

# Organoborates in New Synthetic Reactions

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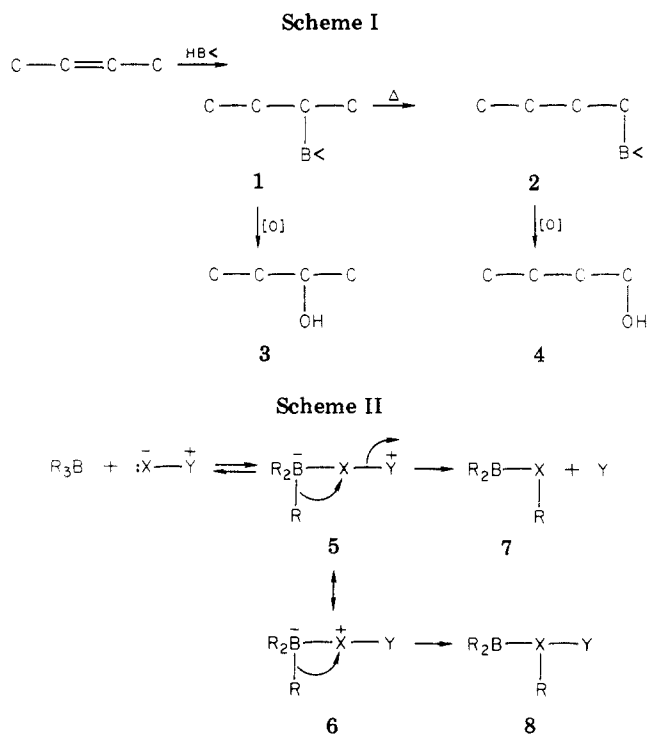
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The facile addition of the boron-hydrogen bond to carbon-carbon multiple bonds of unsaturated organic derivatives yields organoboranes. This hydroboration reaction has various characteristic properties. The reaction is very rapid, usually being complete within a few minutes at temperatures below 25 °C. In general, hydroboration proceeds via a cis addition of the boron-hydrogen moiety to the carbon-carbon multiple bond from the less hindered side, to place the boron atom predominantly at the less substituted carbon atom.<sup>1</sup>

Organoboranes thus obtained have been recognized as synthetically interesting intermediates in organic synthesis. For example, as shown in Scheme I, the organoboranes **1** prepared from 2-butene at room temperature, give the corresponding alcohol **3** upon subsequent alkaline hydrogen peroxide oxidation. The organoborane **1** is, on the other hand, readily isomerized by heating at 150 °C to **2**, which is oxidized under the same conditions to the alcohol **4**. Consequently, two different alcohols can be selectively produced in good yields from an alkene. In spite of having such merit for synthetic applications, organoboranes are chemically inert when compared with other organometallic compounds. For instance, trialkylboranes are remarkably stable toward water, alcohols, and phenols. They do not undergo Grignard-type reactions with carbonyl compounds and are not effective as catalysts in the chain-growth reaction of olefins.

Let us consider the reasons why organoboranes have such characteristic properties. This may be illustrated by considering the following three points: There is a small difference in electronegativity between boron and carbon, and this is regarded as a major reason for the inertness of the organoboranes toward ionic reactions. The second point is the presence of a vacant p orbital on boron, thus making the organoboranes accessible for nucleophile attack to form the tetracoordinated borate complexes **5**, as shown in Scheme II. If the R group on boron in **5** can migrate to X with the concurrent elimination of Y, product **7** is formed. If the contribution of structure **6** is considerable, there is another possibility that a migration of R to X occurs without elimination of Y to give the product **8**. The third point is that the C-B bond length is almost the same length as that of a C-C bond. For example, in trimethylboroxine and trimethylborane, the C-B bond lengths were reported to be 1.57 and 1.56 Å, respectively. Consequently, we must take note of such a steric requirement of organoboranes in their reactions.

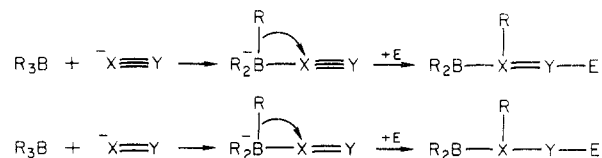
For the past 16 years, we have been investigating organic synthesis using organoboranes and have found



that organoboranes are versatile intermediates. The alkyl groups are used as carbanions, alkyl radicals, and carbocation sources for synthetic reactions of a wide variety of organic compounds. In this Account, synthetic applications (carried out by our research group), of tetracoordinated organoborates, easily obtained from organoboranes, are reviewed.

## Synthesis via Alkynylborates

As shown in Scheme II, the organoborates formed by the reaction of organoboranes with basic or nucleophilic species are able to make new R-X bonds by 1,2-migration reactions. The following modified patterns of reaction are also expected:



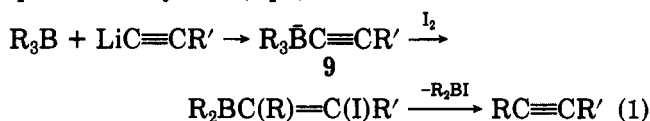
The first example of syntheses using 1-alkynyltriorganoborates that we explored was the reaction with iodine. This reaction provides a general synthetic procedure for internal alkynes.<sup>2</sup> When 1-alkynyltriorganoborates, readily prepared from lithium acetylides and trialkylboranes, are treated with iodine, the cor-

(1) (a) Brown, H. C. "Hydroboration"; Benjamin: Reading, MA, 1980. (b) Brown, H. C. "Organic Syntheses via Boranes"; Wiley: New York, 1975. (c) Cragg, G. M. L. "Organoboranes in Organic Synthesis"; Marcel Dekker: New York, 1973.

(2) Suzuki, A.; Miyaura, N.; Abiko, S.; Itoh, M.; Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* 1973, 95, 3080.

