme 29,


Charge transfer complex
+ R3Cu2Li
1/2 R4Cu2Li2 + (RCu)n
R = Me, Me(2-thienyl)

Scheme 29

step a_4) from the Cu(III) species **66** affords the enolate **64**, although the exact nature of **M** in the species **64** is still an open question. Intermediate **66** can also arise by way of an initial charge transfer complex (**67**, Scheme 29, step $b_1 \rightarrow b_2$ or *via* $b_3 \rightarrow a_3$).[55] Still more direct would be the nucleophilic addition of the reagent to the β carbon atom of the substrate[56] without the intervention of a single electron transfer step (Scheme 29, step $a_1 \rightarrow c_1 \rightarrow c_2$). Direct carbocupration to give an α–cuprioketone (**69**, Scheme 29, step d_1 or *via* steps $a_1 \rightarrow c_1 \rightarrow d_2$) followed by rearrangement to the thermodynamically more stable lithium enolate (Scheme 29, step d_3) is another alternative.[57]

The notion of an early intermediate complex (beyond that of simple Li^+ coordination) has gained considerable momentum since its original formulation. Infrared spectroscopic studies of reactions involving unsaturated esters[58] and, in particular, low-temperature ^1H and ^{13}C NMR studies of the reaction of Gilman's reagent, Me_2CuLi[59] (**1**) and of the mixed lower order cuprate Me(2-thienyl)CuLi[60] with cinnamate esters (**70**) provide cogent evidence for binding between copper and the π* MO of the enone. Thus, addition of **70** and **1** in THF-d_8 at -70°C gave an intermediate species in which the ^{13}C labelled C_2 carbon shifted upfield by 55 ppm to give a quartet of signals at 53.7, 52.6, 51.0 and 49.9 ppm which were ascribed to an intermediate π-complex.[60,61]



70

These shifts are in the range of coordination shifts (~ 60 ppm) for trigonal alkene-transition metal complexes of Ni, Pd and Pt.[62,63] Since diastereoisomerism would be expected to yield only two π–complexes (i.e., only two signals) the additional signals must be related either to *E, Z* isomerism, solvent association or aggregation state.[59,60]

The study described here involved measurements of the ^{13}C NMR spectra of solutions generated during the addition of metallocuprates to cyclohex-2-ene-1-one (**32**) at low temperature with the aim of observing resonances due to the copper containing species formed following the delivery of R_3M (M = Si or Sn) from $(R_3M)_n(Me)CuLi_{n-1}\cdot LiCN$ to **32**. The logical byproduct of ligand transfer is the LO cyanocuprate MeCu(CN)Li (**16**) which should be observable over time.

When reactions of **32** with $PhMe_2Si(Me)Cu(CN)Li_2$ (**43**) or $Me_3Sn(Me)Cu(CN)Li_2$ (**56**) were monitored by ^{13}C NMR spectroscopy at -85°C the appearance and gradual increase of a peak at -13.5 ppm corresponding to **16** was readily discerned.There was also evidence for the involvement of a π–complex between higher order silyl- (**29** and **43**) as well as HO stannylcuprate (**56**) and cyclohex-2-ene-1-one (**32**).

The ^{13}C NMR spectra of the cuprates and cyclohex-2-ene-1-one are complex. Some features, however, are prominent and facilitate interpretation. These are particularly the methyl signals and the signals of the C_2 carbon of the enone as illustrated in Figure 36a. On addition of $(PhMe_2Si)_3CuLi_2$ (**29**) at -85°C to **32** the resonances for C_2 (120.9 ppm) and C_3 (150.7 ppm) of **32** disappear and several closely spaced signals are generated that are initially centered around 60 ppm (59.2 and 61.7 ppm) and around 35 ppm (32.7 and 33.8 ppm). Coincident with these new signals, four major (-2.37, -2.69, -4.4, -5.14 ppm) and two minor (3.9, 4.0 ppm) resonances attributable to silyl bound methyls appear. As the solution is allowed to stand at -70°C, the high field methyl resonances at -4.4 and -5.14 ppm disappear while those at 3.9 and 4.0 ppm grow. This

is accompanied by a decrease in the signal intensities near 60 and 35 ppm and an increase at 38.6 and 23.7 ppm. The signals originally obtained for the nitrile carbons (159.4 ppm) are replaced by another at 152 ppm. Workup of this reaction yields **33** (Scheme 30). It is attractive to attribute the signals centered at 35 and 60 ppm to C_2 and C_3 of a copper-alkene-π–complex (**68**, Scheme 29, R = $PhMe_2Si$) while the signals at 38.6 and 23.7 ppm are attributed to the C_2 and C_3 of the enolate **64** (Scheme 29, R = $PhMe_2Si$). The signal due to the C_3 carbon of the product appears at 26 ppm. The upfield methyl shifts at -2.37 and -2.67 and -4.4 and -5.14 are assigned to the silicon bound methyls in the α–cuprioketone, **69** (Scheme 29) and the copper-alkene-π–complex, **68** respectively (Scheme 29, R = $PhMe_2Si$). The signal due to the carbonyl (C_1) is difficult to distinguish from the baseline noise due to long relaxation decay of the quaternary carbon.

Similarly, the low-temperature ^{13}C NMR spectrum of $PhMe_2Si(Me)Cu(CN)Li_2$ and **32** shows four major signals at -2.37, -2.67, -4.40 and -5.14 ppm and two minor signals at 3.9 and 4.0 ppm (Figure 36b). The important feature is the appearance of signal at -13.5 ppm corresponding to MeCu(CN)Li (**16**) as a result of exclusive silyl group transfer from the silylcuprate to cyclohexenone. The appearance of **16** suggests that under these conditions, some addition of **43** to **32** has occurred. It also allows one to deduce that lithium is coordinated to the enolate product, **64** (Scheme 29, M = Li). One set of doublets (3.9 and 4.0 ppm) may be attributed to the silyl bound methyls in the common enolate adduct (**64**, Scheme 29). The corresponding signals for C_2 of the adduct appear around 40 ppm while those for C_3 absorb at 24 ppm. These signals are close to that expected for the silyated enolate corresponding to **64** (R = $PhMe_2Si$). The broad signal for the nitrile (159.4 ppm) is replaced by another at 151.3 ppm as the reaction progresses. The other remaining set of signals around 60 and 35 ppm are hypothesized to be due to a copper-alkene π–complex (corresponding to the adduct **68**, Scheme 29).[59-61]

The formation of a chiral center on mixing a silylcuprate (**29**) with **32** is a straight-forward basis for the presence of two signals for silyl bound methyls in the ^{13}C NMR spectrum corresponding to the enolate **64** (3.9 and 4.0 ppm) and the copper-alkene π–complex **68** (-4.4 and -5.14 ppm; Scheme 29). The presence of lithium salts

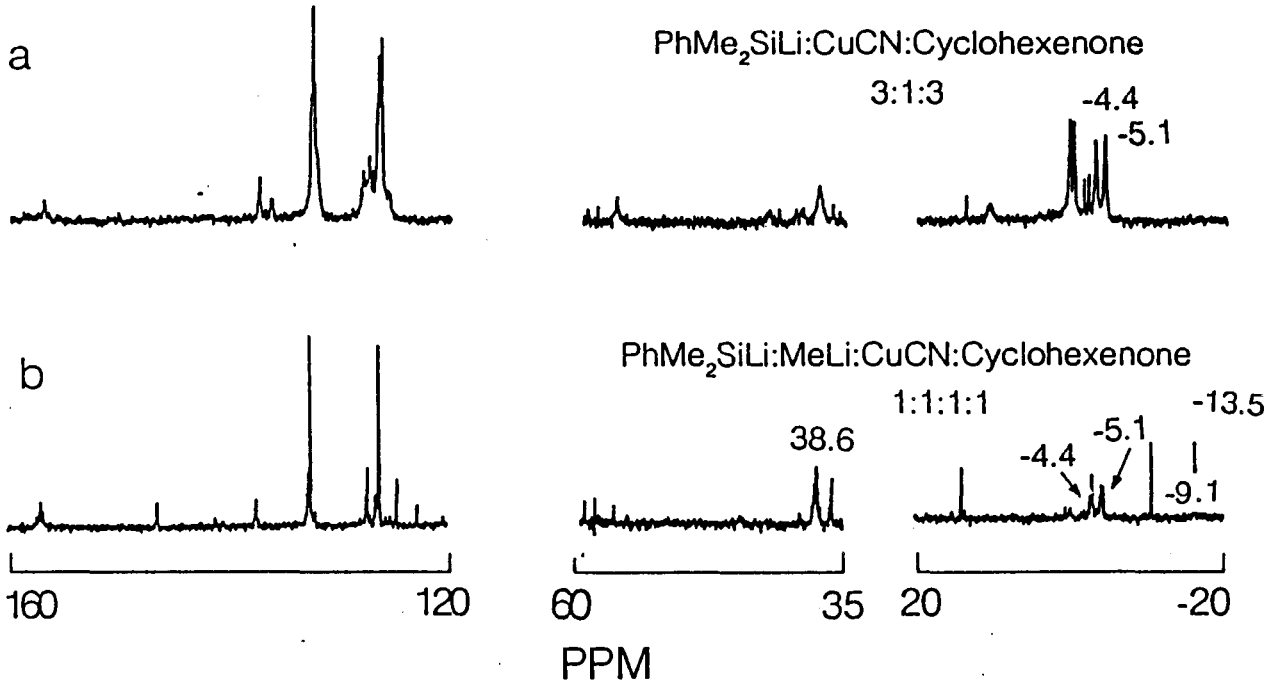


Figure 36. ^{13}C NMR spectra of (a) $(PhMe_2Si)_3CuLi_2$ + 3.0 equiv 32 (b) $PhMe_2Si(Me)Cu(CN)Li_2$ + 32; the spectra were run at -85°C.

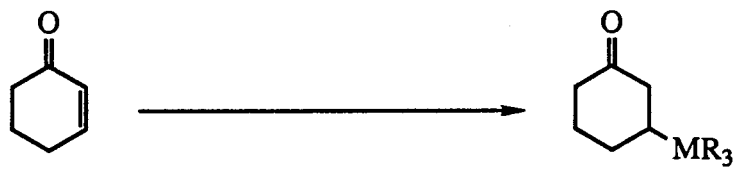
in the solutions of these cuprates may be responsible for the appearance of additional signals at -2.4 and -2.7 ppm. Coordination with these salts may result in the formation of a stable adduct **69** (Scheme 29) since no signals were obtained around -2.0 ppm in solutions free of LiCl. Alternatively, the aggregation state of the silylcuprates and the π-complexes could vary and hence give rise to species the enone carbons in different magnetic environments.

Similar results were obtained by using the HO homocuprate **28** and the HO stannylcuprate **56**. In the latter case signals near 35 ppm along with a doublet centered at 12 ppm were produced on initial mixing at -85°C and these signals disappeared as signals for stannylated enolate (38 ppm) and MeCu(CN)Li (δ -13.5) appeared.

On the basis of this preliminary spectroscopic information, it is proposed that conjugate addition of mixed metallocuprates to α,β-unsaturated ketones involves initial formation of an intermediate copper(I)-olefin-π-complex **68** which is stable at very low temperatures. In the presence of lithium salts appreciable amounts of α–cuprioketone (**69**) is also produced. Warming the solutions leads to exclusive delivery of the metallo anion with simultaneous formation of the LO alkylcyanocuprate.

In accordance with our NMR results, it was found that solutions of $PhMe_2Si(Me)Cu(CN)Li_2$ (**43**), $Me_3Sn(Me)Cu(CN)Li_2$ (**56**) and $Bu_3Sn(Me)Cu(CN)Li_2$ (**61**) deliver a $PhMe_2Si$ or R_3Sn (R = Me, Bu) group

Scheme 30. Reaction of metalocuprates with **32.**



32

33 M = Si; R_3 = $PhMe_2$
70 M = Sn; R_3 = Bu or Me

43	$PhMe_2Si(Me)CuCNLi$	94%
44	2 $PhMe_2SiLi$:MeLi:CuCN	91%
45	3 $PhMe_2SiLi$:MeLi:CuCN	87%
56	$Me_3SnCu(Me)(CN)Li_2$	92%
61	$Bu_3SnCu(Me)(CN)Li_2$	96%

exclusively *via* 1,4-addition to cyclohex-2-en-1-one (**32**) to give 3-silyated (**33**) or 3-stannylated (**70**) cyclohexanones respectively (Scheme 30).[32,46] 3-Methyl-cyclohexanone which would be produced from 1,4-addition of a methyl group was not observed.

Thus, the transferability of R_3Si or R_3Sn anions bound to copper is higher than that of the methyl ligands. The preference for R_3M (M = Si or Sn) transfer presumably reflects the kinetic reactivities of higher order mixed metallocuprates, as well as the stability of the resulting lower order reagent formed [i.e., Me(Cu)CNLi].

Conclusion

These studies indicate that higher order cuprates containing silyl or stannyl and alkyl anionic ligands (e.g., $R_3Si(R')CuLi{\cdot}LiX$ (**41**) and $R_3Sn(R')CuLi{\cdot}Li$ (**42**) are similar to alkyl cuprates (**17**) with respect to their tendencies to readily exchange ligands between copper centers. These studies also present evidence that such mixed cuprates transfer silyl and stannyl ligands in preference to alkyl ligands in reactions with α,β-enones. The formation of a copper(I)-alkene complex as an initial step of the conjugate addition of homo-trialkylsilylcuprates, homo-trialkylstannylcuprates as well as mixed stannyl- or mixed silylcuprates to enones has been demonstrated but additional work using a ^{13}C labelled enone is required to firmly establish the suggested parallel.

Final comments

One of the overriding questions regarding the nature of metallocuprates is the aggregation state of the solution species. If one uses a chiral ligand R* to prepare

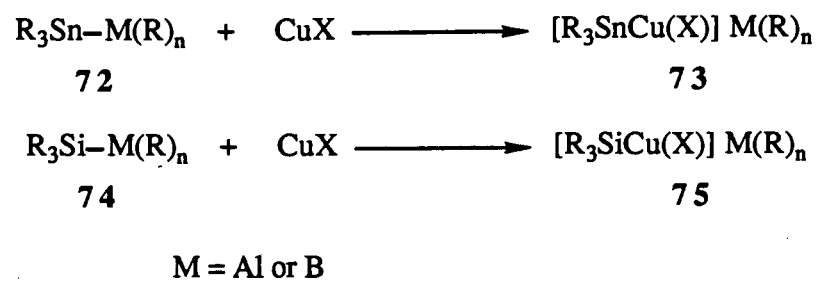
$R^*(R_3M)Cu(CN)Li_2$ then if the R* is optically pure and the species is monomeric one should obtain signals for the ^{13}C and ^{1}H spectra of the species (i.e., same δ for R and S). If the R* is optically pure and the species is dimeric, a single signal should appear for each magnetically nonequivalent atom. If the R* is racemic and the species is monomeric then one signal should appear for each magnetically nonequivalent atom. If, on the other hand the species is dimeric then atoms magnetically equivalent in the monomer would appear nonequivalent in the dimer and give more than one signal due to the diastereoisomeric species that are possible (different signals for RR, SS and RS and SR).

IN SITU GENERATION OF ACTIVATED METALLOCUPRATES

During the evolution of stoichiometric lithium-based stannyl- and silylcuprates in synthetic chemistry,[27-32] one aspect of their chemistry that has been invariant is their mode of preparation.[27,28] Both lower order and higher order stannyl- and silylcuprates are routinely prepared from Cu(I) salts and 1 or 2 equivalents of R_3MLi (M = Sn or Si). When the Cu(I) salts are cuprous halides 2.0 equivalents of R_3MLi are required to induce *ate* formation. When CuCN is used direct *ate* formation occurs. This contrasts with organometallic chemistry outside the organocopper arena where preformed organometallic complexes are commonly produced *via* ligand exchange between metal centers.[1]

As reported in the previous section ligand exchange [e.g., $R_2Cu(CN)Li_2$ and $(R_3M)_2Cu(CN)Li_2$, M = Si or Sn] readily occurs between silylcopper or stannylcopper derivatives and alkylcopper systems. The equilibria established by the many combinations examined led to the view that exchange between anionic organic ligands such as R_3Si, R_3Sn and alkyl associated with cuprous ion is indeed facile. On the basis of these observations, it was decided to examine the chemistry associated with ligand migration on copper where ligands with different electropositive metals are involved.

Specifically, it was envisioned to prepare derivatives of trialkylstannyl and trialkylsilyl anions in which the counter ion is a metal-containing species capable of exerting an effect as an electrophilic additive. An example of the type of reaction we hoped to achieve is shown in Scheme 31.



Scheme 31

These reactions were of interest because, if successful, they would allow the *in situ* generation of activated stannyl (**73**) and silylcuprates (**75**) directly from trialkylstannyl- (**72**) and trialkylsilyl metalloids (**74**) respectively, thereby bypassing the generation of thermally labile stannyl- or silylcuprates. Mixed ligand cuprates such as **73** and **75** would, by analogy to activated alkylcuprates, possess increased reactivity toward organic substrates. If the stannyl and silylcuprates are indeed activated by the presence of the electrophilic $M(R)_n$ group, the literature did not give an indication of this at the onset of our work.

Certainly, one of the recent and most encouraging aspects of organocuprate chemistry has been the improvement made in reactivity when other species are added to the reactions of lower or higher order alkylcuprates.[6] Phosphorus-containing compounds (e.g., phosphines and phosphites, etc.) have been utilized for decades to solubilize the cuprous(I) salts and also to act as stabilizing ligands. Recently, however, the use of electrophilic species such as $BF_3{\cdot}Et_2O$, Et_2AlCl, $ZnBr_2$, $MgBr_2$, $TiCl_4$ and Me_3SiCl with Gilman cuprates (R_2CuLi, **2**) has significantly expanded the scope of this methodology.[6] In general, these electron-deficient reagents tend to increase both the rates and yields of cuprate reactions. Since no changes in protocols for cuprate use are necessary, aside from the introduction of additive, it is not surprising that the frequency of their use continues to grow.[2,6]

Although commonly used, little is actually known about the role of these Lewis acids in the reactivity modification. It is presumed that these additives function by Lewis acid-base complexation with the substrate while the cuprate remains unperturbed. However, it has been recently shown by low-temperature NMR spectroscopy that the addition of Lewis acids such as $BF_3 \cdot Et_2O$ and Me_3SiCl leads to formation of modified cuprates.[64,65] Thus, addition of $BF_3 \cdot Et_2O$ to a solution of $Me_2Cu(CN)Li_2$ (**17**) leads to immediate association of the nitrile ligand of the cuprate with the additive. It also sequesters MeLi from the cuprate cluster to form $MeLi \cdot BF_3$ and the lower order cuprate MeCu(CN)Li (**16**, Scheme 32).[64]

$$\underset{\mathbf{17}}{Me_2Cu(CN)Li_2} + BF_3\,Et_2O \longrightarrow MeLi.BF_3.Et_2O + \underset{\mathbf{16}}{MeCu(CN)Li}$$

Scheme 32

Similarly, Me_3SiCl reacts with the higher order cuprate **17** to give Me_3SiCN and the corresponding lower order cuprate **1** (Scheme 33).[65]

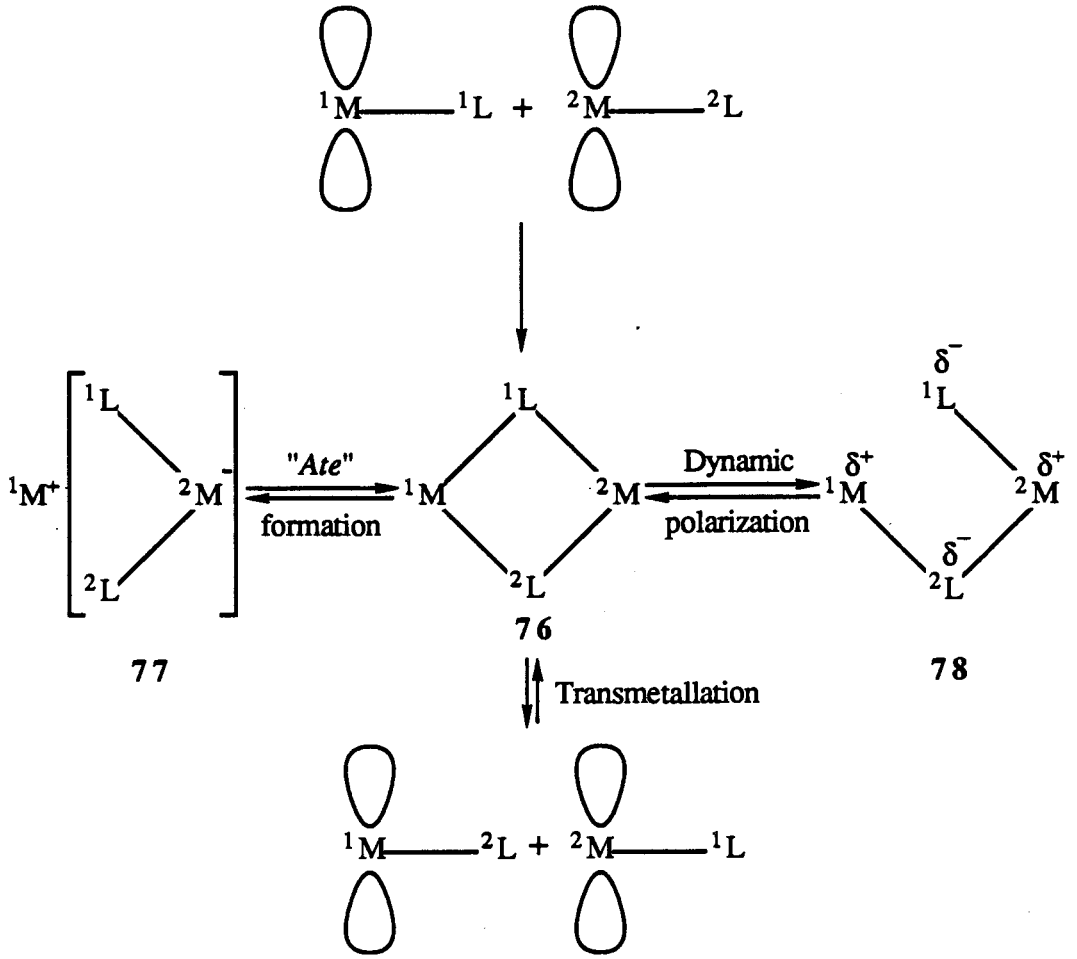
$$\underset{\mathbf{17}}{Me_2Cu(CN)Li_2} + Me_3SiCl \longrightarrow Me_3SiCN + LiCl + \underset{\mathbf{1}}{Me_2CuLi}$$

Scheme 33

Our reasons for expecting the desired ligand exchange (Scheme 31) to occur lay in the strong tendency of organodimetallics containing coordinatively unsaturated metals to form bridged complexes[1] (**76**) through three-center-two-electron bonds. Where

participating metals are identical, such associations are of little synthetic consequence. When the metals are different, however, it can lead to transmetallation, *ate* formation or complexes in which the charge has been reversed on ^2M compared to that in *ate* formation (Scheme 34).[1]

When the electronegativities of ^1M and ^2M are substantially different, the more



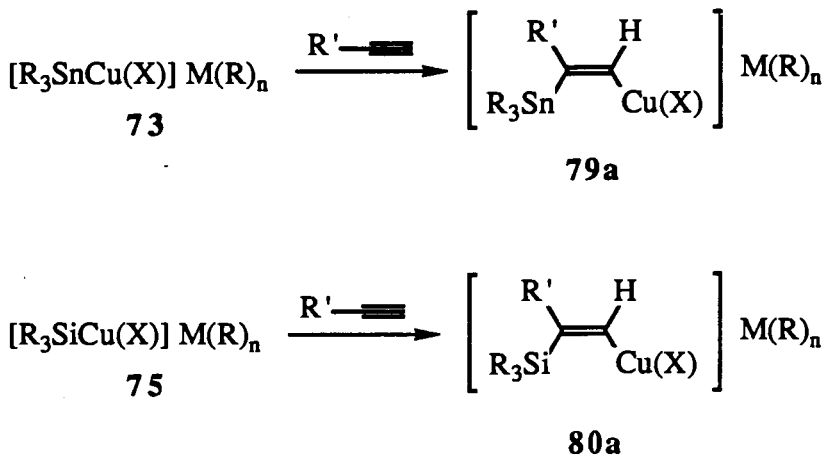
Scheme 34

electronegative metal is reported to attract both bridging ligands, i.e., ^{1}L and ^{2}L, inducing *ate* formation as shown in **77**. *Ate* formation increases the nucleophilicity of the ^{2}M-^{2}L moiety, as in the conversion of organocoppers[2] to lower order, (R_2CuLi),[2,4] or higher order, ($R_2Cu(CN)Li_2$),[2,7,8] cuprates. *Ate* formation is also responsible for increasing the nucleophilicity of carbon-metal adducts during the conversion of organoboron and organoaluminum compounds into organoborates[66] and organoaluminates.[67] It can also suppress undesirable electrophilicity of the ^{2}M center, such as the B and Al atoms of organoboranes and organoalanes, respectively.[1]

Alternatively, transmetallation can result from dissociation of the bridged species **76** into two new coordinatively unsaturated species.[1,68] This is a very general process in organometallic chemistry.

Finally, polarization[69] within **76** through three-center-two-electron bridging of the two metal centers can occur as shown in **78**. The ^{2}M center in **78** is both coordinatively unsaturated and positively charged. Such metal centers are more electrophilic than in the unpolarized monomer.

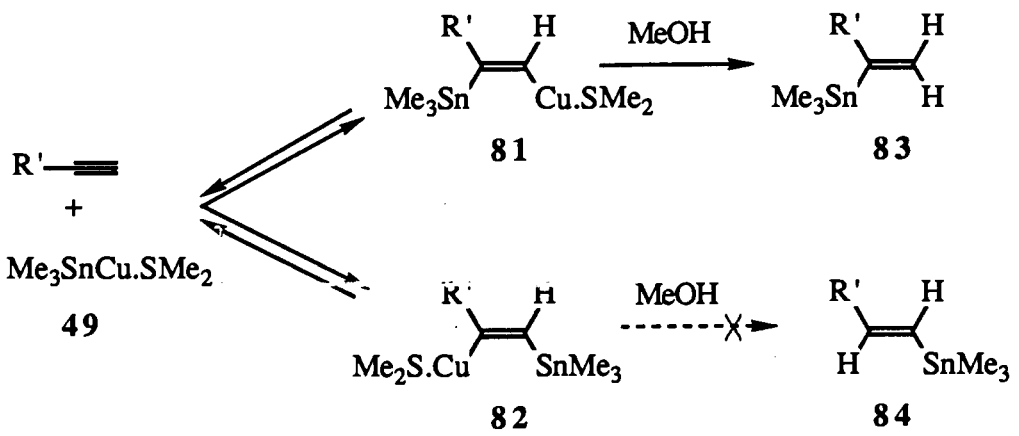
Since the types of species (**73** and **75**) expected to be produced in Scheme 31 were logical intermediates in the cuprous ion catalyzed reaction of stannyl and silyl metalloids with 1-alkynes, we adopted the reaction in Scheme 35 as a test of the aforementioned strategy of *in situ* activation.



Scheme 35

Cu(I) MEDIATED METALLOMETALLATION OF 1-ALKYNES

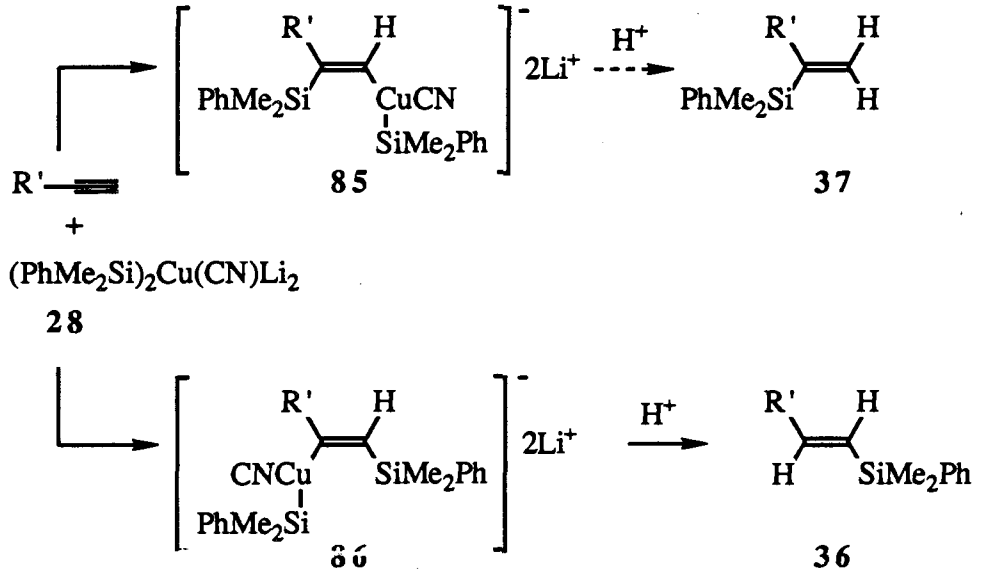
The first synthetically useful metallometallations of 1-alkynes were those involving the addition of the stannylcopper reagent **49** to 1-alkynes (Scheme 36).[28c,30e-h]



Scheme 36

These reactions give products possessing the regiochemistry shown in **83** almost entirely devoid of **84**.[30g] The presumptive initial adducts (**81** and **82**) were reported to require consumption of the vinyl-copper center by *in situ* protonolysis, presumably to overcome an unfavorable adduct → alkyne equilibrium.[28a,30g] Attempted capture of the intermediate vinyl-copper compounds with electrophiles other than proton was unsuccessful.[30e-h]

Parallel with the development of stannylcupration, addition of silylcuprates (**28**) to 1-alkynes was investigated (Scheme 37).[30a-d] In the resulting adducts (**85** and **86**) subsequent capture of the vinyl-copper bond with both proton and carbon electrophiles was achieved and yielded vinyl silanes (**36** >> **37**) possessing regiochemistry opposite to that observed in the case of stannylcuprations.[30a-d]

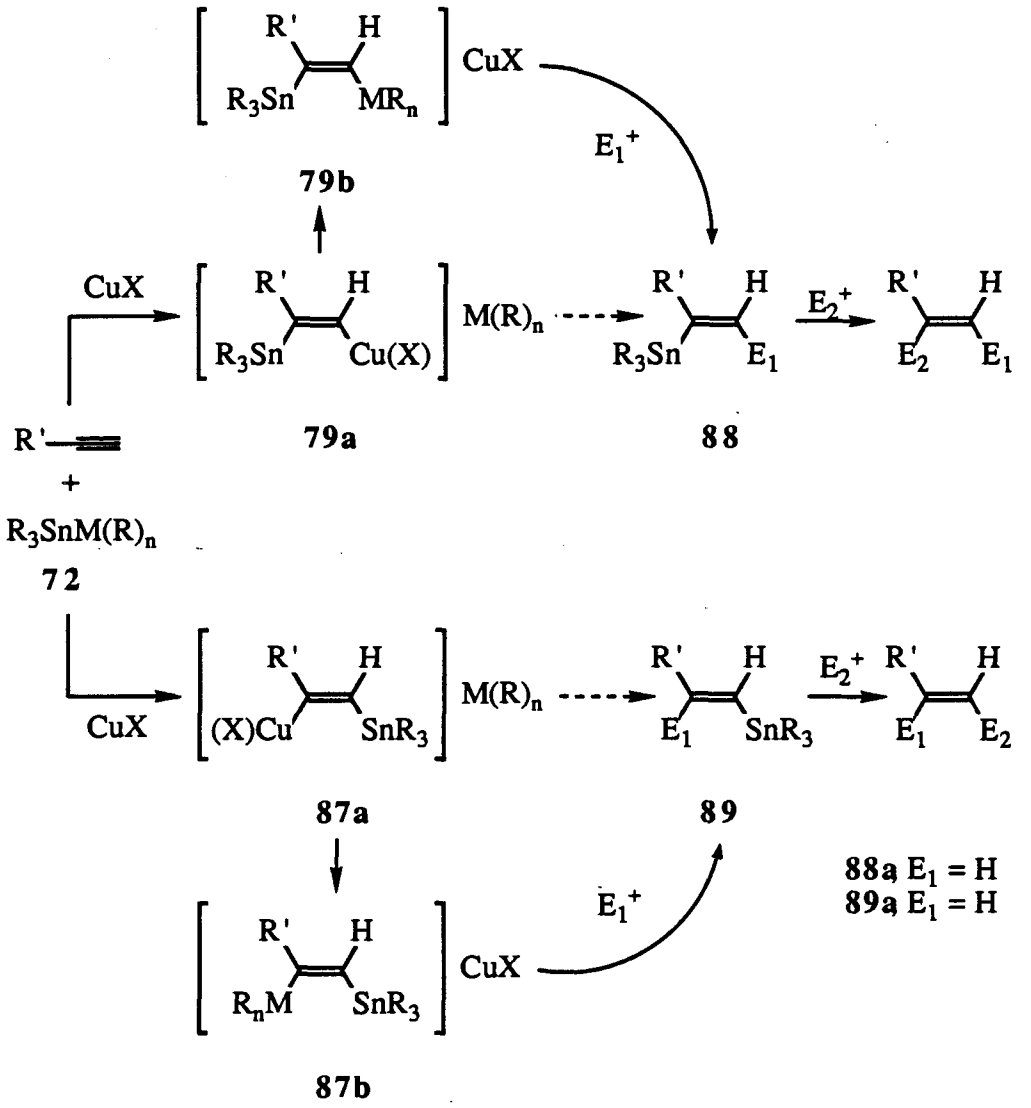


Scheme 37

Regiochemical control is a challenge because additions of Si-Cu and Sn-Cu reagents to 1-alkynes are reversible.[28a,30g] Thus, the first step in Schemes 36 and 37 is reported to be thermodynamically unfavourable, and the stannylcupration (Scheme 36) is reported to proceed to completion only when an alcohol is present *in situ* to hydrolyze the vinyl carbon-copper bond in the intermediate **81**.[30g] Assuming a reversible reaction, the regiochemistry in metallocupration reactions would probably be dictated by the greater ease of protodecupration of **81** and **85** than of its regioisomer **82** and **86** respectively. Thus, other factors must be at work to explain why stannylcupration yields 2-stannylated alkenes (**83**) form 1-alkynes whereas silylcupration yields 1-silylalkenes (**36**).

Metallometallation of 1-alkynes has been developed as an extention of stannyl- and silylcuprations of 1-alkynes (Scheme 38, shown for stannylmetallation only). Such reactions have been sucessfully extended to bimetallic reagents derived from Sn-Al,[48b,c,70] Sn-Mg,[70] Sn-Zn,[70] Sn-Mn,[71] Sn-B,[48a,72] Sn-Si,[73] Sn-Sn,[74] Si-Al,[75] Si-Mg,[75] Si-Zn,[75,76] Si-Si[77] and Si-Mn.[71,78] Additions are very slow without added catalysts; Cu(I) and Pd(0) complexes have emerged as the most effective catalysts in terms of yields and regiochemical bias. In the case of Cu(I) catalysis one can postulate **79a** and **87a** as the initial adducts. For Cu^+ to behave as a catalyst, subsequent reaction of the vinyl carbon-copper bonds in **79a** and **87a** must occur to give the products (**79b** and **87b**, respectively) of transmetallation by $M(R)_n$. The reactivities of these final adducts (**79b** and **87b**) require electrophilic consumption of the more reactive organometallic center prior to isolation and yield **88** and **89** respectively. Reaction of the second vinyl organometallic center with an electrophile commonly involves electrophilic addition in case of silicon[79] or transmetallation in case of tin.[80] Thus, the utility of metallometallation lies in the simultaneous generation of two stereo- and regiodefined vinyl organometallics of differential reactivity.

Several problems beset the stannyl and silylmetallations of 1-alkynes shown in Table III. Reactions utilizing reagents wherein $M(R)_n$ = Al,[70,75] Mg[70,75] and Zn[74,75,76] are reported to require a three fold excess of reagent to achieve high alkyne consumption. The use of excess reagent leads to the formation of by-products which are



Scheme 38

Table III. Addition of Silyl- or Stannylmetalloids to 1-alkynes.

	Reagent	Catalyst	Conditions	%yield	88a	89a
1	$Bu_3SnAlEt_2$	CuCN	THF, 0°C	87	62	38
2	$Bu_3SnMgMe$	CuCN	THF, 0°C	70	30	70
3	$(Bu_3Sn)_2Zn$	$Pd(PPh_3)_4$	THF, 0°C	70	95	5
4	$(Bu_3Sn)_2Zn$	$Pd(PPh_3)_4$	TMEDA,0°C	50	50	50
5	$(Bu_3Sn)_2Zn$	CuCN	TMEDA,0°C	83	83	17
6	Bu_3SnBEt_3Li	CuCN	THF, 0°C MeOH	40	35	65
7	$Me_3SnSiMe_3$	$Pd(PPh_3)_4$	60-70°C 48h	65	90	10
8	$Me_3SnSnMe_3$	$Pd(PPh_3)_4$	85°C	29	NA	
9	$Me_3SnSnMe_3$	$Pd(PPh_3)_4$	THF, 25°C	82	NA	
10	$PhMe_2SiAlEt_2$	$RhCl(PPh_3)_3$	THF, 0°C	70	9	91
11	$PhMe_2SiMgMe$	CuI	THF, 0°C	86	1	99
12	$PhMe_2SiBEt_3Li$	CuCN	THF, 0°C MeOH	89	39	61
13	$(Me_3Si)_3MnMgMe$		THF, 0°C	66	33	67
14	$Ph_3SiZnEt_2Li$	CuI	THF, 25°C	90	-	100
15	$PhMe_2SiZn^tBu_2Li$	CuCN	THF, 25°C	92	99	1
16	$(PhMe_2Si)_2Zn$	$RuCl_2(PPh_3)_2$	THF, 0°C	75	80	20

not easily separated from the vinylsilane[30a,c,46] or stannane[48] products. Regiospecificity is high for some stannylmetallations (Scheme 38, Table III) **88a/89a**, Sn-Zn[70] (95/5), Sn-Si[73] (90/10) but low for others Sn-Al[70] (62/38), Sn-Mg[70] (30/70), and Sn-B[72] (35/65). Only for the Sn-Zn and Sn-Si cases is the regiochemical bias synthetically useful. Control of regiochemistry in the addition of $R_3Si\text{-}M(R)_n$ and $R_3Sn\text{-}M(R)_n$ reagents to 1-alkynes is a goal that has been pursued only for silicon-zinc reagents. Nozaki and co-workers[75] reported that the Cu^+ catalyzed addition of $Ph_3SiZnEt_2Li$ to 1-alkynes gave only regioisomer **89a**. A related reagent[76] possessing larger zinc alkyl groups, $PhMe_2SiZn^tBu_2Li$, added to 1-alkynes to give almost exclusively (>99:1) the alternate regioisomer, **88a**.[76]

Proposed work

It is proposed to study the scope and mechanism of copper catalyzed addition of stannyl and silylmetalloids to 1-alkynes with an aim to:

i) determine if metallocuprates containing electrophilic cationic metals are activated towards electrophilic consumption of the vinyl copper bond in the expected adducts.

ii) achieving regiochemical control.

iii) determining the synthetic potential and utility of the expected vinyl metal bonds in the adducts.

iv) determine the compatibility of metallometallations with polar functional groups.

Applications of the developed chemistry to the synthesis of pheromomes.

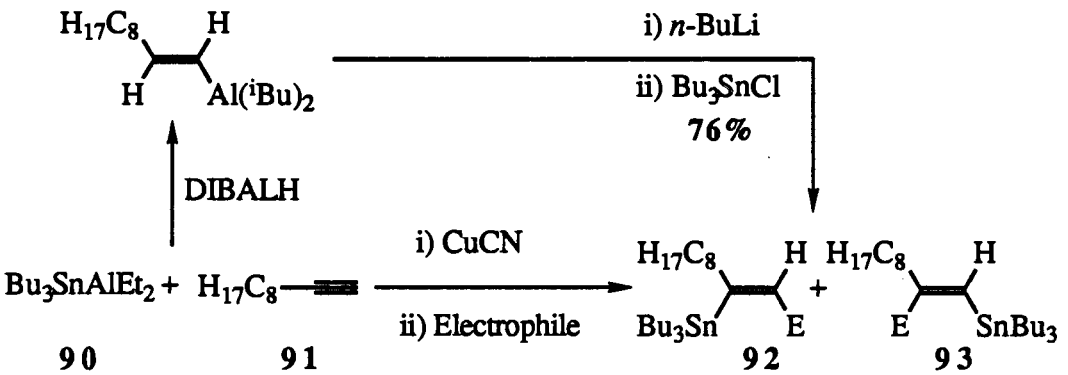
Effect of Method of Preparation of Trialkylstannylithium on the Efficiency of Stannylalumination and Stannylboronation

Capture of R_3SnLi by methyl iodide provided a facile assay of the efficiency of R_3SnLi preparation (Table IV). Reaction of Bu_3SnH[81] with LDA (entry 5)[49a] at low temperature and reaction of $Me_3SnSnMe_3$ with MeLi (entry 6) were clearly the most efficient.[30d]

Table IV. Efficiency of Production of R_3SnLi Observed Upon Quenching with MeI

Entry	Reactants and Conditions	% yield of R_3SnMe	By-Products(% yield).
1	$SnCl_2$, 3BuLi, THF, 0°C, 15min.	33	Bu_4Sn (45%), Bu_3SnCl (15%).
2	Bu_3SnCl, Li (wire) THF, 0°C, 24h.	48	Bu_6Sn_2 (30%), Bu_4Sn (30%), Bu_3SnCl (4%).
3	Me_3SnCl, Li (dis) THF, 0°C, 8h.	70	Me_6Sn_2 (30%).
4	Bu_3SnH, BuLi, THF, 0°C, 15min.	4	Bu_4Sn.
5	Bu_3SnH, LDA, THF, -30°C, 15min.	90	Bu_6Sn_2 (8%).
6	$Me_3SnSnMe_3$, MeLi -40°C, THF, 20min.	80	

Reaction of Bu_3SnLi with Et_2AlCl in THF gave solutions of $Bu_3SnAlEt_2$ (**90**) which, in the presence of Cu^+ salts, reacted with 1-decyne (**91**) to give, after protonolysis, the vinyl stannanes **92a** and **93a** (Scheme 39, Table V). *In situ* addition of a proton source was not necessary to achieve high conversion of alkyne to product in these reactions. Indeed, the more efficient the reaction yielding Bu_3SnLi, the more efficient the subsequent stannylalumination of 1-decyne (Table V, compare entries 1 and 2; 3 and 4; and 5 and 6). Vinyl stannanes (**92a** and **93a**) were separated by preparative gas chromatography and their structures deduced by ^1H, ^{13}C and ^{119}Sn NMR



Electrophile			
HCl	**92a**, E = H	90%	**93a**, E = H
^2HCl	**92b**, E = ^2H	92%	**93b**, E = ^2H
CH_2=$CHCH_2Br$	**92c**, E = CH_2CH=CH_2	89%	
MeI	**92d**, E = Me	76%	**93d**, E = Me
$PhCH_2Br$	**92e**, E = CH_2Ph	84%	
PhI	**92f**, E = Ph	79%	

Scheme 39

spectroscopy as well as GC-MS. Evidence for the structure and stereochemistry of **92a** and **93a** was provided by the magnitude of the coupling constants ($^3J_{Sn-H}$ ~ 140 Hz for **92a** and ~ 70 Hz for **93a**) between the ^{117}Sn and ^{119}Sn isotopes and ^1H. These values are typical of vinyl stannanes having trialkylstannyl groups *trans* and*cis* , respectively to vinyl hydrogens.[50] *Cis* addition to the alkyne was confirmed by the disappearance of the high field[70] vinyl hydrogen signal in the ^1H NMR spectrum of **92b** when the reaction of **90** ($Bu_3SnAlEt_2$) with **91** (1-decyne) was quenched with ^2HCl. Regioisomer **93a** was prepared independently by hydroalumination[67] of **91** with DIBALH, transmetallation (*n*-BuLi) and reaction of the alkenylalanate with Bu3SnCl (Scheme 39). Proton magnetic resonance and mass spectra as well as the gas chromatographic retention time of this sample were indistinguishable from those of **93a** obtained by metallometallation (Scheme 39).

Effect of Catalyst on Stannylalumination

Use of Pd°, Pd^{2+} or Cu^+ complexes as catalysts resulted in efficient addition of $Bu_3SnAlEt_2$ (**90**) to 1-decyne, **91** (Table V). Addition of **91** to THF solutions of **90** at -30°C in the presence of Cu^+ salts resulted in high yields of vinyl stannanes **92a** and **93a** with a synthetically useful regiochemical bias favoring **92a**. Use of CuCN gave higher yields and higher regiochemical bias than CuBr·Me_2S (Table V, compare entry 2 with 8). Regioisomer **93a** was favored (90:10) when CuI was used as the catalyst (compare entry 2 with 4). Catalysts based on Pd° generally gave mixtures of **92a** and **93a** which were rich in **93a** (Table V, entries 5-7). Yields and regiochemical bias were lower for palladium catalysts than for CuCN.

