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A NEW STEREOSPECIFIC CROSS-COUPLING BY THE PALLADIUM-CATALYZED REACTION OF 1-ALKENYLBORANES
WITH 1-ALKENYL OR 1-ALKYNYL HALIDES

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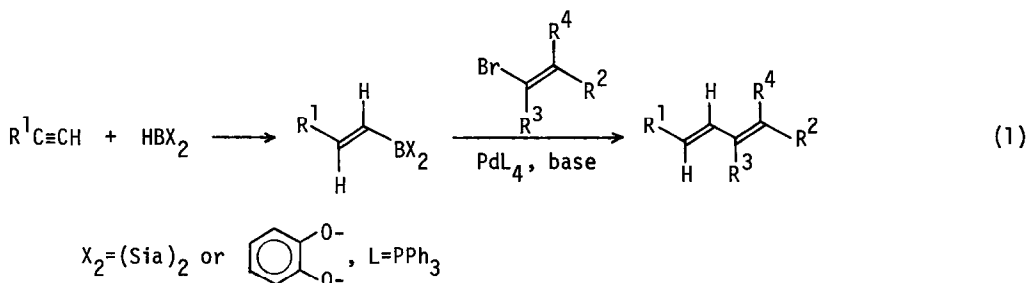
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Summary: The representative (E)-1-alkenyldisiamylboranes and (E)-1-alkenyl-1,3,2-benzodioxaboroles readily obtainable via hydroboration of 1-alkynes react with 1-alkenyl halides or 1-alkynyl halides in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium and base to give corresponding conjugated (E)-dienes or (E)-enynes with high regio- and stereo-specificity in good yields, respectively.

Stereoselective syntheses of conjugated (E,E)- and (E,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 for the preparation of conjugated dienes have appeared utilizing organoaluminum,¹ boron,² copper,³ magnesium,⁴ silver,⁵ mercury,⁶ and zirconium⁷ reagents. However, the scope of many of these reactions is limited by the nature of the organometallic involved or the procedure employed, e.g. they require stoichiometric amounts of palladium catalyst,^{2,3,5} and some of them can be best utilized only for the synthesis of symmetrical dienes^{5,6} or unfunctionalized dienes because of the reducing property of organometallic compounds.¹

In our continuous investigations of organic syntheses using organoboranes, we have now discovered a novel cross-coupling reaction of 1-alkenylboranes readily obtainable via hydroboration of alkynes with 1-alkenyl halides in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium and base as shown below (eq. 1). This reaction provides a highly stereo- and regiospecific synthesis of conjugated dienes from organoboranes.

When we attempted to carry out the coupling reaction of such alkenylboranes with 1-alkenyl halides in the presence of the palladium complex, it failed to provide the desired products, as Negishi and Baba previously reported.¹ For example, the reaction of an equimolar amount of (E)-1-hexenyldisiamylborane in THF with (E)-1-bromo-2-phenylethene in the presence of 1 mole % of



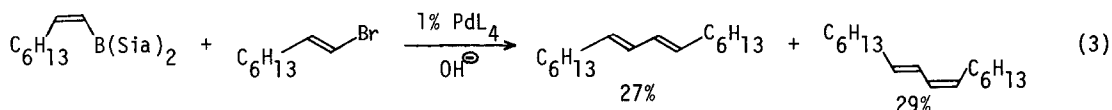
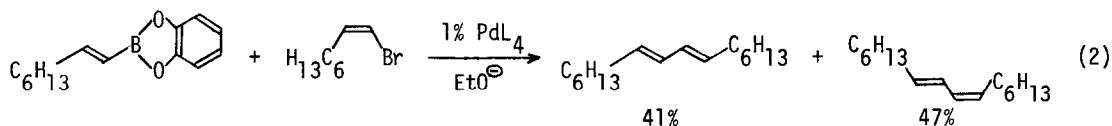
tetrakis(triphenylphosphine)palladium gave (E,E)-1-phenyl-1,3-octadiene in a yield of only 2% together with other products. However, we found that the addition of bases such as sodium methoxide, ethoxide, acetate and hydroxide to the mixture brings about a rapid and clean reaction. Addition of two fold excess of aqueous 2N-sodium hydroxide to the above reaction mixture followed by refluxing for 2 h produced the expected diene in a yield of 59%. Furthermore, use of 1,3,2-benzodioxaborole as a hydroborating reagent increased the yield of the diene to 80%. In general, aqueous sodium hydroxide for alkenyldisiamylboranes in THF and sodium ethoxide in ethanol for alkenylbenzodioxaboroles in benzene respectively gave the most favorable results. The representative results are summarized in Table 1.

