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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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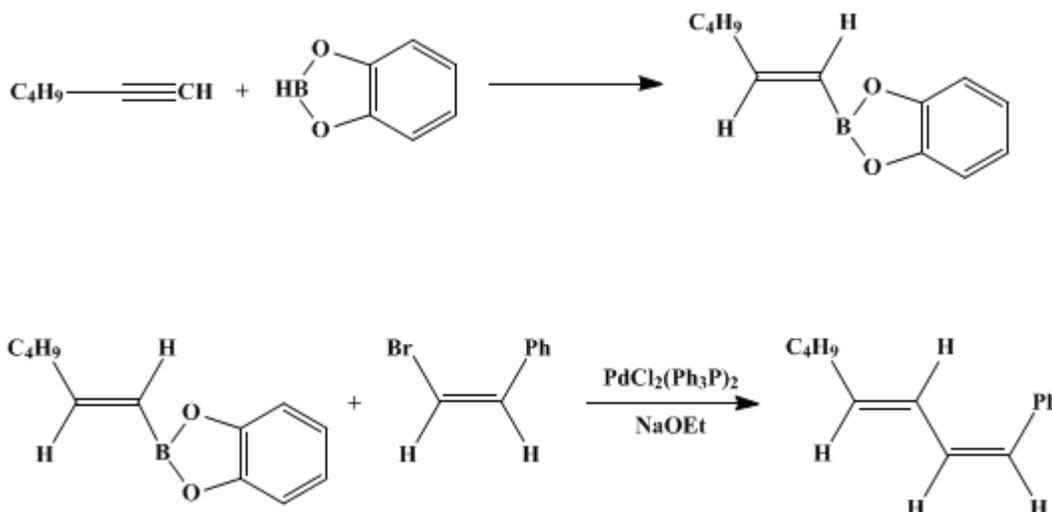
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 8, p.532 (1993); Vol. 68, p.130 (1990).

PALLADIUM-CATALYZED REACTION OF 1- ALKENYLBORONATES WITH VINYLIC HALIDES: (1*Z*,3*E*)-1- PHENYL-1,3-OCTADIENE

[Benzene, 1,3-octadienyl-, (*Z*,*E*)-]



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Discussion Addendum: *Org. Synth.* **2011**, *88*, 202

1. Procedure

A. (*E*)-1-Hexenyl-1,3,2-benzodioxaborole. A 25-mL, three-necked, round-bottomed flask is equipped with a magnetic stirring bar, a thermometer, a rubber septum, a 10-mL addition funnel, and a reflux condenser. The apparatus is connected through the condenser to a nitrogen source and an oil bubbler (Note 1). The flask is charged with 4.9 g (60 mmol) of 1-hexyne (Note 2) through the addition funnel. While the solution is stirred slowly, 6.7 mL (60 mmol) of catecholborane (Note 3) is injected by syringe through the septum cap. The exothermic reaction is maintained at 60–70°C by intermittent cooling in an ice–water bath. The reaction mixture is allowed to cool to room temperature and is stirred for 15 min. The rubber septum is replaced by a glass stopper, and the mixture is heated to 60°C and stirred for an additional 2 hr. The flask is cooled to room temperature, the condenser is replaced by a short-path distillation head, and the mixture is distilled at reduced pressure to give 9.5–10.5 g (78–87%) of clear, colorless product, bp 75–76°C (0.10 mm) [lit.² bp 82°C (0.25 mm)] (Note 4).

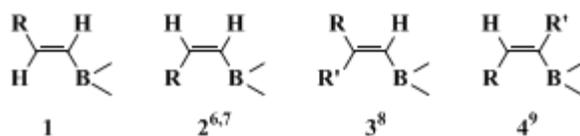
B. (1*Z*,3*E*)-1-Phenyl-1,3-octadiene. A 500-mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar, a reflux condenser to which a nitrogen inlet tube and oil bubbler are attached, a glass stopper, and an addition funnel is flushed with nitrogen and charged with 9.5 g (47 mmol) of (*E*)-1-hexenyl-1,3,2-benzodioxaborole and 200 mL of benzene (Note 5). The solution is stirred and 8.4 g (46 mmol) of (*Z*)-β-bromostyrene (Note 6), 50 mL of 2 M sodium ethoxide in ethanol (Note 7), and finally 0.28 g (0.4 mmol) of dichlorobis(triphenylphosphine)palladium(II) (Note 8) are added. The mixture is refluxed for 3 hr. The light-brown solution containing a white precipitate of sodium bromide is cooled to room temperature, treated with 60 mL of 3 M sodium hydroxide and 6 mL of 30% hydrogen peroxide, and stirred at room temperature for 1 hr (Note 9). The organic layer is separated, washed 4 times with 50 mL of 3 M sodium hydroxide (Note 10), and dried over anhydrous magnesium sulfate. The drying agent is removed by filtration and the filtrate is concentrated on a rotary evaporator. The residual oil is distilled under reduced pressure (Note 11) to give 7.0 g (82%) of (1*Z*,3*E*)-1-phenyl-1,3-octadiene as a clear, colorless liquid, bp 80°C (0.15 mm) (Note 12).

