An Efficient Route to Benzo[b]thiophene Quinones, Quinone Bisketals, and Quinone Monoketals via Anodic Oxidation of Methoxylated Benzo[b]thiophenes. Studies Directed at the Synthesis of Functionalized Benzo[b]thiophene-4,7-quinones

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A convenient route to 4- and 7-methoxybenzo[b]thiophenes has been developed in the course of electrochemical studies of these molecules. The anodic oxidations of 4-methoxy-, 5-bromo-4-methoxy-, 5-methyl-4-methoxy-, and 6-bromo-7-methoxybenzo[b]thiophene, **17a–d**, respectively, in methanolic potassium hydroxide at a platinum anode have been investigated. The products obtained from the oxidation of these compounds were temperature dependent. This temperature dependence was most extensively studied for **17a** wherein oxidation at or below room temperature, followed by workup, gave primarily 4,7-dimethoxybenzo[b]thiophene. However, oxidation of **17a** in methanol at ca. 65 °C gave primarily the quinone bisketal. In a similar manner oxidation of **17b,c** gave the respective bisketals of benzo[b]thiophene-4,7-quinones in good yields. Extended acidic hydrolyses of these quinone bisketals afforded the corresponding quinones in 78–95% yield. Milder conditions for the hydrolyses afforded monoketals of benzo[b]thiophene-4,7-quinones, the products from **17b,c** being formed with high regioselectivity. Other chemistry of these quinone bis- and monoketals, initially directed at a synthesis of Caldariellaquinone, is presented and discussed.

Introduction

Benzo[b]thiophene-4,7-quinones have been of interest for more than 50 years, due in large measure to their isosteric relationship to naphthoquinones. Derivatives of this parent ring system have been prepared and their biological activity examined.[1,2] Although naphthoquinones are widely distributed in nature,[3] naturally occurring thianaphtha-4,7-quinones were unknown until the late 1970s when caldariellaquinone, **1**, was isolated from the extremely thermophilic and acidophilic bacteria *Caldariella acidophilia*.[4,5]

The structure proposed for caldariellaquinone is **1**.[5] While the assignments of the basic ring system and the thiomethyl ether and polyprenyl side chains are reasonably secure, the alternative structure **2** cannot be rigorously ruled out. Recent anodic oxidation studies[6] in our group

1 2

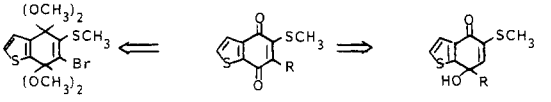
R = -(CH2CH2-CH(CH3)-CH2)5-CH2CH2CH(CH3)2 (CH3 on the CH)

suggested a facile entry into the benzo[b]thiophene-4,7-quinone ring systems. We report herein these anodic oxidation results and some studies directed at the synthesis of caldariellaquinone.[7]

Electrochemical and Synthetic Studies

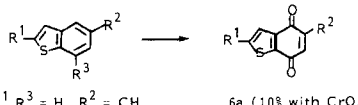
Initially, two approaches were considered for the synthesis of **1**. One of these involved preparation of the quinone bisketal **3**, conversion of the vinyl bromide to its cuprate derivative,[8] coupling with an allylic halide, and the reduction of the double bond to give the required isoprenoid side chain (Scheme I). A second general strategy was preparation of the *p*-quinol **4** from the appropriate monoketal, followed by a dienone–phenol rearrangement and oxidation to afford **1**. While bisketals of benzoquinones and naphthoquinones can be readily prepared by electrochemical oxidation of the respective 1,4-dimethoxy aromatic derivatives,[9] there have been no reports of related oxidations in benzo[b]thiophenes.

Scheme I. Synthetic Strategies to Caldariellaquinone



3 1 4

The 4,7-dimethoxybenzo[b]thiophenes required for the exploratory anodic oxidation studies are not so readily available as the corresponding 1,4-dimethoxy aromatic systems. While they could be prepared from reduction of the corresponding quinones followed by methylation of the resulting hydroquinones, the benzo[b]thiophene-4,7-quinones themselves are usually not available in good yield from readily available precursors. Thus, 5-methylbenzo[b]thiophene, **5a**, can be oxidized with chromium oxide to the quinone **6a** in only 10% yield,[1] while Fremy's salt



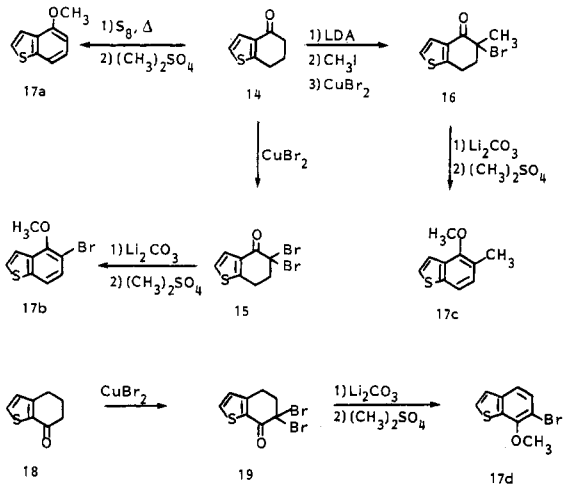
5a, R^1,R^3 = H, R^2 = CH_3 6a (10% with CrO_3)
b, R^1 = C_6H_5, R^2 = H, R^3 = OH b (31% with Fremy's salt)

oxidation of **5b** affords **6b** in 31% yield.[10] An additional problem associated with the Fremy's salt oxidation is the competing formation of *o*-quinones.[10] Perhaps the most

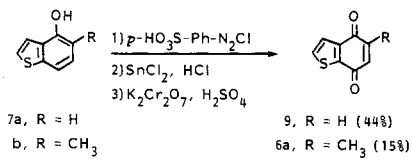
(1) Tarbell, D. S.; Fukushima, D. K.; Dam, H. *J. Am. Chem. Soc.* **1945**, *67*, 1643.
(2) Kitchen, R.; Sandin, R. B. *J. Am. Chem. Soc.* **1945**, *67*, 1645.
(3) Ramasarma, T. *Adv. Lipid Res.* **1968**, *6*, 108.
(4) DeRosa, M.; Gambacorta, A.; Minale, L. *J. Chem. Soc., Chem. Commun.* **1975**, 392.
(5) DeRosa, M.; DeRosa, S.; Gambacorta, A.; Minale, L.; Thompson, R. H.; Worthington, R. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 653.
(6) Jackson, D. K.; Swenton, J. S. *Synth. Commun.* **1977**, *7*, 333. Dolson, M. G.; Swenton, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 2361.
(7) A preliminary report of some of this work has been published: Chenard, B. L.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1979**, 1172.
(8) Chenard, B. L.; Manning, M. J.; Raynolds, P. W.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 378.
(9) For a comprehensive discussion, see: Henton, D. R.; McCreery, R. L.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 369.
(10) For a review of Fremy's salt oxidation, see: Zimmer, H.; Lankin, D. C.; Hargon, S. W. *Chem. Rev.* **1971**, *71*, 229.

