

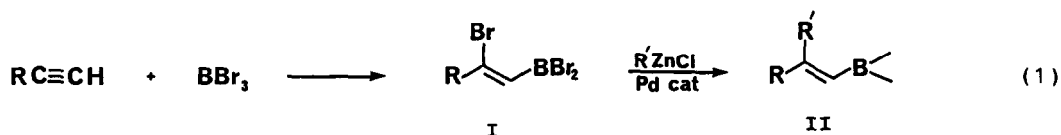
ORGANIC SYNTHESIS USING HALOBORATION REACTIONS 11. A FORMAL CARBO-
BORATION REACTION OF 1-ALKYNES AND ITS APPLICATION TO THE DI-
AND TRISUBSTITUTED ALKENE SYNTHESIS

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Summary: The cross-coupling reaction of organozinc chlorides with (Z)-2-bromo-1-alkenylboranes prepared by the bromoboration reaction of 1-alkynes with tribromoborane, proceeds in the presence of a palladium catalyst to give 2,2-disubstituted alkenylboranes, which can be used for the di- or tri-substituted alkene synthesis directly.

Carbometallation of 1-alkynes¹ has been regarded as the most reliable and straightforward method for the stereoselective synthesis of 2,2-disubstituted alkenylmetals, which are versatile intermediates for the stereoselective synthesis of trisubstituted alkenes. However, the drawback to such reactions as carbocupration¹, zirconium-assisted methylalumination², carbozincation³, and allylmetallations by allylic derivatives of Zn⁴ and B⁵ is the fact that they are operative only when alkyl- or allylmetals are used as the carbometallation reagent. We wish to report here a conceptually novel route to 2,2-disubstituted alkenylboranes (II), which involves the palladium catalyzed cross-coupling reaction of organozinc chlorides with (Z)-2-bromo-1-alkenyldibromoboranes (I) (eq.1).



Though the bromoboration reaction of 1-alkyne with tribromoborane proceeds under mild conditions with high stereoselectivity⁶, the resulting I is sensitive toward the attack of nucleophiles⁷, which made it difficult to use I for the further transformation. We have found that, in the presence of Pd catalyst, I reacts with organozinc compounds at the bromo moiety while the undesired β -elimination can be suppressed sufficiently. The formation of II was confirmed by the isolation of disubstituted alkene (III) after the protonolysis. Furthermore, II can be used for the synthesis of tri-substituted alkene directly by the cross-coupling reaction with organic halides. Thus, the addition of base and organic halides to the reaction

Table 1. The Synthesis of Di- and Trisubstituted Alkenes^a

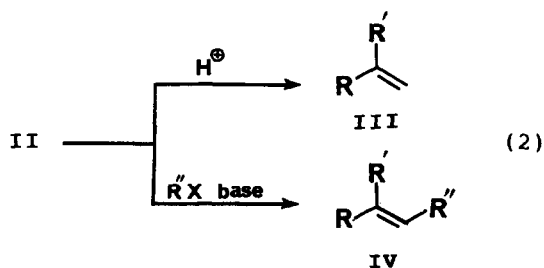
RC≡CH, R=	R'ZnCl, R'=	R''-X	Base(eq.) ^b	Product ^c	Yield, % ^d (I.P.) ^e
Hex	Bu	PhI	A(10)		65(97)
Hex	Bu	H [⊕] _f	—		70
Hex	Bu		B(20)		56(98)
Hex	Bu	Hex-1-ene-I	B(30)		52(99)
	Me ₃ Si-	H [⊕] _f	—		63 ^g
	p-Tol	H [⊕] _f	—		68 ^g
Oct	Me	H [⊕] _f	—		78
Hex	Me ₃ SiCH ₂ ^h	PhI	C(10)		73 ^g (99)
Oct	Me ₃ SiCH ₂ ^h	H [⊕] _f	—		92 ^l
Oct	Me ₃ SiCH ₂ ^h	H [⊕] _i	—		89 ^g
Hex	Me ₃ SiCH ₂ ^h	BuC≡CBr	C(70)		59 ^g (99)
Hex	Ph		B(20)		65 ^g (99)
Bu	Ph	H [⊕] _f	—		71
	Ph	PhCH ₂ Cl	B(20)		60 ^g (99)
	Ph	PhCH ₂ Cl	B(20)		77 ^g (99)
Hex	Me ₃ Si-	PhI	B(10)		73 ^g (100)

Table 1 continued.

