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A STEREOSELECTIVE ROUTE TO ALKENYL SULFIDES THROUGH THE PALLADIUM-CATALYZED CROSS-COUPLING REACTION OF 9-ALKYL-9-BBN WITH 1-BROMO-1-PHENYLTHIOETHENE OR (E)- AND (Z)-2-BROMO-1-PHENYLTHIO-1-ALKENES

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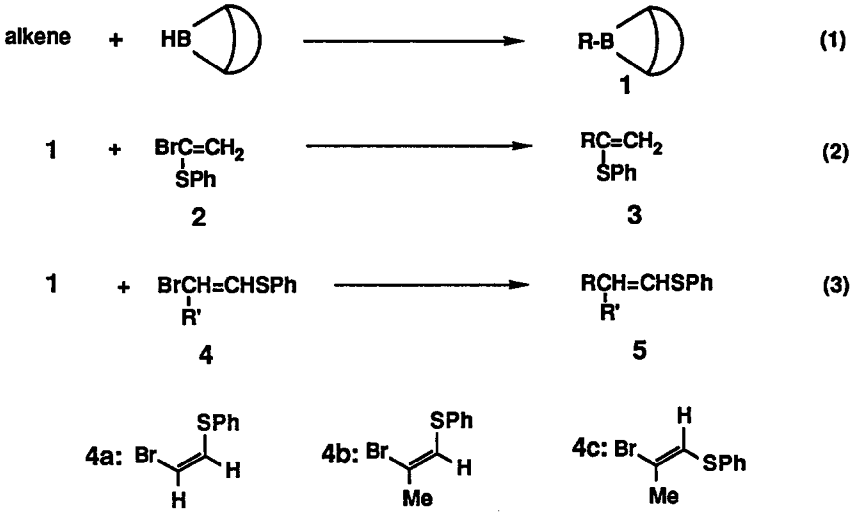
Summary: The reaction of 9-alkyl-9-BBNs with 1-bromo-1-phenylthioethene or (E)- and (Z)-2-bromo-1-phenylthio-1-alkenes takes place readily in the presence of $Pd(PPh_3)_4$ and sodium hydroxide to afford stereodefined vinylic sulfides in excellent yields.

Elegant synthetic studies by Naso and his co-workers[1] have demonstrated the potential usefulness of (E)- and (Z)-1-bromo-2-phenylthioethenes as efficient building blocks for the synthesis of stereodefined double bonds by sequential cross-coupling reaction with Grignard reagents. Such bromo(phenylthio)-ethenes have several advantages in terms of their practical use for cross-coupling reactions. The rate of coupling with the carbon-bromine bond is reasonably faster than that with the carbon-sulfur bond which completely avoids the formation of symmetrical coupling product. (E)- and (Z)-2-Bromo-1-phenylthio-1-alkenes[2] are readily available and most importantly, both stereoisomers are easily separable by chromatography. We report here a cross-coupling reaction of 9-alkyl-9-borabicyclo[3.3.1]nonanes (9-R-9-BBN) with these bromo(phenylthio)alkenes (**2** and **4**) to afford vinylic sulfides (**3** and **5**)[3], stereoselectively, as depicted in Eqs. 2 and 3. Vinylic sulfides are synthetically equivalent to carbonyl groups[4] and converted to the stereodefined alkenes by the nickel-catalyzed cross-coupling reactions with alkyl, aryl, and alkenyl Grignard reagents[5], respectively.

We have reported previously[6] that alkylboranes can be cross-coupled with aryl and 1-alkenyl halides in the presence of a catalytic amount of $PdCl_2(dppf)$ and base such as aqueous sodium hydroxide. The same procedure was extended to the bromo(phenylthio)alkenes, but unsatisfactory results were obtained. For instance, the reaction of 9-octyl-9-BBN with 1-bromo-1-phenylthioethene (**2**) in the presence of 3 mol% of $PdCl_2(dppf)$ and aqueous sodium hydroxide gave 2-phenylthio-1-decene in only 21%. Presumably, the step of reductive elimination or transmetallation might be retarded by intramolecular coordination[7] of sulfur to palladium. However, when $Pd(PPh_3)_4$ was employed as a catalyst, the yield of 2-phenylthio-1-decene was improved to 87 %. The conditions were also suitable for 2-bromo-1-phenylthio-1-alkenes (**4a-c**) (Eq. 2), to give the corresponding coupling products (**5a**, **5b**, and **5c**: R=octyl) in yields of 96, 85, and 90%, respectively.

