Evaluation of Furan Photooxygenation as a Device for Construction of the Zaragozic Acid (Squalestatin) Core

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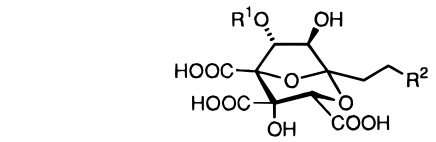
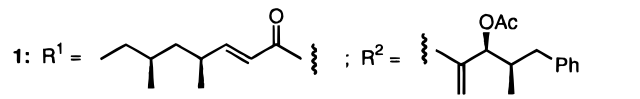
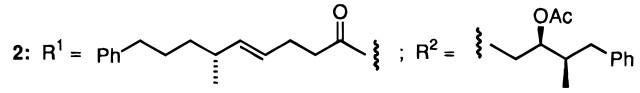
A practical application of the photooxygenation chemistry of 3-substituted furans to construction of the zaragozic acid/squalestatin backbone is described. Although addition of 3-lithiofuran to the tartrate-derived aldehyde **7** proceeds without chelation control to give a 1:1 mixture of diastereomeric alcohols **8**, it is demonstrated initially that ready conversion to the polyfunctional intermediate **10** is possible by sequential treatment of **9** with singlet oxygen, sodium borohydride, and triisopropylsilyl triflate. The actual enantiocontrolled route consisted of oxidation of **8** to the ketone and Wittig olefination of the latter in advance of asymmetric dihydroxylation with AD-mix-β. Once this series of transformations had been accomplished, formation of the target product **30** was realized by an entirely comparable photooxygenation.

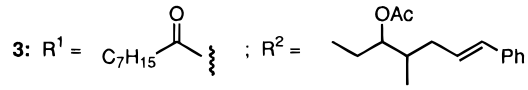
The treatment of hypercholesterolemia, initiated more than two decades ago,[1] initially focused on inhibiting HMG CoA reductase, an enzyme broadly involved in endogenous steroid biosynthesis.[2] More recently, chiefly as a consequence of the isolation from fungi of the zaragozic acids[3] and the squalestatins,[4] attention has turned instead to squalene synthase. This enzyme catalyzes the head-to-head coupling of farnesyl pyrophosphate to squalene[5] and serves as the specific control point for cholesterol biosynthesis.[6] This therapeutic application, as well as reputed anticancer[7] and antifungal properties,[4a] have prompted considerable synthetic interest in these highly oxygenated 2,8-dioxabicyclo[3.2.1]-octanes. Successful routes to **1**[8] and **2**[9,10] have been reported, and model studies abound.[11]

Despite these remarkable successes, shorter routes to these targets would prove highly desirable.[12] To this end, the process of furan photooxygenation[13,14] has now been examined in developmental form as a means for economizing on the requisite number of steps needed to arrive at **1**−**3**. Scheme 1 illustrates the retro-synthetic analysis in its most simplified form. Thus, the extensively func-









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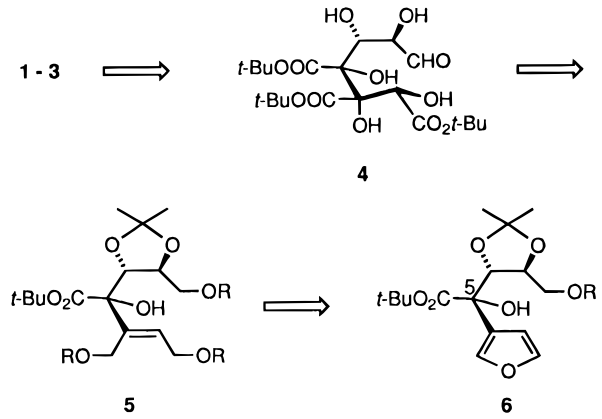
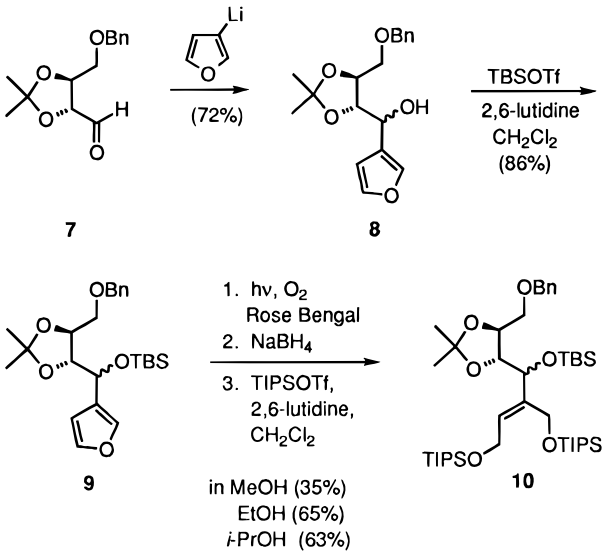
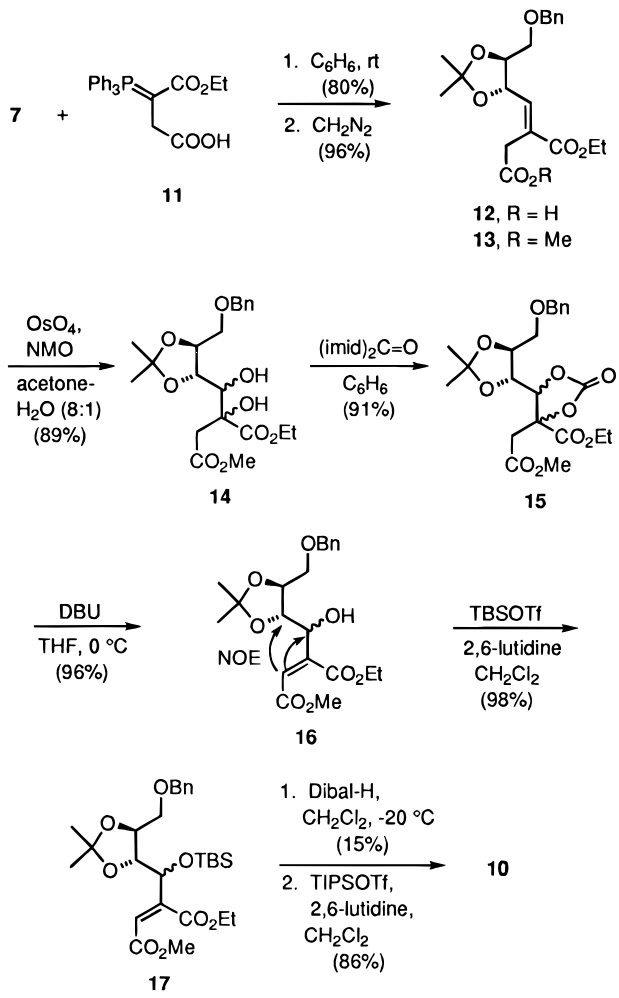
Scheme 1



Scheme 2



Scheme 3



tionalized intermediate **4** can potentially be reached by combined oxidation of the three−CH_2OR groups, vicinal dihydroxylation of the double bond, and acetal hydrolysis. Rapid access to **5** was viewed to be possible by singlet oxygenation/reduction of **6**, itself anticipated to be available by coupling of 3-lithiofuran to a suitable tartrate-derived electrophilic partner. In this way, the entire lower half of **4** would arise conveniently from the furan building block introduced in this manner. A prerequisite would be the ability to set the stereocenter properly at C-5 (zaragozic acid numbering), a process already recognized to be controllable by means of the hydroxyl protecting groups (see below).

Results and Discussion

In order to establish concept feasibility, the preliminary study outlined in Scheme 2 was carried out first. Condensation of the known aldehyde **7**[15] with 3-lithiofuran[16] gave alcohol **8** as a 1:1 diastereomeric mixture. Following silylation of the hydroxyl functionality, **9** was photooxygenated in ethanol containing rose bengal as the sensitizer. The reaction temperature was maintained below −55 °C in order to preserve the integrity of the resulting endoperoxide. Direct reduction with sodium borohydride[14] and capping of the resulting diol with triisopropylsilyl groups afforded **10** in 59% overall yield. Comparable yields were obtained in ethanol or isopropyl alcohol, while the use of methanol led to a considerable reduction in overall yield.