Table V. Addition of $Bu_3SnAlEt_2$ to 1-Decyne.[a]

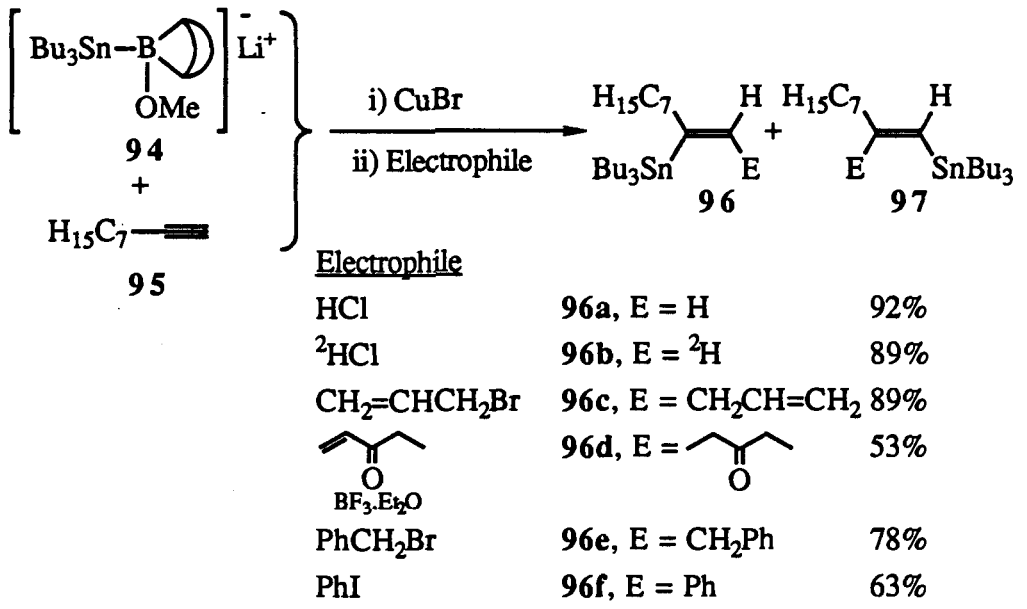
Entry	$Bu_3SnM(R)_n$	$Bu_3SnM(R)_n$ Alkyne	Catalyst (solvent)	Temp	92a	93a	%yield 92a+93a (alkyne unreacted)	Bu_4Sn	Bu_6Sn_2 ↓
1	$Bu_3SnAlEt_2$[b]	3:1	CuCN(THF)	-30°C	81	19	85(15)	52	8
2	$Bu_3SnAlEt_2$[c]	3:1	CuCN(THF)	-30°C	91	9	quant.	6	41
3	$Bu_3SnAlEt_2$[b]	3:1	CuI(THF)	-30°C	19	81	21(58)	50	7
4	$Bu_3SnAlEt_2$[c]	3:1	CuI(THF)	-30°C	10	90	51(22)	12	23
5	$Bu_3SnAlEt_2$[b]	3:1	$Pd(PPh_3)_4$ (THF)	0°C	35	65	36(28)	38	14
6	$Bu_3SnAlEt_2$[c]	3:1	$Pd(PPh_3)_4$ (THF)	0°C	15	85	44(21)	17	33
7	$Bu_3SnAlEt_2$[c]	3:1	$Pd(PPh_3)_2Cl_2$ 2DIBALH (THF)	-30°C	35	65	59(11)	15	17
8	$Bu_3SnAlEt_2$[c]	3:1	CuBr.Me_2S (THF)	-30°C	85	15	32(28)	12	31
9	$Bu_3SnAlEt_2$[b]	3:1	CuCN(HMPA)	0°C	6	94	45(51)	45	1
10	$Bu_3SnAlEt_2$[c]	3:1	CuCN(HMPA)	0°C	6	94	56(18)	22	37
11	$Bu_3SnAlEt_2$[c]	2:1	CuCN(THF)	-30°C	90	10	90(7)	11	28
12	$Bu_3SnAlEt_2$[c]	2:1 (inv)	CuCN(THF)	-30°C	76	24	57(24)	3	52
13	$Bu_3SnAlEt_2$[c]	1:1	CuCN(THF)	-30°C	92	8	31(53)	28	8
14	$Bu_3SnAlEt_2$[c]	1:1 (inv)	CuCN(THF)	-30°C	80	20	11(82)	0	48
15	$Bu_3SnAlEt_2$[d]	1:1.2	CuCN(THF)	-30°C	87	13	59(5)	15	15
16	$Bu_3SnAlEt_2$[d]	1:1.2 (inv)	CuCN(THF)	-30°C	90	10	21(43)	17	18

[a]See Scheme 39 for numbering. [b]Bu_3SnLi prepared from $SnCl_2$ and BuLi. [c]Bu_3SnLi prepared from Bu_3SnH and LDA. [d]Half of the theoretical amount of alkyne was added, followed by CuCN (5 mol %), then the remaining amount of alkyne.

Effect of the Mode of Addition of Reagents on Stannylalumination and Stannylboronation

A solution of **91** was added to a cold (-30°C) THF solution of **90** followed by the Cu^+ catalyst; it was then quenched with 1M HCl. This solution yielded vinyl stannane products (**92a** >> **93a**) of higher regiochemical purity than when the reaction was conducted by adding solutions of **90** to **91** (Table V, compare entry 11 with 12, 13 with 14, and 15 with 16).When the alkyne was added in one portion to the organometallic reagent it was necessary to use excess tin reagent to achieve high alkyne consumption (Table V, entries 2, 11 and 13). The excess reagent was eventually converted to hexaalkylditin and tetraalkyltin. Slow addition of alkyne to 1.2 equivalents of **90** at -30°C resulted in high alkyne consumption and minimal formation of hexabutylditin (Table V, entry 16). Excess 1-alkyne can presumably provide a proton, which can react with the intermediate generated. Normant has recently shown that slow addition of 1-alkynes to organometallics at low temperature improved yields of carbocupration reactions.[82]

Similarly, copper (I) catalyzed addition of [(Bu_3Sn-9-BBN•OMe)Li^+] (**94**) to 1-nonyne (**95**), followed by quenching with 1M HCl yielded vinyl stannanes (**96a** and **97a**) with high regiochemical bias (Scheme 40) in favour of **96a**. Use of ^{2}HCl as the quenching agent gave high yields of **96b**, confirming the *syn* mode of addition of **94** to the alkyne (**95**). Use of CuBr•Me_2S gave higher yields and higher regiochemical bias than CuCN. Regioisomer **97a** was favoured (60:40) when phenyl acetylene was used as the alkyne. As observed for stannylalumination (*vide supra*) yields and regiochemical bias were lower for palladium catalysts than for CuBr•Me_2S.



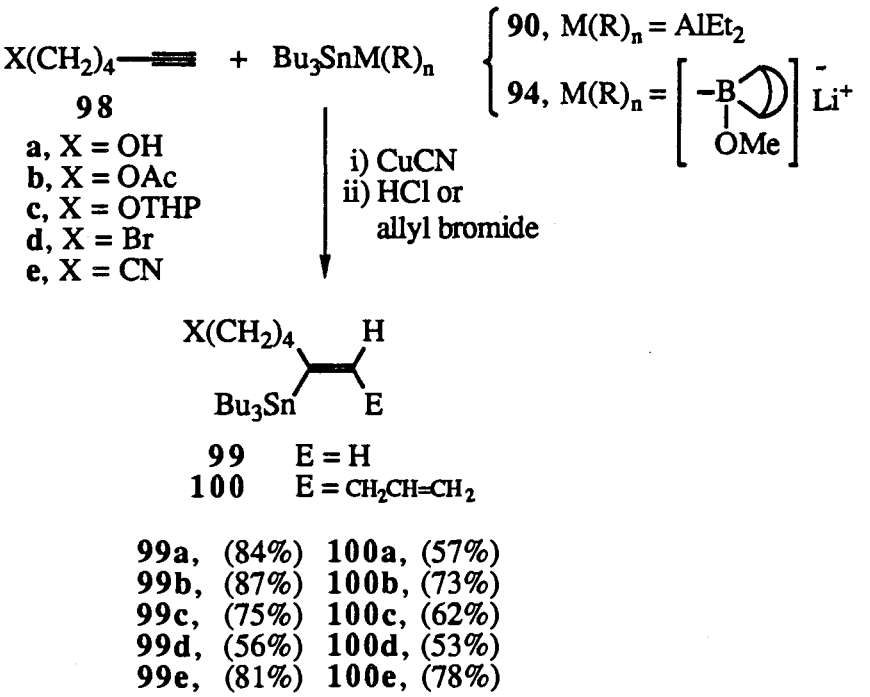
Scheme 40

Effect of Solvent on Stannylalumination and Stannylboronation

Addition of polar aprotic solvents such as dimethylformamide (DMF) or dimethylsulphoxide (DMSO) had no effect on the course of Cu(I) catalyzed stannylalumination. Addition of HMPA, surprisingly, reversed the regiochemistry of the reaction. The latter reactions were conducted by adding HMPA to cold THF solutions of Bu3SnLi followed by addition of Et2AlCl, 1-decyne (**91**) and CuCN. After consumption of **91** ceased the reaction was quenched with 1M HCl to yield vinyl stannane **93a** (Scheme 39) as the major regioisomer (94:6) (Table V, compare entry 1 with 9 and 2 with 10).

Compatibility of Polar Functional Groups with Stannylalumination and Stannylboronation

That stannylalumination and stannylboronation are compatible with polar functional groups was shown by the efficient reaction of $Bu_3SnAlEt_2$ (**90**) and [$(Bu_3Sn\text{-}9\text{-}BBN{\bullet}OMe)^-Li^+$] (**94**) with 5-hexyne-1-ol (**98a**), 5-hexyne-1-acetate (**98b**), 1-(tetrahydro-pyranyloxy)-5-hexyne (**98c**), 1-bromo-5-hexyne (**98d**) and 1-cyano-5-hexyne (**98e**) in the presence of Cu(I) catalysis to yield vinyl stannanes **99a - e** (Scheme 41). In case of 1-bromo-5-hexyne, a product arising from intramolecular cyclization resulting from the formation of the other regioisomer was also obtained. The only other tin containing product in these reactions were hexabutylditin which was easily separated



Scheme 41

by chromatography on silica. Furthermore, *in situ* protonolysis of the presumptive 1,2-dimetallo adduct, **79a** or **87a** (Scheme 38) is not necessary to achieve high consumption of alkyne if a reactive coupling reagent is added to the reaction.[83] Thus, addition of **94** to the functionalized alkynes (**98a-e**) with CuBr•Me_2S as the catalyst, followed by the addition of one equivalent of CuBr•Me_2S as the coupling agent and allyl bromide as the electrophile,[83] gave decent yields of **100a-e** with only minor contamination of the other regioisomer thereby making the entire process extremely versatile (Scheme 41).

Reactions of 1,2-*cis*-Dimetallo-1-Alkenes with Electrophiles.

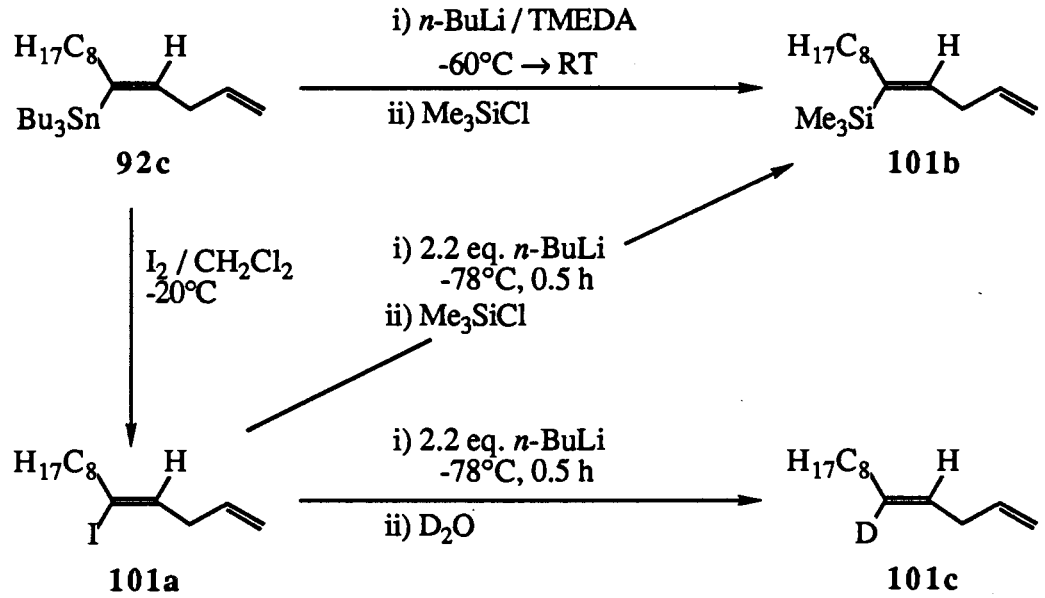
The dimetallic adducts generated in the reaction of $Bu_3SnAlEt_2$ (**90**) with **91** underwent either transmetallation with *n*-BuLi or Pd(0) catalyzed cross-coupling reactions exclusively at the vinyl-aluminum bond (Scheme 39). For instance, stannylalumination of 1-decyne catalyzed by CuCN, followed by transmetallation of the vinylalane moiety with *n*-BuLi resulted in the intermediate alanate. Reaction of the alanate with excess allyl bromide[84] in THF or methyl iodide in HMPA gave good yields of **92c** and mixtures of **92d** and **93d**, respectively. Addition of 3 mole% of $Pd(PPh_3)_2Cl_2$-2.0 DIBALH (diisobutyl aluminum hydride)[85] to the adduct derived from the addition of **90** to **91** under CuCN catalysis followed by addition of allyl bromide, benzyl bromide or iodobenzene[86] gave excellent yields of **92c**, **92e** or **92f** in high stereo- and regiochemical purity (Scheme 39).

Likewise, addition of 1-nonyne (**95**) to cold THF solutions of [(Bu_3Sn-9-BBN•OMe)$^-Li^+$] (**94**) followed by CuBr•Me_2S and use of allyl bromide[87a] and ethyl vinyl ketone in the presence of BF_3•Et_2O (1.0 equivalent) as the electrophile gave

modest yields of **96c** and **96d** respectively (Scheme 40). Addition of the mixture resulting from reaction of **94** and **95** to a solution of 5 mole% of $Pd(PPh_3)_4$ and allyl bromide,[87b] benzyl bromide,[87c] iodobenzene[87d] as the electrophiles and NaOMe as the base gave **96c, e-f** respectively in high regio and stereochemical purity (Scheme 40). No products arising from cross-coupling reactions of vinylstannane were observed.

Synthesis of Trisubstituted Alkenes.

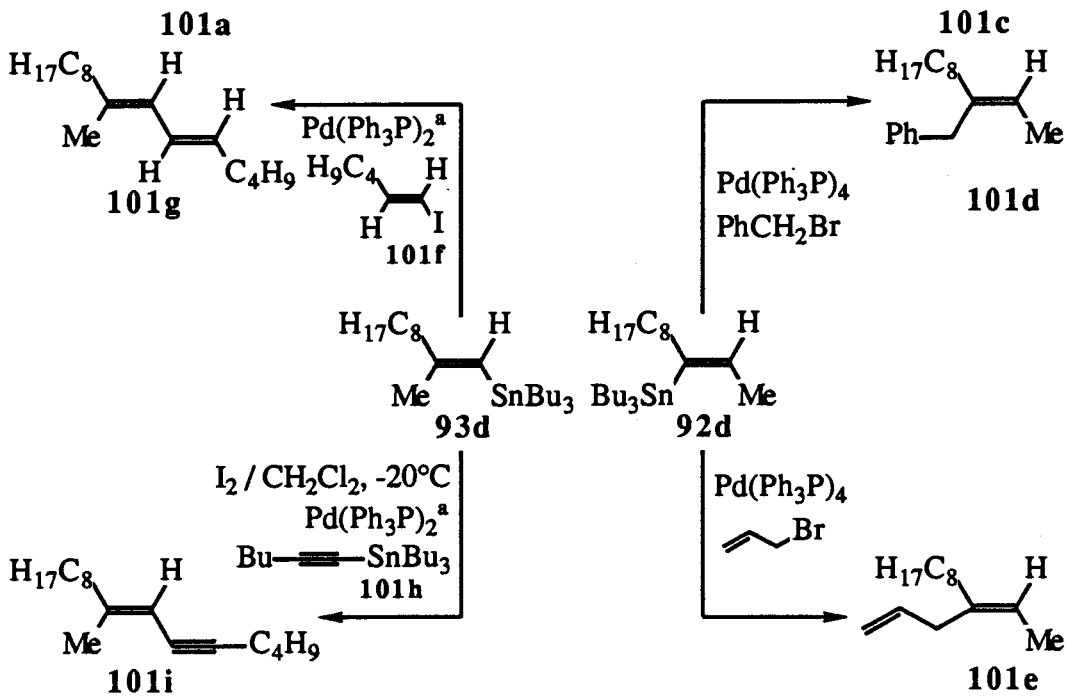
Vinylstannanes **92c, 92d** and **93d** were further reacted with electrophiles under transmetallation conditions to afford olefins **101a - i** (Schemes 42 and 43). In each case the reactions resulted in cross-coupled products derived from retention of configuration with respect to the vinyl-tin bond. In the case of **92c** (Scheme 42), reaction with I_2 in CH_2Cl_2 smoothly produced the vinyliodide, **101a**, which underwent facile metal-halogen exchange with excess *n*-BuLi.[88] Addition of Me_3SiCl gave **101b** in good yield



Scheme 42

whereas quenching the reaction with ^2H_2O gave an excellent yield of **101c**. Olefin **101b** was also synthesized in moderate yield by treatment of **92c** with *n*-BuLi / TMEDA[73b] followed by trapping of the vinyl anion with Me3SiCl. The low yield of product in this reaction is attributed to poor transmetallation due to steric congestion of the tributylstannyl group.[73,89]

Oxidative addition of either benzyl bromide or allyl bromide at Pd(Ph3P)4 followed by coupling with vinylstannane **92d** (Scheme 43) in refluxing THF gave excellent yields of **101d** and **101e**, respectively.[90] The vinyl stannane **93d** also underwent facile coupling with (*E*)-1-iodo-hexene (**101f**) under Pd(0) catalysis to yield stereochemically pure 1,3-diene, **101g**.[91] Palladium catalyzed cross-coupling of



[a] $Pd(Ph_3P)_2$ prepared from reaction of $Pd(Ph_3P)_2Cl_2$ with two equiv. of DIBALH

Scheme 43

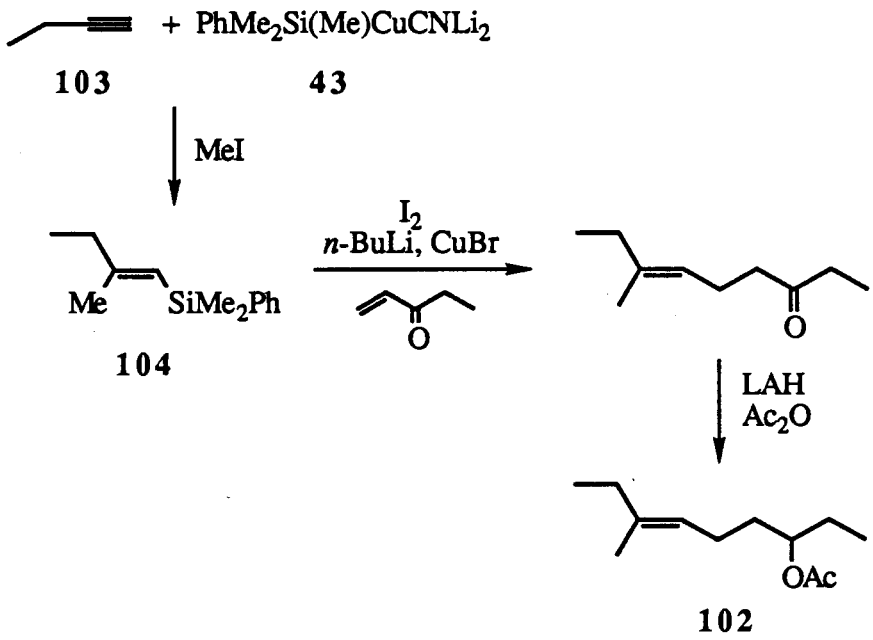
the iodide derived from **93d** with 1-hexynl-*n*-tributylstannane (**101h**) cleanly gave stereo-defined 1,3-enyne, **101i**.[92] The rate of the coupling reaction was sensitive to catalyst. High ratios of phosphine ligand to palladium slowed the reaction.[92] Hence, the coordinatively unsaturated Pd(0) catalyst derived from reduction of $(Ph_3P)_2PdCl_2$ with 2.0 equivalents of DIBALH[85] was used for cross-coupling reactions during the synthesis of **101g** and **101i.**

Synthesis of the pheromone of the Square-Necked grain beetle

The square-necked grain beetle, *Cathartus quadricollis* , is a cosmopoliton pest of stored grain products. In North America this shiny, reddish-brown beetle is abundant chiefly in the Southern United States and infests a variety of stored commodities such as corn and peanuts. The beetle is also found in the wild and attacks a large variety of plant seed pods. In morphology and habit, *C. quadricollis* is similar to other grain-infesting beetles of the genera *Cryptolestes* and *Oryzaephilis* but is larger and strong flyer.[93] The major differences between *C. quadricollis* and the other cucujids studied to date is that the aggregation pheromone of this species appears to be a single component, and is assigned the structure 7-methyl-(6*E*)-nonen-3-yl acetate (**102**, Scheme 44).[94] It was envisioned that addition of bimetallic reagents to 1-butyne followed by sequential quenching of the vinylbimetallic adduct with MeI and ethyl vinyl ketone should result in the formation of the keto- intermediate in a single step. Reduction followed by acetylation would give the desired product of correct stereo and regiochemistry.

Thus, addition of $PhMe_2Si(Me)Cu(CN)Li_2$ (**43**) to 1-butyne (**103**) followed by electrophilic capture of the vinylsilyl-copper intermediate with MeI in HMPA/THF resulted in the formation of **104**.[46a] Iodonation-transmetallation[79] followed by

conversion of the vinyllithium to the vinylcopper species and addition to ethyl vinyl ketone yielded the ketone which was reduced to the alcohol and then to the pheromone (**102**, Scheme 44) in two steps in overall yield of 53%. The same precursor was also synthesized from the addition of **94** to 1-butyne followed by addition of ethyl vinyl ketone in the presence of $BF_3 \cdot Et_2O$. Transmetallation of the vinylstannane and subsequent coupling with MeI completed this sequence.



Scheme 44

Mechanistic Studies

In the previous section, it was demonstrated that under Cu(I) catalysis bimetallic reagents derived from Sn or Si add efficiently to 1-alkynes. These additions yield organometallics that contain two carbon-metal bonds of differential reactivity. The chemistry ensuing from this methodology has yielded powerful new methods for

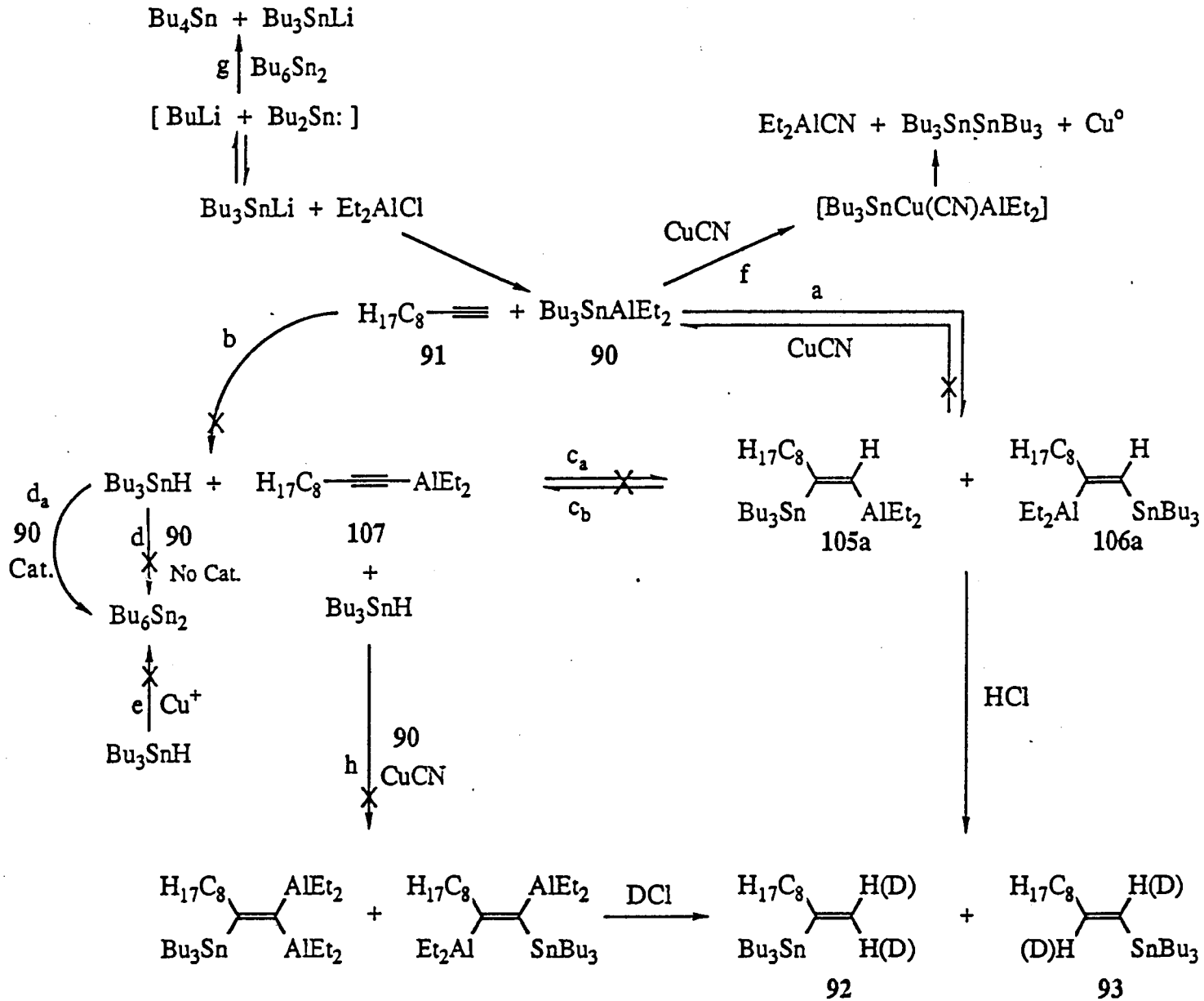
stereospecific synthesis of trisubstituted olefins under mild conditions and in the presence of polar functional groups.[48] Although regiochemical control of metallo-metallations was possible, the mechanistic features of this reaction are not fully understood.

In this section we describe chemical and spectroscopic studies aimed at elucidation of the mechanism of the addition of trialkylstannyl- and silylmetalloids to 1-alkynes. Specifically, we examined the ^{2}H, ^{7}Li, ^{11}B, ^{13}C, ^{29}Si and ^{119}Sn NMR spectra of species generated in solution when trimethylstannyl or dimethylphenylsilyl lithium were reacted with salts of electrophilic aluminum or boron and finally with 1-^{2}H-octyne.

Results and discussion

The formation of hexabutylditin and tetrabutyltin as side products as well as the incomplete consumption of 1-alkyne even with three equivalents of $Bu_3SnAlEt_2$ (**90**) and [(Bu_3Sn-9-BBN•OMe)$^{-}Li^{+}$] (**94**) suggested that stannylalumination and stannylboronation were competing with other processes. The mechanistic possibilities shown in Scheme 45, **a-h**, (shown for $Bu_3SnAlEt_2$) illustrate the wide variety of processes that have literature precedant in related systems.

The reversibility of process **a** was investigated by conducting the addition of **90** and **91** using an equimolar ratio of reactants and allowing the reaction to proceed until no further consumption of alkyne was observed. At this point an equivalent amount of 1-^{2}H-**91** was added and the reaction allowed to proceed for a time equivalent to that for the initial reaction. Protolytic work-up of the reaction followed by analysis of the vinylstannane adducts by ^{1}H NMR and GC-MS revealed no ^{2}H incorporation in either vinyl stannane (**92** and **93**). These results suggest that the addition of **91** to **90** is not


Bu4Sn + Bu3SnLi
g
Bu6Sn2
[BuLi + Bu2Sn:]
Bu3SnLi + Et2AlCl
Et2AlCN + Bu3SnSnBu3 + Cu°
[Bu3SnCu(CN)AlEt2]
CuCN
f
a
H17C8
91
+ Bu3SnAlEt2
90
CuCN
b
da
90
Cat.
Bu3SnH +
H17C8
AlEt2
107
ca
cb
H17C8
H
Bu3Sn
AlEt2
105a
+
H17C8
H
Et2Al
SnBu3
106a
d 90
No Cat.
Bu6Sn2
e Cu+
Bu3SnH
+
Bu3SnH
h 90
CuCN
HCl
H17C8
AlEt2
Bu3Sn
AlEt2
+
H17C8
AlEt2
Et2Al
SnBu3
DCl
H17C8
H(D)
Bu3Sn
H(D)
92
+
H17C8
H(D)
(D)H
SnBu3
93

Scheme 45

reversible under these reaction conditions (i.e., **105a** and **106a** are not converted to **90** and **91**).

Process **b** was shown to be inoperative by conducting the reaction of **90** with 1-^{2}H-**91** in the presence of CuCN followed by protolytic workup and examination of the ^{2}H content of unreacted **91**. No dimunition of ^{2}H in **91** was observed in this experiment. Thus, $Bu_3SnAlEt_2$ (**90**) did not remove the C_1 hydrogen from **91**. This experiment also suggests that the conversion of **105a** and **106a** to $C_8H_{17}C{\equiv}CAlEt_2$ (**107**) as shown in process $\mathbf{c_b}$ is not occurring. To check the forward process $\mathbf{c_a}$ reaction of Bu_3SnH (**58**) with **107** in the presence of Cu^{+1} was examined. Recovery of only 1-decyne from this reaction suggests that process $\mathbf{c_a}$ is not operative.

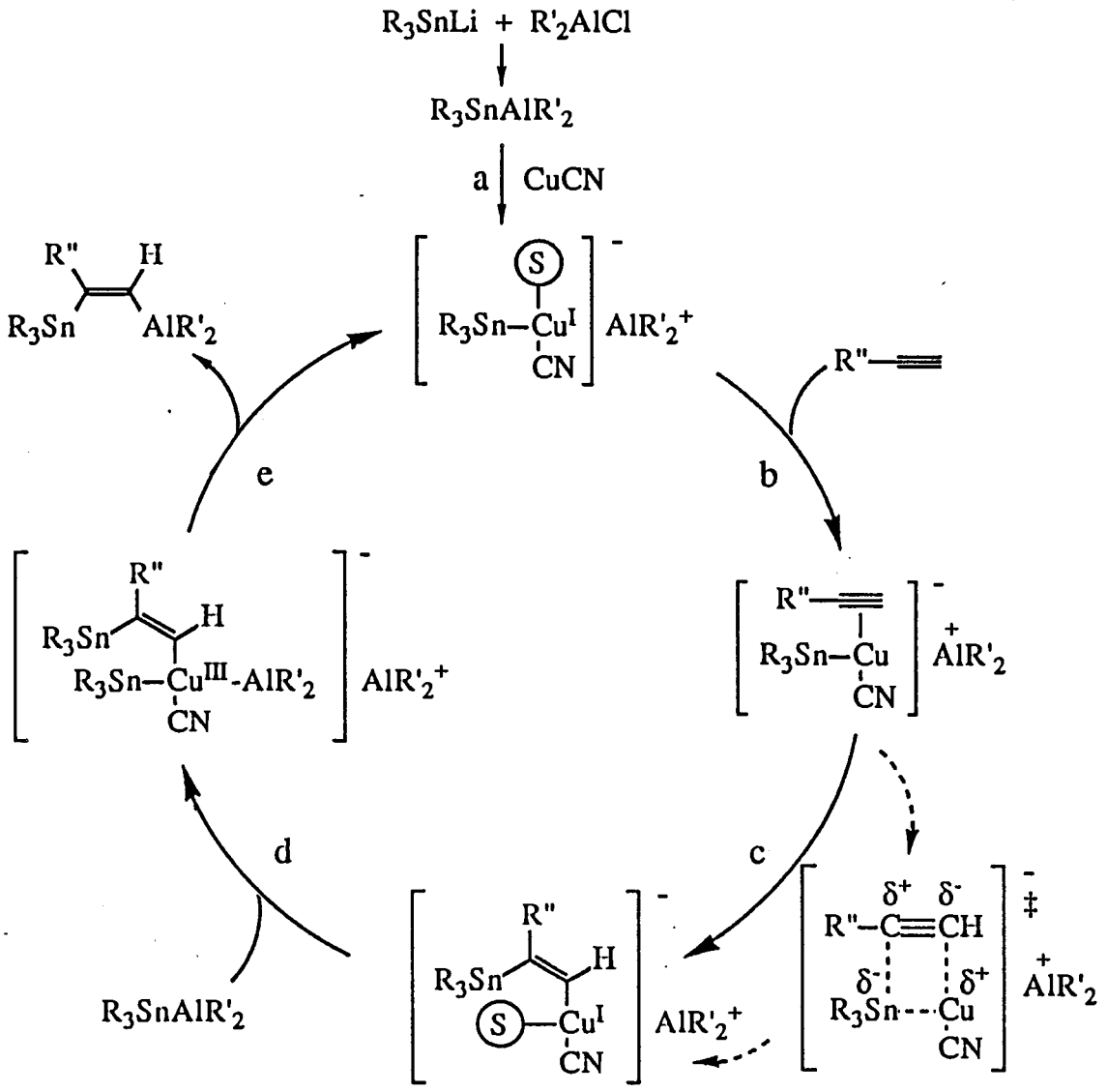
To investigate if process **d** occurs, $Bu_3SnAlEt_2$ (**90**) was reacted with Bu_3SnH (**58**). Without added catalyst no hexabutylditin was observed over 24 h. Metallometallations are normally complete in 3 h. When either CuCN, CuI, $Pd(PPh_3)_2Cl_2$ or $Pd(Ph_3P)_4$ were added to THF solutions of $Bu_3SnAlEt_2$ (**90**) containing Bu_3SnH (**58**, process $\mathbf{d_a}$) the only product detected (GC) was $Bu_3SnSnBu_3$. No hexabutylditin was obtained when copper catalysts were reacted with Bu_3SnH alone (process **e**) but reaction of $Bu_3SnAlEt_2$ (**90**) with CuI and $Pd(Ph_3P)_4$ gave hexabutylditin in 69 and 77% yield respectively. Thus, hexabutylditin can be formed by reaction of $Bu_3SnAlEt_2$ with catalyst in the absence of 1-alkyne. These results are consistent with formation of hexabutylditin *via* reductive elimination from a stannyl-alumino-cuprate as shown in process **f**. The formation of tetrabutyltin from decomposition of alkali stannides in the presence of hexabutylditin (process **g**) is a known process.[94]

The possiblity that process **h** is taking place was examined by conducting the reaction of **107** (prepared from $C_8H_{17}C{\equiv}CLi$ and $ClAlEt_2$)with $Bu_3SnAlEt_2$ (**90**) in the presence of CuCN. No vinyl stannanes were obtained from quenching this reaction

after 24 h. An independent check of reaction **h** involved reaction of **90** (method **b**, Table IV) with **91** in a 1:1 molar ratio followed by quenching with ^{2}HCl. Incorporation of only one ^{2}H into each of the vinyl stannane products **92** and **93** (^{1}H NMR) ruled out the operation of this process.

In the case of Sn-Al reagents the preparative synthetic procedure which was found to give good yields of products involved addition of the trialkylstannyllithium and diethylaluminum chloride to the reaction solution prior to cuprous ion. Monitoring these solutions by ^{119}Sn and ^{13}C NMR (*vide infra*) revealed that reaction between Me_3SnLi and Et_2AlCl occurred prior to addition of the Cu^{+}salt. The initial reagent is formulated as $Me_3SnAlEt_2$ (**54**), although cuprous ion is undoubtedly an integral part of the reactive species. The mechanism (Scheme 46) considered to be operative involves oxidative addition (**a**) of $R_3SnAlR'_2$ to CuCN to generate a three coordinate Cu(I) species. This is followed by insertion (**b**) of the alkyne, a step which does not involve a change in the oxidation state of copper. This, in turn, is followed by rearrangement (**c**) to a vinyltin-cuprate adduct with oxidation of the copper(I) to Cu(III) through addition (**d**) of a second equivalent of $R_3SnAlR'_2$. The next logical step is reductive elimination (**e**) of the vinyl-stannyl-aluminum adduct to regenerate the initial Cu(I) complex, thereby making the process catalytic.

In the case of CuBr catalyzed stannyl- or silylmetallations, the initial step involves transmetallation to yield a stannyl- or silylcopper reagent and metallic electrophile as shown in Scheme 47 (step **a**). Silyl- (**38**) and stannylcopper (**49**) reagents are highly reactive toward 1-alkynes due to the presence of an empty coordination site and the partial positive charge on copper (step **b**). Species polarized as in **38** or **49** would be expected to react with 1-alkynes to produce vinyl-silyl or stannylcopper adducts in which the silyl-



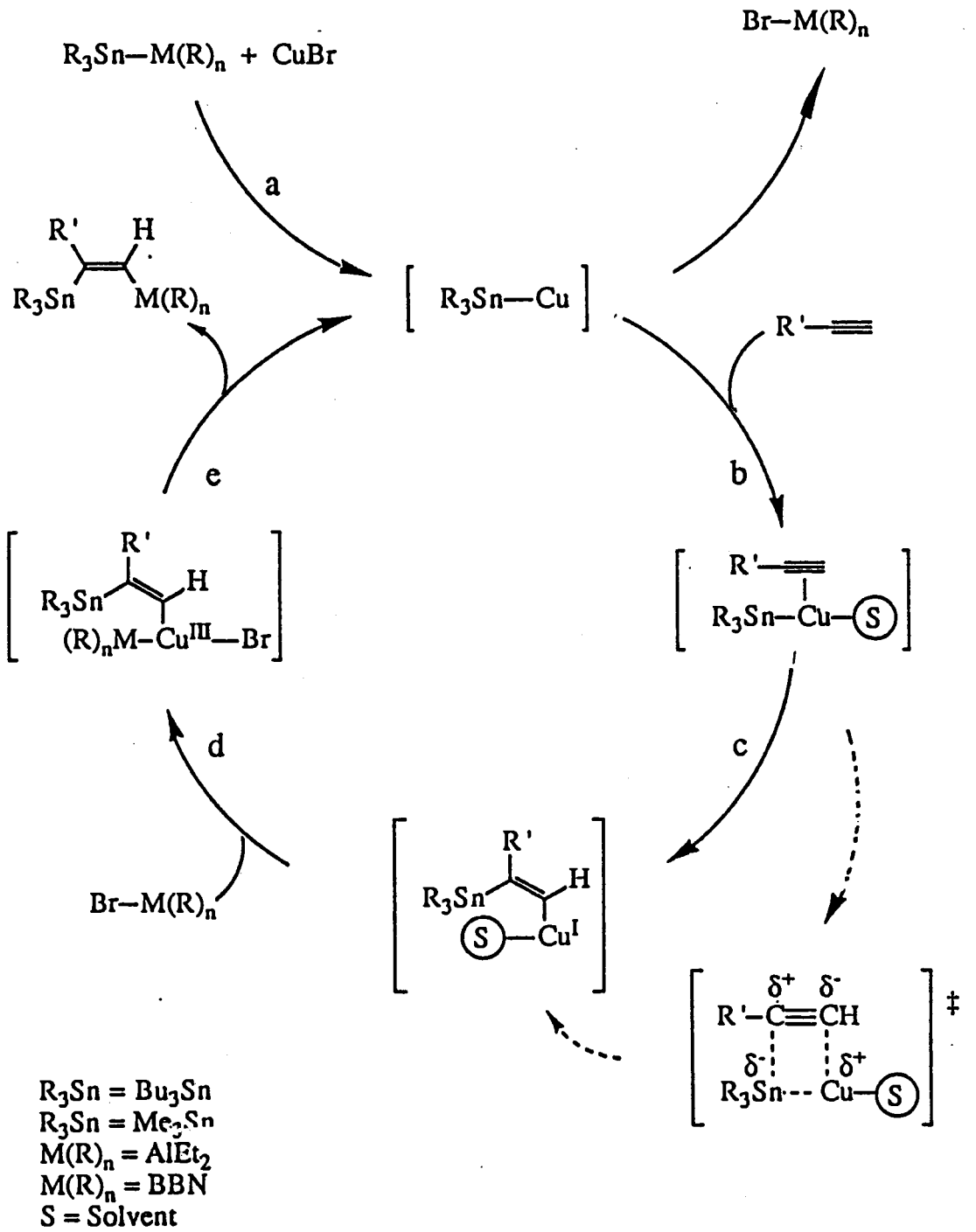
$R_3SnAlR'_2$ = $Bu_3SnAlEt_2$
$R_3SnAlR'_2$ = $Mc_3SnAlEt_2$
S = Solvent

Scheme 46

or stannyl- group is attached to the more substituted center of the alkyne (step **c**).

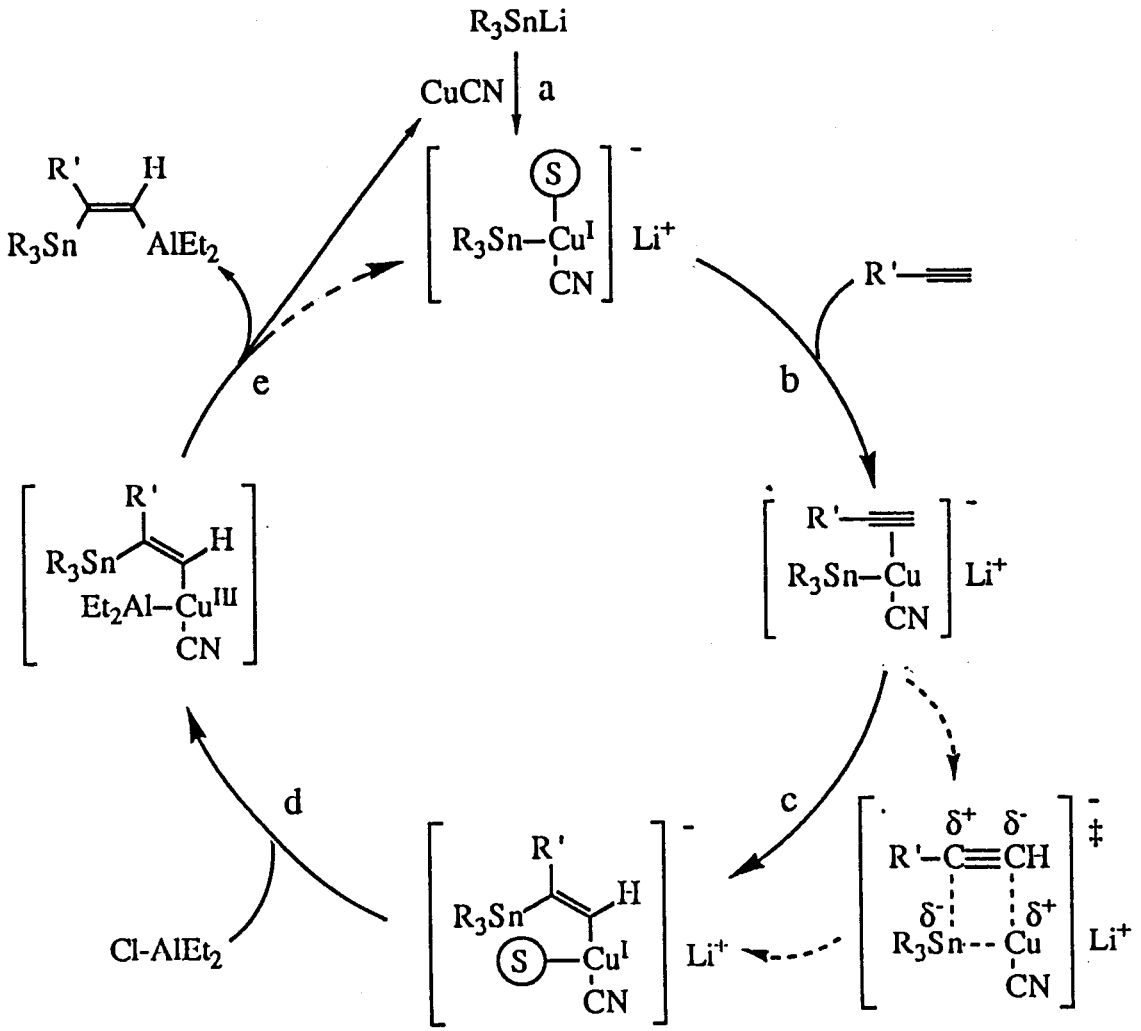
Transmetallation of the vinyl-copper bond by metallic electrophile (step **d**) generated *in*

situ followed by reductive elimination (step e) would result in the eventual production of 2-metallated-1-alkenes (Scheme 47).



Scheme 47

Stannylalumination also proceeds well when diethylaluminum chloride is added to the reaction mixture after the trialkylstannate anion, Cu^+ salt and alkyne (Scheme 48). In this case we consider the reaction to proceed *via* initial formation of the LO trialkylstannylcyanocuprate (**48, a**). Complexation of this species with alkyne (**b**) followed by rearrangement (**c**) to a vinyltin-cuprate adduct yields a Cu(I) species.



$R_3Sn = Bu_3Sn$
$R_3Sn = Me_3Sn$
S = Solvent

Scheme 48

Reaction of this complex with diethylaluminum chloride (**d**) would give a Cu(III) species with an expected propensity for reductive elimination (**e**) to the catalytic Cu^+ species and the vinyl-stannyl-aluminum adduct in which the silicon or the tin moiety is at more substituted end of alkyne. Indeed, quenching the vinylstannyl-copper or the vinylsilyl-copper adduct generated in the reaction of "R_3MCu" (M = Sn or Si, i.e., **26**, **38** or **48**, **49**) with 1-nonyne by either MeOH, Et_2AlCl, Br-9-BBN led to the exclusive formation of 2-stannyl- or 2-silyated alkenes. A rationale for the observed mode of addition is provided by the electronic effects governing the transition state as shown in Schemes 47 and 48 (step **c**). Quantum mechanical and molecular orbital calculations have shown that the electron density distribution in case of 1-propyne[95] to be in the direction that one expects an anion to attack at the central carbon atom resulting in the formation of 2-metallated alkenes.

It can be envisioned that steric environment around the copper moiety can also dictate the regiochemistry in silyl- and stannylcuprations of 1-alkynes. The latter consideration is important was suggested by the observation that addition of highly coordinating solvent like HMPA to $R_3Si(Cu)(CN)Li$ (**26**) resulted in the formation of the reverse regioisomer (i.e., 1-silyated alkene). That LO cuprates possess a sterically demanding Cu center has been suggested from our NMR studies on (**26**), R_3SiCu (**38**), $R_3Sn(Cu)(CN)Li$ (**48**) and R_3SnCu (**49**). The ^{13}C, ^{29}Si and ^{119}Sn NMR spectra of these reagents consists of several broad lines indicative of oligomeric species in solution. In highly coordinating solvents like HMPA these cuprates tend to be less aggregated as seen by appearance of sharp signals in the ^{13}C NMR spectra of **26** (Figure 18). According to this proposal the change in regioselectivity on the addition of HMPA to **26** and 1-octyne (Scheme 12) was due to deaggregation of this reagent in this solvent. Further support of this hypothesis comes from the exclusive formation of 1-silyated alkenes on the addition of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) to 1-alkynes which was shown

alkenes on the addition of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**) to 1-alkynes which was shown to be less aggregated in THF. Thus, it is envisioned that the additions of mixed stannyl- $(R_3Sn)Cu(R')(CN)Li_2$ (**56**) or mixed silylcuprates $(R_3Si)Cu(R')(CN)Li_2$ (**43**) can result in the formation of either regioisomer depending upon the steric bulk of R'..

