Synthesis of (+)-Juruenolide C: Use of Sequential 5-*Exo-Digonal* Radical Cyclization, 1,5-Intramolecular Hydrogen Transfer, and 5-*Endo-Trigonal* Cyclization

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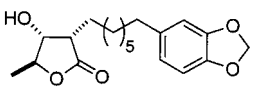
Acetylenic alcohol **10** was converted successively into silane **11** and phenylseleno carbonate **14**. On treatment with Ph_3SnH, the latter underwent 5-*exo-digonal* radical cyclization, intramolecular hydrogen transfer, and 5-*endo-trigonal* cyclization, yielding **15**. Conversion of the lactone into the lactol benzyl ether **17**, carbon−silicon bond cleavage, and regeneration of the lactone carbonyl gave (+)-juruenolide C (**1**).

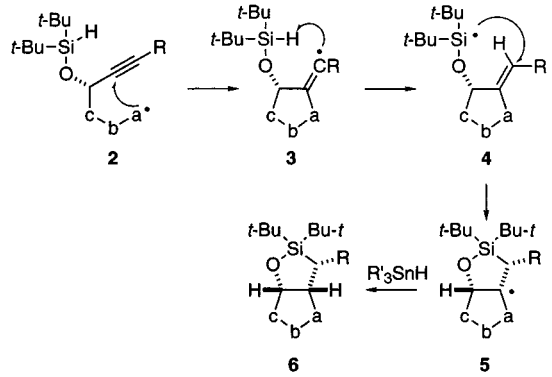
The γ-lactone juruenolide C (**1**) was isolated[1,2] from seedlings and micropropagated leaves of *Virola surinamensis*—a myristicaceous tree that thrives on river banks in Amazonia. The compound is a member of a group of related substances differing in the length of the chain that connects the piperonyl and lactone units.[1,4] The amount of **1** in the plant source appears to be related to the growth rate,[1] although the mechanistic basis for this is not known. Compound **1** has been found to have antifungal activity against *Cladiosporium cladisporioides*, but it is 10 times less potent than nystatin.[4]



1

Simple, naturally occurring γ-lactones bearing three contiguous substituents with the 3α,4α,5β relationship found in **1** appear to be rare.[5] This particular stereochemistry is precisely that which is directly accessible[6] by appropriate modification of the general radical cascade[7] summarized in Scheme 1, where the chain linking the radical center to the acetylene can carry substituents and/or incorporate heteroatoms. Previous work in this laboratory has illustrated some synthetic applications of this sequence, but in examples where stereochemical adjustment of the final cascade product was required;[7b] in the present case, no such modifications are needed, and we report a short route to (+)-**1**.

Scheme 1



Analysis of structure **1** in terms of the general method summarized in Scheme 1 shows that appropriate starting materials are the known aldehyde **7**[8] and the acetylene **8**. Previous work[7a,c] had indicated that a triethylsilyl protecting group (see **7**) was suitable, as it can be removed (see below) in the presence of the *t*-Bu_2SiH group that plays a central role in the radical cascade (see Scheme 1). The acetylene **8** was readily made (CBr_4, Ph_3P, Et_3N, −78 °C to room temperature, 87%; BuLi, −78

(1) (a) Lopes, N. P.; França, S. de C.; Pereira, A. M. S.; Maia, J. G. S.; Kato, M. J.; Cavalheiro, A. J.; Gottlieb, O. R.; Yoshida, M. *Phytochemistry* **1994**, *35*, 1469−1470. (b) Lopes, N. P.; Blumenthal, E. E. de A.; Cavalheiro, A. J.; Kato, M. J.; Yoshida, M. *Phytochemistry* **1996**, *43*, 1089−1092.

(2) The absolute stereochemistry was assigned by comparison with that of juruenolide (see ref 3).

(3) Vieira, P. C.; Yoshida, M.; Gottlieb, O. R.; Filho, H. F. P.; Nagem, T. J.; Filho, R. B. *Phytochemistry* **1983**, *22*, 711−714.

(4) Lopes, N. P.; Kato, M. J.; Yoshida, M. *Phytochemistry* **1999**, *51*, 29−33.

(5) For some other examples, retrieved by a search of the Beilstein database, see ref 3 and: (a) Hikino, H.; Nomoto, K.; Takemoto, T. *Phytochemistry* **1971**, *10*, 3173−3178. (b) Epstein, W. W.; Gaudioso, L. A. *J. Org. Chem.* **1979**, *44*, 3113−3117. (c) Ravi, B. N.; Wells, R. J. *Aust. J. Chem.* **1982**, *35*, 105−112. (d) Huneck, S.; Tønsberg, T.; Bohlmann, F. *Phytochemistry* **1986**, *25*, 453−459. (e) Maeda, M.; Kodama, T.; Tanaka, T.; Yoshizumi, H.; Takemoto, T.; Nomoto, K.; Fujita, T. *Tetrahedron Lett.* **1987**, *28*, 633−636. (f) Magri, F. M. M.; Kato, M. J.; Yoshida, M. *Phytochemistry* **1996**, *43*, 669−672. (g) Lopes, N. P.; Silva, D. H. S.; Kato, M. J.; Yoshida, M. *Phytochemistry* **1998**, *49*, 1405−1410.

