# Convenient One-Pot Synthesis of Vinylic Sulfides from Thioalkynes via a Catalytic Hydroboration–Coupling Sequence

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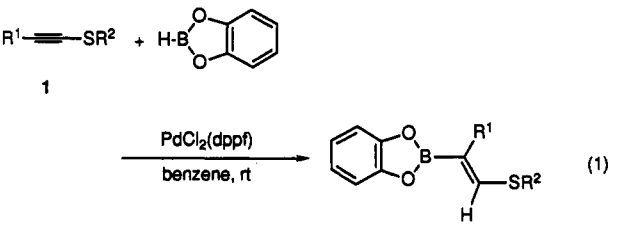
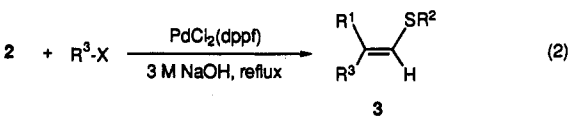
A variety of vinylic sulfides are stereospecifically synthesized by the catalytic hydroboration of thioacetylenes with catecholborane followed by cross-coupling of the resulting boron derivatives with organic halides. The use of the same palladium catalyst for both stages allows the whole transformation to be carried out in one flask. The synthetic utility of the method is demonstrated by the transformation of vinylic sulfides into diene, indole, and naphtho[*b*]furan derivatives.

1-Alkenyl sulfides are valuable precursors for the synthesis of ketones or aldehydes by hydrolysis with mercury(II) chloride,[1] the synthesis of 1-alkenyl sulfoxides[2] (which can serve as dienophiles in the Diels–Alder reaction or as Michael acceptors), and the synthesis of a variety of alkenes and dienes *via* the nickel-catalyzed cross-coupling reaction of the C–S bond with Grignard reagents.[3] However, there are only a few stereoselective syntheses of 1-alkenyl sulfides. The coupling reactions of 1-alkenyl halides with metal thioalkoxides in the presence of a transition-metal catalyst provide vinylic sulfides in excellent yields with high stereoselectivity.[4] Another route to vinylic sulfides involves cross-coupling reactions between β-(alkylthio)alkenyl halides and organometallic reagents such as alkyl, aryl, and 1-alkenylmagnesium[5] or boron[6] reagents. These routes, however, require stereodefined alkenyl halides, which cannot always be obtained with high stereoselectivity.

We now wish to report a one-pot, two-step procedure that allows the synthesis of stereodefined 1-alkenyl sulfides with various structures. The method demonstrates the synthetic utility of two novel reactions from our group: the catalytic hydroboration of thioalkynes (eq 1)[7] and the cross-coupling reaction of 1-alkenylborane compounds with organic halides (eq 2);[8] both of which are catalyzed by a palladium complex.




## Discussion

We have found that $NiCl_2$(dppe) and $NiCl_2$(dppf) are the most effective catalysts for the hydroboration of thioacetylenes with catecholborane (1,3,2-benzodioxaborole).[7] However, the nickel catalyst does not allow the hydroboration and cross-coupling reactions to take place in the same flask since nickel complexes are not effective for the cross-coupling reactions of **2** with organic halides. Our results also indicate that phosphine-based palladium complexes, such as $Pd(PPh_3)_4$ and $PdCl_2$(dppf), are good catalysts for the hydroboration of thioacetylenes. Although the palladium-catalyzed hydroboration is slower than the nickel-catalyzed reaction, these palladium catalysts are sufficiently effective to permit the preparation of quantitative yields of **2** after an overnight reaction period. The use of either one of these palladium complexes provides the same synthetic efficiency for both stages; however, $PdCl_2$(dppf) provides slightly higher yields of the sulfides than does $Pd(PPh_3)_4$.

The use of base is essential for the boron cross-coupling reaction.[8] The coupling proceeds smoothly in benzene in the presence of 3 equiv of aqueous sodium hydroxide and the 3 mol % of palladium catalyst used for the hydroboration stage. Although the C–B bonds of vinylic boronates are usually insensitive to protonolysis with an aqueous base, the protonolysis of **2** occurs to some extent on prolonged heating. The use of a two-phase system and the preparation of **2** from 2 equiv of the thioalkyne are sufficient to completely consume the organic halide coupling partner. However, the cross-couplings of some boron derivatives **2** having a phenyl or vinyl group on the α carbon to boron were unsuccessful because of extremely fast protodeboronation with aqueous base.