In order to establish that arrival at **10** was notably expedient and to confirm the structural assignment, the alternate route shown in Scheme 3 was developed. Wittig reagent **11**, readily available from maleic anhydride, triphenylphosphine, and ethanol,[17] is now recognized to afford 2-alkylidenesuccinic acid monoethyl esters stereoselectively, with the R group of the original aldehyde positioned uniquely cis to the acetic acid substituent in the product.[18] In the present example, the formation of **12** proved to be equally dependable (80%). Following esterification, the dihydroxylation of **13** proceeded smoothly to give diol **14** as a 1:1 mixture of diastereomers. This intermediate was then converted into cyclic carbonate **15** with carbonyldiimidazole.[19] As hoped for, the carbonate was readily cleaved with DBU even at 0 °C to give the desired allylic alcohol **16** exclusively (96%). NOE studies revealed convincingly that olefin geometry had been properly set. When attempts to effect the dihydroxylation of **16** with osmium tetraoxide proved to

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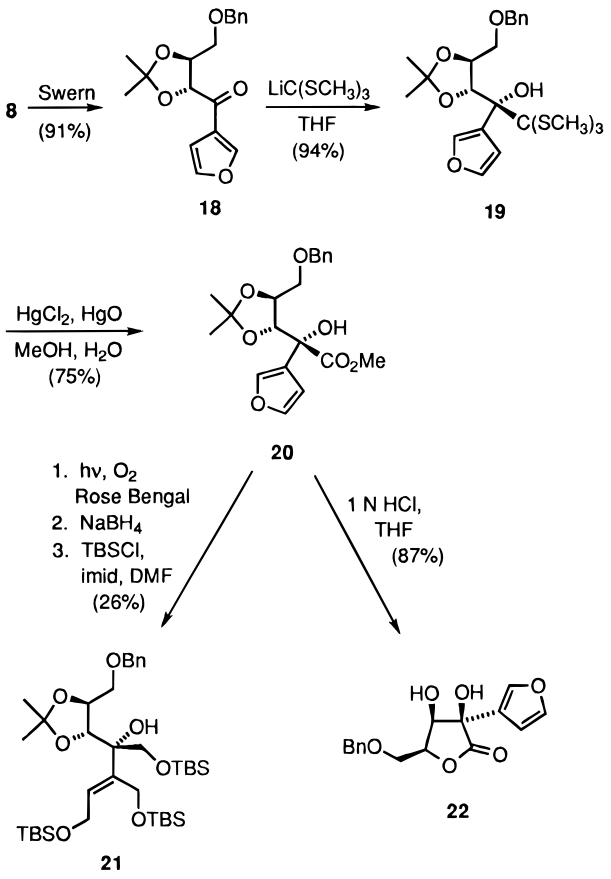
Scheme 4



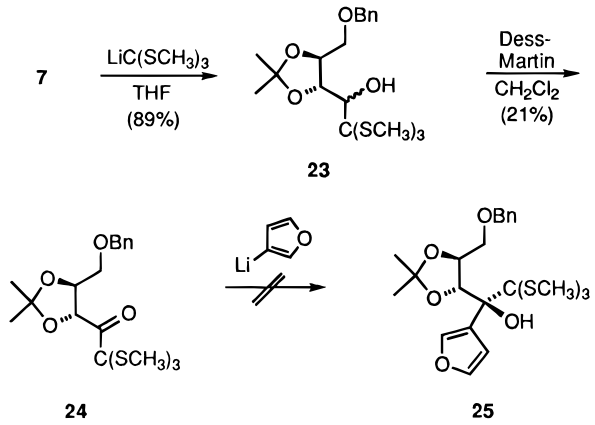
be highly inefficient, recourse was made to protection of the free hydroxyl as the *tert*-butyldimethylsilyl ether. However, this ploy did not remedy matters, and reductive chemistry was undertaken in order to facilitate the necessary production of a diol at this site.

The conversion of **16** to **10** proved to be far more problematical than expected because of the overwhelming tendency of derivatives of **16** to undergo S_N2' attack during ester reduction with elimination of the allylic oxygen functionality. In the end, the TBS ether **17** was treated with diisobutylaluminum hydride at −78 °C → −20 °C, and the unpurified diol so produced was directly silylated. The resulting product (13%) proved to be identical with **10** in all respects.

Consequently, these early studies provided several key pieces of information: (a) a 3-substituted furan can be introduced without risking loss of configuration; (b) photooxygenation of the furan ring can be accomplished without interference from other nearby oxygenated substituents; and (c) sodium borohydride reduction of the endoperoxide can be achieved without reductive elimination of the oxygen center residing at C-5. Armed with this information, we embarked on proper incorporation of the carboxylic acid unit resident at C-5.

To this end, **8** was oxidized to **18** under Swern conditions (91%) or with the Dess−Martin periodinane[20] in 85% yield (Scheme 4). Treatment of **18** with lithiated tris(methylthio)methane[21] resulted in cleanly diastereoselective 1,2-addition to the carbonyl group. This single product was transformed into the oily methyl ester **20**

Scheme 5



by hydrolysis with mercuric chloride and mercuric oxide in aqueous methanol.[22] Hydrolysis of **20** with 1 N hydrochloric acid in THF provided the highly crystalline lactone **22**, X-ray crystallographic analysis of which established that the improper configuration had been set at C-5 (Figure 1, supporting information).[23] This finding proves that nucleophilic attack on **18** follows the Felkin−Ahn model and takes place *without* chelation control. It is noteworthy that an identical preference for the Felkin−Ahn model has been reported for aldehyde **7** in its reaction with a range of nucleophiles.[15] In contrast, the attack of Grignard reagents on the less conformationally rigid di-MOM-protected congener of **7** occurs with chelation control, giving rise to products with the opposite configuration.[24]

In addition to this required modification in the synthetic protocol, we came to recognize that borohydride-promoted cleavage of the endoperoxide from **20** also resulted in reduction of the ester functionality, such that ultimate silylation gave rise to **21** in modest yield.

Two approaches were subsequently investigated for generating intermediates with the proper C-5 configuration. The first of these consisted merely of reversing the sequence of additions (Scheme 5). Although the addition of lithio tris(methylthio)methane to **7** proceeded efficiently, the abundance of sulfur atoms present in **23** introduced complications during the subsequent oxidation to ketone **24**. For example, recourse to the Dess-Martin periodinane provided **24** in only 21% yield. Efforts to optimize this transformation were not implemented when it was made clear that the addition of 3-furyllithium to **24** failed completely to give rise to **25**.

Pursuit of the second alternative pathway shown in Scheme 6 proved to be very rewarding. Methylation of **18** proceeded in excellent yield to furnish alkene **26,** which underwent highly diastereoselective dihydroxylation with AD-mix-β[25] to furnish a 21:1 mixture of diols **27** and **28**. The stereochemical assignment was confirmed through $LiAlH_4$ reduction of **20** to afford diol **28** selectively.

With **27** in hand, it proved an easy matter to silylate its primary hydroxyl group selectively as in **29** (98%).

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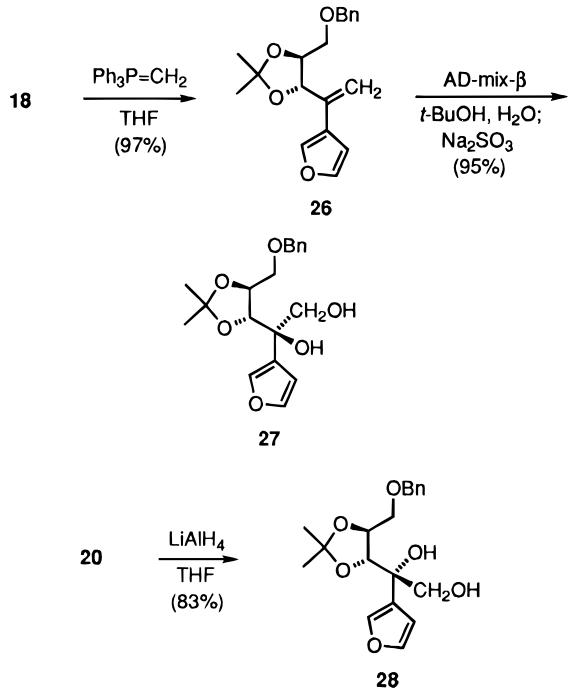
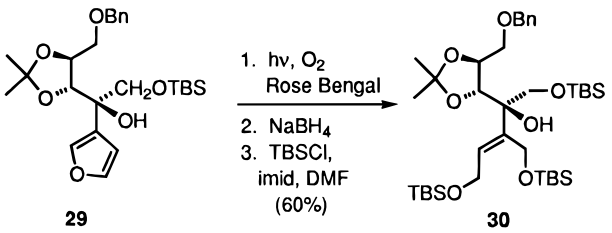
Scheme 6



Scheme 7



Submission of this intermediate to the photooxygenation sequence led to the formation of **30** (Scheme 7), which was easily distinguishable from **21** on the basis of its ^{1}H and ^{13}C NMR spectral features.