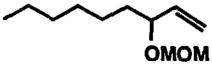
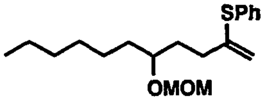
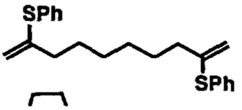
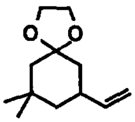
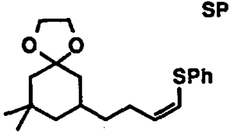
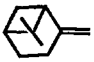
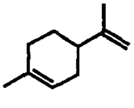
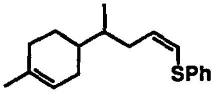
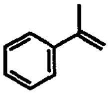
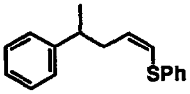
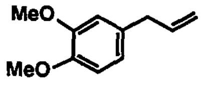
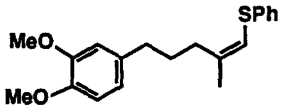
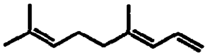
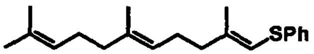
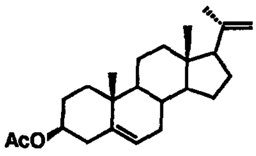
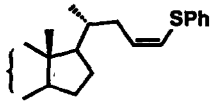
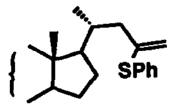


The results of the coupling reaction between a variety of bromo(phenylthio)alkenes (**2** and **4**) and 9-alkyl-9-BBNs (**1**) obtained in situ by hydroboration of alkenes are summarized in Table 1.

The following observation and interpretations may be worth noting. (1) The cross-coupling in each case occurs regioselectively at the bromine position and no coupling products at the sulfur position were obtained even under conditions using an excess of 9-alkyl-9-BBNs or a prolonged reaction. (2) The reaction proceeds via retention of configuration and isometrically pure vinylic sulfides were obtained without any difficulty. The isomeric purity in each case exceeds 98%. (3) The present reaction take place only with primary alkyl-9-BBNs and was not utilized for secondary alkyl-9-BBNs.[8] Although the coupling reaction of alkyl groups having sp^3 carbon containing β-hydrogens have been severely limited due to the competitive side reactions caused by β-hydride elimination[9], the isomerization of alkyl groups or the formation of alkenes did not take place here. However, in one case, an isomerized coupling product was obtained. Namely, the reaction of 9-(2-phenylpropyl)-9-BBN with **2** gave 3-phenyl-2-phenylthio-1-pentene (41%), contaminated with 3-methyl-3-phenyl-2-phenylthio-1-butene (31%) which may be formed by the apparent isomerization of palladium to the benzylic carbon[10] before reductive elimination, whereas the same reaction with **4a** gave a normal coupling product (Entry 6). (5) The reaction can be extended readily to the relatively large alkenes such as a side chain of steroid (Entries 9 and 10).

Representative procedure. To a solution of β-pinene (2 mmol) in THF (1 ml) was added a solution of 9-BBN (4.2 ml of 0.5M solution in THF, 2.1 mmol)[11] at 0 °C. The mixture was warmed up slowly to room temperature, and then was stirred for 3 h to give a solution of 9-(pina-10-yl)-9-BBN. Benzene (12 ml), $Pd(PPh_3)_4$ (0.06 mmol), (Z)-1-bromo-2-phenylthioethene (2.2 mmol), and an aqueous sodium

Table 1. Synthesis of Vinylic Sulfides.

