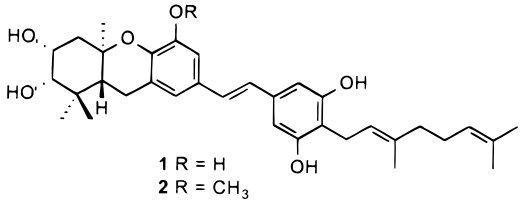
Synthesis of Schweinfurthin C, a Geranylated Stilbene from *Macaranga schweinfurthii*

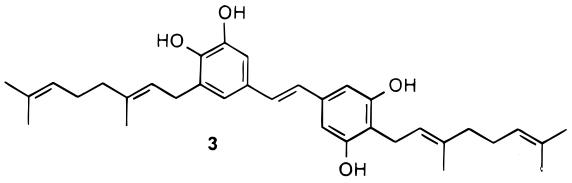
Edward M. Treadwell, Steven C. Cermak, and David F. Wiemer*

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242-1294

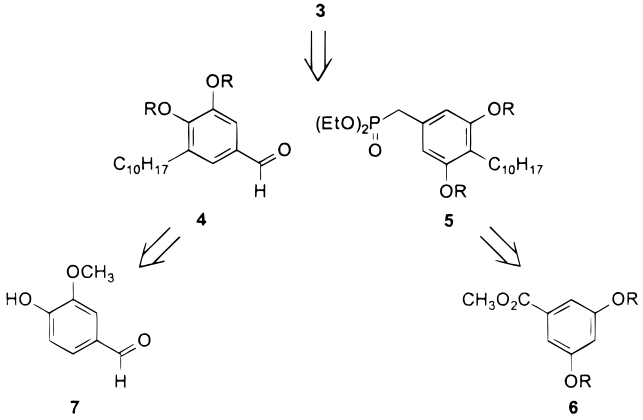
Received June 1, 1999

As part of a program investigating natural sources of potential anticancer agents, Beutler et al. have studied a cytotoxic extract of the plant *Macaranga schweinfurthii* Pax from Cameroon.[1] Application of a bioassay-guided fractionation sequence to this extract yielded three novel geranylated stilbenes, compounds that they named schweinfurthins A−C (**1**−**3**). Our interests in isolation[2] and synthesis[3] of prenylated aromatic compounds led us to undertake synthesis of these natural products, a task that has grown more compelling because isolation of more of the natural materials has not been straightforward.[4] In this paper, we report the first total synthesis of schweinfurthin C.





Synthesis of stilbenes is readily accomplished through Wittig-type assembly of the central olefin.[5] Because schweinfurthin C is not quite symmetrical, application of such an approach to this synthesis would require preparation of two geranylated phenols bearing different substitution patterns (**4** and **5**). In terms of retrosynthetic analysis, the "right half" of schweinfurthin C can be readily traced to a resorcinol derivative such as compound **6**, and assembly of the key intermediate **5** could be based on directed ortho metalation.[6,7] While commercial vanillin (**7**) is an attractive precursor to the "left half" of schweinfurthin C, addition of the geranyl substituent to this aromatic compound is made somewhat more difficult by the need for regiocontrolled elaboration of the unsymmetrical starting material.



Our synthesis of the key "right half" intermediate began with the commercial ester **8**. After protection of the phenolic groups by reaction with sodium hydride and MOMCl,[8] standard reduction of the protected ester **9** gave benzyl alcohol **10**.[9] Reaction with TBSCl proceeded smoothly to afford compound **11**, but when the protected ether **11** was treated with *n*-BuLi and geranyl bromide (**12**), the aromatic alkylation product was not isolated. Instead, an unexpected product (**13**) arising from benzylic lithiation was obtained in modest yield (21%).[6d,10] When metalation was conducted with *n*-BuLi and TMEDA, reaction with geranyl bromide gave a mixture of compounds **13** and **14** in low yield. However, when metalation was carried out with *n*-BuLi, TMEDA, and CuCN,[9] presumably forming an intermediate cuprate, subsequent reaction with geranyl bromide gave a single product isomeric to compound **13**. The symmetry of that product was evident in its spectral data, allowing unambiguous identification of the desired phenol derivative **14**. After cleavage of the silyl group by reaction with TBAF to obtain alcohol **15**, formation of the mesylate (**16**) and displacement with NaI gave benzylic iodide **17**. A final

(1) Beutler, J. A.; Shoemaker, R. H.; Johnson, T.; Boyd, M. R. *J. Nat. Prod.* **1998**, *61*, 1509−1512.

(2) (a) Ampofo, S. A.; Roussis, V.; Wiemer, D. F. *Phytochemistry* **1987**, *26*, 2367−2370. (b) Green, T. P.; Treadwell, E. M.; Wiemer, D. F. *J. Nat. Prod.* **1999**, *62*, 367−368.

(3) Blunt, S. B.; Chen, T. B.; Wiemer, D. F. *J. Nat. Prod.* **1998**, *61*, 1400−1403.

(4) Beutler, J. A. Personal communication, 1999.

(5) (a) Bachelor, F. W.; Loman, A. A.; Snowdon, L. R. *Can. J. Chem.* **1970**, *48*, 1554−1557. (b) Moody, C. J.; Warrellow, G. J. *J. Chem. Soc., Perk. Trans. 1* **1990**, 2929−2936. (c) Cushman, M.; Nagarathnam, D.; Gopal, D.; Chakraborti, A. K.; Lin, C. M.; Hamel, E. *J. Med. Chem.* **1991**, *34*, 2579−2588.

(6) (a) Winkle, M. R.; Ronald, R. C. *J. Org. Chem.* **1982**, *47*, 2101−2108. (b) Napolitano, E.; Giannone, E.; Fiaschi, R.; Marsili, A. *J. Org. Chem.* **1983**, *48*, 3653−3657. (c) Sneickus, V. *Chem. Rev.* **1990**, *90*, 879−933. (d) Thayumanavan, S.; Basu, A.; Beak, P. *J. Am. Chem. Soc.* **1997**, *119*, 8209−8216.

(7) Gschwend, H. W.; Rodiguez, H. R. *Org. React.* **1979**, *26*, 1−360.

(8) Townsend, C. A.; Davis, S. G.; Christensen, S. B.; Link, J. C.; Lewis, C. P. *J. Am. Chem. Soc.* **1981**, *103*, 6885−6888.

(9) Falck, J. R.; Reddy, K. K.; Chandrasekhar, S. *Tetrahedron Lett.* **1997**, *38*, 5245−5248.