In summary, the strategy of applying the photooxygenation of furans to enantiocontrolled construction of the zaragozic acid/squalestatin core has met with success. When advancing from acetonide **7**, seven distinct laboratory steps passing through **8**, **18**, and **26**−**30** are required to complete the sequence. In contemplating the di-MOM equivalent of **7** as the starting material, one less step would be necessary if chelation control were to operate at a useful level. In line with precedent,[7b] **30** is recalcitrant to dihydroxylation of its double bond under a variety of conditions. A change in protect-ing groups is clearly warrranted.

Experimental Section

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at the indicated field strengths. High resolution mass spectra were obtained at The Ohio State University Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. All separations were effected under flash chromatography on Merck silica gel HG_{254}. The organic extracts were dried over anhydrous magnesium sulfate. Solvents were reagent grade and in many cases dried before use.

(4*S*,5*S*)-5-[(Benzyloxy)methyl]-α-3-furyl-2,2-dimethyl-1,3-dioxolane-4-methanol (8). *n*-Butyllithium (30.0 mL of 1.6 M in hexanes, 48.0 mmol) was added during 20 min to a cold (−78 °C), magnetically stirred solution of 3-bromofuran (7.05 g, 48.0 mmol) in dry THF (120 mL) under N_2. After 10 min, a solution of **7** (8.00 g, 32.0 mmol) in dry THF (12 mL) was introduced, and stirring was maintained for 1.5 h at this temperature. Following quenching with saturated NH_4Cl solution (30 mL), the separated aqueous layer was extracted with ethyl acetate (2 × 50 mL), and the combined organic phases were washed with water (30 mL) and brine (30 mL), dried, and evaporated. Chromatography of the residue on silica gel (elution with 20% ethyl acetate in hexanes) gave **8** (7.23 g, 72%) as a pale yellow oil: IR (film, cm^{-1}) 3440, 1500, 1450; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (br s, 1 H), 7.40−7.20 (m, 6 H), 6.38 (d, J = 1.8 Hz, 0.5 H), 6.37 (d, J = 1.4 Hz, 0.5 H), 4.81 (d, J = 5.4 Hz, 0.5 H), 4.60−4.40 (m, 2.5 H), 4.15 (dt, J = 8.0, 4.8 Hz, 1 H), 4.00 (dd, J = 7.9, 5.4 Hz, 1 H), 3.43 (d, J = 4.8 Hz, 2 H), 2.16 (br s, 1 H), 1.43 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 143.1, 139.7, 137.5, 128.4, 127.8, 127.7, 127.6, 113.9, 109.4, 108.7, 81.0, 76.9, 73.5, 70.6, 67.0, 27.1, 26.9; MS m/z (M^+) calcd 318.1468, obsd 318.1463.

[[(4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-3-furylmethoxy]-*tert*-butyldimethylsilane (9). A solution of **8** (860 mg, 2.70 mmol) and 2,6-lutidine (0.31 mL, 2.7 mmol) in dry CH_2Cl_2 (10 mL) was treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.47 mL, 2.7 mmol) at rt under N_2. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with saturated $NaHCO_3$ solution (20 mL), water (20 mL), and brine (20 mL), and then dried. Following solvent evaporation, the residue was chromatographed on silica gel (elution with 10% ethyl acetate in hexanes) to deliver **9** as a colorless oil (1.00 g, 86%): IR (film, cm^{-1}) 1490, 1475; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.20 (m, 7 H), 6.36 (t, J = 1.3 Hz, 0.5 H), 6.30 (t, J = 1.2 Hz, 0.5 H), 4.87 (d, J = 5.0 Hz, 0.5 H), 4.77 (d, J = 5.4 Hz, 0.5 H), 4.59 (d, J = 12.5 Hz, 0.5 H), 4.55 (d, J = 12.3 Hz, 0.5 H), 4.49 (d, J = 12.3 Hz, 0.5 H), 4.49 (d, J = 12.5 Hz, 0.5 H), 4.28 (ddd, J = 10.3, 6.7, 2.4 Hz, 0.5 H), 4.00 (ddd, J = 10.3, 6.6, 2.6 Hz, 0.5 H), 3.88 (dd, J = 10.3, 5.0 Hz, 0.5 H), 3.85 (dd, J = 10.3, 5.4 Hz, 0.5 H), 3.50 (dd, J = 10.4, 2.6 Hz, 0.5 H), 3.48 (dd, J = 10.4, 2.4 Hz, 0.5 H), 3.40 (dd, J = 10.4, 6.6 Hz, 0.5 H), 3.33 (dd, J = 10.4, 6.7 Hz, 0.5 H), 1.42 (s, 3 H), 1.41 (s, 3 H), 0.86 (s, 4.5 H), 0.84 (s, 4.5 H), 0.06 (s, 1.5 H), 0.03 (s, 1.5 H), −0.04 (s, 1.5 H), −0.07 (s, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 143.0, 142.6, 139.8, 139.6, 138.1, 128.3, 127.8, 127.6, 127.5, 126.5, 125.1, 109.8, 109.5, 108.9, 80.7, 80.1, 77.6, 76.8, 73.4, 73.3, 71.7, 71.1, 68.4, 27.3, 27.1, 26.9, 25.8, 25.7, 18.1, −4.8, −5.0, −5.1; MS m/z (M^+) calcd 432.2326, obsd 432.2332.

[(*E*)-2-[[(4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl](*tert*-butyldimethylsiloxy)methyl]-2-butenylene]bis(triisopropylsilane) (10). Into a dry ice/acetone-cooled solution of **9** (150 mg, 0.35 mmol) and rose bengal (10 mg, 9.8 μmol) in ethanol (10 mL) was bubbled oxygen with concomitant irradiation from a 600 W tungsten lamp. After 20 min, the reaction mixture was poured onto sodium borohydride (52 mg, 1.4 mmol) in ethanol (2 mL) precooled to the same temperature, with subsequent warming to 0 °C during 1.5 h. The solvent was evaporated under reduced pressure, and the unstable diol was rapidly filtered through silica gel (elution with 30% ethyl acetate in hexanes), concentrated (94 mg), and immediately dissolved in CH_2Cl_2 (5 mL) containing 2,6-lutidine (0.053 mL, 0.46 mmol). Triisopropylsilyl trifluoromethanesulfonate (0.12 mL, 0.46 mmol) was added at rt, and the solution was stirred for 30 min prior to dilution with CH_2Cl_2 (5 mL), washed with saturated $NaHCO_3$ solution (5 mL), water (5 mL), and brine (5 mL), dried, and concentated. Chromatography of the residue on silica gel (elution with 5% ethyl acetate in hexanes) gave **10** as a colorless oil (157 mg, 59%); IR (film, cm^{-1}) 1465; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60−7.30 (m, 5 H), 5.74 (d, J = 5.5 Hz, 0.5 H), 5.68 (d, J = 5.5 Hz, 0.5 H), 4.57 (d, J = 12.5 Hz, 0.5 H), 4.50 (s, 1 H), 4.47 (d, J = 12.5 Hz, 0.5 H), 4.50−4.00 (m, 6 H), 3.87 (dd, J = 8.0, 4.8 Hz, 0.5 H), 3.82 (dd, J = 8.1, 5.0 Hz, 0.5 H), 3.60 (dd, J = 10.4, 2.1 Hz, 0.5 H), 3.56 (dd, J = 10.4, 2.7 Hz, 0.5 H) 3.43 (dd, J = 10.4, 7.1 Hz, 0.5 H), 3.38 (dd, J = 10.4, 6.5 Hz, 0.5 H), 1.37 (s, 3 H), 1.33 (s, 3 H), 1.15−0.90 (m, 42 H), 0.84 (s, 4.5 H), 0.82 (s, 4.5 H), 0.02 (s, 1.5 H), −0.02 (s, 1.5 H), −0.03 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.5,

138.3, 137.4, 130.8, 129.0, 128.2, 127.7, 127.6, 127.4, 109.1, 108.8, 80.0, 79.0, 77.2, 76.7, 73.7 73.4, 73.3, 72.7, 72.0, 71.4, 60.1, 59.8, 27.2, 27.0, 26.0, 25.8, 18.2, 18.0, 12.0, 11.9, −4.6, −4.7, −4.8, −5.0; MS *m*/*z* (M^+) calcd 764.5263, obsd 764.5263. Anal. Calcd for $C_{42}H_{80}O_6Si_3$: C, 65.91; H, 10.54. Found: C, 65.82; H, 10.51.

