so a true mutation fraction can be calculated. Duplicate samples are tested, and triplicate platings are obtained from each sample. Thus a total of six selective plate counts and six bacterial survival counts are available for each sample tested. To mimic animal metabolism, samples are also incubated with Aroclor 1254 induced rat liver postmitochondrial supernatant (PMS). All samples were tested to a concentration of 300 mg/mL or their maximum solubility. There is no single parameter that can describe a complex dose–response relationship between test agent concentration and induced mutant fraction. For simplicity we have chosen to use the maximum slope from dose–response curves as a measure of mutagenic activity of the sample. The 99% confidence limits for each slope were calculated on the basis of the Poisson counting statistics of the data.

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An Efficient One-Pot Method for the Preparation of Polysubstituted Benzothiophenes[†]

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A one-pot method for the transformation of an aryl bromide, an internal alkyne, and sulfur dichloride into a polysubstituted benzothiophene, in high yield, is described. The method involves the generation and trapping of a zirconocene complex of a substituted benzyne.

Heterocycles are, perhaps, the most frequently used class of compounds in the pharmaceutical industry.[2] Accordingly, a tremendous body of literature on their structure, properties, and synthesis has appeared.[3] While myriad means for the preparation of heterocyclic compounds exist, new methods of higher efficiency and greater generality which utilize readily available precursors are in great demand. We have been concerned with the development of new tactics for the construction of heterocyclic compounds and have recently reported new methods for the preparation of benzisothiazoles,[4a] butenolides,[4b] and pyrroles[4c] using organozirconium-based strategies.[4d] We now report an experimentally simple, general, high-yield synthesis of polysubstituted benzothiophenes.

Benzothiophenes are most frequently constructed via cyclization reactions beginning with thiophenol precursors[5] or by the annulation of an aromatic ring onto a thiophene moiety.[6] While these strategies have merit for the preparation of benzothiophenes of specific substitution patterns, they lack generality and, hence, cannot be used to prepare many polysubstituted variants. In our study of the coupling of nitriles with zirconocene complexes of substituted benzynes,[4a] we observed excellent to complete regioselectivity in metallacycle formation. For the analogous coupling of an unsymmetric alkyne with a zirconium complex of an unsymmetrical benzyne, four regioisomers are possible. Of these possibilities, we felt, based on the above-mentioned work, that only **1a** and/or **1b** (for R^1 larger than R^2) would be produced (Scheme I). In order to induce the formation of a single regioisomer, we sought to differentiate R^3 from R^4 to the greatest extent possible without sacrificing the generality of the transformation. One obvious means to accomplish this would employ a terminal alkyne as the substrate. This possibility, however, is untenable, since, unlike many of the related zirconocene complexes that we have prepared and studied,[4d,7] the benzyne complexes do not undergo clean coupling reactions with terminal alkynes. It was decided, therefore, to employ the trimethylsilyl group as a proton surrogate for two reasons. First, protodesilylation of vinylsilanes is well-precedented.[8] Second, in earlier work on the regiochemical course of the intermolecular cross-coupling of two different alkynes, we observed that, for internal alkynes in which one substituent was a trialkylsilyl group, this trialkylsilyl group always ended up on the 2-carbon in the product zirconacycles.[9] In practice, for cases in which $R^1 = R^2$ or $R^2 = H$, only a single regioisomeric zirconacycle is formed[10] (Scheme II). As we had observed previously, modification of the conditions of Nugent and Fagan[11] allows the clean, high-yield conversion of the intermediate zirconacycles without need for their isolation or purification. Note that in entries 4–15 a commercially available bromoarene and alkyne are converted in a one-pot procedure to the substituted benzothiophene in 60–80% isolated yield as is shown in Table I. In cases 3, 6, 9, 12, and 15, proto-

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[†] This paper is dedicated to Professor Frederick D. Greene, friend, colleague, and gifted teacher, in recognition of his 27 years of service as Editor of *The Journal of Organic Chemistry*.

[1] Camille & Henry Dreyfus Teacher–Scholar Awardee, 1989–94; American Cancer Society Junior Faculty Research Awardee 1987–89; Eli Lilly Grantee 1988–90; Alfred P. Sloan Research Fellow, 1988–90; Union Carbide Innovation Recognition Program Awardee, 1989.