0022-3263/83/1948-4312$01.50/0

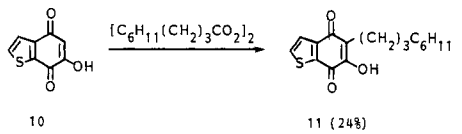
Scheme II. Synthesis of Functionalized Benzo[b]thiophenes



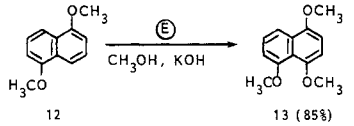
expedient entry into benzo[b]thiophene-4,7-quinones is the classical diazo coupling/reduction/oxidation sequence as illustrated for quinones **9** and **6a**. While this sequence



afforded **9**[11] in 44% overall yield, **6a** was formed in only 15% overall yield.[2] Furthermore, even with the quinone unit available, the introduction of carbon functionality on the quinone bearing ring is nontrivial as illustrated by the conversion of **10** to **11**.[12]

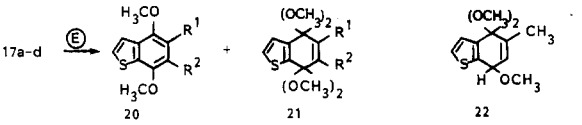


In view of the difficulty of preparing functionalized benzo[b]thiophene-4,7-quinones, a good route to these quinones was required before approaches to the synthesis of **1** could be evaluated. We had recently reported that anodic oxidation of monomethoxylated naphthalene derivatives often afforded dimethoxylated naphthalenes in excellent yield (e.g., **12** to **13**).[6] Since 4-methoxylated-5-



substituted benzo[b]thiophenes are readily available via the procedure outlined in Scheme II, the extension of our naphthalene oxidations to the benzo[b]thiophenes could be easily examined.

Anodic oxidation of **17a** in 1% methanolic hydroxide at room temperature gave two products, **20a** and **21a**, in yields of 21% and 36%, respectively. The ratio of the products was markedly temperature dependent: at −30 °C the ratio of **20a** to **21a** was 46:16, while anodic oxidation in this solvent system heated to reflux gave exclusively **21a** in 78% yield. In the higher temperature oxidation the ultraviolet spectra showed isospectic points at 247 and 237 nm, implying that **22** is eliminating methanol to afford **20a**, which is rapidly oxidized to the bisketal. Thus, a readily available benzo[b]thiophene could be converted to its quinone bisketal via a one-pot four-electron oxidation.

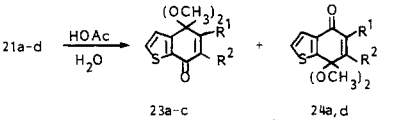


a, $R^1 = R^2 = H$; b, $R^1 = Br$, $R^2 = H$; c, $R^1 = CH_3$, $R^2 = H$; d, $R^1 = H$, $R^2 = Br$

Similarly, the higher temperature anodic oxidation of **17b** in a divided cell gave **21b** in 60% recrystallized yield. The yield in this particular reaction was markedly improved (80%) when the solvent for the anodic oxidation was changed to 1% methanolic sodium methoxide. Similarly, anodic oxidation of **17d** afforded **21d** in 76% yield. The methyl derivative **17c** was reluctant to undergo the four-electron oxidation even in methanol heated to reflux. Careful workup of this anodic oxidation afforded a crude oil that showed spectroscopic properties consistent with structure **22**. However, if **17c** was anodically oxidized, the electrolysis mixture concentrated at 50 °C, and the material further electrolyzed, **21c** was obtained in 85% yield. These results, together with the temperature dependence of the products noted for **17a**, suggest that the overall four-electron oxidation derives from a two-electron oxidation to afford intermediates such as **22**, followed by elimination of methanol and further oxidation of these products to the quinone bisketals.

Chemistry of Benzo[b]thiophene-4,7-quinone Bisketals

With the major obstacle—accessibility of benzo[b]-thiophene-4,7-quinone bisketals—overcome, some of the chemical transformations of the bisketals were studied. Complete hydrolysis of **21a–c** to the respective quinones was easily accomplished in yields of 78%, 77%, and 95%, respectively. Acidic hydrolyses of **21b,c** under mild conditions gave regiospecifically the respective monoketals **23b,c** in yields of 92% and 95%.[13] The structural assignments were confirmed by sodium borohydride reduction of the monoketals and ^1H NMR studies analogous to those reported previously.[13] The parent system **21a**, while undergoing clean monohydrolysis, showed no regioselectively; the two possible monoketals were formed in nearly equal amounts.



a, $R^1 = R^2 = H$; b, $R^1 = Br$, $R^2 = H$; c, $R^1 = CH_3$, $R^2 = H$; d, $R^1 = H$, $R^2 = Br$; e, $R^1 = H$, $R^2 = SCH_3$

Since **1** has a thiomethyl ether at C_5, the introduction of this group was examined next. Reaction of **21b** with *n*-butyllithium at −70 °C followed by addition of dimethyl disulfide yielded **25**. Apparently, metal–halogen exchange was followed by rapid deprotonation of the α-position of the thiophene ring and subsequent sulfenylation of this position. However, if the metal–halogen exchange was conducted at −90 °C and the dimethyl disulfide added within 15 s followed by acidic hydrolysis, the desired

(11) Fieser, L. F.; Kennelly, R. G. *J. Am. Chem. Soc.* **1935**, *57*, 1611.
(12) Hartough, H. D.; Meusil, S. L. "Compounds with Condensed Thiophene Rings"; Interscience: New York, 1954; p 105.
(13) For an extensive discussion of monohydrolysis conditions, see: Henton, D. R.; Anderson, D. K.; Manning, M. J.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 3422.

product **26** was obtained in 75% yield. The acidic α-hydrogen on the thiophene ring would also complicate the cuprate formation that was considered as a method for introduction of the required aliphatic side chain in **1**. Thus, the α-position of the thiophene ring was blocked with a trimethylsilyl group, which could be removed under mild acid conditions at a later stage of the synthesis. In practice, it was most convenient to convert **21b** to **27** without isolation of intermediates. Finally, **27** was converted to **28** via standard reactions. While the bromination reaction was accompanied by some protiodesilylation, the methylation products **28** and **29** were easily separated by silica gel chromatography.