2. Notes

1. All glassware was predried in an oven at 130°C for 3 hr, assembled while hot, and allowed to cool under a stream of nitrogen.
2. The preparation of 1-hexyne is described in *Org. Synth., Coll. Vol. IV*, 1963, 117. The checkers obtained 1-hexyne from Aldrich Chemical Company, Inc., and distilled it prior to use.
3. Catecholborane (1,3,2-benzodioxaborole) with a purity of 95% was purchased from Aldrich Chemical Company, Inc. and purified by distillation under nitrogen, bp 58°C (52 mm). For the distillation and handling of air and moisture-sensitive compounds, see ^{3,4,5}. Catecholborane is a liquid at room temperature, and the neat material is 9.0 M in catecholborane.³ The preparation of catecholborane from borane and catechol has been reported.³
4. The submitters report bp 86–87°C (0.3 mm). (*E*)-1-Hexenyl-1,3,2-benzodioxaborole is quite air-stable, but it can slowly hydrolyze to boronic acid and turn brown on repeated use in air. The submitters recommend storing it at refrigerator temperature in a bottle purged with nitrogen and capped with a rubber septum. Alternatively, the crude 1-hexenyl-1,3,2-benzodioxaborole can be used the next coupling reaction without purification. In this case, the unreacted 1-hexyne should be removed under reduced pressure (0.1 mm for 30 min), because it also reacts with (*Z*)- β -bromostyrene to afford (1*Z*)-1-phenyl-1-octen-3-yne. In this manner the expected diene was obtained in a yield of 86%.
5. Benzene was obtained from Fisher Scientific Company and redistilled before use.
6. (*Z*)- β -Bromostyrene was prepared by the procedure described in *Org. Synth., Coll. Vol. VII*, 1990, 172.
7. The sodium ethoxide solution was prepared by dissolving 2.3 g of sodium in 50 mL of anhydrous ethanol and was used immediately.
8. The palladium catalyst is prepared as follows. A 100-mL, one-necked, round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser connected to a nitrogen inlet is flushed with nitrogen and charged with 1.00 g (5.64 mmol) of palladium chloride (Johnson Matthey, Inc.), 3.25 g (12.4 mmol) of triphenylphosphine (Aldrich Chemical Company, Inc.), and 30 mL of benzonitrile (Aldrich Chemical Company, Inc.). The mixture is stirred, gradually heated to 180°C, and held at that temperature for 20 min. The clear, red solution that results is allowed to cool slowly to room temperature and stand overnight. The bright-yellow crystals that precipitate are collected by filtration, washed with three 10-mL portions of ether, and dried at reduced pressure to give 3.90 g (5.55 mmol) of dichlorobis(triphenylphosphine)palladium(II).
9. This operation removes most of the palladium-containing compounds. Any unreacted 1-hexenylboronate is oxidized to hexenal.
10. Catechol must be washed out completely because it is difficult to remove by distillation. A solution of catechol in aqueous sodium hydroxide turns dark brown on treatment with hydrogen peroxide or on standing in air.
11. The residual oil can be purified before distillation by filtering it through a short (20-cm) silica gel column (70–230 mesh) using hexanes as an eluant. This effectively removes traces of catechol and palladium-containing compounds.
12. Gas chromatographic analysis of the product (Hewlett-Packard fused silica, crosslinked, methylsilicone capillary column, 25 m \times 20 mm, column temperature 100–270°C, injection temperature 250°C) shows that the product is over 99% chemically and isomerically pure. (*Z,E*)-1-Phenyl-1,3-octadiene shows the following spectral properties: IR (neat) cm^{-1} : 1640, 1595, 1490, 985; ¹H NMR (CDCl_3) δ : 0.89 (t, 3 H, $J = 7.1$), 1.25–1.45 (m, 4 H), 2.05–2.20 (m, 2 H), 5.87 (d of t, 1 H, $J = 7.1$, 15, $\text{PhC}=\text{C}=\text{CH}$), 6.21 (d of d, 1 H, $J = 11.2$, 11.6, $\text{PhC}=\text{CH}$), 6.30 (d, 1 H, $J = 11.6$, $\text{PhCH}=\text{C}$), 6.60 (d of d, 1 H, $J = 11.2$, 15, $\text{PhC}=\text{C}-\text{CH}=\text{C}$), and 7.15–7.40 (m, 5 H, aromatic).