1-Ethyl Hydrogen [(*E*)-[(4*S*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]methylene]succinate (12). A solution of **7** (4.53 g, 18.1 mmol) in dry benzene (120 mL) was treated with **11** (7.367 g, 18.1 mmol) and stirred under N_2 at 25 °C for 24 h. The solvent was evaporated, and the residue was chromatographed on silica gel (elution with 30 → 50% ethyl acetate in hexanes) to give **12** (5.45 g, 80%) as a yellowish oil: IR (film, cm^{-1}) 1714, 1663, 1497; ^1H NMR (300 MHz, $CDCl_3$) δ 10.16 (m, 1 H), 7.31 (m, 5 H), 6.89 (d, J = 8.0 Hz, 1 H), 4.69 (t, J = 8.0 Hz, 1 H), 4.58 (d, J = 12.0 Hz, 1 H), 4.52 (d, J = 12.0 Hz, 1 H), 4.22 (q, J = 7.2 Hz, 1 H), 4.21 (q, J = 7.2 Hz, 1 H), 4.00 (dt, J = 8.0, 4.1 Hz, 1 H), 3.65 (dd, J = 10.8, 4.1 Hz, 1 H), 3.59 (dd, J = 10.8, 4.1 Hz, 1 H), 3.52 (d, J = 17.2 Hz, 1H), 3.43 (d, J = 17.2 Hz, 1 H), 1.44 (s, 6 H), 1.28 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 176.3, 166.1, 140.0, 137.7, 128.7, 128.3, 127.7, 110.3, 79.7, 74.4, 73.6, 68.4, 61.3, 32.7, 26.8. 26.7, 14.0; MS *m*/*z* (M^+) calcd 378.1678, obsd 378.1671; $[\alpha]^{24}_D$ −34.7 (*c* 0.80, $CHCl_3$).

1-Ethyl Methyl [(*E*)-[(4*S*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]methylene]succinate (13). To a mixture of **12** (3.18 g, 8.40 mmol) and triethylamine (3.51 mL, 25.2 mmol) in 1,1-dimethoxyethane (60 mL) was added *N*-methyl-*N*-nitrosourea (2.60 g, 25.2 mmol) with stirring at 0 °C. After 2 days at rt, the solution was diluted with ethyl acetate (60 mL), washed twice with saturated $NaHCO_3$ solution (25 mL), water (25 mL), and brine (25 mL), and then dried and concentrated. Purification of the residue on silica gel (elution with 20% ethyl acetate in hexanes) gave **13** as a colorless oil (3.16 g, 96%): IR (film, cm^{-1}) 1742, 1715, 1664, 1497; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H), 6.84 (d, J = 8.2 Hz, 1 H), 4.68 (t, J = 8.2 Hz, 1 H), 4.59 (d, J = 12.0 Hz, 1 H), 4.53 (d, J = 12.0 Hz, 1 H), 4.22 (q, J = 7.1 Hz, 1 H), 4.21 (q, J = 7.1 Hz, 1 H), 4.00 (dt, J = 8.2, 4.1 Hz, 1 H), 3.66 (dd, J = 10.9, 3.6 Hz, 1 H), 3.62 (s, 3 H), 3.59 (dd, J = 10.9, 4.5 Hz, 1 H), 3.48 (d, J = 16.8 Hz, 1 H), 3.38 (d, J = 16.8 Hz, 1 H), 1.45 (s, 6 H), 1.28 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.8, 166.2, 139.7, 137.8, 129.3, 128.3, 127.6, 127.5, 110.2, 79.9, 74.3, 73.6, 68.5, 61.2, 51.9, 32.6, 26.9, 14.1; MS *m*/*z* (M^+) calcd 392.1835, obsd 392.1836; $[\alpha]^{21}_D$ −57.8 (*c* 1.00, $CHCl_3$).

1-Ethyl Methyl 2-[[(4*S*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]hydroxymethyl]maleate (14). A solution of **13** (3.18 g, 8.05 mmol) and *N*-methylmorpholine *N*-oxide (1.42 g, 25.2 mmol) in acetone−water (8:1, 150 mL) was treated with osmium tetraoxide (20 mg, 0.08 mmol) and stirred for 1 week at rt. The reaction mixture was cooled to 0 °C, quenched with saturated $NaHSO_3$ solution (40 mL), and freed of acetone under reduced pressure. The product was extracted into ethyl acetate (3 × 120 mL), dried, and concentrated. Purification of the product by chromatography on silica gel (elution with 30% ethyl acetate in hexanes) afforded **14** as a colorless, oily mixture of diastereomers (3.05 g, 89%). This mixture was used without further purification.

Separation was achieved by a second chromatography as above (elution with 20% ethyl acetate in hexanes).

For the less polar isomer: IR (film, cm^{-1}) 3505, 1797, 1743, 1688, 1475; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H), 4.57 (s, 2 H), 4.25 (q, J = 7.1 Hz, 2 H), 4.20 (dt, J = 8.6, 4.6 Hz, 1 H), 4.17 (dd, J = 10.5, 8.6 Hz, 1 H), 3.67 (s, 3 H), 3.64 (dd, J = 10.4, 4.9 Hz, 1 H), 3.56 (dd, J = 10.4, 4.3 Hz, 1 H), 3.55 (d, J = 10.5 Hz, 1 H), 3.29 (d, J = 16.5 Hz, 1 H), 2.72 (d, J = 16.5 Hz, 1 H), 1.38 (s, 3 H), 1.37 (s, 3 H), 1.31 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.1, 171.1, 137.8, 128.3, 127.5, 109.9, 76.3, 75.8, 75.2, 73.3, 72.8, 69.9, 62.5, 51.7, 41.4, 27.1, 26.7, 13.9; MS *m*/*z* (M^+) calcd 426.1890, obsd 426.1883; $[\alpha]^{23}_D$ −10.7 (*c* 0.80, $CHCl_3$).

For the more polar isomer: IR (film, cm^{-1}) 3485, 1798, 1714, 1493; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 5 H), 4.61 (d, J = 12.2 Hz, 1 H), 4.55 (d, J = 12.2 Hz, 1 H), 4.28 (q, J = 7.1 Hz, 2 H), 4.40−4.15 (m, 1 H), 4.01 (t, J = 8.0 Hz, 1 H), 3.75 (d, J = 8.0 Hz, 1 H), 3.71 (dd, J = 9.7, 3.2 Hz, 1 H), 3.68 (s, 3 H), 3.58 (dd, J = 9.7, 5.8 Hz, 1 H), 3.09 (d, J = 16.5 Hz, 1 H), 2.91 (d, J = 16.5 Hz, 1 H), 1.39 (s, 6 H), 1.31 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 173.3, 171.1, 137.2, 128.2, 127.7, 127.6, 109.7, 78.6, 77.5, 76.9, 75.9, 73.4, 70.5, 62.0, 51.6, 39.3, 26.8, 26.6, 13.8; MS *m*/*z* (M^+) calcd 426.1890, obsd 426.1894; $[\alpha]^{23}_D$ −2.0 (*c* 0.69, $CHCl_3$).