The present cross-coupling reaction is evidently applicable to representative (E)-1-alkenylboranes ($R^1 = \text{Ph, Butyl, Hexyl}$) and is useful for the synthesis of (E,E)-dienes. The reaction in each case is stereospecific, supporting the assumption that such a reaction proceeds through retention of configuration both in (E)-1-alkenylboranes and (E)-1-alkenyl bromides (entries 1-8).

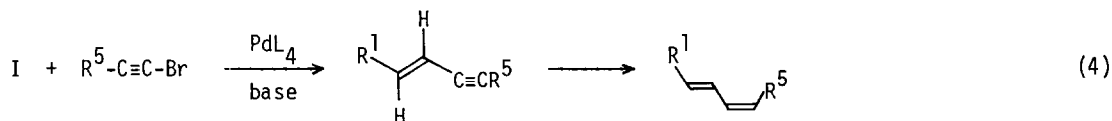
The following procedure for the preparation of (E)-2-methyl-2,4-nonadiene is representative. A dry 50 ml-flask equipped with a magnetic stirring bar, a septum inlet, and a reflux condenser was flushed with nitrogen. In the flask was placed a mixture of tetrakis(triphenylphosphine)-palladium⁸ (0.054 g, 0.05 mmol) in 10 ml of benzene and 1-bromo-2-methyl-1-propene (0.985 g, 5 mmol) under nitrogen gas. After stirring for 30 min at room temperature, (E)-1-hexenyl-1,3,2-benzodioxaborole⁹ (5.5 ml of 1 M solution in benzene, 5.5 mmol) and sodium ethoxide in ethanol (5 ml of 2 M solution, 10 mmol) were added, and the solution was immediately warmed to reflux temperature. After refluxing for 2 h, the residual organoborane was oxidized by an addition of 3N aqueous sodium hydroxide (0.3 ml) and 30% hydrogen peroxide (0.3 ml) for 1 h at room temperature, and the product was extracted with hexane. Analysis of extracts by GLC (SE-30) indicated that 4.05 mmol (81%) of (E)-2-methyl-2,4-nonadiene had been formed. An analytically pure sample was obtained by preparative GLC (15% SE-30 on Uniport-B, 2m): n_D^{20} 1.4697. ¹H NMR (CCl₄, TMS); δ , 0.90 (t, 2H), 1.1-1.5 (m, 4H), 1.72 (s, 6H), 1.8-2.2 (m, 2H), 5.42 (dt, J=7 and 14 Hz, 1H), 5.67 (d, J=10 Hz, 1H), and 6.12 (dd, J=10 and 14 Hz, 1H) ppm. IR (neat); 3030, 1625, 1380, 995, 965, and 875 cm^{-1} .