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[10] In one case (entry 9) 4% of the 3-trimethylsilyl-substituted regioisomer is formed, see Table I.

[11] Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310.

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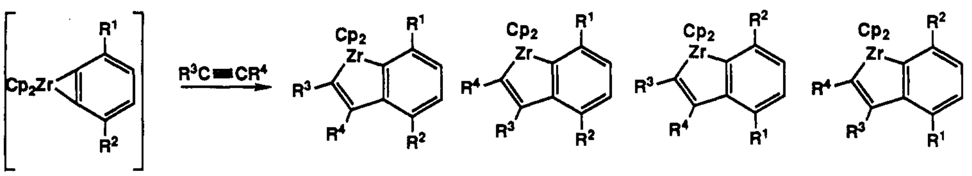
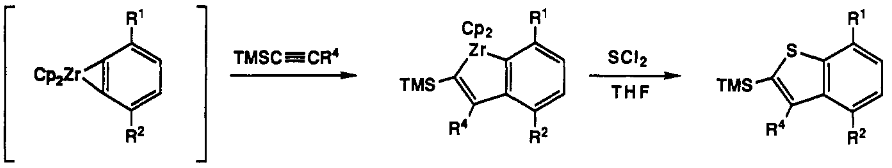
Scheme I

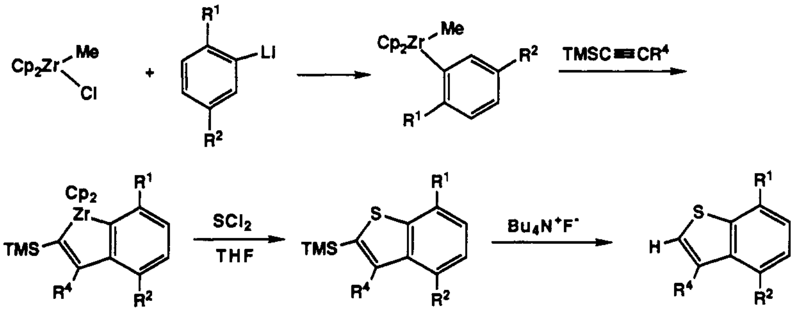


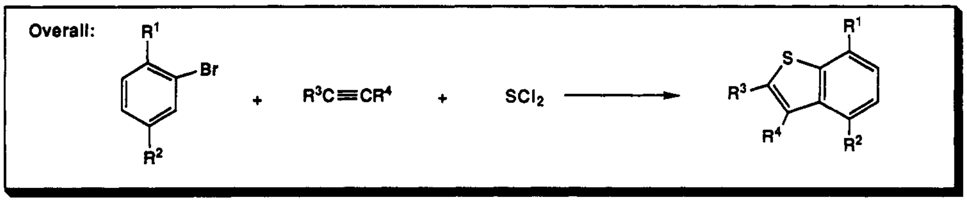
1a 1b 1c 1d

Scheme II



Scheme III





desilylation could be accomplished in >90% yield simply by treatment of the trimethylsilyl-substituted benzothiophene with tetrabutylammonium fluoride in THF.[12] As can be seen, this experimentally simple procedure provides a rapid means for the preparation of a large number of tri- and tetrasubstituted thiophenes in good to excellent overall yield and, as such, should see much use by medicinal and pharmaceutical chemists.

We are continuing our work in the development of transition metal-mediated methods for the preparation of a variety of other heterocyclic and carbocyclic organic compounds and will report our results in due course.

Experimental Section

All manipulations of air- or moisture-sensitive compounds were performed using standard Schlenk techniques (argon atmosphere) or in a Vacuum Atmospheres Co. dry box (nitrogen atmosphere). Argon used in the Schlenk work was purified by passage through columns of BASF-RS-11 (Chemalog) and Linde 4 Å molecular sieves. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker WM-250, a Varian XL-300, a Varian XL-400, or a Varian VXR-500 Fourier transform spectrometer. Infrared (IR) spectra were recorded on an IBM IR/30S or a Mattson Cygnus Starlab 100 Fourier transform spectrometer. Electron-impact high-resolution mass determinations (HRMS) were recorded on a Finnegan MAT System 8200 spectrometer. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

Flash chromatography was carried out using Merck Kieselgel 60 (230–400 mesh) silica gel. Spinning plate chromatography was performed with a Harrison Research Chromatotron using either 2 or 4 mm thick plates poured with Merck Kieselgel 60 PF254 silica gel.

