Stereocontrolled Elaboration of Natural (−)-Polycavernoside A, a Powerfully Toxic Metabolite of the Red Alga *Polycavernosa tsudai*

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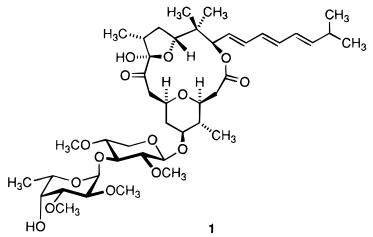
Abstract: A stereoselective total synthesis of natural levorotatory polycavernoside A (**1**) has been achieved. Initial investigations produced the properly activated disaccharide unit **18b** via the conjoining of building blocks originating from L-fucose and D-xylose. This objective was followed by preparation of the phenylsulfonyl-substituted tetrahydropyran **23** and aldehyde **30**. After proper linking of these key compounds, important information had to be garnered on the sequence of steps that would ultimately result in successful access to **1**. Although oxidation to generate α-diketone **35** and unmasking of the C-13 hydroxyl did give rise efficiently to lactol **36**, this functionality did not pave the way for ensuring macrolactonization. When this sequence of steps was reversed, it was indeed possible to arrive at the heavily functionalized precursor **44**. However, numerous experiments failed to result in the requisite activation of C-16 for attachment of the trienyl side chain. However, if the *E*-vinyl iodide was elaborated in advance of α-diketone generation, glycosidation, and complete side chain construction, arrival at **1** proceeded without unsurmountable complications to furnish the targeted marine toxin.

Drawing upon the powerful capabilities of chemical spectroscopy, Yasumoto and co-workers were able to define the gross structural features of polycavernoside A (**1**) in 1993.[1] A strong sense of urgency surrounded this effort because the widely consumed red alga *Polycavernosa tsudai*, which is the source of this powerful human toxin, had never previously induced poisoning and death. For unknown reasons, the onset of lethal metabolite production proved to be seasonal, occurring only during the months of April and May.[2] Fortunately, this phenomenon has declined more recently. From 2.6 kg of dried material collected at Tanguisson Beach on Guam, 400 μg of the natural product was obtained as a colorless solid. Five structurally related compounds have subsequently been secured in lesser amounts.[1,3]



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Although the absolute configuration of **1** could not be defined with such small quantities in hand, polycavernoside A was nevertheless revealed to be a structurally novel 13-membered macrolactone disaccharide fitted with a trienyl side chain. Detailed inspection of this small group of bioactive marine toxins reveals significant structural deviation from known macrolides. The 3,5,7,13,15-pentahydroxy-9,10-dioxotricosanoic acid carbon backbone is unprecedented, although the smaller trioxatridecane ring is similar in principle to the trioxadodecane network present in the aplysiatoxins.[4] The presence of an α-dicarbonyl moiety bears some remote resemblance to the tricarbonyl immunosuppressive agents rapamycin[5] and FK-506.[6] Particularly atypical is the lack of unsaturation within the macrolide ring. The polyene appendage that is conserved among all congeners may serve as a lipophilic "anchor" for attachment to a cell membrane.

The high degree of methylation of the disaccharide conforms to its algal origin. Beyond this, it would seem reasonable to hypothesize that the structural variants present in the sugar region may contribute to the heightened toxicity of these algal metabolites.

Results and Discussion

Deduction of Absolute Stereochemistry. Enantioselective Synthesis of the Disaccharide Component. For the reasons discussed above, polycavernoside A (**1**) emerged as an attractive target molecule. Preliminary disclosure has, in fact, been made of completed independent syntheses of **1** by the groups of Murai[7] and Paquette.[8] Before initiating such an effort, it was mandatory that the absolute stereochemistry of the entire structure be

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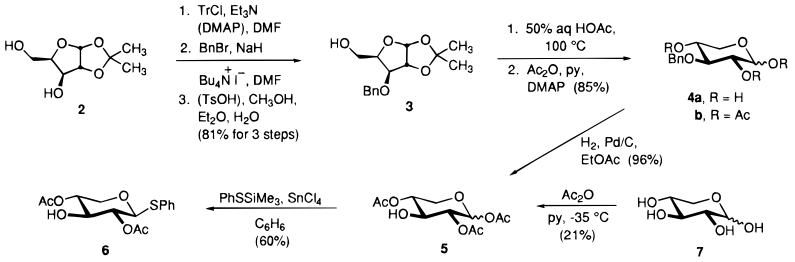
Scheme 1



deduced. The Hokkaido University team proceeded to couple *O*-methylated derivatives of natural L-fucose, unnatural D-fucose, and natural D-xylose with synthetic variants of the tetrahydrofuran (THF) ring[9] and to correlate the ^{1}H NMR features of the diastereoisomers so produced.[10] The chemical shifts and splitting patterns, when compared with those of **1**, were diagnostic and conclusive.

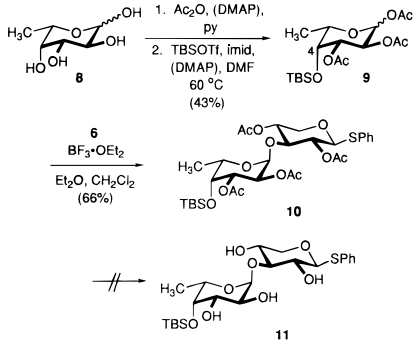
Our approach to this dilemma consisted of comparing the structural homology of an "unraveled" view of polycavernoside A with the Celmer model[11] of macrolide stereostructure,[12,13] and to synthesize the complete disaccharide ready for attachment to the aglycone from sugars usually found in marine biota. More specifically, the unique glycosidic building block was elaborated by linking a 2,3-di-*O*-methyl-α-L-fucopyranose $1 \rightarrow 3$ to a 2,4-di-*O*-methyl-α-D-xylopyranose.[14]

At the outset, sulfide **6** was considered to be the acceptor glycoside of choice; therefore, its preparation was explored from two directions (Scheme 1). Initially, the starting point took the form of commercially available 1,2-*O*-isopropylidene-α-D-xylofuranose (**2**). After its conversion into **3** by a series of precedented steps,[15,16] subsequent warming in 50% aqueous acetic acid was used to effect hydrolysis of the isopropylidene protecting group and allow for equilibration to the pyranose form **4a**. Esterification with acetic anhydride gave rise to **4b** (85% from 3), thereby permitting chemoselective removal of the benzyl group as in **5** (97%). the thioglycosidation of this intermediate with phenylthiotrimethylsilane and $SnCl_4$ in dry benzene according to the directives prescribed by others[17,18] made **6** available without complication.

A more expeditious route to **5** can be realized by taking advantage of the selectivity with which D-xylose (**7**) undergoes acetylation with acetic anhydride in pyridine at −35 °C.[19] However, we were unable to improve upon the 21% yield realized in the developmental stages by the original authors. Nevertheless, the inexpensive nature of **7** and the ease with which the C-3 hydroxyl can be differentiated from the other three equatorial OH groups were adequate compensation.

The process of elaborating a suitable glycosyl donor began by converting L-fucose (**8**) into **9**. Initial selective acetylation of the equatorial hydroxyls was followed by silylation of the lone remaining OH group (Scheme 2). The structural features of the crystalline α-anomer were clearly apparent on the basis of its ^{1}H NMR spectrum. One feature was the unmistakable

Scheme 2



deshielding of H-1, H-2, and H-3 (δ 6.29, 5.44, and 5.25 ppm) relative to that experienced by H-4 (δ 3.96). The selective formation of **10** after coupling to **6** in the presence of boron trifluoride etherate[19] requires that C−O bond formation occur exclusively via axial addition to the oxonium ion intermediate. Given this initial indication of feasibility, it seemed reasonable to advance **10** to compound **11** before penultimate *O*-methylation. However, this conversion could not be realized satisfactorily because saponification of the acetate groups was unavoidably met with migration of the silyl functionality.[20] For lack of a practical solution to this problem, our attention was redirected toward the acquisition of **15**.

This initiative began with peracetylated L-fucose,[21] involved its conversion to the thioglycoside with thiophenol and tin(IV) chloride,[22] and culminated with saponification to deliver **12b** (Scheme 3). The anomers were separated at the **12a** stage and the more dominant β form was singly advanced for reasons of practicality. Intermediate **12** was transformed into its 3,4-acetonide, thereby making possible selective *O*-methylation of the C-2 carbinol. Hydrolytic removal of the protecting group[23] furnished diol **13** in 83% overall yield. Preferential methylation at C-3 was mediated by the stannylene acetal,[24] for which cesium

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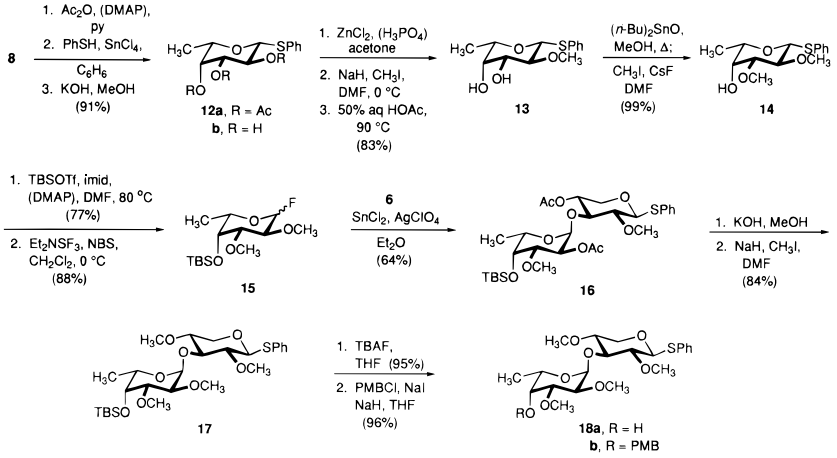
Scheme 3

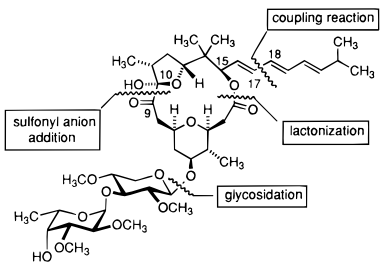


fluoride served as the activating/cleaving agent of choice. The substitution pattern present in **14** was corroborated by semiselective DEPT-45 experiments.[25] Silylation of the axial alcohol gave the fully protected pyran, which could be converted uneventfully into fluoride **15** with diethylaminosulfur trifluoride and *N*-bromosuccinimide.[26]

To test our "second generation" approach, **15** was admixed with **6** under Mukaiyama conditions,[27] and disaccharide **16** was isolated as the only detectable isomer (64%). The coupling pattern for each of the hydrogens, most notably the anomeric proton (δ 4.88, $J = 3.4$ Hz), was consistent with this structural assignment. Once **17** was in hand, three-bond-coupling interaction between H-2 and H-4 of the xylose component to the methoxyl carbons was observed, and H-2 and H-3 in the furanose ring were similarly correlated. In addition, the full range of NMR data for **17** corresponded very closely to that of this subunit in polycavernoside A.[1]

Given initial indications of potential complications surrounding removal of the *tert*-butyldimethylsilyl protecting group after glycosidation with **17**, it was considered appropriate to make the *p*-methoxybenzyl derivative **18b** available for use in subsequent studies (vide infra).

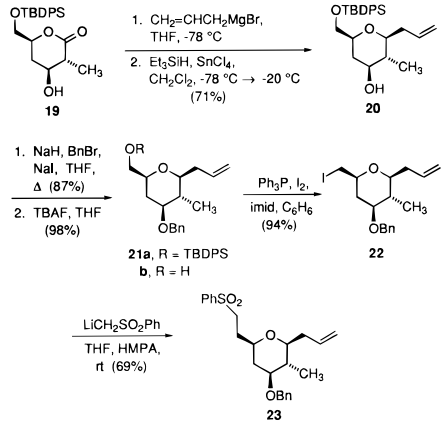
Retrosynthetic Analysis of the Aglycone Segment. The polycavernoside A structure offers several major challenges to anyone contemplating its synthesis. The first is construction of the 14-membered lactone core, the success of which will depend critically on attainment by the seco acid precursor of a conformation properly suited to ring closure. Another key question surrounds the feasibility of establishing the provocative α-dicarbonyl linkage across the C-9/C-10 bond. Our initial investigation contemplated the use of a dithiane subunit as the



nucleophilic carbonyl synthon of this union.[13] However, favorable coupling could not be achieved despite deployment of a substantial array of variants. In this study, the specific objective was to make matters operative by making recourse to a softer nucleophile. Beyond the added concern for stereoselective introduction of the multiple stereogenic centers, it was envisioned that the sensitive trienyl functionality be introduced late in the synthesis. Of the several ploys conceivably adaptable to elaboration of this polyolefinic appendage, the possibility of uniting C-17 to C-18 seemed most conveniently workable.

Synthesis of the Sulfonyl-Substituted Tetrahydropyran. Disconnection of **1** at the lactone site and across the C-9 and C-10 bond fragments the target into a functionalized tetrahydropyranylacetic acid among other subunits. To be in a position later to implement the planned nucleophilic addition, the choice was made to pursue the generation of **23** (Scheme 4). The acquisition of this phenyl sulfone began with the known lactone **19**, whose enantioselective synthesis from L-malic acid was developed earlier by Fukui and co-workers.[28]

Scheme 4



To achieve economy in the overall number of synthetic steps, **19** was condensed directly without hydroxyl protection with excess allylmagnesium bromide at −78 °C. The resulting sensitive hemiacetal was subjected without delay to chemoselective ionic reduction with triethylsilane (TES) in the presence of stannic chloride.[27g] This methodology served to orient the

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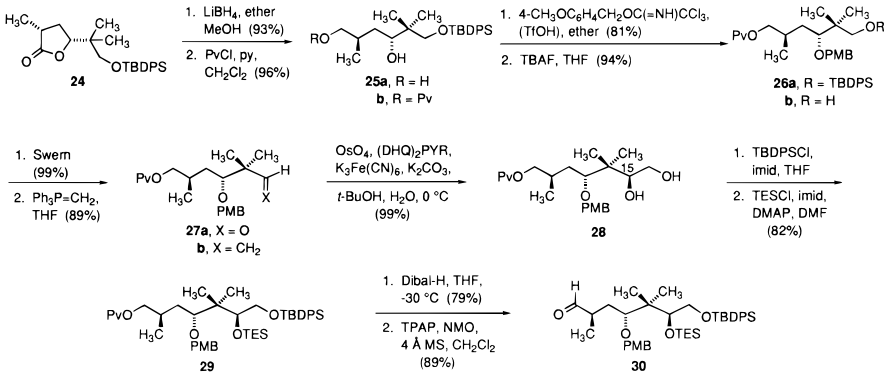
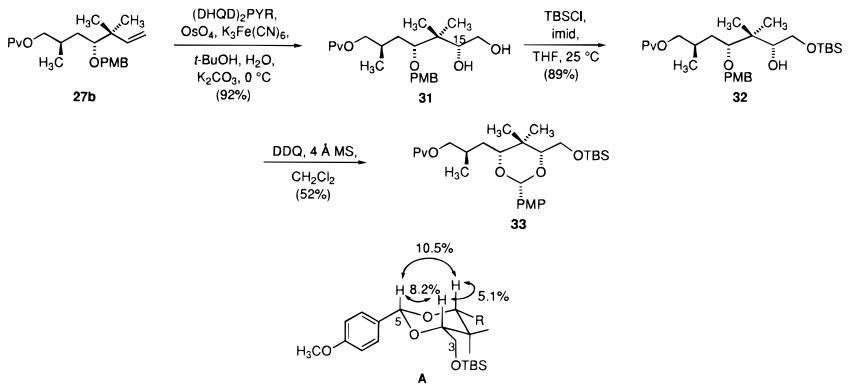
Scheme 5



Scheme 6



allyl group in **20** equatorially in a distinctively diastereoselective manner. Once the secondary alcohol had been transformed into a benzyl ether, desilylation to give **21b** and the formation of iodide **22** proceeded very efficiently.[29] The latter step was implemented for the purpose of enhancing the response of this building block to S_N2 displacement.[30,31] Indeed, the alkylation of lithiated methyl phenyl sulfone with **22** proceeded quite effectively.

