Benzannulation of Aromatic Heterocycles. A Regiocontrolled Method for Construction of Substituted Benzo- and Dibenzofurans and Benzo- and Dibenzothiophenes

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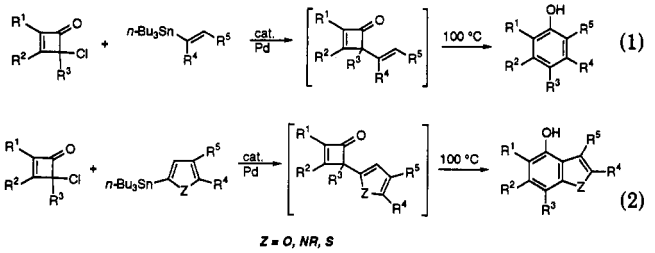
Received February 12, 1993

4-Chloro-2,3-disubstituted-2-cyclobutenones undergo palladium-catalyzed cross-coupling with oxygen and sulfur heteroaryl tin reagents, and upon thermolysis at 100 °C, good to high yields of substituted benzannulated heteroaromatics are formed. Relying on the control inherent in the construction of 4-chloro-2,3-disubstituted-2-cyclobutenones, regioisomeric substituted heteroaromatics are easily prepared.

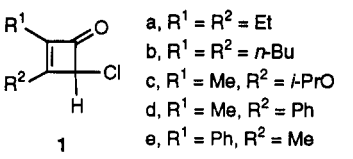
Introduction

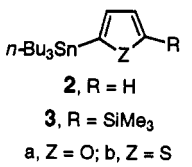
A new method for the regiocontrolled synthesis of highly substituted phenols was recently described,[1] whereby 2,3-disubstituted-4-chloro-2-cyclobutenones, prepared by regiospecific transformations of substituted cyclobutenediones, undergo palladium-catalyzed cross-coupling with vinyl- and arylstannanes and vinylzirconium reagents to form 4-R_{unsat}-2-cyclobutenones. Without isolation, on thermolysis at 100 °C, these substrates were transformed into substituted phenols in high yield (eq 1). The ability to easily annulate a substituted phenol ring onto an unsaturated organostannane, if applied to a stannylated heteroaromatic, could provide a novel method for the synthesis of substituted aromatic benzoheterocycles where the placement of substituents about the heterocycle ring is not limited by traditional directing effects associated with electrophilic substitution or lithiation (eq 2). Documented within are efforts aimed at the realization of this goal for oxygen and sulfur five-membered ring heteroaromatics. Because of the unique biological importance of nitrogen heteroaromatics (indoles, carbazoles, quinolines, isoquinolines) and the nitrogen protection and deprotection issues that attend their synthesis, they will be dealt with in a separate publication.

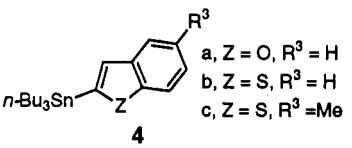


Results and Discussion

Starting Materials. A variety of 2,3-disubstituted-4-chloro-2-cyclobutenones (1) were prepared, in a regiocontrolled fashion, following established procedures.[1,2] Pending a more complete study of the regiochemistry of the cross-coupling of 4-chloro-2,3,4-trisubstituted-2-cyclobutenones with unsaturated organostannanes and related mild nucleophiles (organoboron, organozinc, etc.), attention was restricted to 4-chloro-2,3-disubstituted-2-cyclobutenones where cross-coupling at the least-substituted terminus of the putative π-allylpalladium intermediate was anticipated.[1,2] Oxygen and sulfur heteroarylstannanes were prepared using well-established technology or minor modifications of known procedures (2-(tri-*n*-butylstannyl)furan (**2a**),[3] 2-(tri-*n*-butylstannyl)thiophene (**2b**)[4,5]). 5-(Trimethylsilyl)-2-(tri-*n*-butylstannyl)furan (**3a**) was prepared following the procedure described for 2,5-bis(trimethylstannyl)furan.[3,6] This reaction sequence was extended to 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)thiophene (**3b**) prepared following the procedure described for 2,5-bis(trimethylstannyl)thiophene.[3,7] 2-(Tri-*n*-butylstannyl)benzofuran (**4a**) was easily prepared in good yield by treating benzofuran with *n*-BuLi and TMEDA[8,9] in ether solution at −78 °C and a quenching with *n*-Bu_3SnCl. 2-(Tri-*n*-butylstannyl)benzothiophene (**4b**) and 2-(tri-*n*-butylstannyl)-5-methylbenzothiophene (**4c**) were prepared following standard lithiation procedures.







(1) Krysan, D. J.; Gurski, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1992**, *114*, 1412.
(2) Edwards, J. P.; Krysan, D.; Liebeskind, L. S. *J. Org. Chem.* **1993**, in press.
(3) Seitz, D. E.; Lee, S. H.; Hanson, R. N.; Bottaro, J. C. *Synth. Commun.* **1983**, *13*, 121.
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(5) Peters, D.; Hörnfeldt, A.-B.; Gronowitz, S. *J. Heterocycl. Chem.* **1990**, *27*, 2165.
(6) Lukevics, E.; Erchak, N. P.; Popelis, J.; Dipans, I. *Zh. Obshch. Khim.* **1977**, *47*, 802.
(7) Lee, S. H.; Hanson, R. N.; Seitz, D. E. *Tetrahedron Lett.* **1984**, *23*, 431.
(8) Gschwend, H. W.; Rodriquez, H. R. *Heteroatom-Facilitated Lithiations*; Organic Reactions; John Wiley and Sons: New York, 1979; Vol. 26.
(9) Chadwick, D. J.; Willbe, C. *J. Chem. Soc., Perkin Trans. 1* **1977**, 887.

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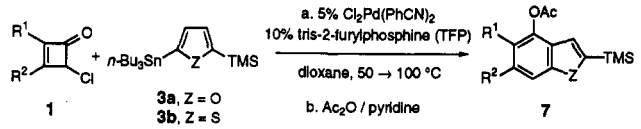
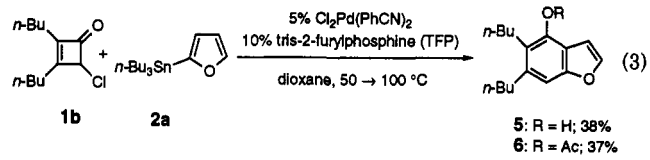
Table I. Cross-Coupling of Heteroarylstannanes with 4-Chloro-2,3-disubstituted-2-cyclobutenones



1 | 3a, Z = O; 3b, Z = S | 7

entry	R^1	R^2	Z	product	yield (%)
1	Et	Et	O	**7a**	71
2	*n*-Bu	*n*-Bu	O	**7b**	65
3	Me	*i*-PrO	O	**7c**	78
4	Et	Et	S	**7d**	58

Furan Benzannulation Studies. Initial attempts to benzannulate 2-(tri-*n*-butylstannyl)furan via Stille cross-coupling with 4-chlorocyclobutenones were not encouraging. In the presence of 5 mol% of $(PhCN)_2PdCl_2$ and 10 mol% of tris-2-furylphosphine (TFP),[10,11] compound **1b** reacted with 2-(tri-*n*-butylstannyl)furan in dioxane at 50 °C for 4 h and then at 100 °C for an additional 4 h to give the corresponding benzofuran derivative **5** in only 38% yield (eq 3). The 4-hydroxybenzofuran product **5**



(3)

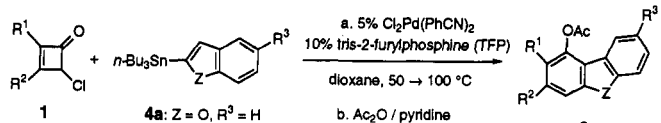
1b **2a** | **5**: R = H; 38% | **6**: R = Ac; 37%

was quite labile and decomposed upon standing. However, direct acetylation of the phenol in the reaction mixture with 2.0 equiv of Ac_2O/pyridine led in 37% yield to the analogous and stable phenol acetate **6** that could be fully characterized and stored (eq 3).