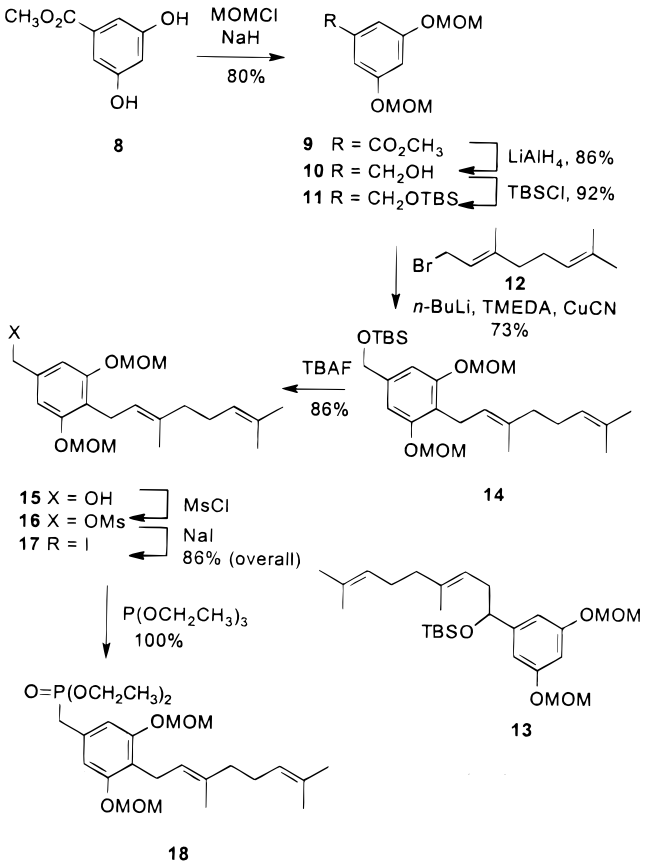
(10) (a) Harris, T. D.; Roth, G. P. *J. Org. Chem.* **1979**, *44*, 2004−2007. (b) Court, J. J.; Hlasta, D. J. *Tetrahedron Lett.* **1996**, *37*, 1335−1338. (c) Ludt, R. E.; Crowther, G. P.; Hauser, C. R. *J. Org. Chem.* **1970**, *35*, 1288−1296.

(11) (a) Bates, R. W.; Gabel, C. J. *Tetrahedron Lett.* **1993**, *34*, 3547−3550. (b) Manners, G. D.; Wong, R. Y. *J. Chem. Soc., Perk. Trans. 1* **1981**, 1849−1854. (c) Daves, G. D., Jr.; Moore, H. W.; Schwab, D. E.; Olsen, R. K.; Wilczynski, J. J.; Folkers, K. *J. Org. Chem.* **1967**, *32*, 1414−1417. (d) Yamada, S.; Ono, F.; Katagiri, T.; Tanaka, J. *Synth. Commun.* **1975**, *5*, 181−184.

(12) Asakawa, Y.; Kondo, K.; Tori, M.; Hashimoto, T.; Ogawa, S. *Phytochemistry* **1991**, *30*, 219−234.

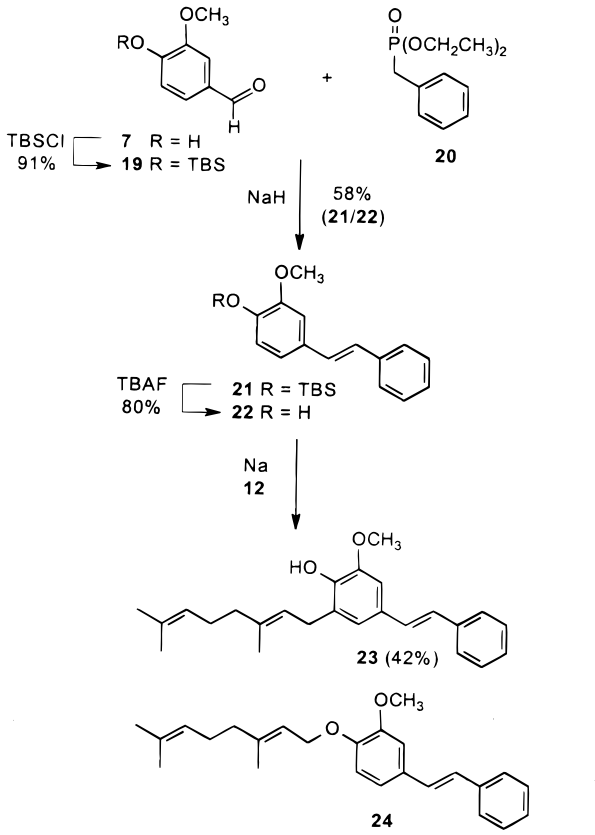
10.1021/jo9908795 CCC: $18.00
Published on Web 11/12/1999

Arbuzov reaction with $(EtO)_3P$ gave the desired phosphonate **18**.



A priori, compound **18** could be used to prepare schweinfurthin C through either a linear strategy based on condensation with a minimally substituted aldehyde or via a convergent approach where an intact "right half" was employed in stilbene formation. Despite the attraction of a convergent sequence in terms of cumulative yield, a linear sequence appeared to offer some advantages in terms of the minimal number of protection steps required and the opportunities for regiocontrol. In particular, C-alkylation of a vanillin derivative through reaction with an allylic halide would be expected[11,12] to afford only the ortho alkylation product, while a directed ortho metalation strategy would have to contend with at least two potential directing groups. Thus, a linear approach based on initial assembly of the stilbene and subsequent addition of the geranyl chain was investigated in a model system.

For construction of the model stilbene, vanillin (**7**) was first treated with TBSCl to obtain the protected aldehyde **19**.[13] Condensation of this aldehyde with phosphonate **20** gave the protected stilbene **21** along with some of the phenol **22**, and subsequent reaction with TBAF completed formation of the phenol. Reaction of phenol **22** with sodium metal and geranyl bromide gave the C-alkylated product **23** in 42% yield, along with ~46% of recovered starting material. The O-alkylated product **24** was occasionally observed as a minor byproduct, but it was readily identified by the relatively downfield resonances of both C-1 in the ^{13}C NMR spectrum and the C-1 hydrogens in the ^1H NMR spectrum. Because recycling the starting material is at least theoretically possible, these results encouraged examination of a similar strategy with phosphonate **18**.



Condensation of aldehyde **19** with phosphonate **18** gave a mixture of stilbene products with (**25**) and without (**26**) the silyl group, and complete conversion to the phenol **26** was brought about by treatment of compound **25** with TBAF. Despite the successful transformation observed with the model compound **22**, reaction of phenol **26** with sodium metal and geranyl bromide proved problematic. While traces of the desired C-alkylated product **27** were observed, in the best case only 14% of this product was isolated. Instead, the major product of this reaction was the O-alkylated isomer (**28**) and little starting material was recovered. Thus, we were pressed to explore an alternate sequence for preparation of schweinfurthin C.

