Synthesis of Zaragozic Acid A/Squalestatin S1

K. C. Nicolaou,* Eddy W. Yue, Susan La Greca, Alan Nadin, Zhen Yang, James E. Leresche, Tatsuo Tsuri, Yoshimitsu Naniwa, and Francesco De Riccardis

Abstract: A novel synthetic approach to the construction of the zaragozic acids, which was used for the asymmetric synthesis of zaragozic acid A/squalestatin S1 (**1**), is described. Fragment **5**, representing the tricarboxylic acid core portion, is assembled in three key steps: 1) Stille coupling to establish the carbon framework; 2) enantioselective dihydroxylation to introduce the absolute stereochemistry; and 3) diastereoselective dihydroxylation to complete the required carbon–oxygen connectivity. The convergency of this synthesis is demonstrated by the dithiane addition of a variety of C1 side chains (e.g., **78**) to advanced intermediate **5**. A multievent acid-catalyzed rearrangement yielded the zaragozic acid core **86**, which was converted to an intermediate obtained from degradation of zaragozic acid A. A second-generation synthesis of the core of the zaragozic acids is also described. When aldehyde **90** was used instead of **5**, both the yield and diastereoselectivity of the dithiane addition reaction were improved, although the degree of convergency was slightly lower.

Keywords
asymmetric syntheses · enzyme inhibitors · squalestatins · total syntheses · zaragozic acids

Introduction

Despite declining since the mid 1950's, coronary heart disease (CHD) remains the largest single cause of death in many industrialized nations.[1] There is a clear connection between the incidence of CHD and high levels of low density lipoprotein (LDL) cholesterol in the bloodstream,[2] and much effort has been made to reduce serum LDL cholesterol levels in the population, particularly by education about dietary intake of cholesterol. However, approximately half of the human body's requirement for cholesterol is met by endogenous synthesis, mainly in hepatic tissue, and in recent years attention has been focused on controlling amounts of LDL cholesterol from this source.[3] The discovery of inhibitors of HMG CoA reductase,[4] the first key regulatory enzyme in the sterol biosynthetic pathway, resulted in the development of a number of clinically useful agents (e.g., Mevacor[5]) for the control of high LDL cholesterol levels. However, the inevitable consequence of inhibiting an early enzyme in a branched biosynthetic pathway is that its action may be felt more widely throughout the pathway and undesirable side effects may occur.[6] The first *pathway-specific* step on the biosynthetic pathway to cholesterol, catalyzed by squalene synthase (EC 2.5.1.21), is the reductive dimerization of two farnesyl pyrophosphate (FPP) molecules via presqualene pyrophosphate to form squalene,[7] and this represents an ideal point at which to inhibit cholesterol biosynthesis.

[*] Prof. Dr. K. C. Nicolaou, E. W. Yue, S. La Greca, A. Nadin, Z. Yang, J. E. Leresche, T. Tsuri, Y. Naniwa and F. De Riccardis
Department of Chemistry, The Scripps Research Institute
10666 N. Torrey Pines Rd., La Jolla, California 92037 (USA)
Telefax: Int code + (619) 554-6738
and
Department of Chemistry and Biochemistry, University of California
San Diego, 9500 Gilman Drive, La Jolla, California 92093 (USA)

During programs in which fungal extracts were screened for inhibitors of squalene synthase, researchers at Merck and Glaxo independently discovered the same class of natural products, named the zaragozic acids[8] and squalestatins,[9] respectively (e.g., zaragozic acid A/squalestatin S1, **1**, Fig. 1). These compounds are competitive inhibitors of mouse, rat, and HepG2 squalene synthase,[8a, 9a] and are much more potent than earlier designed substrate analogues. For example, the K_i for zaragozic acid A is 78 pM for rat microsomal squalene synthase;[8a] previous inhibitors were several orders of magnitude less potent.[7] Furthermore, zaragozic acid A/squalestatin S1 (**1**), has been shown to reduce serum cholesterol levels in marmosets at an oral dose of 10 mg kg^{-1} d^{-1} for eight weeks,[10] with no attenuation of response. The zaragozic acids also display potent antifungal activity.[9a] Zaragozic acid A has been shown to be an inhibitor of *ras*-farnesyl transferase, which has implications in the development of anticancer agents, particularly for colon and pancreatic cancer.[11] Consequently, a large number of analogues have been prepared[12] and the components of the natural products necessary for biological activity are being elucidated.

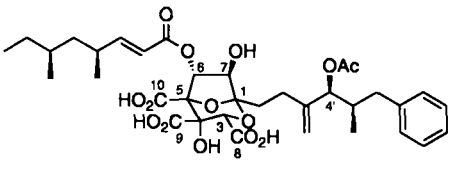

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Fig. 1. Zaragozic acid A/squalestatin S1 (**1**).

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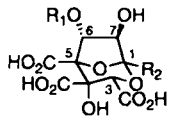
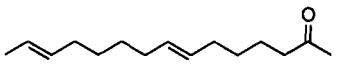
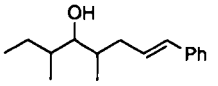
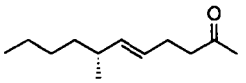
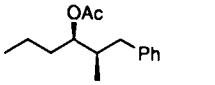
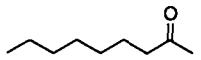
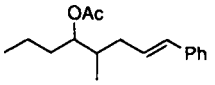
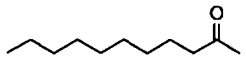
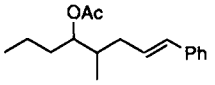
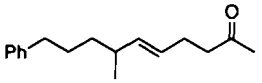
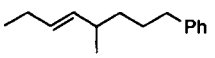
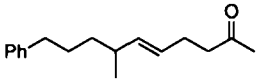
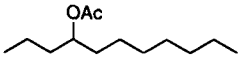
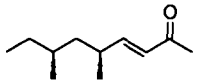
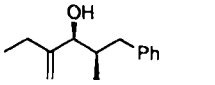
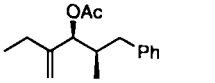
Table 1. Zaragozic acids B–F (**2a–2f**) and squalestatins S2 and H1 (**3a** and **3b**).



Compound	R_1	R_2
Zaragozic Acid B (**2a**)		
Zaragozic Acid C (**2b**)		
Zaragozic Acid D (**2c**)		
Zaragozic Acid D_2 (**2d**)		
Zaragozic Acid E (**2e**)		
Zaragozic Acid F (**2f**)		
Squalestatin S2 (**3a**)		
Squalestatin H1 (**3b**)	H	

The seven zaragozic acids and the majority of the 27 naturally occurring squalestatins all contain a unique, highly oxygenated 4,6,7-trihydroxy-2,8-dioxobicyclo-[3.2.1]-octane-3,4,5-tricarboxylic acid "core", with variation only in the C1 alkyl side chain and the C6 acyl side chain (Table 1). Although there are a few examples of 2,8-dioxobicyclo-[3.2.1]-octane skeletons in nature,[13] and many more as synthetic intermediates,[14] there are none known so densely oxygenated nor functionalized as the core of the zaragozic acids.[15] In view of their therapeutic potential and remarkable chemical structures, the zaragozic acids have attracted attention from many synthetic chemists, which has concentrated mainly on synthesizing models of the bicyclic core,[16] but four total syntheses have also now been reported.[17] Herein we describe in detail our studies on the zaragozic acids.[18]

Results and Discussion

1. **Retrosynthesis**: Our general synthetic strategy is shown in Figure 2, exemplified with zaragozic acid A (**1**). The zaragozic acids are clearly composed of three distinct modules, comprising the C6 acyl side chain, the C1 alkyl side chain, and, most strikingly, the tricarboxylic acid core. Uppermost in our minds was the desire to design a synthetic scheme in which this modularity could be exploited to enable the synthesis of a wide range of naturally occurring zaragozic acids/squalestatins and a range of designed synthetic analogues. Introduction of a wide variety of C6 acyl side chains (e.g., **4**) clearly presents no problem and construction of the C1–C7 bond by addition of an acyl anion equivalent, for example **6**, to an aldehyde **5** would, in principle, provide attractive modules for the C1 side chain and the tricarboxylic acid core, respectively. The presence of two 1,2-diol functionalities (C3–C4 and C5–C6) in **5** suggested to us the possibility of making **5** in three key steps (Fig. 3)—a Stille coupling[19] to assemble the carbon framework and two dihydroxylations, the first enantioselective, to establish the required carbon–oxygen connectivity. With this, the problem was reduced to a technical matter of adjusting the oxidation states of C8, C9, and C10 to the acid, C7 to the aldehyde, and C3, C4, C5, and C6 to the alcohol by suitable manipulation of protecting groups.

2. **Degradative Studies**: With a ready supply of zaragozic acid A (**1**),[20] we were in the fortunate position of being able to obtain information about the planned end of the synthesis before

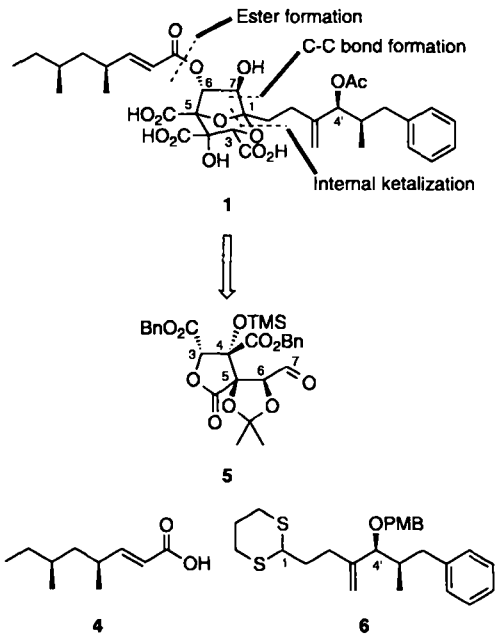


Fig. 2. Retrosynthetic analysis of zaragozic acid A/squalestatin S1 (**1**).

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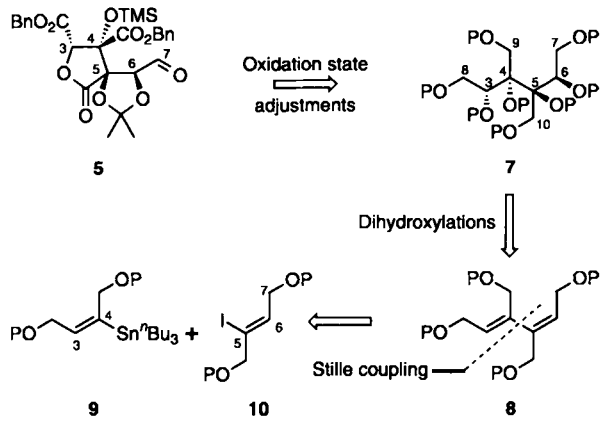
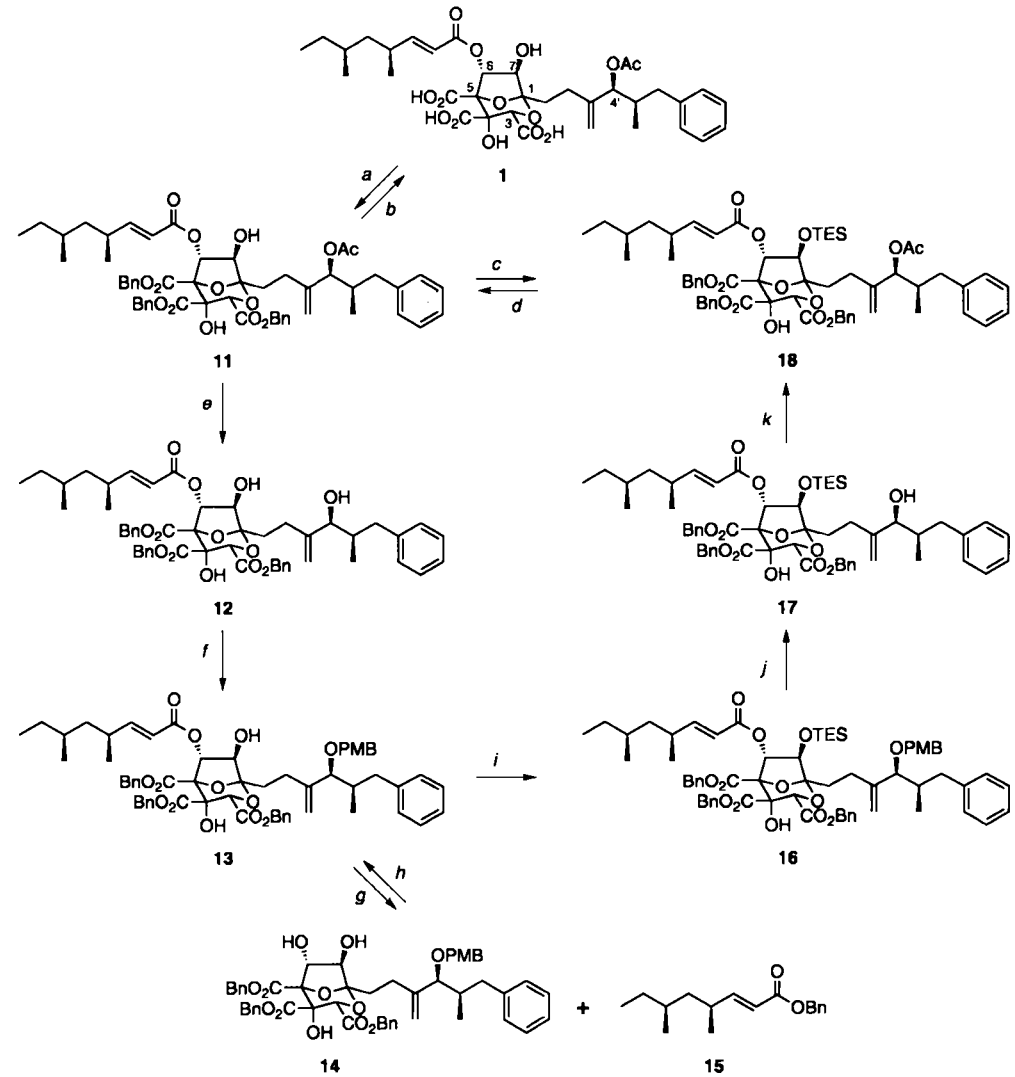


Fig. 3. Retrosynthetic analysis of the aldehyde **5**. P = protecting group.

reaching it with valuable synthetic material. It was clear from the outset that the three carboxylic acids needed to be protected as esters, to provide more tractable late-stage intermediates. However, with the presence of two other esters in the natural product (C6 and C4′), it was imagined that simple esters (e.g., methyl) could not be cleaved selectively. Studies of the medicinal chemistry of the zaragozic acids have shown the convenience with which the three carboxyls can be manipulated as *tert*-butyl esters.[8, 9, 12] In principle, benzyl esters can also be cleaved selectively by hydrogenolysis, and we began to investigate this route (Scheme 1).[21] Accordingly, zaragozic acid A (**1**) was benzylated with *N,N′*-dicyclohexyl-*O*-benzylisourea (DCBI)[22] in refluxing toluene to give the tribenzyl ester **11** in 99% yield. We then tried to remove the three benzyl esters. Transfer hydrogenolysis with Pearlman's catalyst ($Pd(OH)_2$) and 1,4-cyclohexadiene in refluxing dioxane effected removal of the benzyl esters, in the presence of the α,β-unsaturated ester, the acetate, and the olefin, but caused some epimerization at the C4′ stereocenter. A wide range of other conditions with this catalyst led to similar or inferior results. However, when the nonbasic Pd/C catalyst was used, pure zaragozic acid A (**1**) was obtained in 50% yield after reverse phase HPLC purification.

Attention was then focused on the manipulation of the four hydroxyl groups (C4, C4′, C6 and C7). We anticipated that the sterically hindered C4 hydroxyl would not pose a problem during the manipulation of the other hydroxyl groups. Furthermore, the C6 acyl side chain appeared compatible with any transformations planned for the end of the synthesis; thus we were able to incorporate it at an earlier stage. Analysis of molecular models indicated different steric environments between C7 and C4′; this lead us to pursue selective acylation at C4′. Consequently, the C4′ acetate of **11** was removed selectively with 3% HCl/MeOH[8b] to give the triol **12** in 51% yield (with 37% recovered starting material). Longer reaction times led to significant methanolysis of the relatively unhindered C3 benzyl ester



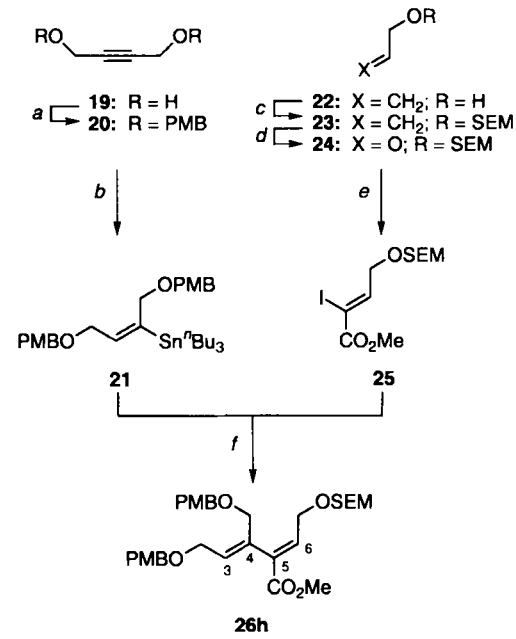
Scheme 1. Retrosynthetic and synthetic studies with **1**. Reagents and conditions: a) DCBI (4.2 equiv), toluene, reflux, 2 h, 99%; b) 10% Pd/C (1.0 wt equiv), 1,4-cyclohexadiene, 1,4-dioxane, 110 °C, 2 h, >70% crude, 50% after HPLC (reverse phase C18: MeOH/0.1% AcOH (4:1), flow rate 9 mL min^{-1}, retention time 13.8 min); c) TESOTf (1.1 equiv), pyridine (1.5 equiv), CH_2Cl_2, 22 °C, 10 min, 95%; d) TBAF (1.2 equiv), THF, 0 °C, 15 min, 85%; e) 3% HCl/MeOH, 22 °C, 2 h, 51% (plus 37% recovered **11**); f) $Cl_3CC(OPMB)=NH$ (2.0 equiv), CSA (0.2 equiv), CH_2Cl_2, cyclohexane, 22 °C, 3 h, 68% (plus 26% recovered **12**); g) 1. LiOH·H_2O (10 equiv), THF/H_2O (2:1), 22 °C, 12 h; 2. DCBI (4.4 equiv), toluene, reflux, 2 h, 42% (**14**), 62% (**15**); h) 1. **15** (1.0 equiv), LiOH (15 equiv), THF/MeOH/H_2O (2:1:1), 22 °C, 4 h; 2. **14** (1.0 equiv), EDC (1.25 equiv), DMAP (0.6 equiv), CH_2Cl_2, 22 °C, 10.5 h, 47% (3:2 mixture of acyl C6 (**13**) and acyl C7, respectively) (plus 20% recovered **14**); i) TESOTf (1.1 equiv), pyridine (1.5 equiv), CH_2Cl_2, 22 °C, 20 min, 79%; j) DDQ (1.2 equiv), CH_2Cl_2/H_2O (20:1), 22 °C, 1 h, 98%; k) Ac_2O (2.5 equiv), pyridine (3.0 equiv), DMAP (0.1 equiv), CH_2Cl_2, 22 °C, 4 h, 99%. DCBI = *N,N′*-dicyclohexyl-*O*-benzylisourea, TESOTf = triethylsilyl trifluoromethanesulfonate, TBAF = tetrabutylammonium fluoride, PMB = *p*-methoxybenzyl, CSA = (±)-10-camphorsulfonic acid, EDC = 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.

(vide infra). However, the acetate could not be reintroduced selectively, giving predominantly the (C4′, C7) bisacetate, so that the C7 alcohol needed to be protected before reintroduction of the acetate at C4′. After considerable experimentation, it was found that a *p*-methoxybenzyl (PMB) ether could be placed selectively on the C4′ hydroxyl of **12** with PMB-trichloroacetimidate in the presence of a catalytic amount of (±)-10-camphorsulfonic acid (**12** → **13**, 68% plus 26% recovered starting material).

We anticipated at the outset of these studies that the C6 hydroxyl (being outside the "bowl-shaped" core) could be selectively acylated with the C6 acyl side chain in the presence of the C7 hydroxyl. In order to test this hypothesis, the C6 acyl side chain was hydrolyzed with lithium hydroxide (which also caused cleavage of the C3 and C5 benzyl esters). After workup with DCBI, triol **14** was obtained in 42% yield, together with **15** (62% yield), the benzyl ester of the C6 acyl side chain. Reintroduction of the C6 acyl side chain, however, proceeded with only modest selectivity to give a 3:2 mixture of C6:C7 acylated products in 47% yield.[23] However, the C7 acylated product could be readily separated by flash column chromatography, hydrolyzed, and recycled.

Having differentiated the C4′ hydroxyl from the C7 hydroxyl, it was necessary to mask the C7 hydroxyl with a protecting group before the PMB ether on C4′ was removed. Since it was already known that a TES group could be used at C7 (**18** → **11**), it followed that this was an appropriate protecting group. Accordingly, **13** was sequentially silylated with TESOTf, deprotected with DDQ, and acetylated with acetic anhydride to give **18** via intermediates **16** and **17** in 77% overall yield (3 steps).

Consequently, these synthetic studies provided the following important pieces of information: 1) triol **14** was a viable late-stage intermediate; 2) a PMB ether could be selectively placed at C4′; and 3) the three carboxylic acids could be conveniently protected as benzyl esters. With this information, we embarked on the syntheses of the fragments **4**, **5**, and **6**.



Scheme 2. Synthesis of diene **26h**. Reagents and conditions: a) NaH (2.5 equiv), PMBCl (2.5 equiv), nBu$_4$NI (0.4 equiv), DMF, 22 °C, 8 h, 94%; b) nBu$_3$SnH (1.1 equiv), Pd(PPh$_3$)$_2$Cl$_2$ (0.015 equiv), THF, 22 °C, 17 h, 94%; c) SEM-Cl (1.1 equiv), N(iPr)$_2$Et (2.2 equiv), CH_2Cl_2, 22 °C, 2 h, 98%; d) O_3, CH_2Cl_2/MeOH (10:1), Me_2S (6.0 equiv), −78 °C, 20 min, 98%; e) Methyl iodo(triphenylphosphoranylidene) acetate (0.8 equiv), benzene, 22 °C, 24 h, 78% ((*Z*/*E*) ratio 30:1); f) **21** (1.1 equiv), **25** (1.0 equiv), Pd(CH$_3$CN)$_2$Cl$_2$ (0.15 equiv), DMF, 22 °C, 3 d, 70%. SEM = 2-(trimethylsilyl)ethoxymethyl.

3. **The Enantioselective Dihydroxylation**: A number of dienes were synthesized by routes analogous to that illustrated for **26h** (Scheme 2) and evaluated as substrates for the Sharpless asymmetric dihydroxylation (AD) reaction.[24] 2-Butyne-1,4-diol (**19**) was protected as its bisPMB ether by treatment with NaH and PMBCl in DMF to give **20** in 94% yield and then hydrostannylated with nBu$_3$SnH and Pd(PPh$_3$)$_4$ to give vinylstannane **21**.[25] Allyl alcohol **22** was protected as a SEM ether to give **23**, oxidized with ozone to give the aldehyde **24**, and subjected to a Wittig reaction with methyl iodo(triphenylphosphoranylidene)acetate[26] to give vinyl iodide **25** as a 30:1 mixture of (*Z*/*E*) stereoisomers. The Stille coupling of vinylstannane **21** and vinyl iodide **25** in DMF using Pd(MeCN)$_2$Cl$_2$ (15%) as the catalyst proceeded smoothly to give the (*Z*,*E*) diene **26h** in 70% yield. It was found to be essential to degas the DMF carefully and conduct the reaction in the absence of light to achieve optimal yields.

The results of the asymmetric dihydroxylation for dienes **26a**–**k** are shown in Table 2. Our initial choice of protecting groups for the C8, C9, and C10 hydroxyl groups (R = Ac, R′ = TPS) was not successful because the diene **26a** did not undergo AD with AD-mix β,[24] even when left at room temperature for a long time (Table 2, entry 1). Reducing the methyl ester to an acetoxy-protected hydroxymethyl group did not result in dihydroxylation, but instead accelerated decomposition of the starting material (entry 2). Changing the protecting groups at C8 and C9 to either MOM or benzyl ethers still did not result in dihydroxylation (entries 3 and 4). However, *simply by changing the C7 hydroxymethyl protecting group to a smaller and more polar one (SEM or MEM), dihydroxylation was observed for the first time, even at 0 °C* (entries 5–9). We attributed this dramatic change in reactivity to steric requirements in the "binding pocket" of the AD catalyst, which appears, in this instance, unable to accommodate a large TPS group in the "north-eastern" quadrant (Fig. 4), but able to accommodate a smaller, linear protecting group such as MEM or SEM. The best combination of protecting groups for the dihydroxylation appeared to be for **26g** (R = MOM, R′ = SEM, R″ = CO_2Me) but difficulties in removing the MOM protecting group led us to try R = PMB. This gave equally satisfactory results with R′ = SEM (**26h**) or R′ = MEM (**26i**) (entries 8 and 9); in practice the SEM group was superseded by the MEM group for reasons of economy. Changing the chiral ligand from (DHQD)$_2$PHAL to (DHQ)$_2$PYR[24] resulted in a less satisfactory reaction with **26i** (entry 10). When the chiral ligand was changed to the pseudo-enantiomeric (DHQ)$_2$PHAL (AD-mix α) (entry 11), the dihydroxylation of **26h** proceeded with slightly reduced yield and enantioselectivity. We had hoped for a favorable attractive interaction between the phenyl ring and the "south-western" quadrant but, disappointingly, the benzyl ester **26j** (entry 12) proved a slightly poorer substrate for the dihydroxylation. The acid **26k** did not react at all (entry 13). Although the yield in the AD of **26h** or **26i** was quite low, the reaction was extremely dependable, and could be performed on scales exceeding 0.2 mol. The enantiomeric excess for the dihydroxylation step (83% *ee* for **27h** and 75% *ee* for **27i**) was determined by NMR analysis of the Mosher's esters[27] of the derived allylic alcohols (e.g., **29a** or **29b**). The absolute configuration, which remained uncertain for some time because of our reluctance to decide the relative size of the various substituents on the diene, was finally established by X-ray crystallographic analysis of **32** (Fig. 7) (vide infra).[28]

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26a-k **27a-k**

Table 2. Asymmetric dihydroxylation of dienes **26a–k**

Entry	R	R′	R″	Reaction conditions [a,b]	Recovered diene (%)	Diol (%)	*ee* (%)
1	Ac	TPS	CO_2Me	A	**26a** (88)	**27a** (0)	–
2	Ac	TPS	CH_2OAc	A	**26b** (65)	**27b** (0)	–
3	MOM	TPS	CO_2Me	A	**26c** (72)	**27c** (0)	–
4	Bn	TPS	CO_2Me	A	**26d** (72)	**27d** (0)	–
5	Ac	SEM	CO_2Me	B	**26e** (63)	**27e** (21)	75
6	Ac	MEM	CO_2Me	B	**26f** (40)	**27f** (20)	ND
7	MOM	SEM	CO_2Me	B	**26g** (47)	**27g** (48)	61
8	PMB	SEM	CO_2Me	B	**26h** (44)	**27h** (30)	83
9	PMB	MEM	CO_2Me	B	**26i** (47)	**27i** (25)	75
10	PMB	MEM	CO_2Me	B [c]	**26i** (48)	**27i** (8)	ND
11	PMB	SEM	CO_2Me	B [d]	**26h** (54)	**27h** (18)	68 [e]
12	PMB	MEM	CO_2Bn	B	**26j** (49)	**27j** (24)	70
13	PMB	MEM	CO_2H	B	**26k** (77)	**27k** (0)	–

[a] All reactions were performed in tBuOH/H_2O (1:1); [b] Reaction conditions A: AD-mix β (2.0–2.8 g mmol^{-1} diene), $MeSO_2NH_2$ (1.5–2.0 equiv), 0–25 °C, 19–72 h; Reaction conditions B: "super" AD-mix β (1.4 g mmol^{-1} diene ["super" AD-mix β is $K_3Fe(CN)_6$ (3.0 equiv), K_2CO_3 (3.0 equiv), $(DHQD)_2PHAL$ (0.10 equiv), $K_2OsO_2(OH)_4$ (0.01 equiv)]), $MeSO_2NH_2$ (2.0–3.0 equiv), 0 °C, 24–72 h; [c] $(DHQ)_2PYR$ (0.10 equiv) was used instead of $(DHQD)_2PHAL$; [d] $(DHQ)_2PHAL$ (0.10 equiv) was used instead of $(DHQD)_2PHAL$; [e] The *ee* was in the opposite sense to experiments conducted with $(DHQD)_2PHAL$. TPS = *tert*-butyldiphenylsilyl, ND = not determined.

At the outset of these studies, no examples of the AD of dienes with electron-withdrawing groups at the 2-position had been reported, and we were both surprised and pleased that the proximal C5–C6 double bond was dihydroxylated exclusively and with good enantioselectivity in the sense required for the natural product. However, a rationalization of these facts was not obvious from consideration of the Sharpless mnemonic device.[24] Indeed, counter-intuitively, the diene **26** needs to fit into the binding pocket such that the largest, branched C3–C4 substituent on C5 is placed in the small, "north-west" quadrant (Fig. 4). It is also interesting to note that in contrast to the work of Corey,[29] which has shown that an allylic PMB group can promote the AD, the C3–C4 olefin (with *two* allylic PMB groups) was not dihydroxylated.

Molecular dynamics calculations[30] were performed on dienes **26a** and **26i**, and the lowest energy conformations are shown in Figure 5. These show clearly that the two olefins of the diene are approximately coplanar, but the methyl ester is twisted almost completely out of conjugation. This is presumably a result of the competing effects of allylic strain and the loss of olefin–ester conjugation.[31] It is also notable that the two allylic hydroxymethyl substituents (OAc for **26a** and OPMB for **26i**) are approximately orthogonal to the plane of the C3–C4 olefin; this maximizes hyperconjugative stabilization. In contrast, the C5–C6 olefin only has one such electron-withdrawing hydroxymethyl group (OTPS for **26a** and OMEM for **26i**). These two features suggest that, contrary to superficial expectations, the C5–C6 olefin is more electron-rich than the C3–C4 olefin, and therefore intrinsically more reactive towards AD.

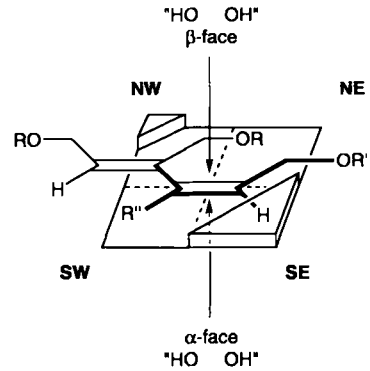


Fig. 4. Sharpless mnemonic device applied to the AD of dienes **26** (ref. [24]).

Furthermore, inspection of **26i** (Fig. 5) shows that the C3–C4 olefin is extremely hindered, but that one face of the C5–C6 olefin appears quite accessible. Further evidence for the hindered nature of the C3–C4 olefin was obtained when acetonide **28a** and **28b** (Scheme 3) failed to undergo AD or standard dihydroxylation, even with a stoichiometric amount of OsO_4 for several weeks (vide infra). Both olefins in **26i** appear severely hindered (Fig. 5). It is also interesting to note that the diene in **26i** appears to have the s-*trans* conformation, whereas in **26a** it appears to be s-*cis*. Inspection of the Sharpless mnemonic device shows that an s-*cis* conformation about C4–C5 would place the bulky C3–C8 unit inside the "binding pocket" of the catalyst; this may possibly prevent dihydroxylation. In contrast, the s-*trans* conformation (Fig. 4) places the C3–C8 unit outside the binding pocket. Clearly, as with other complicated polyunsaturated substrates subjected to the AD reaction, a subtle balance of steric and electronic effects dictates the site of dihydroxylation.

With satisfactory, if not quite rationalized, conditions for the enantioselective dihydroxylation now in hand, we turned our attention to the dihydroxylation of the C5–C6 double bond.

4. The Diastereoselective Dihydroxylation: The diol (**27h**, R_1 = SEM; **27i**, R_1 = MEM) was protected as an acetonide using 2-methoxypropene and a catalytic amount of PPTS (Scheme 3).

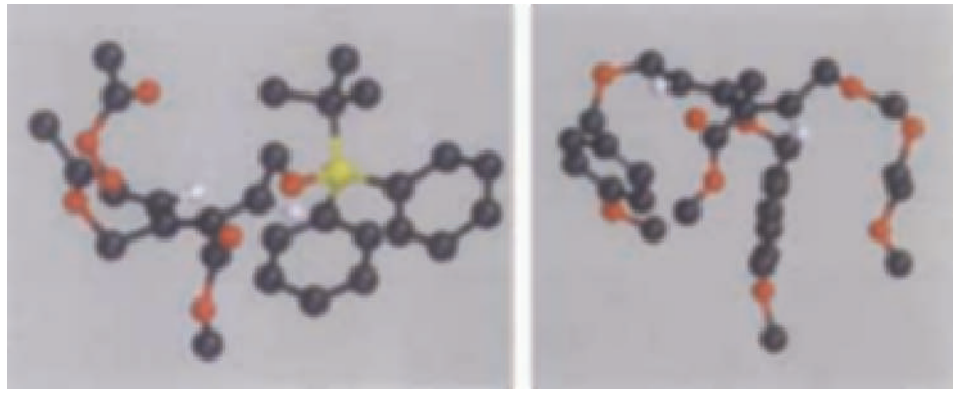
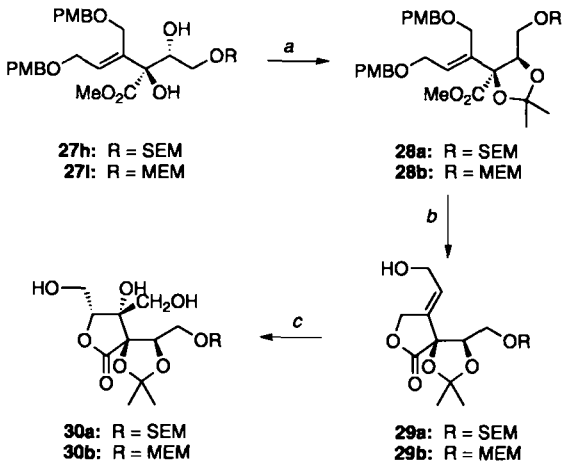
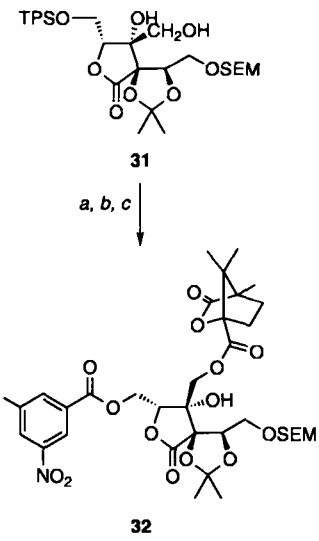


Fig. 5. Lowest energy conformations of dienes **26a** and **26i**.



Scheme 3. Synthesis of lactones **30a** and **30b**. Reagents and conditions: a) 2-Methoxypropene (5.0 equiv), PPTS (0.2 equiv), CH_2Cl_2, 0 °C, 12 h, 88% (**27h** → **28a**); 77% (**27i** → **28b**); b) DDQ (3.0 equiv), $CHCl_3/H_2O$ (20:1), 22 °C, 12 h, 86% (**28a** → **29a**); 78% (**28b** → **29b**); c) OsO_4 (0.05 equiv), NMO (3.0 equiv), *t*BuOH/THF/H_2O (1:1:1), 0 °C, 18 h, 83% (**29a** → **30a**); 100% (**29b** → **30b**). NMO = 4-methylmorpholine *N*-oxide.



Scheme 4. Synthesis of camphanate derivative **32**. Reagents and conditions: a) (−)-Camphanic acid chloride (3.0 equiv), pyridine, 22 °C, 6 h, 73%; b) TBAF (1.2 equiv), AcOH (2.0 equiv), THF, 0 °C, 1 h, 84%; c) 2,4-dinitrobenzoyl chloride (3.0 equiv), DMAP (0.1 equiv), pyridine, 22 °C, 1 h, 75%.

It was hoped that the C3–C4 double bond could be dihydroxylated selectively, but, disappointingly, it was found to be resistant to either standard dihydroxylation or the AD (vide supra). Consequently, we decided to try and increase the reactivity by removing the PMB protecting groups to generate a less sterically hindered allylic alcohol. This was also expected to yield the lactone **29a** or **29b**, which had the added advantage of providing severe steric hindrance to attack at the *re* face of the olefin. These predictions proved correct when dihydroxylation (0.01 equiv OsO_4, NMO, 0 °C, 2 h) provided the triol **30a** or **30b** as a single diastereoisomer in quantitative yield (Scheme 3). It is noteworthy that the *N*-methylmorpholine generated during the dihydroxylation slowly catalyzed translactonization, which could be brought to completion by addition of triethylamine in the workup. This serendipitous translactonization both released the C8 hydroxyl for oxidation and protected the C3 hydroxyl in the desired oxidation state. A similar translactonization has been reported by Roberts et al. in a related system.[16d] The relative stereochemistry at C3 and C4 of triol **30a** was determined by X-ray crystallography (Fig. 6). In order to determine the absolute configuration, **31** (Scheme 5) was derivatized by the following sequence of reactions to give **32** (Scheme 4): 1) esterification of the C9 hydroxyl with (−)-camphanic acid chloride; 2) desilylation of the C8 hydroxyl with TBAF; and 3) esterification of the C8 hydroxyl with 3,5-dinitrobenzoyl chloride. The initial mixture of diastereoisomers of **32** (approximately 10:1) was recrystallized three times to homogeneity (500 MHz ^{1}H NMR analysis). Crystals were then grown by allowing a solution of **32** in hot heptane/ethyl acetate to evaporate slowly.The crystal structure of **32** is shown in Figure 7.

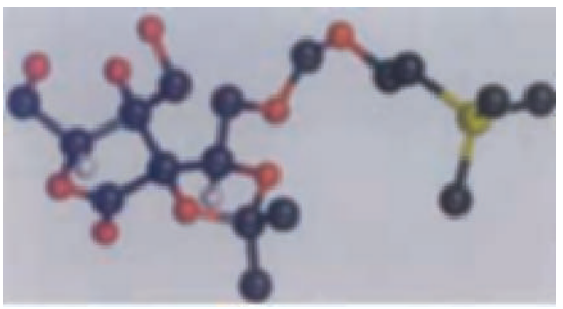


Fig. 6. Representation of the X-ray crystal structure of **30a**.

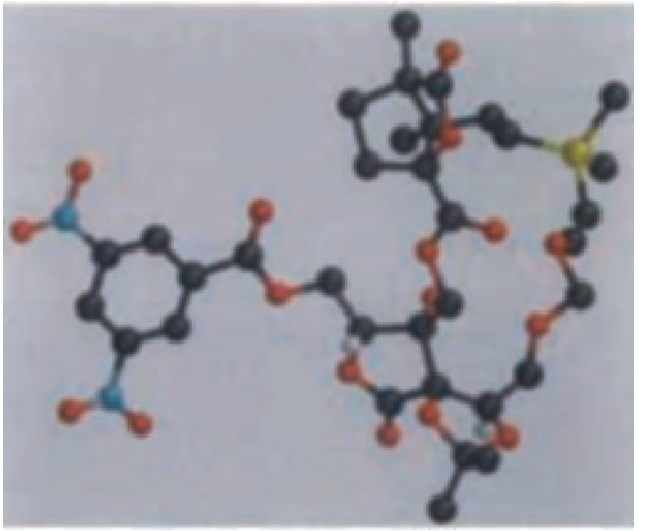


Fig. 7. Representation of the X-ray crystal structure of **32**.