To what might the low isolated yields of benzofurans **5** and **6** be attributed? Akita and others discovered that π-electron-rich aromatic heterocycles such as furan, thiophene, pyrrole, and their benzo analogs participate in a palladium-catalyzed C-2 arylation reaction with aryl halides.[12] A similar susceptibility of the C2–C3 double bond of the benzofuran products depicted in eq 3 to reaction with the π-allylpalladium intermediate could account for the observed low yields. To test this possibility, 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)furan (**3a**) and 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)thiophene (**3b**) were prepared in order to hinder reaction at the C2–C3 double bond of the anticipated product with palladium(II) species. This device proved useful. When 4-chloro-2-cyclobutenones **1a–c** and compounds **3a** and **3b** were treated with 5% $(PhCN)_2PdCl_2$ and 10% TFP at 50 °C for 3–4 h and then at 100 °C for 4 h, good isolated yields of the benzofuran and benzothiophene products shown in Table I were obtained. Products were conveniently isolated as the phenol acetates by treatment of the reaction mixtures with Ac_2O/pyridine.

Benzofuran and Benzothiophene Annulations. The synthesis of polycyclic aromatic heterocycles should be feasible starting with 2-(tri-*n*-butylstannyl)benzofuran and its analogs. When a dioxane solution of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**), 2-(tri-*n*-butylstannyl)-benzofuran (**4a**), 5 mol% $(PhCN)_2PdCl_2$, and 10 mol% TFP was heated to 50 °C for 12 h and then at 100 °C for 4 h, compound **8a** was obtained in 94% yield (entry 1, Table II) after acetylation of the reaction mixture (2.0 equiv of Ac_2O/pyridine at 100 °C for 4 h). This reaction sequence was extended to other 4-chloro-2,3-disubstituted-2-cyclobutenones, and as illustrated in Table II, a number of highly substituted dibenzofuran derivatives could be prepared using the cross-coupling of 4-chlorocyclobutenones **1** and 2-(tri-*n*-butylstannyl)benzofuran (**4a**).

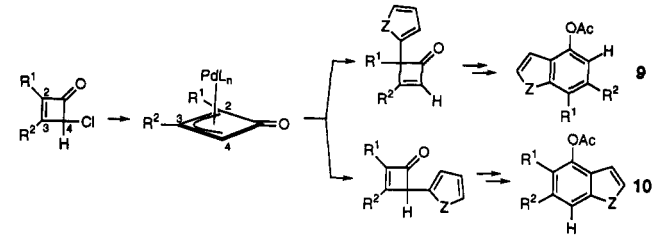
Table II. Cross-Coupling of 4a–c with 4-Chloro-2,3-disubstituted-2-cyclobutenones 1



1 | **4a**: Z = O, R^3 = H; **4b**: Z = S, R^3 = H; **4c**: Z = S, R^3 = Me | **8**

entry	R^1	R^2	Z	R^3	product	yield (%)
1	Et	Et	O	H	**8a**	94
2	*n*-Bu	*n*-Bu	O	H	**8b**	65
3	Me	*i*-PrO	O	H	**8c**	84
4	Me	Ph	O	H	**8d**	75
5	Ph	Me	O	H	**8e**	89
6	Et	Et	S	H	**8f**	85
7	*n*-Bu	*n*-Bu	S	H	**8g**	61
8	Me	*i*-PrO	S	H	**8h**	82
9	Me	Ph	S	H	**8i**	63
10	Ph	Me	S	H	**8j**	51
11	Et	Et	S	Me	**8k**	92
12	*n*-Bu	*n*-Bu	S	Me	**8l**	58
13	Me	Ph	S	Me	**8m**	60
14	Ph	Me	S	Me	**8n**	63

Scheme I

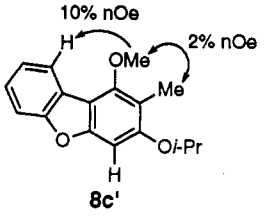


The method was extended to the synthesis of other polycyclic aromatic heterocycles. Reaction of 2-(tri-*n*-butylstannyl)benzothiophene (**4b**) with 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) in the presence of 5% $(PhCN)_2PdCl_2$ and 10% of TFP followed by esterification with 2.0 equiv of Ac_2O/pyridine afforded an 85% yield of product **8f**. Additional results of the reaction of **4b** with other 4-chloro-2,3-disubstituted-2-cyclobutenones **1** are summarized in Table II. High yields of other sulfur-containing heteroaromatics were also obtained by analogous reaction of 5-methyl-2-(tri-*n*-butylstannyl)benzothiophene (**4c**) with 4-chloro-2,3-disubstituted-2-cyclobutenones and are listed in Table II.

As demonstrated in Table II, regioisomeric heteroaromatic compounds could be readily prepared from regiodefined 4-chloro-2,3-disubstituted-2-cyclobutenones **1**. For instance, the cross-coupling of **4a**, **4b**, and **4c** with the regioisomeric 4-chlorocyclobutenones **1d** and **1e** provided a direct route to generate isomeric trisubstituted heteroaromatics **8d** and **8e**, **8i** and **8j**, and **8m** and **8n** (Table II, entries 4 and 5, 9 and 10, 13 and 14).

Two different products (**9** and **10**) could result from the cross-coupling of 4-chloro-2,3-disubstituted-2-cyclobutenones with heteroarylstannanes depending on the site of cross-coupling (Scheme I). Only product **10** was observed in each reaction, and consistent with earlier studies,[1,13]

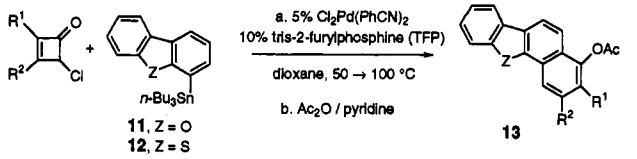
(10) Farina, V.; Roth, G. P. *Tetrahedron Lett.* **1991**, *32*, 4243.
(11) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.
(12) Aoyagi, Y.; Inoue, A.; Koizumi, I.; Hashimoto, R.; Tokunaga, K.; Gohma, K.; Komatsu, J.; Sekine, K.; Miyafuji, A.; Kunoh, J.; Honma, R.; Akita, Y.; Ohta, A. *Heterocycles* **1992**, *33*, 257.



8c'

Figure 1. Determination of Product Regiochemistry by NOE.

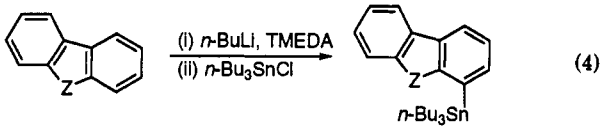
Table III. Cross-Coupling of 11 and 12 with 4-Chloro-2,3-disubstituted-2-cyclobutenones



entry	R^1	R^2	Z	product	yield (%)
1	Et	Et	O	**13a**	76
2	Me	Ph	O	**13b**	60
3	Et	Et	S	**13c**	78
4	Me	Ph	S	**13d**	62

carbon–carbon bond formation occurred at the least-substituted allylic terminus. An NOE difference experiment performed on the phenol methyl ether 8c' derived from phenol acetate 8c by hydrolysis and methylation with K_2CO_3/MeI supported the structure assignment (Figure 1). Irradiation at 3.96 ppm (OCH_3 absorption) induced a 2% enhancement of the CH_3 singlet at 2.25 ppm and a 10% enhancement of the H-9 absorption centered at 7.98 pm. Irradiation at 2.25 ppm (arylCH_3) caused a 2% enhancement of the methyl ether absorption at 3.96 ppm.

