Total Synthesis of Brevetoxin A: Part 3: Construction of GHIJ and BCDE Ring Systems

K. C. Nicolaou,* Guo-qiang Shi, Janet L. Gunzner, Peter Gärtner, Paul A. Wallace, Michael A. Ouellette, Shuhao Shi, Mark E. Bunnage, Konstantinos A. Agrios, Chris A. Veale, Chan-Kou Hwang, John Hutchinson, C. V. C. Prasad, William W. Ogilvie, and Zhen Yang[a]

Abstract: Successful syntheses of highly complex intermediates **2** (GHIJ ring system) and **3** (BCDE ring system) for the total synthesis of brevetoxin A (**1**) are described. Several of our methodologies were utilized to achieve this goal: i) hydroxy epoxide cyclizations of intermediates **22** and **30** (rings I and H, respectively); ii) hydroxy dithioketal cyclization of **45** (ring G); and, iii) palladium-catalyzed coupling with bis(cyclic ketene acetal phosphate) **68** (rings B and D). With the knowledge gained from our previous model studies, **2** and **3** were expected to be pivotal intermediates on the synthetic route to brevetoxin A.

Keywords: brevetoxin A · synthetic methods · total synthesis

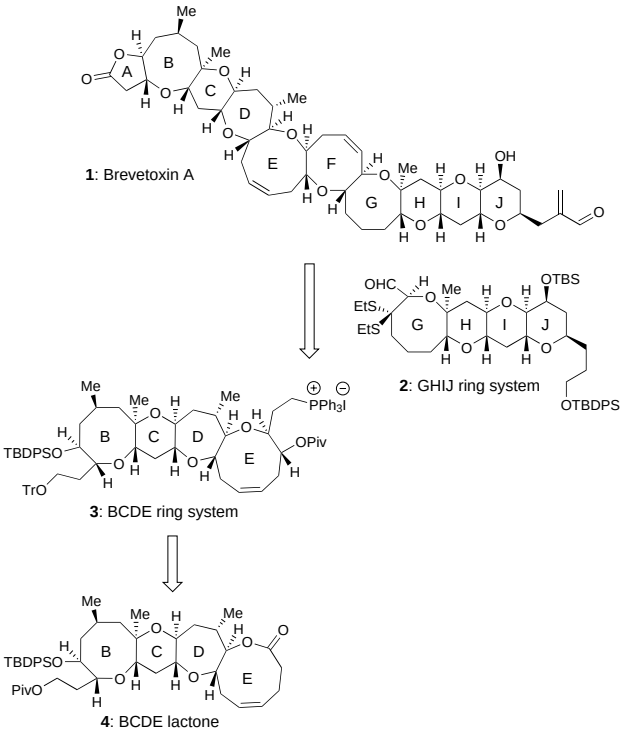
Introduction

In the preceding paper[1] we described chemistry which provided support for our projected total synthesis of brevetoxin A (**1**), and that this could be achieved by way of intermediates **2** (GHIJ ring system) and **3** (BCDE ring system) (Scheme 1). In this article, we present the construction of key intermediates **2** and **4** (a precursor of **3**) in enantiomerically and diastereomerically pure form from readily available starting materials on multigram scale.

Results and Discussion

Synthesis of GHIJ ring system 2

The synthesis of the GHIJ ring system **2** proceeded along similar lines to those already described by us for the HIJ ring system[2] of brevetoxin B, and for the FGHIJ ring system[3] of brevetoxin A (**1**). However, the new sequence includes sufficient modifications and improvements to warrant a full discussion herein.



Scheme 1. Structures of brevetoxin A (**1**) and intermediates **2**, **3**, and **4**.

[*] Prof. Dr. K. C. Nicolaou, Dr. G.-Q. Shi, J. L. Gunzner, Dr. P. Gärtner, Dr. P. A. Wallace, M. A. Ouellette, Dr. S. Shi, Dr. M. E. Bunnage, Dr. K. A. Agrios, Dr. C. A. Veale, Dr. C.-K. Hwang, Dr. J. Hutchinson, Dr. C. V. C. Prasad, Dr. W. W. Ogilvie, Dr. Z. Yang
Department of Chemistry and The Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, CA 92037 (USA)
Fax: (+1) 619-784-2469
E-mail: kcn@scripps.edu
and
Department of Chemistry and Biochemistry
University of California, San Diego
9500 Gilman Drive, La Jolla, CA 92093 (USA)

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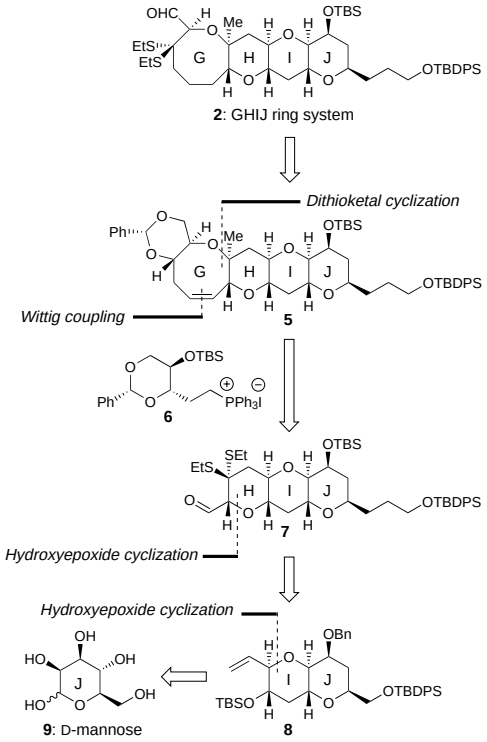
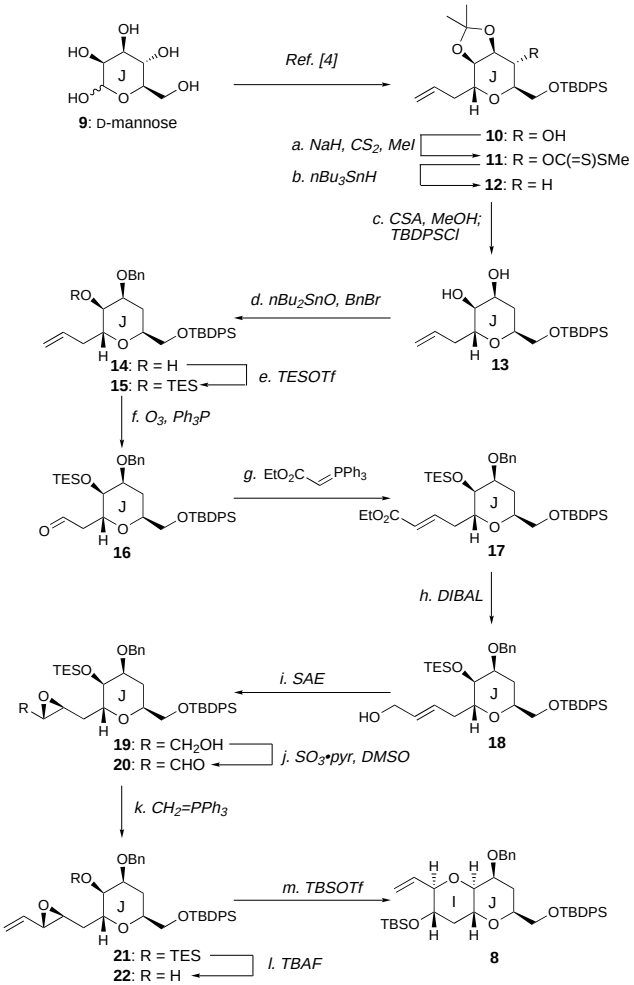
Scheme 2 outlines the retrosynthetic analysis that led to the design of the present construction of **2**. Thus, functional group manipulations allowed the generation of **5** as a possible precursor to **2**. The eight-membered ring (ring G) of **5** was dismantled by sequential retro hydroxydithioketal cyclization, and a Wittig coupling, unraveling phosphonium salt **6** and dithioketal aldehyde **7** as viable precursors. Sequential hydroxyepoxide ring closures then traced intermediate **7** to D-mannose (**9**) via bicyclic system **8**.



Scheme 2. Retrosynthetic analysis and strategic bond disconnections for GHIJ ring system **2**.

Construction of the GHIJ ring system **2** proceeded through intermediates **8**, **34**, and **7**, as summarized in Schemes 3–6. Thus D-mannose (**9**) was converted to bicyclic key intermediate **8** as shown in Scheme 3. The transformation of **9** to **10** has



Scheme 3. Construction of IJ ring system **8**. Reagents and conditions: a) 2.0 equiv of NaH, 0.1 equiv of imidazole, THF, 0 °C, 0.5 h; 3.0 equiv of CS_2, 3.0 equiv of MeI, 0 → 25 °C, 4 h, 69 %; b) 4.0 equiv of nBu$_3$SnH, 0.4 equiv of AIBN, benzene, 80 °C, 5 min, 92 %; c) 0.05 equiv of CSA, MeOH, 60 °C, 48 h; 1.0 equiv of TBDPSCl, 2.0 equiv of imidazole, CH_2Cl_2, 0 °C, 1 h, 91 %; d) 1.1 equiv nBu$_2$SnO, MeOH, 60 °C, 1 h, 1.5 equiv of BnBr, 1.5 equiv of nBu$_4$NBr, benzene, 80 °C, 5 h, 81 %; e) 1.2 equiv of TESOTf, 1.3 equiv of 2,6-lutidine, CH_2Cl_2, 0 °C, 4 h, 95 %; f) O_3, CH_2Cl_2, −78 °C, 2 h; then 1.2 equiv of Ph_3P, −78 → 25 °C, 18 h; g) 1.5 equiv of $Ph_3PCH{=}CO_2Me$, benzene, 25 °C, 17 h, 80 % for two steps, h) 2.7 equiv of DIBAL, CH_2Cl_2, −78 °C, 3 h, 100 %; i) 0.3 equiv of (+)-DET, 0.25 equiv of Ti(iOPr)$_4$ 1.5 equiv of tBuOOH, 4 Å, MS CH_2Cl_2, −25 °C, 19 h, 89 %; j) 5.0 equiv of $SO_3 \cdot$ pyr, 5.0 equiv of Et_3N, CH_2Cl_2:DMSO (1:1), 0 °C, 2 h; k) 1.5 equiv of $Ph_3P^+CH_3Br^-$, 1.4 equiv of NaHMDS, THF, 0 → 25 °C, 1 h, 88 % for two steps; l) 1.1 equiv of TBAF, THF, −20 → 0 °C, 1 h; 1.1 equiv of TBDPSCl, 1.5 equiv of imidazole, CH_2Cl_2:DMF (20:1), 0 °C, 3 h, 88 %; m) 0.24 equiv of TBSOTf, CH_2Cl_2, −78 °C, 10 min; then 1.4 equiv of 2,6-lutidine, 1.05 equiv of TBSOTf, −78 → 25 °C, 30 min, 88 %. AIBN = 2,2′-azobisisobutyronitrile; CSA = 10-camphorsulfonic acid, DET = diethyl tartrate, DIBAL = diisobutylaluminum hydride, DMSO = dimethylsulfoxide, MS = molecular sieves, NaHMDS = sodium bis(trimethylsilyl) amide, SAE = Sharpless Asymmetric Epoxidation; TBAF = tetra-*n*-butylammonium fluoride, TBDPS = *tert*-butyldiphenylsilyl, TBS = *tert*-butyldimethylsilyl, TES = triethylsilyl, Tf = trifluoromethane sulfonate, DMF = *N*,*N*-dimethylformamide.

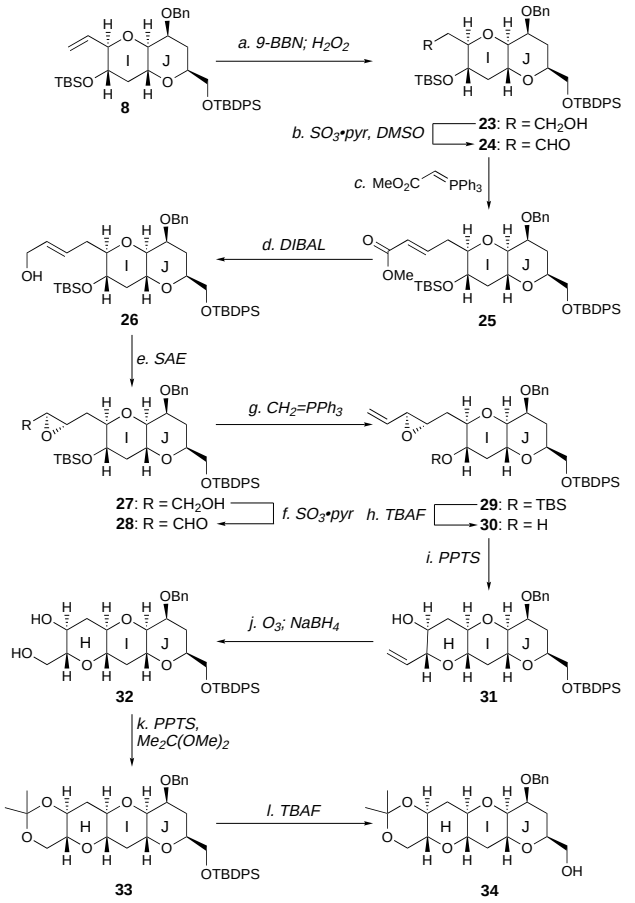
previously been described by us.[4] Compound **10** was then deoxygenated by conversion to xanthate ester **11** (NaH-CS_2; then MeI, 69 % yield), and reduction of the latter compound (nBu$_3$SnH, AIBN, PhH, 80 °C) to afford **12** (92 % yield).[5] The yield for the reduction step was remarkably increased over the

Abstract in Greek:

Σε αυτο το αρθρο περιγραφεται η επιτυχης συνθεση των εξαιρετικα πολυπλοκων πολυκυκλικων ενδιαμεσων **2** (GHIJ) και **3** (BCDE) για την ολικη συνθεση της μπρεβετοξινης A. Μεθοδολογιες που αναπτυχθηκαν στα εργαστηρια μας και χρησιμοποιηθηκαν για την πραγματωση αυτου του στοχου περιλαμβανουν: 1. τις ενδομοριακες κυκλοποιησεις υδροξυ–εποξειδιων που αναγνωριζουμε χαρακτηριστικα στα ενδιαμεσα **22** και **30** (δακτυλιοι I και H αντιστοιχα). 2. την ενδομοριακη υδροξυ–θειοκεταλικη κυκλοποιηση του ενδιαμεσου **45** (δακτυλιος G) και, 3. την, καταλυομενη απο παλαδιο, συζευξη της δι(κυκλικης φωσφωρικης κετενο–ακεταλης) **68** (δακτυλιοι B και D). Η γνωση που αποκομηθηκε απο το περιγραφομενο μοντελο, οδηγησε στην αναγνωριση των ενδιαμεσων **2** και **3** ως πρωταρχικων στοιχειων για την ολικη συνθεση της μπρεβετοξινης A.

standard experimental protocol by adding a benzene solution of **11** and AIBN to a refluxing solution of excess nBu$_3$SnH. The acetonide group was removed from **12** by the action of CSA in methanol at 60 °C, conditions that led to concomitant removal of the silyl group. The triol so obtained was selectively silylated at the primary position with TBDPSCl-imidazole in CH_2Cl_2, furnishing diol **13** in 91 % yield from **12**. Selective monobenzylation of **13** was achieved by using the method of Nashed[6] (nBu$_2$SnO, BnBr, nBu$_4$NBr) to yield **14** in 81 % yield (plus 14 % of the regioisomer of **14** which could be refunneled back into the sequence by i) ozonolysis; ii) hydrogenolysis; iii) reaction with $Ph_3P{=}CHCO_2Me$; iv) monobenzylation; and, v) TES protection, 36 % yield of **17**). Protection of the remaining hydroxyl group in **14** with TESOTf and 2,6-lutidine (95 %), followed by ozonolysis and exposure to Ph_3P, furnished aldehyde **16** via intermediate **15**. Wittig reaction of aldehyde **16** with $Ph_3P{=}CHCO_2Me$ yielded smoothly the *E*-olefin **17** (80 % yield from **15**), together with 10 % of the corresponding *Z*-olefin. The latter compound was recycled by an ozonolysis – olefination sequence to provide an additional 8 % yield of **17**. The ester group in **17** was reduced with DIBAL to afford allylic alcohol **18** (100 %) which was subjected to Sharpless asymmetric epoxidation[7] [(+)-DET, Ti(OiPr)$_4$, tBuOOH] leading to epoxide **19** in 89 % yield (only trace amounts, less than 2 %, of the epimeric epoxide was observed). Oxidation of the hydroxyl group in **19** with $SO_3\cdot$pyridine[8] in the presence of DMSO and Et_3N furnished aldehyde **20**, which reacted with the ylide generated from $Ph_3P^+CH_3Br^-$ and NaHMDS to afford vinyl epoxide **21** in 88 % overall yield from **19**. Removal of the TES group from **21** by exposure to TBAF afforded hydroxy epoxide **22** (88 % after selective mono-reprotection of the primary hydroxyl group in the fully desilylated by-product: TBDPSCl, imidazole, DMF), which set the stage for closure of ring I. The anticipated cyclization and subsequent protection was carried out using a one-pot procedure. This involved initial addition of 0.24 equivalents of TBSOTf, which in situ generated a catalytic amount of TfOH, thereby initiating the ring closure.[9] Subsequently, an excess amount of 2,6-lutidine and an additional 1.05 equivalents of TBSOTf were added to ensure complete silylation, furnishing IJ ring system **8** in 88 % yield.

The transformation of intermediate **8** to the tricyclic system (HIJ) **34** is summarized in Scheme 4. Thus, hydroboration of **8** with 9-BBN, followed by the usual basic H_2O_2 workup gave alcohol **23** (89 % yield), which was oxidized to aldehyde **24** by the action of $SO_3\cdot$pyridine activated by DMSO. Treatment of **24** with $Ph_3P{=}CHCO_2Me$ (86 % yield of **25** from **23**), followed by DIBAL reduction (88 % yield of **26**) and Sharpless asymmetric epoxidation[7] [(+)-DET, Ti(OiPr)$_4$, tBuOOH, 97 % yield, ca. 7:1 ratio of diastereomeric epoxides by ^{1}H NMR] afforded **27**. A second oxidation with $SO_3\cdot$pyridine activated by DMSO afforded aldehyde **28**, which was reacted with $Ph_3P{=}CH_2$ to give vinyl epoxide **29** in 84 % overall yield from **27**. Selective removal of the TBS group was effected with TBAF, leading to hydroxy epoxide **30** (72 %, plus 26 % dihydroxy compound; silylating the dihydroxy material with TBDPSCl-imidazole raised the total yield of **30** to 94 %). At this stage, the unwanted minor epoxide isomer,



Scheme 4. Construction of HIJ ring system **36**. Reagents and conditions: a) 5.5 equiv of 9-BBN, THF, 0 °C, 4 h; 22 equiv of $NaHCO_3$, 15 equiv of 30 % H_2O_2, 0 °C, 4 h, 89 %; b) 5.0 equiv of $SO_3\cdot$pyr, 5.0 equiv of Et_3N, CH_2Cl_2:DMSO (1:1), 0 °C, 2 h; c) 1.5 equiv of $Ph_3PCHCOOMe$, benzene, 25 °C, 11 h, 86 % for two steps; d) 2.9 equiv of DIBAL, CH_2Cl_2, −78 °C, 3 h, 88 %; e) 0.30 equiv of (+)-DET, 0.25 equiv of Ti(iOPr)$_4$, 2.4 equiv of *tert*-BuOOH, 4 Å MS, CH_2Cl_2, −25 °C, 18 h, 97 %; f) 5.0 equiv of $SO_3\cdot$pyr, 5.0 equiv of Et_3N, CH_2Cl_2:DMSO (1:1), 0 °C, 1 h; g) 2.0 equiv of $CH_3P^+Ph_3Br^-$, 1.5 equiv of NaHMDS, THF, 0 °C, 15 min, 84 % for two steps; h) 1.7 equiv of TBAF, THF, 0 °C, 3 h; 1.2 equiv of TBDPSCl, 2.0 equiv of imidazole, CH_2Cl_2, 0 °C, 1 h, 94 %; i) 0.57 equiv of PPTS, 4 Å MS, CH_2Cl_2, 25 °C, 18 h; j) O_3, CH_2Cl_2:MeOH (1:3), −78 °C, 1 h; then 4.1 equiv of $NaBH_4$, −78 → 25 °C, 2 h; k) 15 equiv of 2,2-dimethoxypropane, 0.05 equiv of PPTS, CH_2Cl_2, 25 °C, 28 h; l) 1.4 equiv of TBAF, THF, 25 °C, 3 h, 81 % for four steps. 9-BBN = borabicyclo[3.3.1]nonane, PPTS = pyridinium *p*-toluenesulfonate, pyr = pyridine.

and other impurities were removed by flash column chromatography (silica gel).

Exposure of hydroxy epoxide **30** to PPTS in CH_2Cl_2 resulted in clean ring closure, furnishing tricyclic system **31**, which was subjected to ozonolysis with $NaBH_4$ workup to afford diol **32**. Acetonide formation [$Me_2C(OMe)_2$, PPTS] gave compound **33**, from which the TBDPS group was removed by exposure to TBAF, furnishing primary alcohol **34** in 81 % overall yield from **30**. Two-carbon extension of the side chain on ring J was accomplished by the following sequence (Scheme 5): i) oxidation of **34** with $SO_3\cdot$pyridine and DMSO to aldehyde **35**; ii) olefination of **35** with $Ph_3P{=}CHCO_2Me$ furnishing α,β-unsaturated ester **36** (90 % yield for two steps); iii) selective reduction of the conjugated double bond with Raney Ni(W2) to give ester **37**; iv) LAH

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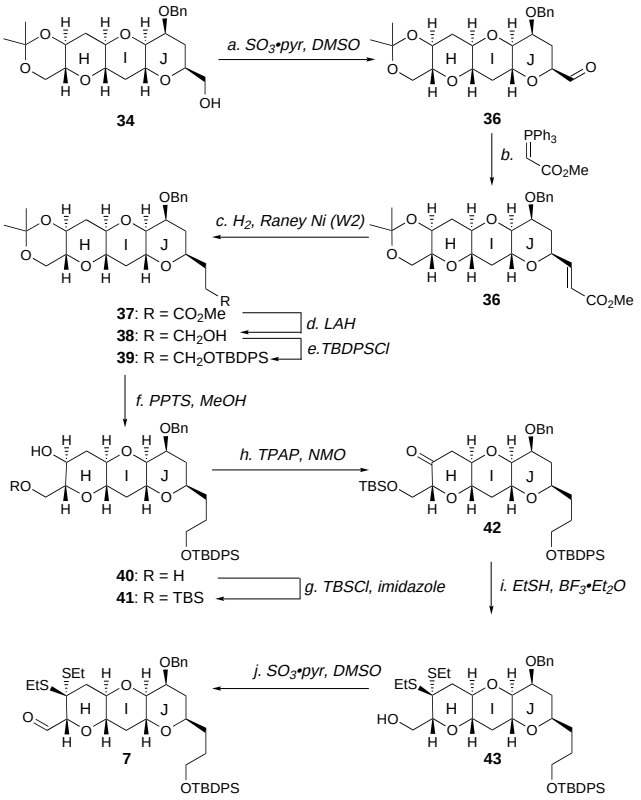
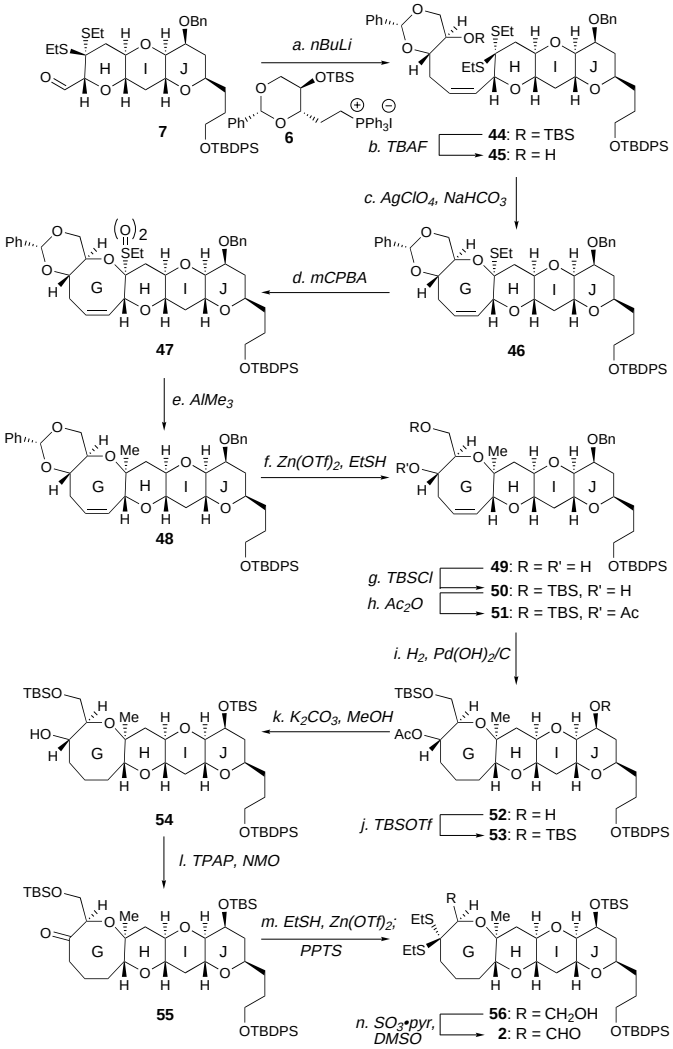


Scheme 5. Construction of HIJ ring system **7**. Reagents and conditions: a) 5.0 equiv of $SO_3 \cdot$ pyr, 5.0 equiv of Et_3N, CH_2Cl_2:DMSO (1:1), 0 °C, 1 h; b) 1.5 equiv of $Ph_3P{=}PCHCO_2Me$, toluene, 25 °C, 5 h, 90 % for three steps; c) H_2, Raney-Ni (W2), EtOAc, 25 °C, 1 h; d) 1.2 equiv of LAH, Et_2O, 0 °C, 1.5 h; e) 1.8 equiv of TBDPSCl, 4.5 equiv of imidazole, CH_2Cl_2, 25 °C, 4 h, 90 % for two steps; f) 0.1 equiv of PPTS, MeOH:CH_2Cl_2 (20:1), 25 °C, 6 h; g) 1.1 equiv of TBSCl, 2.8 equiv of imidazole, CH_2Cl_2, 0 °C, 4.5 h; (h) 1.5 equiv of NMO, 0.1 equiv of TPAP, 4 Å MS, CH_2Cl_2, 0 °C, 2 h, 85 % for three steps; i) 2.5 equiv of EtSH, 1.2 equiv of $BF_3 \cdot Et_2O$, CH_2Cl_2, −78 →0 °C, 1.5 h, 94 %; j) 5.0 equiv of $SO_3 \cdot$ pyr, 5.0 equiv of Et_3N, CH_2Cl_2:DMSO (1:1), 0 °C, 1 h, 91 %. LAH = lithium aluminum hydride; NMO = 4-methylmorpholine-*N*-oxide; TPAP = tetra-*n*-propylammonium perruthenate;



Scheme 6. Construction of GHIJ ring system **2**. Reagents and conditions: a) 1.1 equiv of **6**, 1.2 equiv of *n*BuLi, THF, −78 °C, 20 min; then 12 equiv of HMPA, 1.0 equiv of **7**, −78 →25 °C, 1.5 h, 88 %; b) 1.1 equiv of TBAF, THF, 25 °C, 7 h, 83 %; c) 2.0 equiv of $AgClO_4$, 10.0 equiv of $NaHCO_3$, SiO_2, 4 Å MS, $MeNO_2$, 25 °C, 3 h, 92 %; d) 2.0 equiv of *m*CPBA, 3.0 equiv of $NaHCO_3$, CH_2Cl_2, 0 °C, 2 h, 94%; e) 3.0 equiv of $AlMe_3$, CH_2Cl_2, −78 °C, 1 h, 94 %; f) 4.5 equiv of EtSH, 0.1 equiv of $Zn(OTf)_2$, 1.6 equiv of $NaHCO_3$, CH_2Cl_2, 25 °C, 4 h, 92 %; g) 1.1 equiv of TBSCl, 1.3 equiv of imidazole, CH_2Cl_2, 25 °C, 1 h, 92 %; h) 1.1 equiv of Ac_2O, 1.2 equiv of Et_3N, 0.2 equiv of 4-DMAP, CH_2Cl_2, 25 °C, 2 h, 95 %; i) H_2, 20 % $Pd(OH)_2$/C, AcOH, 25 °C, 48 h; j) 2.1 equiv of TBSOTf, 2.2 equiv of 2,6-lutidine, CH_2Cl_2, 0 °C, 0.5 h, 87 % for two steps; k) 0.5 equiv of K_2CO_3, MeOH, 25 °C, 4 h, 93 %; l) 0.05 equiv of TPAP, 2.0 equiv of NMO, CH_2Cl_2, 25 °C, 1 h, 94 %; m) 38 equiv of EtSH, 0.3 equiv of $Zn(OTf)_2$, 0.8 equiv of $NaHCO_3$, CH_2Cl_2, 25 °C, 2.5 h; 0.6 equiv of PPTS, MeOH, 25 °C, 4 h, 92 %; n) 4.0 equiv of $SO_3 \cdot$ pyr, 5.0 equiv of Et_3N, DMSO:CH_2Cl_2 (1:7), CH_2Cl_2, 0 °C, 1.5 h, 85 %. *m*CPBA = *m*-chloroperbenzoic acid; 4-DMAP = 4-*N*,*N*-dimethylaminopyridine; HMPA = hexamethyphosphoramide.

reduction of ester **37** to alcohol **38**; and, v) silylation of **38** with TBDPSCl-imidazole (90 % yield for three steps). We were now ready to continue the elaboration on the left side of the molecule as drawn. The acetonide protecting group was removed from **39** by treatment with PPTS in methanol, and the resulting diol **40** was selectively silylated with TBSCl-imidazole to afford the hydroxy silyl ether **41**, which was oxidized with TPAP-NMO furnishing ketone **42** in 85 % overall yield from **39**. The dithioketal was installed on ring H by exposure of **42** to EtSH and $BF_3 \cdot Et_2O$ in CH_2Cl_2 (−78 →0 °C), and was accompanied by cleavage of the TBS group to afford primary alcohol **43**. Oxidation of **43** with $SO_3 \cdot$ pyridine and DMSO then gave aldehyde **7** in 85 % overall yield from **42**.

