Organoboron compounds in new synthetic reactions
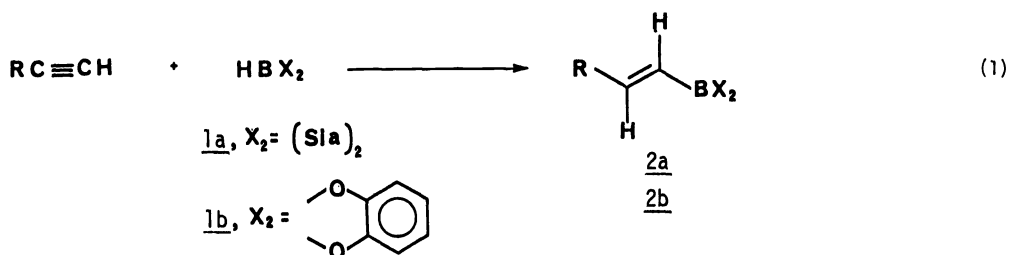
Akira Suzuki

Department of Applied Chemistry, Faculty of Engineering, Hokkaido University,
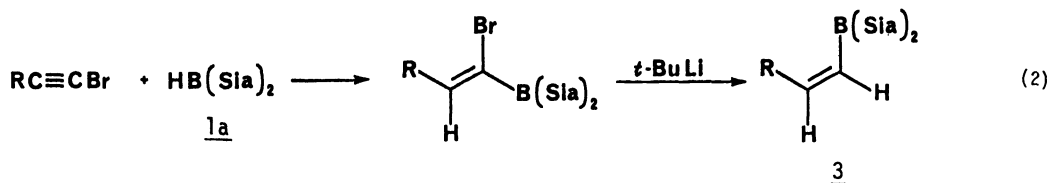Sapporo 060, Japan

Abstract - A general and convenient method for the stereo- and regiospe-
cific synthesis of conjugated alkadienes, alkenynes, arylated alkenes, and
other olefinic compounds is described. The reaction of (E)- or (Z)-1-
alkenyldisiamylboranes, or 2-(E)-1-alkenyl-1,3,2-benzodioxaboroles easily
obtainable by hydroboration, with either (E)- or (Z)-1-alkenyl halides in
the presence of a catalytic amount of tetrakis(triphenylphosphine)palla-
dium and bases such as sodium alkoxides gives the corresponding (E,E)-,
(E,Z)-, (Z,E)-, or (Z,Z)-conjugated alkadienes stereo- and regiospecifi-
cally, while retaining the configurations of both the starting alkenyl-
boranes and haloalkenes. The reaction of (E)- and (Z)-1-alkenyldisiamyl-
boranes with 1-haloalkynes similarly provides a stereo- and regiospecific
synthesis of conjugated (E)- and (Z)-alkenynes. A mechanism of this cross-
coupling reaction, which involves the transmetallation between a 1-alkenyl-
borane and an alkoxopalladium(II) complex generated through the metathet-
ical displacement of a halogen atom from RPd(II)X with sodium alkoxide,
is proposed. The versatility of this method has been demonstrated by the
stereospecific synthesis of natural products bearing conjugated alkadiene
or alkenyne structures, e.g., trans(C_{10})-allofarnesene, bombykol and its
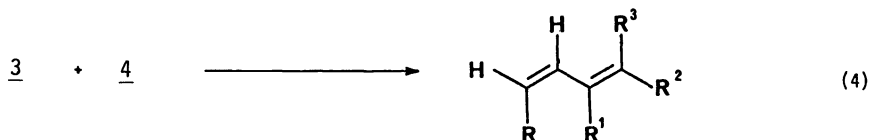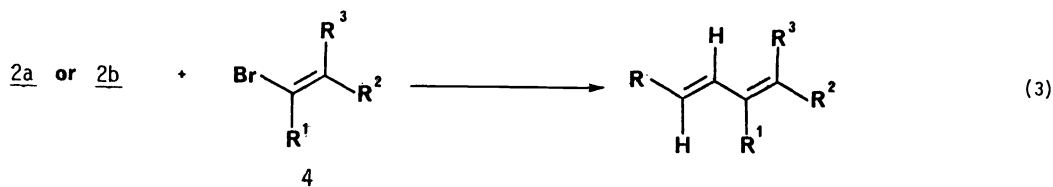three geometrical isomers, humulene, and trisporol B.

I INTRODUCTION

The stereo- and regiospecific syntheses of conjugated alkadienes are of great importance in
organic chemistry in themselves, as well as in their utilization in other reactions such as
the Diels-Alder reaction. A number of new methods for the preparation of conjugated dienes
have been recently developed utilizing organometallic compounds, Mg, Al, B, Si, Cu, Ag, Hg,
and Zr reagents. Although these methods have their own excellence, the scope of many of
these reagents has still been limited by the nature of the organometallic involved or the
procedure employed. For instance, some of the mothods can only be applicable for the synthe-
sis of symmetrical dienes, or because of the highly reducing property of the organometallics,
the method can be used only for the synthesis of unfunctionalized dienes, or, in some cases,
stoichiometric amounts of transition-metal compounds are necessary.

Among these procedures, the most promising ones of preparing conjugated dienes or enynes in
a stereospecific manner are perhaps those based on the direct cross-coupling reaction of
stereodefined alkenylmetallics with stereodefined haloalkenes or haloalkynes with the aid of
a catalytic amount of transition-metal complexes. On the other hand, it is well-known that
stereodefined 1-alkenyldiorganoboranes are readily prepared by the monohydroboration of
alkynes; e.g., diorganoboranes such as disiamylborane (1a) and catecholborane (1b) permit the
monohydroboration of terminal alkynes, thus making readily available the corresponding (E)-
1-alkenyldiorganoboranes (2) with high stereoselectivity, more than 99% (eq. 1) (ref. 1).
Highly pure (Z)-1-alkenyldiorganoboranes (3) (purity, more than 98%) are prepared without
any difficulty via the monohydroboration of 1-halo-1-alkynes with disiamylborane or dicyclo-
hexylborane, followed by treatment with tert-butyllithium (eq. 2) (ref. 2).

$$RC{\equiv}CH \quad + \quad HBX_2 \quad \longrightarrow \quad \text{(product)} \tag{1}$$

1a, X_2= $(Sia)_2$

1b, X_2 =

2a
2b

$$RC{\equiv}CBr \ + \ HB(Sia)_2 \ \longrightarrow \ \underset{H}{\overset{R}{>}}{=}{\overset{Br}{\underset{B(Sia)_2}{<}}} \ \xrightarrow{\textit{t}\text{-BuLi}} \ \underset{H}{\overset{R}{>}}{=}{\overset{B(Sia)_2}{\underset{H}{<}}} \qquad (2)$$

$$\underset{1a}{}$$

$$\underline{3}$$

Consequently, if such 1-alkenyldiorganoboranes react with 1-alkenyl halides stereo- and regioselectively, these reactions provide direct and convenient synthetic procedures for stereodefined conjugated alkadienes (eqs. 3 and 4) or alkenynes. In spite of the efforts by many workers to find such reactions, there were no successful reports when we started this work.