1-Ethyl Methyl 2-[[(4*S*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]hydroxymethyl]maleate, Cyclic Carbonate (15). A solution of **14** (1.84 g, 4.31 mmol) in dry benzene (20 mL) was treated at 0 °C under N_2 with *N*,*N*′-carbonyldiimidazole (840 mg, 5.18 mmol), and stirring was continued for 5 h at rt. The reaction mixture was washed with water (10 mL), dried, and concentrated. Chromatography of the residue on silica gel (elution with 15% ethyl acetate in hexanes) provided 1.78 g (91%) of **15** as a colorless, oily 1:1 mixture of diastereomers: IR (film, cm^{-1}) 1827, 1746, 1687, 1496; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33 (m, 5 H), 4.84 (s, 0.5 H), 4.62 (d, J = 6.0 Hz, 0.5 H), 4.59 (d, J = 6.0 Hz, 0.5 H), 4.59 (d, J = 5.8 Hz, 0.5 H), 4.57 (d, J = 6.9 Hz, 0.5 H), 4.57 (d, J = 5.8 Hz, 0.5 H), 4.34 (q, J = 7.1 Hz, 1 H), 4.30 (q, J = 7.1 Hz, 0.5 H), 4.29 (q, J = 7.1 Hz, 0.5 H), 4.40−4.18 (m, 1 H), 4.05 (dd, J = 9.6, 6.9 Hz, 0.5 H), 3.98 (d, J = 8.3 Hz, 0.5 H), 3.77 (dd, J = 9.8, 4.5 Hz, 0.5 H), 3.74 (dd, J = 10.9, 2.9 Hz, 0.5 H), 3.70 (s, 3 H), 3.61 (dd, J = 10.9, 4.8 Hz, 0.5 H), 3.57 (dd, J = 9.8, 6.5 Hz, 0.5 H), 3.44 (d, J = 17.4 Hz, 0.5 H), 3.36 (s, 1 H), 3.08 (d, J = 17.4 Hz, 0.5 H), 1.44 (s, 1.5 H), 1.42 (s, 3 H), 1.38 (s, 1.5 H), 1.33 (t, J = 7.1 Hz, 1.5 H), 1.29 (t, J = 7.1 Hz, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 169.0, 168.7, 168.5, 168.4, 152.6, 151.6, 137.7, 137.5, 128.4, 127.9, 127.7, 111.4, 111.3, 82.6, 82.2, 81.5, 80.0, 78.5, 77.1, 74.7, 73.7, 73.6, 72.7, 69.5, 69.4, 63.1, 52.3, 52.2, 36.4, 36.3, 27.2, 27.0, 26.8, 25.8, 13.8; MS *m*/*z* (M^+) calcd 452.1682, obsd 452.1684.

Anal. Calcd for $C_{22}H_{28}O_{10}$: C, 58.40; H, 6.24. Found: C, 58.33; H, 6.38.

1-Ethyl Methyl [[(4*S*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]hydroxymethyl]maleate (16). To a solution of **15** (638 mg, 1.41 mmol) in dry THF (20 mL) was added DBU (0.084 mL, 0.56 mmol) with stirring at 0 °C under N_2. After 1 h, the mixture was partitioned between ethyl acetate (20 mL) and saturated NH_4Cl solution (20 mL). The aqueous layer was extracted with ethyl acetate (20 mL), and the combined organic phases were washed with saturated NH_4Cl solution (10 mL), water (10 mL), and brine (10 mL) prior to drying and solvent evaporation. The residue was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to give **16** as a colorless oil (551 mg, 96%): IR (film, cm^{-1}) 3454, 1728, 1654, 1497; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (m, 5 H), 6.28 (d, J = 1.5 Hz, 0.5 H), 6.19 (d, J = 1.6 Hz, 0.5 H), 4.58 (s, 1 H), 4.57 (s, 1 H), 4.60−4.50 (m, 1 H), 4.26 (q, J = 7.1 Hz, 1 H), 4.25 (q, J = 7.1 Hz, 1 H), 4.25−4.10 (m, 1 H), 4.07 (dd, J = 8.2, 2.7 Hz, 0.5 H), 3.94 (dd, J = 7.6, 6.6 Hz, 0.5 H), 3.74 (s, 3 H), 3.68 (dd, J = 10.0, 4.9 Hz, 0.5 H), 3.67 (dd, J = 9.9, 5.0 Hz, 0.5 H), 3.61 (dd, J = 10.0, 5.6 Hz, 0.5 H), 3.56 (dd, J = 9.9, 5.6 Hz, 0.5 H), 1.41 (s, 1.5 H), 1.39 (s, 3 H), 1.38 (s, 1.5 H), 1.28 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 166.6, 165.5, 165.3, 147.8, 146.5, 137.4, 128.4, 127.8, 127.7, 127.6, 122.1, 121.9, 110.0, 109.9, 80.1, 79.4, 77.3, 75.7, 73.7, 72.0, 70.5, 70.1, 69.9, 61.5, 61.4, 51.9, 51.8, 29.3, 26.9, 26.8, 26.7, 13.8; MS *m*/*z* (M^+) calcd 408.1784, obsd 408.1787.

Anal. Calcd for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91. Found: C, 61.47; H, 7.02.

1-Ethyl Methyl [[(4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl](*tert*-butyldimethylsiloxy)-methyl]maleate (17). A solution of **16** (199 mg, 0.49 mmol) and 2,6-lutidine (0.23 mL, 1.95 mmol) in dry CH_2Cl_2 (10 mL) was treated with *tert*-butyldimethylsilyl triflate (0.34 mL, 1.46 mmol), stirred at rt under N_2 for 1.5 h, and washed sequentially with saturated $NaHCO_3$ solution (5 mL), water (5 mL), and brine (5 mL) prior to drying and solvent evaporation. The residue was purified by chromatography on silica gel (elution with 20% ethyl acetate in hexanes), and **17** was obtained as a colorless oil (250 mg, 98%): IR (film, cm^{-1}) 1732; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.20 (m, 5 H), 6.18 (d, J = 1.3 Hz, 0.5 H), 6.17 (d, J = 1.3 Hz, 0.5 H), 4.75 (dd, J = 4.3, 1.3 Hz, 0.5

H), 4.63−4.55 (m, 0.5 H), 4.61 (d, J = 12.4 H, 0.5 H), 4.60 (d, J = 12.2 Hz, 0.5 H), 4.53 (d, J = 12.4 Hz, 0.5 H), 4.51 (d, J = 12.2 Hz, 0.5 H), 4.23 (q, J = 7.1 Hz, 2 H), 4.35−4.05 (m, 1 H), 3.97 (dd, J = 8.2, 4.3 Hz, 0.5 H), 3.88 (dd, J = 7.5, 5.4 Hz, 0.5 H), 3.74 (s, 1.5 H), 3.73 (s, 1.5 H), 3.75−3.60 (m, 0.5 H), 3.66 (dd, J = 10.5, 2.6 Hz, 0.5 H), 3.55 (d, J = 10.3, 6.1 Hz, 0.5 H), 3.47 (dd, J = 10.5, 6.8 Hz, 0.5 H), 1.39 (s, 1.5 H), 1.38 (s, 3 H), 1.37 (s, 1.5 H), 1.29 (t, J = 7.1 Hz, 1.5 H), 1.27 (t, J = 7.1 Hz, 1.5 H), 0.89 (s, 4.5 H), 0.87 (s, 4.5 H), 0.11 (s, 1.5 H), 0.06 (s, 3 H), 0.04 (s, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 166.4, 166.3, 165.5, 165.4, 148.7, 147.3, 138.1, 128.3, 127.6, 127.5, 122.9, 121.9, 109.8, 109.6, 78.7, 78.6, 77.5, 76.2, 73.4, 72.9, 71.7, 71.6, 70.9, 61.5, 61.4, 51.9, 27.1, 27.0, 26.6, 25.8, 25.7, 18.1, 18.0, 13.9, 13.8, −4.8, −4.9, −5.1, −5.2; MS m/z (M^+) calcd 522.2649, obsd 522.2668.

Conversion of 17 to 10. A cold (−78 °C), magnetically stirred solution of **17** (58 mg, 0.11 mmol) in dry toluene (3 mL) was blanketed with N_2 and treated dropwise with diisobutylaluminum hydride (0.55 mL of 1.0 M in hexanes, 0.55 mmol). After 30 min, an additional equivalent quantity of reducing agent was added, and the temperature was raised to −20 °C during 1.5 h. The reaction mixture was quenched with saturated potassium sodium tartrate solution, and the organic phase was dried and concentrated. Rapid filtration of the residue through silica gel (50% ethyl acetate in hexanes as eluent) gave the diol as an unstable colorless oil (8 mg, 15%), which was immediately dissolved in dry CH_2Cl_2 (2 mL), treated sequentially with 2,6-lutidine (0.008 mL, 0.067 mmol) and triisopropylsilyl triflate (0.014 mL, 0.0050 mmol) under N_2 at rt, and stirred for 30 min. The reaction mixture was washed with saturated $NaHCO_3$ solution, dried, and evaporated. The product was purified chromatographically as above (elution with 5% ethyl acetate in hexanes) to give 11 mg (86%) of **10**, identical in all respects to the material described earlier.