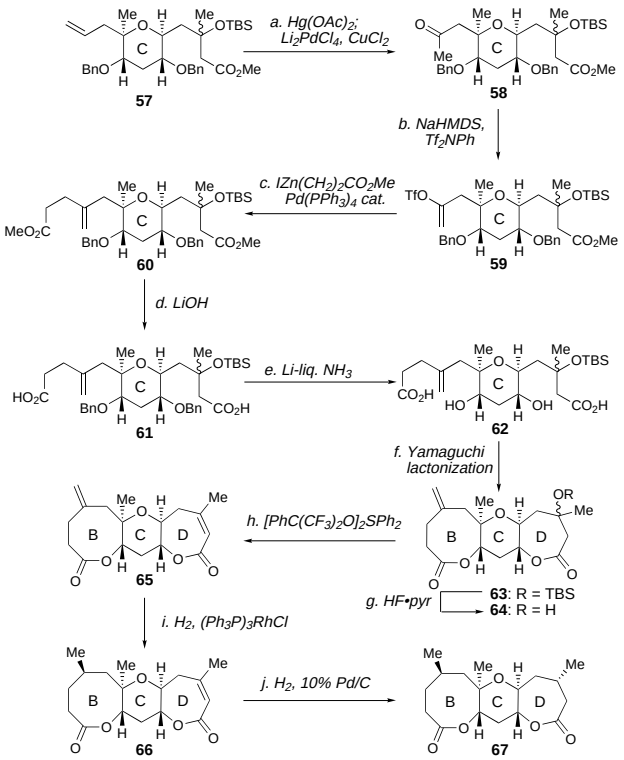
Our next goal was the construction of ring G. Scheme 6 details the sequence that was used to convert **7** to **2**. Previous conditions for Wittig couplings involving β,β'-dithioketal aldehydes, such as **7**, suffered from β-elimination side-products. Adding an excess of HMPA (12 equivalents) to the reaction mixture of **7** and the ylide derived from phosphonium iodide **6** and *n*BuLi (THF, −78 °C), however, resulted in a pleasant increase in yield to 88 % for the desired *Z*-olefin **44**. The silyl group was then removed from the coupling product **44** (1.1 equivalents of TBAF, THF, 83 % yield), and the resulting hydroxy dithioketal (**45**) was subjected to the standard ring-closure conditions[10] ($AgClO_4$, $NaHCO_3$, SiO_2, 4 Å MS, $MeNO_2$) to afford the desired oxocene system **46** (92 % yield). Activation of the sulfur towards nucleophilic attack by oxidation to the corresponding

sulfone (2.0 equivalents of *m*CPBA, CH_2Cl_2, 0 °C, 94% yield) was followed by reaction with $AlMe_3$ to afford the oxocene system **48** (94% yield), in which the methyl group was delivered from the bottom face of the molecule as drawn, and presumably through the intermediacy of an oxocarbonium ion. The assignment of stereochemistry at the methyl-bearing center was based on NMR data for **48**, and those of closely related compounds previously synthesized in these laboratories. The action of $Zn(OTf)_2$/EtSH/$NaHCO_3$ on **48** resulted in the removal of the benzylidene group and formation of the diol **49** (92%), which was differentially protected by sequential treatment with TBSCl/imidazole (primary silyl ether **50**, 92%), and Ac_2O/4-DMAP (secondary acetate **51**, 95%). Hydrogenation of the double bond in ring G of **51** was carried out in the presence of 20% $Pd(OH)_2/C$, which resulted in concomitant debenzylation (ring J), furnishing hydroxy compound **52**. The newly liberated hydroxyl group was now available for masking with a more suitable protecting group for the steps ahead. A TBS group was, therefore, introduced by treatment with TBSOTf and 2,6-lutidine, and the product (**53**, 87% yield for two steps) was deacetylated with K_2CO_3 in MeOH, furnishing secondary alcohol **54** (93% yield). Oxidation of **54** (TPAP/NMO, 94% yield), followed by simultaneous dithioketal formation and primary TBS cleavage [EtSH/$Zn(OTf)_2$] resulted in the formation of hydroxydithioketal **56** (92% yield) via ketone **55**. Finally, $SO_3 \cdot$pyridine and DMSO-mediated oxidation of **56** gave the desired GHIJ fragment **2** in 87% yield.

Construction of BCDE system 4

The synthesis of the desired BCDE ring system **4** (Scheme 1) began with D-glucose and proceeded through key intermediates **67** (see Scheme 7) and **73** (see Scheme 8). A first generation synthesis of the BCD key intermediate **67** was described in paper 1[11] of this series. The second-generation approach discussed here (Scheme 7), and partially in paper 1 of this series[11], includes a number of more practical steps that, along with the new synthetic technology developed for the construction of ring E, allowed the production of BCDE ring system **4** in multigram quantities.

The elaboration of rings B and D as lactones around ring C is shown in Scheme 7 . Thus, **57** (**51**, paper 1, Scheme 7) was subjected to Wacker-type oxidation ([$Hg(OAc)_2$], followed by addition of $PdCl_2$, LiCl and $CuCl_2$) to furnish methyl ketone **58** in 84% yield.[12] Regioselective enol triflate formation (NaHMDS/Tf_2NPh, 86% yield), followed by Pd-catalyzed coupling with the homoenolate equivalent $IZn(CH_2)_2CO_2Me$[13] gave compound **60** in 94% yield. Hydrolysis of the methyl esters in **60** with LiOH afforded dicarboxylic acid **61**, from which the benzyl groups were cleaved by the action of lithium in liquid ammonia, leading to dihydroxydicarboxylic acid **62**. Double Yamaguchi lactonization[14] of **62** (2,4,6-trichlorobenzoyl chloride/Et_3N; 4-DMAP, 80 °C) then led smoothly to bis(lactone) **63** in 78% overall yield form **60**. The TBS group was removed from **63** by the action of HF in pyridine (CH_2Cl_2, 0 °C), and the resulting tertiary alcohol (**64**) was subjected to dehydration with Martin's sulfurane[15] ([$PhC(CF_3)_2O]_2SPh_2$) to afford compound **65** (89% yield for two steps). The next task was the reduction of the two C=C bonds, with control over the configurations at the resulting methyl-bearing stereocenters. Semiempirical calculations on **65** (Figure 1) revealed a minimum energy conformation



Scheme 7. Synthesis of BCDE fragment **3**. Second-generation construction of BCD bis-lactone **67**. Reagents and conditions: a) 1.2 equiv of $Hg(OAc)_2$, MeOH, 25 °C, 2 h; then 0.1 equiv of $PdCl_2$, 0.2 equiv of LiCl, 3.0 equiv of $CuCl_2$, MeOH, 65 °C, 2 h, 84%; b) 1.2 equiv of NaHMDS, 1.2 equiv of $PhNTf_2$, THF, −78 → 0 °C, 1.5 h, 86%; c) 2.0 equiv of $IZn(CH_2)_2CO_2Me$, 0.05 equiv of [$Pd(PPh_3)_4$], DMA:benzene (1:9), 25 °C, 2 h, 94%; d) 10.0 equiv of LiOH, THF:H_2O:MeOH (3:1:1), 60 °C, 9 h; e) 12.0 equiv of Li, liq. NH_3, EtOH, −78 °C, 15 min; f) 2.1 equiv of 2,4,6-trichlorobenzoyl chloride, 4.0 equiv of Et_3N, THF, 0 °C, 1 h; then 6.0 equiv of 4-DMAP, benzene, 80 °C, 5 h, 78% for three steps; g) HF · pyr, CH_2Cl_2, 0 °C, 2 h; h) 1.5 equiv of [$PhC(CF_3)_2O]_2SPh_2$ (Martin's sulfurane), CH_2Cl_2, 0 °C, 15 min, 89% for two steps; i) H_2, 0.05 equiv of $(Ph_3P)_3RhCl$, benzene, 25 °C, 5 h, 99%, ca. 4:1 ratio of diastereoisomers in favor of **66**; j) H_2, 10% Pd/C, EtOAc, 25 °C, 12 h, 95%, ca. 19:1 ratio of diastereoisomers in favor of **67**. DMA = *N*,*N*-dimethylacetamide.

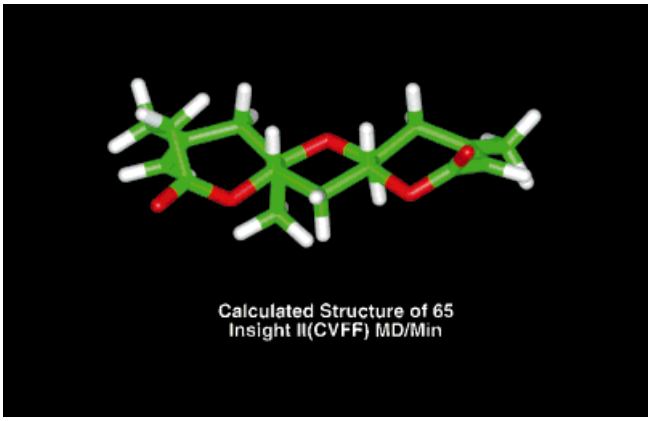


Figure 1. Computer-generated, minimized structure of **65**. The atoms are colored according to the following code: carbon, green; hydrogen, white; oxygen, red.

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(Figure 2) that suggested facial differentiation of the two double bonds. An adaptation of a very similar conformation was later verified by X-ray crystallographic analysis. Specifically, it was anticipated that the lactone moiety may, through chelation, direct delivery of hydrogen from the bottom face of

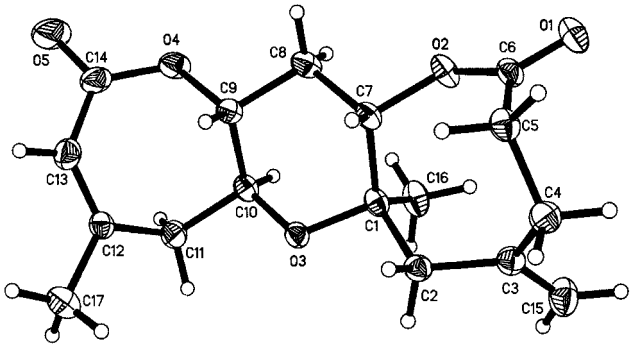
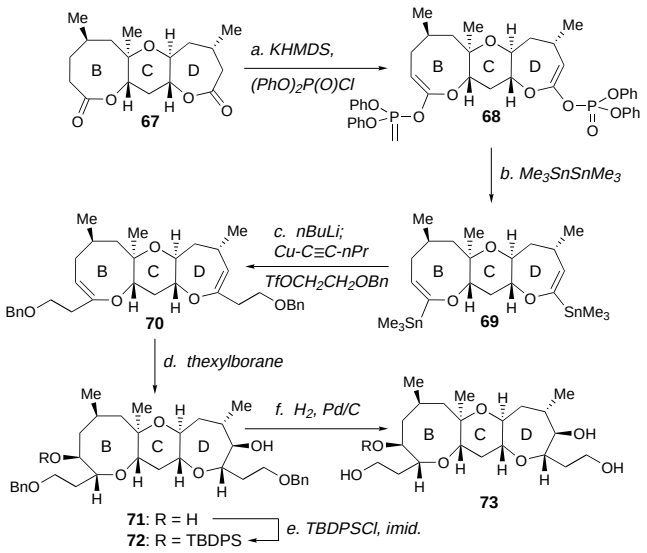


Figure 2. X-Ray structure of **65**.

the *exo*cyclic double bond as drawn, through the use of the appropriate catalyst. Based on this conformation, we also made the prediction that catalytic hydrogenation of the other endocyclic double bond may proceed from the top face of the molecule as drawn, due to steric factors, thus setting the correct stereochemistry at that center as well. To our delight, this goal was achieved by a stepwise hydrogenation sequence, first, in the presence of Wilkinson's catalyst[16] [$(Ph_3P)_3RhCl$] to afford **66** with satisfactory facial selectivity (ca. 4:1 ratio of diastereoisomers in favor of **66**, 99% combined yield), and then in the presence of 10% Pd/C, to give compound **67** with even higher facial selectivity (ca. 19:1 in favor of **67**, 95% combined yield). Compound **67** was secured in diastereomerically pure form by flash column chromatography (silica gel).

Scheme 8 depicts the new strategy for the conversion of the bis(lactone) **67** to the desired bis(enol ether) **73** which proved greatly superior to our previous strategy which utilized bis(thionolactone) intermediates corresponding to **67**.[17] Thus, application of the cyclic ketene acetal phosphate technology for transforming lactones to cyclic ethers,[18] resulted in an efficient sequence for accomplishing this objective: i) KHMDS/$(PhO)_2P(O)Cl$, **67** → **68** (85%); ii) $Me_3SnSnMe_3$, [$Pd(PPh_3)_4$] cat., LiCl, **68** → **69** (81% yield); and, iii) *n*BuLi, then CuC≡C*n*Pr, HMPT; then $TfOCH_2CH_2OBn$, **69** → **70** (65% yield). The conversion of **70** to **73** via **71** and **72** has already been described in paper 1[11] of this series.

In Scheme 9, the final drive towards the targeted BCDE intermediate **4** is presented. Engagement of the two hydroxyl groups branching from ring D as a ketal with cyclohexanone dimethylketal and PPTS, furnished compound **74** (87% yield) which was treated with PivCl and 4-DMAP to afford **75** (100% yield). Cleavage of the ketal with CSA in methanol regenerated the diol system on the right side of the molecule (97% yield), which was easily differentiated by reaction with TrCl·4-DMAP[19] at 40 °C, furnishing trityl ether **77** (99% yield) via **76**. The secondary hydroxyl group in **77** was

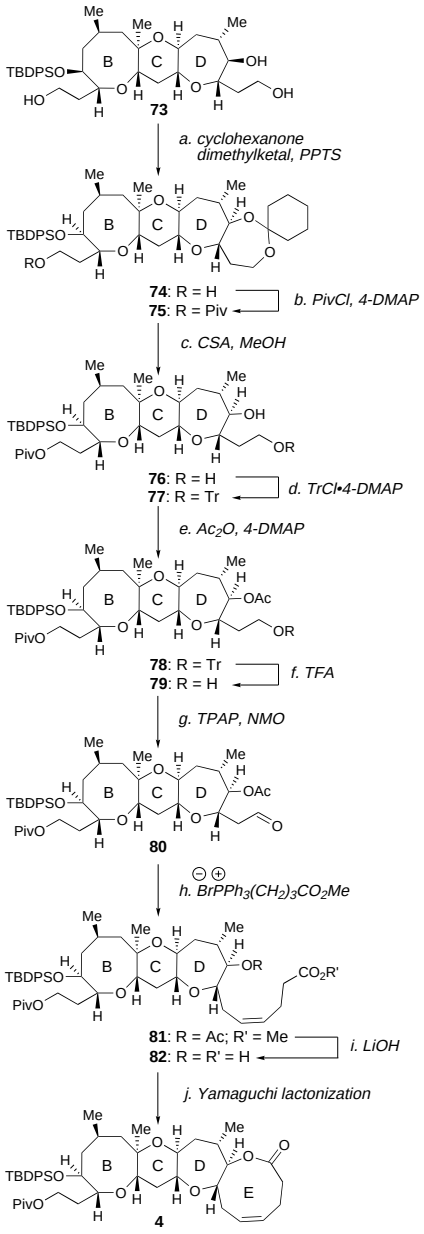


Scheme 8. Synthesis of the BCDE fragment **4**. Construction of compound **73**. Reagents and conditions: a) 4.0 equiv of KHMDS, 6.0 equiv of $(PhO)_2P(O)Cl$, 6.0 equiv of HMPA, THF, −78 °C, 1 h, 85%; b) 8.0 equiv of $Me_3SnSnMe_3$, 6.0 equiv of LiCl, 0.15 equiv of $Pd(PPh_3)_4$, THF, 75 °C, 2 h, 81%; c) 3.2 equiv of *n*BuLi, 3.5 equiv of CuC≡C*n*Pr, 7.1 equiv of HMPT, THF, −78 → −40 °C, 1 h; then 6.8 equiv of $TfOCH_2CH_2OBn$, THF, −78 → 25 °C, 14 h, 65%; d) 4.0 equiv of thexylborane, THF, −20 → 0 °C, 17 h; then 20.0 equiv of 30% H_2O_2, 20.0 equiv of aq. NaOH, 0 °C, 2 h, 86%; e) 1.3 equiv of TBDPSCl, 3.0 equiv of imidazole, DMF, 25 °C, 24 h, 90% (five recycles); f) H_2, 10% Pd/C, MeOH, 25 °C, 24 h, 97%. DMF = *N*,*N*-dimethylformamide; HMPT = hexamethylphosphorous triamide; KHMDS = potassium bis(trimethylsilyl) amide.

acetylated (Ac_2O, 4-DMAP, 99% yield), and the trityl ether was removed with TFA, furnishing primary alcohol **79** (96% yield). Oxidation of **79** with TPAP/NMO[20] allowed the generation of aldehyde **80** (87% yield), which reacted with the ylide generated from phosphonium salt $Br^-PPh_3^+(CH_2)_3CO_2Me$[21] and KHMDS in THF to afford *Z*-olefin **81** (94% yield). Exposure of **81** to LiOH cleaved the ester and acetate protecting groups, furnishing hydroxy acid **82** in high yield. Finally, Yamaguchi lactonization[14] (2,4,6-trichlorobenzoyl chloride, Et_3N; then 4-DMAP, 80 °C) led to BCDE fragment **4** in 86% overall yield from **81**.

Conclusion

The efficient synthetic routes developed for the construction of the brevetoxin A (**1**) key fragments GHIJ (**2**) and BCDE (**4**) made available these key intermediates in multigram quantities. With these compounds in hand, and with the knowledge gained from the model studies presented in papers 1[11] and 2[1] of this series, the stage was now set for our final journey towards brevetoxin A (**1**). In the following article,[22] we describe the closing stages of the total synthesis of brevetoxin A, that were more complex than anticipated, and required even further model studies to map out the very final pathway.



Scheme 9. Synthesis of the BCDE fragment **4**. Final stages. Reagents and conditions: a) 1.1 equiv of cyclohexanone dimethylketal, 0.1 equiv of PPTS, DMF, 25 °C, 13 h, 87 %; b) 1.3 equiv of PivCl, 1.4 equiv of 4-DMAP, CH_2Cl_2, 25 °C, 2 h, 100 %; c) 0.1 equiv of CSA, MeOH:CH_2Cl_2 (2:1), 25 °C, 1 h, 97 %; d) 1.5 equiv of TrCl·4-DMAP, CH_2Cl_2, 40 °C, 36 h, 99 %; e) 2.0 equiv of Ac_2O, 3.0 equiv of Et_3N, 0.1 equiv of 4-DMAP, CH_2Cl_2, 25 °C, 1 h, 99 %; f) 1.5 equiv of TFA, MeOH:CH_2Cl_2 (1:25), 25 °C, 30 min, 96 %; g) 0.1 equiv of TPAP, 2.0 equiv of NMO, CH_2Cl_2, 25 °C, 1 h, 87 %; h) 2.5 equiv of $^-Br^+PPh_3(CH_2)_3CO_2Me$, 2.0 equiv of KHMDS, THF, −78 °C, 2 h, 94 %; i) 11.5 equiv of LiOH, THF:H_2O:MeOH (5:1:1), 0 °C, 4 h; j) 1.8 equiv of 2,4,6-trichlorobenzoyl chloride, 4.0 equiv of Et_3N, THF, 0 °C, 1 h; then 4.0 equiv of 4-DMAP, benzene, 80 °C, 2 h, 86 % for two steps. Tr = triphenylmethyl.

Experimental Section

General techniques: See paper 1 in this series.[1]

Olefin 15: A solution of alcohol **14** (118.2 g, 0.229 mol) in CH_2Cl_2 (1.5 L) was cooled to 0 °C and treated with 2,6-lutidine (34.8 mL, 0.299 mol) and TESOTf (72.6 g, 0.275 mol) for 4 h. The mixture was concentrated, and the residue was dissolved in ether (1.5 L), and washed with water (0.5 L), 10 % aqueous potassium bisulfate solution (0.5 L), saturated aqueous $NaHCO_3$ solution (0.5 L), and brine (0.5 L). The organic layer was dried ($MgSO_4$) and concentrated to afford **15** (136.6g, 95 %). **15**: colorless oil; $R_f = 0.78$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +19.7$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2953$, 1462, 1109, 817, 738, 500 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.65-7.63$ (m, 4H, ArH), 7.40–7.24 (m, 11H, ArH), 5.80 (ddd, $J = 17.0$, 10.0, 7.0 Hz, 1H, =CH), 5.06–5.01 (m, 2H, $=CH_2$), 4.56 (s, 2H, OCH_2Ph), 3.89–3.85 (m, 2H, OCH), 3.74–3.66 (m, 3H, OCH), 3.63 (dt, $J = 8.5$, 3.5 Hz, 1H, OCH), 2.32–2.19 (m, 2H, $CH_2CH=CH_2$), 1.98 (dt, $J =$ 13.0, 8.5 Hz, 1H, C*H*H), 1.76 (dt, $J = 13.0$, 3.5 Hz, 1H, C*H*H), 1.04 (s, 9H, *t*BuSi), 0.93 (t, $J = 8.5$ Hz, 9H, $(CH_3CH_2)_3Si$), 0.59 (q, $J = 8.5$ Hz, 6H, $(CH_3CH_2)_3Si$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.6$, 135.6, 134.9, 133.7, 129.5, 128.2, 127.6, 127.4, 116.7, 75.7, 74.1, 71.3, 70.4, 65.9, 35.1, 28.6, 26.8, 19.2, 6.9, 5.0; HRMS, calcd for $C_{38}H_{54}O_4Si_2$ ($[M + Cs^+]$) 763.2615, found 763.2631.