$$\underline{2a} \ \textbf{or} \ \underline{2b} \ + \ \underset{R^1}{\overset{R^3}{Br{\frown}R^2}} \ \longrightarrow \ (3)$$

$$\underline{4}$$

$$\underline{3} \ + \ \underline{4} \ \longrightarrow \ (4)$$

At the initial stage of our exploration, we considered that the reason of difficulty in the coupling seemed to be based on the following feature. The common mechanism of transition-metal-catalyzed cross-coupling reactions (ref. 3) between organometallic compounds and organic halides involves sequential (a) oxidative addition, (b) transmetallation, and (c) reductive elimination. One of the major reasons why 1-alkenylboranes cannot react with 1-alkenyl or 1-alkynyl halides appears to be the step (b), namely the transmetallation process between RMX (M=transition metal; X=halogen) and organoboranes does not occur readily, because of the weak carbanion character of organic groups in the organoboranes. Therefore, if the organoborates formed readily from 1-alkenylboranes and basic species such as alkoxide, acetate, and hydroxide ions are used instead of alkenylboranes themselves, there may be a possibility that the transmetallation takes place more readily.

II SYNTHESIS OF CONJUGATED ALKADIENES AND ALKENYNES (ref. 4)

When we attempted to carry out the coupling reaction of $\underline{6}$ with $\underline{5b}$, prepared by the hydro-boration of 1-hexyne with catecholborane, in the presence of tetrakis(triphenylphosphine)-palladium, it failed to obtain the expected diene ($\underline{7}$) in any noticeable amount and $\underline{6}$ was recovered (Table I), as Negishi and Baba previously reported (ref. 5). However, we found that the addition of bases to the mixture brings dramatically about a rapid and clean coupling reaction. The optimum conditions for the synthesis of ($\underline{E,E}$)-alkadienes were examined by the cross-coupling between $\underline{5a}$ (or $\underline{5b}$) and $\underline{6}$ (eq. 5), the results of which are summarized in Table I. As a typical example of the synthesis, the preparation of $\underline{9}$ is shown in eq. 6.
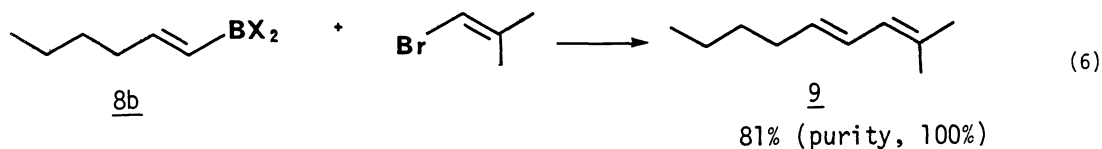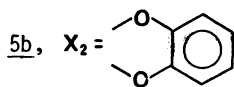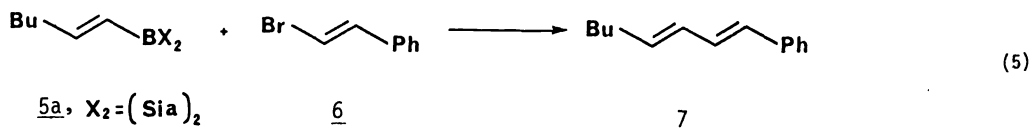
$$Bu{\diagdown}{\diagup}{\diagdown}BX_2 \ + \ Br{\diagdown}{\diagup}{\diagdown}Ph \ \longrightarrow \ Bu{\diagdown}{\diagup}{\diagdown}{\diagup}{\diagdown}Ph \qquad (5)$$

$$\underline{5a}, \ X_2=(Sia)_2 \qquad\qquad \underline{6} \qquad\qquad\qquad \underline{7}$$

$$\underline{5b}, \ X_2 = \underset{O}{\overset{O}{<}}\hexagon$$

$$\diagdown{\diagup}{\diagdown}{\diagup}{\diagdown}BX_2 \ + \ Br{\diagdown}{\diagup}{\diagdown} \ \longrightarrow \ \diagdown{\diagup}{\diagdown}{\diagup}{\diagdown}{\diagup}{\diagdown}{\diagup}{\diagdown} \qquad (6)$$

$$\underline{8b} \qquad\qquad\qquad\qquad\qquad\qquad \underline{9}$$

$$81\% \ (purity, \ 100\%)$$

TABLE 1. Cross-Coupling of <u>5</u> with <u>6</u> (eq. 5)[a]

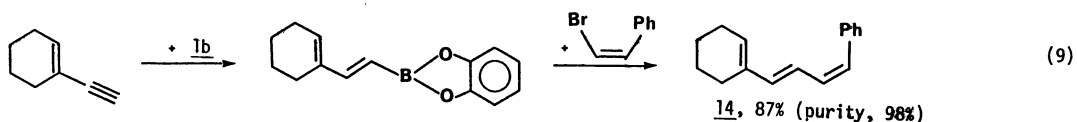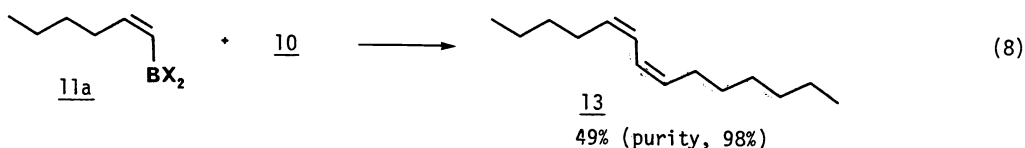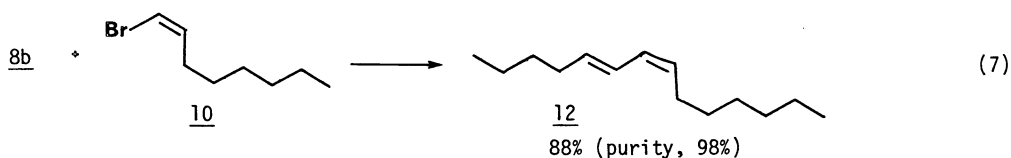| <u>5</u>	Catalyst[b] (mol%)	Base (equivalent)[c]	Solvent	Reaction time, h	Yield (%) of <u>7</u>[d]
<u>5b</u>	PdL$_4$(3)	None	THF	6	0
<u>5b</u>	PdL$_4$(3)	None	benzene	6	0
<u>5a</u>	PdL$_4$(3)	2M NaOMe(2)-MeOH	THF	2	59
<u>5a</u>	PdL$_4$(3)	2M NaOEt(2)-EtOH	THF	2	73
<u>5a</u>	PdL$_4$(3)	2M NaOH (2)-H$_2$O	THF	2	59
<u>5b</u>	PdL$_4$(1)	2M NaOEt(2)-EtOH	THF	2	44
<u>5b</u>	PdL$_4$(3)	2M NaOEt(2)-EtOH	THF	4	78
<u>5b</u>	PdL$_4$(1)	2M NaOMe(2)-MeOH	benzene	2	61
<u>5b</u>	PdL$_4$(1)	2M NaOEt(2)-EtOH	benzene	2	86
<u>5b</u>	PdL$_4$(1)	2M NaOPh(2)-MeOH	benzene	2	73
<u>5b</u>	PdL$_4$(1)	2M NaOH (2)-H$_2$O	benzene	2	86
<u>5b</u>	PdL$_4$(1)	2M KOAc (2)-H$_2$O	benzene	2	27
<u>5b</u>	PdL$_4$(1)	Et$_3$N (5)	benzene	5	4
<u>5b</u>	PdCl$_2$:L$_2$(1)	2M NaOEt(2)-EtOH	benzene	2	86
<u>5b</u>	Pd(OAc)$_2$(1)	2m NaOEt(2)-EtOH	benzene	2	10