5. The Oxidations: The oxidations of C7, C8 and C9 were not as uneventful as we had hoped. Our initial attempts to oxidize simultaneously the C8 and C9 positions on **30a** or **30b** were unsuccessful and gave only complex mixtures of lactones and other products. This led us to consider the longer, but efficient and effective, stepwise procedure shown in Scheme 5 for the C7-SEM derivative **30a**. Silylation of the triol was highly selective for the C8 hydroxyl to give exclusively the diol **31**. Dess–Martin oxidation,[32] Pinnick oxidation,[33] and esterification with DCBI gave the ester **35**. Desilylation with TBAF gave the diol **36**. The oxidation of **36** to the aldehyde with standard oxidizing agents (Dess–Martin periodinane, Swern, PCC, and TPAP) or to the acid (RuO_4) sometimes gave very low yields, particularly on a large scale, and we attributed this to retro-aldol cleavage of the C3–C4 bond. This problem was solved by protecting the tertiary alcohol in a convenient two-step bissilylation–monodesilylation sequence to give the alcohol **38**. Repeating the stepwise oxidation on the C8 hydroxyl and esterification then gave the diester **41a** reliably and in excellent yield. A small amount (5–10%) of desilylated material (**41b**) was formed in the esterification step. This could be isolated, but generally the mixture was used without further purification. The SEM and TMS groups were removed

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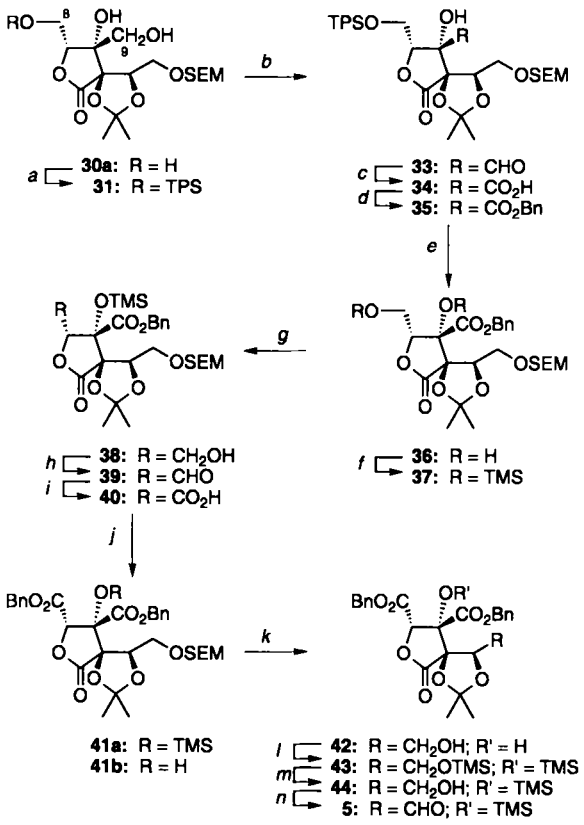
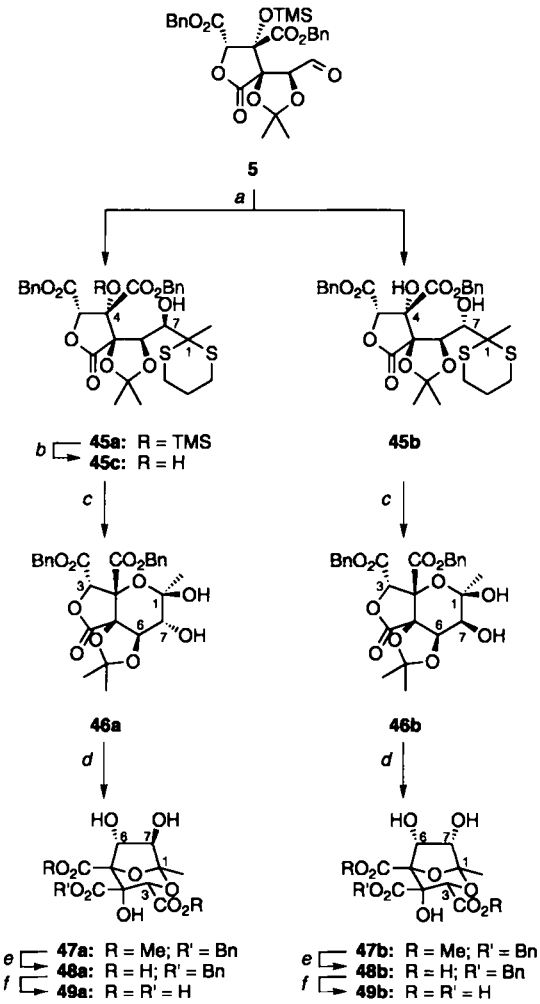
with TFA in dichloromethane in good yield.[34, 35] Finally, the C4 OH of **42** was reprotected as a TMS ether by another bissilylation–monodesilylation sequence and the C7 hydroxyl was oxidized to the aldehyde **5**. Protection was necessary to avoid lactolization. The 13 step sequence of reactions from diol **31** to aldehyde **5** could be performed with only three chromatographic purifications and gave overall yields in excess of 50%.



Scheme 5. Synthesis of aldehyde **5**. Reagents and conditions: a) TPSCl (1.05 equiv), imidazole (2.0 equiv), DMAP (0.05 equiv), DMF, 22 °C, 12 h, 89%; b) Dess–Martin periodinane (3.0 equiv), CH_2Cl_2, 22 °C, 24 h, 89%; c) $NaClO_2$ (3.0 equiv), NaH_2PO_4 (1.05 equiv), 2-methyl-2-butene (4.2 equiv), *t*BuOH/H_2O (4:1), 22 °C, 3 h; d) DCBI (1.5 equiv), toluene, 100 °C, 1 h, 96% (2 steps); e) TBAF (1.2 equiv), AcOH (2.0 equiv), THF, 0 °C, 2 h, 97%; f) $CH_3N(TMS)COCF_3$ (3.5 equiv), 100 °C, 2 h; g) PPTS (0.014 equiv), CH_2Cl_2/MeOH (10:1), 22 °C, 5 min; h) Dess–Martin periodinane (1.2 equiv), CH_2Cl_2, 22 °C, 2 h, 97% (3 steps); i) $NaClO_2$ (3.0 equiv), NaH_2PO_4 (1.05 equiv), 2-methyl-2-butene (4.2 equiv), *t*BuOH/H_2O (4:1), 22 °C, 3 h; j) DCBI (1.3 equiv), toluene, 60 °C, 3 h, 60% (**41a**, 2 steps), 16% (**41b**, 2 steps); k) TFA (50 equiv), CH_2Cl_2, 0 °C, 1–2 h, 25% (**41a** → **42**), 42% (**44**); 88% (**41b** → **42**); l) $CH_3N(TMS)COCF_3$, 80 °C, 1 h; m) PPTS (0.15 equiv), CH_2Cl_2/MeOH (10:1), 22 °C, 5 min; n) Dess–Martin periodane (2.1 equiv), CH_2Cl_2, 22 °C, 30 min, 93% (3 steps).

With the correct oxidation states now set, and **5** available in quantities of several grams by this route, attention was turned to coupling it with a C1 module.

6. Coupling of Aldehyde 5 with Methyl Dithiane and Rearrangement to the Bicyclic Core: As a model for the C1 side chain of the zaragozic acids, we elected to use methyl dithiane as a simple acyl anion equivalent. Thus, deprotonation of methyl dithiane with *n*-butyllithium under standard conditions[36] and addition of aldehyde **5** gave a mixture of the desired adduct **45a** (formally resulting from *anti*-Cram addition) and the epimer **45b** in an approximate 1:1 ratio (Scheme 6). Intriguingly, only the epimer **45b** was desilylated under the reaction conditions, possibly as a result of internal migration of the TMS group from C4 to C7 and subsequent desilylation. Our attempts to influence the diastereoselectivity by adding $MgBr_2$ or $MgCl_2$[37] or by changing the solvent (ether or THF) gave inferior results. The desired (7*R*) diastereoisomer **45a** was desilylated and the dithiane was hydrolyzed with $Hg(ClO_4)_2/CaCO_3$ in good yield to give the lactol **46a** as a single anomer.[38] The hydrolysis of the dithiane was far less efficient if the TMS group protecting the C4 OH



Scheme 6. Synthesis of model systems **49a** and **49b** from **5**. Reagents and conditions: a) 1. 2-Methyl-1,3-dithiane (1.5 equiv), *n*BuLi (1.5 equiv), THF, −40 °C, 1.5 h; 2. **5** (1.0 equiv), −78 °C, 5 min, **45a** (30%) and **45b** (34%); b) 2% HCl in MeOH, CH_2Cl_2, 22 °C, 5 min, 76%; c) $Hg(ClO_4)_2$ (1.6 equiv), $CaCO_3$ (1.7 equiv), THF/H_2O (5:1), 22 °C, 2 h, 72% (**45c** → **46a**); 76% (**45b** → **46b**); d) 2% HCl in MeOH, 68 °C, 18 h, 40% (**46a** → **47a**); 54% (**46b** → **47b**); e) LiOH·H_2O (20 equiv), THF/H_2O (1:1), 22 °C, 19 h, >90%; f) H_2, Pd/C, MeOH, 22 °C, 5 h, 100%.

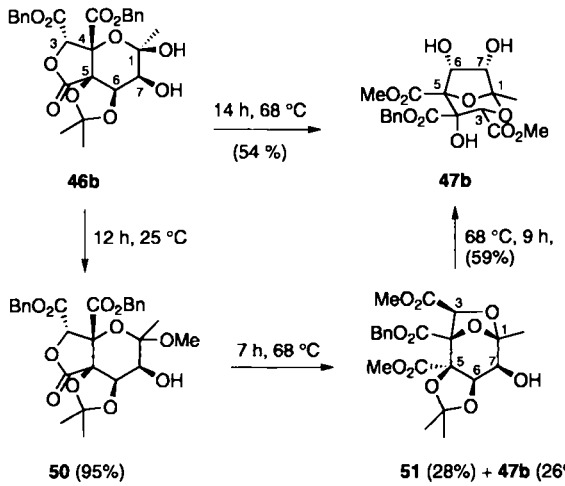
was left in place. Presumably, the free hydroxyl group at C4 assists the hydrolysis of the intermediate thionium ion; this accounts for the particular ease of the conversion in this instance. The Stork reagent[39] [(bis(trifluoroacetoxy)iodo)benzene] and "Claycop"[40] ($Cu(NO_3)_2$ on K-10 clay) were both found to be ineffective. Our attempts to invert the C7 stereocenter were unsuccessful, probably because of intramolecular participation of the adjacent dithiane, severe steric hindrance, or both.

The lactol **46a** contains the correctly oxygenated carbon framework of the zaragozic acid core, and all that remained was to remove the acetonide, open the internal lactol and lactone protecting groups, and trust that the desired bicyclic ketal **47a**

would be more thermodynamically stable than the many other possible products. Extensive degradation chemistry[8, 9, 12] had demonstrated that the bicyclic core was particularly strong, and a recent report on the interconversion of ascorbic acid derivatives[41] suggested experimental conditions that might be effective for this transformation.[42] In the event, heating **46a** with 2% HCl/MeOH for 18 h at 68 °C resulted in the exclusive formation of the bicyclic core **47a** in 56% yield in which all the desired transformations had occurred as planned. In addition, the C3 benzyl ester had been transesterified to a methyl ester. This latter event was not unanticipated, as other experiments on derivatives of the diester **41b** had shown that the C3 ester was far more susceptible than the C4 ester towards hydrolysis, and degradation chemistry[8b, 18] had demonstrated the C4 ester of the zaragozic acids to be far less reactive than either the C3 or the C5 ester. The stereochemistry at C7 was confirmed by the coupling constant $J = 2.3$ Hz (H6–H7) and by NOE measurements.[43] Similarly, the C7 epimer **47b** was made in an analogous manner, and the H6–H7 coupling constant ($J = 6.3$ Hz) and NOE measurements confirmed the stereochemical assignments.[43]

The two methyl esters of **47a** were selectively hydrolyzed with LiOH to give the diacid **48a**. The benzyl ester was removed by hydrogenolysis to give the water-soluble triacidtriol **49a**, a complex molecule with a remarkably simple ^{1}H NMR spectrum [500 MHz, 320 K, D_2O: $\delta = 5.51$ (d, $J = 2.0$ Hz, 1H, H-6), 5.03 (s, 1H, H-3), 4.25 (d, $J = 2.0$ Hz, 1H, H-7) and 1.80 (s, 3H, CH_3)]. The same experiments on **47b** gave **49b** [500 MHz, 298 K, D_2O: $\delta = 5.30$ (d, $J = 7.0$ Hz, 1H, H-6), 4.47 (s, 1H, H-3), 4.32 (d, $J = 7.0$ Hz, 1H, H-7) and 1.50 (s, 3H, CH_3)].

A few experiments were conducted to try to determine whether a clear order of events occurred in the cascade rearrangement (Scheme 7). The lactol **46b** was treated with 2% HCl/MeOH at room temperature for 12 h to yield the methyl glycoside **50**. After 7 h at 68 °C, the reaction mixture was much more complex by TLC analysis but contained two major components, the desired bicyclic compound **47b** (26% yield) and the acetonide **51** (28% yield), in which the lactone ring had been opened, the C3 hydroxyl had ketalized onto C1,[41] and the C3 ester had been transesterified with methanol. When **51** was resubmitted to the reaction conditions, further rearrangement occurred to give the desired compound **47b** in 59% yield. This suggested that the slowest event in the rearrangement cascade



Scheme 7. Some intermediates along the rearrangement pathway of **46b** to **47b**. Reaction conditions: 2% HCl in MeOH for all reactions.

was the hydrolysis of the acetonide. A number of alternative solvents (tBuOH/H_2O, THF/H_2O and BnOH) were employed but did not effect the rearrangement cleanly. Camphorsulfonic acid (0.55 M in MeOH) was found to be an effective but less convenient replacement for 2% HCl/MeOH.

7. Synthesis of the C1 Alkyl Side Chain 6: Having successfully demonstrated the appropriateness of our overall strategy for the synthesis of the zaragozic acids, we turned our attention to the synthesis of the C1 alkyl and C6 acyl side chains.[44] The key disconnection in the retrosynthesis of the C1 alkyl side chain (Fig. 8) was expected to be a three-carbon homologation of the aldehyde **52**. We planned to make **52** from (*Z*)-1-hydroxy-4-phenyl-2-butene (**54**) by a Sharpless asymmetric epoxidation and subsequent opening of the epoxide **53**.

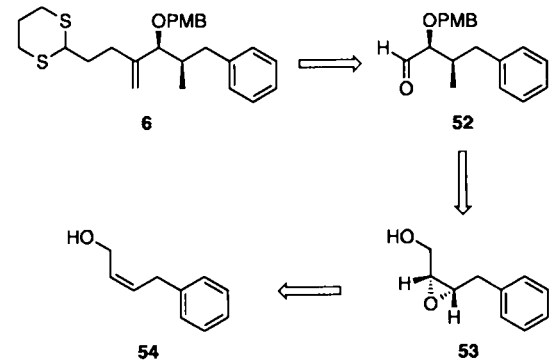


Fig. 8. Retrosynthetic analysis of side chain **6**.

The synthesis of aldehyde **52** is shown in Scheme 8. Initially, we synthesized **54** with a modified Horner–Emmons reaction between 2-phenylacetaldehyde (**56**) and phosphonate **55**.[45] This gave exclusively the *cis* α,β-unsaturated ester (by ^{1}H NMR analysis), which was reduced to the allylic alcohol **54** with DIBALH in 99% yield. In a more cost-effective route, **54** was synthesized by a Wittig reaction between phosphonium bromide **58** and aldehyde **59**[46] followed by desilylation with TBAF to give the allylic alcohol **54** in 90% yield (2 steps). Sharpless epoxidation[47] of **54** gave the epoxide **55** in 83% yield and 81% *ee*.[48] Despite some precedent,[49] we were not able to open the epoxide **55** at C5′ with good regioselectivity and elected instead to protect the primary hydroxyl as a *p*-methoxybenzyl ether. This approach allowed us to use an "ate" complex ($AlMe_3$ and nBuLi)[50] to open the epoxide **61** regioselectively at C5′ (regioselectivity >95:5 by ^{1}H NMR analysis) to give **62**, and to take advantage of the PMB group in subsequent manipulations. Oxidation of the PMB ether **63** with DDQ in the absence of water[51] gave the unstable acetal **63**, which was immediately reduced with DIBALH to give the primary alcohol **64** as a single regioisomer. Swern oxidation afforded the aldehyde **52** in 98% yield.

Homologation of **52** with 2-(1,3-dioxolan-2-yl)ethylmagnesium bromide gave the acetal **65** as a 1:1 mixture of diastereoisomers in 73% yield (Scheme 9).[52] Oxidation with Dess–Martin periodinane gave the ketone **66** and Tebbe methylenation[53] gave the olefin **67** in 78% yield (2 steps). The olefin **67** was recrystallized from cyclohexane to afford material of 98% *ee*.[54] Finally, transthioacetalization[55] of **67** gave the dithiane **6** in 64% yield (8% overall yield from **54** in 10 steps), ready for coupling with the aldehyde **5**.

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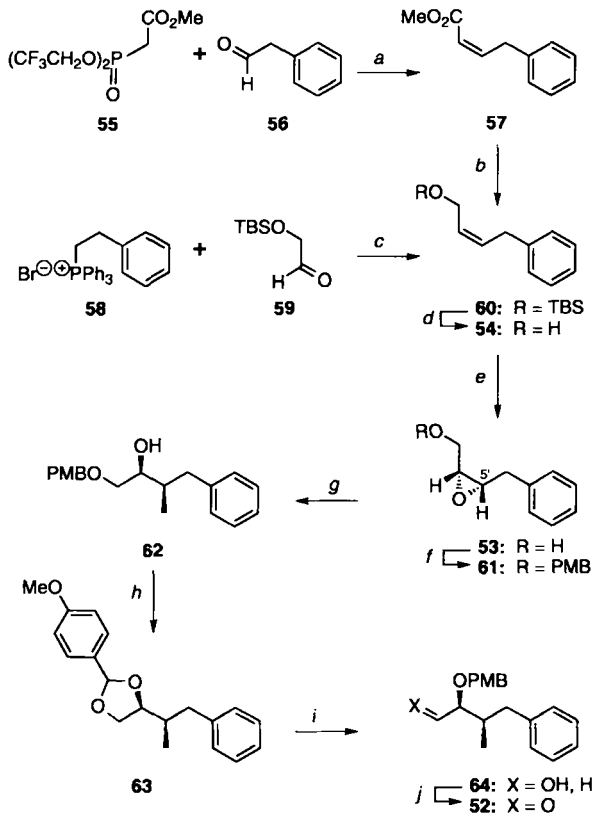
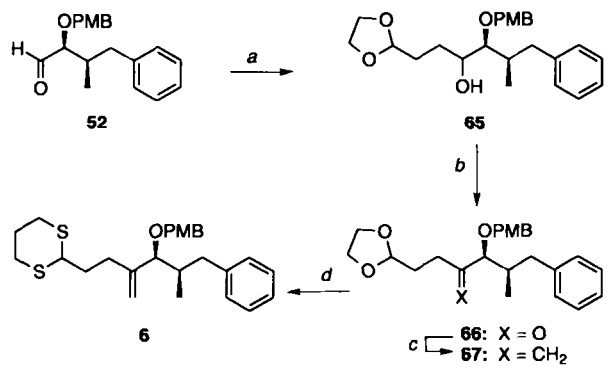
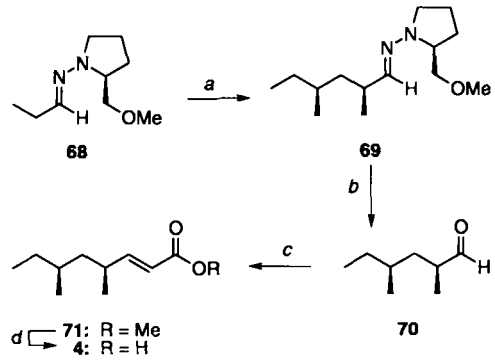


Scheme 8. Synthesis of aldehyde **52**. Reagents and conditions: a) **55** (1.0 equiv), **56** (1.0 equiv), KHMDS (1.0 equiv), 18-crown-6 (5.0 equiv), THF, −78 °C, 30 min, 87%; b) DIBALH (4.4 equiv), CH_2Cl_2, −78 °C, 15 min, 99%; c) **58** (1.0 equiv), **59** (1.0 equiv), NaHMDS (1.0 equiv), CH_2Cl_2/THF (1:1.2), −78 °C → 22 °C, 1 h, 99%; d) TBAF (1.05 equiv), THF, 0 °C, 30 min, 90%; e) *t*BuOOH (2.0 equiv), $Ti(OiPr)_4$ (0.1 equiv), diisopropyl D-tartrate (0.14 equiv), 4 Å M. S. (0.67 wt equiv), CH_2Cl_2, −20 °C, 20 h, 83%, 81% *ee*; f) PMBCl (1.25 equiv), NaH (1.2 equiv), $nBu_4N^+I^-$ (0.04 equiv), THF, reflux, 30 min, 73%; g) $Al(CH_3)_3$ (2.0 equiv), *n*BuLi (0.3 equiv), toluene, −20 °C, 20 h, 89%; h) DDQ (1.3 equiv), CH_2Cl_2, 4 Å M. S. (0.20 wt equiv), 22 °C, 5 h, 53%; i) DIBALH (1.2 equiv), CH_2Cl_2, −78 °C → 22 °C, 2 h, 81%; j) $(COCl)_2$ (1.5 equiv), DMSO (2.0 equiv), Et_3N (4.0 equiv), CH_2Cl_2, −78 °C, 2 h, 98%. NaHMDS = sodium bis(trimethylsilyl)amide, KHMDS = potassium bis(trimethylsilyl)amide, M. S. = molecular sieves.



Scheme 9. Synthesis of dithiane **6**. Reagents and conditions: a) 2-(1,3-Dioxolan-2-yl)ethylmagnesium bromide (3.0 equiv), THF, 35 °C, 6 h, 73%; b) Dess–Martin periodinane (1.2 equiv), CH_2Cl_2, 22 °C, 20 min, 92%; c) Tebbe reagent (1.4 equiv), THF, 22 °C, 1 h, 85%; d) DIBALH (3.2 equiv), 1,3-propanedithiol (1.6 equiv), benzene, 22 °C, 20 h, 64%.

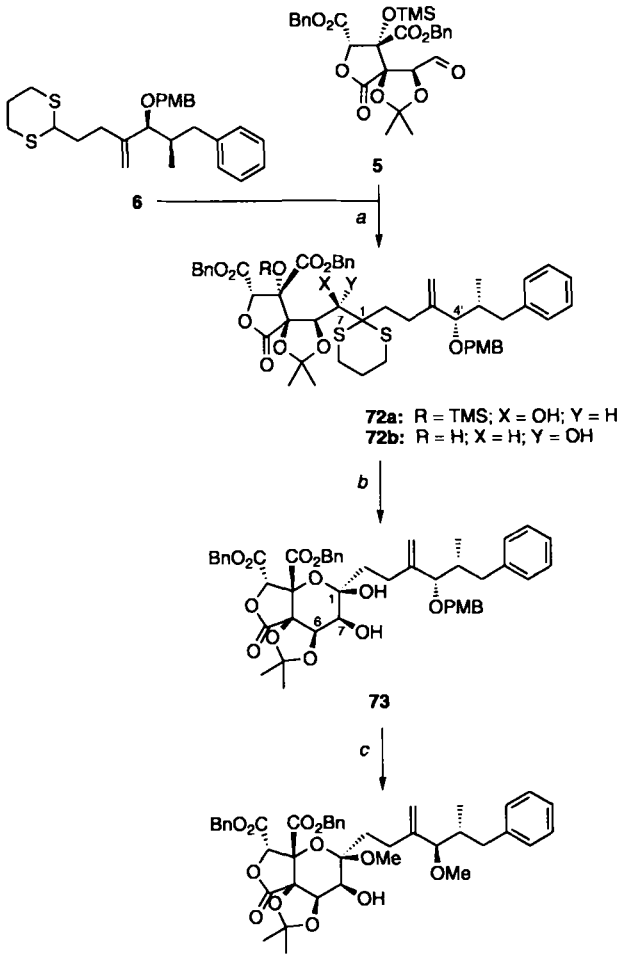
8. Synthesis of the C6 Acyl Side Chain 4: The C6 acyl side chain was synthesized as shown in Scheme 10. Our initial plans to alkylate the enolate derivative of (4*R*,5*S*)-3-oxopropyl-4-methyl-5-phenyl-2-oxazolidinone[56] with the commercially available (*S*)-1-iodo-2-methylbutane gave disappointing mixtures of diastereoisomers, presumably because of "mismatching" of the two chiral partners. Oppolzer's chiral sultam auxiliary[57] also gave disappointing results. However, Enders' hydrazone **68**[58] [prepared from propanal and (*S*)-1-amino-2-(methoxymethyl)pyrrolidine (SAMP)] could be alkylated with much higher diastereoselectivity (92% *de*). Ozonolysis of the crude hydrazone **69** provided the aldehyde **70** and Wittig olefination gave the ester **71** (30% yield overall from **68**). Hydrolysis of the ester afforded acid **4** in 90% yield, which was identical in all respects to a sample obtained by degradation of the natural product (vide supra).



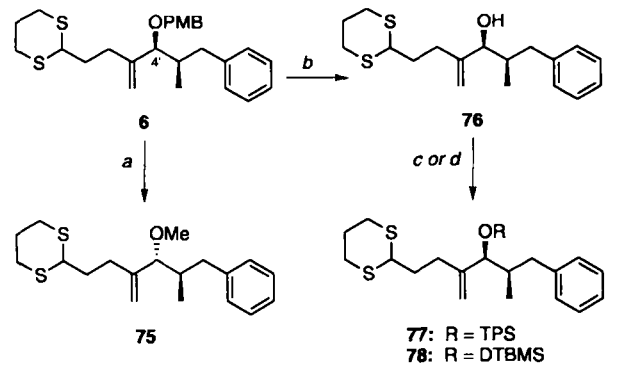
Scheme 10. Synthesis of C6-acyl side chain **4**. Reagents and conditions: a) iPr_2NH (1.1 equiv), *n*BuLi (1.05 equiv), THF, 0 °C, 15 min, then **68** (1.0 equiv), 0 °C, 4 h, then *n*BuLi (1.05 equiv), −20 °C, 2 h, then (*S*)-1-iodo-2-methylbutane (1.2 equiv), −100 °C to −50 °C, 1.25 h; b) O_3, CH_2Cl_2, −78 °C, 30 s; c) $Ph_3P{=}CHCO_2CH_3$ (1.2 equiv), CH_2Cl_2, 22 °C, 3 h, 30% overall from **68**, 92% *de*; d) $LiOH \cdot H_2O$ (3.0 equiv), $MeOH/H_2O$ (2:1), 22 °C, 3 h, 90%.

9. Coupling of Various C1 Alkyl Side Chains, Successful Rearrangement, and Completion: Following the conditions established with methyl dithiane, the C1 side chain **6** was lithiated and added to aldehyde **5**, to give, as before, an approximate 1:1 mixture of diastereoisomers **72a** and **72b** (Scheme 11). The more polar one, which had lost the C4 TMS group and was assumed to have the (7*S*) stereochemistry, was treated with mercury perchlorate solution to remove the dithiane protecting group. The resulting lactol **73** was treated with 2% HCl/MeOH and stirred at room temperature overnight. The ^1H NMR of the crude reaction mixture showed that in addition to the formation of the methyl glycoside, the PMB group had undergone S_N2 displacement with methanol to give **74**. This unwelcome result was also observed with the C1 side chain fragment (**6** → **75**, Scheme 12). Other attempts at the rearrangement (*t*BuOH/H_2O/HCl, BnOH/HCl) were unsuccessful, or gave the same result (0.55 M CSA in MeOH).

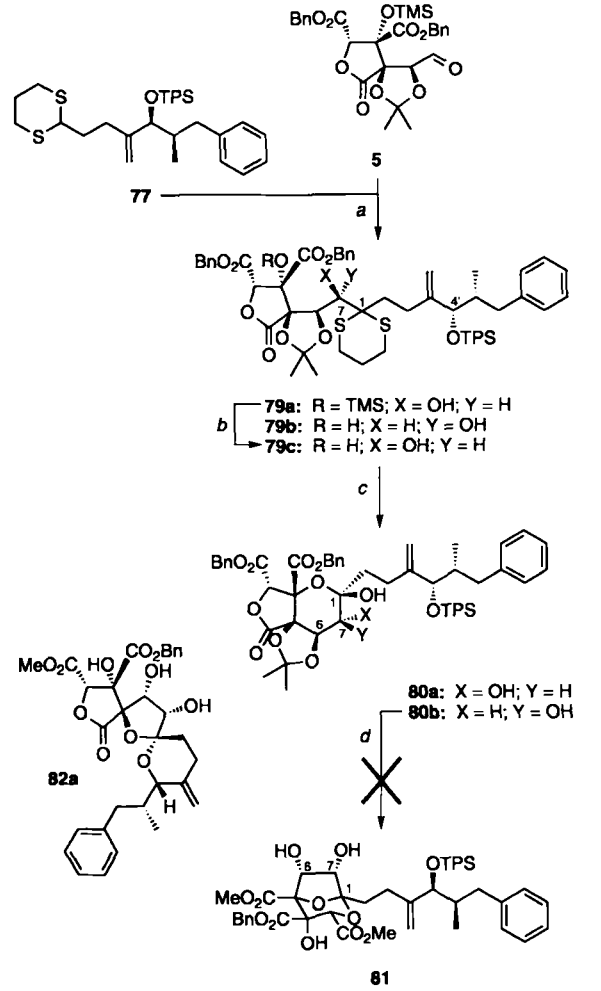
Consequently, the suitability of other protecting groups was investigated (Scheme 12). The PMB group was removed with DDQ to give **76** in 70% yield, and the TPS group was introduced in 98% yield to give dithiane **77**. This was lithiated and added to the aldehyde **5**, and the adducts **79a** and **79c** were converted to the lactol **80a** and **80b** (Scheme 13). Exposure of **80b** to the rearrangement conditions resulted in the formation of a new product, tentatively identified as the spiroketal **82a**, in which the TPS ether and the acetonide protecting groups had been removed but the lactone remained unopened. Molecular dynamics calculations (Insight-Discover, modified AMBER forcefield)[59] suggested that the (1*R*) diastereoisomer **82a** was more stable than the other possible spiroketal **82b** by 2.7 kcal mol^{-1} (Fig. 9), and this stereochemistry was assumed for **82a**. Spiroketal **82a** was resubmitted to the reaction condi-



Scheme 11. Unsuccessful rearrangement of the PMB ether **73**. Reagents and conditions: a) 1. **6** (5.0 equiv), *n*BuLi (5.0 equiv), THF, −23 °C, 1 h; 2. **5** (1.0 equiv), −78 °C, 5 min, 29% (**72a**), 21% (**72b**); b) $Hg(ClO_4)_2$ (1.2 equiv), $CaCO_3$ (1.3 equiv), THF/H_2O (5:1), 67% (**72b**→**73**); c) 2% HCl/MeOH, 22 °C, 12 h, 40%.



Scheme 12. Protection of the C4′ hydroxyl. Reagents and conditions: a) 2% HCl/MeOH, 60 °C, 12 h, 78%; b) DDQ (1.3 equiv), CH_2Cl_2/H_2O (20:1), 22 °C, 30 min, 70%; c) TPSCl (1.2 equiv), imidazole (2.0 equiv), DMAP (0.05 equiv), DMF, 60 °C, 12 h, 98%; d) DTBMSOTf (5.9 equiv), 2,6-lutidine (12.0 equiv), DMAP (2.0 equiv), 70 °C, 8 h, 87%. DTBMS = di-*tert*-butylmethylsilyl.



Scheme 13. Unsuccessful rearrangement of lactol **80b**. Reagents and conditions: a) 1. **77** (1.7 equiv), *n*BuLi (1.6 equiv), THF, −25 °C, 1.5 h; 2. **5** (1.0 equiv), THF, −78 °C, 5 min, 23% (**79a**), 29% (**79b**); b) 2% HCl-MeOH/CH_2Cl_2 (1:3), 22 °C, 5 min, 95%; c) $Hg(ClO_4)_2$ (1.6 equiv), $CaCO_3$ (1.7 equiv), THF/H_2O (5:1), 22 °C, 2 h, 80% (**79c**→**80a**); 93% (**79b**→**80b**); d) 2% HCl/MeOH, 78 °C, 21 h, 0%.

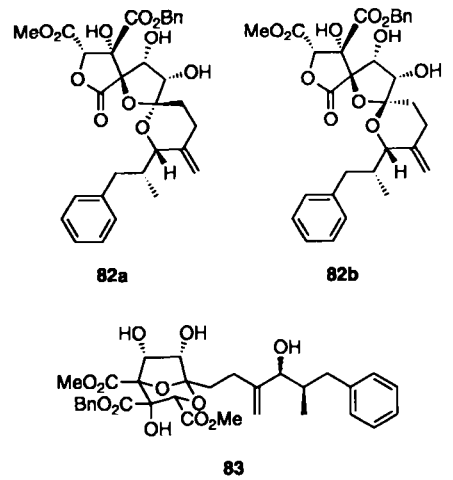


Fig. 9. Calculated energies of spiroketals **82a** ($E = 127.26$ kcal mol^{-1}) and **82b** ($E = 129.92$ kcal mol^{-1}) and rearranged core **83** ($E = 137.51$ kcal mol^{-1}).

tions, but did not rearrange further to the dioxabicyclo[3.2.1]octane skeleton. Indeed, molecular dynamics calculations suggest that the lowest energy conformation of **82a** is considerably lower in energy than the lowest energy conformation of the desired core structure **83** (Fig. 9).

The rarely used di-*tert*-butylmethylsilyl (DTBMS) group is known to be extremely stable to acidic conditions.[60] This silyl protecting group is no longer commercially available, and was synthesized by the method of Barton.[61] Dithiane **78** was formed in 87% yield by heating **76** with a neat solution of

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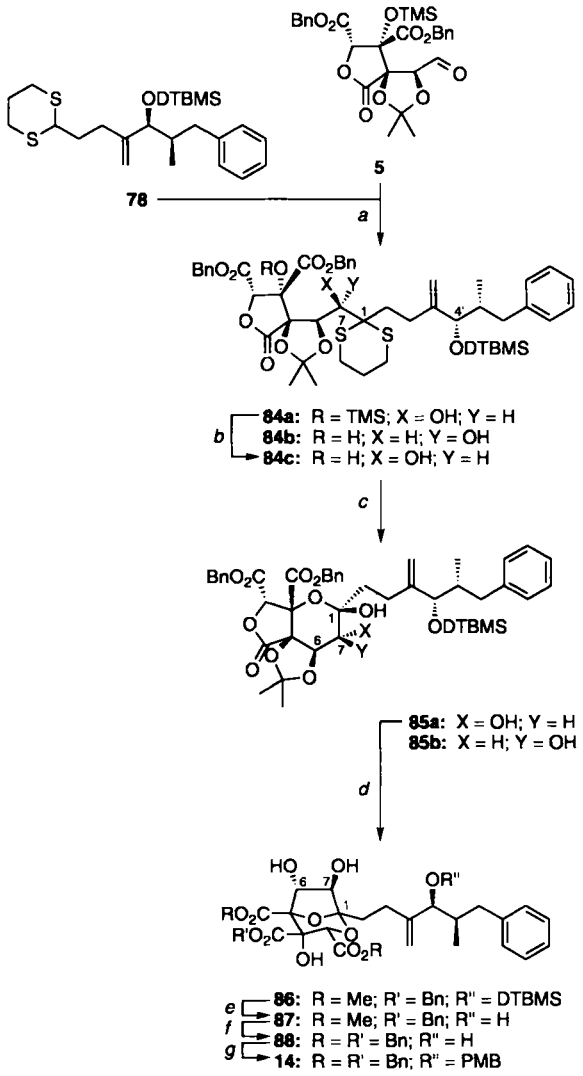
DTBMSOTf (10 equiv), 2,6-lutidine, and DMAP at 70 °C for 8 h (Scheme 12). The dithiane was lithiated, added to the aldehyde **5**, and the desired (7*R*) diastereoisomer **84a** was desilylated and converted to the lactol **85a** (Scheme 14). Lactol **85a** was submitted to the rearrangement conditions, and this time the silyl protecting group survived to afford the desired intermediate **86**. The DTBMS group was then removed using 49% aqueous HF in nitromethane (1:10)[62] to give **87**. All other conditions investigated (TBAF, TBAF on silica gel, HF·py, CsF, HF/MeCN, HCl, HF/urea, BF_3 in CH_2Cl_2,[61] $BF_3 \cdot OEt_2$) either failed to remove the DTBMS group or caused varying degrees of destruction.

The two methyl esters present in **87** (one introduced by nucleophilic opening of the lactone; the other by transesterification of the C3 benzyl ester) were then hydrolyzed and replaced with benzyl esters. This was necessary to avoid concomitant hydrolytic cleavage of the C6 acyl side chain at the end of the synthesis. The resulting tetraol **88** was then treated with PMB



Scheme 14. Synthesis of key intermediate **14**. Reagents and conditions: a) 1. **78** (1.2 equiv), *n*BuLi (1.2 equiv), THF, −25 °C, 1.5 h; 2. **5** (1.0 equiv), THF, −78 °C, 5 min, 40% (**84a**), 32% (**84b**); b) 2% HCl-MeOH/CH_2Cl_2 (2:3), 22 °C, 5 min, 99%; c) $Hg(ClO_4)_2$ (1.2 equiv), $CaCO_3$ (1.3 equiv), THF/H_2O (5:1), 22 °C, 2.5 h, 83% (**84c** → **85a**); 80% (**84b** → **85b**); d) 1.8% HCl/MeOH, 78 °C, 21 h, 45%; e) 49% aqueous HF/$MeNO_2$ (1:10), 0 °C, 24 h, 30%; f) 1. LiOH·H_2O (10.0 equiv), THF/H_2O (2:1), 22 °C, 1 h; 2. DCBI (4.8 equiv), THF, 55 °C, 1.5 h, 68% (2 steps); g) CSA (0.1 equiv), $Cl_3CC(OPMB)=NH$ (1.0 equiv), CH_2Cl_2, 22 °C, 45 min, 21% (**14**), 36% (**88**).

trichloroacetimidate and a small amount of CSA to give predominantly **14** in which the allylic hydroxyl had been protected. Other isomers in which the C6 and C7 positions had been protected were conveniently separated by flash column chromatography and recycled. Comparison of the spectral data of **14** with a sample obtained by degradation of the natural product indicated that the two samples were indistinguishable.

10. Redesign of the Aldehyde 5: Unfortunately our choice of the initial aldehyde **5** for the tricarboxylic acid module suffered from a number of problems. Firstly, we were not able to control the diastereoselectivity at C7 in the coupling of the C1 fragment. Secondly, the aldehyde was not stable to chromatography, with the practical consequence that, in the event of premature quenching of the dithiane anion by adventitious moisture, we could not recover the aldehyde from the reaction mixture. Thirdly, the C3 benzyl ester was prone to attack of the dithiane anion, particularly in small-scale reactions. This last problem could be solved by using the di-*tert*-butyl ester **89** (Fig. 10) but this solution suffered from low yields in the *tert*-butyl esterifications. This led us to consider **90** as a more suitable coupling partner. In this molecule, the C8 oxidation state is reduced and the TMS group replaced with a benzylidene acetal, which, it was hoped, would influence the approach of the C1 anion to the aldehyde.

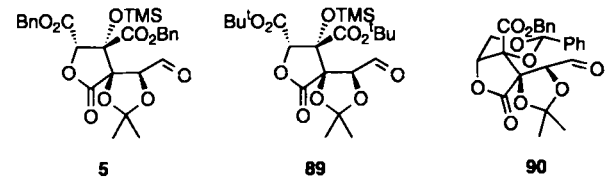
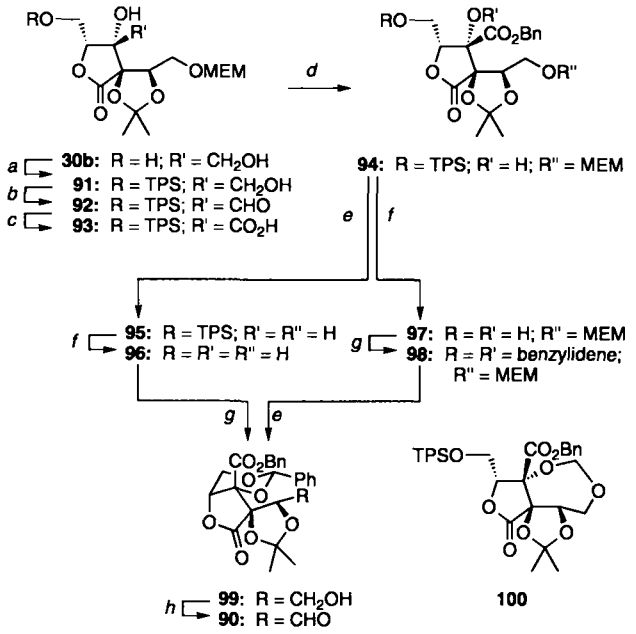
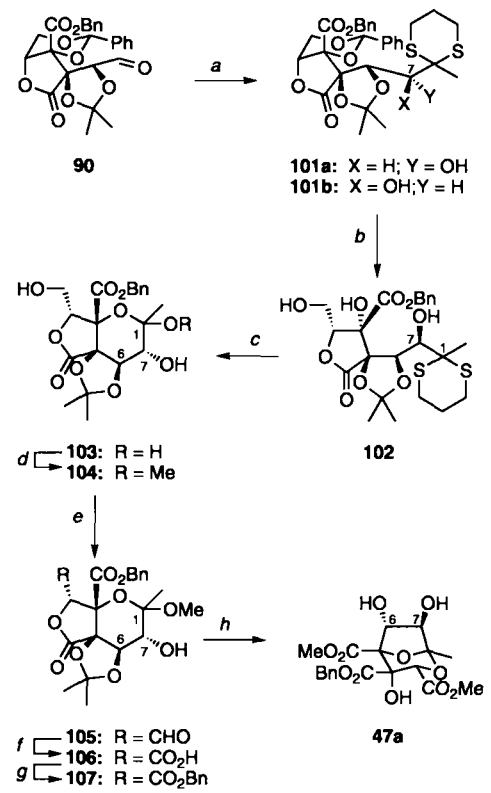


Fig. 10. Alternative key intermediates **89** and **90**.