(6) For other routes to 4-hydroxy-3,5-disubstituted γ-lactones with 3α,4α,5β relative stereochemistry, see, for example: (a) Heathcock, C. H.; Young, S. D.; Hagen, J. P.; Pirrung, M. C.; White, C. T.; VanDerveer, D. *J. Org. Chem.* **1980**, *45*, 3846−3856. (b) Kozikowski, A. P.; Ghosh, A. K. *J. Org. Chem.* **1984**, *49*, 2762−2772. (c) Schlessinger, R. H.; Tata, J. R.; Springer, J. P. *Tetrahedron Lett.* **1987**, *28*, 5423−5426. (d) Mulzer, J.; Schulze, T.; Strecker, A.; Denzer, W. *J. Org. Chem.* **1988**, *53*, 4098−4103. (e) Rotella, D. P.; Li, X. *Heterocycles* **1990**, *31*, 1205−1211. (f) Hanessian, S.; Léger, R.; Alpegiani, M. *Carbohydr. Res.* **1992**, *228*, 145−156. (g) Mukai, C.; Kataoka, O.; Hanaoka, M. *J. Org. Chem.* **1993**, *58*, 2946−2952.

(7) (a) Clive, D. L. J.; Yang, W.; MacDonald, A.; Wang, Z.; Cantin, M. *J. Org. Chem.* **2001**, *66*, 1966−1983 and references cited therein. (b) Sannigrahi, M.; Mayhew, D. L.; Clive, D. L. J. *J. Org. Chem.* **1999**, *64*, 2776−2788. (c) Clive, D. L. J.; Yang, W. *J. Chem. Soc., Chem. Commun.* **1996**, 1605−1606. (d) Clive, D. L. J.; Cantin, M. *J. Chem. Soc., Chem. Commun.* **1995**, 319−320.

(8) Cainelli, G.; Panunzio, M.; Bandini, E.; Martelli, G.; Spunta, G. *Tetrahedron* **1996**, *52*, 1685−1698.

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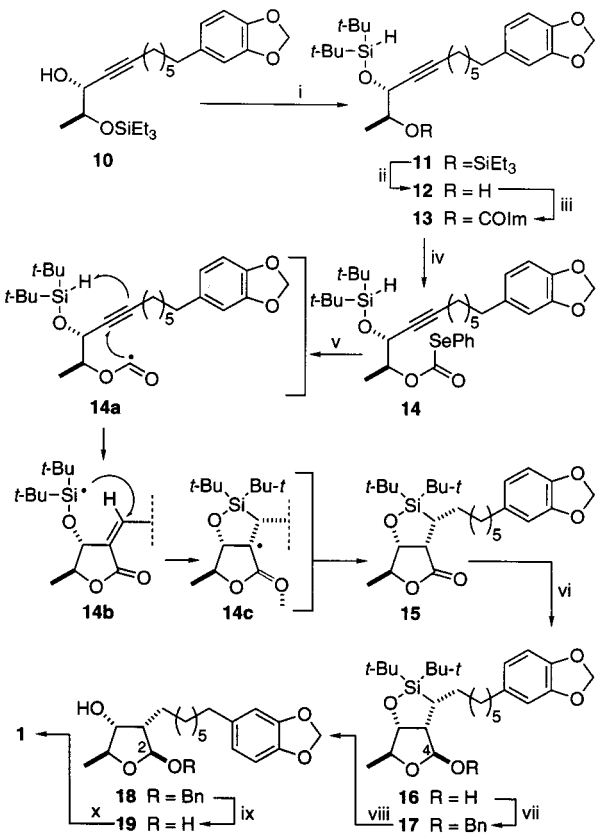
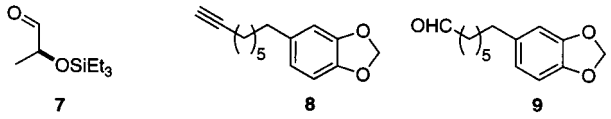
Scheme 2

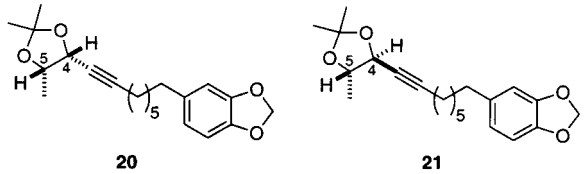


[a] Key: (i) *t*-Bu_2SiHCl, imidazole, CH_2Cl_2, 18 h, 82%; (ii) CF_3CO_2H, THF−water, 2 h, 87%; (iii) Im_2CO, $ClCH_2CH_2Cl$, 4 h; (iv) PhSeH, $ClCH_2CH_2Cl$, reflux, 12 h, 74% from **12**; (v) Ph_3SnH, AIBN, addition over 7 h, PhH, reflux, 79%; (vi) DIBAL-H, PhMe, −78 °C, 15 min, ca. 100%; (vii) BnOH, CH_2Cl_2, $TsOH·H_2O$, 10 min, 98% from **15**; (viii) Bu_4NF, THF−DMF, 60 °C, 4 h, 71%; (ix) Pd/C, MeOH, H_2 (balloon), 15 min; (x) Fétizon's reagent, PhH, reflux, 4 h, 53% from **17**.