Elaboration of the Electrophilic Partner. Expecting that lactone **24** previously synthesized in this laboratory[13] would outperform other chiral precursors to the C-10/C-17 stor of **1**, we set about to reduce it to diol **25a** with lithium borohydride (Scheme 5). Subsequent monoesterification with pivaloyl chloride and pyridine proceeded almost quantitatively to deliver **25b**. Protection of the secondary hydroxyl moiety with *p*-methoxybenzyl trichloroacetimidate under triflic acid catalysis[32] was followed by fluoride ion-induced desilylation. This sequence led to terminal carbinol **26b**, which on Swern oxidation gave rise to carboxaldehyde **27a**. Because **27a** is a nonepimerizable intermediate, it is not vulnerable to possible deleterious action by basic reagents. Accordingly, we did not have to exercise particular care during the ensuing Wittig olefination deployed to generate the homologated terminal alkene **27b**.

This option was exercised to permit proper elaboration of the configuration at C-15. Although other probe experiments soon revealed that this is no trivial matter, the protocol involving reagent-controlled dihydroxylation[33] with $(DHQ)_2PYR$ proved ideally suited to the task, affording **28** in 99% yield. Although it seemed reasonable to conclude that the 15*S* diastereomer was in hand, added proof was considered highly desirable. Oxidative cyclization of **28** to a 1,3-dioxolane would generate the *trans* isomer whose anticipated dynamic NMR behavior would only complicate matters further. This possibility could be countered, however, by subjecting **27b** to dihydroxylation with 2,5-diphenyl-4,6-pyrimidenediyl hydroquinidine diether ($(DHQD)_2$-PYR), a chiral ligand recognized to deliver the diol of opposite absolute configuration.[33,34] The strategy is that **31** so formed would, after regiocontrolled silylation, prove amenable to cyclization with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (Scheme 6). The stereodisposition of the substituents in **33** was certain to favor an all-equatorial disposition as shown in **A**. Indeed, nuclear Overhauser effect (NOE) experiments on this acetal gave the indicated results, thereby confirming that **31** possesses the 15*R* configuration and, indirectly, that **28** is our requisite intermediate.

The next transformation in the synthetic pathway was the fully regioselective introduction of two different silyl protecting groups as in **29**. The pivaloyl group in **29** was cleaved subsequently with diisobutylaluminum hydride, and the alcohol so formed was oxidized with tetra-*n*-proylammonium perruthenate (TPAP).[35] The fully elaborated aldehyde *30* resulted.

Proper Timing of More Advanced Functionalization. The Macrolactonization Step. Deprotonation of **23** with *n*-butyllithium and reaction of this salt with **30** in THF at −78 °C furnished an alcohol (76% yield) whose oxidation with the Dess−Martin periodinane reagent[36] delivered keto sulfone **34**

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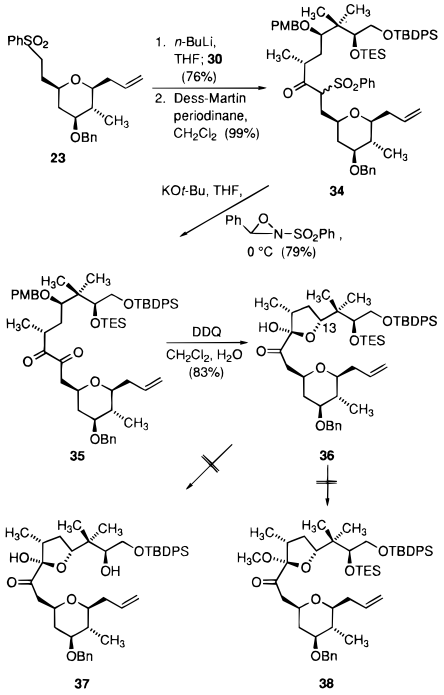
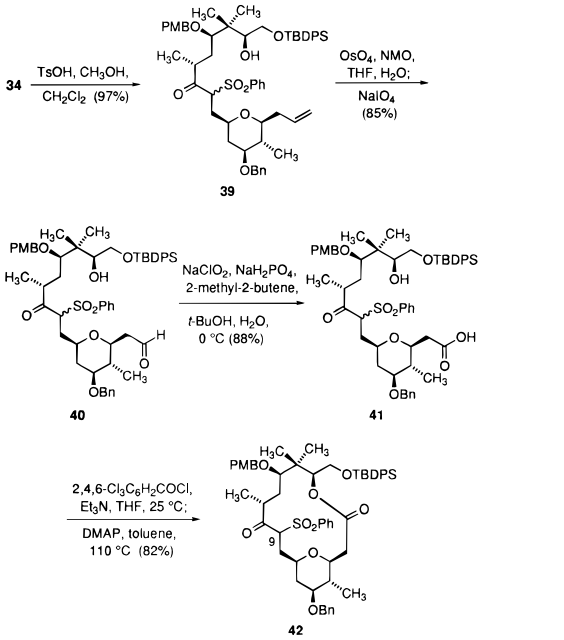
Scheme 7



Scheme 8



quantitatively (Scheme 7). After arrival at this coupling product, it seemed reasonable to attempt to advance by unmasking the α-dicarbonyl functionality, liberating the C-13 hydroxyl, and thereby making allowance for intramolecular cyclization to form a hemiacetal. When **34** was deprotonated with potassium *tert*-butoxide and exposed to the Davis oxaziridine,[37] oxidative desulfonylation took place to give **35** exclusively. Of perhaps greater significance was the finding that subsequent reaction of **35** with DDQ gave **36** in 83% yield. Exclusive formation of the five-membered ring lactol, a key step in the overall scheme, was deduced principally on the basis of the coupling constants observed for H-13. The doublet of doublets arising from spin−spin interactions with the C-12 methylene protons (J = 11.2 and 5.5 Hz) proved to be very similar to the pattern exhibited by polycavernoside A (J = 11.6 and 5.3 Hz).[1] Later work by Murai who had witnessed six-membered acetalization revealed that the magnitudes of the H-13/H-12 coupling constants in that series were distinctively different ($J \approx 12$ and 0−2 Hz).[7]

We next turned to the possibility of accessing **37** by chemoselective removal of the triethylsilyl group in **36**. However, attempts ranging from mildly acidic conditions to various fluoride-promoted methods were unsuccessful. Because it was plausible that the unprotected lactol was at the root of this problem, effort was expended to prepare methyl ether **38**. When we were unable to accomplish this step, we decided to undertake the necessary macrolactonization before chemical modification of the phenylsulfonyl group.

In this alternative scenario, removal of the TES substituent was straightforward (Scheme 8). Once the C-15 hydroxyl had been deprotected as in **39**, the capacity to cleave the allylic double bond efficiently (85% yield) was most welcome. Subjection of **40** to chemoselective oxidation with sodium chlorite[38] then provided carboxylic acid **41** in readiness for macrocyclization under modified Yamaguchi conditions.[39] An added benefit to the process was the production of a single C-9 diastereomer of **42**, presumably as the direct consequence of concomitant enolate equilibration. In light of impending chemistry that would erase the chirality of this center, no effort was expended to define the precise configuration.

Arrival at the Target. Having synthesized lactone **42**, we were anxious to determine whether the oxidative desulfonylation protocol used successfully in Scheme 7 before macrolide formation would prove equally dependable in a macro-ring setting. In fact, the α-diketone **43** was smoothly elaborated. This yellow foamy substance lent itself to efficient DDQ-promoted removal of the *p*-methoxybenzyl (PMB) group (Scheme 9). The resulting carbinol enters readily into intramolecular cyclization, such that **44** was obtained in 63% yield. The NOE results recorded for this intermediate (see formula) ensure without ambiguity the stereochemistry at C-10. Particularly informative is the rather strong interaction observed between H-8 and H-11 (9.8%). The requisite spatial proximity demanded by this observation can be realized uniquely in the desired stereoisomer.

Encouraged by the success of this substrate-controlled reaction, we decided to explore in a preliminary way a possible means for attachment of the trienyl side chain. Because most options require the involvement of aldehyde **46**, it was first shown that desilylation to provide alcohol **45** was not at all problematic. However, attempted oxidation of **45** by a variety of methods failed to afford this advanced intermediate. The application of several such reagents invariably led to wholesale destruction of the system. Apparently, the presence of the hemiacetal renders the macrocycle vulnerable to their latent oxidizing capability.

Our prior negative experience with lactol protection (e.g., **36** → **38**) caused us once again to consider postponement of the C-9 unveiling. This option required removal of the *tert*-butyldiphenylsilyl protecting group in **42** in advance of conversion to aldehyde **48** (Scheme 10). The second of these steps was particularly well served by making recourse to the Dess−

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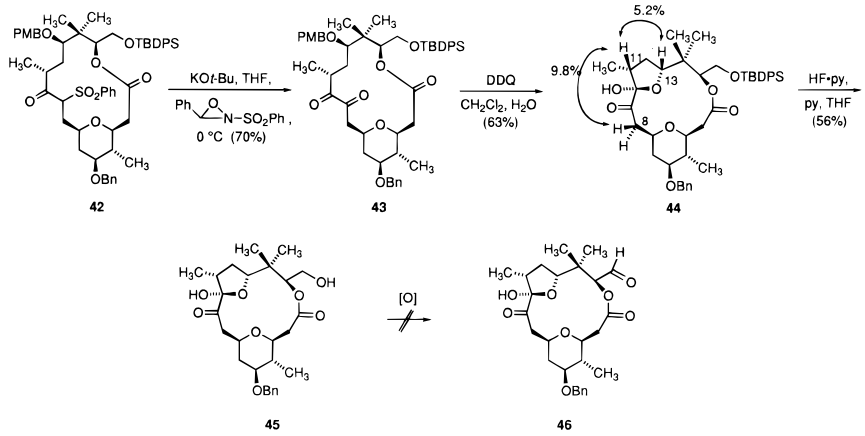
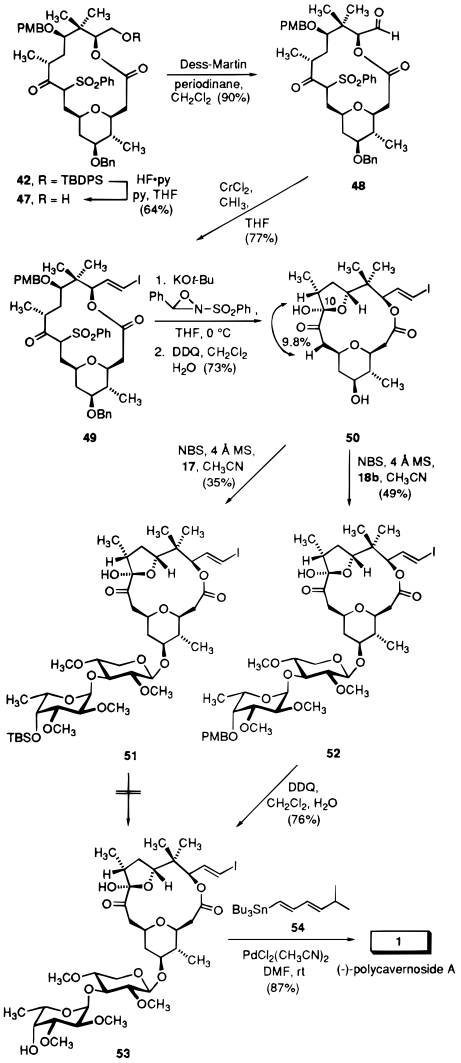
Scheme 9



Martin periodinane (90%). The smooth operation of this step stands in stark contrast to the rapid degradation observed during the numerous attempts to obtain **46** from **45**.

Scheme 10



Inspection of the retrosynthetic plan for polycavernoside A reveals that a one-carbon homologation with incorporation of C-17 in a way predisposed to establish *E* geometry across the C-16/C-17 double bond was now required. Iodovinylation of **48** with the Takai reagent ($CrCl_2-CHI_3$)[40] gave the desired **49** in 77% yield without detectable epimerization at C-15. The oxidative desulfonylation protocol used previously was successful in delivering the corresponding α-diketone as a yellow foam. Because of the lability of this intermediate, it was treated immediately with DDQ in wet dichloromethane to provide **50** in 73% overall yield. As before, a single diastereomer was formed during the transannular cyclization.

Glycosidation of aglycone **50** with **17** by means of Nicolaou methodology[41] gave **51** in 35% yield. We expected that subsequent desilylation of **51** would give rise to **53**, thereby providing for completion of the synthesis via a projected Stille coupling. However, removal of the *tert*-butyldimethylsilyl (TBS) group in **51** unexpectedly proved to be very difficult. All attempts to effect this deprotection maneuver resulted in extensive degradation. When **18b** was brought instead into the glycosidation step, a 3:1 mixture of **52** and its α-anomer was produced in 49% yield. After chromatographic separation, the conversion of **52** into carbinol **53** with DDQ proceeded uneventfully.

Dienylstannane **54** was readily obtained by iodide-tin exchange involving (*E*,*E*)-1-iodo-5-methyl-1,3-hexadiene.[7] Although **54** was unstable to silica gel, its purification was readily achieved by reverse-phase chromatography as recommended by Farina.[42] When attempts to accomplish the final cross-coupling of **53** to **54** with $Pd_2(dba)_3{\cdot}CHCl_3$[43] or various Cu(I) salts[44] were discovered to be totally ineffective, recourse was made instead to bis(acetonitrile)dichloropalladium(II) in dimethylformamide (DMF)[45] as catalyst. These conditions were conducive to the efficient formation of (−)-polycavernoside A (**1**). The 500 MHz ^1H and 125 MHz ^{13}C NMR spectra of the material produced in this manner (in CD_3CN) were compared directly with those of the natural toxin and corresponded well as expected. In addition, the negative optical rotation was in close accord to the reported value.[7]

In summation, we have devised and executed a highly convergent total synthesis of (−)-polycavernoside A, thereby confirming its global structure and absolute configuration. The macrocyclic framework was assembled by sequential coupling

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of an α-sulfonyl carbanion to an aldehyde, lactonization, and oxidative desufonylation. The route was punctuated by a palladium-catalyzed Stille coupling. We note in particular that the capacity to assemble the several building blocks in the described manner might well be exploited to produce new congeners of **1** for biological evaluation. The very late stages at which the disaccharide and trienyl side chain are introduced appear notably serviceable for gaining access to specifically designed analogues.[46]

Experimental Section

General. THF and ether were distilled from sodium benzophenone ketyl under nitrogen just before use. For CH_2Cl_2 and benzene, the drying agent was calcium hydride. All reactions were performed under a N_2 atmosphere. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} aluminum-backed plates. All chromatographic purifications were performed on E. Merck silica gel 60 (230−400 mesh) using the indicated solvent systems. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker instruments at 300 and 75 MHz, respectively, except where noted. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, Georgia. The organic extracts were dried over anhydrous $MgSO_4$. IR spectra were recorded with a Perkin-Elmer 1320 spectrometer and optical rotations were measured with a Perkin-Elmer model 241 polarimeter. The high-resolution mass spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center.

Phenyl 2,4-Di-*O*-acetyl-1-thio-D-xylopyranoside (6). Triacetate **5** (650 mg, 2.98 mmol) and phenylthiotrimethylsilane (0.85 mL, 4.47 mmol) were stirred in the presence of tin(IV) chloride (0.17 mL, 1.45 mmol) for 15 min before the addition of BF_3•OEt_2 (0.73 mL, 5.96 mmol). After an additional 20 min of stirring, saturated NH_4Cl solution was introduced to give a biphasic mixture that was extracted with ethyl acetate. The combined organic layers were dried, concentrated, and purified (SiO_2, elution with 50% ethyl acetate in hexanes) to provide 647 mg (66%) of **6**.