Tetrahydrofuran (THF) and benzene were distilled from sodium benzophenone ketyl. Yields refer to isolated yields of greater than 95% purity as determined by capillary GC and ^{1}H NMR. Cp_2ZrCl_2 was purchased from Boulder Scientific Inc., Mead, CO. Alkynes were purified before use by passage through a short column of neutral alumina (ICN Alumina N, Akt. I). Sulfur dichloride was purchased from Aldrich Chemical Co. and distilled at atmospheric pressure, and the fraction boiling between 59 and 60 °C was collected. All the zirconium reagents were prepared as previously described.[4a] All other reagents were available from commercial sources and were used without further purification.

Typical Procedure for the Preparation of Benzo[*b*]thiophenes. Method A (Using Diphenylzirconocene). Preparation of 2,3-Dimethylbenzo[*b*]thiophene.[13] To a solution of diphenylzirconocene (0.563 g, 1.50 mmol) in THF (10 mL) at −78 °C was added 2-butyne (0.0972 g, 1.80 mmol). The reaction mixture was warmed to room temperature and heated at 80 °C for 16 h. The solution was then cooled to −78 °C, sulfur dichloride (0.185 g, 1.80 mmol) was added, and the reaction solution was stirred for 5 min and quenched with aqueous HCl (1 N, 0.05 mL) to remove the excess SCl_2. The reaction mixture was transferred to a round-bottom flask using THF, the solvent was removed by rotary evaporation, and the residue was washed with pentane (2 × 10 mL). The pentane solution was passed through a short silica gel column (ca. 3 cm), and the filtrate was concen-

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trated to give the product (0.230 g, 1.43 mmol) in 95% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3 H), 2.46 (s, 3 H), 7.24–7.26 (dd, J = 8.0 Hz, 8.0 Hz, 1 H), 7.30–7.33 (dd, J = 7.2 Hz, 7.2 Hz, 1 H), 7.55–7.57 (d, J = 8.0 Hz, 1 H), 7.71–7.73 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.30, 13.74, 121.07, 121.96, 123.38, 123.73, 126.97, 133.64, 138.04, 140.95; IR (neat) 3061, 3029, 2857, 1686, 1580, 1545, 1383, 1341, 1156, 1076, 932, 849, 714 cm^{-1}; HRMS calcd for $C_{10}H_{10}S$ 162.0503, found 162.0503 ± 0.0008 amu.

2,3-Diethylbenzo[*b*]thiophene:[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, J = 7.0 Hz, 3 H), 1.32 (t, J = 7.0 Hz, 3 H), 2.80 (q, J = 7.3 Hz, 2 H), 2.88 (q, J = 7.1 Hz, 2 H), 7.22–7.26 (m, 1 H), 7.30–7.34 (m, 1 H), 7.62–7.64 (d, J = 7.2 Hz, 1 H), 7.75–7.77 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.62, 16.22, 19.57, 21.74, 121.14, 122.31, 123.25, 123.67, 132.49, 138.40, 140.13, 141.28; IR (neat) 3061, 3026, 2967, 2872, 1582, 1458, 1435, 1375, 1175, 1063, 839, 708, 691, 660 cm^{-1}; HRMS calcd for $C_{12}H_{14}S$ 190.0816, found 190.0816 ± 0.0006 amu.

3-Methyl-2-(trimethylsilyl)benzo[*b*]thiophene: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.41 (s, 9 H), 2.51 (s, 3 H), 7.30–7.36 (m, 2 H), 7.69–7.72 (d, J = 8.4 Hz, 1 H), 7.83–7.85 (d, J = 7.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.03, 14.40, 121.58, 122.20, 123.63, 124.05, 134.66, 138.71, 141.84, 142.73; IR (KBr) 3053, 2956, 1509, 1458, 1424, 1378, 1251, 1032, 840, 794 cm^{-1}; HRMS calcd for $C_{12}H_{16}SSi$ 220.0742, found 220.0742 ± 0.0004 amu.