The stage was set for the anodic oxidation of **28** and the introduction of the alkyl side chain. While oxidation of the thiomethyl ether side chain in **28** was a concern, this was unwarranted since the anodic oxidation of **28** gave **30** in 85% yield.[14] Unfortunately, the successes achieved thus far were overshadowed by the failure of **30** to undergo the cuprate coupling reaction under a variety of conditions and with a variety of substrates. The major problem apparently rests with elimination of the thiomethyl ether group under the metal–halogen exchange conditions since ^{1}H NMR of crude reaction mixtures from both metal–halogen exchange reactions and attempted cuprate additions showed substantial loss of this functionality. These nontrivial difficulties caused this approach to be abandoned.

Next, the quinol route (Scheme I) was briefly explored. Addition of methyl Grignard and *n*-butyllithium to **23b** followed by acidic hydrolysis afforded the sensitive quinols **31** and **32**, respectively. However, attempts to convert these quinols to alkylated hydroquinones under acidic conditions gave complex reaction mixtures. While reaction of **32** with potassium *tert*-butoxide followed by silver oxide oxidation did produce 5-bromo-6-butylbenzo[*b*]thiophene-4,7-quinone, the yield was only 30%. In view of these difficulties, work was discontinued on this approach.

An alkyl side chain could be introduced into the benzo[*b*]thiophene ring by the classical procedure of Fieser;[16] however, the yields for the resulting quinones were miserable. A comparison of the ultraviolet and ^{1}H NMR spectra of **34a** and **34b** in the manner described by Thomson[5] supports the original assignment of **1** as the correct regioisomer for caldariellaquinone; however, firm evidence for this regiochemical assignment is still lacking.

(14) Anodic oxidation of 2-(methylthio)-1,4-dimethoxybenzo[*b*]thiophene also forms the corresponding quinone bisketal in good yield.
(15) Scheffer, J. R.; Wong, Y.-F. *J. Am. Chem. Soc.* **1980**, *102*, 6604.

Summary

Anodic oxidation of readily available 4- or 7-methoxybenzo[*b*]thiophenes affords the bisketals of benzo[*b*]thiophene-4,7-quinones in excellent yields. This comprises the method of choice for preparation of the quinone bisketals, the quinone monoketals, and the quinones of benzo[*b*]thiophene-4,7-quinones. The quinone bis- and monoketals or benzo- and naphthoquinone have proven to be especially versatile synthetic intermediates,[17] and these heterocyclic counterparts may be of similar value. Attempts to introduce carbon functionality into the benzo[*b*]thiophene-4,7-quinone ring having a thiomethyl ether linkage via organolithium or organocuprate chemistry failed, thus terminating this approach to caldariellaquinone. General, efficient methods for alkylation of these quinones still remain an important unsolved problem.

Experimental Section[18]

15 and 17b. Cupric bromide (30 g, 133 mmol) was suspended in EtOAc (80 mL) and heated to reflux. A solution of **14**[11] (5.0 g, 32.9 mmol) in $CHCl_3$ (10 mL) was added to the refluxing solution through the condenser along with an additional 70 mL of $CHCl_3$. After refluxing for 8 h, the green suspension was cooled and filtered, and the solvent was removed at reduced pressure to leave a dark oil which solidified. This material was filtered through neutral alumina (activity III, 1.5 × 10 cm column, Et_2O as eluant) without collecting fractions to give the light yellow

(16) Misiti, D.; Moore, H. W.; Folkers, K. *Biochemistry* **1965**, *4*, 1156.
(17) For a recent discussion, see: Swenton, J. S. *Acc. Chem. Res.* **1983**, *16*, 74.
(18) The following abbreviations have been used throughout the Experimental Section: *n*-butyllithium (*n*-BuLi), chloroform ($CHCl_3$), dimethylformamide (DMF), dimethyl sulfoxide (Me_2SO), ethanol (EtOH), ether (Et_2O), ethyl acetate (EtOAc), hexane (H), hydrochloric acid (HCl), lithium diisopropylamide (LDA), methanol (CH_3OH), methylene chloride (CH_2Cl_2), potassium hydroxide (KOH), petroleum ether (PE), tetrahydrofuran (THF). All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Measurements with standard samples indicate that the reported melting points are probably 1–2 °C lower than the correct value. Infrared spectra were taken primarily on a Perkin-Elmer Model 283B grating spectrometer with some spectra being recorded on a Perkin-Elmer Infracord and are reported in reciprocal centimers. ^{1}H NMR spectra were recorded at 60 MHz unless otherwise noted and are reported in δ units. Apparent multiplicities are reported, and in some cases signals reported as triplets are, in fact, closely spaced doublet of doublets. ^{13}C NMR spectra (tetramethylsilane reference) were recorded on a Bruker WP80 instrument at 20 MHz in deuteriochloroform by Mr. Carl Engelman and B. L. Chenard. Mass spectra and exact mass measurements were obtained by Mr. C. R. Weisenberger on a Consolidated Electronics MS-9 double-focusing instrument and a Krapos MS-30 double-beam, double-focusing mass spectrometer with automatic data acquisition. Ultraviolet spectra were recorded on a Carey Model 15 instrument with maxima reported in nanometers with extinction coefficients in parentheses. Tetrahydrofuran was freshly distilled from benzophenone/sodium immediately prior to use. All organolithium reactions were performed with freshly titrated reagents in rigorously dried apparatus under dry nitrogen. Analytical samples were determined by Scandinavian Microanalytical Laboratory. Aluminum oxide and silica gel were from E. Merck Co. Workup as usual consisted of extraction of the product (CH_2Cl_2 or Et_2O), drying over calcium sulfate, and concentration in vacuo, followed by vacuum drying.

dibromide. A sample recrystallized from H had mp 91.5–92 °C: IR (KBr) 3180 (m), 3095 (m), 1700 (s), 1520 (s), 1435 (m), 1430 (m), 1420 (m), 1405 (s), 1277 (s), 1240 (s), 1085 (m), 1060 (m), 1025 (m), 923 (s), 890 (m), 828 (m), 800 (s), 775 (m), 735 (s), 700 (s), 680 (m) cm^{-1}; ^1H NMR (CCl_4) δ 7.18 (AB q, $\Delta\nu$ = 18 Hz, J = 5 Hz, 2 H), 3.11 (s, 4 H); exact mass calcd for $C_8H_6OSBr_2$ m/e 307.8507, obsd m/e 307.8515.