For the α-anomer: colorless oil; $R_f = 0.28$; IR ($CHCl_3$, cm^{-1}) 1746, 1210, 1037; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.22 (m, 5 H), 5.79 (d, $J = 5$ Hz, 1 H), 4.95−4.84 (m, 2 H), 4.13−4.00 (m, 2 H), 3.91−3.85 (m, 1 H), 2.17 (s, 3 H), 2.13 (s, 3 H), 1.95 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 170.3, 133.3, 131.7, 129.1, 127.6, 85.5, 73.4, 71.5, 69.8, 59.8, 20.90, 20.88; $[\alpha]^{23}_D$ +141 (*c* 0.64, $CHCl_3$).

For the β-anomer: colorless oil; $R_f = 0.21$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.45 (m, 2 H), 7.33−7.27 (m, 3 H), 4.87−4.80 (m, 2 H), 4.73 (d, $J = 8.7$ Hz, 1 H), 4.23 (dd, $J = 11.6$, 5.0 Hz, 1 H), 3.78 (dd, $J = 8.3$, 8.3 Hz, 1 H), 3.35 (dd, $J = 11.6$, 9.0 Hz, 1 H), 2.46 (br s, 1 H), 2.16 (s, 3 H), 2.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.3, 132.6, 132.4, 129.0, 128.1, 86.2, 73.4, 72.4, 71.3, 65.5, 20.9, 20.8; HRMS (EI) *m*/*z* (M^+) calcd 326.0824, obsd 326.0825; $[\alpha]^{20}_D$ −24.2 (*c* 1.02, $CHCl_3$).

Anal. Calcd for $C_{15}H_{18}O_6S$: C, 55.20; H, 5.56. Found: C, 55.14; H, 5.56.

1,2,3-Tri-*O*-acetyl-4-*O*-(*tert*-butyldimethylsilyl)-L-fucopyranose (9). To a solution of L-fucose (8.89 g, 54.2 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 0.662 g, 5.43 mmol) in pyridine (50 mL) at room temperature was added acetic anhydride (15.3 mL, 0.162 mmol) in two portions. A third equivalent was introduced after 2 h. The solution was stirred for an additional 1.5 h before dilution with water and extraction with ether and ethyl acetate. Drying of the organic layers and concentration in vacuo provided a crude oil that was chromatographed (SiO_2, elution with 50% ethyl acetate in hexanes) to remove undesired partially acetylated starting material. A pure sample of triacetate was also obtained in this manner and shown to be an epimeric mixture ($\alpha:\beta = 4.6:1$), the α-anomer of which was characterized: colorless prisms, mp 134.5−135.5 °C (from ether); IR ($CHCl_3$, cm^{-1}) 3610, 1750, 1372, 1244; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.29 (d, $J =$ 3.7 Hz, 1 H), 5.39 (dd, $J = 10.8$, 3.8 Hz, 1 H), 5.26 (dd, $J = 10.8$, 3.0 Hz, 1 H), 4.17 (q, $J = 6.7$ Hz, 1 H), 3.98 (d, $J = 1.0$ Hz, 1 H), 2.13 (s, 3 H), 2.11 (s, 3 H), 1.99 (s, 3 H), 1.28 (d, $J = 6.7$ Hz, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 169.9, 169.2, 90.0, 70.5, 70.2, 68.4, 66.4, 20.8, 20.8, 20.5, 16.0; HRMS (EI) *m*/*z* ($M^+ - C_2H_3O_2$) calcd 231.0869, obsd 231.0872.

Anal. Calcd for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25. Found: C, 49.68; H, 6.05.

The mixture of triacetates and peracetylated L-fucose was warmed (60 °C) with imidazole (3.11 g, 45.7 mmol), 4-(*N*,*N*-dimethylamino)-pyridine (0.559 g, 4.58 mmol), and *tert*-butyldimethylsilyl triflate (10.49 mL, 45.7 mmol) in DMF (14 mL) for 6 h. Dilution of the cooled solution with saturated $NaHCO_3$ solution and extraction of the mixture with ether was followed by drying of the organic layers, evaporation of the solvent under reduced pressure, and chromatography of the residue (SiO_2, elution with 20% ethyl acetate in hexanes) to provide peracetylated L-fucose (5.86 g, 33%) as an oil and the desired triacetate **9** (9.51 g, 43%); colorless oil; IR ($CHCl_3$, cm^{-1}) 1752, 1372, 1253, 1240; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.29 (d, $J = 4$ Hz, 1 H), 5.44 (dd, $J = 11$, 4 Hz, 1 H), 5.25 (dd, $J = 11$, 2 Hz, 1 H), 4.10 (q, $J = 7$ Hz, 1 H), 3.96 (d, $J = 2$ Hz, 1 H), 2.12 (s, 3 H), 2.08 (s, 3 H), 1.99 (s, 3 H), 1.19 (d, $J = 7$ Hz, 3 H), 0.95 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 169.9, 169.4, 90.4, 71.8, 70.7, 69.4, 66.5, 25.9 (3 C), 21.2, 21.0, 20.6, 18.3, 17.1, −4.38 (2 C); HRMS (EI) *m*/*z* ($M^+ - C_2H_3O_2$) calcd 345.1733, obsd 345.1737; $[\alpha]^{22}_D$ −94.5 (*c* 0.83, $CHCl_3$).

Phenyl 2,3,4-Tri-*O*-acetyl-1-thio-L-fucopyranoside (12a). A solution of L-fucose (5.04 g, 30.7 mmol), acetic anhydride (14.5 mL, 153 mmol), and DMAP (50 mg, 0.41 mmol) in pyridine (12 mL) was stirred at room temperature for 12 h, diluted with ethyl acetate, and washed successively with saturated $NaHCO_3$ solution, 10% HCl, and brine. The organic layer was dried and concentrated in vacuo to provide a crude oil. This oil was taken up in benzene (30 mL) before being treated with thiophenol (3.79 mL, 36.8 mmol) and tin(IV) chloride (21.5 mL, 1 M in CH_2Cl_2, 21.5 mmol). Stirring for 1.5 h was followed by dilution with ethyl acetate and washing of the organic layer with 10% HCl and brine. Drying and solvent evaporation left a yellow oil, an aliquot of which was purified by silica gel chromatography (elution with 35% ethyl acetate in hexanes) to provide both anomers of **12a** as colorless oils.

For the α-anomer: $R_f = 0.38$; IR ($CHCl_3$, cm^{-1}) 1750, 1369, 1030; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.39 (m, 2 H), 7.33−7.22 (m, 3 H), 5.93 (d, $J = 5$ Hz, 1 H), 5.38−5.25 (m, 3 H), 4.61 (q, $J = 7$ Hz, 1 H), 2.16 (s, 3 H), 2.09 (s, 3 H), 2.01 (s, 3 H), 1.13 (d, $J = 7$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.2, 169.9, 133.3, 131.8, 129.1, 127.5, 85.6, 70.9, 68.6, 68.2, 65.5, 20.8, 20.7, 20.6, 15.9; $[\alpha]^{23}_D$ −225 (*c* 0.47, $CHCl_3$).

For the β-anomer: $R_f = 0.30$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.48 (m, 2 H), 7.35−7.28 (m, 3 H), 5.26 (d, $J = 3$ Hz, 1 H), 5.20 (d, $J = 10$ Hz, 1 H), 5.05 (dd, $J = 10$, 3 Hz, 1 H), 4.70 (d, $J = 10$ Hz, 1 H), 3.83 (q, $J = 7$ Hz, 1 H), 2.14 (s, 3 H), 2.08 (s, 3 H), 1.97 (s, 3 H), 1.24 (d, $J = 7$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 170.1, 169.4, 132.9, 132.4, 128.8, 127.9, 86.5, 73.2, 72.4, 70.4, 67.4, 20.8, 20.8, 20.6, 16.5; HRMS (EI) *m*/*z* ($M^+ - C_6H_5S$) calcd 273.0974, obsd 273.0968; $[\alpha]^{22}_D$ −6.72 (*c* 0.66, $CHCl_3$).

Anal. Calcd for $C_{18}H_{22}O_7S$: C, 56.53; H, 5.80. Found: C, 56.41; H, 5.96.

Phenyl 2-*O*-Methyl-1-thio-β-L-fucopyranoside (13). The β-anomer of **12a** from above was dissolved in methanol (100 mL) and stirred with potassium hydroxide (1.03 g, 18.4 mmol) which had been introduced in aliquots of 0.1 equiv. The resulting turbid mixture was agitated for an additional 5 h before concentration under reduced pressure and purification of the oil so obtained by silica gel chromatography (elution with 10% methanol−chloroform) to afford the triol as a white foam (7.18 g, 91% for three steps).

Zinc(II) chloride (5.85 g, 42.9 mmol) and phosphoric acid (0.05 mL) in acetone (80 mL) was slowly added to a suspension of the triol (7.18 g, 28.0 mmol) in acetone (80 mL). The resulting solution was stirred for 10 h before potassium hydroxide (1 g) was added and the mixture was concentrated in vacuo. The residue was treated with water and extracted with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$ solution and brine before drying. The solvent

(46) For application of this coupling to the preparation of analogues of **1**, see Barriault, L.; Boulet, S. L.; Fujiwara, K.; Murai, A.; Paquette, L. A.; Yotsu-Yamashita, M. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2069.

was removed under reduced pressure, and the residue was chromatographed (SiO_2, elution with 40% ethyl acetate in hexanes) to furnish the acetonide as a colorless oil (6.9 g, 83%).

A portion of the acetonide (5.80 g, 19.6 mmol) in DMF (55 mL) was treated with methyl iodide (2.44 mL, 39.1 mmol) and sodium hydride (704 mg, 29.4 mmol) at 0 °C. The low temperature was maintained for 30 min before removal of the ice bath. Stirring for an additional hour was immediately followed by quenching with saturated $NaHCO_3$ solution and water. After extraction of the mixture with ether, the combined organic layers were washed with brine, dried, and concentrated in vacuo to provide a yellow oil.

The crude oil was warmed to 100 °C in a 50% aqueous AcOH solution (150 mL) for 2 h. Removal of the solvent under reduced pressure and filtration of the residue through silica gel (elution with ethyl acetate) provided **13** as a colorless oil (5.28 g, 99%); IR ($CHCl_3$, cm^{-1}) 3600−3200, 1463, 1175; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55−7.51 (m, 2 H), 7.32−7.22 (m, 3 H), 4.51 (d, $J = 9.7$ Hz, 1 H), 3.75 (br d, $J = 3.2$ Hz, 1 H), 3.64 (s, 3 H), 3.62−3.58 (m, 2 H), 3.27 (dd, $J = 9.4$ Hz, 1 H), 2.65 (s, 2 H), 1.33 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.8, 131.7, 128.8, 127.4, 87.2, 79.9, 75.4, 74.4, 71.8, 61.2, 16.6; HRMS (EI) *m/z* (M^+) calcd 270.0926, obsd 270.0928; $[\alpha]^{24}_D$ +22.9 (*c* 1.06, $CHCl_3$).

Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.76; H, 6.71. Found: C, 57.80; H, 6.85.

Phenyl 2,3-Di-*O*-methyl-1-thio-*β*-L-fucopyranoside (14). A solution of **13** (406 mg, 1.50 mmol) in methanol (6 mL) was refluxed in the presence of di-*n*-butyltin oxide (392 mg, 1.58 mmol) for 2 h. Concentration of the mixture left a white solid to which DMF (3 mL), methyl iodide (0.47 mL, 7.51 mmol), and cesium fluoride (342 mg, 2.25 mmol) were added. The mixture was stirred for 12 h, at which point the foamy solution was diluted with 10% HCl (5 mL) and extracted with ethyl acetate. The combined organic layers were dried and concentrated to leave a residue which was chromatographed (SiO_2, elution with 60% ethyl acetate in hexanes) to provide **14** as a colorless oil (424 mg, 99%); IR ($CHCl_3$, cm^{-1}) 3569, 1479, 1440, 1381; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59−7.53 (m, 2 H), 7.32−7.21 (m, 3 H), 4.48 (d, $J = 9.3$ Hz, 1 H), 3.85 (dd, $J = 3.1$, 1.0 Hz, 1 H), 3.57 (s, 3 H), 3.59−3.52 (m, 1 H), 3.50 (s, 3 H), 3.29 (dd, $J = 9.0$, 9.0 Hz, 1 H), 3.22 (dd, $J = 8.8$, 3.1 Hz, 1 H), 2.04 (br s, 1 H), 1.36 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.8, 132.0, 128.8, 127.3, 87.2, 85.0, 78.4, 74.2, 68.6, 61.1, 57.6, 16.7; HRMS (EI) *m/z* (M^+) calcd 284.1082, obsd 284.1081; $[\alpha]^{25}_D$ +9.56 (*c* 1.13, $CHCl_3$).

Phenyl 4-*O*-(*tert*-Butyldimethylsilyl)-2,3-di-*O*-methyl-1-thio-*β*-L-fucopyranoside. A warm (80 °C) solution of **14** (3.34 g, 11.7 mmol), imidazole (1.60 g, 23.5 mmol), and DMAP (287 mg, 2.35 mmol) in DMF (8 mL) was treated with *tert*-butyldimethylsilyl triflate (3 mL, 13.1 mmol) in three aliquots at 1-h intervals. Continued heating for 14 h was followed by cooling and quenching of the reaction mixture with saturated $NaHCO_3$ solution. After extraction with ether, the combined organic layers were washed with water and saturated NH_4Cl solution, dried, and concentrated. The residue was chromatographed (SiO_2, elution with 15% ethyl acetate in hexanes) to provide the silyl ether of **14** as a colorless oil (3.61 g, 77%); IR ($CHCl_3$, cm^{-1}) 1584, 1472, 1440, 1368, 1250; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.55 (m, 2 H), 7.29−7.18 (m, 3 H), 4.41 (d, $J = 9.5$ Hz, 1 H), 3.80 (d, $J = 2.6$ Hz, 1 H), 3.52 (q, $J = 6.4$ Hz, 1 H), 3.46 (s, 3 H), 3.44 (s, 3 H), 3.36 (dd, $J = 9.4$, 9.4 Hz, 1 H), 3.06 (dd, $J = 9.2$, 2.7 Hz, 1 H), 1.28 (d, $J = 6.4$ Hz, 3 H), 0.92 (s, 9 H), 0.058 (s, 3 H), 0.054 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.7, 131.7, 128.6, 126.9, 86.6, 86.3, 77.5, 75.3, 71.2, 60.6, 58.5, 26.0, 18.6, 17.7, −4.13, −4.96; HRMS (EI) *m/z* (M^+) calcd 398.1947, obsd 398.1939; $[\alpha]^{25}_D$ +123 (*c* 0.50, $CHCl_3$).

Anal. Calcd for $C_{20}H_{34}O_4SSi$: C, 60.26; H, 8.60. Found: C, 60.61; H, 8.69.

4-*O*-(*tert*-Butyldimethylsilyl)-2,3-di-*O*-methyl-L-fucopyranosyl Fluoride (15). To a solution of silylated **14** (250 mg, 0.627 mmol) and diethylaminosulfur trifluoride (91 μL, 0.690 mmol) in cold (0 °C) CH_2Cl_2 (5 mL) was added *N*-bromosuccinimide (117 mg, 0.658 mmol). The orange solution was stirred for 15 min, diluted with triethylamine (1 mL) and ethyl acetate, washed with water, dried, and concentrated. The residue was purified by chromatography (SiO_2, elution with 15% ethyl acetate in hexanes containing 1% triethylamine) to provide **15** as a colorless oil (170 mg, 88%). The instability of **15** in most solvents limited its characterization to the α-anomer; colorless oil; $R_f = 0.28$; ^1H NMR (300 MHz, $CDCl_3$) δ 5.68 (dd, $J = 54.5$ Hz, 2.7 Hz, 1 H), 4.03 (q, $J = 6.5$ Hz, 1 H), 3.90 (d, $J = 2.2$ Hz, 1 H), 3.59 (ddd, $J = 25.2$, 10.1, 2.7 Hz, 1 H), 3.54 (s, 3 H), 3.47 (s, 3 H), 3.44 (dd, $J = 7.5$, 2.6 Hz, 1 H), 1.23 (d, $J = 6.5$ Hz, 3 H), 0.93 (s, 9 H), 0.13 (s, 3H), 0.074 (s, 3 H).