Aldehyde 16: Ozone was bubbled through a solution of olefin **15** (137.5 g, 0.218 mol) in CH_2Cl_2 (1.5 L) at −78 °C until a pale blue color appeared (ca. 2 h). Triphenylphosphane (69.0 g, 0.263 mol) was added, and the mixture was stirred for 18 h at 25 °C. The solvent was distilled off, and the residue was coevaporated with benzene to give crude **16** (211 g) which was used for the next step without further purification. For analytical purposes, a small amount of this mixture was purified by flash chromatography (silica gel, 3:7, ether:hexanes). **16**: colorless oil; $R_f = 0.18$ (silica gel, 1:9, EtOAc:hexanes); $[\alpha]_D^{25} = +30.3$ ($c = 0.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3067$, 2953, 1727 (CO), 1463, 1426, 1242, 1112, 817, 737, 504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.51$ (dd, $J = 3.5$, 2.0 Hz, 1H, CHO), 7.62–7.59 (m, 4H, ArH), 7.39–7.24 (m, 11H, ArH), 4.54 (AB, $J = 6.5$ Hz, 2H, OCH_2Ph), 4.36 (ddd, $J = 9.5$, 7.5, 4.5 Hz, 1H, OCH), 3.81–3.75 (m, 3H, OCH), 3.67 (dt, $J = 3.0$, 3.0 Hz, 1H, OCH), 3.56 (dd, $J = 7.0$, 2.5 Hz, 1H, OCH), 2.58 (ddd, $J = 16.0$, 4.5, 2.0 Hz, 1H, C*H*HCHO), 2.41 (ddd, $J = 16.0$, 9.0, 3.5 Hz, 1H, C*H*HCHO), 2.10 (ddd, $J = 14.0$, 5.5, 4.0 Hz, 1H, C*H*H), 1.75 (ddd, $J =$ 14.0, 5.0, 3.5 Hz, 1H, C*H*H), 1.02 (s, 9H, *t*Bu), 0.92 (t, $J = 8.0$ Hz, 9H, $(CH_2CH_3)_3Si$), 0.57 (q, $J = 8.0$ Hz, 6H, $(CH_2CH_3)_3Si$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 201.3$, 138.3, 135.6, 133.7, 129.6, 128.3, 127.7, 127.6, 127.5, 76.8, 74.7, 72.3, 71.3, 68.7, 64.7, 45.7, 28.6, 26.8, 19.2, 6.9, 5.0; HRMS, calcd for $C_{37}H_{52}O_5Si_2Cs$ ($[M + Cs^+]$) 765.2408, found 765.2385.

***α,β*-Unsaturated ester 17**: A solution of crude aldehyde **16** (211 g) in benzene (1.5 L) was treated with Ph_3PCHCO_2Me (109.5 g, 0.327 mol) at 25 °C for 17 h. The mixture was concentrated, and the residue was dissolved in a minimum amount of CH_2Cl_2 followed by ether (1 L) and hexanes (1 L). The precipitate (Ph_3PO) was filtered, washed with a mixture of ether:-hexanes (1:1), and the filtrate was concentrated and purified by flash column chromatography (silica gel, 3:7, ether:hexanes) to afford *trans*-**17** (120.2 g, 80 % from **15**) and *cis*-**17** (15.0 g, 10 % from **15**). *trans*-**17**: colorless oil; $R_f = 0.34$ (silica gel, 3:1, ether:hexanes); $[\alpha]_D^{25} = +17.7$ ($c = 1.3$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2950$, 1724 (CO), 1658, 1431, 1110, 817, 737, 612, 500 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.65-7.63$ (m, 4H, ArH), 7.41–7.26 (m, 11H, ArH), 6.97 (dt, $J = 15.5$, 7.5 Hz, 1H, C*H*=$CHCO_2CH_3$), 5.87 (d, $J = 15.5$ Hz, 1H, CH=C*H*CO_2CH_3), 4.58, 4.54 (AB, $J = 12.0$ Hz, 2H, OCH_2Ph), 3.96–3.91 (m, 2H, OCH), 3.78–3.60 (m, 4H, OCH), 3.68 (s, 3H, CO_2CH_3), 2.49–2.44 (m, 1H, C*H*HCH=CH), 2.39–2.33 (m, 1H, C*H*HCH=CH), 2.04 (ddd, $J = 13.5$, 7.0, 6.5 Hz, 1H, C*H*H), 1.76 (dt, $J = 13.5$, 4.5 Hz, 1H, C*H*H), 1.05 (s, 9H, *t*BuSi), 0.94 (t, $J =$ 8.0 Hz, 9H, $(CH_3CH_2)_3Si$), 0.60 (q, $J = 8.0$ Hz, 6H, $(CH_3CH_2)_3Si$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 166.6$, 145.6, 138.4, 135.6, 133.7, 133.6, 129.6, 129.5, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 122.9, 74.4, 73.5, 71.8, 71.5, 70.8, 65.3, 51.3, 33.8, 28.6, 26.8, 19.2, 6.9, 5.0; HRMS, calcd for $C_{40}H_{56}O_6Si_2$ ($[M + Cs^+]$) 821.2670, found 821.2637. *cis*-**17**: colorless oil; $R_f = 0.45$ (silica gel, 3:7, ether:hexanes); $[\alpha]_D^{25} = +22.7$ ($c = 5.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} =$ 3043, 2932, 1722 (CO), 1648, 1433, 1113, 819, 737, 702, 612, 504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.69-7.67$ (m, 4H, ArH), 7.44–7.27 (m, 11H, ArH), 6.36 (dt, $J = 11.5$, 6.5 Hz, 1H, C*H*=$CHCO_2CH_3$), 5.86 (d, $J =$ 6.5 Hz, 1H, CH=C*H*CO_2CH_3), 4.59 (AB, $J = 11.4$ Hz, 2H, OCH_2Ph), 3.99–3.90 (m, 2H, OCH), 3.83–3.68 (m, 7H, OCH and CO_2CH_3), 3.07–3.01 (m, 1H, C*H*HCH=CH), 2.90–2.83 (m, 1H, C*H*HCH=CH), 2.00 (dt, $J = 13.0$, 8.0 Hz, 1H, C*H*H), 1.79–1.73 (m, 1H, C*H*H), 1.07 (s, 9H, *t*Bu), 0.97 (t, $J =$ 8.0 Hz, 9H, $(CH_3CH_2)_3Si$) 0.63 (q, $J = 8.0$ Hz, 6H, $(CH_3CH_2)_3Si$); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 166.7$, 146.9, 138.6, 135.6, 133.7, 133.6, 129.5, 128.2, 127.6, 127.5, 127.3, 120.3, 75.5, 74.6, 71.4, 71.0, 70.7, 65.9, 51.0, 30.2, 28.7, 26.8, 19.2, 6.9, 5.0; HRMS, calcd for $C_{40}H_{56}O_6Si_2$ ($[M + Na^+]$) 711.3513, found 711.3533.

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Allylic alcohol 18: A solution of *trans*-**17** (18.8 g, 0.027 mol) in CH_2Cl_2 was cooled to −78 °C, treated with DIBAL (74 mL, 1.0 M solution in CH_2Cl_2, 0.074 mol) and stirred for 3 h. The reaction mixture was poured into a mixture of ice (100 g), saturated aqueous sodium potassium tartrate solution (100 mL), and ether (400 mL), while vigorously stirring. The resulting mixture was stirred for an additional 4 h, the layers were separated, and the aqueous layer was extracted with ether (400 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to afford allylic alcohol **18** (18.0 g, 0.027 mol, 100 %). **18**: oil; $R_f = 0.35$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +15.9$ ($c = 0.6$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3421$ (OH), 3066, 2951, 2879, 1462, 1427, 1365, 1240, 1110, 1009, 972, 818, 738, 703, 613, 504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.66-7.64$ (m, 4 H ArH), 7.41–7.24 (m, 11 H, ArH), 5.71–5.63 (m, 2 H, C*H*=C*H*CH_2OH), 4.56 (s, 2 H, OCH_2Ph), 4.03 (d, $J = 4.5$ Hz, 2 H, HOCH_2), 3.91 (dd, $J = 10.0$, 6.0 Hz, 1 H, OCH), 3.86 (dt, $J = 9.0$, 5.0 Hz, 1 H, OCH), 3.78–3.63 (m, 4 H, OCH), 2.31 (dt, $J = 14.0$, 6.5 Hz, 1 H, CH=CHC*H*H), 2.22 (ddd, $J = 14.0$, 9.0, 4.0 Hz, 1 H, CH=CHC*H*H), 1.98 (dt, $J = 13.0$, 7.5 Hz, 1 H, C*H*H), 1.76 (dt, $J = 13.0$, 3.5 Hz, 1 H, C*H*H), 1.51 (br s, 1 H, OH), 1.05 (s, 9 H, *t*Bu), 0.94 (t, $J = 8.0$ Hz, 9 H, (CH_3CH_2)$_3$Si), 0.59 (q, $J = 8.0$ Hz, 6 H, (CH_3CH_2)$_3$Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.5$, 135.6, 133.7, 131.2, 129.6, 129.1, 128.2, 127.6, 127.4, 75.4, 74.3, 71.4, 71.0, 70.6, 65.7, 63.6, 33.5, 28.7, 26.8, 19.2, 6.9, 5.0; HRMS, calcd for $C_{39}H_{56}O_5Si_2$ ([M + Cs^+]) 793.2721, found 793.2750.

Epoxide 19: *tert*-Butyl hydroperoxide (48.8 mL, 5.0 M solution in isooctane, 0.244 mol) was added to a mixture of (+)-diethyl-D-tartrate (10.1 g, 0.049 mol), 4 Å molecular sieves (21 g), and titanium isopropoxide (11.6 g, 0.041 mol) in CH_2Cl_2 (400 mL) at −25 °C. The reaction mixture was stirred for 30 min. A solution of allylic alcohol **18** (108 g, 0.163 mol) in CH_2Cl_2 (200 mL) was treated with 4 Å molecular sieves (11 g) for 0.5 h at 25 °C and added to the peroxide-tartrate mixture at −25 °C. The resulting mixture was stirred at −25 °C for 19 h. After addition of EtOAc (500 mL) and saturated aqueous sodium sulfate (500 mL), the mixture was stirred for 1 h, filtered through Celite 545, and the layers were separated. The aqueous layer was extracted with EtOAc (500 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated. The residue was purified by flash column chromatography (silica gel, 2:1, ether:hexanes) to afford epoxide **19** (98.2 g, 89 %). **19**: oil; $R_f = 0.39$ (silica gel, 2:1, ether:hexanes); $[\alpha]_D^{25} = +16.4$ ($c = 0.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max}$ 3450 (OH), 2954, 2872, 1455, 1428, 1361, 1240, 1112, 823, 738, 701, 613 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.64-7.62$ (m, 4 H ArH), 7.40–7.24 (m, 11 H, ArH), 4.55, 4.52 (AB, $J = 12.0$ Hz, 2 H, OCH_2Ph), 3.96–3.91 (m, 2 H, OCH), 3.80–3.74 (m, 2 H, OCH), 3.69 (dd, $J = 10.0$, 5.5 Hz, 1 H, OCH), 3.62–3.58 (m, 2 H, OCH), 3.52 (ddd, $J = 12.0$, 7.0, 4.5 Hz, 1 H, OCH), 3.05–3.03 (m, 1 H, OCH), 2.92 (dt, $J = 4.5$, 2.5 Hz, 1 H, OCH), 1.98 (dt, $J = 14.0$, 7.0 Hz, 1 H, C*H*H), 1.88 (ddd, $J = 14.0$, 9.5, 5.0 Hz, 1 H, C*H*H), 1.72 (dt, $J = 14.0$, 4.0 Hz, 1 H, C*H*H), 1.66 (ddd, $J = 14.0$, 6.0, 4.0 Hz, 1 H, C*H*H), 1.55 (br s, 1 H, OH), 1.03 (s, 9 H, *t*Bu), 0.91 (t, $J = 8.0$ Hz, 9 H, (CH_3CH_2)$_3$Si), 0.57 (q, $J = 8.0$ Hz, 6 H, (CH_3CH_2)$_3$Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.5$, 135.6, 133.7, 129.6, 128.3, 127.6, 127.5, 74.4, 72.6, 71.6, 71.5, 70.8, 65.6, 61.9, 57.7, 53.6, 32.5, 28.6, 26.9, 19.2, 6.9, 5.0; HRMS, calcd for $C_{39}H_{56}O_6Si_2$ ([M + Cs^+]) 809.9495, found 809.9484.

Epoxy aldehyde 20: To a solution of epoxide **19** (144.3 g, 0.213 mol) in CH_2Cl_2 (600 mL) at 0 °C was added DMSO (600 mL), Et_3N (107.9 g, 1.066 mol), and SO_3·pyridine complex (169.6 g, 1.066 mol) in three portions. The reaction mixture was stirred for 2 h, poured into H_2O (600 mL), and extracted with EtOAc (2 L). The combined organic extracts were washed with 10 % aqueous potassium bisulfate solution (1 L), saturated aqueous $NaHCO_3$ solution (1 L), and brine (1 L), dried ($MgSO_4$), concentrated, and coevaporated (2 ×) with benzene to give crude aldehyde **20** (143.9 g) which was used in the next step without further purification. For analytical purposes, a small amount of the crude aldehyde **20** was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to afford aldehyde **20**. **20**: oil; $R_f = 0.67$ (silica gel, 2:1, ether:hexanes); $[\alpha]_D^{25} = +47.3$ ($c = 3.2$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3066$, 2916, 1729 (CO), 1590, 1462, 1362, 1240, 1111, 817, 740, 614, 494 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.89$ (d, $J = 6.5$ Hz, 1 H, CHO), 7.64 (d, $J = 7.0$ Hz, 4 H ArH), 7.41–7.24 (m, 11 H, ArH), 4.57, 4.53 (AB, $J = 11.5$ Hz, 2 H, OCH_2Ph), 4.02–3.95 (m, 2 H, OCH), 3.84 (dt, $J = 12.0$, 6.0 Hz, 1 H, OCH), 3.73 (dd, $J = 10.5$, 5.5 Hz, 1 H, OCH), 3.65 (dt, $J = 6.5$, 3.0 Hz, 1 H, OCH), 3.57 (dd, $J = 6.5$, 2.5 Hz, 1 H, OCH), 3.36 (dt $J = 5.5$, 1.5 Hz, 1 H, OCH), 3.16 (dd, $J = 6.5$, 1.5 Hz, 1 H, OCH), 2.08–2.02 (m, 1 H, C*H*H), 1.86 (t, $J = 5.8$ Hz, 2 H, C*H*H), 1.76 (ddd, $J = 13.5$, 5.0, 3.0 Hz, 1 H, C*H*H), 1.04 (s, 9 H, *t*Bu), 0.93 (t, $J = 8.0$ Hz, 9 H, (CH_3CH_2)$_3$Si), 0.59 (q, $J = 8.0$ Hz, 6 H, (CH_3CH_2)$_3$Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 198.2$, 138.3, 135.5, 133.6, 129.6, 128.3, 127.6, 127.5, 74.5, 72.0, 71.9, 71.1, 65.0, 58.5, 54.5, 32.6, 28.5, 26.8, 19.2, 6.9, 5.0.

Olefin 21: A mixture of triphenylmethylphosphonium bromide (114.3 g, 0.320 mol) in THF (600 mL) was treated with NaHMDS (298 mL, 1 M solution in THF, 0.298 mol) at 0 °C for 1 h. To the yellow suspension was added a solution of crude aldehyde **20** (143.9 g) in THF (600 mL), and the mixture was stirred for 1 h at 25 °C. Acetone (150 mL) was added, and the mixture was poured into H_2O (600 mL) and ether (600 mL). The layers were separated, the aqueous layer was extracted with ether (600 mL), and the combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica gel, 2:8, ether:hexanes) to afford olefin **21** (125.9 g, 88 % for two steps). **21**: oil; $R_f = 0.73$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +16.5$ ($c = 3.8$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} =$ 2954, 2877, 1461, 1427, 1361, 1240, 1110, 819, 737, 701, 611, 504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.63-7.62$ (m, 4 H ArH), 7.39–7.24 (m, 11 H, ArH), 5.47 (ddd, $J = 17.5$, 10.0, 7.5 Hz, 1 H, CH_2=C*H*), 5.39 (dd, $J =$ 17.5, 2.0 Hz, 1 H, C*H*H=CH), 5.19 (dd, $J = 10.0$, 2.0 Hz, 1 H, C*H*H=CH), 4.54 (s, 2 H, OCH_2Ph), 3.95 (dt, $J = 9.5$, 5.0 Hz, 1 H, OCH), 3.89 (dd, $J =$ 10.0, 6.5 Hz, 1 H, OCH), 3.75 (dt, $J = 10.5$, 4.5 Hz, 1 H, OCH), 3.70 (dd, $J =$ 10.0, 6.0 Hz, 1 H, OCH), 3.61–3.59 (m, 2 H, OCH), 3.07 (dd, $J = 7.5$, 2.0 Hz, 1 H, OCH), 2.96 (ddd, $J = 6.5$, 4.5, 2.0 Hz, 1 H, OCH), 2.00 (dt, $J = 14.0$, 7.0 Hz, 1 H, C*H*H), 1.89 (ddd, $J = 14.0$, 9.5, 4.5 Hz, 1 H, C*H*H), 1.73 (dt, $J =$ 14.0, 4.2 Hz, 1 H, C*H*H), 1.62 (ddd, $J = 14.0$, 6.0, 4.5 Hz, 1 H, C*H*H), 1.02 (s, 9 H, *t*Bu), 0.91 (t, $J = 8.0$ Hz, 9 H, (CH_3CH_2)$_3$Si), 0.57 (q, $J = 8.0$ Hz, 6 H, (CH_3CH_2)$_3$Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.4$, 135.6, 133.7, 129.5, 128.2, 127.6, 119.1, 74.3, 72.8, 71.5, 71.4, 70.7, 65.5, 58.3, 57.8, 33.0, 28.4, 26.8, 19.2, 6.9, 5.0; HRMS, calcd for $C_{40}H_{56}O_5Si_2$ ([M + Cs^+]) 805.2721, found 805.2739.

Hydroxy epoxide 22: A solution of epoxide **21** (125 g, 0.186 mol) in THF (1.2 L) was treated with TBAF (204 mL, 1.0 M solution in THF, 0.204 mol) at −20 °C. The reaction mixture was warmed to 0 °C over 1 h, concentrated, and diluted with EtOAc (1 L). The solution was washed successively with H_2O, 5 % aqueous potassium bisulfate solution (500 mL), saturated aqueous $NaHCO_3$ solution (500 mL), and brine (500 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica gel, 3:7, ether:hexanes) to afford hydroxy epoxide **22** (73.6 g, 71 %) and a dihydroxy epoxide (10.8 g, 0.034 mol) in which both silyl ethers were cleaved. A solution of the dihydroxy epoxide (10.8 g, 0.034 mol) and imidazole (3.5 g, 0.051 mol) in DMF (50 mL) and CH_2Cl_2 (1 L) was treated with TBDPSCl (10.2 g, 0.037 mol) at 0 °C for 3 h. The reaction mixture was concentrated, dissolved in ether, and washed with H_2O (500 mL), 5 % aqueous potassium bisulfate solution (500 mL), saturated aqueous $NaHCO_3$ solution (500 mL), and brine (500 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (silica gel, 1:9, ether:hexanes, gradient with ether) provided an additional amount of **22** (18.0 g, 17 %). **22**: oil; $R_f = 0.26$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +22.5$ ($c = 0.4$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3464$ (OH), 2931, 2860, 1428, 1110, 740, 702, 612, 504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.66$ (m, 4 H ArH), 7.44–7.27 (m, 11 H, ArH), 5.56–5.49 (m, 1 H, CH_2=C*H*), 5.42 (d, $J = 17.0$ Hz, 1 H, C*H*H=CH), 5.22 (d, $J = 10.0$ Hz, 1 H, C*H*H=CH), 4.63, 4.49 (AB, $J =$ 12.0 Hz, 2 H, OCH_2Ph), 3.97 (dt, $J = 8.5$, 4.0 Hz, 1 H, OCH), 3.94–3.91 (m, 1 H, OCH), 3.83 (dt, $J = 11.0$, 6.0 Hz, 1 H, OCH), 3.77 (dt, $J = 7.5$, 3.5 Hz, 1 H, OCH), 3.72–3.69 (m, 1 H, OCH), 3.61 (dd, $J = 8.5$, 5.5 Hz, 1 H, OCH), 3.13 (d, $J = 7.5$ Hz, 1 H, OCH), 3.02–2.99 (m, 1 H, OCH), 2.48 (t, $J = 4.5$ Hz, 1 H, C*H*H), 1.99–1.92 (m, 2 H, C*H*H, OH), 1.86 (dt, $J = 14.0$, 4.0 Hz, 1 H, C*H*H), 1.71 (dt, $J = 14.5$, 5.0 Hz, 1 H, C*H*H), 1.07 (s, 9 H, *t*Bu); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 137.6$, 135.7, 135.5, 135.4, 133.5, 133.4, 129.6, 128.5, 127.9, 127.8, 127.7, 127.6, 127.5, 119.1, 73.5, 71.9, 70.8, 70.5, 69.1, 65.3, 58.3, 57.4, 32.7, 28.1, 26.8, 19.2; HRMS, calcd for $C_{34}H_{42}O_5Si$ ([M + Cs^+]) 691.1856, found 691.1869.

TBS-protected alcohol 8: A solution of hydroxy epoxide **22** (79.2 g, 0.142 mol) in CH_2Cl_2 (1 L) was treated with TBSOTf (8 mL, 0.034 mol) at −78 °C. After stirring for 10 min, 2,6-lutidine (23.3 mL, 0.199 mol) was added, followed by TBSOTf (34.8 mL, 0.150 mol), and the mixture was warmed to 25 °C. After 30 min, the mixture was diluted with ether (2 L), washed with H_2O, 5 % aqueous potassium bisulfate solution (1 L), saturated aqueous $NaHCO_3$ solution (1 L), and brine (1 L), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica gel, 3:7, ether:hexanes) to afford TBS-protected alcohol **8**

(83.9 g, 88%). **8**: oil; $R_f = 0.77$ (silica gel, 1:2, EtOAc:benzene); $[\alpha]_D^{25} = +52.4$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2930, 2857, 1471, 1428, 1253, 1104, 836, 777, 737, 702, 613, 506\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.66–7.64 (m, 4H, ArH), 7.39–7.24 (m, 11H, ArH), 5.92 (ddd, $J = 17.0, 10.5, 5.5$ Hz, 1H, CH_2=C*H*), 5.33 (d, $J = 17.0$ Hz, 1H, C*H*H=CH), 5.18 (d, $J = 10.5$ Hz, 1H, C*H*H=CH), 4.73, 4.59 (AB, $J = 12.5$ Hz, 2H, OCH_2Ph), 4.07–3.92 (m, 4H, OCH), 3.67 (dt, $J = 11.0, 4.5$ Hz, 1H, OCH), 3.58 (dd, $J = 9.0, 5.5$ Hz, 1H, OCH), 3.37 (ddd, $J = 10.5, 9.0, 4.5$ Hz, 1H, OCH), 3.13 (dd, $J = 9.5, 2.5$ Hz, 1H, OCH), 2.23–2.17 (m, 2H, C*H*H), 1.82 (ddd, $J = 15.0, 7.0, 2.5$ Hz, 1H, C*H*H), 1.47 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.05 (s, 9H, *t*BuSi), 0.85 (s, 9H, *t*BuSi), 0.04 (s, 3H, CH_3Si), 0.01 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.1, 136.1, 135.5, 133.8, 129.5, 128.2, 127.6, 127.1, 116.2, 83.0, 80.0, 73.1, 72.5, 72.2, 70.5, 64.2, 63.3, 40.0, 29.9, 26.8, 25.7, 19.2, 17.9, -4.2, -4.6$; HRMS, calcd for $C_{40}H_{56}O_5Si_2$ ($[M + Cs^+]$) 805.2721, found 805.2737.

Alcohol 23: A solution of olefin **8** (98 g, 0.146 mol) in THF (300 mL) was treated with 9-BBN (804 mL, 1.0 M solution in THF, 0.804 mol) at 0 °C for 4 h. The mixture was added to a solution of $NaHCO_3$ (275 g, 3.274 mol) in H_2O (3.8 L) followed by careful addition of hydrogen peroxide (223 mL, 30% w/w solution in H_2O, 2.184 mol). After the mixture was stirred for 4 h, ether (1 L) was added, the layers were separated, and the aqueous layer was extracted with ether (500 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash column chromatography (silica gel, 3:7, ether:hexanes) to afford alcohol **23** (105.7 g, contains about 15% w/w of an impurity derived from 9-BBN, 0.130 mol, 89%) which was used without further purification in the next step. For analytical purposes, a small amount of crude alcohol **23** was purified by flash column chromatography (silica gel, 3:7, ether:hexanes). **23**: oil; $R_f = 0.44$ (silica gel, 1:2, EtOAc:hexanes); $[\alpha]_D^{25} = +55.2$ ($c = 0.8$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3454$ (OH), 2923, 2857, 1470, 1428, 1253, 1103, 837, 777, 737, 702, 613, 506 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.65-7.62$ (m, 4H, ArH), 7.45–7.19 (m, 11H, ArH), 4.58 (s, 2H, OCH_2Ph), 4.03–3.93 (m, 3H, OCH), 3.87–3.74 (m, 3H, OCH), 3.65 (ddd, $J = 11.0, 6.5, 4.5$ Hz, 1H, OCH), 3.44–3.39 (m, 1H, OCH), 3.34 (dt, $J = 9.0, 2.5$ Hz, 1H, OCH), 3.09 (dd, $J = 9.5, 3.0$ Hz, 1H, OCH), 2.24 (dd, $J = 15.0, 3.5$ Hz, 1H, C*H*H), 2.18 (dt, $J = 11.5, 4.5$ Hz, 1H, C*H*H), 2.06–1.87 (m, 2H, C*H*H, OH), 1.77 (ddd, $J = 15.0, 6.0, 3.0$ Hz, 1H, C*H*H), 1.73–1.63 (m, 1H, C*H*H), 1.38 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.05 (s, 9H, *t*BuSi), 0.85 (s, 9H, *t*BuSi), 0.06 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 138.4, 135.4, 133.6, 133.5, 129.5, 129.4, 128.1, 127.5, 127.2, 82.9, 79.8, 72.8, 72.1, 71.8, 69.6, 63.9, 63.0, 61.0, 39.6, 33.6, 28.9, 26.7, 25.6, 19.1, 17.7, -4.2, -4.9$; HRMS, calcd for $C_{40}H_{58}O_6Si_2$ ($[M + Cs^+]$) 823.2826, found 823.2858.