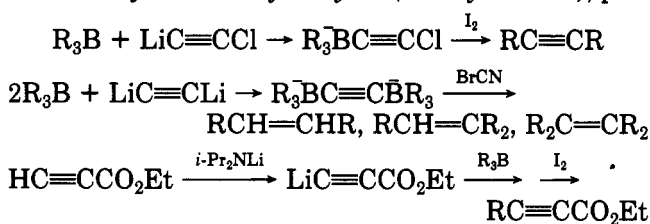
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responding internal alkynes are obtained in almost quantitative yields (eq 1). The reaction is considered



to proceed through  $\beta$  attack and migration followed by elimination. Probably, the most general method previously available for the synthesis of internal alkynes involves the reaction of alkali metal acetylides with organic halides or sulfates. However, such a synthesis is only satisfactory for primary alkyl halides or sulfates, which readily undergo nucleophilic substitution reactions. In the case of secondary alkyl halides or sulfates, elimination reactions also take place competitively. On the other hand, our procedure easily permits the introduction not only of both primary and secondary alkyl groups but also of aryl groups in excellent yields. One may wonder if the reaction is applicable for the preparation of terminal alkynes from monolithium acetylide and trialkylboranes. This is rather difficult, as ethynyltrialkylborates thus formed are subject to disproportionation, leading to a mixture of the diboron derivatives and acetylene. However, Midland and Brown<sup>3</sup> overcame this difficulty by using monolithium acetylide-ethylenediamine instead of monolithium acetylide itself.

It has been observed that the 1-alkynyltriorganoborate-iodine reaction is also useful for the synthesis of conjugated alkadiynes<sup>4</sup> and alkenynes.<sup>5</sup> Negishi and his co-workers synthesized the pheromone bombykol by this procedure.<sup>5</sup> Moreover, the reaction of iodine with ate complexes, obtained from trialkylboranes and lithium 2-chloroethyne, gives the corresponding symmetric alkynes.<sup>6</sup> Ethynediylbis(trialkylborates), pre-



pared from dilithium acetylide and 2 mol of trialkylboranes, have been found to be interesting intermediates in the reaction with cyanogen bromide. By controlling the amounts of cyanogen bromide, di-, tri-, and tetraalkylethenes are produced, respectively, in good yields with relatively high distribution ratios of the expected products.<sup>7</sup> In the case where ethyl propynoate or ethynyl aryl ketones are used as substrates, a modified procedure is required, because an addition of butyllithium to the carbon-oxygen double bonds occurs competitively in the lithium acetylide forming step. Thus, by using lithium diisopropylamide as a base, the expected ethyl 2-alkynoates or 1-alkynyl aryl ketones are prepared in good yields.<sup>8</sup> In addition, 1-alkynyltrialkylborates afford the corresponding alkenes upon

(3) Midland, M. M.; Brown, H. C. *J. Org. Chem.* 1974, 39, 731.

(4) Pelter, A.; Smith, K.; Tabata, M. *J. Chem. Soc., Chem. Commun.* 1975, 857.

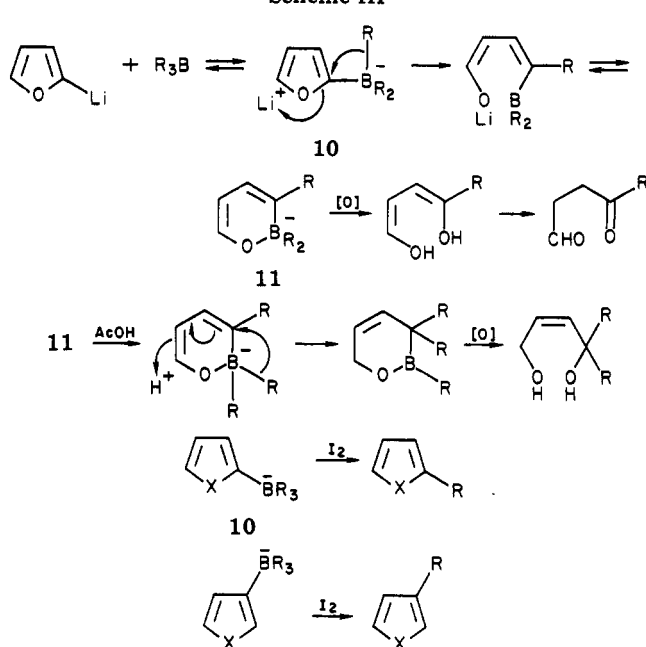
(5) Negishi, E.; Lew, G.; Yoshida, T. *J. Chem. Soc., Chem. Commun.* 1973, 874.

(6) Yamada, K.; Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* 1975, 1961.

(7) Miyaura, N.; Abiko, S.; Itoh, M.; Suzuki, A. *Synthesis* 1975, 669.

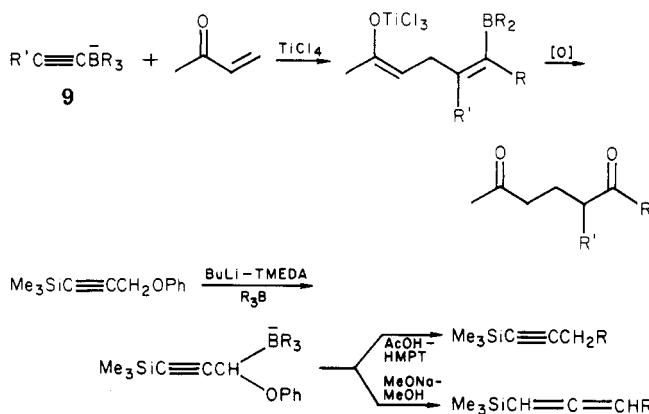
(8) Miyaura, N.; Yamada, K.; Itoh, M.; Suzuki, A. *Synthesis* 1977, 679.