°C, 95%)[9] from the known aldehyde **9**,[10,11] which was itself easily prepared by standard methods.[10]



Treatment of acetylene **8** with BuLi and reaction with aldehyde **7** gave (59%) the acetylenic alcohol **10** (Scheme 2) as the major (ca 2.5:1) product, whose stereochemistry was assigned by analogy with related[12] acetylide additions. The assignment was confirmed by desilylation and conversion of the resulting diol into the ketal **20**. The minor alcohol (**10′**, not shown in Scheme 2) from the acetylide addition was likewise converted into ketal **21**. ^1H NMR analysis of both ketals showed that $J_{4,5}$ for **20** was 5.5 Hz, and the corresponding value for **21** was 8.1 Hz. Published coupling constants for suitable model compounds[13,14] show that $J_{4,5}$ is typically ca. 5−6 Hz for cis substitution (cf. **20**) and ca. 7−8 Hz for trans substitution (cf. **21**) on the dioxolane ring. Later in the synthesis (see below), the stereochemistry was again confirmed by TROESY NMR measurements on compound **17**.



Silylation of **10** with *t*-Bu_2SiHCl then afforded **11** in 82% yield. In the two steps leading to **10** and **11**, some O → O migration of the Et_3Si group was observed. Selective removal of the Et_3Si group (CF_3CO_2H, THF−water, 87%) gave alcohol **12**, which was not susceptible to silyl migration. The free hydroxyl of **12** was acylated with 1,1′-carbonyldiimidazole (Im_2CO), and the resulting carbamate **13** was treated with PhSeH in refluxing $ClCH_2CH_2Cl$. The desired phenylseleno carbonate **14** could then be isolated in 74% overall yield.[15] Attempts to convert **12** into the corresponding chloroformate, for subsequent reaction with PhSeNa, gave erratic results, but the route via **13** is reliable. Slow addition of a benzene solution of Ph_3SnH and AIBN to a refluxing solution of phenylseleno carbonate **14** in the same solvent served to generate the expected acyl radical (**14** → **14a**) and initiate the desired cascade of transformations (**14a** → **14b** → **14c**), ultimately affording lactone **15** (79%).

At this point, we experienced some difficulty in cleaving the carbon−silicon bond of **15**, but soon found that conversion of the lactone into a lactol ether allowed smooth desilylation. Reduction of lactone **15** (DIBAL-H) and conversion of the resulting lactol **16**[16] into the corresponding benzyl ether (BnOH, $TsOH·H_2O$, 98% overall) gave material (**17**) that underwent the desired C−Si cleavage (**17** → **18**) when treated with Bu_4NF in warm THF−DMF (ca. 71%). Benzyl ether **17** was a single isomer, and the indicated stereochemistry was confirmed by TROESY measurements. Hydrogenolysis of crude **18** released the lactol functional group (**18** → **19**[17]), and oxidation with Fétizon's reagent gave (+)-juruenolide C (**1**). We had initially converted **16** into the derived *O*-methyl ethers [epimeric at C(4)] but were unable to regenerate the lactols efficiently after C−Si cleavage;[18] use of a benzyl ether solved this problem.

Our synthetic **1** had ^1H and ^{13}C NMR spectra that were identical, within experimental error, with the published data, but the optical rotation differed from the reported value. We found $[\alpha]_{546}$ +26 (*c* 0.3, MeOH) [lit.[1a] $[\alpha]^{25}_{546}$

(9) Grandjean, D.; Pale, P.; Chuche, J. *Tetrahedron Lett.* **1994**, *35*, 3529−3530. Cf. Clive, D. L. J.; He, X.; Postema, M. H. D.; Mashimbye, M. J. *J. Org. Chem.* **1999**, *64*, 4397−4410.

(10) Rotherham, L. W.; Semple, J. E. *J. Org. Chem.* **1998**, *63*, 6667−6672.

(11) Aldehyde **9** was made by PCC oxidation (92−95%) of the corresponding alcohol; the procedure of ref 10 calls for Swern oxidation (95%).

(12) Cf. Hirama, M.; Shigemoto, T.; Itô, S. *J. Org. Chem.* **1987**, *52*, 3342−3346.

(13) Models for trans ketal: Mukai, C.; Kim, J. S.; Sonobe, H.; Hanaoka, M. *J. Org. Chem.* **1999**, *64*, 6822−6832. Compounds **5a**−**c** of this publication were used as the models.

(14) Model for cis ketal: Yadav, J. S.; Chander, M. C.; Reddy, K. K. *Tetrahedron Lett.* **1992**, *33*, 135−138. Compound **10** of this publication was used as the model.