3-Methylbenzo[*b*]thiophene:[14] ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 7.03 (s, 1 H), 7.30–7.38 (m, 2 H), 7.68–7.71 (d, J = 9.3 Hz, 1 H), 7.82–7.84 (d, J = 7.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.85, 121.45, 121.67, 122.71, 123.79, 124.03, 132.06, 139.62, 140.23; IR (neat) 3052, 2923, 2855, 1461, 1443, 1427, 1265, 835, 770, 754, 740, 728 cm^{-1}; HRMS calcd for C_9H_8S 148.0346, found 148.0341 ± 0.0004 amu.

Method B (Coupling Reactions with Symmetrical Alkynes Using in Situ Prepared Aryl(alkyl)zirconocene Precursors). Preparation of 7-Methoxy-2,3-dimethylbenzo[*b*]thiophene.[15] To a solution of 2-bromoanisole (0.385 g, 2.00 mmol) in THF (10 mL) at −78 °C was added *n*-butyllithium (1.20 mL of a 1.68 M solution in hexane, 2.02 mmol). The reaction mixture was allowed to stir for 15 min and was then cannula-transferred into a solution of zirconocene (methyl) chloride (0.570 g, 2.10 mmol) in THF (10 mL) at −78 °C. To this was added 2-butyne (0.130 g, 2.40 mmol), and the resulting solution was heated overnight in a sealed flask at 80 °C to give a yellow solution. This was cooled to −78 °C, and sulfur dichloride (0.156 mL, 2.4 mmol) was added. The solution was allowed to stir for 5 min, and the solvent was then removed to give a yellow solid. This was washed with pentane (2 × 20 mL), and the pentane washings were concentrated to give a crude product (0.350 g), which was recrystallized from pentane to yield 0.274 g (1.42 mmol, 71%) of pure product: mp 110–110.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.27 (d, J = 1.2 Hz, 3 H), 2.47 (d, J = 1.2 Hz, 3 H), 3.96 (s, 3 H), 6.69–6.72 (d, J = 8.0 Hz, 1 H), 7.19–7.31 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.57, 13.79, 55.55, 103.75, 114.02, 125.06, 126.35, 127.47, 134.01, 142.89, 154.14; IR (KBr) 3000, 2964, 2915, 2838, 1555, 1474, 1460, 1438, 1351, 1049, 1041, 779, 721 cm^{-1}; HRMS calcd for $C_{11}H_{12}OS$ 192.0609, found 192.0609 ± 0.0005 amu.

Method C (Coupling Reactions with 1-(Trimethylsilyl)propyne). Preparation of 3,7-Dimethyl-2-(trimethylsilyl)benzo[*b*]thiophene. To a solution of 2-bromotoluene (0.248 g, 1.43 mmol) in THF (5 mL) at −78 °C was added *n*-butyllithium (0.851 mL of a 1.68 M solution in hexane, 1.43 mmol). The reaction mixture was allowed to stir for 15 min and was then cannula-transferred into a solution of zirconocene (methyl) chloride (0.413 g, 1.51 mmol) in THF (10 mL) at −78 °C. To this was added 1-(trimethylsilyl)propyne (0.25 mL, 1.7 mmol), and the resulting solution was allowed to warm to room temperature and was then heated at 75–80 °C overnight. At this point, the solvent was removed in vacuo to give a yellow solid that was dissolved in benzene (10 mL). The suspension of LiBr was cannula-filtered to remove lithium salts, benzene was removed in vacuo, and THF (10 mL) was added. The solution was cooled to −78 °C, sulfur dichloride (0.108 mL, 1.71 mmol) was added, and the reaction solution was allowed to stir for 5 min. The reaction mixture was transferred to a round-bottom flask using THF, and the solvent was removed by rotary evaporation to give a yellow solid, which was washed with pentane (2 × 20 mL). The combined pentane washings were concentrated to give 0.260 g of crude product. This was purified either by spinning plate chromatography using pentane as eluent or by recrystallization from pentane to yield 0.233 g (1.00 mmol, 69%) of pure product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.51 (s, 9 H), 2.59 (s, 3 H), 2.65 (s, 3 H), 7.20–7.22 (d, J = 7.2 Hz, 1 H), 7.37–7.40 (dd, J = 7.0 Hz, 8.0 Hz, 1 H), 7.64–7.66 (d, J = 8.8 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 0.04, 14.73, 20.19, 119.26, 124.22, 124.29, 131.77, 133.90, 139.49, 141.75, 142.86; IR (KBr) 3063, 3026, 1574, 1510, 1392, 1377, 1263, 1251, 843, 695, 624 cm^{-1}; HRMS calcd for $C_{13}H_{18}SSi$ 234.0898, found 234.0898 ± 0.0009 amu.