Polycyclic Systems. Facile deprotonation of dibenzofuran and dibenzothiophene occurs at the position ortho to the O and S atoms using *n*-BuLi and TMEDA in ether.[8] Quenching of the lithiates with *n*-Bu_3SnCl gave 4-(tri-*n*-butylstannyl)dibenzofuran (11) and 4-(tri-*n*-butylstannyl)-dibenzothiophene (12) (eq 4). Compounds 11 and 12



(4)

Z = O 11

Z = S 12

underwent palladium-catalyzed cross-coupling with 4-chloro-2,3-disubstituted-2-cyclobutenones 1 providing good yields of products 13 (Table III).

Conclusions

Good yields of substituted polycyclic oxygen and sulfur heteroaromatic compounds can be readily obtained by the palladium-catalyzed cross-coupling of a variety of 2,3-disubstituted-4-chloro-2-cyclobutenones and heteroarylstannanes under mild reaction conditions. Regioisomeric substituted heteroaromatics are easily prepared by the substituent control inherent in the construction of 4-chloro-2,3-disubstituted-2-cyclobutenones.

(13) Sheffy, F. K.; Godschalx, J.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833.

Experimental Section

Materials and Methods. Thin-layer chromatography (TLC) was effected using precoated 0.25-mm silica gel 60F-254 plates from EM Reagents and with visualization by one of the following methods: UV light, phosphomolybdic acid, vanillin, and anisaldehyde stain. Routine column chromatography was carried out using flash grade silica gel 60 (EM Science) with compressed air as the source of positive pressure unless stated otherwise. Tetrahydrofuran and ether were distilled from sodium and benzophenone under nitrogen or argon. Methylene chloride, acetonitrile, triethylamine, and TMSCl were distilled from calcium hydride. Dioxane was purchased from Aldrich in Sure-Seal bottles and degassed before use. Air-sensitive reactions were conducted under an atmosphere of argon or nitrogen in flame or oven-dried glassware using standard airless techniques.

Bis(benzonitrile)palladium dichloride was purchased from Alfa and used as received. Tris(2-furyl)phosphine (TFP) was prepared according to a literature method.[14] 5-Methylbenzo[*b*]thiophene was purchased from Lancaster. **2-(Tri-*n*-butylstannyl)thiophene (2b)** was prepared according to the procedure reported by Gronowitz et al.[5]

Preparation of Heteroarylstannanes. 2-(Tri-*n*-butylstannyl)furan (2a).[3] Furan (4.16 g, 61.10 mmol, 1.0 equiv) was dissolved in 120 mL of ether and cooled to −78 °C. TMEDA (10.14 mL, 67.22 mmol, 1.1 equiv) was introduced. After *n*-BuLi (26.89 mL, 2.5 M in hexanes, 67.22 mmol, 1.1 equiv) was added, the solution was stirred under N_2 at −78 °C for 1 h. The reaction was allowed to warm to room temperature and stirred for 3 h and then cooled to −78 °C. *n*-Bu_3SnCl was added dropwise via syringe and stirred for 1.5 h at −78 °C. The reaction was quenched with 10% of aqueous NH_4Cl (25 mL) and extracted with 3 × 70 mL ether. The combined ether layers were dried over Na_2SO_4 and concentrated to an oil. The resulting crude oil was purified by distillation to give 17.03 g (78%) of a clear yellow oil: bp 90–92 °C/0.025 mmHg; IR ($CHCl_3$, cm^{-1}) 1466, 1140; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.71 (d, *J* = 1.2 Hz, 1H), 6.54 (d, *J* = 3.3 Hz, 1H), 6.40 (m, 1H), 1.63–1.49 (m, 6H), 1.40–1.22 (m, 6H), 1.12–1.00 (m, 6H), 0.91 0.85 (t, *J* = 7.5 Hz, 9H). Anal. Calcd for $C_{16}H_{30}OSn$: C, 53.81; H, 8.47. Found: C, 53.91; H, 8.51.

5-(Trimethylsilyl)-2-(tri-*n*-butylstannyl)furan (3a) was prepared following the procedure described for the preparation of 2,5-bis(trimethylstannyl)furan.[3,6] Furan (6.11 g, 89.75 mmol, 1.0 equiv) and TMEDA (16.25 mL, 107.70 mmol, 1.2 equiv) were dissolved in 100 mL of THF and cooled to −78 °C. *n*-BuLi (43.08 mL, 2.5 M in hexanes, 107.7 mmol, 1.2 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature for 2.5 h and then cooled to −78 °C. TMSCl (11.39 mL, 89.75 mmol, 1.0 equiv) was added and the mixture was stirred for 1.5 h at −78 °C. After an additional 1.2 equiv of 2.5 M *n*-BuLi (43.08 mL, 107.70 mmol, 1.2 equiv) was added, the reaction mixture was warmed to room temperature for 2 h and then cooled to −78 °C. *n*-Bu_3SnCl (29.21 mL, 107.70 mmol, 1.2 equiv) was added dropwise and the reaction mixture was stirred for an additional 1.5 h at −78 °C. The reaction was quenched with 10% aqueous NH_4Cl (30 mL) and extracted with Et_2O (3 × 70 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to an oil. The resulting orange oil was purified by distillation to give 34.45 g (89%) of a yellow oil: bp 137–139 °C/0.18 mmHg; IR (CH_2Cl_2, cm^{-1}) 1540, 1466; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.63 (d, *J* = 2.7 Hz, 1H), 6.53 (d, *J* = 2.7 Hz, 1H), 1.61–1.51 (m, 6H), 1.38–1.26 (m, 6H), 1.08–1.03 (m, 6H), 0.88 (t, *J* = 7.2 Hz, 9H), 0.24 (s, 9H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 165.0, 164.5, 120.6, 118.7, 28.9, 27.1, 13.6, 10.1, −1.6. Anal. Calcd for $C_{19}H_{38}OSiSn$: C, 53.16; H, 8.92. Found: C, 53.22; H, 8.91.

5-(Trimethylsilyl)-2-(tri-*n*-butylstannyl)thiophene (3b). 2-(Trimethylsilyl)thiophene (5.00 g, 31.99 mmol, 1.0 equiv) and TMEDA (6.03 mL, 39.99 mmol, 1.25 equiv) were dissolved in 100 mL of THF and cooled to −78 °C. *n*-BuLi (15.99 mL, 2.5 M in hexanes, 39.99 mmol, 1.25 equiv) was added dropwise and the reaction mixture was warmed to room temperature for 3 h. The mixture was cooled to −78 °C, *n*-Bu_3SnCl (10.41 mL, 38.39 mmol, 1.2 equiv) was added dropwise, and the reaction mixture was

(14) Allen, D. W.; Hutley, B. G.; Mellor, R. T. J. *J. Chem. Soc., Perkin Trans. 2* **1972**, 63.

stirred for 1 h at −78 °C. The reaction was quenched with 10% aqueous NH_4Cl (20 mL) and warmed to room temperature. The mixture was extracted with Et_2O (3 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to an orange oil. The resulting orange oil was purified by distillation to give 12.70 g (89%) of a yellow oil: bp 143–144 °C/0.15 mmHg; IR (CH_2Cl_2, cm^{-1}) 1484, 1466; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, J = 2.7 Hz, 1H), 7.41 (d, J = 2.7 Hz, 1H), 1.69–1.61 (m, 6H), 1.56–1.43 (m, 6H), 1.37–1.20 (m, 6H), 1.17–1.02 (m, 9H), 0.46 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.7, 142.0, 136.1, 134.7, 29.0, 27.3, 13.6, 10.9, 0.2; HRMS (EI) calcd for $C_{19}H_{38}SSiSn$ 446.1485, found 446.1486.