(15) Cf. Tian, F.; Montchamp, J.-L.; Frost, J. W. *J. Org. Chem.* **1996**, *61*, 7373−7381.

(16) Compound **16** is a single lactol, but the indicated C(4) stereochemistry is an arbitrary assignment.

(17) We did not establish if the material was a single isomer or a mixture of two; the indicated C(2) stereochemistry is arbitrary.

(18) We tried the following conditions: $TsOH·H_2O$−THF−water, room temperature; CF_3CO_2H−THF−water, 0 °C or at room temperature; AcOH−THF−water, room temperature.

+3.7 (MeOH)]. The optical purity of our synthetic juruenolide C rests on the optical purity of alcohol **10**; that compound was found to have an ee of >98% (see Supporting Information). The magnitude of the optical rotation previously reported for **1** is, however, a tentative value,[1a] as insufficient material was available for a reliable measurement. If the dextrorotatory nature of the compound is accepted, our synthesis confirms the assigned absolute configuration.

Experimental Section

General Procedures. Unless stated to the contrary, the general procedures used previously[19] were followed. The symbols s′, d′, t′, and q′ used for ^{13}C NMR signals indicate zero, one, two, or three attached hydrogens, respectively. The expression "apparent triplet" indicates nonbinomial relative intensity of the signals.

5-(7-Octynyl)-1,3-benzodioxole (8). (a) 5-(8,8-Dibromo-7-octenyl)-1,3-benzodioxole. A solution of CBr_4 (4.63 g, 13.96 mmol) in CH_2Cl_2 (25 mL) was added dropwise to a stirred and cooled (−20 °C) solution of Ph_3P (3.66 g, 14.0 mmol) in CH_2Cl_2 (25 mL). Stirring was continued for 15 min at −20 °C, and the reaction flask was then transferred to a cold bath at −78 °C. A solution of aldehyde **9** (1.50 g, 6.35 mmol) and Et_3N (0.87 mL, 6.35 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 10 min at −78 °C. The cold bath was removed, and stirring was continued for 2 h. The mixture was filtered through a pad (2 × 3 cm) of flash chromatography silica gel, using Et_2O as a rinse. Evaporation of the combined filtrates and flash chromatography of residue over silica, using 5% EtOAc−hexane, gave 5-(8,8-dibromo-7-heptenyl)-1,3-benzodioxole (2.28 g, 92%) as a yellowish oil: FTIR ($CHCl_3$ cast) 3010, 1502 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 1.28−1.40 (m, 8 H), 1.58 (m, 2 H), 2.09 (q, J = 7.0 Hz, 2 H), 2.51 (t, J = 7.0 Hz, 2 H), 5.92 (s, 2 H), 6.41 (t, J = 7.0 Hz, 1 H), 6.60−6.78 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 27.7 (t′), 28.8 (t′), 28.9 (t′), 31.6 (t′), 33.0 (t′), 35.6 (t′), 88.6 (s′), 100.7 (t′), 108.1 (d′), 108.9 (d′), 121.1 (d′), 136.6 (s′), 138.9 (d′), 145.5 (s′), 147.5 (s′); exact mass m/z calcd for $C_{15}H_{18}{}^{79}Br^{81}BrO_2$ 389.95530, found 389.96536.

(b) 5-(7-Octynyl)-1,3-benzodioxole (8). *n*-BuLi (2.5 M in hexanes, 3.70 mL, 9.25 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of the above dibromoalkene (1.445 g, 3.7 mmol) in dry THF (35 mL). Stirring at −78 °C was continued for 1 h, the cold bath was removed, and stirring was continued for 2 h. Saturated aqueous NH_4Cl (5 mL) and Et_2O (20 mL) were added, and the organic layer was washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using 25% PhMe-hexane, gave **8** (0.809 g, 95%) as a colorless oil: FTIR ($CHCl_3$ cast) 3297, 2116 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) 1.28−1.64 (m, 8 H), 1.95 (t, J = 2.5 Hz, 1 H), 2.19 (td, J = 7.0, 2.5 Hz, 2 H), 2.53 (apparent t, J = 7.0 Hz, 2 H), 5.92 (s, 2 H), 6.60−6.78 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.4 (t′), 28.4 (t′), 28.6 (t′), 28.6 (t′), 31.6 (t′), 35.6 (t′), 68.2 (d′), 84.7 (s′), 100.7 (t′), 108.0 (d′), 108.8 (d′), 121.0 (d′), 136.6 (s′), 145.4 (s′), 147.5 (s′); exact mass m/z calcd for $C_{15}H_{18}O_2$ 230.13068, found 230.13067.