Scheme III



treatment with propionic acid.<sup>9</sup>

As previously mentioned, 1-alkynyltrialkylborates **9** have become increasingly important in the formation of carbon-carbon bonds. Such borate complexes are readily attacked by electrophiles such as iodine cation and proton to give intermediates, which have potential synthetic utility. However, alkynylborates **9** cannot react with weak electrophiles such as  $\alpha,\beta$ -unsaturated carbonyl compounds. Most recently, we found that  $\alpha,\beta$ -unsaturated carbonyl compounds react with **9** in the presence of  $\text{TiCl}_4$  followed by the usual alkaline hydrogen peroxide oxidation to produce  $\delta$ -dicarbonyl compounds.<sup>10</sup> The reaction of ate complexes (obtained



from trialkylboranes and (trimethylsilyl)propargyl phenyl ether) with a mixture of acetic acid and hexamethylphosphoric triamide (HMPT) gives (trimethylsilyl)acetylenes,<sup>11</sup> whereas (trimethylsilyl)allenes are selectively formed upon treatment with sodium methoxide in methanol.<sup>12</sup> These trimethylsilyl derivatives are useful precursors to yield functionalized organic compounds.<sup>13</sup>

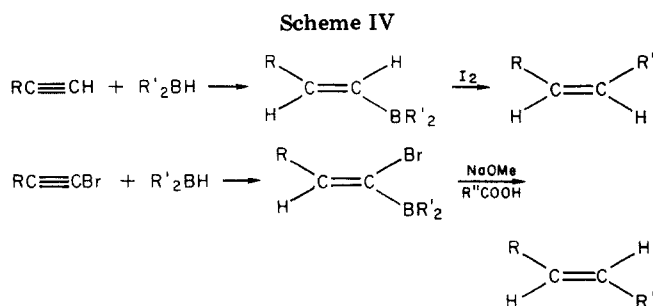
(9) Yoshinari, T.; Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* 1974, 2961.

(10) Hara, S.; Kishimura, K.; Suzuki, A. *Chem. Lett.* 1980, 221.

(11) Yogo, T.; Koshino, J.; Suzuki, A. *Synth. Commun.* 1979, 9, 809.

(12) Yogo, T.; Koshino, J.; Suzuki, A. *Tetrahedron Lett.* 1979, 1781.

(13) Koshino, J.; Yogo, T.; Suzuki, A. *Synth. Commun.* 1981, 11, 769.



### Synthesis via Alkenylborates

About a decade ago, we sought to find a method for the synthesis of  $\gamma$ -keto aldehydes from organoboranes and 2-lithiofuran. As depicted in Scheme III, the ate complex **10** was expected to be converted into a  $\gamma$ -keto aldehyde through the intermediate **11**. But unexpectedly this reaction afforded the (*Z*)-alkenediol, probably via the reaction pathway shown in Scheme III.<sup>14</sup> Recently, we have found that the ate complex **10** gives the corresponding 2-alkylfuran by reaction with iodine.<sup>15</sup> This reaction has significant applicability for the introduction of both primary and secondary alkyl groups to the furan nucleus. By the same procedure, 2-alkylthiophenes,<sup>16</sup> 2-alkyl-1-methylpyrroles,<sup>16</sup> 3-alkylfurans,<sup>17</sup> and 3-alkylthiophenes<sup>17</sup> are also prepared in good yields. A similar type of reaction has also been reported by Levy and co-workers.<sup>18</sup>

An interesting reaction of 1-alkenyldialkylboranes, readily obtainable by the monohydroboration of 1-alkynes with dialkylboranes, was first discovered by Zweifel and his co-workers (Scheme IV). 1-Alkenyldialkylboranes, upon treatment with iodine in the presence of bases, give the corresponding (*Z*)-alkenes.<sup>19</sup> On the other hand, treatment of (1-bromo-1-alkenyl)dialkylboranes (formed by monohydroboration of 1-bromo-1-alkynes with dialkylboranes) with sodium methoxide followed by protonolysis with a carboxylic acid gives the corresponding (*E*)-alkenes.<sup>19</sup> Conjugated (*E,Z*)-alkadienes<sup>20</sup> and (*E,E*)-alkadienes<sup>21</sup> could be obtained by the modified Zweifel's procedure.

In connection with such a reaction of 1-alkenylborates, we attempted the isopropenylation of C=C bonds. Our first expectation was that an organoborane would react with isopropenyllithium to form the tetraordinated organoborate, iodination of which, followed by elimination of the B-I moiety, gives the isopropenyl derivative. As anticipated, the reaction was found to take place smoothly to afford corresponding products in good yields.<sup>22</sup>

Recently, a highly convenient synthesis of (1-alkylethenyl)lithium derivatives from [(2,4,6-triisopropyl-

(14) Suzuki, A.; Miyaura, N.; Itoh, M. *Tetrahedron* 1971, 27, 2775.

(15) Akimoto, I.; Suzuki, A. *Synthesis* 1979, 146.

(16) Sotoyama, T.; Hara, S.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1979, 52, 1865.

(17) Akimoto, I.; Sano, M.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1981, 54, 1587.

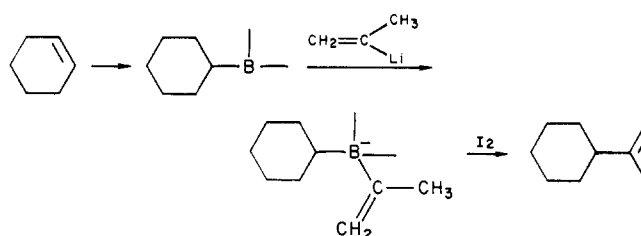
(18) (a) Levy, A. B. *J. Org. Chem.* 1978, 43, 4684. (b) Marinelli, E. R.; Levy, A. B. *Tetrahedron Lett.* 1979, 2313. (c) Levy, A. B. *Ibid.* 1979, 4021.

(19) (a) Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* 1967, 89, 3652. (b) Zweifel, G.; Arzoumanian, H. *Ibid.* 1967, 89, 5086. (c) *Ibid.* 1971, 93, 6309.

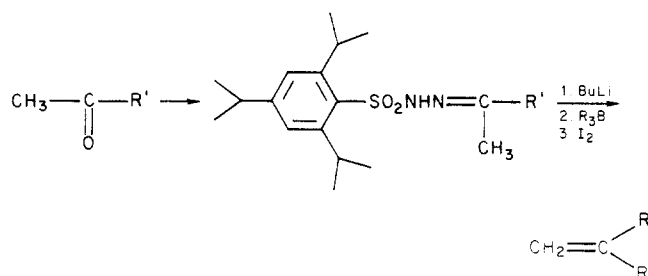
(20) Zweifel, G.; Polston, N. L.; Whitney, C. C. *J. Am. Chem. Soc.* 1968, 90, 6243.