Representative syntheses of vinylic sulfides are summarized in Table I. Although the sequence of hydrobo-

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(1) Trost, B. M.; Hiroi, K.; Kurozumi, S. *J. Am. Chem. Soc.* **1975**, *97*, 438–440.

(2) Durst, T. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ed.; Pergamon Press: Oxford, 1979; Vol. 3, pp 121–156.

(3) (a) Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* **1979**, 43–46. (b) Wenkert, E.; Ferreira, T. W.; Michelott, E. L. *J. Chem. Soc. Chem. Commun.* **1979**, 637–638 and ref 5.

(4) (a) Murahashi, S.; Yamamoto, M.; Yanagisawa, K.-i.; Mita, M.; Kondo, K. *J. Org. Chem.* **1979**, *44*, 2408–2417. (b) FOA, M.; Santi, R.; Garavaglia, F. *J. Organomet. Chem.* **1981**, *206*, C29–C32.

(5) (a) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, J. *J. Chem. Soc. Chem. Commun.* **1982**, 647–649. (b) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, J. *J. Chem. Soc. Perkin Trans. 1* **1985**, 1115–1119.

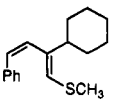
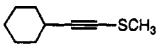
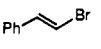
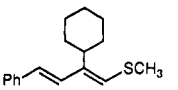
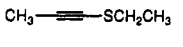
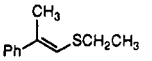
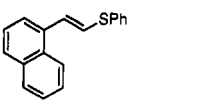
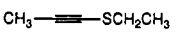
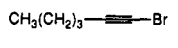
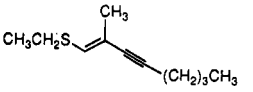
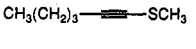
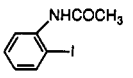
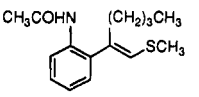
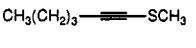
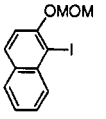
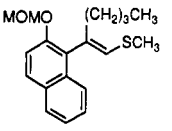
(6) (a) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1987**, 25–28. (b) Hoshino, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1988**, *29*, 3983–3987. (c) Ishiyama, T.; Miyaura, N.; Suzuki, A. *Org. Synth.* **1992**, *71*, 89–95.

(7) Gridnev, I. D.; Miyaura, N.; Suzuki, A. *Organometallics* **1993**, *12*, 589–592.

(8) (a) Miyaura, N.; Yamada, Y.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972–980. (b) Miyaura, N.; Maeda, K.; Suginome, H.; Suzuki, A. *J. Org. Chem.* **1982**, *47*, 2117–2120. (c) Satoh, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1986**, 1329–1332. (d) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314–321. (e) Suzuki, A. *Pure Appl. Chem.* **1985**, *57*, 1749–1758. (f) Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419–422.

0022-3263/93/1958-5351$04.00/0 

**Table I. One-Pot Synthesis of Alkenyl Sulfides[a]**

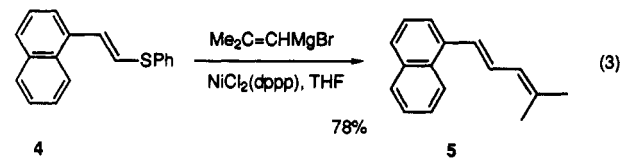
| entry | thioacetylene | halide | product | yield, %[b] |
|---|---|---|---|---|
| 1 |  |  |  | 85 |
| 2 |  |  |  | 72 |
| 3 |  | Ph-I |  | 90 |
| 4 |  |  |  | 90[c] |
| 5 |  |  |  | 73 |
| 6 |  |  |  | 80 |
| 7 |  |  |  | 71 |

[a] The catalytic hydroboration of thioalkyne (2 equiv) with catecholborane (2 equiv) in the presence of $PdCl_2$(dppf) (3 mol %) was followed by the cross-coupling reaction with an organic halide (1 equiv). [b] Isolated yields based on the amount of organic halide used. [c] The Ni-catalyzed hydroboration was followed by cross-coupling with a Pd catalyst; see the text.