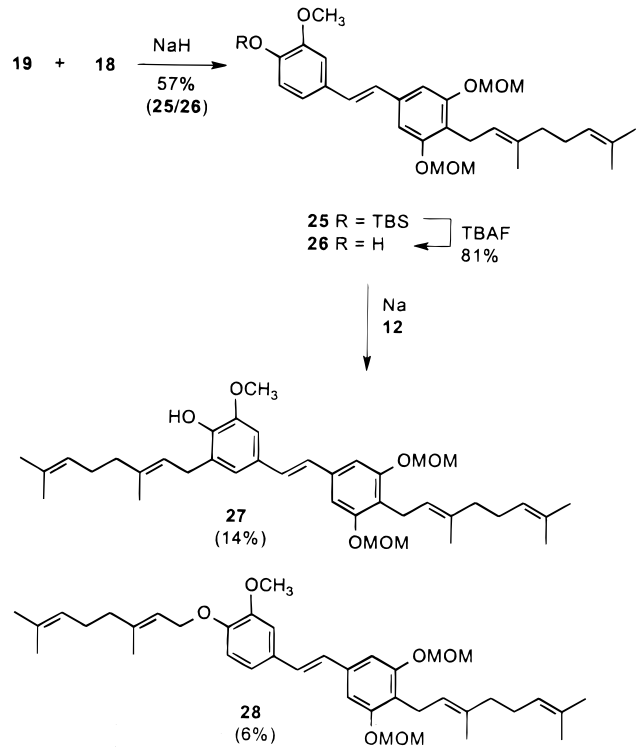
To pursue a more convergent approach to this natural product, to allow regiocontrolled introduction of the geranyl chain, and to simplify the eventual deprotection of the phenols, we chose to begin this sequence with the known aldehyde **29**,[14] which is readily prepared from vanillin.[15] After reduction with $LiAlH_4$ and reaction of the resulting alcohol (**30**) with TESCl to obtain the silyl ether **31**, halogen−metal exchange[16] was attempted. Upon treatment with *n*-BuLi followed by geranyl bromide, the desired C-alkylated product **32** was obtained in 54% yield. Cleavage of the silyl ether gave alcohol **33**,

(13) Singh, S. B.; Pettit, G. R. *Synth. Commun.* **1987**, *17*, 877−892.

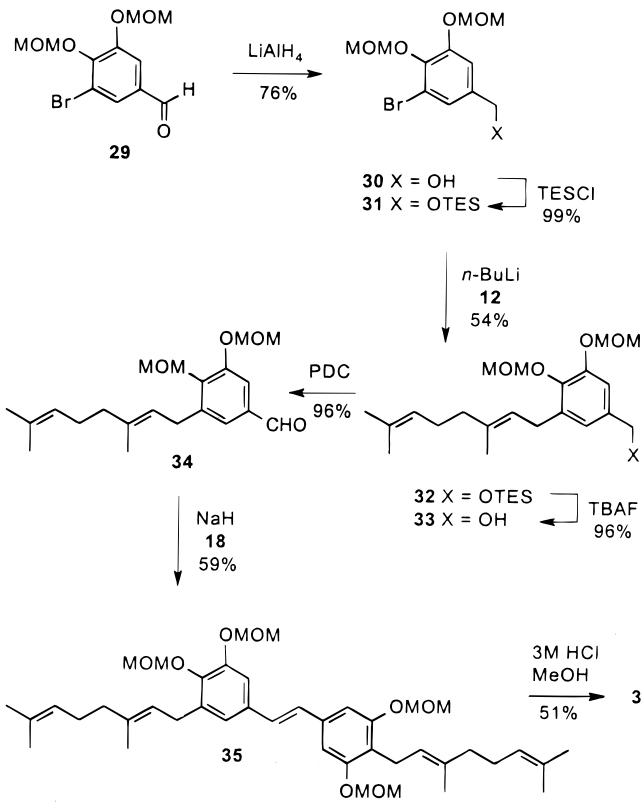
(14) Stafford, J. A.; Valvano, N. L. *J. Org. Chem.* **1994**, *59*, 4346−4349.

(15) (a) Manchand, P. S.; Belica, P. S.; Wong, H. S. *Synth. Commun.* **1990**, *20*, 2659−2666. (b) Lange, R. G. *J. Org. Chem.* **1962**, *27*, 2037−2039.

(16) (a) Jones, R. G.; Gilman, H. *Org. React.* **1951**, *6*, 339−366. (b) Tanaka, H.; Hiroo, M.; Ichino, K.; Ito, K. *Chem. Pharm. Bull.* **1989**, *37*, 1441−1445.



and oxidation with PDC to the aromatic aldehyde **34** provided the key "left half" intermediate for this approach.



Condensation of aldehyde **34** and phosphonate **18** gave the desired stilbene **35** as a single olefin isomer. Deprotection of compound **35** was accomplished by hydrolysis in 3 M HCl in methanol in ~50% yield. Given that this final deprotection required hydrolysis of four MOM groups, it may not be surprising that this reaction gave generally modest yields. However, the material prepared in this manner proved identical to the natural material in direct TLC comparisons with an authentic sample as well as in comparison of ^{1}H and ^{13}C NMR data with literature values.[1] Thus, the first synthesis of this natural product is now complete.

Schweinfurthin C is clearly the least complicated example of this small family of natural products, and in contrast to schweinfurthins A and B, it did not demonstrate significant anticancer activity in the NCI screens. Nevertheless, this synthesis of schweinfurthin C establishes strategies that can be applied in syntheses of the more complex members of this family and provides an intermediate in phosphonate **18** that would be useful for preparation of either schweinfurthin A or B. Our efforts to extend this work to allow preparation of related natural products and to identify the molecular targets for the cytotoxic geranylated stilbenes will be reported in due course.

Experimental Section

Tetrahydrofuran (THF) and diethyl ether were distilled from sodium/benzophenone immediately prior to use, DMF was distilled from molecular sieves, and CH_2Cl_2 and Et_3N were distilled from CaH. All nonaqueous reactions were conducted in oven-dried or flame-dried glassware, under an atmosphere of argon or nitrogen, with magnetic stirring. Oil-free NaH was prepared by washing mineral oil dispersions five times with an equal volume of pentane. Flash chromatography was carried out on silica gel with 40 μm average particle diameter. NMR spectra were recorded at 300 MHz for ^{1}H with $CDCl_3$ as solvent and $(CH_3)_4Si$ (^{1}H) or $CDCl_3$ (^{13}C, 77.0 ppm) as internal standards unless otherwise noted. ^{31}P NMR chemical shifts are reported in ppm relative to 85% H_3PO_4 (external standard). Low-resolution (70 eV), high-resolution, and FAB mass spectra were obtained at the University of Iowa Mass Spectrometry Facility. Elemental analyses were performed by Atlantic Microlab, Inc. (Norcross, GA).

***tert*-Butyl[(3,5-bis(methoxymethoxy)benzyl)oxy]dimethylsilane (11).** To a solution of alcohol **10**[9] (2.74 g, 12.0 mmol) in CH_2Cl_2 (50 mL) at 0 °C were added TBSCl (2.80 g, 18.6 mmol) and imidazole (3.32 g, 48.8 mmol), and the reaction was stirred for 12 h. The resulting solution was quenched by addition of H_2O and EtOAc. After the aqueous layer was extracted with EtOAc, the combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to afford compound **11** (3.77 g, 92%) as a clear oil. An analytical sample was prepared by flash column chromatography (9:1 hexanes/EtOAc): ^{1}H NMR δ 6.68 (d, J = 2.4 Hz, 2H), 6.61 (t, J = 2.4 Hz, 1H), 5.14 (s, 4H), 4.68 (s, 2H), 3.46 (s, 6H), 0.95 (s, 9H), 0.10 (s, 6H); ^{13}C NMR δ 158.2 (2C), 144.1, 107.1 (2C), 103.3, 94.4 (2C), 64.6, 55.8 (2C), 25.9 (3C), 18.3, −5.4 (2C); EIMS m/z (relative intensity) 342 (M^+, 1), 285 (15), 223 (19), 89 (100). Anal. Calcd for $C_{17}H_{30}O_5Si$: C, 59.62; H, 8.83. Found: C, 59.84; H, 9.01.