(21) Negishi, E.; Yoshida, T. *J. Chem. Soc., Chem. Commun.* 1973, 606.

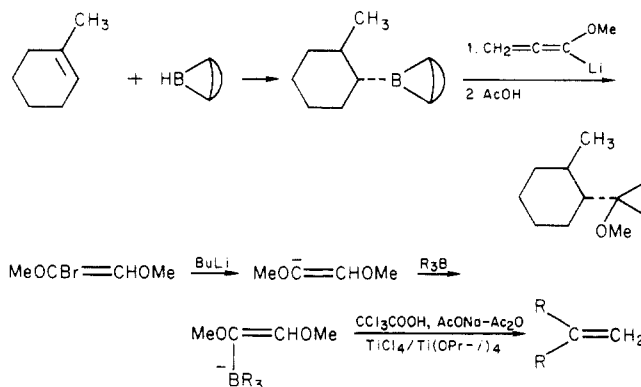
(22) Tagami, H.; Miyaura, N.; Itoh, M.; Suzuki, A. *Chem. Lett.* 1974, 1411.



phenyl)sulfonyl]hydrazones (trisyldiazones) of methyl ketones was reported.<sup>23</sup> In order to apply this method to the formation of C-C bonds, we tried the reaction of ate complexes (derived from trialkylboranes and (1-alkylethenyl)lithium derivatives, which are formed by treatment of trisyldiazones with butyllithium) with iodine and found that the reaction proceeds to give 1,1-dialkylethenes in excellent yields.<sup>24</sup>



The reaction of (1-bromo-1-alkenyl)dialkylboranes with lead(IV) acetate or (diacetoxyiodo)benzene gave 1-bromo-1,2-dialkylethenes.<sup>25</sup> Methoxycyclopropanes are synthesized upon treatment of ate complexes (prepared from *B*-alkyl-9-borabicyclo[3.3.1]nonanes and 1-lithio-1-methoxy-1,2-propadiene) with acetic acid.<sup>26</sup>



1,1-Dialkylethenes are prepared from (1,2-dimethoxyethenyl)trialkylborates by reaction with trichloroacetic acid and then with a mixture of sodium acetate-acetic anhydride and  $\text{TiCl}_4/\text{Ti}(\text{OPr-}i)_4$ .<sup>27</sup> The reaction of alkyl fluorosulfates with (1,2-dimethoxyethenyl)trialkylborates gives the corresponding ketones.<sup>28</sup>

### Synthesis via Copper(I) Methyltrialkylborates

Although reaction details are not given in this Account, we discovered that organoboranes undergo

(23) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* 1978, 43, 147.

(24) Avasthi, K.; Baba, T.; Suzuki, A. *Tetrahedron Lett.* 1980, 21, 945.

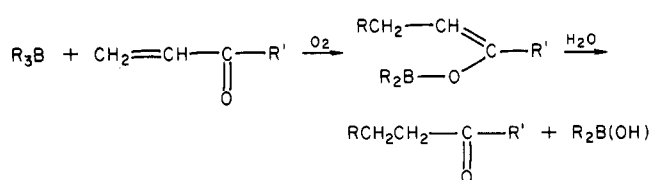
(25) Masuda, Y.; Arase, A.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1980, 53, 1652.

(26) Yoshinari, T.; Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* 1980, 21, 537.

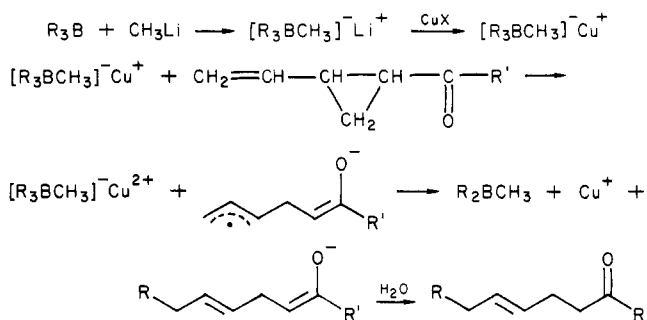
(27) Yogo, T.; Suzuki, A. *Chem. Lett.* 1980, 591.

(28) Koshino, J.; Yogo, T.; Suzuki, A. *Chem. Lett.* 1981, 1059.

Scheme V



Scheme VI



spontaneous 1,4-addition reactions in the presence of oxygen to numerous  $\alpha,\beta$ -unsaturated carbonyl and related compounds such as methyl vinyl ketone (Scheme V),<sup>29</sup> acetylacetylene,<sup>30</sup> 1,3-butadiene monoxide,<sup>31</sup> and 3,4-epoxy-1-butyne.<sup>32</sup> However, ethyl acrylate and acrylonitrile did not react with organoboranes under such reaction conditions, while vinyl phenyl ketone and 1-acyl-2-vinylcyclopropane<sup>33</sup> gave the corresponding products in poor yields. This may be due to the polymerization of substrates or to the fact that the unstable intermediates initially formed are subject to other reactions.

In order to overcome these obstacles, we attempted various experiments, one of which is the reaction of copper(I) methyltrialkylborate, the alkyl groups of which are considered to be more anionic than those of the corresponding trialkylborane. Consequently, we examined the reaction of substrates such as acrylonitrile and 1-acyl-2-vinylcyclopropane with lithium methyltrialkylborates, readily prepared from trialkylboranes and methyllithium. The reason we chose methyllithium as the alkylating agent for trialkylboranes was the B-C bond dissociation energy between boron and methyl group was known to be the largest among B-alkyl bonds.<sup>34</sup> Contrary to our expectation, it was shown that lithium methyltrialkylborates did not react with acrylonitrile. Therefore, we next examined the reaction of the substrate with copper(I) methyltrialkylborates, obtainable with no difficulty via metathesis between lithium methyltrialkylborates and cuprous halides. The reaction of copper(I) methyltrialkylborates with acrylonitrile gives the corresponding 1,4-addition products which are converted by hydrolysis with water

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(30) Suzuki, A.; Nozawa, S.; Itoh, M.; Brown, H. C.; Kabalka, G. W. *J. Am. Chem. Soc.* 1970, 92, 3503.