[a]All the reactions were conducted at boiling temperature of the solvent using 10% excess of <u>5b</u> or 50% excess of <u>5a</u>.

[b]L is triphenylphosphine and in parenthesis the amount of the catalyst used is shown in mol% per <u>6</u>.
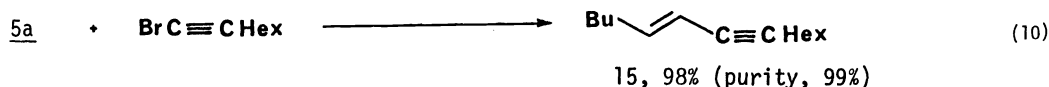
[c]Equivalents per <u>6</u>.

[d]Determined by GLC, based on <u>6</u> by using an internal standard.

Next, we examined the reactions of B-(<u>E</u>)-1-hexenyl-1,3,2-benzodioxaborole (<u>8b</u>) and (<u>Z</u>)-1-hexenyldisiamylborane (<u>11a</u>) with (<u>Z</u>)-1-octenyl bromide (<u>10</u>) as coupling partners in order to check the utility of the coupling for the synthesis of (<u>E,Z</u>)- and (<u>Z,Z</u>)-dienes. Thus, when such reactions were carried out in benzene containing 2 equivalents of NaOEt in EtOH at 80 °C for 2 h, using 3 mol% of Pd(PPh$_3$)$_4$, the expected products (<u>12</u> and <u>13</u>) were produced in 88% and 49% yield, respectively. The isomeric purity of the both products is more than 98% (eqs. 7 and 8). These results clearly indicate that this Pd-catalyzed alkenyl-alkenyl cross-coupling reaction proceeds smoothly under the reaction conditions analogous to the synthesis of (<u>E,E</u>)-dienes, while retaining the original configuration of both the starting alkenyl-boranes and the haloalkenes. The usefulness of the method is illustrated by the stereospecific synthesis of <u>14</u> from 1-cyclohexenylethyne (eq. 9).

<u>8b</u>   +   [structure]   <u>10</u>   →   [structure]   <u>12</u>   88% (purity, 98%)   (7)

[structure] <u>11a</u> BX$_2$ +   <u>10</u>   →   [structure]   <u>13</u>   49% (purity, 98%)   (8)

[structure]   + <u>1b</u> →   [structure]   + [structure]   →   [structure]   <u>14</u>, 87% (purity, 98%)   (9)

The reaction with (E)-1-alkenyl-1,3,2-benzodioxaboroles always gives the dienes in ca. 90% yields, while the coupling with (Z)-1-alkenyldisiamylboranes gives less than 50% yields of the corresponding dienes.

The ready coupling of alkenylboranes with haloalkenes encouraged us to examine the extention of this method for the cross-coupling of alkenylboranes with haloalkynes. It was found that unlike the alkenyl-alkenyl coupling, 1-alkenyl-1,3,2-benzodioxaboroles were quite inert to haloalkynes, and all the attempts to obtain the cross-coupling enynes were unsuccessful. We found, however, that 1-alkenyldisiamylboranes react with haloalkynes to give such cross-coupling enynes. Thus the reaction of (E)-1-hexenyldisiamylborane (5a) with 1-bromooctyne gives 15 in 98% yield with an isomeric purity of 99% (eq. 10).

$$\underline{5a} \quad + \quad BrC\equiv CHex \quad \longrightarrow \quad Bu\diagdown\diagup{}_{C\equiv CHex} \qquad (10)$$

$$\underline{15},\ 98\%\ (\text{purity},\ 99\%)$$

The principal features of this reaction, which are important for delineating the mechanism, are as follows. (a) Only catalytic amounts of palladium complexes (1-3 mol%) are required. (b) The coupling reactions are highly regio- and stereospecific and take place while retaining the original configurations of both the starting alkenylboranes and the haloalkenes. The isomeric purity of the products generally exceeds 97%. (c) A base is required to carry out a successful coupling. On the role of bases, we considered at the initial stage of the investigation to increase the carbanion character of the alkenyl groups in organoboranes by their coordination with the boron atoms, thereby facilitating the transfer of alkenyl groups
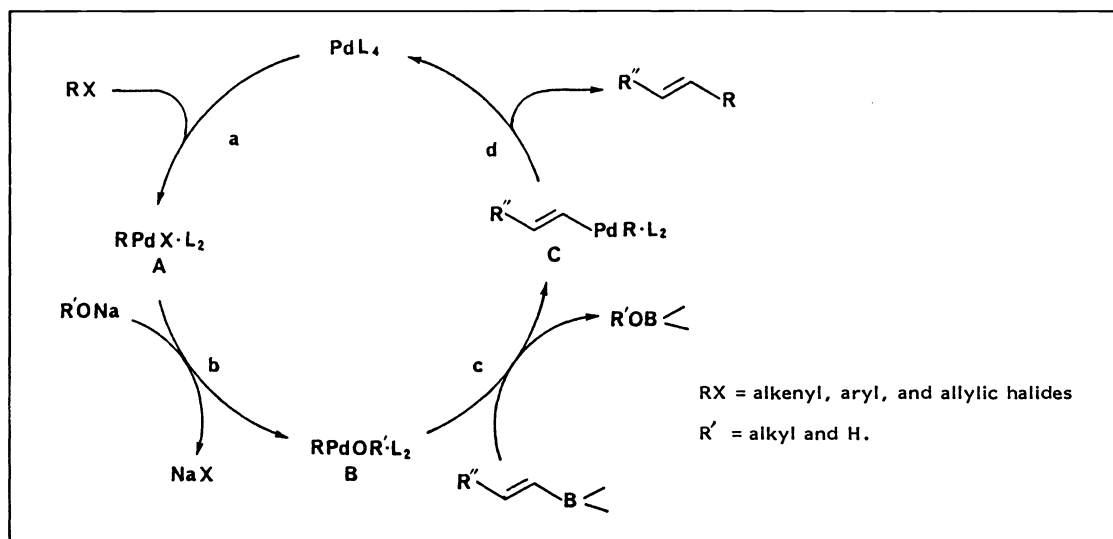
$$Bu\diagdown\diagup\overset{Me}{\underset{\ominus}{\underset{|}{B}}}(Sia)_2 \quad + \quad \underline{6} \quad \xrightarrow{PdL_4} \quad Bu\diagdown\diagup\diagdown\diagup_{Ph} \qquad (11)$$