Entry	Alkene	2 or 4	Product	Yield(%)[a]
1		2		64
2		2		64[b]
3		4a		81
4		4a		73
5		4a		90[c]
6		4a		89
7		4b		85
8		4c		78
9		4a		89[d]
10		2		75[d]

a) Isolated yields based on alkenes employed. b) Two equivs of 9-BBN and 2 were used. c) A 50% excess of limonene against 9-BBN and 4a was used, and the yield was based on 4a. d) During the coupling reaction, a part of 3-acetoxy group was saponificated. Therefore the mixture was reacetylated with acetic anhydride and pyridine before isolation.

hydroxide solution (2 ml of 3M solution) were added, and then the mixture was refluxed for 5 h. After the reaction was completed, the reaction mixture was diluted with hexane, and the organic phase was separated and dried over $MgSO_4$. The product was isolated by chromatography over silica gel with hexane to give a oil, 0.399 g (73 %). The assigned (Z) configuration was confirmed by the magnitude (J=9.23 Hz)[1b] of the coupling constant of two olefinic protons (δ, 5.80 and 6.20) and by the absence of a band at 955 cm^{-1} in the IR spectrum[1b].

Reference and Notes

1. (a) E. Fiandanese, G. Marchese, F. Naso, and L. Ronzini, J. Chem. Soc., Chem. Commun., 647 (1982); (b) J. Chem. Soc., Perkin Trans. 1, 1115 (1985).
2. E. Angeletti, F. Motanari, and A. Negrini, Gazz. Chem. Ital., **87**, 1086 (1957), and see also references 1b and 3.
3. We reported previously the synthesis of conjugated 1-phenylthio-1,3-alkadienes or 1,3,5-alkatrienes by the cross-coupling reaction of 1-alkenylboron compounds with **2** or **4**; T. Ishiyama, N. Miyaura, and A. Suzuki, Chem. Lett., 25 (1987).
4. E. J. Corey, B. W. Erickson, and R. Noyori, J. Am. Chem. Soc., **93**, 1724 (1973); H. Takahashi, K. Oshima, H. Yamanoto, and H. Nozaki, ibid., **95**, 5803 (1973); B. M. Trost, K. Hiroi, and S. Kurozumi, ibid., **97**, 438 (1975); A. J. Mura, D. A. Benett, and T. Cohen, Tetrahedron Lett., 4433 (1975); A.J. Mura, G. Majetich, P. A. Grieco, and T. Cohen, ibid., 4437 (1975).
5. H. Okamura, M. Mita, and H. Takei, Tetrahedron Lett., 43 (1979); E. Wenkert, T. W. Ferreira, and E. L. Michelott, J. Chem. Soc., Chem. Commun., 637 (1979); E. Wenkert, and T. W. Ferreira, ibid., 840 (1982); E. Wenkert, M. H. Leftin, and E. L. Michelotti, ibid., 617 (1984); Y. Ikeda, K. Furuta, N. Meguriya, N. Ikeda, and H. Yamamoto, J. Am. Chem. Soc., **104**, 7663 (1982); Y. Ikeda, J. Ukai, N. Ikeda, and H. Yamamoto, Tetrahedron, **43**, 731 (1987).
6. N. Miyaura, T. Ishiyama, M. Ishikawa, and A. Suzuki, Tetrahedron Lett., **27**, 6369 (1986).
7. G. Yoshida, H. Kurosawa, and R. Okawara, J. Organomet. Chem., **113**, 85 (1976); T. Chivers, and P. L. Timmes, ibid., **118**, C37 (1976); K. Miki, Y. Kai, N. Yasuoka, and N. Kasai, ibid., **135**, 53 (1977); The reaction between **4** and R-9-BBNs may proceed more readily than **2**.
8. Although we have found most recently that the reaction of sec-alkylboron compounds such as tricyclohexyl or tri(2-butyl)boranes with iodobenzene affords sec-alkylbenzenes in moderate yields under some conditions, the reactions with **2** and **4** under such conditions were failed.
9. T. Hayashi, M. Konishi, Y. Kobori, M. Kumada, T. Higuchi, and K. Hirotsu, J. Am. Chem. Soc., 106, 158 (1984) and references cited therein.
10. R. F. Heck,"Palladium Reagents in Organic Syntheses" , Academic Press, New York (1985).
11. 9-BBN in THF is a commercial product from Aldrich Chem. which was used without further purification.

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