Phenyl 2,4-Di-*O*-acetyl-3-*O*-[4-*O*-(*tert*-butyldimethylsilyl)-2,3-di-*O*-methyl-α-L-fucopyranosyl)-1-thio-*β*-D-xylopyranoside (16). A solution of **15** (193 mg, 0.627 mmol) in ether (5 mL) was added to a vigorously stirred suspension of **6** (170 mg, 0.521 mmol), silver perchlorate (114 mg, 0.521 mmol), and tin(II) chloride (104 mg, 0.521 mmol) in ether (5 mL). The reaction mixture was stirred for 45 min before dilution with brine and extraction with ether. The combined ether layers were dried and concentrated, and the residue was chromatographed (SiO_2, elution with 20% ethyl acetate in hexanes) to afford **16** as a white solid, mp 138−140 °C (from ether−hexanes) (207 mg, 64%); IR ($CHCl_3$, cm^{-1}) 1240, 1236, 1196, 1134; ^1H NMR (300 MHz, $CDCl_3$) δ 7.63−7.59 (m, 2 H), 7.05−6.91 (m, 3 H), 5.27 (dd, $J = 8.4$, 8.4 Hz, 1 H), 5.02 (ddd, $J = 8.8$, 7.9, 5.1 Hz, 1 H), 4.88 (d, $J = 3.4$ Hz, 1 H), 4.64 (d, $J = 8.6$ Hz, 1 H), 4.02 (dd, $J = 11.7$, 5.0 Hz, 1 H), 3.67 (q, $J = 6.4$ Hz, 1 H), 3.59 (dd, $J = 10.1$, 3.3 Hz, 1 H), 3.56 (dd, $J = 7.9$, 7.9 Hz, 1 H), 3.44 (d, $J = 0.9$ Hz, 1 H), 3.41 (dd, $J = 10.3$, 0.9 Hz, 1 H), 3.32 (s, 3 H), 3.24 (s, 3 H), 2.93 (dd, $J = 11.7$, 8.8 Hz, 1 H), 1.89 (s, 3 H), 1.75 (s, 3 H), 1.15 (d, $J = 6.5$ Hz, 3 H), 1.05 (s, 9 H), 0.21 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 168.7, 133.4 (2 C), 133.1, 129.1 (2 C), 128.1, 100.0, 86.3, 81.0, 80.1, 78.8, 72.9, 70.5, 70.4, 68.5, 65.4, 58.9, 58.7, 26.4 (3 C), 20.8, 20.7, 18.9, 17.1, −3.71, −4.68; HRMS (EI) *m/z* ($M^+ - C_6H_5S$) calcd 505.2469, obsd 505.2467; $[\alpha]^{24}_D$ −99.0 (*c* 0.92, $CHCl_3$).

Anal. Calcd for $C_{29}H_{46}O_{10}SSi$: C, 56.65; H, 7.55. Found: C, 57.07; H, 7.62.

Phenyl 3-*O*-[4-*O*-(*tert*-butyldimethylsilyl)-2,3-di-*O*-methyl-α-L-fucopyranosyl]-2,4-di-*O*-methyl-1-thio-*β*-D-xylopyranoside (17). Disaccharide **16** (101 mg, 0.164 mmol) was stirred for 15 min in methanol (5 mL) in the presence of potassium hydroxide (7 mg, 0.125 mmol). The solvent was evaporated, and the residue was redissolved in DMF (1 mL), cooled to 0 °C, and treated successively with methyl iodide (102 μL, 1.64 mmol) and sodium hydride (10 mg, 0.411 mmol). The ice bath was removed, and after 1 h of stirring, water was carefully introduced. The mixture was extracted with ether, and the combined organic layers were dried and concentrated to leave a residue that was purified by silica gel chromatography (elution with 25% ethyl acetate in hexanes) to furnish **17** as a colorless oil (77 mg, 84%); IR ($CHCl_3$, cm^{-1}) 3000, 2933, 2857, 1463, 1365, 1253, 1101, 1028, 970; ^1H NMR (300 MHz, C_6D_6) δ 7.58−7.55 (m, 2 H), 7.05−6.92 (m, 3 H), 5.46 (d, $J = 3.6$ Hz, 1 H), 4.53 (d, $J = 9.3$ Hz, 1 H), 4.23 (q, $J = 6.5$ Hz, 1 H), 3.83 (dd, $J = 11.4$, 5.1 Hz, 1 H), 3.78 (dd, $J = 8.9$, 8.9 Hz, 1 H), 3.75−3.70 (m, 2 H), 3.61 (s, 3 H), 3.54 (dd, $J = 10.1$, 2.6 Hz, 1 H), 3.31 (s, 3 H), 3.29 (s, 3 H), 3.27 (dd, $J = 9.1$, 9.1 Hz, 1 H), 3.09 (ddd, $J = 9.4$, 9.4, 5.1 Hz, 1 H), 3.00 (s, 3 H), 2.85 (dd, $J = 11.4$, 9.6 Hz, 1 H), 1.29 (d, $J = 6.5$ Hz, 3 H), 1.09 (s, 9 H), 0.25 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 135.0, 132.1, 129.0, 127.4, 98.5, 88.6, 83.8, 81.0, 79.9, 78.64, 78.60, 73.0, 67.1, 66.4, 60.4, 59.4, 58.5, 57.4, 26.4, 19.0, 17.4, −3.63, −4.60; HRMS (EI) *m/z* (M^+) calcd 558.2683, obsd 558.2702; $[\alpha]^{24}_D$ −17.1 (*c* 1.01, $CHCl_3$).

Anal. Calcd for $C_{27}H_{46}O_8SSi$: C, 58.03; H, 8.30. Found: C, 57.89; H, 8.50.

Phenyl 3-*O*-(2,3-di-*O*-methyl-α-L-fucopyranosyl)-2,4-di-*O*-methyl-1-thio-*β*-D-xylopyranoside (18a). A solution of **17** (239 mg, 429 μmol) and *tert*-butylammonium fluoride (TBAF) (1.28 mL of 1.0 M in THF, 1.28 μmol) in THF (5 mL) was stirred for 48 h and concentrated. Chromatography of the residue on silica gel (elution with ethyl acetate) gave **18a** as a white foam (181 mg, 95%); IR (film, cm^{-1}) 3482, 1099; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.46 (m, 2 H), 7.30−7.22 (m, 3 H), 5.31 (d, $J = 3.0$ Hz, 1 H), 4.55 (d, $J = 9.1$ Hz, 1 H), 4.24 (q, $J = 6.7$ Hz, 1 H), 4.14 (dd, $J = 4.5$, 11.1 Hz, 1 H), 3.88 (br s, 1 H), 3.68 (t, $J = 8.4$ Hz, 1 H), 3.60 (s, 3 H), 3.56−3.50 (m, 2 H), 3.52 (s, 3 H), 3.48 (s, 3 H), 3.35 (s, 3 H), 3.33−3.16 (m, 3 H), 2.33 (br s, 1 H), 1.24 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.3, 131.3 (2 C), 128.5 (2 C), 127.0, 97.2, 87.7, 82.3, 79.3, 79.0, 77.3, 77.1, 68.7,

65.9, 64.8, 59.8, 59.4, 57.4, 56.8, 15.6; HRMS (EI) *m/z* (M^+) calcd 444.1818, obsd 444.1830; $[\alpha]^{20}_D$ −70.4 (*c* 2.26, $CHCl_3$).

Anal. Calcd for $C_{21}H_{32}O_8S$: C, 56.73; H, 7.26. Found: C, 56.88; H, 7.30.

Phenyl 3-*O*-[4-*O*-(*p*-methoxybenzyl)-2,3-di-*O*-methyl-α-L-fucopyranosyl]-2,4-di-*O*-methyl-1-thio-*β*-D-xylopyranoside (18b). A solution of **18a** (57 mg, 128 mmol) and THF (3 mL) was treated with sodium iodide (212 mg, 1.28 μmol), sodium hydride (19.2 mg of 80% in oil, 641 μmol), and *p*-methoxybenzyl chloride (60 mg, 384 μmol), heated at 65 °C for 30 min, and allowed to cool to room temperature. The reaction mixture was quenched with saturated NH_4Cl solution (5 mL) and extracted with ether (three times). The combined organic layers were dried and concentrated to leave a residue which was purified by flash chromatography (SiO_2, elution with 50% ethyl acetate in hexanes) to provide **18b** as a colorless oil (69 mg, 96%); IR (film, cm^{-1}) 1612, 1098; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 1.9, 7.9 Hz, 2 H), 7.35−7.24 (m, 5 H), 6.86 (d, *J* = 7.9 Hz, 2 H), 5.34 (d, *J* = 3.8 Hz, 1 H), 4.86 (d, *J* = 11.4 Hz, 1 H), 4.59 (d, *J* = 11.1 Hz, 1 H), 4.58 (d, *J* = 9.2 Hz, 1 H), 4.16−4.11 (m, 2 H), 3.79 (s, 3 H), 3.77−3.66 (m, 3 H), 3.60 (s, 3 H), 3.60−3.56 (m, 1 H), 3.56 (s, 3 H), 3.51 (s, 3 H), 3.34 (s, 3 H), 3.30−3.16 (m, 3 H), 1.08 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 133.8, 131.7 (2 C), 130.8, 129.9 (2 C), 128.8 (2 C), 127.4, 113.5 (2 C), 98.5, 97.6, 88.0, 82.6, 81.3, 78.9, 78.0, 77.7, 75.7, 74.1, 66.2, 66.1, 60.1, 59.6, 57.9, 55.2, 16.6; HRMS (EI) molecular ion too fleeting for accurate mass measurement; $[\alpha]^{20}_D$ −150.6 (*c* 2.25, $CHCl_3$).

Anal. Calcd for $C_{29}H_{40}O_9S$: C, 61.68; H, 7.14. Found: C, 61.94; H, 7.28.

(2*S*,3*R*,4*S*,6*S*)-2-Allyl-6-[(*tert*-butyldiphenylsiloxy)methyl]tetrahydro-3-methyl-2*H*-pyran-4-ol (20). A solution of 15.00 g (37.6 mmol) of **19**[28] in 200 mL of THF was treated at −78 °C with 112.9 mL (112.9 mmol) of 1 M allylmagnesium bromide in ether, stirred for 5 min, quenched with 100 mL of saturated NH_4Cl solution, and allowed to warm to room temperature. The product was extracted into ether (ca. 50 mL of 1 M HCl was added to break the emulsion), and the combined organic phases were washed with brine, dried, and concentrated. The residual yellowish hemiacetal was dried at high vacuum for 2 h, admixed with 42.60 g (376.3 mmol) of triethylsilane dissolved in 200 mL of CH_2Cl_2, cooled to −78 °C, and treated with 41.4 mL (41.4 mmol) of a 1 M solution of tin tetrachloride in CH_2Cl_2. The reaction mixture was allowed to warm gradually to −20 °C for 80 min and quenched with 100 mL of water and 50 mL of 1 M HCl. The product was extracted into CH_2Cl_2 and ether, and the combined organic phases were dried and concentrated. The residue was purified by chromatography (SiO_2, elution with 15% ether in petroleum ether) to furnish 11.43 g (71%) of **20** as a colorless oil; IR (film, cm^{-1}) 3355, 1113; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72−7.66 (m, 4 H), 7.45−7.34 (m, 6 H), 6.00−5.87 (m, 1 H), 5.11−5.00 (m, 2 H), 3.76 (dd, *J* = 5.4, 10.3 Hz, 1 H), 3.61 (dd, *J* = 5.1, 10.3 Hz, 1 H), 3.55−3.47 (m, 1 H), 3.37 (td, *J* = 4.6, 10.4 Hz, 1 H), 3.06 (ddd, *J* = 3.0, 7.0, 9.9 Hz, 1 H), 2.44 (dm, *J* = 14.0 Hz, 1 H), 2.21 (m, 1 H), 2.04 (ddd, *J* = 1.9, 4.7, 12.3 Hz, 1 H), 1.51 (br, 1 H), 0.56−0.40 (m, 2 H), 1.06 (s, 9 H), 0.98 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.7 (4 C), 135.7, 133.7 (2 C), 129.5 (2 C), 127.6 (4 C), 116.3, 80.4, 76.0, 73.6, 66.9, 43.1, 37.6, 37.1, 26.8 (3 C), 19.3, 12.6; FAB MS *m/z* (M^+ + H) calcd 425.25, obsd 425.19; $[\alpha]^{21}_D$ −25.3 (*c* 0.79, $CHCl_3$).

Anal. Calcd for $C_{26}H_{36}O_3Si$: C, 73.54; H, 8.54. Found: C, 73.81; H, 8.59.

[[(2*S*,4*S*,5*R*,6*S*)-6-Allyl-4-(benzyloxy)tetrahydro-5-methyl-2*H*-pyran-2-yl]methoxy]-*tert*-butyldiphenylsilane (21a). A suspension of 80% sodium hydride in mineral oil (2.40 g, 80.1 mmol) was placed in a 250-mL flask, washed once with 20 mL of THF, and treated with a solution of **20** (11.33 g, 26.7 mmol) in 80 mL of THF followed by 12.0 g (80.1 mmol) of flame-dried sodium iodide. The reaction mixture was refluxed for 5 min, treated with 9.1 g (53.0 mmol) of benzyl bromide, and refluxed for an additional 20 min before cooling, dilution with 200 mL of ether, quenching with water, and extraction with ether. The combined organic layers were washed with brine, dried, and concentrated. The residue was chromatographed (SiO_2, gradient elution with 2−5% ether in petroleum ether) to furnish 11.93 g (87%) of **21a** as a colorless oil; IR (film, cm^{-1}) 1454, 1428, 1113; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78−7.69 (m, 4 H), 7.49−7.27 (m, 11 H), 6.00−5.89 (m, 1 H), 5.52−5.02 (m, 2 H), 4.68 (d, *J* = 11.6 Hz, 1 H), 4.46 (d, *J* = 11.6 Hz, 1 H), 3.80 (dd, *J* = 5.5, 10.4 Hz, 1 H), 3.66 (dd, *J* = 5.0, 10.4 Hz, 1 H), 3.52−3.43 (m, 1 H), 3.16 (td, *J* = 6.0, 10.4 Hz, 1 H), 3.09 (ddd, *J* = 2.9, 7.0, 9.9 Hz, 1 H), 2.46 (dm, *J* = 12.0 Hz, 1 H), 2.29−2.17 (m, 2 H), 1.55−1.46 (m, 1 H), 1.31 (q, *J* = 11.6 Hz, 1 H), 1.09 (s, 9 H), 0.99 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.7, 135.7 (4 C), 135.2, 133.8 (2 C), 129.6 (2 C), 128.3 (2 C), 127.7 (2 C), 127.6 (5 C), 116.2, 80.7, 80.4, 76.0, 70.4, 67.1, 41.1, 37.3, 33.5, 26.8 (3 C), 19.3, 13.0; HRMS (EI) *m/z* ($M^+ - C_4H_9$) calcd 457.2199, obsd 457.2201; $[\alpha]^{21}_D$ +34.0 (*c* 1.04, $CHCl_3$).

Anal. Calcd for $C_{33}H_{42}O_3Si$: C, 77.00; H, 8.22. Found: C, 77.18; H, 8.29.