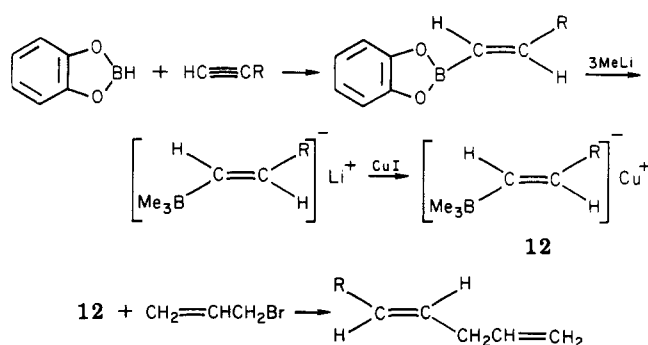
(31) Suzuki, A.; Miyaura, N.; Itoh, M.; Brown, H. C.; Holland, G. W. *J. Am. Chem. Soc.* 1971, 93, 2792.

(32) Suzuki, A.; Miyaura, N.; Itoh, M.; Brown, H. C.; Jacob, P. *Synthesis*, 1973, 305.

(33) Sasaki, N.; Miyaura, N.; Itoh, M.; Suzuki, A. *Synthesis* 1975, 317.

(34) (a) Finch, A.; Gardner, P. J.; Pearn, E. J.; Whatts, G. B. *Trans. Faraday Soc.* 1967, 63, 1880. (b) Skinner, H. A. *Adv. Organomet. Chem.* 1964, 2, 49.

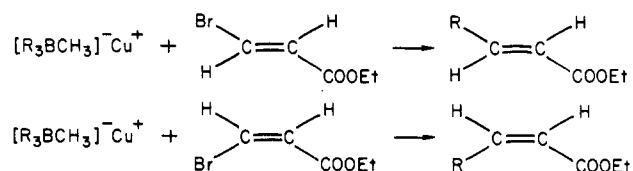
Scheme VII



into alkyl cyanides in about 90% yields.<sup>35</sup> Such cuprous borates also react smoothly with 1-acyl-2-vinylcyclopropane to afford the corresponding  $\gamma,\delta$ -unsaturated ketones in good yields (ca. 80%).<sup>35</sup> As one of the possible reaction routes, the mechanism involving a redox process of copper ions may be considered (Scheme VI).

Ate complexes also react with benzylic halides<sup>36</sup> and aroyl chlorides<sup>37</sup> to give the corresponding cross-coupling products in good yields. The same type of cross-coupling takes place in the reaction of copper(I) methyltrialkylborates with allyl halides to yields 1-alkenes,<sup>38</sup> and terminal allenes are prepared upon treatment with propargyl halides.<sup>38</sup> Next, the reaction of allyl bromide with copper(I) 1-alkenyltrimethylborates was examined in an attempt to synthesize 1,4-alkadienes. Copper(I) 1-alkenyltrimethylborates are readily produced by the procedure depicted in Scheme VII. The ate-complexes 12 react easily with allyl bromide to give the expected 1,4-alkadienes in greater than 90% yield.<sup>39</sup>

The reaction of cuprous methyltrialkylborates with  $\beta$ -bromoacrylates is also interesting. Reaction with (*E*)- $\beta$ -bromoacrylate occurs smoothly to afford the corresponding  $\alpha,\beta$ -unsaturated esters, which are selectively *E* isomers. On the other hand, (*Z*)- $\beta$ -alkyl-



acrylates are selectively produced from (*Z*)- $\beta$ -bromoacrylate. Although the reaction mechanism is not clear, this evidence seems to suggest that the reaction proceeds through retention of configuration by a *cis* addition and *trans* elimination process.<sup>40</sup> (*E*)- $\alpha,\beta$ -Unsaturated carboxylic esters can also be obtained by reaction of such borate complexes with ethyl propiolate.<sup>41</sup> The same type of reaction between copper(I) methyl-

(35) Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* 1976, 255.

(36) Miyaura, N.; Itoh, M.; Suzuki, A. *Synthesis* 1976, 618.

(37) Sasaki, N.; Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* 1977, 173.

(38) Miyaura, N.; Itoh, M.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1977, 50, 2199.

(39) Yano, T.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1980, 53, 1471.

(40) Sasaki, N.; Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* 1977, 3369.

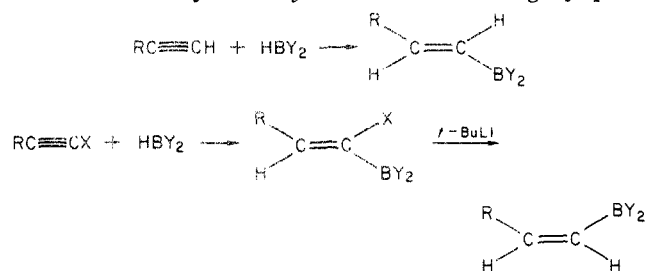
(41) Yamada, K.; Miyaura, N.; Itoh, M.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1977, 50, 3431.

trialkylborates and 1-(1-pyrrolidinyl)-6-chloro-1-cyclohexene affords the corresponding alkylation products, which are readily hydrolyzed to 2-alkylcyclohexanones.<sup>42</sup>

### Synthesis via the Palladium-Catalyzed Reaction of 1-Alkenylboranes in the Presence of Bases

Stereoselective syntheses of conjugated (*E,E*)-, (*E,Z*)-, and (*Z,Z*)-dienes are of considerable importance in organic chemistry in themselves as well as in their utilization in other reactions such as the Diels-Alder reaction. Recently a number of new methods utilizing organoaluminum,<sup>43</sup> boron,<sup>44</sup> copper,<sup>45</sup> magnesium,<sup>46</sup> silver,<sup>47</sup> mercury,<sup>48</sup> and zirconium<sup>49</sup> reagents for the preparation of conjugated dienes, have appeared. However, the scope of many of these reactions is limited by the nature of the organometallic compound involved or the procedure employed, e.g., they require stoichiometric amounts of metal compounds, and some of them can be best utilized only for the synthesis of symmetric dienes or unfunctionalized dienes because of the reducing property of organometallic derivatives.