$$\underline{16} \qquad\qquad\qquad\qquad\qquad\qquad\qquad \underline{7}$$

$$R\,PdX\cdot L_n \ + \ NaOMe \ \xrightarrow{\ -X^-\ } \ R\,Pd\,OMe\cdot L_n \ \xrightarrow{\ -CH_2O\ } \ R\,Pd\,H\cdot L_n \ \longrightarrow \ R\,H \ + \ Pd\,L_4 \qquad (12)$$

$$\underset{\underline{17}}{Hex\diagdown\diagup_{BX_2}} \ + \ \underset{\underline{18}}{Cl\diagup\overset{Cl}{\underset{Cl}{\diagdown}}Pd\,Y\cdot(PPh_3)_2} \ \longrightarrow \ Hex\diagdown\diagup\diagdown\overset{Cl}{\underset{Cl}{\diagup}}Cl \qquad (13)$$
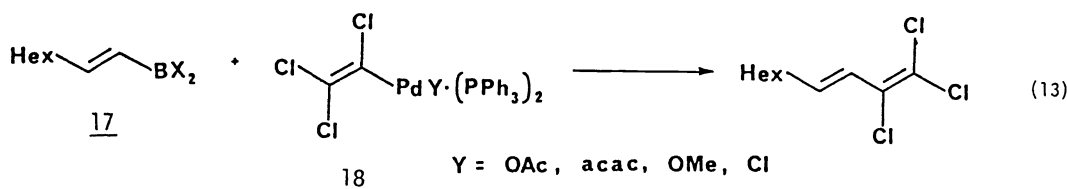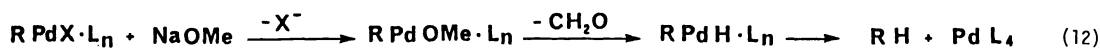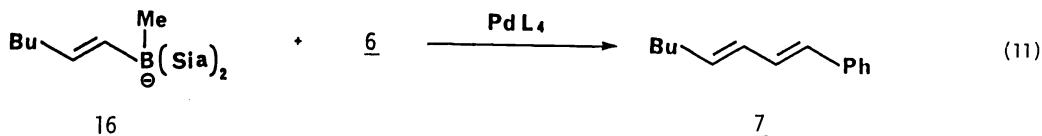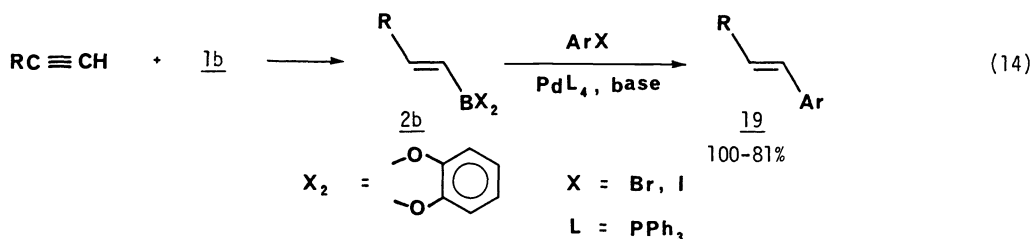
$$Y = OAc,\ acac,\ OMe,\ Cl$$

Figure 1   Catalytic cycle for the coupling reaction of haloalkenes and haloalkynes with alkenylboranes.

from the boron to the palladium in the transmetallation step. In order to check this possibility, lithium (1-hexenyl)methyldisiamylborate (16) was examined to react with 6 in the presence of tetrakis(triphenylphosphine)palladium (eq. 11). The yield of the coupling product (7), however, was found to be only 9%. This evidence indicates that the base does not function in such a way in the coupling. (d) In some cases, small amounts of the reduction products (5%) arising from the starting haloalkenes were detected. The formation of such products may be attributable to the alkoxopalladium(II) intermediate formed by metathetical displacement, as depicted in eq. 12 (ref. 6). (e) In order to confirm the possibility if alkoxopalladium(II) complexes are real intermediates, the reaction of 17 with 18 possessing different types of ligands was tested (eq. 13), and we found that the reaction takes place at room temperature when the complexes bearing Pd-O bands are used, whereas the reaction does not proceed smoothly with the Pd-Cl complexes. The mechanism of this cross-coupling reaction, which accommodates all the above features of the reaction, is outlined in Figure 1.
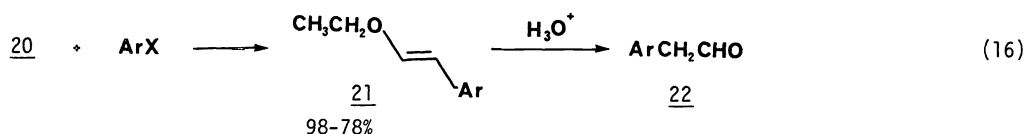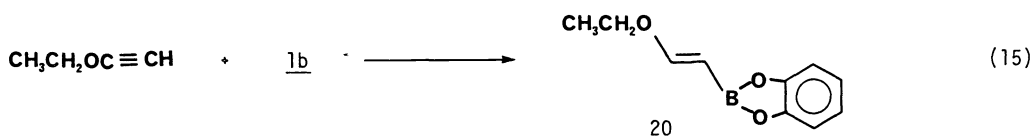
III SYNTHESIS OF ARYLATED ALKENES (ref. 7)

The good results in the cross-coupling reaction described above led us to explore the reaction with aryl halides, which also have sp^2 C-halogen bonds. B-1-Alkenyl-1,3,2-benzodioxaboroles (2b) readily react with aryl halides under the similar conditions mentioned above to afford the corresponding arylated alkenes (19) in excellent yields (eq. 14). In the absence of base we failed to obtain the products in any noticeable amounts. In general, aqueous sodium hydroxide and sodium ethoxide in ethanol are satisfactory bases. Lewis bases,

$$RC \equiv CH \quad + \quad \underline{1b} \quad \longrightarrow \quad \begin{matrix} R \\ \diagdown \\ \diagup \\ BX_2 \end{matrix} \quad \xrightarrow[\text{PdL}_4,\ \text{base}]{ArX} \quad \begin{matrix} R \\ \diagdown \\ \diagup \\ Ar \end{matrix} \quad (14)$$

$$\underline{2b} \qquad\qquad \underline{19}$$
$$100\text{-}81\%$$

$$X_2 \ = \ \begin{matrix} -O \\ -O \end{matrix} \bigcirc \qquad X \ = \ Br,\ I$$

$$L \ = \ PPh_3$$

such as triethylamine, did not accelerate the reaction. The reaction proceeds with retention of configuration with respect to alkenylboranes. No difficulty was encountered with derivatives of benzene having functional groups such as OMe, ester, and halogen. However, aryl chlorides are inert for the coupling. Consequently, the reaction of B-(E)-1-hexenylborane with p-chlorobromobenzene produces only p-chloro(1-hexenyl)benzene in quantitative yield. Not only p-substituted benzenes but also o-substituted derivatives give good results. For instance, the coupling between B-(E)-1-hexenyl-1,3,2-benzodioxaborole and o-methoxybromobenzene gives the product in 81% yield.