(2*S*,4*S*,5*R*,6*S*)-6-Allyl-4-(benzyloxy)tetrahydro-5-methyl-2*H*-pyran-2-methanol (21b). A solution of 10.96 g (21.3 mmol) of **21a** in 80 mL of THF was treated with 31.9 mL (31.9 mmol) of a 1 M solution of TBAF in THF. The reaction mixture was stirred for 1.5 h before dilution with ether and aqueous workup. The combined organic phases were dried and concentrated, and the residue was purified by column chromatography on silica gel (gradient elution with 20−40% ether in petroleum ether) to furnish 5.78 g (98%) of **21b** as a colorless oil; IR (film, cm^{-1}) 3442, 1454, 1072; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.27 (m, 5 H), 5.96−5.82 (m, 1 H), 5.11−5.03 (m, 2 H), 4.66 (d, *J* = 11.5 Hz, 1 H), 4.43 (d, *J* = 11.5 Hz, 1 H), 3.63−3.53 (m, 2 H), 3.49−3.41 (m, 1 H), 3.22−3.08 (br m, 2 H), 2.47 (dm, *J* = 14.7 Hz, 1 H), 2.26−2.17 (m, 2 H), 2.03 (ddd, *J* = 1.9, 4.6, 12.3 Hz, 1 H), 1.76−1.42 (m, 1 H), 1.31 (q, *J* = 11.4 Hz, 1 H), 0.99 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 134.8, 128.4 (2 C), 127.7 (2 C), 127.6, 116.6, 80.5, 80.0, 75.6, 70.5, 66.0, 41.2, 37.2, 32.8, 12.9; HRMS (EI) *m/z* (M^+) calcd 276.1725, obsd 276.1715; $[\alpha]^{20}_D$ +75.41 (*c* 1.11, $CHCl_3$).

Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.62; H, 8.71.

(2*S*,3*R*,4*S*,6*R*)-2-Allyl-4-(benzyloxy)-6-iodomethyltetrahydro-3-methyl-2*H*-pyran (22). A solution of 1.00 g (3.62 mmol) of alcohol **21b**, 1.42 g (5.42 mmol) of triphenylphosphine, and 0.37 g (5.4 mmol) of imidazole in 50 mL of benzene was cooled to 10 °C and treated with 1.38 g (5.42 mmol) of iodine (added in portions for 10 min) with vigorous magnetic stirring. The cooling bath was removed and stirring was continued for an additional 1.5 h, during which time an amorphous precipitate that originally deposited on the walls of the flask was transformed into a suspension. The reaction mixture was quenched with 10 mL of 25% sodium thiosulfate solution, and the product was extracted into ether. The combined organic phases were washed with brine, dried, and concentrated. Chromatographic purification of the residue on silica gel (elution with 3% ether in petroleum ether) afforded 1.31 g (94%) of **22** as a colorless oil; IR (film, cm^{-1}) 1354, 1074; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.27 (m, 5 H), 6.05−5.91 (m, 1 H), 5.12−5.04 (m, 2 H), 4.67 (d, *J* = 11.5 Hz, 1 H), 4.44 (d, *J* = 11.5 Hz, 1 H), 3.41−3.32 (m, 1 H), 3.24−3.06 (m, 4 H), 2.49−2.33 (m, 2 H), 2.27−2.18 (m, 1 H), 1.57−1.41 (m, 1 H), 1.26 (q, *J* = 11.4 Hz, 1 H), 0.98 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 135.0, 128.4 (2 C), 127.7 (2 C), 127.6, 116.4, 81.0, 79.9, 74.8, 70.6, 40.9, 37.2, 36.7, 12.8, 9.0; HRMS (EI) *m/z* ($M^+ - C_3H_5$) calcd 345.0351, obsd 345.0309; $[\alpha]^{20}_D$ +57.52 (*c* 1.33, $CHCl_3$).

Anal. Calcd for $C_{17}H_{23}IO_2$: C, 52.86; H, 6.00. Found: C, 52.65; H, 6.06.

(2*S*,3*R*,4*S*,6*S*)-2-Allyl-4-(benzyloxy)tetrahydro-3-methyl-6-[2-(phenylsulfonyl)ethyl]-2*H*-pyran (23). A solution of 5.07 g (32.5 mmol) of methyl phenyl sulfone in 70 mL of THF was cooled to −78 °C and treated with 21.0 mL (32.5 mmol) of a 1.5 M solution of *n*-butyllithium in hexanes. The reaction mixture was stirred for 25 min before the addition of 1.88 mL of hexamethylphosphoric triamide (HMPA) and a solution of 4.18 g (10.8 mmol) of **22** in 70 mL of THF. The reaction mixture was allowed to warm gradually to room temperature and stirred for an additional 8 h before aqueous workup and extraction with ether. The combined organic phases were dried and concentrated, and the residue was purified by chromatography (SiO_2, elution with 30% ether in petroleum ether) to furnish 3.09 g (69%) of **23** as a white solid, mp 57 °C (from ether−petroleum ether); IR (film, cm^{-1}) 1450, 1357, 1305, 1137, 1075; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97−7.89 (m, 2 H), 7.69−

7.54 (m, 3 H), 7.38−7.27 (m, 5 H), 5.87−5.73 (m, 1 H), 5.06−4.99 (m, 2 H), 4.62 (d, J = 11.5 Hz, 1 H), 4.40 (d, J = 11.5 Hz, 1 H), 3.37−3.27 (m, 2 H), 3.21 (dd, J = 5.8, 9.9 Hz, 1 H), 3.17−3.04 (m, 1 H), 2.95 (ddd, J = 2.8, 7.6, 10.1 Hz, 1 H), 2.42−2.33 (m, 1 H), 2.16−1.99 (m, 2 H), 1.99−1.77 (m, 2 H), 1.46−1.32 (m, 1 H), 1.20 (q, J = 11.3 Hz, 1 H), 0.93 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 138.4, 135.0, 133.6, 129.3 (2 C), 128.4 (2 C), 128.0 (2 C), 127.7 (2 C), 127.6, 116.4, 80.6, 80.0, 72.9, 70.6, 52.8, 41.2, 37.2, 37.0, 29.2, 12.9; HRMS (EI) m/z ($M^+ - C_3H_5$) calcd 341.1575, obsd 341.1517; $[\alpha]^{20}_D$ +51.2 (c 0.215, $CHCl_3$).

Anal. Calcd for $C_{24}H_{30}O_4S$: C, 69.53; H, 7.29. Found: C, 69.40; H, 7.30.

(2*R*,4*R*)-6-(*tert*-Butyldiphenylsiloxy)-4-hydroxy-2,5,5-trimethylhexyl Pivalate (25b). A cold (0 °C), magnetically stirred solution of **24**[13] (1.26 g, 3.07 mmol) in ether (30 mL) was treated with methanol (148 mg, 4.61 mmol) and lithium borohydride (100 mg, 4.61 mmol), stirred at room temperature for 30 min, and quenched with saturated NH_4Cl solution. The product was extracted into ether (three times), and the combined organic layers were dried and concentrated. The residue was purified by flash chromatography (SiO_2, elution with 50% ethyl acetate in hexanes) to provide **25a** as a colorless oil (1.13 g, 93%); IR (film, cm^{-1}) 3346, 1589, 1111; ^{1}H NMR (300 MHz, C_6D_6) δ 7.79−7.72 (m, 4 H), 7.24−7.20 (m, 6 H), 3.69 (dd, J = 1.3, 10.2 Hz, 1 H), 3.58 (d, J = 9.8 Hz, 1 H), 3.51 (d, J = 9.8 Hz, 1 H), 3.60−3.43 (m, 1 H), 3.36 (dd, J = 7.3, 10.6 Hz, 1 H), 1.89−1.84 (m, 1 H), 1.52−1.32 (m, 1 H), 1.29−1.27 (m, 1 H), 1.13 (s, 9 H), 0.89 (s, 3 H), 0.86 (d, J = 6.5 Hz, 3 H), 0.75 (s, 3 H) (two OH not observed); ^{13}C NMR (75 MHz, C_6D_6) δ 136.1 (2 C), 136.0 (2 C), 133.5, 133.4, 130.2, 130.1, 128.1 (4 C), 76.7, 72.9, 68.9, 39.4, 37.3, 34.9, 27.0 (3 C), 21.9, 19.5; HRMS (EI) m/z (M^+ + H) calcd 414.2590, obsd 414.2687; $[\alpha]^{20}_D$ +16.6 (c 1.50, $CHCl_3$).

Anal. Calcd for $C_{25}H_{38}O_3Si$: C, 72.41; H, 9.24. Found: C, 72.55; H, 9.28.

This material was dissolved in CH_2Cl_2 (30 mL) and treated sequentially with pyridine (1.35 g, 17.0 mmol) and pivaloyl chloride (515 mg, 4.26 mmol) at 25 °C. After overnight stirring, saturated NH_4Cl solution was introduced, the product was extracted into CH_2Cl_2 (three times), and the combined organic phases were washed with 2 N HCl, saturated $NaHCO_3$ solution, and brine before drying. The solvent was removed under reduced pressure and the residue was chromatographed (SiO_2, elution with 30% ether in hexanes) to afford **25b** (1.36 g, 96%) as a colorless oil; IR (film, cm^{-1}) 3506, 1728, 1478, 1427; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68−7.65 (m, 4 H), 7.45−7.27 (m, 6 H), 4.00 (dd, J = 10.6, 5.5 Hz, 1 H), 3.90 (dd, J = 10.6, 6.8 Hz, 1 H), 2.67 (d, J = 9.5 Hz, 1 H), 3.53 (d, J = 10.0 Hz, 1 H), 3.47 (d, J = 10.0 Hz, 1 H), 3.19 (br s, 1 H), 2.21−2.04 (m, 1 H), 1.55−1.42 (m, 1 H), 1.26−1.17 (m, 1 H), 1.20 (s, 9 H), 1.07 (s, 9 H), 0.98 (d, J = 6.7 Hz, 3 H), 0.87 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 135.7 (2 C), 135.6 (2 C), 132.7 (2 C), 129.9 (2 C), 129.8 (2 C), 127.8 (2 C), 75.4, 73.3, 70.1, 38.8, 38.7, 35.0, 29.5, 27.2 (3 C), 26.9 (3 C), 22.3, 19.2, 19.1, 16.1; HRMS (EI) m/z ($M^+ - C_9H_{18}O_2$) calcd 340.1858, obsd 340.1891; $[\alpha]^{20}_D$ +19.1 (c 0.98, $CHCl_3$).

Anal. Calcd for $C_{30}H_{46}O_4Si$: C, 72.24; H, 9.30. Found: C, 72.12; H, 9.30.

(2*R*,4*R*)-6-(*tert*-Butyldiphenylsiloxy)-4-[(*p*-methoxybenzyl)oxy]-2,5,5-trimethylhexyl Pivalate (26a). A solution of **25b** (945 mg, 1.89 mmol) in ether (20 mL) was treated successively with *p*-methoxybenzyl trichloroacetimidate (1.36 g, 4.73 mmol) and triflic acid (189 μL of 0.1 M in ether, 18.9 mmol) at room temperature. After the reaction mixture had been stirred for 1 h, saturated $NaHCO_3$ solution was introduced and the product was extracted into ethyl acetate. The combined organic phases were washed with brine, dried, and freed of solvent. Flash chromatography of the residue (SiO_2, elution with 10% ether in hexanes) gave 953 mg (81%) of **26a** as a colorless oil; IR (film, cm^{-1}) 1728, 1513, 1247, 1160; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69−7.66 (m, 4 H), 7.50−7.40 (m, 6 H), 7.14 (d, J = 8.4 Hz, 2 H), 6.83 (d, J = 8.4 Hz, 2 H), 4.54 (s, 2 H), 4.00−3.86 (m, 2 H), 3.81 (s, 3 H), 3.63 (d, J = 10.1 Hz, 1 H), 3.58 (d, J = 9.8 Hz, 1 H), 3.41 (d, J = 9.8 Hz, 1 H), 2.08−2.02 (m, 1 H), 1.66−1.57 (m, 1 H), 1.32−1.19 (m, 1 H), 1.21 (s, 9 H), 1.12 (s, 9 H), 1.01 (d, J = 6.6 Hz, 3 H), 0.91 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 158.9, 135.8 (4 C), 133.7 (2 C), 131.4, 129.6 (2 C), 128.8 (4 C), 127.6 (2 C), 113.6 (2 C), 80.2, 74.3, 70.4, 69.9, 55.2, 41.1, 38.8, 34.6, 29.9, 27.2 (3 C), 27.0 (3 C), 21.8, 20.2, 19.4, 16.5; HRMS (EI) molecular ion too fleeting for accurate mass measurement; $[\alpha]^{20}_D$ +10.1 (c 0.99, $CHCl_3$).

Anal. Calcd for $C_{38}H_{54}O_5Si$: C, 73.74; H, 8.80. Found: C, 73.85; H, 8.70.

(2*R*,4*R*)-6-Hydroxy-4-[(*p*-methoxybenzyl)oxy]-2,5,5-trimethylhexyl Pivalate (26b). A solution of **26a** (239 mg, 372 μmol) and tetra-*n*-butylammonium fluoride (1.16 mL of 0.1 M in THF, 1.16 mmol) in THF (4 mL) was stirred for 3 days. After concentration, the brown residue was purified by flash chromatography (SiO_2, elution with 50% ether in hexanes) to afford **26b** as a colorless oil (133 mg, 94%); IR (film, cm^{-1}) 3473, 1726, 1513, 1465; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 8.5 Hz, 2 H), 6.81 (d, J = 8.5 Hz, 2 H), 4.54 (s, 2 H), 3.91 (d, J = 6.2 Hz, 2 H), 3.78 (s, 3 H), 3.60 (d, J = 10.8 Hz, 1 H), 3.40 (dd, J = 9.3, 2.0 Hz, 1 H), 3.30 (d, J = 10.8 Hz, 1 H), 2.72 (br s, 1 H), 2.07−2.00 (m, 1 H), 1.74−1.65 (m, 1 H), 1.34−1.26 (m, 1 H), 1.20 (s, 9 H), 1.02 (s, 3 H), 0.96 (d, J = 6.7 Hz, 3 H), 0.84 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 159.5, 130.5, 129.2 (2 C), 113.8 (2 C), 84.0, 74.4, 70.4, 69.6, 55.2, 39.6, 38.8, 35.0, 30.2, 27.2 (3 C), 23.1, 20.7, 16.5; HRMS (EI) m/z (M^+) calcd 380.2563, obsd 380.2549; $[\alpha]^{20}_D$ +5.4 (c 1.1, $CHCl_3$).

(2*R*,4*R*)-5-Formyl-4-[(*p*-methoxybenzyl)oxy]-2,5-dimethylhexyl Pivalate (27a). Oxalyl chloride (7.39 g, 57.6 mmol) dissolved in CH_2Cl_2 (140 mL) was cooled to −78 °C, treated with dimethyl sulfoxide (DMSO) (9.0 g, 115 mmol), and stirred for 10 min. A solution of **26b** (18.37 g, 48 mmol) was introduced via cannula at this temperature, and the reaction mixture was stirred for 1 h before the addition of triethylamine (19.4 g, 192 mmol) and gradual warming to 0 °C. After stirring had been maintained for 30 min, the mixture was poured into saturated NH_4Cl solution (200 mL) and extracted with CH_2Cl_2 (three times). The combined organic phases were washed with saturated $NaHCO_3$ solution and brine, dried, and concentrated. Purification of the residue by flash chromatography on silica gel (elution with 20% ether in hexanes) gave **27a** as a colorless oil (18.13 g, 99%); IR (film, cm^{-1}) 1728, 1613, 1514, 1249; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.61 (s, 1 H), 7.21 (d, J = 8.6 Hz, 2 H), 6.84 (d, J = 8.6 Hz, 2 H), 4.49 (s, 2 H), 3.90 (d, J = 6.2 Hz, 2 H), 3.77 (s, 3 H), 3.64 (dd, J = 9.6, 2.2 Hz, 1 H), 2.08−1.90 (m, 1 H), 1.70−1.60 (m, 1 H), 1.25−1.20 (m, 1 H), 1.19 (s, 9 H), 1.11 (s, 3 H), 1.04 (s, 3 H), 0.96 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 178.3, 159.1, 134.7, 129.1 (2 C), 113.7 (2 C), 80.4, 73.4, 69.3, 55.1, 51.1, 38.8, 35.0, 29.8, 27.1 (3 C), 19.1, 17.6, 16.3; HRMS (EI) m/z (M^+) calcd 378.2406, obsd 378.2394; $[\alpha]^{20}_D$ +5.2 (c 1.30, $CHCl_3$).