2-(Tri-*n*-butylstannyl)benzofuran (4a). Benzofuran (2.00 g, 16.93 mmol, 1.0 equiv) and TMEDA (3.07 mL, 20.32 mmol, 1.2 equiv) were dissolved in 60 mL of ether and cooled to −78 °C. *n*-BuLi (8.12 mL, 2.5 M in hexanes, 20.32 mmol) was added dropwise via syringe. The reaction mixture was allowed to warm to room temperature and stirred for 3 h under argon. The solution was cooled to −78 °C and *n*-Bu_3SnCl (5.5 mL, 20.32 mmol, 1.2 equiv) was added dropwise. The reaction mixture was stirred for an additional 1.5 h at −78 °C and then quenched with 10% aqueous NH_4Cl (15 mL). The solution was allowed to warm to room temperature. After the mixture was extracted with ether (3 × 70 mL), the combined ether layers were dried ($MgSO_4$) and concentrated to an oil. The resulting yellow oil was purified by column chromatography on flash silica gel (hexanes eluant, R_f = 0.30) to afford 4.85 g (70%) of **4a** as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 1466, 1439; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.70–7.63 (m, 2H), 7.35–7.30 (m, 2H), 7.05 (s, 1H), 1.79–1.71 (m, 6H), 1.58–1.45 (m, 6H), 1.34–1.29 (m, 6H), 1.05 (t, J = 7.2 Hz, 9H). Anal. Calcd for $C_{20}H_{32}OSn$: C, 59.00; H, 7.92. Found: C, 58.96; H, 7.92.

2-(Tri-*n*-butylstannyl)benzothiophene (4b). Prepared as described for **4a**. An ether solution (60 mL) of benzothiophene (4.42 g, 32.96 mmol, 1.0 equiv) and TMEDA (5.97 mL, 39.55 mmol, 1.2 equiv) was treated with *n*-BuLi (15.82 mL, 2.5 M in hexanes, 39.55 mmol, 1.2 equiv) at −78 °C followed by *n*-Bu_3SnCl (10.73 mL, 39.55 mmol, 1.2 equiv) quench. Workup and purification by flash silica gel chromatography (1:10 EtOAc/hexanes, R_f = 0.72) gave 12.05 g (86%) of **4b** as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 1453, 1412; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.89–7.79 (m, 2H), 7.38 (s, 1H), 7.33–7.25 (m, 2H), 1.68–1.56 (m, 6H), 1.41–1.31 (m, 6H), 1.24–1.05 (m, 6H), 0.89 (t, J = 7.2 Hz, 9H). Anal. Calcd for $C_{20}H_{32}SSn$: C, 56.76; H, 7.62. Found: C, 56.93; H, 7.65.

5-Methyl-2-(tri-*n*-butylstannyl)benzothiophene (4c). Prepared as described for **4a**. An ether solution (40 mL) of 5-methylbenzothiophene (2.59 g, 16.47 mmol, 1.0 equiv) and TMEDA (3.29 mL, 20.59 mmol, 1.25 equiv) was treated with *n*-BuLi (8.73 mL, 2.5 M in hexanes, 20.59 mmol, 1.25 equiv) at −78 °C followed by *n*-Bu_3SnCl quench. Workup and purification by flash silica gel chromatography (hexanes eluant, R_f = 0.32) gave 7.02 g (92%) of **4c** as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 1493, 1465, 1418; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.85 (d, J = 7.8 Hz, 1H), 7.71 (s, 1H), 7.43 (s, 1H), 7.19 (d, J = 7.8 Hz, 1H), 2.56 (s, 3H), 1.78–1.67 (m, 6H), 1.54–1.40 (m, 6H), 1.30–1.23 (m, 6H), 1.06–1.01 (m, 9H). Anal. Calcd for $C_{21}H_{34}SSn$: C, 57.69; H, 7.84. Found: C, 57.75; H, 7.83.

4-(Tri-*n*-butylstannyl)dibenzofuran (11). An ether solution (80 mL) of dibenzofuran (4.03 g, 24.00 mmol, 1.0 equiv) and TMEDA (4.53 mL, 30.00 mmol, 1.25 equiv) was treated with 2.5 M *n*-BuLi in hexanes (12.00 mL, 30.00 mmol, 1.25 equiv) at −78 °C followed by *n*-Bu_3SnCl quench. Workup and purification by flash silica gel chromatography (hexanes, R_f = 0.29) gave 6.95 g (63%) of **11** as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 1580, 1468; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.96–7.89 (m, 2H), 7.55–7.40 (m, 3H), 7.34–7.29 (m, 2H), 1.69–1.55 (m, 6H), 1.41–1.31 (m, 6H), 1.25–1.14 (m, 6H), 0.9 (t, J = 7.5 Hz, 9H). Anal. Calcd for $C_{24}H_{34}OSn$: C, 63.05; H, 7.50. Found: C, 63.21; H, 7.51.

4-(Tri-*n*-butylstannyl)dibenzothiophene (12). An ether solution (50 mL) of dibenzothiophene (3.51 g, 19.05 mmol, 1.0 equiv) and TMEDA (3.59 mL, 23.81 mmol, 1.25 equiv) was treated with 2.5 M *n*-BuLi in hexanes (9.52 mL, 23.81 mmol, 1.25 equiv) at −78 °C followed by *n*-Bu_3SnCl quench. Workup and purification by flash silica gel chromatography (hexanes eluant, R_f = 0.33) gave 6.13 g (68%) of **12** as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 1465, 1370; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.15–8.08 (m, 2H), 7.86–7.83 (m, 1H), 7.52–7.38 (m, 4H), 1.67–1.48 (m, 6H), 1.46–1.16 (m, 12H), 0.9 (t, J = 7.5 Hz, 9H). Anal. Calcd for $C_{24}H_{34}SSn$: C, 60.91; H, 7.24. Found: C, 60.52; H, 7.28.

Preparation of 4-Chlorocyclobutenones. 4-Chlorocyclobutenones were prepared according to literature procedures (4-chloro-2,3-diethyl-2-cyclobutenone (**1a**),[2] 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**),[15] 4-chloro-2-methyl-3-(1-methylethoxy)-2-cyclobutenone (**1c**),[1] 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (**1d**),[1] and 4-chloro-3-methyl-2-phenyl-2-cyclobutenone (**1e**)[1]).

Palladium-Catalyzed Cross-Coupling of 4-Chlorocyclobutenones with 2-Stannylated Heteroaryls Followed by Thermolysis to Benzoheteroaryls. 5,6-Di-*n*-butyl-4-hydroxybenzofuran (5). A dioxane solution (3 mL) of 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**) (0.35 g, 1.61 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)furan (0.63 g, 1.77 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (0.03 g, 5 mol%) and TFP (0.04 g, 10 mol%) was heated to 50 °C for 4 h then at 100 °C for an additional 4 h. The reaction mixture was cooled to room temperature and quenched with 10 mL of water followed by extraction with ether (3 × 20 mL). The combined ether layers were dried (Na_2SO_4), filtered, and concentrated to an oil. The crude product was purified by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.43) to give 0.150 g (38%) of **5** as an unstable yellow solid: mp 55–56 °C (CH_2Cl_2/hexanes); IR ($CHCl_3$, cm^{-1}) 3618, 1592; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.45 (s, 1H), 6.97 (s, 1H), 6.73 (s, 1H), 5.06 (br, s, 1H), 2.68 (t, 4H), 1.65–1.50 (m, 8H), 0.96 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 154.5, 146.3, 143.0, 138.9, 119.6, 114.3, 104.4, 102.7, 33.7, 33.1, 32.5, 25.4, 23.0, 22.6, 13.9. The instability of this compound precluded a full analysis. Complete data were obtained for the analogous phenol acetate, described below.