With the earlier intermediate **30b** as starting material, the C8 hydroxyl was selectively silylated to give **91**, the C9 hydroxyl oxidized and the resulting acid **93** esterified with DCBI to give **94** in 82% overall yield (Scheme 15). Our attempts to remove the MEM group at this stage met with some resistance. Zinc bromide in wet dichloromethane[63] worked but gave only a small amount of the desired product **95** (38%) and a significant amount (24%) of the seven-membered acetal by-product **100**. The reaction rate was increased substantially by performing the reaction in an ultrasound bath, which also stopped formation of the acetal by-product **100** and gave an increased yield (53% of **95** plus 35% of recovered starting material). If the reaction was allowed to go to completion, the yield of the product **95** was substantially lower. Treatment of **94** with PPTS in refluxing *t*-butanol[64] for two days effected removal of the MEM group to give **95** in 66% yield, conditions that remarkably left the TPS group intact. Finally, treatment of **94** with TMSCl/NaI in MeCN at −35 °C[65] provided the best conditions for removal of the MEM group (78% of **95** plus 20% recovered starting material). Compound **95** was then desilylated to give the desired triol **96** in 87% yield. Triol **96** was crystalline, and two recrystallizations from dichloromethane increased the enantiomeric excess from 78% to >98% (measured by making the *bis*Mosher's esters). Treatment of the triol **96** with benzaldehyde dimethyl acetal and a catalytic amount of CSA gave the benzylidene acetal **99** as a single diastereoisomer in 85% yield. Alternatively, the MEM protecting group could be removed after formation of the benzylidene acetal (via intermediates **97** and **98**), although



Scheme 15. Synthesis of aldehyde **90**. Reagents and conditions: a) TPSCl (1.6 equiv), imidazole (1.6 equiv), DMAP (0.07 equiv), DMF, 22 °C, 3 h, 89%; b) Dess–Martin periodinane (1.1 equiv), CH_2Cl_2, 22 °C, 12 h; c) $NaClO_2$ (3.0 equiv), NaH_2PO_4 (1.2 equiv), 2-methyl-2-butene (4.2 equiv), *t*BuOH/H_2O (1:1), 22 °C, 2 h; d) DCBI (1.5 equiv), toluene, 110 °C, 1 h, 93% (3 steps); e) TMSCl (2.0 equiv), NaI (2.0 equiv), −30 °C, 1.5 h, 71% (**94** → **95**); 66% (**98** → **99**) (plus 26% recovered **98**); f) TBAF (1.2 equiv), AcOH (2.0 equiv), THF, 0 °C, 1.5 h, 97% (**94** → **97**); 87% (**95** → **96**); g) $PhCH(OMe)_2$ (3.0 equiv), CSA (0.25 equiv), CH_2Cl_2, 18 h, 22 °C, 79% (**96** → **99**) (plus 6% recovered **96**); 85% (**97** → **98**); h) Dess–Martin periodinane (3.0 equiv), CH_2Cl_2, 22 °C, 1 h, 90%.

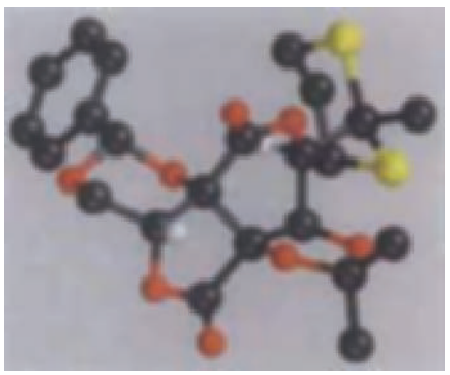


Scheme 16. Synthesis of the model system **47a** from aldehyde **90**. Reagents and conditions: a) 1. 2-Methyl-1,3-dithiane (2.6 equiv), *n*BuLi (2.5 equiv), THF, −40 → −25 °C, 1.5 h; 2. **90** (1.0 equiv), THF, −78 °C, 5 min, 47% (**101a**), 16% (**101b**); b) $Zn(OTf)_2$ (3.9 equiv), EtSH, CH_2Cl_2, ultrasound bath, 22 °C, 8 h, 89% (**101a** → **102**); c) $Hg(ClO_4)_2$ (1.8 equiv), $CaCO_3$ (1.9 equiv), THF/H_2O (5:1), 22 °C, 0.5 h, 81%; d) 2% HCl/MeOH, 22 °C, 6 h, 82% (plus 11% recovered **103**); e) PCC (10 equiv), Celite (1.0 wt equiv), 3 Å M. S. (1.2 wt equiv), CH_2Cl_2, 22 °C, 2.5 h, 65%; f) $NaClO_2$ (3.0 equiv), NaH_2PO_4 (1.5 equiv), 2-methyl-2-butene (9.1 equiv), *t*BuOH/H_2O (5:1), 22 °C, 3.5 h; g) DCBI (1.6 equiv), toluene, 110 °C, 35 min, 92% (2 steps); h) 2% HCl/MeOH, 80 °C, 19 h, 64%.

this route did not offer increased enantiomeric purity. Finally, oxidation of **99** with Dess–Martin periodinane gave the aldehyde **90** in 92% yield.

Addition of methyl dithiane anion under the same conditions described for aldehyde **5** gave a 3:1 mixture of two diastereoisomers, **101a** and **101b**, respectively (Scheme 16). The diastereoisomers were readily separated by column chromatography and the major one, **101a**, was converted to the known bicyclic core **47a** in order to confirm the stereochemistry at C7. Removal of the benzylidene acetal with $Zn(OTf)_2$ and ethanethiol[66] gave triol **102** in 89% yield. Hydrolysis of the dithiane protecting group gave the lactol **103**. Conversion of the lactol to the methyl glycoside and oxidation and esterification gave the dibenzyl ester **107**, the first probable intermediate in the cascade rearrangement. Subjection of this to the rearrangement conditions (2% HCl/MeOH) then gave the bicyclic core **47a**, proving that the aldehyde **90** did indeed favor formation of the desired (7*R*) diastereoisomer, **101a**. Further proof of this was obtained from the crystal structure of lactone **108** (Fig. 11), isolated together with a small amount of the minor diastereoisomer **101b** from a dithiane addition reaction that had been allowed to warm to −35 °C. The crystal structure clearly shows the (7*R*) stereochemistry; presumably the minor diastereoisomer **101b** was unable to lactonize because of severe steric interactions between the dithiane moiety and the phenyl ring of the benzylidene acetal.

Although routes to the zaragozic acids involving the aldehyde **90** as the tricarboxylic acid core fragment are inevitably less convergent because the oxidations of C8 are performed after the coupling with the C1 side chain, the advantages stemming from its improved stability and diastereoselectivity more than compensated.[67]



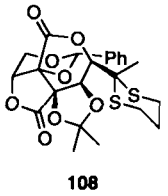


Fig. 11. Representation of the X-ray crystal structure of **108**.

Conclusion

The described chemistry demonstrates an effective and flexible strategy for the synthesis of the zaragozic acids/squalestatins.[68] A simple model of the fully oxygenated bicyclic "core" was made by a multi-event acid-catalyzed rearrangement of an advanced intermediate. This was obtained from a late-stage coupling of a simple C1 side chain model with a C3–C7 tricarboxylate fragment **5** or **90**. Although a greater degree of convergency in the synthetic scheme is embodied in **5**, a number of practical problems and low diastereoselectivity were overcome

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by the design of **90**. The complex oxygenation pattern present in the zaragozic acids was readily attained by sequential enantio- and diastereoselective dihydroxylations of a heavily substituted prochiral diene. A number of synthetic analogues have been prepared by means of the chemistry described in this paper, and their biological activities will be reported in due course.

Experimental Procedure

General Techniques: All nonaqueous reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. When appropriate, intermediates were azeotropically dried with benzene or toluene before use. Tetrahydrofuran (THF) and diethyl ether (ether) were distilled from sodium/benzophenone, dichloromethane and benzene from calcium hydride, and toluene from sodium. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise noted. All aqueous solutions used in workup procedures are saturated unless otherwise noted. Most reagents were purchased at the highest available commercial quality and were used without further purification unless otherwise stated.

All reactions were monitored by thin layer chromatography carried out on 0.25 mm E. Merck silica gel plates ($60F_{254}$) using UV light as visualizing agent and ethanolic *p*-anisaldehyde solution (2.7%), aqueous cerium(IV) sulfate (1%)-phosphomolybdic acid (1.6%) solution, iodine, or basic $KMnO_4$ and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin layer chromatography separations were carried out on E. Merck silica gel plates (60 F_{254} 0.25 or 0.50 mm).

NMR spectra were recorded at ambient temperature on Bruker AMX-500, AMX-400 or AM-300 instruments and calibrated with the residual undeuterated solvent as the internal reference. The following abbrevations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; app, apparent. IR spectra were recorded on a Perkin–Elmer 1600 series FT-IR spectrometer or Mattson Galaxy 2020 FT-IR. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-2SE mass spectrometer under fast atom bombardment (FAB) conditions or on a Hewlett–Packard GC-MS under electron ionization (EI). Melting points (M.p.) are uncorrected and were recorded on a Thomas Hoover capillary melting point apparatus. The nomenclature used to name intermediates was based on CAS guidelines, although for the sake of simplicity the carbon numbering of zaragozic acid A (**1**) (Fig. 1) was used elsewhere.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-3,4-bis-*C*-(carboxyl)-11-ethanoate-10-methylene-12-(phenylmethyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid (zaragozic acid A, 1). A solution of tribenzyl ester **11** (12.6 mg, 13.1 μmol) in 1,4-dioxane (1 mL) and 1,4-cyclohexadiene (0.25 mL) was treated with 10% palladium on carbon (12.6 mg, 100 wt%). The reaction mixture was refluxed for 3 h, cooled to room temperature, filtered through Celite, and washed with ether (2 × 5 mL). The filtrate was concentrated to give a crude oil. Purification by HPLC (reverse phase C18, 4:1 MeOH:0.1% aqueous AcOH, flow rate 9 mL min^{-1}, retention time 13.8 min) gave zaragozic acid A (**1**) (4.4 mg, 50%) as a white foam. $[\alpha]_D^{22} = +18.3$ (*c* 0.60 in $CHCl_3$); $R_f = 0.27$ (silica, *n*-butanol:acetic acid:H_2O 4:1:0.5); IR (thin film): $\tilde{\nu}_{max} = 3450$, 3022, 2964, 2929, 1732, 1650, 1454, 1377, 1251, 1216, 1182, 1138, 1024 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD): $\delta = 7.27-7.24$ (m, 2H, Ph), 7.19–7.13 (m, 3H, Ph), 6.85 (dd, $J = 15.5$, 8.5 Hz, 1H, C*H*=CHCO$_2$R), 6.32 (brs, 1H, H-6), 5.84 (d, $J = 15.6$ Hz, 1H, CH=C*H*CO$_2$R), 5.18 (brs, 1H, H-3), 5.09 (d, $J = 4.7$ Hz, 1H, C*H*(OAc)), 5.02 (s, 1H, C=C*H*H'), 4.96 (s, 1H, C=CH*H*'), 4.00 (s, 1H, H-7), 2.70 (dd, $J = 13.2$, 6.0 Hz, 1H, CH(CH$_3$)C*H*H'Ph), 2.51–2.39 (m, 2H, C*H*(CH$_3$)CH=CH, C*H*H'C(=CH$_2$)), 2.41 (dd, $J = 13.2$, 8.9 Hz, 1H, CH(CH$_3$)CH*H*'Ph), 2.36–2.29 (m, 1H, CH*H*'C(=CH$_2$)), 2.27–2.22 (m, 1H, C*H*(CH$_3$)CH$_2$Ph), 2.10 (s, 3H, OAc), 2.06–2.00 (m, 2H, C*H*$_2$CH$_2$C(=CH$_2$)), 1.38–1.30 (m, 3H, CH$_3$C*H*H'C*H*(CH$_3$)C*H*H'), 1.16–1.11 (m, 2H, CH$_3$CH*H*'CH(CH$_3$)CH*H*'), 1.03 (d, $J = 6.6$ Hz, 3H, CH(C*H*$_3$)CH=CH), 0.89–0.84 (m, 9H, C*H*$_3$CH$_2$CH(C*H*$_3$), CH(C*H*$_3$)CH$_2$Ph); ^{13}C NMR (125 MHz, CD_3OD): $\delta = 172.7$, 172.2, 170.3, 168.6, 166.6, 157.6, 147.8, 141.7, 130.3, 129.4, 127.0, 120.0, 111.5, 106.9, 91.2, 82.7, 81.1, 80.2, 76.7, 75.7, 44.5, 41.0, 37.8, 35.7, 35.0, 33.2, 30.9, 26.5, 21.0, 20.6, 19.3, 14.2, 11.6; FAB HRMS calcd for $C_{35}H_{46}O_{14}Cs$ (M + Cs)$^+$: 823.1942; found $m/z = 823.1937$.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-11-ethanoate-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (11).

Method A: from zaragozic acid A (1). A solution of zaragozic acid A (**1**) (0.5 g, 0.72 mmol) in toluene (5 mL) was treated with DCBI (0.96 g, 3.0 mmol). The reaction mixture was refluxed for 2 h, cooled to room temperature, and concentrated in vacuo. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4 → 2:3) gave tribenzyl ester **11** (0.69 g, 99%) as a white foam.

Method B: from silyl ether 18. A solution of silyl ether **18** (6.2 mg, 5.8 μmol) in THF (0.2 mL) at 0 °C was treated with TBAF (1.0 M in THF, 6.9 μL, 6.9 μmol). The reaction mixture was stirred at 0 °C for 15 min and then diluted with water (2 mL) and ether (2 mL). The aqueous phase was separated and extracted with ether (2 mL) and the combined organic extracts were washed with NH_4Cl (5 mL) and then water (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19 → 1:4) gave diol **11** (4.7 mg, 85%) as a white foam. $[\alpha]_D^{22} = +2.2$ (*c* 0.43 in $CHCl_3$); $R_f = 0.29$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3468$, 3026, 2963, 2929, 1768, 1736, 1650, 1455, 1379, 1244, 1217 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.30-7.22$ (m, 15H, Ph), 7.15–7.11 (m, 5H, Ph), 6.78 (dd, $J = 15.6$, 8.8 Hz, 1H, C*H*=CHCO$_2$R), 5.75 (d, $J = 2.1$ Hz, 1H, H-6), 5.35 (d, $J = 15.6$ Hz, 1H, CH=C*H*CO$_2$R), 5.23 (s, 1H, H-3), 5.20 (d, $J = 12.0$ Hz, 1H, OC*H*H'Ph), 5.16 (d, $J = 12.1$ Hz, 1H, OC*H*H'Ph), 5.07 (d, $J = 5.0$ Hz, 1H, C*H*(OAc)), 5.00 (d, $J = 12.1$ Hz, 2H, OCH*H*'Ph, OCH*H*'Ph), 4.95 (d, $J = 7.9$ Hz, 2H, C=CH$_2$), 4.89 (d, $J = 12.1$ Hz, 1H, OC*H*H'Ph), 4.80 (d, $J = 12.1$ Hz, 1H, OCH*H*'Ph), 3.97 (d, $J = 2.0$ Hz, 1H, H-7), 3.85 (s, 1H, C4-OH), 3.14 (s, 1H, C7-OH), 2.66 (dd, $J = 13.4$, 5.6 Hz, 1H, CH(CH$_3$)C*H*H'Ph), 2.42–2.27 (m, 3H, C*H*(CH$_3$)CH=CH, C*H*$_2$C(=CH$_2$)), 2.34 (dd, $J = 13.6$, 9.1 Hz, 1H, CH(CH$_3$)-CH*H*'Ph), 2.11–2.05 (m, 3H, C*H*$_2$CH$_2$C(=CH$_2$), C*H*(CH$_3$)CH$_2$Ph), 2.07 (s, 3H, OAc), 1.37–1.23 (m, 3H, CH$_3$C*H*H'C*H*(CH$_3$)C*H*H'), 1.15–1.08 (m, 2H, CH$_3$CH*H*'CH(CH$_3$)CH*H*'), 1.03 (d, $J = 6.6$ Hz, 3H, CH(C*H*$_3$)CH=CH), 0.85–0.80 (m, 9H, C*H*$_3$CH$_2$CH(C*H*$_3$), CH(C*H*$_3$)CH$_2$Ph); ^{13}C NMR (125 MHz, CD_3OD): $\delta = 172.1$, 170.2, 167.8, 166.4, 166.0, 157.9, 147.6, 141.6, 136.5, 136.0, 136.0, 130.3, 130.2, 129.9, 129.9, 129.8, 129.8, 129.8, 129.7, 129.7, 129.7, 129.6, 129.6, 129.5, 129.5, 129.4, 129.4, 129.4, 129.3, 127.0, 119.8, 111.7, 107.2, 91.2, 82.3, 81.0, 80.0, 76.6, 76.2, 69.2, 68.7, 68.4, 44.4, 40.9, 37.8, 35.7, 34.8, 33.3, 31.0, 26.5, 21.0, 20.8, 19.1, 14.3, 11.6; FAB HRMS calcd for $C_{56}H_{64}O_{14}Cs$ (M + Cs)$^+$: 1093.3350; found $m/z = 1093.3350$.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (12). A solution of acetate **11** (300 mg, 0.31 mmol) in 3% HCl/MeOH (8 mL) was stirred at room temperature for 2 h. The reaction mixture was quenched with $NaHCO_3$ (10 mL) and concentrated in vacuo. The aqueous phase was extracted with ether (3 × 10 mL) and the combined organic extracts were washed with brine (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4 → 1:3 → 3:7 → 2:3) gave the desired triol **12** (145 mg, 51%), unreacted acetate **11** (111 mg, 37%), and the C3 methyl ester of the desired triol **12** (21 mg, 8%) as white foams. $[\alpha]_D^{22} = -7.2$ (*c* 0.21 in $CHCl_3$); $R_f = 0.14$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3489$, 2961, 2925, 1739, 1648, 1498, 1457, 1380, 1263, 1023 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.32-7.23$ (m, 15H, Ph), 7.18–7.09 (m, 5H, Ph), 6.77 (dd, $J = 15.6$, 8.8 Hz, 1H, C*H*=CHCO$_2$R), 5.73 (brs, 1H, H-6), 5.33 (d, $J = 15.6$ Hz, 1H, CH=C*H*CO$_2$R), 5.22 (d, $J = 12.4$ Hz, 1H, OC*H*H'Ph), 5.21 (s, 1H, H-3), 5.16 (d, $J = 12.0$ Hz, 1H, OC*H*H'Ph), 5.11 (s, 1H, C=C*H*H'), 5.00 (s, 1H, C=CH*H*'), 4.95 (d, $J = 12.0$ Hz, 1H, OCH*H*'Ph), 4.90 (d, $J = 11.9$ Hz, 1H, OCH*H*'Ph), 4.80 (d, $J = 12.1$ Hz, 1H, OC*H*H'Ph), 4.73 (d, $J = 12.1$ Hz, 1H, OCH*H*'Ph), 4.06 (d, $J = 5.1$ Hz, 1H, C*H*(OH)CH(CH$_3$)), 3.96 (d, $J = 1.9$ Hz, 1H, H-7), 3.92 (brs, 1H, C4-OH), 3.19 (brs, 1H, C7-OH), 2.74 (dd, $J = 13.4$, 5.6 Hz, 1H, CH(CH$_3$)C*H*H'Ph), 2.61 (brs, 1H, CH(O*H*)CH(CH$_3$)), 2.53–2.47 (m, 1H, C*H*(CH$_3$)CH=CH), 2.38 (dd, $J = 13.4$, 9.3 Hz, 1H, CH(CH$_3$)CH*H*'Ph), 2.32–2.28 (m, 2H, C*H*$_2$C(=CH$_2$)), 2.18–2.07 (m, 2H, C*H*$_2$CH$_2$C(=CH$_2$)), 1.94–1.89 (m, 1H, C*H*(CH$_3$)CH$_2$Ph), 1.36–1.25 (m, 3H, CH$_3$C*H*H'C*H*(CH$_3$)C*H*H'), 1.14–1.08 (m, 2H, CH$_3$CH*H*'CH(CH$_3$)CH*H*'), 1.02 (d, $J = 6.6$ Hz, 3H, CH(C*H*$_3$)CH=CH), 0.84–0.82 (m, 9H, C*H*$_3$CH$_2$CH(C*H*$_3$), CH(C*H*$_3$)CH$_2$Ph); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.1$, 166.9, 166.0, 164.3, 157.9, 151.3, 141.3, 134.5, 129.2, 129.0, 128.7, 128.5, 128.5, 128.2, 125.7, 117.8, 111.5, 106.0, 88.3, 82.4, 81.6, 75.3, 74.7, 68.2, 67.8, 67.7, 43.2, 40.2, 38.0, 34.5, 33.6, 31.9, 30.0, 29.7, 26.3, 20.3, 18.8, 13.5, 11.1; FAB HRMS calcd for $C_{54}H_{62}O_{13}Na$ (M + Na)$^+$: 941.4088; found $m/z = 941.4095$.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-11-*O*-[(4-methoxyphenyl)methyl]-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (13).

Method A: from triol 12. A solution of triol **12** (322 mg, 0.36 mmol) in dichloromethane (7.5 mL) and cyclohexane (7.5 mL) was treated with PMB trichloroacetimidate (208 mg, 0.74 mmol) and CSA (17 mg, 73.1 μmol). The reaction mixture was stirred at room temperature for 12 h and then diluted with ether (5 mL) and $NaHCO_3$ (5 mL). The aqueous phase was separated and extracted with ether (2 × 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude yellow oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:9 → 1:4 → 3:7) gave the desired ether **13** (255 mg, 68%) and unreacted triol **12** (86 mg, 26%) as a white foam.

Method B: from triol 14. A solution of benzyl ester **15** (7.0 mg, 26.9 μmol) in THF (1 mL), methanol (0.5 mL), and water (0.5 mL) was treated with LiOH·H_2O (17 mg, 0.41 mmol). The reaction mixture was stirred at room temperature for 4 h, diluted with ether (3 mL), and acidified with aqueous HCl (0.1 M, 10 drops) to pH 3. The reaction mixture was extracted with ether (3 × 4 mL) and the combined organic

extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude residue. The crude acid was dissolved in dichloromethane (2 mL) and treated with triol **14** (10 mg, 11.3 μmol), EDC (6.5 mg, 34.0 μmol), and DMAP (2.0 mg, 16.4 μmol). The reaction mixture was stirred at room temperature for 10.5 h and then diluted with water (3 mL) and ether (3 mL). The aqueous phase was separated and extracted with ether (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4 → 1:2) gave the desired C6 ester **13** (3.3 mg, 28%), C7 ester (2.2 mg, 19%), and recovered triol **14** (2.0 mg, 20%) as white foams. $[\alpha]_D^{22} = -12.0$ (c 0.12 in $CHCl_3$); $R_f = 0.39$ (silica, ethyl acetate:petroleum ether, 3:7); IR (thin film): $\tilde{\nu}_{max} = 2959, 2924, 1768, 1737, 1512, 1456, 1249, 1178, 1151, 1030\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.32-7.23$ (m, 16H, Ph), 7.21–7.18 (m, 2H, Ph), 7.13–7.10 (m, 2H, Ph), 7.06 (d, $J = 7.0$ Hz, 2H, $CH_3OC_6H_4$), 6.86 (d, $J = 8.6$ Hz, 2H, $CH_3OC_6H_4$), 6.79 (dd, $J = 15.6$, 8.7 Hz, 1H, $CH{=}CHCO_2R$), 5.76 (d, $J = 1.9$ Hz, 1H, H-6), 5.36 (d, $J = 15.6$ Hz, 1H, $CH{=}CHCO_2R$), 5.25 (s, 1H, H-3), 5.21 (d, $J = 12.0$ Hz, 1H, $OCHH'Ph$), 5.15 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.06 (s, 2H, $C{=}CH_2$), 5.00 (d, $J = 12.2$ Hz, 1H, $OCHH'Ph$), 4.97 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.87 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.78 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.45 (d, $J = 11.4$ Hz, 1H, $CH_3OC_6H_4CHH'$), 4.11 (d, $J = 11.5$ Hz, 1H, $CH_3OC_6H_4CHH'$), 3.98 (d, $J = 2.1$ Hz, 1H, H-7), 3.85 (brs, 1H, C4-OH), 3.80 (s, 3H, OCH_3), 3.49 (d, $J = 5.9$ Hz, 1H, $CH(OCH_2Ar)$), 3.17 (brs, 1H, C7-OH), 2.65 (dd, $J = 13.5$, 5.6 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.41–2.34 (m, 2H, $CH(CH_3)CH{=}CH$, $CHH'C(=CH_2)$), 2.27 (dd, $J = 13.3$, 9.1 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.33–2.09 (m, 3H, $CH_2CHH'C(=CH_2)$), 1.97–1.93 (m, 1H, $CH(CH_3)CH_2Ph$), 1.36–1.27 (m, 3H, $CH_3CHH'CH(CH_3)CHH'$), 1.13–1.08 (m, 2H, $CH_3CHH'CH(CH_3)CHH'$), 1.03 (d, $J = 6.6$ Hz, 3H, $CH(CH_3)CH{=}CH$), 0.83–0.81 (m, 9H, $CH_3CH_2CH(CH_3)$, $CH(CH_3)CH_2Ph$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.7, 166.9, 165.8, 164.5, 158.9, 157.9, 146.1, 141.2, 134.8, 134.6, 134.4, 131.0, 129.4, 129.2, 129.0, 128.7, 128.5, 128.1, 125.6, 117.8, 113.6, 112.4, 105.9, 88.5, 85.3, 81.8, 75.3, 74.7, 70.1, 68.5, 67.7, 67.4, 55.2, 43.2, 40.1, 37.6, 34.5, 34.2, 31.9, 29.7, 24.4, 20.3, 18.8, 14.6, 11.1$; FAB HRMS calcd for $C_{62}H_{70}O_{14}Cs$ ($M + Cs$)$^+$: 1171.3820; found m/z = 1171.3856.

(7*S*)-2,7-Anhydro-8,9,10,12,13-pentadeoxy-11-*O*-[(4-methoxyphenyl)methyl]-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (14).

Method A: from ester 13. A solution of ester **13** (122 mg, 0.12 mmol) in THF (5 mL) and water (3 mL) was treated with $LiOH \cdot H_2O$ (49 mg, 1.2 mmol). The reaction mixture was stirred at room temperature for 12 h, quenched with aqueous HCl (1 M, 2 mL), and diluted with ethyl acetate (5 mL). The organic phase was separated, dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. A solution of the crude material in toluene (5 mL) was treated with DCBI (167 mg, 0.53 mmol). The reaction mixture was refluxed for 2 h, cooled to room temperature, and again concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19 → 1:1) gave tribenzyl ester **14** (44 mg, 42%) as a white foam and benzyl ester **15** (19 mg, 62%) as a colorless oil.

Method B: from tribenzyl ester 88. A solution of tribenzyl ester **88** (5.5 mg, 7.2 μmol) in dichloromethane (0.2 mL) was treated with a solution of PMB trichloroacetimidate in dichloromethane (26.5 mM, 0.27 mL, 7.2 μmol) and a solution of CSA in dichloromethane (35.0 mM, 20 μL, 0.7 μmol). The reaction mixture was stirred at room temperature for 45 min and then purified directly by preparative TLC (acetone:CH_2Cl_2 1:9) to give the allylic PMB ether **14** (1.3 mg, 21%), identical to a sample prepared by degradation of the natural product (**13** → **14**), unreacted **88** (2 mg, 36%) and mixtures of other PMB ethers (2 mg, ca. 30%). $[\alpha]_D^{22} = -20.9$ (c 0.55 in $CHCl_3$); $R_f = 0.29$ (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max} = 3487, 3330, 3027, 2929, 2853, 1746, 1617, 1512, 1454, 1246, 1034\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.30-7.13$ (m, 20H, Ph), 7.07 (d, $J = 7.1$ Hz, 2H, $CH_3OC_6H_4$), 6.86 (d, $J = 8.6$ Hz, 2H, $CH_3OC_6H_4$), 5.28 (d, $J = 12.2$ Hz, 1H, $OCHH'Ph$), 5.17 (s, 1H, H-3), 5.14 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.08 (s, 2H, $C{=}CH_2$), 5.06 (s, 1H, H-6), 4.99 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.97 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.85 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.82 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 4.45 (d, $J = 11.4$ Hz, 1H, $CH_3OC_6H_4CHH'$), 4.14 (d, $J = 11.4$ Hz, 1H, $CH_3OC_6H_4CHH'$), 4.05 (s, 1H, H-7), 3.79 (s, 3H, OCH_3), 3.78 (s, 1H, C4-OH), 3.50 (d, $J = 6.1$ Hz, 1H, $CH(OCH_2Ar)$), 3.46 (brs, 1H, C6-OH), 2.65 (dd, $J = 13.5$, 5.7 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.46 (brs, 1H, C7-OH), 2.39–2.32 (m, 1H, $CHH'C(=CH_2)$), 2.27 (dd, $J = 13.5$, 9.0 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.20–2.09 (m, 4H, $CH_2CHH'C(=CH_2)$, $CH(CH_3)$), 0.85 (d, $J = 6.6$ Hz, 3H, $CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.9, 166.1, 159.0, 146.1, 141.2, 134.8, 134.7, 134.5, 130.9, 129.4, 129.2, 128.6, 128.5, 128.4, 128.2, 125.6, 113.7, 112.8, 105.8, 91.3, 85.4, 82.3, 78.6, 75.2, 74.7, 70.1, 68.4, 67.7, 67.4, 55.3, 49.2, 40.0, 37.6, 33.9, 33.7, 29.7, 25.5, 24.9, 24.3, 14.8$; FAB HRMS calcd for $C_{52}H_{54}O_{13}Cs$ ($M + Cs$)$^+$: 1019.2619; found m/z = 1019.2640.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-11-*O*-[(4-methoxyphenyl)-methyl]-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-6-*O*-(triethylsilyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (16). A solution of diol **13** (19.0 mg, 18.3 μmol) in dichloromethane (0.5 mL) was treated with pyridine (2.2 μL, 27.4 μmol) and triethylsilyl trifluoromethanesulfonate (4.5 μL, 20.1 μmol). The reaction mixture was stirred at room temperature for 10 min and then diluted with water (5 mL) and ether (5 mL). The aqueous phase was separated and extracted with ether (5 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude yellow oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19 → 1:9 → 1:4) gave silyl ether **16** (16.6 mg, 79%) as a white foam. $[\alpha]_D^{22} = +1.2$ (c 0.57 in $CHCl_3$); $R_f = 0.56$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 2958, 2916, 2876, 1772, 1734, 1513, 1457, 1248, 1180, 1128\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.33-7.19$ (m, 17H, Ar), 7.13–7.08 (m, 5H, Ar), 6.87 (d, $J = 8.7$ Hz, 2H, $CH_3OC_6H_4$), 6.85 (dd, $J = 15.6$, 8.4 Hz, 1H, $CH{=}CHCO_2R$), 6.29 (d, $J = 1.8$ Hz, 1H, H-6), 5.62 (dd, $J = 15.6$, 0.86 Hz, 1H, $CH{=}CHCO_2R$), 5.26 (s, 1H, H-3), 5.13 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.08 (s, 2H, $C{=}CH_2$), 5.02 (d, $J = 10.2$ Hz, 1H, $OCHH'Ph$), 5.01 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.00 (d, $J = 13.6$ Hz, 1H, $OCHH'Ph$), 4.88 (d, $J = 11.8$ Hz, 1H, $OCHH'Ph$), 4.56 (d, $J = 11.8$ Hz, 1H, $OCHH'Ph$), 4.48 (d, $J = 11.5$ Hz, 1H, $CH_3OC_6H_4CHH'$), 4.13 (d, $J = 11.5$ Hz, 1H, $CH_3OC_6H_4CHH'$), 4.13 (d, $J = 1.8$ Hz, 1H, H-7), 3.86 (brs, 1H, C4-OH), 3.80 (s, 3H, OCH_3), 3.52 (d, $J = 5.9$ Hz, 1H, $CH(OCH_2Ar)$), 2.67 (dd, $J = 13.5$, 5.3 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.48–2.35 (m, 2H, $CH(CH_3)CH{=}CH$, $CHH'C(=CH_2)$), 2.29 (dd, $J = 13.5$, 9.6 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.25–2.17 (m, 2H, $CHH'CHH'C(=CH_2)$), 2.07–1.96 (m, 2H, $CHH'CH_2C(=CH_2)$, $CH(CH_3)CH_2Ph$), 1.37–1.24 (m, 3H, $CH_3CHH'CH(CH_3)CHH'$), 1.13–1.08 (m, 2H, $CH_3CHH'CH(CH_3)CHH'$), 1.01 (d, $J = 6.7$ Hz, 3H, $CH(CH_3)CH{=}CH$), 0.84–0.80 (m, 9H, $CH_3CH_2CH(CH_3)$, $CH(CH_3)CH_2Ph$), 0.77 (t, $J = 8.0$ Hz, 9H, $Si(CH_2CH_3)_3$), 0.46 (q, $J = 7.9$ Hz, 6H, $Si(CH_2CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.8, 166.1, 164.6, 164.2, 158.9, 157.0, 146.2, 141.1, 134.9, 134.3, 134.2, 131.1, 129.3, 129.2, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3, 128.1, 125.6, 118.2, 113.6, 112.3, 105.9, 90.0, 85.6, 81.8, 78.6, 74.9, 74.5, 70.1, 68.8, 67.9, 67.2, 55.2, 43.2, 40.1, 37.5, 34.5, 33.7, 31.9, 29.7, 24.5, 20.1, 18.8, 14.5, 11.2, 6.5, 4.4$; FAB HRMS calcd for $C_{68}H_{84}O_{14}SiCs$ ($M + Cs$)$^+$: 1285.4685; found m/z = 1285.4698.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-6-*O*-(triethylsilyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (17). A solution of ether **16** (36.0 mg, 31.2 μmol) in dichloromethane (5 mL) and water (0.25 mL) was treated with DDQ (8.5 mg, 37.5 μmol). The two-phase reaction mixture was stirred vigorously at room temperature for 1 h and then diluted with water (5 mL) and ether (5 mL). The aqueous phase was separated and extracted with ether (5 mL). The combined organic extracts were washed with $NaHCO_3$ (4 × 5 mL) until the yellow color disappeared, and then with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude residue. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19 → 1:4) gave diol **17** (31.8 mg, 98%) as a white foam. $[\alpha]_D^{22} = +9.1$ (c 0.60 in $CHCl_3$); $R_f = 0.40$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3470, 3031, 2959, 2922, 1737, 1649, 1456, 1379, 1259, 1178, 1125, 1027\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.33-7.14$ (m, 18H, Ph), 7.07–7.05 (m, 2H, Ph), 6.83 (dd, $J = 15.7$, 8.6 Hz, 1H, $CH{=}CHCO_2R$), 6.26 (d, $J = 1.6$ Hz, 1H, H-6), 5.59 (d, $J = 15.6$ Hz, 1H, $CH{=}CHCO_2R$), 5.21 (s, 1H, H-3), 5.14 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.14 (s, 1H, $C{=}CHH'$), 5.01 (d, $J = 11.6$ Hz, 1H, $OCHH'Ph$), 5.02 (s, 1H, $C{=}CHH'$), 4.96 (d, $J = 12.2$ Hz, 1H, $OCHH'Ph$), 4.96 (d, $J = 12.2$ Hz, 1H, $OCHH'Ph$), 4.79 (d, $J = 11.9$ Hz, 1H, $OCHH'Ph$), 4.48 (d, $J = 11.9$ Hz, 1H, $OCHH'Ph$), 4.09 (brs, 1H, 4-OH), 4.07 (d, $J = 1.8$ Hz, 1H, H-7), 3.89 (s, 1H, $CH(OH)$), 2.78 (dd, $J = 13.4$, 5.8 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.75 (brs, 1H, $CH(OH)$), 2.57–2.51 (m, 1H, $CH(CH_3)CH{=}CH$), 2.43 (dd, $J = 13.4$, 9.1 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.39–2.27 (m, 2H, $CH_2C(=CH_2)$), 2.14–2.08 (m, 1H, $CHH'CH_2C(=CH_2)$), 1.99–1.90 (m, 2H, $CHH'CH_2C(=CH_2)$, $CH(CH_3)CH_2Ph$), 1.37–1.23 (m, 3H, $CH_3CHH'CH(CH_3)CHH'$), 1.12–1.07 (m, 2H, $CH_3CHH'CH(CH_3)CHH'$), 1.01 (d, $J = 6.6$ Hz, 3H, $CH(CH_3)CH{=}CH$), 0.86–0.80 (m, 9H, $CH_3CH_2CH(CH_3)$, $CH(CH_3)CH_2Ph$), 0.79 (t, $J = 8.0$ Hz, 9H, $Si(CH_2CH_3)_3$), 0.47 (q, $J = 8.0$ Hz, 6H, $Si(CH_2CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 167.9, 166.3, 164.5, 164.0, 157.0, 151.6, 141.4, 134.7, 134.3, 134.1, 129.2, 129.0, 128.9, 128.7, 128.6, 128.5, 128.3, 128.1, 125.6, 118.2, 111.2, 106.0, 89.7, 82.6, 78.5, 76.5, 74.9, 74.6, 68.4, 68.0, 67.5, 43.2, 40.2, 38.0, 34.5, 33.3, 31.9, 29.7, 26.9, 20.1, 18.8, 13.4, 11.2, 6.5, 4.4$; FAB HRMS calcd for $C_{60}H_{76}O_{13}SiCs$ ($M + Cs$)$^+$: 1165.4110; found m/z = 1165.4120.

[5(2*E*,4*S*,6*S*),7*S*]-2,7-Anhydro-8,9,10,12,13-pentadeoxy-11-ethanoate-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-6-*O*-(triethylsilyl)-5-(4,6-dimethyl-2-octenoate)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (18).

Method A: from diol 11. A solution of diol **11** (6.9 mg, 7.2 μmol) in dichloromethane (0.2 mL) was treated with pyridine (0.9 μL, 10.8 μmol) and TESOTf (1.8 μL, 7.9 μmol). The reaction mixture was stirred at room temperature for 10 min and then diluted with water (5 mL) and ether (5 mL). The aqueous phase was separated and extracted with ether (5 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude yellow oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19 → 1:4) gave silyl ether **18** (7.3 mg, 95%) as a white foam.