Aldehyde 24: To a solution of crude alcohol **23** (110.8 g, content ca. 85% w/w, 0.136 mol), DMSO (400 mL), and Et_3N (95.4 mL, 0.682 mol) in CH_2Cl_2 (400 mL) at 0 °C was added $SO_3 \cdot$pyridine complex (108.5 g, 0.682 mol) in three portions. The reaction mixture was stirred for 2 h, diluted with EtOAc (2 L), washed successively with H_2O, 10% aqueous potassium bisulfate solution, saturated aqueous $NaHCO_3$ solution, and brine, dried ($MgSO_4$), and concentrated. The residue was coevaporated twice with benzene to give crude aldehyde **24** (110.5 g) which was used in the next step without further purification. For analytical purposes, a small amount of crude aldehyde **24** was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether). **24**: oil; $R_f = 0.68$ (silica gel, 2:1, ether:hexanes); $[\alpha]_D^{25} = +47.6$ ($c = 0.7$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2954, 2930, 2857, 1730$ (CO), 1472, 1428, 1253, 1104, 837, 777, 738, 702, 613, 506 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.78$ (dd, $J = 3.0, 2.0$ Hz, 1H, CHO), 7.68–7.65 (m, 4H, ArH), 7.40–7.21 (m, 11H, ArH), 4.61, 4.58 (AB, $J = 12.5$ Hz, 2H, OCH_2Ph), 4.08–4.03 (m, 1H, OCH), 4.00–3.94 (m, 2H, OCH), 3.86 (d, $J = 3.0$ Hz, 1H, OCH), 3.69–3.64 (m, 2H, OCH), 3.41 (ddd, $J = 11.0, 9.0, 4.5$ Hz, 1H, OCH), 3.13 (dd, $J = 10.0, 3.0$ Hz, 1H, OCH), 2.77 (ddd, $J = 16.0, 3.5, 1.5$ Hz, 1H, C*H*H), 2.46 (ddd, $J = 16.0, 10.0, 3.5$ Hz, 1H, C*H*H), 2.23 (dt, $J = 11.5, 4.5$ Hz, 1H, C*H*H), 2.18 (dd, $J = 14.5, 3.0$ Hz, 1H, C*H*H), 1.83–1.77 (m, 1H, C*H*H), 1.47 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.07 (s, 9H, *t*BuSi), 0.87 (s, 9H, *t*BuSi), 0.08 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 201.2, 138.8, 135.5, 133.8, 133.7, 129.5, 128.2, 127.6, 127.1, 127.0, 80.3, 78.1, 73.1, 72.0, 69.9, 64.0, 63.1, 46.2, 39.6, 29.5, 26.8, 25.7, 19.2, 17.8, -4.1, -4.8$; HRMS, calcd for $C_{40}H_{56}O_6Si_2$ ($[M + Cs^+]$) 821.2670, found 821.2694.

***α,β*-Unsaturated ester 25**: A solution of crude aldehyde **24** (110.5 g) in benzene (1 L) was treated with methyl (triphenylphosphoranylidene)acetate (68.3 g, 0.204 mol) at 25 °C for 11 h. The reaction mixture was concentrated and purified by flash column chromatography (silica gel, 1:49, ether:hexanes, gradient with ether) to afford ester **25** (97.9 g, 86% for two steps). **25**: colorless oil; $R_f = 0.51$ (silica gel, 3:7, ether:hexanes); $[\alpha]_D^{25} = +69.7$ ($c = 0.6$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2952, 2930, 2857, 1726$ (CO), 1658, 1470, 1429, 1255, 1102, 1046, 837, 777, 738, 702, 613, 506 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.66$ (m, 4H, ArH), 7.41–7.23 (m, 11H, ArH), 7.04 (dt, $J = 16.0, 8.0$ Hz, 1H, C*H*=CHCO$_2$Me), 5.91 (d, $J = 16.0$ Hz, 1H, CH=C*H*CO$_2$Me), 4.67 (dd, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.58 (dd, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.06–4.03 (m, 1H, OCH), 4.00–3.92 (m, 2H, OCH), 3.90–3.84 (m, 1H, OCH), 3.74 (s, 3H, CO_2CH_3), 3.66–3.60 (m, 1H, OCH), 3.40–3.35 (m, 1H, OCH), 3.20 (t, $J = 8.5$ Hz, 1H, OCH), 3.06 (d, $J = 9.5$ Hz, 1H, OCH), 2.70–2.64 (m, 1H, C*H*H), 2.30 (dt, $J = 15.0, 7.5$ Hz, 1H, C*H*H), 2.22–2.14 (m, 2H, C*H*H), 1.84–1.75 (m, 1H, C*H*H), 1.42 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.07 (s, 9H, *t*BuSi), 0.88 (s, 9H, *t*BuSi), 0.07 (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.9, 146.2, 139.0, 135.6, 133.8, 129.6, 129.5, 128.2, 127.6, 127.1, 122.8, 81.3, 80.3, 73.1, 72.0, 71.9, 69.9, 64.1, 63.3, 51.4, 39.8, 34.7, 29.6, 26.9, 25.7, 19.3, 17.9, −3.9, −4.7; HRMS, calcd for $C_{43}H_{60}O_7Si_2$ ($[M + Cs^+]$) 877.2932, found 877.2904.

Allylic alcohol 26: A solution of ester **25** (96.4 g, 0.115 mol) in CH_2Cl_2 (1 L) was treated with DIBAL (328 mL, 1.0 M solution in CH_2Cl_2, 0.328 mol) at −78 °C for 3 h. The reaction mixture was poured into a mixture of ice (750 g), saturated aqueous sodium potassium tartrate (750 mL) and EtOAc (1.5 L) and stirred vigorously for 4 h. The organic layer was separated, washed with 10% aqueous potassium bisulfate (500 mL), saturated aqueous $NaHCO_3$ (500 mL), and brine (500 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether) to afford allylic alcohol **26** (80.6 g, 88%). **26**: colorless oil; $R_f = 0.33$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +61.6$ ($c = 3.2$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3438$ (OH), 2930, 2856, 1470, 1428, 1254, 1102, 1050, 836, 776, 737, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.66$ (m, 4H, ArH), 7.41–7.26 (m, 11H, ArH), 5.80–5.69 (m, 2H, CH=CH), 4.70 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.60 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.10–3.97 (m, 5H, OCH), 3.89 (d, $J = 3.0$ Hz, 1H, OCH), 3.65 (dt, $J = 10.5, 4.5$ Hz, 1H, OCH), 3.39 (ddd, $J = 10.5, 9.0, 5.0$ Hz, 1H, OCH), 3.13 (dt, $J = 8.5, 3.0$ Hz, 1H, OCH), 3.06 (dd, $J = 9.5, 3.0$ Hz, 1H, OCH), 2.56–2.52 (m, 1H, C*H*H), 2.22–2.15 (m, 3H, C*H*H), 1.80 (ddd, $J = 15.0, 6.0, 3.0$ Hz, 1H, C*H*H), 1.60 (br s, 1H, OH), 1.42 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.06 (s, 9H, *t*BuSi), 0.88 (s, 9H, *t*BuSi), 0.07 (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.0, 135.5, 133.7, 131.1, 129.5, 129.1, 128.1, 127.5, 127.1, 127.0, 82.1, 80.1, 73.0, 71.9, 69.6, 64.0, 63.6, 63.4, 39.7, 34.5, 29.5, 26.8, 25.7, 19.2, 17.8, -4.0, -4.7$; HRMS, calcd for $C_{42}H_{60}O_6Si_2$ ($[M + Cs^+]$) 849.2983, found 849.2961.

Epoxide 27: A solution of allylic alcohol **26** (74.7 g, 93.8 mmol) in CH_2Cl_2 (300 mL) was treated with 4 Å molecular sieves (40 g) for 0.5 h at 25 °C. This mixture was added to a mixture of (+)-diethyl-D-tartrate (5.7 g, 27.6 mmol), 4 Å molecular sieves (41 g), titanium isopropoxide (6.7 g, 23.6 mmol), and *tert*-butyl hydroperoxide (45 mL, 5.0 M solution in isooctane, 225 mmol) in CH_2Cl_2 (300 mL) at −25 °C for 18 h. After addition of EtOAc (350 mL) and saturated aqueous sodium sulfate (135 mL), the reaction mixture was stirred for 1 h and filtered through celite 545. The aqueous layer was separated and extracted with EtOAc (2 × 250 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated. The residue was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether) to afford epoxide **27** (74.1 g, 97%) as a mixture of two isomers (ca. 7:1 by ^1H NMR). **27**: oil; $R_f = 0.29$ (silica gel, 2:1, ether:hexanes); $[\alpha]_D^{25} = +56.1$ ($c = 1.8$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3449$ (OH), 2954, 2930, 2857, 1472, 1428, 1252, 1104, 1052, 837, 777, 737, 702, 613, 505 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.65$ (m, 4H, ArH), 7.42–7.25 (m, 11H, ArH), 4.68 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.61 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.06–3.84 (m, 5H, OCH), 3.70–3.58 (m, 2H, OCH), 3.48–3.40 (m, 1H, OCH), 3.25–3.18 (m, 1H, OCH), 3.17–3.14 (m, 1H, OCH), 3.10–3.05 (m, 1H, OCH), 2.94–2.90 (m, 1H, OCH), 2.25–2.18 (m, 2H, C*H*H), 1.92–1.75 (m, 3H, C*H*H), 1.56 (br s, 1H, OH), 1.41 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.06 (s, 9H, *t*BuSi), 0.86 (s, 9H, *t*BuSi), 0.07 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.9, 135.5, 135.4, 133.7, 133.6, 129.5, 128.2, 128.1, 127.5, 127.1, 127.0, 80.3, 80.0, 73.0, 72.1, 71.9, 69.6, 64.0, 63.2, 61.7, 57.9, 53.3, 39.7, 33.6, 29.4, 26.8, 25.7, 19.2, 17.8, -4.1, -4.8$; HRMS, calcd for $C_{42}H_{60}O_7Si_2$ ($[M + Cs^+]$) 865.2932, found 865.2954.

Epoxy aldehyde 28: To a solution of epoxide **27** (82.0 g, 0.101 mol), DMSO (500 mL), and Et_3N (72 mL, 0.504 mol) in CH_2Cl_2 (500 mL) at 0 °C was

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added $SO_3 \cdot$pyridine complex (80.0 g, 0.503 mol) in three portions. The reaction mixture was stirred at 0 °C for 1 h, diluted with EtOAc (1 L), and washed successively with H_2O (500 mL), 10% aqueous potassium bisulfate (500 mL), saturated aqueous $NaHCO_3$ (500 mL), and brine (500 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was coevaporated twice with toluene to give crude aldehyde **28** (81.8 g) which was used in the next step without further purification. For analytical purposes a small amount of crude aldehyde **28** was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether). **28**: colorless oil; $R_f = 0.53$ (silica gel, 2:1, ether:hexanes); $[\alpha]_D^{25} = +79.2$ ($c = 1.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2954, 2930, 2857, 1730$ (CO), 1471, 1428, 1254, 1103, 1051, 837, 778, 738, 703, 506 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.96$ (d, $J = 6.0$ Hz, 1H, CHO), 7.68–7.65 (m, 4H, ArH), 7.42–7.24 (m, 11H, ArH), 4.67 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.62 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.07–3.94 (m, 3H, OCH), 3.90–3.89 (m, 1H, OCH), 3.67 (dt, $J = 11.0, 4.5$ Hz, 1H, OCH), 3.45 (ddd, $J = 10.5, 9.0, 4.5$ Hz, 1H, OCH), 3.41 (dt, $J = 5.5, 1.5$ Hz, 1H, OCH), 3.25 (dt, $J = 8.5, 3.0$ Hz, 1H, OCH), 3.14 (dd, $J = 6.0, 2.0$ Hz, 1H, OCH), 3.09 (dd, $J = 9.5, 3.0$ Hz, 1H, OCH), 2.23–2.19 (m, 2H, C*H*H), 2.06 (ddd, $J = 14.5, 5.5, 3.0$ Hz, 1H, C*H*H), 1.90–1.79 (m, 2H, C*H*H), 1.42 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.07 (s, 9H, *t*BuSi), 0.86 (s, 9H, *t*BuSi), 0.08 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 198.4, 138.9, 135.6, 135.5, 133.7, 129.6, 129.5, 128.2, 127.6, 127.2, 127.1, 127.0, 80.1, 80.0, 73.0, 72.1, 70.0, 69.6, 64.0, 63.2, 58.4, 54.3, 39.7, 33.4, 29.5, 26.8, 25.7, 19.2, 17.8, −4.0, −4.8$.

Olefin 29: A solution of aldehyde **28** (81.8 g, 0.101 mol) in THF (500 mL) was added to a mixture of triphenylmethylphosphonium bromide (72.2 g, 0.202 mol) and NaHMDS (152 mL, 1M solution in THF, 0.152 mol) in THF (500 mL) at 0 °C. The reaction mixture was stirred for 15 min and quenched by pouring into a mixture of ice (250 g), H_2O (250 mL), and EtOAc (500 mL). The organic layer was separated, washed with 10% aqueous potassium bisulfate (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether) to afford olefin **29** (68.6 g, 84% for two steps). **29**: colorless oil; $R_f = 0.44$ (silica gel, 3:7, ether:hexanes); $[\alpha]_D^{25} = +61.7$ ($c = 2.7$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2954, 2931, 2857, 1471, 1428, 1254, 1104, 1052, 837, 777, 738, 702, 612, 506$ cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.68–7.66$ (m, 4H, ArH), 7.42–7.26 (m, 11H, ArH), 5.57 (ddd, $J = 17.5, 10.0, 7.5$ Hz, 1H, C*H*=CH_2), 5.45 (d, $J = 17.5$ Hz, 1H, CH=C*H*H), 5.26 (d, $J = 10.0$ Hz, 1H, CH=C*H*H), 4.70 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.61 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.09–4.04 (m, 1H, OCH), 4.01–3.96 (m, 2H, OCH), 3.90 (d, $J = 2.5$ Hz, 1H, OCH), 3.68 (dt, $J = 10.5, 4.5$ Hz, 1H, OCH), 3.45 (dt, $J = 10.$, 4.5 Hz, 1H, OCH), 3.25 (dt, $J = 8.5, 3.0$ Hz, 1H, OCH), 3.13–3.06 (m, 3H, OCH), 2.34–2.19 (m, 2H, C*H*H), 1.93 (ddd, $J = 14.0, 5.5, 2.5$ Hz, 1H, C*H*H), 1.86–1.80 (m, 2H, C*H*H), 1.43 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.07 (s, 9H, *t*BuSi), 0.87 (s, 9H, *t*BuSi) 0.08 (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.0, 135.9, 135.6, 135.5, 133.8, 133.7, 129.5, 128.1, 127.6, 127.1, 127.0, 119.0, 80.4, 80.1, 73.0, 72.1, 72.0, 69.8, 64.1, 63.3, 58.1, 57.8, 39.8, 34.2, 29.6, 26.8, 25.7, 19.2, 17.9, −4.1, −4.7$; HRMS, calcd for $C_{43}H_{60}O_6Si_2$ ($[M + Cs^+]$) 861.2983, found 861.2953.

Hydroxy epoxide 30: A solution of epoxide **29** (69.8 g, 86.2 mmol) in THF (500 mL) was treated with TBAF (145 mL, 1.0M solution in THF, 0.145 mol) at 0 °C for 3 h. The reaction mixture was diluted with EtOAc (1 L), washed with H_2O (250 mL), 10% aqueous potassium bisulfate (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica gel, 1:9, EtOAc:hexanes, gradient with EtOAc) to afford hydroxy epoxide **30** (38.5 g, 72%) and a dihydroxy epoxide (both silyl protecting groups were cleaved) (8.6 g, 26%) which was reprotected to yield additional hydroxy epoxide **30** (11.7 g, 22%). **30**: colorless oil; $R_f = 0.57$ (silica gel, 2:1, EtOAc:hexanes); $[\alpha]_D^{25} = +60.0$ ($c = 0.4$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3432$ (OH), 2933, 2855, 1461, 1425, 1107, 1035, 823, 737, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.68–7.64$ (m, 4H, ArH), 7.42–7.22 (m, 11H, ArH), 5.55 (ddd, $J = 17.0, 10.0, 7.5$ Hz, 1H, C*H*=CH_2), 5.47 (dd, $J = 17.0, 2.0$ Hz, 1H, CH=C*H*H), 5.28 (dd, $J = 10.0, 2.0$ Hz, 1H, CH=C*H*H), 4.68 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.58 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.15–4.10 (m, 1H, OCH), 4.00 (q, $J = 7.0$ Hz, 1H, OCH), 3.91–3.88 (m, 2H, OCH), 3.64–3.56 (m, 2H, OCH), 3.27 (ddd, $J = 9.0, 5.5, 3.0$ Hz, 1H, OCH), 3.16 (dd, $J = 7.5, 2.5$ Hz, 1H, OCH), 3.11 (dd, $J = 9.5, 2.5$ Hz, 1H, OCH), 3.04 (dt, $J = 6.5, 4.5$ Hz, 1H, OCH), 2.25 (dt, $J = 11.5, 4.0$ Hz, 1H, C*H*H), 2.19–2.11 (m, 1H, C*H*H), 1.90–1.73 (m, 3H, C*H*H), 1.58 (br s, 1H, OH), 1.41 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.06 (s, 9H, *t*BuSi); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.1, 135.5, 135.3, 133.8, 133.7, 129.6, 129.5, 128.1, 127.6, 127.1, 127.0, 126.9, 119.5, 80.5, 80.0, 73.2, 72.4, 72.3, 68.4, 63.9, 63.5, 58.3, 57.2, 38.6, 34.2, 30.1, 26.9, 19.2$; HRMS, calcd for $C_{37}H_{46}O_6Si$ ($[M + Cs^+]$) 747.2118, found 747.2146.

Alcohol 31: To a solution of hydroxy epoxide **30** (47.5 g, 77.3 mmol) in CH_2Cl_2 (1.5 L) and 4 Å molecular sieves (5 g) was added pyridinium *p*-toluenesulfonate (11.0 g, 43.8 mmol), and the reaction mixture was stirred at 25 °C for 18 h. After concentration, the residue was treated with EtOAc (500 mL) and filtered through celite 545. The filtrate was washed with H_2O (250 mL), 10% aqueous potassium bisulfate solution (250 mL), saturated aqueous $NaHCO_3$ (250 mL) and brine (250 mL). The organic layer was dried ($MgSO_4$) and concentrated to give alcohol **31** (44.8 g). For analytical purposes, a small amount of the crude material was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether). **31**: colorless oil; $R_f = 0.30$ (silica gel, 1:1, EtOAc:hexanes); $[\alpha]_D^{25} = +40.9$ ($c = 2.6$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3431$ (OH), 2934, 2859, 1460, 1427, 1106, 1042, 930, 825, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67–7.63$ (m, 4H, ArH), 7.41–7.22 (m, 11H, ArH), 5.84 (ddd, $J = 17.5, 10.5, 7.0$ Hz, 1H, C*H*=CH_2), 5.45 (d, $J = 17.5$ Hz, 1H, CH=C*H*H), 5.38 (d, $J = 10.5$ Hz, 1H, CH=C*H*H), 4.67 (d, $J = 12.0$ Hz, 1H, OC*H*HPh), 4.58 (d, $J = 12.0$ Hz, 1H, OC*H*HPh), 4.12 (dd, $J = 10.5, 7.5$ Hz, 1H, OCH), 4.00 (q, $J = 7.0$ Hz, 1H, OCH), 3.90–3.86 (m, 2H, OCH), 3.68 (ddd, $J = 11.5, 9.5, 4.5$ Hz, 1H, OCH), 3.55 (dd, $J = 9.0, 7.5$ Hz, 1H, OCH), 3.47–3.42 (m, 1H, OCH), 3.16–3.01 (m, 3H, OCH), 2.44 (dt, $J = 11.5, 4.0$ Hz, 1H, C*H*H), 2.25 (dt, $J = 11.5, 4.0$ Hz, 1H, C*H*H), 2.15 (dt, $J = 14.5, 3.0$ Hz, 1H, C*H*H), 1.84 (ddd, $J = 15.0, 7.5, 3.0$ Hz, 1H, C*H*H), 1.57 (br s, 1H, OH), 1.54 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.43 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.05 (s, 9H, *t*BuSi); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.9, 135.5, 135.3, 133.8, 133.7, 129.6, 129.5, 128.1, 127.6, 127.1, 119.9, 83.8, 80.6, 76.6, 76.1, 73.2, 72.4, 72.1, 68.8, 63.8, 63.7, 37.4, 35.6, 29.9, 26.8, 19.2$.

Diol 32: A solution of crude alcohol **31** (44.8 g) in CH_2Cl_2 (150 mL) and MeOH (450 mL) was treated with ozone at −78 °C until a pale blue color appeared (ca. 1 h). Sodium borohydride (12.0 g, 317.2 mmol) was added in small portions, and the mixture was stirred at 25 °C for 2 h. The reaction mixture was concentrated, and the residue was dissolved in EtOAc (500 mL) and washed with 10% aqueous potassium bisulfate (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL). The solution was dried ($MgSO_4$) and concentrated to afford crude diol **32** (44.7 g) which was used in the next step without further purification. For analytical purposes, a small amount of the crude material was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether). **32**: colorless foam; mp = 80–100 °C; $R_f = 0.27$ (silica gel, 2:1, EtOAc:hexanes); $[\alpha]_D^{25} = +42.1$ ($c = 0.7$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3406$ (OH), 2933, 2860, 1461, 1428, 1108, 1042, 910, 825, 735, 702, 612, 505 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67–7.64$ (m, 4H, ArH), 7.44–7.21 (m, 11H, ArH), 4.67 (d, $J = 12.0$ Hz, 1H, OC*H*HPh), 4.57 (d, $J = 12.0$ Hz, 1H, OC*H*HPh), 4.13 (dd, $J = 10.5, 7.5$ Hz, 1H, OCH), 4.00 (q, $J = 6.5$ Hz, 1H, OCH), 3.89–3.86 (m, 3H, OCH), 3.82–3.78 (m, 1H, OCH), 3.74–3.64 (m, 2H, OCH), 3.23 (dt, $J = 9.0, 4.5$ Hz, 1H, OCH), 3.12 (dd, $J = 9.5, 2.5$ Hz, 1H, OCH), 3.06–2.98 (m, 2H, OCH), 2.45 (br s, 1H, OH), 2.40 (dt, $J = 11.5, 4.5$ Hz, 1H, C*H*H), 2.26 (br s, 1H, OH), 2.20 (dt, $J = 11.5, 4.0$ Hz, 1H, C*H*H), 2.14 (dd, $J = 15.0, 3.5$ Hz, 1H, C*H*H), 1.84 (ddd, $J = 15.0, 7.5, 3.0$ Hz, 1H, C*H*H), 1.53 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.39 (q, $J = 11.5$ Hz, 1H, C*H*H), 1.06 (s, 9H, *t*BuSi); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.8, 135.5, 133.7, 129.6, 129.5, 128.1, 127.6, 127.1, 81.3, 80.5, 76.5, 76.2, 73.2, 72.4, 72.1, 66.3, 63.8, 63.6, 62.7, 38.1, 35.5, 29.8, 26.8, 19.2$; HRMS, calcd for $C_{36}H_{46}O_7Si$ ($[M + Cs^+]$) 751.2067, found 751.2044.

Acetonide 33: A solution of crude diol **32** (44.7 g), 2,2-dimethoxypropane (139 mL, 1.15 mol) and pyridinium *p*-toluenesulfonate (1.0 g, 4.0 mmol) in CH_2Cl_2 (1 L) was stirred at 25 °C for 28 h. The reaction mixture was concentrated, and the residue was dissolved in EtOAc (500 mL) and washed successively with 10% aqueous potassium bisulfate (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL). The organic layer was dried ($MgSO_4$) and concentrated to furnish crude acetonide **33** (47.2 g) which was used in the next step without further purification. For analytical purposes, a small amount of the crude material was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether). **33**: colorless foam; mp = 55–60 °C; $R_f = 0.70$ (silica gel, 2:1, EtOAc:hexanes); $[\alpha]_D^{25} = +39.3$ ($c = 0.6$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2937, 2878, 1461, 1428, 1377, 1270, 1200, 1105, 1026, 860, 826, 738, 702, 612,$

506 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.63$ (m, 4H, ArH), 7.43–7.21 (m, 11H, ArH), 4.65 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.57 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.14–4.11 (m, 1H, OCH), 4.00 (q, $J = 6.5$ Hz, 1H, OCH), 3.94–3.85 (m, 3H, OCH), 3.76–3.61 (m, 3H, OCH), 3.24–3.03 (m, 4H, OCH), 2.25 (dt, $J = 11.5$, 4.0 Hz, 1H, C*H*H), 2.19 (dt, $J = 12.0$, 4.5 Hz, 1H, C*H*H), 2.13 (dd, $J = 15.0$, 3.0 Hz, 1H, C*H*H), 1.86–1.80 (m, 1H, C*H*H), 1.59–1.30 (m, 2H, C*H*H), 1.50 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.06 (s, 9H, *t*BuSi); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.9$, 135.5, 133.6, 129.5, 128.1, 127.6, 127.5, 127.1, 127.0, 99.2, 80.8, 77.2, 76.9, 74.8, 73.2, 72.3, 72.1, 69.3, 63.8, 63.6, 62.6, 35.5, 35.2, 29.9, 29.1, 26.8, 19.2, 19.0; HRMS, calcd for $C_{39}H_{50}O_7Si$ ($[M + Cs^+]$) 791.2380, found 791.2356.

Alcohol 34: A solution of crude acetonide **33** (47.2 g) in THF (500 mL) was treated with TBAF (107.5 mL, 1.0 M solution in THF, 107.5 mmol) at 25 °C for 3 h. The reaction mixture was concentrated, and the residue was dissolved in EtOAc (500 mL) and washed with H_2O (250 mL), 10% aqueous potassium bisulfate solution (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, EtOAc:hexanes, gradient with EtOAc) to provide alcohol **34** (26.3 g, 62.5 mol, 81% from **30**). **34**: colorless oil; $R_f = 0.30$ (silica gel, 2:1, EtOAc:hexanes); $[\alpha]_D^{25} = +53.5$ ($c = 0.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3453$ (OH), 2932, 2879, 1458, 1378, 1270, 1202, 1100, 1061, 1025, 915, 860, 734, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.34-7.26$ (m, 5H, ArH), 4.78 (d, $J = 12.0$ Hz, 1H, OC*H*HPh), 4.61 (d, $J = 12.0$ Hz, 1H, OC*H*HPh), 4.22 (dd, $J = 12.0$, 9.0 Hz, 1H, OCH), 4.05–3.90 (m, 4H, OCH), 3.73–3.63 (m, 2H, OCH), 3.51 (dd, $J = 11.5$, 3.0 Hz, 1H, OCH), 3.27–3.14 (m, 4H, OCH), 2.35–2.27 (m, 3H, C*H*H and OH), 2.01 (ddd, $J = 15.0$, 7.5, 3.0 Hz, 1H, C*H*H), 1.88 (dd, $J = 15.0$, 3.5 Hz, 1H, C*H*H), 1.64–1.36 (m, 2H, C*H*H) 1.51 (s, 3H, CH_3), 1.42 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.5$, 128.3, 127.5, 127.4, 99.3, 80.8, 77.4, 77.0, 74.8, 73.0, 72.9, 71.9, 69.3, 63.5, 63.3, 62.6, 35.5, 35.3, 31.2, 29.1, 19.1; HRMS, calcd for $C_{23}H_{32}O_7$ ($[M + H^+]$) 421.2226, found 421.2242.