4-Acetoxy-5,6-di-*n*-butylbenzofuran (6). A dioxane solution (3 mL) of 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**) (0.349 g, 1.63 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)furan (0.639 g, 1.79 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (0.031 g, 5 mol%) and TFP (0.038 g, 10 mol%) was heated to 100 °C for 6 h. Analysis by TLC indicated consumption of starting material (R_f = 0.43, 1:4 EtOAc/hexanes). Ac_2O (0.33 g, 3.26 mmol) and pyridine (0.26 g, 3.26 mmol) were added, and the reaction mixture was stirred for 4 h at 100 °C and quenched with 10 mL of water. The reaction mixture was extracted with ether (3 × 20 mL), the combined ether layers were dried (Na_2SO_4), filtered, concentrated to an oil, and purified by column chromatography on silica gel (R_f = 0.58, 1:4 EtOAc/hexanes) to give 0.174 g (37%) of **6** as a yellow oil: IR ($CHCl_3$, cm^{-1}) 1760, 1466; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.49 (d, J = 1.8 Hz, 1H), 7.25 (s, 1H), 6.52 (d, J = 1.8 Hz, 1H), 2.76–2.60 (m, 4H), 2.40 (s, 3H), 1.68–1.41 (m, 8H), 0.98 (t, J = 7.2 Hz, 6H). Anal. Calcd for $C_{18}H_{24}O_2$: C, 74.97; H, 8.39. Found: C, 74.90; H, 8.41.

4-Acetoxy-5,6-diethyl-2-(trimethylsilyl)benzofuran (7a). A dioxane solution (4 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.280 g, 1.77 mmol, 1.0 equiv) and 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)furan (**3a**) (0.834 g, 1.95 mmol, 1.0 equiv) with $(PhCN)_2PdCl_2$ (34 mg, 5 mol%) and TFP (41 mg, 10 mol%) was heated to 50 °C for 4 h and then at 100 °C for 4 h. Acetylation with pyridine (0.28 g, 3.54 mmol) and Ac_2O (0.36 g, 3.54 mmol) at 100 °C for an additional 4 h, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.48) gave 0.382 g (71%) of **7a** as a yellow oil: IR (CH_2Cl_2, cm^{-1}) 1758, 1466; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.28 (s, 1H), 6.71 (s, 1H), 2.78 (q, J = 7.5 Hz, 2H), 2.66 (q, J = 7.5 Hz, 2H), 2.43 (s, 3H), 1.29 (t, J = 7.5 Hz, 3H), 1.14 (t, J = 7.5 Hz, 3H), 0.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.2, 163.0, 157.6, 140.8, 139.8, 127.5, 119.7, 112.7, 108.1, 25.8, 20.7, 19.5, 15.4, 14.7, −1.9. Anal. Calcd for $C_{17}H_{24}O_3Si$: C, 67.07; H, 7.95. Found: C, 67.17; H, 7.97.

4-Acetoxy-5,6-di-*n*-butyl-2-(trimethylsilyl)benzofuran (7b). A dioxane solution (4 mL) of 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**) (0.386 g, 1.80 mmol, 1.0 equiv) and 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)furan (**3a**) (0.850 g, 1.98 mmol, 1.0 equiv) with $(PhCN)_2PdCl_2$ (34 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 4 h and then 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica

(15) Stone, G. B.; Liebeskind, L. S. *J. Org. Chem.* **1990**, *55*, 4614.

gel chromatography (1:4 EtOAc/hexanes, R_f = 0.54) gave 0.422 g (65%) of **7b** as a yellow oil: IR (CH_2Cl_2, cm^{-1}) 1762, 1629, 1584; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.25 (s, 1H), 6.71 (s, 1H), 2.75–2.63 (m, 4H), 2.41 (s, 3H), 1.65–1.41 (m, 8H), 1.00–0.94 (m, 6H), 0.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.7, 163.6, 158.1, 141.7, 139.4, 127.0, 120.4, 113.4, 110.1, 34.3, 33.5, 33.3, 26.8, 23.6, 23.3, 21.4, 14.6, 14.5, −1.2. Anal. Calcd for $C_{21}H_{32}O_2Si$: C, 69.95; H, 8.95. Found: C, 70.06; H, 8.99.

4-Acetoxy-5-methyl-6-(1-methylethoxy)-2-(trimethylsilyl)-benzofuran (7c). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-(1-methylethoxy)-2-cyclobutenone (**1c**) (0.324 g, 1.86 mmol, 1.0 equiv) and 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)-furan (**3a**) (0.877 g, 2.05 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (36 mg, 5 mol%) and TFP (43 mg, 10 mol%) was heated to 50 °C for 4 h and then at 100 °C for 4 h. Acetylation and workup as above and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.67) gave 0.465 g (78%) of **7c** as a yellow oil: IR (CH_2Cl_2, cm^{-1}) 1764, 1632; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.96 (s, 1H), 6.75 (s, 1H), 4.54 (hept, J = 6.0 Hz, 1H), 2.40 (s, 3H), 2.12 (s, 3H), 1.38 (d, J = 6.0 Hz, 6H), 0.35 (s, 9H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.6, 161.8, 157.6, 154.8, 141.2, 115.0, 114.7, 112.6, 94.4, 70.9, 21.9, 20.5, 9.4, −1.9. Anal. Calcd for $C_{17}H_{24}O_4Si$: C, 63.72; H, 7.55. Found: C, 63.78; H, 7.56.

4-Acetoxy-5,6-diethyl-2-(trimethylsilyl)benzothiophene (7d). A dioxane solution (4 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.284 g, 1.79 mmol, 1.0 equiv) and 5-(trimethylsilyl)-2-(tri-*n*-butylstannyl)thiophene (**3b**) (0.877 g, 1.97 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (34 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 4 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.47) gave 0.333 g (58%) of **7d** as a yellow oil: IR (CH_2Cl_2, cm^{-1}) 1766, 1621, 1544; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.58 (s, 1H), 7.13 (s, 1H), 2.77 (q, J = 7.5 Hz, 2H), 2.67 (q, J = 7.5 Hz, 2H), 2.45 (s, 3H), 1.29 (t, J = 7.5 Hz, 3H), 1.15 (t, J = 7.5 Hz, 3H), 0.34 (s, 9H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.3, 143.1, 142.7, 142.0, 140.1, 132.8, 129.5, 125.9, 119.2, 25.8, 20.7, 19.7, 15.4, 14.4, −0.4. Anal. Calcd for $C_{17}H_{24}O_2SiS$: C, 63.70; H, 7.55. Found: C, 63.79; H, 7.55.

Typical Procedure for Palladium-Catalyzed Cross-Coupling of 4-Chlorocyclobutenones and 2-Stannylated Benzoheteroaryls Followed by Rearrangement to Dibenzoheteroaryls. 1-Acetoxy-2,3-diethyldibenzofuran, 8a. A dioxane solution (3 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.224 g, 1.41 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)-benzofuran, (**4a**) (0.632 g, 1.55 mmol, 1.1 equiv) was prepared in a 25-mL round-bottomed flask and degassed under nitrogen for 15 min. The solution was treated with a solid mixture of $(PhCN)_2PdCl_2$ (27 mg, 5 mol%) and TFP (33 mg, 10 mol%). The mixture was stirred for 10 min at room temperature until all the solids had dissolved and then heated to 50 °C. After 12 h, TLC showed consumption of starting material (R_f = 0.64 for the coupled product, 1:4 EtOAc/hexanes). The reaction mixture was heated to 100 °C for an additional 4 h and then treated with Ac_2O (0.29 g, 2.82 mmol) and pyridine (0.22 g, 2.82 mmol) for 4 h at 100 °C to effect esterification. After cooling to room temperature, 10 mL of 10% aqueous KF solution was added followed by 20 mL of aqueous $CuSO_4$ solution to remove pyridine. The mixture was extracted with 3 × 25 mL of ether and the combined ether layers were dried ($MgSO_4$), filtered, and concentrated to an orange oil that was purified by column chromatography on flash silica gel (R_f = 0.64, 1:4 EtOAc/hexanes) to give 0.374 g (94%) of **8a** as a white solid: mp 62–63 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1756, 1607; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.71 (d, J = 7.5 Hz, 1H), 7.57 (d, J = 8.1 Hz, 1H), 7.43 (t, J = 7.5 Hz, J = 8.1 Hz, 1H), 7.38 (s, 1H), 7.34 (t, J = 7.5 Hz, J = 8.1 Hz, 1H), 2.87 (q, J = 7.5 Hz, 2H), 2.73 (m, 2H), 2.56 (s, 3H), 1.39 (t, J = 7.5 Hz, 3H), 1.25 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz, only 17 C observed) δ 168.9, 156.0, 155.4, 142.9, 128.6, 126.6, 122.7, 122.4, 121.2, 115.4, 111.4, 109.1, 26.1, 20.7, 19.5, 15.3, 14.7. Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.40; H, 6.45.