On the other hand, it is well-known that stereodefined 1-alkenyldialkylboranes are readily prepared by the monohydroboration of alkynes; i.e., dialkylboranes such as disiamylborane and catecholborane permit the monohydroboration of terminal acetylenes; this makes the corresponding (*E*)-1-alkenyldialkylboranes with high stereoselectivity readily available.<sup>1b</sup> Highly pure



(*Z*)-1-alkenyldialkylboranes (more than 99%) are prepared via monohydroboration of 1-halo-1-alkynes with disiamylborane and dicyclohexylborane, followed by treatment with *tert*-butyllithium.<sup>50</sup> Consequently, if such 1-alkenyldialkylboranes react with 1-alkenyl halides or 1-alkynyl halides, it provides convenient synthetic procedures for conjugated dienes or enynes. In spite of the efforts by many workers to find such cross-coupling reactions, there were no successful reports. Accordingly, we intended to explore the reaction.

(42) Yamada, K.; Yano, T.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1979, 52, 275.

(43) (a) Baba, S.; Negishi, E. *J. Am. Chem. Soc.* 1976, 98, 6729. (b) Negishi, E. "New Applications of Organometallic Reagents in Organic Synthesis"; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; p 93.

(44) (a) Zweifel, G.; Polston, N. L.; Whitney, C. C. *J. Am. Chem. Soc.* 1968, 90, 6243. (b) Zweifel, G.; Polston, N. L. *Ibid.* 1970, 92, 4068. (c) Negishi, E.; Yoshida, T. *J. Chem. Soc., Chem. Commun.* 1972, 606. (d) Negishi, E.; Lew, G.; Yoshida, T. *Ibid.* 1973, 874. (e) Brown, H. C.; Ravindran, N. *J. Org. Chem.* 1973, 38, 1617. (f) Yamamoto, Y.; Yatagai, H.; Murayama, K.; Sonoda, S.; Murahashi, S-I. *J. Am. Chem. Soc.* 1977, 99, 5652. (g) Zweifel, G.; Backlund, S. J. *J. Organomet. Chem.* 1978, 156, 159. (h) Campbell, J. B., Jr.; Brown, H. C. *J. Org. Chem.* 1980, 45, 549.

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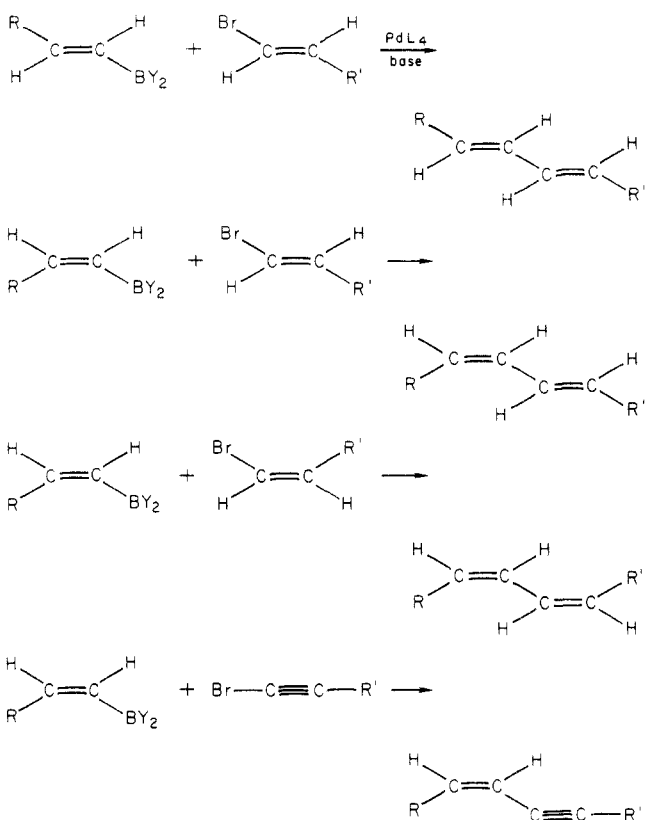
(48) Larock, R. C. *Angew. Chem., Int. Ed. Engl.* 1978, 17, 27.

(49) Okukado, N.; Vanhorn, D. E.; Klima, W. L.; Negishi, E. *Tetrahedron Lett.* 1978, 1027.

(50) Campbell, J. B., Jr.; Molander, G. A. *J. Organomet. Chem.* 1978, 156, 71.

The common mechanism of transition-metal-catalyzed cross-coupling reactions<sup>51</sup> between organometallic compounds and organic halides involves sequential (a) oxidative addition, (b) transmetalation, and (c) reductive elimination. A principal reason why 1-alkenylboranes cannot react with 1-alkenyl and 1-alkynyl halides seems to be step b, because the transmetalation process between R'<sup>2</sup>PdX and 1-alkenylboranes does not occur smoothly, due to the weak carbanion character of organic groups in organoboranes. However, we thought that if the organoborates formed from 1-alkenylboranes and basic species such as alkoxide, acetate, and hydroxide ions were used instead of alkenylboranes themselves, there is a possibility that the transmetalation could take place readily.