The dibromide was dissolved in DMF (100 mL), and Li_2CO_3 (15 g) was added under a nitrogen atmosphere. The solution was heated to 100 °C for 6 h, cooled, and filtered; water (100 mL) and Et_2O (150 mL) were added. The layers were acidified to pH 1 and separated. The Et_2O layer was washed with water (2 × 50 mL), and the phenol was extracted into 5% aqueous KOH (3 × 50 mL). This solution was acidified with concentrated HCl and back-extracted with Et_2O (3 × 40 mL). Workup as usual gave the known phenol[19] as a light brown solid. This material was dissolved in acetone (100 mL) under nitrogen, and K_2CO_3 (9.1 g) and dimethyl sulfate (4.7 mL) were added. This solution was refluxed for 8 h, cooled, and filtered, and the solvent was removed at reduced pressure. Dissolution in CH_3OH (20 mL) and addition of sodium hydroxide (8 g) followed by stirring for 45 min decomposed excess dimethyl sulfate. Workup as usual gave **17b** as a dark oily solid. Sublimation (53 °C, 0.1 mm) gave 6.1 g (76% overall) of pure **17b** as a white crystalline solid: mp 53–54 °C; IR (KBr) 1459 (m), 1442 (m), 1418 (s), 1329 (s), 1229 (m), 1159 (m), 1018 (s), 887 (m), 823 (s), 801 (m), 776 (s), 720 (m), 715 (s) cm^{-1}; ^1H NMR (CCl_4) δ 7.35 (m, 4 H), 3.95 (s, 3 H); exact mass calcd for C_9H_7OSBr m/e 241.9402, obsd m/e 241.9401.

4-Oxo-5-methyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene. To a solution of lithium diisopropylamine prepared at −78 °C from *n*-BuLi (42.5 mL, 65.8 mmol) and diisopropylamine (9.2 mL, 65.8 mmol) in THF (50 mL) was added **14** (10.0 g, 65.8 mmol), with the system being maintained under nitrogen. The yellow solution was warmed to −30 to −20 °C for 10 min to make the enolate followed by cooling to −78 °C and addition of methyl iodide (12.3 mL, 198 mmol) via syringe. Stirring was continued for 10 min at −78 °C followed by warming to room temperature for 1 h. Workup gave 10.72 g of a yellow oil. Medium-pressure chromatography (EM Reagents-Lobar prepacked size C, 10% Et_2O/PE) of 5.8 g of crude product proceeded as follows: 650 mL, nil; 260 mL, 326 mg of dimethylated material; 80 mL, 50 mg of a mixture of mono- and dimethylated products; 1000 mL, 3.5 g of pure monomethylated compound.

The chromatography was repeated on the remaining material for a total yield of 680 mg (5.7%) of 4-oxo-5,5-dimethyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene as a pale yellow liquid: IR (neat) 2980 (s), 2930 (s), 1665 (s), 1525 (s), 1470 (m), 1450 (m), 1400 (s), 1295 (s), 1240 (s), 1215 (m), 1040 (m), 920 (s), 890 (m), 830 (m), 715 (s) cm^{-1}; ^1H NMR (CCl_4) δ 7.12 (AB q, $\Delta\nu$ = 19 Hz, J = 6 Hz, 2 H), 3.00 (t, J = 6 Hz, 2 H), 2.00 (t, J = 6 Hz, 2 H), 1.18 (s, 6 H); exact mass calcd for $C_{10}H_{12}OS$ m/e 180.0609, obsd m/e 180.0613.

The title compound (6.8 g, 62%) was obtained as an off-white solid: mp 30–32 °C (lit.[2] mp 35–36 °C); IR (neat) 3970 (m), 2940 (s), 2860 (m), 1670 (s), 1530 (s), 1455 (m), 1435 (m), 1405 (s), 1270 (m), 1245 (s), 1225 (m), 925 (s), 845 (m), 730 (s), 715 (s) cm^{-1}; ^1H NMR (CCl_4) 7.10 (AB q, $\Delta\nu$ = 21 Hz, J = 5 Hz, 2 H), 3.05 (4-line m, 2 H), 2.7–1.85 (m, 3 H), 1.25 (d, J = 7 Hz, 3 H); exact mass calcd for $C_9H_{10}OS$ m/e 166.0452, obsd m/e 166.0455.

17c. Essentially as described for **15**, $CuBr_2$ (2.7 g, 12 mmol) in EtOAc (15 mL) was reacted with 4-oxo-5-methyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (1.0 g, 6 mmol) to afford after subsequent reactions 854 mg (79% overall) of pure **17c** as a colorless oil [IR (neat) 2930 (m), 1450 (s), 1420 (s), 1325 (s), 1250 (s), 1215 (s), 1152 (m), 1030 (s), 1020 (s), 895 (s), 837 (s), 785 (s), 712 (s) cm^{-1}; ^1H NMR (CCl_4) δ 7.4–6.85 (m, 4 H), 3.76 (s, 3 H), 2.3 (s, 3 H); exact mass calcd for $C_{10}H_{10}OS$ m/e 178.0452, obsd m/e 178.0458].

19. Essentially as described for **17b**, cupric bromide (12.3 g, 55.2 mmol), EtOAc (35 mL), and **18**[19] (2.0 g, 13.1 mmol) in $CHCl_3$ (15 mL) were reacted at 80 °C for 14 h to afford after recrystallization from Et_2O/H pale yellow saltlike crystals: mp 99–101 °C; IR (KBr) 1678 (s), 1530 (m), 1438 (s), 1420 (s), 1390 (s), 1335 (s), 1280 (s), 1235 (s), 1032 (s), 1020 (m), 850 (s), 823 (m), 770 (m), 750 (s), 718 (m), 700 (s), 638 (s), 608 (s), 540 (m) cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.33 (AB, q, $\Delta\nu$ = 66 Hz, J = 5 Hz, 2 H), 3.05 (m, 4 H); exact mass calcd for $C_8H_6OSBr_2$ m/e 309.8486, obsd m/e 309.8457.