Most recently, it has been revealed that the cross-coupling reaction with aryl halides provides a convenient synthetic procedure for benzo[b]heterocycles (ref. 8). Previously, we reported that vinylic ethers (21) can be synthesized in high yields by the coupling of aryl halides with (2-ethoxyethenyl)-1,3,2-benzodioxaborole (20) in the presence of 1 mol% of a palladium complex such as $PdCl_2(PPh_3)_2$, $Pd(OAc)_2(PPh_3)_2$, or $Pd(PPh_3)_4$ and a base. The intermediates (21) thus obtained can readily be hydrolyzed to give aldehydes (22) (eqs. 15 and 16) (ref. 9). By applying this reaction to o-heteroatom-substituted aryl halides, followed by

$$CH_3CH_2OC \equiv CH \quad + \quad \underline{1b} \quad \longrightarrow \quad \begin{matrix} CH_3CH_2O \\ \diagdown \\ \diagup \\ B \begin{smallmatrix} O \\ O \end{smallmatrix} \bigcirc \end{matrix} \qquad (15)$$

$$\underline{20}$$

$$\underline{20} \quad + \quad ArX \quad \longrightarrow \quad \begin{matrix} CH_3CH_2O \\ \diagdown \\ \diagup \\ Ar \end{matrix} \quad \xrightarrow{H_3O^+} \quad ArCH_2CHO \qquad (16)$$

$$\underline{21} \qquad\qquad\qquad \underline{22}$$
$$98\text{-}78\%$$

treatment with acid, the corresponding benzoheterocyclic compounds are prepared in excellent yields, two examples of which are depicted in eqs. 17 and 18 (ref. 8).

$$R = Me \ (91\%) \qquad\qquad R = Me \ (99\%)$$
$$R = Hex \ (88\%) \qquad\qquad R = Hex \ (99\%)$$

(17)

(18)
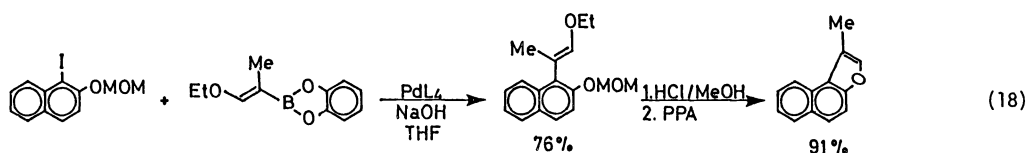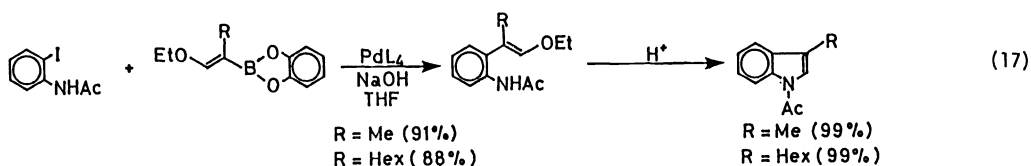
The same type of reaction between arylboronic acids and haloarenes occurs without any diffi-culty to provide a straightforward synthesis of biaryls (eq. 19) (ref. 10).

(19)

99-66%
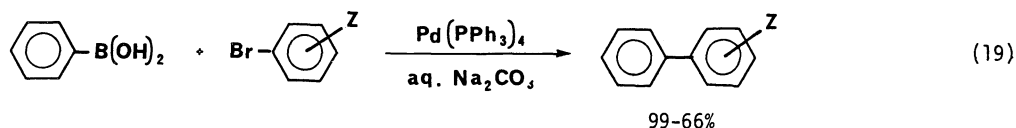
IV SYNTHESIS OF 1,4-ALKADIENES AND ALLYLIC BENZENES (ref. 11)

It was confirmed that the cross-coupling reaction takes place cleanly with organic halides with sp^2 carbon- or sp carbon-halogen bonds, namely with vinylic or acetylenic halides. Next, we examined the reaction with alkyl halides, and found that although simple alkyl halides cannot react with 1-alkenylboranes, allylic or banzylic bromides react readily to yield the corresponding coupling products (eq. 20). In the reaction with 1-bromo-2-butene,

(20)
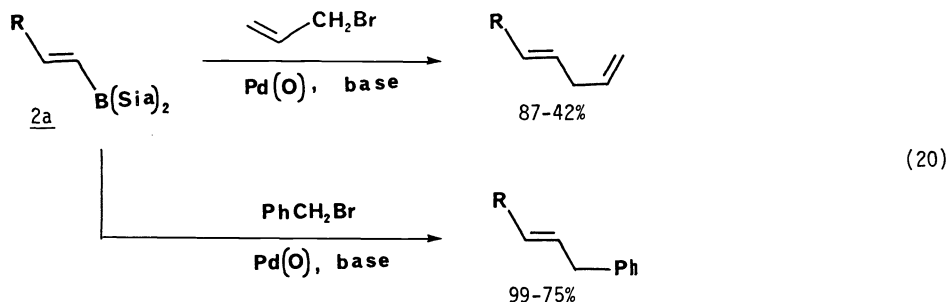
the carbon-carbon bond formation occurred at two positions, the ratio of straight to branched chain dienes was 72:28, in accordance with the mechanism involving π-allylpalladium inter-mediates (ref. 6b).

V MISCELLANEOUS REACTIONS

In this section, other synthetic methods related to the palladium-catalyzed cross-coupling reaction of 1-alkenylboranes will be described.

Palladium-catalyzed "head-to-tail" cross-coupling

A different type of reaction, "head-to-tail" cross-coupling, occurs between (E)-1-alkenyl-1,3,2-benzodioxaboroles (2b) and aryl or 1-alkenyl iodides in the presence of palladium black (3 mol%) readily prepared by reduction of $Pd(OAc)_2$ with diborane, and triethylamine to give the "head-to-tail" products (23) together with small amounts of the usual "head-to-head" products (eq. 21) (ref. 12).

(21)

94-61%

X = I;   R^1 = Ar or 1-alkenyl
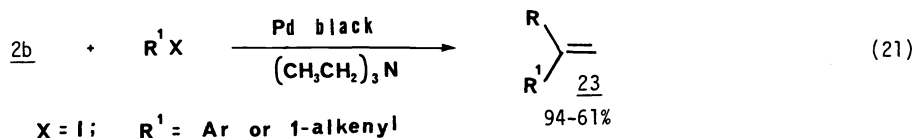
This coupling is considered to proceed through a different pathway involving (i) addition of an organopalladium iodide to the C=C bond of 1-alkenylborane, (ii) isomerization of the intermediate, and (iii) the elimination of $IPdBX_2$ (ref. 3a, 6b, and 13). The reaction is effectively applied for the synthesis of methylenecycloalkenes, one example of which is shown in eq. 22 (ref. 14).