3. Discussion

The procedure described here is an example of a general method for preparing conjugated alkadienes by the palladium-catalyzed reaction of 1-alkenylboranes or boronates with vinylic halides. Hydroboration of 1-alkynes with catecholborane is a standard method for obtaining (*E*)-1-alkenylboronates (**1**).^{2,3} Several different types of alkenylboranes and boronates (**2–4**) are now available as reagents for the cross-coupling reaction with vinyl halides.



These alkenylboron derivatives react not only with 1-alkenyl halides but also with a variety of other organic halides, including 1-bromo-1-alkynes,⁶ aryl halides,^{7,8,9} and allylic or benzylic halides,¹⁰ in the presence of a palladium catalyst and base. Both Pd(PPh₃)₄ and PdCl₂(PPh₃)₂ are excellent catalysts for most of the reactions. A base is generally required for successful coupling. Sodium ethoxide (2 equiv) in ethanol–benzene, which is used in the procedure described here, gives high yields with most 1-bromo-1-alkenes. For 1-iodo-1-alkenes, aqueous sodium hydroxide in tetrahydrofuran¹¹ or aqueous 4 M potassium hydroxide (3 equiv) in benzene⁸ can give better results. Alkoxides and hydroxides normally accelerate the reaction, but the choice of base depends on its compatibility with the particular organic halide. For the coupling reaction with 3-halo-2-cyclohexen-1-one¹² a relatively weak base, such as sodium acetate in methanol, works well. The reaction with 1-bromo-2-phenylthio-1-alkenes¹³ is successfully carried out using aqueous potassium hydroxide. For the reaction of (*E*)-2-ethoxyvinylborane with aryl halides,¹⁴ a suspension of sodium hydroxide in tetrahydrofuran gives better results than homogeneous base. The versatility of these methods has been reviewed.^{15,16}

In addition to alkenylboron compounds, alkenylalane,^{17 18 19} alkenylzirconium,^{20 21} alkenyltin,²² alkenylcopper,^{23 24} and alkenylmagnesium²⁵ reagents are reported to undergo a related alkenyl–alkenyl coupling reaction to give 1,3-alkadienes.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

(E)-1-alkenylboronates

ethanol (64-17-5)

Benzene (71-43-2)

methanol (67-56-1)

ether (60-29-7)

sodium acetate (127-09-3)

benzotrile (100-47-0)

sodium hydroxide (1310-73-2)

sodium bromide (7647-15-6)

nitrogen (7727-37-9)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

palladium (7440-05-3)

Catechol (120-80-9)

hydrogen peroxide (7722-84-1)

palladium chloride (7647-10-1)

magnesium sulfate (7487-88-9)

borane (7440-42-8)

Tetrahydrofuran (109-99-9)

1-Hexyne (693-02-7)

triphenylphosphine (603-35-0)

CATECHOLBORANE,

1,3,2-benzodioxaborole (274-07-7)

(Z)- β -Bromostyrene (103-64-0)

dichlorobis(triphenylphosphine)palladium(II) (13965-03-2)

1-hexenyl-1,3,2-benzodioxaborole

1-hexenylboronate

hexenal

(1Z,3E)-1-Phenyl-1,3-octadiene,
(Z,E)-1-Phenyl-1,3-octadiene (39491-66-2)

Benzene, 1,3-octadienyl-, (Z,E)- (39491-66-2)

(E)-1-Hexenyl-1,3,2-benzodioxaborole (37490-22-5)

(1Z)-1-phenyl-1-octen-3-yne

(E)-2-ethoxyvinylborane