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Title	PALLADIUM(0)-CATALYZED REACTION OF 9-ALKYL-9-BORABICYCLO[3.3.1]NONANE WITH 1-BROMO-1-PHENYLTHIOETHENE: 4-(3-CYCLOHEXENYL)-2-PHENYLTHIO-1-BUTENE
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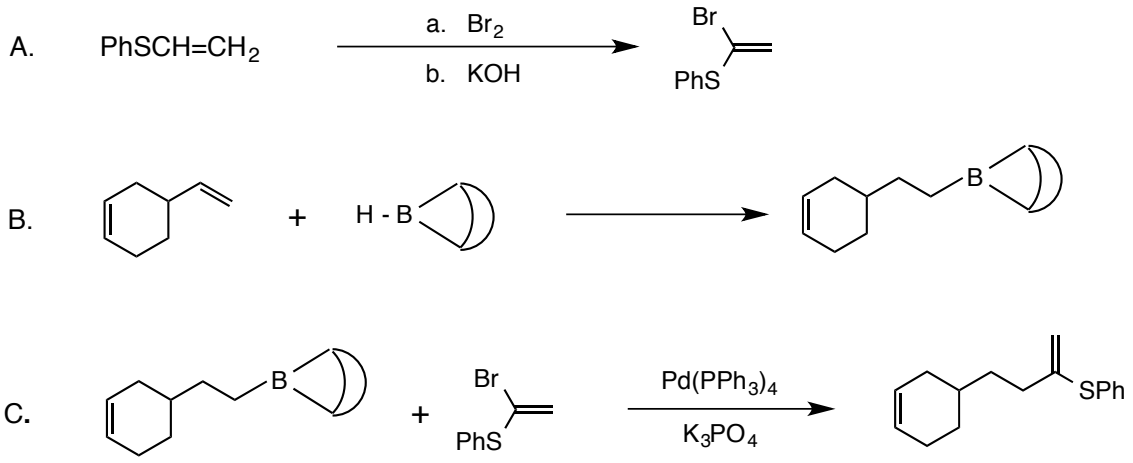
Palladium(0)-Catalyzed Reaction of 9-Alkyl-9-borabicyclo-[3.3.1]nonane with 1-Bromo-1-phenylthioethene: 4-(3-Cyclohexenyl)-2-phenylthio-1-butene



Submitted by Tatsuo Ishiyama, Norio Miyaura, and Akira Suzuki.1

1. Procedure

A. 1-Bromo-1-phenylthioethene. A 300 mL, two-necked, round-bottomed flask is fitted with a magnetic stirring bar, a pressure-equalizing dropping funnel, and a reflux condenser to which a nitrogen inlet tube and an oil bubbler are attached, is flushed with nitrogen. In the flask are placed 13.6 g (100 mmol) of phenyl vinyl sulfide (Note 1) and 80 mL of ether (Note 2), and then cooled to ca. -78°C with a dry ice-methanol bath. Bromine (16.0 g, 100 mmol) is added dropwise over 30 min to the stirred solution. After warming up to room temperature, 40 mL of absolute ethanol, followed by a solution of 8 g (143 mmol) of potassium hydroxide in 80 mL of absolute ethanol are added dropwise to the resulting slightly red solution over 30 min. The light brown solution containing white precipitate of potassium bromide is stirred at room temperature for 2 hr. The precipitate is filtered off and the solvent is removed thoroughly by rotary evaporation. The residue is treated with 200 mL of ether and 200 mL of water. Then, the organic layer is separated, washed with brine (50 mL), and dried over anhydrous magnesium sulfate. After the evaporation of solvent by rotary evaporation, the residual oil is distilled under reduced pressure to give 17.2 g (80 %) of 1-bromo-1-phenylthioethene (Note 3) as a colorless liquid, bp 49-50° C (0.07 mm).

B. 9-[2-(3-Cyclohexenyl)ethyl]-9-BBN. A 500 mL, three-necked, round-bottomed flask is equipped with a magnetic stirring bar, a thermometer, a reflux condenser, a pressure-equalizing addition funnel capped with rubber septum. The apparatus is connected through the condenser to a nitrogen source and an oil bubbler and flushed with nitrogen (Note 4). The flask is charged with 35 ml of tetrahydrofuran (Note 5) and 8.32 g (77 mmol) of 4-vinyl-1-cyclohexene (Note 6) and cooled to 0。C. While stirring, a 0.5 M solution of 9-BBN in tetrahydrofuran (154 mL, 77 mmol)(Note 7) which is transferred via cannula to the addition funnel is added dropwise over 1 hr maintaining the temperature at 0 to 5。C. The reaction mixture is stirred for 1 hr at 0。C and for 1.5 hr at room temperature. The solution obtained is used in the next step without further treatment (Note 8).