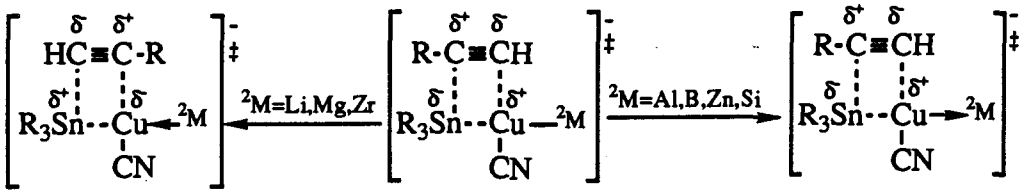
Regioselectivity in metallometallations is influenced by the catalyst employed as well as by the metals and steric bulk of the alkyl groups in the bismetalloid. According to Scheme 46, a change in regiochemistry in the cuprous ion catalyzed silyl- or stannylmetallations of 1-alkynes is due to a change in the regioselectivity in step **c**. The differences in electronegativities of the metalloid partners would be expected to give the bond connecting them some polar character and the direction of this polarity would be expected to be dictated by the nature of appended ligands (denoted ^2M). The metalloids known to participate in stannylmetallations are B, Si, Cu, Zn, Al, Zr, and Mg (written in order of decreasing electronegativity). In the case of copper catalyzed stannylmetallations, tin should be more electronegative than copper associated with the attached metal (^2M) in those cases where the latter is strongly electronegative. In cases where ^2M is weakly electronegative it is possible that the copper would be more electron rich and the polarity of the tin-copper bond could reverse (Scheme 49).

According to this proposal, it is envisioned that the metal partners of tin with low electronegativity (Mg, Zr, Al) will be better donors to the copper center in the proposed addition complex (Step **c**, Scheme 46) and that this will enhance addition in the reverse mode (Mg > Zr > Al). For those metals less electronegative than copper this trend certainly seems evident. Additions of stannylaluminum reagents give normal regiochemistry while addition of stannylmagnesium reagents proceed with reverse regiochemistry.[70] It is expected that at low temperature Sn-Zr will give good regioslectivity in favor of reverse addition. Also, bulky[74] ligands on ^2M should result in the opposite regioisomer **93a**. On the other hand, metalloids with high electronegativity

(Zn, Si, B) will act to enhance addition in the normal mode (B > Si > Zn). The Sn-Zn,[70] Sn-Si[73] and Sn-B[72] additions are reported to give excellent regioselectivity in favor of the normal addition product **92a** (i.e., 2-stannyl-1-alkenes).

Reversal of regioselectivity of stannylaluminations in the presence of HMPA would, in this proposal, be attributable to its ability to efficiently complex ^{2}M, thus, accentuating the negative charge on copper and favoring generation of the regioisomer **93a** (1-stannyl-1-alkenes). **93a** can also result from the addition of less aggregated trialkylstannylcopper species to 1-alkynes.

Thus, it is possible to envision a change in regiochemistry for stannylalumination in the presence of HMPA or bulky ligands without requiring either stannyl- or silylcupration or subsequent steps to be reversible.



Scheme 49

Spectroscopic studies

Metallometallations are usually conducted by addition of 1-alkyne to the preformed bimetallic reagent, followed by addition of cuprous salt. This sequence of

reagent addition prevents formation of dimer by-products which can arise if the cuprous salt is added to the bimetallic reagents prior to alkyne. Since stannyl- or silylmetalloids do not react with alkynes without the Cu(I) catalyst, it was envisioned that the Sn-Cu-metalloid sequence of addition would generate the same species as those involving the Sn-metalloid-Cu sequence of addition. Thus, both sequences would result in the *in situ* generation of stannyl- or silylcuprates from stannyl- or silylmetalloids as shown in Scheme 31.

The ^{13}C NMR spectra of solutions resulting from the reaction of Et_2AlCl with Me_3SnLi (**47**) at -70°C in THF exhibited a singlet at -7.5 ppm due to the methyl carbons bound to tin in $Me_3SnAlEt_2$ (**54**) alongwith a singlet for Me_4Sn at -9.3 ppm (Me_3SnLi was prepared from the cleavage of Me_6Sn_2 with MeLi, Figure 37a). The ^{119}Sn NMR spectra of this solution revealed a broad signal for $Me_3SnAlEt_2$ (**54**) at -126 ppm with respect to Me_4Sn (0.0 ppm, an internal reference). This signal broadening may be attributed to the coupling of tin to quadrupolar aluminum. The ^{7}Li NMR exhibited a sharp signal at 0.0 ppm implying the formation of LiCl in these solutions. Addition of a THF solution of CuCN•2LiCl (1.0 equivalent) to **54** resulted in the formation of a new species exhibiting a broad ^{13}C signal at -4.5 ppm (Figure 37b). The chemical shift of this signal corresponded to that obtained earlier for the solutions generated by mixture of equimolar amounts of Me_3SnLi (**47**) and CuCN•2LiCl (Figure 33b). More remarkable was the obsevation that admixture of equimolar ratios of $Me_3SnCu(CN)Li$ (**48**) and Et_2AlCl (Figure 37c) resulted in the same chemical shifts as obtained earlier (Figure 37b). Similarly, the ^{119}Sn NMR chemical shifts from both the reagent combinations [i.e., $Me_3SnCu(CN)Li$ (**48**, δ -150 ppm)-Et_2AlCl and $Me_3SnAlEt_2$ (**54**, δ -126)-CuCN•2LiCl were identical indicating that same species ($Me_3SnCu(CN)AlEt_2$, δ -156, step **a** in Scheme 46] is obtained when the ratio of stannyl anion to copper cation and aluminum cation is 1:1:1.

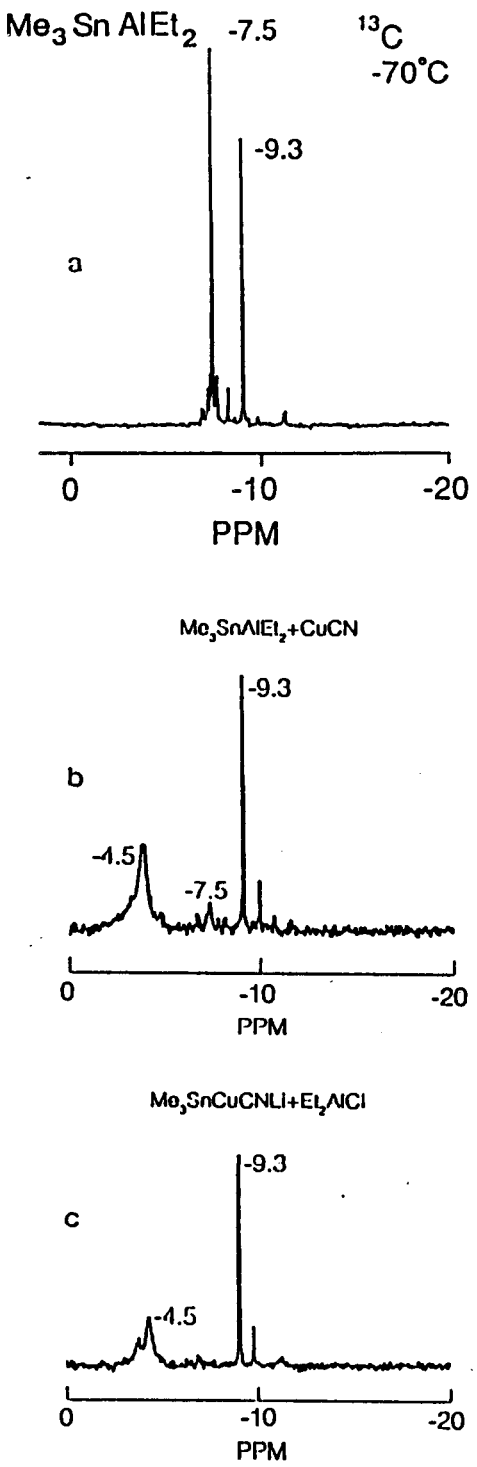


Figure 37. ^{13}C NMR spectra of (a) $Me_3SnAlEt_2$ (b) $Me_3SnAlEt_2$ + CuCN (c) $Me_3SnCu(CN)Li$ + Et_2AlCl; the spectra were run at -70°C.

Addition of 1-^{2}H-octyne to the clear solution of $Me_3SnAlEt_2$ (**54**) followed by CuCN (step **b**, Scheme 46) resulted in the formation of a wine red solution that exhibited a ^{119}Sn NMR signal at -50.0 ppm. This signal is very close to the one obtained for the vinyl-tin (δ -53.0) in species **79a** (Scheme 38, where $M(R)_n$ = Li, *vide infra*). The ^{2}H NMR exhibited a broad signal at 4.1 ppm indicating the formation of a vinylic carbon. Addition of a further equivalent of $Me_3SnAlEt_2$ (**54**, step **d**, Scheme 46) resulted in the appearance of a new vinyl ^{2}H peak at 7.2 ppm which we attribute to the vinytin-aluminum adduct, **79b** (step **e**, Scheme 46).

We next focussed attention on addition of stannylcuprate (**48**) to 1-alkynes. The ^{119}Sn NMR spectra of solutions generated from the addition of one equivalent of $Me_3SnCu(CN)Li$ (**48**, δ -151, step **a**, Scheme 48) to 1-^{2}H-octyne (step **b**, Scheme 48) at -50°C resulted in the appearance of signals for a vinyltin-copper adduct at -53.0 ppm. The ^{2}H signal of the 1-^{2}H-octyne (1.45 ppm) shifted to 4.1 ppm. Addition of one equivalent of Et_2AlCl (step **d**, Scheme 48) resulted in a downfield shift of the ^{2}H signal to 7.1 ppm (Figure 38). It should be recalled that this signal has the same chemical shift as that obtained by the addition of **54** to 1-^{2}H-octyne followed by CuCN (*vide supra*). These NMR results cogently attest to the involvement of a vinylstannyl-copper species such as **79a** that are converted to a species formulated as **79b** (Scheme 38 or step **e**, Schemes 46 and 48).

The unusual upfield shift of the vinyl-^{2}H (vinyl protons generally absorb around 6-7 ppm) obtained for vinyltin-copper species (**79a**, Scheme 38 and also shown in step **c**, Schemes 46 and 48) can be understood in terms of changes in the π electron density at carbon due to metal-alkyne coordination. According to the Dewar-Chatt-Duncanson model,[96] metal coordination to an alkyne should result in net shielding of the vinyl carbon ^{13}C and ^{1}H chemical shifts as a result of perturbation due to π-backbonding.[97] This may be attributed to an increase in electron density. On the other hand, perturbation

due to σ-bonding should result in net deshielding of the chemical shifts of the attendent carbon and proton due to a decrease in electron density. Appearance of the vinyl-^{2}H signal at around 4 ppm during addition of stannylcopper (**48** and **49**) and silylcopper (**26, 27** and **28**) to 1-alkynes (similar upfield shifts at δ 3.3 were obtained) suggests that π-back bonding is more dominant in the alkyne complexes of Cu^I. This may be attributed to the full d^{10} electron configuration of Cu(I) complexes which favours the transfer of electron density from the filled d orbitals of copper to the empty π*-orbitals of the alkyne. Addition of metallic electrophiles (e.g., Et_2AlCl or Br-9-BBN) should result

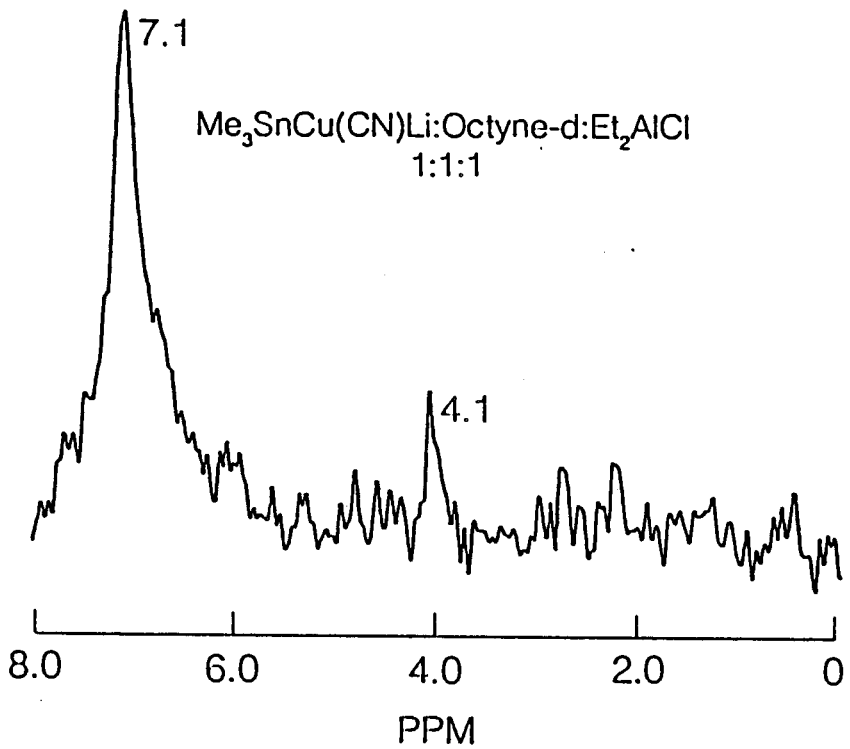


Figure 38. ^{2}H NMR spectra of $Me_3SnCu(CN)Li$ + 1-^{2}H-octyne + Et_2AlCl; the spectra were run at -70°C.

in the downfield shift of the vinyl-carbon as well as vinyl-^{2}H due to transfer of electron density to the electron deficient metal.

Copper(I) catalyzed stannylboronation of 1-alkynes by low-temperature NMR spectroscopy (Scheme 50) was next studied. Reaction of equimolar ratios of Me_3SnLi (**47**, δ ^{119}Sn, -187.7) and 9-BBN•OMe (δ ^{11}B, 55.4) resulted in the formation of $(Me_3Sn\text{-}9\text{-}BBN\bullet OMe)^{-}Li^{+}$ (**55**). This species exhibited a broad ^{119}Sn NMR signal at -109.5 ppm at -50°C due to the quadrupolar coupling caused by boron (^{10}B, natural abundance: 19.58%, spin: 3; ^{11}B, natural abundance: 80.42, spin: 3/2).[98] Cooling the solution to -85°C resulted in considerable sharpening of the signal. The ^{11}B spectrum exhibited a broad signal at 2.3 ppm. This value is reported for boron compounds bound to four ligands. Addition of 1-^{2}H-octyne to the preformed reagent, $[(Me_3Sn\text{-}9\text{-}BBN\bullet OMe)^{-}Li^{+}]$ (**55**) followed by $CuBr\bullet Me_2S$ resulted in the formation of the vinyltin-boron adduct as indicated by the appearance of vinyltin (^{119}Sn, δ -50.7) and vinyl-^{2}H NMR (5.7 ppm) signals attributable to this species.

The ^{119}Sn NMR spectra obtained from the addition of 1-^{2}H-octyne to Me_3SnCu (**49**, Figure 40a, step **b**, Scheme 47) exhibited a singlet at -59.0 ppm (figure 40b). This signal is attributed to the vinyltin-copper adduct, **79a** (Scheme 38, where $M(R)_n$ = Li, step **c**, Scheme 47). The ^{2}H NMR exhibited a broad signal at 6.1 ppm indicating the formation of a vinylic species (Figure 41a, Scheme 50). Remarkably, addition of an equivalent of Br-9-BBN (δ, ^{11}B, 84.0, step **d**, Scheme 49) followed by an equivalent of NaOMe resulted in the formation of the same intermediate which was obtained earlier for Cu(I) catalyzed stannylboration of 1-^{2}H-octyne (Scheme 50).

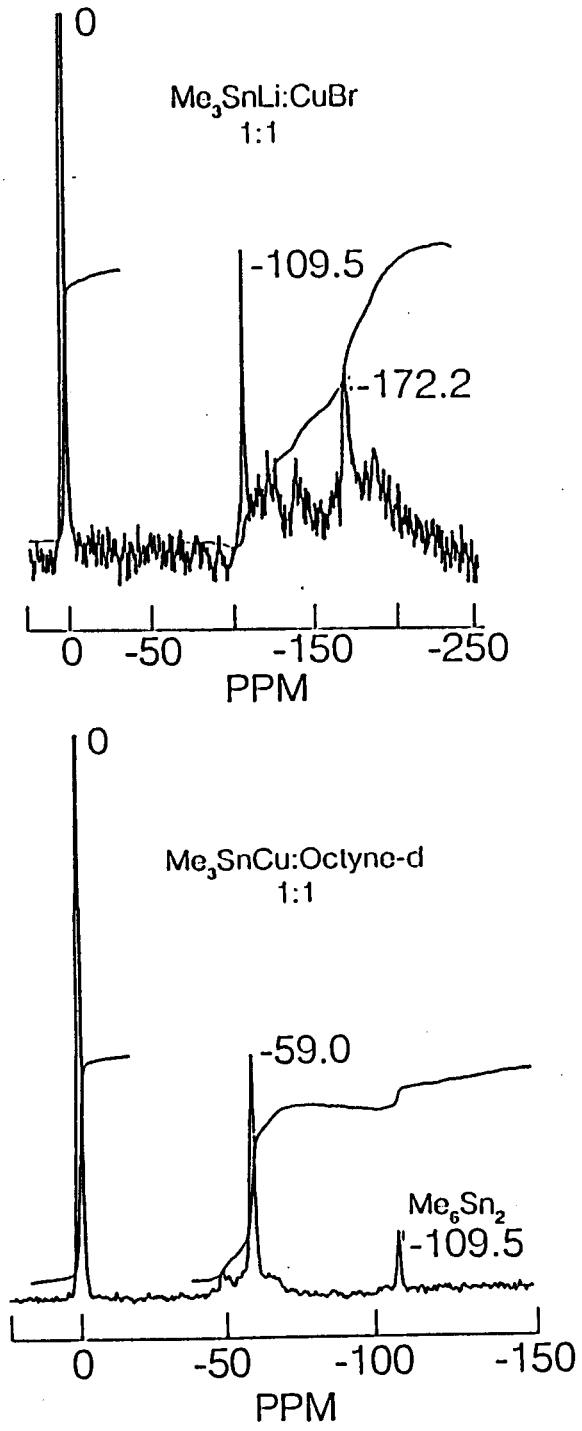


Figure 39. ^{119}Sn NMR of (a) Me3SnCu (b) Me3SnCu + 1-^{2}H-octyne; the spectra were run at -50°C.

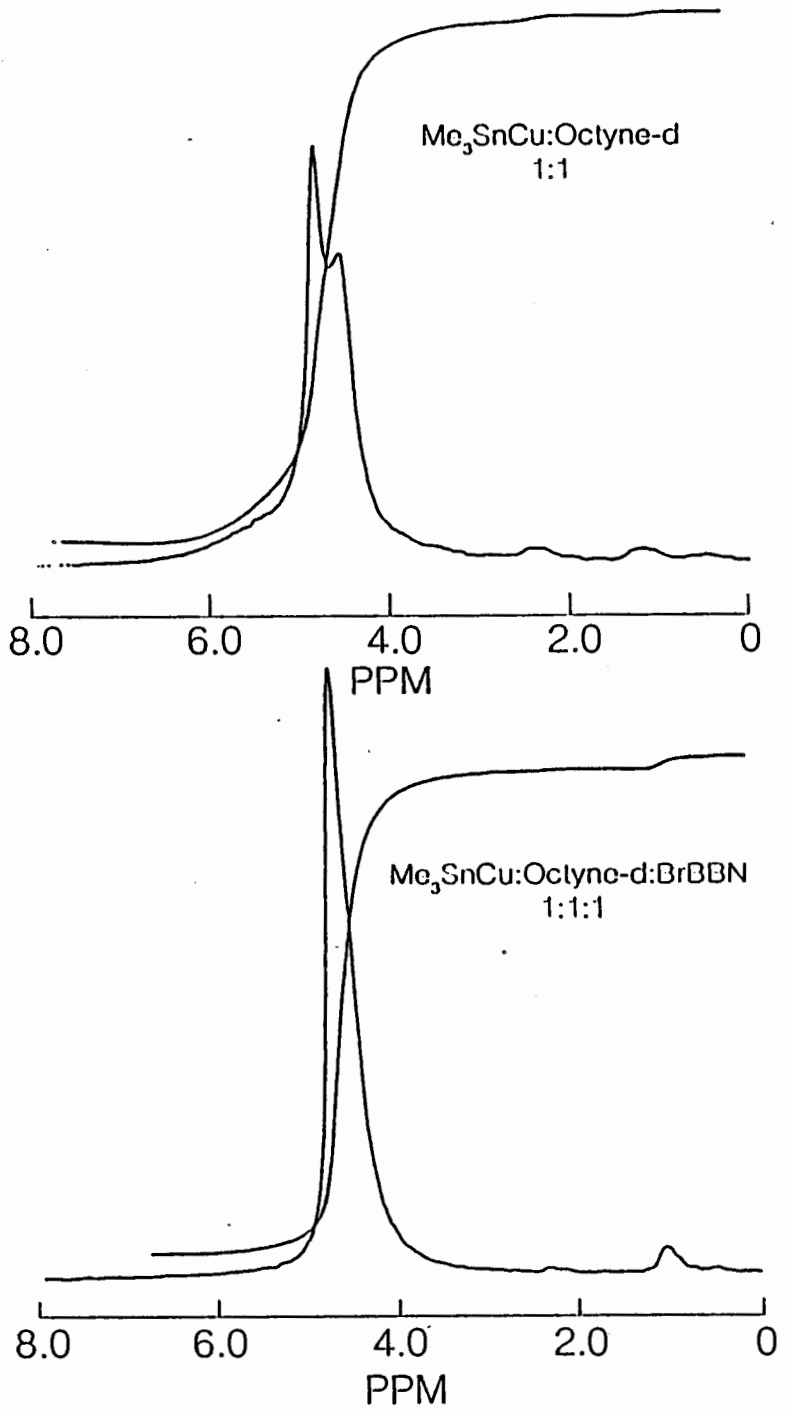
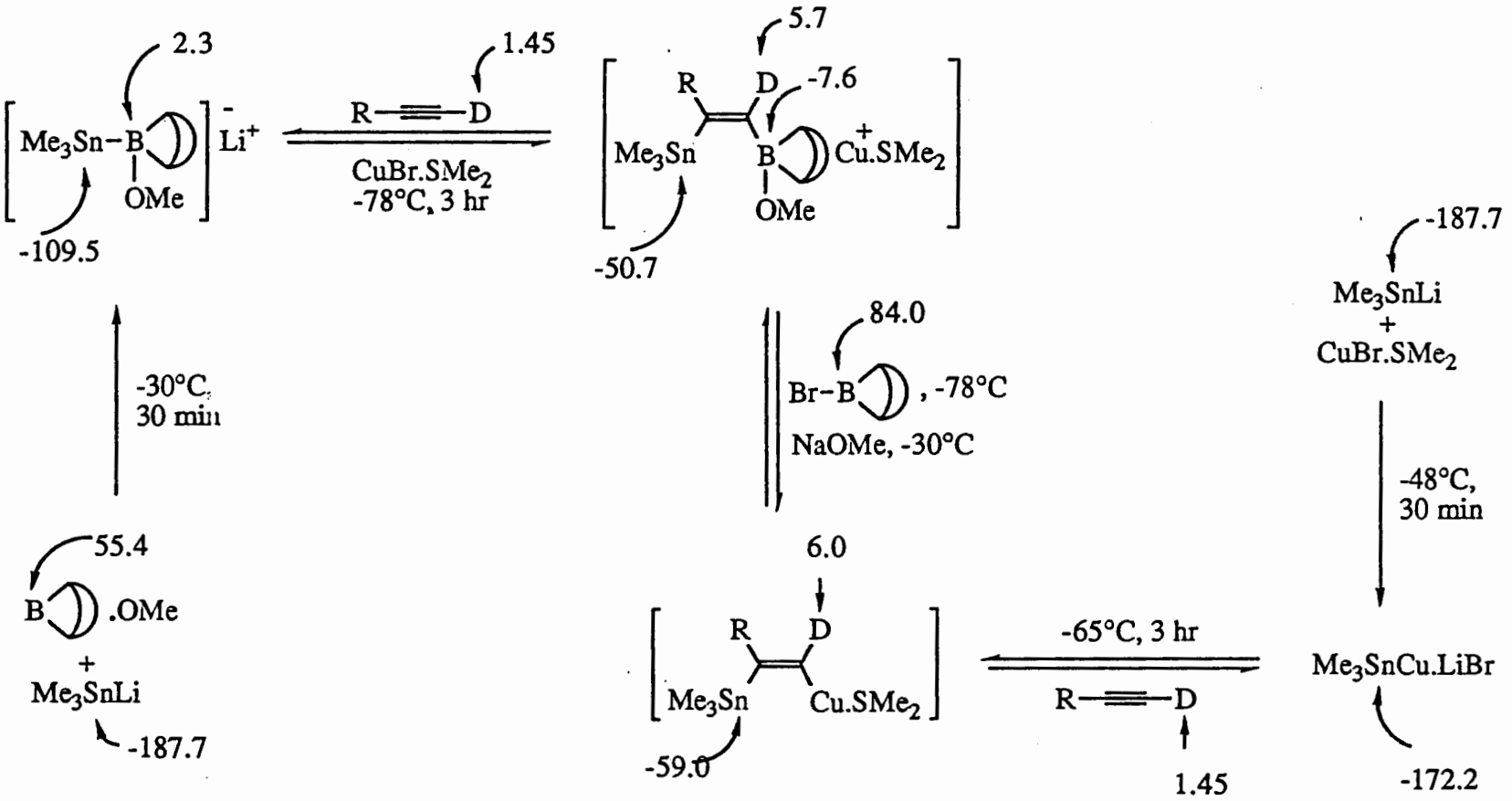


Figure 40. ^{2}H NMR of (a) Me3SnCu + 1-^{2}H-octyne (b) Me3SnCu + 1-^{2}H-octyne + Br-9-BBN + NaOMe; the spectra were run at -70°C.


2.3
1.45
5.7
-7.6
-109.5
-50.7
84.0
-187.7
55.4
6.0
-59.0
1.45
-172.2
-30°C,
30 min
CuBr.SMe2
-78°C, 3 hr
Br-B , -78°C
NaOMe, -30°C
-48°C,
30 min
-65°C, 3 hr
.OMe
+
Me3SnLi
CuBr.SMe2
Me3SnCu.LiBr

Scheme 50

Conclusion

Thus, in conclusion copper (I) catalyzed metallometallation of 1-alkynes can be visualized as initial metallocuprations of 1-alkynes followed by transmetallation of the vinylmetallo-copper adduct by metallic electrophile generated *in situ* in the reaction mixture. These reactions are compatible with polar functional groups. *In situ* addition of a proton source is not necessary to achieve high conversion of alkyne as the 1,2-dimetallo-adducts generated can be easily captured by electrophiles.

EXPERIMENTAL

All glassware and syringes were dried in an oven overnight at 120°C, and glassware was flame dried under vacuum and flushed with argon immediately prior to use. Syringes were flushed with argon and kept under positive argon pressure while cooling until use. Transfer of reagents was performed by with syringes equipped with stainless steel needles. Reactions were carried out in three-necked round bottom flasks equipped with filtration units and teflon-coated magnetic stirring bars. Usual workup involved quenching of the reaction with 1N HCl, extraction of the organic layer with Et_2O (2 x 5 mL), back-washing the combined organic extracts with satd. NH_4Cl (2 x 5 mL) and drying of the organic layer over anhydrous $MgSO_4$.

Transfer of CuCN and CuBr•Me_2S took place in a glove bag. CuBr•Me_2S was purified by the method of House.[99a] All alkyllithiums were freshly titrated before use.[99b]

Tetrahydrofuran was freshly distilled over potassium benzophenone-ketyl. Hexamethylphosphoramide and diisopropylamine were distilled over calcium hydride and stored over activated 3 A molecular sieves. Unless otherwise stated, other chemicals obtained from commercial sources were used without further purification.

Low-temperature ^{119}Sn NMR experiments were conducted on a Bruker WM-400 spectrometer with an operating frequency of 149.197 MHz. A typical set of parameters utilized a spectral width of 50000 Hz, 8K of memory, 11 Hz/data point, an acquisition time of 0.09 s and a 55° pulse of 35 μs. The decoupler was turned on during acquisition and off during the relaxation delay (4 s) in order to supress the negative nOe of ^{119}Sn. A

line broadening of 20 Hz was applied to all spectra. Spectra were recorded in THF that contained Me_4Sn as internal reference.

Low-temperature ^{29}Si NMR experiments were conducted on a Bruker WM-400 spectrometer with an operating frequency of 79.495 MHz. A typical set of parameters utilized a spectral width of 20000 Hz, 8K of memory, 2.44 Hz/data point, an acquisition time of 0.204 s and a 15° pulse of 10 μs. The decoupler was turned on during acquisition and off during the relaxation delay (4 s) in order to supress the negative nOe of ^{29}Si. A line broadening of 20 Hz was applied to all spectra. Spectra were recorded in THF that contained Me_4Si as internal reference.

^{13}C NMR spectra (> -30°C) were obtained on Bruker WM-400 spectrometer at a frequency of 100.61 MHz. Parameters for the ^{13}C spectral acquisition typically involved a spectral width of 22000 Hz, 32K of memory, 1.32 Hz/data point, an acquisition time of 0.75 s and a 13.5° pulse of 9 μs. The spectra were recorded in THF solutions unless otherwise specified and were referenced to THF, α = 26.0 ppm, β = 68.2 ppm. Inverse-gated decoupling was employed.

^{13}C NMR spectra were also obtained on Varian XL-300 spectrometer (run at temperatures < -30°C) with an operating frequency of 75.46 MHz. Parameters for the ^{13}C spectral acquisition typically involved a spectral width of 15000 Hz, 32K of memory, an acquisition time of 0.4 s and a 60° pulse of 12 μs. The spectra were recorded in THF solutions unless otherwise specified and were referenced to THF, α = 25.3 ppm, β = 67.41 ppm.

Low-temperature ^{7}Li NMR spectra were obtained on a Varian XL-300 spectrometer with an operating frequency of 116.6 MHz with a sweep width of 20000 Hz, 16K of memory, 1.25 Hz/data point, an acquisition time of 0.4 s and a 55° pulse of 12 μs.

A line broadening of 10 Hz was applied to all spectra. ^{7}Li chemical shifts were referenced with respect to 0.5M LiCl/CD_3OD (δ 0 ppm) in a capillary insert.

Low-temperature ^{1}H NMR spectra were recorded on a Varian XL-300 spectrometer in THF-d8 and were referenced to Me_4Sn (δ 0). Low-temperature ^{11}B NMR spectra were recorded on a Bruker WM-400 spectrometer with $BF_3 \cdot Et_2O$ (δ 0) as internal standard.

A vacuum-jacketed glass dewar measuring 7.5 x 16.0 cm (id 5.5 cm) was designed with tapering bottom to fit in the cup of the vortex mixer. All NMR samples were stirred while cooling at the indicated temperatures in this dewar.

^{1}H NMR and ^{119}Sn spectra of isolated products were recorded on a Bruker WM-400 spectrometer in $CDCl_3$ with $CHCl_3$ (δ 7.25) and Me_4Sn (δ 0) respectively, as internal standards. The tin-proton coupling constants (J_{Sn-H}) are given as an average of the ^{117}Sn and ^{119}Sn values.

Gas chromatographic analyses utilized a Hewlett-Packard 5880A instrument equipped with a with a flame ionization detector and employing a J/W fused silica DB-1 capillary column (15 m x 0.25 mm), with a linear temperature gradient. The purity of all the title compounds was >95% as judged by gas chromatographic analysis with dodecane as an internal standard. Chromatographic purifications were carried out with E.M. Merck silica gel (60, particle size 0.040-0.063 mm). Low resolution mass spectra were obtained with an HP 5985B GC-MS system with electron-impact ionization at 70 eV while the high resolution mass spectra were obtained on a Kratos MS50 RFA mass spectrometer (University of British Columbia, regional facility). For compounds containing a Bu_3Sn group, molecular mass measurements are based on ^{120}Sn and use

the (M^+- Bu) peak. Infrared (IR) spectra were recorded in THF solutions with Perkin-Elmer Model 283 spectrophotometer.

PREPARATION OF TRIALKYLSILYLCUPRATES

^{29}Si NMR Sample Preparations

Preparation of $PhMe_2SiLi$ (25) in THF: Dimethylphenylsilyl chloride (3.6 g, 21.0 mmol) was stirred with small pieces of lithium (0.450 g, 64.0 mmol) in THF (20 mL) at -5°C in an ice/salt bath.[33a] Reaction was initiated by immersion of the reaction flask in a sonicator for 30 min and then stirred overnight at -5°C. Dimethylphenylsilyllithium was titrated according to the procedure of Fleming *et al.*[27b]

Preparation of LiCl-Free $PhMe_2SiLi$ (25) in THF: According to the procedure of Gilman,[33a] to a solution of 1,2-diphenyl-1,1,2,2-tetramethyldisilane (prepared according to the procedure of Gilman[33b]) (4.6 g, 17.0 mmol) in THF (10 mL) were added small pieces of lithium (24 mg, 34.0 mmol). The reaction was initiated in a sonicator bath for 30 min and then stirred overnight at -5°C. The resultant green solution gave a negative halogen test.

Preparation of $PhMe_2SiLi$ (25) in DMS: 1,2-Diphenyl-1,1,2,2-tetramethyldisilane[33b] (3.6 g, 21.0 mmol) was stirred with small pieces of lithium (0.450 g, 64.0 mmol) in THF (20 mL) at - 5°C in an ice/salt bath. The reaction was initiated by immersion of the reaction flask in a sonicator for 30 min and then stirred overnight at -5°C. THF was removed under vacuum and replaced with an equal volume of DMS. This procedure was repeated three times. Dimethylphenylsilyllithium was titrated according to the procedure of Fleming *et al.*[27b]

Generation of Silylcuprates from CuCN

Preparation of $PhMe_2SiCu(CN)Li$ (26): CuCN (0.18 g, 2.0 mmol) was placed in a 10 mm NMR tube, equipped with an argon inlet. The tube was repeatedly (3x) evacuated and purged with argon. Me_4Si (0.5 mL) was injected, the reaction was cooled to -50°C and dimethylphenylsilyllithium in THF (1.8 mL, 2.0 mmol) added dropwise. The solution was stirred on a vortex mixer at -50°C in a custom built dewar for 20 min. The NMR spectrum was then immediately recorded.

Preparation of $(PhMe_2Si)_2Cu(CN)Li_2$ (28): A THF solution of $PhMe_2SiLi$ (**25**, 1.8 mL, 2.0 mmol) was added to a 10 mm NMR tube containing a THF solution of $PhMe_2SiCu(CN)Li$ (**26**, *vide supra*) at -50°C. The deep red solution was stirred for 20 min at -50°C prior to examination by NMR and IR spectroscopy.

Preparation of $(PhMe_2Si)_2CuLi_2$ (29): To a THF solution of $(PhMe_2Si)_2Cu(CN)Li_2$ (**28**, 2.0 mmol) prepared as outlined above was added a THF solution of $PhMe_2SiLi$ (**25**, 1.8 mL, 2.0 mmol) at -50°C. The reaction was stirred for 20 min at -50°C before examination by NMR and IR spectroscopy.

Preparation of $(PhMe_2Si)_3CuLi_2$ (29) with excess $PhMe_2SiLi$ (25): To a THF solution of $(PhMe_2Si)_3CuLi_2$ (**29**, 2.0 mmol) prepared as outlined above was added a THF solution of $PhMe_2SiLi$ (**25**, 1.8 mL, 2.0 mmol) at -50°C. The reaction was stirred for 20 min at -50°C before examination by NMR spectroscopy.

Regeneration of $(PhMe_2Si)_2Cu(CN)Li_2$, 28 from 29: CuCN (0.09 g, 1.0 mmol) was added to the solution of **29** (2.0 mmol). The reaction was stirred for 20 min at -50°C before examination by NMR spectroscopy.

Regeneration of $PhMe_2SiCu(CN)Li$ (26) from 28: CuCN (0.18 g, 2.0 mmol) was added to the NMR tube containing silylcyanocuprate **28**. The reaction was stirred for 20 min at -50°C and then examined by NMR spectroscopy.

Generation of Silylcuprates from $CuBr{\cdot}Me_2S$

Preparation of $(PhMe_2Si)Cu$ (38): $CuBr{\cdot}Me_2S$ (0.41 g, 2.0 mmol) was placed in a 10 mm NMR tube, equipped with an argon inlet. The tube was repeatedly (3x) evacuated and purged with argon. Me_4Si (0.5 mL) was injected, the solution was cooled to -50°C and dimethylphenysilyllithium in THF (**25**, 1.8 mL, 2.0 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer at -50°C in the custom built dewar for 20 min. The NMR spectrum was then immediately recorded.

Preparation of $(PhMe_2Si)_2CuLi$ (27): A THF solution of $PhMe_2SiLi$ (1.8 mL, 2.0 mmol) was added to a 10 mm NMR tube containing a THF solution of $PhMe_2SiCu$ (**38**, 2.0 mmol, *vide supra*) at -50°C. The resultant deep red solution was stirred for 20 min at -50°C prior to examination by NMR spectroscopy.

Preparation of $(PhMe_2Si)_3CuLi_2$ (29): To a THF solution of $(PhMe_2Si)_2CuLi$ (2.0 mmol) prepared as outlined above, was added a THF solution of

$PhMe_2SiLi$ (1.8 mL, 2.0 mmol) at -50°C. The reaction mixture was stirred for 20 min at -50°C before examination by NMR spectroscopy.

Preparation of $(PhMe_2Si)_3CuLi_2$ (29) with excess $PhMe_2SiLi$ (25): To a THF solution of $(PhMe_2Si)_3CuLi_2$ (**29**, 2.0 mmol), prepared as above from $CuBr{\bullet}Me_2S$, was added a THF solution of $PhMe_2SiLi$ (1.8 mL, 2.0 mmol) at -50°C. The reaction mixture was stirred for 20 min at -50°C before examination by NMR spectroscopy.

Regeneration of $(PhMe_2Si)_2CuLi$ (27) from 29 prepared from $CuBr{\bullet}Me_2S$: $CuBr{\bullet}Me_2S$ (0.205 g, 1.0 mmol) was added to 2.0 mmol of the solution generated by mixing $PhMe_2SiLi$ (**25**) and $CuBr{\bullet}Me_2S$ in a 3:1 ratio. The reaction mixture was stirred for 20 min at -50°C before examination by NMR spectroscopy.

Regeneration of $PhMe_2SiCu$ (38) from 27: $CuBr{\bullet}Me_2S$ (0.41 g, 2.0 mmol) was added to the NMR tube containing silylcuprate (**27**, 2.0 mmol). The reaction was stirred for 20 min at -50°C and then examined by NMR spectroscopy.

Generation of Mixed Silylcuprates

Preparation of $PhMe_2Si(Me)Cu(CN)Li_2$ (43) by Reaction of $PhMe_2SiLi$ (25) and $MeCu(CN)Li$ (16): CuCN (0.18 g, 2.0 mmol) was added to a 10 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (1.4 mL, 2.0 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on the vortex mixer in a custom built dewar for 10 min.

Dimethylphenylsilyllithium (**25**) in THF (1.8 mL, 2.0 mmol) was added dropwise to this clear solution at -50°C. The reaction turned deep red in color. The NMR spectrum was recorded immediately.

Preparation of 43 by Reaction of $PhMe_2SiCu(CN)Li$ (26) and MeLi: MeLi (1.4 mL, 2.0 mmol) was added to a solution of **26** (2.0 mmol, *vide supra*) at -50°C. The reaction mixture was stirred on a vortex mixer at -50°C in a custom built dewar for 20 min. The NMR spectrum was immediately recorded.

Preparation of 43 by Reaction of $(PhMe_2Si)_2Cu(CN)Li_2$ (28) and $Me_2Cu(CN)Li_2$ (17): CuCN (0.09 g, 1.0 mmol) was added to a flask, equipped with an argon inlet. The solution was cooled to -50°C where MeLi (1.4 mL, 2.0 mmol) was introduced dropwise to generate a clear solution of **17**. After 10 min this solution was transferred *via* a pre-cooled cannula into cuprate **28** (2.0 mmol, *vide supra*) which was also maintained at below -50°C. The resulting deep red solution was stirred for 20 min before recording the NMR spectrum.

Preparation of $(PhMe_2Si)_2(Me)CuLi_2$ (44) by Reaction of $PhMe_2SiLi$ (25) and MeCu(CN)Li (16): CuCN (0.09 g, 1.0 mmol) was added to a 10 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.7 mL, 1.0 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Dimethylphenylsilyllithium (**25**) in THF (1.8 mL, 2.0 mmol) was added dropwise to this clear solution at -78°C. The reaction turned deep red in color. The NMR spectrum was recorded immediately.

Preparation of 44 from Reaction of $(PhMe_2Si)_2Cu(CN)Li_2$ (28) and MeLi: MeLi in Et_2O (1.4 mL, 2.0 mmol) was introduced dropwise *via* a syringe

Preparation of 44 from Reaction of $(PhMe_2Si)_2Cu(CN)Li_2$ (28) and MeLi: MeLi in Et_2O (1.4 mL, 2.0 mmol) was introduced dropwise *via* a syringe to a solution of **28** (2.0 mmol) at -78°C. The resulting deep red solution was stirred for 20 min before recording the NMR spectrum.

Preparation of $PhMe_2Si(Me)_2CuLi_2$ (45) by Reaction of $PhMe_2SiLi$ (25) MeLi and CuCN: CuCN (0.09 g, 1.0 mmol) was added to a 10 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.7 mL, 1.0 mmol) in Et_2O was added *via* a syringe followed by dimethylphenylsilyllithium (**25**) in THF (2.7 mL, 3.0 mmol) at -78°C. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. The reaction turned deep red in color. The NMR spectrum was recorded immediately.

Preparation of 45 by Reaction of $(PhMe_2Si)_3CuLi_2$ (29) and MeLi: MeLi in Et_2O (0.7 mL, 1.0 mmol) was introduced dropwise *via* a syringe to a solution of **29** (1.0 mmol, *vide supra*) at -78°C. The resulting deep red solution was stirred for 20 min before recording the NMR spectrum.

^{13}C and ^{1}H NMR Sample Preparation

Preparation of CuCN•2LiCl: THF (11.0 mL) was added to a mixture of CuCN (0.98 g, 11.0 mmol) and LiCl (0.95 g, 22.0 mmol) in a round bottomed flask under argon. A clear faint yellow solution was obtained after 0.5 h of stirring. This

solution was used as the Cu(I)CN source for all the ^{13}C and ^{1}H NMR sample preparations unless otherwise specified.

Preparation of CuBr•2LiCl: THF (11.0 mL) was added to a mixture of CuBr•Me_2S (2.25 g, 11.0 mmol) and LiCl (0.95 g, 22.0 mmol) in a round bottomed flask under argon. A clear dark yellow solution was obtained after 0.5 h of stirring. This solution was used as the Cu(I)Br source for all the ^{13}C and ^{1}H NMR sample preparations.

Generation of Silylcuprates from CuCN

Preparation of 26: The above THF solution of CuCN (0.5 mL, 0.5 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 26 in THF/HMPA: A solution of CuCN in THF (0.5 mL, 0.5 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise followed by addition of HMPA (0.5 mL) *via* a syringe. The reaction was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 28: The above THF solution of CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 29: The above THF solution of CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF (0.9 mL, 0.75 mmol) added dropwise. The reaction was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 29 with excess 25: The above THF solution of CuCN (0.125 mL, 0.125 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise. The reaction was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 26 for ^{1}H NMR analysis: The above THF solution of CuCN (0.5 mL, 0.5 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF-d8 (0.6 mL, 0.5 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 28 and 29 for ^{1}H NMR analysis: These solutions were prepared in THF-d8 as described above.

Generation of LiCl-free Silylcuprates from CuCN

Preparation of $PhMe_2SiCu(CN)Li$ (26): CuCN (0.06 g, 0.66 mmol) was placed in a 5 mm NMR tube, equipped with an argon inlet and a capillary insert containing 1M solution of LiCl in MeO^2H. The tube was repeatedly (3x) evacuated and purged with argon. LiCl-free dimethylphenysilyllithium in THF (0.6 mL, 0.66 mmol) added dropwise at -70°C. The solution was stirred on a vortex mixer at -70°C in a custom built dewar for 20 min. The NMR spectrum was then immediately recorded.

Preparation of 28 and 29: These were prepared precisely as described above. Both the solutions were green in color. Addition of LiCl resulted in the familiar red silylcuprates.

Generation of Silylcuprates from $CuBr{\bullet}Me_2S$

Preparation of $PhMe_2SiCu$ (38): $CuBr{\bullet}Me_2S$ (0.5 mL, 0.5 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The reaction was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise. The solution was stirred on a vortex mixer in a custom built dewar for 20 min. The slurry was used as such.

Preparation of $(PhMe_2Si)_2CuLi$ (27): This cuprate was generated as described above. Thus, $CuBr{\bullet}Me_2S$ (0.25 mL, 0.25 mmol) was added to a 5 mm NMR

tube, equipped with an argon inlet. The reaction was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise. The solution was stirred on a vortex mixer in a custom built dewar for 20 min before examination of the NMR spectrum.

Preparation of $(PhMe_2Si)_3CuLi_2$ (29): $CuBr{\cdot}Me_2S$ (0.125 mL, 0.125 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The reaction was cooled to -78°C and dimethylphenylsilyllithium in THF (0.9 mL, 0.75 mmol) added dropwise. The solution was stirred on a vortex mixer in a custom built dewar for 20 min before examination of the NMR spectrum.

Generation of Silylcuprates from CuBr in DMS

Preparation of $(PhMe_2Si)_2CuLi$ (27) in DMS: $CuBr{\cdot}Me_2S$ (0.05 g 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The reaction was cooled to -78°C and dimethylphenylsilyllithium in DMS (0.45 mL, 0.5 mmol) added dropwise. The solution was stirred on a vortex mixer (*vide supra*). The spectra were recorded at -85°C immediately. In a separate set of experiments, solutions of silylcuprate **27** in DMS were prepared in a flask equippped with a filtration unit. The silylcuprate was filtered under argon *via* a cannula to the pre-cooled 5 mm NMR tube. Both the solutions exhibited same resonances in the ^{13}C NMR spectra. For the ^{13}C analysis the samples were prepared without filtration whereas the ^{7}Li NMR samples were filtered prior to examination by NMR spectroscopy.

Preparation of LiCl-free $(PhMe_2Si)_2CuLi$ (27) in THF: $CuBr{\cdot}Me_2S$ (0.05 g 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The reaction was cooled to -78°C and LiCl-free dimethylphenylsilyllithium in THF (0.45 mL, 0.5 mmol) added dropwise. The solution was stirred on a vortex mixer. The spectra were recorded at -85°C immediately.

Preparation of $(PhMe_2Si)_2CuLi{\cdot}LiI$ (39) in DMS: $(PhMe_2Si)_2CuLi{\cdot}LiI$ was prepared as above except for the substitution of CuI (0.047 g 0.25 mmol) for $CuBr{\cdot}Me_2S$.

Preparation of $(PhMe_2Si)_3CuLi_2$ (29) in DMS:
Dimethylphenylsilyllithium in DMS (0.45 mL, 0.5 mmol) was added to the silylcuprate **27** (0.5 mmol) at -78°C. The solution was stirred on a vortex mixer (*vide supra*). The spectra were recorded at -85°C immediately.

Generation of Mixed Silylcuprates

Preparation of 43 by Reaction of 25 and 16: CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.18 mL, 0.25 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Upon addition of dimethylphenylsilyllithium in THF (0.3 mL, 0.25 mmol) dropwise to this clear solution at -78°C the reaction turned deep red. The NMR spectrum was recorded immediately.