(2*S*,3*R*)-11-(1,3-Benzodioxol-5-yl)-2-[(triethylsilyl)oxy]-4-undecyn-3-ol (10). *n*-BuLi (2.5 M in hexanes, 0.40 mL, 1.0 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of acetylene **8** (0.220 g, 0.95 mmol) in dry THF (5 mL). The mixture was stirred at −78 °C for 30 min, and then a solution of aldehyde **7** (0.180 g, 0.95 mmol) in dry THF (1.5 mL) was added dropwise over 5 min. Stirring at −78 °C was continued for 3 h, and then saturated aqueous NH_4Cl (1 mL) and Et_2O (10 mL) were added. The aqueous layer was extracted with Et_2O, and the combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2 × 15 cm), using 10% EtOAc−hexane, gave alcohol **10** (0.236 g, 59%) as a colorless oil. The other isomer that was formed was not obtained pure, and was discarded. Compound **10** had: $[\alpha]_D$ −21.26 (*c* 1.35, $CHCl_3$); FTIR ($CHCl_3$ cast) 3571, 2933 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) 0.62 (q, J = 7.9 Hz, 6 H), 0.97 (t, J = 7.9 Hz, 9 H), 1.23 (d, J = 6.2 Hz, 3 H), 1.25−1.61 (m, 8 H), 2.21 (td, J = 6.9, 2.5 Hz, 2 H), 2.38 (d, J = 4.7 Hz, 1 H), 2.53 (apparent t, J = 7.5 Hz, 2 H), 3.90 (dq, J = 6.2, 3.6 Hz, 1 H), 4.27 (m, 1 H), 5.91 (s, 2 H), 6.60−6.78 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 4.9 (t′), 6.8 (q′), 17.8 (q′), 18.7 (t′), 28.5 (t′), 28.6 (t′), 28.7 (t′), 31.6 (t′), 35.6 (t′), 67.1 (d′), 71.0 (d′), 78.0 (s′), 86.8 (s′), 100.7 (t′), 108.0 (d′), 108.4 (d′), 121.0 (d′), 136.6 (s′), 145.4 (s′), 147.5 (s′); exact mass (electrospray) m/z calcd for $C_{24}H_{38}NaO_4Si$ 441.243708, found 441.243724.

In a similar experiment, done on almost the same scale, a portion of the crude product from the acetylide addition was desilylated and the diol mixture was ketalized (see the Supporting Information). The ketals were separated chromatographically, and their ratio, determined by isolation, was 2.5:1.

(5*R*,6*S*)-5-[8-(1,3-Benzodioxol-5-yl)-1-octynyl]-3-(1,1-dimethylethyl)-8,8-diethyl-2,2,6-trimethyl-4,7-dioxa-3,8-disiladecane (11). *t*-Bu_2SiHCl (0.16 mL, 0.79 mmol) was added dropwise to a stirred solution of alcohol **10** (0.261 g, 0.62 mmol) and imidazole (0.110 g, 1.61 mmol) in CH_2Cl_2 (2.5 mL). After 18 h, water (2 mL) and CH_2Cl_2 (10 mL) were added, and the organic layer was separated and washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1 × 15 cm), using 5% EtOAc−hexane, gave **11** (0.287 g, 82%) as a colorless oil: $[\alpha]_D$ −11.97 (*c* 0.81, CH_2Cl_2); FTIR (CH_2Cl_2 cast) 2095 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) 0.62 (q, J = 7.5 Hz, 6 H), 0.97 (t, J = 7.5 Hz, 9 H), 1.02 (s, 9 H), 1.03 (s, 9 H), 1.24 (d, J = 6.0 Hz, 3 H), 1.28−1.62 (m, 8 H), 2.19 (dt, J = 7.0, 1.5 Hz, 2 H), 2.53 (apparent t, J = 7.0 Hz, 2 H), 3.81 (dq, J = 6.0, 4.5 Hz, 1 H), 4.11 (s, 1 H), 4.27 (dt, J = 4.5, 1.5 Hz, 1 H), 5.92 (s, 2 H), 6.60−6.74 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 4.9 (t′), 6.9 (q′), 18.6 (q′), 18.7 (t′), 19.9 (s′), 20.3 (s′), 27.3 (q′), 27.5 (q′), 28.5 (t′), 28.7 (two overlapping t′), 31.6 (t′), 35.6 (t′), 71.6 (d′), 72.5 (d′), 79.9 (s′), 85.8 (s′), 100.7 (t′), 108.0 (d′), 108.8 (d′), 121.0 (d′), 136.7 (s′), 145.4 (s′), 147.5 (s′); exact mass (electrospray) m/z calcd for $C_{32}H_{56}NaO_4Si_2$ 583.361487, found 583.361501.