(22)

71%
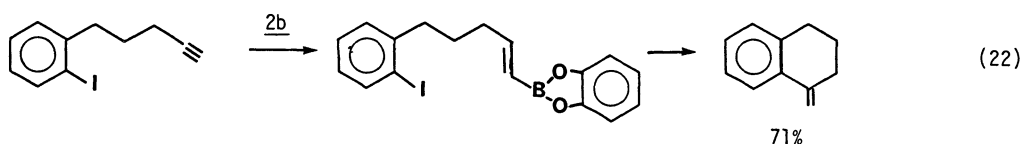
Synthesis of α,β-unsaturated carboxylic esters via the Pd-catalyzed carbonylation of l-alkenylboranes

α,β-Unsaturated carboxylic ester synthesis from alkynes, carbon monoxide and alcohols with the aid of transition-metal catalysts is important in industrial or laboratory application. The alkynes are mainly hydrocarboxylated in accordance with Markownikoff rule in such a reaction (ref. 6b and 15). 1-Alkenylboranes, especially 1-alkenyl-1,3,2-benzodioxaboroles have been found to react with carbon monoxide in the presence of palladium chloride (1-3 mol%) as well as sodium acetate in methanol to give the corresponding α,β-unsaturated esters with retention of configuration with respect to the alkenylboranes in good yields (eq. 23) (ref. 16).

(23)

95-70%
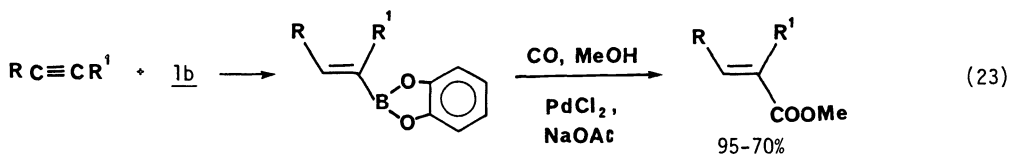
Cross-coupling of l-alkenylboranes with β-halocycloenones

The cross-coupling reactions of 1-alkenylboranes with various organic halides mentioned in the Sections II, III, and IV, provides useful, and in some cases, superior alternatives to those employing previously established methods. However, as these reactions need relatively strong bases such as sodium alkoxides and hydroxide, these cannot be applicable to organic halides like β-halocycloenones highly susceptible to strong bases. Fortunately, as a result of the exploration, it has been recently ascertained that unlike the previous Pd-catalyzed coupling reactions, relatively weak bases such as sodium acetate in methanol are effective to achieve high yield and stereoselectivity (eq. 24) (ref. 17). Under these conditions,

(24)

X = Br, Cl

24

100-77% (purity, 99%)
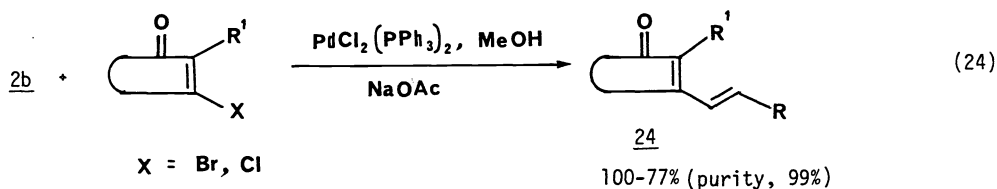
cyclohaloenones are stable and inert to nucleophilic displacement of halogen atoms with bases. Moreover, we have not observed the formation of any dimers derived from dienones (24), which may be unavoidable by-products in the Claisen-Schmidt condensation method. Although all the Pd complexes examined were effective, both $Pd(OAc)_2$ and $PdCl_2(PPh_3)_2$ are recommended. As one of the characteristics of the reaction, it should be pointed out that β-chlorocycloenones as well as bromo derivatives are effectively employed.

Synthesis of ethyl 2,4-alkadienoates from ethyl β-bromoacrylates

In connection with alkali-sensitive organic halides, we attempted the reaction of β-bromoacrylate and its derivatives. In 1975, Heck and Dieck (ref. 18) reported that 1-hexenyl-boronic acid reacts readily with methyl acrylate under the influence of $Pd(OAc)_2$ to give methyl 2,4-nonadienoate in a good yield. However, this synthesis has a disadvantage, because it requires a stoichiometric amount of palladium. On the other hand, irrespective of many efforts to find a procedure to obtain conjugated alkadienoates through the cross-coupling of 1-alkenylboranes with β-acrylate, no successful reports have been appeared (ref. 19). It has recently become apparent that such a coupling of (E)-β-bromoacrylate (25) with B-(E)-1-alkenyl-1,3,2-benzodioxaboroles (2b) occurs smoothly to produce the expected products (26) in good yields, when the reaction is carried out in the presence of $Pd(OAc)_2(PPh_3)_2$ (3 mol%) and Na_2CO_3 in aqueous ethanol at the reflux temperature (eq. 25) (ref. 20). In the case of (Z)-

β-bromoacrylate (<u>28</u>), the above conditions give a mixture of <u>29</u> and <u>30</u>, whereas the reaction using Pd(OAc)$_2$(dppf) [dppf: 1,1'-bis(diphenylphosphino)ferrocene] and Na$_2$CO$_3$ at room temperature provides a satisfactory result, as shown in eq. 26.


$$\text{(25)}$$

89-66% (purity, 97%)

$$\text{(26)}$$

73% (purity, 95%)
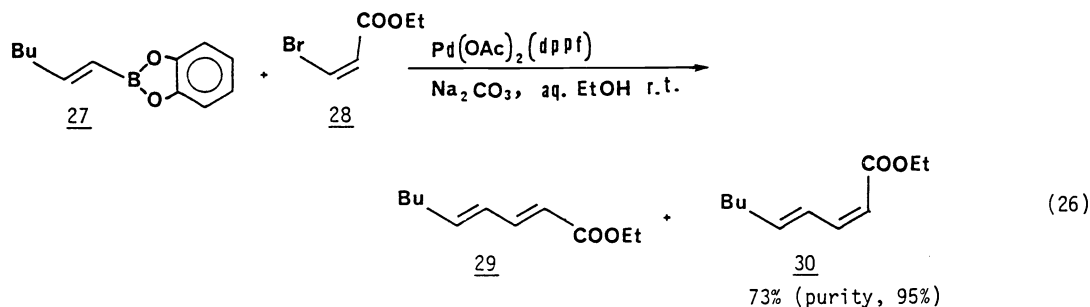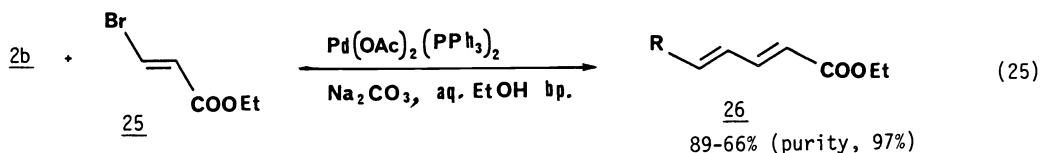
VI SYNTHETIC APPLICATIONS

In order to substantiate the versatility of the present stereodefined synthesis of conjugated alkadienes and alkenynes, we tried the syntheses of natural products with such structures, including bombykol and its three geometrical isomers (ref. 21), <u>trans</u>(C$_{10}$)-allofarnesene (ref. 22), humulene (ref. 23), and the benzyl ether of trisporol B (ref. 24). The synthetic procedures of bombykol itself, <u>trans</u>(C$_{10}$)-allofarnesene, and trisporol B are described here.