Preparation of 43 by Reaction of 26 and MeLi: CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -70°C and dimethylphenylsilyllithium in THF (0.3 mL, 0.25 mmol) was added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. MeLi (0.18 mL, 0.25 mmol) in Et_2O was added *via* a syringe at -78°C. The spectra were recorded immediately.

Preparation of 43 by Reaction of 17 and 28: CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and dimethylphenylsilyllithium in THF (0.6 mL, 0.5 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. In a separate vial, MeLi (0.36 mL, 0.5 mmol) was added to a THF solution of CuCN (0.25 mL, 0.25 mmol) at -50°C. After 10 min of stirring, the solution of **17**, precooled to -78°C, was transferred *via* a cannula into cuprate **28**, which was also maintained at -78°C. The resulting deep red solution was stirred for 20 min before recording the NMR spectrum

Preparation of $(PhMe_2Si)_2(Me)CuLi_2$ (44) by Reaction of $PhMe_2SiLi$ (25) and MeCu(CN)Li (16): CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.18 mL, 0.25 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Dimethylphenylsilyllithium (**25**) in THF (0.6 mL, 0.5 mmol) was added dropwise to this clear solution at -78°C. The resulting deep red solution was examined by NMR immediately.

Preparation of 44 by Reaction of $(PhMe_2Si)_2Cu(CN)Li_2$ (28) and MeLi: MeLi in Et_2O (0.36 mL, 0.5 mmol) was introduced dropwise *via* a syringe to a solution of **28** (0.05 mmol, *vide supra*) at -78°C. The resulting deep red solution was stirred for 20 min before recording the NMR spectrum.

Preparation of $PhMe_2Si(Me)_2CuLi_2$ (45) by Reaction of $PhMe_2SiLi$ (25) MeLi and CuCN: CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C. and MeLi (0.36 mL, 0.5 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Upon addition of dimethylphenylsilyllithium (**25**) in THF (0.3 mL, 0.25 mmol) dropwise to this clear solution at -78°C the reaction turned deep red. The NMR spectrum was recorded immediately.

Preparation of 45 by Reaction of $(PhMe_2Si)_3CuLi_2$ (29) and MeLi: MeLi in Et_2O (0.7 mL, 1.0 mmol) was introduced dropwise *via* a syringe to a solution of **29** (1.0 mmol, *vide supra*) at -78°C. The resulting deep red solution was stirred for 20 min before recording the NMR spectrum.

Preparation of ^{13}C NMR Samples for Reactions of 43 with 32: $PhMe_2SiLi$ (0.3 mL, 0.25 mmol) was added dropwise at -85°C to a THF solution of MeCu(CN)Li (0.25 mmol, *vide supra*) under argon. The resulting deep red solution was stirred for 10 min after which **32** (0.024 mL, 0.25 mmol) was added *via* a syringe. The reaction was stirred for 10 min before recording the NMR spectrum.

Preparation of ^{13}C NMR Samples for Reaction of 29 with 32: 32 (0.024 mL, 0.25 mmol) was added *via* a syringe at -85°C to a THF solution of

$(PhMe_2Si)_3CuLi_2$, **29** (0.25 mmol, *vide supra*). The reaction was stirred for 10 min before recording the NMR spectrum.

Preparation of 3-trialkylsilyl cyclohexanone

Typical Procedure for Reactions of $PhMe_2SiLi$/CuCN Solutions with 32, Synthesis of 33: $PhMe_2SiLi$ (1.25 mL, 1.0 mmol) was added dropwise at -45°C to CuCN (0.089 g, 1.0 mmol) in THF (2 mL) under argon. The resulting deep red solution was stirred for 0.5 h after which **32** (0.08 mL, 0.82 mmol) was added *via* a syringe. All reactions were stirred for a further 0.5 h and then quenched with satd. NH_4Cl/10% NH_4OH. The usual workup involved extraction of the organic phase with Et_2O (2 x 2 mL) and washing with brine (2 x 2 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concetrated *in vacuo*. Column chromatography (4:1 hexanes:EtOAc) yielded 3-(dimethylphenylsilyl)-cyclohexanone (**33**). The ratios of 1,2- *vs* 1,4-addition products and the overall yields are reported in text. The ^1H NMR and IR data for **33** matched those reported by Fleming *et al.*[32c] for this compound. $^{13}C\{^1H\}$ ($CDCl_3$) δ 212.5 (*C*=O), 136.6 (*ipso*), 133.8, 129.2, 127.8, 42.3, 41.8, 29.7, 27.5, 26.0, -5.4 (Si*C*H3), -5.5 (Si*C*H3); MS m/e (rel. intensity) 232 (M^+, 20), 217 (15), 189 (5), 156 (22), 135 (100); Anal. calc. $C_{14}H_{20}OSi$ 232.1283 found 232.1282.

Typical Procedure for Reactions of $PhMe_2SiLi$/ $CuBr{\bullet}Me_2S$ with 32: $PhMe_2SiLi$ (1.25 mL, 1.0 mmol) was added dropwise at -45°C to $CuBr{\bullet}Me_2S$ (0.10 g, 0.5 mmol) in THF (2 mL) under argon. The resulting deep red solution was stirred for 0.5 h after which **32** (0.04 mL, 0.41 mmol) was added *via* a syringe. All

reactions were stirred for a further 0.5 h and then quenched. Standard workup and the spectral data for **33** are as reported above.

Typical Procedure for Reactions of $PhMe_2SiLi$/MeLi/ CuCN Solutions with 32, Synthesis of 33: $PhMe_2SiLi$ (1.25 mL, 1.0 mmol) was added dropwise at -70°C to a solution of MeCu(CN)Li [(1.0 mmol, prepared from the addition of MeLi in Et_2O (0.7 mL, 1.0 mmol) and CuCN (0.089 g, 1.0 mmol in THF (2 mL) at -50°C)] in THF (2 mL) under argon. The resulting deep red solution was stirred for 0.5 h after which **32** (0.08 mL, 0.82 mmol) was added *via* a syringe. All reactions were stirred for a further 0.5 h and then quenched. Standard workup and the spectral data for **33** are as reported above.

Preparation of 1-(Dimethylphenylsilyl)-cyclohex-2-en-1-ol (34): Cyclohex-2-en-1-one (0.08 mL, 0.82 mmol) was added dropwise to a solution of $PhMe_2SiLi$ (1.25 mL, 1.0 mmol) at -45°C in THF (2 mL) under argon. The solution turned yellow upon completion of addition. The reaction was stirred for 0.5 h and then quenched with satd. NH_4Cl/10% NH_4OH. The usual workup followed by column chromatography (4:1 hexanes:EtOAc) gave 62% of **34** as a colorless oil. IR (NaCl) 3460 (OH), 1440 (Ph*Me*$_2$Si) cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 7.2-7.7 (m, 5H, Ph), 5.9 (ddd, *J* = 10, 5, 3 Hz, 1H, CH_2HC=C), 5.7 (dt, *J* = 10, 3 Hz, 1H, C=C*H*), 1.4-2.1 (m, 6H, ring CH_2), 1.18 (bs, 1H, O*H*), 0.38 (s, 3H, SiCH_3), 0.36 (s, 3H, SiCH_3); $^{13}C\{^1H\}$ ($CDCl_3$) δ 136.4 (*ipso*), 134.6, 130.4, 130.2, 129.2, 127.7, 64.2 (*C*OH), 32.7, 25.2, 17.5, -5.8 (Si*C*H$_3$), -6.0 (Si*C*H$_3$); MS m/e (rel. intensity) 232 (M^+, 5), 214 (M^+-18, 20), 199 (15), 135 (100); Anal. calc. $C_{14}H_{20}OSi$ 232.1284 found 232.1286.

Typical Procedure for Silylcupration with "$PhMe_2SiCu$"

Reaction of $PhMe_2SiLi$ with 35a: 1-Octyne (0.24 g, 2.2 mmol) was added dropwise to a solution of $PhMe_2SiLi$ (2.6 mL, 2.2 mmol) at -45°C in THF (3 mL) under argon. The reaction was stirred for 0.5 h and then quenched with ^2H_2O (5 mL). It was gradually warmed to room temperature. The usual workup yielded octyne-1-^2H (70% incorporation as calculated from GC-MS analysis).

For **35a:** MS m/e (rel. intensity) 95 (M^+-15, 30), 81 (100), 67 (52).

For **35b:** MS m/e (rel. intensity) 96 (M^+-15, 25), 95 (17.5), 82 (100), 81 (28), 68 (40).

Synthesis of 36 and 37: CuCN (0.197 g, 2.2 mmol) was placed in a flask equipped with an argon inlet. The flask was repeatedly (3x) evacuated and purged with argon. THF (5 mL) was injected, the reaction was cooled to -50°C and dimethylphenylsilyllithium in THF (2.6 mL, 2.2 mmol) added dropwise. The resulting deep red solution was stirred for 0.5 h after which 1-Octyne (0.24 g, 2.2 mmol) was added dropwise. The reaction was stirred for additional 0.5 h and then quenched with H_2O (5 mL) for the preparation of **36a** and **37a**, whereas ^2H_2O (5 mL) was used as the quenching agent for the generation of **36b**. The reactions were warmed gradually to room temperature. The usual workup followed by column chromatography (hexanes) yielded the vinyl silanes which were analyzed by ^1H NMR and GC-MS analysis to determine the amount of ^2H incorporated. The ratios of **36** to **37** and the overall yields are reported in the text.

For **36a:** IR (NaCl) 1620, 1440, 1250, 1120, 995 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 7.1-7.5 (m, 5H, Ph), 6.17 (dt, *J* = 18, 6 Hz, 1H, *H*C=CSi), 5.85 (dt, *J* = 18, 1.5 Hz, 1H, C=C*H*Si), 2.7 (tdd, *J* = 7, 6, 1.5 Hz, 2H, allylic), 1.2-1.42 (m, 8H, CH_2), 0.95 (t, *J* = 7 Hz, 3H, CH_3), 0.3 (s, 6H, SiCH_3); $^{13}C\{^1H\}$ ($CDCl_3$) δ 149.5 (*C*=CSi), 139.4 (C=*C*Si), 133.8 (*ipso*), 128.7, 127.6, 127.2, 36.8, 36.7, 31.7, 28.8, 28.6, 22.5, 13.9 (Si*C*H_3); MS m/e (rel. intensity) 246 (M^+, 9), 231 (70), 161 (35), 135 (50), 121 (100); Anal. calc. $C_{16}H_{26}Si$ 246.1803 found 246.1809.

For **36b**: 400 MHz ^1H NMR ($CDCl_3$) δ 7.1-7.5 (m, 5H, Ph), 5.85 (brt *J* = 1.5 Hz, 1H, C=C*H*Si), 2.7 (td, *J* = 7, 1.5 Hz, 2H, allylic), 1.2-1.42 (m, 8H, CH_2), 0.95 (t, *J* = 7 Hz, 3H, CH_3), 0.3 (s, 6H, SiCH_3); MS m/e (rel. intensity) 247 (M^+, 12), 232 (100), 162 (80), 148 (40), 135 (60), 122 (80), 121 (80); Anal. calc. $C_{16}H_{25}DSi$ 247.1866 found 247.1874.

For **37a:** 400 MHz ^1H NMR ($CDCl_3$) δ 5.9 (dt, *J* = 7, 1.5 Hz, 2H, vinyl); MS m/e (rel. intensity) 246 (M^+, 45), 231 (45), 161 (35), 135 (100), 121 (35).

Gilman Tests. All cuprates prepared in 10 mm NMR tubes were subjected to Gilman test. An equal volume of Michler's ketone (1% solution) in dry benzene was added to the cuprate at 0°C. H_2O (1 mL) was introduced after 10 min and the reaction was allowed to warm to room temperature. After vigorous stirring, a 2% solution of I_2 in glacial acetic acid was added dropwise. A persistent blue color in the organic layer is considered a positive test (confirmation of free RLi).[42]

PREPARATION OF TRIALKYLSTANNYLCUPRATES

^{119}Sn NMR sample preparation

Preparation of Me_3SnLi (47): According to the procedure of Still *et al.*[49a] MeLi (7.15 mL, 10.0 mmol) was added dropwise at -45°C to Me_6Sn_2 (3.27 g, 10.0 mmol) in THF (10 mL) under argon. The resulting pale yellow solution was stirred for 0.5 h and titrated according to procedure of Gilman[99b] before being used in the preparations of cuprates.

Generation of stannylcuprates from CuCN

Preparation of $Me_3SnCu(CN)Li$ (48): CuCN (0.09 g, 1.0 mmol) was placed in a 10 mm NMR tube, equipped with an argon inlet. The tube was repeatedly (3x) evacuated and purged with argon. The reaction was cooled to -70°C and trimethyltinlithium in THF (2.0 mL, 1.0 mmol) was added dropwise. The orange slurry was stirred on a vortex mixer at -78°C in a custom built dewar for 20 min. The NMR spectrum was then immediately recorded.

Preparation of $(Me_3Sn)_2Cu(CN)Li_2$ (51): A THF solution of Me_3SnLi (2.0 mL, 1.0 mmol) was added to a 10 mm NMR tube containing a THF solution of $Me_3SnCu(CN)Li$ at -78°C. The orange colored solution was stirred for 20 min at -78°C prior to examination by NMR and IR spectroscopy.

Preparation of $(Me_3Sn)_3CuLi_2$ (50): To a THF solution of $(Me_3Sn)_2Cu(CN)Li_2$ (1.0 mmol) prepared as outlined above was added a THF solution of Me_3SnLi (2.0 mL, 1.0 mmol) at -78°C. The reaction was stirred for 20 min at -78°C before examination by NMR and IR spectroscopy.

Preparation of $(Me_3Sn)_3CuLi_2$ (50) with excess 47: To a THF solution of $(Me_3Sn)_3CuLi_2$ (1.0 mmol, *vide supra*) was added a THF solution of Me_3SnLi (2.0 mL, 1.0 mmol) at -78°C. The reaction was stirred for 20 min at -78°C before examination by NMR and IR spectroscopy.

Regeneration of $(Me_3Sn)_2Cu(CN)Li_2$ (51) from 50: CuCN (0.045 g, 0.05 mmol) was added to the stannylcuprate **50**. The reaction was stirred for 20 min at -78°C before examination by NMR spectroscopy.

Regeneration of $Me_3SnCu(CN)Li$ (48) from 51: CuCN (0.09 g, 1.0 mmol) was added to the NMR tube containing stannylcyanocuprate **51**. The reaction was stirred for 20 min at -78°C and then examined by NMR spectroscopy.

Generation of Stannylcuprates from $CuBr \cdot Me_2S$

Preparation of Me_3SnCu (49): $CuBr \cdot Me_2S$ (0.205 g, 1.0 mmol) was placed in a 10 mm NMR tube, equipped with an argon inlet. The tube was repeatedly (3x) evacuated and purged with argon. The solution was cooled to -78°C and trimethyltinlithium in THF (2.0 mL, 1.0 mmol) was added dropwise. A red slurry was

obtained. The reaction mixture was stirred on a vortex mixer at -78°C in a custom built dewar for 20 min. The NMR spectrum was immediately recorded without filtration.

Preparation of $(Me_3Sn)_2CuLi$ (52): A THF solution of Me_3SnLi (2.0 mL, 1.0 mmol) was added to a 10 mm NMR tube containing a THF solution of Me_3SnCu **49** (1.0 mmol, *vide supra*) at -78°C. The resultant deep red colored solution was stirred for 20 min at -78°C prior to examination by NMR spectroscopy.

Preparation of $(Me_3Sn)_3CuLi_2$ (50): To a THF solution of $(Me_3Sn)_2CuLi$ (1.0 mmol) prepared as outlined above, was added a THF solution of Me_3SnLi (2.0 mL, 1.0 mmol) at -78°C. The reaction mixture was stirred for 20 min at -78°C before examination by NMR spectroscopy.

Preparation of $(Me_3Sn)_3CuLi_2$ (50) with excess Me_3SnLi (47): To a THF solution of $(Me_3Sn)_3CuLi_2$ (**50**, 1.0 mmol) prepared as outlined above, was added a THF solution of Me_3SnLi (2.0 mL, 1.0 mmol) at -78°C. The reaction mixture was stirred for 20 min at -78°C before examination by NMR spectroscopy.

Regeneration of $(Me_3Sn)_2CuLi$ (52) from 50: $CuBr{\bullet}Me_2S$ (0.10 g, 0.5 mmol) was added to 1.0 mmol of the solution generated by mixing Me_3SnLi (**47**) and $CuBr{\bullet}Me_2S$ in a 3:1 ratio. The reaction mixture was stirred for 20 min at -78°C before examination by NMR spectroscopy.

Regeneration of Me_3SnCu (49) from 52: $CuBr{\bullet}Me_2S$ (0.205 g, 1.0 mmol) was added to the NMR tube containing stannylcuprate **52** (1.0 mmol). The reaction was stirred for 20 min at -78°C and then examined by NMR spectroscopy.

Generation of Mixed Stannylcuprates

Preparation of $Me_3Sn(Me)Cu(CN)Li_2$ (56) by Reaction of Me_3SnLi (47) and MeCu(CN)Li (16): CuCN in THF (0.09 g, 1.0 mmol) was added to a 10 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.71 mL, 1.0 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Trimethyltinlithium in THF (2.0 mL, 1.0 mmol) was added dropwise to this clear solution at -78°C. The reaction turned clear yellow in color. The spectra were recorded immediately.

Preparation of 56 by Reaction of $Me_3SnCu(CN)Li$ (48) and MeLi: MeLi in Et_2O (0.71 mL, 1.0 mmol) was added to the orange solution of **48** (1.0 mmol, prepared as above) at -78°C. The clear yellow solution was stirred on a vortex mixer at -78°C in a custom built dewar for 20 min. The NMR spectrum was then immediately recorded.

Preparation of 56 by Reaction of $(Me_3Sn)_2Cu(CN)Li_2$ (51) and $Me_2Cu(CN)Li_2$ (17): CuCN (0.09 g, 1.0 mmol) was added to a flask, equipped with an argon inlet. The solution was cooled to -50°C where MeLi (1.4 mL, 2.0 mmol) was introduced dropwise generating a clear solution in 10 min. It was then transferred *via* a cannula into cuprate **51** (1.0 mmol, prepared as above) which was also maintained at below -78°C. The resulting yellow solution was stirred for 20 min before recording the NMR spectrum

^{1}H and ^{13}C NMR Sample Preparation

Generation of Stannylcuprates from CuCN

Preparation of 48: A THF solution of Me3SnLi (0.5 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and a solution of CuCN in THF (0.25 mL, 0.25 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately. Inverse addition of the reagents gave similar spectral results.

Preparation of 51: A THF solution of Me3SnLi (0.5 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and a solution of CuCN in THF (0.125 mL, 0.125 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately. Similar spectral results were obtained when the order of mixing of reagents was reversed.

Preparation of 50: A THF solution of Me3SnLi (0.5 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and a solution of CuCN in THF (0.08 mL, 0.08 mmol) added dropwise. The reaction was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately. Inverse addition of the reagents gave similar spectral results.

Preparation of 50 with excess 47: A THF solution of Me3SnLi (0.5 mL, 0.25 mmol) was added to a solution of stannylcuprate **50** at -78°C. The reaction was

stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately. Inverse addition of the reagents gave similar spectral results.

Preparation of 48 for ^{1}H NMR analysis: The above THF solution of CuCN (0.25 mL, 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and trimethyltinlithium in THF-d8 (0.5 mL, 0.25 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Preparation of 50 and 51 for ^{1}H NMR analysis: These solutions were prepared in THF-d8 as described above for **48**.

Generation of Stannylcuprates from CuBr•Me$_2$S

Preparation of Me$_3$SnCu (49): CuBr•Me$_2$S (0.25 mL 0.25 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The reaction was cooled to - 78°C and trimethyltinlithium in THF (0.5 mL, 0.25 mmol) added dropwise. The solution was stirred on a vortex mixer in a custom built dewar for 20 min. A deep red slurry was obtained. The spectra were recorded without filteration.

Preparation of (Me$_3$Sn)$_3$Cu$_2$Li (53): CuBr•Me$_2$S (0.17 mL 0.166 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The reaction was cooled to -78°C and trimethyltinlithium in THF (0.5 mL, 0.25 mmol) was added dropwise. The solution was stirred on a vortex mixer in a custom built dewar for 20 min. The slurry was used as such.

Preparation of $(Me_3Sn)_3CuLi_2$ (50): Trimethyltinlithium in THF (0.5 mL, 0.25 mmol) was added dropwise to a solution of **53** (0.25 mmol) at -78°C. The solution was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Generation of Mixed Stannylcuprates

Preparation of 56 by Reaction of 47 and 16: CuCN in THF (0.4 mL, 0.4 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.3 mL, 0.4 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Trimethyltinlithium in THF (1.0 mL, 0.4 mmol) was added dropwise to this clear solution at -78°C. The reaction turned yellow in color. The spectra were recorded immediately.

Preparation of 56 by Reaction of 17 and 51: CuCN in THF (0.4 mL, 0.4 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and trimethyltinlithium in THF (1.0 mL, 0.4 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min. In a separate vial, **17** (prepared as above) precooled to -78°C, was transferred *via* a cannula into cuprate **51**, which was also maintained at -78°C. The resulting yellow solution was stirred for 20 min before recording the NMR spectrum.

Preparation of $Me_3Sn(Me)_2CuLi_2$ (57) by Reaction of 48 and MeLi: CuCN in THF (0.4 mL, 0.4 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -78°C and Me_3SnLi (1.0 mL, 0.4 mmol) in THF was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. MeLi (0.6 mL, 0.8 mmol) in Et_2O was added dropwise to this orange suspension at -78°C. The reaction turned clear yellow in color. The spectra were recorded immediately.

Preparation of 57 by Reaction of 56 and MeLi: CuCN in THF (0.4 mL, 0.4 mmol) was added to a 5 mm NMR tube, equipped with an argon inlet. The solution was cooled to -50°C and MeLi (0.3 mL, 0.4 mmol) in Et_2O was added *via* a syringe. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 10 min. Trimethyltinlithium in THF (1.0 mL, 0.4 mmol) was added dropwise to this clear solution at -78°C. The reaction turned yellow in color. MeLi (0.3 mL, 0.4 mmol) in Et_2O was then added *via* a syringe to yield a clear yellow solution. The spectra were recorded immediately.

Reaction of 51with MeLi: MeLi in Et_2O (0.15 mL, 0.2 mmol) was added dropwise to a THF solution of **51** (0.4 mmol) at -78°C. The solution was stirred on a vortex mixer in a custom built dewar for 20 min. The spectra were recorded immediately.

Reaction of 50 with 56: A THF solution of $(Me_3Sn)_3CuLi_2$ (0.25 mmol) was prepared in a 5 mm NMR tube as described above. The solution was cooled to -78°C and a solution of $Me_3Sn(Me)Cu(CN)Li_2$ in THF (0.25 mmol) added dropwise. The reaction mixture was stirred on a vortex mixer in a custom built dewar for 20 min.

Reaction of 58 with 17, generation of 60: Bu_3SnH (0.13 mL 0.5 mmol) was added dropwise at -85°C to $Me_2Cu(CN)Li_2$ (0.5 mmol, *vide supra*). NMR was recorded on the resulting yellow solution after stirring for 10 min.

Reaction of 58 with 17, generation of 61: Bu_3SnH (0.13 mL 0.5 mmol) was added dropwise at -85°C to the above solution. After the evolution of H_2 subsided (5 min) NMR was recorded on the resulting yellow solution.

Preparation of 3-trialkylstannyl cyclohexanone

Typical Procedure for Reactions of Me_3SnLi/MeLi/CuCN Solutions with 32, Synthesis of 70: Me_3SnLi (2.0 mL, 1.0 mmol) was added dropwise at -78°C to a solution of MeCu(CN)Li (**16**, 1.0 mmol, generated from the reaction of MeLi in Et_2O (0.75 mL, 1.0 mmol) and CuCN (0.09 g, 1 mmol) in THF (2 mL) under argon. The resulting solution was stirred for 0.5 h after which **32** (0.08 mL, 0.82 mmol) was added *via* a syringe. The reaction was stirred for a further 0.5 h and then quenched with satd. NH_4Cl/10% NH_4OH. Workup involved extraction of the organic phase with Et_2O (2 x 2 mL) and washing with brine (2 x 2 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concetrated *in vacuo*. Column chromatography (4:1 hexanes:EtOAc) yielded 3-(trimethylstannyl)-cyclohexanone (**70**) in > 90% isolated yield. The ^1H NMR and IR data for **70** matched those reported by Still[48a] for this compound. $^{13}C\{^1H\}$ ($CDCl_3$) δ 212.2 (*C*=O), 45.8, 42.1, 30.8, 29.4, 25.2, -11.7 (Sn*C*H_3); MS m/e (rel. intensity) 246 (M^+-15, 20); Anal. calc. $C_9H_{18}OSn$ 246.1283 found 246.1282.

Reaction of Bu_3SnH/ $Me_2Cu(CN)Li_2$ with 32, Synthesis of 71: Bu_3SnH (0.27 mL, 1.0 mmol) was added dropwise at -78°C to a solution of $Me_2Cu(CN)Li_2$ (**17**, 1.0 mmol, generated from the reaction of MeLi in Et_2O (0.75 mL, 1.0 mmol) and CuCN (0.045 g, 0.5 mmol) in THF (2 mL) under argon. The resulting yellow solution was stirred for 0.5 h after which **32** (0.082 mL, 0.82 mmol) was added *via* a syringe. The reaction was stirred for a further 0.5 h and then quenched with satd. NH_4Cl/10% NH_4OH. The usual workup involved extraction of the organic phase with Et_2O (2 x 2 mL) and washing with brine (2 x 2 mL). The combined extracts were dried over anhydrous $MgSO_4$ and concetrated *in vacuo*. Column chromatography (4:1 hexanes:EtOAc) yielded 3-(tributylstannyl)-cyclohexanone (**71**) in > 96% isolated yield. The ^1H NMR and IR data for **71** matched those reported by Still[48a] for this compound. $^{13}C\{^1H\}$ ($CDCl_3$) δ 211.8 (*C*=O), 46.3, 42.1, 31.0, 30.0, 29.1, 27.3 (*C*$_3$), 13.4, 8.0; MS m/e (rel. intensity) 331 (M^+-56, 70).

Preparation of Bu_3SnH (58): Reduction of Bu_3SnCl with $LiAlH_4$[25] gave Bu_3SnH in 82% chemical yield and 97% purity as measured by gas chromatographic analysis after distillation (bp 49°C @ 0.05 mm Hg). A modified work-up procedure was employed that involved the transfer of the supernatant from the aqueous layer *via* a canula. Removal of Et_2O followed by addition of *n*-hexanes *in vacuo* concentration and distillation under reduced pressure gave oxide-free Bu_3SnH that could be stored in the freezer without noticable decomposition for several months.

Preparation of Trialkylstannyllithium and Quenching with Methyl Iodide, Table IV:

Entry 1: Bu_3SnLi was prepared according to the procedure of Nozaki.[70] Stannous chloride (0.6 g, 3.16 mmol) was stirred in 5 mL of dry THF at 0°C and then *n*-BuLi (3.65 mL, 9.48 mmol) was added dropwise over 30 min. To an aliquot of the deep red solution was added excess MeI in THF at 0°C. The reaction was stirred for 15 min then quenched by addition of NH_4Cl solution and the separated organic layer analyzed by gas chromatography with dodecane as an internal standard. Bu_3SnMe was formed in 33% yield.

Entry 2: A solution of Bu_3SnCl (4.0 g, 12.5 mmol) in 25 mL of THF was added to a suspension of Li clippings (0.35 g, 50 mmol) in 20 mL of THF at 0°C according to the procedure of Soloski.[49b] The reaction was stirred overnight at this temperature and the green solution treated with excess MeI. The yield of Bu_3SnMe was 48% as determined by GC against an internal standard (dodecane).

Entry 3: A Li dispersion (1.4 g, 200 mmol) in *n*-hexane was prepared in a preweighed Schlenk tube under argon. THF (75 mL) was added, followed by Me_3SnCl (10 g, 50 mmol) in 50 mL of THF. The reaction was stirred at 0°C for 8 h. An aliquot was quenched with excess MeI. The yield of Me_3SnLi was calculated from the amount of Me_4Sn detected by gas chromatographic analysis *vs* decane as an internal standard.

Entry 4: *n*-BuLi (0.38 mL, 1.0 mmol), was added to a stirred solution of Bu_3SnH (0.291 g, 1.0 mmol) in 5 mL of THF at 0°C. The reaction was quenched with

MeI after 15 min. Gas chromatographic analysis revealed Bu_4Sn as the major product accompanied by only 4% of Bu_3SnMe (dodecane as internal standard).

Entry 5: Preparation of Bu_3SnLi by the modified procedure of Still[49a] involved addition of BuLi (1.0 mL, 2.5 mmol) to an efficiently stirred solution of diisopropyl amine (0.35 mL, 2.5 mmol) in 5 mL of THF at -10°C. The reaction was stirred for 30 min then $_3SnH$ (0.72 g, 2.5 mmol) was added at -30°C. The reaction turned pale green at this point. The yield of Bu_3SnMe was 90% as determined by gas chromatographic analysis with dodecane as an internal standard.

Entry 6: To an efficiently stirred solution of $Me_3SnSnMe_3$ (1.63 g, 5.0 mmol) in 20 mL of THF was added MeLi (3.6 mL, 5 mmol) while maintaining the temperature below -40°C. After 20 min the reaction was quenched with excess MeI and the yield (80%) of Me_4Sn was calculated as before.

Reaction of 1-Decyne (91) with $Bu_3SnAlEt_2$ (90); Representative Procedures for the Preparation of 2-Tributylstannyl-1-alkenes (92a, 92b, 93a and 93b): The following three procedures are representative of the addition of **91** to **90** (Table V).

(a) Using $SnCl_2$ and *n*-BuLi (Method A): *n*-BuLi (11.4 mL, 28.44 mmol) was added dropwise to a solution of stannous chloride (1.8 g, 9.48 mmol) in 15 mL of dry THF at 0°C. After stirring for 30 min, diethylaluminum chloride (9.48 mL, 9.48 mmol) was added and the reaction stirred for a further 0.5 h. 1-Decyne (0.437 g, 3.16 mmol) and catalyst (0.3 mmol) were then added at -30°C. The reaction was stirred

for 3 h after which it was allowed to warm to 0°C. Normal workup gave vinyl stannanes **92a** and **93a** in the ratios shown in the Table 2.

(b) Using Bu_3SnH and LDA (Method B): Bu_3SnH (1.45 g, 5 mmol) was added to 5 mL of THF containing lithium diisopropyl amide (prepared by dropwise addition of *n*-BuLi (2 mL, 5 mmol) to an efficiently stirred solution of diisopropyl amine (0.70 mL, 5 mmol) in 5 mL of THF at -10°C) while maintaining the temperature below -30°C. After stirring for 0.5 h, Et_2AlCl (5 mL, 5 mmol) was added dropwise at -30°C. The clear solution was further stirred for 0.5 h then 1-decyne (0.22 g, 1.6 mmol) in 5 mL of THF was added dropwise followed by the addition of a catalyst (0.16 mmol). The reaction turned orange at this time. After 3 h the reaction was warmed to 0°C and subjected to normal workup.

(c) General Procedure for Slow Addition Reactions (Method C): To 3.2 mmol of lithium diisopropyl amide in 5 mL of THF was added Bu_3SnH (0.87 g, 3 mmol) in 12 mL THF at -30°C. After stirring for 0.5 h, Et_2AlCl (2.8 mL, 2.8 mmol) in hexane was added dropwise. After stirring for 0.5 h, one half of the 1-decyne to be reacted (0.32 g, 2.3 mmol) was added in 15 mL of THF. This was followed by addition of CuCN (0.022 g, 0.23 mmol) in 5 mL of THF. The remainder of the alkyne was added over 0.75 - 1.0 h. The reaction was stirred at -30°C for 3 h then warmed to 0°C and subjected to normal workup.

The experimental results of the addition of **91** to **90** are summarized in Table V, and the products gave the following spectral data.

2-Tributylstannyl-1-decene (92a, Scheme 39): ^{1}H NMR ($CDCl_3$) δ 0.82 (t, 3H, CH_3, J = 7.5 Hz), δ 0.88 (t, 9H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 22H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.23 (ddt, 2H, C=CCH_2, J = 7.56 Hz, 1.45 Hz, 1.04 Hz), 5.09 (dt, 1H, C=CH, J = 2.9 Hz, 1.04 Hz, $^3J_{Sn-H}$ = 64 Hz), 5.66 (dt, 1H, C=CH, J = 2.9 Hz, 1.45 Hz, $^3J_{Sn-H}$ = 140 Hz). Allylic region decoupled: δ 2.21 (s), 5.09 (d, 1H, C=CH, J = 2.9 Hz), 5.66 (d, 1H, C=CH, J = 2.9 Hz); ^{13}C NMR 156.0 (C=CSnBu3), 124.5 (C=CH_2), 41.4, 32.0, 29.7, 29.5, 29.3, 29.1, 27.4, 22.6, 13.6, 9.7; ^{119}Sn NMR = - 45.6; GC/MS, m/e (relative intensity), 373 (M^+ - 56, 37.5), 291 (100.0). Anal Calcd for $C_{18}H_{37}Sn$: 373.1917. Found: 373.1920; for $C_{14}H_{29}Sn$: 317.1291. Found: 317.1288 .

***E*-Tributylstannyl-1-decene (93a):** ^{1}H NMR ($CDCl_3$) δ 0.8 (t, 3H, CH_3, J = 5.7 Hz), 0.88 (t, 9H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 22H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.2 (dq, 2H, C=CCH_2, J = 5.5 Hz, 2.0 Hz), 5.85 (dt, 1H, C=CH, J = 18.0 Hz, 2.0 Hz, $^2J_{Sn-H}$ = 60 Hz), 5.96 (dt, 1H, C=CH, J = 18.0 Hz, 5.5 Hz, $^3J_{Sn-H}$ = 47 Hz). Allylic region decoupled, 2.2 (s, 2H), 5.85 (d, 1H, C=CH, J = 18.0 Hz), 5.96 (d, 1H, C=CH, J = 18.0 Hz); ^{13}C NMR 155.3 (C=CSnBu3), 121.4 (C=CH), 42.2, 31.9, 29.5, 29.3, 28.2, 27.3, 24.4, 22.7, 13.6, 10.0; ^{119}Sn NMR = - 50.1; GC/MS, m/e (relative intensity), 373 (M^+ - 56, 31.25), 291 (100.0). Anal Calcd for $C_{18}H_{37}Sn$: 373.1917. Found: 373.1916; for $C_{14}H_{29}Sn$: 317.1291. Found: 317.1290.

Independent preparation of 93a (Scheme 39): To 1-Decyne (0.138 g, 1.0 mmol) in 5 mL of *n*-hexanes DIBALH (1 mL, 1.0 mmol) was added dropwise with stirring . The reaction was refluxed for 2 h after which time the solvent was removed under vacuum. THF (5 mL) was then added and the solution was cooled to -78°C whereupon *n*-BuLi (0.8 mL, 2.0 mmol) and HMPA (2 mL) were added. The reaction

was stirred for 0.5 h then Bu_3SnCl (0.65 g, 2.0 mmol) was added and the reaction further stirred for an hour at -78°C and 2 h at 0°C. Normal workup gave 0.32 g (76%) of (**93a**). Bu_4Sn was the other product detected.

Preparation of 92b and 93b (Scheme 39): The reaction was conducted as described above (Method B), but was quenched by stirring with ^2HCl for 0.5 h and then processed in the usual fashion.

***Z*-1-Deuterio-2-tributylstannyl-1-decene (92b):** ^1H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 7.0 Hz), 0.9 (t, 3H, CH_3, J = 7.7 Hz), 1.2-1.4 (m, 22H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.24 (dt, 2H, C=CCH_2, J = 7.66 Hz, 1.5 Hz), 5.66 (t, 1H, C=CH, J = 1.5 Hz, $^3J_{Sn-H}$ = 140 Hz); GC/MS, m/e (relative intensity), 374 (M^+ - 56, 97). Anal Calcd for $C_{14}H_{28}Sn^2H$: 318.1354. Found: 318.1350.

***Z*-2-Deuterio-1-tributylstannyl-1-decene (93b):** ^1H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 7.0 Hz), 0.9 (t, 3H, CH_3, J = 5.7 Hz), 1.2-1.4 (m, 22H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.2 (dt, 2H, C=CCH_2, J = 5.5 Hz, 3.0 Hz), 5.85 (t, 1H, C=CH, J = 3.0 Hz, $^2J_{Sn-H}$ = 60 Hz); GC/MS, m/e (relative intensity), 374 (M^+ - 56, 100). Anal Calcd for $C_{14}H_{28}Sn^2H$: 318.1354. Found: 318.1361.

Reaction of 1-Nonyne (95) with [(Bu3Sn-9-BBNOMe)$^-$]Li$^+$ (94); Representative Procedures for the Preparation of 2-Tributylstannyl-1-alkenes (96a, 97a, 96b and 97b): The following procedure is representative of the addition of **95** to **94**, (Scheme 40).

Bu_3SnH (1.5 g, 5.8 mmol) in THF (10 mL) was added to 5 mL of THF containing lithium diisopropyl amide (prepared by dropwise addition of *n*-BuLi (2.5 mL, 6.0 mmol) to an efficiently stirred solution of diisopropyl amine (0.84 mL, 6.0 mmol) in 5 mL of THF at -10°C) while maintaining the temperature below -30°C. After stirring for 0.5 h, B-methoxy-9-borabicyclo[3.3.1]nonane (11.6 mL, 5.8 mmol) was added dropwise at -78°C. The clear solution was warmed to 0°C and further stirred for 0.5 h. The reaction was cooled to -78°C and then 1-nonyne (0.38 g, 3.0 mmol) in 5 mL of THF was added dropwise followed by the addition of a catalyst (0.3 mmol). The reaction turned orange at this point. After 3 h at -65°C, a coupling agent was added. Stirring was continued for 1 h and then the reaction was quenched and oxidized with NaOH (15 mL and H_2O_2 (5 mL). The resulting solution was filtered through celite and then subjected to column purification. Spectral data for the various products are listed below:

2-Tributylstannyl-1-nonene (96a, Scheme 40): ^1H NMR ($CDCl_3$) δ 0.82 (t, 3H, CH_3, J = 7.5 Hz), δ 0.88 (t, 9H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.23 (ddt, 2H, C=CCH_2, J = 7.56 Hz, 1.45 Hz, 1.04 Hz), 5.09 (dt, 1H, C=CH, J = 2.9 Hz, 1.04 Hz, $^3J_{Sn-H}$ = 64 Hz), 5.66 (dt, 1H,

C=CH, J = 2.9 Hz, 1.45 Hz, $^{3}J_{Sn-H}$ = 140 Hz); ^{13}C NMR 156.0 (C=CSnBu3), 124.5 ($C=CH_2$), 41.4, 32.0, 29.5, 29.3, 29.1, 27.4, 22.6, 13.6, 9.7; ^{119}Sn NMR = - 45.6; GC/MS, m/e (relative intensity), 361 (M^+ - 56, 37.5), 291 (100.0).

***E*-Tributylstannyl-1-nonene (97a):** ^{1}H NMR ($CDCl_3$) δ 0.8 (t, 3H, CH_3, J = 5.7 Hz), 0.88 (t, 9H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.2 (dq, 2H, $C=CCH_2$, J = 5.5 Hz, 2.0 Hz), 5.85 (dt, 1H, C=CH, J = 18.0 Hz, 2.0 Hz, $^{2}J_{Sn-H}$ = 60 Hz), 5.96 (dt, 1H, C=CH, J = 18.0 Hz, 5.5 Hz, $^{3}J_{Sn-H}$ = 47 Hz); ^{13}C NMR 155.3 (C=CSnBu3), 121.4 (C=CH), 42.2, 31.9, 29.3, 28.2, 27.3, 24.4, 22.7, 13.6, 10.0; ^{119}Sn NMR = - 50.1; GC/MS, m/e (relative intensity), 361 (M^+ - 56, 31.25), 291 (100.0).

***Z*-1-Deuterio-2-tributylstannyl-1-nonene (96b):** ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 7.0 Hz), 0.9 (t, 3H, CH_3, J = 7.7 Hz), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.24 (dt, 2H, $C=CCH_2$, J = 7.66 Hz, 1.5 Hz), 5.66 (t, 1H, C=CH, J = 1.5 Hz, $^{3}J_{Sn-H}$ = 140 Hz); GC/MS, m/e (relative intensity), 362 (M^+ - 56, 97).

***Z*-2-Deuterio-1-tributylstannyl-1-nonene (97b):** ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 7.0 Hz), 0.9 (t, 3H, CH_3, J = 5.7 Hz), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.2 (dt, 2H, $C=CCH_2$, J = 5.5 Hz, 3.0 Hz), 5.85 (t, 1H, C=CH, J = 3.0 Hz, $^{2}J_{Sn-H}$ = 60 Hz); GC/MS, m/e (relative intensity), 362 (M^+ - 56, 100).

Bu_4Sn and $Bu_3SnSnBu_3$ were identified by NMR and gas chromatographic comparison with authentic samples.

In the absence of a catalyst but otherwise under the same conditions the reaction did not produce vinylstannanes.

General Procedure for the Preparation of Disubstituted Vinylstannanes (Scheme 39): 1-Decyne (0.69 g, 5.0 mmol) in 5 mL of THF was added to a solution of **90** at -30°C (10 mmol, *vide supra*) in 20 mL of THF. This was followed by addition of CuCN (0.045 g, 0.5 mmol) at which point the reaction turned orange. After stirring for 3 h at -30°C it was warmed to 0°C (wine red in color) and subjected to two separate sets of conditions as described below:

(a) Transmetallation with *n*-BuLi: Preparation of 92c, 92d and 93d: *n*-BuLi (2.4 mL, 6.0 mmol) was added at -78°C to 1,2-dimetallo-1-alkene (prepared as described above). After stirring for 30 min an excess of allyl bromide (**92c**, 2x) or MeI (2x) in HMPA (5 mL, **92d** and **93d**) was added. The reaction was left to stir overnight. Usual workup followed by silica gel chromatography (*n*-hexanes as eluant) gave the desired products in >98% stereoisomeric purity.

5-Tributylstannyl-4(*Z*)-1-tridecadiene (92c): 1.6 g (68%); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 22H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.23 (dt, 2H, C=CCH_2, J = 7.0 Hz, 1.5 Hz), 2.73 (ddt, 2H, C=CCH_2C=C, J = 7.0 Hz, 2.0 Hz, 1.5 Hz), 4.99 (ddt, 1H, HC=CH*cis*, J = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, J = 17.0 Hz, 2.0 Hz), 5.8 (ddt, 1H, HC=CH_2, J = 17.0

Hz, 10.0 Hz, 6.0 Hz), 5.96 (ddt, 1H, C=CHCH$_2$, J = 7.0 Hz, 2.0 Hz, 1.5 Hz, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 156.0 (C=CSnBu3), 148.0 (C=CH), 139.5 (HC=CH$_2$), 138.0 (C=CH$_2$), 115.0 (C=CCH$_2$C=C), 41.4, 32.0, 29.6, 29.3, 29.2, 29.1, 27.4, 22.6, 13.6, 9.7; ^{119}Sn NMR = - 52.1; GC/MS, m/e (relative intensity), 413 (M^+ - 56, 100); Anal Calcd for $C_{21}H_{43}Sn$: 413.1354. Found: 413.1361.

2-Tributylstannyl-1(Z)-undecene (92d): 0.85 g (38%); ^{1}H NMR (CDCl3) δ 0.88 (t, 12H, CH3, J = 7.0 Hz), 1.2-1.4 (m, 22H, CH$_2$), 1.45-1.6 (m, 8H, CH$_2$), 1.96 (d, 3H, CH3, J = 7.0 Hz), 2.23 (dt, 2H, C=CCH$_2$, J = 7.0 Hz, 1.9 Hz), 6.1 (qt, 1H, C=CH, J = 7.0, 1.9 Hz, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 145.2 (C=CSnBu3), 134.0 (C=CH), 40.8, 30.7, 29.3, 29.2, 27.8, 26.8, 24.2, 15.5, 14.0, 10.2; ^{119}Sn NMR = - 45.0; GC/MS, m/e (relative intensity), 387 (M^+ - 56, 100); Anal Calcd for $C_{19}H_{39}Sn$: 387.2199. Found: 387.2139.

Tributylstannyl-2-methyl-1(Z)-decene (93d): 0.85 g (38%); ^{1}H NMR (CDCl3) δ 0.88 (t, 12H, CH3, J = 6.6 Hz), 1.2-1.4 (m, 22H, CH$_2$), 1.45-1.6 (m, 8H, CH$_2$), 1.78 (s, 3H, CH3), 2.23 (dt, 2H, C=CCH$_2$, J = 6.7 Hz, 2.0 Hz), 5.45 (s, 1H, $^3J_{Sn-H}$ = 75 Hz); ^{13}C NMR δ 155.3 (C=CSnBu3), 121.3 (C=CH), 42.2, 32.0, 29.5, 29.3, 29.2, 28.2, 27.3, 24.4, 22.7, 19.7, 13.6, 10.0; ^{119}Sn NMR = - 49.0; GC/MS, m/e (relative intensity), 387 (M^+ - 56, 100); Anal Calcd for $C_{19}H_{39}Sn$: 387.2199. Found: 387.2169.

b) Palladium-Catalyzed Cross-Coupling Reactions of 1,2-Dimetallo-1-alkenes, Preparation of 92c, 92e and 92f: To 0.74 g (1 mmol) of Pd(PPh3)2Cl2 in 20 mL of THF were sequentially added DIBALH (2 mL, 2 mmol; 25°C, 30 min), *cis* 1,2-dimetallo-vinyl adduct (10 mmol, prepared in a separate flask as

described above) and the electrophilic coupling reagent (15.0 mmol). The reactions were stirred at overnight at room temperature. Usual workup followed by silica gel chromatography (*n*-hexanes as eluant) gave the bifunctionalized vinylstannanes. Cross-coupled products derived from reaction of the vinylstannyl bonds were not detected.

For **92c**: 2.1 g (89%).

1-Phenyl-3-tributylstannyl-2(Z)-undecene (92e): 2.17 g (84%); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 22H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.25 (dt, 2H, C=CCH_2, J = 7.0 Hz, 2.0 Hz), 3.4 (d, 2H, C=CCH_2Ph, J = 7.0 Hz), 6.2 (tt, 1H, C=CCHCH_2, J = 7.0 Hz, 2.0, $^3J_{Sn-H}$ = 140 Hz), 7.15-7.4 (m, 5H, Ph); ^{119}Sn NMR = - 50.1; GC/MS, m/e (relative intensity), 463 (M^+ - 56, 100).