17d. Essentially as described for **17b**, **19** (3.5 g, 11.4 mmol), Li_2CO_3 (5.3 g, 72 mmol), and DMF (30 mL) were heated at 100 °C for 12 h. This phenol was isolated by flash chromatography on silica gel (2 × 5 cm column, 4% EtOAc/PE as eluant). Elution proceeded as follows: 40 mL, nil; 180 mL, 1.69 g (65%) of 6-bromo-7-hydroxybenzo[*b*]thiophene as a white solid [mp 109–110 °C; IR (KBr) 3350 (m), 1550 (m), 1500 (m), 1458 (s), 1340 (s), 1280 (s), 1220 (s), 1020 (s), 830 (s), 800 (s), 770 (s), 700 (m), 690 (m), 610 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.31 (m, 4 H), 5.89 (s, 1 H); exact mass calcd for C_8H_5BrSO m/e 227.9245, obsd m/e 227.9216].

In a manner similar to that for **17b**, the crude phenol from above (1.38 g, 6.0 mmol), K_2CO_3 (2.18 g, 15.8 mmol), acetone (40 mL), and dimethyl sulfate (1.14 mL, 12.02 mmol) were heated at reflux for 10.5 h. Workup as for **17b** gave 1.43 g (98%) of **17d** as a colorless oil: IR (neat) 3100 (w), 2940 (m), 1553 (m), 1495 (s), 1460 (s), 1430 (s), 1370 (s), 1345 (s), 1230 (s), 1210 (m), 1130 (m), 1085 (m), 1040 (s), 855 (s), 835 (s), 800 (s), 780 (s), 700 (s), 643 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (m, 4 H), 3.98 (s, 3 H); exact mass calcd for C_9H_7BrSO m/e 241.9401, obsd m/e 241.9405.

Anodic Oxidations.[9] A procedure is given for **21a**. For the remaining systems, only the isolation procedure and spectroscopic data are provided.

21a. Anodic oxidation of **17a** (1.0 g, 6.1 mmol) in 1% KOH/CH_3OH (100 mL) heated to reflux was conducted in a single cell with an initial potential of 1.7 V and gradually increased to 2.15 V (vs. Pt). The initial current was 0.5 A, and the final current was 0.1 A (4800 C, 49% current efficiency). The CH_3OH was removed in vacuo, and the product was extracted with Et_2O (30 mL). The organic phase was washed with saturated Na_2CO_3 (3 × 15 mL), dried, and concentrated. The residue was chromatographed on activity III neutral alumina (2.5 × 10 cm column, 5% Et_2O/PE as eluant). Elution proceeded as follows: 20 mL, nil; 60 mL, 115 mg of **20a** and **21a**; 500 mL of 10% Et_2O/PE, 1.22 g (78%) of **21a**, which was triturated with Et_2O/PE to give **21a** as a white solid: mp 45–46 °C; IR (KBr) 1376 (m), 1300 (m), 1272 (m), 1209 (m), 1120 (s), 1075 (vs), 969 (s), 889 (m), 769 (m) cm^{-1}; ^1H NMR (CCl_4) δ 7.1 (AB q, $\Delta\nu$ = 16 Hz, J = 5 Hz, 2 H), 6.10 (s, 2 H), 3.20 (s, 6 H), 3.12 (s, 6 H); exact mass calcd for $C_{12}H_{16}O_4S$ m/e 256.0769, obsd m/e 256.0774.

20a. Anodic oxidation of **17a** (0.5 g, 3.1 mmol) gave a mixture of **20a** and **21a**. This mixture was dissolved in 3:1 acetone/water (20 mL), CF_3CO_2H (0.5 mL) was added, and the reaction mixture was stirred at room temperature for 3 h. Workup gave a mixture of **20a** and benzo[*b*]thiophene-4,7-quinone, which was separated by chromatography on silica gel (2 × 15 cm column 5% Et_2O/PE as eluant). The elution proceeded as follows: 40 mL, nil; 140 mL, 276 mg (46%) of **20a** as a white solid, mp 89–91 °C. A sample triturated with Et_2O/PE had mp 90.5–92 °C: IR (KBr) 1515 (s), 1465 (s), 1440 (s), 1272 (s), 1268 (s), 1080 (m), 1055 (s), 815 (m), 780 (m), 730 (m), 715 (m), 710 (m) cm^{-1}; ^1H NMR (CCl_4) δ 7.30 (AB q, $\Delta\nu$ = 9 Hz, J = 5 Hz, 2 H), 6.48 (s, 2 H), 3.90 (s, 3 H), 3.82 (s, 3 H); exact mass calcd for $C_{10}H_{10}O_2S$ m/e 194.0402, obsd m/e 194.0407.

Continued elution gave the following: 60 mL, nil; 140 mL, 79 mg (15.6%) of the quinone as a yellow solid. A sample triturated with Et_2O/PE had mp 127–130 °C (lit.[11] mp 130–131 °C).

21b. Anodic oxidation of **17b** (0.5 g, 2.0 mmol) in a divided cell in 1% methanolic sodium methoxide (60 mL) followed by workup and trituration with PE gave 500 mg of **21b** as a pale yellow solid. The mother liquors were chromatographed on neutral alumina (activity III, 2 × 10 cm column, 10% Et_2O/PE as eluant) to give 43 mg of **21b**, 543-mg (79%) total yield. The analytical sample was prepared by recrystallization from H (mp 118–119 °C) and sublimation (60–70 °C, 0.5 mm): IR (KBr) 1311 (s), 1224 (m), 1128 (s), 1080 (vs), 1070 (vs), 998 (m), 782 (m), 769 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.25 (AB q, $\Delta\nu$ = 19 Hz, J = 5 Hz, 2 H), 6.8 (s, 1 H), 3.3 (s, 6 H), 3.03 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 140.6, 136.9, 136.5, 130.8, 127.4, 125.1, 97.3, 96.3, 51.6, 51.1. Anal. Calcd for $C_{12}H_{15}O_4Br$: C, 42.99; H, 4.51. Found: C, 43.06; H, 4.51.

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21c. Oxidation of **17c** (370 mg, 2.0 mmol) in 1% KOH/CH_3OH (60 mL) at ambient temperature (potential gradually being raised to 2.15 V to maintain a current of 0.55 A) was performed until the UV absorption at 305 nm was gone (775 C). The CH_3OH was removed at reduced pressure and at 80 °C. If the reaction is stopped at this point and worked up and the residue chromatographed on silica gel, 4,7-dimethoxy-5-methylbenzothiophene may be isolated as a colorless solid: mp 56–57 °C; IR (neat) 2930 (m), 1510 (s), 1450 (s), 1415 (s), 1350 (m), 1330 (s), 1228 (s), 1116 (s), 1035 (s), 1020 (m), 869 (s), 780 (m), 710 (s) cm^{-1}; ^1H NMR (CCl_4) δ 7.25 (s, 2 H), 6.45 (s, 1 H), 3.83 (s, 3 H), 3.72 (s, 3 H), 2.30 (s, 3 H); exact mass calcd for $C_{11}H_{12}O_2S$ m/e 208.0558, obsd m/e 208.0563.