Method B: from allylic alcohol 17. A solution of allylic alcohol **17** (20.0 mg, 19.4 μmol) in dichloromethane (1 mL) was treated with pyridine (4.7 μL, 58.1 μmol), acetic anhydride (4.6 μL, 48.4 μmol), and DMAP (0.2 mg, 1.9 μmol). The reaction mixture was stirred at room temperature for 4 h and then diluted with $NaHCO_3$ (3 mL) and ether (5 mL). The organic phase was separated and washed

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with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude residue. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19 → 1:9 → 1:4) gave acetate **18** (20.7 mg, 99%) as a white foam. $[\alpha]_D^{22} = +19.5$ (c 0.55 in $CHCl_3$); $R_f = 0.18$ (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max} = 3461, 2959, 1769, 1737, 1649, 1457, 1374\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$ plus one drop of D_2O): $\delta = 7.32-7.24$ (m, 15H, Ph), 7.18–7.13 (m, 5H, Ph), 6.86 (dd, $J = 15.6$, 8.6 Hz, 1H, $CH{=}CHCO_2R$), 6.30 (d, $J = 1.8$ Hz, 1H, H-6), 5.57 (dd, $J = 15.6$, 0.8 Hz, 1H, $CH{=}CHCO_2R$), 5.26 (s, 1H, H-3), 5.14 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.12 (d, $J = 5.4$ Hz, 1H, $CH(OAc)$), 5.05 (d, $J = 11.9$ Hz, 1H, $OCHH'Ph$), 5.01 (d, $J = 12.1$ Hz, 1H, $OCHH'Ph$), 5.01 (s, 1H, $C{=}CHH'$), 5.00 (d, $J = 11.9$ Hz, 1H, $OCHH'Ph$), 4.97 (s, 1H, $C{=}CHH'$), 4.91 (d, $J = 11.8$ Hz, 1H, $OCHH'Ph$), 4.59 (d, $J = 11.8$ Hz, 1H, $OCHH'Ph$), 4.11 (d, $J = 1.9$ Hz, 1H, H-7), 3.89 (brs, 1H, C4-OH), 2.70 (dd, $J = 13.4$, 5.3 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.49–2.35 (m, 3H, $CH(CH_3)CH{=}CH$, $CH_2C(=CH_2)$), 2.33 (dd, $J = 13.5$, 9.4 Hz, 1H, $CH(CH_3)CHH'Ph$), 2.17–2.10 (m, 2H, $CHH'CH_2C(=CH_2)$, $CH(CH_3)CH_2Ph$), 2.08 (s, 3H, OAc), 2.03–1.98 (m, 1H, $CHH'CH_2C(=CH_2)$), 1.38–1.27 (m, 3H, $CH_3CHH'CH(CH_3)CHH'$), 1.14–1.07 (m, 2H, $CH_3CHH'CH(CH_3)CHH'$), 1.03 (d, $J = 6.7$ Hz, 3H, $CH(CH_3)CH{=}CH$), 0.84–0.81 (m, 9H, $CH_3CH_2CH(CH_3)$, $CH(CH_3)CH_2Ph$), 0.79 (t, $J = 8.0$ Hz, 9H, $Si(CH_2CH_3)_3$), 0.48 (q, $J = 7.9$ Hz, 6H, $Si(CH_2CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.2, 168.9, 166.1, 164.6, 164.1, 157.0, 145.6, 140.3, 134.9, 134.2, 129.2, 129.0, 128.9, 128.6, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 125.9, 118.2, 111.8, 105.7, 90.0, 82.0, 79.3, 78.6, 74.8, 74.4, 68.8, 67.9, 67.2, 43.2, 39.9, 36.6, 34.5, 33.8, 31.9, 29.7, 25.2, 21.1, 20.1, 18.8, 13.8, 11.2, 6.5, 4.4$; FAB HRMS calcd for $C_{62}H_{78}O_{14}SiCs$ ($M + Cs$)$^+$: 1207.4215; found $m/z = 1207.4215$.

1,4-[Bis(4-methoxyphenyl)methoxy]-2-butyne (20). A suspension of washed sodium hydride (60% dispersion in mineral oil, 14.8 g, 369 mmol) in DMF (100 mL) was treated slowly with a solution of 2-butyne-1,4-diol **19** (12.7 g, 148 mmol) in DMF (25 mL) over a period of 30 min. The reaction mixture was stirred at room temperature until H_2 evolution ceased and then treated with tetrabutylammonium iodide (2.19 g, 5.92 mmol) and a solution of PMBCl (57.8 g, 369 mmol) in DMF (20 mL) over a period of 2 h. The reaction mixture was stirred at room temperature for 12 h, poured slowly into ice water (500 mL), and extracted with ether (3 × 400 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 30:70 → 35:65) gave alkyne **20** (45.0 g, 94%) as a colorless oil. $R_f = 0.30$ (silica, ether:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max} = 3000, 2936, 2839, 1611, 1512, 1463, 1349, 1247, 1070, 823\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.32-7.29$ (m, 4H, $CH_3OC_6H_4$), 6.91–6.88 (m, 4H, $CH_3OC_6H_4$), 4.56 (s, 4H, $CH_3OC_6H_4CH_2$), 4.22 (s, 4H, $CH_2C{\equiv}CCH_2$), 3.81 (s, 6H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.8, 130.1, 129.8, 114.2, 82.9, 71.6, 57.5, 55.7$; FAB HRMS calcd for $C_{20}H_{22}O_4Na$ ($M + Na$)$^+$: 349.1416; found $m/z = 349.1423$.

(*E*)-2-(1,1,1-Tributylstannyl)-1,4-[bis(4-methoxyphenyl)methoxy]-2-butene (21). A solution of alkyne **20** (45.0 g, 138 mmol) in THF (350 mL) was treated dropwise with bis(triphenylphosphine)palladium(II) chloride (1.45 g, 2.07 mmol) and tributyltin hydride (40.8 mL, 152 mmol). The reaction mixture was stirred at room temperature for 17 h and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:9) gave vinyl stannane **21** (77.0 g, 90%) as a colorless oil. $R_f = 0.32$ (silica, ether:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max} = 2922, 2853, 1612, 1512, 1463, 1302, 1250, 1083, 821\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.30-7.25$ (m, 4H, $CH_3OC_6H_4$), 6.91–6.88 (m, 4H, $CH_3OC_6H_4$), 5.79–5.76 (m, 1H, CH=C), 4.45 (s, 2H, $CH_3OC_6H_4CH_2$), 4.43 (s, 2H, $CH_3OC_6H_4CH_2$), 4.16–4.15 (m, 2H, C=C(Sn)CH_2O), 4.03 (d, $J = 5.7$ Hz, 2H, $OCH_2CH{=}C$), 3.82 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 1.51–1.45 (m, 6H, $Sn(CH_2CH_2CH_2CH_3)_3$), 1.35–1.28 (m, 6H, $Sn(CH_2CH_2CH_2CH_3)_3$), 0.90 (t, $J = 7.3$ Hz, 9H, $Sn(CH_2CH_2CH_2CH_3)_3$), 0.89 (t, $J = 8.3$ Hz, 6H, $Sn(CH_2CH_2CH_2CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.6, 159.5, 148.6, 135.4, 130.8, 130.7, 129.9, 129.8, 114.2, 114.0, 72.6, 72.2, 71.7, 67.3, 55.6, 29.6, 27.8, 14.1, 10.6$; FAB HRMS calcd for $C_{32}H_{50}O_4SnCs$ ($M + Cs$)$^+$: 751.1785; found $m/z = 751.1761$.

1-[[2-(Trimethylsilyl)ethoxy]methoxy]-2-propene (23). A solution of allyl alcohol **22** (18.3 g, 315 mmol) in dichloromethane (350 mL) and diisopropylethylamine (115 mL, 660 mmol) at 0 °C was treated dropwise with SEMCl (50.0 g, 0.30 mol) over a period of 30 min. The reaction mixture was stirred at 0 °C for 1 h, warmed to room temperature and stirred for 3 h, diluted with dichloromethane (200 mL) and washed with NH_4Cl (2 × 200 mL), water (2 × 300 mL), and brine (300 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:97 → 5:95) gave compound **23** (49.6 g, 88%) as a colorless oil. $R_f = 0.71$ (silica, ether:petroleum ether 3:97); IR (thin film): $\tilde{\nu}_{max} = 3082, 2954, 2881, 1649, 1408, 1249, 1059, 920, 836\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.95-5.87$ (m, 1H, $CH_2{=}CH$), 5.30–5.26 (m, 1H, $CHH'{=}C$), 5.19–5.16 (m, 1H, $CHH'{=}C$), 4.68 (s, 2H, OCH_2O), 4.07–4.05 (m, 2H, $CH_2{=}CHCH_2$), 3.64–3.60 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 0.95–0.92 (m, 2H, $CH_2Si(CH_3)_3$), 0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 134.9, 117.5, 94.5, 68.7, 65.6, 18.6, -1.0$.

[[2-(Trimethylsilyl)ethoxy]methoxy]acetaldehyde (24). A solution of olefin **23** (25.0 g, 133 mmol) in dichloromethane (250 mL) and methanol (50 mL) at −78 °C was treated with ozone until the reaction mixture turned blue. Oxygen was passed through the reaction mixture for 20 min; the latter was then quenched with dimethyl sulfide (58.5 mL, 798 mmol), warmed to room temperature, stirred for 12 h, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7 → 4:6) gave aldehyde **24** (25.3 g, 100%) as a colorless oil. $R_f = 0.40$ (silica, ether:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max} = 2953, 2893, 1739, 1415, 1379, 1250, 1060, 836\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.64$ (t, $J = 0.8$ Hz, 1H, CHO), 4.68 (s, 2H, OCH_2O), 4.11 (d, $J = 0.8$ Hz, 2H, $CHOCH_2$), 3.61–3.57 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 0.87–0.84 (m, 2H, $CH_2Si(CH_3)_3$), −0.06 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 200.5, 95.7, 73.6, 66.2, 18.4, -1.0$; FAB HRMS calcd for $C_8H_{19}O_3Si$ ($M + H$)$^+$: 191.1103; found $m/z = 191.1105$.

(*Z*)-2-Iodo-4-[[2-(trimethylsilyl)ethoxy]methoxy]-2-butenoic acid methyl ester (25). A solution of the aldehyde **24** (21.0 g, 11 mmol) in benzene (600 mL) at 0 °C was treated with methyl iodo(triphenylphosphoranylidene)acetate [26] (76.2 g, 166 mmol). The reaction mixture was warmed to room temperature, stirred for 12 h, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 2:3) gave vinyl iodide **25** (38.7 g, 94%, 30:1 mixture of (*Z*/*E*) isomers) as a colorless oil. $R_f = 0.40$ (silica, ether:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max} = 2952, 2889, 1723, 1621, 1435, 1246, 1108, 1057, 1037, 858\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.49$ (t, $J = 5.0$ Hz, 1H, C=CH), 4.71 (s, 2H, OCH_2O), 4.24 (d, $J = 5.0$ Hz, 2H, $C{=}CHCH_2O$), 3.82 (s, 3H, CO_2CH_3), 3.64–3.61 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 0.96–0.92 (m, 2H, $CH_2Si(CH_3)_3$), 0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 163.1, 150.8, 119.6, 95.3, 72.4, 65.9, 54.2, 18.5, -0.9$; FAB HRMS calcd for $C_{11}H_{21}O_4ISiNa$ ($M + Na$)$^+$: 395.0152; found $m/z = 395.0160$.

(*E*,*Z*)-5-[(4-Methoxyphenyl)methoxy]-3-[[(4-methoxyphenyl)methoxy]methyl]-2-[2-[[2-(trimethylsilyl)ethoxy]methoxy]ethylidene]-3-pentenoic acid methyl ester (26h). A solution of vinyl iodide **25** (11.2 g, 30.1 mmol) in DMF (75 mL) was treated with bis(acetonitrile)palladium(II) chloride (1.17 g, 4.52 mmol) and freeze–thaw degassed. A solution of vinyl stannane **21** (22.3 g, 36.1 mmol) in DMF (75 mL), which was also freeze–thaw degassed, was cannulated into the solution of the vinyl iodide **25**. The reaction mixture was stirred at room temperature in the absence of light for 3 d. The reaction mixture was quenched with 10% NH_4OH (500 mL), diluted with ether (250 mL), and stirred vigorously for 30 min. The aqueous phase was separated and extracted with ether (3 × 250 mL). The combined organic extracts were washed with water (2 × 300 mL) and brine (500 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7 → 1:1) gave diene **26h** (12.1 g, 70%) as a colorless oil. $R_f = 0.26$ (silica, ether:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 2951, 2861, 1722, 1612, 1513, 1463, 1248, 1174, 1035, 835\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.27-7.25$ (m, 2H, $CH_3OC_6H_4$), 7.20–7.17 (m, 2H, $CH_3OC_6H_4$), 6.96 (t, $J = 6.4$ Hz, 1H, H-6), 6.89–6.83 (m, 4H, $CH_3OC_6H_4$), 5.60 (t, $J = 6.2$ Hz, 1H, H-3), 4.67 (s, 2H, OCH_2O), 4.44 (s, 2H, $CH_3OC_6H_4CH_2$), 4.34 (s, 2H, $CH_3OC_6H_4CH_2$), 4.33 (d, $J = 6.4$ Hz, 2H, H-7), 4.13 (d, $J = 6.2$ Hz, 2H, $CH_3OC_6H_4CH_2OCH_2$), 4.11 (s, 2H, $CH_3OC_6H_4CH_2OCH_2$), 3.80 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.71 (s, 3H, CO_2CH_3), 3.63–3.60 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 0.94–0.90 (m, 2H, $CH_2Si(CH_3)_3$), 0.00 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 167.1, 159.7, 159.6, 141.1, 135.1, 132.3, 130.6, 130.5, 129.92, 129.90, 129.7, 114.2, 114.1, 95.0, 72.5, 72.4, 67.3, 65.9, 65.7, 65.3, 55.7, 52.4, 18.5, -1.0$; FAB HRMS calcd for $C_{31}H_{44}O_8SiNa$ ($M + Na$)$^+$: 595.0703; found $m/z = 595.0729$.

[2*S*-2(1*R*)-*E*]-2-Hydroxy-2-[1-hydroxy-2-[[2-(trimethylsilyl)ethoxy]methoxy]ethyl]-5-[(4-methoxyphenyl)methoxy]-3-[[(4-methoxyphenyl)methoxy]methyl]-3-pentenoic acid methyl ester (27h). A solution of $K_3Fe(CN)_6$ (6.39 g, 19.4 mmol) and K_2CO_3 (2.69 g, 19.4 mmol) in *t*-butanol (30 mL) and water (30 mL) was treated with $(DHQD)_2PHAL$ (500 mg, 64.3 μmol). The reaction mixture was stirred at room temperature for 45 min, treated with $K_2OsO_2(OH)_4$ (23.7 mg, 64.3 μmol), cooled to 0 °C, treated with methanesulfonamide (918 mg, 9.66 mmol), and stirred for 30 min. The reaction mixture was poured into a second flask containing the diene **26h** (3.69 g, 6.44 mmol) and stirred at 0 °C for 3 d. The reaction mixture was quenched at 0 °C with Na_2SO_3 (6.81 g, 54.0 mmol) and stirred for 15 min. The reaction mixture was diluted with water (15 mL) and extracted with ethyl acetate (4 × 75 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4 → 1:1) gave desired diol **27h** (1.17 g, 30%, 83% *ee*) and unreacted diene **26h** (1.73 g, 44%) as yellow oils.

Data for **27h**: $[\alpha]_D^{22} = +10.6$ (c 1.25 in $CHCl_3$, 83% *ee*); $R_f = 0.33$ (silica; ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max} = 3493, 2951, 1738, 1612, 1514, 1454, 1301, 1247, 1108, 1034, 835\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.22$ (d, $J = 8.7$ Hz, 2H, $CH_3OC_6H_4$), 7.20 (d, $J = 8.7$ Hz, 2H, $CH_3OC_6H_4$), 6.86 (d, $J = 8.7$ Hz, 2H, $CH_3OC_6H_4$), 6.85 (d, $J = 8.7$ Hz, 2H, $CH_3OC_6H_4$), 6.24 (t, $J = 6.1$ Hz, 1H, CH=C), 4.64 (ABq, $J_{AB} = 6.7$ Hz, $\Delta\nu_{AB} = 13.6$ Hz, 2H, OCH_2O), 4.39 (s, 2H, $CH_3OC_6H_4CH_2$), 4.37–4.34 (m, 1H, H-6), 4.33 (ABq, $J_{AB} = 11.5$ Hz, $\Delta\nu_{AB} = 9.9$ Hz, 2H, $CH_3OC_6H_4CH_2$), 4.08 (d, $J = 6.1$ Hz, 2H, $OCH_2CH{=}C$), 4.02 (ABq, $J_{AB} = 11.1$ Hz, $\Delta\nu_{AB} = 34.5$ Hz, 2H, $CH{=}CCH_2O$), 3.88 (s, 1H, C5-OH), 3.81–3.79 (m, 1H, H-7), 3.79 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.74 (s, 3H, CO_2CH_3), 3.65–3.55 (m, 3H, $OCH_2CH_2Si(CH_3)_3$ and H'-7), 3.20 (d, $J = 6.3$ Hz, 1H, C6-OH), 0.91 (t, $J = 8.4$ Hz, 2H, $CH_2Si(CH_3)_3$), −0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.9, 159.7, 135.6, 131.9, 130.4, 130.3, 130.0, 129.9,$

114.3, 114.2, 96.0, 80.9, 73.5, 72.8, 72.5, 69.6, 66.4, 65.9, 64.6, 55.7, 53.7, 18.5, −1.0; FAB HRMS calcd for $C_{31}H_{46}O_{10}SiNa$ $(M + Na)^+$: 629.2758; found m/z = 629.2541.

[2*S*-2(1*R*)-*E*]-2-Hydroxy-2-[1-hydroxy-2-[[2-(methoxy)ethoxy]methoxy]ethyl]-5-[(4-methoxyphenyl)methoxy]-3-[[(4-methoxyphenyl)methoxy]methyl]-3-pentenoic acid methyl ester (27i). A solution of $K_3Fe(CN)_6$ (209 g, 0.63 mol), K_2CO_3 (87 g, 0.63 mol), and $(DHQD)_2PHAL$ (8.24 g, 10.6 mmol) in *t*-butanol (1000 mL) and water (1000 mL) was stirred at room temperature for 1 h, treated with $K_2OsO_2(OH)_4$ (0.78 g, 2.12 mmol), cooled to 0 °C, treated with methansulfonamide (60 g, 0.63 mol), stirred for 30 min, treated with the diene **26i** (112 g, 0.21 mol), and stirred at 0 °C for 3 d. The reaction mixture was quenched with Na_2SO_3 (315 g) and warmed to room temperature. The reaction mixture was diluted with water (1000 mL) and ethyl acetate (2000 mL). The aqueous phase was separated and extracted with ethyl acetate (3 × 500 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:2 → 1:0) gave diol **27i** (30 g, 25%, 75% *ee*) and unreacted diene **26i** (53 g, 47%) as yellow oils. $[\alpha]_D^{22} = +14.7$ (*c* 1.00 in $CHCl_3$, 75% *ee*); $R_f = 0.39$ (silica, ethyl acetate); IR (thin film): $\tilde{\nu}_{max}$ = 3459, 2934, 2883, 1736, 1662, 1617, 1587, 1513, 1460, 1401, 1362, 1300, 1247, 1175, 1089, 1034 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): 7.24–7.20 (m, 4H, $CH_3OC_6H_4$), 6.87–6.85 (m, 4H, $CH_3OC_6H_4$), 6.25 (t, J = 6.1 Hz, 1H, CH=C), 4.68 (ABq, J_{AB} = 6.9 Hz, $\Delta\nu_{AB}$ = 8.7 Hz, 2H, OCH_2O), 4.39 (s, 2H, $CH_3OC_6H_4CH_2$), 4.40–4.37 (m, 1H, H-6), 4.34 (ABq, J_{AB} = 11.4 Hz, $\Delta\nu_{AB}$ = 9.3 Hz, 2H, $CH_3OC_6H_4CH_2$), 4.09 (d, J = 6.1 Hz, 2H, OCH_2CH=C), 4.02 (ABq, J_{AB} = 11.1 Hz, $\Delta\nu_{AB}$ = 34.9 Hz, 2H, CH=CCH_2O), 3.84 (s, 1H, C5-OH), 3.802 (s, 3H, OCH_3), 3.799 (s, 3H, OCH_3), 3.78–3.76 (m, 1H, H-7), 3.76 (s, 3H, CO_2CH_3), 3.73–3.64 (m, 3H, H′-7 and $OCH_2CH_2OCH_3$), 3.51 (t, J = 4.5, 2H, CH_2OCH_3), 3.36 (s, 3H, CH_2OCH_3), 3.92 (d, J = 7.0 Hz, 1H, CH(*OH*)); ^{13}C NMR (125 MHz, $CDCl_3$): 173.4, 159.2, 135.1, 131.4, 130.0, 129.8, 129.4, 129.4, 73.0, 72.3, 72.1, 71.7, 69.0, 66.9, 66.0, 64.1, 58.9, 55.2, 53.2; FAB HRMS calcd for $C_{29}H_{40}O_{11}Cs$ $(M + Cs)^+$: 697.1625; found m/z = 697.1625.

(4*R*,5*S*,*E*)-5-[[3-[(4-Methoxyphenyl)methoxy]-1-[[(4-methoxyphenyl)methoxy]methyl]-1-propenyl]-2,2-dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-1,3-dioxacyclopentane-5-carboxylic acid, methyl ester (28a). A solution of diol **27h** (1.55 g, 2.55 mmol) and PPTS (128 mg, 0.511 mmol) in dichloromethane (35 mL) at 0 °C was treated with 2-methoxypropene (1.22 mL, 12.8 mmol). The reaction mixture was stirred at 0 °C for 3 h, treated with an additional amount of 2-methoxypropene (0.50 mL, 5.23 mmol), and stirred at 0 °C for 4 h. The reaction mixture was quenched at 0 °C with $NaHCO_3$ (35 mL) and warmed to room temperature. The aqueous phase was separated and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7 → 4:6) gave acetonide **28a** (1.45 g, 88%) as a colorless oil. $[\alpha]_D^{22} = +55.6$ (*c* 1.22 in $CHCl_3$, 83% *ee*); $R_f = 0.38$ (silica, ether:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max}$ = 2951, 1731, 1613, 1514, 1455, 1372, 1246, 1174, 1060, 856 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.23 (d, J = 8.3 Hz, 2H, $CH_3OC_6H_4$), 7.18 (d, J = 8.3 Hz, 2H, $CH_3OC_6H_4$), 6.86 (d, J = 8.3 Hz, 2H, $CH_3OC_6H_4$), 6.84 (d, J = 8.3 Hz, 2H, $CH_3OC_6H_4$), 6.19 (dd, J = 6.5, 5.9 Hz, 1H, CH=C), 5.00 (dd, J = 8.2, 4.2 Hz, 1H, H-6), 4.63 (s, 2H, OCH_2O), 4.40 (s, 2H, $CH_3OC_6H_4CH_2$), 4.29 (s, 2H, $CH_3OC_6H_4CH_2$), 4.10 (dd, J = 13.4, 6.5 Hz, 1H, OC*H*H′CH=C), 4.07 (dd, J = 13.4, 5.9 Hz, 1H, OCH*H*′CH=C), 3.88 (ABq, J_{AB} = 11.6 Hz, $\Delta\nu_{AB}$ = 20.1 Hz, 2H, CH=CCH_2O), 3.79 (s, 6H, OCH_3 and OCH_3), 3.68 (s, 3H, CO_2CH_3), 3.64–3.55 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 3.51 (dd, J = 10.2, 4.2 Hz, 1H, H-7), 3.43 (dd, J = 10.2, 8.2 Hz, 1H, H′-7), 1.53 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 0.91 (t, J = 8.4 Hz, 2H, $CH_2Si(CH_3)_3$), 0.00 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.6, 159.61, 159.60, 133.2, 130.5, 130.21, 130.20, 129.8, 129.7, 114.2, 114.1, 110.8, 95.3, 86.8, 79.6, 72.8, 72.4, 68.0, 66.2, 65.6, 65.4, 55.6, 53.2, 28.4, 26.4, 18.4, −1.0; FAB HRMS calcd for $C_{34}H_{50}O_{10}SiNa$ $(M + Na)^+$: 669.3071; found m/z = 669.3080.

(4*R*,5*S*,*E*)-5-[[3-[(4-Methoxyphenyl)methoxy]-1-[[(4-methoxyphenyl)methoxy]methyl]-1-propenyl]-4-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-1,3-dioxacyclopentane-5-carboxylic acid methyl ester (28b). A solution of diol **27i** (30 g, 0.053 mol) in dichloromethane (400 mL) at 0 °C was treated with 2-methoxypropene (50 mL, 0.52 mol) and PPTS (0.71 g, 2.82 mmol). The reaction mixture was warmed to room temperature, stirred for 8 h, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:2) gave acetonide **28b** (25 g, 77%). $[\alpha]_D^{22} = +51.6$ (*c* 9.35 in $CHCl_3$, 75% *ee*); $R_f = 0.34$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max}$ = 2936, 2879, 1735, 1612, 1514, 1462, 1372, 1249, 1175, 1071, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.15 (m, 4H, $CH_3OC_6H_4$), 6.87–6.81 (m, 4H, $CH_3OC_6H_4$), 6.18 (dd, J = 6.6, 5.8 Hz, 1H, CH=C), 4.99 (dd, J = 8.2, 4.4 Hz, 1H, H-6), 4.66 (ABq, J_{AB} = 6.9 Hz, $\Delta\nu_{AB}$ = 3.1 Hz, 2H, OCH_2O), 4.38 (s, 2H, $CH_3OC_6H_4CH_2$), 4.27 (s, 2H, $CH_3OC_6H_4CH_2$), 4.09 (dd, J = 13.2, 6.6 Hz, 1H, C*H*H′CH=C), 4.05 (dd, J = 13.2, 5.8 Hz, 1H, CH*H*′CH=C), 3.87 (ABq, J_{AB} = 11.7 Hz, $\Delta\nu_{AB}$ = 10.7 Hz, 2H, CH=CCH_2O), 3.77 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.67 (s, 3H, CO_2CH_3), 3.64–3.62 (m, 2H, $OCH_2CH_2OCH_3$), 3.54 (dd, J = 10.3, 4.4 Hz, 1H, H-7), 3.48–3.46 (m, 2H, CH_2OCH_3), 3.40 (dd, J = 10.3, 8.2 Hz, 1H, H′-7), 3.33 (s, 3H, CH_2OCH_3), 1.51 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.5, 159.6, 159.5, 133.2, 130.4, 130.2, 130.0, 129.8, 129.7, 114.1, 114.0, 110.7, 95.9, 86.8, 79.5, 72.8, 72.4, 72.0, 68.0, 67.2, 66.1, 65.4, 59.2, 55.6, 53.1, 28.4, 26.4; FAB HRMS calcd for $C_{32}H_{44}O_{11}Cs$ $(M + Cs)^+$: 737.1938; found m/z = 737.1954.

(4*R*,5*S*,*E*)-9-(2-Hydroxyethylidene)-2,2-dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (29a). A solution of the acetonide **28a** (7.45 g, 11.5 mmol) in chloroform (300 mL) and water (15 mL) was treated with DDQ (7.85 g, 34.6 mmol). The reaction mixture was stirred vigorously at room temperature for 12 h. The reaction mixture was quenched with $NaHCO_3$ (300 mL) and extracted with ethyl acetate (3 × 300 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 3:7 → 4:6) gave the lactone **29a** (3.70 g, 86%) as a colorless oil. $[\alpha]_D^{22} = -34.2$ (*c* 2.95 in $CHCl_3$, 83% *ee*); $R_f = 0.53$ (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 3454, 2958, 2893, 1770, 1462, 1377, 1217, 1198, 1061, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.82–5.79 (m, 1H, C=CH), 5.07 (dd, J = 13.7, 1.3 Hz, 1H, C*H*H′-lactone ring), 4.89 (dd, J = 13.7, 2.0 Hz, 1H, CH*H*′-lactone ring), 4.60 (ABq, J_{AB} = 6.5 Hz, $\Delta\nu_{AB}$ = 7.6 Hz, 2H, OCH_2O), 4.55 (dd, J = 7.7, 5.7 Hz, 1H, H-6), 4.28 (d, J = 5.2 Hz, 2H, CH_2OH, coincident peaks), 3.79 (dd, J = 9.7, 5.7 Hz, 1H, H-7), 3.61–3.51 (m, 3H, $OCH_2CH_2Si(CH_3)_3$ and H′-7), 2.04 (brs, 1H, CH_2OH), 1.63 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 0.91 (app.t, J = 8.1 Hz, 2H, $CH_2Si(CH_3)_3$), 0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.3, 133.9, 128.3, 112.4, 95.7, 81.9, 81.0, 69.4, 66.6, 66.2, 60.4, 27.6, 25.8, 18.5, −1.0; FAB HRMS calcd for $C_{17}H_{30}O_7SiNa$ $(M + Na)^+$: 397.1659; found m/z = 397.1643.

(4*R*,5*S*,*E*)-9-(2-Hydroxyethylidene)-4-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-1,3,7-trioxaspiro[4.4]nonan-6-one (29b). A solution of the acetonide **28b** (48.9 g, 0.081 mol) in chloroform (1550 mL) and water (77 mL) was treated with DDQ (55.2 g, 0.24 mol). The reaction mixture was stirred at room temperature for 16 h and then diluted with with ethyl acetate (1000 mL) and $NaHCO_3$ (1500 mL). The aqueous phase was separated and extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, methanol:dichloromethane 1:99 → 1:24) gave lactone **29b** (21 g, 78%). $[\alpha]_D^{22} = -48.7$ (*c* 2.81 in $CHCl_3$, 75% *ee*); $R_f = 0.16$ (silica, ethyl acetate:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max}$ = 3450, 2938, 2892, 1779, 1460, 1376, 1217, 1076, 872 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.76 (ddd, J = 7.6, 4.9, 2.1 Hz, 1H, C=CH), 5.04 (dd, J = 13.7, 1.4 Hz, 1H, C*H*H′-lactone ring), 4.90 (dd, J = 13.7, 2.1 Hz, 1H, CH*H*′-lactone ring), 4.61 (ABq, J_{AB} = 6.7 Hz, $\Delta\nu_{AB}$ = 8.4 Hz, 2H, OCH_2O), 4.51 (dd, J = 8.1, 5.6 Hz, 1H, H-6), 4.20–4.24 (m, 2H, CH_2OH), 3.72 (dd, J = 9.6, 5.6 Hz, 1H, H-7), 3.62–3.58 (m, 3H, $OCH_2CH_2OCH_3$ and H′-7), 3.51 (app.t, J = 4.4 Hz, 2H, CH_2OCH_3), 3.34 (s, 3H, OCH_3), 2.94 (brdd, J = 5.4, 5.2 Hz, 1H, OH), 1.58 (s, 3H, CH_3), 1.52 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.4, 133.3, 128.8, 112.2, 96.3, 81.8, 80.7, 72.0, 69.5, 67.6, 66.7, 60.2, 59.4, 27.4, 25.7; FAB HRMS calcd for $C_{15}H_{24}O_8Cs$ $(M + Cs)^+$: 465.0526; found m/z = 465.0539.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-8,9-bis(hydroxymethyl)-2,2-dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (30a). A solution of lactone **29a** (2.24 g, 5.98 mmol) in THF (35 mL) and *t*-butanol (35 mL) was treated with NMO (2.10 g, 17.9 mmol). The reaction mixture was cooled to 0 °C and treated with osmium tetroxide (1.54 mL, 0.299 mmol, 4.76 wt% in H_2O), stirred at 0 °C for 24 h, quenched with solid Na_2SO_3 (3.01 g, 23.9 mmol), stirred for 15 min, treated with Florisil (3.45 g), and again stirred for 15 min. It was then filtered through Celite and the filtrate was concentrated in vacuo to give a crude oil, which was diluted with ethyl acetate (100 mL) and washed with a mixture of aqueous HCl (1 M, 30 mL) and brine (90 mL). The aqueous phase was separated and extracted with ethyl acetate (3 × 75 mL). The combined organic extracts were washed with a mixture of $NaHCO_3$ (40 mL) and brine (30 mL). This aqueous phase was likewise separated and extracted with ethyl acetate (3 × 75 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. The crude oil (2.42 g, 99%) was used in the next step without any further purification. Pure compound could be obtained, however, by flash column chromatography (silica, ethyl acetate:petroleum ether 2:3 → 1:1) to yield the triol **30a** (2.04 g, 83%) as a white solid. $[\alpha]_D^{22} = +38.9$ (*c* 1.50 in $CHCl_3$, 83% *ee*); $R_f = 0.33$ (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 3388, 2952, 2895, 1788, 1384, 1250, 1217, 1059, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 4.97 (brs, 1H, C4-OH), 4.85 (dd, J = 7.0, 3.4 Hz, 1H, H-6), 4.75 (s, 2H, OCH_2O), 4.48 (dd, J = 5.9, 3.9 Hz, 1H, H-3), 4.13 (dd, J = 11.6, 3.4 Hz, 1H, H-7), 4.08 (dd, J = 11.9, 3.9 Hz, 1H, CHC*H*H′OH), 4.05 (dd, J = 11.9, 5.9 Hz, 1H, CHCH*H*′OH), 3.89 (ABq, J_{AB} = 29.6 Hz, $\Delta\nu_{AB}$ = 26.9 Hz, 2H, C(OH)CH_2OH), 3.86 (dd, J = 11.6, 7.0 Hz, 1H, H′-7), 3.69–3.61 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.47 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 0.95–0.92 (m, 2H, $CH_2Si(CH_3)_3$), 0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.1, 111.2, 95.6, 84.5, 83.3, 80.0, 78.0, 66.3, 65.5, 62.6, 59.7, 27.0, 25.4, 18.5, −1.0; FAB HRMS calcd for $C_{17}H_{32}O_9SiNa$ $(M + Na)^+$: 431.1713; found m/z = 431.1720.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-8,9-bis(hydroxymethyl)-4-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-1,3,7-trioxaspiro[4.4]nonan-6-one (30b). A solution of allylic alcohol **29b** (11 g, 33.0 mmol) and NMO (11.6 g, 0.10 mol) in *t*-butanol

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(193 mL), THF (193 mL) and water (3.8 mL) at 0 °C was treated with osmium tetroxide (2.5 wt% in *t*-butanol, 16.8 mL, 1.34 mmol). The reaction mixture was stirred at 0 °C for 6 h, quenched with Na_2SO_3 (16.7 g), stirred for 15 minutes, treated with Florisil (20 g), again stirred for 15 min, warmed to room temperature, and filtered, and the filtrate was concentrated in vacuo to give a crude oil. A solution of the crude lactone in ethyl acetate (300 mL) was treated with triethylamine (5 mL). The reaction mixture was stirred at room temperature for 5 min and washed with aqueous HCl (1 M, 100 mL), $NaHCO_3$ (300 mL), and brine (300 mL). The aqueous phases were sequentially extracted with more ethyl acetate (3 × 300 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give the triol **30b** (12.5 g, 100%) as a red oil. The triol was usually used in the next step without any further purification. Pure compound could be obtained, however, by flash column chromatography (silica, ethyl acetate:petroleum ether 1:1 → 3:1). $[\alpha]_D^{22} = +43.3$ (*c* 1.36 in $CHCl_3$, 75% *ee*); $R_f = 0.19$ (silica, ethyl acetate); IR (thin film): $\tilde{\nu}_{max} = 3395, 2940, 2893, 1784, 1457, 1377, 1114, 1058, 862\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 4.93$ (s, 1H, C4-OH), 4.85 (dd, $J = 7.1, 3.5$ Hz, 1H, H-6), 4.80 (ABq, $J_{AB} = 6.8$ Hz, $\Delta\nu_{AB} = 5.4$ Hz, 2H, OCH_2O), 4.48 (dd, $J = 5.8, 4.1$ Hz, 1H, H-3), 4.16 (dd, $J = 11.4, 3.5$ Hz, 1H, H-7), 4.11–4.07 (m, 1H, CH_2OH), 4.06–4.03 (m, 2H, $CHCH_2OH$), 3.95 (dd, $J = 11.7, 5.9$ Hz, 1H, C(OH)CHH'OH), 3.89 (dd, $J = 11.4, 7.1$ Hz, 1H, H'-7), 3.87–3.81 (m, 3H, C(OH)CHH'OH and CH_2OH), 3.77–3.70 (m, 2H, $OCH_2CH_2OCH_3$), 3.58 (app.t, $J = 4.5$ Hz, 2H, CH_2OCH_3), 3.39 (s, 3H, OCH_3), 1.46, (s, 3H, CH_3), 1.42 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 174.1, 111.2, 96.5, 84.6, 83.6, 79.9, 78.0, 72.2, 67.8, 65.8, 62.5, 59.5, 59.4, 27.0, 25.4$; FAB HRMS calcd for $C_{15}H_{26}O_{10}Na$ $(M + Na)^+$: 389.1424; found $m/z = 389.1429$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-9-hydroxymethyl-2,2-dimethyl-8-[[[(1,1-dimethylethyl)-diphenylsilyl]oxy]methyl]-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (31). A solution of the triol **30a** (641 mg, 1.60 mmol) in DMF (7 mL) was treated with imidazole (218 mg, 3.20 mmol), DMAP (10.0 mg, 81.9 μmol), and TPSCl (428 μL, 1.65 mmol). The reaction mixture was stirred at room temperature for 12 h, poured into a mixture of aqueous HCl (1 M)/brine (1:3, 20 mL), and extracted with ethyl acetate (3 × 25 mL). The combined organic extracts were washed with a mixture of $NaHCO_3$/brine (1:1, 20 mL) and brine (20 mL). They were then dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7 → 2:3) gave diol **31** (930 mg, 89%) as a clear oil. $[\alpha]_D^{22} = +35.4$ (*c* 0.88 in $CHCl_3$, 83% *ee*); $R_f = 0.33$ (silica, ether:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3415, 2953, 2893, 2859, 1789, 1463, 1428, 1376, 1249, 1218, 1119, 1061, 859\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.69–7.65$ (m, 4H, Ph), 7.47–7.39 (m, 6H, Ph), 4.93 (s, 1H, C4-OH), 4.89 (dd, $J = 7.2, 3.3$ Hz, 1H, H-6), 4.76 (ABq, $J_{AB} = 6.9$ Hz, $\Delta\nu_{AB} = 4.7$ Hz, 2H, OCH_2O) 4.45 (dd, $J = 5.3, 3.8$ Hz, 1H, H-3), 4.18 (dd, $J = 11.6, 3.3$ Hz, 1H, H-7), 4.13 (dd, $J = 11.5, 5.3$ Hz, 1H, CHH'OSi), 4.08 (dd, $J = 11.5, 3.8$ Hz, 1H, CHH'OSi), 3.95 (dd, $J = 12.0, 6.3$ Hz, 1H, CHH'OH), 3.89 (dd, $J = 11.6, 7.2$ Hz, 1H, H'-7), 3.88 (dd, $J = 12.0, 6.1$ Hz, 1H, CHH'OH), 3.70–3.61 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 2.98 (dd, $J = 6.3, 6.1$ Hz, 1H, CH_2OH), 1.49 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.05 (s, 9H, $SiC(CH_3)_3$), 0.94 (app.t, $J = 8.4$ Hz, 2H, $CH_2Si(CH_3)_3$), 0.01 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.8, 136.0, 135.9, 132.2, 131.9, 130.7, 128.5, 128.4, 111.1, 95.5, 84.5, 82.8, 80.0, 78.2, 66.0, 65.3, 62.6, 61.9, 27.1, 27.0, 25.4, 19.5, 18.4, −1.0$; FAB HRMS calcd for $C_{33}H_{50}O_9Si_2Cs$ $(M + Cs)^+$: 779.2048; found $m/z = 779.2060$.

(4*R*,5*R*,8*R*,9*S*)-9-[[[(−)-Camphanyl]oxy]methyl]-9-hydroxy-2,2-dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-8-[(3,5-dinitrobenzoyl)methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (32). A solution of **31** (233 mg, 0.36 mmol) in pyridine (2.5 mL) was treated with DMAP (4.4 mg, 36 μmol) and (−)-camphanic acid chloride (234 mg, 1.08 mmol). The reaction mixture was stirred at room temperature for 6 h and then diluted with dichloromethane (10 mL) and water (10 mL). The aqueous phase was separated and extracted with dichloromethane (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, petroleum ether:ethyl acetate 9:1 → 5:1) gave the camphate ester (173 mg, 73%). A solution of the camphate ester (216 mg, 0.26 mmol) in THF (3.4 mL) at 0 °C was treated with acetic acid (30 μL, 0.53 mmol) and TBAF (1.0 M in THF, 0.31 mL, 0.31 mmol). The reaction mixture was stirrred at 0 °C for 1 h, warmed to room temperature, and diluted with water (10 mL) and ethyl acetate (10 mL). The aqueous phase was separated and extracted with ethyl acetate. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:1) gave the diol (129 mg, 84%). A solution of the diol (129 mg, 0.22 mmol) in pyridine (1.5 mL) was treated with DMAP (2.7 mg, 22 μmol) and 3,5-dinitrobenzoyl chloride (151 mg, 0.66 mmol). The reaction mixture was stirred at room temperature for 1 h and then diluted with water (10 mL) and dichloromethane (10 mL). The aqueous phase was separated and extracted with dichloromethane (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:5 → 1:3) gave the diester **32** (128 mg, 75%) as a white crystalline solid. Diester **32** was recrystallized three times from hot heptane/ethyl acetate. Single crystals of **32** were grown by allowing a solution of **32** in hot heptane/ethyl acetate to partially evaporate slowly overnight. M.p. 146–147 °C (heptane/ethyl acetate); $[\alpha]_D^{22} = +50.2$ (*c* 0.84 in $CHCl_3$); $R_f = 0.89$ (silica, ethyl acetate:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3352, 3104, 2957, 2894, 1792, 1741, 1629, 1548, 1459, 1381, 1346, 1312, 1274, 1219, 1164, 1104, 1058\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.25–9.24$ (m, 1H, Ar), 9.19–9.18 (m, 2H, Ar), 5.20 (d, $J = 12.2$ Hz, 1H, C(OH)CHH'O), 5.11 (br d, $J = 12.5$ Hz, 1H, CHCHH'O), 5.00–4.96 (m, 2H, C4-OH and CHCHH'O), 4.89 (d, $J = 6.5$ Hz, 1H, OCHH'O), 4.85–4.82 (m, 2H, OCHH'O and H-6), 4.75 (dd, $J = 12.6, 8.7$ Hz, 1H, H-3), 4.41 (d, $J = 12.1$ Hz, 1H, C(OH)CHH'O), 4.19 (dd, $J = 11.4, 4.3$ Hz, 1H, H-7), 4.06 (dd, $J = 11.4, 2.0$ Hz, 1H, H'-7), 3.68 (d, $J = 8.6$ Hz, 1H, OCHH'$CH_2Si(CH_3)_3$), 3.66 (d, $J = 8.6$ Hz, 1H, OCHH'$CH_2Si(CH_3)_3$), 2.46 (ddd, $J = 13.2, 10.9, 4.2$ Hz, 1H, CH_2), 2.10 (ddd, $J = 13.4, 9.4, 4.4$ Hz, 1H, CH_2), 1.96 (ddd, $J = 13.1, 10.9, 4.4$ Hz, 1H, CH_2), 1.72 (ddd, $J = 13.2, 9.4, 4.0$ Hz, 1H, CH_2), 1.52 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.10 (s, 6H, CH_3 and CH_3), 0.98 (s, 3H, CH_3), 0.99–0.96 (m, 2H, $CH_2Si(CH_3)_3$), 0.03 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 177.4, 172.5, 167.3, 162.1, 148.5, 133.1, 129.5, 122.4, 110.5, 95.1, 90.6, 83.9, 82.4, 77.7, 76.8, 66.2, 65.4, 65.0, 62.9, 54.6, 54.3, 30.8, 28.7, 26.5, 24.7, 17.8, 16.7, 16.6, 9.5, −1.5$; FAB HRMS calcd for $C_{34}H_{46}N_2O_{17}SiCs$ $(M + Cs)^+$: 915.1620; found $m/z = 915.1640$.