1-Phenyl-2-tributylstannyl-1(Z)-decene (92f): 2.0 g (79%); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9 H, CH_3, J = 7.0 Hz), 0.9 (t, 3H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 12H, CH_2), 1.45-1.6 (m, 18H, CH_2), 2.25 (dt, 2H, C=CCH_2, J = 7.0 Hz, 1.5 Hz), 6.15 (t, 1H, C=CH, J = 1.5 Hz, $^3J_{Sn-H}$ = 135 Hz), 7.1-7.4 (m, 5H, Ph); ^{119}Sn NMR = - 47.0; GC/MS, m/e (relative intensity), 449 (M^+ - 56, 100).

General Procedure for the Preparation of Disubstituted Vinylstannanes (Scheme 40) 1-Nonyne (0.38 g, 3.0 mmol) in 5 mL of THF was added to a solution of **94** at -65°C (5.8 mmol, *vide supra*) in 20 mL of THF. This was followed by addition of CuBr (0.06 g, 0.3 mmol) at which point the reaction turned orange. After stirring for 3 h at -65°C CuBr (0.6 g, 3.0 mmol) was added and the reaction allowed to stir further for an hr. Allyl bromide (0.8 mL, 9.0 mmol) was then

added and the reaction was warmed to 0°C (wine red in color). Oxidation with NaOH(15 mL) and H_2O_2 (5 mL), followed by column purification (hexanes as the eluant) resulted in the desired products in the yields reported in Scheme 40.

In cases where Pd° was the coupling agent, the initial reaction solution containing the 1,2-dimetallo adduct was added *via* a canula to a solution of the electrophile (6.0 mmol) in 5 mL of THF and Pd° (0.15 mmol) at room temperature. The palladium catalyzed reactions were stirred further for overnight. All reactions were subjected to normal workup followed by flash chromatography to give the indicated products whose spectral data are reported below:

5-Tributylstannyl-4(*Z*)-1-dodecadiene (96c): 1.16 g (89%); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12H, CH_3, *J* = 7.0 Hz), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.23 (dt, 2H, C=CCH_2, *J* = 7.0 Hz, 1.5 Hz), 2.73 (ddt, 2H, C=CCH_2C=C, *J* = 7.0 Hz, 2.0 Hz, 1.5 Hz), 4.99 (ddt, 1H, HC=CH*cis*, *J* = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, *J* = 17.0 Hz, 2.0 Hz), 5.8 (ddt, 1H, HC=CH_2, *J* = 17.0 Hz, 10.0 Hz, 6.0 Hz), 5.96 (ddt, 1H, C=CHCH_2, *J* = 7.0 Hz, 2.0 Hz, 1.5 Hz, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 156.0 (C=CSnBu3), 148.0 (C=CH), 139.5 (HC=CH_2), 138.0 (C=CH_2), 115.0 (C=CCH_2C=C), 41.4, 32.0, 29.3, 29.2, 29.1, 27.4, 22.6, 13.6, 9.7; ^{119}Sn NMR = - 52.1; GC/MS, m/e (relative intensity), 399 (M^+ - 56, 100).

3-Keto-7-tributylstannyl-6(*Z*)-tetradecene (96d): 0.8 g (53%); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 12H, CH_3, *J* = 7.0 Hz), 1.02 (t, 3H, CH_3), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.08 (q, 2H, CH_2), 2.15 (t, 2H, CH_2), 2.25 (dt, 2H, C=CCH_2, *J* = 7.0 Hz, 2.0 Hz), 5.92 (tt, 1H, C=CHCH_2, *J* = 7.0 Hz, 2.0,

$^3J_{Sn-H}$ = 140 Hz); IR (cm^{-1}) 2966, 1726, 1455; ^{119}Sn NMR = - 57.3; GC/MS, m/e (relative intensity), 443 (M^+ - 56, 100).

1-Phenyl-3-tributylstannyl-2(Z)-decene (96e): 1.18 g (78%); ^1H NMR ($CDCl_3$) δ 0.88 (t, 12H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 20H, CH_2), 1.45-1.6 (m, 8H, CH_2), 2.25 (dt, 2H, C=CCH_2, J = 7.0 Hz, 2.0 Hz), 3.4 (d, 2H, C=CCH_2Ph, J = 7.0 Hz), 6.2 (tt, 1H, C=$CCHCH_2$, J = 7.0 Hz, 2.0, $^3J_{Sn-H}$ = 140 Hz), 7.15-7.4 (m, 5H, Ph); ^{119}Sn NMR = - 50.1; GC/MS, m/e (relative intensity), 449 (M^+ - 56, 100).

1-Phenyl-2-tributylstannyl-1(Z)-nonene (96f): 0.92g (63%); ^1H NMR ($CDCl_3$) δ 0.88 (t, 9 H, CH_3, J = 7.0 Hz), 0.9 (t, 3H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 12H, CH_2), 1.45-1.6 (m, 18H, CH_2), 2.25 (dt, 2H, C=CCH_2, J = 7.0 Hz, 1.5 Hz), 6.15 (t, 1H, C=CH, J = 1.5 Hz, $^3J_{Sn-H}$ = 135 Hz), 7.1-7.4 (m, 5H, Ph); ^{119}Sn NMR = - 47.0; GC/MS, m/e (relative intensity), 435 (M^+ - 56, 100).

Stannylalumination of Functionalized 1-Alkynes (Scheme 41)

Preparation of 6-Acetoxy-1-hexyne (98b): Pyridine (5.45 g, 0.069 mol), Ac_2O (6.9 g, 0.068 mol) and 5-hexyn-1-ol (**98a**, 6.7 g, 0.069 mol) were stirred together for 3 h at room temperature after which time the reaction was worked up in the normal manner. Vacuum distillation yielded 9.25 g (97%) of the acetate. (bp 61°C @ 10 mm Hg). GC analysis revealed a purity of 97%. ^1H NMR ($CDCl_3$) δ 1.62 (pentet, 2H, CH_2, J = 6.6 Hz), 1.77 (pentet, 2H, CH_2, J = 6.6 Hz), 1.96 (t, 1H, CCH, J = 1.9 Hz), 2.1 (s, 3H, $COCH_3$), 2.22 (dt, 2H, $CCCH_2$, J = 6.6 Hz, 1.9 Hz), 4.1 (t, 2H, OCH_2, J = 6.6 Hz); GC /MS, m/e (relative intensity), CI (isobutane) 141 (M^+ +1, 100).

Preparation of 6-Tetrahydopyranyloxy-1-hexyne (98c): To 5-hexyne-1-ol (**98a**, 5.0 g, 0.50 mol) and freshly distilled dihydropyran (10.5 g, 0.125 mol) were added 4 drops o conc. HCl and the mixture stirred overnight at room temperature. Ether (30 mL) was then added and the mixture shaken with 10% NaOH solution until neutral. Usual workup followed by vacuum distillation yielded 8.4 g (91%) of the protected alcohol (bp 108°C @ 17 mm Hg). GC analysis revealed a purity of 98%. ^{1}H NMR ($CDCl_3$), δ 1.2-1.8 (m, 10H, CH_2), 1.96 (t, 1H, CCH, J = 1.9 Hz), 2.22 (dt, 2H, $CCCH_2$, J = 6.6 Hz, 1.9 Hz), 3.38 (ddd, 1H, OCH_2CH_2), 3.5 (dt, 1H, CH_2 on OTHP), 3.75 (ddd, 1H, OCH_2CH_2), 3.85 (dt, 1H, CH_2 on OTHP), 4.1 (tt, 1H, OCHO); GC /MS, m/e (relative intensity), 182 (M^+, 100).

Preparation of 1-Bromo-5-hexyne (98d): PBr_3 (4.86 mL, 0.05 mmol) was added dropwise to 5-hexyne-1-ol (**98a**, 13.72 g, 0.14 mol) in 50 mL of anhydrous Et_2O at -5°C. The reaction was stirred for 2 h and then warmed to room temperature. It was then quenched by pouring onto ice-cold $NaHCO_3$ solution. Usual workup followed by distillation gave 19.8 g (88%) of the bromide (bp 68°C @ 21 mm Hg). GC analysis revealed a purity of 92%. ^{1}H NMR ($CDCl_3$) δ 1.73 (pentet, 2H, CH_2, J = 6.6 Hz), 1.96 (t, 1H, CCH, J = 1.9 Hz), 2.02 (pentet, 2H, CH_2, J = 6.6 Hz), 2.30 (dt, 2H, $CCCH_2$, J = 6.6 Hz, 1.9 Hz), 3.5 (t, 2H, $BrCH_2$, J = 6.6 Hz); GC/MS, m/e (relative intensity), CI (isobutane) 163 (M^+ + 2, 12.5), 161 (M^+, 14.6).

Preparation of 6-Hydroxy-2-tributylstannyl-1-hexene (99a): To an efficiently stirred solution of lithium diisopropyl amide (5.8 mmol) in 5 mL of THF was added Bu_3SnH (1.69 g, 5.8 mmol) in 5 mL THF at -30°C. After stirring for 30 min Et_2AlCl (5.8 mL, 5.8 mmol) was added and the reaction was further stirred for 30 min. 5-Hexyne-1-ol, **98a** (0.29 g, 3.0 mmol), in 5 mL THF was added dropwise followed

by CuCN (0.026 g, 0.3 mmol). The reaction turned light orange at this point and was stirred at -30°C for 3 h, and then overnight at room temperature. The usual workup, followed by chromatography on silica gel (hexane:ethyl acetate, 96:4, as eluant) gave 0.97 g (84%) of a mixture of **99a** and **100a** (2:1). ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 14H, CH_3, J = 6.7 Hz), 1.32 (q, 18H, CH_2, J = 6.7 Hz), 1.47 (m, 12H, CH_2), 1.55 (m, 3H, OCH_2CH_2), 2.7-3.2 (m, 3H, $C=CH_2$), 3.6 (m, 3H, OCH_2), 5.1 (dt, 1H, C=CH, J = 4.2, 1.1, $^3J_{Sn-H}$ = 64 Hz), 5.7 (dt, 1H, C=CH, J = 4.2, 2.9, $^3J_{Sn-H}$ = 140 Hz), 5.9 (m, 0.5H, C=CH); ^{13}C NMR δ 155.2 ($C=CSnBu_3$), 149.2 ($C=CSnBu_3$), 127.7 ($C=CH_2$), 125.0 ($C=CH_2$), 62.9 (C-OH), 62.8 (C-OH), 40.9, 37.5, 32.4, 32.3, 32.2, 29.3, 29.2, 29.1, 27.5, 27.2, 25.6, 25.1, 13.6, 9.6; GC/MS, m/e (relative intensity), For **99a**: 333 (M^+-56, 100). For **100a**: 333 (M^+-56, 40); Anal calcd for $C_{14}H_{29}OSn$: 333.1241 Found: 333.1239.

Preparation of 6-Acetoxy-2-tributylstannyl-1-hexene (99b): 1-Acetoxy-5-hexyne (**98b**, 0.39 g, 2.8 mmol), in 10 mL THF was added dropwise to an efficiently stirred solution of $Bu_3SnAlEt_2$ (3.0 mmol, *vide supra*) followed by CuCN (0.012 g, 0.14 mmol). The reaction was stirred at and further stirred for 2 h. Usual workup, followed by silica gel chromatography (hexane:ethyl acetate, 95:5, as eluant) gave 1.05 g (87.5%) of **99b** in 99% purity as measured by GC analysis. ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 6.6 Hz), 1.32 (q, 12H, CH_2, J = 6.6 Hz), 1.5 (m, 8H, CH_2), 1.6 (t, 2H, CH_2O, J = 6.7 Hz), 2.1 (s, 3H, $COCH_3$), 2.3 (tt, 2H, $C=CCH_2$, J = 6.6 Hz, 1.9 Hz), 4.1 (t, 2H, CH_2O, J = 6.6 Hz), 5.1 (dt, 1H, C=CH, J = 5.0, 1.2, $^3J_{Sn-H}$ = 63 Hz), 5.7 (dt, 1H, C=CH, J = 5.0, 2.9, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 154.9 ($C=CSnBu_3$), 125.2 ($C=CH_2$), 64.4 (OCH_2), 40.8, 29.1, 28.3, 27.3, 25.9, 20.9, 13.6, 9.6; ^{119}Sn NMR = - 44.7; GC/MS, m/e (relative intensity), 375 (M^+-56, 61); Anal calcd for $C_{16}H_{31}O_2Sn$: 375.1346. Found: 375.1353.

Preparation of 6-Tetrahydropyranyloxy-2-tributylstannyl-1-hexene (99c): A solution of $Bu_3SnAlEt_2$ (5.8 mmol) in 10 mL of THF was prepared as described above. 6-Tetrahydropyranyloxy-1-hexyne (**98c**, 0.546 g, 3.0 mmol), in 5 mL THF was added dropwise with stirring, followed by CuCN (0.02 g, 0.3 mmol). The reaction was stirred at -30°C for 3 h after which time it turned clear yellow. The reaction was then warmed to room temperature and subjected to the usual workup. This was followed by chromatography on silica gel (hexane:ethyl acetate, 99:1, as eluant) to give 1.05 g (75%) of **95c** in >99% purity. ^1H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 6.6 Hz), 1.32 (q, 12H, CH_2, J = 6.6 Hz), 1.5 (m, 8H, CH_2), 1.6 (t, 2H, CH_2O, J = 6.7 Hz), 2.3 (tt, 2H, C=CCH_2, J = 6.6 Hz, 1.9 Hz), 3.38 (ddd, 1H, OCH_2CH_2), 3.5 (tt, 1H, CH_2 on OTHP), 3.75 (ddd, 1H, OCH_2CH_2), 3.85 (tt, 1H, CH_2 on OTHP), 4.6 (tt, 1H, OCHO), 5.1 (dt, 1H, C=CH, J = 3.0, 1.2, $^3J_{Sn-H}$ = 64 Hz), 5.7 (dt, 1H, C=CH, J = 3.0, 1.2, $^3J_{Sn-H}$ = 140 Hz); ^{13}C NMR 155.4 (C=CSnBu3), 124.8 (C=CH_2), 98.7 (OCHO), 67.4 (OCH_2), 62.1 (OCH_2), 41.1, 30.8, 29.5, 29.1, 27.3, 26.3, 25.5, 19.6, 13.6, 9.6; GC/MS, m/e (relative intensity) 417 (M^+-56, 2.3); Anal calcd for $C_{19}H_{37}O_2Sn$: 417.1816. Found: 417.1808.

Preparation of 6-Bromo-2-tributylstannyl-1-hexene (99d). 1-Bromo-5-hexyne (**98d**, 0.48g, 3 mmol) was added to a solution of $Bu_3SnAlEt_2$ (5.8 mmol) in 10 mL of THF followed by CuCN (0.02 g, 0.3 mmol). The reaction was stirred at -30°C for 3 h, then warmed to room temperature. The usual workup, followed by chromatography on silica gel (hexane, as eluant) gave 0.75 g (56%) of **99d** and 30% of the cyclized product (**100d'**) presumably arising from the intramolecular cyclization of the trans regioisomer (**100d**). ^1H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 6.6 Hz), 1.32 (q, 12H, CH_2, J = 6.7 Hz), 1.40 (m, 8H, CH_2), 1.85 (t, 4H, CH_2, J = 6.7 Hz), 2.3 (tt, 4H, C=CCH_2, J = 6.6 Hz, 1.9 Hz), 3.41 (t, 4H, CH_2Br, J = 6.6 Hz), 5.1 (dt,

1.5H, C=CH, J = 3.0, 1.2, $^3J_{Sn-H}$ = 64 Hz), 5.7 (dt, 1.5H, C=CH, J = 3.0, 1.9, $^3J_{Sn-H}$ = 140 Hz); For cyclized product: ^{1}H NMR ($CDCl_3$) δ 5.9 (brs, 0.5H, C=CH, $^2J_{Sn-H}$ = 66 Hz); ^{13}C NMR δ 155.4 (C=CSnBu3), 125.3 ($C=CH_2$), 40.3 (CH_2Br), 32.4, 30.6, 29.1, 27.4, 27.3, 13.6, 9.6; GC/MS, m/e (relative intensity) For **99d**: 395 (M^+-56, 2); For **100d'**: 315 (M^+-80, 75); Anal calcd for $C_{14}H_{28}BrSn$: 395.0397. Found: 395.0398.

Preparation of 6-Cyano-2-tributylstannyl-1-hexene (99e): 1-Cyano-5-hexyne (**98e**, 0.24 g, 2.2 mmol), in 10 mL THF was added dropwise to an efficiently stirred solution of Bu3SnBBN·OMe (3.0 mmol, *vide supra*) followed by CuBr (0.04 g, 0.22 mmol). The reaction was stirred at -70°C for 3 h.CuBr 90.4 g, 2.2 mmol) was then added followed by the addition of MeOH after 2 h of stirring. Usual workup, followed by silica gel chromatography (hexane:ethyl acetate, 95:5, as eluant) gave 0.48 g (81.5%) of **99e** in 99% purity as measured by GC analysis. ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 6.6 Hz), 1.32 (q, 12H, CH_2, J = 6.6 Hz), 1.5 (m, 8H, CH_2), 1.6 (t, 2H, CH_2CN J = 6.7 Hz), 2.3 (tt, 2H, $C=CCH_2$, J = 6.6 Hz, 1.9 Hz), 5.1 (dt, 1H, C=CH, J = 5.0, 1.2, $^3J_{Sn-H}$ = 63 Hz), 5.7 (dt, 1H, C=CH, J = 5.0, 2.9, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 154.9 (C=CSnBu3), 125.2 ($C=CH_2$), 64.4 (OCH_2), 40.8, 29.1, 28.3, 27.3, 25.9, 20.9, 13.6, 9.6; ^{119}Sn NMR = - 44.7; GC/MS, m/e (relative intensity), 342 (M^+-56, 100).

General procedure for the preparation of disubstituted functionalzed vinyl stannanes - Preparation of 9-Hydroxy-5-tributylstannyl-4(*E*)-2-nonadiene (99f): To an efficiently stirred solution of lithium diisopropyl amide (4.0 mmol) in 5 mL of THF was added Bu3SnH (1.0 mL, 3.8

mmol) in 5 mL THF at -30°C. After stirring for 30 min 9-BBNOMe (0.6 mL, 3.5 mmol) was added and the reaction was further stirred for 30 min. 5-Hexyne-1-ol (**98a**) (0.22 g, 2.2 mmol), in 5 mL THF was added dropwise followed by CuBr (0.04 g, 0.22 mmol). The reaction turned light orange at this point and was stirred at -70°C for 3 h, and then added CuBr (0.4 g, 2.2 mmol). After i hr of stirring allyl bromide (0.23 g, 6.0 mmol) was added. The reaction was stirred overnight at room temperature. The usual workup, followed by chromatography on silica gel (hexane:ethyl acetate, 6:1, as eluant) gave 0.53 g (57%) of **99f** .^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 6.7 Hz), 1.32 (q, 12H, CH_2, J = 6.7 Hz), 1.47 (m, 8H, CH_2), 1.55 (m, 2H, OCH_2CH_2), 2.32 (dt, 2H, CH_2, J = 6.7 Hz, 1.5 Hz), 2.73 (ddt, 2H, C=CCH_2C=C, J = 7.0 Hz, 2.0 Hz, 1.5 Hz), 3.6 (m, 2H, OCH_2), 4.99 (ddt, 1H, HC=CH*cis*, J = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, J = 17.0 Hz, 2.0 Hz), 5.8 (ddt, 1H, HC=CH_2, J = 17.0 Hz, 10.0 Hz, 6.0 Hz), 5.96 (ddt, 1H, C=$CHCH_2$, J = 7.0 Hz, 2.0 Hz, 1.5 Hz, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 155.2 (C=$CSnBu_3$), 139.5 (HC=CH_2), 127.7 (C=CH_2),115.0 (C=CCH_2C=C), 62.9 (C-OH), 40.9, 37.5, 32.4, 32.3, 32.2, 29.3, 29.2, 29.1, 27.5, 27.2, 25.6, 25.1, 13.6, 9.6; GC/MS, m/e (relative intensity), For **99f**: 373 (M^+-56, 100).

Preparation of 9-Acetoxy-5-tributylstannyl-4(*E*)-2-nonadiene (99g): 1.26 g (73%) of **99g** in 99% purity as measured by GC analysis. ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, J = 6.6 Hz), 1.32 (q, 12H, CH_2, J = 6.6 Hz), 1.5 (m, 8H, CH_2), 1.6 (t, 2H, CH_2O, J = 6.7 Hz), 2.1 (s, 3H, $COCH_3$), 2.3 (tt, 2H, C=CCH_2, J = 6.6 Hz, 1.9 Hz), 2.73 (ddt, 2H, C=CCH_2C=C, J = 7.0 Hz, 2.0 Hz, 1.5 Hz), 4.1 (t, 2H, CH_2O, J = 6.6 Hz), 4.99 (ddt, 1H, HC=CH*cis*, J = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, J = 17.0 Hz, 2.0 Hz), 5.7 (dt, 1H, C=CH, J = 5.0, 2.9, $^3J_{Sn-H}$ = 138 Hz); ^{13}C NMR δ 154.9 (C=$CSnBu_3$), 125.2 (C=CH_2), 115.0

($C{=}CCH_2C{=}C$), 64.4 (OCH_2), 40.8, 29.1, 28.3, 27.3, 25.9, 20.9, 13.6, 9.6; ^{119}Sn NMR = - 44.7; GC/MS, m/e (relative intensity), 415 (M^+-56, 100).

Preparation of 9-Tetrahydropyranyloxy-5-tributylstannyl-4(*E*)-2-nonadiene (99h): 0.81 g (53%) of **99h** in >99% purity. ^1H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, *J* = 6.6 Hz), 1.32 (q, 12H, CH_2, *J* = 6.6 Hz), 1.5 (m, 8H, CH_2), 1.6 (t, 2H, CH_2O, *J* = 6.7 Hz), 2.3 (tt, 2H, $C{=}CCH_2$, *J* = 6.6 Hz, 1.9 Hz), 2.73 (ddt, 2H, $C{=}CCH_2C{=}C$, *J* = 7.0 Hz, 2.0 Hz, 1.5 Hz), 3.38 (ddd, 1H, OCH_2CH_2), 3.5 (tt, 1H, CH_2 on OTHP), 3.75 (ddd, 1H, OCH_2CH_2), 3.85 (tt, 1H, CH_2 on OTHP), 4.1 (t, 2H, CH_2O, *J* = 6.6 Hz), 4.6 (tt, 1H, OCHO), 4.99 (ddt, 1H, HC=CH*cis*, *J* = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, *J* = 17.0 Hz, 2.0 Hz), 5.7 (dt, 1H, C=CH, *J* = 3.0, 1.2, $^3J_{Sn\text{-}H}$ = 140 Hz); ^{13}C NMR 155.4 ($C{=}CSnBu_3$), 124.8 ($C{=}CH_2$), 115.0 ($C{=}CCH_2C{=}C$), 98.7 (OCHO), 67.4 (OCH_2), 62.1 (OCH_2), 41.1, 30.8, 29.5, 29.1, 27.3, 26.3, 25.5, 19.6, 13.6, 9.6; GC/MS, m/e (relative intensity) 457 (M^+-56, 52.3).

Preparation of 9-Bromo-5-tributylstannyl-4(*E*)-2-nonadiene (99i). 0.78 g (53%); ^1H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, *J* = 6.6 Hz), 1.32 (q, 12H, CH_2, *J* = 6.7 Hz), 1.40 (m, 8H, CH_2), 1.85 (t, 4H, CH_2, *J* = 6.7 Hz), 2.3 (tt, 4H, $C{=}CCH_2$, *J* = 6.6 Hz, 1.9 Hz), 2.73 (ddt, 2H, $C{=}CCH_2C{=}C$, *J* = 7.0 Hz, 2.0 Hz, 1.5 Hz), 3.41 (t, 4H, CH_2Br, *J* = 6.6 Hz), 4.99 (ddt, 1H, HC=CH*cis*, *J* = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, *J* = 17.0 Hz, 2.0 Hz), 5.7 (dt, 1.5H, C=CH, *J* = 3.0, 1.9, $^3J_{Sn\text{-}H}$ = 140 Hz); ^{13}C NMR δ 155.4 ($C{=}CSnBu_3$), 125.3 ($C{=}CH_2$), 115.0 ($C{=}CCH_2C{=}C$), 40.3 (CH_2Br), 32.4, 30.6, 29.1, 27.4, 27.3, 13.6, 9.6; GC/MS, m/e (relative intensity) 435 (M^+-56, 48).

Preparation of 9-Cyano-5-tributylstannyl-4(*E*)-2-nonadiene (99j). 1.02 g (78%); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 9H, CH_3, *J* = 6.6 Hz), 1.32 (q, 12H, CH_2, *J* = 6.7 Hz), 1.40 (m, 8H, CH_2), 1.85 (t, 4H, CH_2, *J* = 6.7 Hz), 2.3 (tt, 4H, $C{=}CCH_2$, *J* = 6.6 Hz, 1.9 Hz), 2.73 (ddt, 2H, $C{=}CCH_2C{=}C$, *J* = 7.0 Hz, 2.0 Hz, 1.5 Hz), 3.41 (t, 4H, CH_2Br, *J* = 6.6 Hz), 4.99 (ddt, 1H, HC=CH*cis*, *J* = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, HC=CH*trans*, *J* = 17.0 Hz, 2.0 Hz), 5.7 (dt, 1.5H, C=CH, *J* = 3.0, 1.9, $^3J_{Sn\text{-}H}$ = 140 Hz); ^{13}C NMR δ 155.4 ($C{=}CSnBu_3$), 125.3 ($C{=}CH_2$), 115.0 ($C{=}CCH_2C{=}C$), 40.3 (CH_2CN), 32.4, 30.6, 29.1, 27.4, 27.3, 13.6, 9.6; GC/MS, m/e (relative intensity) 382 (M^+-56, 100).

Preparation of Trisubstituted Alkenes (Schemes 42 and 43)

Preparation of 5-Iodo-4(*Z*)-1-tridecadiene (101a): To a solution of **92c** (1.4 g, 3 mmol) in CH_2Cl_2 (10 mL) was added a solution of I_2 in CH_2Cl_2 dropwise at -50°C until a faint coloration persisted. The reaction was warmed to -20°C and quenched with satd. NH_4Cl. The vinyl iodide was extracted into pentane and combined extracts were washed with water and sodium thiosulphate and then dried over potassium carbonate. silica gel chromatography with hexane as the eluant gave **101a** in 72% (0.65 g) yield; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3H, CH_3, *J* = 7.1 Hz), 1.26-1.4 (m, 12H, CH_2), 2.23 (dt, 2H, $C{=}CCH_2$, *J* = 7.0 Hz, 2.0 Hz), 2.73 (dt, 2H, $C{=}CCH_2C{=}C$, *J* = 6.0 Hz, 2.0 Hz), 4.99 (dq, 1H, C=CH*cis*, *J* = 10.0, 2.0 Hz), 5.02 (dq, 1H, C=CH*trans*, *J* = 17.0, 2.0 Hz), 5.8 (ddt, 1H, $CH_2HC{=}CCH_2$, *J* = 17.0,

10.0, 6.0 Hz), 6.96 (tt, 1H, C=CH, *J* = 6.0 Hz, 2.0 Hz); GC/MS, m/e (relative intensity), 306 (M^+, 40).

Preparation of 101b and 101c from 101a: *n*-BuLi (1.5 mL, 3.6 mmol) was added to **101a** (0.49 g, 1.6 mmol) at -78°C. After 0.5 h the reaction was quenched with excess Me_3SiCl (**101b**) or ^2H_2O (**101c**) and slowly warmed to room temperature. Usual workup followed by column chromatography with *n*-hexanes as eluant gave the desired products in the yields listed below.

5-Trimethylsilyl-4(*Z*)-1-tridecadiene (101b): 0.3 g (78%); ^1H NMR ($CDCl_3$) δ 0.15 (s, 9H, CH_3Si), 0.87 (t, 3H, CH_3, *J* = 7.1 Hz), 1.26-1.4 (m, 12H, CH_2), 2.23 (dt, 2H, $C{=}CCH_2$, *J* = 7.0 Hz, 2.0 Hz), 2.73 (dt, 2H, $C{=}CCH_2HC{=}C$, *J* = 6.0 Hz, 2.0 Hz), 4.99 (dq, 1H, C=CH*cis*, *J* = 10.0, 2.0 Hz), 5.02 (dq, 1H, C=CH*trans*, *J* = 17.0, 2.0 Hz), 5.8 (ddt, 1H, $CH_2HC{=}CH_2$, *J* = 17.0, 10.0, 6.0 Hz), 5.96 (tt, 1H, C=CH, *J* = 6.0 Hz, 2.0 Hz); ^{13}C NMR δ 148.5 ($C{=}CSiMe_3$), 139.3 ($C{=}CH_2$), 137.5 (C=CH), 137.4 ($C{=}CHCH_2$), 114.8 ($C{=}CHCH_2CH{=}C$), 38.4, 36.2, 32.0, 29.5, 29.4, 29.3, 22.7, 13.6, 0.3; GC/MS, m/e (relative intensity), 252 (M^+, 100). Anal Calcd for $C_{16}H_{32}Si$: 252.2273. Found: 252.2281.

5-Deuterio-4(*E*)-1-tridecadiene (101c) 0.25 g (87%); ^1H NMR ($CDCl_3$) δ 0.87 (t, 3H, CH_3, *J* = 7.1 Hz), 1.26-1.4 (m, 12H, CH_2), 2.20 (dt, 2H, $C{=}CCH_2$, *J* = 7.0 Hz, 2.0 Hz), 2.73 (dt, 2H, $C{=}CCH_2HC{=}C$, *J* = 6.0 Hz, 2.0 Hz), 5.0 (dq, 1H, C=CH*cis*, *J* = 10.0, 2.0 Hz), 5.02 (dq, 1H, C=CH*trans*, *J* = 17.0, 2.0 Hz), 5.40 (tt, 1H, C=CH, *J* = 6.0 Hz, 2.0 Hz), 5.8 (ddt, 1H, $CH_2HC{=}CH_2$, *J* = 17.0, 10.0, 6.0 Hz); ^{13}C NMR δ 137.6 ($HC{=}CH_2$), 131.9 (C=CD), 127.5 (C=CH), 114.8 ($C{=}CHCH_2CH{=}C$), 36.7, 32.5, 31.9, 29.5, 29.3, 29.2, 22.6, 14.1; GC/MS, m/e

(relative intensity), 181 (M^+, 52). Anal Calcd for $C_{13}H_{23}{}^2H$: 181.1941. Found: 181.1933.

101b was also prepared from **92c** *via* transmetallation with *n*-BuLi. Thus, to a solution of **92c** (1.17 g, 2.5 mmol) in 5 mL of THF, was added *n*-BuLi (1.2 mL, 3 mmol) in 5 mL of TMEDA at -60°C. The reaction was stirred at this temperature for 2 h and then warmed to room temperature. After stirring further for 1 h, Me_3SiCl (0.6 mL, 5 mmol) was added slowly at -78°C. The reaction was warmed to room temperature and worked up as usual. silica gel chromatography with hexane as the eluant gave **101b** in 63% (0.39 g) yield.

General Procedure for Palladium Catalyzed Cross-Coupling Reactions:

Preparation of 101d and 101e: To a Schlenk tube at room temperature was sequentially added $Pd(Ph_3P)_4$ (5 mole%) in 5 mL of benzene, benzylbromide (6 mmol) or allyl bromide (6 mmol) and vinylstannane **92d** (2.36 g, 5.0 mmol). The reaction was refluxed until palladium metal precipitated (24 h). The reaction was cooled to room temperature and partitioned between Et_2O (20 mL) and satd. KF (20 mL). After 0.5 h of vigorous stirring, Bu_3SnF was removed by filtration, the organic layer was separated, washed with brine and dried. The solvent was evaporated and the crude mixture passed through a silica gel column (hexanes:ethyl acetate, 99:1, as eluant) to give **101d** or **101e**.

1-Phenyl-2(*Z*)-(1-propenyl)-1-nonene (101d): ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 3H, CH_3, J = 7.0 Hz), 1.2-1.5 (m, 12H, CH_2), 1.4 (d, 3H, CH_3, J = 6.6 Hz), 2.1 (dt, 2H, C=CCH_2, J = 7.0 Hz, 1.9 Hz), 3.3 (s, 2H, C=CCH_2Ph), 5.5 (qt, 1H, C=CH, J = 6.6, 1.9 Hz), 7.0-7.5 (m, 5H, Ph); ^{13}C NMR δ 149.6, 136.1, 129.0, 128,2, 126.0, 110.9, 65.8, 43.0, 35.5, 31.9, 29.4, 29.3, 29.2, 22.7, 22.6, 14.0; GC/MS, m/e (relative intensity), 244 (M^+, 12.3). Anal Calcd for $C_{18}H_{28}$: 244.2191. Found: 244.2187.

4(*Z*)-(1-Propenyl)-1-dodecene (101e): ^{1}H NMR ($CDCl_3$) δ 0.9 (t, 3H, CH_3, J = 7.0 Hz), 1.2-1.5 (m, 12H, CH_2), 1.6 (d, 3H, CH_3, J = 7.0 Hz), 1.95 (dt, 2H, C=CCH_2, J = 7.0 Hz, 1.5 Hz), 2.8 (ddd, 2H, C=CCH_2C=C, J = 7.0 Hz, 2.0 Hz, 1.5 Hz), 4.99 (ddd, 1H, C=CH*cis*, J = 10.0 Hz, 2.0 Hz, 1.5 Hz), 5.02 (dq, 1H, C=CH*trans*, J = 17.0, 2.0 Hz), 5.3 (qt, 1H, C=CH, J = 7.0 Hz, 1.5 Hz), 5.75 (ddt, 1H, HC=CCH_2, J = 17.0 Hz, 10.0 Hz, 7.0 Hz); GC/MS, m/e (relative intensity), 194 (M^+, 100).

Preparation of (*E*)-1-Iodo-1-hexene (101f): This compound was prepared by the known procedure.[91b] ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3H, CH_3, J = 7.0 Hz), 1.26-1.4 (m, 4H, CH_2), 1.98-2.0 (dt, 2H, J = 7.0 Hz, 1.9 Hz), 5.95 (dt, 1H, C=CHI, J = 15.0, 1.8 Hz), 6.5 (dt, 1H, CH=CHI, J = 14.8, 7 Hz). ^{13}C NMR 146.6, 73.9, 35.6, 30.5, 21.9, 13.7.

Preparation of 8-Methyl-5(*E*), 7(*E*)-hexadecadiene (101g): To a solution of "$Pd(Ph_3P)_2$" (0.05 mmol) in 5 mL of THF, (generated *in situ* by the reaction of DIBALH (0.1 mL, 0.1 mmol) and $Pd(Ph_3P)_2Cl_2$ (0.037g, 0.05 mmol in THF), were sequentially added **93d**, (0.50 g, 1.2 mmol) and **101f** (0.211g, 1.0 mmol) at room temperature. The homogeneous reaction mixture turned black in 24 h. The reaction

mixture was diluted with ether and stirred with satd. KF. After filtration of Bu_3SnF, the reaction was worked up as usual and the crude product purified by column chromatography (hexane as eluant) to give 0.14 g (88%) of **101g**. ^1H NMR ($CDCl_3$) δ 0.86 (t, 6H, CH_3, J = 7.0 Hz), 1.02-1.4 (m, 16H, CH_2), 1.9 (s, 3H), 2.3 (dt, 2H, $C{=}CCH_2$, J = 7.0 Hz, 1.6 Hz), 2.9 (dq, 2H, $C{=}CCH_2$, J = 7.0, 1.6 Hz), 5.5 (ddt, 1H, HC=CH-C, J = 18.0 Hz, 10.0 Hz, 1.6 Hz), 5.8 (dt, 1H, C=CH-HC=C, J = 10.0 Hz, 1.6 Hz), 6.0 (ddt, 1H, CH=CH-C, J = 18.0 Hz, 10.0 Hz, 7.0 Hz); ^{13}C NMR δ 142.6 (C=CHCH=C), 132.7 (C=CHCH=C), 129.6 (C=CHCH=C), 123.5 (C=CHCH=C), 33.2, 32.7, 31.9, 29.9, 29.3, 22.6, 17.6, 14.1; GC/MS, m/e (relative intensity) 280 (M^+, 35.0). The spectral data matched those published for this compound.[91]

Preparation of 1-Hexynyltributylstannane (101h): To a solution of 1-hexyne (0.82 g, 10.0 mmol) in Et_2O (15 mL) was added dropwise *n*-BuLi (3.8 mL, 10.0 mmol) at -30°C. After 30 min Bu_3SnCl (3.25 g, 10.0 mmol) was added. The reaction was warmed to room temperature and then subjected to normal work-up. Bulb-to-bulb distillation (bath temperature, 65°C @ 0.03 mm Hg) gave 3.5 g (95%); ^1H NMR ($CDCl_3$) δ 0.86 (t, 9H, CH_3, J = 7.0 Hz), 0.89 (t, 3H, CH_3, J = 7.0 Hz), 1.2-1.4 (m, 12H, CH_2), 1.4-1.5 (m, 10H, CH_2), 2.20 (t, 2H, CH_2, J = 7.0 Hz); ^{119}Sn = - 68.2; GC/MS, m/e (relative intensity), 315 (M^+ - 56, 100).

Preparation of 8-Methyl-7(*E*)-hexadecen-5-yne (101i): To a solution of **93d** (0.211 g, 1.0 mmol, prepared as described earlier) and **101h** (0.44 g, 1.2 mmol) at room temperature was added "$Pd(Ph_3P)_2$" (0.05 mmol) in 5 mL of THF, (generated *in situ* by the reaction of 2 equivalents of DIBALH and one equivalent of $Pd(Ph_3P)_2Cl_2$ in THF). The homogeneous reaction mixture turned black within an hour. The black reaction mixture was added to 25 mL of water and this aqueous mixture was extracted with ether (3 x 25 mL) which was back extracted with brine (1 x

25 mL) and dried over potassium carbonate. The dried extracts were filtered through alumina and concentrated under reduced pressure. The crude product was purified by column chromatography (hexane as eluant) to give 0.155g (88%) of **101i.** ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 6H, CH_3, J = 6.7 Hz), 1.26-1.4 (m, 12H, CH_2), 1.54-1.64 (m, 4H, CH_2), 1.9 (s, 3H, CH_2), 2.1 (dt, 2H, $CCCH_2$, J = 6.7 Hz, 1.8 Hz), 2.23 (dt, 2H, $C{=}CCH_2$, J = 6.7 Hz, 1.9 Hz), 5.7 (t, 1H, C=CH-CC, J = 1.9 Hz); ^{13}C NMR δ 142.9 (C=CHCC), 120.1 (C=CH), 110.1. 88.6, 79.3, 39.1, 32.7, 32.5, 31.0, 22.1, 22.0, 19.0, 13.7, 13.5; GC/MS, m/e (relative intensity) 278 (M^+, 23.0).

Synthesis of Square-Necked Grain beetle pheromone:

Synthesis of 104: CuCN (0.36 g, 4.0 mmol) was placed in a flask equipped with an argon inlet. The flask was repeatedly (3x) evacuated (vacuum pump) and purged with argon. THF (10 mL) was injected, the reaction was cooled to -50°C when MeLi (2.84 mL, 4.0 mmol) was added slowly keeping the temperature below -50°C. The reaction was stirred for 0.5 h and dimethylphenylsilyllithium in THF (4.2 mL, 4.0 mmol) added dropwise. The resulting deep red solution was stirred for 0.5 h after which 1-butyne (0.20 g, 4.0 mmol) was added dropwise. The reaction mixture was stirred for additional 2.0 h and then quenched with MeI (2.0 mL) in HMPA (3.0 mL). The reaction mixture was warmed gradually to room temperature. The usual workup followed by column chromatography (hexanes) yielded 0.728 g of **104** (90%) in > 95% purity as judged by capillary g.c analysis. IR (NaCl) 1620, 1440, 1250, 1120, 995 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 7.1-7.5 (m, 5H, Ph), 5.35 (dt, J = 18, 1.5 Hz, 1H, C=C*H*Si), 2.7 (tdd, J = 7, 6, 1.5 Hz, 2H, allylic), 1.85 (s, 3H, $C{=}CCH_3$), 0.95 (t, J = 7 Hz, 3H,

CH_3), 0.3 (s, 6H, SiCH_3); $^{13}C\{^1H\}$ ($CDCl_3$) δ 159.5 (*C*=CSi), 140.4 (C=*C*Si), 133.8 (*ipso*), 128.6 127.7, 118.8, 35.1, 22.0, 12.5, -0.9 (Si*C*H_3); MS m/e (rel. intensity) 204.3 (M^+, 30), 189.2 (100), 135 (80), 121 (60); Anal. calc. $C_{13}H_{20}Si$ 204.1337 found 204.1334.

Synthesis of 102: Synthesis of **102** was achieved by converting the vinyl silane adduct to vinyl iodide and then cuprate followed by 1,4-addition of ethyl vinyl ketone by known procedures. Reduction of the crude material followed by acetylation completed the sequence. The following spectral data was obtained:

(*E*)-7-Methyl-6-nonen-3-ol: Conversion of vinylsilane to iodide (I_2 in CH_2Cl_2) followed by purification by flash chromatography resulted in the vinyl iodide. Addition of 1.2 equiv. *n*-BuLi followed by 1 equiv. of CuBr and 1.2 equiv. of ethyl vinyl ketone gave the vinyl ketone on workup. LAH reduction gave the alcohol. IR (cm^{-1}) 3360, 2975, 1460, 1120, 970, 850; 400 MHz ^1H NMR ($CDCl_3$) δ 5.15 (dt, *J* = 18, 1.5 Hz, 1H, C=C*H*), 3.5 (1H, CHO*H*), 2.10 (m, 2H, allylic), 2.7 (tdd, *J* = 7, 6, 1.5 Hz, 2H, allylic), 1.65 (s, 3H, C=CCH_3), 1.4-1.5 (m, 2H, CH_2), 0.95 (t, *J* = 7 Hz, 3H, CH_3); MS CI (isobutane), m/e (rel. intensity) 157 (M^++ 1, 100); Anal. calc. $C_{10}H_{20}O$ C, 76.86; H, 12.86, found C, 76.74; H, 12.92.

(*E*)-3-Methyl-7-acetoxy-3-nonene (102): Conversion of the alcohol to the acetate **102** with acetic anhydride in pyridine yielded >95% of **102** in > 95% purity (gc analysis). IR (cm^{-1}) 2975, 1735, 1460, 1020, 955; 400 MHz ^1H NMR ($CDCl_3$) δ 5.10 (dt, *J* = 18, 1.5 Hz, 1H, C=C*H*), 4.9 (1H, CHO*H*, pentet, *J* = 6.8 Hz), 2.0 (s, 3H, $COCH_3$), 2.13 (tdd, *J* = 7, 6, 1.5 Hz, 4H, allylic), 1.4-1.5 (m, 4H, CH_2), 1.01 (t, 3H, C=CCH_3, *J* = 7 Hz), 0.85 (t, *J* = 7 Hz, 3H, CH_3); MS CI (isobutane), m/e (rel.

intensity) 199 (M^++ 1, 5); Anal. calc. $C_{12}H_{22}O_2$ C, 72.68; H, 11.18, found C, 72.85; H, 11.62.

Reaction of 1-Decynyldiethyl Aluminum with Tributyltin Hydride: To a solution of 1-decynyldiethyl aluminum (**107**) in THF (prepared from 1-decyne (0.138 g, 1.0 mmol) in 5 mL of THF, *n*-BuLi (0.40 mL, 1.04 mmol) and Et_2AlCl (1.0 mL, 1.0 mmol); 0°C, 0.5 h), Bu_3SnH (0.291 g, 1.0 mmol) was added dropwise and the reaction mixture stirred overnight at 0°C. Only 1-decyne and Bu_3SnH were recovered. Vinyl stannane products were not detected by gas chromatographic analysis after the normal workup.

Reaction of $Bu_3SnAlEt_2$ and Tributylstannyl Hydride: To a THF solution of $Bu_3SnAlEt_2$ (1.0 mmol) prepared by Method **b** was added Bu_3SnH (0.291 g, 1.0 mmol) at 0°C and the reaction mixture was stirred at this temperature. Only Bu_3SnH was obtained upon the usual workup. Formation of hexabutylditin was not observed even after 24 h.

Reaction of $Bu_3SnAlEt_2$ with Tributylstannyl Hydride in the Presence of Catalyst: $Bu_3SnAlEt_2$ (1.0 mmol) was prepared according to Method **b**. Bu_3SnH (0.291 g, 1.0 mmol) and CuCN (0.004 g, 0.05 mmol) in 5 mL of THF were added to this solution at 0°C. After stirring for 0.5 h, the reaction mixture was quenched with 1N HCl and subjected to normal work-up. Hexabutylditin (0.04 g, 69%) was obtained as the only product after bulb to bulb distillation.

Reaction of Tributyltin Hydride with CuCN: No reaction was observed when Bu_3SnH was reacted with CuCN in THF under argon at 0°C for 12 h.

Reaction of $Bu_3SnAlEt_2$ with CuCN: CuCN (0.004 g, 0.05 mmol) was added to a solution of $Bu_3SnAlEt_2$ (1.0 mmol, Method **b**) in in 5 mL of THF. The solution immediately turned red. Workup after 30 min, yielded 69% of hexabutylditin.

Reaction of 1-Decynyldiethyl Aluminum with $Bu_3SnAlEt_2$: Decynyldiethyl aluminum (**107**) was transferred *via* a canula to a THF solution of $Bu_3SnAlEt_2$ (1.0 mmol) while maintaining the temperature at 0°C. The reaction mixture was stirred overnight at 0°C after which it was subjected to normal workup to give 1-decyne.

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$$K_2 = \frac{k_2}{k_{-2}} = \frac{[\,(PhMe_2Si)_3CuLi_2\,]}{[\,(PhMe_2Si)_2CuLi\,]\,[\,PhMe_2SiLi\,]} = 32 \pm 16$$

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THE SYNTHESIS OF SULFONIUM MIMICS OF THE PRESUMPTIVE CARBOCATION INTERMEDIATES IN THE DIMERIZATION OF FARNESYL PYROPHOSPHATE TO SQUALENE BY SQUALENE SYNTHETASE

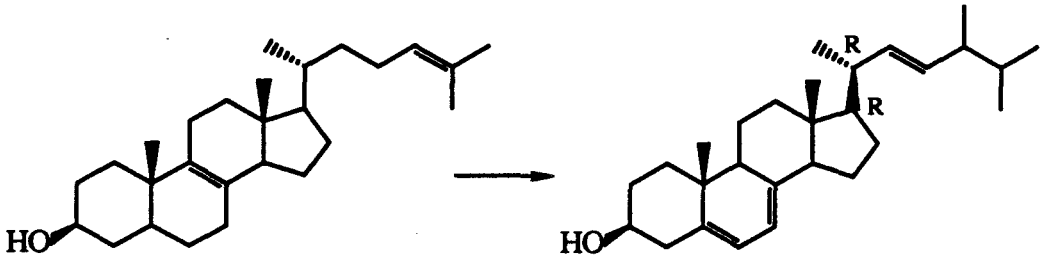
Introduction

Excellent inhibition of enzymes may be achieved by administration of mimics of presumptive intermediates that bind to catalytic sites but are not transformed. The efficiency of intermediate mimics as inhibitors is due to the superior ability of enzymes to stabilize intermediates formed during a catalyzed process.[1] Regulation of sterol biosynthesis in man is a therapeutically valuable goal.[2] A promising approach is the inhibition of enzymes involved in sterol biosynthesis. Indeed the hypocholesteremic agents most recently approved for human use are inhibitors of β-hydroxy-β-methylglutaryl CoA reductase, a regulatory enzyme early in the sterol biosynthetic process.[3] As most other inhibitors of sterol biosynthesis they were discovered as natural products and not by design.

