

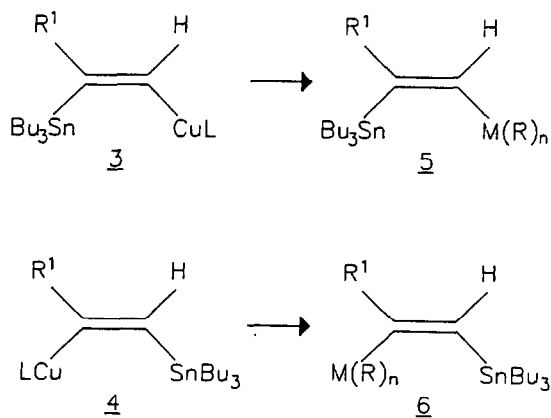
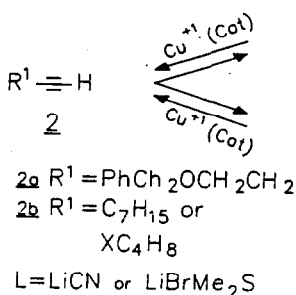
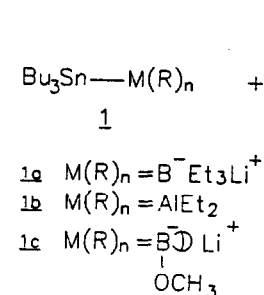
REGIOSELECTIVE SYNTHESIS AND CROSS COUPLING REACTIONS
 of 1,2-BOROSTANNYL-1-ALKENES

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Summary: The copper (I) catalyzed addition of $\text{Bu}_3\text{Sn}^\ominus\text{B}(\text{OCH}_3)^\oplus\text{Li}^\ominus$ to 1-alkynes yields lithium[2-tri-*n*-butylstannyl-(*Z*)-1-alkenyl]-1-borates which may be selectively coupled via organopalladium or organocuprate chemistry with a variety of electrophiles, exclusively at the vinyl boron bond. Products of opposite regiochemistry are obtained when $\text{BF}_3 \cdot \text{Et}_2\text{O}$ is added to the initial reaction and the reaction solution is refluxed.

Bismetalation of 1-alkynes with unsymmetrical bimetallic reagents yields *cis*-1,2-dimetallo-1-alkenes in which the vinyl metal bonds possess differential reactivity. Further elaboration of these dimetallo adducts by replacement of the carbon-metal bonds by carbon-carbon bonds would provide a facile and versatile route to trisubstituted alkenes¹. Two metals for which much chemistry of this type is available are tin² and boron³.

Recently the conversion of 1-alkyne, (2a) to lithium[1-tri-*n*-butylstannyl-(*E*)-1-alkenyl]-2-borate was achieved by the addition of $\text{Bu}_3\text{Sn}^\ominus\text{BEt}_2\text{Li}^\oplus$ (1a) in the presence of copper (I) cyanide⁴. It was suggested that the reaction proceeded *via* reversible stannylcupration^{6,7} to yield 3 and 4, a process we have recently considered to be involved in the copper (I) catalyzed addition of (1b)⁸ to 1-alkynes.