(4*R*,5*R*,8*R*,9*S*)-9-Formyl-9-hydroxy-2,2-dimethyl-8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (33). A solution of the diol **31** (1.47 g, 2.27 mmol) in dichloromethane (50 mL) was treated with Dess–Martin periodinane (2.88 g, 6.81 mmol). The reaction mixture was stirred at room temperature for 12 h, diluted with ether (50 mL), quenched with 25% $Na_2S_2O_3$ in aqueous $NaHCO_3$ (25 mL), and stirred vigorously for 15 min. The aqueous phase was separated and extracted with ether (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 2:8 → 3:7) gave the aldehyde **33** (1.41 g, 96%) as a colorless oil. $[\alpha]_D^{22} = +63.9$ (*c* 0.82 in $CHCl_3$, 83% *ee*); $R_f = 0.33$ (silica, ether:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3361, 3072, 2953, 2891, 1796, 1731, 1463, 1428, 1384, 1249, 1112, 1057, 836\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.93$ (s, 1H, CHO), 7.66–7.63 (m, 4H, Ph), 7.47–7.40 (m, 6H, Ph), 5.06 (dd, $J = 7.1, 5.1$ Hz, 1H, H-3), 4.94 (s, 1H, C4-OH), 4.85 (dd, $J = 4.3, 3.6$ Hz, 1H, H-6), 4.71 (s, 2H, OCH_2O), 4.00 (dd, $J = 11.7, 3.6$ Hz, 1H, H-7), 3.96 (dd, $J = 10.7, 7.1$ Hz, 1H, CHH'OSi), 3.92 (dd, $J = 10.7, 5.1$ Hz, 1H, CHH'OSi), 3.83 (dd, $J = 11.7, 4.3$ Hz, 1H, H'-7), 3.67-3.64 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.49 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.02 (s, 9H, $SiC(CH_3)_3$), 0.99–0.96 (m, 2H, $CH_2Si(CH_3)_3$), 0.04 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 197.2, 172.5, 136.0, 135.9, 132.6, 132.5, 130.5, 128.33, 128.30, 111.9, 95.3, 86.2, 82.1, 80.3, 77.7, 66.2, 64.4, 60.2, 27.2, 27.0, 25.7, 19.4, 18.4, −1.0$; FAB HRMS calcd for $C_{33}H_{48}O_9Si_2Cs$ $(M + Cs)^+$: 777.1891; found $m/z = 777.1862$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-2,2-dimethyl-8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid (34). A solution of the aldehyde **33** (3.39 g, 5.25 mmol) in *t*-butanol (30 mL) and water (7.5 mL) was treated with 2-methyl-2-butene (2.0 M in THF, 11.0 mL, 22.0 mmol) and $NaH_2PO_4 \cdot H_2O$ (761 mg, 5.51 mmol). The reaction mixture was stirred at room temperature for 15 min, treated with $NaClO_2$ (1.42 g, 15.8 mmol), and stirred for 3 h. The reaction mixture was cooled to 0 °C, quenched with aqueous HCl (1 M, 100 mL), and extracted with dichloromethane (4 × 300 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to provide the acid **34** (3.47 g, 100%) as a colorless oil. The crude acid was usually used in the next step without any further purification. $R_f = 0.55$ (silica, CH_2Cl_2:MeOH:[H_2O:AcOH (3:1)] 90:10:1.5); IR (thin film): $\tilde{\nu}_{max} = 3332, 2957, 2894, 1790, 1731, 1472, 1428, 1384, 1251, 1113, 1059, 836\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.69–7.62$ (m, 4H, Ph), 7.49–7.41 (m, 6H, Ph), 6.20 (s, 1H, C4-OH), 4.95–4.93 (m, 2H, H-6 and H-3), 4.84 (ABq, $J_{AB} = 6.8$ Hz, $\Delta\nu_{AB} = 11.4$ Hz, 2H, OCH_2O), 4.34 (dd, $J = 12.4, 2.5$ Hz, 1H, H-7), 4.23 (dd, $J = 12.4, 3.5$ Hz, 1H, H'-7), 4.21–4.17 (m, 2H, CH_2OSi), 3.77–3.66 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.48 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.02 (s, 9H, $SiC(CH_3)_3$), 0.95 (app.t, $J = 8.3$ Hz, 2H, $CH_2Si(CH_3)_3$), 0.02 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.8, 170.2, 136.1, 135.9, 132.1, 131.6, 130.7, 128.5, 128.4, 112.0, 95.7, 84.6, 82.0, 80.2, 77.8, 66.6, 64.2, 62.2, 27.1, 27.0, 25.5, 19.5, 18.3, −1.0$; FAB HRMS calcd for $C_{33}H_{48}O_{10}Si_2Cs$ $(M + Cs)^+$: 793.1840; found $m/z = 793.1852$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-2,2-dimethyl-8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (35). A solution of the acid **34** (3.47 g, 5.25 mmol) in toluene (90 mL) was treated with DCBI (3.30 g, 10.5 mmol). The reaction mixture was heated at 100 °C for 1.5 h, cooled to room temperature, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:9 → 2:8) gave benzyl ester **35** (3.77 g, 96% from **33**) as a colorless oil. $[\alpha]_D^{22} = +31.3$ (*c* 3.35 in $CHCl_3$, 83% *ee*); $R_f = 0.55$ (silica, ether:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3331, 3070, 2953, 2882, 1797, 1741, 1472, 1428, 1376, 1275, 1111, 939, 837\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.67–7.63$ (m, 4H, Ph), 7.45–7.43 (m, 2H, Ph), 7.40–7.36 (m, 9H, Ph), 5.54 (s, 1H, C4-OH), 5.20 (ABq, $J_{AB} = 12.3$ Hz, $\Delta\nu_{AB} = 32.1$ Hz, 2H, CH_2Ph), 5.15 (t, $J = 5.2$ Hz, 1H, H-3), 4.95 (dd, $J = 6.3, 5.3$ Hz, 1H, H-6), 4.71 (ABq, $J_{AB} = 6.8$ Hz, $\Delta\nu_{AB} = 24.8$ Hz, 2H, OCH_2O), 4.14 (dd, $J = 11.3, 5.3$ Hz, 1H, H-7),

4.08 (d, J = 5.2 Hz, 2H, CH_2OSi), 3.98 (dd, J = 11.3, 6.3 Hz, 1H, H'-7), 3.67–3.63 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.44 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.05 (s, 9H, $SiC(CH_3)_3$), 0.98–0.95 (m, 2H, $CH_2Si(CH_3)_3$), 0.04 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.3, 168.4, 135.5, 135.4, 134.4, 132.2, 131.9, 130.0, 129.9, 128.6, 128.4, 127.82, 128.80, 111.6, 95.0, 85.4, 81.0, 80.2, 77.8, 67.9, 65.6, 64.7, 61.1, 27.1, 26.6, 25.2, 19.0, 17.9, −1.5; FAB HRMS calcd for $C_{40}H_{54}O_{10}Si_2Cs$ $(M + Cs)^+$: 883.2310; found m/z = 883.2351.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-8-hydroxymethyl-2,2-dimethyl-4-[[[2-(trimethylsilyl)-ethoxy]methoxy]methyl]-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (36). A solution of benzyl ester **35** (3.77 g, 5.03 mmol) in THF (50 mL) at 0 °C was treated with acetic acid (0.578 mL, 10.1 mmol) and TBAF (1.0 M in THF, 6.03 mL, 6.03 mmol). The reaction mixture was stirred at 0 °C for 2 h, quenched with water (50 mL), and extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 2:8 → 4:6) gave diol **36** (2.49 g, 97%) as a colorless oil. $[\alpha]_D^{22}$ = + 45.2 (c 0.84 in $CHCl_3$, 83% *ee*); R_f = 0.42 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3451, 3301, 2952, 2895, 1789, 1740, 1458, 1377, 1277, 1192, 1057, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.33 (m, 5H, Ph), 5.88 (s, 1H, C4-OH), 5.23 (s, 2H, CH_2Ph), 5.03 (dd, J = 4.7, 4.6 Hz, 1H, H-3), 4.88 (dd, J = 5.9, 5.6 Hz, 1H, H-6), 4.67 (ABq, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 28.6 Hz, 2H, OCH_2O), 4.10 (dd, J = 11.4, 5.6 Hz, 1H, H-7), 4.07 (dd, J = 12.6, 4.6 Hz, 1H, CHH'OH), 4.02 (dd, J = 12.6, 4.7 Hz, 1H, CHH'OH), 3.94 (dd, J = 11.4, 5.9 Hz, 1H, H'-7), 3.64–3.56 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 2.89 (br s, 1H, CH_2OH), 1.40 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 0.93–0.90 (m, 2H, $CH_2Si(CH_3)_3$), 0.00 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.0, 169.0, 134.9, 129.2, 129.1, 129.0, 112.2, 95.5, 85.9, 81.4, 81.3, 78.3, 68.5, 66.3, 65.0, 60.3, 27.5, 25.7, 18.4, −1.0; FAB HRMS calcd for $C_{24}H_{36}O_{10}SiCs$ $(M + Cs)^+$: 645.1132; found m/z = 645.1145.

(4*R*,5*R*,8*S*,9*S*)-8-Formyl-2,2-dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]-methyl]-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (39). A solution of diol **36** (432 mg, 0.843 mmol) in *N*-methyl-*N*-(trimethylsilyl)-trifluoroacetamide (0.55 mL, 2.95 mmol) was heated at 100 °C for 2 h. The reaction mixture was cooled to room temperature and concentrated in vacuo to give a crude oil. A solution of the crude bissilyl ether **37** [R_f = 0.73 (silica, ether:petroleum ether 1:1)] in dichloromethane (28 mL) and methanol (2.8 mL) was treated with PPTS (30.7 mg, 0.122 mmol). The reaction mixture was stirred at room temperature for 5 min, quenched with phosphate buffer solution (pH 7, 20 mL), and extracted with dichloromethane (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo to give the alcohol **38** (0.49 g, 100%) as a colorless oil [R_f = 0.36 (silica, ether:petroleum ether 1:1)]. A solution of the crude alcohol **38** (490 mg, 0.843 mmol) in dichloromethane (50 mL) was treated with Dess–Martin periodinane (429 mg, 1.01 mmol). The reaction mixture was stirred at room temperature for 2 h, diluted with ether (100 mL), and filtered through Celite. The filtrate was washed with 25% $Na_2S_2O_3$ in aqueous $NaHCO_3$ (30 mL). The aqueous phase was separated and extracted with ether (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7 → 4:6) gave aldehyde **39** (0.48 g, 97% from **36**) as a colorless oil. $[\alpha]_D^{22}$ = +18.9 (c 1.60 in $CHCl_3$, 83% *ee*); R_f = 0.48 (silica, ether:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 3361, 3072, 2953, 2891, 1796, 1731, 1463, 1428, 1384, 1249, 1112, 1057, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.67 (s, 1H, CHO), 7.44–7.34 (m, 5H, Ph), 5.31 (s, 1H, H-3), 5.25 (ABq, J_{AB} = 12.0 Hz, $\Delta\nu_{AB}$ = 40.6 Hz, 2H, CH_2Ph), 4.87 (dd, J = 6.3, 6.3 Hz, 1H, H-6), 4.66 (ABq, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 49.7 Hz, 2H, OCH_2O), 4.00 (d, J = 6.3 Hz, 2H, H-7, H'-7, coincident peaks), 3.67–3.53 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.43 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 0.93–0.90 (m, 2H, $CH_2Si(CH_3)_3$), 0.05 (s, 9H, $OSi(CH_3)_3$), 0.01 (s, 9H, $CH_2Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 195.5, 172.0, 167.5, 134.5, 129.63, 129.60, 129.2, 112.1, 95.3, 85.5, 85.1, 84.8, 79.4, 69.3, 65.7, 65.5, 27.0, 25.2, 18.5, 1.9, −0.9; FAB HRMS calcd for $C_{27}H_{42}O_{10}Si_2Na$ $(M + Na)^+$: 605.2214; found m/z = 605.2239.

(4*R*,5*R*,8*S*,9*S*)-2,2-Dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (41a) and (4*R*,5*R*,8*S*,9*S*)-9-hydroxy-2,2-dimethyl-4-[[[2-(trimethylsilyl)ethoxy]methoxy]methyl]-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (41b). A stirred solution of the aldehyde **39** (250 mg, 0.429 mmol) in *t*-butanol (3.6 mL) and water (0.9 mL) was treated with 2-methyl-2-butene (2.0 M in THF, 0.90 mL, 1.80 mmol) and $NaH_2PO_4 \cdot H_2O$ (62.0 mg, 0.450 mmol). The reaction mixture was stirred at room temperature for 15 min, treated with $NaClO_2$ (116 mg, 1.29 mmol), and stirred for 3 h. The reaction mixture was cooled to 0 °C, quenched with aqueous HCl (1 M, 10 mL), and extracted with dichloromethane (4 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give acid **40** (257 mg, 100%) [R_f = 0.48 (silica, CH_2Cl_2:MeOH:[H_2O:AcOH (3:1)]90:10:1.5)] which was used in the next step without any further purification. A solution of the crude acid **40** (257 mg, 0.429 mmol) in toluene (17 mL) was treated with DCBI (175 mg, 0.558 mmol). The reaction mixture was heated to 60 °C for 3 h, cooled to room temperature, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 2:8 → 3:7) gave dibenzyl ester **41a** (178 mg, 60% over 2 steps) and the desilylated dibenzyl ester **41b** (41.0 mg, 16% over 2 steps) as colorless oils.

Data for **41a**: $[\alpha]_D^{22}$ = + 28.1 (c 2.70 in $CHCl_3$, 83% *ee*); R_f = 0.25 (silica, ether:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 2953, 2896, 1804, 1763, 1456, 1383, 1252, 1191, 1060, 849 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.33 (m, 10H, Ph), 5.42 (s, 1H, H-3), 5.22 (ABq, J_{AB} = 12.2 Hz, $\Delta\nu_{AB}$ = 86.2 Hz, 2H, CH_2Ph), 5.19 (ABq, J_{AB} = 12.0 Hz, $\Delta\nu_{AB}$ = 25.5 Hz, 2H, CH_2Ph), 4.81 (dd, J = 9.1, 2.4 Hz, 1H, H-6), 4.68 (ABq, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 26.0 Hz, 2H, OCH_2O), 4.04 (dd, J = 11.2, 2.4 Hz, 1H, H-7), 3.98 (dd, J = 11.2, 9.1 Hz, 1H, H'-7), 3.69–3.55 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.44 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 0.94 (app.t, J = 8.5 Hz, 2H, $CH_2Si(CH_3)_3$), 0.13 (s, 9H, $OSi(CH_3)_3$), 0.02 (s, 9H, $CH_2Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.0, 167.8, 166.1, 134.7, 134.5, 129.4, 129.3, 129.25, 129.20, 129.1, 129.0, 112.1, 95.2, 85.8, 85.4, 80.8, 80.5, 69.0, 68.3, 65.9, 65.5, 27.1, 25.5, 18.5, 2.4, −0.9; FAB HRMS calcd for $C_{34}H_{48}O_{11}Si_2Cs$ $(M + Cs)^+$: 821.1790; found m/z = 821.1821.

Data for **41b**: $[\alpha]_D^{22}$ = + 60.7 (c 0.70 in $CHCl_3$, 83% *ee*); R_f = 0.20 (silica, ether:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max}$ = 3302, 2951, 1801, 1774, 1745, 1455, 1384, 1273, 1216, 1178, 1063, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.28 (m, 8H, Ph), 7.26–7.23 (m, 2H, Ph), 5.62 (d, J = 1.5 Hz, 1H, H-3), 5.57 (d, J = 1.5 Hz, 1H, C4-OH), 5.18 (s, 2H, CH_2Ph), 5.11 (ABq, J_{AB} = 24.1 Hz, $\Delta\nu_{AB}$ = 27.0 Hz, 2H, CH_2Ph), 4.84 (dd, J = 6.1, 4.4 Hz, 1H, H-6), 4.69 (ABq, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 11.3 Hz, 2H, OCH_2O), 4.02 (dd, J = 11.5, 6.1 Hz, 1H, H-7), 3.86 (dd, J = 11.5, 4.4 Hz, 1H, H'-7), 3.65–3.55 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 1.40 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 0.95–0.91 (m, 2H, $CH_2Si(CH_3)_3$), 0.02 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.3, 168.2, 165.2, 135.2, 134.5, 129.3, 129.2, 129.11, 129.07, 128.9, 112.1, 95.6, 86.0, 80.75, 80.73, 78.4, 69.0, 68.2, 66.5, 64.2, 27.8, 25.8, 18.5, −0.9; FAB HRMS calcd for $C_{31}H_{40}O_{11}SiCs$ $(M + Cs)^+$: 749.1394; found m/z = 749.1429.

(4*R*,5*R*,8*S*,9*S*)-9-Hydroxy-4-hydroxymethyl-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro-[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (42) and (4*R*,5*R*,8*S*,9*S*)-4-hydroxymethyl-2,2-dimethyl-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]-nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (44) from silyl ether 41a. A solution of benzyl ester **41a** (178 mg, 0.258 mmol) in dichloromethane (25 mL) at 0 °C was treated with trifluoroacetic acid (0.994 mL, 12.9 mmol). The reaction mixture was warmed to room temperature, stirred for 1 h, diluted with toluene (25 mL), and concentrated in vacuo until approximately 2 mL of solution remained. The reaction mixture was azeotropically distilled with toluene (2 × 10 mL) to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:1) gave alcohol **44** (60.0 mg, 42%) and diol **42** (31 mg, 25%) as colorless oils.

Data for **44**: $[\alpha]_D^{22}$ = + 52.5 (c 0.99 in $CHCl_3$, 83% *ee*); R_f = 0.47 (silica, ether:petroleum ether 3:1); IR (thin film): $\tilde{\nu}_{max}$ = 3535, 2957, 1802, 1763, 1747, 1254, 1178, 1068, 849 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 10H, Ph), 5.35 (d, J = 11.9 Hz, 1H, CHH'Ph), 5.34 (s, 1H, H-3), 5.19 (ABq, J_{AB} = 12.0 Hz, $\Delta\nu_{AB}$ = 17.2 Hz, 2H, CH_2Ph), 5.07 (d, J = 11.9 Hz, 1H, CHH'Ph), 4.69 (t, J = 5.8 Hz, 1H, H-6), 4.01 (d, J = 5.8 Hz, 2H, CH_2OH), 1.44 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 0.13 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.0, 168.0, 166.5, 134.22, 134.20, 129.41, 129.40, 129.3, 129.23, 129.20, 129.1, 112.0, 85.5, 85.1, 82.9, 80.3, 69.1, 68.5, 61.0, 27.3, 25.8, 2.4; FAB HRMS calcd for $C_{28}H_{34}O_{10}SiCs$ $(M + Cs)^+$: 691.0976; found m/z = 691.0951.

Diol 42 from alcohol 41b. A solution of compound **41b** (104 mg, 0.169 mmol) in dichloromethane (15 mL) at 0 °C was treated with trifluoroacetic acid (0.651 mL, 8.45 mmol). The reaction mixture was warmed to room temperature, stirred for 2 h, diluted with toluene (10 mL), and concentrated in vacuo until approximately 2 mL of solution remained. The reaction mixture was azeotropically distilled with toluene (2 × 10 mL) to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:1 → 3:2) gave diol **42** (72.0 mg, 88%) as a colorless oil. $[\alpha]_D^{22}$ = + 81.8 (c 1.20 in $CHCl_3$, 83% *ee*); R_f = 0.33 (silica, ether:petroleum ether 3:1); IR (thin film); $\tilde{\nu}_{max}$ = 3473, 3229, 2991, 2943, 1799, 1771, 1745, 1456, 1385, 1274, 1217, 1177, 1069 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.20 (m, 10H, Ph), 6.46 (s, 1H, C4-OH), 5.62 (s, 1H, H-3), 5.19 (ABq, J_{AB} = 12.1 Hz, $\Delta\nu_{AB}$ = 25.7 Hz, 2H, CH_2Ph), 5.10 (ABq, J_{AB} = 12.1 Hz, $\Delta\nu_{AB}$ = 44.3 Hz, 2H, CH_2Ph), 4.77 (dd, J = 3.6, 2.4 Hz, 1H, H-6), 4.20 (dd, J = 13.3, 3.6 Hz, 1H, CHH'OH), 3.97 (br dd, J = 13.3, 2.4 Hz, 1H, CHH'OH), 3.07–2.97 (br s, 1H, CH_2OH), 1.42 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6, 169.1, 165.3, 135.2, 134.5, 129.3, 129.2, 129.04, 129.0, 128.9, 111.9, 84.6, 81.1, 80.5, 79.9, 69.1, 68.2, 59.0, 27.0, 25.5; FAB HRMS calcd for $C_{25}H_{26}O_{10}Cs$ $(M + Cs)^+$: 619.0580; found m/z = 619.0596.

(4*S*,5*R*,8*S*,9*S*)-4-Formyl-2,2-dimethyl-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (5). A solution of diol **42** (0.614 g, 1.26 mmol) in *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (2.2 mL) was heated at 80 °C for 1 h. The reaction mixture was concentrated in vacuo and diluted with dichloromethane (44 mL) and methanol (4 mL). The reaction mixture was treated with PPTS (47 mg, 0.19 mmol), stirred at room temperature for 5 min, and poured into phosphate buffer solution (pH 7, 120 mL). The aqueous phase was separated and extracted with dichloromethane (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give the primary alcohol **43** (0.705 g, 100%) as a colorless oil. A solution of the crude primary alcohol

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43 in dichloromethane (70 mL) was treated with Dess–Martin periodinane (1.13 g, 2.67 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with ether (150 mL), and poured into a 25% $Na_2S_2O_3/NaHCO_3$ solution (150 mL). The aqueous phase was separated and extracted with ether (2 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give the aldehyde **5** (0.655 g, 93% for 3 steps) as a colorless oil. The aldehyde was unstable to silica gel chromatography and usually used in the next step without any further purification. $[\alpha]_D^{22} = +29.6$ (*c* 1.51 in $CHCl_3$, 83% *ee*); $R_f = 0.20$ (silica, ethyl acetate:petroleum ether 1:6); IR (thin film): $\tilde{\nu}_{max} = 2936$, 2857, 1806, 1764, 1738, 1456, 1384, 1351, 1254, 1222, 1191, 1144, 1085 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.53$ (d, $J = 0.7$ Hz, 1H, CHO), 7.36–7.34 (m, 10H, Ph), 5.34 (d, $J = 12.1$ Hz, 1H, C*H*H'Ph), 5.23 (s, 2H, CH_2Ph), 5.21 (s, 1H, H-3), 5.15 (d, $J = 12.1$ Hz, 1H, CH*H*'Ph), 4.80 (d, $J = 0.7$ Hz, 1H, H-6), 1.51 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 0.14 (s, 9H, $Si(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 192.0$, 171.6, 168.5, 166.4, 133.9, 128.9, 128.8, 128.7, 128.6, 128.5, 114.1, 88.4, 85.3, 84.0, 79.5, 68.7, 68.5, 26.7, 25.8, 1.6; FAB HRMS calcd for $C_{28}H_{32}O_{10}SiNa$ $(M + Na)^+$: 579.1662; found $m/z = 579.1669$.

[4*R*,4-(1*R*),5*R*,8*S*,9*S*]-4-[Hydroxy(2-methyl-1,3-dithian-2-yl)methyl]-2,2-dimethyl-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (45a) and [4*R*,4-(1*S*),5*R*,8*S*,9*S*]-9-hydroxy-4-[hydroxy(2-methyl-1,3-dithian-2-yl)methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (45b). A solution of 2-methyl-1,3-dithiane (81 μL, 0.68 mmol) at −40 °C in THF (20 mL) was treated with *n*-butyllithium (1.60 M in hexane, 0.42 mL, 0.67 mmol). The reaction mixture was warmed to −25 °C, stirred for 1.5 h, and then cooled to −78 °C. A solution of the aldehyde **3** (249 mg, 0.45 mmol) in THF (2 mL) was cooled to −78 °C and cannulated rapidly into the solution of the lithiated dithiane. The reaction mixture was stirred at −78 °C for 5 min, quenched with a solution of acetic acid in THF (0.5 M in THF, 1.5 mL, 0.75 mmol), and warmed to room temperature. The reaction mixture was diluted with NH_4Cl (20 mL) and ether (20 mL). The aqueous phase was separated and extracted with ether (2 × 30 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:8 → 1:5) gave dithiane **45a** (94 mg, 30%) and dithiane **45b** (94 mg, 34%) as colorless oils.

Data for **45a**: $[\alpha]_D^{22} = +30.3$ (*c* 0.30 in $CHCl_3$, 83% *ee*); $R_f = 0.58$ (silica, ethyl acetate:petroleum ether 1:3); IR (thin film): $\tilde{\nu}_{max} = 3476$, 2940, 1798, 1748, 1454, 1383, 1264, 1216, 1169, 1142, 1095 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.35$–7.31 (m, 10H, Ph), 5.56 (d, $J = 1.5$ Hz, 1H, H-7), 5.48 (s, 1H, H-3), 5.26 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.24 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.20 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 5.14 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 4.86 (d, $J = 1.5$ Hz, 1H, H-6), 4.83 (s, 1H, C7-OH), 3.15 (ddd, $J = 13.5$, 11.5, 3.0 Hz, 1H, CH_2), 2.98 (ddd, $J = 13.5$, 11.5, 3.0 Hz, 1H, CH_2), 2.65–2.55 (m, 2H, CH_2), 2.10–2.05 (m, 1H, CH_2), 1.91–1.82 (m, 1H, CH_2), 1.53 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 0.26 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.7$, 168.8, 165.8, 134.5, 134.1, 128.5, 128.4, 128.3, 126.9, 110.9, 84.7, 81.4, 80.6, 79.4, 70.7, 68.4, 67.6, 53.2, 26.8, 26.3, 25.8, 25.1, 23.8, 23.3, 2.2; FAB HRMS calcd for $C_{33}H_{42}O_{10}S_2SiCs$ $(M + Cs)^+$: 823.1043; found $m/z = 823.1030$.

Data for **45b**: $[\alpha]_D^{22} = +11.3$ (*c* 0.15 in $CHCl_3$, 83% *ee*); $R_f = 0.30$ (silica, ethyl acetate:petroleum ether 1:3); IR (thin film): $\tilde{\nu}_{max} = 3225$, 3064, 1800, 1770, 1743, 1498, 1456, 1424, 1375, 1349, 1271, 1216, 1172, 1060, 1003 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.34$–7.26 (m, 10H, Ph), 7.06 (brs, 1H, C4-OH), 5.63 (brs, 1H, H-3), 5.22 (s, 2H, CH_2Ph), 5.15 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.10 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 4.85 (d, $J = 9.0$ Hz, 1H, H-7), 4.58 (d, $J = 9.0$ Hz, 1H, H-6), 4.32 (brs, 1H, C7-OH), 2.98–2.86 (m, 2H, CH_2), 2.63–2.54 (m, 2H, CH_2), 1.99–1.94 (m, 1H, CH_2), 1.85–1.78 (m, 1H, CH_2), 1.51 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.6$, 168.3, 165.1, 134.7, 134.3, 128.5, 128.4, 128.3, 128.2, 111.8, 85.9, 81.1, 80.6, 78.5, 69.8, 68.2, 67.4, 52.9, 26.8, 26.6, 25.9, 24.6, 23.6, 22.8; FAB HRMS calcd for $C_{30}H_{34}O_{10}S_2Cs$ $(M + Cs)^+$: 751.0648; found $m/z = 751.0660$.

[4*R*,4-(1*R*),5*R*,8*S*,9*S*]-9-Hydroxy-4-[hydroxy(2-methyl-1,3-dithian-2-yl)methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (45c). A solution of dithiane **45a** (56 mg, 0.081 mmol) in dichloromethane (4 mL) was treated with 2% HCl/MeOH (1 mL). The reaction mixture was stirred at room temperature for 5 min and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4) gave the dithiane **45c** (38 mg, 76%) as a colorless oil. $[\alpha]_D^{22} = +35.0$ (*c* 0.04 in $CHCl_3$, 83% *ee*); $R_f = 0.24$ (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max} = 3263$, 2982, 2936, 1798, 1771, 1743, 1498, 1456, 1423, 1384, 1351, 1275, 1216, 1176, 1147, 1066 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.35$–7.23 (m, 10H, Ph), 6.24 (brs, 1H, C4-OH), 5.62 (brs, 1H, H-3), 5.60 (brs, 1H, H-7), 5.22 (d, $J = 12.1$ Hz, 1H, C*H*H'Ph), 5.18 (d, $J = 12.2$ Hz, 1H, C*H*H'Ph), 5.12 (d, $J = 12.1$ Hz, 1H, CH*H*'Ph), 5.01 (d, $J = 12.2$ Hz, 1H, CH*H*'Ph), 4.49 (brs, 1H, H-6), 3.52 (brs, 1H, C7-OH), 2.96–2.91 (m, 2H, CH_2), 2.63–2.59 (m, 2H, CH_2), 2.10–2.05 (m, 1H, CH_2), 1.87–1.77 (m, 1H, CH_2), 1.52 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.0$, 168.0, 164.9, 134.5, 134.1, 128.6, 128.5, 128.4, 128.3, 111.7, 84.4, 80.8, 80.2, 76.9, 68.3, 67.6, 65.9, 52.3, 26.3, 26.1, 25.6, 25.1, 23.6, 23.4; FAB HRMS calcd for $C_{30}H_{34}O_{10}S_2Cs$ $(M + Cs)^+$: 751.0648; found $m/z = 751.0661$.

(3a*R*,4*R*,5*R*,6a*S*,7*S*,9a*R*)-Dihydro-4,5-dihydroxy-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl) ester (46a). A solution of the dithiane **45a** (38 mg, 0.061 mmol) in THF (2.4 mL) was treated with $CaCO_3$ (10.6 mg, 0.106 mmol) and aqueous $Hg(ClO_4)_2$ (0.20 M in H_2O, 0.485 mL, 0.097 mmol). The reaction mixture was stirred at room temperature for 2 h, treated with ether (10 mL), and stirred for 10 min. The precipitate was removed by filtration and the filtrate was dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:2) gave lactol **46a** (23.5 mg, 72%) as a white foam. $[\alpha]_D^{22} = +10.9$ (*c* 0.11 in $CHCl_3$, 83% *ee*); $R_f = 0.20$ (silica, ethyl acetate:petroleum ether 1:3); IR (thin film): $\tilde{\nu}_{max} = 3470$, 3065, 3033, 2991, 2941, 1805, 1748, 1658, 1498, 1455, 1384, 1356, 1304, 1271, 1246, 1181, 1141, 1126, 1088, 1056 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.38$–7.26 (m, 10H, Ph), 5.85 (s, 1H, H-3), 5.29 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.22 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.14 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 5.13 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 4.67 (d, $J = 6.0$ Hz, 1H, H-6), 4.06 (brdd, $J = 6.0$, 6.0 Hz, 1H, H-7), 3.52 (brs, 1H, C1-OH), 2.15 (brd, $J = 6.0$ Hz, 1H, C7-OH), 1.52 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.29 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.2$, 166.3, 166.1, 134.5, 134.4, 128.5, 128.3, 128.0, 126.9, 113.7, 98.4, 82.9, 81.3, 80.5, 80.1, 73.9, 68.2, 67.6, 26.0, 24.8, 23.7; FAB HRMS calcd for $C_{27}H_{28}O_{11}Cs$ $(M + Cs)^+$: 661.0686; found $m/z = 661.0655$.

(3a*R*,4*S*,5*R*,6a*S*,7*S*,9a*R*)-Dihydro-4,5-dihydroxy-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl)ester (46b). The procedure described for lactol **46a** gave lactol **46b** from **45b** in 76% yield as a white foam. $[\alpha]_D^{22} = +86.5$ (*c* 0.20 in $CHCl_3$, 83% *ee*); $R_f = 0.18$ (silica, ethyl acetate:petroleum ether 1:3); IR (thin film): $\tilde{\nu}_{max} = 3424$, 1804, 1761, 1728, 1595, 1453, 1382, 1285, 1215, 1078 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.38$–7.26 (m, 10H, Ph), 5.87 (s, 1H, H-3), 5.29 (d, $J = 12.1$ Hz, 1H, C*H*H'Ph), 5.24 (d, $J = 12.5$ Hz, 1H, C*H*H'Ph), 5.21 (d, $J = 12.1$ Hz, 1H, CH*H*'Ph), 5.20 (d, $J = 12.5$ Hz, 1H, CH*H*'Ph), 4.92 (d, $J = 7.4$ Hz, 1H, H-6), 4.44 (d, $J = 12.7$ Hz, 1H, 7-OH), 4.08 (dd, $J = 12.7$, 7.4 Hz, 1H, H-7), 3.80 (brs, 1H, C1-OH), 1.56 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.6$, 168.4, 166.7, 134.2, 133.9, 128.6, 128.4, 128.3, 114.0, 99.1, 83.1, 79.7, 77.6, 74.9, 69.2, 67.9, 66.5, 25.8, 25.1, 24.2; FAB HRMS calcd for $C_{27}H_{28}O_{11}Cs$ $(M + Cs)^+$: 661.0686; found $m/z = 661.0672$.

(7*S*)-2,7-Anhydro-8-deoxy-4-*C*-(methoxycarbonyl)-3-*C*-[(phenylmethoxy)carbonyl]-L-*glycero*-D-*altro*-7-octulo-7,4-furanosonic acid methyl ester (47a).

Method A: from lactol 46a. A solution of lactol **46a** (6.5 mg, 12 μmol) in 2% HCl/MeOH (1.4 mL) was heated in a sealed tube at 68 °C for 18 h. The reaction mixture was concentrated in vacuo to give a crude oil. Purification by preparative TLC (ethyl acetate) gave **47a** (2.1 mg, 40%) as a white solid.

Method B: from lactol 107. A solution of benzyl ester **107** (6.3 mg, 11.6 μmol) in 2% HCl/MeOH (1.5 mL) was heated at 80 °C for 19 h. The reaction mixture was concentrated in vacuo to give a crude oil. Purification by preparative TLC (ethyl acetate:petroleum ether 5:1) gave the bicycle **47a** (3.2 mg, 64%), identical to a sample prepared from **46a**. $[\alpha]_D^{22} = -10.0$ (*c* 0.08 in $CHCl_3$, 83% *ee*); $R_f = 0.25$ (silica, ethyl acetate); IR (thin film): $\tilde{\nu}_{max} = 3466$, 2919, 2851, 1748, 1444, 1266, 1169, 1045 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.48$–7.35 (m, 5H, Ph), 5.39 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.28 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 5.16 (d, $J = 2.3$ Hz, 1H, H-6), 5.15 (s, 1H, H-3), 4.16 (d, $J = 2.3$ Hz, 1H, H-7), 3.72 (s, 3H, CO_2CH_3), 3.59 (s, 3H, CO_2CH_3), 1.72 (s, 3H, C1-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.1$, 166.9, 166.7, 134.6, 129.0, 128.7, 128.5, 105.1, 91.5, 83.4, 78.2, 75.2, 74.4, 68.6, 52.9, 52.4, 22.0; FAB HRMS calcd for $C_{19}H_{22}O_{11}Na$ $(M + Na)^+$: 449.1060; found $m/z = 449.1072$.

(7*S*)-2,7-Anhydro-8-deoxy-4-*C*-(methoxycarbonyl)-3-*C*-[(phenylmethoxy)carbonyl]-D-*glycero*-D-*altro*-7-octulo-7,4-furanosonic acid methyl ester (47b). The same procedure as described for **47a** gave bicycle **47b**, from **46b**, in 54% yield as a white foam. $[\alpha]_D^{22} = -8.3$ (*c* 0.35 in $CHCl_3$, 83% *ee*); $R_f = 0.20$ (silica, ethyl acetate:petroleum ether 1:5); IR (thin film): $\tilde{\nu}_{max} = 3429$, 2924, 2854, 1749, 1445, 1382, 1270, 1234, 1171, 1107 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.47$–7.38 (m, 5H, Ph), 5.39 (d, $J = 11.9$ Hz, 1H, C*H*H'Ph), 5.32 (dd, $J = 6.3$, 6.3 Hz, 1H, H-6), 5.28 (d, $J = 11.9$ Hz, 1H, CH*H*'Ph), 4.69 (s, 1H, H-3), 4.32 (dd, $J = 6.3$, 6.3 Hz, 1H, H-7), 3.75 (s, 1H, C4-OH), 3.72 (s, 3H, C5-CO_2CH_3), 3.57 (s, 3H, C3-CO_2CH_3), 3.08 (d, $J = 6.3$ Hz, 1H, C6-OH), 3.03 (d, $J = 6.3$ Hz, 1H, C7-OH), 1.72 (s, 3H, C1-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.1$, 166.5, 166.4, 134.5, 129.1, 128.7, 128.6, 109.0, 92.4, 74.6, 73.9, 71.0, 68.7, 52.8, 52.5, 19.3; FAB HRMS calcd for $C_{19}H_{22}O_{11}Na$ $(M + Na)^+$: 449.1060; found $m/z = 449.1065$.

Data for **(3a*R*,4*S*,5*R*,6a*S*,7*S*,9a*R*)-Dihydro-4-hydroxy-5-methoxy-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl)ester (50)**: $R_f = 0.30$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3404$, 2953, 2926, 1807, 1770, 1728, 1272, 1084, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.35$–7.25 (m, 10H, Ph), 5.73 (s, 1H, H-3), 5.26 (d, $J = 12.5$ Hz, 1H, C*H*H'Ph), 5.25 (d, $J = 12.5$ Hz, 1H, C7-OH), 5.22 (d, $J = 12.5$ Hz, C*H*H'Ph), 5.12 (d, $J = 12.5$ Hz, 1H, CH*H*'Ph), 5.09 (d, $J = 12.5$ Hz, 1H, CH*H*'Ph), 4.92 (d, $J = 7.5$ Hz, 1H, H-6), 4.04 (dd, $J = 12.5$, 7.5 Hz, 1H, H-7), 3.11 (s, 3H, OCH_3), 1.53 (s, 3H, C1-CH_3), 1.37 (s, 3H, CH_3), 1.36 (s, 3H, CH_3);

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3, 169.9, 164.3, 134.5, 133.7, 128.8, 128.6, 128.4, 113.5, 103.3, 82.7, 79.6, 78.9, 74.2, 69.3, 67.6, 67.4, 48.5, 26.0, 24.9, 18.4; FAB HRMS calcd for $C_{28}H_{30}O_{12}Cs$ $(M + Cs)^+$: 675.0842; found m/z = 675.0854.