Preparation of 3,7-Dimethylbenzo[*b*]thiophene.[16] To a solution of 3,7-dimethyl-2-(trimethylsilyl)benzo[*b*]thiophene (0.300 g, 1.28 mmol) in THF was added tetrabutylammonium fluoride solution in THF (5.0 mL of 1 M solution, and the reaction mixture was allowed to stir for 3 h. At this point ether (30 mL), water (5 mL), and aqueous HCl (1 N, 10 mL) were added. The two layers were separated, and the water layer was washed with ether (5 mL). The combined organic layers were washed with saturated sodium bicarbonate and brine and were dried over anhydrous magnesium sulfate. The resulting solution was concentrated to yield a pure white solid (0.198 g, 1.22 mmol) in 95% yield: mp 33–33.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (d, J = 1.9 Hz, 3 H), 2.55 (s, 3 H), 7.05 (s, 1 H), 7.13–7.15 (d, J = 7.3 Hz, 1 H), 7.29–7.34 (dd, J = 7.0 Hz, 8.0 Hz, 1 H), 7.54–7.57 (d, J = 8.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.14, 20.14, 119.30, 121.02, 124.28, 124.39, 132.14, 132.85, 139.54, 140.45; IR (KBr) 3093, 2973, 2915, 1473, 1390, 1381, 1058, 836, 782, 755, 725 cm^{-1}; HRMS calcd for $C_{10}H_{10}S$ 162.0532, found 162.0499 ± 0.0008 amu.

2,3,7-Trimethylbenzo[*b*]thiophene:[17] mp 49–50 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.28 (s, 3 H), 2.49 (s, 3 H), 2.50 (s, 3 H), 7.05–7.07 (d, J = 7.5 Hz, 1 H), 7.24–7.29 (dd, J = 7.5 Hz, 7.5 Hz, 1 H), 7.41–7.44 (d, J = 7.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.53, 13.75, 20.14, 118.75, 123.84, 124.25, 127.70, 131.36, 133.20, 138.13, 140.89 IR (KBr) 3021, 2914, 2856, 1561, 1473, 1437, 1379, 1054, 775, 725 cm^{-1}; HRMS calcd for $C_{11}H_{12}S$ 176.0660, found 176.0658 ± 0.0006 amu. Anal. Calcd: 74.97; H, 6.87. Found: C, 75.10; H, 6.90.

2,3-Diethyl-7-methylbenzo[*b*]thiophene: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, J = 7.0 Hz, 3 H), 1.34 (t, J = 8.2 Hz, 3 H), 2.52 (s, 3 H), 2.79 (q, J = 7.6 Hz, 2 H), 2.89 (q, J = 6.8 Hz, 2 H), 7.05–7.07 (d, J = 7.2 Hz, 1 H), 7.25–7.28 (dd, J = 7.0 Hz, 7.0 Hz, 1 H), 7.47–7.49 (d, J = 8.0 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.60, 17.13, 20.63, 21.08, 22.63, 119.68, 124.49, 125.06, 132.58, 134.10, 139.24, 140.80, 141.68; IR (neat) 3063, 3029, 2967, 1579, 1473, 1463, 1377, 1166, 1058, 782, 732 cm^{-1}; HRMS calcd for $C_{13}H_{16}S$ 204.0973, found 204.0972 ± 0.0007 amu.