(2*S*,3*R*)-11-(1,3-Benzodioxol-5-yl)-3-[[bis(1,1-dimethylethyl)silyl]oxy]-4-undecyn-2-ol (12). CF_3CO_2H[20] (75 μL, 0.97 mmol) was added dropwise to a stirred solution of silane **11** (205 mg, 0.37 mmol) in THF (2.4 mL) and water (0.4 mL). After 2 h, saturated aqueous $NaHCO_3$ (1 mL) and Et_2O (5 mL) were added. The layers were separated, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1 × 15 cm), using 15% EtOAc−hexane, gave **12** (142 mg, 87%) as a colorless oil: FTIR (CH_2Cl_2 cast) 2101 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) 1.01 (s, 9 H), 1.03 (s, 9 H), 1.24 (d, J = 6.5 Hz, 3 H), 1.27−1.62 (m, 8 H), 2.21 (dt, J = 7.0, 2.0 Hz, 2 H), 2.29 (d, J = 5.0 Hz, 1 H), 2.52 (apparent t, J = 7.5 Hz, 2 H), 3.81 (m, 1 H), 4.11 (s, 1 H), 4.36 (dt, J = 4.0, 2.0 Hz, 1 H), 5.92 (s, 2 H), 6.60−6.74 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) 17.8 (q′), 18.7 (t′), 19.8 (s′), 21.2 (s′), 27.29 (q′), 27.34 (q′), 28.5 (t′), 28.6 (t′), 28.7 (t′), 31.6 (t′), 35.6 (t′), 70.8 (d′), 71.3 (d′), 77.5 (s′), 87.7 (s′), 100.7 (t′), 108.0 (d′), 108.8 (d′), 121.0 (d′), 136.7 (s′), 145.4 (s′), 147.5 (s′); exact mass (electrospray) m/z calcd for $C_{26}H_{42}NaO_4Si$ 469.275008, found 469.275388.

Imidazole-1-carboxylic Acid (1*S*,2*R*)-*O*-[10-(1,3-Benzodioxol-5-yl)-2-[[bis(1,1-dimethylethyl)silyl]oxy]-1-methyl-3-decynyl] Ester (13) and *Se*-Phenyl (1*S*,2*R*)-*O*-[10-(1,3-Benzodioxol-5-yl)-2-[[bis(1,1-dimethylethyl)silyl]oxy]-1-methyl-3-decynyl]carbonoselenoate (14). The following method for making the selenocarbonate is based on the procedure given in ref 15.

A solution of alcohol **12** (19 mg, 0.0582 mmol) in $ClCH_2CH_2Cl$ (1 mL) was added to a stirred solution of Im_2CO (24 mg, 0.1480 mmol) in $ClCH_2CH_2Cl$ (1 mL). After 4 h, PhSeH

(19) Clive, D. L. J.; Wickens, P. L.; Sgarbi, P. W. M. *J. Org. Chem.* **1996**, *61*, 7426−7437.

(20) Cf. Jones, T. K.; Reamer, R. A.; Desmond, R.; Mills, S. G. *J. Am. Chem. Soc.* **1990**, *112*, 2998−3017.

(46 mg, 0.286 mmol) in $ClCH_2CH_2Cl$ (1 mL) was added to the resulting imidazole-1-carboxylic acid (1*S*,2*R*)-*O*-[10-(1,3-benzodioxol-5-yl)-2-[[bis(1,1-dimethylethyl)silyl]oxy]-1-methyl-3-decynyl] ester (**13**), and the solution was refluxed overnight. The mixture was cooled to room temperature, and water and CH_2Cl_2 were added. The organic layer was separated, washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (0.5 × 15 cm), using 15% EtOAc−hexane, gave **14** (26 mg, 74%) as a colorless oil: FTIR ($CDCl_3$ cast) 1726 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) 1.02 (s, 18 H), 1.40 (d, J = 6.5 Hz, 3 H), 1.27−1.60 (m, 8 H), 2.19 (dt, J = 7.0, 2.0 Hz, 2 H), 2.52 (apparent t, J = 7.5 Hz, 2 H), 4.10 (s, 1 H), 4.63 (m, 1 H), 5.08 (dq, J = 6.5, 2.0 Hz, 1 H), 5.92 (s, 2 H), 6.60−6.74 (m, 3 H), 7.32−7.40 (m, 3 H), 7.58−7.63 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) 14.2 (q′), 18.6 (t′), 20.0 (s′), 20.3 (s′), 27.3 (q′), 27.5 (q′), 28.4 (t′), 28.7 (two overlapping t′), 31.7 (t′), 35.7 (t′), 68.1 (d′), 76.2 (s′), 78.0 (d′), 87.3 (s′), 100.7 (t′), 108.1 (d′), 108.9 (d′), 121.1 (d′), 126.3 (s′), 129.0 (d′), 129.3 (d′), 135.8 (d′), 136.7 (s′), 145.5 (s′), 147.5 (s′), 166.5 (s′); exact mass (electrospray) m/z calcd for $C_{33}H_{46}NaO_4{}^{80}SeSi$ 653.217744, found 653.217657.

The intermediate (1*S*,2*R*)-*O*-[10-(1,3-benzodioxol-5-yl)-2-[[bis(1,1-dimethylethyl)silyl]oxy]-1-methyl-3-decynyl] ester (**13**) had: ^1H NMR ($CDCl_3$, 360 MHz) δ 1.02 (s, 18 H), 1.47 (d, J = 6.9 Hz, 3 H), 1.25−1.40 (m, 8 H), 2.19 (dt, J = 7.0, 2.0 Hz, 2 H), 2.53 (t, J = 7.5 Hz, 2 H), 4.10 (s, 1 H), 4.70−4.73 (m, 1 H), 5.12−5.20 (m, 1 H), 5.92 (s, 2 H), 6.60−6.73 (m, 3 H), 7.08 (br s, 1 H), 7.43 (br s, 1 H), 8.17 (br s, 1 H).