The focus of the current work is the rational design of inhibitors of enzymes involved in the biosynthesis of cholesterol that function after the formation of farnesyl pyrophosphate but are not involved in the biosynthesis of the ubiquinones (electron transfer agents that are important in cell respiration). Unlike enzymatic carbon-carbon bond formation leading to nucleic acids, proteins, carbohydrates and lipids that utilize reactions proceeding through enolate equivalents, the enzymes involved in the advanced

stages of sterol biosynthesis utilize cationic processes for carbon-carbon bond formation.[4]

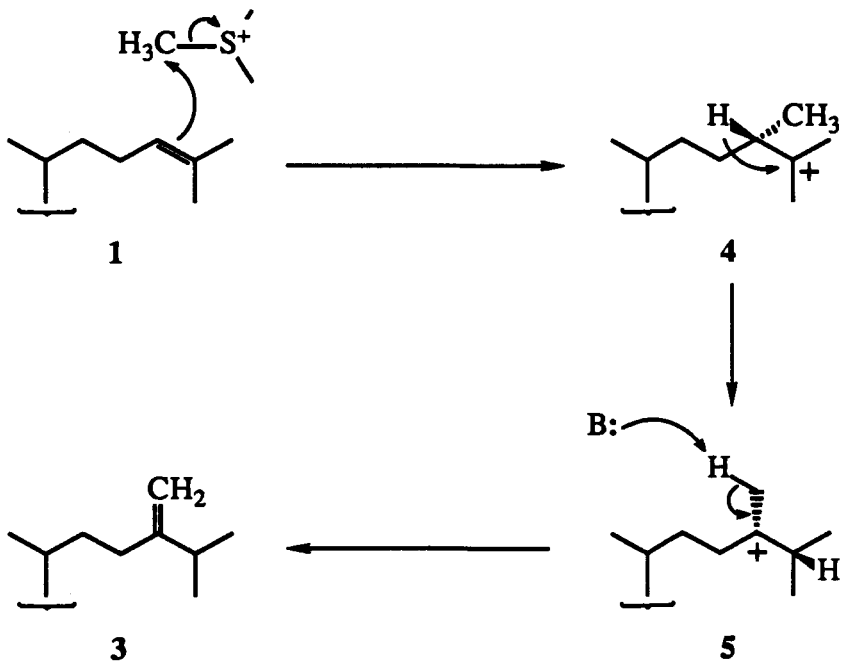
Work in our and other laboratories during the last decade has made it apparent that efficient inhibition of the latter enzymes can be achieved by administering sulfonium and ammonium analogs of the presumptive cationic intermediates.[5,6] Initial investigations were aimed at design of ammonium and sulfonium intermediate analogues of carbocations presumed to be involved in the alkylation of the side chain of zymosterol (**1**) during biosynthesis of ergosterol (**2**) by the yeast *Saccharomyces cerevisae*.[5]



1 **2**

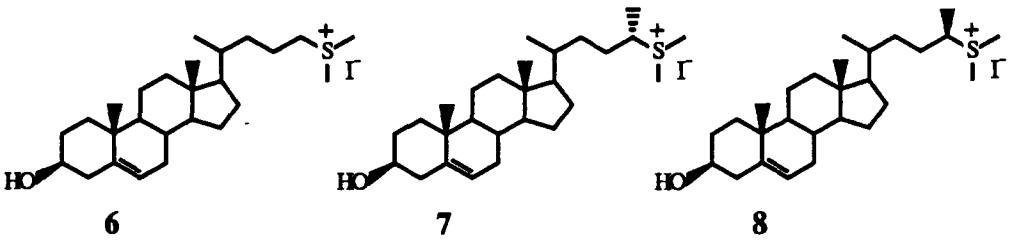
The enzyme responsible for this alkylation converts **1** to fucosterol **3** (Scheme 1). The mechanism suggested for yeast 24-sterol methyltransferase (24-SMT) involves generation of cationic intermediates **4** and **5**. Heteroatom analogues of these species containing sulfur[5d] (**6**, **7** and **8**) or nitrogen[5a-c] (**9** and **10**) were excellent inhibitors both *in vitro* and *in vivo* (Scheme 2). The most efficient mimics were those containing a sulfonium moiety at position 25 (compounds **6**, **7**, and **8**). Inhibitor **7** bound yeast 24-SMT 25,000 times more tightly than the natural substrate for this enzyme and effectively inhibited the enzyme at nanomolar concentrations (K_i ~2 nM).[5d] The superior ability of

7 compared to 8 as an inhibitor of 24-SMT suggested the stereochemistry of alkylation was as illustrated in 4.[5d]

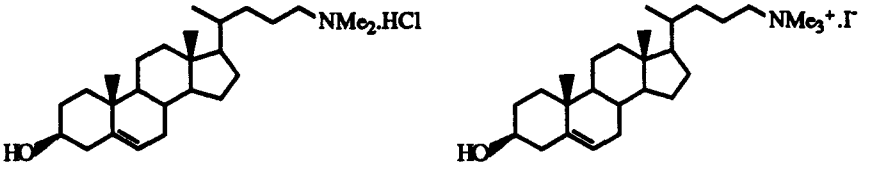


Scheme 1

It has also been shown by Benveniste[7] that 24-methyl 25-azacycloartenol (**11**), 25- azacycloartenol (**12**) and 25-methyl-25-azacycloartenol (**13**) as well as arsonium and sulfonium analogs of **4** were potent inhibitors of cycloartenol 24-sterol methyltransferase in microsomes of maize seedlings (Scheme 3).



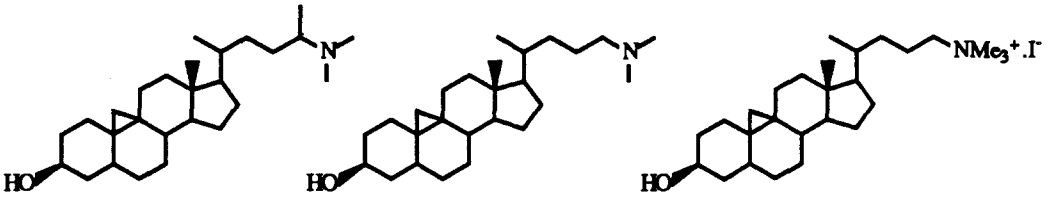
6 7 8



9 10

Scheme 2

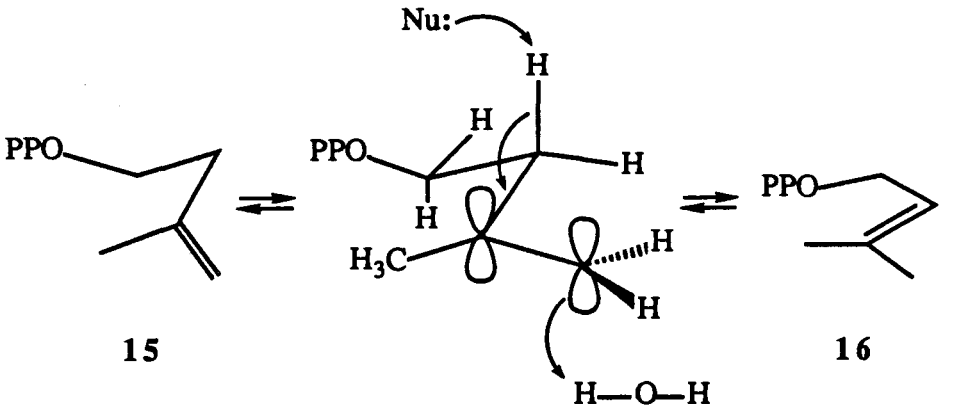
Kinetic evidence suggests that the ionic heteroatom analogues of **4** exhibit their inhibitory power as reversible competitive inhibitors simply through Coulombic attraction between the positively charged heteroatom and nucleophile(s) responsible for stabilization of the presumptive carbocation intermediate.[5d,7]

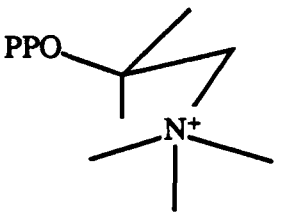


11 12 13

Scheme 3

This approach has led to the design of an ammonium inhibitor (**14**) for the dimethyl allyl pyrophosphate (**15**) to isopentenyl pyrophosphate (**16**) transformation[8] (Scheme 4).

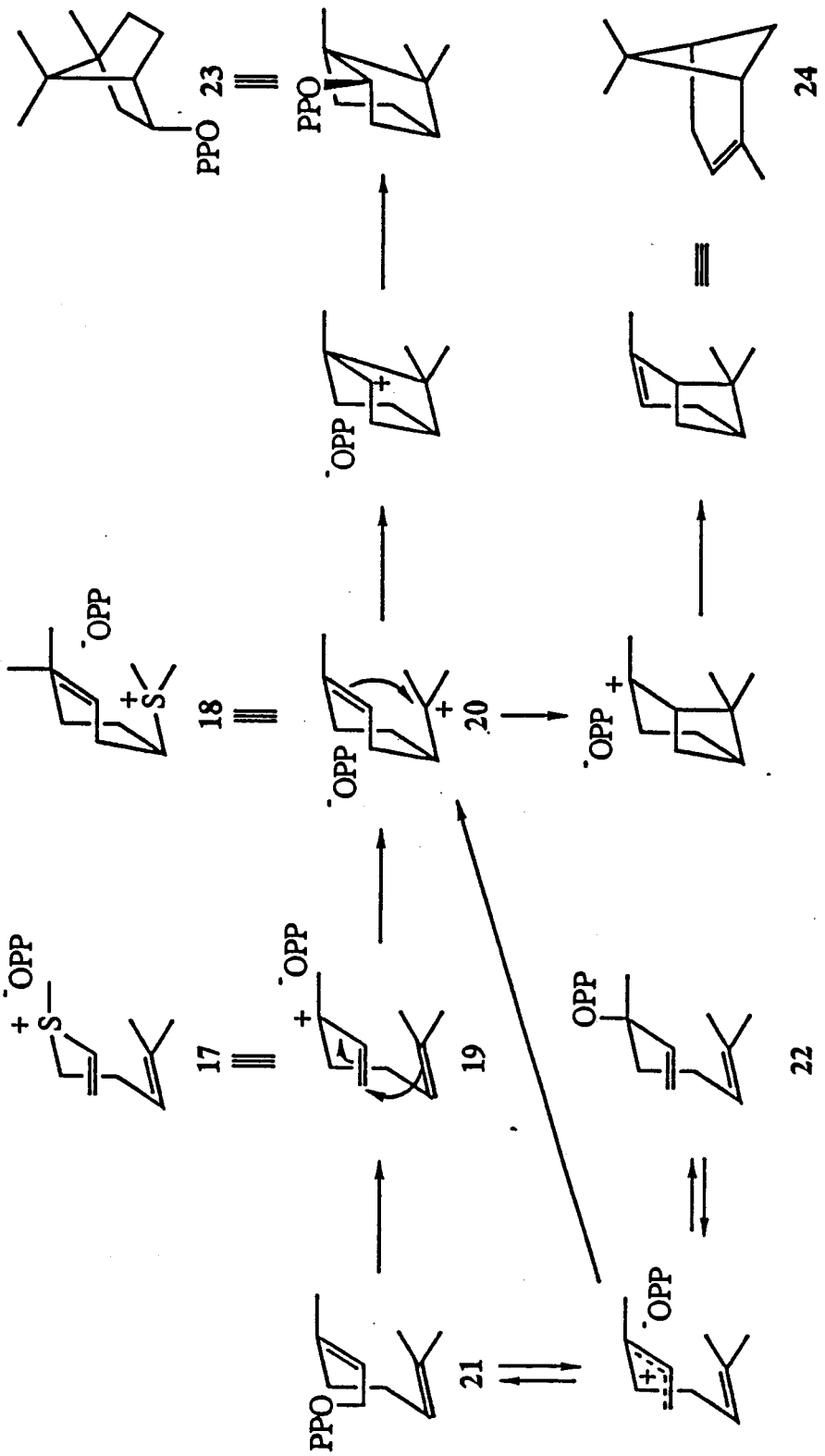




14

Scheme 4

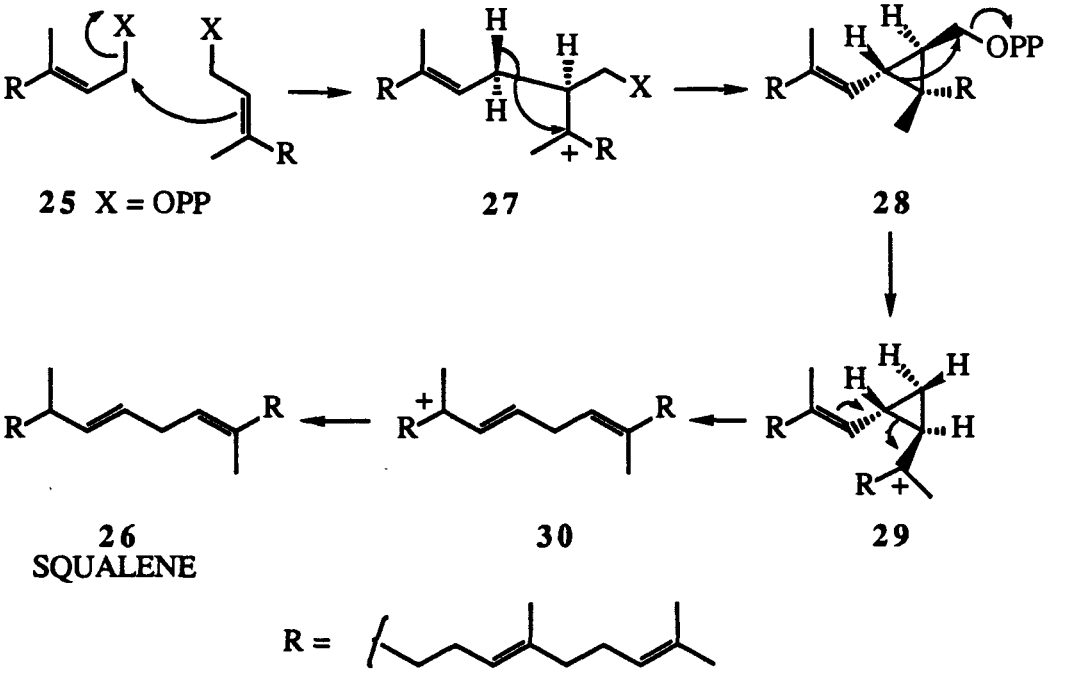
Similarly, sulfonium mimics (**17** and **18**) of presumptive cationic intermediates (**19** and **20**) were efficient inhibitors of bornyl pyrophosphate cyclase and α-pinene cyclase.[9] These enzymes accept geranyl pyrophosphate, **21**, or linalyl pyrophosphate, **22**, as substrates and produce bornyl pyrophosphate, **23**, and α-pinene, **24**, respectively (Scheme 5). Inhibition by each sulfonium mimic is synergized (3-10 x)



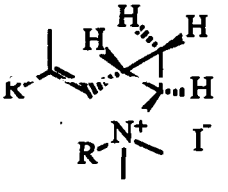
Scheme 5

by the addition of inorganic pyrophosphate confirming tight active site binding to the postulated ion pair.

Squalene synthetase is a relatively small microsomal protein[10] that catalyses the 1'-1 condensation of two molecules of farnesyl pyrophosphate (**25**) to yield squalene (**26**). The transformations considered to be involved are the insertion of C_1 of one farnesyl pyrophosphate into the C_2-C_3 double bond of a second to generate intermediate



Scheme 6



31

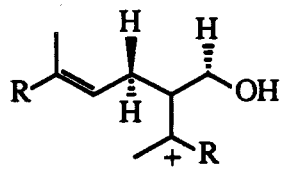
27 which rearranges to presqualene alcohol pyrophosphate, **28** (Scheme 6). Further rearrangement of **28** *via* a cyclopropyl carbinyl rearrangement yields intermediate **29**. Ring opening of **29** yields allylic cation **30**. Hydride reduction of the latter completes the enzymatic transformation. Since the rearrangement of primary cyclopropylcarbinyl cation **28** to its tertiary isomer **29** was neither kinetically nor thermodynamically favoured in solution it was assumed that squalene synthetase exerts strict control upon cationic intermediates to achieve the regiocontrol required for biosynthesis of squalene. It was suggested that regiocontrol was, in fact, achieved as a natural consequence of the orientation between the positively and negatively charged partners in the tight ion pair generated upon cleavage of the carbon-oxygen bond in **28**. An ammonium analog, **31**, of intermediate, **29**, has been shown to be an efficient inhibitor of squalene.[11]

The preceeding examples reveal that ammonium and sulfonium analogues of presumptive carbocationic intermediates are efficient inhibitors of enzymes presumed to mediate processes *via* such intermediates. In all cases it is presumed that the positively charged intermediates generated during the enzymatic reactions are stabilized by nucleophilic sites located near the cationic carbons generated and that these nucleophilic sites bind to the sulfonium and ammonium intermediate mimics through Coulombic interactions.

Proposed work

The present study was undertaken to prepare the sulfonium ions **32, 33** and **34** which are analogues of the cationic intermediates **27, 29** and **30** respectively, presumed to be stabilized by squalene synthetase (Scheme 7). It was anticipated that **32-34** would be efficient inhibitors of this enzyme. Although there are several preparations of squalene

synthetase which could be studied, attention would be centered on the enzyme available from yeast. The inhibition would be followed by incorporation of radiolabelled farnesyl pyrophosphate into squalene.[12]



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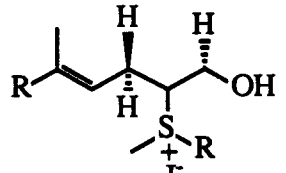
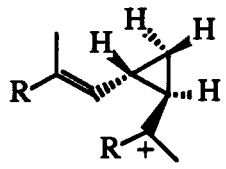


32



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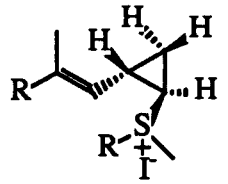

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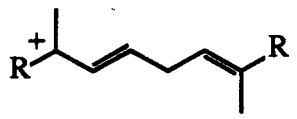
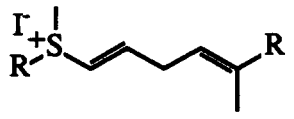
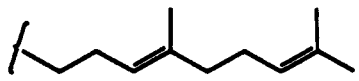


30



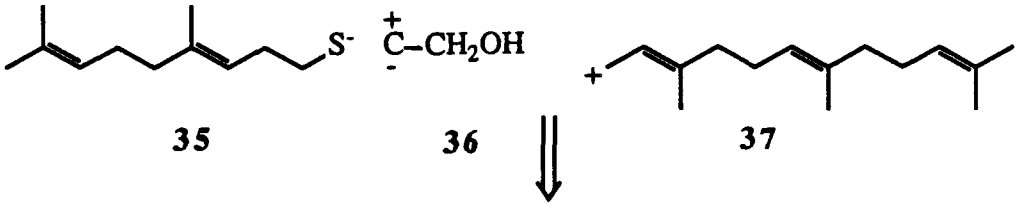
34

R = 

Scheme 7

Results and discussion

Retrosynthetic analysis of **32** reveals that it can be prepared from fragments **35**, **36** and **37**. Fragment **35** is a homologated geraniol (**38**) derivative, whereas fragment **37** is a farnesol (**39**) derivative. The connecting fragment (**36**) can be visualized to be derived from an α-haloester (Scheme 8).

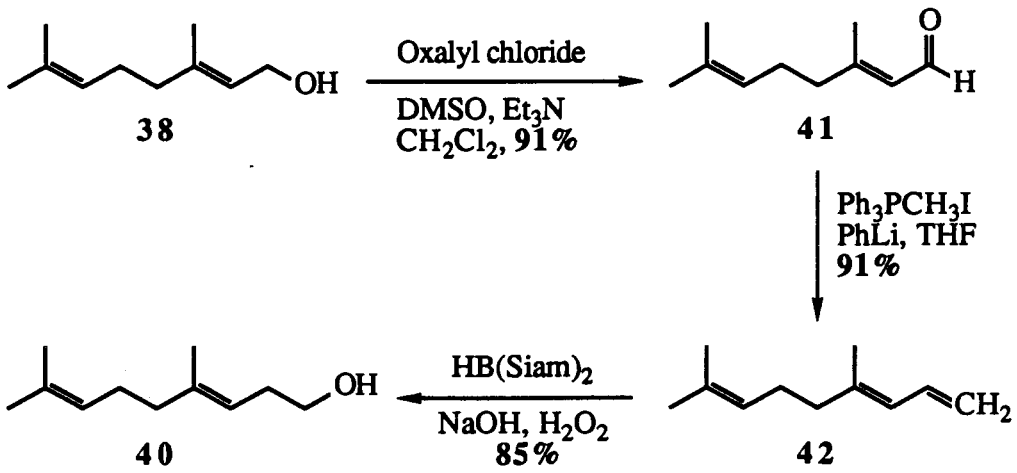


35 **36** **37**

32

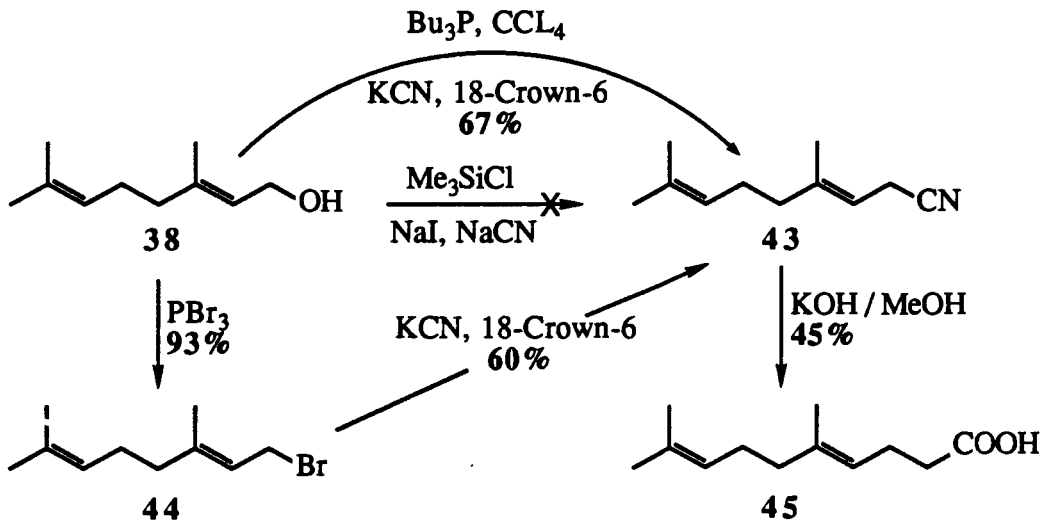
Scheme 8

The thiol corresponding to **35** was prepared from geraniol (**38**) *via* homogeraniol (**40**). The latter was prepared from **38** by the method developed by Leopold.[13] Thus, Swern oxidation[14a] of geraniol to geranial (**41**) produced less than 2% *Z* isomer. The aldehyde was converted to triene, **42**, by Wittig reaction using methyl triphenyl phosphonium iodide and phenyl lithium as the base.[15] Hydroboration[16a] of **42** with freshly prepared disamyl borane[16b] gave **40** in 85% yield (Scheme 9).



Scheme 9

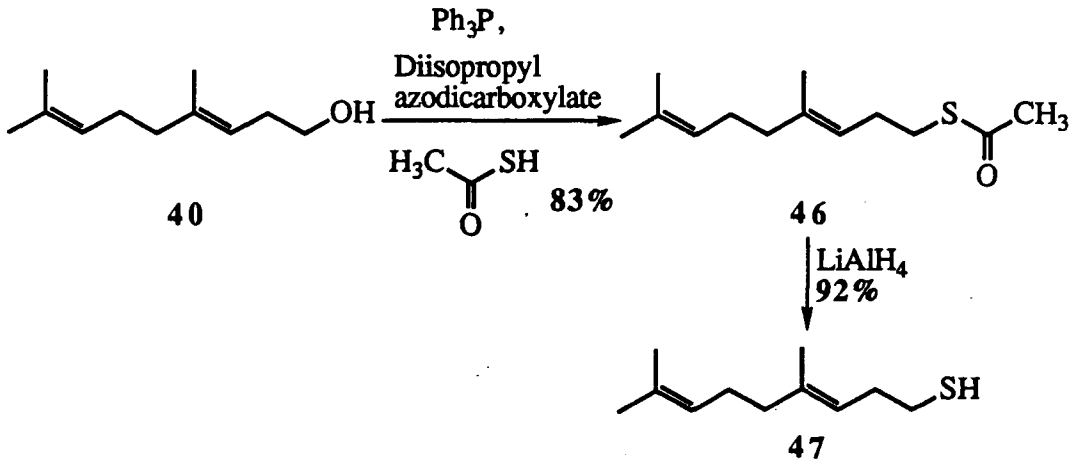
Alternate strategies to prepare homogeraniol (**40**) *via* geranyl cyanide (**43**) were less satisfactory. The direct conversion of geraniol to geranyl cyanide failed in our hands (Scheme 10).[17] Although preparation of **43** from geranyl bromide (**44**)[18] was



Scheme 10

successful,[19] it was abandoned because hydrolysis of the former gave appreciable amounts of the *Z* isomer of **45** (Scheme 10).[20]

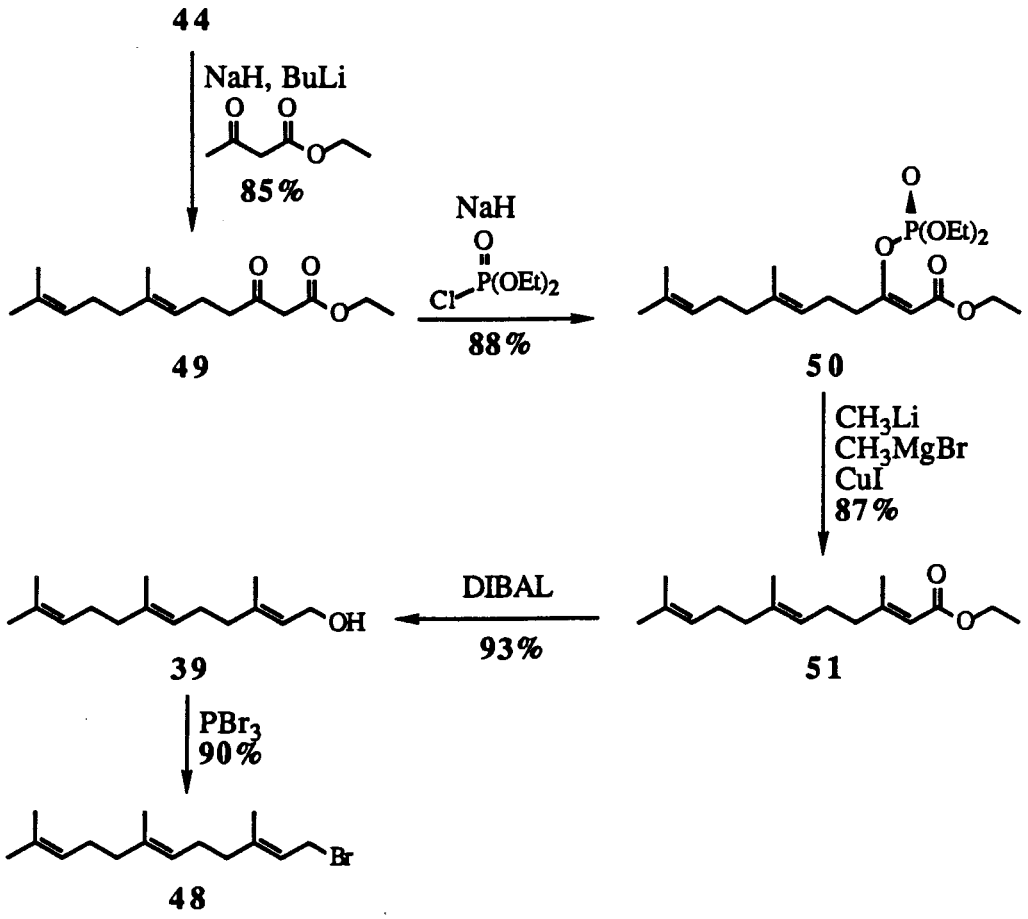
Homogeraniol (**40**) was converted to thiolacetate, **46**, by the Mitsunobu reaction.[21] Preformation of the adduct between triphenyl phosphine and diisopropyl azodicarboxylate is essential for the success of this reaction.[22] Reduction of **46** by lithium tetrahydridoaluminate gave the required thiol (**47**) in 53% overall yield (Scheme 11).[23]



Scheme 11

Farnesyl bromide (**48**) was prepared from *E,E*-farnesol, **39**, in an overall yield of 54% (Scheme 12).[18] The latter was prepared by the method of Weiler.[24] At the time this work was undertaken, *E,E*-farnesol was not commercially available.It is now available from Aldrich in 98% isomeric purity. Ethyl acetoacetate was successively treated with sodium hydride, *n*-butyl lithium and geranyl bromide, **44**, to give **49** in 85% yield.[24a] Treatment of **49** with sodium hydride and diethyl phosphochloridate gave enolphosphonate **50**[24b] which was treated with mixed methyl cuprate, (formed by treatment of cuprous iodide with methyl lithium and methyl magnesium bromide) to give

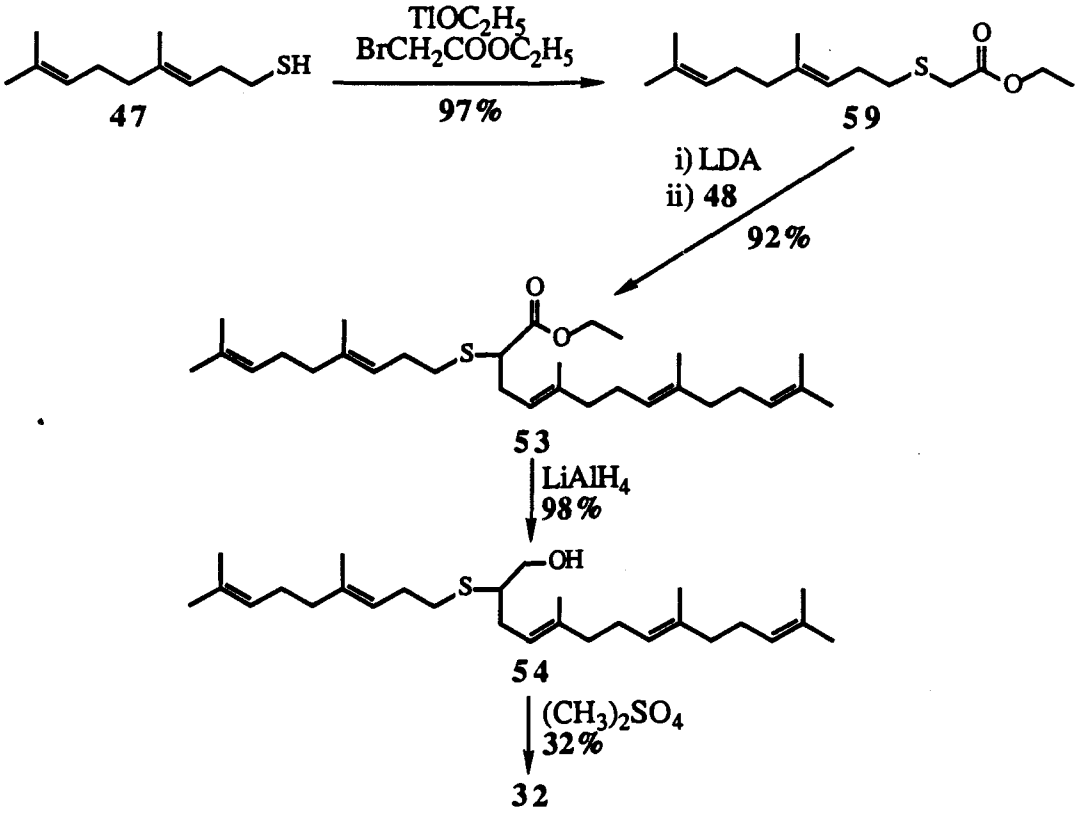
ethyl farnesoate, **51**.[24c] Reduction of **51** with diisobutylaluminium hydride gave *E,E* - farnesol, **39**, in 93% yield.[25] This was then converted to **48** in 90% yield by the procedure of Osbond.[18]



Scheme 12

Synthesis of sulfonium analogue **32** proceeded in 55% overall yield by coupling **47** and **48** (Scheme 13). Thiol **47** was treated with thallium ethoxide[26a] and ethyl-α-bromo acetate according to the procedure of Detty[26b] to produce **52** in nearly quantitative yield.

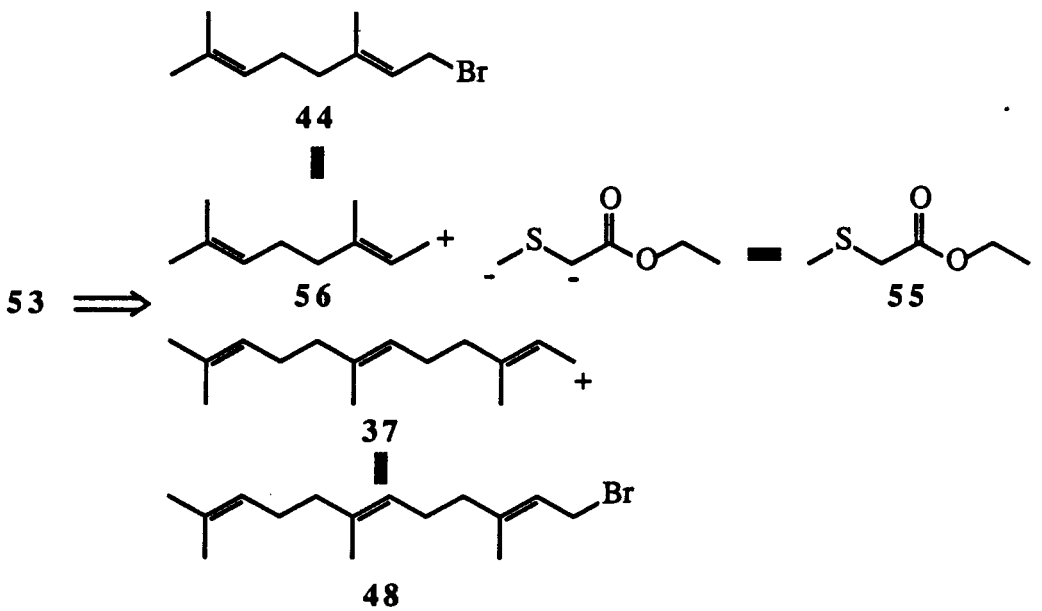
Treatment of **52** with lithium diisopropylamide[27] followed by addition of **48** gave **53** in excellent yield. Use of the thallium salt of thiol **47** (a soft base) avoided the 1,2-addition reactions characteristic of the harder sodium and lithium thiolates. Reduction[23] of **53** with lithium tetrahydridoaluminate gave alcohol **54** in 98% yield. Methylation[9] of **54** with dimethyl sulfate gave **32** in 32% yield as a viscous oil (Scheme 13).



Scheme 13

Future directions

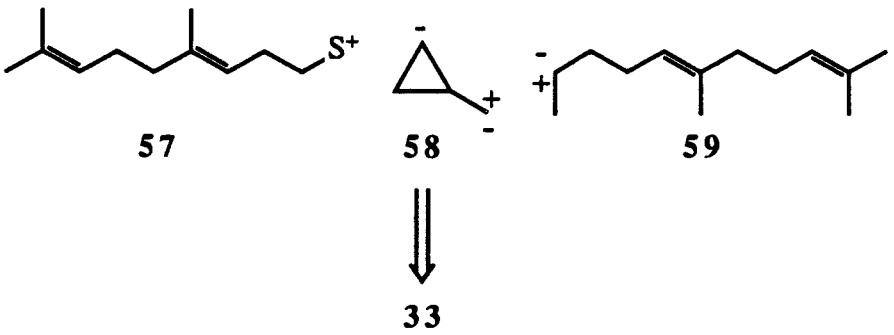
Direct synthesis of **53** can also be envisioned as shown in Scheme 14. Thus, the dianion of thiomethyl ethyl acetate (**55**) can be generated by reaction with one equivalent of NaH and one equivalent of *n*-butyl lithium.[24a] To this solution can be added one equivalent of geranyl bromide, **44**, followed by one equivalent of farnesyl bromide, **48**. It is visualized that reaction of geranyl bromide (**44**) and farnesyl bromide (**48**) with dianion of **55** would be a facile process and should lead to the formation of **53** directly from **44** and **48** in relatively fewer steps than the sequence in Scheme 13.



Scheme 14

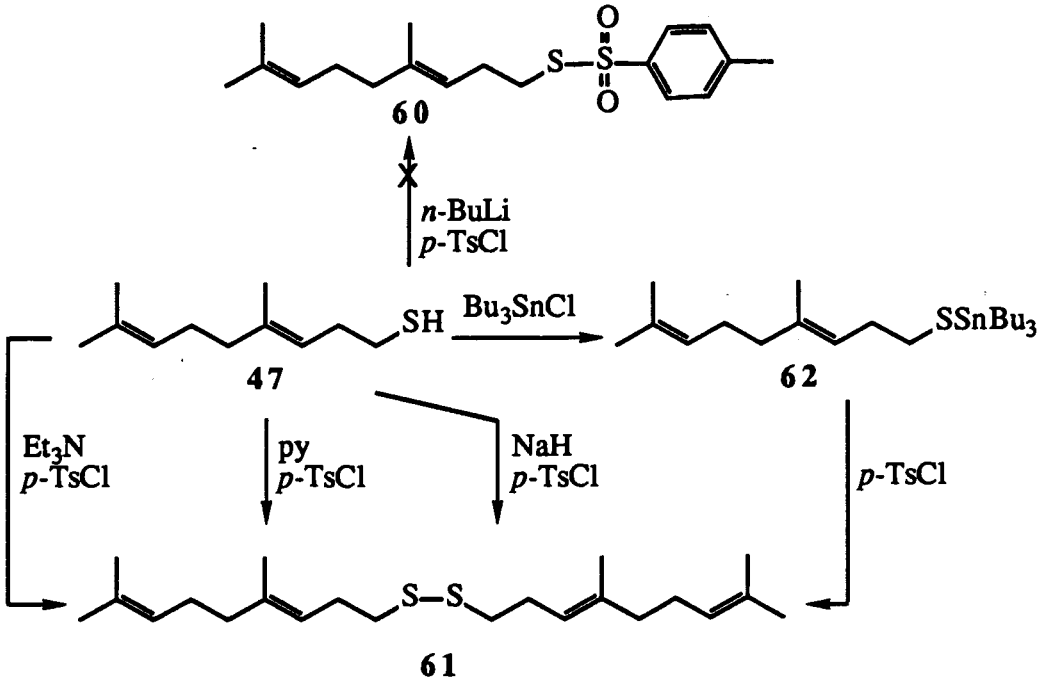
SYNTHESIS OF CYCLOPROPYL SULFONIUM ION MIMIC, 33

Retrosynthetic analysis of sulfonium ion **33** revealed it could be fabricated from the umpulong (**57**) of **35**, a cyclopropyl carbinyl fragment (**58**) and a ylide (**59**) derived from farnesol (Scheme 15).



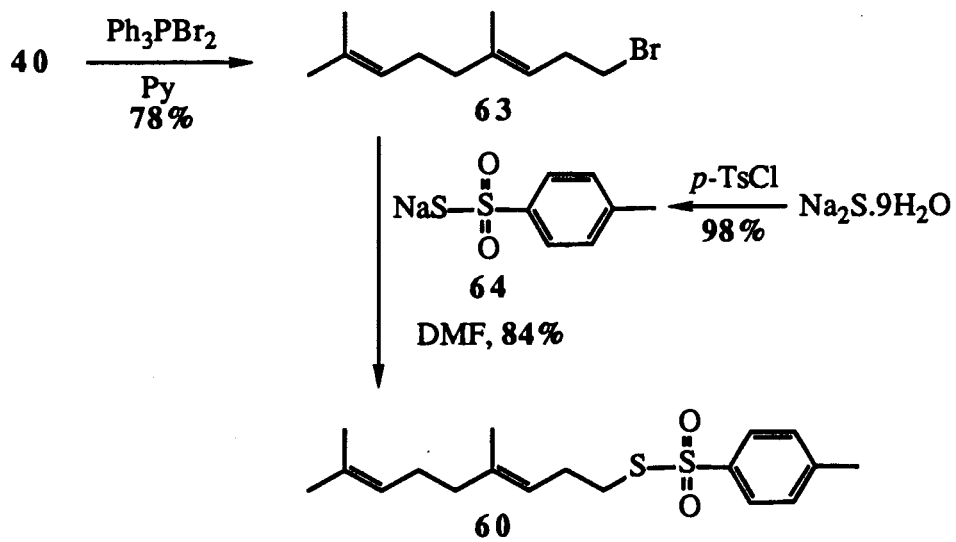
Scheme 15

Umpulong of thiolate, **35**, was envisioned as being derived from the thiosulfonate ester, **60**. All attempts to synthesize **60** from thiol **47** and *p*-toluene sulfonyl chloride failed (Scheme 16)[28] and resulted in mostly disulfide, **61**. Presumably if **60** was formed from the anion of **47** and *p*-toluene sulfonyl chloride, it reacted with remaining thiolate to produce **61**. Inverse addition of the reagents did not significantly alter the outcome of this process. Formation of the thiosulfonate ester *via* the tributyltin intermediate **62**[28b] was also unsuccessful in our hands. Thus, reaction of **62** with with *p*-toluene sulfonyl chloride yielded a complex mixture containing **61** along with a variety of tin containing products (Scheme 16).