Aldehyde 35: To a solution of alcohol **34** (26.3 g, 62.5 mmol), DMSO (150 mL), and Et_3N (45.0 mL, 0.313 mol) in CH_2Cl_2 (150 mL) at 0 °C was added $SO_3 \cdot$pyridine complex (49.8 g, 0.313 mol) in three portions. The reaction mixture was stirred for 1 h, diluted with EtOAc (500 mL), and washed with H_2O (250 mL), 10% aqueous potassium bisulfate (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL). The organic layer was dried ($MgSO_4$) and concentrated to give crude aldehyde **35** (26.2 g) which was used in the next step without further purification. For analytical purposes, a small amount of the crude material was purified by flash column chromatography (silica gel, 1:9, EtOAc:hexanes, gradient with EtOAc). **35**: colorless foam; mp = 190–193 °C; $R_f = 0.65$ (silica gel, 2:1, EtOAc:hexanes); $[\alpha]_D^{25} = +106.0$ ($c = 2.1$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2875$, 1742 (CO), 1453, 1375, 1270, 1203, 1103, 954, 863, 739, 698, 599 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 9.83$ (d, $J = 0.5$ Hz, 1H, CHO), 7.34–7.26 (m, 5H, ArH), 4.57 (s, 2H, OCH_2Ph), 4.16 (ddd, $J = 11.5$, 10.0, 4.5 Hz, 1H, OCH), 4.09 (d, $J = 6.5$ Hz, 1H, OCH), 3.95–3.94 (m, 1H, OCH), 3.92 (dd, $J = 11.0$, 5.5 Hz, 1H, OCH), 3.70 (t, $J = 11.0$ Hz, 1H, OCH), 3.65 (ddd, $J = 11.5$, 9.5, 4.0 Hz, 1H, OCH), 3.27–3.15 (m, 4H, OCH), 2.51 (ddd, $J = 14.5$, 3.5, 1.0 Hz, 1H, C*H*H), 2.47 (dt, $J = 11.5$, 4.5 Hz, 1H, C*H*H), 2.28 (dt, $J = 11.5$, 4.5 Hz, 1H, C*H*H), 1.97 (ddd, $J = 14.0$, 7.0, 1.5 Hz, 1H, C*H*H), 1.61 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.53 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.51 (s, 3H, CH_3), 1.42 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.1$, 128.1, 127.3, 127.1, 99.1, 79.7, 77.3, 76.7, 76.0, 74.7, 71.3, 71.1, 69.1, 66.4, 62.4, 35.2, 35.0, 30.9, 29.0, 18.9; HRMS, calcd for $C_{23}H_{30}O_7$ ($[M + H^+]$) 419.2070, found 419.2086.

***α,β*-Unsaturated ester 36**: A solution of crude aldehyde **35** (26.2 g) in toluene (600 mL) was treated with methyl (triphenylphosphoranylidene)acetate (31.4 g, 93.9 mmol) at 25 °C for 5 h. The reaction mixture was concentrated, and the residue was dissolved in EtOAc (250 mL) and washed with 10% aqueous potassium bisulfate (150 mL), saturated aqueous $NaHCO_3$ (150 mL), and brine (150 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:9, EtOAc:hexanes, gradient with EtOAc) to afford **36** (26.8 g, 56.5 mmol, 90% from **34**). **36**: colorless foam; m.p. = 165–182 °C; $R_f = 0.41$ (silica gel, 1:1 EtOAc:hexanes); $[\alpha]_D^{25} = +64.8$ ($c = 0.9$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2945$, 2880, 1722 (CO), 1439, 1376, 1273, 1176, 1096, 1061, 861, 740, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.31-7.22$ (m, 6H, ArH, C*H*=CHCO$_2$Me), 5.96 (dd, $J = 16.0$, 2.0 Hz, 1H, CH=C*H*CO$_2$Me), 4.73 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.61 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.56–4.52 (m, 1H, OCH), 4.05 (ddd, $J = 11.5$, 9.5, 4.5 Hz, 1H, OCH), 3.98 (d, $J = 2.5$ Hz, 1H, OCH), 3.91 (dd, $J = 11.0$, 5.5 Hz, 1H, OCH), 3.73–3.62 (m, 5H, OCH), 3.25–3.15 (m, 4H, OCH), 2.34 (dt, $J = 11.0$, 4.5 Hz, 1H, C*H*H), 2.27 (dt, $J = 11.5$, 4.5 Hz, 1H, C*H*H), 2.14–2.02 (m, 2H, C*H*H), 1.59 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.52–1.44 (m, 1H, C*H*H) 1.51 (s, 3H, CH_3), 1.42 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 166.6$, 148.8, 138.6, 128.0, 127.0, 126.9, 119.6, 99.1, 80.4, 77.2, 76.7, 74.7, 72.0, 71.9, 70.5, 69.2, 64.0, 62.4, 51.4, 35.1, 34.2, 29.0, 18.9; HRMS, calcd for $C_{26}H_{34}O_8$ ($[M + H^+]$) 475.2332, found 475.2347.

Saturated ester 37: Raney-Nickel W2 (45 g) was washed with methanol and EtOAc and added to a solution of **36** (26.4 g, 55.6 mmol) in EtOAc (1 L). The reaction mixture was stirred under hydrogen atmosphere at 25 °C for 1 h, filtered through celite 545, and concentrated to give crude ester **37** (26.4 g) which was used without further purification in the next step. For analytical purposes, a small amount of the crude material was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether). **37**: colorless foam; m.p. 109–111 °C; $R_f = 0.48$ (silica gel, 1:1, EtOAc:hexanes); $[\alpha]_D^{25} = +53.7$ ($c = 1.1$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2944$, 2878, 1737 (CO), 1454, 1373, 1268, 1200, 1176, 1095, 1065, 1022, 860, 736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.34-7.26$ (m, 5H, ArH), 4.75 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.64 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 3.93–3.82 (m, 4H, OCH), 3.73–3.63 (m, 5H, OCH), 3.28–3.15 (m, 4H, OCH), 2.73–2.65 (m, 1 H C*H*H), 2.37 (t, $J = 7.5$ Hz, 2H, CH_2), 2.31–2.23 (m, 2H, C*H*H), 1.98–1.87 (m, 2H, C*H*H), 1.80–1.71 (m, 1H, C*H*H), 1.62 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.51 (s, 3H, CH_3), 1.48–1.41 (m, 1H, C*H*H), 1.42 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 174.0$, 139.0, 128.2, 127.2, 127.1, 99.2, 80.9, 77.2, 77.0, 74.8, 72.6, 72.3, 71.8, 69.3, 62.6, 62.5, 51.5, 35.5, 35.3, 33.1, 31.4, 29.1, 27.7, 19.0; HRMS, calcd for $C_{26}H_{36}O_8$ ($[M + Cs^+]$) 609.1465, found 609.1484.

Alcohol 38: A solution of crude ester **37** (26.4 g) in ether (500 mL) was treated with lithium aluminum hydride (2.5 g, 65.9 mmol) at 0 °C for 1.5 h. The reaction mixture was poured into a mixture of ice (250 g) and 10% aqueous potassium bisulfate (250 mL) and stirred for 1 h. The organic layer was washed with saturated aqueous $NaHCO_3$ (250 mL) and brine (250 mL). The organic layer was dried ($MgSO_4$) and concentrated to give crude alcohol **38** (23.7 g) which was used in the next step without further purification. For analytical purposes, a small amount of this material was purified by flash column chromatography (silica gel, 1:9, EtOAc:hexanes, gradient with EtOAc). **38**: colorless oil; $R_f = 0.20$ (silica gel, 1:1, EtOAc:hexanes); $[\alpha]_D^{25} = +45.4$ ($c = 1.1$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3452$ (OH), 2940, 1455, 1374, 1273, 1200, 1178, 1105, 1064, 1014, 912, 860, 734, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.32-7.22$ (m, 5H, ArH), 4.69 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.61 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 3.92–3.82 (m, 4H, OCH), 3.67 (t, $J = 10.5$ Hz, 1H, OCH), 3.62 (ddd, $J = 11.5$, 9.5, 4.0 Hz, 1H, OCH), 3.57 (dd, $J = 6.0$, 4.5 Hz, 1H, OCH), 3.23–3.11 (m, 4H, OCH), 2.47 (m, 1H, OCH), 2.27–2.21 (m, 3H, C*H*H), 1.92–1.82 (m, 2H, C*H*H), 1.64–1.39 (m, 6H, C*H*H) 1.47 (s, 3H, CH_3), 1.39 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 138.8$, 128.0, 127.1, 127.0, 99.1, 80.7, 77.1, 76.8, 74.6, 72.6, 72.3, 72.0, 69.1, 62.4, 62.3, 35.3, 35.1, 32.6, 30.0, 29.0, 28.9, 18.9; HRMS, calcd for $C_{25}H_{36}O_7$ ($[M + Cs^+]$) 581.1515, found 581.1531.

TPS-protected alcohol 39: A solution of crude alcohol **38** (23.7 g) and imidazole (17.1 g, 251.2 mmol) in CH_2Cl_2 (500 mL) was treated with TBDPSCl (26 mL, 100.0 mmol) at 25 °C for 4 h. The reaction mixture was concentrated, and the residue was dissolved in EtOAc (250 mL), washed with H_2O (150 mL), 10% aqueous potassium bisulfate (150 mL), saturated aqueous $NaHCO_3$ (150 mL), and brine (150 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:49, ether:hexanes, gradient with ether) to provide TPS-protected alcohol **39** (34.5 g, 50.2 mmol, 90% from **36**). **39**: oil; $R_f = 0.33$ (silica gel, 4:6, ether:hexanes); $[\alpha]_D^{25} = +32.7$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2935$, 2863, 1460, 1428, 1379, 1270, 1200, 1104, 1017, 860, 823, 735, 702, 504 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.65$ (m, 4H, ArH), 7.41–7.25 (m, 11H, ArH), 4.71 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 4.63 (d, $J = 13.0$ Hz, 1H, OC*H*HPh), 3.94–3.86 (m, 3H, OCH), 3.82–3.80 (m, 1H, OCH), 3.74–3.64 (m, 4H, OCH), 3.26–3.13 (m, 4H, OCH), 2.33–2.23 (m, 3H, C*H*H), 1.90–1.89 (m, 2H, C*H*H), 1.67–1.40 (m, 5H, C*H*H), 1.51 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.04 (s, 9H, *t*BuSi); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.1$, 135.5, 134.0, 129.5, 128.2, 128.1, 127.6, 127.5, 127.2, 127.1, 99.2, 80.9, 77.2, 77.1, 76.7, 74.8, 72.8, 72.4, 69.3, 63.7, 62.6, 62.4, 35.6, 35.3, 32.8, 29.8, 29.2, 28.6, 26.8, 19.1; HRMS, calcd for $C_{41}H_{54}O_7Si$ ($[M + Cs^+]$) 819.2693, found 819.2669.

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Diol 40: A solution of **39** (5.8 g, 8.44 mmol) in CH_2Cl_2 (20 mL) and MeOH (380 mL) was treated with pyridinium *p*-toluenesulfonate (0.25 g, 0.99 mmol) at 25 °C for 6 h. The reaction mixture was poured into H_2O (400 mL) and EtOAc (400 mL). The organic layer was separated, washed with 10% aqueous potassium bisulfate (250 mL), saturated aqueous $NaHCO_3$ (250 mL), and brine (250 mL), dried ($MgSO_4$), and concentrated to afford crude diol **40** (5.2 g). **40**: oil; $R_f = 0.39$ (silica gel, 3:97, methanol:ether); $[\alpha]_D^{25} = +30.5$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3400, 3060, 2920, 2860, 1650, 1455, 1420, 1100, 1040, 900, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.20$ (m, 15H, ArH), 4.73 (d, $J =$ 12.5 Hz, 1H, OC*H*HPh), 4.60 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 3.89–3.71 (m, 6H, OCH), 3.68 (t, $J = 6.0$ Hz, 2H, OCH), 3.21 (dt, $J = 9.0$, 4.5 Hz, 1H, OCH), 3.13 (dd, $J = 9.5$, 3.0 Hz, 1H, OCH), 3.08 (dd, $J = 6.5$, 4.0 Hz, 1H, OCH), 3.04 (dd, $J = 9.0$, 4.0 Hz, 1H, OCH), 2.85 (br s, 1H, OH), 2.54 (br s, 1H, OH), 2.41 (dt, $J = 11.5$, 4.5 Hz, 1H, C*H*H), 2.31 (br m, 1H, C*H*H), 2.24 (dt, $J = 11.0$, 4.0 Hz, 1H, C*H*H), 1.88 (d, $J = 3.0$ Hz, 2H, C*H*H), 1.80 (br s, 1H, C*H*H), 1.68–1.53 (m, 3H, C*H*H), 1.42 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.05 (s, 9H, *t*BuSi); HRMS, calcd for $C_{38}H_{50}O_7Si$ ($[M+H^+]$) 647.3404, found 647.3381.

Secondary alcohol 41: A solution of crude diol **40** (5.2 g) in CH_2Cl_2 (30 mL) was treated with imidazole (1.6 g, 23.5 mmol) and TBSCl (1.44 g, 9.6 mmol) at 0 °C for 4.5 h. The solvent was evaporated, and the residue was dissolved in EtOAc (50 mL) and washed with H_2O (25 mL), 10% aqueous potassium bisulfate (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and brine (25 mL). The organic layer was dried ($MgSO_4$) and concentrated to give crude secondary alcohol **41** (6.3 g). **41**: oil; $R_f = 0.47$ (silica gel, 1:1, ether:-hexanes); $[\alpha]_D^{25} = +14.6$ ($c = 1.1$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3450, 3080, 2920, 2860, 1450, 1250, 1110, 1090, 1040, 840, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.20$ (m, 15H, ArH), 4.74 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.60 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 3.97 (dd, $J = 10.0$, 4.5 Hz, 1H, OCH), 3.92 (d, $J = 3.0$ Hz, 1H, OH), 3.88 (dt, $J = 11.0$, 4.5 Hz, 1H, OCH), 3.82–3.74 (m, 3H, OCH), 3.71 (d, $J = 1.5$ Hz, 1H, OCH), 3.68 (t, $J = 5.5$ Hz, 2H, OCH), 3.63 (d, $J = 2.0$ Hz, 1H, OCH), 3.28 (dt, $J = 8.5$, 4.5 Hz, 1H, OCH), 3.14 (dd, $J = 9.5$, 3.0 Hz, 1H, OCH), 3.07 (m, 1H, OCH), 2.42 (dt, $J = 11.5$, 4.5 Hz, 1H, C*H*H), 2.33 (m, 1H, C*H*H), 2.21 (dt, $J = 11.0$, 3.5 Hz, 1H, C*H*H), 1.88 (t, $J = 3.5$ Hz, 2H, C*H*H), 1.53–1.68 (m, 4H, C*H*H), 1.39 (q, $J = 11.0$ Hz, 1H, C*H*H), 1.04 (s, 9H, *t*BuSi), 0.91 (s, 9H, *t*BuSi), 0.11 (s, 3H, CH_3), 0.11 (s, 3H, CH_3); HRMS, calcd for $C_{44}H_{64}O_7Si_2$ ($[M-t\mathrm{Bu}^-$) 703.3486, found 703.3448.

Dithioketal 43: To a solution of alcohol **41** (6.3 g) in CH_2Cl_2 (100 mL) at 0 °C was added 4 Å molecular sieves (2 g), TPAP (0.3 g, 0.85 mmol), and NMO (1.5 g, 12.8 mmol). The reaction mixture was stirred at 0 °C for 2 h and filtered through celite 545. The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:9, ether:hexanes, gradient with ether) to afford ketone **42** (5.42 g, 85% for three steps). A solution of ketone **42** (4.9 g, 6.46 mmol) in CH_2Cl_2 (50 mL) was treated with EtSH (1.2 mL, 16.1 mmol) and $BF_3 \cdot Et_2O$ (1.0 mL, 7.75 mmol) at −78 °C. The reaction mixture was warmed to 0 °C over 1.5 h and diluted with EtOAc (200 mL). The solution was washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 4:6, ether:hexanes) to afford dithioketal **43** (4.56 g, 94%). **43**: oil; $R_f = 0.50$ (silica gel, 1:1, ether:-hexanes); $[\alpha]_D^{25} = +33.8$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3450, 3080, 2960, 2920, 2860, 1490, 1440, 1430, 1100, 910, 840, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.20$ (m, 15H, ArH), 4.70 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.59 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 3.99 (dd, $J = 10.0$, 10.0 Hz, 1H, OCH), 3.89 (d, $J = 3.0$ Hz, 1H, OCH), 3.86 (dt, $J = 11.0$, 4.5 Hz, 1H, OCH), 3.79–3.71 (m, 3H, OCH), 3.67 (t, $J = 6.0$ Hz, 2H, OCH), 3.60 (dt, $J = 11.0$, 4.0 Hz, 1H, OCH), 3.18 (dd, $J = 9.5$, 2.5 Hz, 1H, OCH), 3.12 (dt, $J = 12.0$, 4.0 Hz, 1H, OCH), 2.69–2.61 (m, 4H, CH_2S), 2.44 (dd, J = 13.0, 4.0 Hz, 1H, C*H*H), 2.26 (m, 2H, C*H*H), 2.17 (d, $J = 8.5$ Hz, 1H, C*H*H), 1.87 (m, 2H, C*H*H), 1.66–1.52 (m, 4H, C*H*H), 1.24 (t, $J = 7.0$ Hz, 6H, CH_3CH_2S), 1.03 (s, 9H, *t*BuSi); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 139.1, 135.5, 134.0, 129.5, 128.1, 127.5, 127.1, 96.1, 85.4, 80.9, 77.7, 74.9, 73.0, 72.3, 63.7, 62.5, 62.1, 59.7, 40.3, 35.4, 32.7, 29.9, 28.6, 26.8, 23.8, 23.2, 19.2, 14.2, 13.8; HRMS, calcd for $C_{42}H_{58}O_6S_2Si$ ($[M+H^+]$) 751.3522, found 751.3549.

Aldehyde 7: A solution of alcohol **43** (2.16 g, 2.87 mmol) in CH_2Cl_2 (14 mL) was treated with DMSO (14 mL), Et_3N (2.0 mL, 14.3 mmol), and $SO_3 \cdot$ pyridine complex (2.28 g, 14.3 mmol) at 0 °C for 1 h. The mixture was diluted with EtOAc (500 mL) and washed with H_2O (250 mL) and brine (250 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 3:1, ether:hexanes) to afford aldehyde **7** (1.95 g, 91%). **7**: $R_f = 0.30$ (silica gel, 3:7, ether:hexanes); $[\alpha]_D^{25} = +40.2$ ($c = 2.1$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3080, 3020, 2960, 2620, 2850, 2720, 1740, 1590, 1440, 1430, 1100, 910, 820, 740, 710 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) $\delta = 9.98$ (d, $J = 1.5$ Hz, 1H, CHO), 7.70–7.20 (m, 15H, ArH), 4.68 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.58 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.04 (d, $J = 1.5$ Hz, 1H, OCH), 3.89 (d, $J =$ 3.0 Hz, 1H, OCH), 3.85 (dt, $J = 11.0$, 4.5 Hz, 1H, OCH), 3.82–3.71 (m, 1H, OCH), 3.66 (t, $J = 6.0$ Hz, 2H, OCH), 3.64–3.61 (m, 1H, OCH), 3.19 (dd, $J = 9.5$, 3.0 Hz, OCH), 3.14–3.08 (m, 1H, OCH), 2.72–2.62 (m, 4H, CH_2S), 2.45 (dd, $J = 13.0$, 4.0 Hz, 1H, C*H*H), 2.28 (m, 2H, C*H*H), 1.91 (dd, $J = 13.0$, 11.0 Hz, 1H, C*H*H), 1.87 (t, $J = 2.5$ Hz, 2H, CH_2), 1.70–1.50 (m, 4H, C*H*H), 1.25 (t, $J = 7.5$ Hz, 3H, CH_3), 1.24 (t, $J = 7.5$ Hz, 3H, CH_3), 1.02 (s, 9H, *t*BuSi); HRMS calcd for $C_{42}H_{56}O_6S_2Si$ ($[M+H^+]$) 749.3366, found 749.3315.

Olefin 44: A solution of phosphonium salt **5** (18.1 g, 0.025 mol) in THF (600 mL) was treated dropwise with *n*-butyllithium (16 mL, 1.6 M in hexanes, 0.026 mol) at −78 °C and stirred for 20 min. After addition of HMPA (46 mL, 0.257 mol), and a solution of aldehyde **7** (16 g, 0.022 mol) in THF (200 mL) at −78 °C, the mixture was stirred at −78 °C for 30 min, and then at 25 °C for 1 h. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (300 mL) and extracted with EtOAc (3 × 100 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to give olefin **44** (19.8 g, 88%). **44**: oil; $R_f = 0.75$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = -4.1$ ($c = 1.1$, CH_2Cl_2); IR (film) $\tilde{\nu}_{max} =$ 2955, 2929, 2856, 1456, 1428, 1389, 1360, 1259, 1106, 1049, 838, 778, 735, 700, 613, 505 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.68-7.66$ (m, 4H, ArH), 7.49–7.26 (m, 16H, ArH), 5.98–5.92 (m, 1H, CH=C*H*–CH_2), 5.73 (dd, $J = 9.0$, 8.5 Hz, 1H, CH–C*H*=CH), 5.48 (s, 1H, PhCH), 4.74 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.63 (d, $J = 12.5$ Hz, 1H, OC*H*HPh), 4.40 (d, $J = 8.5$ Hz, 1 H OCH), 4.19 (d, $J = 6.0$ Hz, 1H, OCH), 3.94–3.80 (m, 3H, OCH), 3.69–3.56 (m, 5H, OCH), 3.22 (dd, $J = 9.5$, 2.5 Hz, 1H, OCH), 3.17 (ddd, $J = 11.5$, 9.0, 4.0 Hz, 1H, OCH), 2.97 (dd, $J = 15.0$, 8.5 Hz, 1H, OCH), 2.71–2.58 (m, 4H, CH_2S), 2.48 (dd, $J = 13.0$, 4.0 Hz, 1H, C*H*H), 2.35–2.26 (m, 3H, C*H*H), 1.91 (s, 2H, C*H*H), 1.77 (dd, $J = 13.0$, 11.0 Hz, 1H, C*H*H), 1.69–1.56 (m, 5H, C*H*H), 1.28 (t, $J = 7.5$ Hz, 3H, $C(SCH_2CH_3)_2$), 1.09 (t, $J = 7.5$ Hz, 3H, $C(SCH_2CH_3)_2$), 1.06 (s, 9H, *t*BuSi), 0.91 (s, 9H, *t*BuSi), 0.15 (s, 3H; CH_3Si), 0.10 (s, 3H; CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 137.8, 135.5, 134.0, 132.0, 129.5, 128.7, 128.2, 128.1, 127.6, 127.2, 127.1, 127.0, 126.0, 100.8, 82.3, 81.8, 81.0, 77.6, 74.8, 73.1, 72.3, 71.6, 66.9, 63.7, 62.8, 62.7, 40.9, 35.6, 32.7, 30.7, 29.8, 28.7, 26.8, 25.7, 23.4, 22.6, 19.2, 17.9, 14.0, 13.8, −4.2, −4.7; HRMS, calcd for $C_{60}H_{84}O_8S_2Si_2$ ($[M+Cs^+]$) 1185.4201, found 1185.4249.

Hydroxy dithioketal 45: A solution of dithioketal **44** (10 g, 9.5 mmol) in THF (100 mL) was treated with TBAF (10.5 mL of 1.0 M in THF, 10.5 mmol) and stirred at 25 °C for 7 h. After addition of a saturated aqueous NH_4Cl solution (100 mL), the mixture was extracted with EtOAc (4 × 100 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 3:7, EtOAc:hexanes) to afford hydroxy dithioketal **45** (7.38 g, 83%). **45**: $R_f = 0.54$ (silica gel, 3:7, EtOAc:hexanes); $[\alpha]_D^{25} = +30.1$ ($c = 3.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} =$ 3447, 2929, 1097, 734, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.72-7.65$ (m, 4H, ArH), 7.52–7.24 (m, 16H, ArH), 6.04–5.98 (m, 1H, =CH), 5.85 (dd, $J = 11.0$, 8.0 Hz, 1H, =CH), 5.49 (s, 1H, PhCH), 4.73 (d, $J = 12.5$ Hz, 1H, PhC*H*HO), 4.64 (d, $J =$ 12.5 Hz, 1H, PhC*H*HO), 4.47 (d, $J = 8.0$ Hz, 1H), 4.24 (dd, $J = 11.0$, 4.0 Hz, 1H), 3.96–3.89 (m, 2H), 3.85–3.79 (m, 1H), 3.74–3.64 (m, 5H), 3.62–3.56 (m, 1H), 3.27 (ddd, $J = 12.0$, 8.0, 4.0 Hz, 1H), 3.21 (dd, $J = 9.5$, 2.5 Hz, 1H), 3.04 (d, $J = 4.0$ Hz, 1H), 2.83–2.75 (m, 1H), 2.72–2.61 (m, 6H), 2.51 (dd, $J = 13.0$, 4.0 Hz, 1H), 2.37–2.26 (m, 2H), 1.91 (br s, 2H), 1.86–1.79 (m, 1H), 1.72–1.55 (m, 3H), 1.30 (t, $J = 7.5$ Hz, 3H), 1.19 (t, $J =$ 7.5 Hz, 3H), 1.06 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 139.1, 137.7, 135.5, 134.0, 133.9, 132.6, 129.4, 129.2, 128.8, 128.1, 127.5, 127.1, 127.0, 126.5, 126.0, 100.9, 81.4, 80.9, 80.8, 77.7, 74.5, 73.0, 72.2, 72.2, 70.6, 66.3, 63.6, 62.5, 62.0, 40.4, 35.4, 32.6, 32.5, 29.7, 28.6, 26.8, 23.7, 22.6, 19.1, 13.8, 13.7; HRMS (FAB) calcd for $C_{54}H_{70}O_8S_2Si$ ($[M+Cs^+]$) 1071.3336, found 1071.3377.