(3*R*,3a*S*,6*S*,6a*R*)-3-[6-(1,3-Benzodioxol-5-yl)hexyl]-2,2-bis(1,1-dimethylethyl)tetrahydro-6-methylfuro[3,4-*d*]-1,2-oxasilol-4(2*H*)-one (15). A solution of Ph_3SnH (15 mg, 0.040 mmol) and AIBN (1 mg, 0.006 mmol) in PhH (2.5 mL) was added over 7 h by a syringe pump to a stirred and refluxing solution of phenylseleno carbonate **14** (20 mg, 0.033 mmol) in PhH. Refluxing was continued for 1 h after the end of addition, and the mixture was then cooled to room temperature. Evaporation of the solvent and flash chromatography of the residue over silica gel (0.5 × 15 cm), using 20% EtOAc−hexane, gave **15** (13 mg, 79%) as a colorless oil: $[\alpha]_D$ 10.88 (*c* 2.7, CH_2Cl_2); FTIR ($CDCl_3$ cast) 1768 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) 1.02 (s, 18 H), 1.30−1.80 (m, 10 H), 2.31 (m, 1 H), 2.53 (t, J = 7.5 Hz, 2 H), 3.19 (dd, J = 10.0, 5.3 Hz, 1 H), 4.26 (d, J = 5.3 Hz, 1 H), 4.62 (q, J = 6.9 Hz, 1 H), 5.92 (s, 2 H), 6.60−6.73 (m, 3 H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) 18.9 (q′), 20.5 (s′), 21.4 (s′), 25.1 (t′), 25.3 (d′), 27.6 (q′), 27.8 (q′), 29.1 (t′), 29.4 (t′), 31.6 (t′), 31.7 (t′), 35.7 (t′), 43.8 (d′), 81.9 (d′), 82.6 (d′), 100.6 (t′), 108.0 (d′), 108.8 (d′), 121.0 (d′), 136.8 (s′), 145.4 (s′), 147.4 (s′), 175.8 (s′); exact mass (electrospray) m/z calcd for $C_{27}H_{42}NaO_5Si$ 497.269923, found 497.270380.

(3*R*,3a*S*,6*S*,6a*R*)-3-[6-(1,3-Benzodioxol-5-yl)hexyl]-2,2-bis(1,1-dimethylethyl)hexahydro-6-methylfuro[3,4-*d*]-1,2-oxasilol-4-ol (16) and (3*R*,3a*S*,4*S*,6*S*,6a*R*)-3-[6-(1,3-Benzodioxol-5-yl)hexyl]-2,2-bis(1,1-dimethylethyl)-hexahydro-6-methyl-4-(phenylmethoxy)furo[3,4-*d*]-1,2-oxasilole (17). DIBAL-H (1 M in PhMe, 26 μL, 0.026 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of lactone **15** (12 mg, 0.025 mmol) in PhMe (1 mL). After 15 min, the reaction was complete (TLC control, silica, 30% EtOAc−hexane), and MeOH (0.1 mL) was added, followed by water (0.1 mL) and Celite (0.2 g). The cooling bath was removed, and stirring was continued for 15 min. The mixture was filtered through a pad (2 × 1 cm) of Celite, using EtOAc as a rinse. Evaporation of the filtrate gave the sensitive lactol **16**[16] (12 mg, 100%), which was used immediately in the next step. Attempted flash chromatography over silica gel caused decomposition.

BnOH (10 mg, 9.2 mmol) in CH_2Cl_2 (0.5 mL) was added to a stirred solution of the above lactol (12 mg, 0.025 mmol) in CH_2Cl_2 (1 mL), followed by a crystal of $TsOH\cdot H_2O$. After 10 min, saturated aqueous $NaHCO_3$ (1 mL) and CH_2Cl_2 (5 mL) were added, and the organic layer was separated, washed with brine, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (0.5 × 15 cm), using 10% EtOAc−hexane, gave **17** (14 mg, 98%) as a colorless oil: FTIR ($CDCl_3$ cast) 1768 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) 1.01 (s, 9 H), 1.02 (s, 9 H), 1.20−1.40 (m, 7 H), 1.50−1.60 (m, 7 H), 2.98 (t, J = 7.5 Hz, 2 H), 2.98 (m, 1 H), 4.20 (d, J = 5.5 Hz, 1 H), 4.47 (q, J = 7.0 Hz, 1 H), 4.51 (ABq, J = 11.5 Hz, $\Delta\nu_{AB}$ = 170.5 Hz, 2 H), 5.15 (d, J = 3.9 Hz, 1 H), 5.92 (s, 2 H), 6.60−6.73 (m, 3 H), 7.25−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125.7 MHz) 20.3 (q′), 21.2 (s′), 21.8 (s′), 25.5 (t′), 28.03 (q′), 28.05 (t′), 28.1 (q′), 29.3 (t′), 29.8 (t′), 31.5 (t′), 31.9 (t′), 35.8 (t′), 52.3 (d′), 69.7 (t′), 84.2 (d′), 87.3 (d′), 100.7 (t′), 105.2 (d′), 108.0 (d′), 108.8 (d′), 121.0 (d′), 127.5 (d′), 128.21 (d′), 128.25 (d′), 136.7 (s′), 138.1 (s′), 145.4 (s′), 147.4 (s′); exact mass (electrospray) m/z calcd for $C_{27}H_{44}O_5Si$ 476.29581, found 476.29526. TROESY NMR measurements showed an NOE between C(4)**H** and C(6)**H**, and between C(3a)**H** and C(6a)**H**.