1-Acetoxy-2,3-di-*n*-butyldibenzofuran (8b). A dioxane solution (4 mL) of 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**) (0.365 g, 1.70 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)-benzofuran (**4a**) (0.761 g, 1.87 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (33 mg, 5 mol%) and TFP (40 mg, 10 mol%) was heated at 50 °C for 12 h and at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.65, 1:4 EtOAc/hexanes, 1:8 EtOAc/hexanes) gave 0.374 g (65%) of **8b** as a pale yellow oil: IR (CH_2Cl_2, cm^{-1}) 1758, 1644, 1607; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.63 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.42–7.37 (m, 1H), 7.30–7.25 (m, 2H), 2.78–2.62 (m, 4H), 2.52 (s, 3H), 1.69–1.28 (m, 8H), 0.99–0.88 (m, 6H); HRMS (EI) calcd for $C_{22}H_{26}O_3$ 338.1882, found 338.1882.

1-Acetoxy-2-methyl-3-(1-methylethoxy)dibenzofuran (8c). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-(1-methylethoxy)-2-cyclobutenone, **2c**, (0.321 g, 1.84 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzofuran (**4a**) (0.824 g, 2.02 mmol, 1.0 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (43 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.62, 1:8 EtOAc/hexanes) gave 0.462 g (84%) of **8c** as a thick yellow oil: IR (CH_2Cl_2, cm^{-1}) 1756, 1646, 1609; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.68 (d, J = 7.5 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.40–7.28 (m, 3H), 4.59 (hept, J = 6.0 Hz, 1H), 2.52 (s, 3H), 2.16 (s 3H), 1.41 (d, J = 6.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.3, 156.6, 155.8, 155.7, 143.5, 125.5, 122.73, 122.67, 120.5, 115.6, 111.1, 110.0, 94.4, 71.1, 22.0, 20.6, 9.3. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.25; H, 6.13.

1-Methoxy-2-methyl-3-(1-methylethoxy)dibenzofuran (8c') for NOE Studies. A solution of 1-acetoxy-2-methyl-3-(1-methylethoxy)dibenzofuran (80.2 mg, 0.27 mmol) in 4 mL of methanol and 2 mL of water was treated with 2 mL of saturated sodium bicarbonate solution then degassed under nitrogen. The suspension was heated to gentle reflux for 15 h and was then cooled to room temperature. The reaction mixture was acidified with 10% hydrochloric acid and extracted with EtOAc (3 × 25 mL). The extract was dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated to form a crude oil that was purified by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.56) to give 64 mg (93%) of 1-hydroxy-2-methyl-3-(1-methylethoxy)-dibenzofuran as a pale yellow solid: mp 85–87 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 3605, 1660, 1610; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01–7.98 (m, 1H), 7.50–7.47 (m, 1H), 7.36–7.27 (m, 2H), 6.73 (s, 1H), 5.21 (s, 1H), 4.59 (hept, J = 6.0 Hz, 1H), 2.25 (s, 3H), 1.39 (d, J = 6.0 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 156.6, 156.2, 155.5, 150.0, 124.8, 123.8, 122.7, 121.4, 110.8, 107.0, 105.9, 90.2, 71.2, 22.2, 8.0. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.70; H, 6.36. A solution of 1-hydroxy-2-methyl-3-(1-methylethoxy)dibenzofuran (58 mg, 0.23 mmol) in 2 mL of acetone was treated with K_2CO_3 (156 mg, 1.13 mmol) and iodomethane (321 mg, 2.30 mmol). The mixture was stirred under nitrogen and heated to gentle reflux for 6 h. The reaction mixture was cooled to room temperature, and the precipitated salts were removed by filtration. The filtrate was concentrated *in vacuo* and the resulting crude product was purified by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.58) to give 58 mg (94%) of 1-methoxy-2-methyl-3-(1-methylethoxy)dibenzofuran (**8c'**) as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 1640, 1608; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99–7.97 (m, 1H), 7.51–7.49 (m, 1H), 7.38–7.30 (m, 2H), 6.89 (s, 1H), 4.60 (hept, J = 6.0 Hz, 1H), 3.96 (s, 3H), 2.25 (s, 3H), 1.41 (d, J = 6.0 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 157.1, 156.1, 155.7, 153.6, 125.1, 123.2, 122.8, 121.5, 115.8, 110.9, 110.2, 93.1, 71.0, 60.3, 22.1, 8.9; HRMS calcd for $C_{17}H_{18}O_3$ 270.1256, found 270.1256.

Description of NOE Experiment. The regiochemistry of **8c'** was determined by the NOE difference method[16] using a Nicolet/GE NT-360 instrument: irradiation at the methyl resonance at 2.25 ppm (12 s, 28 dB, causing ca. 85% reduction in peak intensity), 2% enhancement of the methoxy resonance at 3.96 ppm; irradiation at 3.96 ppm (12 s, 32 dB, causing ca. 85% reduction in peak intensity), 2% enhancement of the methyl resonance at 2.25 ppm and 10% enhancement of H-9 (centered at 7.98 ppm) of the dibenzofuran ring.

1-Acetoxy-2-methyl-3-phenyldibenzofuran (8d). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (**1d**) (0.328 g, 1.70 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)-benzofuran (**4a**) (0.761 g, 1.87 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$

(16) Derome, A. E. *Modern NMR Techniques for Chemistry Research*; Pergamon: New York, 1987; pp 143.

(33 mg, 5 mol%) and TFP (40 mg, 10 mol%) was heated to 50 °C for 12 h and then 4 h at 100 °C. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.65, 1:4 EtOAc/hexanes) gave 0.403 g (75%) of **8d** as a white solid: mp 91–92 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1758, 1644, 1602; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.77 (d, J = 7.5 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.48–7.33 (m, 8H), 2.56 (s, 3H), 2.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.4, 156.2, 154.8, 143.4, 142.4, 141.1, 129.3, 128.1, 127.2, 127.1, 122.8, 122.6, 122.1, 121.4, 116.4, 111.5, 110.7, 20.7, 13.4. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.67; H, 5.14.

1-Acetoxy-3-methyl-2-phenyldibenzofuran (8e). A dioxane solution (4 mL) of 4-chloro-3-methyl-2-phenyl-2-cyclobutenone (**1e**) (0.343 g, 1.78 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzofuran (**4a**) (0.798 g, 1.96 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (34 mg, 5 mol%) and TFP (41 mg, 10 mol%) was heated to 50 °C for 12 h and then 4 h at 100 °C. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.62, 1:4 EtOAc/hexanes, 1:8 EtOAc/hexanes eluant) gave 0.502 g (89%) of **8e** as a white solid: mp 165–167 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1775, 1644, 1607; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.43 (m, 5H), 7.25 (m, 3H), 2.26 (s, 3H), 2.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.6, 156.04, 155.95, 142.3, 137.1, 136.1, 130.0, 129.7, 128.0, 127.2, 126.8, 122.8, 122.3, 121.2, 115.4, 111.4, 110.4, 21.2, 20.2. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: 79.47; H, 5.14.