Mixed thioketal 46: A heterogeneous mixture of hydroxy dithioketal **45** (5.7 g, 6.1 mmol), powdered 4 Å molecular sieves (freshly activated, 5.0 g), silica gel (dried under vacuum, 5.0 g), sodium bicarbonate (dried under

vacuum, 5.2 g, 61 mmol), and silver perchlorate (2.5 g, 12.2 mmol) in dry CH_3NO_2 (distilled from CaH_2, 200 mL) was stirred vigorously at 25 °C for 3 h. After addition of Et_3N (20 mL), the mixture was diluted with ether (300 mL) and filtered through a pad of celite. The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to afford mixed thioketal **46** (4.94 g, 92 %). **46**: $R_f = 0.62$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +134.3$ ($c = 1.5$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2930$, 2856, 1455, 1385, 1111, 735, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.74-7.65$ (m, 4H, ArH), 7.57–7.25 (m, 16H, ArH), 6.00 (ddd, $J = 10.5$, 10.5, 7.0 Hz, 1H, =CH), 5.78 (dd, $J = 10.5$, 7.0 Hz, 1H, =CH), 5.46 (s, 1H, PhCH), 4.76 (d, $J = 12.5$ Hz, 1H, PhC*H*HO), 4.69 (ddd, $J = 9.5$, 9.5, 5.0 Hz, 1H), 4.65 (d, $J = 12.5$ Hz, 1H, PhC*H*HO), 4.18 (d, $J = 7.0$ Hz, 1H), 4.05–4.00 (m, 1H), 4.01 (dd, $J = 10.5$, 5.0 Hz, 1H), 3.95 (br d, $J = 2.5$ Hz, 1H), 3.91 (ddd, $J = 10.0$, 10.0, 4.5 Hz, 1H), 3.88–3.82 (m, 1H), 3.72 (dd, $J = 6.0$, 6.0 Hz, 2H), 3.62 (dd, $J = 10.5$, 10.5 Hz, 1H), 3.57 (ddd, $J = 12.5$, 8.5, 4.0 Hz, 1H), 3.23 (dd, $J = 9.5$, 2.5 Hz, 1H), 3.17 (ddd, $J = 12.5$, 8.5, 4.0 Hz, 1H), 2.82 (ddd, $J = 15.0$, 9.0, 6.0 Hz, 1H), 2.69–2.60 (m, 1H), 2.56–2.47 (m, 3H), 2.40–2.34 (m, 1H), 2.30 (ddd, $J = 11.0$, 4.0, 4.0 Hz, 1H), 1.93 (br s, 2H), 1.81 (dd, $J = 12.0$, 12.0 Hz, 1H), 1.71–1.58 (m, 4H), 1.32 (t, $J = 7.5$ Hz, 3H), 1.08 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta =$ 139.1, 137.5, 135.5, 134.0, 133.9, 131.4, 129.4, 129.3, 129.1, 128.9, 128.2, 128.1, 127.5, 127.1, 127.0, 126.1, 101.5, 91.2, 83.4, 81.8, 80.8, 77.6, 75.5, 73.0, 72.3, 72.2, 69.9, 64.0, 63.7, 62.6, 40.6, 35.4, 32.8, 30.7, 29.8, 28.6, 26.8, 20.7, 19.2, 14.1; HRMS (FAB) calcd for $C_{52}H_{64}O_8SSi$ ($[M + Cs^+]$) 1009.3146, found 1009.3179.

Sulfone 47: A heterogeneous mixture of mixed thioketal **46** (3.5 g, 4.0 mmol) and sodium bicarbonate (1.0 g, 12 mmol) in CH_2Cl_2 (200 mL) was treated with *m*CPBA (2.5 g of 50–60 %, 8.0 mmol) and stirred at 0 °C for 2 h. After addition of dimethyl sulfide (0.2 mL), the mixture was washed with a saturated aqueous NH_4Cl solution (20 mL). The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 3:7, EtOAc:hexanes) to afford sulfone **47** (3.41 g, 94 %). **47**: $R_f = 0.35$ (silica gel, 3:7, EtOAc:hexanes); $[\alpha]_D^{25} = +100.8$ ($c = 4.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2931$, 2857, 1455, 1305, 1097, 909, 734, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.72-7.65$ (m, 4H, ArH), 7.52–7.25 (m, 16H, ArH), 6.22 (dd, $J = 10.0$, 8.0 Hz, 1H, =CH), 6.08 (ddd, $J = 10.0$, 10.0, 8.0 Hz, 1H, =CH), 5.42 (s, 1H, PhCH), 5.16 (ddd, $J = 9.5$, 9.5, 5.0 Hz, 1H), 4.73 (d, $J = 13.0$ Hz, 1H, PhC*H*HO), 4.64 (d, $J = 13.0$ Hz, 1H, PhC*H*HO), 4.43 (d, $J = 8.0$ Hz, 1H), 4.27 (dd, $J = 10.5$, 5.0 Hz, 1H), 3.95–3.91 (m, 3H), 3.89–3.82 (m, 2H), 3.72 (dd, $J = 6.0$, 6.0 Hz, 2H), 3.64 (dd, $J = 10.0$, 10.0 Hz, 1H), 3.26 (dd, $J = 10.0$, 2.5 Hz, 1H), 3.23–3.12 (m, 3H), 2.84 (ddd, $J = 15.0$, 7.0, 7.0 Hz, 1H), 2.64 (dd, $J = 14.0$, 4.5 Hz, 1H), 2.56 (dd, $J = 15.0$, 7.5 Hz, 1H), 2.40–2.31 (m, 2H), 1.94–1.88 (m, 3H), 1.74–1.56 (m, 4H), 1.47 (t, $J = 7.5$ Hz, 3H), 1.07 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.0$, 137.2, 135.5, 134.0, 133.9, 131.1, 129.5, 129.4, 129.0, 129.0, 128.2, 128.2, 127.5, 127.2, 127.0, 126.2, 101.4, 94.2, 82.6, 81.2, 80.9, 78.4, 74.0, 72.9, 72.3, 72.1, 69.1, 67.2, 63.6, 62.6, 45.6, 39.7, 35.2, 32.6, 31.2, 29.8, 28.5, 26.8, 19.2; HRMS (FAB) calcd for $C_{52}H_{64}O_{10}SSi$ ($[M + Cs^+]$) 1041.3044, found 1041.3076.

Benzylidene ketal 48: A solution of sulfone **47** (3.0 g, 3.3 mmol) in CH_2Cl_2 (100 mL) was treated with $AlMe_3$ (5.0 mL, 2.0 M in toluene, 10.0 mmol) at −78 °C and stirred for 1 h. The reaction mixture was quenched with MeOH (10 mL) at −78 °C and warmed up to 25 °C over a period of 20 min. After addition of a saturated sodium potassium tartrate solution (50 mL), the mixture was stirred at 25 °C for 2 h and extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 3:7, EtOAc:hexanes) to afford compound **48** (2.58 g, 94 %). **48**: $R_f = 0.75$ (silica gel, 4:6, EtOAc:hexanes); $[\alpha]_D^{25} = +93.8$ ($c = 2.9$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2930$, 2856, 1380, 1090, 909, 734, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.63$ (m, 4H, ArH), 7.52–7.23 (m, 16H, ArH), 5.95 (ddd, $J = 10.5$, 10.5, 7.0 Hz, 1H, =CH), 5.79 (dd, $J = 10.5$, 7.0 Hz, 1H, =CH), 5.44 (s, 1H, PhCH), 4.73 (d, $J = 12.5$ Hz, 1H, PhC*H*HO), 4.64 (d, $J = 12.5$ Hz, 1H, PhC*H*HO), 4.04–4.01 (m, 2H), 3.98–3.86 (m, 4H), 3.86–3.80 (m, 1H), 3.71–3.68 (m, 2H), 3.62 (dd, $J = 10.0$, 10.0 Hz, 1H), 3.25–3.16 (m, 2H), 3.13–3.05 (m, 1H), 2.89–2.80 (m, 1H), 2.46 (dd, $J = 14.0$, 7.0 Hz, 1H), 2.37–2.27 (m, 2H), 2.12 (dd, $J = 12.0$, 4.5 Hz, 1H), 1.91 (br s, 2H), 1.73–1.56 (m, 4H), 1.48 (ddd, $J = 11.5$, 11.5, 11.5 Hz, 1H), 1.34 (s, 3H), 1.06 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.1$, 137.5, 135.4, 133.9, 133.9, 132.7, 129.4, 128.9, 128.3, 128.2, 128.1, 127.5, 127.1, 127.0, 126.0, 101.4, 83.6, 81.7, 80.9, 77.4, 77.2, 76.7, 76.4, 72.8, 72.3, 72.1, 70.5, 63.6, 62.5, 44.1, 35.5, 32.8, 30.5, 29.8, 28.6, 26.8, 19.1, 17.2; HRMS (FAB) calcd for $C_{51}H_{62}O_8Si$ ($[M + Cs^+]$) 963.3268, found 963.3235.

Diol 49: A heterogeneous mixture of benzylidene ketal **48** (12.2 g, 15 mmol), EtSH (5 mL, 67.5 mmol), $NaHCO_3$ (2 g, 24.0 mmol), and $Zn(OTf)_2$ (0.5 g, 1.4 mmol) in CH_2Cl_2 (50 mL) was stirred at 25 °C for 4 h. The reaction mixture was concentrated, and the residue was purified by flash column chromatography (silica gel, 3:1, EtOAc:hexanes) to give diol **49** (10.0 g, 92 %). **49**: $R_f = 0.25$ (silica gel, 3:1, EtOAc:hexanes); $[\alpha]_D^{25} = +84.9$ ($c = 3.4$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3410$, 2933, 2863, 1101, 1039, 734, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.61$ (m, 4H, ArH), 7.45–7.22 (m, 11H, ArH), 5.96–5.88 (m, 1H, =CH), 5.74 (dd, $J = 11.0$, 6.0 Hz, 1H, =CH), 4.73 (d, $J = 13.0$ Hz, 1H, PhC*H*HO), 4.61 (d, $J = 13.0$ Hz, 1H, PhC*H*HO), 4.06–4.04 (m, 2H), 3.93–3.90 (m, 1H), 3.88 (ddd, $J = 11.0$, 11.0, 4.5 Hz, 1H), 3.85–3.78 (m, 1H), 3.71–3.64 (m, 6H), 3.24–3.17 (m, 1H), 3.17 (dd, $J = 9.5$, 2.5 Hz, 1H), 3.12–3.05 (m, 1H), 2.73–2.65 (m, 1H), 2.50 (d, $J = 4.5$ Hz, 1H), 2.36–2.24 (m, 4H), 2.11 (dd, $J = 12.0$, 4.5 Hz, 1H), 1.89 (dd, $J = 3.0$, 3.0 Hz, 2H), 1.73 (dd, $J = 12.0$, 12.0 Hz, 1H), 1.69–1.53 (m, 2H), 1.47 (ddd, $J = 11.5$, 11.5, 11.5 Hz, 1H), 1.29 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.1$, 135.4, 134.0, 133.9, 132.4, 129.4, 128.1, 127.7, 127.5, 127.1, 127.0, 81.9, 80.9, 77.7, 77.4, 76.6, 74.7, 72.8, 72.3, 72.2, 71.7, 65.0, 63.6, 62.5, 44.4, 35.6, 32.8, 29.8, 28.6, 26.8, 19.1, 17.0; HRMS (FAB) calcd for $C_{44}H_{58}O_8Si$ ($[M + Cs^+]$) 875.2955, found 875.2979.

TBS-protected alcohol 50: A solution of diol **49** (10.0 g, 13.5 mmol) in CH_2Cl_2 (200 mL) was treated with imidazole (1.2 g, 17.5 mmol) and TBSCl (2.14 g, 14.2 mmol) and stirred at 25 °C for 1 h. After addition of a saturated aqueous NH_4Cl solution (50 mL), the mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 4:6, EtOAc:hexanes) to provide TBS-protected alcohol **50** (10.67 g, 92 %). **50**: $R_f = 0.72$ (silica gel, 4:6, EtOAc:hexanes); $[\alpha]_D^{25} = +74.1$ ($c = 3.8$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3459$, 2933, 2860, 1463, 1254, 1106, 836, 702, 505; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.71-7.64$ (m, 4H, ArH), 7.45–7.22 (m, 11H, ArH), 5.96 (ddd, $J = 11.0$, 11.0, 6.0 Hz, 1H, =CH), 5.73 (dd, $J = 11.0$, 6.0 Hz, 1H, =CH), 4.74 (d, $J = 12.5$ Hz, 1H, C*H*HOPh), 4.62 (d, $J = 12.5$ Hz, 1H, C*H*HOPh), 4.05 (br d, $J = 5.5$ Hz, 1H), 4.04–3.99 (m, 1H), 3.95–3.86 (m, 2H), 3.85–3.80 (m, 1H), 3.73–3.63 (m, 4H), 3.63–3.57 (m, 1H), 3.46 (br s, 1H), 3.25–3.15 (m, 2H), 3.13–3.05 (m, 1H), 2.66 (dd, $J = 11.0$, 11.0 Hz, 1H), 2.38–2.25 (m, 4H), 2.09 (dd, $J = 12.0$, 4.5 Hz, 1H), 1.90 (br s, 2H), 1.75–1.55 (m, 3H), 1.48 (ddd, $J = 11.5$, 11.5, 11.5 Hz, 1H), 1.29 (s, 3H), 1.06 (s, 9H), 0.93 (s, 9H);); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 139.1$, 135.4, 134.0. 133.9, 131.6, 129.4, 128.5, 128.1, 127.5, 127.0, 127.0, 82.0, 80.9, 77.7, 77.6, 77.4, 76.7, 72.8, 72.3, 72.2, 70.6, 67.5, 63.6, 62.6, 44.3, 35.6, 32.8, 32.0, 29.8, 28.6, 26.8, 25.8, 19.1, 18.1, 16.7, −5.6, −5.8; HRMS (FAB) calcd for $C_{50}H_{72}O_8Si_2$ ($[M + Cs^+]$) 989.3820, found 989.3859.

Acetate 51: A solution of secondary alcohol **50** (10.5 g, 12.3 mmol), 4-DMAP (0.26 g, 2.11 mmol) and Et_3N (2.1 mL, 15 mmol) in CH_2Cl_2 (200 mL) was treated with acetic anhydride (1.27 mL, 13.5 mmol) and stirred at 25 °C for 2 h. After addition of a saturated aqueous $NaHCO_3$ solution (30 mL), the mixture was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 3:7, EtOAc:hexanes) to afford acetate **51** (10.5 g, 95 %). **51**: $R_f = 0.73$ (silica gel, 3:7, EtOAc:hexanes); $[\alpha]_D^{25} = +94.5$ ($c = 2.9$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2933$, 2859, 1740, 1236, 1105, 1035, 838, 734 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.72-7.62$ (m, 4H, ArH), 7.45–7.22 (m, 11H, ArH), 5.75 (br s, 2H), 4.93 (d, $J = 9.0$ Hz, 1H), 4.74 (d, $J = 12.5$ Hz, 1H), 4.61 (d, $J = 12.5$ Hz, 1H), 4.05 (br s, 1H), 3.97–3.86 (m, 2H), 3.81 (br m, 2H), 3.68 (br m, 2H), 3.54–3.39 (m, 2H), 3.27–3.04 (m, 3H), 2.71–2.62 (m, 1H), 2.39–2.23 (m, 3H), 2.20–2.13 (m, 1H), 2.05 (s, 3H, CO_2CH_3), 1.90 (br s, 2H), 1.78–1.53 (m, 5H), 1.47 (ddd, $J = 11.0$, 11.0, 11.0 Hz, 1H), 1.32 (s, 3H), 1.22 (dd, $J = 7.0$, 7.0 Hz, 1H), 1.04 (s, 9H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 170.0$, 139.1, 135.4, 134.0, 133.9, 133.1, 129.4, 128.1, 127.5, 127.0, 127.0, 126.7, 82.2, 80.9, 77.9, 77.3, 76.8, 75.6, 72.9, 72.3, 72.2, 71.8, 65.2, 63.6, 62.5, 44.1, 35.6, 32.9, 29.8, 29.3, 28.6, 26.8, 25.9, 21.1, 19.1, 18.3, 17.2, −5.3, −5.6; HRMS (FAB) calcd for $C_{52}H_{74}O_9Si_2$ ($[M + Cs^+]$) 1031.3926, found 1031.3973.

TBS-protected secondary alcohol 53: A heterogeneous mixture of acetate **51** (10.0 g, 11.1 mmol) and $Pd(OH)_2$ (20 % w/w on carbon, 2.0 g) in acetic acid (200 mL) was stirred vigorously under hydrogen atmosphere at 25 °C

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for 48 h. The reaction mixture was concentrated, and the residue was filtered through a pad of celite and washed with EtOAc. The filtrate was concentrated to provide crude secondary alcohol **52**. A solution of crude secondary alcohol **52** in CH_2Cl_2 (220 mL) was treated with 2,6-lutidine (2.8 mL, 24.0 mmol) and TBSOTf (5.3 mL, 23.0 mmol) at 0 °C for 30 min. After addition of a saturated aqueous NH_4Cl solution (50 mL), the mixture was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:4, ether:hexanes) to afford TBS-protected secondary alcohol **53** (8.95 g, 87% for two steps). **53**: $R_f = 0.53$ (silica gel, 1:3, ether:hexanes); $[\alpha]_D^{25} = +54.6$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2933, 2858, 1739, 1380, 1246, 1102, 777\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.63$ (m, 4H, ArH), 7.45–7.34 (m, 6H, ArH), 4.69 (dd, $J = 7.5, 7.5$ Hz, 1H), 4.14 (br d, $J = 2.5$ Hz, 1H), 3.91 (ddd, $J = 7.0, 7.0, 2.0$ Hz, 1H), 3.83–3.73 (m, 2H), 3.67 (dd, $J = 6.0, 6.0$ Hz, 2H), 3.49 (dd, $J = 10.5, 2.0$ Hz, 1H), 3.38 (dd, $J = 10.5, 8.0$ Hz, 1H), 3.25 (d, $J = 9.0$ Hz, 1H), 3.20 (ddd, $J = 12.5, 8.5, 4.5$ Hz, 1H), 3.05–2.95 (m, 2H), 2.29 (ddd, $J = 9.5, 9.5, 9.5$ Hz, 1H), 2.22 (ddd, $J = 10.5, 4.0, 4.0$ Hz, 1H), 2.14 (dd, $J = 12.0, 4.0$ Hz, 1H), 2.09–1.93 (m, 3H), 2.04 (s, 3H), 1.83–1.53 (m, 9H), 1.43 (ddd, $J = 11.5, 11.5, 11.5$ Hz, 1H), 1.32 (s, 3H), 1.05 (s, 9H), 0.90 (s, 9H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 170.1, 135.4, 134.0, 129.4, 127.5, 83.8, 80.1, 78.3, 76.7, 76.2, 73.4, 73.1, 72.6, 66.9, 66.0, 63.7, 61.9, 44.6, 35.6, 30.0, 29.0, 28.2, 27.3, 26.8, 25.9, 25.8, 25.5, 21.1, 20.0, 19.1, 18.4, 18.1, 16.9, −3.7, −4.3, −5.3, −5.6$; HRMS (FAB) calcd for $C_{51}H_{84}O_9Si_3$ ($[M + Cs^+]$) 1057.4478, found 1057.4515.

Secondary alcohol 54: A solution of acetate **53** (6.5 g, 7.0 mmol) in MeOH (25 mL) was treated with K_2CO_3 (0.5 g) and stirred at 25 °C for 4 h. The reaction mixture was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:4, EtOAc:hexanes) to afford secondary alcohol **54** (5.8 g, 93%). **54**: $R_f = 0.62$ (silica gel, 1:4, EtOAc:hexanes); $[\alpha]_D^{25} = +53.6$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 3473, 2933, 2859, 1465, 1102, 836, 780, 505\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.73-7.65$ (m, 4H, ArH), 7.45–7.33 (m, 6H, ArH), 4.13 (br d, $J = 2.5$ Hz, 1H), 3.82–3.72 (m, 4H), 3.70–3.64 (m, 3H), 3.55–3.50 (m, 1H), 3.32 (s, 1H), 3.27 (d, $J = 9.0$ Hz, 1H), 3.22–3.15 (m, 1H), 3.03–2.95 (m, 2H), 2.29 (ddd, $J = 9.5, 9.5, 9.5$ Hz, 1H), 2.23 (ddd, $J = 11.0, 4.5, 4.5$ Hz, 1H), 2.05 (dd, $J = 12.0, 4.0$ Hz, 1H), 2.02–1.84 (m, 4H), 1.78–1.50 (m, 8H), 1.42 (ddd, $J = 11.0, 11.0, 11.0$ Hz, 1H), 1.30 (s, 3H), 1.05 (s, 9H), 0.92 (s, 9H), 0.87 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 135.4, 134.0, 129.4, 127.5, 83.5, 80.1, 78.3, 76.6, 75.9, 74.4, 72.6, 72.3, 68.2, 66.9, 63.7, 61.9, 44.8, 35.7, 35.6, 30.0, 29.6, 29.0, 28.3, 27.3, 26.8, 25.8, 25.6, 19.1, 18.1, 16.4, −4.3, −5.3, −5.6, −5.8$; HRMS (FAB) calcd for $C_{49}H_{82}O_8Si_3$ ($[M + Cs^+]$) 1015.4372, found 1015.4411.

Ketone 55: Secondary alcohol **54** (2.9 g, 3.3 mmol) was dissolved in CH_2Cl_2 (100 mL) and treated with NMO (0.77 g, 6.6 mmol) and TPAP (60 mg, 0.17 mmol) at 25 °C for 1 h. The reaction mixture was filtered through a pad of silica gel. The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:3, EtOAc:hexanes) to provide ketone **55** (2.78g, 94%). **55**: $R_f = 0.64$ (silica gel, 1:3, EtOAc:hexanes); $[\alpha]_D^{25} = +56.8$ ($c = 0.2$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2932, 1713, 1463, 1250, 1104, 835\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.70-7.63$ (m, 4H, ArH), 7.45–7.32 (m, 6H, ArH), 4.15 (br d, $J = 2.5$ Hz, 1H), 4.02 (dd, $J = 5.0, 3.5$ Hz, 1H), 3.90–3.70 (m, 3H), 3.68 (dd, $J = 6.0, 6.0$ Hz, 2H), 3.39 (dd, $J = 5.0, 3.5$ Hz, 1H), 3.30 (ddd, $J = 10.5, 8.5, 8.5$ Hz, 1H), 3.19 (ddd, $J = 11.5, 8.0, 4.0$ Hz, 1H), 3.07–2.98 (m, 1H), 3.01 (dd, $J = 9.0, 3.0$ Hz, 1H), 2.28 (ddd, $J = 10.0, 9.0, 9.0$ Hz, 1H), 2.23 (ddd, $J = 11.0, 4.0, 4.0$ Hz, 1H), 2.14 (dd, $J = 12.0, 4.5$ Hz, 1H), 2.04–1.99 (m, 1H), 1.96 (ddd, $J = 14.5, 7.0, 3.0$ Hz, 1H), 1.92–1.82 (m, 2H), 1.80–1.54 (m, 6H), 1.77 (dd, $J = 12.0, 12.0$ Hz, 1H), 1.70 (dd, $J = 14.0, 3.0$ Hz, 1H), 1.47–1.38 (m, 1H), 1.24 (s, 3H), 1.05 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 218.6, 135.4, 134.7, 134.0, 129.4, 128.7, 127.5, 127.3, 84.4, 80.2, 80.0, 78.4, 77.2, 76.4, 72.6, 66.9, 65.8, 63.7, 61.9, 44.8, 35.7, 35.5, 35.2, 30.0, 29.0, 27.9, 27.3, 26.8, 25.8, 25.7, 25.0, 19.1, 18.2, 16.0, −4.5, −5.2, −5.5, −5.5$; HRMS (FAB) calcd for $C_{49}H_{80}O_8Si_3$ ($[M + Cs^+]$) 1013.4215, found 1013.4257.

Hydroxy dithioketal 56: A heterogeneous mixture of ketone **55** (1.27 g, 1.44 mmol), powdered $NaHCO_3$ (100 mg, 1.2 mmol), $Zn(OTf)_2$ (150 mg, 0.4 mmol), and EtSH (4 mL, 54 mmol) in CH_2Cl_2 (4 mL) was stirred at 25 °C for 2.5 h. The reaction mixture was filtered through a pad of silica gel, and the filtrate was concentrated. The residue was dissolved in MeOH (10 mL) and treated with PPTS (0.2 g, 0.8 mmol) at 25 °C for 4 h. The reaction mixture was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:4, EtOAc:hexanes) to afford hydroxy dithioketal **56** (1.16 g, 92%). **56**: $R_f = 0.38$ (silica gel, 1:4, EtOAc:hexanes); IR (thin film): $\tilde{\nu}_{max} = 3427, 1452, 1085, 1027, 733\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67-7.36$ (m, 10H, ArH), 4.13 (br s, 1H), 3.98 (br s, 1H), 3.85 (br s, 1H), 3.79–3.70 (m, 3H), 3.67 (m, 2H), 3.33 (d, $J = 10.0$ Hz, 1H), 3.18 (br s, 1H), 3.03–2.97 (m, 2H), 2.83 (br s, 1H), 2.62–2.74 (br s, 3H), 2.47 (br s, 1H), 2.32–2.21 (m, 2H), 2.10 (br s, 1H), 1.94 (m, 1H), 1.86 (br s, 1H), 1.62–1.53 (m 7H), 1.41 (m, 1H), 1.32–1.18 (m, 11H), 1.05 (s, 9H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 135.4, 134.0, 129.4, 127.5, 82.4, 80.15, 78.3, 76.5, 72.6, 66.8, 65.5, 64.6, 63.7, 61.9, 44.8, 35.6, 30.0, 29.6, 29.0, 27.3, 26.8, 25.8, 24.8, 23.1, 20.9, 19.1, 18.1, 16.5, 13.7, 13.6, −4.3, −5.2$; HRMS (FAB) calcd for $C_{47}H_{76}O_7S_2Si_2$ ($[M + Cs^+]$) 1005.3625, found 1005.3670.

Aldehyde 2: To a solution of primary alcohol **56** (400 mg, 0.46 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added DMSO (1.5 mL, 21.1 mmol), Et_3N (0.32 mL, 2.3 mmol), and $SO_3 \cdot$ pyridine complex (293 mg, 1.84 mmol). The reaction mixture was stirred at 0 °C for 3 h, poured into H_2O (50 mL), and extracted with EtOAc (2 × 25 mL). The combined organic extracts were washed with saturated aqueous NH_4Cl solution (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography (silica gel, 2:8, EtOAc:hexanes) to afford aldehyde **2** (340 mg, 85%): $R_f = 0.15$ (silica gel, 3:7, ether:hexanes); $[\alpha]_D^{25} = +90.4$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2931, 2857, 1733, 1468, 1384, 1251, 1103, 831, 705, 505\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 9.68$ (s, 1H), 7.68–7.64 (m, 4H), 7.44–7.34 (m, 6H), 4.29 (s, 1H), 4.14 (br s, 1H), 3.83–3.73 (m, 2H), 3.67 (dd, $J = 6.0, 6.0$ Hz, 2H), 3.30 (d, $J = 8.5$ Hz, 1H), 3.25–3.15 (m, 1H), 3.05–2.95 (m, 2H), 2.82–2.71 (m, 2H), 2.71–2.62 (m, 2H), 2.50 (br t, $J = 12.5$ Hz, 1H), 2.34–2.25 (m, 2H), 2.23 (ddd, $J = 11.5, 3.5, 3.5$ Hz, 1H), 2.13–2.01 (m, 1H), 1.94 (ddd, $J = 14.0, 7.0, 2.5$ Hz, 1H), 1.85–1.60 (m, 8H), 1.60–1.50 (m, 1H), 1.41 (ddd, $J = 11.5, 11.0, 11.0$ Hz, 1H), 1.26 (dd, $J = 7.0, 7.0$ Hz, 3H), 1.16 (s, 3H), 1.16 (dd, $J = 7.0, 7.0$ Hz, 3H), 1.05 (s, 9H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 197.3, 135.5, 134.0, 129.4, 127.5, 82.9, 82.2, 80.3, 78.7, 76.8, 72.7, 66.9, 63.8, 62.0, 61.2, 44.0, 35.7, 35.6, 30.1, 29.1, 26.8, 25.8, 24.4, 22.6, 21.9, 19.2, 18.2, 15.9, 14.0, 13.8, −4.2, −5.2$; HRMS calcd for $C_{47}H_{74}O_7S_2Si_2$ ($[M + Cs^+]$) 1003.3469, found 1003.3422.