The residue was redissolved in 1% KOH/CH_3OH (60 mL) and further electrolyzed at potentials up to 1.0 V, again to maintain a current of 0.55 A (the total number of C used was 1200, 67% current efficiency). Workup and trituration of the residue with H gave 383 mg of pure **21c**. The pure mother liquors were concentrated, and the residue was chromatographed on neutral alumina (activity III, 2 × 10 cm column, 10% Et_2O/PE as eluant) to give a total of 481 mg (85%) of **21c**: mp 83–86 °C (additional trituration gave mp 86–87 °C); IR (KBr) 3098 (m), 3010 (m), 2960 (m), 2840 (m), 1450 (m), 1308 (m), 1258 (s), 1220 (s), 1132 (s), 1095 (vs), 1085 (vm), 1070 (vs), 1030 (m), 987 (m), 975 (s), 968 (s), 880 (s), 770 (s), 705 (s) cm^{-1}; ^1H NMR (CCl_4) δ 7.18 (AB q, $\Delta\nu$ = 19 Hz, J = 5 Hz, 2 H), 6.02 (q, not cleanly resolved, J = 2 Hz, 1 H), 3.2 (s, 6 H), 2.9 (s, 6 H), 1.8 (d, J = 2 Hz, 3 H); exact mass calcd for $C_{13}H_{18}O_4S$ m/e 270.0926, obsd m/e 270.0931.

22. In a single cell, **17c** (100 mg, 0.56 mmol) was dissolved in 1% KOH/CH_3OH (50 mL) and electrolyzed at −30 °C at potentials to 1.6 V to maintain a current of 0.35 A. The electrolysis was stopped when the UV absorption at 307 nm was almost gone with a final current of 0.08 A. The solution was poured into cold (0 °C) saturated aqueous sodium carbonate solution (100 mL) and extracted with Et_2O (50 mL). Workup gave a yellow oil, which was chromatographed on silica gel (1.5 × 10 cm column, 10% Et_2O/PE as eluant). Elution proceeded as follows: 10 mL, nil; 20 mL, unweighed amount of **17c**; 90 mL, nil; 200 mL, 71 mg of **22**, which was ca. 95% pure as characterized by ^1H NMR [(CCl_4) δ 7.11 (AB q, J = 5 Hz, $\Delta\nu$ = 17 Hz, 2 H), 6.08 (sym m, 1 H), 5.00 (sym m, 1 H), 3.10 (s, 3 H), 2.90 (s, 3 H), 2.85 (s, 3 H), 1.80 (t, J = 1.5 Hz, 3 H); exact mass calcd for $C_{12}H_{16}O_3S$ m/e 240.0820, obsd m/e 240.0825].

21d. The anodic oxidation of **17d** (1.1 g, 4.6 mmol) in 1% methanolic sodium methoxide (60 mL) followed by workup and trituration of the residue with H gave 1.16 g (76%) of **21d** as a white solid. Recrystallization of a sample from Et_2O/H gave mp 81–84 °C: IR (KBr) 3080 (m), 3040 (m), 2935 (m), 2822 (m), 1460 (m), 1435 (m), 1310 (s), 1270 (s), 1240 (s), 1130 (s), 1070 (vs), 980 (s), 880 (s), 765 (s), 750 (s) cm^{-1}; ^1H NMR (CCl_4, 90 Hz) δ 7.15 (AB q, $\Delta\nu$ = 27 Hz, J = 5 Hz, 2 H), 6.68 (s, 1 H), 3.23 (s, 6 H), 3.10 (s, 6 H). Anal. Calcd for $C_{12}H_{15}BrSO_4$: C, 42.99; H, 4.51. Found: C, 43.02; H, 4.49.

30. The anodic oxidation of **28** (300 mg, 0.66 mmol) in 1% KOH/CH_3OH at 0 °C with a potential of 1.65 V vs. Pt (310 C, 48% current efficiency), followed by concentration at room temperature and workup, yielded a white solid, which was crystallized from Et_2O/H to give **30** as white needles (300 mg, 85%): mp 139–141 °C; IR (KBr) 1105 (s), 1080 (vs), 835 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.2 (s, 1 H), 3.15 (s, 12 H), 2.7 (s, 3 H), 0.32 (s, 9 H). The analytical sample was sublimed at 110 °C (0.5 mm). Anal. Calcd for $C_{16}H_{25}O_4S_2SiBr$: C, 42.38; H, 5.56. Found: C, 42.39; H, 5.55.

Hydrolyses of Quinone Bisketals to Monoketals.[13] **23b.** The bisketal **21b** (100 mg, 0.30 mmol) was dissolved in acetone (1 mL), 50% aqueous acetic acid (3 mL) was added, the solution was swirled for 15 min, and then the solution was neutralized with excess solid K_2CO_3. Workup and recrystallization from 10:1 Et_2O/PE gave 80 mg (92%) of pure **23b**: mp 102–103 °C; IR (KBr) 1656 (s), 1424 (s), 1318 (m), 1240 (m), 1101 (s), 1095 (s), 1076 (s), 805 (m), 785 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.5 (AB, q, $\Delta\nu$ = 27 Hz, J = 5 Hz, 2 H), 6.98 (s, 1 H), 3.08 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 176.3, 147.7, 146.3, 139.0, 137.0, 134.2, 127.1, 97.4, 51.8; exact mass calcd for $C_{10}H_9O_3SBr$ m/e 287.9456, obsd m/e 287.9463. Reduction of the monoketal with sodium borohydride in CH_3OH gave the labile alcohol, which confirmed the regiochemistry of the hydrolysis: ^1H NMR ($CDCl_3$) δ 7.20 (AB q, $\Delta\nu$ = 18 Hz, J = 5 Hz, 2 H), 6.89 (d, J = 4 Hz, 1 H), 5.22 (d, J = 4 Hz, 1 H), 3.03 (s, 3 H), 3.0 (s, 3 H), 2.7 (br, 1 H).