Data for **(7*S*)-2,7-Anhydro-8-deoxy-4-*C*-(methoxycarbonyl)-4,5-*O*-(1-methylethylidene)-3-*C*-[(phenylmethoxy)carbonyl]-D-*glycero*-D-*altro*-7-octulo-7,3-pyranosonic acid methyl ester (51)**: $[\alpha]_D^{22}$ = − 21.3 (*c* 0.08 in $CHCl_3$, 83% *ee*); R_f = 0.80 (silica, ethyl acetate:petroleum ether 5:1); IR (thin film): $\tilde{\nu}_{max}$ = 3466, 3063, 3031, 2991, 2954, 1771, 1740, 1438, 1385, 1376, 1322, 1299, 1269, 1232, 1176, 1164, 1125, 1082, 1063, 1024 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$ + one drop of C_6D_6): δ = 7.48–7.27 (m, 5H, Ph), 5.70 (d, *J* = 5.5 Hz, 1H, H-6), 5.39 (d, *J* = 12.0 Hz, 1H, C*H*H'Ph), 5.31 (d, *J* = 12.0 Hz, 1H, CH*H*'Ph), 4.73 (s, 1H, H-3 or C7-OH), 4.72 (s, 1H, H-3 or C7-OH), 4.62 (d, *J* = 5.5 Hz, 1H, H-7), 3.72 (s, 3H, CO_2CH_3), 3.58 (s, 3H, CO_2CH_3), 1.73 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.8, 166.3, 165.4, 134.5, 129.1, 128.7, 128.6, 128.5, 127.5, 126.9, 113.8, 107.8, 25.8, 25.3, 18.9; FAB HRMS calcd for $C_{22}H_{26}O_{11}Cs$ $(M + Cs)^+$: 559.0529; found m/z = 559.0540.

(*Z*)-4-Phenyl-2-butenoic acid methyl ester (57). A solution of bis(2,2,2-trifluoroethyl) (methoxycarbonylmethyl)phosphonate **55** (1.32 g, 4.2 mmol) and 18-crown-6 (5.5 g, 20.8 mmol) in THF (60 mL) at − 78 °C was treated dropwise with potassium bis(trimethylsilyl)amide (1.0 M in THF, 8.3 mL, 4.2 mmol). The reaction mixture was stirred at − 78 °C for 5 min and then treated slowly with phenylacetaldehyde **56** (500 mg, 4.2 mmol) over a period of 15 min. The reaction mixture was stirred at − 78 °C for 30 min and then quenched with NH_4Cl (50 mL), warmed to room temperature and extracted with ether (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude yellow oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19) gave the *cis* α,β-unsaturated ester **57** (634 mg, 87%) as a yellow oil. R_f = 0.17 (silica, ethyl acetate:petroleum ether 1:19); IR (thin film): $\tilde{\nu}_{max}$ = 3028, 2950, 1722, 1645, 1602, 1496, 1437, 1407, 1207, 1168 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.29 (m, 2H, Ph), 7.24–7.21 (m, 3H, Ph), 6.37 (dt, *J* = 11.4, 7.5 Hz, 1H, CH=C*H*CH_2), 5.87 (dt, *J* = 11.4, 1.8 Hz, 1H, C*H*=CHCH$_2$), 4.03 (dd, *J* = 7.6, 1.6 Hz, 2H, C*H*$_2$Ph), 3.76 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.8, 148.3, 139.3, 128.6, 126.3, 119.4, 51.2, 35.1; EI HRMS calcd for $C_{11}H_{12}O_2$: 176.0837; found m/z = 176.0829.

(*Z*)-1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-4-phenyl-2-butene (60). A solution of (2-bromoethyl)benzene (27.5 mL, 200 mmol) in benzene (44 mL) was treated with triphenylphosphine (58.1 g, 220 mmol). The reaction mixture was refluxed for 24 h and then cooled to room temperature. The upper phase of the two phase mixture containing excess triphenylphosphine and benzene was decanted and the reaction mixture was diluted with more benzene (50 mL). The reaction mixture was refluxed for 20 min and the decantation procedure was repeated with benzene (50 mL). The remaining lower phase was concentrated in vacuo to give, after drying in vacuo at 140 °C for 12 h, the yellow phosphonium salt **58** (87.6 g, 92%). A solution of the phosphonium salt **58** (124.3 g, 278 mmol) in dichloromethane (500 mL) and THF (600 mL) at 0 °C was treated with sodium bis(trimethylsilyl)amide (1.0 M in THF, 278 mL, 278 mmol). The red suspension was cooled to − 78 °C and a solution of (*tert*-butyldimethylsilyloxy)acetaldehyde **59** [45] (48.4 g, 278 mmol) in THF (300 mL) was added slowly over a period of 20 min. The reaction mixture was warmed to room temperature, stirred for 1 h, and diluted with water (200 mL). The reaction mixture was concentrated in vacuo and rediluted with water (300 mL) and ether (500 mL). The organic phase was separated and washed with water (400 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude orange solid. The solid was dried in vacuo at room temperature for 24 h and then diluted with ether:petroleum ether (1:1) (400 mL). The insoluble triphenylphosphine oxide was filtered and this extraction procedure was repeated with ether:petroleum ether (1:1) (2 × 400 mL). Purification by flash column chromatography (silica, ether:petroleum ether 1:99) gave silyl ether **60** (72.9 g, 99%) as a yellow oil. R_f = 0.48 (silica, ethyl acetate:petroleum ether 1:19); IR (thin film): $\tilde{\nu}_{max}$ = 3026, 2955, 2928, 2856, 1494, 1472, 1462, 1254, 1100, 1081 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.28 (m, 2H, Ph), 7.21–7.18 (m, 3H, Ph), 5.68–5.62 (m, 2H, CH=CH), 4.34 (d, *J* = 5.5 Hz, 2H, CH_2OSi), 3.41 (d, *J* = 6.7 Hz, 2H, C*H*$_2$Ph), 0.92 (s, 9H, $SiC(CH_3)_3$), 0.09 (s, 6H, $Si(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.4, 130.5, 129.1, 128.4, 128.3, 126.0, 59.3, 33.8, 26.0, 18.4, − 5.1; FAB HRMS calcd for $C_{16}H_{25}OSi$ $(M-H)^+$: 261.1675; found m/z = 261.1682.

(*Z*)-4-Phenyl-2-buten-1-ol (54).

Method A: from ester 57. A solution of *cis* α,β-unsaturated ester **57** (120.0 mg, 0.68 mmol) in dichloromethane (1 mL) at − 78 °C was treated with DIBALH (1.0 M in CH_2Cl_2, 3.0 mL, 3.0 mmol). The reaction mixture was stirred at − 78 °C for 15 min and then quenched with ethyl acetate (5 mL) and sodium potassium tartrate (5 mL). The reaction mixture was warmed to room temperature and stirred for 1 h. The aqueous phase was separated and extracted with ethyl acetate (5 mL). The combined organic extracts were washed with sodium potassium tartrate (3 × 5 mL), water (5 mL), and brine (10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude yellow oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4) gave allylic alcohol **54** (100 mg, 99%) as a yellow oil.

Method B: from silyl ether 60. A solution of silyl ether **60** (72.9 g, 0.28 mol) in THF (550 mL) at 0 °C was treated slowly with TBAF (1.0 M in THF, 292 mL, 0.29 mol) over a period of 30 min. The reaction mixture was stirred at 0 °C for 30 min and then quenched with NH_4Cl (300 mL). The reaction mixture was concentrated in vacuo and diluted with ether (300 mL). The aqueous phase was separated and extracted with ether (400 mL). The combined organic extracts were washed with water (500 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to yield a crude black oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:9) gave allylic alcohol **54** (37.8 g, 90%) as a yellow oil. R_f = 0.38 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3329, 3025, 2921, 1654, 1602, 1495, 1453, 1029 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.28 (m, 2H, Ph), 7.22–7.18 (m, 3H, Ph), 5.76–5.74 (m, 2H, CH=CH), 4.32 (d, *J* = 4.9 Hz, 2H, CH_2OH), 3.45 (d, *J* = 5.5 Hz, 2H, C*H*$_2$Ph), 1.55–1.4 (brs, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.1, 131.0, 129.3, 128.5, 128.3, 126.1, 58.5, 33.6; EI HRMS calcd for $C_{10}H_{10}$ $(M-H_2O)^+$: 130.0783; found m/z = 130.0786.

(2*R*,3*S*)-2-Hydroxymethyl-3-phenylmethyloxirane (53). A suspension of 4 Å activated molecular sieves (27.0 g, 67 wt%) in dichloromethane (800 mL) at − 20 °C was treated with a solution (−)-diisopropyl-D-tartrate (8.9 g, 38.1 mmol) in dichloromethane (10 mL) and titanium(IV) isopropoxide (7.7 g, 27.2 mmol). The reaction mixture was then treated slowly with a solution of *t*-butylhydroperoxide (5.5 M in decane, 98.9 mL, 0.55 mol) (which had been prestirred over activated 4 Å molecular sieves (40 g)) over a period of 10 min. The reaction mixture was stirred at − 20 °C for 30 min and then treated slowly with a solution of allylic alcohol **54** (40.3 g, 0.27 mol) in dichloromethane (200 mL) (which had also been prestirred with activated 4 Å molecular sieves (20 g)) over a period of 20 min. The reaction mixture was kept in a − 20 °C freezer for 20 h without stirring, and then warmed to 0 °C and diluted with water (150 mL). After stirring at room temperature for 45 min, it was treated with 30% aqueous NaOH saturated with NaCl (30 mL). After stirring the reaction mixture for 30 min, a phase separation occurred and the lower organic phase was separated. The aqueous phase was separated and extracted with dichloromethane (2 × 180 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4 → 3:7) gave the epoxy alcohol **53** (37.0 g, 83%, 81% *ee* according to ^{1}H and ^{19}F NMR analysis of the Mosher's ester) as a yellow oil. $[\alpha]_D^{22}$ = + 12.1 (*c* 0.45 in $CHCl_3$, 81% *ee*); R_f = 0.15 (silica, ether:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3412, 2983, 2926, 1603, 1495, 1451, 1035 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.32 (m, 2H, Ph), 7.27–7.25 (m, 3H, Ph), 3.97 (m, 1H, C*H*H'OH), 3.85 (m, 1H, CH*H*'OH), 3.30 (m, 1H, C*H*CH$_2$OH), 3.24 (m, 1H, C*H*CH$_2$Ph), 3.01 (dd, *J* = 14.8, 6.5 Hz, 1H, C*H*H'Ph), 2.85 (dd, *J* = 14.8, 6.3 Hz, 1H, CH*H*'Ph), 1.69 (m, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.3, 128.7, 128.6, 126.7, 60.7, 57.4, 56.9, 34.2; FAB HRMS calcd for $C_{10}H_{12}O_2Na$ $(M + Na)^+$: 187.0735; found m/z = 187.0740.

(2*R*,3*S*)-2-[[(4-Methoxyphenyl)methoxy]methyl]-3-phenylmethyloxirane (61). A suspension of washed NaH (60% in mineral oil, 5.6 g, 0.14 mol) in THF (120 mL) was treated with a solution of epoxyalcohol **55** (19.2 g, 0.12 mol) in THF (30 mL). The reaction mixture was stirred at room temperature for 2 min and then treated with PMBCl (19.8 mL, 0.15 mol) and tetrabutylammonium iodide (1.7 g, 4.7 mmol). The reaction mixture was refluxed for 30 min, cooled to room temperature, and quenched with NH_4Cl (150 mL) and water (40 mL). The reaction mixture was extracted with ether (2 × 300 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:4) gave epoxide **61** (33.2 g, 73%) a white solid. M.p. 36–44 °C; $[\alpha]_D^{22}$ = + 4.5 (*c* 0.82 in $CHCl_3$, 81% *ee*); R_f = 0.19 (silica, ethyl acetate:petroleum ether 1:9); IR (thin film): $\tilde{\nu}_{max}$ = 2910, 2858, 1612, 1512, 1457, 1301, 1248, 1176, 1091, 1034 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.25 (m, 7H, Ar), 6.89 (d, *J* = 8.6 Hz, 2H, $CH_3OC_6H_4$), 4.60 (d, *J* = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.50 (d, *J* = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 3.81 (s, 3H, OCH_3), 3.78 (dd, *J* = 11.0, 4.6 Hz, 1H, C*H*H'Ph), 3.67 (dd, *J* = 10.9, 6.1 Hz, 1H, CH*H*'Ph), 3.28–3.21 (m, 2H, CHOH), 2.89 (dd, *J* = 14.7, 6.5 Hz, 1H, OC*H*H'), 2.80 (dd, *J* = 14.8, 6.0 Hz, 1H, OCH*H*'); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 137.4, 129.8, 129.4, 128.7, 128.6, 126.6, 113.7, 73.0, 67.7, 56.3, 55.3, 55.2, 34.3; FAB HRMS calcd for $C_{18}H_{20}O_3Cs$ $(M + Cs)^+$: 417.0467; found m/z = 417.0478.

(2*S*,3*R*)-1-[(4-Methoxyphenyl)methoxy]-3-methyl-4-phenylbutan-2-ol (62). A solution of trimethylaluminum (2.0 M in hexane, 85.0 mL, 0.17 mol) in toluene (80 mL) at 0 °C was treated with *n*-butyllithium (2.5 M in hexane, 10.2 mL, 25.5 mmol). The reaction mixture was cooled to − 20 °C and treated with epoxide **61** (24.4 g, 85.8 mmol). The reaction mixture was stirred at − 20 °C for 20 h and acidified with aqueous HCl (1 M) at 0 °C to pH 7. The reaction mixture was extracted with ethyl acetate (2 × 200 mL). The combined organic extracts were washed with $NaHCO_3$ (200 mL) and water (200 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:4) gave secondary alcohol **62** (22.9 g, 89%) as a yellow oil. $[\alpha]_D^{22}$ = + 1.1 (*c* 0.45 in $CHCl_3$, 81% *ee*); R_f = 0.72 (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 3463, 3026, 2909, 2864, 1611, 1512, 1457, 1368, 1301, 1248, 1176, 1094, 1036 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.24 (m, 4H, Ar), 7.18–7.16 (m, 3H, Ar), 6.88 (d, *J* = 8.4 Hz, 2H, $CH_3OC_6H_4$), 4.48 (d, *J* = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.45 (d, *J* = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 3.81 (s, 3H, OCH_3), 3.74–3.72 (m, 1H, C*H*OH), 3.47 (dd, *J* = 15.4, 9.5 Hz, 1H, OC*H*H'C(OH)), 3.45 (dd, *J* = 20.0, 9.1 Hz, 1H, OCH*H*'C(OH)), 2.82 (dd, *J* = 13.3,

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6.5 Hz, 1H, C*H*H'Ph), 2.43 (dd, J = 13.3, 8.6 Hz, 1H, CH*H*'Ph), 2.26 (d, J = 3.2 Hz, 1H, OH), 1.89–1.84 (m, 1H, C*H*(CH_3)), 0.88 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 140.8, 129.9, 129.4, 129.1, 128.2, 125.8, 113.8, 73.0, 72.8, 72.2, 55.2, 39.6, 37.6, 14.0; FAB HRMS calcd for $C_{19}H_{24}O_3Cs$ (M + Cs)$^+$: 433.0780; found m/z = 433.0796.

(2*S*,3*R*)-2-[(4-Methoxyphenyl)methoxy]-3-methyl-4-phenylbutan-1-ol (64). A solution of alcohol **62** (30.0 g, 100 mmol) in dichloromethane (900 mL) was treated with activated 4 Å molecular sieves (6.0 g, 20 wt%). The reaction mixture was stirred at room temperature for 20 min and then treated with a solution of DDQ (28.4 g, 0.13 mol) in dichloromethane (which had been prestirred with activated 4 Å molecular sieves (1.0 g)). The resultant green slurry was stirred at room temperature for 5 h, diluted with ether (500 mL), and filtered. The filtrate was washed with $NaHCO_3$ (2 × 500 mL), filtered through Celite, dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:9) gave acetal **63** (15.8 g, 53%) as an oil. Pure acetal could not be obtained owing to decomposition and this material was usually used directly in the next step. A solution of the acetal **63** (15.8 g, 53.0 mmol) in dichloromethane (250 mL) at −78 °C was treated with DIBALH (1.0 M in CH_2Cl_2, 63.6 mL, 63.6 mmol). The reaction mixture was warmed to room temperature over a period 2 h. The reaction mixture was then cooled to −78 °C and quenched with methanol (15 mL), NH_4Cl (140 mL), and water (20 mL). The reaction mixture was warmed to room temperature and extracted with ethyl acetate (2 × 200 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:2) gave primary alcohol **64** (12.9 g, 81%) as a yellow oil. $[\alpha]_D^{22}$ = −1.4 (*c* 0.35 in $CHCl_3$, 81% *ee*); R_f = 0.58 (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 3430, 3025, 2932, 1611, 1512, 1458, 1301, 1247, 1176, 1037 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 4H, Ph), 7.21–7.18 (m, 1H, Ph), 7.13 (d, J = 7.2 Hz, 2H, $CH_3OC_6H_4$), 6.91 (d, J = 8.5 Hz, 2H, $CH_3OC_6H_4$), 4.63 (d, J = 11.1 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.53 (d, J = 11.1 Hz, 1H, $CH_3OC_6H_4CHH'$), 3.82 (s, 3H, OCH_3), 3.72–3.67 (m, 2H, CH_2OH), 3.47–3.44 (m, 1H, C*H*(OCH_2Ar)), 2.93 (dd, J = 13.3, 4.7 Hz, 1H, C*H*H'Ph), 2.30 (dd, J = 13.3, 9.9 Hz, 1H, CH*H*'Ph), 2.13–2.08 (m, 1H, C*H*(CH_3)), 1.87 (dd, J = 7.2, 5.2 Hz, 1H, OH), 0.89 (d, J = 6.9 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 141.0, 130.6, 129.3, 129.0, 128.2, 125.8, 113.8, 82.8, 72.1, 62.2, 55.2, 38.7, 36.5, 14.8; FAB HRMS calcd for $C_{19}H_{24}O_3Cs$ (M + Cs)$^+$: 433.0780; found m/z = 433.0780.

(2*S*,3*R*)-2-[(4-Methoxyphenyl)methoxy]-3-methyl-4-phenylbutanal (52). A solution of oxalyl chloride (8.4 μL, 96.5 μmol) in dichloromethane (0.8 mL) at −78 °C was treated with dimethylsulfoxide (9.1 μL, 0.13 mmol). After stirring at −78 °C for 20 min, the reaction mixture was treated with a solution of alcohol **64** (19.3 mg, 64.3 μmol) in dichloromethane (0.5 mL). After stirring at −78 °C for 1 h, the reaction mixture was treated with triethylamine (35.8 μL, 0.26 mmol), stirred at −78 °C for 1 h, and warmed to room temperature. The reaction mixture was diluted with water (5 mL) and extracted with ether (10 mL). The organic phase was washed with NH_4Cl (5 mL), water (2 × 5 mL) and brine (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:19) gave aldehyde **52** (19 mg, 98%) as a yellow oil. $[\alpha]_D^{22}$ = −28.3 (*c* 0.78 in $CHCl_3$, 81% *ee*); R_f = 0.30 (silica, ethyl acetate:petroleum ether 1:9); IR (thin film): $\tilde{\nu}_{max}$ = 2935, 1731, 1611, 1513, 1458, 1376, 1302, 1249, 1176, 1070, 1037 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.66 (d, J = 1.6 Hz, 1H, CHO), 7.31–7.25 (m, 4H, Ph), 7.21–7.20 (m, 1H, Ph), 7.09 (d, J = 7.0 Hz, 2H, $CH_3OC_6H_4$), 6.90 (d, J = 8.6 Hz, 2H, $CH_3OC_6H_4$), 4.63 (d, J = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.41 (d, J = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 3.82 (s, 3H, OCH_3), 3.61 (dd, J = 3.4, 1.7 Hz, 1H, C*H*(OCH_2Ar)), 2.76 (dd, J = 13.5, 7.8 Hz, 1H, C*H*H'Ph), 2.56 (dd, J = 13.5, 7.4 Hz, 1H, CH*H*'Ph), 2.30–2.25 (m, 1H, C*H*(CH_3)), 0.95 (d, J = 6.9 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.2, 159.4, 139.9, 129.7, 129.5, 129.1, 128.3, 126.1, 113.8, 84.8, 72.4, 55.2, 39.4, 37.3, 14.3; FAB HRMS calcd for $C_{19}H_{22}O_3Cs$ (M + Cs)$^+$: 431.0623; found m/z = 431.0626.

[2(4*S*,5*R*)]-2-[3-Hydroxy-4-[(4-methoxyphenyl)methoxy]-5-methyl-6-phenylhexyl]-1,3-dioxolane (65). A solution of freshly prepared 2-(1,3-dioxolan-2-yl)ethylmagnesium bromide (1.0 M in THF, 20 mL, 20 mmol) in THF (20 mL) at room temperature was treated dropwise with a solution of aldehyde **52** (2.0 g, 6.7 mmol) in THF (10 mL). The reaction mixture was stirred at 35 °C for 6 h and then quenched with NH_4Cl (20 mL) and water (3.0 mL). The reaction mixture was concentrated in vacuo and extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were washed with water (40 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:1) gave the alcohol **65** (1.96 g, 73%) as an inseparable mixture of diastereoisomeric oils. $[\alpha]_D^{22}$ = −4.8 (*c* 0.45 in $CHCl_3$, 81% *ee*); R_f = 0.48 (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 3479, 2957, 2881, 1611, 1513, 1456, 1403, 1301, 1248, 1035 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) (multiple peaks due to mixture of diastereoisomers): δ = 7.31–7.27 (m, 4H, Ar), 7.21–7.13 (m, 3H, Ar), 6.90 (d, J = 8.4 Hz, 2H, $CH_3OC_6H_4$), 4.89 (t, J = 4.6 Hz, 1H, CH($O)_2$), 4.67 (d, J = 10.9 Hz, 0.7H, $CH_3OC_6H_4CH_2$), 4.57 (d, J = 11.1 Hz, 0.94H, $CH_3OC_6H_4CH_2$), 4.52 (d, J = 11.1 Hz, 0.36H, $CH_3OC_6H_4CH_2$), 3.99–3.96 (m, 2H, $OCH_2C'H_2O$), 3.88–3.85 (m, 2H, $OCH_2C'H_2O$), 3.81 (s, 3H, OCH_3), 3.73–3.69 (m, 1H, C*H*(OCH_2Ar)), 3.24–3.20 (m, 1H, C*H*(OH)), 2.89 (dd, J = 13.6, 5.5 Hz, 0.67H, CH_2Ph), 2.75 (dd, J = 13.3, 6.4 Hz, 0.33H, CH_2Ph), 2.56–2.49 (m, 1H, CH_2Ph), 2.37 (s, 1H, OH), 2.23–2.17 (m, 0.3H, C*H*(CH_3)), 2.13–2.05 (m, 0.7H, C*H*(CH_3)), 1.92–1.83 (m, 1H, C*H*H'CH(OH)), 1.80–1.70 (m, 1H, CH*H*'CH(OH)), 1.70–1.52 (m, 2H, CH_2CH_2CH(OH)), 0.98 (d, J = 6.8 Hz, 0.81H, CH_3), 0.90 (d, J = 6.8 Hz, 2.19H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) (multiple peaks due to mixture of diastereoisomers): δ = 159.2, 141.0, 130.6, 129.3, 129.2, 129.1, 128.2, 128.2, 125.8, 125.8, 113.8, 113.8, 85.1, 84.0, 74.4, 73.2, 71.5, 71.4, 64.9, 64.9, 64.8, 55.2, 40.9, 40.2, 37.2, 36.2, 30.4, 30.0, 28.8, 26.9, 14.5, 14.3; FAB HRMS calcd for $C_{24}H_{32}O_5Cs$ (M + Cs)$^+$: 533.1304; found m/z = 533.1293.

[2(4*S*,5*R*)]-2-[4-[(4-Methoxyphenyl)methoxy]-5-methyl-3-oxo-6-phenylhexyl]-1,3-dioxolane (66). A solution of the alcohol **65** (1.8 g, 4.5 mmol) in dichloromethane (5 mL) was treated with Dess–Martin periodinane (2.2 g, 5.2 mmol). The reaction mixture was stirred at room temperature for 20 min, diluted with ether (25 mL), poured into a solution of $NaHCO_3$ (25 mL) containing $Na_2S_2O_3$ (6.5 g), and stirred vigorously for 5 min. The organic phase was separated and washed with $NaHCO_3$ (25 mL) and water (25 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7) gave ketone **66** (1.65 g, 92%) as a yellow oil. $[\alpha]_D^{22}$ = −29.5 (*c* 0.32 in $CHCl_3$, 81% *ee*); R_f = 0.31 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 2882, 1716, 1612, 1513, 1457, 1249, 1138, 1035 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.25 (m, 4H, Ph), 7.20–7.18 (m, 1H, Ph), 7.10 (d, J = 7.6 Hz, 2H, $CH_3OC_6H_4$), 6.90 (d, J = 8.4 Hz, 2H, $CH_3OC_6H_4$), 4.89 (t, J = 4.2 Hz, 1H, CH($O)_2$), 4.56 (d, J = 11.2 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.23 (d, J = 11.2 Hz, 1H, $CH_3OC_6H_4CHH'$), 3.92–3.89 (m, 2H, $OCH_2C'H_2O$), 3.83–3.81 (m, 2H, $OCH_2C'H_2O$), 3.82 (s, 3H, OCH_3), 3.68 (d, J = 3.8 Hz, 1H, C*H*(OCH_2Ar)), 2.69 (dd, J = 13.5, 7.5 Hz, 1H, C*H*H'Ph), 2.57–2.51 (m, 3H, CH_2CO, CH*H*'Ph), 2.24–2.22 (m, 1H, C*H*(CH_3)), 1.98–1.94 (m, 2H, CH_2CH_2C=O), 0.88 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 212.0, 159.2, 140.2, 129.9, 129.5, 129.0, 128.3, 126.0, 113.7, 103.1, 86.1, 72.3, 64.8, 64.8, 55.2, 39.6, 38.1, 32.7, 27.0, 14.3; FAB HRMS calcd for $C_{24}H_{30}O_5Cs$ (M + Cs)$^+$: 531.1148; found m/z = 531.1162.

[2(4*S*,5*R*)]-2-[4-[(4-Methoxyphenyl)methoxy]-5-methyl-3-methylene-6-phenylhexyl]-1,3-dioxolane (67). A solution of ketone **66** (1.5 g, 3.8 mmol) in THF (8.5 mL) at 0 °C was treated with Tebbe reagent (0.5 M in toluene, 10.6 mL, 5.3 mmol). The reaction mixture was warmed to room temperature, stirred for 1 h, quenched with NaOH (0.1 M, 1 mL), and stirred vigorously. The deep red solution was dried ($MgSO_4$), filtered through Celite, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:3) gave olefin **67** (1.27 g, 85%) as a white solid. The solid was recrystallized from cyclohexane (0 °C, 24 h) to give enantiomerically enriched product **67** (0.96 g, 76%, 98% *ee* according to ^{1}H and ^{19}F NMR analysis of the Mosher's ester of **67**). M.p. 46–48 °C (cyclohexane); $[\alpha]_D^{22}$ = −36.4 (*c* 0.35 in $CHCl_3$, 98% *ee*); R_f = 0.53 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 2932, 2875, 1611, 1513, 1454, 1247, 1137, 1065, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.23 (m, 4H, Ph), 7.18-7.14 (m, 1H, Ph), 7.09 (d, J = 7.3 Hz, 2H, $CH_3OC_6H_4$), 6.88 (d, J = 8.4 Hz, 2H, $CH_3OC_6H_4$), 5.08 (s, 2H, C=CH_2), 4.91 (t, J = 4.7 Hz, 1H, CH($O)_2$), 4.47 (d, J = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.14 (d, J = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 3.99–3.96 (m, 2H, $OCH_2C'H_2O$), 3.88–3.85 (m, 2H, $OCH_2C'H_2O$), 3.81 (s, 3H, OCH_3), 3.49 (d, J = 6.3 Hz, 1H, C*H*(OCH_2Ar)), 2.69 (dd, J = 13.5, 5.2 Hz, 1H, C*H*H'Ph), 2.25 (dd, J = 13.5, 9.5 Hz, 1H, CH*H*'Ph), 2.21–2.16 (m, 1H, C*H*H'C(=CH_2)), 2.08–2.02 (m, 1H, CH*H*'C(=CH_2)), 1.97–1.94 (m, 1H, C*H*(CH_3)), 1.89–1.85 (m, 2H, CH_2CH_2C(=CH_2)), 0.86 (d, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.9, 146.4, 141.1, 130.9, 129.3, 129.0, 128.1, 125.6, 113.6, 112.4, 104.1, 85.8, 69.9, 64.8, 55.2, 39.9, 37.6, 31.9, 25.1, 14.8; FAB HRMS calcd for $C_{25}H_{32}O_4Cs$ (M + Cs)$^+$: 529.1355; found m/z = 529.1355.

[2(4*S*,5*R*)]-2-[4-[(4-Methoxyphenyl)methoxy]-5-methyl-3-methylene-6-phenylhexyl]-1,3-dithiane (6). A solution of DIBALH (1.0 M in CH_2Cl_2, 28.3 mL, 28.3 mmol) in benzene (21 mL) at 0 °C was treated with 1,3-propanedithiol (1.4 mL, 14.1 mmol). The reaction mixture was stirred at 0 °C for 10 min and then treated with a solution of acetal **67** (3.5 g, 8.8 mmol) in benzene (5 mL). The reaction mixture was stirred at room temperature for 20 h, cooled to 0 °C, quenched with methanol (4.3 mL, 0.12 mol), water (2.15 mL, 0.11 mol), and ether (55 mL), and stirred for 10 min. The reaction mixture was dried ($MgSO_4$), filtered through Celite, and washed with NaOH (3 M, 10 mL) and brine (10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:9) gave dithiane **6** (2.4 g, 64%) as a yellow oil. $[\alpha]_D^{22}$ = −33.6 (*c* 0.17 in $CHCl_3$, 98% *ee*); R_f = 0.64 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 2904, 1611, 1512, 1454, 1247, 1176, 1065, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.23 (m, 4H, Ph), 7.18–7.15 (m, 1H, Ph), 7.10 (d, J = 7.3 Hz, 2H, $CH_3OC_6H_4$), 6.88 (d, J = 8.4 Hz, 2H, $CH_3OC_6H_4$), 5.09 (d, J = 6.4 Hz, 2H, C=CH_2), 4.47 (d, J = 11.4 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.14, (d, J = 11.3 Hz, 1H, $CH_3OC_6H_4CHH'$), 4.06 (t, J = 6.8 Hz, 1H, SCHS), 3.81 (s, 3H, OCH_3), 3.48 (d, J = 6.5 Hz, 1H, C*H*(OCH_2Ar)), 2.87–2.84 (m, 4H, $SCH_2CH_2CH_2S$), 2.68 (dd, J = 13.4, 5.3 Hz, 1H, C*H*H'Ph), 2.30–2.15 (m, 4H, CH*H*'Ph, CH_2C(=CH_2), $SCH_2CHH'CH_2S$), 1.98–1.86 (m, 4H, C*H*(CH_3), CH_2CH_2C(=CH_2), $SCH_2CHH'CH_2S$), 0.85 (d, J = 6.5 Hz, 3H, CH_3);

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.9, 146.0, 141.1, 130.9, 129.3, 129.1, 128.1, 125.7, 113.6, 113.0, 85.8, 70.0, 55.2, 47.1, 40.0, 37.6, 33.5, 30.3, 27.8, 26.0, 14.8; FAB HRMS calcd for $C_{26}H_{34}O_2S_2Cs$ $(M + Cs)^+$: 575.1055; found m/z = 575.1061.

(*E*,4*S*,6*S*)-4,6-Dimethyl-2-octenoic acid methyl ester (71). A solution of diisopropylamine (45 μL, 0.32 mmol) in THF (0.6 mL) at 0 °C was treated with *n*-butyllithium (1.6 M in hexane, 0.19 mL, 0.31 mmol). The reaction mixture was stirred at 0 °C for 15 min and then treated dropwise with hydrazone **68** (50 mg, 0.29 mmol). The reaction mixture was stirred at 0 °C for 4 h, cooled to −20 °C, and treated again with *n*-butyllithium (1.6 M in hexane, 0.19 mL, 0.31 mmol). The reaction mixture was stirred at −20 °C for 2 h, cooled to −100 °C, and treated with (*S*)-1-iodo-2-methylbutane (46 μL, 0.35 mmol). The reaction mixture was slowly warmed to −78 °C, stirred for 45 min, warmed to −50 °C, and stirred for 30 min. The reaction mixture was quenched with NH_4Cl (4 mL) and diluted with ether (5 mL). The aqueous phase was separated and extracted with ether (5 mL). The combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give hydrazone **69** as a crude oil. The crude hydrazone **69** was immediately dissolved in dichloromethane (3 mL) and treated with ozone at −78 °C until the hydrazone was consumed, ~30 s (time varies with scale). Oxygen was passed through the reaction mixture for ~30 s (time varies with scale), warmed to room temperature, dried ($MgSO_4$), filtered, and concentrated in vacuo to give aldehyde **70** as a crude oil. The crude aldehyde **70** was immediately dissolved in dichloromethane (3 mL) and treated with methyl (triphenylphosphoranylidene)acetate (118.0 mg, 0.35 mmol). The reaction mixture was stirred at room temperature for 3 h, filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:pentane 1:49) gave α,β-unsaturated ester **71** (16 mg, 30% for 3 steps, 92% *de* according to ^{1}H NMR analysis) as a yellow oil. $[\alpha]_D^{22}$ = + 34.9 (*c* 0.32 in $CHCl_3$, 92% *de*); R_f = 0.55 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 2960, 2924, 1728, 1656, 1459, 1272, 1182 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.82 (dd, J = 15.7, 8.5 Hz, 1H, C*H*=CH(CO_2CH_3)), 5.78 (d, J = 15.7 Hz, 1H, CH=C*H*(CO_2CH_3)), 3.73 (s, 3H, OCH_3), 2.42–2.38 (m, 1H, C*H*(CH_3)CH=CH), 1.39–1.26 (m, 3H, $CH_3CHH'CH(CH_3)CHH'$), 1.13–1.09 (m, 2H, $CH_3CHH'CH(CH_3)CHH'$), 1.03 (d, J = 6.6 Hz, 3H, CH(CH_3)CH=CH), 0.86–0.82 (m, 6H, $CH_3CH_2CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.5, 155.1, 119.2, 51.4, 43.4, 34.3, 31.9, 29.8, 20.4, 18.8, 11.2; FAB HRMS calcd for $C_{11}H_{20}O_2Na$ $(M + Na)^+$: 207.1361; found m/z = 207.1367.

(*E*,4*S*,6*S*)-4,6-Dimethyl-2-octenoic acid (4). A solution of ester **71** (6 mg, 32.6 μmol) in methanol (0.2 mL) and water (0.1 mL) was treated with $LiOH \cdot H_2O$ (4.1 mg, 97.8 μmol). The reaction mixture was stirred at room temperature for 3 h, diluted with water (1 mL), and acidified with aqueous HCl (1 M, 1 mL) to pH 3. The reaction mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:4) gave α,β-unsaturated acid **4** (5 mg, 90%) as a yellow oil. $[\alpha]_D^{22}$ = + 46.4 (*c* 0.06 in $CHCl_3$, 92% *de*); R_f = 0.62 (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max}$ = 2962, 2919, 2681, 1696, 1694, 1459, 1418, 1288 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.93 (dd, J = 15.6, 8.5 Hz, 1H, C*H*=CH(CO_2H)), 5.79 (d, J = 15.6 Hz, 1H, CH=C*H*(CO_2H), 2.46–2.42 (m, 1H, C*H*(CH_3)CH=CH), 1.43–1.27 (m, 3H, $CH_3CHH'CH(CH_3)CHH'$), 1.16–1.10 (m, 2H, $CH_3CHH'CH(CH_3)CHH'$), 1.05 (d, J = 6.7 Hz, 3H, CH(CH_3)CH=CH), 0.87–0.84 (m, 6H, $CH_3CH_2CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.2, 157.6, 118.6, 43.1, 34.3, 31.8, 29.7, 20.1, 18.7, 11.1; FAB HRMS calcd for $C_{10}H_{19}O_2$ $(M + H)^+$: 171.1385; found m/z = 171.1391.

[2(4*S*,5*R*)]-2-[4-Hydroxy-5-methyl-3-methylene-6-phenylhexyl]-1,3-dithiane (76). A solution of ether **6** (0.55 g, 1.2 mmol) in dichloromethane (5 mL) and water (0.25 mL) was treated with DDQ (0.34 g, 1.5 mmol). The reaction mixture was stirred at room temperature for 30 min and then diluted with water (5 mL) and ether (5 mL). The aqueous phase was separated and extracted with ether (10 mL). The combined organic extracts were washed with $NaHCO_3$ (4 × 10 mL) until the yellow color disappeared, and then with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:9) gave allylic alcohol **76** (280 mg, 70%) as a yellow oil. $[\alpha]_D^{22}$ = − 9.0 (*c* 0.54 in $CHCl_3$, 98% *ee*); R_f = 0.13 (silica, ethyl acetate:petroleum ether 1:9); IR (thin film): $\tilde{\nu}_{max}$ = 3462, 2928, 1450, 1423 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.27 (m, 2H, Ph), 7.23–7.18 (m, 3H, Ph), 5.12 (s, 1H, C=C*H*H'), 4.97 (s, 1H, C=CH*H'*), 4.03 (t, J = 6.8 Hz, 1H, SCHS), 3.94 (d, J = 4.6 Hz, 1H, C*H*OH), 2.89–2.80 (m, 4H, $SCH_2CH_2CH_2S$), 2.76 (dd, J = 13.4, 6.3 Hz, 1H, C*H*H'Ph), 2.46 (dd, J = 13.4, 8.7 Hz, 1H, CH*H'*Ph), 2.29–2.23 (m, 1H, C*H*H'C(=CH_2)), 2.16–2.09 (m, 2H, CH*H'*C(=CH_2), $SCH_2CHH'CH_2S$), 1.99–1.94 (m, 1H, C*H*(CH_3)), 1.93–1.85 (m, 3H, $CH_2CH_2C(=CH_2)$, $SCH_2CHH'CH_2S$), 0.83 (d, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.5, 140.9, 129.1, 128.2, 125.8, 110.4, 77.0, 46.9, 40.2, 37.8, 33.6, 30.3, 30.2, 28.6, 25.9, 13.1; FAB HRMS calcd for $C_{18}H_{26}OS_2Na$ $(M + Na)^+$: 345.1323; found m/z = 345.1319.

[2(4*S*,5*R*)]-2-[5-Methyl-4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-3-methylene-6-phenylhexyl]-1,3-dithiane (77). A solution of allylic alcohol **76** (94 mg, 0.29 mmol) in DMF (0.2 mL) was treated with imidazole (40 mg, 0.59 mol), TPSCl (91 μL, 0.35 mmol), and DMAP (1.7 mg, 13.9 μmol). The reaction mixture was heated at 60 °C for 12 h, cooled to room temperature, and diluted with ether (5 mL). The organic phase was washed with water (4 × 5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 0:1 → 1:20) gave silyl ether **77** (160 mg, 98%) as a yellow oil. $[\alpha]_D^{22}$ = + 21.6 (*c* 1.5 in $CHCl_3$, 98% *ee*); R_f = 0.26 (silica, ethyl acetate:petroleum ether 1:19); IR (thin film): $\tilde{\nu}_{max}$ = 3070, 2931, 2856, 1428, 1112, 1061 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73–7.71 (m, 2H, Ph), 7.67–7.65 (m, 2H, Ph), 7.45–7.34 (m, 6H, Ph), 7.23–7.20 (m, 2H, Ph), 7.15–7.12 (m, 1H, Ph), 7.02–7.00 (m, 2H, Ph), 4.99 (s, 1H, C=C*H*H'), 4.82 (d, J = 1.3 Hz, 1H, C=CH*H'*), 4.04 (d, J = 5.4 Hz, 1H, CH(OSi)), 4.00–3.96 (m, 1H, SCHS), 2.83 (brs, 4H, $SCH_2CH_2CH_2S$), 2.63 (dd, J = 13.3, 3.5 Hz, 1H, C*H*H'Ph), 2.35–2.28 (m, 1H, C*H*H'C(=CH_2)), 2.13–2.08 (m, 2H, CH*H'*C(=CH_2), $SCH_2CHH'CH_2S$), 2.04 (dd, J = 13.2, 11.0 Hz, 1H, CH*H'*Ph), 1.89–1.84 (m, 2H, C*H*(CH_3), $SCH_2CHH'CH_2S$), 1.81–1.73 (m, 2H, $CH_2CH_2C(=CH_2)$), 1.10 (s, 9H, $SiC(CH_3)_3$), 0.73 (d, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.2, 141.5, 136.3, 136.2, 134.2, 133.9, 129.5, 129.0, 128.1, 127.4, 127.3, 125.5, 111.9, 81.3, 47.3, 39.8, 39.6, 33.1, 30.3, 28.4, 27.2, 26.0, 19.6, 14.4; FAB HRMS calcd for $C_{34}H_{44}OS_2SiNa$ $(M + Na)^+$: 583.2501; found m/z = 583.2488.