(3*E*)-1-*tert*-Butyldimethylsilyloxy-4,8-dimethyl-1-(3,5-bis(methoxymethoxy)phenyl)-3,7-nonadiene (13). To a solution of protected alcohol **11** (1.02 g, 2.97 mmol) in THF (30 mL) at 0 °C was added *n*-BuLi (1.31 mL, 2.50 M in hexane, 3.27 mmol) dropwise over 15 min. After 3 h, the solution was cooled to −78 °C, and geranyl bromide (0.59 mL, 3.0 mmol) was added. The reaction was stirred for 1 h and then allowed to warm to room temperature over 30 min and stirred for 30 min. The resulting solution was quenched by addition of H_2O and stirred for 1 h. This mixture was extracted with EtOAc, and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (9:1 hexanes/EtOAc) to afford compound **13** (298 mg, 21%) as a yellow oil: ^{1}H NMR δ 6.67 (d, J = 3.9 Hz, 2H), 6.58 (t, J = 3.9 Hz, 1H), 5.21−5.07 (m, 2H), 5.14 (s, 4H), 4.56 (s, 1H), 3.47 (s, 6H), 2.42−2.24 (m, 2H), 2.09−1.93 (m, 4H), 1.68 (s, 3H), 1.60 (s, 3H), 1.54 (s, 3H), 0.88 (s, 9H), 0.02 (s, 3H), −0.09 (s, 3H); ^{13}C NMR δ 157.9 (2C), 148.5, 136.9, 131.3, 124.4,

120.6, 107.3 (2C), 103.2, 94.5 (2C), 75.1, 55.9 (2C), 39.8, 39.5, 26.7, 25.8 (3C), 25.6, 18.2, 17.6, 16.3, −4.7, −5.0; EIMS *m/z* (relative intensity) 478 (M^+, 4), 355 (100), 69 (98); HRMS calcd for $C_{27}H_{46}O_5Si$ 478.3116, found 478.3115.

***tert*-Butyl[(4-(2*E*-3,7-dimethyl-2,6-octadienyl)-3,5-bis-(methoxymethoxy)benzyl)oxy]dimethylsilane (14).** To a solution of protected alcohol **11** (1.42 g, 4.15 mmol) and TMEDA (1.30 mL, 8.6 mmol) in THF (15 mL) at −20 °C was added *n*-BuLi (2.20 mL, 2.15 M in hexane, 4.73 mmol) dropwise over 10 min. After 50 min, CuCN (379 mg, 4.23 mmol) was added as a solid in one portion. After another 50 min at −20 °C, the solution was added via cannula into a solution of geranyl bromide (0.82 mL, 4.1 mmol) in THF (15 mL), which was cooled to −78 °C. After 2 h at −78 °C, the reaction mixture was allowed to warm to room temperature followed by the addition of H_2O and the resulting solution stirred for 45 min. The resulting blue/green solution was extracted with EtOAc, and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The resulting oil was purified by flash column chromatography (95:5 hexanes/EtOAc) to afford compound **14** (1.46 g, 73%) as a yellow oil: ^{1}H NMR δ 6.77 (s, 2H), 5.24−5.18 (tm, J = 7.2 Hz, 1H), 5.17 (s, 4H), 5.09−5.04 (tm, J = 6.8 Hz, 1H), 4.69 (s, 2H), 3.46 (s, 6H), 3.39 (d, J = 6.9 Hz, 2H), 2.08−2.01 (m, 2H), 1.98−1.93 (m, 2H), 1.78 (s, 3H), 1.64 (s, 3H), 1.57 (s, 3H), 0.95 (s, 9H), 0.10 (s, 6H); ^{13}C NMR δ 155.6 (2C), 140.6, 134.3, 131.1, 124.4, 122.9, 118.6, 105.7 (2C), 94.5 (2C), 64.9, 55.8 (2C), 39.8, 26.7, 25.9 (3C), 25.6, 22.5, 18.3, 17.6, 16.0, −5.3 (2C); EIMS, *m/z* (relative intensity) 478 (M^+, 2), 355 (48), 69 (94), 45 (100); HRMS calcd for $C_{27}H_{46}O_5Si$ 478.3116, found 478.3110. Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68. Found: C, 67.48; H, 9.77.

4-((2*E*)-3,7-Dimethyl-2,6-octadienyl)-3,5-bis(methoxymethoxy)benzyl Alcohol (15). To a solution of protected alcohol **14** (473 mg, 0.99 mmol) in THF (20 mL) was added dropwise TBAF (1.0 mL, 1.0 M in THF, 1.0 mmol), and the reaction mixture was stirred at room temperature for 3 h. The resulting solution was quenched by addition of H_2O and EtOAc. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting liquid was purified by flash column chromatography (4:1 hexanes/EtOAc) to afford compound **15** (310 mg, 86%) as a clear oil: ^{1}H NMR δ 6.76 (s, 2H), 5.22−5.17 (tm, J = 7.3 Hz, 1H), 5.17 (s, 4H), 5.08−5.03 (tm, J = 6.7 Hz, 1H), 4.58 (s, 2H), 3.45 (s, 6H), 3.38 (d, J = 6.9 Hz, 2H), 2.51 (br s, 1H), 2.07−2.00 (m, 2H), 1.96−1.92 (m, 2H), 1.78 (s, 3H), 1.64 (s, 3H), 1.56 (s, 3H); ^{13}C NMR δ 155.6 (2C), 140.1, 134.5, 131.1, 124.3, 122.6, 119.2, 106.3 (2C), 94.2 (2C), 65.1, 55.9 (2C), 39.7, 26.6, 25.5, 22.4, 17.5, 16.0; EIMS *m/z* (relative intensity) 364 (M^+, 4), 241 (100), 233 (63), 69 (69); HRMS calcd for $C_{21}H_{32}O_5$ 364.2251, found 364.2250. Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.08; H, 8.86.

4-((2*E*)-3,7-Dimethyl-2,6-octadienyl)-3,5-bis(methoxymethoxy)benzyl Iodide (17). To a solution of alcohol **15** (837 mg, 2.3 mmol) and Et_3N (0.42 mL, 3.0 mmol) in CH_2Cl_2 (60 mL) at 0 °C was added methanesulfonyl chloride (0.23 mL, 3.0 mmol) dropwise. After the reaction mixture was stirred at 0 °C for 1 h, it was extracted sequentially with H_2O, saturated $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4), filtered, and concentrated in vacuo. The yellow residue was dissolved in acetone (40 mL), and solid NaI (1.04 g, 6.91 mmol) was added in one portion. The solution was stirred at room temperature for 22 h as a precipitate formed. The resulting orange solution was added to a solution of saturated $NaHCO_3$ and extracted with EtOAc. The combined organic layers were then washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The resulting brown oil was purified by flash column chromatography (9:1 hexanes/EtOAc) to afford iodide **17** (937 mg, 86%) as a yellow oil: ^{1}H NMR δ 6.79 (s, 2H), 5.20−5.16 (tm, J = 7.3 Hz, 1H), 5.17 (s, 4H), 5.08−5.03 (tm, J = 6.9 Hz, 1H), 4.39 (s, 2H), 3.46 (s, 6H), 3.35 (d, J = 6.9 Hz, 2H), 2.08−2.00 (m, 2H), 1.97−1.92 (m, 2H), 1.77 (s, 3H), 1.63 (s, 3H), 1.56 (s, 3H); ^{13}C NMR δ 155.5 (2C), 137.8, 134.6, 131.1, 124.2, 122.2, 120.0, 108.3 (2C), 94.3 (2C), 55.9 (2C), 39.7, 26.6, 25.6, 22.5, 17.5, 16.0, 6.4; EIMS, *m/z* (relative intensity) 347 (M^+ − 127, 46), 69 (81), 46 (100); HRMS calcd for $C_{21}H_{31}O_4$ (M^+ − I) 347.2223, found 347.2241.