(4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl 3-Furyl Ketone (18). A solution of oxalyl chloride (4.7 mL, 54 mmol) in dry CH_2Cl_2 (100 mL) at −78 °C under N_2 was treated dropwise with DMSO (4 mL, 58.5 mmol) and stirred for 10 min. Following the addition of **8** (9.3 g, 29.2 mmol) in CH_2Cl_2 (50 mL) and a 30-min wait, triethylamine (18.76 mL, 135 mmol) was introduced and the reaction mixture was allowed to warm to rt during 1.5 h and diluted with water. The organic phase was washed with brine, dried, and concentrated to leave a residue that was chromatographed on silica gel (elution with 10% ethyl acetate in hexanes) to give **18** as a colorless oil (8.4 g, 91%): IR (film, cm^{-1}) 1666, 1560, 1511; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (br s, 1 H), 7.43 (br s, 1 H), 7.40−7.20 (m, 5 H), 6.84 (br s, 1 H), 4.65 (d, J = 7.2 Hz, 1 H), 4.64 (s, 2 H), 4.45 (ddd, J = 7.2, 5.2, 3.2 Hz, 1 H), 3.82 (dd, J = 10.8, 3.2 Hz, 1 H), 3.68 (dd, J = 10.8, 5.2 Hz, 1 H), 1.53 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 193.0, 149.6, 143.0, 137.4, 127.9, 127.2, 124.4, 110.7, 108.6, 80.5, 76.2, 73.1, 69.6, 26.5, 25.8; MS m/z (M^+) calcd 316.1311, obsd 316.1315; $[\alpha]^{26}_D$ −39.1 (c 1.44, $CHCl_3$).

Trimethyl (α*R*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-α-3-furyl-2,2-dimethyl-trithio-1,3-dioxolane-4-orthoglycolate (19). A cold (−78 °C), magnetically stirred solution of tris(methylthio)methane (0.37 mL, 2.76 mmol) in dry THF (10 mL) was treated with *n*-butyllithium (1.72 mL of 1.6 M in hexanes, 2.76 mmol) under N_2. After 15 min, a solution of **18** (436 mg, 1.38 mmol) in dry THF (2 mL) was introduced, and stirring was maintained at −78 °C for 1 h and at −20 °C for 30 min. The reaction mixture was quenched with saturated NH_4Cl solution (5 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layers were washed with brine (5 mL), dried, and evaporated to leave a residue that was chromatographed on silica gel (elution with 10% ethyl acetate in hexanes) to give 609 mg (94%) of **19** as a colorless oil: IR (film, cm^{-1}) 3450; ^{1}H NMR (300 MHz, C_6D_6) δ 7.66 (dd, J = 1.5, 0.9 Hz, 1 H), 7.35−7.00 (m, 6 H), 6.86 (dd, J = 1.5, 0.4 Hz, 1 H), 5.00 (d, J = 4.9 Hz, 1 H), 4.45 (d, J = 12.3 Hz, 1 H), 4.40 (d, J = 12.3 Hz, 1 H), 4.11 (ddd, J = 8.0, 4.7, 3.5 Hz, 1 H), 3.96 (s, 1 H), 3.82 (dd, J = 10.3, 3.5 Hz, 1 H), 3.72 (dd, J = 10.3, 4.7 Hz, 1 H), 1.93 (s, 9 H), 1.40 (s, 3 H), 1.27 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 142.7, 141.1, 128.5, 127.9, 127.8, 125.4, 113.5, 110.1, 82.0, 80.9, 79.1, 78.5, 73.6, 71.9, 27.1, 27.0, 15.4; MS m/z (M^+) calcd 455.1021, obsd 455.1008; $[\alpha]^{25}_D$ +10.6 (c 1.31, $CHCl_3$).

Methyl (α*R*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-α-3-furyl-2,2-dimethyl-1,3-dioxolane-4-glycolate (20). A mixture of **19** (7.16 g, 16.2 mmol), mercuric oxide (5.61 g, 25.9 mmol), and mercuric chloride (16.7 g, 61.4 mmol) in methanol−water (12:1, 440 mL) was stirred at 60 °C for 2 h. After filtration, the mercury salts were rinsed with CH_2Cl_2 (220 mL), and the combined filtrates were concentrated under reduced pressure. The residue was partitioned between water (200 mL), and CH_2Cl_2 (160 mL), and the aqueous layer was further extracted with CH_2Cl_2 (2 × 160 mL). The combined organic layers were washed with NH_4OAc (3 × 100 mL) and NH_4Cl solutions (2 × 100 mL), dried, and evaporated. Chromatography of the residue on silica gel (elution with 20% ethyl acetate in hexanes) gave 4.55 g (75%) of **20** along with 1.21 g (23%) of ketone **18**.

For **20**: colorless oil; IR (film, cm^{-1}) 3515, 1780; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (dd, J = 1.7, 0.8 Hz, 1 H), 7.40−7.20 (m, 6 H), 6.48 (dd, J = 1.7, 0.8 Hz, 1 H), 4.53 (s, 2 H), 4.28 (s, 2 H), 3.73 (s, 3 H), 3.43 (dd, J = 10.8, 2.7 Hz, 1 H), 3.36 (dd, J = 10.9, 4.3 Hz, 1 H), 1.41 (s, 3 H), 1.38 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 172.4, 142.9, 140.7, 137.8, 128.3, 127.8, 127.6, 124.0, 110.3, 109.6, 81.8, 76.4, 75.0, 73.4, 70.7, 53.1, 27.2, 26.8; MS m/z (M^+) calcd 376.1522, obsd 376.1506; $[\alpha]^{24}_D$ −17.0 (c 1.22, $CHCl_3$).

(α*S*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-α-[(*tert*-butyldimethylsiloxy)-methyl]-α-[(*E*)-3-(*tert*-butyldimethylsiloxy)-1-[(*tert*-butyldimethylsiloxy)methyl]propenyl]-2,2-dimethyl-1,3-dioxolane-4-methanol (21). A slow stream of O_2 was passed through a solution of **20** (165 mg, 0.44 mmol) and rose bengal (10 mg) in ethanol (10 mL). This solution was cooled to −78 °C, irradiated with a tungsten lamp for 10 min, and poured into a precooled (-78 °C) mixture of sodium borohydride (52 mg, 1.39 mmol) in ethanol (2 mL). The temperature was raised to 0 °C during 1.5 h, at which point the mixture was concentrated to 25% of its volume under reduced pressure and diluted with ethyl acetate (75 mL). The organic phase was washed with brine (2 × 20 mL), dried, and concentrated to leave a residue that was dissolved in dry DMF (2 mL) and treated with *tert*-butyldimethylsilyl chloride (211 mg, 1.4 mmol) and imidazole (191 mg, 2.8 mmol). This mixture was stirred at rt for 2.5 days, diluted with ethyl acetate (75 mL), and washed with brine (2 × 20 mL) prior to drying and concentration under reduced pressure. Flash chromatography of the residue on silica gel (elution with 10% ethyl acetate in hexanes) afforded **21** (80 mg, 26%) as a colorless oil: IR (film, cm^{-1}) 3539; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.24 (m, 5 H), 5.93 (t, J = 5.7 Hz, 1 H), 4.59 (s, 2 H), 4.36 (dd, J = 5.6, 1.9 Hz, 2 H), 4.27 (d, J = 11.6 Hz, 1 H), 4.19 (d, J = 11.6 Hz, 1 H), 4.17 (ddd, J = 5.9, 5.9, 2.6 Hz, 1 H), 4.07 (d, J = 8.3 Hz, 1 H), 3.83 (d, J = 10.1 Hz, 1 H), 3.73 (dd, J = 10.4, 2.6 Hz, 1 H), 3.57 (dd, J = 10.4, 6.2 Hz, 1 H), 3.55 (d, J = 10.1 Hz, 1 H), 3.26 (s, 1 H), 1.37 (s, 6 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.065 (s, 6 H), 0.061 (s, 6 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.3, 136.8, 132.6, 128.2, 127.6, 127.4, 108.7, 78.6, 76.8, 75.8, 73.3, 71.6, 67.2, 60.3, 58.7, 27.1, 26.9, 25.94, 25.85, 18.3, 18.2, −5.15, −5.18, −5.4, −5.46, −5.52; MS m/z molecular ion too elusive to be accurately mass measured.