[2(4*S*,5*R*)]-2-[5-Methyl-4-[[bis(1,1-dimethylethyl)methylsilyl]oxy]-3-methylene-6-phenylhexyl]-1,3-dithiane (78). A solution of allylic alcohol **76** (150 mg, 0.47 mmol) in 2,6-lutidine (0.65 mL) was treated with DMAP (114.2 mg, 0.93 mmol) and DTBMSOTf (1.43 g, 4.67 mmol). The reaction mixture was heated at 70 °C for 8 h, cooled to room temperature, and diluted with water (20 mL) and ether (20 mL). The aqueous phase was separated and extracted with ether (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:99) gave silyl ether **78** (194 mg, 87%) as a yellow oil. $[\alpha]_D^{22}$ = + 2.3 (*c* 0.84 in $CHCl_3$, 98% *ee*); R_f = 0.36 (silica, ethyl acetate:petroleum ether 1:19); IR (thin film): $\tilde{\nu}_{max}$ = 2933, 2858, 1467, 1385, 1253, 1076 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.25 (m, 2H, Ph), 7.18–7.13 (m, 3H, Ph), 5.10 (s, 1H, C=C*H*H'), 4.96 (s, 1H, C=CH*H'*), 4.12 (d, J = 5.4 Hz, 1H, CH(OSi)), 4.09 (t, J = 6.7 Hz, 1H, SCHS), 2.90–2.80 (m, 4H, $SCH_2CH_2CH_2S$), 2.42–2.34 (m, 1H, C*H*H'Ph), 2.24–2.10 (m, 4H, CH*H'*Ph, $CH_2C(=CH_2)$, $SCH_2CHH'CH_2S$), 2.04–1.85 (m, 4H, C*H*(CH_3), $CH_2CH_2C(=CH_2)$, $SCH_2CHH'CH_2S$), 1.04 (s, 9H, $SiC(CH_3)_3$), 0.97 (s, 9H, $SiC(CH_3)_3$), 0.78 (d, J = 6.7 Hz, 3H, CH_3), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.8, 141.5, 129.1, 128.1, 125.6, 111.6, 81.7, 47.3, 40.2, 39.8, 33.3, 30.4, 28.2, 27.9, 26.0, 21.0, 14.3, −7.7; FAB HRMS calcd for $C_{27}H_{47}OS_2Si$ $(M + H)^+$: 479.2838; found m/z = 479.2829.

[4*R*,4[1*R*,2(4*S*,5*R*)],5*R*,8*S*,9*S*]-4-[Hydroxy[2-[5-methyl-3-methylene-4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-6-phenylhexyl]-1,3-dithian-2-yl]methyl]-2,2-dimethyl-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (79a) and [4*R*,4[1*S*,2(4*S*,5*R*)],5*R*,8*S*,9*S*]-9-hydroxy-4-[hydroxy-[2-[5-methyl-3-methylene-4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-6-phenylhexyl]-1,3-dithian-2-yl]methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (79b). A solution of dithiane **77** (324 mg, 0.58 mmol) in THF (12 mL) at −40 °C in a Schlenk tube was treated with *n*-butyllithium (1.60 M in hexane, 0.36 mL, 0.58 mmol). The reaction mixture was warmed to −25 °C, stirred for 1.5 h, and then cooled to −78 °C. A solution of the aldehyde **5** (195 mg, 0.35 mmol) in THF (2 mL) was cooled to −78 °C and cannulated rapidly into the solution of the lithiated dithiane. The reaction mixture was stirred at −78 °C for 5 min and quenched with a solution of acetic acid in THF (0.5 M in THF, 1.2 mL, 0.60 mmol) and warmed to room temperature. The reaction mixture was diluted with NH_4Cl (40 mL) and ether (20 mL). The aqueous phase was separated and extracted with ether (2 × 30 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:8 → 1:4) gave dithiane **79a** (91 mg, 23%) and dithiane **79b** (106 mg, 29%) as colorless oils.

Data for **79a**: $[\alpha]_D^{22}$ = + 53.5 (*c* 0.85 in $CHCl_3$); R_f = 0.41 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3070, 2958, 2933, 2898, 2857, 1801, 1750, 1456, 1265, 1068 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76–7.66 (m, 4H, Ph), 7.43–7.00 (m, 21H, Ph), 5.58 (d, J = 1.5 Hz, 1H, H-7), 5.51 (s, 1H, H-3), 5.26 (d, J = 12.5 Hz, 1H, OC*H*H'Ph), 5.23 (s, 2H, OCH_2Ph), 5.16 (d, J = 12.5 Hz, 1H, OCH*H'*Ph), 5.01 (d, J = 1.5 Hz, 1H, H-6), 4.99 (brs, 1H, C=C*H*H'), 4.89 (brs, 1H, C7-OH), 4.87 (brs, 1H, C=CH*H'*), 4.03 (d J = 5.5 Hz, 1H, CH(OSi)), 3.17-3.12 (m, 1H, CH_2), 3.02–2.94 (m, 1H, CH_2), 2.64–2.51 (m, 4H, CH_2), 2.38–2.30 (m, 1H, CH_2), 2.22–2.16 (m, 1H, CH_2), 2.06–1.82 (m, 5H, CH_2 and OH), 1.40 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.11 (s, 9H, $SiC(CH_3)_3$), 0.70 (d, J = 6.5 Hz, 3H, CH(CH_3)), 0.25 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.7, 168.9, 165.9, 149.4, 141.5, 136.2, 136.0, 134.5, 134.4, 134.2, 133.8, 129.4, 129.0, 128.5, 128.4, 128.3, 127.9, 127.3, 125.3, 111.2, 110.7, 84.8, 81.6, 81.4, 80.3, 79.5, 71.1, 68.4, 67.6, 58.7, 39.6, 32.7, 27.2, 26.6, 26.2, 25.5, 25.0, 23.7, 19.6, 14.1, 2.33; FAB HRMS calcd for $C_{62}H_{76}O_{11}S_2Si_2Cs$ $(M + Cs)^+$: 1249.3422; found m/z = 1249.3481.

Data for **79b**: $[\alpha]_D^{22}$ = + 40.8 (*c* 0.62 in $CHCl_3$); R_f = 0.22 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3226, 3069, 2959, 2932, 2857, 1803, 1770, 1745, 1455, 1376, 1270, 1217, 1172 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73–7.66 (m, 4H, Ph), 7.44–7.06 (m, 21H, Ph), 5.62 (s, 1H, H-3), 5.23 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.21 (d, J = 12.0 Hz, 1H, OCH*H'*Ph), 5.12 (d,

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J = 12.5 Hz, 1H, OC*H*H'Ph), 5.06 (d, J = 12.5 Hz, 1H, OCH*H*'Ph), 4.96 (d, J = 9.5 Hz, 1H, H-7), 4.94 (brs, 1H, C=C*H*H'), 4.80 (brs, 1H, C=CH*H*'), 4.72 (d, J = 9.5 Hz, 1H, H-6), 4.43 (brs, 1H, OH), 4.07 (d, J = 5.5 Hz, 1H, CH(OSi)), 2.97–2.91 (m, 2H, CH_2), 2.72–2.61 (m, 3H, CH_2), 2.46–2.39 (m, 1H, CH_2), 2.28–2.22 (m, 1H, CH_2), 2.05–1.86 (m, 6H, CH_2 and OH), 1.37 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.12 (s, 9H, $SiC(CH_3)_3$), 0.74 (d, J = 6.5 Hz, 3H, $CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 168.5, 165.2, 148.5, 141.4, 136.2, 136.1, 134.8, 134.3, 134.2, 133.8, 129.5, 129.0, 128.5, 128.4, 128.2, 128.0, 127.3, 125.4, 112.0, 111.7, 85.9, 81.6, 81.1, 80.6, 78.5, 70.2, 68.1, 67.4, 58.6, 39.8, 39.3, 33.7, 27.2, 26.7, 26.5, 25.9, 25.5, 24.5, 23.7, 19.5, 14.6; FAB HRMS calcd for $C_{59}H_{68}O_{11}S_2SiCs$ (M + Cs)$^+$: 1177.3027; found m/z = 1177.2963.

[4*R*,4[1*R*,2(4*S*,5*R*)],5*R*,8*S*,9*S*]-9-Hydroxy-4-[hydroxy[2-[5-methyl-3-methylene-4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-6-phenylhexyl]-1,3-dithian-2-yl]methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (79c). A solution of dithiane **79a** (10.3 mg, 9.22 μmol) in dichloromethane (1.5 mL) was treated with 2% HCl/MeOH (0.5 mL). The reaction mixture was stirred at room temperature for 5 min and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 2:7) gave the dithiane **79c** (9.1 mg, 95%) as a colorless oil. $[\alpha]_D^{22}$ = + 43.3 (c 0.82 in $CHCl_3$, 78% *ee*); R_f = 0.18 (silica, ethyl acetate:petroleum ether 1:5); IR (thin film): $\tilde{\nu}_{max}$ = 3444, 3070, 2932, 2855, 1800, 1770, 1747, 1652, 1496, 1472, 1456, 1427, 1385, 1274, 1216, 1175, 1145, 1112, 1068 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.73–7.65 (m, 4H, Ph), 7.43–7.01 (m, 21H, Ph), 6.21 (brs, 1H, C7-OH), 5.60 (s, 1H, H-3), 5.59 (s, 1H, H-7), 5.23 (d, J = 12.5 Hz, 1H, OC*H*H'Ph), 5.19 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.14 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.00 (d, J = 12.5 Hz, 1H, OCH*H*'Ph), 4.92 (brs, 1H, C=C*H*H'), 4.76 (brs, 1H, C=CH*H*'), 4.53 (brs, 1H, H-6), 4.01 (d, J = 5.5 Hz, 1H, CH(OSi)), 2.96–2.89 (m, 2H, CH_2), 2.63–2.59 (m, 3H, CH_2 and OH), 2.52–2.44 (m, 1H, CH_2), 2.28–2.20 (m, 1H, CH_2), 2.12–2.08 (m, 1H, CH_2), 2.05–1.83 (m, 5H, CH_2), 1.37 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.10 (s, 9H, $SiC(CH_3)_3$), 0.72 (d, J = 7.0 Hz, 3H, $CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 168.0, 164.9, 149.0, 141.4, 136.2, 136.1, 134.5, 134.2, 134.1, 133.8, 129.4, 129.0, 128.5, 128.4, 128.0, 127.3, 127.2, 125.4, 111.7, 111.4, 84.5, 81.6, 80.8, 80.2, 68.3, 67.7, 66.4, 57.7, 39.7, 39.4, 33.8, 29.6, 27.1, 26.3, 26.2, 25.4, 25.1, 23.7, 19.5, 14.4; FAB HRMS calcd for $C_{59}H_{68}O_{11}S_2SiCs$ (M + Cs)$^+$: 1177.3027; found m/z = 1177.3080.

[3a*R*,4*S*,5*R*,5(4*S*,5*R*),6a*S*,7*S*,9a*R*]-Dihydro-4,5-dihydroxy-2,2-dimethyl-5-[5-methyl-3-methylene-4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-6-phenylhexyl]-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl)ester (80b). A solution of dithiane **79b** (10.0 mg, 9.56 μmol) in THF (0.38 mL) was treated with $CaCO_3$ (1.6 mg, 0.016 mmol) and aqueous $Hg(ClO_4)_2$ (0.20 M in H_2O, 0.076 mL, 0.015 mmol). The reaction mixture was stirred at room temperature for 2.5 h, diluted with ether (4 mL), and stirred for 10 min. The precipitate was removed by filtration, and the filtrate was dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:5) gave lactol **80b** (8.5 mg, 93%) as a white foam. $[\alpha]_D^{22}$ = + 52.7 (c 1.83 in $CHCl_3$); R_f = 0.36 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3436, 3068, 2959, 2931, 2856, 1807, 1756, 1732, 1455, 1385, 1278, 1216, 1176, 1082, 1048 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.69–7.62 (m, 4H, Ph), 7.42–7.14 (m, 19H, Ph), 6.99–6.97 (m, 2H, Ph), 5.86 (s, 1H, H-3), 5.29 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.24 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.20 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.09 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 4.92–4.88 (m, 2H, C7-OH and C=C*H*H'), 4.70 (brs, 1H, C=CH*H*'), 4.55 (d, J = 7.0 Hz, 1H, H-6), 4.10 (dd, J = 12.5, 7.0 Hz, 1H, H-7), 3.98 (d, J = 5.5 Hz, 1H, CH(OSi)), 3.45 (brs, 1H, C1-OH), 2.66 (dd, J = 13.5, 3.0 Hz, 1H, CH_2), 2.14–2.00 (m, 2H, CH_2), 1.88–1.75 (m, 3H, CH_2 and OH), 1.57 (s, 3H, CH_3), 1.56–1.53 (m, 1H, CH_2), 1.40 (s, 3H, CH_3), 1.09 (s, 9H, $SiC(CH_3)_3$), 0.73 (d, J = 7.0 Hz, 3H, $CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6, 168.5, 166.5, 147.8, 141.2, 136.1, 134.1, 133.8, 133.6, 129.4, 128.9, 128.8, 128.7, 128.6, 128.3, 128.1, 128.0, 127.3, 125.5, 114.0, 112.0, 100.5, 82.9, 81.6, 79.5, 77.9, 74.7, 69.3, 67.8, 64.8, 39.9, 39.4, 33.7, 27.1, 25.8, 25.1, 23.8, 19.5, 14.8; FAB HRMS calcd for $C_{56}H_{62}O_{12}SiCs$ (M + Cs)$^+$: 1087.3065; found m/z = 1087.3090.

[3a*R*,4*R*,5*R*,5(4*S*,5*R*),6a*S*,7*S*,9a*R*]-Dihydro-4,5-dihydroxy-2,2-dimethyl-5-[5-methyl-3-methylene-4-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-6-phenylhexyl]-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl)ester (80a). The procedure described for lactol **80b** gave lactol **80a** from **79c** in 80% yield as a white foam. $[\alpha]_D^{22}$ = + 16.7 (c 0.30 in $CHCl_3$); R_f = 0.10 (silica, ethyl acetate:petroleum ether 1:5); IR (thin film): $\tilde{\nu}_{max}$ = 3478, 3069, 3031, 2958, 2931, 2856, 1807, 1750, 1455, 1386, 1270, 1216, 1082, 1058 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.67 (d, J = 7.0 Hz, 2H, Ph), 7.62 (d, J = 7.0 Hz, 2H, Ph), 7.41–7.14 (m, 19H, Ph), 6.94 (d, J = 7.0, 2H, Ph), 5.84 (s, 1H, H-3), 5.25 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.17 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.12 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.00 (brs, 1H, C=C*H*H'), 4.95 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 4.73 (brs, 1H, C=CH*H*'), 4.70 (d, J = 6.5 Hz, 1H, H-7), 4.09 (d, J = 6.5 Hz, 1H, H-6), 3.99 (d, J = 5.0 Hz, 1H, CH(OSi)), 3.5 (brs, 1H, C1-OH), 2.61 (dd, J = 13.5, 4.0 Hz, 1H, CH_2), 2.09–2.04 (m, 2H, CH_2), 1.80–1.72 (m, 4H, CH_2 and OH), 1.54 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.07 (s, 9H, $SiC(CH_3)_3$), 0.69 (d, J = 6.5 Hz, 3H, $CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.1, 166.0, 165.9, 148.2, 141.2, 136.2, 136.1, 134.3, 134.1, 134.0, 133.8, 129.5, 128.9, 128.6, 128.5, 128.1, 128.0, 127.9, 127.3, 125.5, 113.7, 112.2, 99.4, 82.9, 81.3, 80.4, 80.2, 80.0, 72.1, 68.4, 67.6, 39.7, 39.5, 34.5, 27.1, 26.0, 25.3, 24.9, 19.5, 14.2; FAB HRMS calcd for $C_{56}H_{62}O_{12}SiCs$ (M + Cs)$^+$: 1087.3065; found m/z = 1087.3118.

Data for **[3*S*,4*S*,5*R*,7*R*,9*S*,9(1*R*),13*S*,14*R*]-4,13,14-Trihydroxy-10-methylene-9-(1-methyl-2-phenylethyl)-2,6,8-trioxadispiro[4.1.5.2]tetradecane-3,4-dicarboxylic acid 3-methyl 4-(phenylmethyl) ester (82a).** R_f = 0.29 (silica, ethyl acetate:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max}$ = 3494, 2926, 2853, 1806, 1756, 1438, 1365, 1264, 1170, 1113, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.23 (m, 10H, Ph), 5.42 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.29 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 4.97 (s, 1H, H-3), 4.91 (brs, 1H, C=C*H*H'), 4.90 (brs, 1H, C=CH*H*'), 4.58 (brd, J = 3.8 Hz, 1H, H-6 or H-7), 4.54 (brs, 1H, H-6 or H-7), 3.89 (s, 1H, C4-OH), 3.86 (s, 3H, CO_2CH_3), 3.75 (d, J = 5.1 Hz, 1H, H-4'), 3.20 (brs, 1H, OH), 3.12 (dd, J = 13.5, 3.9 Hz, 1H, CH_2), 2.40 (dd, J = 13.5, 10.0 Hz, 1H, CH_2), 2.32–2.28 (m, 1H, CH_2), 2.18–2.13 (m, 2H, CH_2 and H-5'), 2.00–1.91 (m, 2H, CH_2Ph), 0.92 (d, J = 6.7 Hz, 3H, CH_3); FAB HRMS calcd for $C_{31}H_{34}O_{11}Cs$ (M + Cs)$^+$: 715.1155; found m/z = 715.1184.

[4*R*,4[1*R*,2(4*S*,5*R*)],5*R*,8*S*,9*S*]-4-[Hydroxy[2-[5-methyl-3-methylene-4-[[bis(1,1-dimethylethyl)methylsilyl]oxy]-6-phenylhexyl]-1,3-dithian-2-yl]methyl]-2,2-dimethyl-6-oxo-9-[(trimethylsilyl)oxy]-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (84a) and [4*R*,4[1*S*,2(4*S*,5*R*)],5*R*,8*S*,9*S*]-9-hydroxy-4-[hydroxy-[2-[5-methyl-3-methylene-4-[[bis(1,1-dimethylethyl)methylsilyl]oxy]-6-phenylhexyl]-1,3-dithian-2-yl]methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (84b). A solution of DTBMS-dithiane **78** (131 mg, 0.27 mmol) in THF (6 mL) at −40 °C in a Schlenk tube was treated with *n*-butyllithium (1.60 M in hexane, 0.18 mL, 0.29 mmol). The reaction mixture was warmed to −25 °C, stirred for 1.5 h, and then cooled to −78 °C. A solution of the aldehyde **5** (127 mg, 0.23 mmol) in THF (2 mL) was cooled to −78 °C and cannulated rapidly into the solution of the lithiated dithiane. The reaction mixture was stirred at −78 °C for 5 min, quenched with a solution of acetic acid in THF (0.5 M in THF, 0.6 mL, 0.3 mmol), and warmed to room temperature. The reaction mixture was diluted with NH_4Cl (20 mL) and ether (20 mL). The aqueous phase was separated and extracted with ether (2 × 30 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:8 → 1:5) gave dithiane **84a** (96 mg, 40%) and dithiane **84b** (70 mg, 32%) as colorless oils.
Data for **84a**: $[\alpha]_D^{22}$ = + 30.9 (c 0.89 in $CHCl_3$); R_f = 0.37 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3396, 2931, 2856, 1799, 1752, 1456, 1374, 1253, 1069 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.16 (m, 15H, Ph), 5.56 (d, J = 2.0 Hz, 1H, H-7), 5.49 (s, 1H, H-3), 5.24 (d, J = 12.5 Hz, 1H, OC*H*H'Ph), 5.22 (s, 2H, OCH_2Ph), 5.14 (d, J = 12.5 Hz, 1H, OCH*H*'Ph), 5.08 (brs, 1H, C=C*H*H'), 5.00 (d, J = 2.0 Hz, 1H, H-6), 4.96 (brs, 1H, C7-OH), 4.88 (brs, 1H, C=CH*H*'), 4.14 (d, J = 5.5 Hz, 1H, CH(OSi)), 3.18–3.10 (m, 1H, CH_2), 3.02–2.96 (m, 1H, CH_2), 2.84 (dd, J = 13.0, 3.4 Hz, 1H, CH_2), 2.64–2.61 (m, 2H, CH_2), 2.53–2.17 (m, 4H, CH_2), 2.06–2.02 (m, 1H, CH_2), 1.91–1.87 (m, 3H, CH_2 and OH), 1.40 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.05 (s, 9H, $SiC(CH_3)_3$), 0.98 (s, 9H, $SiC(CH_3)_3$), 0.78 (d, J = 6.5 Hz, 3H, $CH(CH_3)$), 0.26 (s, 9H, $Si(CH_3)_3$), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.7, 168.8, 165.9, 149.9, 141.6, 134.5, 134.1, 129.1, 128.5, 128.4, 128.3, 128.0, 125.5, 111.0, 110.7, 84.8, 81.7, 81.5, 80.3, 79.5, 71.1, 68.4, 67.6, 58.7, 40.1, 40.0, 28.2, 27.9, 26.3, 26.2, 25.5, 24.9, 23.6, 21.0, 13.9, 2.3, −7.7; FAB HRMS calcd for $C_{55}H_{78}O_{11}S_2Si_2Cs$ (M + Cs)$^+$: 1167.3578; found m/z = 1167.3502.
Data for **84b**: $[\alpha]_D^{22}$ = + 18.8 (c 2.03 in $CHCl_3$), R_f = 0.10 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3239, 2932, 2857, 1802, 1770, 1742, 1497, 1457, 1381, 1269, 1216, 1170, 1063 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.17 (m, 15H, Ph), 5.56 (d, J = 2.0 Hz, 1H, H-3), 5.50 (brs, 1H, H-7), 5.24 (d, J = 12.5 Hz, 1H, OC*H*H'Ph), 5.23 (s, 2H, OCH_2Ph), 5.14 (d, J = 12.5 Hz, 1H, OCH*H*'Ph), 5.08 (brs, 1H, C=C*H*H'), 5.00 (d, J = 2.0 Hz, 1H, C4-OH), 4.96 (brs, 1H, H-6), 4.88 (brs, 1H, C=CH*H*'), 4.15 (d, J = 5.0 Hz, 1H, CH(OSi)), 3.16–3.12 (m, 1H, CH_2), 3.02–2.97 (m, 1H, CH_2), 2.84 (dd, J = 13.5, 3.5, 1H, CH_2), 2.66–2.61 (m, 2H, CH_2), 2.53–2.34 (m, 3H, CH_2), 2.26–2.17 (m, 2H, CH_2), 2.08–2.00 (m, 1H, OH), 1.91–1.83 (m, 2H, CH_2), 1.40 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.05 (s, 9H, $SiC(CH_3)_3$), 0.98 (s, 9H, $SiC(CH_3)_3$), 0.79 (d, J = 6.5 Hz, 3H, $CH(CH_3)$), 0.08 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5, 168.5, 165.2, 149.1, 141.5, 134.7, 134.3, 129.1, 128.5, 128.4, 128.2, 128.0, 125.5, 111.8, 111.7, 85.9, 81.5, 81.1, 80.5, 78.6, 70.3, 68.1, 67.5, 58.5, 40.2, 39.6, 33.9, 28.2, 27.9, 26.7, 26.6, 25.9, 25.6, 24.5, 23.7, 20.9, −7.8; FAB HRMS calcd for $C_{52}H_{70}O_{11}S_2SiCs$ (M + Cs)$^+$: 1095.3183; found m/z = 1095.3154.

[4*R*,4[1*R*,2(4*S*,5*R*)],5*R*,8*S*,9*S*]-9-Hydroxy-4-[hydroxy[2-[5-methyl-3-methylene-4-[[bis(1,1-dimethylethyl)methylsilyl]oxy]-6-phenylhexyl]-1,3-dithian-2-yl]methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-8,9-dicarboxylic acid bis(phenylmethyl) ester (84c). A solution of dithiane **84a** (48 mg, 0.046 mmol) in dichloromethane (3 mL) was treated with 2% HCl/MeOH (2 mL). The reaction mixture was stirred at room temperature for 5 min and concentrated in vacuo to give a crude oil. Purification by flash column chromatography gave the dithiane **84c** (44 mg, 99%) as a colorless oil. $[\alpha]_D^{22}$ = + 33.2 (c 0.73 in $CHCl_3$); R_f = 0.38 (silica, ethyl acetate:petroleum ether 1:2); IR (thin film): $\tilde{\nu}_{max}$ = 3446, 3299, 2956, 2931, 2856, 1800, 1770, 1746, 1456, 1387, 1275, 1216, 1175, 1145, 1068, 1029 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.27 (m, 15H, Ph), 6.22 (s, 1H, C4-OH), 5.63 (s, 1H,

H-3), 5.59 (s, 1H, H-7), 5.22 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.17 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.13 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.07 (brs, 1H, C=C*H*H'), 5.00 (d, J = 12.0 Hz, 1H, OCH*H*'Ph) 4.91 (s, 1H, C=CH*H*'), 4.56 (s, 1H, H-6), 4.12 (d J = 5.5 Hz, 1H, CH(OSi)), 2.97–2.90 (m, 2H, CH_2), 2.84 (dd, J = 13.5, 3.5 Hz, 1H, CH_2), 2.67–2.62 (m, 2H, CH_2), 2.50–2.45 (m, 1H, CH_2), 2.38–2.28 (m, 1H, CH_2), 2.20–1.80 (m, 6H, CH_2 and OH), 1.38 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.05 (s, 9H, $SiC(CH_3)_3$), 0.98 (s, 9H, $SiC(CH_3)_3$), 0.79 (d, J = 7.0 Hz, 3H, $CH(CH_3)$), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 168.0, 164.9, 149.6, 141.5, 134.5, 134.1, 129.0, 128.5, 128.4, 128.0, 125.5, 111.7, 111.2, 84.5, 81.8, 80.8, 80.2, 76.6, 77.0, 68.3, 67.7, 66.3, 57.7, 40.0, 39.8, 33.9, 28.2, 27.9, 26.3, 26.0, 25.4, 25.1, 23.7, 21.0, 14.2, −7.7; FAB HRMS calcd for $C_{52}H_{70}O_{11}S_2SiCs$ $(M + Cs)^+$: 1095.3183; found m/z = 1095.3133.

[3a*R*,4*R*,5*R*,5(4*S*,5*R*),6a*S*,7*S*,9a*R*]-Dihydro-4,5-dihydroxy-2,2-dimethyl-5-[5-methyl-3-methylene-4-[[bis(1,1-dimethylethyl)methylsilyl]oxy]-6-phenylhexyl]-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl)ester (85 a). A solution of the dithiane **84c** (42.6 mg, 0.044 mmol) in THF (1.4 mL) was treated with $CaCO_3$ (5.9 mg, 0.059 mmol) and aqueous $Hg(ClO_4)_2$ (0.20 M in H_2O, 0.265 mL, 0.053 mmol). The reaction mixture was stirred at room temperature for 2.5 h, treated with ether (4 mL), and stirred for 10 min. The precipitate was removed by filtration and the filtrate dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography gave lactol **85a** (32 mg, 83%) as a white foam. $[\alpha]_D^{22}$ = +19.1 (c 0.43 in $CHCl_3$); R_f = 0.43 (silica, ethyl acetate:petroleum ether 1:2); IR (thin film): $\tilde{\nu}_{max}$ = 3474, 2931, 2855, 1807, 1752, 1454, 1385, 1270, 1215, 1082 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.10 (m, 15H, Ph), 5.87 (s, 1H, H-3), 5.30 (d, J = 12.5 Hz, 1H, C*H*H'Ph), 5.20–5.14 (m, 3H, CH_2Ph and OH), 5.08 (brs, 1H, C=C*H*H'), 4.99 (d, J = 12.5 Hz, 1H CH*H*'Ph), 4.87 (brs, 1H, C=CH*H*'), 4.74 (d, J = 6.5 Hz, 1H, H-6), 4.22 (d, J = 6.0 Hz, 1H, H-7), 4.06 (d, J = 5.5 Hz, 1H, CH(OSi)), 2.74 (dd, J = 13.5, 3.5 Hz, 1H, CH_2), 2.20–1.67 (m, 6H, CH_2 and OH), 1.61 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.02 (s, 9H, $SiC(CH_3)_3$), 0.92 (s, 9H, $SiC(CH_3)_3$), 0.75 (d, J = 6.5 Hz, 3H, $CH(CH_3)$), 0.03 (s, 3H, $SiCH_3$); FAB HRMS calcd for $C_{49}H_{64}O_{12}SiCs$ $(M + Cs)^+$: 1005.3221; found m/z = 1005.3291.

[3a*R*,4*S*,5*R*,5(4*S*,5*R*),6a*S*,7*S*,9a*R*]-Dihydro-4,5-dihydroxy-2,2-dimethyl-5-[5-methyl-3-methylene-4-[[bis(1,1-dimethylethyl)methylsilyl]oxy]-6-phenylhexyl]-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl)ester (85 b). The procedure described for lactol **85a** gave lactol **85b** from **84b** in 80% yield as a white foam. $[\alpha]_D^{22}$ = +43.3 (c 1.22 in $CHCl_3$); R_f = 0.42 (silica, ethyl acetate:petroleum ether 1:4); IR (thin film): $\tilde{\nu}_{max}$ = 3438, 2961, 2932, 2856, 1808, 1755, 1737, 1456, 1386, 1278, 1217, 1081, 1031 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.11 (m, 15H, Ph), 5.87 (s, 1H, H-3), 5.29 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.24 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.20 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.16 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.08 (brs, 1H, C=C*H*H'), 4.93 (d, J = 6.0 Hz, 1H, C7-OH), 4.91 (s, 1H, C=CH*H*'), 4.47 (d, J = 13.0 Hz, 1H, H-6), 4.19 (dd, J = 13.0, 6.0 Hz, 1H, H-7), 4.10 (d, J = 5.5 Hz, 1H, CH(OSi)), 3.63 (brs, 1H, C1-OH), 2.80 (dd, J = 13.5, 3.5 Hz, 1H, CH_2), 2.26–1.66 (m, 6H, CH_2 and OH), 1.57 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.04 (s, 9H, $SiC(CH_3)_3$), 0.96 (s, 9H, $SiC(CH_3)_3$), 0.80 (d, J = 7.0 Hz, 3H, $CH(CH_3)$), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.6, 168.5, 166.6, 148.5, 141.3, 134.1, 129.0, 128.8, 128.7, 128.6, 128.3, 128.1, 125.6, 114.0, 111.7, 100.6, 82.9, 81.9, 79.6, 77.9, 74.8, 69.3, 67.9, 64.7, 40.2, 39.6, 34.0, 28.1, 27.8, 26.3, 25.8, 25.1, 23.4, 20.9, 14.7, −7.9; FAB HRMS calcd for $C_{49}H_{64}O_{12}SiNa$ $(M + Na)^+$: 895.4065; found m/z = 895.4043.

(7*S*)-2,7-Anhydro-8,9,10,12,13-pentadeoxy-4-*C*-(methoxycarbonyl)-10-methylene-11-*O*-[bis(1,1-dimethylethyl)methylsilyl]-3-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid methyl ester (86). A solution of lactol **85a** (19 mg, 0.022 mmol) in methanol (0.3 mL) and 2% HCl/MeOH (2.5 mL) was heated in a sealed tube at 78 °C for 21 h. The reaction mixture was concentrated in vacuo to give a crude oil. Purification by preparative TLC (ether) gave the bicycle **86** (7.6 mg, 45%) as a white foam. $[\alpha]_D^{22}$ = −6.9 (c 0.29 in $CHCl_3$); R_f = 0.42 (silica, ether); IR (thin film): $\tilde{\nu}_{max}$ = 3449, 2931, 2856, 1747, 1455, 1253, 1118, 1081 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.15 (m, 10H, Ph), 5.38 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.29 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.19 (s, 1H, H-3), 5.15 (d, J = 2.5 Hz, 1H, H-6), 5.11 (s, 1H, C=C*H*H'), 4.96 (s, 1H, C=CH*H*'), 4.18 (d, J = 2.5 Hz, 1H, H-7), 4.15 (d, J = 5.0 Hz, 1H, CH(OSi)), 3.71 (s, 3H, CO_2CH_3), 3.58 (s, 3H, CO_2CH_3), 2.83 (dd, J = 14.0, 4.0 Hz, 1H, CH_2), 2.51–2.42 (m, 1H, CH_2), 2.30–2.19 (m, 3H, CH_2), 2.15–2.10 (m, 1H, CH_2), 1.93–1.87 (m, 1H, $CH(CH_3)$), 1.04 (s, 9H, $SiC(CH_3)_3$), 0.96 (s, 9H, $SiC(CH_3)_3$), 0.79 (d, J = 6.5 Hz, 3H, CH_3), 0.07 (s, 3H, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.0, 166.8, 148.8, 141.5, 134.6, 129.0, 128.9, 128.6, 128.5, 128.0, 125.5, 111.1, 105.8, 91.4, 82.4, 81.2, 78.6, 75.3, 74.5, 68.6, 52.9, 52.3, 40.0, 39.8, 33.4, 28.1, 27.8, 24.0, 21.0, 20.9, 14.1, −7.8; FAB HRMS calcd for $C_{41}H_{58}O_{12}SiCs$ $(M + Cs)^+$: 903.2752; found m/z = 903.2775.

(7*S*)-2,7-Anhydro-8,9,10,12,13-pentadeoxy-4-*C*-(methoxycarbonyl)-3-*C*-[(phenylmethoxy)carbonyl]-10-methylene-12-(phenylmethyl)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid methyl ester (87). A solution of bicycle **86** (3.0 mg, 0.004 mmol) in nitromethane (0.5 mL) was treated with 49% aqueous HF solution (0.05 mL). The reaction mixture was stirred at 0 °C for 24 h, quenched with $NaHCO_3$ (2 mL), and extracted with ethyl acetate (3 × 1 mL). The organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by preparative TLC (ethyl acetate:petroleum ether 4:1) gave the tetraol **87** (1 mg, 30%) as a yellow oil. $[\alpha]_D^{22}$ = −9 (c 0.83 in $CHCl_3$); R_f = 0.32 (silica, ethyl acetate:petroleum ether 3:1); IR (thin film): $\tilde{\nu}_{max}$ = 3607, 3484, 3084, 3064, 3027, 2956, 2931, 2854, 1749, 1645, 1604, 1558, 1453, 1439, 1375, 1265, 1241, 1187, 1146, 1122, 1101, 1030 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.42 (m, 2H, Ph), 7.38–7.33 (m, 3H, Ph), 7.28–7.23 (m, 2H, Ph), 7.17–7.13 (m, 3H, Ph), 5.33 (d, J = 12.0 Hz, 1H, OC*H*H'Ph), 5.23 (d, J = 12.0 Hz, 1H, OCH*H*'Ph), 5.17 (s, 1H, H-3), 5.11 (d, J = 1.6 Hz, 1H, H-6), 5.09 (brs, 1H, C=C*H*H'), 5.03 (brs, 1H, C=CH*H*'), 4.17 (d, J = 1.6 Hz, 1H, H-7), 3.99 (d, J = 6.5 Hz, 1H, H-4'), 3.95 (brs, 1H, OH), 3.63 (s, 3H, CO_2CH_3), 3.48 (s, 3H, CO_2CH_3), 2.72 (dd, J = 13.4, 4.7 Hz, 1H, CH_2), 2.53–2.47 (m, 1H, CH_2), 2.33–2.15 (m, 4H, CH_2), 1.95–1.89 (m, 1H, $CH(CH_3)$), 0.84 (d, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.0, 167.3, 166.8, 150.3, 140.9, 134.8, 129.2, 128.7, 128.6, 128.2, 125.7, 112.5, 106.2, 91.5, 82.9, 79.1, 78.5, 75.4, 74.7, 68.4, 52.9, 52.4, 39.9, 38.3, 33.6, 25.1, 14.3; FAB HRMS calcd for $C_{32}H_{38}O_{12}Cs$ $(M + Cs)^+$: 747.1418; found m/z = 747.1435.

(7*S*)-2,7-Anhydro-8,9,10,12,13-pentadeoxy-10-methylene-3,4-bis-*C*-[(phenylmethoxy)carbonyl]-12-(phenylmethyl)-L-*erythro*-L-*glycero*-D-*altro*-7-trideculo-7,4-furanosonic acid phenylmethyl ester (88). A solution of dimethyl ester **87** (3.8 mg, 6.2 μmol) in THF (0.3 mL) and water (0.15 mL) was treated with $LiOH \cdot H_2O$ (2.6 mg, 0.06 mmol). The reaction mixture was stirred at room temperature for 1 h and quenched by adding aqueous HCl (1 M, 1 mL). The aqueous phase was separated and extracted with ethyl acetate (3 × 2 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. A solution of the crude acid in THF (0.5 mL) was treated with DCBI (8.7 mg, 27 μmol) and heated at 55 °C for 1.5 h. The reaction mixture was concentrated in vacuo to give a crude oil. Purification by preparative TLC (ethyl acetate:petroleum ether 3:1) gave tribenzyl ester **88** (3.2 mg, 68%, 2 steps) as a yellow oil. $[\alpha]_D^{22}$ = −8.8 (c 0.80 in $CHCl_3$); R_f = 0.43 (silica, ethyl acetate:petroleum ether 3:1); IR (thin film): $\tilde{\nu}_{max}$ = 3477, 3063, 3031, 2961, 2931, 2854, 1747, 1632, 1556, 1497, 1454, 1384, 1352, 1276, 1187, 1155, 1122, 1028 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.09 (m, 20H, Ph), 5.23 (d, J = 12.1 Hz, 1H, OC*H*H'Ph), 5.18 (s, 1H, H-3), 5.10 (d, J = 12.1 Hz, 1H, OCH*H*'Ph), 5.06 (brs, 1H, C=C*H*H'), 5.05 (d, J = 2.3 Hz, 1H, H-6), 5.02 (brs, 1H, C=CH*H*'), 4.95 (d, J = 12.1 Hz, 1H, OC*H*H'Ph), 4.92 (d, J = 12.1 Hz, 1H, OCH*H*'Ph), 4.72 (d, J = 12.2 Hz, 1H, OC*H*H'Ph), 4.68 (d, J = 12.2 Hz, 1H, OCH*H*'Ph), 4.13 (d, J = 2.3 Hz, 1H, H-7), 3.95 (brd, J = 6.5 Hz, 1H, H-4'), 3.93 (brs, 1H, OH), 2.70 (dd, J = 13.5, 4.9 Hz, 1H, CH_2), 2.51–2.45 (m, 1H, CH_2), 2.32–2.27 (m, 1H, CH_2), 2.24 (dd, J = 13.5, 9.7 Hz, 1H, CH_2), 2.15–2.11 (m, 2H, CH_2), 1.90–1.88 (m, 1H, $CH(CH_3)$), 0.82 (d, J = 6.6 Hz, 3H, $CH(CH_3)$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.6, 166.5, 166.0, 150.5, 141.0, 134.6, 129.2, 128.6, 128.5, 128.4, 128.2, 125.7, 112.6, 106.1, 91.3, 83.0, 78.8, 78.6, 75.3, 74.8, 68.1, 67.9, 67.7, 39.9, 38.2, 33.5, 25.4, 14.2; FAB HRMS calcd for $C_{44}H_{46}O_{12}Cs$ $(M + Cs)^+$: 899.2044; found m/z = 899.2065.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-9-hydroxymethyl-4-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-8-[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (91). A solution of crude triol **30b** (12.5 g, 0.033 mmol) in DMF was treated with DMAP (183 mg, 1.50 mmol), imidazole (4.09 g, 0.060 mol), and TPSCl (9.3 mL, 0.036 mol). The reaction mixture was stirred at room temperature for 3 h, poured into a mixture of aqueous HCl (1 M)/brine (1:3) (200 mL), and extracted with ethyl acetate (3 × 200 mL). The combined organic extracts were washed with aqueous $NaHCO_3$/brine (1:1) (100 mL) and brine (100 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 3:1 → 1:1) gave the diol **91** (15.1 g, 75%) as a yellow oil. $[\alpha]_D^{22}$ = +41.6 (c 1.07 in $CHCl_3$, 75% *ee*); R_f = 0.18 (silica, ether:petroleum ether 3:1); IR (thin film): $\tilde{\nu}_{max}$ = 3414, 2935, 2890, 1787, 1472, 1428, 1375, 1217, 1114, 1061, 856 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69–7.65 (m, 4H, Ph), 7.49–7.40 (m, 6H, Ph), 4.90 (dd, J = 7.1, 3.4 Hz, 1H, H-6), 4.89 (s, 1H, C4-OH), 4.82 (s, 2H, OCH_2O), 4.45 (dd, J = 5.2, 3.8 Hz, 1H, H-3), 4.21 (dd, J = 11.5, 3.4 Hz, 1H, H-7), 4.13 (dd, J = 11.5, 5.2 Hz, 1H, C*H*H'OSi), 4.09 (dd, J = 11.5, 3.8 Hz, 1H, CH*H*'OSi), 3.96 (dd, J = 12.2, 7.3 Hz, 1H, C*H*H'OH), 3.92 (dd, J = 11.5, 7.1 Hz, 1H, H'-7), 3.87 (dd, J = 12.2, 6.6 Hz, 1H, CH*H*'OH), 3.79–3.71 (m, 2H, $OCH_2CH_2OCH_3$), 3.57 (app.t, J = 4.6 Hz, 2H, CH_2OCH_3), 3.38 (s, 3H, OCH_3), 2.85 (dd, J = 7.3, 6.6 Hz, 1H, CH_2OH), 1.50 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.06 (s, 9H, $SiC(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.9, 136.1, 136.0, 132.2, 131.9, 130.82, 130.80, 128.53, 128.50, 111.2, 96.4, 84.6, 82.7, 80.1, 78.2, 72.2, 67.7, 65.7, 62.7, 62.0, 59.5, 27.2, 27.1, 25.4, 19.5; FAB HRMS calcd for $C_{31}H_{44}O_{10}SiNa$ $(M + Na)^+$: 627.2601; found m/z = 627.2571.