2,3-Diethyl-7-methoxybenzo[*b*]thiophene: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (t, J = 7.4 Hz, 3 H), 1.33 (t, J = 7.6 Hz, 3 H), 2.77 (q, J = 7.6 Hz, 2 H), 2.88 (q, J = 7.5 Hz, 2 H), 3.96 (s, 3 H), 6.71 (m, 1 H), 7.26–7.31 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 15.58, 17.06, 20.65, 22.60, 56.40, 104.34, 114.91, 125.86, 127.52, 133.86, 142.50, 142.86, 155.26; IR (neat) 3063, 2967, 2933, 2872, 1597, 1572, 1475, 1376, 1261, 1057, 865, 781, 723, 686, 621 cm^{-1}; HRMS calcd for $C_{13}H_{16}OS$ 220.0922, found 220.0922 ± 0.0007 amu.

7-Methoxy-3-methyl-2-(trimethylsilyl)benzo[*b*]thiophene: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.41 (s, 9 H), 2.49 (s, 3 H), 4.00 (s, 3 H), 6.74–6.77 (m, 1 H), 7.32–7.35 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 0.07, 14.65, 55.62, 103.85, 114.36, 125.17, 131.51, 134.70, 139.09, 143.89, 154.38; IR (neat) 3063, 2957, 2838, 1595, 1512, 1470, 1439, 1377, 1053, 945, 777, 766, 631, 590 cm^{-1}; HRMS calcd for $C_{13}H_{18}OSSi$ 250.0848, found 250.0847 ± 0.0007 amu.

7-Methoxy-3-methylbenzo[*b*]thiophene:[18] mp 77–77.5 °C (lit. mp 76–77 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (b s, 3 H), 3.99 (s, 3 H), 6.77–6.80 (m, 1 H), 7.05–7.06 (b s, 1 H), 7.33–7.35 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.00, 55.55, 104.09, 114.45,

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Table I

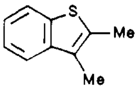
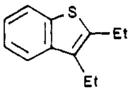
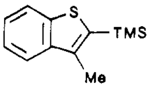
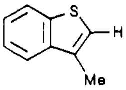
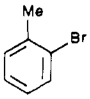
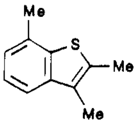
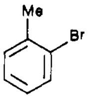
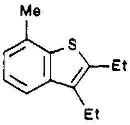
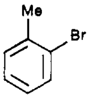
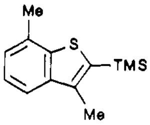
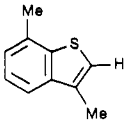
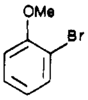
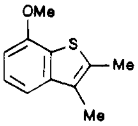
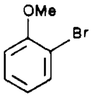
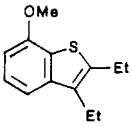
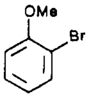
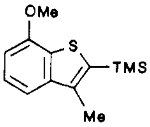
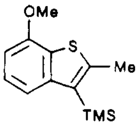
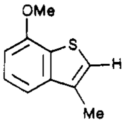
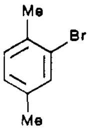
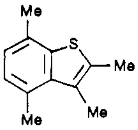
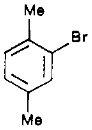
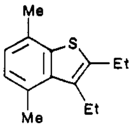
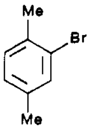
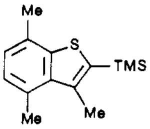
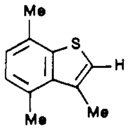
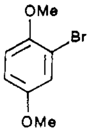
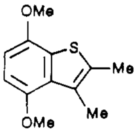
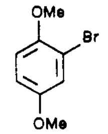
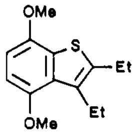
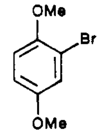
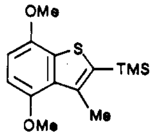
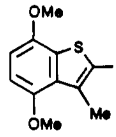
entry	precursor	alkyne	product	yield, %	desilylated product	yield, %
1	Cp_2ZrPh_2	MeC≡CMe		95		
2	Cp_2ZrPh_2	EtC≡CEt		91		
3	Cp_2ZrPh_2	MeC≡CTMS		88		92
4		MeC≡CMe		72		
5		EtC≡CEt		71		
6		MeC≡CTMS		69		95
7		MeC≡CMe		71		
8		EtC≡CEt		80		
9		MeC≡CTMS	 (22)  (1)	71		98
10		MeC≡CMe		78		
11		EtC≡CEt		67		
12		MeC≡CTMS		75		93
13		MeC≡CMe		60		