(2*R*,4*R*)-4-[(*p*-Methoxybenzyl)oxy]-2,5,5-trimethyl-6-heptenyl Pivalate (27b). To a suspension of methyltriphenylphosphonium iodide (29.1 g, 72 mmol) in THF (450 mL) was added potassium hexamethyldisilazide (144 mL of 0.5 M in toluene, 72 mmol) at 0 °C. After 20 min of stirring, a solution of **27a** (18.13 g, 48 mmol) in THF (50 mL) was introduced via cannula, and the reaction mixture was stirred at 0 °C for an additional 20 min before being quenched with saturated NH_4Cl solution. The product was extracted into ether (three times), and the combined organic phases were dried and concentrated. The residue was chromatographed on silica gel (elution with 10% ether in hexanes) to provide **27b** as a colorless oil (16.02 g, 89%); IR (film, cm^{-1}) 1728, 1248, 1162; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.6 Hz, 2 H), 6.86 (d, J = 8.6 Hz, 2 H), 5.91 (dd, J = 16.8, 10.5 Hz, 1 H), 5.02−4.96 (m, 2 H), 4.58 (d, J = 10.8 Hz, 1 H), 4.51 (d, J = 10.8 Hz, 1H), 3.88 (dd, J = 5.8, 5.0 Hz, 2 H), 3.79 (s, 3 H), 3.20 (dd, J = 9.7, 2.0 Hz, 1 H), 2.00−1.95 (m, 1 H), 1.58−1.49 (m, 1 H), 1.27−1.20 (m, 1 H), 1.19 (s, 9 H), 1.06 (s, 3 H), 1.04 (s, 3 H), 0.93 (d, J = 7.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4, 159.0, 146.0, 131.2, 129.1 (2 C), 113.7 (2 C), 111.7, 84.2, 74.6, 69.7, 55.2, 42.4, 38.8, 35.4, 29.9, 27.2 (3 C), 24.1, 22.8, 16.5; HRMS (EI) m/z (M^+) calcd 377.2692, obsd 377.2731; $[\alpha]^{20}_D$ +17.6 (c 1.83, $CHCl_3$).

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.35; H, 9.64. Found: C, 73.20; H, 9.51.

(2*R*,4*R*,6*S*)-6,7-Dihydroxy-4-[(*p*-methoxybenzyl)oxy]-2,5,5-trimethylheptyl Pivalate (28). To a well stirred mixture of $(DHQ)_2PYR$ (6.3 mg, 7.2 μmol), osmium tetraoxide (45 μL of 0.16 M in THF, 7.17 μmol), potassium ferricyanide (707 mg, 2.15 mmol), and K_2CO_3 (296 mg, 2.15 mmol) in *tert*-butyl alcohol-water (1:1, 8 mL) was added **27b**

(270 mg, 717 μmol) dissolved in the same solvent system (3 mL at 0 °C). The mixture was stirred overnight at this temperature, treated with sodium sulfite (1.2 g), and after 20 min extracted several times with CH_2Cl_2. The combined organic layers were dried and concentrated. Flash chromatography of the residue on silica gel (gradient elution with 50% ethyl acetate in hexanes to 100% ethyl acetate) gave **28** as a colorless, oily mixture (>25:1) of diastereomers (293 mg, 99%); IR (film, cm^{-1}) 3440, 1727, 1514, 1248, 1171; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22 (d, J = 8.5 Hz, 2 H), 6.85 (d, J = 8.5 Hz, 2 H), 4.55 (s, 2 H), 3.90 (d, J = 6.2 Hz, 2 H), 3.70 (s, 3 H), 3.71 (dd, J = 3.0, 7.8 Hz, 1 H), 3.61−3.51 (m, 2 H), 3.36 (dd, J = 1.6, 9.3 Hz, 1 H), 2.03−1.95 (m, 1 H), 1.79−01.73 (m, 1 H), 1.39−1.32 (m, 1 H), 1.18 (s, 9 H), 1.03 (s, 3 H), 0.94 (d, J = 6.7 Hz, 3 H), 0.83 (s, 3 H) (two OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3, 159.3, 129.9, 129.1 (2 C), 113.8 (2 C), 94.4, 86.2, 75.8, 74.8, 63.2, 55.1, 40.5, 38.7, 34.8, 30.2, 27.1 (3 C), 21.7, 20.9, 16.3; HRMS (EI) m/z (M^+) calcd 410.2668, obsd 410.2669; $[\alpha]^{20}_D$ +15.3 (c 1.00, $CHCl_3$).

(2*R*,4*R*,6*S*)-7-(*tert*-Butyldiphenylsiloxy)-4-[(*p*-methoxybenzyl)-oxy]-2,5,5-trimethyl-6-(triethylsiloxy)heptyl Pivalate (29). A solution of **28** (293 mg, 717 μmol), *tert*-butyldiphenylsilyl chloride (295 mg, 1.07 mmol), and imidazole (195 mg, 2.87 mmol) in THF (15 mL) was stirred for 5 h, quenched with saturated NH_4Cl solution, and extracted with ether (three times). The combined organic phases were dried and concentrated to leave a residue, purification of which by flash chromatography (SiO_2, elution with 20% ether in hexanes) afforded 636 mg of a colorless oil.

This oil was dissolved in DMF (10 mL), treated in turn with triethylsilyl chloride (324 mg, 2.15 mmol), DMAP (87 mg, 717μmol), and imidazole (195 mg, 2.86 mmol), stirred for 5 h, quenched with saturated NH_4Cl solution, and extracted with 1:1 ether−hexanes (three times). The combined organic layers were processed in the predescribed manner to furnish 439 mg (81% over two steps) of **29** as a colorless oil; IR (film, cm^{-1}) 1729, 1109; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71−7.67 (m, 4 H), 7.44−7.34 (m, 6 H), 7.22 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 4.49 (s, 2 H), 3.89 (dd, J = 1.6, 5.9 Hz, 2 H), 3.86−3.80 (m, 2 H), 3.80 (s, 3 H), 3.63−3.58 (m, 1 H), 3.48 (dd, J = 2.0, 9.4 Hz, 1 H), 2.05−1.90 (m, 1 H), 1.70−1.60 (m, 1 H), 1.35−1.25 (m, 1 H), 1.21 (s, 9 H), 1.09 (s, 9 H), 1.06−0.85 (m, 15 H), 0.79 (s, 3 H), 0.72−0.60 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4, 158.8, 135.8 (2 C), 135.7 (2 C), 133.6, 133.5, 131.5, 129.6 (2 C), 129.5 (2 C), 128.5 (2 C), 127.6 (2 C), 113.6 (2 C), 81.2, 78.9, 73.9, 69.8, 66.8, 55.2, 43.4, 38.8, 34.8, 30.3, 27.2 (3 C), 26.9 (3 C), 20.3 (2 C), 19.1, 16.4, 7.1 (3 C), 5.5 (3 C); FAB MS m/z (M^+ + H) calcd 763.47 obsd 763.41; $[\alpha]^{20}_D$ +13.7 (c 2.06, $CHCl_3$).

Anal. Calcd for $C_{45}H_{70}O_6Si_2$: C, 70.82; H, 9.25. Found: C, 70.64; H, 9.11.

(2*R*,4*R*,6*S*)-7-(*tert*-Butyldiphenylsiloxy)-4-[(*p*-methoxybenzyl)-oxy]-2,5,5-trimethyl-6-(triethylsiloxy)heptanal (30). A solution of **29** (509 mg, 667 μmol) in THF (10 mL) was cooled to −78 °C, treated with diisobutylaluminum hydride (2.67 mL of 1.0 M in hexanes, 2.67 mmol), warmed to −40 °C, stirred for 1 h at this temperature, and quenched slowly with acetone (1 mL) and tartaric acid (10 mL of 1 M in water). The reaction mixture was stirred for 1 h at room temperature before extraction with ether (three times). The combined organic phases were washed with brine, dried, and freed of solvent to leave a residue that was purified by flash chromatography on silica gel (elution with 50% ether in hexanes). Obtained was 357 mg (79%) of the primary alcohol as a colorless gum; IR (film, cm^{-1}) 3358, 1110; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (m, 4 H), 7.43−7.32 (m, 6 H), 7.15 (d, J = 8.6 Hz, 2 H), 6.80 (d, J = 8.6 Hz, 2 H), 4.42−4.36 (m, 2 H), 3.85 (dd, J = 10.8, 2.8 Hz, 1 H), 3.78 (s, 3 H), 3.70 (dd, J = 6.3, 2.8 Hz, 1 H), 3.55 (dd, J = 10.8, 6.2 Hz, 1 H), 3.48−3.41 (m, 3 H), 1.80−1.75 (m, 1 H), 1.66 (br s, 1 H), 1.60−1.45 (m, 1 H), 1.30−1.18 (m, 1 H), 1.07 (s, 9 H), 1.05−0.88 (m, 12 H), 0.86 (s, 3 H), 0.76 (s, 3 H), 0.73−0.60 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 135.8 (2 C), 135.7 (2 C), 133.5, 133.4, 131.1, 129.6, 129.5, 128.2 (2 C), 127.6 (4 C), 113.6 (2 C), 81.4, 79.8, 74.6, 69.2, 67.2, 55.2, 43.4, 34.8, 33.2, 26.9 (3 C), 20.4 (2 C), 19.1, 16.9, 7.1 (3 C), 5.4 (3 C); HRMS (EI) m/z (M^+ − C_4H_9OH) calcd 604.3585, obsd 604.3589; $[\alpha]^{20}_D$ −0.5 (c 1.88, $CHCl_3$).

The alcohol above (102 mg, 150 μmol) was dissolved in CH_2Cl_2 (2 mL), treated with tetra-*n*-propylammonium perruthenate (2.6 mg, 7.5 μmol), *N*-methylmorpholine *N*-oxide (NMO) (26 mg, 225 μmol), and powdered 4-Å molecular sieves (75 mg), stirred for 1 h, and concentrated. The black residue was purified by flash chromatography on silica gel (elution with 20% ether in hexanes) to provide **30** as a colorless gum (90 mg, 89%); IR (film, cm^{-1}) 1723, 1513, 1247, 1107; ^1H NMR (300 MHz, $CDCl_3$) δ 9.44 (d, J = 2.9 Hz, 1 H), 7.71−7.67 (m, 4 H), 7.46−7.36 (m, 6 H), 7.21 (d, J = 8.6 Hz, 2 H), 6.83 (d, J = 8.6 Hz, 2 H), 4.45 (d, J = 10.5 Hz, 1 H), 4.37 (d, J = 10.5 Hz, 1 H), 3.84−3.76 (m, 2 H), 3.80 (s, 3 H), 3.60 (dd, J = 4.8, 9.9 Hz, 1 H), 3.50 (dd, J = 2.5, 10.5 Hz, 1 H), 2.38−2.34 (m, 1 H), 2.07−1.98 (m, 1 H), 1.42 (ddd, J = 2.5, 6.5, 9.0 Hz, 1 H), 1.11 (s, 9 H), 1.02−0.92 (m, 15 H), 0.85 (s, 3 H), 0.68−0.51 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 159.0, 136.0 (4 C), 133.6, 133.5, 131.0, 129.9 (2 C), 129.1 (4 C), 127.9 (2 C), 113.8 (2 C), 82.4, 78.8, 74.3, 66.9, 55.4, 44.6, 43.9, 33.4, 27.2 (3 C), 20.7, 20.5, 19.3, 14.3, 7.3 (3 C), 5.6 (3 C); HRMS m/z (M^+ − $C_6H_{15}Si$) calcd 618.3741, obsd 618.3779; $[\alpha]^{20}_D$ +14.8 (c 1.02, $CHCl_3$).

(4*R*,6*R*,8*S*)-1-[(2*S*,4*S*,5*R*,6*S*)-6-Allyl-4-(benzyloxy)tetrahydro-5-methyl-2*H*-pyran-2-yl]-9-(*tert*-butyldiphenylsiloxy)-8-hydroxy-6-[(*p*-methoxybenzyl)oxy]-4,7,7-trimethyl-2-(phenylsulfonyl)-3-nonanone (39). A solution of **34** (232 mg, 213 μmol) and *p*-toluenesulfonic acid (4 mg, 21.3 μmol) in methanol (5 mL) was stirred for 1 h, quenched with saturated $NaHCO_3$ solution (5 mL), and concentrated. After extraction with CH_2Cl_2 (three times), the combined organic layers were dried and freed of solvent under reduced pressure. The residue was purified by flash chromatography on silica gel (elution with 50% ether in hexanes) to provide **39** as a white foam (201 mg, 97%); IR (film, cm^{-1}) 3566, 1715, 1612, 1308, 1111; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78−7.26 (m, 22 H), 5.88 (m, 2 H), 5.83−5.60 (m, 1 H), 5.03−4.87 (m, 2 H), 4.79−4.59 (m, 3 H), 4.35 (m, 1 H), 3.79 (s, 3 H), 3.78−3.43 (m, 4 H), 3.20−2.75 (m, 4 H), 2.31−2.29 (m, 1 H), 2.20−1.80 (m 4 H), 1.70−1.50 (m, 2 H), 1.40−1.20 (m, 2 H), 1.16−0.75 (m, 20 H), 0.70 and 0.65 (2 s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.5, 205.2, 159.1, 159.0, 138.4, 138.3, 137.0, 136.9, 135.5, 135.4, 134.5, 134.0, 133.9, 133.1, 133.0, 132.9, 129.3, 129.2, 127.9, 127.6, 127.5, 116.9, 116.6, 113.8, 91.9, 81.7, 80.2, 79.9, 79.7, 79.6, 75.1, 74.7, 74.5, 72.7, 70.9, 70.4, 70.3, 69.9, 69.6, 64.9, 64.7, 60.2, 55.1, 45.3, 44.5, 40.9, 40.5, 40.2, 37.1, 36.9, 34.3, 33.6, 32.9, 32.4, 26.8, 20.9, 19.2, 19.1, 19.0, 18.9, 18.8, 15.3, 14.3, 14.1, 12.6, 12.5; FAB MS m/z (M^+ − OH) calcd 957.33, obsd 957.43; $[\alpha]^{20}_D$ +10.7 (c 2.01, $CHCl_3$).

(2*S*,3*R*,4*S*,6*S*)-4-(Benzyloxy)-6-(4*R*,6*R*,8*S*)-9-(*tert*-butyldiphenylsiloxy)-8-hydroxy-6-[(*p*-methoxybenzyl)oxy]-4,7,7-trimethyl-3-oxo-2-(phenylsulfonyl)nonyl]tetrahydro-3-methyl-2*H*-pyran-2-acetaldehyde (40). A solution of **39** (452 mg, 464 μmol), osmium tetraoxide (11.8 mg, 46.4 μmol), and *N*-methylmorpholine *N*-oxide (109 mg, 927 μmol) in THF−water (5:1, 6 mL) was stirred for 4 h, at which point sodium periodate (298 mg, 1.39 μmol) was introduced and agitation was continued for another 3 h. The reaction mixture was quenched with saturated sodium sulfite solution (3 mL), stirred for 30 min, and extracted with ether (three times). The usual workup including flash chromatography on silica gel (elution with 30% ethyl acetate in hexanes) furnished 403 mg (89%) of **40** as a white foam; IR (film, cm^{-1}) 3430, 1719, 1079; ^1H NMR (300 MHz, $CDCl_3$) δ 9.71 and 9.61 (m, 1 H), 7.79−7.25 (m, 22 H), 6.93−6.88 (m, 2 H), 4.73−4.55 (m, 3 H), 4.42−4.32 (m, 1 H), 3.82−3.40 (m, 8 H), 3.30−2.80 (m, 3 H), 2.65−2.23 (m, 2 H), 2.15−1.80 (m, 3 H), 1.75−1.55 (m, 2 H), 1.50−0.60 (m, 25 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 200.7, 159.2, 159.1, 138.2, 138.1, 136.7, 135.5, 135.4, 134.2, 134.1, 133.2, 133.1, 133.0, 131.0, 130.8, 129.8, 129.7, 129.3, 127.5, 113.9, 113.8, 113.6, 82.1, 82.0, 79.3, 79.1, 76.8, 76.6, 75.2, 74.8, 74.8, 74.5, 72.9, 71.5, 70.6, 70.4, 69.6, 64.9, 64.8, 55.2, 47.0, 46.7, 45.3, 44.3, 41.6, 41.4, 41.0, 37.1, 37.0, 33.9, 33.7, 33.1, 32.4, 26.8, 19.3 (2 C), 19.1, 19.0, 15.4, 14.4, 14.1, 12.9, 12.7; FAB MS m/z (M^+) calcd 976.45, obsd 976.35; $[\alpha]^{20}_D$ −2.6 (c 1.53, $CHCl_3$).