(4*R*,5*R*,8*R*,9*S*)-9-Formyl-9-hydroxy-4-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-8-[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-1,3,7-trioxaspiro[4.4]nonan-6-one (92). A solution of compound **91** (1.14 g, 1.89 mmol) in dichloromethane (40 mL) was treated with Dess–Martin periodinane (878 mg, 2.08 mmol). The reaction mixture was stirred at room temperature for 12 h, diluted with ether (80 mL), quenched with 25% $Na_2S_2O_3$ in aqueous $NaHCO_3$ (20 mL), and stirred for 15 min. The aqueous phase was extracted with ether (3 × 80 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 1:1) gave aldehyde **92** (1.04 g, 91%) as a colorless oil. $[\alpha]_D^{22}$ = +60.0 (c 0.54

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in $CHCl_3$, 75% *ee*); $R_f = 0.38$ (silica, ether:petroleum ether 3:1); IR (thin film): $\tilde{\nu}_{max} = 3376, 2934, 2859, 1793, 1731, 1462, 1428, 1376, 1216, 1113, 825\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 9.91$ (s, 1H, CHO), 7.65–7.61 (m, 4H, Ph), 7.47–7.38 (m, 6H, Ph), 5.03 (dd, $J = 6.8$, 5.2 Hz, 1H, H-3), 4.87 (brs, 1H, C4-OH), 4.83 (dd, $J = 4.5$, 3.5 Hz, 1H, H-6), 4.75 (ABq, $J_{AB} = 6.8$ Hz, $\Delta\nu_{AB} = 9.0$ Hz, 2H, OCH_2O), 4.01 (dd, $J = 11.7$, 3.5 Hz, 1H, H-7), 3.95 (dd, $J = 10.7$, 6.8 Hz, 1H, C*H*H'OSi), 3.90 (dd, $J = 10.7$, 5.2 Hz, 1H, CH*H'*OSi), 3.84 (dd, $J = 11.7$, 4.5 Hz, 1H, H'-7), 3.77–3.69 (m, 2H, $OCH_2CH_2OCH_3$), 3.58–3.56 (m, 2H, CH_2OCH_3), 3.39 (s, 3H, OCH_3), 1.48 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.01 (s, 9H, $SiC(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 197.3$, 172.6, 136.0, 135.9, 132.6, 132.5, 130.5, 128.4, 128.3, 111.9, 96.2, 86.1, 82.2, 80.3, 77.7, 72.1, 67.9, 64.7, 60.2, 59.4, 27.2, 27.0, 25.7, 19.4; FAB HRMS calcd for $C_{31}H_{42}O_{10}SiNa$ $(M + Na)^+$: 625.2445; found $m/z = 625.2472$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-4-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-8-[[[(1,1-dimethylethyl)diphenylsilyl]oxy]methyl]-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (94). A solution of the aldehyde **92** (2.50 g, 4.15 mmol) in *t*-butanol (25 mL) and water (7.5 mL) was treated with 2-methyl-2-butene (2.0 M in THF, 8.72 mL, 17.4 mmol) and $NaH_2PO_4 \cdot H_2O$ (0.602 g, 4.36 mmol). The reaction mixture was stirred at room temperature for 15 min, treated with $NaClO_2$ (1.13 g, 12.5 mmol), and stirred for 5 h. The reaction mixture was cooled to 0 °C, quenched with aqueous HCl (1 M, 100 mL), and extracted with dichloromethane (4 × 250 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to provide the acid **93** in quantitative yield as a colorless oil. The crude acid was used in the next step without any further purification. A solution of the crude acid **93** in toluene (75 mL) was treated with DCBI (1.96 g, 6.23 mmol). The reaction mixture was heated at 100 °C for 2 h, cooled to room temperature, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 25:75 → 30:70) gave MEM ether **94** (2.77 g, 94% from **92**) as a colorless oil. $[\alpha]_D^{22} = +26.3$ (*c* 2.40 in $CHCl_3$, 75% *ee*); $R_f = 0.31$ (silica, ether:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3335, 2934, 2890, 1790, 1742, 1457, 1376, 1275, 1192, 1119, 1056, 824\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.65–7.60$ (m, 4H, Ph), 7.45–7.42 (m, 2H, Ph), 7.38–7.34 (m, 9H, Ph), 5.42 (s, 1H, C4-OH), 5.17 (ABq, $J_{AB} = 12.3$ Hz, $\Delta\nu_{AB} = 25.8$ Hz, 2H, CH_2Ph), 5.11 (dd, $J = 5.3$, 4.9 Hz, 1H, H-3), 4.92 (dd, $J = 6.7$, 5.0 Hz, 1H, H-6), 4.75 (ABq, $J_{AB} = 6.9$ Hz, $\Delta\nu_{AB} = 30.1$ Hz, 2H, OCH_2O), 4.14 (dd, $J = 11.2$, 5.0 Hz, 1H, H-7), 4.07 (dd, $J = 11.4$, 4.9 Hz, 1H, C*H*H'OSi), 4.04 (dd, $J = 11.4$, 5.3 Hz, 1H, CH*H'*OSi), 3.97 (dd, $J = 11.2$, 6.7 Hz, 1H, H'-7), 3.74–3.66 (m, 2H, $OCH_2CH_2OCH_3$), 3.54 (app.t, $J = 4.6$ Hz, 2H, CH_2OCH_3), 3.38 (s, 3H, OCH_3), 1.42 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.03 (s, 9H, $SiC(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$); $\delta = 172.8$, 169.0, 136.0, 135.9, 134.9, 132.7, 132.3, 130.53, 130.50, 129.1, 128.9, 128.4, 128.3, 112.1, 96.2, 85.8, 81.3, 80.9, 78.4, 72.1, 68.5, 67.7, 65.4, 61.7, 59.5, 27.5, 27.1, 25.7, 19.6; FAB HRMS calcd for $C_{38}H_{48}O_{11}SiCs$ $(M + Cs)^+$: 841.2020; found $m/z = 841.2039$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-4-hydroxymethyl-2,2-dimethyl-8-[[[(1,1-dimethylethyl)-diphenylsilyl]oxy]methyl]-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (95). A solution of MEM ether **94** (16.2 g, 23.0 mmol) in acetonitrile (300 mL) was treated with sodium iodide (3.43 g, 23.0 mmol). The reaction mixture was cooled to −30 °C and treated with TMSCl (2.92 mL, 23.0 mmol), stirred at −30 °C for 1 h, treated with an additional amount of sodium iodide (3.43 g, 23.0 mmol) and TMSCl (2.92 mL, 23.0 mmol), and stirred for 30 min. The reaction mixture was quenched with $NaHCO_3$ (500 mL) and ethyl acetate (300 mL) and warmed to room temperature. The aqueous phase was separated and extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 3:1 → 2:1) gave the diol **95** (10.1 g, 71%) and unreacted MEM ether **94** (3.85 g, 24%).

Data for **95**: $[\alpha]_D^{22} = +37.7$ (*c* 0.69 in $CHCl_3$, 75% *ee*); $R_f = 0.47$ (silica, ethyl acetate:petroleum ether 1:2); IR (thin film): $\tilde{\nu}_{max} = 3511, 3231, 2932, 2891, 2858, 1789, 1742, 1461, 1428, 1375, 1276, 1217, 1186, 1113, 1055\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.66–7.63$ (m, 4H, Ph), 7.43–7.26 (m, 11H, Ph), 6.30 (s, 1H, C4-OH), 5.22–5.14 (m, 3H, CH_2Ph and H-3 or H-6), 4.84 (dd, $J = 4.0$, 4.0 Hz, 1H, H-3 or H-6), 4.24 (ddd, $J = 13.0$, 3.7, 3.7 Hz, 1H, C*H*H'O), 4.10–4.05 (m, 2H, CH_2O), 3.97 (ddd, $J = 13.0$, 5.6, 3.3 Hz, 1H, CH*H'*O), 3.13 (dd, $J = 8.9$, 4.0 Hz, 1H, C7-OH), 1.27 (s, 3H, CH_3), 1.04 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.2$, 169.0, 135.5, 135.4, 135.3, 134.3, 132.3, 132.1, 129.9, 128.6, 128.2, 127.7, 110.9, 84.6, 81.4, 80.6, 79.1, 68.0, 61.5, 59.1, 26.6, 26.3, 25.0, 19.1; FAB HRMS calcd for $C_{34}H_{40}O_9SiCs$ $(M + Cs)^+$: 753.1496; found $m/z = 753.1465$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-4,8-bis(hydroxymethyl)-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (96). A solution of silyl ether **95** (14.4 g, 23.2 mmol) in THF (308 mL) at 0 °C was treated with acetic acid (2.64 mL, 46.2 mmol) and TBAF (1.0 M in THF, 26.1 mL, 26 mmol). The reaction mixture was stirred at 0 °C for 30 min, warmed to room temperature, and poured into brine (500 mL) and ethyl acetate (300 mL). The aqueous phase was separated and extracted with ethyl acetate (4 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 2:1) gave the triol **96** (7.73 g, 87%) as a white crystalline solid. Recrystallization from hot dichloromethane gave enantiomerically enriched triol **96** (>98% *ee*). M.p. 118–119 °C (dichloromethane); $[\alpha]_D^{22} = +88.2$ (*c* 1.14 in $CHCl_3$, >98% *ee*); $R_f = 0.15$ (silica, ethyl acetate:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3262, 1792, 1734, 1700, 1662, 1653, 1559, 1506, 1456, 1374, 1276, 1217, 1186, 1059\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.41–7.36$ (m, 5H, Ph), 6.80 (s, 1H, C4-OH), 5.28 (d, $J = 12.2$ Hz, 1H, C*H*H'Ph), 5.21 (d, $J = 12.2$, 1H, CH*H'*Ph), 5.08 (dd, $J = 4.8$, 4.8 Hz, 1H, H-3 or H-6), 4.81 (dd, $J = 4.2$, 2.8 Hz, 1H, H-3 or H-6), 4.27 (ddd, $J = 13.2$, 4.2, 3.0 Hz, 1H, C*H*H'OH), 4.12–4.02 (m, 2H, CH_2OH), 3.95 (ddd, $J = 13.2$, 10.0, 2.8 Hz, 1H, CH*H'*OH), 3.40 (dd, $J = 10.0$, 2.8 Hz, 1H, OH), 2.56 (dd, $J = 7.9$, 5.2 Hz, 1H, OH), 1.41 (s, 3H, CH_3), 1.27 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.1$, 169.0, 134.1, 128.8, 128.7, 128.4, 128.3, 111.0, 84.4, 81.4, 80.9, 79.0, 68.1, 60.0, 58.7, 26.1, 24.9; FAB HRMS calcd for $C_{18}H_{22}O_9Cs$ $(M + Cs)^+$: 515.0318; found $m/z = 515.0336$.

(4*R*,5*R*,8*R*,9*S*)-9-Hydroxy-8-hydroxymethyl-4-[[[2-(methoxy)ethoxy]methoxy]-methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (97). A solution of compound **94** (2.11 g, 2.98 mmol) in THF (40 mL) at 0 °C was treated with acetic acid (0.34 mL, 5.96 mmol) and TBAF (1.0 M in THF, 3.57 mL, 3.57 mmol). The reaction mixture was stirred at 0 °C for 1.5 h, quenched with water (40 mL) at 0 °C, and extracted with ethyl acetate (3 × 80 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:1) gave diol **97** (1.36 g, 97%) as a colorless oil. $[\alpha]_D^{22} = +47.4$ (*c* 1.80 in $CHCl_3$, 75% *ee*); $R_f = 0.33$ (silica, ethyl acetate:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3332, 2939, 1790, 1741, 1455, 1377, 1185, 1020, 866\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.40–7.32$ (m, 5H, Ph), 5.75 (s, 1H, C4-OH), 5.23 (ABq, $J_{AB} = 12.2$ Hz, $\Delta\nu_{AB} = 9.7$ Hz, 2H, CH_2Ph), 5.01 (dd, $J = 4.7$, 4.4 Hz, 1H, H-3), 4.88 (dd, $J = 6.2$, 5.3 Hz, 1H, H-6), 4.72 (ABq, $J_{AB} = 6.8$ Hz, $\Delta\nu_{AB} = 33.2$ Hz, 2H, OCH_2O), 4.13 (dd, $J = 11.4$, 5.3 Hz, 1H, H-7), 4.08 (dd, $J = 12.6$, 4.4 Hz, 1H, C*H*H'OH), 4.03 (dd, $J = 12.6$, 4.7 Hz, 1H, CH*H'*OH), 3.96 (dd, $J = 11.4$, 6.2 Hz, 1H, H'-7), 3.70–3.64 (m, 2H, $OCH_2CH_2OCH_3$), 3.52 (app.t, $J = 4.5$ Hz, 2H, CH_2OCH_3), 3.36 (s, 3H, OCH_3), 2.81 (brs, 2H, CH_2OH), 1.40 (s, 3H, CH_3), 1.25 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.9$, 169.0, 134.9, 129.3, 129.2, 129.1, 112.2, 96.2, 85.8, 81.5, 81.2, 78.4, 72.0, 68.6, 67.8, 65.2, 60.3, 59.4, 27.5, 25.7; FAB HRMS calcd for $C_{22}H_{30}O_{11}Na$ $(M + Na)^+$: 493.1686; found $m/z = 493.1665$.

(5*R*,2'*S*,4'a*R*,7'*R*,7'a*S*)-Dihydro-5-[[[2-(methoxy)ethoxy]methoxy]methyl]-2,2-dimethyl-6'-oxo-2'-phenyl-spiro[1,3-dioxolane-4,7'(6'*H*)-[7a*H*]furo[3,2-*d*][1,3]dioxin]-7'a-carboxylic acid phenylmethyl ester (98). A solution of diol **97** (770 mg, 1.64 mmol) in dichloromethane (35 mL) was treated with CSA (95.0 mg, 0.410 mmol) and benzaldehyde dimethyl acetal (0.737 mL, 4.91 mmol). The reaction mixture was stirred at room temperature for 12 h and treated with more CSA (15.0 mg, 0.0646 mmol) and benzaldehyde dimethyl acetal (75.0 μL, 0.500 mmol). After stirring for 2 h, the same portions of CSA and benzaldehyde dimethyl acetal were added and this was repeated one more time. The reaction mixture was quenched with triethylamine (150 μL), diluted with ethyl acetate (150 mL), and washed with water (2 × 35 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 2:8 → 3:7) gave compound **98** (783 mg, 85%) as a colorless oil. $[\alpha]_D^{22} = +51.2$ (*c* 4.01 in $CHCl_3$, 75% *ee*); $R_f = 0.26$ (silica, ethyl acetate:petroleum ether 2:8); IR (thin film): $\tilde{\nu}_{max} = 2938, 2888, 1795, 1741, 1455, 1384, 1277, 1199, 1062, 909, 861\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.44–7.27$ (m, 10H, Ph), 5.35 (ABq, $J_{AB} = 12.0$ Hz, $\Delta\nu_{AB} = 66.6$ Hz, 2H, OCH_2Ph), 5.30 (s, 1H, C*H*Ph), 4.98 (dd, $J = 9.5$, 2.6 Hz, 1H, H-6), 4.91 (d, $J = 1.4$ Hz, 1H, H-3), 4.62 (ABq, $J_{AB} = 6.7$ Hz, $\Delta\nu_{AB} = 27.4$ Hz, 2H, OCH_2O), 4.51 (d, $J = 13.7$ Hz, 1H, CHC*H*H'O), 4.16 (dd, $J = 13.7$, 1.4 Hz, 1H, CHCH*H'*O), 4.12 (dd, $J = 11.3$, 9.5 Hz, 1H, H-7), 4.03 (dd, $J = 11.3$, 2.6 Hz, 1H, H'-7), 3.62–3.53 (m, 2H, $OCH_2CH_2OCH_3$), 3.40 (app.t, $J = 4.6$ Hz, 2H, CH_2OCH_3), 3.32 (s, 3H, OCH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.0$, 166.5, 136.3, 134.8, 129.9, 129.5, 129.3, 129.2, 128.7, 126.2, 112.2, 98.4, 96.0, 84.7, 83.2, 78.9, 72.6, 72.0, 68.7, 67.1, 66.0, 65.2, 59.3, 27.1, 25.2; FAB HRMS calcd for $C_{29}H_{34}O_{11}Cs$ $(M + Cs)^+$: 691.1156; found $m/z = 691.1186$.

(5*R*,2'*S*,4'a*R*,7'*R*,7'a*S*)-Dihydro-5-hydroxymethyl-2,2-dimethyl-6'-oxo-2'-phenyl-spiro[1,3-dioxolane-4,7'(6'*H*)-[7a*H*]furo[3,2-*d*][1,3]dioxin]-7'a-carboxylic acid phenylmethyl ester (99).

Method A: from triol 96. A solution of triol **96** (406 mg, 1.06 mmol) in dichloromethane (20 mL) was treated with CSA (60 mg, 0.26 mmol) and benzaldehyde dimethyl acetal (0.44 mL, 3.19 mmol). The reaction mixture was stirred at room temperature for 18 h and then poured into $NaHCO_3$ (30 mL) and extracted with ethyl acetate (4 × 40 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:2 → 2:1) gave alcohol **99** (394 mg, 79%) and unreacted triol **96** (25 mg, 6%) as colorless oils.

Method B: from benzylidene acetal 98. A solution of benzylidene acetal **98** (845 mg, 1.51 mmol) in acetonitrile (18 mL) at −40 °C was treated with sodium iodide (273 mg, 1.82 mmol) and TMSCl (0.230 mL, 1.82 mmol). The reaction mixture was stirred at −40 °C for 1 h, quenched with water (20 mL), and concentrated in vacuo. The reaction mixture was extracted with ethyl acetate (3 × 35 mL) and the combined organic extracts were washed with sodium thiosulfate (30 mL) and brine (30 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 3:7) gave

desired alcohol **99** (471 mg, 66%) and unreacted benzylidene **98** (221 mg, 26%) as an inseparable mixture of white foams. $[\alpha]_D^{22} = +82.5$ (c 2.52 in $CHCl_3$, >98% *ee*); $R_f = 0.65$ (silica, ethyl acetate:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 2927, 1794, 1741, 1384, 1276, 1189, 1061\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.45-7.28$ (m, 10H, Ph), 5.45 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.31 (s, 1H, C*H*Ph), 5.29 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 4.93 (br s, 1H, H-3), 4.88 (dd, $J = 5.5, 5.5$ Hz, 1H, H-6), 4.54 (dd, $J = 14.0, 1.5$ Hz, 1H, CHC*H*H'O), 4.15 (dd, $J = 13.5, 1.5$ Hz, 1H, CHCH*H*'O), 4.12–4.02 (m, 2H, CH_2OH), 1.44 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.5, 166.1, 135.4, 134.4, 129.7, 129.1, 128.8, 128.7, 128.5, 125.7, 111.3, 98.3, 84.4, 83.0, 79.8, 71.9, 68.3, 64.8, 60.1, 26.5, 24.7$; FAB HRMS calcd for $C_{25}H_{26}O_9Cs$ ($M + Cs$)$^+$: 603.0631; found $m/z = 603.0631$.

(5*S*,2'*S*,4'a*R*,7'*R*,7'a*S*)-5-Formyldihydro-2,2-dimethyl-6'-oxo-2'-phenyl-spiro[1,3-dioxolane-4,7'(6'*H*)-[7a*H*]furo[3,2-*d*][1,3]dioxin]-7'a-carboxylic acid, phenylmethyl ester (90). A solution of alcohol **99** (394 mg, 0.84 mmol) in dichloromethane (50 mL) was treated with Dess–Martin periodinane (1.14 g, 2.69 mmol). The reaction mixture was stirred at room temperature for 1 h, diluted with ether (100 mL), and poured into 25% $Na_2S_2O_3$/$NaHCO_3$ (100 mL). The aqueous phase was separated and extracted with ether (2 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ether:petroleum ether 3:7) gave the aldehyde **90** (355 mg, 90%) as a white foam. $[\alpha]_D^{22} = +81.4$ (c 1.03 in $CHCl_3$, >98% *ee*); $R_f = 0.19$ (silica, ether:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 2924, 1790, 1738, 1456, 1378, 1273, 1217, 1190, 1074\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.64$ (d, $J = 2.0$ Hz, 1H, CHO), 7.44–7.18 (m, 10H, Ph), 5.48 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.27 (s, 1H, C*H*Ph), 5.23 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 5.04 (d, $J = 2.0$ Hz, 1H, H-3), 4.97 (br s, 1H, H-6), 4.56 (d, $J = 13.5$ Hz, 1H, CHC*H*H'O), 4.18 (dd, $J = 13.5, 1.5$ Hz, 1H, CHCH*H*'O), 1.46 (s, 3H, CH_3), 1.39 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 191.8, 171.1, 165.5, 135.1, 134.1, 129.6, 129.0, 128.9, 128.8, 128.3, 125.8, 114.1, 98.5, 86.1, 82.4, 82.2, 72.1, 68.3, 64.8, 26.2, 25.0$; FAB HRMS calcd for $C_{25}H_{24}O_9Cs$ ($M + Cs$)$^+$: 601.0475; found $m/z = 601.0470$.

Data for **[3a*R*,7a*S*,8*R*,10a*R*]-8-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]methyl]dihydro-2,2-dimethyl-10-oxo-10*H*-1,3-dioxolo[4,5-*e*]furo[3,4-*d*][1,3]dioxepin-7a(8*H*)-carboxylic acid phenylmethyl ester (100)**: $R_f = 0.76$ (silica, ethyl acetate:petroleum ether 1:2); IR (thin film): $\tilde{\nu}_{max} = 3229, 3040, 2930, 2856, 1791, 1745, 1588, 1460, 1428, 1379, 1271, 1214, 1175, 1106, 1058\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.80-7.60$ (m, 4H, Ph), 7.50–7.20 (m, 11H, Ph), 5.32 (d, $J = 6.0$ Hz, 1H, OC*H*H'O), 5.19–5.12 (m, 3H, CH_2Ph and H-3 or H-6), 5.02 (dd, $J = 5.0, 5.0$ Hz, 1H, H-3 or H-6), 4.71 (d, $J = 6.0$ Hz, 1H, OCH*H*'O), 4.31 (dd, $J = 13.5, 6.0$ Hz, 1H, CH_2), 4.06 (dd, $J = 11.5, 4.0$ Hz, 1H, CH_2), 4.02 (dd, $J = 13.5, 4.0$ Hz, 1H, CH_2), 3.96 (dd, $J = 11.5, 7.0$ Hz, 1H, CH_2), 1.44 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.03 (s, 9H, $SiC(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.1, 165.1, 135.5, 135.4, 130.0, 129.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.5, 127.4, 112.6, 94.4, 86.0, 83.9, 83.7, 79.2, 67.9, 67.5, 61.7, 29.6, 26.6, 26.0, 25.0$; FAB HRMS calcd for $C_{35}H_{40}O_9SiNa$ ($M + Na$)$^+$: 655.2339; found $m/z = 655.2330$.

[5*R*,5(1*R*),2'*S*,4'a*R*,7'*R*,7'a*S*]-Dihydro-5-[hydroxy(2-methyl-1,3-dithian-2-yl)methyl]2,2-dimethyl-6'-oxo-2'-phenyl-spiro[1,3-dioxolane-4,7'(6'*H*)-[7a*H*]furo[3,2-*d*][1,3]dioxin]-7'a-carboxylic acid phenylmethyl ester (101a) and [5*R*,5(1*S*),2'*S*,4'a*R*,7'*R*,7'a*S*]-dihydro-5-[hydroxy(2-methyl-1,3-dithian-2-yl)methyl]-2,2-dimethyl-6'-oxo-2'-phenyl-spiro[1,3-dioxolane-4,7'(6'*H*)-[7a*H*]furo[3,2-*d*][1,3]dioxin]-7'a-carboxylic acid phenylmethyl ester (101b). A solution of 2-methyl-1,3-dithiane (0.78 mL, 6.51 mmol) in THF (100 mL) at −40 °C was treated with *n*-butyllithium (1.60 M in hexane, 3.95 mL, 6.32 mmol). The reaction mixture was warmed to −25 °C, stirred for 1.5 h, cooled to −78 °C, treated with a solution of the aldehyde **90** (1.18 g, 2.54 mmol) in THF (20 mL), stirred at −78 °C for 5 min, quenched with a solution of acetic acid in THF (0.5 M in THF, 14 mL, 7 mmol), and warmed to room temperature. The reaction mixture was diluted with NH_4Cl (100 mL) and ether (150 mL). The aqueous phase was separated and extracted with ether (2 × 150 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (silica, ethyl acetate:petroleum ether 1:8 → 1:5)) gave dithiane **101a** (687 mg, 47%) and dithiane **101b** (242 mg, 16%) as colorless oils.

Data for **101a**: $[\alpha]_D^{22} = +46.3$ (c 0.37 in $CHCl_3$, 75% *ee*); $R_f = 0.29$ (silica, ether:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3556, 2928, 1796, 1742, 1453, 1383, 1219, 1051, 1033\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.43-7.32$ (m, 10H, Ph), 5.65 (s, 1H, C*H*Ph), 5.52 (s, 1H, H-6), 5.36 (m, 2H, CH_2Ph), 4.96 (s, 1H, H-3), 4.53–4.50 (m, 2H, OH and CHC*H*H'O), 4.51 (s, 1H, H-7), 4.04 (d, $J = 13.0$ Hz, 1H, CHCH*H*'O), 2.32–1.85 (m, 6H, CH_2), 1.44 (s, 6H, CH_3 and CH_3), 1.38 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.4, 166.0, 136.2, 134.2, 129.7, 129.0, 128.9, 128.7, 128.4, 126.4, 113.2, 98.8, 86.6, 82.5, 76.2, 72.7, 68.7, 65.1, 64.9, 52.8, 26.6, 26.3, 25.6, 24.9, 24.0, 22.5$; FAB HRMS calcd for $C_{30}H_{34}O_9S_2Cs$ ($M + Cs$)$^+$: 735.0697; found $m/z = 735.0723$.

Data for **101b**: $[\alpha]_D^{22} = +37.8$ (c 1.49 in $CHCl_3$, 75% *ee*); $R_f = 0.37$ (silica, ether:petroleum ether 1:1); IR (thin film): $\tilde{\nu}_{max} = 3556, 2928, 1797, 1740, 1455, 1383, 1254, 1219, 1064\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.46-7.37$ (m, 10H, Ph), 5.48 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.39 (s, 1H, C*H*Ph), 5.24 (d $J = 12.0$ Hz, 1H, CH*H*'Ph), 5.07 (d, $J = 9.0$ Hz, 1H, H-6), 4.91 (s, 1H, H-3), 4.75 (dd, $J = 9.0, 5.0$ Hz, 1H, H-7), 4.59 (d, $J = 14.0$ Hz, 1H, CHC*H*H'O), 4.21 (dd, $J = 14.0, 1.5$ Hz, 1H, CHCH*H*'O), 3.24 (m, 2H, CH_2), 2.94 (d, $J = 5.0$ Hz, 1H, C7-OH), 2.45 (m, 2H, CH_2), 1.97–1.73 (m, 2H, CH_2), 1.44 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.3, 165.9, 135.3, 134.1, 129.7, 129.1, 128.9, 128.7, 128.5, 126.5, 125.2, 111.3, 97.7, 85.1, 83.7, 81.0, 79.1, 71.7, 68.2, 64.6, 50.7, 29.6, 28.9, 26.9, 26.4, 25.8, 24.3, 24.2$; FAB HRMS calcd for $C_{30}H_{34}O_9S_2Cs$ ($M + Cs$)$^+$: 735.0697; found $m/z = 735.0728$.

[4*R*,4(1*R*),5*R*,8*R*,9*S*]-9-Hydroxy-8-hydroxymethyl-4-[hydroxy(2-methyl-1,3-dithian-2-yl)methyl]-2,2-dimethyl-6-oxo-1,3,7-trioxaspiro[4.4]nonan-9-carboxylic acid phenylmethyl ester (102). A solution of dithiane **101a** (82 mg, 0.14 mmol) in dichloromethane (20 mL) was treated with ethanethiol (1.3 mL) and $Zn(OTf)_2$ (200 mg, 0.55 mmol). The reaction mixture was placed in an ultrasound bath for 8 h and then diluted with dichloromethane (50 mL), washed with NH_4Cl (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography gave the triol **102** (62.1 mg, 89%) as a colorless oil. $[\alpha]_D^{22} = +44.8$ (c 0.67 in $CHCl_3$, 75% *ee*); $R_f = 0.45$ (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max} = 3456, 2934, 1787, 1738, 1383, 1278, 1218, 1186, 1081, 891\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.39-7.36$ (m, 5H, Ph), 6.43 (s, 1H, C4-OH), 5.67 (s, 1H, H-6), 5.25 (ABq, $J_{AB} = 12.2$ Hz, $\Delta\nu_{AB} = 77.7$ Hz, 2H, CH_2Ph), 5.12 (dd, $J = 4.7, 4.6$ Hz, 1H, H-3), 4.48 (d, $J = 6.1$ Hz, 1H, H-7), 4.04 (ddd, $J = 12.6, 8.1, 4.7$ Hz, 1H, C*H*H'OH, 3.98 (ddd, $J = 12.6, 8.1, 4.6$ Hz, 1H, CH*H*'OH), 3.81 (d, $J = 6.1$ Hz, 1H, C7-OH), 2.98–2.91 (m, 2H, SC*H*H'CH_2C*H*H'S), 2.67–2.63 (m, 2H, SCH*H*'CH_2CH*H*'S), 2.21 (br dd, $J = 8.1, 8.1$ Hz, 1H, CH_2OH), 2.12–2.09 (m, 1H, SCH_2C*H*H'CH_2S), 1.89–1.81 (m, 1H, SCH_2CH*H*'CH_2S), 1.55 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.5, 169.5, 134.8, 129.3, 129.2, 128.8, 112.2, 85.1, 82.2, 81.8, 77.6, 68.8, 67.0, 60.5, 53.0, 26.9, 26.7, 26.3, 25.7, 24.4, 24.0$; FAB HRMS calcd for $C_{23}H_{30}O_9S_2Cs$ ($M + Cs$)$^+$: 647.0229; found $m/z = 647.0257$.

(3a*R*,4*R*,6a*S*,7*R*,9a*R*)-Dihydro-4,5-dihydroxy-7-hydroxymethyl-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-carboxylic acid phenylmethyl ester (103). A solution of the triol **102** (230 mg, 0.45 mmol) in THF (20 mL) was treated with $CaCO_3$ (85 mg, 0.85 mmol) and aqueous $Hg(ClO_4)_2$ (0.20 M in H_2O, 4.0 mL, 0.80 mmol). The reaction mixture was stirred at room temperature for 0.5 h, diluted with ether (50 mL), and filtered through a short column of silica to give the lactol **103** (160 mg, 81%) as a colorless oil. $R_f = 0.20$ (silica, ethyl acetate:petroleum ether 2:3); IR (thin film): $\tilde{\nu}_{max} = 3452, 2926, 1774, 1742, 1377, 1215, 1090, 1085\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.42-7.30$ (m, 5H, Ph), 5.30–5.10 (m, 3H, CH_2Ph, H-3), 4.67 (d, $J = 6.0$ Hz, 1H, H-6), 4.21 (dd, $J = 10.5, 6.0$ Hz, 1H, H-7), 4.19 (s, 1H, CH_2OH), 4.09–3.98 (m, 2H, $CHCH_2OH$), 2.35 (d, $J = 10.5$ Hz, 1H, C7-OH) 1.57 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.5, 167.3, 134.4, 128.6, 128.5, 128.0, 113.4, 98.6, 86.4, 83.0, 82.2, 81.3, 80.4, 73.7, 68.1, 60.0, 25.9, 24.9, 23.8$; FAB HRMS calcd for $C_{20}H_{24}O_{10}Cs$ ($M + Cs$)$^+$: 557.0424; found $m/z = 557.0425$.

(3a*R*,4*R*,6a*S*,7*R*,9a*R*)-Dihydro-4-hydroxy-7-hydroxymethyl-5-methoxy-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-carboxylic acid phenylmethyl ester (104). A solution of lactol **103** (156 mg, 0.35 mmol) in 2% HCl/MeOH (2 mL) was stirred at room temperature for 6 h. The reaction mixture was quenched with triethylamine (0.1 mL) and the solvent was concentrated in vacuo to give a crude oil. Purification by flash column chromatography gave the methyl glycoside **104** (127 mg, 82%) and unreacted **103** (17 mg, 11%). $R_f = 0.20$ (silica, ethyl acetate:petroleum ether 3:2); IR (thin film): $\tilde{\nu}_{max} = 3508, 2946, 2874, 1790, 1748, 1456, 1379, 1215, 1035\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.42-7.30$ (m, 5H, Ph), 5.26 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.18 (d, $J = 12.5$ Hz, 1H, CH*H*'Ph), 5.17 (dd, $J = 7.0, 4.5$ Hz, 1H, H-3), 4.63 (d, $J = 6.5$ Hz, 1H, H-6), 4.35 (dd, $J = 10.5, 6.5$ Hz, 1H, H-7), 4.09–3.97 (m, 2H, CH_2OH), 3.20 (s, 3H, OCH_3), 2.12 (d, $J = 10.5$ Hz, 1H, C7-OH), 1.50 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.5, 167.2, 134.3, 128.7, 128.2, 113.3, 101.9, 82.5, 81.8, 81.3, 79.4, 74.4, 68.1, 48.7, 28.5, 26.0, 24.9, 19.1$; FAB HRMS calcd for $C_{21}H_{26}O_{10}Cs$ ($M + Cs$)$^+$: 571.0580; found $m/z = 571.0587$.

(3a*R*,4*R*,6a*S*,7*S*,9a*R*)-7-Formyldihydro-4-hydroxy-5-methoxy-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-carboxylic acid phenylmethyl ester (105). A solution of methyl glycoside **104** (42 mg, 93 μmol) in dichloromethane (2.5 mL) was treated with activated 3 Å molecular sieves (50 mg), pre-dried Celite (40 mg), and PCC (199 mg, 0.93 mmol). The reaction mixture was stirred at room temperature for 2.5 h and then filtered through a short column of silica. Purification by preparative TLC gave the aldehyde **105** (27.2 mg, 65%). NB. Aldehyde **105** exists partly in the hydrated form. $R_f = 0.8$ (silica, ethyl acetate:petroleum ether 4:1); IR (thin film): $\tilde{\nu}_{max} = 3486, 2993, 2945, 1805, 1747, 1380, 1271, 1186, 1086, 1038\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 9.65$ (s, 1H, CHO), 7.43–7.33 (m, 5H, Ph), 5.58 (s, 0.5H, H-3), 5.33 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.23 (d, $J = 12.0$ Hz, 1H, CH*H*'Ph), 5.21 (s, 0.2H, H-3), 4.92 (d, $J = 7.0$ Hz, 0.3H, $CH(OH)_2$), 4.66 (d, $J = 7.0$ Hz, 0.7H, H-6), 4.64 (d, $J = 6.5$ Hz, 0.3H, H-6), 4.32 (dd, $J = 10.0, 6.5$ Hz, 0.7H, H-7), 4.27 (dd, $J = 10.0, 7.0$ Hz, 0.3H, H-7), 3.20 (s, 1H, OCH_3), 3.12 (s, 2H, OCH_3), 2.17 (d, $J = 10.0$ Hz, 1H, C7-OH), 1.55 (s, 2H, CH_3), 1.50 (s, 1H, CH_3), 1.42 (s, 3H, CH_3), 1.33 (s, 2H, CH_3), 1.32 (s, 1H, CH_3); FAB HRMS calcd for $C_{21}H_{25}O_{10}$ ($M + H$)$^+$: 437.1448; found $m/z = 437.1455$.

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(3a*R*,4*R*,6a*S*,7*S*,9a*R*)-Dihydro-4-hydroxy-5-methoxy-2,2,5-trimethyl-9-oxo-5*H*,9*H*-1,3-dioxolo[4,5-*c*]furo[3,4-*b*]pyran-6a,7(7*H*)-dicarboxylic acid bis(phenylmethyl) ester (107). A solution of aldehyde **105** (15 mg, 0.033 mmol) in *t*-butanol (0.35 mL) and water (75 μL) at 0 °C was treated with a solution of 2-methyl-2-butene (2.0 M in THF, 0.15 mL, 0.30 mmol), $NaClO_2$ (9 mg, 0.10 mmol) and NaH_2PO_4 (5.7 mg, 0.048 mmol). The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction mixture was poured into aqueous HCl (2.0 N, 1 mL) and extracted with ethyl acetate. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give the acid **106** as a crude oil. The acid **106** was dissolved in toluene (3 mL), treated with DCBI (17 mg, 0.054 mmol) and heated at 110 °C for 35 min. The reaction mixture was concentrated in vacuo to give a crude oil. Purification by preparative TLC gave benzyl ester **107** (17 mg, 92%, 2 steps). $R_f = 0.50$ (silica, ethyl acetate:petroleum ether 3:7); IR (thin film): $\tilde{\nu}_{max} = 3302, 2924, 2868, 1784, 1725, 1377, 1273, 1051\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.35-7.26$ (m, 10H, Ph), 5.70 (s, 1H, H-3), 5.32 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.13 (d, $J = 12.0$ Hz, 1H, C*H*H'Ph), 5.11 (d, $J = 12.0$ Hz, 1H, CH*H'*Ph), 5.08 (d, $J = 12.0$ Hz, 1H, CH*H'*Ph), 4.63 (d, $J = 7.0$ Hz, 1H, H-6), 4.22 (dd, $J = 7.0$, 5.5 Hz, 1H, H-7), 3.08 (s, 3H, OCH_3), 2.12 (d, $J = 5.5$ Hz, 1H, C7-OH), 1.49 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.1, 166.4, 164.4, 134.7, 134.2, 128.6, 128.4, 113.5, 101.8, 82.3, 81.1, 80.0, 79.6, 74.5, 48.6, 26.1, 24.8, 18.7$; FAB HRMS calcd for $C_{28}H_{30}O_{11}Cs$ $(M + Cs)^+$: 675.0842; found $m/z = 675.0844$.

(3a*R*,5a*R*,8*S*,9a*S*,12*R*,12a*R*)-Tetrahydro-2,2-dimethyl-12-(2-methyl-1,3-dithian-2-yl)-8-phenyl-4*H*,10*H*-1,3-dioxolo[4′,5′]pyrano[3′,4′:3,4]furo[3,2-*d*][1,3]dioxin-4,10-dione (108). $[\alpha]_D^{22} = 0.00$ (*c* 0.79 in $CHCl_3$); $R_f = 0.46$ (silica, ethyl acetate:petroleum ether 1:2); IR (thin film): $\tilde{\nu}_{max} = 2992, 2934, 1805, 1770, 1457, 1377, 1189, 1107\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.43-7.31$ (m, 5H, Ph), 5.76 (s, 1H, C*H*Ph), 5.47 (d, $J = 2.0$ Hz, 1H, H-6), 5.40 (d, $J = 2.0$ Hz, 1H, H-7), 4.97 (s, 1H, H-3), 4.57 (d, $J = 14.0$ Hz, 1H, CHC*H*H'O), 4.47 (d, $J = 14.0$ Hz, 1H, CHCH*H'*O), 2.57–2.41 (m, 4H, $SCH_2CH_2CH_2S$), 1.80–1.76 (m, 2H, $SCH_2CH_2CH_2S$), 1.70 (s, 3H, CH_3), 1.46 (s, 6H, CH_3 and CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.3, 163.6, 135.3, 130.1, 128.4, 126.1, 114.7, 98.7, 97.5, 85.2, 79.5, 77.3, 73.3, 72.5, 67.8, 64.9, 26.7, 26.6, 26.4, 23.8, 23.4$; FAB HRMS calcd for $C_{23}H_{26}O_8S_2Cs$ $(M + Cs)^+$: 627.0123; found $m/z = 627.0135$.

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