ration of thioalkynes with catecholborane followed by cross-coupling with either vinyl-, aryl-, or alkynyl halides can be successfully used for the synthesis of vinyl sulfides, the hydroboration of terminal alkynes with the palladium catalyst fails to provide **2**. Thus, the synthesis shown in entry 4 is the only reaction that requires the isolation of boron intermediate **2** which was prepared by the $NiCl_2$(dppp)-catalyzed hydroboration reaction.[7] The catalytic hydroborations of thioacetylenes proceed regio- and stereospecifically through syn-addition with the boron atom adding adjacent to the carbon $\beta$ to sulfur. This configuration is conserved during the cross-coupling reaction with aryl, alkynyl, or vinylic halides. The stereochemistry of the vinylic halides is also retained during this stage (entries 1 and 2). The cross-coupling with 2-aminoiodobenzene is very slow, presumably because of the formation of a stable N–Pd chelate in the oxidative adduct, but the corresponding acetamide produces a high yield of the coupling product (entry 6).

In order to demonstrate the synthetic utility of the vinylic sulfides thus prepared, we have carried out further synthetic transformations of these compounds. For example, the coupling reaction of vinylic sulfides and alkyl, aryl, and 1-alkenylmagnesium reagents in the presence of a nickel catalyst is known to provide good yields of the corresponding alkenes or polyenes.[3] Thus, the reaction of sulfide **4** and (2-methylpropenyl)magnesium bromide in the presence of $NiCl_2$(dppp) gives **5** in 78% yield (eq 3).

The vinylic sulfide is synthetically equivalent to a carbonyl compound.[1] The use of aromatic halides having an *o*-acetylamino or a protected hydroxy group for the present coupling reaction provides valuable precursors for heterocyclic compounds. Vinylic sulfide **6** is readily converted into *N*-acetyl-3-butylindole (**7**) in 82% yield by treatment with mercury(II) chloride (eq 4).



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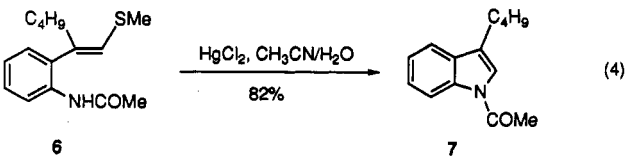
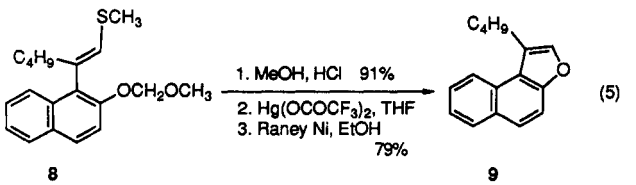


(4)

Analogously, compound **8** can be easily converted to the corresponding naphtho[*b*]furan **9** by treatment with mercury(II) trifluoroacetate (eq 5). The MOM group is removed before the cyclization with mercury(II) trifluoroacetate since the direct cyclization of **8** with $HgX_2$ (X = Cl, OAc, $OCOCF_3$) is unsuccessful. The cyclization product is contaminated with an appreciable amount of 3-butyl-2-(methylthio)naphtho[*b*]furan. However, treat-



(5)

ment of the crude reaction mixture with excess of Raney nickel[9] furnishes **9** in 79% yield.

In conclusion, the sequence of catalytic hydroboration of thioalkynes followed by cross-coupling of the resulting boron derivatives with organic halides provides a new method for the synhtesis of various stereodefined vinylic sulfides. Because the simple experimental procedure does not require the isolation of the boron intermediates and allow the synthesis of a wide range of vinylic sulfides using catalytic amounts of the palladium complex, we anticipate additional synthetic applications of our method.

## Experimental Section

For general experimental information, see ref 7.