Table I (Continued)

entry	precursor	alkyne	product	yield, %	desilylated product	yield, %
14		EtC≡CEt		74		
15		MeC≡CTMS		69		96

121.77, 125.20, 128.96, 132.51, 141.57, 154.66; IR (KBr) 3067, 2963, 2934, 2838, 1568, 1474, 1437, 1355, 1047, 785, 773, 745, 718 cm^{-1}; HRMS calcd for $C_{10}H_{10}OS$ 178.0452, found 178.0452 ± 0.0005 amu. Anal. Calcd: C, 67.40; H, 5.66. Found: C, 67.27; H, 5.75.

2,3,4,7-Tetramethylbenzo[*b*]thiophene:[19] mp 66–67 °C (lit. mp 67.5 °C); ^1H NMR (300 MHz, CDCl$_3$) δ 2.44 (s, 3 H), 2.45 (s, 3 H), 2.49 (s, 3 H), 2.72 (s, 3 H), 6.89–6.97 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 14.09, 15.17, 19.85, 21.32, 123.37, 127.00, 129.07, 129.19, 130.37, 132.51, 138.59, 138.90; IR (KBr) 2913, 2873, 1554, 1477, 1433, 1385, 1363, 1010, 814 cm^{-1}; HRMS calcd for $C_{12}H_{14}S$ 190.0816, found 190.0815 ± 0.0004 amu. Anal. Calcd: C, 75.76; H, 7.42. Found: C, 75.50; H, 7.54.

2,3-Diethyl-4,7-dimethylbenzo[*b*]thiophene: ^1H NMR (300 MHz, CDCl$_3$) δ 1.19 (t, J = 6.9 Hz, 3 H), 1.35 (t, J = 7.5 Hz, 3 H), 2.46 (s, 3 H), 2.71 (s, 3 H), 2.86 (m, 4 H), 6.90–6.93 (d, J = 7.5 Hz, 1 H), 6.97–7.00 (d, J = 7.5 Hz, 1 H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 16.17, 16.30, 19.95, 20.84, 20.95, 21.73, 123.21, 127.29, 129.01, 129.92, 134.78, 137.92, 139.03, 140.80; IR (neat) 3004, 2932, 2870, 1732, 1570, 1470, 1381, 839, 829, 804 cm^{-1}; HRMS calcd for $C_{14}H_{18}S$ 218.1129, found 218.1129 ± 0.0010 amu.

3,4,7-Trimethyl-2-(trimethylsilyl)benzo[*b*]thiophene: mp 74–75 °C; ^1H NMR (300 MHz, CDCl$_3$) δ 0.41 (s, 9 H), 2.49 (s, 3 H), 2.73 (s, 3 H), 2.76 (s, 3 H), 6.96–7.01 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 0.06, 19.18, 19.84, 21.65, 124.11, 126.96, 129.61, 131.31, 133.55, 139.88, 141.23, 144.09; IR (KBr) 2958, 2941, 2915, 1504, 1451, 1437, 1310, 1245, 843, 840, 752, 735, 658 cm^{-1}; HRMS calcd for $C_{14}H_{20}SSi$ 248.1055, found 248.1055 ± 0.0004 amu. Anal. Calcd: C, 67.71; H, 8.12. Found: C, 67.53; H, 8.25.

3,4,7-Trimethylbenzo[*b*]thiophene:[19] mp 53–54 °C (lit. mp 53–53.5 °C); ^1H NMR (300 MHz, CDCl$_3$) δ 2.47 (s, 3 H), 2.61–2.62 (d, J = 1.5 Hz, 3 H), 2.71 (s, 3 H), 6.96–6.98 (m, 3 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 18.70, 19.80, 20.97, 121.58, 124.23, 126.67, 129.90, 131.33, 134.47, 137.45, 141.78; IR ((KBr) 2961, 2926, 1479, 1436, 1168, 851, 766, 741 cm^{-1}; HRMS calcd for $C_{11}H_{12}S$ 176.0660, found 176.0660 ± 0.0004 amu.