Synthesis of bombykol

Bombykol is a well-known pheromone, which was first isolated and synthesized by Butenandt <u>et al.</u> Since then, the synthesis has been, even recently, reported (ref. 25). We attempted to synthesize bombykol by the cross-coupling of the boronic acid (<u>31</u>) with (<u>Z</u>)-1-pentenyl bromide (<u>32</u>) readily obtainable by the Brown's hydroboration-bromination method. As depicted in Scheme 1, the reaction provides bombykol in 82% yield stereo- and regiospecifically. Other three geometrical isomers are also obtained readily by the same procedure (ref. 21).

Scheme 1
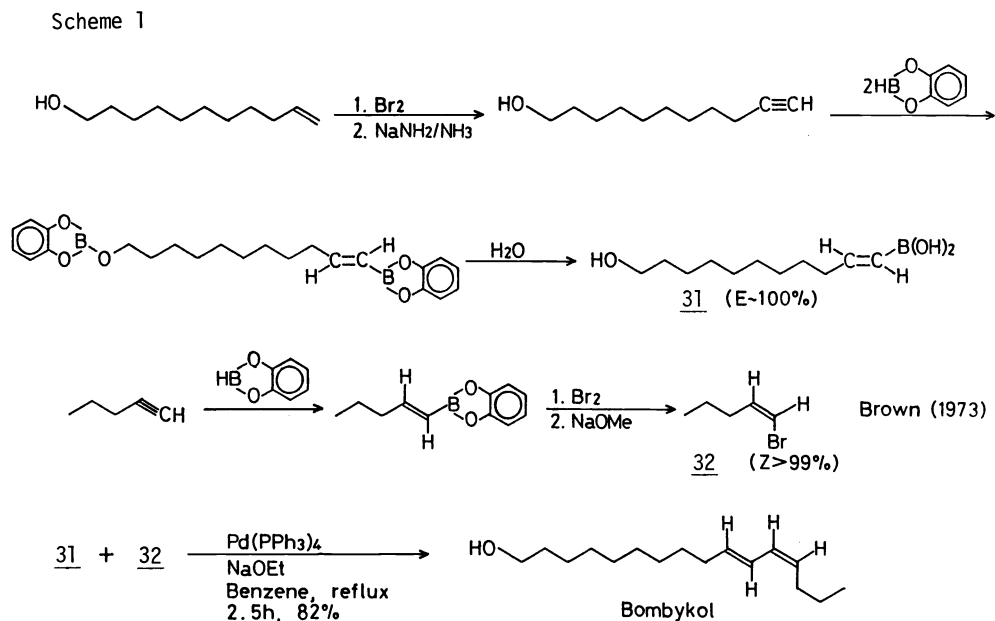
Synthesis of trans(C₁₀)-allofarnesene

An acyclic sesquiterpene, <u>trans</u>(C_{10})-allofarnesene (<u>34</u>), isolated from <u>Perilla frutscens</u> Makino, which has four double bonds in the molecule, was also synthesized by using geraniol as the starting material (Scheme 2) (ref. 22). In this case, the isomeric purity of <u>34</u> (ca. 94%) was not high, compared with other examples. This was thereafter proved to be not an essential disadvantage of the Cross-coupling reaction, because <u>33</u> was found to isomerize readily to the corresponding (<u>E</u>)-isomer.

Scheme 2
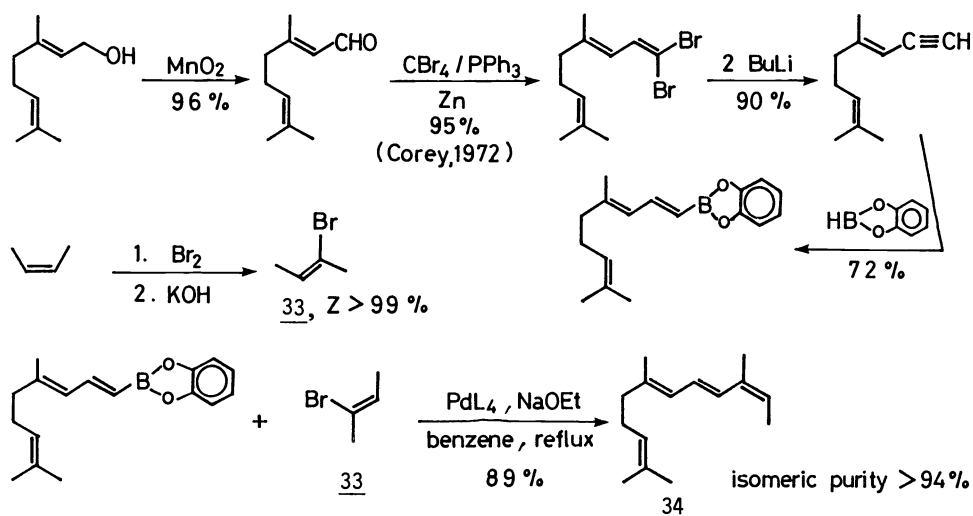
Synthesis of the benzyl ether of trisporol B

Trisporol B (<u>37</u>, Bzl=H), a prohormone of <u>Blakeslea trispora</u>, was first synthesized by White <u>et al</u>. (ref. 26), and Trost and Ornstein (ref. 27) reported recently the synthesis of methyl trisporate B. Most recently, we have succeeded in obtaining the benzyl ether of Trisporol B by the cross-coupling reaction (ref. 24). The (<u>Z</u>)-δ-iodo-γ,δ-unsaturated ketone acetal (<u>36</u>), a necessary fragment of the coupling, is synthesized by the haloboration of propyne, followed by treatment with methyl vinyl ketone, which has been recently revealed (Scheme 3) (ref. 28). The cross-coupling reaction in the presence of tetrakis(triphenylphosphine)palladium and sodium ethoxide gives <u>37</u>, as outlined in Scheme 3 (ref. 24). The present procedure is stereo- and regiospecific, thus providing a better overall yield, compared to those obtained by the previous methods.