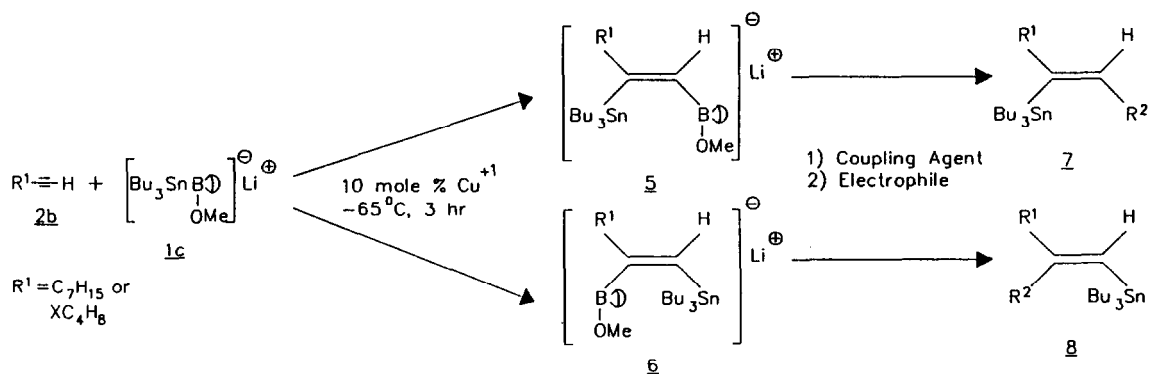






















The major problem besetting the reported addition of 1a to 1-alkyne 2a is the requirement for in situ proteolytic consumption of the vinyl boron center of the bimetallic adducts 5 and 6 presumably^{4,6,7} to overcome an unfavorable adduct = alkyne equilibrium. A second drawback to the reported reaction was the absence of methodology to generate either possible regioisomeric adduct.

We report that the copper (I) catalyzed addition of stannylborate reagent 1c to 1-alkynes can yield either regioisomeric 1,2-borostannyl-1-alkene (5 or 6) with high regiochemical bias (Table 1). Furthermore in situ protonolysis of the 1,2-dimetallo adduct, 5 is not necessary to achieve high consumption of alkyne if a reactive coupling reagent is added to the reaction^{5,8}. We also report the selective conversion of the vinyl carbon-boron bond in the adduct to a carbon-carbon bond by both organopalladium⁹ and organocuprate¹⁰ cross coupling reactions. Various functional groups (entries A-F) can be tolerated under the reaction conditions thereby making the overall process extremely versatile.

In a typical procedure B-methoxy-9-borabicyclo[3.3.1]nonane¹¹ (5.8 mmol) was added to Bu₃SnLi¹² (5.8 mmol) in 5 mL of dry THF at -78°C. The reaction was warmed to 0°C and stirred for 30 min. The ¹¹B NMR spectrum revealed the formation of the "ate" complex 1c (δ5.1 ppm)¹³. The reaction was cooled to -78°C and 1-alkyne (2.9 mmol) in 5 mL of THF was added, followed by 10 mol% CuBr·(CH₃)₂S (entries A-G and K) or CuCN (entries H-J). The reaction was maintained at -65°C for 3 h, after which time a coupling reagent (CuBr·Me₂S, CuCN, Pd(Ø₃P)₄ or "Pd(Ø₃P)₂"⁹ (prepared in situ by the addition of 2 equivalents of DIBAH to a solution of Pd(Ø₃P)₂Cl₂ in THF at room temperature) was added. Stirring was continued for 1hr, then an electrophile (6 mmol) was added and the reaction warmed slowly to room temperature. In cases where Pd⁹ was the coupling agent, the initial reaction solution containing the 1,2-dimetallo adducts (5 or 6) was added via a canula to a solution of the electrophile (6 mmol) in 5 mL of THF and Pd⁹ (0.15 mmol) at room temperature. The palladium catalysed reactions were stirred further for overnight. All reactions were subjected to usual workup followed by flash chromatography to give the indicated products whose structures were confirmed by GC/MS, ¹H, ¹³C and ¹¹⁹Sn NMR.

Addition of 1c to 1-alkyne (2b) using CuBr·Me₂S as the catalyst, followed by the addition of one equivalent of CuBr·Me₂S¹⁰ as the coupling agent and allyl bromide as the electrophile, gave 7a in high yield and excellent regiochemical purity (>90%, entries A-D and G). A duplicate reaction employing 1N HCl in MeOH as the electrophile gave 7b in excellent yields (entries A-G). Likewise, use of ethyl vinyl ketone in the presence of BF₃·Et₂O (1.0 equiv.) as the electrophile gave 7c (entry G). In contrast, when one equivalent of CuCN was used as the coupling agent, the reaction with allyl bromide gave a (2:1) mixture of 7a and 8a (entry H). Addition of CuCN as the coupling agent, followed by protonolysis

Table 1: Addition of $\left[\text{Bu}_3\text{SnB}(\text{O})\text{OMe} \right] \text{Li}^\oplus$ to 1-alkynes and further reactions with electrophiles.