1-Acetoxy-2,3-diethyldibenzothiophene (8f). A dioxane solution (4 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.293 g, 1.84 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzothiophene (**4b**) (0.860 g, 2.02 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (43 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.63, 1:4 EtOAc/hexanes, 1:8 EtOAc/hexanes eluant) gave 0.469 g (85%) of **8f** as a pale yellow solid: mp 113–114 °C (EtOAc/hexanes); IR (CH_2Cl_2, cm^{-1}) 1766, 1610; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.07–8.05 (m, 1H), 7.83–7.80 (m, 1H), 7.59 (s, 1H), 7.43–7.40 (m, 2H), 2.84 (q, J = 7.5 Hz, 2H), 2.70 (m, 2H), 2.57 (s, 3H), 1.33 (t, J = 7.5 Hz, 3H), 1.22 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz, only 17 C observed) δ 169.2, 145.1, 142.3, 139.4, 138.4, 133.7, 130.9, 126.0, 124.4, 123.2, 122.6, 120.0, 25.8, 21.0, 19.7, 15.2, 14.4. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08. Found: C, 72.52; H, 6.09.

1-Acetoxy-2,3-di-*n*-butyldibenzothiophene (8g). A dioxane solution (4 mL) of 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**) (0.390 g, 1.82 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzothiophene (**4b**) (0.846 g, 2.00 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.63, 1:4 EtOAc/hexanes) gave 0.394 g (61%) of **8g** as a pale yellow solid: mp 75–76 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1767, 1609; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.07–8.04 (m, 1H), 7.82–7.79 (m, 1H), 7.57 (s, 1H), 7.42–7.38 (m, 2H), 2.79–2.62 (m, 4H), 2.56 (s, 3H), 1.72–1.41 (m, 8H), 1.02–0.96 (m, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz, only 21 C observed) δ 169.1, 145.3, 141.3, 139.4, 138.2, 133.7, 129.8, 125.9, 124.3, 123.2, 122.6, 120.7, 33.4, 32.8, 32.3, 26.4, 23.1, 22.7, 21.0, 13.9, 13.8. Anal. Calcd for $C_{22}H_{26}O_2S$: C, 74.54; H, 7.39. Found: C, 74.54; H, 7.41.

1-Acetoxy-2-methyl-3-(1-methylethoxy)dibenzothiophene (8h). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-(1-methylethoxy)-2-cyclobutenone (**1c**) (0.321 g, 1.84 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzothiophene (**4c**) (0.857 g, 2.02 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (43 mg, 10 mol%) was heated to 50 °C for 12 h and then 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.59, 1:4 EtOAc/hexanes, 1:8 EtOAc/hexanes eluant) gave 0.475 g (82%) of **8h** as a pale yellow solid: mp 119–120 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1771, 1611; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.10 (d, J = 8.1 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.45–7.38 (m, 2H), 7.21 (s, 1H), 4.60 (hept, J = 6.0 Hz, 1H), 2.54 (s, 3H), 2.18 (s, 3H), 1.41 (d, J = 6.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.3, 155.9, 145.8, 138.63, 138.55, 134.0, 125.2, 124.4, 122.7, 122.4, 121.0, 118.2, 103.7, 70.9, 22.0, 20.8, 9.6. Anal. Calcd for $C_{18}H_{18}O_3S$: C, 68.77; H, 5.77. Found: C, 68.74; H, 5.82.

1-Acetoxy-2-methyl-3-phenyldibenzothiophene (8i). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (**1d**) (0.349 g, 1.81 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzothiophene (**4b**) (0.843 g, 1.99 mmol, 1.0 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (R_f = 0.62, 1:4 EtOAc/hexanes) gave 0.380 g (63%) of **8i** as a pale yellow solid: mp 122–123 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1769, 1602; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.22–8.19 (m, 1H), 7.86–7.83 (m, 1H), 7.66 (s, 1H), 7.49–7.39 (m, 7H), 2.58 (s, 3H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.4, 145.7, 142.1, 140.8, 139.8, 138.0, 133.5, 129.5, 129.3, 128.1, 127.2, 126.4, 124.8, 124.5, 123.7, 122.7, 121.5, 20.9, 13.7. Anal. Calcd for $C_{21}H_{16}O_2S$: C, 75.88; H, 4.85. Found: C, 76.00; H, 4.92.

1-Acetoxy-3-methyl-2-phenyldibenzothiophene (8j). A dioxane solution (3 mL) of 4-chloro-3-methyl-2-phenyl-2-cyclobutenone (**1e**) (0.306 g, 1.59 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)benzothiophene (**4b**) (0.740 g, 1.75 mmol, 1.0 equiv) with $(PhCN)_2PdCl_2$ (30 mg, 5 mol%) and TFP (37 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.60) gave 0.270 g (51%) of **8j** as a pale yellow solid: mp 136–137 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1769, 1609; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.06–8.03 (m, 1H), 7.84–7.81 (m, 1H), 7.66 (s, 1H), 7.46–7.26 (m, 7H), 2.23 (s, 3H), 2.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 168.8, 144.5, 139.9, 139.4, 136.5, 136.2, 133.8, 132.2, 129.8, 128.1, 127.3, 126.3, 126.0, 124.5, 123.5, 122.6, 121.3, 20.9, 20.5. Anal. Calcd for $C_{21}H_{16}O_2S$: C, 75.88; H, 4.85. Found: C, 75.97; H, 4.90.

1-Acetoxy-2,3-diethyl-8-methyldibenzothiophene (8k). A dioxane solution (4 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.290 g, 1.83 mmol, 1.0 equiv) and 5-methyl-2-(tri-*n*-butylstannyl)benzothiophene (**4c**) (0.879 g, 2.01 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.62) gave 0.474 g (83%) of **8k** as a pale yellow solid: mp 97–98 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1766, 1609; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.84 (s, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.56 (s, 1H), 7.22 (d, J = 8.1 Hz, 1H), 2.85–2.63 (m, 4H), 2.57 (s, 3H), 2.49 (s, 3H), 1.32 (t, J = 7.5 Hz, 3H), 1.20 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.1, 145.0, 142.1, 138.8, 136.4, 133.9, 133.8, 130.7, 127.4, 125.9, 123.6, 122.2, 120.0, 25.8, 21.7, 21.0, 19.7, 15.1, 14.4. Anal. Calcd for $C_{19}H_{20}O_2S$: C, 73.04; H, 6.45. Found: C, 72.95; H, 6.46.

1-Acetoxy-2,3-di-*n*-butyl-8-methyldibenzothiophene (8l). A dioxane solution (4 mL) of 4-chloro-2,3-di-*n*-butyl-2-cyclobutenone (**1b**) (0.388 g, 1.80 mmol, 1.0 equiv) and 5-methyl-2-(tri-*n*-butylstannyl)benzothiophene (**4c**) (0.868 g, 1.99 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.77; 1:10 EtOAc/hexanes eluant) gave 0.382 g (58%) of **8l** as a pale yellow solid: mp 56–57 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1767, 1609; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.88 (s, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.56 (s, 1H), 7.24 (d, J = 8.1 Hz, 1H), 2.80–2.64 (m, 4H), 2.58 (s, 3H), 2.51 (s, 3H), 1.74–1.44 (m, 8H), 1.05–0.98 (m, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.0, 145.2, 114.1, 138.7, 136.4, 134.0, 133.8, 129.7, 127.4, 125.9, 123.7, 122.2, 120.7, 33.4, 32.8, 32.3, 26.4, 23.1, 22.8, 21.7, 21.0, 13.9, 13.8. Anal. Calcd for $C_{23}H_{28}O_2S$: C, 74.96; H, 7.66. Found: C, 74.78; H, 7.61.