C. 4-(3-Cyclohexenyl)-2-phenylthio-1-butene. To the above solution of the borane derivative, 0.809 g (0.70 mmol) of tetrakis(triphenylphosphine)palladium(0) (Note 9), 1.47 g (5.6 mmol) of triphenylphosphine (Note 10), 35 ml of 3 M potassium phosphate in water (Note 11), and finally 15.1 g (70 mmol) of 1-bromo-1-phenylthioethene are added and the resulting mixture is refluxed for 3 hr under stirring. The light brown solution is cooled to room temperature and treated with 6.4 g (105 mmol) of ethanolamine (Note 12) for 1 hr. Then, 100 mL of hexane and 100 mL of water are added. The organic layer is separated, washed with 100 mL of water, and dried over anhydrous magnesium sulfate. The drying agent is removed by filtration and the filtrate is concentrated by rotary evaporation. The addition of 100 mL of hexane to the residual viscous oil containing some solid precipitates the 9-BBN/ethanolamine complex. The solid is filtered off, washed with hexane (50 mL X 3), and the solvent is removed on a rotary evaporator. The crude product is passed through a short silica gel column (60-200 mesh, 60 g) using hexane as an eluent (Note 13). After removal of the hexane, the residue is distilled under reduced pressure to give 13.9 g (81%) of 4-(3-cyclohexenyl)-2-phenylthio-1-butene as colorless liquid, bp 114-116。C (0.04 mm) (Note 14).

2. Notes

1. The preparation of phenyl vinyl sulfide is described in Org. Synth. 1985, 64, 157. The compound is also available from Aldrich Chemical Company, Inc.

2. Ether was distilled from benzophenone ketyl under nitrogen before use.

3. The product is labile at room temperature and should be stored in freezer.

4. All glasswares were pre-dried in an oven at 120。C for 2hr, assembled while hot, and allowed to cool under a stream of nitrogen.

5. Tetrahydrofuran is distilled from benzophenone ketyl under nitrogen before use.

6 4-Vinyl-1-cyclohexene was obtained from Aldrich Chemical Company, Inc., and distilled it prior to use.

7. A 0.5 M solution of 9-BBN in tetrahydrofuran was purchased from Aldrich Chemical Company, Inc., and was used without additional purification. The preparation2 of the reagent by hydroboration of 1,5-cyclooctadiene with borane/tetrahydrofuran complex is reported.

8. If necessary, 9-[2-(3-cyclohexenyl)ethyl]-9-BBN3 can be purified by removal of the solvent and vacuum distillation under nitrogen [bp 103。C (0.035 mm)].

9. The preparation of tetrakis(triphenylphosphine)palladium(0) is described in Inorg. Synth., 1972, 13, 121. It is also available from Aldrich Chemical Company, Inc.

10. Triphenylphosphine was obtained from Nakarai Chemicals, Japan. When the reaction is carried out without additional triphenylphosphine, the yield of coupling product may reduce to 60-70% accompanying by-products, phenyl vinyl sulfide and 4-vinyl-1-cyclohexene, derived from b-hydride elimination.

11. The solution is prepared by dissolving 22.3 g (105 mmol) of potassium phosphate (Nakarai Chemicals, Japan) in water and final volume is adjusted to 35 mL. Although our original method4 used sodium hydroxide as a base, potassium phosphate will be desirable for the extention of the present procedure for the base sensitive compounds. Under such conditions, the reaction with 9-(10-carbo-methoxydecanyl)-9-BBN proceeds similarly without saponification of ester group.

12. Ethanolamine was purchased from Nakarai Chemicals, Japan. The reagent reacts with the resulting 9-BBN residue to give an air stable 1:1 adduct5 which is insoluble in hexane.

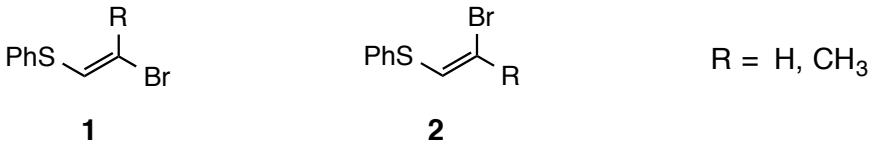
13. This operation effectively removes the remaining palladium-containing compounds, phosphine derivatives, and borane residue.