Actually, we found that (*E*)-1-alkenyldisiamylboranes and (*E*)-1-alkenyl-1,3,2-benzodioxaboroles react with (*E*)-1-alkenyl halides or 1-alkynyl halides in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium and bases to give the corresponding conjugated (*E,E*)-dienes or (*E*)-enynes with high regio- and stereospecificity in good yields.<sup>52</sup> The



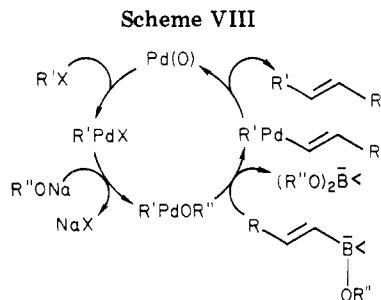
reaction of (*Z*)-1-alkenyldisiamylboranes with (*Z*)- or (*E*)-1-alkenyl bromides under the same conditions gave the conjugated (*Z,Z*)- or (*Z,E*)-alkadienes with high stereospecificity.<sup>53</sup>

The reaction of aryl halides with 1-alkenylboranes provides a convenient new method for the stereoselective synthesis of arylated alkenes under such conditions.<sup>54</sup> The same cross-coupling reaction of 1-alk-

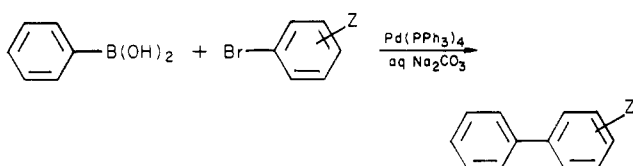
(51) (a) Kochi, J. K. "Organometallic Mechanisms and Catalysis"; Academic: New York, 1978. (b) Collman, J. P.; Hegedus, L. S. "Principles and Applications of Organotransition Metal Chemistry"; University Science Books: Mill Valley, CA, 1980.

(52) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* 1979, 3437.

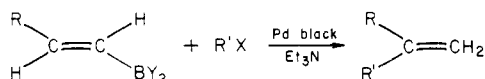
(53) Miyaura, N.; Suginome, H.; Suzuki, A. *Tetrahedron Lett.* 1981, 22, 127.



nylboranes with allylic or benzylic bromides occurs smoothly to give 1,4-alkadienes or allylbenzenes respectively in good yields.<sup>55</sup> The palladium-catalyzed coupling of phenylboronic acid with haloarenes results in the corresponding biaryls in excellent yields.<sup>56</sup>

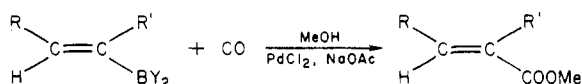


In addition to the "head-to-head" cross-coupling reactions mentioned above, it was found that the reaction of phenyl or 1-alkenyl iodides with (*E*)-1-alkenyl-1,3,2-benzodioxaboroles gives the "head-to-tail" cross-coupling products, 2-phenyl-1-alkenes or 2-alkyl-1,3-alkadienes. The reaction is profoundly affected by catalytic quantities of palladium compounds (Pd black prepared by reduction of Pd(OAc)<sub>2</sub> with diborane is especially effective) in the presence of triethylamine.<sup>57</sup>



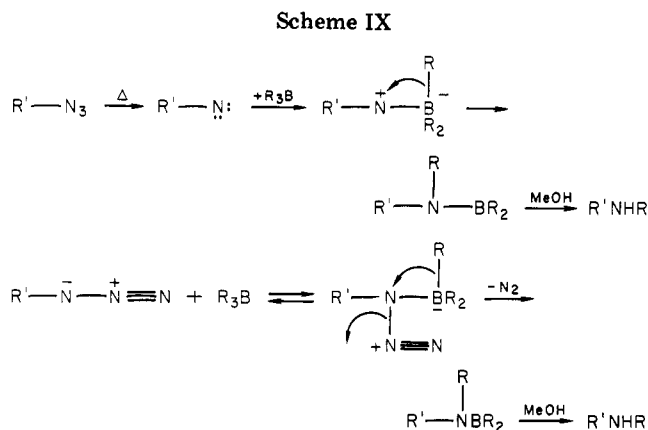
The mechanisms of the palladium-catalyzed "head-to-head" and "head-to-tail" cross-coupling reactions are poorly understood. However, our recent investigation suggested that the "head-to-head" reaction can be accommodated by an oxidative addition of R'X to Pd(0) followed by an exchange with sodium alkoxide, transmetalation with 1-alkenylborates, and reductive elimination as shown in Scheme VIII.<sup>58</sup>

1-Alkenylboranes also react with carbon monoxide in the presence of palladium chloride and sodium acetate in methanol to give  $\alpha,\beta$ -unsaturated carboxylic esters in good yield with retention of configuration with respect to the alkenylboranes.<sup>59</sup>



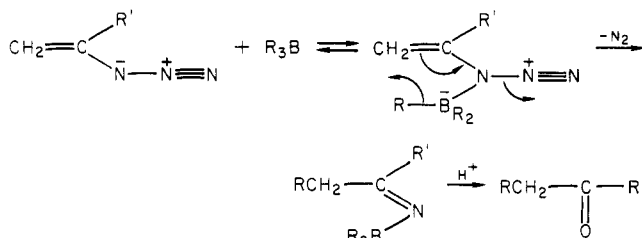
### Miscellaneous Syntheses

There have been many reports on organic syntheses which involve the reactions of tetra-coordinated organoborates, in which  $\alpha$ -carbons have heteroatoms readily



removable as leaving groups (depicted in Scheme II),<sup>1,71</sup> One such synthetic reaction discovered by our research group is the selective synthesis of secondary amines by the reaction of trialkylboranes with alkyl azides. At the time of our initial planning, the desired synthesis was expected to be brought about via the reaction with nitrenes generated by thermal treatment of alkyl azides (Scheme IX). Actually, the secondary amines were produced in good yields, but it was found that the reaction did not proceed through the nitrene intermediate but via the coordination process. The reaction rate was determined to be second order, first order in both the organoborane and the alkyl azide, as shown in Scheme IX.<sup>60</sup> The modified methods using R<sub>2</sub>BCl<sup>61a</sup> and RBCl<sub>2</sub><sup>61b</sup> were reported later.