Diethyl (4-((2*E*)-3,7-Dimethyl-2,6-octadienyl)-3,5-bis(methoxymethoxy)benzyl)phosphonate (18). A solution of iodide **17** (501 mg, 1.06 mmol) in triethyl phosphite (5.0 mL) was heated at reflux for 2.5 h. The solution was allowed to cool to room temperature and placed on a high vacuum line to remove the excess triethyl phosphite. The resulting yellow oil was purified by flash column chromatography (9:1 EtOAc/hexanes) to afford phosphonate **18** (511 mg, 100%) as a yellow oil: ^{1}H NMR δ 6.71 (d, J = 1.8 Hz, 2H), 5.17 (s, 4H), 5.21−5.16 (m, 1H), 5.08−5.04 (tm, J = 6.6 Hz, 1H), 4.04 (dq, J = 6.9, 6.9 Hz, 4H), 3.45 (s, 6H), 3.37 (d, J = 6.9 Hz, 2H), 3.08 (d, J_{PH} = 21.3 Hz, 2H), 2.05−2.00 (m, 2H), 1.97−1.93 (m, 2H), 1.77 (s, 3H), 1.64 (s, 3H), 1.56 (s, 3H), 1.27 (t, J = 6.9 Hz, 6H); ^{13}C NMR δ 155.3 (d, J_{CP} = 3.1 Hz, 2C), 134.1, 130.8, 130.0 (d, J_{CP} = 8.6 Hz), 124.1, 122.5 (d, J_{CP} = 1.8 Hz), 118.5, 109.3 (d, J_{CP} = 3.0 Hz, 2C), 94.1 (2C), 61.7 (d, J_{CP} = 6.7 Hz, 2C), 55.6 (2C), 39.5, 33.5 (d, J_{CP} = 137.3 Hz), 26.4, 25.3, 22.2, 17.3, 16.0 (d, J_{CP} = 6.1 Hz, 2C), 15.7; ^{31}P NMR δ 26.8; EIMS, *m/z* (relative intensity) 483 (M^+ − 1, 2), 46 (100); HRMS calcd for $C_{25}H_{41}O_7P$ 484.2591, found 484.2607.

4-(*tert*-Butyldimethylsilyloxy)-3-methoxybenzaldehyde (19).[13] Diisopropylethylamine (2.15 mL, 12.3 mmol) was added to a solution of vanillin (1.25 g, 8.24 mmol) in DMF (15 mL) at 0 °C, followed by the addition of TBSCl (1.37 g, 9.10 mmol). After the solution was stirred for 130 min, ice-cold H_2O was added, followed by Et_2O and saturated $NaHCO_3$. The resulting layers were separated, and the organic phase was washed with H_2O, saturated $NaHCO_3$, and H_2O. The organic phase was dried ($MgSO_4$) and concentrated in vacuo to yield a clear oil (1.99 g, 91%). The ^{1}H and ^{13}C NMR and the mass spectrum matched literature values.[13,17]

***tert*-Butyldimethylsilyloxy-2-methoxy-4-((*E*)-phenylethenyl)benzene (21).** NaH (458 mg, 19.1 mmol) was added in portions to diethylbenzyl phosphonate (1.71 g, 7.49 mmol) in THF (60 mL) at 0 °C, and the solution was stirred for 30 min. Aldehyde **19** (1.98 g, 7.43 mmol) in THF (15 mL) was then added dropwise and the reaction stirred overnight. The reaction was quenched by addition of H_2O, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash column chromatography (10:1 hexanes/EtOAc) afforded the silylated stilbene **21** (628 mg, 25%) along with phenol **22** (594 mg, 33%). For compound **21**: clear oil; ^{1}H NMR δ 7.48−7.43 (m, 2H), 7.35−7.27 (m, 2H), 7.23−7.17 (m, 1H), 7.02 (d, J = 16.2 Hz, 1H), 7.00 (d, J = 1.6 Hz, 1H), 6.96 (dd, J = 8.1, 1.9 Hz, 1H), 6.93 (d, J = 16.3 Hz, 1H), 6.82 (d, J = 8.1 Hz, 1H), 3.82 (s, 3H), 1.01 (s, 9H), 0.17 (s, 6H); ^{13}C NMR δ 151.0, 145.0, 137.5, 131.2, 128.6, 128.5 (2C), 127.1, 126.7, 126.2 (2C), 120.9, 119.7, 109.7, 55.3, 25.7 (3C), 18.4, −4.7 (2C); EIMS, *m/z* (relative intensity) 340 (M^+, 6), 325 (1), 283 (37), 268 (100). Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29. Found: C, 73.81; H, 8.32.

For compound **22**: white solid; mp 131−132 °C; ^{1}H NMR δ 7.48−7.43 (m, 2H), 7.35−7.29 (m, 2H), 7.24−7.17 (m, 1H), 7.03 (d, J = 16.6 Hz, 1H), 7.01 (d, J = 1.8 Hz, 1H), 7.01 (dd, J = 8.3, 2.1 Hz, 1H), 6.93 (d, J = 16.2 Hz, 1H), 6.90 (d, J = 8.7 Hz, 1H), 5.73 (br s, 1H), 3.87 (s, 3H); ^{13}C NMR δ 146.7, 145.5, 137.5, 129.9, 128.6 (2C), 128.5, 127.2, 126.4, 126.2 (2C), 120.4, 114.5, 108.2, 55.9; EIMS, *m/z* (relative intensity) 226 (M^+, 100), 211 (4), 165 (44).

2-Methoxy-4-((*E*)-phenylethenyl)phenol (22). TBAF (3.1 mL, 1.0 M in THF, 3.1 mmol) was added to a solution of silane **21** (780 mg, 2.29 mmol) in Et_2O (10 mL) at 0 °C. After the solution was stirred for 20 min, the reaction was quenched by addition of saturated NH_4Cl, followed by H_2O. The aqueous layer was extracted with EtOAc, and the organic extract was dried ($MgSO_4$) and concentrated in vacuo to yield compound **22** as a white solid (620 mg, 80%) identical with material obtained above. An analytical sample was prepared by purification by flash column chromatography (6:1 hexanes/EtOAc). Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.20; H, 6.20.