14. Gas chromatographic analysis of the product (Finnigan ITD 800 fused silica capillary, SE 30 column, 0.35 mm X 25 m, column temperature 80-250。C, injection temperature 250。C) shows that the chemical purity is 98.5 %. The spectral data are follows: IR (neat) cm-1: 3030, 2920, 1615, 1590, 1480, 1440, 750, 690; 1H NMR (CDCl3, TMS) d: 1.00-1.90 (m,

6H), 1.90-2.20 (m, 3H), 2.20-2.50 (m, 2H), 4.88 (s, 1H), 5.15 (s, 1H), 5.64 (s, 2H), 7.20-7.50 (m, 5H). The product suffers deterioration at room temperature and should be stored in freezer.

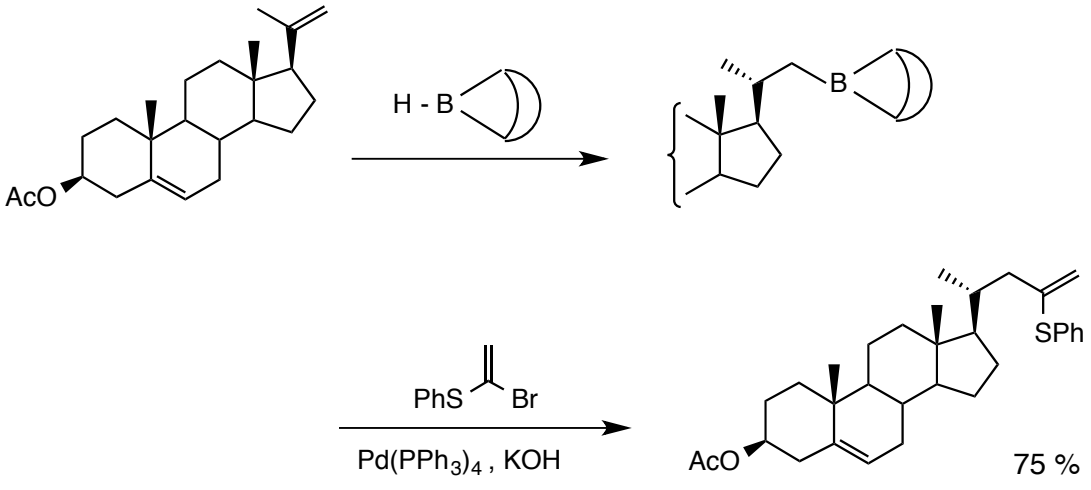
3. Discussion

The reaction described here is an attractive method for the synthesis of alkenyl sulfides via the cross-coupling reaction4 of 9-alkyl-9-BBN with bromo(phenylthio)ethenes induced by palladium catalyst. Bromo(phenylthio)ethene has several advantages in terms of its practical use for cross-coupling reaction. The coupling occurs at the bromine position but no coupling products at the sulfur position are obtained even under conditions using an excess of 9-alkyl-9-BBN which completely avoids the formation of dialkylation products. The reaction is highly stereoselective and readily extended to the coupling with (E)- and (Z)-2-bromo-



1 **2**

1-phenylthio-1-alkene derivatives (1 and 2)6 to afford stereo-defined vinylic sulfides. The generality of the present method was demonstrated by the stereoselective hydroboration of a side chain of steroid, followed by the cross-coupling reaction.



The reactions7 of (E)-, (Z)-1-alkenyl, or 1,3-alkadienylboronic esters with 1 or 2 provide simple routes for stereoselective syntheses of 1,3-alkadienyl and 1,3,5-alkatrienyl phenyl sulfides.

Not only boron derivatives, but also Grignard reagents8 are reported to undergo a related coupling reaction with bromo-(phenylthio)ethene derivatives. Other methods reported for the synthesis of alkenyl sulfides are condensation of carbonyl compounds with 1-methylthioalkylphosphonate esters9 or alkylthio-methyl(trimethyl)silane10, addition11 of organothioalkoxides to alkynes, reduction12 of 1-alkynyl sulfides with metal hydride reagents, and substitution13 of 1-bromo-1-alkenes with sulfur reagents. However, most of these methods may lead to a mixture of geometrical isomers, the separation of which is difficult.

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