Instead of alkyl azides, when vinylic azides such as  $\alpha$ -azidostyrene and 2-azido-1-alkenes are used, a different type of reaction occurs, one in which alkyl group migration takes place from boron to the vinylic carbon followed by hydrolysis to give the corresponding ketones.<sup>62</sup>



Organoboranes have been recently recognized to have a high versatility for the synthesis of organic compounds with various functional groups. However, until most recently, there have been no successful reports on the direct synthesis of carboxylic acids from organoboranes. In order to find a direct synthesis of carboxylic acids, we examined the reactions of organoboranes with sodium cyanide,<sup>63</sup> Meyers' reagents,<sup>63</sup> and catechol dichloromethylene ether.<sup>64</sup> But such reactions were found to yield only symmetric ketones (by two alkyl group migrations) instead of carboxylic acids.

While we made various explorations without success, it was noticed that under basic conditions, O-C bonds, especially phenoxylic O-C bonds, the carbons of which

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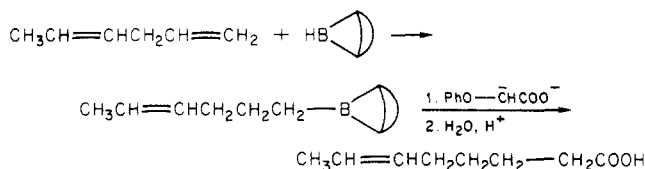
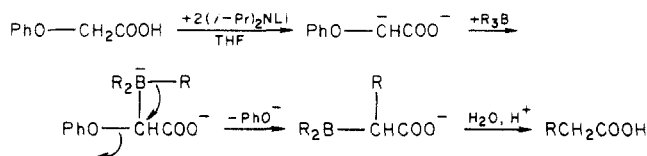
(61) (a) Brown, H. C.; Midland, M. M. *J. Am. Chem. Soc.* **1972**, 94, 2114. (b) Brown, H. C.; Midland, M. M.; Levy, A. B. *Ibid.* **1973**, 95, 2394.

(62) Suzuki, A.; Tabata, M.; Ueda, M. *Tetrahedron Lett.* **1975**, 2195.

(63) Unpublished results.

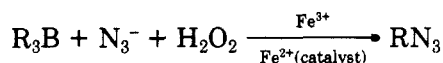
(64) Kawaguchi, T.; Ishidoya, M.; Suzuki, A. *Heterocycles* **1982**, 18, 113.

combine with boron atoms, were easily cleaved. Therefore, we finally investigated the reaction of organoboranes with the dianion of phenoxyacetic acid, which is prepared with no difficulty from lithium diisopropylamide and phenoxyacetic acid and is soluble in tetrahydrofuran. The reaction with trialkylboranes



occurs smoothly, followed by acidification to give corresponding carboxylic acids in excellent yields.<sup>65</sup> The reaction is also applicable to the synthesis of olefinic carboxylic acids via the selective monohydroboration of alkadienes.<sup>65</sup>

Lane reported the synthesis of alkyl chlorides and bromides by the reaction between the trialkylboranes and cupric halides,<sup>66</sup> and we also found that organoboranes on treatment with ferric chloride and thiocyanate in an aqueous tetrahydrofuran solution gave alkyl chlorides and thiocyanates.<sup>67</sup> The reaction was suggested to proceed through a redox process involving iron ions. In the course of our studies on organic synthesis using organoboranes in such a redox process, we attempted to find a synthetic possibility for obtaining azidoalkanes. Unfortunately, the formation of the expected products was not observed in the reaction with ferric azide under similar conditions. This difficulty, however, was found to be overcome by addition of hydrogen peroxide. The reaction provides a convenient



route to azidoalkane synthesis from organoboranes.<sup>68</sup> Although we have not finished a study of the mechanism, a free-radical chain reaction path in which ferrous ions participate may be considered as one of the possibilities.<sup>68</sup>

Many reports have appeared dealing with the syntheses<sup>1</sup> of primary, secondary, and tertiary amines from organoboranes. On the other hand, there are a few examples of similar reactions leading to nitrogen compounds possessing substituents other than hydrogen or alkyl groups attached to nitrogen. Among these are the

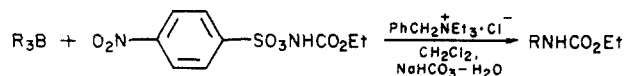
(65) Hara, S.; Kishimura, K.; Suzuki, A. *Tetrahedron Lett.* 1978, 2891.

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(67) Arase, A.; Masuda, Y.; Suzuki, A. *Bull. Chem. Soc. Jpn.* 1974, 47, 2511.

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syntheses of azidoalkanes<sup>68</sup> mentioned above and of *N*-alkyl sulfonamides via the reaction with chloramine-T and its analogues.<sup>69</sup> Most recently, we tried a synthesis of alkylcarbamates from ethyl [(*p*-nitrophenyl)sulfonyl]oxy]carbamate and trialkylboranes under alkaline conditions. The formation of the desired products was found to be unsatisfactory. Finally we found that the reaction proceeds smoothly in an organic-aqueous two-phase system in the presence of phase transfer catalysts such as quaternary ammonium halides to give alkylcarbamates in good yields.<sup>70</sup> This is the first report of a synthetic application of phase transfer catalysis in organic synthesis using organoboranes.



## Concluding Remarks

In summarizing, we wish to emphasize the importance of organoboranes in organic synthesis. Although in this Account novel synthetic reactions employing organoboranes, discovered by our research group, were only reviewed, there have been many interesting reports on organic syntheses using organoboranes and organoborates, carried out by other groups.<sup>1,43b,71</sup> The major advantages of these reactions are as follows: (1) Organoboranes with a wide variety of structures are readily available by the hydroboration of alkenes and alkynes. (2) It is possible to synthesize organoboranes with functional groups. (3) Organoborates are readily prepared. (4) The boron-carbon bonds of organoboranes and organoborates are replaced by substituents or by carbon-carbon bonds. (5) The syntheses using organoboranes and organoborates are usually carried out in "one-pot" preparations. (6) The reactions occur under mild conditions. (7) The reactions are generally regioselective and stereoselective.

"A new continent has been discovered. It requires settlers to develop its riches to contribute to mankind" (Herbert C. Brown<sup>1b</sup>)

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