6-((2*E*)-3,7-Dimethyl-2,6-octadienyl)-2-methoxy-4-((*E*)-phenylethenyl)phenol (23). Small slices of metallic sodium (130 mg, 5.65 mmol) were added to stilbene **22** (309 mg, 1.37 mmol) in Et_2O (35 mL), and the resulting mixture was stirred at room temperature for 2 h. Geranyl bromide (0.5 mL, 2.5 mmol) was then added, and the solution was heated at reflux for

(17) Barclay, L. R. C.; Cromwell, G. R.; Hilborn, J. W. *Can. J. Chem.* **1994**, *72*, 35−41.

approximately 45 h. After the reaction had cooled to room temperature, it was quenched by addition of H_2O, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash column chromatography (10:1 hexanes/EtOAc) afforded the alkylated stilbene **23** (152 mg, 42%) as a yellow oil along with some recovered starting material (135 mg, 44%): ^{1}H NMR δ 7.50−7.44 (m, 2H), 7.35−7.29 (m, 2H), 7.24−7.17 (m, 1H), 7.02 (d, J = 16.3 Hz, 1H), 6.91 (d, J = 16.2 Hz, 1H), 6.90 (br s, 2H), 5.80 (s, 1H), 5.40−5.33 (tm, J = 7.2 Hz, 1H), 5.16−5.09 (tm, J = 6.8 Hz, 1H), 3.87 (s, 3H), 3.38 (d, J = 7.3 Hz, 2H), 2.13−2.03 (m, 2H), 2.03−1.95 (m, 2H), 1.74 (s, 3H), 1.67 (s, 3H), 1.59 (s, 3H); ^{13}C NMR δ 146.4, 143.3, 137.6, 136.3, 131.3, 128.9, 128.9, 128.5 (2C), 127.4, 127.0, 126.1 (2C), 126.0, 124.2, 122.0, 121.1, 105.7, 55.9, 39.7, 27.9, 26.6, 25.6, 17.5, 16.1; EIMS, *m*/*z* (relative intensity) 362 (M^+, 14), 279 (100), 226 (30), 137 (70), 91 (58). Anal. Calcd for $C_{25}H_{30}O_2$: C, 82.82; H, 8.34. Found: C, 82.62; H, 8.37.

***tert*-Butyldimethylsilyloxy-4-((*E*)-4-((2*E*)-3,7-dimethyl-2,6-octadienyl)-3,5-bis(methoxymethoxy)phenylethenyl)-2-methoxybenzene (25).** NaH (28 mg, 1.2 mmol) was added to phosphonate **18** (257 mg, 0.53 mmol) in THF (20 mL) at 0 °C, the ice bath was removed, and the reaction was stirred for 45 min. Aldehyde **19** (154 mg, 0.58 mmol) in THF (2.5 mL) was then added dropwise and the reaction stirred for 10 h. The reaction was quenched by addition of H_2O and the aqueous phase extracted with EtOAc. The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash column chromatography (10:1 hexanes/EtOAc) afforded the silylated stilbene **25** (127 mg, 40%), along with the corresponding phenol **26** (44 mg, 17%). For stilbene **25**: ^{1}H NMR δ 7.05 (d, J = 1.7 Hz, 1H), 7.01 (d, J = 16.3 Hz, 1H), 6.99 (dd, J = 8.1, 1.7 Hz, 1H), 6.96 (s, 2H), 6.93 (d, J = 16.9 Hz, 1H), 6.85 (d, J = 8.1 Hz, 1H), 5.26 (s, 4H), 5.26 (m, 1H), 5.10 (tm, J = 6.4 Hz, 1H), 3.89 (s, 3H), 3.53 (s, 6H), 3.43 (d, J = 7.0 Hz, 2H), 2.10−2.03 (m, 2H), 2.03−1.95 (m, 2H), 1.82 (s, 3H), 1.67 (s, 3H), 1.60 (s, 3H), 1.04 (s, 9H), 0.20 (s, 6H); ^{13}C NMR δ 155.9 (2C), 151.0, 144.9, 136.6, 134.6, 131.3, 131.2, 128.2, 126.9, 124.4, 122.6, 120.9, 119.7, 119.5, 109.6, 106.0 (2C), 94.5 (2C), 55.9 (2C), 55.4, 39.8, 26.7, 25.68 (3C), 25.63, 22.7, 18.4, 17.6, 16.0, −4.7 (2C); EIMS, *m*/*z* (relative intensity) 596 (M^+, 22), 595 (50), 539 (9), 46 (100).

For phenol **26**: ^{1}H NMR δ 7.02 (d, J = 1.6 Hz, 1H), 6.99 (dd, J = 8.1, 1.8 Hz, 1H), 6.97 (d, J = 16.6 Hz, 1H), 6.92 (s, 2H), 6.88 (d, J = 8.1 Hz, 1H), 6.87 (d, J = 16.2 Hz, 1H), 5.72 (br s, 1H), 5.24 (s, 4H), 5.24 (tm, J = 6.9 Hz, 1H), 5.07 (tm, J = 6.9 Hz, 1H), 3.93 (s, 3H), 3.50 (s, 6H), 3.40 (d, J = 7.4 Hz, 2H), 2.07−2.00 (m, 2H), 2.00−1.93 (m, 2H), 1.79 (s, 3H), 1.65 (s, 3H), 1.57 (s, 3H); ^{13}C NMR δ 155.9 (2C), 146.7, 145.5, 136.5, 134.6, 131.2, 129.9, 128.2, 126.6, 124.3, 122.6, 120.4, 119.6, 114.5, 108.1, 105.9 (2C), 94.4 (2C), 55.94 (2C), 55.85, 39.8, 26.7, 25.6, 22.7, 17.6, 16.0; EIMS, *m*/*z* (relative intensity) 482 (M^+, 70), 437 (3), 359 (30), 46 (100); HR FAB-MS calcd for $C_{29}H_{38}O_6Na$ 505.2566, found 505.2578.

2-Methoxy-4-((*E*)-4-(2(*E*)-3,7-dimethyl-2,6-octadienyl)-3,5-bis(methoxymethoxy)phenylethenyl)phenol (26). TBAF (0.20 mL, 1.0 M in THF, 0.2 mmol) was added to silane **25** (119 mg, 0.20 mmol) in THF (15 mL) at 0 °C. After the solution was stirred for 90 min, the reaction was quenched by addition of H_2O and EtOAc, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield compound **26** as a yellow oil (78 mg, 81%), identical with material obtained above.

6-((2*E*)-3,7-Dimethyl-2,6-octadienyl)-4-((*E*)-4-(2(*E*)-3,7-dimethyl-2,6-octadienyl)-3,5-bis(methoxymethoxy)phenylethenyl)-2-methoxyphenol (27). Small slices of metallic sodium (13 mg, 0.54 mmol) were added to phenol **26** (43 mg, 0.089 mmol) in Et_2O (4 mL) and the mixture stirred at room temperaturefor 3 h. Geranyl bromide (0.04 mL, 0.20 mmol) was then added, along with Et_2O (11 mL), and the solution was heated at reflux for 16 h. After the reaction had cooled to room temperature, it was quenched by addition of H_2O, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash column chromatography (12:1 hexanes/EtOAc) afforded the C-alkylated stilbene **27** (8 mg, 14%), along with the O-alkylated product **28** (3 mg, 6%) and unreacted starting material (17 mg, 40%). For compound **27**: yellow oil; ^{1}H NMR (CD_3OD as solvent and internal reference) δ 6.98 (br s, 1H), 6.95 (d, J = 16.2 Hz, 1H), 6.90 (s, 2H), 6.84 (d, J = 16.0 Hz, 1H), 6.83 (br s, 1H), 5.34−5.30 (m, 1H), 5.30−5.04 (m, 3H), 5.22 (s, 4H), 4.85 (s, 6H), 3.89 (s, 3H), 3.36 (d, J = 7.0 Hz, 2H), 3.30 (d, J = 7.0 Hz, 2H), 2.20−2.00 (m, 6H), 2.00−1.90 (m, 2H), 1.77 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H), 1.60 (s, 3H), 1.58 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (CD_3OD as solvent and internal reference) δ 161.9, 157.1, 148.8, 145.3, 138.3, 136.7, 135.2, 132.2, 132.1, 129.91, 129.88, 129.1, 126.8, 125.4 (2C), 124.3, 124.0, 121.9, 120.3, 107.5, 106.9 (2C), 95.7 (2C), 56.4, 56.3 (2C), 40.9 (2C), 28.9, 27.7 (2C), 26.0, 25.8, 23.4, 17.8, 17.7, 16.3, 16.2.