(2*S*,3*R*,4*S*,6*S*)-4-(Benzyloxy)-6-(4*R*,6*R*,8*S*)-9-(*tert*-butyldiphenylsiloxy)-8-hydroxy-6-[(*p*-methoxybenzyl)oxy]-4,7,7-trimethyl-3-oxo-2-(phenylsulfonyl)nonyl]tetrahydro-3-methyl-2*H*-pyran-2-acetic Acid (41). To a mixture of **40** (395 mg, 404 μmol), monobasic sodium phosphate hydrate (557 mg, 4.04 mmol), and β-isoamylene (2.8 g, 40 mmol) in *tert*-butyl alcohol−water (3:1, 4 mL) was added a solution of sodium chlorite (219 mg, 2.42 mmol) in the same medium (4 mL)

at 0 °C. After 10 min of stirring, saturated $NaHSO_3$ solution and brine were introduced, and the product was extracted into ethyl acetate (five times). The combined organic phases were dried and concentrated, and the residue was purified by flash chromatography (SiO_2, elution with 50% ethyl acetate in hexanes) to give **41** as a white foam (353 mg, 88%); IR (film, cm^{-1}) 3572−2784, 1717, 1308, 1111; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85−7.20 (m, 22 H), 7.00−6.85 (m, 2 H), 4.88−4.55 (m, 3 H), 4.45−4.30 (m, 1 H), 3.90−3.57 (m, 7 H),3.50−3.30 (m, 1 H), 3.30−2.75 (m, 4 H), 2.68−2.50 (m, 1 H), 2.40−0.60 (series of m, 29 H) (two OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 172.0, 159.8, 138.2, 137.0, 135.6, 134.0, 133.1, 133.0, 130.1, 130.0, 129.9, 129.8, 129.7, 129.5, 128.6, 128.3, 127.8, 127.7, 127.6, 114.2, 113.9, 83.3, 79.2, 78.7, 75.4, 74.4, 70.8, 70.6, 70.4, 69.9, 64.6, 55.2, 44.3, 41.3, 40.5, 39.0, 38.7, 37.5, 33.2, 32.9, 26.8, 26.7, 19.8, 19.4, 19.1, 14.9, 12.9; FAB MS *m/z* ($M^+ - OH$) calcd 975.56, obsd 975.38; $[\alpha]^{20}_D$ −12.2 (*c* 1.73, $CHCl_3$).

(1*S*,5*S*,7*R*,9*R*,13*S*,15*S*,16*R*)-15-(Benzyloxy)-5-[(*tert*-butyldiphenylsiloxy)methyl]-7-[(*p*-methoxybenzyl)oxy]-6,6,9,16-tetramethyl-11-(phenylsulfonyl)-4,17-dioxabicyclo[11.3.1]heptadecane-3,10-dione (42). A solution of hydroxy acid **41** (555 mg, 0.56 mmol) in THF (1 mL) was treated with 2,4,6-trichlorobenzoyl chloride (409 mg, 1.67 mmol) and triethylamine (282 mg, 2.79 mmol), stirred for 4 h, filtered through a cotton plug, and diluted with toluene (10 mL). This solution of the mixed anhydride was introduced via a syringe pump during a 2-h period into a solution of DMAP (409 mg, 3.35 mmol) in toluene (102 mL) at 110 °C. The syringe was rinsed with toluene (1 mL) and heating was continued for an additional 30 min. The cooled reaction mixture was diluted with saturated sodium bisulfite solution (10 mL) and extracted with ether (three times). After the combined organic phases had been dried and evaporated, the residue was subjected to flash chromatography (SiO_2, elution with 20% ethyl acetate in hexanes) to provide **42** as a diastereomerically pure white foam (445 mg, 82%); IR (film, cm^{-1}) 1733, 1248; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70−7.23 (m, 20 H), 7.06 (d, J = 8.6 Hz, 2 H), 6.69 (d, J = 8.6 Hz, 2 H), 5.04 (dd, J = 2.0, 9.3 Hz, 1 H), 4.91 (dd, J = 3.5, 10.9 Hz, 1 H), 4.60 (d, J = 11.6 Hz, 1 H), 4.40 (d, J = 10.6 Hz, 1 H), 4.35 (d, J = 11.6 Hz, 1 H), 4.30 (d, J = 10.6 Hz, 1 H), 4.10 (dd, J = 9.1, 11.6 Hz, 1 H), 3.85 (dd, J = 2.1, 11.6 Hz, 1 H), 3.82−3.72 (m, 4 H), 3.15−2.95 (m, 4 H), 2.61−2.43 (m, 2 H), 2.15−1.95 (m, 2 H), 1.40−0.85 (series of m, 23 H), 0.80 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 171.5, 159.2, 138.3, 136.8, 135.7 (4 C), 135.5 (2 C), 134.1, 133.7, 133.6, 130.3, 129.7 (2 C), 129.2 (2 C), 129.0 (2 C), 128.7, 128.3 (2 C), 127.6 (2 C), 126.7 (4 C), 113.7 (2 C), 84.4, 81.3, 79.3, 79.2, 75.7, 71.4, 70.4, 68.4, 64.2, 55.2, 44.7, 42.0, 41.9, 40.7, 37.2, 33.4, 33.3, 26.7 (3 C), 24.3, 24.1, 19.0, 13.5, 13.2; FAB MS *m/z* ($M^+ + H$) calcd 975.45, obsd 975.37; $[\alpha]^{20}_D$ −25.9 (*c* 1.08, $CHCl_3$).

(1*S*,5*S*,7*R*,9*R*,13*S*,15*S*,16*R*)-15-(Benzyloxy)-5-(hydroxymethyl)-7-[(*p*-methoxybenzyl)oxy]-6,6,9,16-tetramethyl-11-(phenylsulfonyl)-4,17-dioxabicyclo[11.3.1]heptadecane-3,10-dione (47). A solution of **42** (167 mg, 171 μmol) in THF (1 mL) was treated with the HF−pyridine complex (400 μL) in THF−pyridine (1:3, 3 mL) at 0 °C, stirred for 5 h at room temperature, quenched with saturated $NaHCO_3$ solution (20 mL), and extracted with ether (three times). After drying and solvent evaporation, the residue was chromatographed on silica gel (elution with 50% ethyl acetate in hexanes) to deliver **47** as a colorless foam (77 mg, 64%); IR (film, cm^{-1}) 3469, 1718, 1309, 1251; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 7.4 Hz, 2 H), 7.62−7.46 (m, 4 H), 7.37−7.24 (m, 6 H), 6.92 (d, J = 7.4 Hz, 2 H), 5.10 (dd, J = 2.4, 11.9 Hz, 1 H), 4.67−4.53 (m, 4 H), 4.33 (d, J = 11.6 Hz, 1 H), 4.15−3.69 (series of m, 3 H), 3.80 (s, 3 H), 3.42−3.32 (m, 2 H), 3.15 (br dt, J = 1.2, 9.4 Hz, 1 H), 2.99 (dt, J = 3.8, 10.2 Hz, 1 H), 2.87 (dq, J = 0.6, 10.3 Hz, 2 H), 2.63−2.58 (m, 2 H), 2.23 (t, J = 12.3 Hz, 1 H), 2.00−1.90 (m, 1 H), 1.85−1.80 (m, 1 H), 1.27−1.19 (m, 3 H), 1.22 (s, 3 H), 1.15 (d, J = 6.3 Hz, 3 H), 0.94 (s, 3 H), 0.92 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 170.9, 159.6, 138.2, 137.1, 134.0, 129.6 (2 C), 129.1 (5 C), 128.3 (2 C), 127.7 (2 C), 127.6, 114.2 (2 C), 83.8, 82.1, 79.1, 77.4, 76.7, 71.9, 70.2, 67.5, 59.4, 55.2, 44.6, 42.4, 41.3, 40.1, 36.7, 33.5, 32.4, 26.1, 24.6, 13.6, 12.9; FAB MS *m/z* ($M^+ - OH$) calcd 719.32, obsd 719.38; $[\alpha]^{20}_D$ −81.9 (*c* 2.14, $CHCl_3$).

(1*S*,5*S*,7*R*,9*R*,13*S*,15*S*,16*R*)-15-(Benzyloxy)-7-[(*p*-methoxybenzyl)oxy]-6,6,9,16-tetramethyl-3,10-dioxo-11-(phenylsulfonyl)-4,17-dioxabicyclo[11.3.1]heptadecane-5-carboxaldehyde (48). To a solution of **47** (77 mg, 109 μmol) in CH_2Cl_2 (2 mL) was added the Dess−Martin periodinane (60.2 mg, 141 μmol). The reaction mixture was stirred for 30 min, quenched with saturated $NaHCO_3$ solution (5 mL) and solid sodium thiosulfate (100 mg), stirred for 20 min, and worked up in the usual manner. After chromatography on silica gel (elution with 50% ethyl acetate in hexanes), there was isolated 69 mg (90%) of **48** as a white foam; IR (film, cm^{-1}) 1724, 1513, 1250, 1083; ^1H NMR (300 MHz, $CDCl_3$) δ 9.36 (d, J = 1.7 Hz, 1 H), 7.69−7.60 (m, 3 H), 7.51−7.45 (m, 2 H), 7.38−7.24 (m, 7 H), 6.93 (d, J = 8.7 Hz, 2 H), 4.80 (dd, J = 2.7, 12.5 Hz, 1 H), 4.61 (d, J = 10.2 Hz, 1 H), 4.59 (d, J = 11.6 Hz, 1 H), 4.46 (d, J = 10.8 Hz, 1 H), 4.43 (d, J = 1.7 Hz, 1 H), 4.34 (d, J = 11.6 Hz, 1 H), 3.78 (s, 3 H), 3.40−3.24 (m, 3 H), 3.01 (dt, J = 4.5, 10.6 Hz, 1 H), 2.86 (br t, J = 10.8 Hz, 1 H), 2.72 (dd, J = 1.5, 18.2 Hz, 1 H), 2.58 (dd, J = 8.8, 18.2 Hz, 1 H), 2.49 (t, J = 12.7 Hz, 1 H), 2.16 (t, J = 12.6 Hz, 1 H), 2.05−1.99 (m, 1 H), 1.88−1.79 (m, 1 H), 1.42 (s, 3 H), 1.38−1.11 (m, 3 H), 1.08 (d, J = 6.2 Hz, 3 H), 1.02 (s, 3 H), 0.92 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.1, 194.7, 170.5, 159.5, 138.1, 137.0, 134.1, 130.2 (2 C), 129.2 (2 C), 129.1, 129.0 (2 C), 128.4, 127.7 (4 C), 113.9 (2 C), 85.3, 83.0, 78.9, 77.3, 76.6, 71.6, 70.3, 69.2, 55.3, 45.4, 44.6, 41.3, 39.5, 37.1, 33.7, 32.9, 26.5, 23.8, 13.6, 12.5; FAB MS *m/z* ($M^+ + H$) calcd 735.32, obsd 735.32; $[\alpha]^{20}_D$ −93.9 (*c* 1.65, CH_2Cl_2).

(1*S*,5*R*,7*R*,9*R*,13*S*,15*S*,16*R*)-15-(Benzyloxy)-5-[(*E*)-2-iodovinyl]-7-[(*p*-methoxybenzyl)oxy]-6,6,9,16-tetramethyl-11-(phenylsulfonyl)-4,-17-dioxabicyclo[11.3.1]heptadecane-3,10-dione (49). Chromium dichloride (603 mg, 4.91 mmol) was added to a solution of **48** (69 mg, 98 μmol) and iodoform (579 mg, 1.47 mmol) in THF (5 mL) at 0 °C. The dark solution was stirred for 3 h, diluted with water (3 mL) and saturated sodium thiosulfate solution (3 mL), and extracted with ether (three times). The combined organic phases were dried and concentrated. The residue was subjected to flash chromatography on silica gel (gradient elution with 10−40% ethyl acetate in hexanes) to give **49** as a yellow foam (54 mg, 77% based on 12 mg of recovered **48**); IR (film, cm^{-1}) 1725, 1240, 1092; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73−7.44 (m, 6 H), 7.37−7.21 (m, 6 H), 6.95 (d, J = 9.6 Hz, 2 H), 6.79 (dd, J = 8.7, 16.4 Hz, 1 H), 6.33 (d, J = 14.5 Hz, 1 H), 5.00 (d, J = 8.6 Hz, 1 H), 4.81 (dd, J = 3.1, 11.2 Hz, 1 H), 4.60 (d, J = 11.6 Hz, 1 H), 4.47 (s, 2 H), 4.34 (d, J = 11.6 Hz, 1 H), 3.80 (s, 3 H), 3.78−3.65 (m, 1 H), 3.29−3.12 (m, 3 H), 3.01−2.96 (m, 2 H), 2.56−2.40 (m, 3 H), 2.24−2.15 (m, 1 H), 2.04−1.89 (m, 2 H), 1.69−1.60 (m, 1 H), 1.30−1.25 (m, 1 H), 1.14 (s, 3 H), 1.10 (d, J = 6.4 Hz, 3 H), 0.93 (d, J = 6.4 Hz, 3 H), 0.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 170.6, 159.2, 142.1, 138.2, 134.1, 130.5, 129.3 (2 C), 129.2 (2 C), 129.1, 129.0 (2 C), 128.8 (2 C), 128.4, 128.3, 127.7 (2 C), 114.0 (2 C), 84.1, 80.3, 79.2, 78.2, 75.8, 71.5, 70.3, 68.7, 55.3, 45.0, 42.5, 41.6, 40.4, 37.1, 33.7, 33.2, 25.1, 23.7, 13.5 (2 C); FAB MS *m/z* (M^+) calcd 858.23, obsd 858.41; $[\alpha]^{20}_D$ −72.1 (*c* 0.9, $CHCl_3$).

(1*S*,4*R*,5*R*,7*R*,9*R*,13*S*,14*R*,15*S*)-4,15-Dihydroxy-9-[(*E*)-2-iodovinyl]-5,8,8,14-tetramethyl-10,17,18-trioxatricyclo[11.3.1.1^{4,7}]octadecane-3,11-dione (50). A solution of **49** (24 mg, 28 μmol) in THF (4 mL) was treated with potassium *tert*-butoxide (33.5 μL in 1.0 M in *tert*-butyl alcohol, 33.5 μmol) at 0 °C and stirred for 30 min at this temperature before the addition of the Davis oxaziridine (14.4 mg, 55.8 μmol) in THF (1 mL) via cannula. After an additional 1 h of agitation at 0 °C, the reaction mixture was quenched with saturated NH_4Cl solution (10 mL) and extracted several times with ether. The combined organic phases were dried and concentrated to leave an oil that was dissolved in CH_2Cl_2 and water (18:1, 4 mL), treated with DDQ (190 mg, 840 μmol), and stirred for 20 h. After saturated $NaHCO_3$ solution had been introduced, the product was extracted into CH_2Cl_2 (three times), dried, and concentrated. The residue was purified by flash chromatography on silica gel (elution with 70% ethyl acetate in hexanes) to furnish **50** as a colorless solid (10.6 mg, 73%); IR (film, cm^{-1}) 3482, 1719, 1162; ^1H NMR (300 MHz, $CDCl_3$) δ 6.47 (dd, J = 7.1, 14.4 Hz, 1 H), 6.40 (d, J = 14.4 Hz, 1 H), 5.12 (d, J = 7.1 Hz, 1 H), 4.48 (s, 1 H), 4.15 (dd, J = 5.2, 11.4 Hz, 1 H), 3.79 (br t, J = 10.6 Hz, 1 H), 3.44−3.36 (m, 3 H), 3.05 (dd, J = 9.2, 13.4 Hz, 1 H), 2.76−2.71 (m, 1 H), 2.56 (dd, J = 2.5, 12.5 Hz, 1 H), 2.24 (t, J = 11.8 Hz, 1 H), 2.07−1.97 (m, 3 H), 1.69 (q, J = 11.6 Hz, 1 H), 1.38 (q, J = 11.6 Hz, 1 H), 0.98 (d, J = 6.4 Hz, 3 H), 0.97 (d, J = 6.3 Hz, 3 H), 0.89 (s, 3

H), 0.88 (s, 3 H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 171.2, 140.9, 102.8, 83.0, 82.0, 79.4, 78.9, 74.0, 72.7, 43.4, 42.1, 41.6, 39.5, 39.3, 39.1, 33.5, 19.3, 17.7, 13.3, 12.6; HRMS *m*/*z* (M^+) calcd 522.1114, obsd 522.1112; $[\alpha]^{20}_D$ −47.0 (*c* 0.29, $CHCl_3$).