Next, we attempted to apply this reaction to the synthesis of (E,Z)-dienes via the reaction of (E)-1-alkenylborane with (Z)-1-alkenyl halide (eq. 2) or (Z)-1-alkenylborane¹⁰ with (E)-1-alkenyl halide (eq. 3). Both reactions proceeded smoothly under the same reaction conditions as described before, however, the results were unsatisfactory. For instance, 7,9-hexadecadiene thus obtained was a mixture of (E,E)- and (E,Z)-isomers in a ratio of 1:1, as depicted in eqs. 2 and 3. It appears that the initially formed (E,Z)-diene is isomerized to give the corresponding stable (E,E)-isomer under the palladium-catalyzed reaction conditions.¹¹

Although the direct stereospecific synthesis of (E,Z)-dienes by cross-coupling of alkenylboranes with alkenyl halides is currently under investigation, such a synthesis of (E,Z)-dienes using organoboranes has been reported. Treatment of the borate complexes derived from alkenyldisiamylboranes and alkynyllithium with iodine and sodium hydroxide produces conjugated (E)-enynes readily convertible into the corresponding (E,Z)-dienes via hydroboration-protonolysis.^{2d} The present reaction offers an alternative method for the synthesis of



conjugated (E)-enyne by cross-coupling between 1-alkenyldisiamylboranes (I)¹² and 1-alkynyl bromides in the presence of the palladium complex (eq. 4). As indicated in entries 9-12 in Table 1, it was found that the reaction proceeds smoothly to give the corresponding (E)-enyne in good yields, better than those of the previously reported procedure.^{2d} Each enyne thus obtained was shown by GLC analysis to be a single product, presumably E-isomer, judging from the



IR (955 cm^{-1}) and $^1\text{H NMR}$ ($J_{\text{trans}} = 16\text{ Hz}$) spectra.

Stereospecific formation of (E)-1-alkenylborane compounds via hydroboration of alkynes followed by transfer of the stereodefined alkenyl group to alkyl halides under the conditions mentioned above should provide a simple method for synthesis of stereodefined alkenes. Our preliminary observations suggest that allyl, benzyl or aryl halides are possible substrates for this reaction. These reactions are currently under investigation.

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(12) The corresponding 1-alkenylbenzodioxaboroles failed to provide the desired enynes.

Table 1. Palladium-Catalyzed Cross-Coupling Reaction of (E)-1-Alkenylboranes with 1-Alkenyl or 1-Alkynyl Bromides^{a)}

Entry						$R^5-C\equiv C-Br$	Base ^{b)}	Catalyst ^{c)} mole %	Product ^{d)} and yield, ^{e)} %	Isomeric purity
	R ¹	X ^{f)}	R ²	R ³	R ⁴	R ⁵				
1	Bu	Sia	Ph	H	H		NaOH	3	59 ^{g)}	>96
2	Bu	BDOB	Ph	H	H		NaOEt	1	80	>96
3	Bu	BDOB	H	Ph	H		NaOEt	1	80	~100
4	Bu	BDOB	Me	H	Me		NaOEt	1	81	~100
5	Ph	BDOB	Me	H	Me		NaOEt	1	28	~100
6	Ph	Sia	Me	H	Me		NaOH	3	52 ^{g)}	~100
7	Bu	BDOB	Hex	H	H		NaOEt	1	86	>97
8	Hex	BDOB	Hex	H	H		NaOEt	1	83	>96
9	Bu	Sia				Hex	NaOMe	1	100	>99
10	Bu	Sia				Ph	NaOMe	1	72	>99
11	Ph	Sia				Hex	NaOMe	1	95	>99
12	Me	Sia				Ph	NaOMe	1	91	>96

^{a)}The syntheses of dienes and enynes were carried out in benzene at 80°C for 2 h by using a 10% excess of alkenylboranes, unless otherwise mentioned. ^{b)}As bases, 2N sodium alkoxide in alcohol and 2N aqueous sodium hydroxide were used and the ratio of base/alkenylborane is 2 for all the cases. ^{c)}Pd(PPh₃)₄ was used as the catalyst. ^{d)}The isolated products were adequately characterized by IR, ¹H NMR, mass spectroscopic data and elemental analyses. ^{e)}Based on alkenyl or alkynyl bromides and determined by GLC. ^{f)}Sia = 3-methyl-2-butyl. BDOB = 1,3,2-benzodioxaboryl. ^{g)}THF was used as the solvent, and the reaction was carried out at 65°C for 2 h.

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