Hex		Hex	B(50)		81 ^a (99)
Hex		Bu	B(50)		62 ^a (-) ^j
Hex		PhCH ₂ Br	B(20)		73 ^a (-) ^j
Oct		H [⊕] ^f	—		78 ^a
Hex	BuC≡C ^k	H [⊕] ^f	—		61 ^a
Hex	BuC≡C ^k	Ph I	B(10)		54 ^a (99)

a. Except as otherwise noted, the first cross-coupling was conducted using 3 eq. of the organozinc chloride in THF under reflux for 2 h in the presence of 5 mol% of PdCl₂(PPh₃)₂. b. The second coupling was carried out by refluxing the mixture overnight. Method A: MeOLi in MeOH was used as base. Method B: LiOH in H₂O was used. Method C: MeOLi (powder) was used. c. Compounds reported here were adequately characterized by ¹H NMR, IR, high resolution MS and/or elemental analyses. d. Glpc yied based on 1-octyne used. e. Isomeric purity determined by capillary glpc. f. Protonated with AcOH at room temperature overnight. g. Isolated yield. h. The first coupling was carried out at room temperature for 2 h. i. Protonated with methanolic MeOLi (10 eq.) under reflux overnight. j. Decomposed on glpc. k. Pd(PPh₃)₄ (5 mol%) was used as the catalyst. l. Desilation occurred during the protonolysis.

mixture caused the cross-coupling reaction between II and halides to give trisubstituted alkenes (IV) stereoselectively (eq.2).⁸



All operations can be carried out in one vessel without isolation of intermediates I or II. Because of the generality of the transition metal catalyzed cross-coupling reaction, we can introduce a wide variety of organic groups as R' and R'' in IV, and overcome the limitation of conventional trisubstituted alkene synthesis via carbometallation methods. The versatility of this reaction is shown in Table 1.

The following procedure for the synthesis of (E)-2-butyl-1-phenyl-1-octene is representative: To a stirred solution of boron tribromide (0.25 g,

1.0 mmol) in 3 ml of CH_2Cl_2 was added 1-octyne (0.11 g, 1.0 mmol) at -78°C . The solution was stirred at -78°C for 30 min and at room temperature for another 30 min. After the addition of $\text{PdCl}_2(\text{PPh}_3)_2$ (0.035 g, 0.05 mmol) and a THF solution of butylzinc chloride (3 mmol)⁹, the mixture was heated under reflux for 2 h. Lithium methoxide (5 ml of a 2 M methanolic solution, 10 mmol) and iodobenzene (0.20 g, 1.0 mmol) were added in this order, and then the mixture was heated at 50°C for 14 h with stirring. Glpc analysis showed the formation of (E)-2-butyl-1-phenyl-1-octene in 65 % yield.

The present reaction of trisubstituted alkene synthesis is considered to proceed through two successive cross-coupling reactions catalyzed by the same palladium complex. Unlike other alkenylmetals, the efficient cross-coupling reaction of alkenylboranes with organic halides occurs only when an appropriate base is present.⁸ Such unique reactivity of alkenylboranes toward palladium complex makes the stepwise cross-couplings possible. In the absence of base, the palladium complex catalyzes only the cross-coupling reaction between organozinc compound and I at the bromine position. In the second step, the addition of base and organic halides to the reaction mixture causes the coupling of alkenylborane (II) prepared in the first step, with halides to give trisubstituted alkenes (IV) stereoselectively. Further applications of this reaction are under investigation.

References and Notes

1. For review articles, see: (a) J.F. Normant and A. Alexakis, *Synthesis* **1981**, 841. (b) J.V.N. Prasad and C.N. Pillai, *J. Organometal. Chem.* **1983**, 259, 1.
2. E. Negishi, *Pure and Appl. Chem.* **1981**, 53, 2333.
3. E. Negishi, D.E. Van Horn, T. Yoshida, and C.L. Rand, *Organometallics* **1983**, 2, 563.
4. E. Negishi, *Acc. Chem. Rec.* **1987**, 20, 65 and references cited therein.
5. B.M. Mikhailov, *Organometal. Chem. Rev. A*, **1972**, 8, 1.
6. (a) Y. Satoh, H. Serizawa, S. Hara, and A. Suzuki, *Synthetic Commun.*, **1984**, 14, 313. (b) S. Hara, T. Kato, H. Shimizu, and A. Suzuki, *Tetrahedron Lett.* **1985**, 26, 1065. (c) Y. Satoh, T. Tayano, S. Hara, and A. Suzuki, *Synthesis*, **1985**, 406.
7. M.F. Lappert and B. Prokai, *J. Organometal. Chem.*, **1964**, 1, 384.
8. N. Miyaura, K. Yamada, H. Sugimoto, and A. Suzuki, *J. Am. Chem. Soc.*, **1985**, 107, 972.
9. Butylzinc chloride is prepared simply by the addition of butyllithium to a THF solution of ZnCl_2 .

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