Bis-methyl ester 60: A solution of methyl ester **57** (90.5 g, 0.152 mol) in MeOH (600 mL) was treated with $Hg(OAc)_2$ (57.93 g, 0.182 mol). The reaction mixture was stirred at 25 °C for 2 h and transferred to a mixture of LiCl (1.29 g, 0.030 mol), $PdCl_2$ (2.69 g, 0.015 mol), and $CuCl_2$ (61.16 g, 0.455 mol) in MeOH (200 mL). The reaction mixture was stirred at 65 °C for 2 h, cooled to room temperature, and concentrated. The residue was diluted with ether (4.0 L) and poured into a saturated aqueous $NaHCO_3$ solution (1.0 L) (note: vigorous bubbling). The layers were separated, and the ether layer was washed with brine (500 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica gel, 12:1 → 6:1, hexanes:EtOAc) furnished pure methyl ketone **58** as a mixture of two diastereomers (78.3 g, 84%).

A solution of methyl ketone **58** (78.2 g, 0.128 mol) in THF (400 mL) was added dropwise to a solution of NaHMDS (153.5 mL, 1.0 M in THF, 0.1535 mol) in THF (600 mL) at −78 °C. After stirring for 10 min, a solution of *N*-phenyltrifluoromethanesulfonimide (54.7 g, 0.153 mol) in THF (300 mL) was added by cannula at −78 °C, and the reaction mixture was stirred for 1 h, warmed up to 0 °C over a period of 30 min, and poured into a saturated aqueous $NaHCO_3$ solution (1.0 L). After addition of ether (700 mL), the organic layer was separated, and washed successively with H_2O (200 mL) and brine (500 mL), dried ($MgSO_4$) and concentrated. Flash column chromatography (silica gel, hexanes, 20:1 → 4:1, hexanes: EtOAc (1% Et_3N)) provided pure enol triflate **59** as a mixture of two diastereomers (81.7 g, 86%).

A solution of methyl-3-iodopropionate (47.0 g, 0.220 mol) in PhH (250 mL) was added to a suspension of Zn(Cu) couple (21.55 g, 0.330 mol) in DMA (50 mL) and PhH (250 mL). The reaction mixture was stirred at 90 °C until TLC showed completion of the reaction (ca. 1 h) and then allowed to cool to room temperature. A solution of enol triflate **59** (81.72 g, 0.110 mol) in PhH (200 mL) and $[Pd(Ph_3P)_4]$ (6.32 g, 5.47 mmol) were added successively. The reaction mixture was stirred at 25 °C for 2 h and filtered through a short pad of silica gel (elution with ether). The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, hexanes,

20:1 →10:1, hexanes:EtOAc) to provide pure bis-methyl ester **60** (major diastereomer). **60**: $R_f = 0.72$ (silica gel, 3:7, EtOAc:hexanes); $[\alpha]_D^{25} = -66.5$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2950, 2856, 1739, 1457, 1437, 1350, 1253, 1211, 1159, 1095, 1033, 1006, 898, 836, 774, 737, 698\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.37-7.27$ (m, 10H, ArH), 4.83 (br s, 1H, =CH), 4.76 (br s, 1H, =CH), 4.63 (d, $J = 12.0$ Hz, 1H, C*H*HPh), 4.60 (d, $J = 13.0$ Hz, 1H, C*H*HPh), 4.43 (d, $J = 12.0$ Hz, 1H, C*H*HPh), 4.38 (d, $J = 12.0$ Hz, 1H, C*H*HPh), 3.71 (dd, $J = 9.0$, 9.0 Hz, 1H, OCH), 3.64 (s, 3H, CO_2CH_3), 3.61 (s, 3H, CO_2CH_3), 3.37 (dd, $J = 12.0$, 5.0 Hz, 1H, OCH), 2.99 (ddd, $J = 11.0$, 9.5, 4.5 Hz, 1H, OCH), 2.69 (d, $J = 14.0$ Hz, 1H, C*H*H), 2.54 (ddd, $J = 12.0$, 5.0, 5.0 Hz, 1H, C*H*H), 2.50–2.36 (m, 5H, C*H*H), 2.37 (d, $J = 14.0$ Hz, 1H, C*H*H), 2.29 (d, $J = 14.0$ Hz, 1H, C*H*H), 2.18 (d, $J = 14.0$ Hz, 1H, C*H*H), 1.55 (dd, $J = 14.0$, 9.0 Hz, 1H, C*H*H), 1.50 (ddd, $J = 12.0$, 12.0, 12.0 Hz, 1H, C*H*H), 1.42 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 0.84 (s, 9H, *t*BuSi), 0.04 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 173.7, 171.7, 144.9, 138.7, 138.3, 128.2, 128.2, 127.7, 127.5, 127.4, 127.2, 114.0, 77.0, 76.5, 76.1, 73.9, 70.7, 70.2, 69.9, 51.4, 51.0, 46.2, 45.9, 45.0, 32.6, 32.4, 30.2, 29.0, 25.7, 18.0, 17.0, -2.1, -2.3$; HRMS calcd for $C_{39}H_{58}O_8Si$ ($[M + Cs^+]$) 815.2955, found 815.2978.

Bis-lactone 63: A solution of bis-methyl ester **60** (70.3 g, 0.103 mol) in THF (1.39 L) and MeOH (470 mL) was added to an aqueous solution of $LiOH \cdot H_2O$ (43.27 g, 1.03 mol, 470 mL of H_2O). The reaction mixture was stirred at 60 °C until TLC showed completion of the reaction (ca. 9 h). After concentration, the residue was diluted with H_2O (800 mL) and acidified with CH_3COOH (120 mL). Ether (500 mL) was added, and the layers were separated. The aqueous layer was saturated with NaCl(s) and extracted with ether (1.0 L). The combined organic extracts were dried ($MgSO_4$) and concentrated to provide crude diacid **61** (66.51 g, 99%).

A solution of diacid **61** (66.51 g, 0.102 mol) in EtOH (460 mL) was added to liquid NH_3 (3.1 L). Lithium metal (8.46 g, 1.22 mol), cut into small pieces (0.5 cm), was added in four equal portions, and the reaction mixture was stirred at −78 °C for 10 min. After addition of NH_4Cl(s) (326 g), the reaction mixture was concentrated over a period of 12 h, and the residue was diluted with H_2O (2 L) and acidified with CH_3COOH to pH 4. The aqueous solution was saturated with NaCl(s) and extracted with ether (3 × 750 mL). The ether layer was washed with brine (1 L), dried ($MgSO_4$) and concentrated. The residue was coevaporated with toluene (4 ×) and ether (4 ×) to provide crude bis-hydroxyacid **62** (47.2 g, 98%) as a white powder. A solution of bis-hydroxyacid **62** (47.2 g, 0.10 mol) in THF (525 mL) at 0 °C was treated with Et_3N (55.5 mL, 0.398 mol), followed by the addition of 2,4,6-trichlorobenzoyl chloride (32.7 mL, 0.209 mol) over a period of 20 min. The reaction mixture was stirred at 0 °C for 1 h, and at 25 °C for 30 min, diluted with PhH (3.1 L), and transferred by cannula over 5 h to a solution of 4-DMAP (73.01 g, 0.598 mol) in PhH (1.4 L) at 80 °C. The reaction mixture was stirred overnight and concentrated. The residue was extracted with EtOAc (3 × 1 L) and filtered. The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, hexanes, 6:1:3, hexanes:CH_2Cl_2:EtOAc (elution of less polar isomer), 1:4, hexanes:EtOAc, (elution of more polar isomer)) to afford bis-lactone **63** (33.9 g, 78% for three steps), two diastereomers. **63** (major diastereomer): $R_f = 0.32$ (silica gel, 1:1, EtOAc:hexane); $[\alpha]_D^{25} = +3.0$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2930, 2855, 1739, 1313, 1258, 1234, 1188, 1152, 1110, 1087, 1049, 1002, 840, 774\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.10$ (br s, 1H, =C*H*H), 4.93 (d, $J = 1.5$ Hz, 1H, =C*H*H), 4.34 (dd, $J = 12.5$, 4.5 Hz, 1H, OCH), 4.12 (ddd, $J = 11.0$, 9.5, 6.0 Hz, 1H, OCH), 3.93 (ddd, $J = 10.5$, 10.5, 4.0 Hz, 1H, OCH), 2.80 (s, 2H), 2.79–2.70 (m, 1H), 2.65–2.55 (m, 2H), 2.43 (ddd, $J = 14.5$, 14.5, 5.0 Hz, 1H), 2.41 (d, $J = 14.0$ Hz, 1H), 2.33 (ddd, $J = 12.5$, 5.5, 5.5 Hz, 1H), 2.22–2.08 (m, 3H), 1.58 (dd, $J = 14.0$, 11.0 Hz, 1H), 1.40 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 0.86 (s, 9H, *t*BuSi), 0.15 (s, 3H, CH_3Si), 0.12 (s, 3H, CH_3Si); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 173.4, 169.9, 140.7, 119.0, 76.1, 75.9, 74.8, 71.3, 67.6, 49.8, 48.7, 45.5, 37.5, 32.3, 31.9, 31.5, 25.7, 18.2, 15.9, -2.2$; HRMS calcd for $C_{23}H_{38}O_6Si$ ($[M + H^+]$) 439.2516, found 439.2502.

Bis-olefin 65: A solution of bis-lactone **63** (11.19 g, 0.026 mol) in CH_2Cl_2 (515 mL) was cooled to 0 °C and treated dropwise with HF · pyridine (51.5 mL). The reaction mixture was stirred at 0 °C until TLC showed completion of the reaction (ca. 20 min). The reaction mixture was diluted with CH_2Cl_2 (200 mL) and poured into an aqueous $NaHCO_3$ solution (1.6 g of $NaHCO_3$/1 mL HF · pyridine) at 0 °C. The organic layer was separated, washed with brine (300 mL), dried ($MgSO_4$), and concentrated to afford crude tertiary alcohol **64**. A solution of crude tertiary alcohol **64** (24.7 g, 0.076 mol) in CH_2Cl_2 (285 mL) at 0 °C was treated with a solution of Martin's sulfurane (76.9 g, 0.114 mol) in CH_2Cl_2 (105 mL) for 15 min. The reaction mixture was concentrated and filtered through a pad of silica gel (1:1, hexanes:CH_2Cl_2). The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:9, CH_2Cl_2: hexane → 1:9, CH_2Cl_2:EtOAc) to provide bis-olefin **65** (20.8 g, 89% for two steps). **65**: $R_f = 0.41$ (silica gel, 3:2, EtOAc:hexanes); $[\alpha]_D^{25} = +9.4$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\nu_{max} = 2981, 2930, 1729, 1713, 1644, 1452, 1381, 1266, 1145, 1106, 1053, 913, 870, 733, 607\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.85$ (s, 1H, =CH), 5.11 (s, 1H, =CH), 4.94 (s, 1H, =CH), 4.34 (dd, $J = 12.5$, 4.5 Hz, 1H, OCH), 4.25 (ddd, $J = 11.0$, 9.0, 6.5 Hz, 1H, OCH), 3.97–3.90 (m, 1H, OCH), 2.85 (dd, $J = 19.5$, 6.5 Hz, 1H, C*H*H), 2.78–2.69 (m, 1H, C*H*H), 2.66–2.55 (m, 2H, C*H*H), 2.47–2.37 (m, 2H, C*H*H), 2.43 (d, $J = 15.0$ Hz, 1H, C*H*H), 2.32 (dd, $J = 19.5$, 8.0 Hz, 1H, C*H*H), 2.17 (ddd, $J = 12.0$, 12.0, 12.0 Hz, 1H, C*H*H), 2.12 (d, $J = 15.0$ Hz, 1H, C*H*H), 1.95 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 173.4, 166.2, 151.3, 140.5, 119.1, 117.3, 76.2, 74.5, 74.1, 68.4, 45.2, 41.4, 37.4, 32.3, 31.1, 26.8, 16.0$; HRMS calcd for $C_{17}H_{22}O_5$ ($[M + H^+]$) 307.1545, found 307.1554.

Olefin 66: A solution of bis-olefin **65** (20.8 g, 0.068 mol) in PhH (475 mL) was degassed under freeze-thaw conditions twice. After addition of Wilkinson's catalyst (3.14 g, 3.39 mmol), the reaction mixture was vigorously stirred under hydrogen atmosphere at 25 °C for 5 h. After concentration, the residue was filtered through a pad of silica gel (1:4, EtOAc:hexanes → 1:1, EtOAc:hexanes). The filtrate was concentrated to afford olefin **66** (20.7 g, 99%, ca. 4:1 ratio of diastereomers). **66** (major diastereomer): $R_f = 0.32$ (silica gel, ether); $[\alpha]_D^{25} = +29.2$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2956, 2927, 1733, 1704, 1461, 1381, 1254, 1222, 1167, 1116, 1051, 917, 732\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.85$ (s, 1H, =CH), 4.35 (dd, $J = 12.0$, 4.5 Hz, 1H, OCH), 4.24 (ddd, $J = 11.0$, 9.0, 6.0 Hz, 1H, OCH), 3.93 (ddd, $J = 9.5$, 7.0, 7.0 Hz, 1H, OCH), 2.90–2.80 (m, 2H), 2.47–2.35 (m, 2H), 2.30 (dd, $J = 19.0$, 7.5, Hz, 1H), 2.15 (ddd, $J = 12.0$, 12.0, 12.0 Hz, 1H), 2.02–1.95 (m, 1H), 1.95 (s, 3H, CH_3), 1.68–1.51 (m, 3H), 1.47–1.38 (m, 1H), 1.30 (s, 3H, CH_3), 1.01 (d, $J = 6.5$ Hz, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 173.7, 166.2, 151.0, 117.5, 78.4, 76.0, 74.1, 68.2, 49.3, 41.4, 35.1, 32.4, 28.8, 26.8, 26.6, 25.3, 14.5$; HRMS calcd for $C_{17}H_{24}O_5$ ($[M + Na^+]$) 309.1702, found 309.1711.

Bis-lactone 67: A solution of olefin **66** (16.5 g, 0.054 mol) in EtOAc (630 mL) was treated with 10% Pd/C (2.82 g) under an atmosphere of argon. The reaction mixture was stirred under hydrogen atmosphere at 25 °C for 12 h, filtered through a pad of silica gel (EtOAc), and concentrated. Flash column chromatography (silica gel, 3:2, EtOAc:hexanes) afforded bis-lactone **67** (15.8 g, 95%, ca. 19:1 ratio of diastereomers). **67** (major diastereomer): $R_f = 0.22$ (silica gel, 3:2, EtOAc:hexanes); $[\alpha]_D^{25} = +18.0$ ($c = 1.0$, CH_2Cl_2); IR (thin film): $\tilde{\nu}_{max} = 2927, 2874, 1736, 1459, 1378, 1327, 1251, 1172, 1077, 1044\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 4.34$ (dd, $J = 12.0$, 5.0 Hz, 1H, OCH), 4.08 (ddd, $J = 11.5$, 9.5, 6.0 Hz, 1H, OCH), 3.71 (ddd, $J = 10.0$, 10.0, 4.0 Hz, 1H, OCH), 2.87 (ddd, $J = 12.5$, 12.5, 7.0 Hz, 1H), 2.79 (dd, $J = 14.0$, 2.0 Hz, 1H), 2.63 (ddd, $J = 13.5$, 5.5, 1.0 Hz, 1H), 2.43 (ddd, $J = 12.5$, 7.0, 2.0 Hz, 1H), 2.33–2.26 (m, 2H), 2.11 (ddd, $J = 12.0$, 12.0, 12.0 Hz, 1H), 2.03–1.93 (m, 2H), 1.69–1.51 (m, 4H), 1.43 (ddd, J = 12.0, 7.0, 5.0 Hz, 1H), 1.29 (s, 3H, CH_3), 1.09 (d, $J = 7.5$ Hz, 3H, CH_3), 1.00 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta = 173.9, 172.7, 78.5, 76.6, 75.6, 67.0, 49.3, 41.8, 40.4, 35.0, 32.4, 28.7, 26.5, 25.8, 25.3, 17.7, 14.5$; HRMS calcd for $C_{17}H_{26}O_5$ ($[M + H^+]$) 311.1858, found 311.1848.

Bis-enol phosphate 68: Bis-lactone **67** (2.50 g, 8.04 mmol) was dissolved in THF (150 mL) and added to a solution of diphenyl chlorophosphate (10.0 mL, 48.2 mmol), KHMDS (64.2 mL, 0.5 M in toluene, 32.1 mmol), and HMPA (8.35 mL, 48.2 mmol) in THF (100 mL) at −78 °C. The reaction mixture was stirred at −78 °C until TLC showed completion of the reaction (ca. 1 h), whereupon it was quenched by pouring into a 10% aqueous NH_4OH solution (450 mL). After stirring at 25 °C for 20 min, the solution was saturated with NaCl(s) and extracted into ether (4 × 400 mL). The combined organic extracts were washed with brine (400 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography (silica gel, 3:7, EtOAc:hexanes) provided bis-enol phosphate **68** (5.02 g, 85%). **68**: Colorless oil; $R_f = 0.35$ (silica gel, 2:8, EtOAc:hexanes); IR (thin film): $\tilde{\nu}_{max} = 2955, 1691, 1590, 1489, 1301, 1187, 957, 771\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.35-7.17$ (m, 20H, ArH), 4.77 (ddd, $J = 8.0$, 5.5, 2.5 Hz, 1H, =CH), 4.73 (dd, $J = 7.0$, 2.0 Hz, 1H, =CH), 3.74–3.69 (m, 2H, OCH), 3.59 (ddd, $J = 11.5$, 10.0, 5.0 Hz, 1H, OCH), 2.48 (br m, 1H, =CHC*H*), 2.36–2.28 (m, 1H, =CHC*H*H), 2.21 (dt, $J = 12.0$, 5.0 Hz, 1H, OCHC*H*HCHO),

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2.10–2.00 (m, 1H, CH_3CH), 1.87–1.78 (m, 2H, CH_2), 1.76 (q, J = 12.0 Hz, 1H, OCHC*H*HCHO), 1.66 (dd, J = 14.0, 3.0 Hz, 1H, C*H*H), 1.56–1.48 (m, 2H, C*H*H), 1.30 (s, 3H, CH_3), 1.06 (d, J = 7.0 Hz, 3H, $CHCH_3$), 0.93 (d, J = 7.0 Hz, 3H, $CHCH_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 152.7 (d, $J_{C\text{-}P}$ = 7.8 Hz), 152.1 (d, $J_{C\text{-}P}$ = 7.5 Hz), 150.4, 129.8, 129.3, 125.6, 125.5, 120.2, 120.1, 120.0, 115.6, 97.2, 94.7, 86.7, 80.7, 75.7, 68.8, 50.3, 39.1, 32.7, 32.6, 27.5, 25.4, 24.8, 20.3, 14.0; HRMS (FAB), calcd for $C_{41}H_{44}O_{11}P_2$ ([M + Cs^+]): 907.1413, found 907.1378.

Bis-stannane 69: To a suspension of flame-dried lithium chloride (2.03 g, 48.0 mmol) in THF (50 mL) was added hexamethylditin (21.0 g, 64 mmol), a solution of bis-enol phosphate **68** (5.87 g, 8.0 mmol) in THF (150 mL), and [$Pd(PPh_3)_4$] (1.39 g, 1.20 mmol). The reaction mixture was stirred at 75 °C for 2 h, diluted with hexanes, and filtered through a pad of silica gel (ether). The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:7, CH_2Cl_2:hexanes, 2% Et_3N) to afford bis-stannane **69** (3.91 g, 81%). **69**: R_f = 0.62 (silica gel, 1:9, ether:hexanes); $[\alpha]_D^{25}$ = +24.5 (c = 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 2954, 2919, 1611, 1457, 1376, 1296, 1226, 1118, 1055, 769, 718, 528 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.14 (dd, J = 8.0, 6.0 Hz, 1H, =CH), 4.78 (d, J = 5.0 Hz, 1H, =CH), 3.76 (ddd, J = 10.0, 5.5, 5.5 Hz, 1H, OCH), 3.49 (ddd, J = 12.0, 10.0, 5.0 Hz, 1H, OCH), 3.28 (dd, J = 12.0, 4.5 Hz, 1H, OCH), 2.68 (ddd, J = 14.5, 8.0, 4.5 Hz, 1H), 2.65–2.58 (m, 1H), 2.11–2.04 (m, 1H), 2.02 (ddd, J = 7.0, 4.5, 4.5 Hz, 1H), 1.93 (ddd, J = 14.0, 8.5, 5.5 Hz, 1H), 1.87 (ddd, J = 12.0, 12.0, 12.0 Hz, 1H), 1.76–1.68 (m, 1H), 1.64 (dd, J = 14.0, 4.0 Hz, 1H), 1.55–1.45 (m, 2H), 1.33 (s, 3H, CH_3), 1.02 (d, J = 7.5 Hz, 3H, CH_3), 0.90 (d, J = 7.0 Hz, 3H, CH_3), 0.19 (s, 9H, $(CH_3)_3Sn$), 0.15 (s, 9H, $(CH_3)_3Sn$); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 167.6, 165.8, 127.0, 126.8, 83.1, 79.3, 77.0, 70.4, 49.5, 40.4, 34.4, 32.4, 28.9, 28.6, 23.7, 21.9, 14.6, −9.3, −9.6; HRMS calcd for $C_{23}H_{42}O_3Sn_2$ ([M + Cs^+]) 604.9656, found 604.9672.

Diol 71: Bis-stannane **69** (7.0 g, 11.6 mmol) was dissolved in THF (120 mL) and added to a solution of *n*BuLi (24.0 mL, 1.55 M in hexanes, 37.2 mmol) in THF (60 mL) at −78 °C. The resulting solution was stirred at −78 °C for 30 min. A solution of CuC≡C*n*Pr (5.3 g, 40.6 mmol) and HMPT (15.0 mL, 82.5 mmol) in THF (90 mL) was prepared (after vigorously stirring at 25 °C for 1.5 h) and added to the solution above at −78 °C. The reaction mixture was allowed to warm up to −40 °C over 1 h, cooled to −78 °C again and treated with freshly prepared $TfOCH_2CH_2OBn$ (neat, 22.4 g, 78.9 mmol). The resulting mixture was stirred at −78 °C for 1 h and allowed to warm up to 25 °C over 12 h. Triethylamine (20 mL) was added, and the mixture was stirred for 30 min, before the addition of ether (100 mL), followed by filtration through a pad of silica gel (ether). The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:9, EtOAc:hexanes, 2% Et_3N) to provide bis-enol ether **70** (4.1 g, 65%). 2,3-Dimethyl-2-butene (60.3 mL, 1.0 M solution in THF, 60.3 mmol) was cooled to −20 °C and treated with $BH_3 \cdot$THF (60.3 mL of 1 M in THF, 60.3 mmol). The borane reagent was allowed to form by stirring at −20 °C for 2 h and 0 °C for 2 h. The solution was cooled to −20 °C, and then a solution of bis-enol ether **70** (8.25 g, 15.1 mmol) in THF (120 mL) was added by cannula. The reaction mixture was stirred at −20 °C for 5 h and at 0 °C for 12 h. Then, an aqueous NaOH solution (100 mL, 3 M) was added slowly at 0 °C, followed by a 35% aqueous H_2O_2 solution (45 mL), and the resulting mixture was stirred for 2 h. The aqueous layer was separated and extracted with ether (2 × 200 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and the residue was purified by flash column chromatography (silica gel, hexanes → EtOAc) to afford diol **71** (7.55 g, 86%). **71**: R_f = 0.34 (silica gel, 1:1, EtOAc:hexanes); $[\alpha]_D^{25}$ = −0.5 (c = 1.0, CH_2Cl_2); IR (thin film): ν_{max} = 3423, 2925, 2868, 1455, 1366, 1074, 1028, 912, 736, 699, 608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 10 H, ArH). 4.53 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.52 (s, 2H, CH_2Ph), 4.46 (d, J = 12.0 Hz, 1H, C*H*HPh), 3.67 (ddd, J = 10.5, 6.5, 4.5 Hz, 1H, OCH), 3.64–3.60 (m, 2H, OCH), 3.57 (ddd, J = 9.5, 7.5, 4.5 Hz, 1H, OCH), 3.48 (ddd, J = 7.0, 7.0, 4.0 Hz, 1H, OCH), 3.44–3.37 (m, 3H, OCH), 3.26 (ddd, J = 7.5, 7.5, 3.5 Hz, 1H, OCH), 3.22 (dd, J = 7.5, 6.5 Hz, 1H, OCH), 2.98 (ddd, J = 11.5, 9.5, 4.5 Hz, 1H, OCH), 2.15–1.95 (m, 4H), 1.90–1.82 (m, 3H), 1.78–1.74 (m, 2H), 1.74–1.66 (m, 2H), 1.61 (d, J = 13.5 Hz, 1H), 1.53–1.45 (m, 2H), 1.16 (s, 3H, CH_3), 1.14 (d, J = 7.0 Hz, 3H, CH_3), 1.03 (d, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 138.1, 128.4, 127.7, 127.7, 85.0, 83.0, 82.4, 80.4, 79.7, 75.7, 75.5, 73.1, 73.0, 69.6, 66.8, 66.7, 54.5, 47.7, 36.5, 35.9, 35.0, 34.9, 34.7, 29.7, 28.5, 27.2, 19.9, 16.2; HRMS calcd for $C_{35}H_{50}O_7$ ([M + Cs^+]) 715.2611, found 715.2632.