(1*S*,4*R*,5*R*,7*R*,9*R*,13*S*,14*S*,15*S*)-4-Hydroxy-9-[(*E*)-2-iodovinyl]-15-[[3-*O*-[4-*O*-(*p*-methoxybenzyl)-2,3-di-*O*-methyl-α-L-fucopyranosyl]-2,4-di-*O*-methyl-*β*-D-xylopyranosyl]oxy]-5,8,8,14-tetramethyl-10,-17,18-trioxatricyclo[11.3.1.1^{4,7}]octadecane-3,11-dione (52). Reaction of **50** (32 mg, 361 μmol) with **18b** (68.8 mg, 122 μmol), *N*-bromosuccinimide (43.4 mg, 244 μmol), and pulverized 4-Å molecular sieves (160 mg) in the predescribed manner afforded 21.3 mg (36%) of **52** as an amorphous white solid together with 7.4 mg (13% of the α-anomer.

For **52**: IR (film, cm^{-1}) 1731, 1095; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 2.0 Hz, 1 H), 7.31 (dd, *J* = 1.9, 8.4 Hz, 1 H), 7.27 (br s, 1 H), 6.86 (d, *J* = 8.4 Hz, 1 H), 6.51 (dd, *J* = 7.1, 14.4 Hz, 1 H), 6.43 (d, *J* = 14.4 Hz, 1 H), 5.38 (d, *J* = 3.7 Hz, 1 H), 5.12 (d, *J* = 7.1 Hz, 1 H), 4.84 (d, *J* = 11.5 Hz, 1 H), 4.55 (d, *J* = 11.5 Hz, 1 H), 4.48 (br s, 1 H), 4.28 (d, *J* = 7.7 Hz, 1 H), 4.20−4.10 (m, 2 H), 4.00 (dd, *J* = 5.0, 11.0 Hz, 1 H), 3.89 (s, 3 H), 3.78−3.70 (m, 4H), 3.56 (s, 3 H), 3.55 (s, 3 H), 3.51 (s, 3 H), 3.43−3.38 (m, 2 H), 3.35 (s, 3 H), 3.34−3.30 (m, 2 H), 3.28−3.08 (m, 2 H), 3.03 (dd, *J* = 4.0, 13.4 Hz, 1 H), 2.80−2.60 (m, 1 H), 2.55 (dd, *J* = 2.7, 12.6 Hz, 1 H), 2.23 (t, *J* = 11.4 Hz, 1 H), 2.17−2.10 (m, 1 H), 2.04−1.97 (m, 2 H), 1.69 (q, *J* = 12.0 Hz, 1 H), 1.50 (q, *J* = 11.9 Hz, 1 H), 1.45−1.30 (m, 2 H), 1.12 (d, *J* = 6.5 Hz, 3 H), 1.00 (d, *J* = 6.7 Hz, 6 H), 0.89 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2, 171.2, 133.4, 132.5, 128.7, 113.6, 105.9, 102.8, 97.2, 84.2, 82.9, 82.3, 81.9, 80.9, 80.8, 79.4, 78.1, 77.8, 74.1, 73.6, 66.1, 65.9, 63.1, 60.4, 59.1, 58.0, 56.3, 55.3, 42.1, 41.9, 41.0, 39.6, 39.3, 39.1, 33.5, 19.3, 17.6, 16.6, 13.3, 12.6; FAB MS *m*/*z* (M^+) calcd 976.33, obsd 976.34; $[\alpha]^{20}_D$ −69.1 (*c* 1.19, $CHCl_3$).

For the α-anomer: IR (film, cm^{-1}) 1714, 1258; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (s, 1 H), 7.32 (d, *J* = 7.2 Hz, 1 H), 7.26 (s, 1 H), 6.87 (d, *J* = 8.4 Hz, 1 H), 6.48 (dd, *J* = 7.7, 14.4 Hz, 1 H), 6.40 (d, *J* = 14.4 Hz, 1 H), 5.36 (d, *J* = 3.6 Hz, 1 H), 5.12 (d, *J* = 7.7 Hz, 1 H), 5.05 (d, *J* = 3.5 Hz, 1 H), 4.83 (d, *J* = 11.6 Hz, 1 H), 4.57 (d, *J* = 11.6 Hz, 1 H), 4.39 (s, 1 H), 4.20−4.10 (m, 3 H), 3.89 (s, 3 H), 3.84 (t, *J* = 9.3 Hz, 1 H), 3.76−3.73 (m, 2 H), 3.69 (dd, *J* = 3.6, 13.9 Hz, 1 H), 3.67 (s, 1 H), 3.58−3.47 (m, 2 H), 3.53 (s, 3 H), 3.51 (s, 3 H), 3.45−3.21 (m, 3 H), 3.41 (s, 3 H), 3.36 (s, 3 H), 3.05 (dd, *J* = 9.2, 13.4 Hz, 1 H), 2.74−2.69 (m, 1 H), 2.57 (dd, *J* = 2.2, 12.6 Hz, 1 H), 2.24 (t, *J* = 11.8 Hz, 1 H), 2.07−1.99 (m, 3 H), 1.67 (q, *J* = 11.8 Hz, 1 H), 1.50−1.46 (m, 1 H), 1.31 (q, *J* = 11.8 Hz, 1 H), 1.13 (d, *J* = 6.4 Hz, 3 H), 0.98 (d, *J* = 6.5 Hz, 3 H), 0.97 (d, *J* = 6.2 Hz, 3 H), 0.89 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.1, 171.3, 140.9, 144.3, 132.5, 128.6, 111.6, 102.8, 96.8, 91.7, 82.9, 82.2, 80.6 (2 C), 79.3, 79.1, 78.1, 77.8, 76.6, 75.9, 75.0, 73.8, 73.5, 65.8, 59.7, 58.1 (2 C), 57.7, 56.2, 42.3, 40.9, 39.6, 39.3, 39.1, 36.9, 33.5, 19.3, 17.6, 16.6, 13.3, 13.2 (3 carbons not observed); HRMS (molecular ion too fleeting for accurate mass measurement); $[\alpha]^{20}_D$ −34.7 (*c* 0.47, $CHCl_3$).

(1*S*,4*R*,5*R*,7*R*,9*R*,13*S*,14*S*,15*S*)-15-[[3-*O*-(2,3-Di-*O*-methyl-α-L-fucopyranosyl)-2,4-di-*O*-methyl-*β*-D-xylopyranosyl]oxy]-4-hydroxy-9-[(*E*)-2-iodovinyl]-5,8,8,14-tetramethyl-10,17,18-trioxatricyclo-[11.3.1.1^{4,7}] octadecane-3,11-dione (53). A solution of **52** (17 mg, 17 μmol) in CH_2Cl_2−water (18:1, 1 mL) was treated with DDQ (19.7 mg, 87 μmol), stirred overnight, and poured into saturated $NaHCO_3$ solution (2 mL). The product was extracted into CH_2Cl_2, dried, evaporated, and chromatographed on silica gel (elution with ethyl acetate) to give **53** as a white solid (11.3 mg, 76%); IR (film, cm^{-1}) 3431, 1736, 1707, 1093; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.51−6.38 (m, 2 H), 5.36 (d, *J* = 3.0 Hz, 1 H), 5.12 (d, *J* = 7.1 Hz, 1 H), 4.48 (s, 1 H), 4.29−4.21 (m, 2 H), 4.16 (d, *J* = 5.1, 11.3 Hz, 1 H), 4.01 (dd, *J* = 4.9, 11.4 Hz, 1 H), 3.90 (s, 1 H), 3.74 (br t, *J* = 10.1 Hz, 1 H), 3.62−3.50 (m, 4 H), 3.57 (s, 3 H), 3.54 (s, 3 H), 3.51 (s, 3 H), 3.48−3.37 (m, 1 H), 3.37 (s, 3 H), 3.34−3.22 (m, 2 H), 3.16−3.08 (m, 2 H), 3.01 (dd, *J* = 9.1, 13.5 Hz, 1 H), 2.77−2.69 (m, 1 H), 2.55 (dd, *J* = 2.6, 12.5 Hz, 1 H), 2.23 (t, *J* = 15.2 Hz, 1 H), 2.17−2.11 (m, 1 H), 2.04−1.99 (m, 2 H), 1.69 (q, *J* = 11.6 Hz, 1 H), 1.50 (q, *J* = 12.0 Hz, 1 H), 1.44−1.29 (m, 1 H), 1.26 (d, *J* = 6.5 Hz, 3 H), 0.98 (d, *J* = 6.6 Hz, 6 H), 0.89 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.5, 171.6, 141.4, 106.3, 103.2, 97.6, 84.6, 83.4, 82.8, 82.4, 79.8, 79.7, 79.6, 78.7, 78.5, 77.8, 74.5, 69.5, 65.4, 63.5, 60.8, 59.6, 58.4, 57.7, 42.5, 42.4, 41.4, 40.0, 39.7, 39.5, 33.9, 19.7, 18.1, 16.5, 13.7, 12.9; FAB MS *m*/*z* (M^+ + H) calcd 857.28, obsd 857.13; $[\alpha]^{20}_D$ −85.4 (*c* 0.75, $CHCl_3$).

Polycavernoside A (1). To a solution of (*E*,*E*)-1-iodo-5-methyl-1,3-hexadiene[7,47] (128 mg, 576 μmol) in dry THF (5 mL) cooled to −78 °C was added *tert*-butyllithium (699 μL of 1.65 M in pentane, 1.15 mmol). After 30 min of stirring, tributyltin chloride (170 mg, 523 μmol) was introduced and agitation was maintained for another 30 min before warming to room temperature. Thirty minutes later, water (10 mL) was added and the product was extracted into ether (3 × 10 mL). The combined organic phases were concentrated, the residue was taken up in ether (5 mL), and this solution was stirred for 30 min with potassium fluoride (1 g in 10 mL of water). This mixture was stirred for 20 min and filtered to remove the tin fluoride precipitate. The separated ethereal phase was dried and concentrated. A portion of the residue was purified by reverse-phase chromatography on plates (elution with 10% CH_2Cl_2 in acetonitrile, two elutions) to give **54** as a colorless oil that was used directly; ^{1}H NMR (300 MHz, C_6D_6) δ 6.77 (d, *J* = 9.7, 18.7 Hz, 1 H), 6.26 (d, *J* = 18.7 Hz, 1 H), 6.14 (dd, *J* = 9.7, 14.8 Hz, 1 H), 5.59 (dd, *J* = 6.9, 14.8 Hz, 1 H), 2.24−2.17 (m, 1 H), 1.64−1.51 (m, 8 H), 1.43−1.26 (m, 8 H), 1.10−0.80 (m, 17 H); ^{13}C NMR (75 MHz, C_6D_6) δ 148.2, 141.0, 131.5, 130.5, 31.0 (2 C), 29.9 (3 C), 28.1 (3 C), 15.5, 13.9 (3 C), 9.8 (3 C).

A solution of **53** (1.2 mg, 1.4 μmol) and **54** (5.8 mg, 14 μmol) in previously degassed DMF (0.5 mL) was treated with bis(acetonitrile)-dichloropalladium(II) (42 μL of 0.01 M in DMF, 0.42 μmol), stirred in the dark for 5 h, diluted with water, and extracted with ether−hexanes (1:1, 3 × 10 mL). The combined organic phases were dried, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (elution with ethyl acetate) to give **1** as an amorphous white solid (1.0 mg, 87%); ^{1}H NMR (500 MHz, CD_3CN, CHD_2CN as 1.90 ppm) δ 6.19−6.10 (m, 3 H), 6.03 (dd, *J* = 10.5, 15.6 Hz, 1 H), 5.69 (dd, *J* = 6.9, 15.6 Hz, 1 H), 5.58 (dd, *J* = 7.7, 15.0 Hz, 1 H), 5.21 (d, *J* = 3.3 Hz, 1 H), 5.00 (d, *J* = 7.7 Hz, 1 H), 4.59 (s, 1 H), 4.31 (d, *J* = 7.7 Hz, 1 H), 4.13 (br q, *J* = 6.5 Hz, 1 H), 4.05 (dd, *J* = 4.9, 11.4 Hz, 1 H), 3.93 (dd, *J* = 4.6, 10.8 Hz, 1 H), 3.79 (br s, 1 H), 3.64 (br t, *J* = 10.8 Hz, 1 H), 3.48 (s, 3 H), 3.43 (t, *J* = 8.8 Hz, 1 H), 3.38 (s, 3 H), 3.37 (br d, *J* = 10.1 Hz, 1 H), 3.35 (dd, *J* = 3.3, 10.1 Hz, 1 H), 3.34 (s, 3 H), 3.32 (m, 1 H), 3.31 (s, 3 H), 3.29 (m, 1 H), 3.13 (ddd, *J* = 4.5, 8.4, 10.4 Hz, 1 H), 3.08 (dd, *J* = 10.4, 10.9 Hz, 1 H), 2.96 (dd, *J* = 9.0, 13.8 Hz, 1 H), 2.87 (t, *J* = 9.0 Hz, 1 H), 2.80−2.73 (m, 1 H), 2.70 (d, *J* = 3.1 Hz, 1 H), 2.52 (dd, *J* = 2.7, 12.6 Hz, 1 H), 2.30 (m, 1 H), 2.14 (dd, *J* = 11.2, 12.7 Hz, 1 H), 2.10 (m, 1 H), 2.05 (m, 1 H), 1.99 (ddd, *J* = 5.3, 6.8, 11.5 Hz, 1 H), 1.56 (br q, *J* = 11.5 Hz, 1 H), 1.36 (br q, *J* = 11.5 Hz, 1 H), 1.27 (m, 1 H), 1.07 (d, *J* = 6.5 Hz, 3 H), 0.95 (d, *J* = 6.6 Hz, 6 H), 0.92 (d, *J* = 6.4 Hz, 3 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.79 (s, 3 H), 0.77 (s, 3 H); ^{13}C NMR (125 MHz, CD_3CN, $CD_3{}^{13}CN$ as 118.2 ppm) δ 207.3, 172.1, 143.7, 135.3, 134.8, 130.6, 128.7, 128.1, 106.1, 103.8, 97.8, 85.4, 83.6, 82.6, 79.8 (2 C), 79.2, 78.8 (2 C), 78.1, 74.8, 69.2, 66.0, 63.5, 60.8, 58.7, 58.4, 56.9, 43.1, 42.7, 41.5, 40.4, 40.1, 39.4, 34.3, 31.9, 22.3 (2 C), 19.3, 17.8, 16.4, 13.6, 12.7; $[\alpha]^{25}_D$ −34.5 (*c* 0.09, CH_3CN).

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Supporting Information Available: Experimental details for the preparation of those intermediates associated with unsuccessful alternative routes to **1**, viz. **3**−**5**, **10**, **32**−**36**, **43**−**45**, and **51**, along with copies of the 400 MHz ^{1}H NMR spectra of natural and synthetic **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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