(2*S*,3*R*,4*S*,5*S*)-4-[7-(1,3-Benzodioxol-5-yl)heptyl]-2-methyl-5-(phenylmethoxy)tetrahydrofuran-3-ol (18), (3*S*,4*R*,5*S*)-3-[7-(1,3-Benzodioxol-5-yl)heptyl]tetrahydro-5-methylfuran-2,4-diol (19), and (3*S*,4*R*,5*S*)-3-[7-(1,3-Benzodioxol-5-yl)heptyl]dihydro-4-hydroxy-5-methyl-2(3*H*)-furanone (1). Bu_4NF (1.0 M solution in THF, 50 μL, 0.05 mmol) was added to a stirred, hot (60 °C) solution of (3*R*,3a*S*,4*S*,6*S*,-6a*R*)-3-[6-(1,3-benzodioxol-5-yl)hexyl]-2,2-bis(1,1-dimethylethyl)hexahydro-6-methyl-4-(phenylmethoxy)furo[3,4-*d*]-1,2-oxasilole (**17**) (7.0 mg, 0.0123 mmol) in DMF (2 mL). Stirring was continued for 4 h, and the mixture allowed to cool to room temperature. Water (1 mL) and Et_2O (5 mL) were added, and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with water and brine, dried ($MgSO_4$), and evaporated to afford crude alcohol **18** (3.7 mg, 71%).

Pd/C (10%, 3 mg) was added to a solution of crude alcohol **18** in MeOH (2 mL) and the mixture was stirred under H_2 (balloon) for 15 min. The mixture was filtered through a pad (1 × 2 cm) of Celite, which was washed with MeOH (5 mL). The filtrate was evaporated, and the resulting crude product (unstable to acid) was dissolved in PhH (2.5 mL). Fétizon reagent[21] (20 mg, ca. 0.035 mmol) was added, and the mixture was refluxed for 4 h, cooled, and filtered through a sintered disk. Evaporation of the filtrate and flash chromatography of the residue over silica gel (0.5 × 15 cm), using 30% EtOAc−hexane, gave **1** (2.2 mg, 53% over the last three steps) as a colorless oil, whose ^1H NMR and ^{13}C NMR were identical, within experimental error, to the published[1a] data, the correspondence being particularly clear in the case of the ^{13}C spectrum: ^1H NMR ($CDCl_3$, 360 MHz) δ 1.20−1.83 [m, including d at δ 1.74 (J = 4.5 Hz), 10 H in all], 1.34 (d J = 6.8 Hz, 3 H), 2.52 (t, J = 7.8 Hz, 2 H), 2.60 (dt, J = 9.6, 5.5 Hz, 1 H), 4.19 (br t, J = 4.7 Hz, 1 H), 4.51 (dq, J = 6.76, 1.0 Hz, 1 H), 5.92 (s, 2 H), 6.61 (d, J = 7.9, 1.7 Hz, 1 H), 6.67 (d, J = 1.6 Hz, 1 H), 6.72 (d, J = 7.9 Hz, 1 H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ (values in brackets are the reported[1a] values obtained at 50 MHz in $CDCl_3$) 18.17 (q′) (18.1); 23.36 (t′) (23.3); 27.69 (t′) (27.6); 29.05 (t′) (29.0); 29.27 (t′) (29.2); 29.50 (t′) (29.4); 31.69 (t′) (31.7); 35.68 (t′) (35.6); 43.78 (d′) (43.7); 73.99 (d′) (73.9); 82.36 (d′) (82.4); 100.74 (t′) (100.6); 108.09 (d′) (108.2); 108.90 (d′) (108.8); 121.09 (d′) (121.0); 136.74 (s′) (136.7); 145.47 (s′) (145.4); 147.51 (s′) (147.4); 177.08 (s′) (177.2). The synthetic material had: $[\alpha]^{25}_{546}$ +26 (*c* 0.3, MeOH), $[\alpha]^{25}_{D}$ +16.6 (*c* 0.22, MeOH) [lit.[1a] $[\alpha]^{25}_{546}$ 3.7 (MeOH)].

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Supporting Information Available: NMR spectra of new compounds and experimental procedures for the determination of the relative stereochemistry and optical purity of **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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