For the O-alkylated product **28**: yellow oil; ^{1}H NMR δ 7.02 (d, J = 1.5 Hz, 1H), 7.01 (dd, J = 8.6, 1.5 Hz, 1H), 6.99 (d, J = 16.3 Hz, 1H), 6.94 (d, J = 16.0 Hz, 1H), 6.93 (s, 2H), 6.85 (d, J = 8.3 Hz, 1H), 5.52 (tm, J = 6.5 Hz, 1H), 5.24 (s, 4H), 5.24 (m, 1H), 5.07 (tm, J = 6.5 Hz, 2H), 4.63 (d, J = 6.5 Hz, 2H), 3.93 (s, 3H), 3.50 (s, 6H), 3.40 (d, J = 7.0 Hz, 2H), 2.18−1.90 (m, 8H), 1.79 (s, 3H), 1.73 (s, 3H), 1.67 (s, 3H), 1.64 (s, 3H), 1.60 (s, 3H), 1.57 (s, 3H); ^{13}C NMR δ 155.8 (2C), 149.5, 148.0, 140.5, 136.5, 134.5, 131.6, 131.1, 130.3, 128.0, 126.7, 124.3, 128.8, 122.6, 119.7, 119.6, 119.5, 113.0, 108.8, 105.9 (2C), 94.4 (2C), 65.8, 55.9 (2C), 55.8, 39.7, 39.5, 26.6, 26.2, 25.6 (2C), 22.6, 17.6, 17.5, 16.6, 16.0; HR FAB-MS calcd for $C_{39}H_{54}O_6$ 618.3922, found 618.3902.

5-Bromo-3,4-bis(methoxymethyoxy)benzaldehyde (29).[14] To a solution of 5-bromo-3,4-dihydroxybenzaldehyde[15b] (1.85 g, 8.51 mmol) in DMF (15 mL) at 0 °C was added diisopropylethylamine (3.6 mL, 38 mmol) followed by MOMCl (1.80 mL, 23.7 mmol), and the solution was stirred for 28 h while it warmed to room temperature. The reaction was quenched by addition of H_2O and saturated $NaHCO_3$. Ether was added, the layers were separated, and the organic phase was washed with H_2O, saturated $NaHCO_3$, and brine. After the organic phase was dried ($MgSO_4$) and concentrated in vacuo, compound **29** was obtained as a clear oil (1.79 g, 69%). Both ^{1}H and ^{13}C NMR data were in agreement with literature values.[14]

5-Bromo-3,4-bis(methoxymethoxy)benzyl alcohol (30). Aldehyde **29** (810 mg, 2.65 mmol) in Et_2O (15 mL) was added dropwise to a suspension of $LiAlH_4$ (69.5 mg, 1.83 mmol) in Et_2O (60 mL) at 0 °C, and the remaining aldehyde was transferred with additional Et_2O (4 mL). After the reaction mixture was stirred for 10 min, it was quenched by addition of EtOAc, followed by H_2O, 0.5 M NaOH, and H_2O. The aqueous phase was extracted with EtOAc, and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purification of the resulting oil by flash column chromatography (2:1 hexanes/EtOAc) afforded compound **30** (619 mg, 76%) as a clear oil: ^{1}H NMR δ 7.20 (br s, 1H), 7.07 (br s, 1H), 5.18 (s, 2H), 5.16 (s, 2H), 4.56 (s, 2H), 3.65 (s, 3H), 3.48 (s, 3H), 2.54 (br s, 1H); ^{13}C NMR δ 150.8, 143.1, 138.5, 124.4, 117.7, 114.0, 98.7, 95.1, 63.9, 57.8, 56.3; EIMS, *m*/*z* (relative intensity) 308 (M^++2, 14), 306 (M^+, 14), 246 (5), 244 (5), 230 (100). Anal. Calcd for $C_{11}H_{15}BrO_5$: C, 43.16; H, 4.94. Found: C, 42.76; H, 4.84.

[5-Bromo-3,4-bis(methoxymethoxy)benzyl]triethylsilane (31). TESCl (1.60 mL, 9.41 mmol) was added to alcohol **30** (1.14 g, 3.71 mmol) in CH_2Cl_2 (25 mL) at 0 °C, followed by imidazole (1.04 mg, 15.2 mmol). After the mixture was stirred for 22 h, H_2O and EtOAc were added. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash chromatography (6:1 hexanes/EtOAc) gave compound **31** as a clear oil (1.44 g, 99%): ^{1}H NMR δ 7.18 (d, J = 1.2 Hz, 1H), 7.09 (d, J = 1.3 Hz, 1H), 5.18 (s, 2H), 5.16 (s, 2H), 4.64 (s, 2H), 3.65 (s, 3H), 3.48 (s, 3H), 0.98 (t, J = 7.9 Hz, 9H), 0.65 (q, J = 7.9 Hz, 6H); ^{13}C NMR δ 150.7, 142.7, 138.7, 123.6, 117.4, 113.5, 98.7, 95.1, 63.5, 57.7, 56.0, 6.6 (3C), 4.3 (3C); EIMS, *m*/*z* (relative intensity) 422 (M^+ + 2, 5), 420 (M^+, 4), 215 (100), 213 (99), 117 (50). Anal. Calcd for $C_{17}H_{29}BrO_5Si$: C, 48.57; H, 6.95. Found: C, 48.40; H, 6.90.

[5-((2*E*)-3,7-Dimethyl-2,6-octadienyl)-3,4-bis(methoxymethoxy)benzyl]triethylsilane (32). A solution of silane **31** (177 mg, 0.42 mmol) in Et_2O (10 mL) was treated with *n*-BuLi (0.20 mL, 2.47 M in hexanes, 0.45 mmol) at −78 °C. After the solution was stirred for 20 min, geranyl bromide (0.25 mL, 1.3 mmol) was added dropwise, and the reaction was allowed to warm to room temperature and then stirred for a total of 6 h. The reaction was quenched by addition of H_2O, the aqueous

phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash chromatography (7:1 hexanes/EtOAc) afforded compound **32** (108 mg, 54%) as a clear oil: ^{1}H NMR δ 6.98 (d, J = 1.8 Hz, 1H), 6.80 (d, J = 1.5 Hz, 1H), 5.31 (tm, J = 7.8 Hz, 1H), 5.18 (s, 2H), 5.10 (tm, J = 7.4 Hz, 1H), 5.08 (s, 2H), 4.63 (s, 2H), 3.59 (s, 3H), 3.49 (s, 3H), 3.41 (d, J = 6.9 Hz, 2H), 2.10−2.00 (m, 4H), 1.71 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.65 (q, J = 7.9 Hz, 6H); ^{13}C NMR δ 149.6, 143.6, 137.3, 136.1, 135.6, 131.3, 124.3, 122.5, 120.7, 112.3, 99.0, 95.13, 64.5, 57.4, 56.0, 39.7, 28.3, 26.6, 25.6, 17.6, 16.1, 6.7 (3C), 4.5 (3C); EIMS, *m*/*z* (relative intensity) 478 (M^+, 4), 446 (8), 117 (100). Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68. Found: C, 67.97; H, 9.67.