TPS-monoprotected diol 72: A solution of diol **71** (3.00 g, 5.15 mmol) in DMF (7.5 mL) was treated with imidazole (1.05 g, 15.4 mmol) and TBDPSCl (1.67 mL, 6.42 mmol) at 25 °C for 24 h. The reaction mixture was diluted with ether (50 mL), and washed with saturated aqueous NH_4Cl solution (25 mL) and brine (25 mL). The organic layer was dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (silica gel, hexanes → ether) to provide mono-protected compound **72** (2.54 g, 60%), bis-protected compound (1.80 g, 33%) and starting diol (0.18 g, 6%). **72**: R_f = 0.23 (silical gel, 1:1, ether:hexanes); $[\alpha]_D^{25}$ = +26.9 (c = 1, CH_2Cl_2); IR (thin film): ν_{max} = 3453, 2931, 2862, 1428, 1363, 1312, 1084, 914, 822, 739, 702, 610, 509 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70–7.67 (m, 4H, ArH), 7.45–7.28 (m, 16H, ArH), 4.52 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.50 (s, 2H, CH_2Ph), 4.43 (d, J = 12.0 Hz, 1H, C*H*HPh), 3.69–3.43 (m, 8H, OCH), 3.37 (ddd, J = 9.0, 9.0, 4.5 Hz, 1H, OCH), 3.21 (br m, 1H, OCH), 2.94 (ddd, J = 12.0, 9.0, 4.0 Hz, 1H, OCH), 2.68 (br s, 1H, OH), 2.39–2.30 (m, 1H), 2.09 (ddd, J = 12.0, 5.0, 5.0 Hz, 1H), 2.03–1.93 (m, 2H), 1.88–1.80 (m, 2H), 1.75–1.63 (m, 2H), 1.55–1.35 (m, 6H), 1.12 (d, J = 7.0 Hz, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.04 (s, 9H, *t*BuSi), 0.48 (d, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 138.9, 138.2, 135.9, 134.5, 133.8, 129.6, 129.5, 128.4, 128.3, 127.7, 127.7, 127.6, 127.4, 127.4, 83.6, 82.5, 81.7, 80.5, 79.7, 78.0, 75.6, 73.1, 72.4, 69.6, 66.9, 66.7, 54.1, 46.9, 36.4, 36.0, 34.8, 34.6, 34.1, 27.3, 27.1, 26.6, 21.0, 19.9, 19.4, 16.4; HRMS calcd for $C_{51}H_{68}O_7Si$ ([M + Cs^+]) 953.3789, found 953.3757.

Triol 73: A solution of bis-benzyl ether **72** (6.60 g, 8.04 mmol) in methanol (75 mL) was treated with Pd (10% w/w on carbon, 660 mg). The reaction mixture was stirred under hydrogen atmosphere at 25 °C for 24 h, diluted with EtOAc (200 mL) and filtered through a pad of silica gel. The filtrate was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:9, methanol:EtOAc) to yield triol **73** (5.00 g, 97%). **73**: colorless oil; R_f = 0.14 (silica gel, EtOAc); $[\alpha]_D^{25}$ = +26.1 (c = 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3381, 2932, 2866, 1461, 1428, 1386, 1313, 1080, 912, 820, 738, 704, 613, 508 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.68–7.64 (m, 4H, ArH), 7.46–7.36 (m, 6H, ArH), 3.87–3.76 (m, 2H, OCH), 3.74–3.64 (m, 2H, OCH), 3.62–3.49 (m, 4H, OCH), 3.46–3.40 (m, 1H, OCH), 3.24 (br m, 1H, OH), 3.16–3.03 (m, 2H, OCH), 2.67 (br s, 1H, OH), 2.57 (br s, 1H, OH), 2.24 (ddd, J = 12.0, 5.0, 5.0 Hz, 1H), 2.19–2.12 (m, 1H), 2.04–1.95 (m, 3H), 1.85–1.75 (m, 2H), 1.75–1.65 (m, 2H), 1.58–1.48 (m, 3H), 1.45–1.38 (m, 2H), 1.10 (d, J = 7.5 Hz, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.47 (d, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 135.8, 134.2, 133.5, 129.8, 129.6, 127.7, 127.5, 85.5, 85.2, 81.9, 80.2, 79.7, 77.1, 75.6, 69.7, 60.6, 59.8, 53.7, 46.5, 36.8, 36.0, 35.9, 34.8, 27.3, 27.0, 26.5, 20.3, 19.4, 19.3, 16.4; MS (FAB) calcd for $C_{37}H_{56}O_7Si$ ([M + Cs^+]) 773.2850, found 773.2873.

Cyclohexylidene acetal 74: A solution of triol **73** (5.0 g, 7.8 mmol) in DMF (40 mL) was treated with pyridinium *p*-toluenesulfonic acid (200 mg, 0.80 mmol) and 1,1-dimethoxycyclohexane (1.3 mL, 8.6 mmol). The reaction mixture was stirred at 25 °C for 13 h, diluted with ether (100 mL) and washed with saturated aqueous NH_4Cl (2 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to provide cyclohexylidene acetal **74** (4.9 g, 6.8 mmol, 87%). **74**: white foam; R_f = 0.35 (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25}$ = +27.0 (c = 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}$ = 3495, 2939, 2862, 1459, 1429, 1363, 1273, 1087, 947, 741, 708, 641, 611 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.68–7.64 (m, 4H, ArH), 7.46–7.36 (m, 6H, ArH), 3.73–3.63 (m, 3H, OCH), 3.60–3.50 (m, 4H, OCH), 3.44 (ddd, J = 9.5, 6.0, 6.0 Hz, 1H, OCH), 3.40–3.32 (m, 2H, OCH), 3.09 (ddd, J = 11.5, 9.5, 4.0 Hz, 1H, OCH), 2.21 (ddd, J = 12.0, 4.5, 4.5 Hz, 1H), 2.17–2.03 (m, 2H), 2.00–1.95 (m, 1H), 1.93–1.86 (m, 1H), 1.78–1.37 (m, 19H), 1.05 (s, 3H, CH_3), 1.02 (d, J = 7.5 Hz, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.47 (d, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 135.8, 134.2, 133.5, 129.7, 129.5, 127.6, 127.4, 100.8, 85.6, 84.2, 82.1, 79.5, 78.9, 77.2, 75.7, 70.1, 60.1, 57.2, 53.7, 46.4, 36.9, 36.7, 36.2, 35.0, 35.0, 34.0, 33.2, 27.2, 26.9, 26.5, 25.6, 23.2, 23.0, 20.8, 19.4, 16.5; MS (FAB) calcd for $C_{43}H_{64}O_7Si$ ([M + Cs^+]) 853.3472, found 853.3504.

Pivaloate ester 75: A solution of primary alcohol **74** (4.8 g, 6.7 mmol) in CH_2Cl_2 (50 mL) was treated with 4-DMAP (1.14 g, 9.38 mmol) and trimethyl acetyl chloride (1.03 mL, 8.33 mmol). The solution was stirred at 25 °C for 2 h, and then washed with saturated aqueous NH_4Cl (2 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:9, EtOAc:hexanes) to afford **75** (5.4 g, 6.7 mmol, 100%). **75**: white foam;

$R_f = 0.54$ (silica gel, 4:6, ether:hexanes); $[\alpha]_D^{25} = +33.5$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2937, 2863, 1729, 1458, 1364, 1282, 1157, 1104, 945, 817, 739, 703, 611, 508\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.68-7.62$ (m, 4H, ArH), 7.45–7.34 (m, 6H, ArH), 4.26 (ddd, $J = 10.5, 6.5, 3.5$ Hz, 1H, OCH), 4.03 (ddd, $J = 10.5, 10.5, 5.0$ Hz, 1H, OCH), 3.66 (dd, $J = 12.0, 12.0$ Hz, 1H, OCH), 3.56 (ddd, $J = 12.5, 3.5, 3.5$ Hz, 1H, OCH), 3.51–3.30 (m, 6H, OCH), 3.07 (ddd, $J = 12.5, 10.5, 4.0$ Hz, 1H, OCH), 2.38–2.25 (m, 1H), 2.15–2.02 (m, 1H), 1.90–1.82 (m, 1H), 1.79–1.32 (m, 21H), 1.23 (s, 9H, CO*t*Bu), 1.21 (s, 3H, CH_3), 1.05 (d, $J = 6.5$ Hz, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.48 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta =$ 178.1, 135.8, 134.3, 133.5, 129.7, 129.5, 127.6, 127.4, 100.8, 84.3, 83.7, 82.3, 79.7, 78.9, 77.6, 75.9, 70.1, 60.9, 57.2, 54.0, 46.8, 36.9, 36.6, 35.0, 34.9, 34.1, 33.1, 33.2, 27.3, 27.2, 27.0, 26.9, 26.5, 25.6, 23.2, 23.0, 20.8, 19.3, 16.5; MS (FAB) calcd for $C_{48}H_{72}O_8Si$ ($[M + Cs^+]$) 937.4051, found 937.4085.

Diol 76: A solution of cyclohexylidene acetal **75** (5.4 g, 6.7 mmol) in MeOH (50 mL) and CH_2Cl_2 (25 mL) was treated with 10-camphorsulfonic acid (100 mg, 0.43 mmol) at 25 °C for 1 h. The reaction mixture was neutralized by addition of Et_3N (1 mL) and concentrated. The residue was purified by flash column chromatography (silica gel, 1:1, EtOAc:hexanes) to afford diol **76** (4.7 g, 6.5 mmol, 97%). **76**: white foam; $R_f = 0.34$ (silica gel, ether); $[\alpha]_D^{25} = +37.0$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3390, 2933, 2868, 1726, 1461, 1428, 1370, 1286, 1158, 1082, 914, 819, 739, 704, 612, 507\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.66-7.62$ (m, 4H, ArH), 7.45–7.34 (m, 6H, ArH), 4.21 (ddd, $J = 10.0, 6.5, 3.5$ Hz, 1H, OCH), 4.15–4.04 (m, 1H, OCH), 3.85–3.72 (m, 2H, OCH), 3.55–3.47 (m, 2H, OCH), 3.46–3.38 (m, 2H, OCH), 3.36 (dd, $J = 8.5, 8.5$ Hz, 1H, OCH), 3.25 (dd, $J = 11.0, 6.5$ Hz, 1H, OCH), 3.07 (ddd, $J = 11.5, 9.5, 4.0$ Hz, 1H, OCH), 2.75 (dd, $J = 5.5, 4.0$ Hz, 1H, OH), 2.69 (d, $J = 5.0$ Hz, 1H, OH), 2.35–2.25 (m, 1H), 2.11 (ddd, $J = 11.5, 4.5, 4.5$ Hz, 1H), 2.03–1.92 (m, 2H), 1.85–1.65 (m, 4H), 1.56–1.35 (m, 6H), 1.24 (s, 9H, CO*t*Bu), 1.10 (d, $J = 7.0$ Hz, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.48 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 178.4, 135.8, 134.2, 133.5, 129.7, 129.5, 127.6, 127.4, 84.5, 83.7, 81.9, 80.3, 79.7, 77.5, 75.7, 69.7, 60.9, 60.1, 54.0, 46.8, 38.7, 37.0, 35.9, 35.8, 34.6, 33.1, 27.3, 27.2, 26.9, 26.4, 19.3, 16.4$; MS (FAB) calcd for $C_{42}H_{64}O_8Si$ ($[M + Cs^+]$) 857.3425, found 857.3391.

Trityl ether 77: A solution of diol **76** (4.7 g, 6.5 mmol) in CH_2Cl_2 (30 mL) was treated with TrCl·4-DMAP complex (4.1 mg, 10 mmol) at 40 °C for 36 h. The reaction mixture was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to afford trityl ether **77** (6.2 g, 6.4 mmol, 99%). **77**: white foam; $R_f = 0.40$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +22.5$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} =$ 3486, 3055, 2931, 1726, 1596, 1449, 1428, 1390, 1285, 1155, 1075, 1002, 909, 823, 739, 705, 633, 613, 512 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.70-$ 7.66 (m, 4H, ArH), 7.49–7.25 (m, 21H, ArH), 4.28–4.20 (m, 1H, OCH), 4.08–4.00 (m, 1H, OCH), 3.55–3.25 (m, 7H, OCH), 3.22 (dd, $J = 6.5$, 6.5 Hz, 1H, OCH), 2.97–2.89 (m, 1H, OCH), 2.40 (br s, 1H, OH), 2.33–2.24 (m, 1H), 2.03–1.79 (m, 5H), 1.78–1.60 (m, 2H), 1.58–1.34 (m, 6H), 1.21 (s, 9H, CO*t*Bu), 1.10 (d, $J = 7.0$ Hz, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.05 (s, 9H, *t*BuSi), 0.49 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 178.0, 143.9, 135.7, 134.1, 133.4, 129.6, 129.5, 128.5, 127.7, 127.5, 127.4, 126.9, 86.8, 83.6, 82.6, 81.6, 80.3, 79.2, 77.4, 75.4, 69.4, 61.2, 60.1, 53.8, 46.6, 38.5, 35.8, 35.6, 35.0, 34.5, 33.2, 27.2, 27.1, 26.9, 26.3, 19.4, 19.3, 16.4$; MS (FAB) calcd for $C_{61}H_{78}O_8Si$ ($[M + Cs^+]$) 1099.4520, found 1099.4569.

Acetate 78: A solution of secondary alcohol **77** (6.2 g, 6.4 mmol) in CH_2Cl_2 (30 mL) was treated with Et_3N (2.7 mL, 19 mmol), 4-DMAP (78 mg, 0.64 mmol), and acetic anhydride (1.2 mL, 13 mmol) at 25 °C for 1 h. The reaction mixture was concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to afford acetate **78** (6.4 g, 6.4 mmol, 99%). **78**: white foam; $R_f = 0.58$ (silica gel, 1:1, ether:-hexanes); $[\alpha]_D^{25} = +20.5$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3057, 2933, 1730, 1594, 1450, 1428, 1369, 1240, 1156, 1074, 911, 822, 738, 705, 612, 511\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.72-7.67$ (m, 4H, ArH), 7.50–7.26 (m, 21H, ArH), 4.64 (dd, $J = 6.0, 4.5$ Hz, 1H, AcOCH), 4.21 (ddd, $J =$ 11.5, 8.5, 4.0 Hz, 1H, PivOCH), 4.06 (ddd, $J = 11.0, 7.5, 7.5$ Hz, 1H, PivOCH), 3.73 (ddd, $J = 9.5, 6.0, 3.5$ Hz, 1H, OCH), 3.55–3.45 (m, 2H, OCH), 3.45–3.38 (m, 2H, OCH), 3.26–3.16 (m, 2H, OCH), 2.92 (ddd, $J =$ 11.5, 9.5, 4.0 Hz, 1H, OCH), 2.32–2.22 (m, 1H), 2.18–2.11 (m, 1H), 2.09 (s, 3H, $COCH_3$), 1.92–1.78 (m, 3H), 1.78–1.64 (m, 3H), 1.59–1.49 (m, 3H), 1.48–1.32 (m, 3H), 1.20 (s, 9H, CO*t*Bu), 1.10 (d, $J = 7.0$ Hz, 3H, CH_3), 1.06 (s, 12H, *t*BuSi and CH_3), 0.50 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 178.1, 170.2, 144.3, 135.8, 134.2, 133.5, 129.7, 129.6, 128.7, 127.7, 127.6, 127.5, 126.9, 86.3, 83.5, 81.3, 80.8, 80.6, 80.4, 77.4, 75.5, 69.3, 61.4, 59.9, 53.8, 46.6, 38.6, 35.8, 34.6, 34.4, 33.6, 33.3, 27.2, 26.9, 26.4, 21.3, 19.4, 17.7, 16.5$; MS (FAB) calcd for $C_{63}H_{80}O_9Si$ ($[M + Cs^+]$) 1141.4626, found 1141.4601.

Primary alcohol 79: A solution of trityl ether **78** (5.2 g, 5.2 mmol) in CH_2Cl_2 (50 mL) and MeOH (2 mL) was treated dropwise with trifluoroacetic acid (0.6 mL, 7.8 mmol) at 25 °C until a bright yellow color persisted (ca. 30 min). The reaction mixture was quenched by the addition of Et_3N (1 mL), diluted with CH_2Cl_2 (50 mL), and washed with saturated aqueous $NaHCO_3$ (2×50 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 3:1, ether:hexanes) to afford primary alcohol **79** (3.8 g, 5.0 mmol, 96%). **79**: white foam; $R_f = 0.46$ (silica gel, 3:1, ether:hexanes); $[\alpha]_D^{25} =$ $+38.6$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 3506, 2934, 1732, 1462, 1428, 1370, 1240, 1156, 1109, 1085, 823, 756, 705\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.66-7.62$ (m, 4H, ArH), 7.45–7.34 (m, 6H, ArH), 4.66 (dd, $J = 5.0, 5.0$ Hz, 1H, AcOCH), 4.22–4.08 (m, 2H, OCH), 3.80–3.68 (m, 3H, OCH), 3.50 (dd, $J = 12.0, 5.0$ Hz, 1H, OCH), 3.47–3.40 (m, 2H, OCH), 3.36 (dd, $J = 9.0, 9.0$ Hz, 1H, OCH), 3.07 (ddd, $J = 11.5, 9.5, 4.5$ Hz, 1H, OCH), 2.34–2.26 (m, 1H), 2.19–2.11 (m, 2H), 2.06 (s, 3H, $COCH_3$), 1.88–1.64 (m, 5H), 1.56–1.48 (m, 3H), 1.45–1.36 (m, 3H), 1.24 (s, 9H, CO*t*Bu), 1.12 (d, $J = 7.5$ Hz, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.48 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 178.2, 170.2, 135.7, 134.2, 133.4, 129.6, 129.5, 127.5, 127.4, 83.7, 82.9, 81.6, 80.3, 80.2, 77.3, 75.5, 69.2, 60.8, 60.2, 53.8, 46.7, 38.7, 37.4, 34.7, 34.5, 33.3, 33.1, 27.2, 27.2, 26.8, 26.3, 21.2, 19.3, 17.3, 16.3$; MS (FAB) calcd for $C_{44}H_{66}O_9Si$ ($[M + Cs^+]$) 899.3530, found 899.3563.

Aldehyde 80: To a solution of primary alcohol **79** (4.2 g, 5.5 mmol) in CH_2Cl_2 (50 mL) was added 4 Å MS (5 g), and the mixture was treated with NMO (1.3 g, 11 mmol) and TPAP (96 mg, 0.27 mmol) at 25 °C for 1 h. The reaction mixture was filtered through a pad of silica gel (elution with ether). The filtrate was concentrated to provide aldehyde **80** (3.7 g, 4.8 mmol, 87%). **80**: white foam; $R_f = 0.32$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} =$ $+35.9$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2937, 1731, 1462, 1372, 1284, 1238, 1157, 1093, 819, 753, 704, 609\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta =$ 9.71 (br s, 1H, CHO), 7.66–7.62 (m, 4H, ArH), 7.46–7.34 (m, 6H, ArH), 4.59 (dd, $J = 6.0, 6.0$ Hz, 1H, AcOCH), 4.25 (ddd, $J = 10.0, 6.5, 3.5$ Hz, 1H, OCH), 4.06 (ddd, $J = 10.0, 6.5, 3.5$ Hz, 1H, OCH), 4.01 (ddd, $J = 10.5, 10.5, 5.0$ Hz, 1H, OCH), 3.54 (dd, $J = 11.5, 5.0$ Hz, 1H, OCH), 3.48–3.55 (m, 3H, OCH), 3.15–3.08 (m, 1H, OCH), 2.67 (ddd, $J = 17.0, 10.0, 2.0$ Hz, 1H, C*H*HCHO), 2.54 (dd, $J = 17.0, 3.0$ Hz, 1H, CH*H*CHO), 2.32–2.24 (m, 1H), 2.18–2.04 (m, 2H), 2.06 (s, 3H, $COCH_3$), 1.85 (ddd, $J = 13.0, 10.0, 3.0$ Hz, 1H), 1.75–1.65 (m, 2H), 1.55–1.34 (m, 6H), 1.23 (s, 9H, CO*t*Bu), 1.11 (d, $J = 7.0$ Hz, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.48 (d, $J =$ 7.0 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 199.7, 178.1, 170.1, 135.7, 134.2, 133.4, 129.6, 129.5, 127.5, 127.4, 83.2, 81.3, 80.9, 79.6, 78.5, 77.5, 75.5, 69.1, 60.7, 53.8, 48.5, 46.5, 38.6, 34.9, 34.3, 33.6, 33.2, 27.2, 27.1, 26.8, 26.3, 21.1, 19.3, 17.9, 16.4$; MS (FAB) calcd for $C_{44}H_{64}O_9Si$ ($[M + Cs^+]$) 897.3374, found 897.3349.

Methyl ester 81: A solution of aldehyde **80** (3.7 g, 4.8 mmol) in THF (75 mL) was added by cannula to a mixture of $Br^-Ph_3P^+(CH_2)_3CO_2Me$ (5.3, 12 mmol) and KHMDS (19 mL, 0.5 M solution in toluene, 9.5 mmol) in THF (100 mL) at −78 °C. The reaction mixture was stirred at −78 °C for 2 h, warmed up to 0 °C, quenched by pouring into saturated aqueous NH_4Cl (200 mL), and extracted with CH_2Cl_2 (3×100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:1, ether:hexanes) to afford methyl ester **81** (3.8 g, 4.5 mmol, 94%). **81**: white foam; $R_f = 0.50$ (silica gel, 1:1, ether:hexanes); $[\alpha]_D^{25} = +39.1$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max} = 2956, 1735, 1458, 1430, 1368, 1284, 1239, 1159, 1107, 914, 822, 736, 705, 610\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.67-7.62$ (m, 4H, ArH), 7.46–7.34 (m, 6H, ArH), 4.50–5.38 (m, 2H, CH=CH), 4.63 (dd, $J =$ 5.0, 5.0 Hz, 1H, AcOCH), 4.28 (ddd, $J = 12.5, 8.0, 4.5$ Hz, 1H, OCH), 4.03 (ddd, $J = 10.5, 10.5, 5.0$ Hz, 1H, OCH), 3.67 (s, 3H, CO_2CH_3), 3.51 (dd, $J =$ 11.5, 5.0 Hz, 1H, OCH), 3.49–3.35 (m, 4H, OCH), 3.04–2.96 (m, 1H, OCH), 2.40–2.07 (m, 9H), 2.06 (s, 3H, CH_3CO), 1.83–1.66 (m, 3H), 1.57–1.32 (m, 6H), 1.24 (s, 9H, CO*t*Bu), 1.12 (d, $J = 7.0$ Hz, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.48 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta = 178.0, 173.4, 170.1, 135.7, 134.2, 133.4, 129.6, 129.5, 129.5, 127.6, 127.4, 126.9, 84.3, 83.3, 81.6, 80.8, 80.0, 77.5, 75.5, 69.3, 60.7, 53.9, 51.4, 46.6, 38.6, 34.7, 34.4, 33.8, 33.5, 33.2, 32.9, 27.3, 27.2, 26.9, 26.3, 22.9, 21.2,

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19.3, 17.6, 16.4; MS (FAB) calcd for $C_{49}H_{72}O_{10}Si$ ($[M+Cs^+]$) 981.3949, found 981.3977.

Lactone 4: A solution of methyl ester **81** (3.95 g, 4.65 mmol) in THF (120 mL), MeOH (25 mL), and H_2O (25 mL) was treated with lithium hydroxide (2.2 g, 53.5 mmol) at 0 °C for 4 h. The reaction mixture was neutralized by the addition of HCl (53 mL, 1M) and extracted with ether (3×150 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated, and the residue was azeotroped with toluene (3×50 mL) to afford crude hydroxy acid **82**. A solution of crude hydroxy acid **82** in THF (36 mL) was treated with Et_3N (2.6 mL, 18.6 mmol) and 2,4,6-trichlorobenzoylchloride (1.27 mL, 8.14 mmol) at 0 °C for 1 h. The reaction mixture was slowly added to a solution of 4-DMAP (2.27 g, 18.6 mmol) in PhH (1 L) at 80 °C over 2 h. The mixture was cooled and concentrated, and the residue was purified by flash column chromatography (silica gel, 1:3, EtOAc:hexanes) to afford lactone **4** (3.1 g, 86 % for two steps). **4**: $R_f=0.58$ (silica gel, 1:1, EtOAc:hexanes); $[\alpha]_D^{25}=+14.4$ ($c=1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}_{max}=2956, 2872, 1731, 1461, 1334, 1282, 1246, 1155, 1097, 1036, 1000, 913, 821, 757, 706\ cm^{-1}$; ^1H NMR ($CDCl_3$, 500 MHz): $\delta=7.67-7.63$ (m, 4H, ArH), 7.45–7.34 (m, 6H, ArH), 5.68 (ddd, $J=10.5, 8.0, 8.0$ Hz, 1H, =CH), 5.59 (ddd, $J=10.5, 8.5, 8.5$ Hz, 1H, =CH), 4.55 (dd, $J=8.5, 8.5$ Hz, 1H, OCH), 4.26 (ddd, $J=10.5, 6.5, 3.5$ Hz, 1H, OCH), 4.06 (ddd, $J=10.5, 10.0, 5.0$ Hz, 1H, OCH), 3.70–3.64 (m, 1H, OCH), 3.49 (dd, $J=11.5, 5.0$ Hz, 1H, OCH), 3.47–3.40 (m, 1H, OCH), 3.37 (dd, $J=9.5, 9.5$ Hz, 1H, OCH), 3.33 (dd, $J=9.5, 9.5$ Hz, 1H, OCH), 3.00 (ddd, $J=12.0, 8.5, 4.5$ Hz, 1H, OCH), 2.49–2.38 (m, 1H), 2.39–2.19 (m, 6H), 2.10 (ddd, $J=12.5, 4.5, 4.5$ Hz, 1H), 2.04–1.89 (m, 2H), 1.68 (ddd, $J=14.5, 10.5, 5.0$ Hz, 1H), 1.61 (br d, $J=14.0$ Hz, 1H), 1.57–1.47 (m, 3H), 1.47–1.33 (m, 3H), 1.23 (s, 9H, *t*BuCO), 1.06 (s, 3H, CH_3), 1.05 (d, $J=7.5$ Hz, 3H, CH_3), 1.01 (s, 9H, *t*BuSi), 0.47 (d, $J=7.0$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125.7 MHz): $\delta=178.1, 174.3, 135.8, 134.2, 133.5, 129.7, 129.6, 129.5, 127.6, 127.4, 84.0, 82.9, 81.7, 80.6, 80.5, 77.5, 75.5, 68.7, 61.0, 53.9, 46.8, 38.7, 38.1, 34.2, 33.9, 33.4, 33.2, 33.0, 27.3, 27.2, 26.9, 26.4, 23.7, 19.9, 19.3, 16.2$; HRMS calcd for $C_{46}H_{66}O_8Si$ ($[M+Cs^+]$) 907.3581, found 907.3540.

Molecular dynamics and minimization calculations (CV Force Field) were performed on a SGI Indigo-2 workstation using Insight II (Biosym Technologies, Inc., San Diego, CA). Pictures were created using AVS (AVS Inc., Waltham, MA) and locally developed modules running on a DEC Alpha 3000/500 with a Kubota Pacific Denali graphics card (we thank John Trujillo for his assistance in these modeling studies).

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