23c. The bisketal **21c** (98 mg, 0.36 mmol) was reacted as above, and the product was triturated with hexane to give 77 mg (95%) of **23c** as a pale yellow solid: mp 84.5–86 °C; IR (KBr) 1669 (s), 1435 (s), 1319 (s), 1261 (m), 1089 (s), 1020 (m), 890 (m), 885 (m), 780 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55 (AB, q, $\Delta\nu$ = 27 Hz, J = 5 Hz, 2 H), 6.45 (q, not completely resolved, J = 2 Hz, 1 H), 3.05 (s, 6 H), 2.03 (d, J = 2 Hz, 3 H); exact mass calcd for $C_{11}H_{12}O_3S$ m/e 224.0507, obsd m/e 224.0512. Reduction of the monoketal with sodium borohydride in methanol gave the labile alcohol, which confirmed the assigned regiochemistry: ^1H NMR ($CDCl_3$) δ 7.20 (AB, q, $\Delta\nu$ = 24 Hz, J = 5.5 Hz, 2 H), 6.25–6.20 (m, 1 H), 5.2 (br, 1 H), 2.97 (s, 3 H), 2.92 (s, 3 H), 2.5 (br, 1 H), 2.32 (impurity), 1.82 (m, 3 H). Addition of D_2O to the sample eliminated the signal at δ 2.5. When this sample was irradiated at δ 1.82, the signals at δ 6.25–6.20 and 5.2 collapsed to doublets, J = 3.5, 3.3 Hz, respectively.

26. The metalation was conducted at −90 °C (toluene/liquid nitrogen), using **21b** (0.5 g, 1.5 mmol) in THF (20 mL) and n-BuLi (1.5 mmol). After 10 s of metalation, dimethyl disulfide (0.15 mL, 1.5 mmol) was added all at once. Workup gave a yellow residue which was dissolved in acetone (5 mL) cooled to 0 °C. This was added to a 0 °C solution of 10% HOAc (3 mL), and the solution was stirred for 45 min at 0 °C. Workup gave a yellow oil, which was chromatographed on silica gel (1.5 × 15 cm column, 15% Et_2O/PE as eluant). The elution proceeded as follows: 20 mL, nil; 200 mL, 55 mg of recovered **21b**; 200 mL, 252 mg (75%) of pure **26** as a pale yellow oil, which solidified slowly. A sample recrystallized from Et_2O/H had mp 93–94 °C: IR (CCl_4) 1650 (s), 1429 (s), 1312 (s), 1090 (s), 1068 (m), 845 (m) cm^{-1}; ^1H NMR (CCl_4) δ 7.35 (AB, q, $\Delta\nu$ = 24 Hz, J = 5 Hz, 2 H), 6.1 (s, 1 H), 3.0 (s, 6 H), 2.42 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.7, 164.7, 146.4, 139.9, 132.8, 126.4, 123.2, 98.1, 51.9, 14.1; exact mass calcd for $C_{11}H_{12}O_3S_2$ m/e 256.0223, obsd m/e 256.0233.

27. To a dry, three-necked flask with mechanical stirring under a nitrogen atmosphere were added **21b** (4.0 g, 12 mmol) and dry THF (160 mL). The solution was cooled to −90 °C, and n-BuLi (7.3 mL, 1.65 M in H, 12 mmol) was added over 30 s with vigorous stirring. Within 15 s the reaction was quenched by the addition of dimethyl disulfide (1.08 mL, 12 mmol) all at once via syringe. The reaction was allowed to warm to −78 °C and stirred for 30 min. An additional 7.3 mL of n-BuLi was added to the solution. After stirring of the solution for 25 min at −78 °C, trimethylsilyl chloride (1.52 mL, 12 mmol) was added. The reaction was stirred for 15 min at −78 °C followed by warming to room temperature for 30 min. Saturated aqueous Na_2CO_3 (12 mL) was added, and the THF was removed at reduced pressure. The residue was partitioned between saturated Na_2CO_3 solution (40 mL) and Et_2O (200 mL). Workup as usual gave a dark oil. This oil was dissolved in acetone (200 mL) and cooled to 0 °C. To this solution was added 5% aqueous acetic acid (80 mL, precooled to 0 °C). The resulting mixture was stirred for 40 min at 0 °C followed by quenching with excess solid K_2CO_3. Workup and recrystallization from H gave 2.4 g (62%) of **27** as light yellow flakes: mp 143–147 °C; IR (KBr) 1645 (s), 1532 (m), 1319 (s), 1090 (s), 1015 (m), 1010 (s), 906 (m), 855 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 1 H), 6.25 (s, 1 H), 3.05 (s, 6 H), 2.40 (s, 3 H), 0.35 (s, 9 H). A second recrystallization from Et_2O/H, mp 149–150 °C, gave the analytical sample. Anal. Calcd for $C_{14}H_{20}O_3S_2Si$: C, 51.19; H, 6.14. Found: C, 51.11; H, 6.15.

24e. The conditions were essentially identical with those used in the metalation of **21b**; **21d** (0.5 g, 1.5 mmol) was reacted at −90 °C with n-BuLi (1.49 mmol). The n-BuLi was added over 30 s; after 10 s dimethyl disulfide (0.15 mL, 1.8 mmol) was added all at once. The solution was stirred for an additional 30 min at −90 °C and then warmed to room temperature. Workup afforded 470 mg of an oily yellow solid, which was dissolved in 0 °C acetone and then added to a 0 °C solution of 10% HOAc (2.5 mL). After stirring of the solution for 45 min at 0 °C, workup afforded 340 mg of a yellow solid, which was crystallized from Et_2O/H to afford 240 mg (62%) of white crystals: mp 132–134 °C; IR (KBr) 1640 (s), 1565 (m), 1425 (s), 1400 (s), 1270 (s), 1230 (s), 1135 (m), 1072 (s), 860 (m), 800 (m), 718 (m) cm^{-1}; ^1H NMR (CCl_4, 90 MHz) δ 7.31 (s, 2 H), 6.08 (s, 1 H), 3.10 (s, 6 H), 2.38 (s, 3 H); exact mass

calcd for $C_{11}H_{12}O_3S_2$ m/e 256.0229, obsd m/e 256.0255.