**Reagents.** Thioacetylenes were prepared from the corresponding sodium acetylides and methyl thiocyanate by the method of Brandsma.[10] The syntheses of tetrakis(triphenylphosphine)palladium(0), dichlorobis[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) [$PdCl_2$(dppf)], dichlorobis[1,3-(diphenylphosphino)propane]nickel(II) [$NiCl_2$(dppp)], dichlorobis[1,2-(diphenylphoshino)ethane]nickel(II) [$NiCl_2$(dppe)] were reported previously.[11-13] Catecholborane (1,3,2-benzodioxaborole) was purified by distillation before use.[14]

**Synthesis of Vinylic Sulfides. Typical Procedure.** The general procedure for the synthesis of vinylic sulfides is illustrated by the synthesis of (1*E*,3*S*)-1-(ethylthio)-2-cyclohexyl-4-phenyl-1,3-butadiene. A flask was charged with $PdCl_2$(dppf) (60 mg) and then flushed with nitrogen. Benzene (10 mL), 1,3,2-benzodioxaborole (0.36 mL, 3.3 mmol), and 1-(methylthio)-1-hexyne (3 mmol) were added. The reaction mixture was stirred at rt overnight (ca. 16 h). (*Z*)-β-Bromostyrene (1.5 mmol) and an aqueous NaOH solution (3 M, 9 mmol) were then added. After being stirred for 2 h at reflux, the mixture was extracted with ether. The organic extract was washed twice with water, dried over $MgSO_4$, and concentrated. The residue was chromatographed to give 0.56 g (72%) of pure vinylic sulfide: NMR $^1$H (400 MHz, $CDCl_3$) δ 1.36 (m, 5 H), 1.76 (m, 5 H), 2.05 (s, 3 H), 2.55 (m, 1 H), 5.74 (d, 1 H, $^4J$ = 1.3 Hz), 6.00 (dd, 1 H, $^3J$ = 11.3 Hz, $^4J$ = 1.3 Hz), 6.35 (d, 1 H, $^3J$ = 11.3 Hz), 7.1–7.5 (m, 5 H); $^{13}$C NMR ($CDCl_3$) δ 17.0 ($CH_3$S), 26.3, 26.6, 30.9 (5 $CH_2$ cyclohex) 41.9 (CH), 126.5, 127.9, 128.7, 137.3 ($C_6H_5$), 125.5, 129.1, 129.6, 138.8 (C=C—C=C), HRMS calcd for $C_{17}H_{22}S$ 258.1443, found 258.1414.

The following compounds were prepared by the above method. Samples for analysis were prepared by Kugelrohr distillation or chromatography on silica gel with hexane.

**(*E,E*)-1-(Methylthio)-2-cyclohexyl-4-phenyl-1,3-butadiene**: bp 148 °C (0.04 mmHg); NMR $^1$H (400 MHz, $CDCl_3$) δ 1.2–1.8 (m, 10 H), 2.35 (s, 3 H), 2.56 (m, 1 H), 6.11 (s, 1 H), 6.61 (AB system, 2 H, $^3J$ = 12.7 Hz), 7.1–7.5 (m, 5 H); $^{13}$C NMR ($CDCl_3$) δ 17.7 ($CH_3$S), 26.1, 26.7, 30.4 (5 $CH_2$ cyclohex), 41.0 (CH), 126.2, 126.9, 128.5, 137.8 ($C_6H_5$), 125.4, 126.4, 126.6, 141.2 (C=CC=C); HRMS calcd for $C_{17}H_{22}S$ 258.1443, found, 258.1463.

**(*E*)-1-(Ethylthio)-2-phenylpropene**: bp 130 °C (0.05 mmHg); $^1$H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, 3 H), 2.11 (d, 3 H, $^4J$ = 0.98 Hz), 2.78 (q, 2 H), 6.30 (q, 1 H, $^4J$ = 0.98 Hz), 7.29 (m, 5 H); $^{13}$C NMR ($CDCl_3$) δ 15.7 ($CH_3$), 17.6 ($CH_3$), 28.2 ($CH_2$S), 125.0, 126.5, 128.2, 133.5 ($C_6H_5$), 123.3, 142.1 (C=C); HRMS calcd for $C_{11}H_{14}S$ 178.0816, found 178.0798.

**(*E*)-1-(Ethylthio)-2-methyl-1-octen-3-yne**: $^1$H NMR ($CDCl_3$) δ 0.91 (t, 3 H), 1.29 (t, 3 H), 1.38 (m, 4 H), 1.80 (s, 3 H), 2.29 (t, 2 H), 2.62 (q, 2 H), 6.24 (s, 1 H); HRMS calcd for $C_{11}H_{18}S$ 182.1130, found 182.1151.