1-Acetoxy-2,8-dimethyl-3-phenyldibenzothiophene (8m). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (**1d**) (0.347 g, 1.80 mmol, 1.0 equiv) and 5-methyl-2-(tri-*n*-butylstannyl)benzothiophene (**4c**) (0.866 g, 1.98 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (42 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.55) gave 0.374 g (60%) of **8m** as a white solid: mp 121–123 °C (CH_2Cl_2/

hexanes); IR (CH_2Cl_2, cm^{-1}) 1771; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.03 (s, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.63 (s, 1H), 7.48–7.39 (m, 5H), 7.29 (d, J = 8.4 Hz, 1H), 2.59 (s, 3H), 2.53 (s, 3H), 2.19 (s, 3H). Anal. Calcd for $C_{22}H_{18}O_2S$: C, 76.27; H, 5.24. Found: C, 76.03; H, 5.28.

1-Acetoxy-3,8-dimethyl-2-phenyldibenzothiophene (8n). A dioxane solution (4 mL) of 4-chloro-3-methyl-2-phenyl-2-cyclobutenone (**1e**) (0.354 g, 1.84 mmol, 1.0 equiv) and 5-methyl-2-(tri-*n*-butylstannyl)benzothiophene (**4c**) (0.884 g, 2.02 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (43 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.56) gave 0.401 g (63%) of **8n** as a white solid: mp 156–157 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1771, 1609; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.85 (s, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.64 (s, 1H), 7.46–7.24 (m, 5H), 7.26 (d, J = 8.1 Hz, 1H), 2.47 (s, 3H), 2.23 (s, 3H), 2.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz, only 21 C observed) δ 168.9, 144.5, 140.4, 136.45, 136.37, 134.1, 134.0, 132.1, 129.9, 128.2, 127.8, 127.3, 126.0, 124.0, 122.3, 121.4, 21.8, 21.0, 20.6. Anal. Calcd for $C_{22}H_{18}O_2S$: C, 76.27; H, 5.24. Found: C, 76.35; H, 5.28.

4-Acetoxy-2,3-diethylbenzo[*b*]naphtho[2,1-*d*]furan (13a). A dioxane solution (4 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.292 g, 1.84 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)-dibenzofuran (**4a**) (0.924 g, 2.02 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (35 mg, 5 mol%) and TFP (43 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.49) gave 0.465 g (76%) of **13a** as a pale yellow solid: mp 127–128 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1760, 1513; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.22 (s, 1H), 8.00–7.93 (m, 2H), 7.73 (d, J = 8.1 Hz, 1H), 7.60 (d, J = 8.7 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 2.96 (q, J = 7.5 Hz, 2H), 2.81 (m, 2H), 2.56 (s, 3H), 1.47 (t, J = 7.5 Hz, 3H), 1.28 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.6, 155.9, 151.8, 145.0, 141.9, 132.3, 126.1, 125.0, 124.9, 122.9, 120.7, 120.2, 119.0, 118.3, 117.5, 116.3, 111.9, 25.9, 20.7, 20.3, 15.0, 14.2. Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.07. Found: C, 79.29; H, 6.13.

4-Acetoxy-3-methyl-2-phenylbenzo[*b*]naphtho[2,1-*d*]furan (13b). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (**1d**) (0.334 g, 1.73 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)dibenzofuran (**4a**) (0.871 g, 1.90 mmol) with $(PhCN)_2PdCl_2$ (33 mg, 5 mol%) and TFP (40 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.48) gave 0.379 g (60%) of **13b** as a white solid: mp 220–221 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1761, 1457; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.26 (s, 1H), 8.02–7.99 (m, 2H), 7.71–7.65 (m, 2H), 7.47–7.39 (m, 7H), 2.55 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, only 23 C observed) δ 169.0, 156.1, 152.2, 145.6, 142.1, 141.1, 129.6, 128.2, 127.4, 126.3, 126.0, 125.7, 124.9, 123.0, 120.4, 120.3, 120.0, 119.4, 119.2, 116.2, 111.8, 20.7, 14.6; HRMS (EI) calcd for $C_{25}H_{18}O_3$ 366.1256, found 366.1246.

4-Acetoxy-2,3-diethylbenzo[*b*]naphtho[2,1-*d*]thiophene (13c). A dioxane solution (4 mL) of 4-chloro-2,3-diethyl-2-cyclobutenone (**1a**) (0.278 g, 1.75 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)dibenzothiophene (**4b**) (0.912 g, 1.93 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (34 mg, 5 mol%) and TFP (41 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.52) gave 0.479 g (78%) of **13c** as a white solid: mp 152–153 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1764, 1607; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.17 (dd, J = 7.8 Hz, J = 6.0 Hz, 1H), 8.10 (d, J = 8.7 Hz, 1H), 7.95 (dd, J = 7.8 Hz, J = 6.0 Hz, 1H), 7.85 (s, 1H), 7.67 (d, J = 6.0 Hz, 1H), 7.51–7.47 (m, 2H), 2.90 (q, J = 7.5 Hz, 2H), 2.77 (br, s, 2H), 2.54 (s, 3H), 1.42 (t, J = 7.5 Hz, 3H), 1.24 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 169.6, 145.2, 142.1, 139.0, 136.9, 136.4, 132.4, 132.3, 128.2, 126.0, 124.4, 124.2, 122.8, 121.4, 121.3, 119.4, 118.4, 25.9, 20.7, 20.3, 15.2, 14.2. Anal. Calcd for $C_{22}H_{20}O_2S$: C, 75.83; H, 5.79. Found: C, 75.75; H, 5.80.

4-Acetoxy-3-methyl-2-phenylbenzo[*b*]naphtho[2,1-*d*]thiophene (13d). A dioxane solution (4 mL) of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (0.333 g, 1.73 mmol, 1.0 equiv) and 2-(tri-*n*-butylstannyl)dibenzothiophene (0.900 g, 1.90 mmol, 1.1 equiv) with $(PhCN)_2PdCl_2$ (33 mg, 5 mol%) and TFP (40 mg, 10 mol%) was heated to 50 °C for 12 h and then at 100 °C for 4 h. Acetylation, workup as above, and purification by flash silica gel chromatography (1:4 EtOAc/hexanes, R_f = 0.52) gave 0.410 g (62%) of **13d** as a white solid: mp 217–218 °C (CH_2Cl_2/hexanes); IR (CH_2Cl_2, cm^{-1}) 1764, 1603; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.19–8.16 (m, 2H), 7.95–7.92 (m, 2H), 7.79 (d, J = 8.7 Hz, 1H), 7.49–7.45 (m, 7H), 2.55 (s, 3H), 2.24 (s, 3H). Anal. Calcd for $C_{25}H_{18}O_2S$: C, 78.51; H, 4.74. Found: C, 78.26; H, 4.79.

Acknowledgment. This investigation was supported by Grant No. CA40157, awarded by the National Cancer Institute, DHHS. We acknowledge the use of a VG 70-S mass spectrometer purchased through funding from the National Institutes of Health, S10-RR-02478, a 300-MHz NMR and a 360-MHz NMR purchased through funding from the National Science Foundation, NSF CHE-85-16614 and NSF CHE-8206103, respectively, and a 500-MHz NMR purchased through funding from both the NIH (S10-RR-03519) and NSF (DMB-86-16628). We acknowledge the skilled assistance of Dr. J. Stuart McCallum in conducting the NOE experiment on compound **8c'**. We also acknowledge SmithKline Beecham (Dr. Conrad Kowalski) for a generous gift of squaric acid.