25. The metalation of **21b** (100 mg, 0.39 mmol) was conducted in THF (4 mL) at −70 °C, using *n*-BuLi (0.39 mmol) over 10 min. Dimethyl disulfide (0.04 mL, 0.44 mmol) was added, the solution was stirred for 15 min at −70 °C, and the reaction was quenched with aqueous Na_2CO_3. Workup followed by filtration of the crude product through neutral alumina (activity III, 1.5 × 6 cm column, 10% Et_2O/PE as eluant) gave 92 mg of **25** as a pale yellow oil: IR (neat) 2950 (s), 2845 (s), 1470, 1462, 1450, 1438 (all s, overlapping), 1380 (s), 1305 (s), 1275 (s), 1248 (s), 1210 (s), 1164 (s), 1137 (s), 1080 (s), 980, 962 (overalapping, s) cm^{-1}; ^1H NMR (CCl_4) δ 6.90 (s, 1 H), 6.05 (s, 2 H), 3.20 (s, 6 H), 3.15 (s, 6 H), 2.47 (s, 3 H); exact mass calcd for $C_{13}H_{18}O_4S_2$ m/e 302.0646, obsd m/e 302.0654.

28 and 29. A heterogeneous mixture of **27** (1.0 g, 3.05 mmol), THF (40 mL), and zinc–copper couple (0.62 g, 9.15 mmol) was heated to reflux, and 25% HOAc (12 mL) was added through the condenser. After heating for 1 h, the solution was cooled and filtered, and the filtrate was concentrated. Workup as usual gave the air-sensitive phenol, which was immediately dissolved in CH_2Cl_2 (100 mL). Pyridinium bromide perbromide (0.98 g, 3.05 mmol) was added to the solution, and the reaction mixture was stirred for 30 min (solution color changed from red to yellow). After quenching with saturated $NaHCO_3$ (20 mL), workup gave an air-sensitive oil, which was immediately dissolved in acetone (100 mL). After addition of K_2CO_3 (0.84 g, 6.1 mmol) and dimethyl sulfate (0.43 mL, 4.5 mmol), the mixture was heated to reflux for 5 h, cooled, and filtered. Workup gave a light yellow oil, which was chromatographed on silica gel (12.5 × 25 cm column, 3% Et_2O/PE as eluant). The elution proceeded as follows: 120 mL, nil; 100 mL, 607 mg (51%) of **28** as a colorless oil [^1H NMR (CCl_4) δ 7.31 (s, 12 H), 3.92 (s, 3 H), 3.88 (s, 3 H), 2.35 (s, 3 H), 0.38 (s, 9 H)]. The analytical sample was prepared by molecular distillation (80 °C, 0.1 mmHg). Anal. Calcd for $C_{14}H_{19}O_2S_2SiBr$: C, 42.96; H, 4.89. Found: C, 43.04; H, 4.86.

Continued elution gave 20 mL of an unweighed mixed fraction and 150 mL (250 mg, 24%) of **29** as a clear oil identified by its ^1H NMR [(CCl_4) δ 7.35 (s, 2 H), 3.90 (s, 6 H), 2.35 (s, 3 H); exact mass calcd for $C_{11}H_{11}O_2SBr$ m/e 317.384, obsd m/e 317.389].

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Registry No. **1**, 63693-26-5; **6a**, 63693-33-4; **9**, 73630-87-2; **14**, 13414-95-4; **15**, 25074-27-5; **17a**, 3781-90-6; **17b**, 73630-81-6; **17c**, 73630-82-7; **17d**, 87279-67-2; **18**, 1468-84-4; **19**, 87279-68-3; **20a**, 68452-01-7; **20c**, 87279-69-4; **21a**, 73630-83-8; **21b**, 73630-84-9; **21c**, 73630-85-0; **21d**, 87279-70-7; **22**, 73630-86-1; **23b**, 73630-88-3; **23c**, 73630-89-4; **24e**, 87279-71-8; **25**, 87279-72-9; **26**, 87279-73-0; **27**, 87279-74-1; **28**, 87279-75-2; **29**, 87279-76-3; **30**, 87279-77-4; **31**, 87279-78-5; **32**, 87279-79-6; **33a**, 87279-80-9; **33b**, 87279-81-0; **34a**, 87279-82-1; **34b**, 87279-83-2; 5-bromobenzo[*b*]thiophen-4-ol, 34576-98-2; 4-oxo-5-methyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene, 19995-43-8; 4-oxo-5,5-dimethyl-4,5,6,7-tetrahydrobenzo[*b*]-thiophene, 87279-84-3; 6-bromo-7-hydroxybenzo[*b*]thiophene, 87279-85-4; 4,7-dihydro-4,4-dimethoxy-5-methylbenzo[*b*]thiophen-7-ol, 87279-86-5; 5-bromobenzo[*b*]thiophene-4,7-quinone, 63693-34-5; 5-bromo-4,7-dihydro-4,4-dimethoxy-7-methylbenzo-[*b*]thiophen-7-ol, 87279-87-6; phytol, 7541-49-3; 5-bromo-6-butylbenzo[*b*]thiophene-4,7-quinone, 87279-88-7.

Supplementary Material Available: Experimental procedures and spectroscopic data for benzo[*b*]thiophene-4,7-quinone, 5-bromobenzo[*b*]thiophene-4,7-quinone, 5-methylbenzo[*b*]-thiophene-4,7-quinone, 5-bromo-6-butylbenzo[*b*]thiophene-4,7-quinone, **31**, **32**, **33a**, **33b**, **34b** are given (5 pages). Ordering information is given on any current masthead page.

Synthesis of α-Thiophene Oligomers via 1,3-Butadiynes

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Individual oligomers possessing thiophenes linked by their 2- and 5-positions are conveniently prepared via 1,3-butadiynes. These can be prepared in good yield by the Glaser symmetrical coupling of thienylacetylenes. Following the cyclization of the 1,3-butadiyne unit into a thiophene with sodium sulfide, an oligomer possessing an odd number of thiophene rings is obtained. Oligomers with an even number of rings are accessible from unsymmetrical butadiynes obtained either by the Cadiot–Chodkiewicz procedure, utilizing an odd and an even precursor, or by an organoborane coupling procedure.

Many bithiophene and terthiophene derivatives display interesting biological properties. Most notably, they are toxic to nematodes, and this effect can be greatly enhanced by the presence of ultraviolet light.[1] The most carefully scrutinized of these compounds is α-terthienyl (**3**, n = 1), which has shown photoenhanced activity against nematodes,[1] microorganisms,[2-5] algae,[6] human erythrocytes,[7] insect larvae[8-10] and eggs,[11] in addition to generating skin pigmentation,[12] acting as herbicide,[13] and acting as a seed germination inhibitor.[14] A study of the structure–activity relationship in this type of molecule required significant

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