(3*R*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-4,5-dihydro-3,4-dihydroxy[3,3′-bifuran]-2(3*H*)-one (22). A solution of **20** (825 mg, 2.19 mmol) in THF (20 mL) was treated with 1 N HCl (20 mL), heated at 70 °C for 10 h, cooled, and diluted with saturated $NaHCO_3$ solution (50 mL). The mixture was extracted with ethyl acetate (2 × 50 mL) and the combined organic layers were washed with water (50 mL) and brine (50 mL), dried, and evaporated. Recrystallization of the solid from 30% ethyl acetate in hexanes gave **22** (577 mg, 87%) as colorless needles, mp 100−101 °C; IR (KBr, cm^{-1}) 3500, 3240, 1800; ^{1}H NMR (300 MHz, $CDCl_2$) δ 7.46 (br s, 1 H), 7.42 (br s, 1 H), 7.33 (m, 5 H), 6.46 (br s, 1 H), 4.58 (br s, 2 H), 4.50 (m, 1 H), 4.41 (d, J = 4.4 Hz, 1 H), 4.10−3.75 (m, 2 H), 3.62 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.6, 144.4, 140.9, 137.0, 128.6, 128.1, 127.9, 121.6, 108.5, 78.9, 74.1, 73.9 (2 C), 67.5; MS m/z (M^+) calcd 304.0947, obsd 304.0941; $[\alpha]^{23}_D$ +10.1 (c 1.08, $CHCl_3$).

Anal. Calcd for $C_{16}H_{16}O_6$: C, 63.14; H, 5.30. Found: C, 63.18; H, 5.36.

Trimethyl (4*S*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyltrithio-1,3-dioxolane-4-orthoglycolate (23). To a solution of tris(methylthio)methane (2.0 mL, 15 mmol) in dry THF (50 mL) was added *n*-butyllithium in hexanes (9.4 mL of 1.6 M, 15 mmol) at −78 °C. After 15 min, a solution of **7** (1.88 g, 7.5 mmol) in dry THF (5 mL) was introduced dropwise, and stirring was continued for 1 h at −78 °C. The temperature was raised to −20 °C over 30 min, at which point 30 mL of saturated NH_4Cl solution was added. The separated aqueous phase was extracted with ethyl acetate (2 × 40 mL), and the combined organic layers were dried and evaporated. Flash chromatography of the residue on silica gel (elution with 25% ethyl acetate in hexanes) gave 2.70 g (89%) of **23** as a colorless oil consisting of a 1:1 mixture of diastereomers: IR (film, cm^{-1}) 3464; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.23 (m, 5 H), 4.63 (s, 1 H), 4.57 (s, 1 H), 4.53−4.42 (m, 1 H), 4.25 (t, J = 6.9 Hz, 0.5 H), 4.15 (ddd, J = 5.2, 5.2, 8.5 Hz, 0.5 H), 3.84−3.56 (m, 3 H), 3.26 (d, J = 3.8 Hz, 0.5 H), 3.19 (d, J = 11.0 Hz, 0.5 H), 2.18 (s, 4.5 H), 2.13 (s, 4.5 H), 1.46 (s, 1.5 H), 1.44 (s, 3 H), 1.42 (s, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.3, 137.8, 128.4, 128.3, 128.2, 127.74.127.68, 127.5, 110.3, 109.8, 78.4, 77.8, 77.5, 77.4, 76.6, 74.7, 74.3, 73.6, 73.3, 71.4, 70.1, 27.2, 27.1, 26.8, 26.6, 13.9, 13.5; MS m/z ($M^+ - SCH_3$) calcd 357.1194, obsd 357.1198.

Trimethyl (4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyltrithio-1,3-dioxolane-4-orthoglycolate (24). A solution of **23** (469 mg, 1.16 mmol) in dry CH_2Cl_2 (10 mL) was treated with the Dess−Martin periodinane (591 mg, 1.36 mmol), stirred at rt for 45 min, and diluted with ether (70 mL). The organic phase was washed with saturated $NaHCO_3$/5% $Na_2S_2O_3$ solution (25 mL), water (25 mL), and brine (25 mL), dried, and evaporated. Flash chromatography of the residue on silica gel (elution with 15% ethyl acetate in hexanes) furnished 100 mg (21%) of **24** as a colorless oil: IR (film, cm^{-1}) 1703; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.24 (m, 5 H), 5.25 (d, J = 7.3 Hz, 1 H), 4.65 (d, J = 12.3 Hz, 1 H), 4.54 (d, J = 12.3 Hz, 1 H), 4.42 (ddd, J = 3.4, 6.1 , 7.3 Hz, 1 H), 3.71 (dd, J = 3.4, 10.7 Hz, 1 H), 3.62 (dd, J = 6.1, 10.7 Hz, 1 H), 1.95 (s, 9 H), 1.49 (s, 3 H), 1.48 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 197.7, 137.8, 128.4, 128.1, 127.7, 112.2, 79.5, 79.3, 75.0, 73.4, 69.6, 27.5, 26.2, 13.1; MS m/z ($M^+ - SCH_3$) calcd 355.1038, obsd 355.1039; $[\alpha]^{25}_D$ +10.2 (c 1.5, $CHCl_3$).

(4*S*,5*S*)-4-[(Benzyloxy)methyl]-5-[1-(3-furyl)vinyl]-2,2-dimethyl-1,3-dioxolane (26). A suspension of methyltriphenylphosphonium bromide (1.738 g, 4.87 mmol) in dry THF (10 mL) at 0 °C under N_2 was treated dropwise with *n*-butyllithium (2.76 mL of 1.6 M in hexanes, 4.42 mmol), warmed to rt for 1 h, and recooled to 0 °C during the addition of **18** (700 mg, 2.21 mmol) in THF (5 mL). After 1 h at rt, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The combined organic phases were washed with water and brine prior to drying and concentration. The residue was purified by chromatography on silica gel (elution with 5% ethyl acetate in hexanes) to give 677 mg (97%) of **26** as a colorless oil: IR (film, cm^{-1}) 1453, 1370, 1166; ^1H NMR (200 MHz, C_6D_6) δ 7.69 (t, J = 1.1 Hz, 1 H), 7.26−7.06 (m, 5 H), 7.01 (t, J = 1.8 Hz, 1 H), 6.31 (dd, J = 1.8, 0.8 Hz, 1 H), 5.31 (t, J = 1.2 Hz, 1 H), 5.22 (d, J = 1.4 Hz, 1 H), 4.82 (dd, J = 8.4, 0.8 Hz, 1 H), 4.36, 4.26 (ABq, J = 19.8, 12.2 Hz, 2 H), 4.01 (ddd, J = 6.9, 4.0, 2.9 Hz, 1 H), 3.48 (dd, J = 11.1, 2.9 Hz, 1 H), 3.33 (dd, J = 11.1, 4.0 Hz, 1 H), 1.45 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.7, 139.5, 137.9, 136.5, 128.2, 127.5, 122.9, 113.7, 109.2, 108.8, 80.0, 79.2, 73.4, 69.2, 27.0, 26.8; MS m/z (M^+) calcd 314.1518, obsd 314.1514; $[\alpha]^{23}_D$ −8.3 (c 2.53, EtOAc).