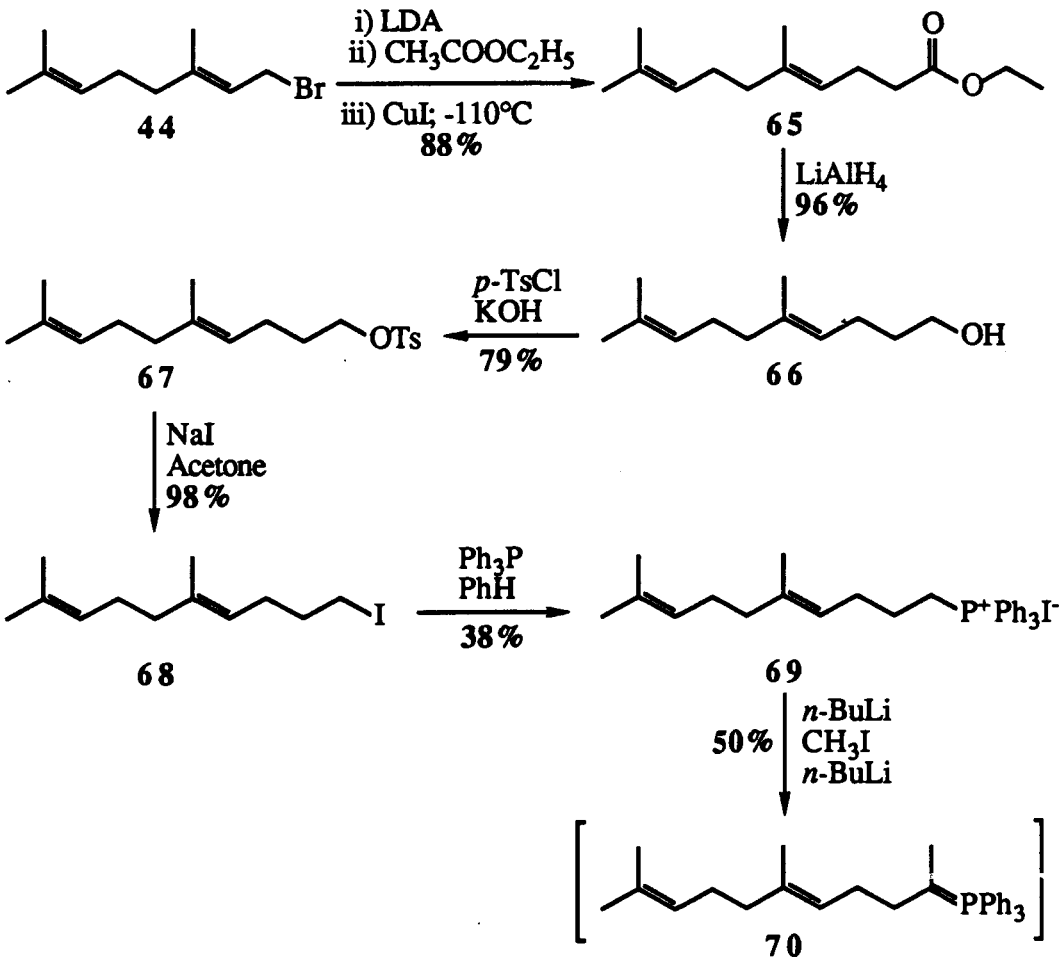
Scheme 16

Synthesis of **60** was achieved *via* reaction of homogeraniol bromide,[29] (**63**) with sodium *p*-toluenesulfonyl thiolate, **64** as shown in Scheme 17.[30]



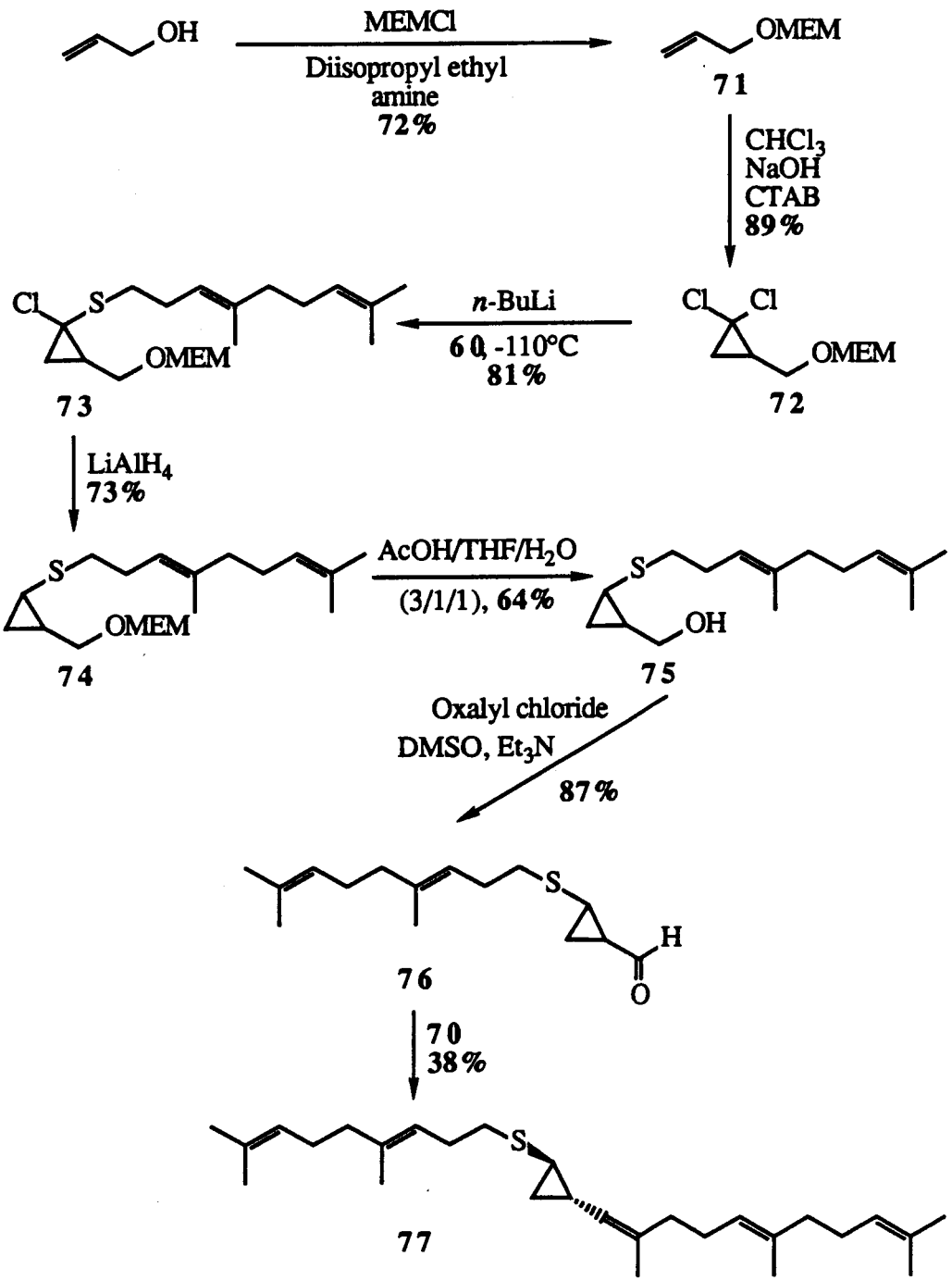
Scheme 17

The ylide corresponding to synthon **59** (Scheme 15) was prepared from geranyl bromide[18] (**44**) by conversion to **65** (Scheme 18).[31] Ester **65** was converted to **66** by reduction with lithium tetrahydridoaluminate. Tosylation[32a] of **66** gave **67** which was converted to the corresponding iodide (**68**) in good yield.[32b] Iodide **68** was treated with triphenyl phosphine[33] in benzene to form the Wittig salt, **69** in 38% yield. The low yield was due to poor crystal formation. In a one pot sequence, **69** was methylated and converted to the corresponding ylide, **70**, according to the procedure of Corey.[34]



Scheme 18

Synthesis of the cyclopropylcarbinyl fragment, **58** (Scheme 15), commenced

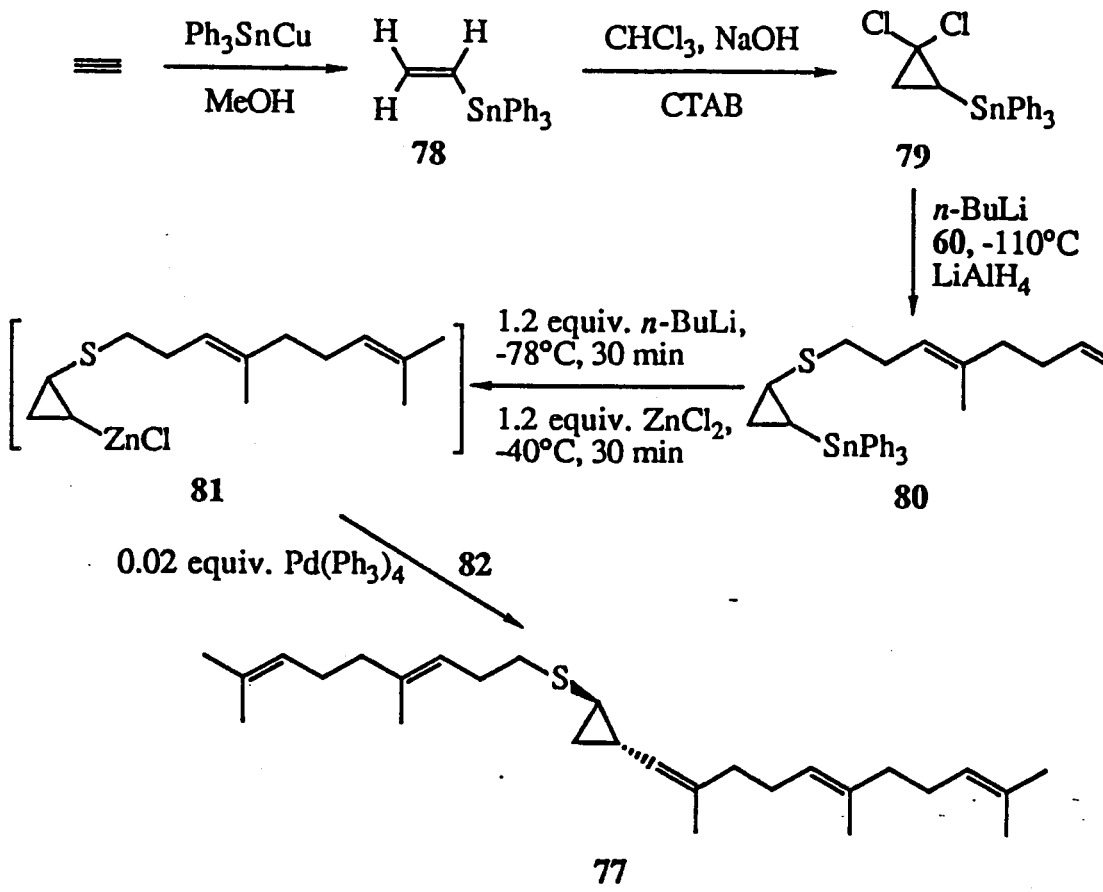


Scheme 19

from the β methoxy-ethoxy-methoxy ether (71) of allyl alcohol (Scheme 19).[35] This was converted to the dichlorocyclo propyl carbinyl intermediate, **72**, by the procedure of Joshi.[36] Reaction of **72** and **60** proceeded smoothly to give **73** using the procedure of deBoer.[37] Dehalogenation of **73** to **74** was achieved by reaction with lithium tetra hydroaluminate. Removal of the β-methoxy-ethoxy-methoxy ether of **74** to give **75** was followed by Swern oxidation to give aldehyde **76** in 56% overall yield.[14] Reaction of **76** and the ylide (**70**, *vide supra*) gave **77** as a 1:1 mixture of *cis,trans* isomers with respect to the two chains attached to the cyclopropane. Chromatographic separation of isomers of **77** was not successful. Often unacceptably low yields (~5%) of the product were obtained along with products whose NMR spectra indicated that the cyclopropane ring had been destroyed, presumably because of the sensitivity of vinylcyclopropyl moiety towards acidic Silica Gel.

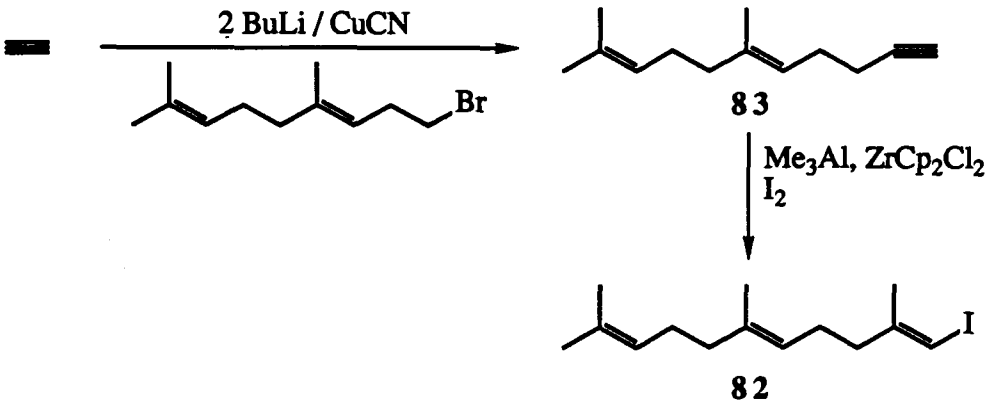
Future directions

The formation of the cyclopropyl sulfonium ion (**33**) can be improved by the addition of Ph_3SnCu to acetylene followed by protonolysis to produce high yields of triphenylstannyl-1-ethene, **78**, as shown in Scheme 20.[38] Addition of the reagents ($CHCl_3$, NaOH, CTAB, *vide supra*)[36] to the alkene, **78**, would result in the corresponding dichloro cyclopropyl intermediate **79**. Introduction of fragment **57** followed by dehalogenation as described above should result in the formation of **80**. Transmetallation of triphenylstannyl moiety followed by conversion of the resultant cyclopropyl-lithium reagent into the corresponding organozinc chloride (**81**) would be achieved using the procedure of Piers.[39] *In situ* $Pd(Ph_3P)_4$ catalyzed coupling of **81** with the vinyl iodide **82** should give **77** of the desired stereochemistry.[39]



Scheme 20

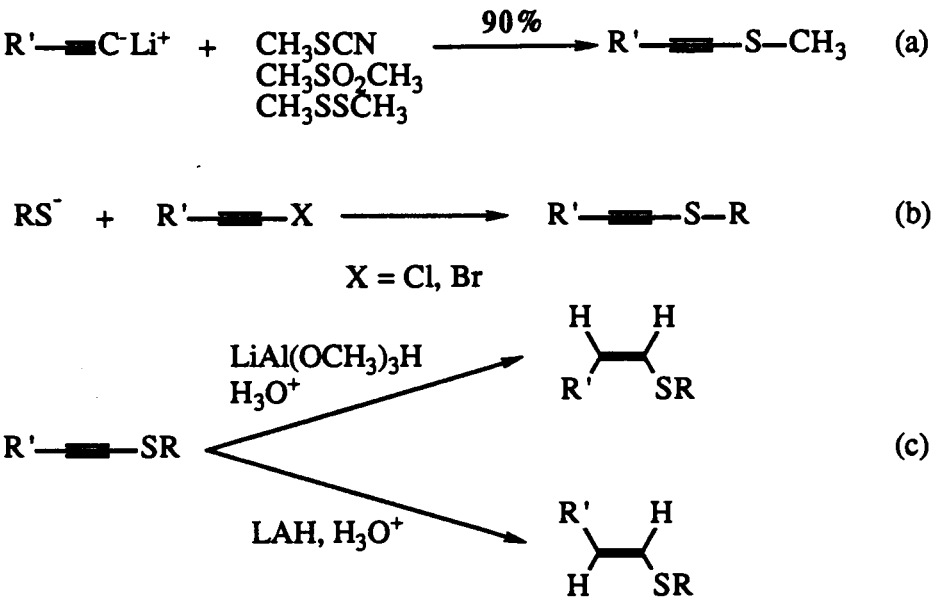
The vinyl iodide, **82**, can be prepared by the dianion of acetylene with coupling of **63** in the presence of CuCN to yield the alkynyl precursor, **83**.[40] Carboalumination-iodination of **83** should result in the stereospecific formation of **82** (Scheme 21).[41] This sequence not only utilizes novel reactions but would also avoid the use of chromatographic separation in the preparation of **77** since the desired stereochemistry is fixed in **80**.



Scheme 21

STEREOSPECIFIC SYNTHESIS OF VINYL SULFONIUM MIMIC, 34

The several methods to stereospecifically prepare vinyl sulfides may be divided into two principle strategies. One involves the creation of an alkynyl sulfide followed by stereospecific reduction. Procedures available to prepare alkynyl sulfides involve the reaction of alkynyl anions with sources of electrophilic sulfur (Scheme 22a),[42] direct displacement of alkynyl halogen by nucleophilic sulfur (Scheme 22b).[42] Reduction of alkynyl sulfides with aluminum hydride reagents is reported to yield *E* or *Z* vinyl sulfides depending upon the reagent used (Scheme 22c).[43]

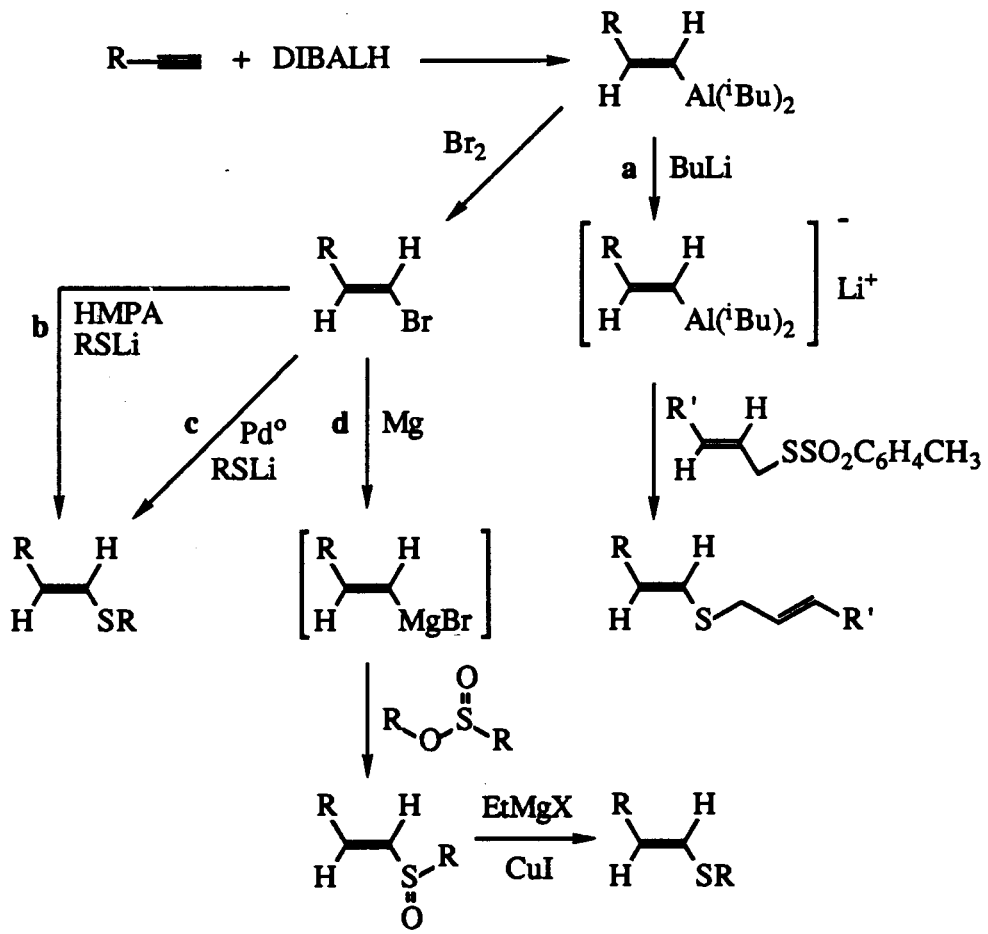


Scheme 22

The second strategy involves reaction of a vinyl organometallic with electrophilic sulfur. Several metals have been successfully applied in this strategy. Thus, diisobutyl-aluminum hydride undergoes stereospecific *cis* hydroalumination with alkynes to give *E*-vinyl alanes (Scheme 23).[43a] These may be converted to vinyl sulfides by a number of routes:

a) Reaction of *E*-vinyl alanes with alkyl lithium reagents yield intermediate alanates which react with electrophilic sulfur.[44b]

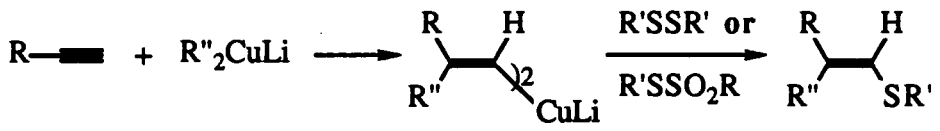
b) Reaction of *E*-vinyl alanes with bromine produce vinyl bromides which may be reacted with nucleophilic sulfur directly in the presence of HMPA (Scheme 23b)[44c] or *via* Pd° catalysis (Scheme 23c).[44d]



Scheme 23

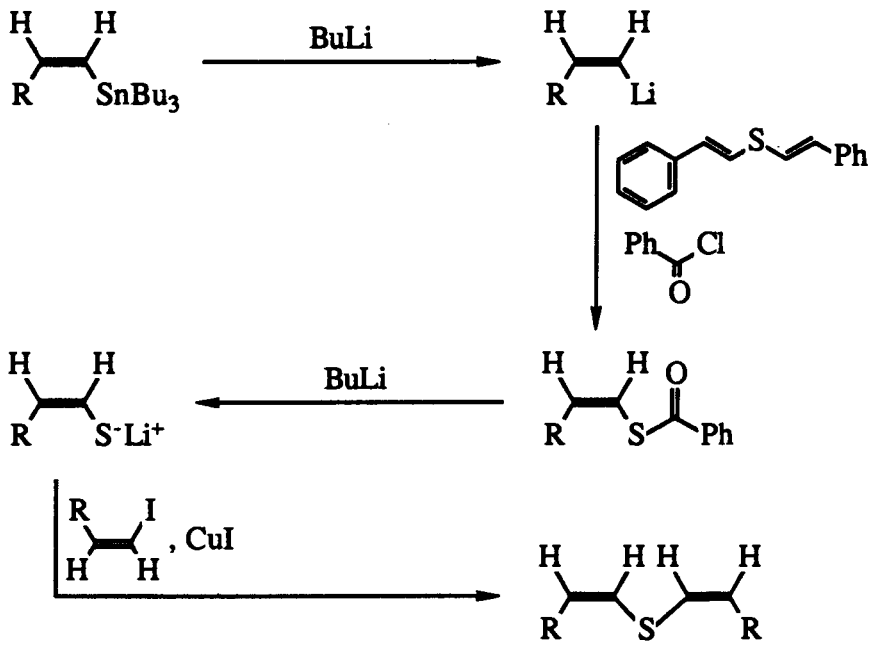
Alternatively, vinyl bromides may be converted to vinyl Grignards (Scheme 23d) and thence to vinyl sulfoxides *via* sulfinic acid esters. Vinyl sulfoxides are easily reduced to vinyl sulfides *via* reaction with ethyl Grignard and cuprous iodide.[44e]

Carbocupration of alkynes also provides a stereospecific route to *E* disubstituted and trisubstituted vinyl cuprates (Scheme 24). These react with both disulfides and thiosulfonate esters to yield vinyl sulfides with retention of stereochemistry.[44f]



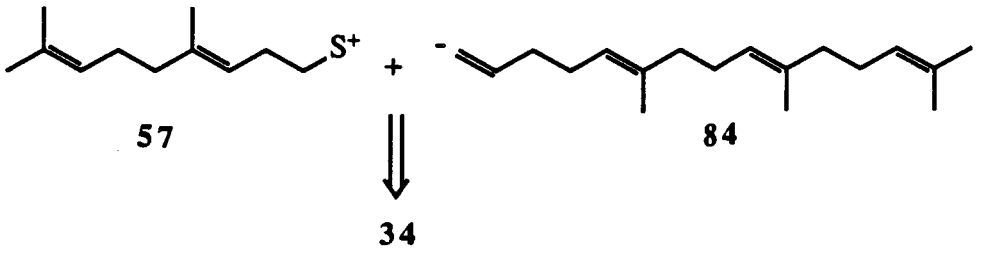
Scheme 24

Recently, Corey has devised a stereospecific route to divinyl sulfides involving stereospecific generation of a vinyl thiolate anion *via* reaction of vinyl lithium intermediates with styrene sulfide. The vinyl thiolates generated coupled stereospecifically with vinyl iodides when reacted as the cuprous thiolates (Scheme 25).[45]



Scheme 25

Retrosynthetic analysis of **34** reveals that this sulfonium mimic of **30** can be prepared by combination of synthon **57** and the vinyl anion equivalent **84** (Scheme 26).

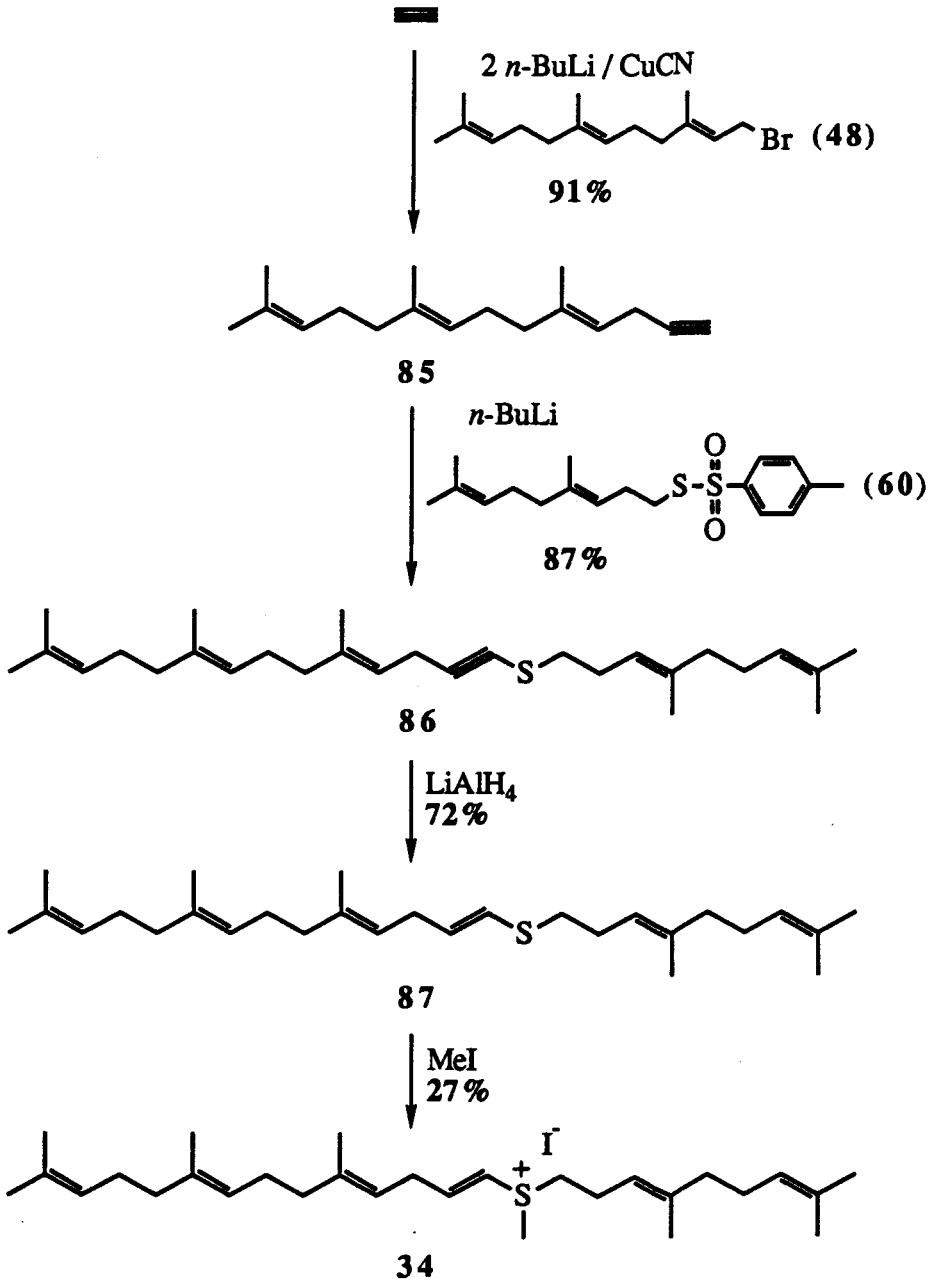


Scheme 26

Reaction of farnesyl bromide (**48**) and dilithioacetylide in the presence of CuCN gave **85**, the required alkynyl precursor of synthon **84** (Scheme 27).[40] Coupling the anion of **85** with thiosulfonate ester **60** yielded the alkynyl sulfide **86** which upon reduction with lithium tetrahydridoaluminate gave the required *E*-vinyl sulfide, **87** (Scheme 27). Methylation of **87** with CH_3I gave the sulfonium ion mimic **34** in 27% yield.

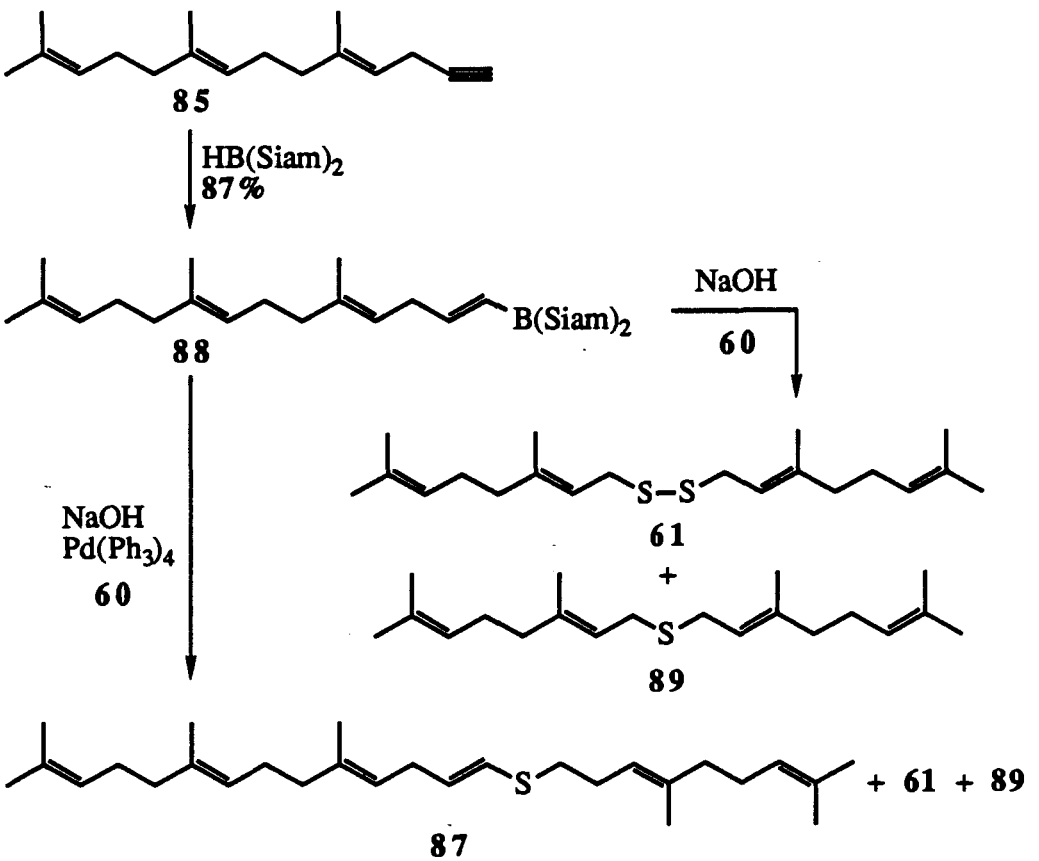
We attempted to react the thiosulfonate ester with vinyl organometallic in order to generate vinyl sulfide **87** directly from the alkynyl precursor **85** (Scheme 28). Reaction of diisobutyl aluminum hydride with **85** gave mixtures of partial and fully reduced products and was abandoned.[44a] Reaction of diisoamyl borane with **85** cleanly gave the vinyl borane product as judged by hydrolytic workup of the initial reaction mixture.[16] Conversion of the presumed *E*-1-vinyl borane (**88**) to vinyl sulfide **87** was attempted under conditions reported by Suzuki[46] for cross coupling reactions of vinyl boranes. One reaction used NaOH to generate a boronate anion which, on reaction with

thiosulfonate ester, **60**, was expected to yield **87**. This reaction consistently gave disulfide (**61**) and



Scheme 27

thioether (89) as the main products, presumably from competing reaction of base with thioester. Addition of $(Ph_3P)_4Pd$ under similar reaction conditions gave the desired vinyl sulfide, albeit in low yield (~15%).



Scheme 28

Future directions

The results to date suggest that vinyl sulfides are formed *via* transition metal catalyzed reaction of thiosulfonates with vinyl boranes. This is consistent with literature on Pd° catalyzed coupling of vinyl boranes with alkenyl halides in the presence of base. Experiments suggested are:

a) Reaction of vinyl boranes with Pd° catalyst in the presence of nonhydroxylic base such as NaOMe or tertiary amines. Since catechol-boranes or 9-BBN function better in Pd° catalyzed cross-coupling reactions than diisoamyl boranes, reactions should be attempted with vinyl boranes derived from the above reagents.

b) To ensure Pd° remains in the proper oxidation state, a reducing species such as $CuBr_2$ should be added to the reaction.

c) In order to achieve oxidative addition of Pd to electrophilic sulfur to obtain RS-Pd-X, perhaps, RSX or RSSR should be used as a sulfur source. Use of a weaker base in Pd° catalyzed cross coupling reaction of vinyl borons with thiosulfonate esters would provide a definite synthetic advantage over the existing routes.

EXPERIMENTAL

^1H NMR spectra were recorded on a Bruker WM-400 spectrometer in $CDCl_3$. Mass spectra were obtained on a Hewlett-Packard 5985B GC/MS system at 70eV. Infrared spectra were recorded neat on a Perkin Elmer Model 599B spectrophotometer. Elemental analyses were performed by Mr. M. Yang of Simon Fraser University, Department of Biological Sciences on a Perkin Elmer Model 240 elemental analyzer. Gas chromatographic analysis were performed on a Hewlett-Packard 5880A instrument using a J and W fused silica DB-1 column (15 m x 0.25 mm i.d.), equipped with a flame ionization detector. Thin layer chromatography was conducted on aluminium sheets precoated with 60 F_{254} Silica Gel (E Merck, Darmstadt). All column chromatography was performed on Silica Gel 60 (230-400 mesh, E Merck, Darmstadt) as described by Still.[47]

Tetrahydrofuran was freshly distilled from potassium benzophenone-ketyl, dimethyl sulfoxide, hexamethyl phosphorous triamide, diisopropyl amine, triethyl amine and dimethyl formamide were distilled from CaH_2 and stored over molecular sieves (3 A). Dichloromethane was distilled from P_2O_5 and stored over molecular sieves (4 A).

Unless otherwise stated all reactions were conducted under argon in flame dried glassware. The general work up procedure was as follows: the reaction mixture was quenched with an ice cold 10% solution of NH_4Cl, the aqueous layer was extracted with ether (3 x 50 mL), the combined organic phase was washed with saturated NaCl solution, dried over anhyd. $MgSO_4$, filtered and concentrated *in vacuo*.

Preparation of (*E*)-3,7-Dimethyl-2,6-octadienal (41). To a stirred solution of oxalyl chloride (29.2 g, 0.23 mol) in CH_2Cl_2 (500 mL) was rapidly added dimethyl sulfoxide (34.3 g, 0.44 mol) in CH_2Cl_2 (100 mL) at -78°C. After stirring for 5 min at the same temperature, geraniol (**38**, 30.8 g, 0.2 mol) was added dropwise over 10 min. After stirring for 15 min, triethylamine (140 mL, 1.0 mol) was added dropwise while maintaining the temperature below -60°C. The mixture was stirred for 5 min, then warmed to rt before addition of 100 mL of water. The aqueous layer was extracted with (2 x 300 mL) portions of CH_2Cl_2. The organic layer was washed with 1% HCl until no longer basic, then washed successively with 50 mL portions of water, 5% Na_2CO_3, water and brine. The combined organic extract was dried over anhyd. $MgSO_4$ and concentrated *in vacuo* to give 34.7 g of the crude product. Flash chromatographic (hexanes/ethyl acetate, 4/1) purification gave 27.6 g (91%) of geranial **41**. Gas chromatographic analysis revealed a purity of 98% with less than 2% *Z* isomer. ^1H NMR ($CDCl_3$) δ 1.56 (s, 3H, vinyl methyl), 1.72 (s, 3H, vinyl methyl), 2.10 (s, 3H, C_3-vinyl methyl), 2.18 (m, 4H, CH_2), 5.15 (t, 1H, C_6-H), 5.82 (d, 1H, C_2-H, J = 10 Hz), 9.2 (d, 1H, C_1-H, J = 10 Hz). MS, m/e (%), 153.2 (0.3), 152.3 (3.2), 94.2 (14.1), 84.2 (25.5), 41.1 (41.6) and 69.1 (100). IR , 2920, 2720, 1680, 1390, 990 and 820.

Preparation of (*E*)-4,8-Dimethyl-1,3,7-nonatriene (42). To methyl triphenylphosphonium iodide (38.9 g, .096 mol) in 250 mL of THF was added of 2.4 M phenyl lithium dropwise at 0°C until a permanent yellow color appeared (1 mL). Then phenyl lithium (37.3 mL, 0.089 mol) was added while keeping the temperature below 0°C. This procedure ensures that the reaction mixture is anhydrous. The deep red solution of ylide containing excess phosphonium salt was stirred for 0.5 h at rt. Geranial (**41**, 13.4 g, 0.088 mol) in THF (40 mL) was added dropwise at 0°C. The reaction was

warmed to rt and stirred overnight after which a light orange suspension was formed. The reaction was quenched by adding 2 mL of methanol. Most of the solvent was evaporated *in vacuo*. and the resulting slurry was diluted with pentane (200 mL) and decanted onto 50 g of Celite. The solids were washed with hot pentane (3 x 50 mL) and filtered through Celite. The resulting yellow solution was filtered through Florosil (50 g) to remove colored impurities. The organic solution was dried over anhyd. $MgSO_4$ and concentrated *in vacuo* to yield 19.96 g of crude product. Distillation yielded 12.1 g (91%) of **42**, b.p. 23-24°C 0.05 mm Hg (Lit. b.p. 22-24°C 0.05 mm Hg). Gas chromatographic analysis revealed a purity of 98% with presence of 1.6% *Z* isomer. ^1H NMR ($CDCl_3$) δ 1.60 (s, 3H, vinyl methyl), 1.68 (s, 3H, vinyl methyl), 1.76 (s, 3H, C_4-vinyl methyl), 2.03-2.14 (m, 4H, CH_2), 4.96-5.11 (m, 3H, C_1, C_7-vinyl H), 5.85 (d, 1H, C_3-vinyl H, J = 10.5 Hz), 6.65 (td, 1H, C_2-vinyl H, J = 10.5 Hz, 16.89 Hz). MS, m/e (%), 151.2 (0.4), 150.2 (3.4), 135.2 (4.1), 81.2 (14.5), 79.2 (15.2), 41.1 (26.1) and 69.1 (100.0). IR , 3035, 1650, 1600, 1450, 1380, 990, 900 and 810.

Preparation of (*E*)-4,8-Dimethyl-3,7-nonadien-1-ol (40). To diborane (50 mL, 50 mmol) in THF at -30°C was added rapidly 2-methyl-2-butene (15.4 g, 0.22 mol). The reaction was stirred at 0°C for 2 h. Concurrently, a solution of **42** (6.75 g, 45 mmol) in THF (20 mL) was added to another flask under argon. The disamyl borane was transferred *via* a canula to the addition funnel of the second flask. The temperature of both reactions was held at 0°C during the 1 hr addition. The reaction was stirred at 0°C for an additional hr, then overnight at rt. Excess disamyl borane was destroyed by addition of methanol (1 mL). After cooling to 0°C, 3 M NaOH (17 mL) was added rapidly. Then 17 mL of 30% H_2O_2 was added while the temperature was maintained below -10°C. The reaction was stirred at rt for 3 h. Usual workup gave 11.11 g of crude product. Distillation yielded 6.37 g (85%) of homogeraniol, **40**, b.p. 65-67°C 0.1mm

Hg. Gas chromatographic analysis revealed a single component. ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 3H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.65 (s, 3H, C_4-vinyl methyl), 1.96-2.07 (m, 4H, CH_2), 2.22-2.27 (q, 2H, C_2-CH_2 J = 6.6 Hz), 3.56 (t, 2H, C_1-CH_2 J = 6.6 Hz), 5.03-5.11 (m, 2H, C_3, C_7-vinyl H). MS, m/e (%), 168.3 (0.1), 125 (33.5), 81.1 (22.7), 69.0 (100), 41.1 (21.5). IR , 3320, 2920, 1665, 1440, 1375, 1110, 1050, 875, 830 and 740.

Synthesis of 1-Bromo-(*E*)-3,7-dimethyl-2,6-octadiene (44). Phosphorus tribromide (3.42 g, 11.9 mmol) was added dropwise to an ice cooled solution of geraniol (**38**, 4.45 g, 28.8 mmol) in 25 mL of anhyd. ether. After 3 hr the reaction was quenched with ice-cold saturated $NaHCO_3$. Usual workup gave 5.8 g (93%) of **44**. Thin layer chromatography using hexane/EtOAc (4/1) as the eluant revealed a single spot. ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 2.0-2.13 (m, 4H, CH_2), 4.2 (d, 2H, C_1-CH_2 J = 7 Hz), 5.04-5.1 (m, 1H, C_6-vinyl H), 5.2 (t, 1H, C_2-vinyl H J = 7 Hz).

Preparation of (*E*)-4,8-Dimethyl-3,7-nonadienonitrile (43). Method A. To an efficiently stirred solution of KCN (0.651 g, 10 mmol) and 18-crown-6 ether (0.132 g, 0.5 mmol) in HMPA (15 mL) was added a solution of geraniol (0.77 g, 5.0 mmol) and tri-*n*- butyl phosphine (1.11 g, 5.5 mmol) in 5 mL of CH_3CN over 10 min. The flask was cooled in an ice/methanol bath and CCl_4 (0.85 g, 5.5 mmol) was added. The reaction was stirred for 3 days after which time it was diluted with Et_2O (200 mL) and washed with 10% aq. citric acid (50 mL). The usual workup and purification by flash chromatography on silica using (4/1), hexane/EtOAc (R_f = 0.23), gave 0.815 g (67%) of nitrile **43**. Gas chromatographic analysis revealed a purity of 97%. ^{1}NMR ($CDCl_3$) δ 1.56 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.72 (s, 3H, vinyl methyl), 2.02-2.19 (m, 4H, CH_2), 3.5 (d, 2H, C_8-CH_2 J = 7.4 Hz), 5.04-5.2 (m, 2H,

vinyl H). MS, m/e (%), 164.3 (0.1), 163.3 (0.9), 162.2 (0.8), 149.2 (0.5), 123.2 (6.5), 67.2 (9.0), 41.1 (25.0) and 69.2 (100). IR , 2926, 2731, 2248, 1701, 1655, 1574, 1515, 1231, 1082, 984 and 827.

Method B. To an efficiently stirred solution of geraniol (1.0 g, 6.5 mmol), NaCN (0.645 g, 13.0 mmol) and NaI (2-5 mg) in CH_3CN (10 mL) was added a solution of Me_3SiCl (1.40 g, 15.0 mmol) in DMF (10 mL). The reaction mixture was refluxed for 8 hr after which time it was poured onto water (100 mL). The usual workup and purification by flash chromatography on silica using (4/1), hexane/EtOAc (R_f = 0.23), gave 0.255 g (21%) of nitrile **43**. The spectral analysis was as reported above.

Method C. To a stirred solution of geranyl bromide, **44**, (5.35 g, 24.6 mmol, prepared as described below) in CH_3CN (20 mL) was sucessively added 18-crown-6-ether (0.25 g, 0.95 mmol) and KCN (4 g, 61.4 mmol). The reaction was stirred in the dark for 6 days after which time it was filtered. The solvent was removed and the residue was titurated with hexane:EtOAc (3:1), to separate the 18-crown-6 ether. The solids were removed by filtration and the filtrate concentrated *in vacuo*. Distillation of the crude product gave 2.4 g (59.7%) of **43**, b.p. 90-91°C 0.2mm Hg. Gas chromatographic analysis revealed a single component. The spectral analysis was identical to that given above.

Synthesis of (*E*)-4,8-Dimethyl-3,7-nonadienoic acid (45). Nitrile, **43** (3.5 g, 21.5 mmol) was dissolved in MeOH (30 mL), and an aqueous KOH solution [4.0 g (71 mmol) in 8 mL of H_2O] was added. The reaction mixture was refluxed for 48 h, cooled, diluted with $NaHCO_3$, extracted with Et_2O, acidified with 2N HCl, filtered and concentrated to give crude homogeranic acid (**45**).as a light brown oil (3.2 g, 82%). ^1H NMR ($CDCl_3$) δ 1.57 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 2.0-2.13

(m, 4H, CH_2), 3.06 (d, 2H, C_1-CH_2 J = 7 Hz), 5.04-5.1 (m, 1H, C_6-vinyl H), 5.2 (t, 1H, C_2-vinyl H J = 7 Hz). IR , 2400-3600, 1725.

Preparation of (*E*)-4,8-Dimethyl-3,7-nonadien-1-thioacetate (46). To an efficiently stirred solution of triphenylphosphine (21 g, 80 mmol) in THF (200 mL) was added diisopropylazodicarboxylate (16.7 g, 80 mmol) at 0°C. The reaction was stirred for 0.5 hr, after which time a thick white precipitate was obtained. A mixture of thiolacetic acid (6.1 g, 80 mmol) and **40** (6.72 g, 40 mmol) in 100 mL THF was added dropwise while the temperature was maintained below 0°C. The reaction was stirred for 1.5 hr at 0°C and then overnight at rt. Solvent was removed *in vacuo* from the clear orange solution and the resulting product purified by flash chromatography using hexane:CH_2Cl_2 (3:1), or hexane:EtOAc (49:1), as eluant. Distillation gave 7.54 g (83%) of **46**, b.p. 65-67°C 0.01mm Hg. Gas chromatographic analysis showed a single component. ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 3H, vinyl methyl), 1.60 (s, 3H, vinyl methyl), 1.67 (s, 3H, C_4-vinyl methyl), 1.95-2.06 (m, 4H, CH_2), 2.22-2.27 (q, 2H, C_2-CH_2 J = 7.3 Hz), 2.31 (s, 3H, $COCH_3$), 2.84-2.87 (t, 2H, C_1-CH_2 J = 7.3 Hz), 5.05-5.12 (m, 2H, C_3, C_7-vinyl H). MS, m/e (%), 226.2 (0.1), 186.2 (0.1), 185.1 (0.6), 184.2 (1.5), 81.1 (59.5), 69.0 (100), 43.1 (42.5), 41.1 (45.3). IR , 3350, 2910, 1690, 1435, 1350, 1130, 1100, 950, 830 and 735. Anal. calcd for $C_{13}H_{22}SO$, C 69.02 H 9.73. Found C 69.22 H9.75.

Preparation of (*E*)-4,8-Dimethyl-3,7-nonadien-1-thiol (47). To a stirred solution of lithium tetrahydridoaluminate (1.22 g, 8.0 equiv) in anhyd. ether (30 mL) was added dropwise a solution of **46** (7.26 g, 32.1 mmol) in 15 mL of anhyd. ether. The reaction was stirred for 0.5 hr, then cooled to 0°C. Excess hydride was destroyed by careful addition of ice-cold 1N HCl. Precipitated salts were removed by filtration through 2 cm of Celite. Usual workup gave 7.5 g of crude product. Distillation

gave 5.42 g (92%) of **47**, b.p. 46°C 0.01mm Hg. Gas chromatographic analysis revealed a purity of 96%. ^{1}H NMR ($CDCl_3$) δ 1.40-1.44 (t, 1H, S*H* *J* = 7.6 Hz), 1.59 (s, 3H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.67 (s, 3H, C_4-vinyl methyl), 1.98-2.02 (m, 2H, C_6-CH_2), 2.04-2.08 (m, 2H, C_5-CH_2), 2.28-2.33 (q, 2H, C_2-CH_2 *J* = 7.1 Hz), 2.49-2,54 (dt, 2H, C_1-CH_2 *J* = 7.1, 7.5 Hz), 5.07-5.11 (m, 2H, C_3, C_7-vinyl H). Irradiation of the triplet at δ 1.40-1.44 resulted in the simplification of the signal at 2.49-2.54 (C_1-CH_2), thus confirming the signal at 1.40-1.44 to be that of the S*H*. MS, m/e (%), 186.2 (0.1), 185.2 (0.2), 141.1 (96.9), 81.1 (36.5), 69.2 (100) and 41.1 (41.0). Isobutylene, CI, m/e (%), 186.0 (12.48), 185.0 (100), 151.0 (20.8), 95.0 (16.64). IR , 2920, 2560 (w), 1735, 1660, 1440, 1285, 1110, 980 and 830.

Synthesis of Ethyl [(*E*)-7,11-dimethyl-3-keto-6,10-dodecadien]-1-oate (49). Ethyl acetoacetate (2.7 g, 21 mmol) was added dropwise to a stirred solution of NaH (1.31 g, 23.5 mmol, 57% mineral oil) in 50 mL of THF at -10°C. The reaction was stirred for 20 min when *n*-BuLi (10 mL, 21 mmol,) was added slowly while the temperature was maintained below -5°C. The resulting yellow solution was stirred for 20 min before the addition of **44** (5 g, 23.1 mmol) in 5 mL of THF. The reaction was stirred for 1 hr before it was quenched with ice-cold saturated NH_4Cl. The usual work up gave 5.8 g of crude product which was distilled, b.p. 112-114°C 0.1mm Hg, to yield 4.6 g (84%) of **49**. Gas chromatographic analysis revealed a purity of 93%. ^{1}H NMR ($CDCl_3$) δ1.30 (t, 3H, OCH_2CH_3 *J* = 10 Hz), 1.62 (s, 6H, vinyl methyl), 1.70 (s, 3H, C_4-vinyl methyl), 1.95-2.10 (m, C_5, C_6-CH_2), 2.30 (q, 2H, C_2-CH_2 *J* = 6.6 Hz), 2.58 (t, 2H, C_1-CH_2 *J* = 6.7 Hz), 3.45 (s, 2H, CO-CH_2-CO), 4.20 (q, 2H, OCH_2CH_3 *J* = 10 Hz), 5.06-5.12 (m, 2H, C_3, C_7-vinyl H). MS, m/e (%), 266 (18.8), 248 (25), 223 (56.2), 205 (18.8), 136 (25), 109 (87.5), 81 (31.2), 69 (100), 41 (62.5). IR , 2920, 1735, 1630, 1450, 1310, 1235, 1035, 910 and 840.