5-((*2E*)-3,7-Dimethyl-2,6-octadienyl)-3,4-bis(methoxymethoxy)benzyl Alcohol (33). TBAF (0.19 mL, 1.0 M in THF, 0.19 mmol) was added dropwise to a solution of silane **32** (83 mg, 0.17 mmol) in THF (10 mL) at 0 °C. After the solution was stirred for 5 h, the reaction was quenched by addition of saturated NH_4Cl. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford a clear oil (60 mg, 96%). Although this material was one spot by TLC, an analytical sample was prepared by purification by flash column chromatography (1.5:1 hexanes/EtOAc): ^{1}H NMR δ 7.01 (d, J = 1.7 Hz, 1H), 6.84 (d, J = 1.4 Hz, 1H), 5.31 (tm, J = 7.1, 1H), 5.19 (s, 2H), 5.10 (s, 2H), 5.10 (m, 1H), 4.59 (s, 2H), 3.60 (s, 3H), 3.50 (s, 3H), 3.42 (d, J = 7.3 Hz, 2H), 2.10−2.00 (m, 4H), 1.71 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H); ^{13}C NMR δ 149.8, 144.1, 136.9, 136.3, 136.2, 131.4, 124.2, 122.4, 121.6, 112.8, 99.0, 95.1, 65.2, 57.4, 56.2, 39.7, 28.3, 26.6, 25.7, 17.7, 16.1; EIMS, *m*/*z* (relative intensity) 364 (M^+, 1), 135 (50), 69 (100). Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 68.94; H, 8.76.

5-((*2E*)-3,7-Dimethyl-2,6-octadienyl)-3,4-bis(methoxymethoxy)benzaldehyde (34). Alcohol **33** (40 mg, 0.11 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a suspension of PDC (85 mg, 0.23 mmol) and 3 Å molecular sieve powder (98 mg) in CH_2Cl_2 (15 mL). After the mixture was stirred at room temperature for 2.5 h, the solution was filtered through silica gel, and the silica gel was washed thoroughly with EtOAc. After concentration in vacuo, the crude product was purified by column chromatography (2:1 hexanes/EtOAc) to afford aldehyde **34** (38 mg, 96%) as a clear oil: ^{1}H NMR δ 9.86 (s, 1H), 7.52 (d, J = 1.5 Hz, 1H), 7.39 (d, J = 1.3 Hz, 1H), 5.33 (tm, J = 7.2 Hz, 1H), 5.25 (s, 2H), 5.23 (s, 2H), 5.14−5.08 (m, 1H), 3.49 (d, J = 8.1 Hz, 2H), 2.13−2.08 (m, 2H), 2.08−2.00 (m, 2H), 1.73 (s, 3H), 1.67 (s, 3H), 1.60 (s, 3H); ^{13}C NMR δ 191.2, 150.1, 150.0, 137.2, 136.6, 132.4, 131.5, 129.0, 124.0, 121.4, 113.6, 98.9, 95.0, 57.5, 56.3, 39.6, 28.2, 26.5, 25.6, 17.6, 16.1; EIMS, *m*/*z* (relative intensity) 362 (M^+, 1), 317 (14), 135 (53), 69 (100). Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.34; H, 8.34

Tetrakis(methoxymethoxy)schweinfurthin C (35). Phosphonate **18** (410 mg, 0.85 mmol) in THF (7 mL) was added to a slurry of NaH (26 mg, 1.09 mmol) in THF (10 mL) at 0 °C, and the reaction mixture was stirred for 30 min. Aldehyde **19** (248 mg, 0.69 mmol) in THF (3 mL) was then added dropwise, the ice bath was removed, and the solution was stirred for 1 h while it warmed to room temperature. After an additional hour at reflux, the reaction was left to stir for 23 h and then quenched by addition of H_2O, and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Repeated purification by flash chromatography (9:1 hexanes/EtOAc) afforded compound **35** (279 mg, 59%) as a clear oil: ^{1}H NMR δ 7.15 (d, J = 1.8 Hz, 1H), 6.97 (d, J = 1.7 Hz, 1H), 6.96 (d, J = 15.6 Hz, 1H), 6.91 (s, 2H), 6.89 (d, J = 16.2 Hz, 1H), 5.34 (tm, J = 7.2 Hz, 1H), 5.24 (s, 2H), 5.23 (s, 4H), 5.23 (m, 1H), 5.12 (s, 2H), 5.07 (m, 2H), 3.61 (s, 3H), 3.54 (s, 3H), 3.50 (s, 6H), 3.43 (d, J = 7.7 Hz, 2H), 3.40 (d, J = 7.8 Hz, 2H), 2.15−2.00 (m, 6H), 2.00−1.90 (m, 2H), 1.79 (s, 3H), 1.75 (s, 3H), 1.68 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 1.57 (s, 3H); ^{13}C NMR δ 155.9 (2C), 149.9, 144.3, 136.4, 136.3, 136.1, 134.7, 133.5, 131.4, 131.2, 128.1, 128.0, 124.4, 124.3, 122.6, 122.5, 121.7, 119.8, 111.6, 106.1 (2C), 98.1, 95.1, 94.5 (2C), 57.5, 56.3, 56.0 (2C), 39.8, 39.7, 28.5, 26.7, 26.6, 25.7, 25.6, 22.7, 17.7, 17.6, 16.3, 16.1; HR FAB-MS calcd for $C_{42}H_{60}O_8Na$ 715.4186, found 715.4184.

Schweinfurthin C (3). To a solution of compound **35** (38 mg, 0.054 mmol) in MeOH (2 mL) was added 3 M HCl (0.5 mL), and the resulting solution was heated at reflux for 24 min. After the reaction mixture had cooled to room temperature, it was quenched by addition of saturated $NaHCO_3$ and then extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash column chromatography (96:4 $CHCl_3$/MeOH) afforded compound **3** as a yellow oil (14 mg, 51%). This material was identical to the natural product in direct TLC comparisons with an authentic sample as well as in comparison of ^{1}H and ^{13}C NMR data with literature values.[1]

Acknowledgment. We thank John A. Beutler for both helpful discussions and an authentic sample of schweinfurthin C. Financial support from the Roy J. Carver Charitable Trust and the University of Iowa Graduate College is gratefully acknowledged.

Supporting Information Available: The ^{1}H and/or ^{13}C data for 10 compounds (**13**, **14**, **17**, **18**, **21**, **23**, **26**−**28**, and **35**). This material is available free of charge via the Internet at http://pubs.acs.org.

JO9908795