(*R*)-1-[[(4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-1-(3-furyl)-1,2-ethanediol (27). A mixture of AD-mix-β (33.6 g) in *tert*-butyl alcohol (120 mL) and water (120 mL) was stirred at rt until both phases were clear. After the mixture was cooled to 0 °C, **26** (7.545 g, 24 mmol) was added in one portion and the heterogeneous slurry was stirred vigorously at 0 °C for 10 h, quenched by addition of sodium sulfite (36 g), warmed to rt, and stirred for 1 h. The product was extracted into ethyl acetate, and the combined organic layers were dried and concentrated. Chromatography of the residue on silica gel (elution with 33% ethyl acetate in hexanes) gave **27** (7.94 g, 95%) as a colorless oil (β/α = 21:1); ^1H NMR (300 MHz, C_6D_6) δ 7.31 (dd, J = 1.7, 0.8 Hz, 1 H), 7.19−7.01 (m, 5 H), 6.92 (t, J = 1.7 Hz, 1 H), 6.06 (dd, J = 1.7, 0.8 Hz, 1 H), 4.36 (ddd, J = 6.3, 4.0, 2.3 Hz, 1 H), 4.24 (d, J = 12.1 Hz, 1 H), 4.23 (d, J = 8.1 Hz, 1 H), 4.14 (d, J = 12.1 Hz, 1 H), 3.77 (d, J = 11.2 Hz, 1 H), 3.52 (d, J = 11.2 Hz, 1 H), 3.31 (br, 1 H), 3.24 (dd, J = 11.0, 2.0 Hz, 1 H), 2.81 (dd, J = 11.0, 4.0 Hz, 1 H), 2.53 (br, 1 H), 1.38 (s, 3 H), 1.31 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 143.2, 139.5, 137.8, 128.2, 127.5, 127.4, 124.6, 109.7, 107.7, 81.0, 76.3, 73.1, 71.3, 69.9, 69.5, 27.0, 26.8; MS m/z (M^+) calcd 348.1573, obsd 348.1563; $[\alpha]^{23}_D$ −20.0 (c 1.28, EtOAc).

Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.49; H, 6.95. Found: C, 64.95; H, 6.85.

(*S*)-1-[[(4*R*,5*S*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-1-(3-furyl)-1,2-ethanediol (28). A cold (0 °C), magnetically stirred solution of **20** (270 mg, 0.72 mmol) in dry THF (3 mL) was treated with lithium aluminum hydride (56 mg, 1.47 mmol), stirred at 0 °C for 30 min and at rt for 30 min, and diluted with ether (20 mL) prior to being quenched with a few drops of 1 N NaOH solution. After 30 min of stirring, anhydrous $MgSO_4$ was introduced. The mixture was agitated for 1 h, filtered, and freed of solvent to leave a residue that was purified chromatographically (silica gel, elution with 30% ethyl acetate in hexanes). There was isolated 208 mg (83%) of **28** as a colorless oil: IR (film, cm^{-1}) 3410; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.28 (m, 7 H), 6.42 (dd, J = 6.8, 1.6 Hz, 1 H), 4.59 (s, 2 H), 4.29 (s, 1 H), 4.12 (d, J = 8.1 Hz, 1 H), 3.87 (ddd, J = 8.1, 7.6, 4.5 Hz, 1 H), 3.81 (br d, J = 12 Hz, 1 H), 3.71 (dd, J = 9.2, 4.5 Hz, 1 H), 3.66 (d, J = 11.3 Hz, 1 H), 3.56 (dd, J = 9.2, 7.6 Hz, 1 H), 2.42 (br s, 1 H), 1.38 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.6, 140.2, 136.7, 128.6, 128.2, 128.0, 126.1, 109.5, 109.3, 81.3, 75.3, 73.9, 73.1, 70.8, 67.9, 26.8, 26.7; MS m/z (M^+) calcd 348.1573, obsd 348.1559.

(α*R*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-α-[(*tert*-butyldimethylsiloxy)methyl]-α-3-furyl-2,2-dimethyl-1,3-dioxolane-4-methanol (29). A solution of **27** (801 mg, 2.3 mmol), *tert*-butyldimethylsilyl chloride (416 mg, 2.76 mmol), and imidazole (235 mg, 3.45 mmol) in DMF (2 mL) was stirred at rt for 15 h, quenched with water (8 mL), and extracted with ether. The combined organic phases were washed with water and brine, dried, and concentrated to leave a residue that was purified by flash chromatography on silica gel (elution with 10% ethyl acetate in hexanes). There was isolated 1.042 g (98%) of **29** as a colorless oil: IR (film, cm^{-1}) 3453; ^1H NMR (200 MHz, C_6D_6) δ 7.56 (dd, J = 1.7, 0.8 Hz, 1 H), 7.25−7.06 (m, 5 H), 7.00 (t, J = 1.7 Hz, 1 H), 6.43 (dd, J = 1.7, 0.8 Hz, 1 H), 4.60 (d, J = 8.3 Hz, 1 H), 4.38 (ddd, J = 6.0, 3.9, 2.1 Hz, 1 H), 4.30, 4.18 (ABq, J = 22.9, 12.0 Hz, 2 H), 3.80, 3.72 (ABq, J = 15.8, 9.2 Hz, 2 H), 3.35 (dd, J = 10.8, 2.1 Hz, 1 H), 2.88 (dd, J = 10.8, 4.0 Hz, 1 H), 2.79 (s, 1 H), 1.48 (s, 3 H), 1.40 (s, 3 H), 0.90 (s, 9 H), −0.10 (s, 3 H), −0.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 142.4, 139.4, 138.0, 128.1, 127.4, 127.3, 126.0, 109.0, 108.8, 77.5, 75.9, 73.0, 71.6, 70.5, 68.1, 27.0, 26.9, 25.7, 18.1, −5.5, −5.7; MS m/z (M^+) 462.2437, obsd 462.2449; $[\alpha]^{23}_D$ −6.5 (c 0.55, EtOAc).

Anal. Calcd for $C_{25}H_{38}O_6Si$: C, 64.90; H, 8.28. Found: C, 65.09; H, 8.33.

(α*R*,4*R*,5*S*)-5-[(Benzyloxy)methyl]-α-[(*tert*-butyldimethylsiloxy)methyl]-α-[(*E*)-3-(*tert*-butyldimethylsiloxy)-1-[(*tert*-butyldimethylsiloxy)methyl]propenyl]-2,2-dimethyl-1,3-dioxolane-4-methanol (30). A solution of **29** (231 mg, 0.50 mmol) in ethanol (8 mL) containing rose bengal (10 mg) was photo-oxygenated at −78 °C in the predescribed manner for 15 min and poured into a precooled (−78 °C) mixture of sodium borohydride (76 mg, 2 mmol) in ethanol (4 mL). After being warmed to 0 °C during 2 h, the reaction mixture was concentrated and extracted with ethyl acetate. The organic solution was washed with brine, dried, and evaporated to leave an oil that was dissolved in DMF (2 mL) and treated with *tert*-butyldimethylsilyl chloride (301 mg, 2.0 mmol) and imidazole (204 mg, 3.0 mmol). The mixture was stirred at rt for 24 h and processed in the predescribed manner

to give after silica gel chromatography (elution with 5% ethyl acetate in hexanes) **30** as a colorless oil (213 mg, 60%): IR (film, cm^{-1}) 3395; ^1H NMR (300 MHz, C_6D_6) δ 7.47−7.14 (m, 5 H), 6.33 (t, J = 5.8 Hz, 1 H), 4.72−4.67 (m, 1 H), 4.58−4.56 (m, 3 H), 4.53 (d, J = 2.8 Hz, 1 H), 4.52 (d, J = 2.8 Hz, 1 H), 4.47, 4.41 (ABq, J = 17.9, 11.9 Hz, 2 H), 4.06, 3.98 (ABq, J = 23.4, 9.8 Hz, 2 H), 3.88 (dd, J = 10.9, 2.3 Hz, 1 H), 3.70 (dd, J = 9.8, 4.7 Hz, 1 H), 3.24 (s, 1 H), 1.54 (s, 3 H), 1.53 (s, 3 H), 1.04 (s, 9 H), 1.01 (s, 9 H), 1.00 (s, 9 H), 0.17 (s, 6 H), 0.13 (s, 6 H), 0.12 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.2, 137.3, 131.2, 128.1, 127.4, 127.2, 109.0, 79.0, 76.1, 75.3, 73.1, 71.7, 67.0, 59.9, 58.8, 27.2, 26.8, 25.8, 25.7, 25.6, 18.2, 18.0, −5.3, −5.4, −5.6, −5.7; MS m/z molecular ion too elusive to be accurately mass measured; $[\alpha]^{23}_D$ −3.2 (c 0.86, EtOAc).

Anal. Calcd for $C_{37}H_{70}O_6Si_3$: C, 62.49; H, 9.92. Found: C, 62.52; H, 9.70.

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Supporting Information Available: Copies of the high-field ^1H and ^{13}C NMR spectra of those compounds for which elemental analyses are not reported and an ORTEP diagram of **22** (31 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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