Scheme 3
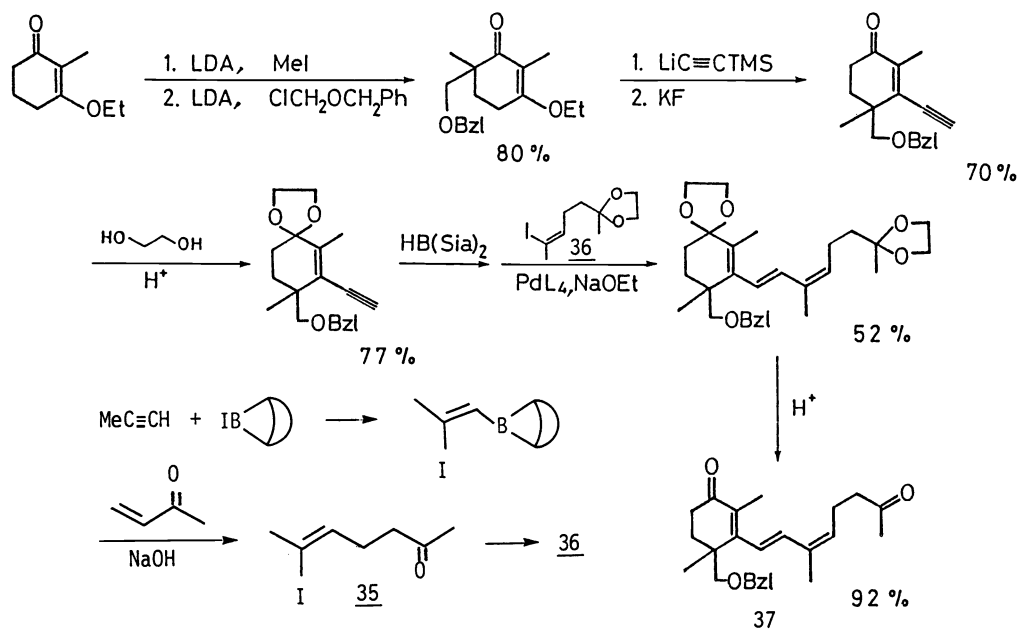
In closing, it should be pointed out that in connection with the development of the cross-coupling reaction mentioned above, the significance of stereoselective synthesis of a variety of vinylic halides has increased. As one of such methodologies, the haloboration reaction of alkynes has become recently apparent to be very useful (refs. 28 and 29). Such results will be reported and discussed elsewhere.

ACKNOWLEDGEMENT

REFERENCES

1. H. C. Brown, Organic Synthesis via Boranes, p. 38 and p. 44, Wiley, New York (1975).
2. J. B. Campbell, Jr., G. A. Molander, J. Organometal. Chem. 156, 71-79 (1978).
3. (a) J. K. Kochi, Organometallic Mechanisms and Catalysis, Academic, New York (1978).
   (b) J. P. Collman, L. S. Hegedus, Principles and Applications of Organotransition Metal Chemistry, University Science Books, Mill Valley, Calif. (1980).
4. (a) N. Miyaura, K. Yamada, A. Suzuki, Tetrahedron Lett. 20, 3437-3440 (1979).
   (b) Idem, Ibid. 22, 127-130 (1981).
   (c) Idem, J. Am. Chem. Soc. 107, 972-980 (1985).
5. S. Baba, E. Negishi, J. Am. Chem. Soc. 98, 6729-6731 (1976).
6. (a) A. Zask, P. Helquist, J. Org. Chem. 43, 1619-1620 (1978).
   (b) P. T. Maitlis, The Organic Chemistry of Palladium, Vols. 1 and 2, Academic, New York (1971).
7. N. Miyaura, A. Suzuki, J. Chem. Soc. Chem. Commun. 866-867 (1979).
8. Unpublished work.
9. N. Miyaura, K. Maeda, H. Suginome, A. Suzuki, J. Org. Chem. 47, 2117-2122 (1982).
10. N. Miyaura, T. Yanagi, A. Suzuki, Synth. Commun. 11, 513-519 (1981).
11. N. Miyaura, T. Yano, A. Suzuki, Tetrahedron Lett. 21, 2865-2868 (1980).
12. N. Miyaura, A. Suzuki, J. Organometal. Chem. 213, C53-C56 (1981).
13. R. F. Heck, Acc. Chem. Res. 12, 146-151 (1979).
14. Unpublished work.
15. I. Wender, P. Pino, Organic Synthesis via Metal Carbonyls, Vol. 2, Wiley, New York (1977).
16. N. Miyaura, A. Suzuki, Chem. Lett. 879-882 (1981).
17. Unpublished work.
18. H. A. Dieck, R. F. Heck, J. Org. Chem. 40, 1083-1090 (1975).
19. (a) H. P. Dang, G. Linstrumelle, Tetrahedron Lett. 19, 191-194 (1978).
    (b) R. C. Larock, M. A. Mitchell, J. Am. Chem. Soc. 100, 180-188 (1978).
20. Unpublished work.
21. (a) N. Miyaura, H. Suginome, A. Suzuki, Tetrahedron Lett. 24, 1527-1530 (1983).
    (b) Idem, Tetrahedron 39, 3271-3277 (1983).
22. N. Miyaura, H. Suginome, A. Suzuki, Bull. Chem. Soc. Jpn. 55, 2221-2223 (1982).
23. N. Miyaura, A. Suzuki, Tetrahedron Lett. 25, 761-764 (1984).
24. Unpublished work.
25. H. J. Bestman, O. Vostrowsky, H. Paulus, W. Billman, W. Stransky, Tetrahedron Lett. 121-124 (1977), and references cited therein.
26. M. P. Prisbylla, K. Takabe, J. D. White, J. Am. Chem. Soc. 101, 762-763 (1979).
27. B. M. Trost, P. L. Ornstein, Tetrahedron Lett. 24, 2833-2836 (1983).
28. Y. Satoh, H. Serizawa, S. Hara, A. Suzuki, J. Am. Chem. Soc. in press.
29. (a) S. Hara, H. Dojo, S. Takinami, A. Suzuki, Tetrahedron Lett. 24, 731-734 (1983).
    (b) S. Hara, Y. Satoh, H. Ishiguro, A. Suzuki, Ibid, 24, 735-738 (1983).
    (c) S. Hara, T. Kato, A. Suzuki, Synthesis 1005-1006 (1983).
    (d) S. Hara, S. Takinami, S. Hyuga, A. Suzuki, Chem. Lett. 345-348 (1984).
    (e) Y. Satoh, H. Serizawa, S. Hara, A. Suzuki, Synth. Commun. 14, 313-319 (1984).
    (f) Y. Satoh, T. Tayano, H. Koshino, S. Hara, A. Suzuki, Synthesis in press.
    (g) S. Hara, T. Kato, H. Shimizu, A. Suzuki, Tetrahedron Lett. 26, 1065-1068 (1985).