Synthesis of Ethyl [(*E*)-7,11-dimethyl-3-(diethoxy phosphonate)-2,6,10-dodecatrien]-1-oate (50). To NaH (0.313 g, 57% mineral oil) in 10 mL of anhyd. ether was added β-keto ester **49** (1.33 g, 5 mmol) in 5 mL ether at 0°C. The reaction was stirred for 20 min before diethylphosphochloridate (0.97 g, 5.6 mmol) was added dropwise. The resulting mixture was stirred for 2 hr and quenched with saturated NH_4Cl. The usual work up proceedure resulted in crude phosphonate ester which was purified by flash chromatography using hexane/EtOAc (3/1). The yield of **50** was 1.76 g (88%). Gas chromatographic analysis revealed a single component. ^1H NMR ($CDCl_3$) δ 1.25 (t, 3H, $COOCH_2CH_3$ J = 7.0 Hz), 1.35 (t, 6H, $P(OCH_2CH_3)_2$ J = 7.0 Hz), 1.60 (s, 6H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.92-2.10 (m, 4H, C_7, C_8-CH_2), 2.24 (q, 2H, C_4-CH_2 J = 7.1 Hz), 2.46 (t, 2H, C_3-CH_2 J = 7.12 Hz), 4.15 (q, 2H, $COOCH_2CH_3$ J = 7.0 Hz), 4.25 (quint, 4H, $P(OCH_2CH_3)_2$ J = 7.0 Hz), 5.05-5.15 (m, 2H, vinyl H), 5.36 (s, 1H, C_1-vinyl H). MS, m/e (%), 402 (12.5), 357 (31.25), 287 (25), 220 (31.25), 155 (100), 99 (50), 69 (43.75) and 41 (37.5). IR , 2940, 2870, 1732, 1670, 1450, 1290, 1210, 1040 and 825.

Preparation of Ethyl [(*E*)-3,7,11-trimethyl-2,6,10-dodecatrien]-1-oate (51). To CuI (1.42 g, 7.46 mmol) in 15 mL THF at -10°C was added dropwise with stirring MeLi (4.7 mL, 7.46 mmol), while the temperature was maintained below -10°C. After 30 min MeMgBr (4.0 mL, 12.43 mmol) was added dropwise at -40°C. The reaction was further stirred for 0.5 h before addition of **50** (1 g, 2.48 mmol) in 5 mL of THF. The reaction was stirred for 1.5 hr before it was warmed to rt. The reaction was quenched by addition of NH_4Cl:NH_4OH (9:1). The usual workup and evaporation of solvent *in vacuo* gave 0.78 g of crude product, which was purified by flash chromatography using hexane/EtOAc, 50/1) as eluant (R_f = 0.29). Gas chromatographic analysis revealed a purity of 94%. The yield of **51** was 0.57 g (87%). ^1H NMR

($CDCl_3$) δ 1.25-1.28 (t, 3H, OCH_2CH_3 J = 7.1 Hz), 1.59 (s, 6H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.95-2.06 (m, 8H, C_4, C_5, C_8, C_9-CH_2), 2.15 (s, 3H, C_3-vinyl methyl), 4.11-4.16 (q, 2H, OCH_2CH_3 J = 7.1 Hz), 5.07-5.09 (m, 2H, vinyl H), 5.66 (s, 1H, C_2-vinyl H). MS, m/e (%), 264 (12.5), 221 (37.5),128 (56.25), 81 (62.5) and 69 (100). IR , 2924, 1725, 1651, 1450, 1230 and 1151.

Synthesis of (*E*,*E*)-3,7,11-Trimethyl-2,6,10-dodecatrien-1-ol (39). DIBALH (40 mL, 40 mmol) was added dropwise to an efficiently stirred solution of **51** (3.55 g, 13.44 mmol) in 25 mL of anhyd. ether at -50°C. The reaction was stirred at the same temperature for 2 hr after which time it was quenched by addition of 300 mL of 10% aqueous tartaric acid. The usual workup, followed by evaporation of the solvent *in vacuo* gave 2.76 g (93%) of *E,E*-farnesol (**39**) in 96% purity. ^1H NMR δ 1.59 (s, 6H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.95-2.12 (m, 8H, C_4, C_5, C_8, C_9-CH_2), 4.13-4.16 (t, 2H, C_1-CH_2 J = 6.15 Hz), 5.06-5.12 (m, 2H, C_6, C_{10}-vinyl H), 5.40-5.43 (t, 1H, C_2-vinyl H J = 6.2 Hz). MS, Isobutylene CI, m/e (%), 221 (12.5), 205 (100), 149 (41.6) and 137 (83.3). IR , 3340 (b), 2940, 1450, 1010 and 850.

Preparation of 1-Bromo-(*E*,*E*)-3,7,11-trimethyl-2,6,10-dodecatriene (48). To a stirred solution of *E,E*-farnesol (**39**, 6.21 g, 0.028 mol) in 25 mL of ether was added dropwise phosphorus tribromide (3.24 g, 0.012 mol) at -10°C. The reaction was stirred for 3 h after which time it was quenched by pouring into an ice-cold saturated solution of $NaHCO_3$. The usual workup, followed by removal of solvent *in vacuo* , yielded 7.16 g (90%) of **48**. TLC using hexane/EtOAc (4/1) revealed a single component (R_f = 0.85). ^1H NMR ($CDCl_3$) δ 1.59 (s, 6H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.75 (s, 3H, C_3-vinyl methyl), 1.95-2.19 (m, 8H, C_4, C_5, C_8, C_9-CH_2), 4.0-4.15 (d, 2H, C_1-CH_2 J = 7.1 Hz), 5.05-5.12 (m, 2H, C_6, C_{10}-vinyl H), 5.5-5.57 (t, 1H, C_2-vinyl H J = 7.1 Hz).

Synthesis of Ethyl [(*E*)-4,8-dimethyl-3,7-nonadien]-1-thioacetate (52). To a Schlenk tube, connected *via* a two-way stopcock to an argon inlet and a vacuum line was added **47** (4.05 g, 22 mmol) in 20 mL of ether/hexane (1/1). To this stirred solution was added thallium ethoxide (5 g, 20 mmol) *via* a syringe. Immediate yellow coloration was observed. The reaction was stirred for 5 min before the solvent was removed under vacuum. The resulting yellow oily residue was washed with ether (2 x 10 mL), the solvent removed under vacuum and the residue redissolved in 50 mL of anhyd. ether. Ethyl-α-bromo acetate (3.32 g, 20 mmol) was added dropwise whereupon a white precipitate of thallous bromide was formed. After stirring for 1 hr at rt the reaction was filtered through 2 cm of Celite. After the removal of solvent, the product was purified by flash chromatography using hexane/dichloromethane (2/1) to give **52** as a single component (R_f=0.325) as the eluant, 5.3 g (97%) of 96% purity as revealed by gas chromatographic analysis. ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 3H, OCH_2CH_3 J = 6.7 Hz), 1.59 (s, 3H, vinyl methyl), 1.66 (s, 3H, vinyl methyl), 1.66 (s, 3H, C_4-vinyl methyl), 1.96-2.1 (m, 4H, CH_2), 2.3 (q, 2H, C_2-CH_2 J = 7.1 Hz), 2.61 (t, 2H, C_1-CH_2 J = 7.1 Hz), 3.25 (s, 2H, -SCH_2CO), 4.2 (q, 2H, OCH_2CH_3 J = 6.6 Hz), 5.06-5.16 (m, 2H, C_3, C_7-vinyl H). MS, m/e (%), 272 (2.0), 270.6 (10.0), 201 (30), 183 (9.0), 150 (22), 107 (29), 81 (58.5), 69 (100) and 41 (41.5). IR 2980, 2960, 1735, 1450, 1380, 1275, 1130, 1030 and 835. Anal. Calcd for $C_{15}H_{26}O_2S$: C, 66.66, H, 9.63. Found: C, 66.46, H, 9.90.

Synthesis of Ethyl-[2-(4',8'-dimethyl-3'(*E*),7'-nonadienyl-thio)-5,9,13-trimethyl-4(*E*),8,12-tetradecatrien]oate (53). To diisopropylamine (0.5 mL, 3.5 mmol) in 5 mL THF was added dropwise at 0°C, *n*-BuLi (1.7 mL, 3.5 mmol) in hexane. The reaction was stirred for 15 min before addition of **52** (0.94 g, 3.5 mmol) in 5 mL of THF. The resulting mixture was stirred for 2.5 hr at 0°C then cooled to -50°C

and stirred for an additional 0.5 hr. Farnesyl bromide (**48**, 1.4 g, 5 mmol) was then added. The reaction was stirred for 1 hr at -50°C and warmed to rt whereupon it was quenched by pouring onto ice-cold saturated NH_4Cl solution. The usual work up and purification by flash chromatography using hexane/CH_2Cl_2 (2/1) gave 1.52 g (92%) of **53** (R_f = 0.34) as eluant. ^1H NMR ($CDCl_3$) δ 1.27 (t, 3H, -$COOCH_2CH_3$ J = 7.1 Hz), 1.59 (s, 15H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.92-2.08 (m, 12H, C_5', C_6', C_6, C_7, C_{10}, C_{11}-CH_2), 2.25-2.62 (m, 6H, C_1', C_2, C_3-CH_2), 3.23-3.27 (m, 1H, SCHCOO), 4.16-4.19 (m, 2H, $COOCH_2CH_3$), 5.06-5.13 (m, 5H, C_3', C_7', C_4, C_8, C_{12} vinyl H). Irradiation of signal at δ 4.16-4.19 resulted in a singlet at δ 1.27 (triplet originally) and simplified the signal at δ 3.23-3.27. This showed the vicinal coupling between CH_2 and CH_3 and long range coupling of CH_1 with SCHCOO. MS, m/e (%), 475 (0.2), 474 (0.6), 405 (4.8), 183 (3.0), 95 (14.8), 81 (25.9), 69 (100.0) and 41 (57.0). IR , 2930, 1735, 1450, 1380, 1150, 1110 and 1040. Anal. Calcd for $C_{30}H_{50}O_2S$: C, 75.90, H, 10.55. Found: C, 75.64, H, 10.74.

Synthesis of 2-[(4',8'-dimethyl-3'(*E*),7'-nonadienyl-thio)-(5,9,13-trimethyl-4(*E*),8(*E*),12-tetradecatrien)]-1-ol (54). To an efficiently stirred solution of $LiAlH_4$ (0.039 g, 1.04 mmol) in 7 mL of ether was added thioacetate **53** (0.49 g, 1.04 mmol). The reaction was stirred for 1 hr before it was quenched by careful addition of ice-cold 1N HCl. The precipitated salts were removed by filtration through 2 cm of Celite and the filtrate subjected to normal work up procedure to give 4.33 g (98%) of **54**. Thin layer chromatography using hexane/EtOAc (4/1) as eluant revealed a single component. ^1H NMR ($CDCl_3$) δ 1.59 (s, 12H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.95-2.1 (m, 12H, C_5', C_6', C_6, C_7, C_{10}, C_{11}-CH_2), 2.22-2.31 (m, 4H, C_2', C_3-CH_2), 2.48-2.55 (m, 2H, C_1-CH_2), 2.75-2.79 (m, 1H, $SCHCH_2OH$ J = 12.5, 6.80, 4.62 Hz), 3.44-3.50 (ddd, 1H, HCH_aOH J = 11.8,

6.2, 5.8 Hz), 3.63-3.69 (ddd, 1H, HCH_bOH *J* = 11.4, 7.1, 4.54 Hz), 5.06-5.14 (m, 5H, vinyl H). MS, m/e (%), 432 (6.5), 363 (80.54), 213 (6.5), 183 (4.4), 81 (15.2), 69 (100.0), and 41 (17.4). IR , 3440, 2920, 2860, 1450, 1380, 1030 and 835. Anal. Calcd for $C_{28}H_{48}OS$ C, 77.78, H, 11.11. Found C, 77.53, H, 11.36.

Synthesis of 32. The thiol (**54**, 0.21g, 0.5 mmol) was dissolved in acid-free dimethyl sulfate (5 mL, distilled under vacuum) in a sealed test tube for 2 h at 90°C. Following complete consumption of the thiol, as judged by TLC on Silica Gel (hexane/EtOAc, 4/1), the resulting dark solution was washed several times with anhyd. Et_2O and the insoluble residue dissolved in H_2O (10 mL). The material was precipitated by addition of perchloric acid and recrystallized from water containing a few percent of perchloric acid to give (0.07 g, 32%) of the sulfonium salt, **32**. ^1H NMR (CD_3OD) δ 1.64 (brs, 15H, vinyl methyl), 1.67 (brs, 6H, vinyl methyl), 2.3-2.5 (m, 16H, C_2', C_3, C_5', C_6', C_6, C_7, C_{10}, C_{11}-CH_2), 2.7 (m, 2H, C_1-CH_2), 2.8 (m, 1H, $SCHCH_2OH$), 2.95 (s, CH_3), 3.57 (ddd, 1H, HCH_aOH *J* = 11.8, 6.2, 5.8 Hz), 3.74 (ddd, 1H, HCH_bOH *J* = 11.4, 7.1, 4.54 Hz), 5.06-5.14 (m, 5H, vinyl H). MS, FAB, (Xenon/sulfolane) m/e 447 (M^+, 100).

Attempted syntheses of 60. Synthesis of thiosulfonate ester **60** using *p*-toluene sulfonyl chloride in combination with NaH, Py or Et_3N and thiol **47** was attempted. The major product was disulfide **61**. A general procedure follows:

Normal addition: Thiol **47** (0.368 g, 2 mmol) was added dropwise to a suspension of NaH (0.14 g, 2.5 mmol, 57% oil) in 5 mL of THF. After 30 min of stirring, *p*-toluene sulfonyl chloride (0.38 g, 2 mmol) in 10 mL of THF, was added dropwise. The reaction was stirred for 3 hr and then subjected to normal work up.

Purification of the product by flash chromatography using hexane/CH_2Cl_2 (3/1) as eluant yielded 0.51 g (76%) of disulfide **61** and 0.05 g (7.4%) of **60**.

Inverse addition: The reaction was conducted in the same manner as above except that the sodium salt of **47** was added to the *p*-toluene sulfonyl chloride. No appreciable change in yield was observed (10%).

Spectral data for **61**: ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 6H, vinyl methyl), 1.61 (s, 6H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.95-2.10 (m, 8H, C_6, C_6', C_5, C_5'-CH_2), 2.35 (q, 4H, C_2, C_2'-CH_2 J = 7.0 Hz), 2.55-2.6 (t, 2H, C_1, C_1'-CH_2 J = 7.1 Hz), 5.04-5.1 (m, 4H, Vinyl H). MS, Isobutylene CI, m/e (%), 367 (30.0), 339 (30.0), 241 (25.0), 225 (32.5), 207 (52.5), 185 (22.5), 183 (100.0), 151 (25.0).

Preparation of Tri-*n*-butyl-(*E*,*E*)-4,8-dimethyl-3,7-nonadien-1-thio)stannane (62). To an efficiently stirred solution of thiol **47** (6.07 g, 33 mmol) and triethylamine (4 g, 39.0 mmol) in 200 mL of CCl_4, was added dropwise *n*-Bu_3SnCl (10.73 g, 33.0 mmol). The reaction was stirred overnight at rt, filtered and the filtrate washed with 5% aqueous acetic acid, then water (50 mL). The organic layer was separated and dried over anhyd. Na_2SO_4. Flash evaporation of the solvent gave needle shaped white crystals, which were recrystallized from hexane. ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 9H, CH_3, J = 7.1 Hz), 1.2-1.4 (m, 12H, CH_2), 1.4-1.5 (m, 6H, CH_2), 1.59 (s, 6H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.95-2.10 (m, 4H, C_6, C_5, -CH_2), 2.35 (q, 2H, C_2, -CH_2 J = 7.0 Hz), 2.55-2.6 (t, 2H, C_1, -CH_2 J = 7.1 Hz), 5.04-5.1 (m, 2H, Vinyl H). MS, m/e (%), 416 (M^+ - 57, 22).

Preparation of Sodium thio-*p*-toluenesulfonate (64). To $Na_2S{\cdot}9H_2O$ (24 g, 0.1 mol) in 20 mL of water cooled to 0°C was added to *p*-toluene sulfonyl chloride (19.05 g, 0.1 mol) while the temperature was maintained below 5°C. After

completion of addition, the reaction was warmed to 85°C until all deposited sulfur dissolved. Solvent was removed under reduced pressure and the resulting powder washed with 50 mL of ether then extracted with hot absolute EtOH. The product was recrystallized using absolute EtOH and the crystals dried over P_2O_5 at 120°C for 12 hr. This procedure yielded 24 g (98%) of **64**. ^1H NMR (D_2O) δ 2.39 (s, 3H, phenyl-CH_3), 7.35-7.78 (AA'BB', 4H, phenyl H). IR , 1330, 1200, 1090, 980, and 800(b).

A similar procedure was used to prepare $NaSSO_2CH_3$. ^1H NMR (D_2O) δ 2.77 (s).

Synthesis of 1-Bromo-4,8-dimethyl-3(*E*),7-nonadiene (63). Bromine was added dropwise to an efficiently stirred ice-cooled solution of triphenylphosphine (3.2 g, 12.2 mmol) in 20 mL of CH_2Cl_2 until a permanent yellow color appeared. A few milligrams of triphenylphophine were added to consume excess Br_2 (i.e., until no yellow coloration remained). At this point 2.0 mL of pyridine was added and the reaction stirred for 10 min. Homogeraniol (**40**, 2.0 g, 12 mmol) in 20 mL of CH_2Cl_2 was added dropwise over 30 min. The reaction was warmed to rt and stirred for 1 hr then filtered. The precipitate was washed with pentane, filtered, and further washed with water (2 x 50 mL). The solvent was dried over anhyd. $MgSO_4$, concentrated *in vacuo* and the residue subjected to column chromatography using hexane as eluant. The yield of **63** (R_f = 0.47) was 2.1 g (78%). Gas chromatographic analysis revealed a purity of 99%. ^1H NMR ($CDCl_3$) δ 1.57 (s, 3H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.65 (s, 3H, vinyl methyl), 1.96-2.13 (m, 4H, C_5, C_6-CH_2), 2.53-2.62 (q, 2H, C_2-CH_2 J = 6.67 Hz), 3.32-3.38 (t, 2H, C_1-CH_2 J = 6.66 Hz), 5.03-5.11 (m, 2H, vinyl H). MS, m/e (%), 230 (7.0), 217 (25.0), 215 (25.0), 189 (14.0), 187 (14.0), 123 (11.6), 69 (100.0).

Synthesis of (4,7-Dimethyl-3(*E*),7-nonadien-1-thio)-*p*-toluenesulfonate (60). To an efficiently stirred solution of $NaSSO_2C_6H_5CH_3$ (**64**, 2.45 g, 10 mmol) in 30 mL of DMF was added homogeranyl bromide (**63**, 2.31 g, 10 mmol) in 10 mL of DMF. The reaction was stirred at rt for 3 days after which time it was quenched by pouring into 100 mL of water. The usual workup and purification by column chromatography using hexane/CH_2Cl_2 (1/1) as eluant gave 2.83 g (84%) of thiotosylate **60**. Gas chromatographic analysis revealed a purity of 91% and the presence of 3% of disulfide **61**. ^1H NMR ($CDCl_3$) δ 1.55 (s, 3H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.92-2.06 (m, 4H, C_5, C_6-CH_2), 2.28-2.35 (q, 2H, C_2-CH_2 J = 6.7 Hz), 2.46 (s, 3H, phenyl-CH_3), 2.97-3.02 (t, 2H, C_1-CH_2 J = 6.7 Hz), 4.9-5.08 (m, 2H, vinyl H), 7.32-7.84 (AA'BB', 4H, phenyl H). MS, m/e (%), 339 (6.3), 255 (25.2), 183 (100.0), 117 (43.7), 115 (38), 69 (87.5). IR , 2920, 1670, 1600, 1500, 1450(b), 1330(b), 1150, 1080, and 830.

Preparation of Ethyl 5,9-dimethyl-4(*E*),8-decadienoate (65). To diisopropylamine (4.65 g, 46 mmol) in 30 mL THF at -65°C was added dropwise *n*-BuLi (17.7 mL, 46 mmol). The reaction was stirred for 1.5 hr after which time it was transferred *via* syringe to another flask containing a mixture of ethyl acetate (4.1 g, 46 mmol) and CuI (17.5 g, 92 mmol) in 175 mL of THF at -110°C. The reaction was warmed to -30°C, whereupon geranyl bromide **44** (5 g, 23 mmol) in 60 mL of THF was added slowly to maintain the temperature at -30°C. The reaction was stirred for 1 hr at the same temperature after which time it was subjected to the normal workup procedure. Distillation yielded 4.52 g (88%) of **65**. Gas chromatographic analysis showed a purity of 91%. ^1H NMR ($CDCl_3$) δ 1.22- 1.25 (t, 3H, $COOCH_2CH_3$ J = 7.1 Hz), 1.58 (s, 3H, vinyl methyl), 1.60 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.94-2.05 (m, 4H, CH_2), 2.3 (s, 4H, C_1, C_2-CH_2), 4.08-4.13 (q, 2H, $COOCH_2CH_3$ J = 7.1

Hz), 5.04-5.10 (m, 2H, vinyl H). MS, m/e (%), 224.2 (1.9), 219 (0.5), 210.3 (1.8), 209.3 (10.2), 94.1 (84.6), 100.1 (92.7), 81.1 (97.4) and 95.2 (100.0). IR , 2980, 2920, 1740, 1450, 1370, 1150, 1050 and 835.

Preparation of 5,9-Dimethyl-4(*E*),8-decatrien-1-ol (66). To an efficiently stirred solution of $LiAlH_4$ (0.68 g, 17.84 mmol) in 20 mL of ether was added dropwise **65** (4.04 g, 18 mmol) in 30 mL of ether. After 30 min excess hydride was destroyed by careful addition of 1N HCl. The solution was filtered through 2 cm of Celite. Usual workup procedure gave 3.12 g (95%) of **65** in 98% purity as measured by gas chromatographic analysis. ^1H NMR ($CDCl_3$) δ 1.58 (s, 3H, vinyl methyl), 1.59 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.95-2.09 (m, 8H, C_2, C_3, C_6, C_7-CH_2), 3.61-3.64 (t, 2H, C_1-CH_2 J = 6.6 Hz), 5.05-5.13 (m, 2H, vinyl H). MS, m/e (%), 183.2 (0.1), 182.2 (0.7), 139.2 (100.0), 95.1 (84.1), 69.1 (76.2) and 67.2 (71.5).

Preparation of 5,9-Dimethyl-4(*E*),8-decadien-1-*p*-toluene sulfonate (67). Powdered KOH (13 g, 232 mmol) was added in 5 g portions to a solution of **66** (3.07 g, 16.86 mmol) and *p*-toluene sulfonyl chloride (3.69 g, 19.25 mmol) in 40 mL of ether at -30°C. The resulting suspension was stirred for 2 hr at 0°C after which time it was quenched by pouring onto ice water (50 mL). The usual workup yielded 4.45 g (79%) of **67** as found by gas chromatographic analysis. This material was used in the next reaction without further purification. ^1H NMR ($CDCl_3$) δ 1.57 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.87-2.08 (m, 8H, C_2, C_3, C_6, C_7-CH_2), 2.43 (s, 3H, phenyl-CH_3), 3.99 (t, 2H, C_1-CH_2 J = 7.1 Hz), 4.92-5.07 (m, 2H, vinyl H), 7.3-7.8 (AA'BB', 4H, phenyl H). MS, m/e (%), 337.3 (0.2), 336.3 (0.8), 322.6 (0.2), 321.3 (0.7), 121.1 (92.7), 95.1 (100.0) and 69.1 (84.1). IR , 2920, 1450, 1350(b), 1180, 960(w) and 835.

Synthesis of 1-Iodo-5,9-dimethyl-4(*E*),8-decadiene (68). A solution of NaI (4.32 g, 28.8 mmol) in 40 mL of acetone was brought to reflux under argon with stirring. To this solution was added **67** (4.38 g, 13 mmol). After 1 hr at reflux the reaction was worked up in the usual fashion using pentane for extraction. The product was purified by column chromatography using hexane as eluant. The yield of **68** (R_f = 0.45) was 3.72 g (98%). Gas chromatographic analysis revealed a purity of 90%. ^1H NMR ($CDCl_3$) δ 1.57 (s, 3H, vinyl methyl), 1.59 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.82-1.86 (q, 2H, C_2-CH_2 J = 7 Hz),1.95-2.12 (m, 6H, C_3, C_6, C_7 - CH_2), 3.15-3.20 (t, 2H, C_1-CH_2 J = 7.0 Hz), 5.03-5.10 (m, 2H, vinyl H). MS, m/e (%), 293.1 (0.2), 292.2 (1.4), 279.2 (0.1), 249.0 (69.2), 95.0 (88.8), 69.0 (100.0) and 41.1 (65.1).

Synthesis of (*E*)-5,9-Dimethyl-4,8-decadienyl)-1-triphenylphosphonium iodide (69). A solution of **68** (1.55 g, 5.3 mmol) and triphenylphosphine (1.7 g, 6.5 mmol) in 2 mL of benzene was placed in the dark for 5 days. The resulting solution was added to 100 mL of ether with rapid stirring. Fine white crystals were obtained which were filtered and washed with ether (3 x 10 mL). Recrystallization using benzene/ether (1/1) gave 1.12 g (38%) of **69**. ^1H NMR (C_6D_6) δ 1.59 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.76 (s, 3H, vinyl methyl), 2.09-2.21 (m, 6H, C_3, C_6, C_7-CH_2), 2.70-2.78 (q, 2H, C_2-CH_2 J = 7.0 Hz), 4.55-4.65 (m, 2H, C_1-CH_2), 5.17-5.25 (m, 2H, C_4, C_8-vinyl H), 7.19 (m, 15H, phenyl H). MS, FAB, (xenon/sulfolane) (%), 427 (M^+,100.0), 289 (37.5), 275 (25.0), 262 (72.9).

Preparation of 71. To a freshly distilled solution of β-ethoxy-methoxy methyl chloride (4.98 g, 0.039 mmol) in 150 mL of CH_2Cl_2 was added diisopropyl amine (5.1

g, 0.039 mmol) at 0°C. The reaction was stirred for 10 min after which allyl alcohol (2.09 g, 0.036 mmol) was added over 0.5 hr. The reaction was stirred for 18 hr and worked up in usual fashion. Distillation gave 3.78 g (72%) of **71**, b.p. 60-61°C 17 mm Hg. Gas chromatographic analysis revealed a single component. ^{1}H NMR ($CDCl_3$) δ 3.4 (s, 3H, OCH_3), 3.55-3.75 (AA'BB', 4H, OCH_2CH_2O), 4.10 (td, 2H, C_3-CH_2 *J* = 6.5 Hz, 3.0 Hz), 4.76 (s, 2H, OCH_2O), 5.17-5.32 (m, 2H, vinyl H), 5.88-5.98 (ddt, 1H, C_2-vinyl H *J* = 18 Hz, 10 Hz, 6.5 Hz). MS, Isobutylene CI, m/e (%), 147 (14.6), 89 (100.0). IR , 2910, 2890, 2150, 1450, 910 and 745.

Preparation of 72. To a solution of **71** (9.34 g, 0.064 mol) in 25 mL of $CHCl_3$ was added acetyl trimethylammonium bromide (0.2 g, 0.55 mmol) and a chilled 50% NaOH solution (125 g of NaOH and 125 mL of water). The two phase suspension was stirred vigorously and analyzed periodically by gas chromatography (linear temperature program from 40°-200°C at 10°/min) over 3 days. After this time the reaction ceased and mixture was diluted with 100 mL of water and the $CHCl_3$ layer separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic extracts washed with water to which $MgSO_4$ was added to break an emulsion during washing. The organic layer was dried over anhyd.$MgSO_4$, the solvent removed *in vacuo* and the residue distilled to yield 12.3 g (89%) of **72**, b.p. 58°-59°C 0.025 mm Hg. Gas chromatographic analysis revealed a single component. ^{1}H NMR ($CDCl_3$) δ 1.20-1.25 (t, 1H, cyclopropyl H *J* = 8.89 Hz), 1.63-1.67 (dt, 1H, cyclopropyl H *J* = 8.9 Hz, 2.9 Hz), 1.92-2.0 (dddd, 1H, cyclopropyl H *J* = 5.6 Hz, 4.5 Hz, 2.7 Hz and 2.2 Hz); 3.37 (s, 3H, OCH_3), 3.55-3.60 (AA'BB, 2H, OCH_2CH_2-CH_2), 3.6-3.65 (dd, 1H, carbinyl H_a *J* = 9.8 Hz, 8.4 Hz), 3.73-3.77 (AA'BB, 3H, OCH_2CH_2O and carbinyl H_b), 4.74-4.76 (s, 2H, OCH_2O). MS, Isobutylene CI, m/e (%), 231 (10.41), 229 (18.75), 125

(37.5), 123 (56.25), 105 (100). IR , 2890, 1455, 1400, 1155, 1055 and 755. Anal. calcd for $C_8H_{14}O_3Cl_2$ C, 41.92, H, 6.61. Found C, 41.89, H, 6.16.

Preparation of 73. Dichlorocyclopropyl derivative **72** (0.5 g, 2.31 mmol) was added to 15 mL of ether and the reaction cooled to -100°C (liquid N_2/EtOH slurry). *n*-BuLi (1.25 mL, 3 mmol) was added dropwise to maintain the temperature below -100°C. After stirring for 2 h at -100°C thiotosylate **60** (1.23 g, 3.65 mmol) was added dropwise and the temperature was kept below -100°C. The reaction was stirred for 30 min and then warmed to rt whereupon it was diluted with 5 mL of water and extracted with pentane (3 x 10 mL). The extract was dried over anhyd.Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography using hexane/EtOAc (6/1) (R_f = 0.32) as eluant. Two fractions were collected.

Fraction 1 (0.08g, 0.34 mmol) , suggested as $BuSC_{11}H_{19}$, was confirmed by ^1H NMR ($CDCl_3$) δ 0.94 (t, 3H, Bu-CH_3 *J* = 7.2 Hz), 1.4 (sixtet, 2H, Bu-CH_2 *J* = 7.2 Hz), 1.57 (m, 4H, Bu-CH_2), 1.57 (s, 3H, vinyl methyl), 1.59 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.97-2.1 (m, 4H, C_5, C_6-CH_2), 2.28 (q, 2H, C_2-CH_2 *J* = 7.1 Hz), 2.54 (q, 2H, C_1 -CH_2 *J* = 7.1 Hz), 5.07-5.2 (m, 2H, C_3, C_7-CH_2).

Fraction 2 (0.7g, 1.87 mmol) and the major one was **73**. ^1H NMR ($CDCl_3$) δ 1.35 (t, 1H, cyclopropyl H *J* = 9.0 Hz), 1.60 (m, 1H, cyclopropyl H), 1.62 (s, 3H, vinyl methyl), 1.98-2.2 (m, 5H, C_5, C_6-CH_2 and cyclopropyl H), 2.38 (q, 2H, C_2-CH_2 *J* = 7 Hz), 2.86 (t, 2H, C_1-CH_2 *J* = 7.1 Hz), 3.4 (s, 3H, OCH_3), 3.55-3.6 (AA'BB', 2H, OCH_2CH_2O), 3.62-3.65 (dd,1H, carbinyl H_a , *J* 9.8 Hz, 8.5 Hz), 3.73-3.8 (m, 3H, OCH_2CH_20 and carbinyl H_b), 4.78 (s, 2H, OCH_2O), 5.07-5.10 (m, 2H, vinyl H).

Since cyclopropyl proton signals were obscured by other signals, the ^{1}H NMR spectrum was obtained in C_6D_6. ^{1}H NMR (C_6D_6) δ 0.74 (t,1H, cyclopropyl H J = 6 Hz), 1.35 (dd, 1H, cyclopropyl H J = 6 Hz, 8 Hz), 1.59 (s, 3H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.74 (s, 3H, vinyl methyl), 1.99-2.24 (m, 5H, C_5, C_6-CH_2 and cyclopropyl H), 2.4 (q, 2H, C_2-CH_2 J = 7 Hz), 2.98 (dt, 2H, C_1-CH_2 J = 7 Hz, 2 Hz), 3.15 (s, 3H, OCH_3), 3.40 (t, 2H, OCH_2CH_2O J = 5 Hz), 3.56 (dd, 1H, carbinyl H_a, J = 9.4 Hz, 8 Hz), 3.62-3.74 (m, 3H, OCH_1CH_2O and carbinyl H_b), 4.65 (s, 2H, OCH_2O), 5.3 (m, 2H, vinyl H).

Confirmation of the assignment of the signal at δ 1.98 to be to H_a and those at δ 0.74 and δ 1.35 to be due to H_b was achieved by spin decoupling experiments. Irradiation at δ 0.74 reduced the dd at δ 1.35 to a doublet (J = 8 Hz). This also simplified the multiplet at δ 1.98-2.20. Irradiation at δ 1.98 reduced the triplet at δ 0.74 to a doublet (J = 6 Hz) and the dd to a doublet (J = 6 Hz). The dd at δ 3.56 was also reduced to a doublet (J = 9.4 Hz) and the signal δ 3.62-3.74 was simplified.

MS, m/e (%) 377 (20.8), 341 (25), 301 (97.9), 265 (45.8), 151 (100). Anal. calcd for for $C_{19}H_{33}O_3SCl$ C, 60.55, H, 8.76. Found C, 60.61, H, 8.69.

Synthesis of 74. To of $LiAlH_4$ (0.15g, 4 mmol)in 5 mL of dry Et_2O, **73** (1.13g, 3.0 mmol) was added and the mixture refluxed for 3 h. It was then quenched carefully with water and extracted with pentane. Usual workup followed by column chromatographic purification (hexane/EtOAc, 6/1) gave 75% (0.77g) of the desired product. ^{1}H NMR (C_6D_6) δ 0.54 (dt,1H, cyclopropyl H J = 6 Hz, 8Hz), 0.74 (td,1H, cyclopropyl H J = 6 Hz, 8Hz), 1.35 (dt, 1H, cyclopropyl H J = 6 Hz, 8 Hz), 1.59 (s, 3H, vinyl methyl), 1.61 (s, 3H, vinyl methyl), 1.74 (s, 3H, vinyl methyl), 1.99-2.24 (m, 5H, C_5, C_6-CH_2 and cyclopropyl H), 2.4 (q, 2H, C_2-CH_2 J = 7 Hz), 2.98 (dt,

2H, C_1-CH_2 J = 7 Hz, 2 Hz), 3.15 (s, 3H, OCH_3), 3.40 (t, 2H, OCH_2CH_2O J = 5 Hz), 3.56 (dd, 1H, carbinyl H_a, J = 9.4 Hz, 8 Hz), 3.62-3.74 (m, 3H, OCH_1CH_2O and carbinyl H_b), 4.65 (s, 2H, OCH_2O), 5.3 (m, 2H, vinyl H). MS, m/e (%) 342 (43.8), 303 (100), 287 (40.3),253 (76.3), 69 (100).

Synthesis of 77. The synthesis of this cyclopropyl analog (**77**) commenced with the preparation of the cyclopropyl alcohol derivative (**75**) and subsequent oxidation using the procedure developed by Swern *et al.*[14] Wittig olefination of the aldehyde with the phosphonium ylide (**70**, generated *in situ*) from the phosphonium iodide (**70**) completed the sequence. Thus, **74**, (0.34g, 1.0 mmol) was added to 6 mL of a mixture of THF:H_2O:AcOH (1:1:3) at rt. After stirring for 4 h, the reaction was extracted with pentane. Usual workup followed by removal of solvent yielded **75** which was immediately oxidized to the aldehyde **76**. To a stirred solution of oxalyl chloride (0.292 g, 2.3 mmol) in CH_2Cl_2 (5 mL) was rapidly added dimethyl sulfoxide (0.343 g, 4.4 mmol) in CH_2Cl_2 (1 mL) at -78°C. After stirring for 5 min at the same temperature, **75**, 0.508 g, 2.0 mmol) was added dropwise over 10 min. After stirring for 15 min, triethylamine (1.4 mL, 0.1 mmol) was added dropwise while maintaining the temperature below -60°C. The mixture was stirred for 5 min, then warmed to rt before addition of 1 mL of water. The aqueous layer was extracted with (2 x 3 mL) portions of CH_2Cl_2. The organic layer was washed with 1% HCl until no longer basic, then washed successively with 5 mL portions of water, 5% Na_2CO_3, water and brine. The combined organic extract was dried over anhyd. $MgSO_4$ and concentrated *in vacuo* to give 0.44 g (87%) of the crude product. ^1H NMR ($CDCl_3$) δ 1.48-1.52 (m, 1H, cyclopropyl H), 1.57 (s, 6H, vinyl methyl), 1.57-1.62 (m, 1H, cyclopropyl H), 1.67 (s, 3H, vinyl methyl), 1.98-2.1 (m, 4H, C_5, C_6-CH_2), 2.21-2.26(m, 1H, cyclopropyl H), 2.38 (q, 2H, C_2-CH_2 J = 7 Hz), 2.41 (m, 1H, cyclopropyl H), 2.86 (t, 2H, C_1-CH_2 J = 7.1

Hz), 5.07-5.10 (m, 2H, vinyl H) 9.25 (d, 1H, C*H*O, *J 3 Hz).* MS, m/e (%) 254 (20.2), 151.0 (20.8), 95.0 (16.64). IR , 2920, 1725, 1440, 1320, 1285, 1110, 980 and 830. Anal. Calcd for $C_{15}H_{26}OS$ C, 70.86, H, 10.20. Found C, 70.53, H, 10.16.

A solution of 0.54g (0.97 mmol) of **69** in 3 mL of anhydrous THF was cooled to O°C. *n*-BuLi (0.97 mmol, 0.4 mL) was added, and the resulting solution was allowed to warm to rt. Stirring was continued for 10 min, methyl iodide (0.14g, 0.97 mmol) was added dropwise, and the resulting solution was stirred for 30 min at rt. The reaction mixture was cooled to O°C, and a second portion of *n*-BuLi (0.97 mmol, 0.42 mL) was added. The solution was allowed to warm to rt and then stirred for 10 min. The reaction mixture was cooled to -45°C, and 0.248 g (0.98 mmol) of **76** was added *via* a syrnge. Stirring was continued for 15 min at this temperature. Et_2O (1 mL) was added and the solution allowed to warm to O°C. After 0.5 h of stirring, absolute EtOH (1 mL) was added. The resulting clear yellow solution was allowed to warm to rt and was stirred overnight. The solution was then poured onto 10 mL of Et_2O and extracted with water until the aqueous layer was pH 7. Usual workup followed by flash chromatography on Silica Gel (benzene/hexane, 1/1) resulted in four fractions. Those fractions containing the pure *trans* isomer (**77**) were pooled to yield 0.08g (0.196 mmol, 20% from **76**) R_f = 0.56; ^1H NMR ($CDCl_3$) δ 0.7-1.1 (m, 1H, cyclopropyl H), 1.59 (s, 12H, vinyl methyl), 1.57-1.60 (m, 1H, cyclopropyl H), 1.61 (s, 3H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.95-2.1 (m, 10H,-CH_2), 2.22-2.31 (m, 4H, C_2, C_3-CH_2), 2.48-2.55 (m, 2H, C_1-CH_2), 2.21-2.26 (m, 1H, cyclopropyl H), 2.38 (q, 2H, C_3-CH_2 *J* = 7 Hz), 2.41 (m, 1H, cyclopropyl H), 4.64 (d, 1H, vinyl H, *J* 9 Hz, 1Hz), 5.07-5.10 (m, 4H, vinyl H). MS, m/e (%) 435 (20.2)..

Those fractions containing the pure *cis* isomer (**77**) were pooled to yield 0.08g (0.196 mmol, 20% from **76**) R_f = 0.61; ^1H NMR ($CDCl_3$) δ 0.7-1.1 (m, 1H,

cyclopropyl H), 1.59 (s, 12H, vinyl methyl), 1.57-1.60 (m, 1H, cyclopropyl H), 1.64 (s, 9H, vinyl methyl), 1.95-2.1 (m, 10H,-CH_2), 2.22-2.31 (m, 4H, C_2, C_3-CH_2), 2.48-2.55 (m, 2H, C_1-CH_2), 2.21-2.26 (m, 1H, cyclopropyl H), 2.38 (q, 2H, C_3-CH_2 J = 7 Hz), 2.41 (m, 1H, cyclopropyl H), 4.54 (d, 1H, vinyl H, J 9 Hz, 1Hz), 5.07-5.10 (m, 4H, vinyl H). MS, m/e (%) 435 (34.2).

Synthesis of 5,9,13-trimethyl-4(*E*),8,12-tetradecatrien-1-yne (85). A stream of dry acetylene (passed successively over $CaCl_2$, and two dry ice acetone traps) was used to saturate 50 mL of anhyd.THF at -50°C. The temperature was lowered to -78°C and *n*-BuLi (3.05 mL, 6.4 mmol) was added dropwise while the temperature was maintained below -70°C. The reaction was stirred for 30 min then CuCN (0.286 g, 3.2 mmol) in 10 mL of THF was added in one portion. The tan suspension was further stirred for 30 min at -78°C and then at 0°C for 1 hr when it was cooled again to -70°C. Farnesyl bromide **48** (0.71 g, 2.5 mmol) in 5 mL of anhyd.THF, was then added dropwise. The reaction was stirred at this temperature for 1 hr after which time it was warmed to 0°C and further stirred for 1 hr. The usual work up and column chromatography using hexane as eluant (R_f =0.37) gave 0.55 g (96.49%) of **85**. Gas chromatographic analysis showed a single component. ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 6H, vinyl methyl), 1.62 (s, 3H, vinyl methyl), 1.67 (s, 3H, vinyl methyl), 1.95-1.97 (t, 1H, acetylene H J = 2.7 Hz), 1.98-2.10 (m, 8H, C_6, C_7, C_{10}, C_{11}- CH_2), 2.88-2.91 (ddt, 2H, C_3-CH_2 J = 6.8 Hz, 2.7 Hz, 0.808 Hz), 5.08-5.15 (m, 2H, C_8, C_{12}-vinyl H), 5.17-5.2 (dt, 1H, C_4-vinyl H J = 0.8 Hz, 2.7 Hz), MS, m/e (%), 230 (3.3), 215 (20), 187 (26.6), 136 (26.6), 105 (20), 91 (33.3), 81 (46.6), 69 (100). Anal. Calcd for $C_{17}H_{26}$ C, 88.69, H, 11.30. Found C, 88.65, H, 11.31.

Preparation of 86. To alkyne **85** (0.143 g, 0.625 mmol) in 5 mL of THF under argon and cooled to -5°C was added with stirring *n*-BuLi 0.26 mL, 0.625 mmol)

dropwise while the temperature was maintained at -5°C. The reddish orange solution obtained was stirred for 30 min then thiotosylate **60** (0.17 g, 0.5 mmol) was added dropwise. The reaction was stirred for 1 hr after which time it was subjected to normal work up and column chromatogrphy using hexane/CH_2Cl_2 (15/1) as eluant. The yield of **86** (R_f =0.29) was 0.17 g (82%). ^1H NMR ($CDCl_3$) δ 1.60 (s, 6H, vinyl methyl), 1.62 (s, 9H, vinyl methyl), 1.70 (s, 6H, vinyl methyl), 1.97-2.15 (m, 12H, $C_{5'}$, $C_{6'}$, C_6, C_7, C_{10}, C_{11}-CH_2), 2.45 (dt, 2H, $C_{2'}$-CH_2 *J* = 7.1 Hz, 7.0 Hz), 2.67 (t, 2H, $C_{1'}$-CH_2 *J* = 7.1 Hz), 5.08-5.2 (m, 5H, vinyl H). MS, Isobutylene, CI, m/e (%) 413 (42.8), 335 (14.3), 317 (9.5), 275 (23.8), 221 (19.0), 207 (14.3), 185 (23.8), 151 (100). MS, m/e (%) 412 (5.0), 373 (7.5), 344 (12.5), 333 (15), 303 (27.5), 275 (25), 259 (20), 207 (30), 183 (70), 165 (45), 135 (15), 109 (20), 81 (52.5), 69 (100). IR 2980, 2940, 2150, 1670, 1450, 1380, 1600, 1150 and 820. Anal. Calcd for $C_{28}H_{44}S$ C, 81.55, H, 10.67. Found C, 81.57, H, 10.61.

Preparation of 87. To a suspension of $LiAlH_4$ (0.6 g, 4.0 equiv.) in 10 mL of anhyd.ether was added dropwise **86** (6.62 g, 16.0 mmol) in 10 mL of ether over a period of 30 min. The reaction was refluxed for 18 hr then cooled to 0°C. Excess hydride was destroyed by careful addition of 1 N HCl. The precipitated salts were removed by filtration through 2 cm of Celite. The filtrate was washed with saturated NaCl solution and dried over anhyd.$MgSO_4$. Removal of the solvent *in vacuo* followed by flash column chromatography using hexane/CH_2Cl_2 (15/1) as eluant gave 6.0 g (90%) of **87**. ^1H NMR ($CDCl_3$) δ 1.6 (s, 6H, vinyl methyl), 1.62 (s, 9H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.98-2.10 (m, 12H, $C_{5'}$, $C_{6'}$, C_6, C_7, C_{10}, C_{11}-CH_2), 2.4 (dt, 2H, $C_{2'}$-CH_2 *J* = 7 Hz), 2.72 (t, 2H, $C_{1'}$-CH_2 *J* = 7 Hz), 3.10 (ddd, 2H, C_3-CH_2 *J* = 11 Hz, 6 Hz, 1.8 Hz), 5.1-5.2 (m, 5H, vinyl H), 5.8 (q, 1H, C_2-vinyl H *J* = 18 Hz, 7 Hz), 6.1 (d, 1H, C_1-vinyl H *J* = 18 Hz, 1.9 Hz). MS, m/e (%) 414 (57.5), 396 (27.5),

329 (45), 314 (52.5), 239 (30), 211 (50), 109 (27.5), 81 (25), 69 (100). Anal. Calcd for $C_{28}H_{46}S$ C, 81.15, H, 11.11. Found C, 81.17, H, 11.21.

Synthesis of 34. The sulfide **87** (0.6 g, 1.6 mmol) was added to 2 mL of dry methyl iodide in a schlenk tube, and the reaction mixture was allowed to stand at rt for overnight. It was then heated with ether, methanol and ethyl acetate to remove excess methyl iodide and dissolve the oily residue. Crystallization occured upon cooling to yield 0.16 g (27%) of the desired product. ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 6H, vinyl methyl), 1.62 (s, 9H, vinyl methyl), 1.67 (s, 6H, vinyl methyl), 1.9 (s, 3H, S-methyl), 2.20 (m, 12H, $C_{5'}$, $C_{6'}$, C_6, C_7, C_{10}, C_{11}-CH_2), 2.4 (dt, 2H, $C_{2'}$-CH_2 J = 7 Hz), 2.72 (t, 2H, $C_{1'}$-CH_2 J = 7 Hz), 3.15 (ddd, 2H, C_3-CH_2 J = 11 Hz, 6 Hz, 1.8 Hz), 5.1-5.2 (m, 5H, vinyl H), 5.8 (q, 1H, C_2-vinyl H J = 18 Hz, 7 Hz), 6.1 (d, 1H, C_1-vinyl H J = 18 Hz, 1.9 Hz). MS, FAB (Xenon/sulfolane) 429 (M^+, 100).

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