4,7-Dimethoxy-2,3-dimethylbenzo[*b*]thiophene: mp 110–110.5 °C; ^1H NMR (300 MHz, CDCl$_3$) δ 2.41 (s, 3 H), 2.47 (s, 3 H), 3.83 (s, 3 H), 3.90 (s, 3 H), 6.54–6.64 (m, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 13.68, 14.06, 55.87, 55.98, 103.20, 105.47, 128.41, 128.44, 132.02, 132.20, 148.40, 150.50; IR (KBr) 2937, 2916, 2836, 1596, 1553, 1486, 1257, 1115, 1045, 822, 795, 788, 701 cm^{-1}; HRMS calcd for $C_{12}H_{14}O_2S$ 222.0715, found 222.0715 ± 0.0005 amu. Anal. Calcd: C, 64.84; H, 6.35. Found: C, 64.75; H, 6.21.

2,3-Diethyl-4,7-dimethoxybenzo[*b*]thiophene: ^1H NMR (400 MHz, CDCl$_3$) δ 1.18 (t, J = 7.4 Hz, 3 H), 1.31 (t, J = 7.0 Hz, 3 H), 2.85 (q, J = 7.6 Hz, 2 H), 2.94 (q, J = 7.4 Hz, 2 H), 3.86 (s, 3 H), 3.91 (s, 3 H), 6.57–6.59 (d, J = 7.6 Hz, 1 H), 6.63–6.65 (d, J = 7.6 Hz, 1 H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 16.66, 17.09, 22.18, 22.34, 56.51, 56.71, 103.84, 105.87, 129.56, 132.04, 135.10, 140.95, 149.30, 151.10; IR (neat) 2967, 2872, 2836, 1774, 1582, 1543, 1483, 1437, 1057, 791, 758, 720, 695 cm^{-1}; HRMS calcd for $C_{14}H_{18}O_2S$ 250.1028, found 250.1027 ± 0.0010 amu.

4,7-Dimethoxy-3-methyl-2-(trimethylsilyl)benzo[*b*]thiophene: mp 89.5–90 °C; ^1H NMR (300 MHz, CDCl$_3$) δ 0.39 (s, 9 H), 2.68 (s, 3 H), 3.85 (s, 3 H), 3.93 (s, 3 H), 6.60 (s, 1 H), 6.61 (s, 1 H); ^{13}C NMR (67 MHz, CDCl$_3$) δ 0.12, 17.79, 55.68, 55.81, 103.86, 104.95, 133.04, 133.18, 134.29, 140.46, 148.52, 151.15; IR (KBr) 3034, 3024, 2877, 2853, 1596, 1579, 1505, 1490, 1469, 1462, 1452, 1438, 1371, 1057, 1028, 840, 829, 797, 719 cm^{-1}; HRMS calcd for $C_{14}H_{20}O_2SSi$ 280.0953, found 280.0953 ± 0.0009 amu. Anal. Calcd: C, 59.98; H, 7.20. Found: C, 60.02, 7.33.

4,7-Dimethoxy-3-methylbenzo[*b*]thiophene: mp 89–90 °C; ^1H NMR (300 MHz, CDCl$_3$) δ 2.59–2.60 (d, J = 2.2 Hz, 3 H), 3.86 (s, 3 H), 3.93 (s, 3 H), 6.64 (s, 2 H), 6.88–6.89 (d, J = 2.2 Hz, 1 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 17.32, 55.84, 55.92, 103.99, 105.04, 120.75, 130.91, 131.62, 133.86, 148.50, 151.35; IR (KBr) 2985, 2975, 2865, 1599, 1582, 1517, 1509, 1505, 1461, 1454, 1433, 1257, 1053, 1024, 792, 768, 711 cm^{-1}; HRMS calcd for $C_{11}H_{12}O_2S$ 208.0558, found 208.0558 ± 0.0007 amu. Anal. Calcd: C, 63.44; H, 5.81. Found: C, 63.24; H, 5.71.

Acknowledgment. We would like to thank Eli Lilly, the American Cancer Society, the National Institutes of Health (Grant GM-34917), and Firmenich SA for their generous financial assistance.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for Table I entries 3, 5, 6, 8, 9, 11, and 14 (7 pages). Ordering information is given on any current masthead page.

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[19] Cagniant, P. F.; Cagniant, D. *Bull. Soc. Chim. Fr.* **1964**, 2423.