**2-[(*E*)-2-(Phenylthio)ethenyl]naphthalene**: [(*E*)-2-(Phenylthio)ethenyl]-1,3,2-benzodioxaborole was prepared in 93% yield by the catalytic hydroboration of phenylthioacetylene (1 equiv) with catecholborane (1 equiv) in benzene at rt for 5 h in the presence of $NiCl_2$(dppp) (3 mol %).[7] The vinylboronate thus obtained (1.5 mmol) was coupled with 1-iodonaphthalene (1 mmol) in refluxing benzene for 2 h in the presence of aqueous NaOH (3 M, 3 mmol) and $PdCl_2$(dppf) (3 mol %) to give a 90% yield of the title compound: mp 47 °C; $^1$H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, 1 H, $^3J$ = 15.1 Hz), 7.20–7.50 (m, 9 H), 7.56 (d, 1 H, $^3J$ = 7.4 Hz), 7.76 (d, 1 H, $^3J$ = 7.7 Hz), 7.82 (d, 1 H, $^3J$ = 7.3 Hz), 8.06 (d, 1 H, $^3J$ = 7.4 Hz); HRMS calcd for $C_{18}H_{14}S$ 262.0817, found 262.0812.

**2-[(*E*)-1-(Methylthio)hexen-2-yl]acetanilide**: mp 111 °C; $^1$H NMR ($CDCl_3$) δ 0.88 (t, 3 H), 0.94 (m, 4 H), 2.15 (s, 3 H), 2.34 (s, 3 H), 2.43 (t, 2 H), 5.95 (s, 1 H), 6.8–7.3 (m, 4 H), 8.0 (broad s, 1 H); $^{13}$C NMR ($CDCl_3$) δ 13.8 ($CH_3$), 17.1 ($CH_3$S), 24.4 ($CH_3$-CO), 22.5, 29.5, 33.4 (3 $CH_2$), 121.2 (CH=), 135.8 (C=), 123.7, 127.6, 128.6, 128.8, 132.8, 134.8 ($C_6H_4$), 167.8 (C=O); HRMS calcd for $C_{15}H_{21}NOS$ 263.1344, found 263.1365.

**2-[(*E*)-1-(Methylthio)hexen-2-yl]-3-(methoxymethoxy)-naphthalene**: $^1$H NMR ($CDCl_3$) δ 0.89 (t, 3 H), 1.23 (m, 4 H), 2.39 (s, 3 H), 2.68 (t, 2 H), 3.50 (s, 3 H), 5.22 (s, 2 H), 5.85 (s, 1 H), 7.43 and 7.55 (m, 6 H); $^{13}$C NMR ($CDCl_3$) δ 13.8 ($CH_3$), 17.1 ($CH_3$S), 23.0, 29.6, 34.0 (3 $CH_2$), 56.0 ($CH_3$O), 95.2 ($OCH_2$O), 116.3 (CH=), 134.6 (C=), 123.6, 125.3, 125.9, 127.1, 127.6, 127.9, 128.23, 129.6, 133.6, 151.2 ($C_{10}H_6$); HRMS calcd for $C_{19}H_{24}O_2S$ 316.1498, found 316.1493.

**Nickel-Catalyzed Cross-Coupling Reaction (eq 3).** An oven-dried flask was charged with $NiCl_2$(dppp) (40 mg), sulfide **4** (519 mg, 2 mmol), and THF (10 mL) and flushed with nitrogen. The solution of (2-methoxypropenyl)magnesium bromide in THF (1.55 M, 4.5 mmol) was then added. After being refluxed for 6 h, the reaction mixture was diluted with ether, washed with water, and dried over $MgSO_4$. The isolation of the product was accomplished by chromatography over silica gel with hexane to give 0.324 g (78%) of (*E*)-1-naphthyl-4-methyl-1,3-pentadiene: $^1$H NMR (400 MHz, $CDCl_3$) δ 1.86 (s, 3 H), 1.87 (s, 3 H), 6.15 (d, 1 H, $^3J$ = 11.0 Hz), 7.03 (dd, 1 H, $^3J$ = 11.0, 15.6 Hz), 7.18 (d, 1 H, $^3J$ = 15.6 Hz), 7.45 (m, 3 H), 7.65 (d, 1 H, $^3J$ = 7.3 Hz), 7.70 (d, 1 H, $^3J$ = 7.3 Hz), 7.80 (dd, 1 H, $^3J$ = 7.8 Hz, $^4J$ = 2.0 Hz), 8.13 (dd, 1 H, $^3J$ = 7.3 Hz, $^4J$ = 1.4 Hz); $^{13}$C NMR ($CDCl_3$) δ 18.6 ($CH_3$), 26.3 ($CH_3$), 125.5, 125.7, 126.2, 126.8, 127.49, 128.0, 128.5, 129.0, 129.1, 131.0 ($C_{10}H_7$), 122.9, 123.6, 127.3, 133.7 (C=CC=C); HRMS calcd for $C_{16}H_{16}$ 208.1252, found 208.1253.