Entry	R ¹	Coupling Agent & Conditions	Electrophile	R ² ; Yield (Z+B) (%)	Z : B
A	HOC ₄ H ₈	1 eq. CuBr.Me ₂ S -78°C, 1hr	a;  b; HCl/MeOH	a;  : 57% b; H : 68%	100: 0 100: 0
B	THPOC ₄ H ₈	"	a;  b; HCl/MeOH	a;  : 62% b; H : 73%	100: 0 100: 0
C	CNC ₄ H ₈	"	a;  b; HCl/MeOH	a;  : 78% b; H : 81%	96: 4 100: 0
D	AcOC ₄ H ₈	"	a;  b; HCl/MeOH	a;  : 73% b; H : 77%	100: 0 100: 0
E	BrC ₄ H ₈	"	a;  b; HCl/MeOH	a;  : 53% b; H : 54%	70: 30 70: 30
F	C ₆ H ₅	"	a;  b; HCl/MeOH	a;  : 80% b; H : 82%	40: 60 46: 54
G	C ₇ H ₁₅	"	a;  b; HCl/MeOH c; 	a;  : 89% b; H : 92% c;  : 53%	92: 8 98: 2 96: 4
H	"	1 eq. CuCN -30°C, 1hr	a;  b; HCl/MeOH	a;  : 75% b; H : 80%	60: 40 66: 34
I	"	Pd(Φ ₃ P) ₄	a; 	a;  : 78%	92: 8
J	"	Pd(Φ ₃ P) ₂ ⁺² NaOMe, RT.	d; ΦI	d; Φ : 63%	96: 4
K	"	1.3eq. BF ₃ .Et ₂ O -78°C → reflux	b; AcOH	b; H : 62%	9: 91

with 1N HCl in MeOH gave **7b** and **8b** in the same ratio (entry H). Addition of the mixture resulting from the reaction of **2b** and **1c** to a solution of 5 mole % Pd(ϕ_3 P)₄ and allyl bromide (6 mmol) yielded **7a** in good yield (entry I). Use of "Pd(ϕ_3 P)₂" as catalyst, iodobenzene^{9,14} as the electrophile and NaOMe as the base gave **7d** (entry J). Addition of BF₃·Et₂O¹⁵ alone as the coupling agent reversed⁴ the regiochemistry of the products (entry K). Thus, treatment of the reaction mixture resulting from addition of **2b** to **1c** with 1.3 equiv. of BF₃·Et₂O at -78°C followed by heating to reflux (56°C, THF) overnight and subsequent protonolysis by AcOH gave a mixture of **7c:8c** (9:91, entry K). We suspect that this reaction involves Cu⁺¹ catalysed addition of species¹⁵ different than **1c**.

The use of 1,2-dimetallo-1-alkenes in synthesis is under active investigation in our laboratory¹⁶.

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13. The adduct was also prepared by treating a solution of BrBBN·Me₂S (δ 11.7 ppm) with Bu₃SnLi and further reaction of Bu₃SnB(ϕ) (δ 56.2 ppm) with NaOMe. This adduct also gave a ¹¹B NMR signal at δ 5.2 ppm.
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15. a) H.C. Brown, N.G. Bhatt and S. Rajagopalan, *Organometallics*, **5**, (1986) 816 b) P. Jacob, III., H.C. Brown, *J. Am. Chem. Soc.*, **98**, (1976) 7832. c) Addition of BF₃·Et₂O to the reaction mixture resulting from addition of **2b** and **1c** gives precipitates of LiBF₄ and copper salts.
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