**Synthesis of *N*-Acetyl-3-butylindole (7)**: To a solution of sulfide **6** (130 mg, 0.5 mmol) in acetonitrile (6 mL) and 2 mL of water was added $HgCl_2$ (1 g, 3.7 mmol), and the reaction mixture was then refluxed for 3 h. After concentration of the reaction mixture, the product was extracted with $CH_2Cl_2$ from the residue. Chromatography on silica gel eluting with methylene chloride gave 85 mg (82%) of *N*-acetyl-3-butylindole: mp 42 °C; $^1$H NMR ($CDCl_3$) δ 0.90 (t, 3 H), 1.1–1.8 (m, 4 H), 2.54 (s, 3 H), 2.61 (t, 2 H), 7.09 (s, 1 H), 7.25 (m, 2 H), 7.48 (m, 1 H), 8.39 (m, 1 H); $^{13}$C NMR ($CDCl_3$) δ 13.9 ($CH_3$), 24.7 ($CH_3CO$), 22.7, 29.7, 31.3 (3 $CH_2$), 116.6, 118.9, 121.5, 123.2, 123.3, 125.0, 130.6, 135.8 ($C_8H_5N$), 168.0 (C=O); HRMS calcd for $C_{14}H_{17}ON$ 215.1310, found 215.1311.

**Synthesis of 1-Butylnaphtho[2.1-*b*]furan (9).** Sulfide **8** (630 mg, 2 mmol) in methanol (10 mL) was treated with concd HCl (1 mL) at rt for 3 h. The reaction mixture was diluted with ether, washed twice with water, and dried over $MgSO_4$. The concentrated residue was chromatographed on silica gel eluting with benzene to give 490 mg (91%) of 1-[1-(methylthio)hexen-2-yl]-2-naphthol.

To a solution of the β-naphthol thus obtained (490 mg, 1.82 mmol) in THF (10 mL) was added a solution of $Hg(OCOCF_3)_2$ (2 g, 4.6 mmol) in THF. After the reaction mixture stirred at reflux temperature for 3 h, the solvent was evaporated in vacuo, and the residue was flushed through a short column of silica gel with methylene chloride. The eluate was washed with water and dried over $MgSO_4$. An ethanol solution of the concentrated residue (20 mL) was treated with 2 g of freshly prepared Raney Ni at rt for 6 h. After filtration and evaporation of solvent in vacuo, the product was isolated by chromatography on silica gel eluting with benzene to give 305 mg (79%) of 1-butylnaphtho-

(9) Pettit, G. R.; Van Tamelen, E. E. *Org. React.* **1962**, *12*, 356–529.
(10) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: Amsterdam, 1971.
(11) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121–123.
(12) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158–168.
(13) Booth, G.; Chatt, J. *J. Chem. Soc.* **1965**, 3239.
(14) (a) Brown, H. C. *Organic Syntheses via Boranes*; Wiley: New York, 1975; pp 63–64. (b) Miyaura, N.; Suzuki, A. *Org. Synth.* **1990**, *68*, 130–137.

[2,1-*b*]furan **9**: $^1$H NMR ($CDCl_3$) $\delta$ 0.85 (t, 3 H), 1.1–1.9 (m, 4 H), 2.92 (t, 2 H), 7.2–8.3 (m, 7 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.01 ($CH_3$), 22.73, 25.78, 31.20 (3 $CH_2$), 112.73, 123.02, 123.35, 123.95, 125.30, 126.15, 129.02, 140.60, 142.52 ($C_{12}H_7O$); HRMS calcd for $C_{16}H_{16}O$ 224.1202, found 224.1197.

**Supplementary Material Available:** Copies of NMR spectra (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.