Total Synthesis of Zaragozic Acid A (Squalestatin S1). Synthesis of the Relay Compound

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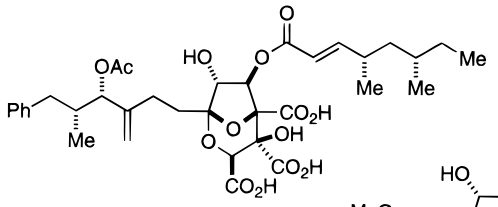
Received August 7, 1996[⊗]

Compound **2** has been prepared from the 1,6-anhydropyranohexose **3**. The key process for elaborating the 1,7-dioxabicyclo[3.2.1]octane core of the zaragozic acids is addition of an organometallic reagent to lactone **6** and treatment of the resulting 1,2,3-trihydroxy-6-oxo ethylene acetal with acid. Use of the cerium(III) reagent of 4-bromo-1-butene in this process provided **7** in excellent yield, unaccompanied by the isomeric 1,6-anhydropyranose isomer. The remaining two carboxy groups of the zaragozic acid core were added by addition of the lithium enolate of **8** to formaldehyde, to obtain **9**, and cerium(III)-mediated addition of vinyllithium to ketone **10**. The latter addition was shown by 2D ^{1}H NMR experiments to provide the relative configuration found in the zaragozic acids. Similar stereoselective additions were observed with 2-furyllithium and (5-methyl-2-furyl)-lithium, but the resulting adducts are resistant to ozonolysis. The synthesis of **2** completes a total synthesis of zaragozic acid A (squalestatin S1) (**1**).

In the preceding article, we reported the interconversion of the natural squalene synthase inhibitor zaragozic acid A (squalestatin S1, **1**) with the dimethyl acetal tri-*tert*-butyl ester **2**.[1] In this article, we report the synthesis of **2** from methyl α-D-glucopyranoside, thus completing a total synthesis of **1**.



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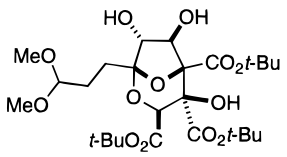

2

Our plan for the synthesis of **2**, involving rearrangement of a suitably constructed hexose to a 1,6-anhydrofuranose, has been previously discussed, and model studies that delineate the structural requirements and reaction conditions for such a rearrangement have been described.[2] For the actual synthesis of intermediate **2**, we started with 1,6-anhydro-2,3-di-*O*-benzyl-*β*-D-ribohexopyranos-4-ulose (**3**), available in five steps and 48% overall yield from methyl α-D-glucopyranoside.[3] As shown in Scheme 1, ketone **3** undergoes the Tamao reaction[4] in a highly stereoselective fashion to give diol **4**, which is quantitatively protected as the *tert*-butyldiphenylsilyl ether (**5**).[5,6] Compound **5** reacts with trifluoroacetic acid (TFA) in acetic anhydride to give a triacetate, resulting from the opening of the anhydropyranose and the esterification of the three hydroxy groups. The crude triacetate is saponified by treatment with sodium methoxide in methanol and the resulting mixture of triols treated with acetone and *p*-toluenesulfonic acid to provide the 5,6-acetonide of a hexofuranose. The hemiacetal is converted into the desired lactone **6** by oxidation with pyridium dichromate (PDC).[7] Addition of the Grignard reagent prepared from homoallyl bromide and magnesium leads to elimination of the benzyloxy group *β* to the carbonyl. This problem was circumvented by transmetalation to the cerium reagent.[8] Although the addition is very slow at −78 °C, monoaddition can be accomplished by keeping the solution at −50 °C. Above this temperature, substantial amounts of bis-addition are observed. The crude addition product is treated with 2 N hydrochloric acid in tetrahydrofuran to obtain the disubstituted 1,6-anhydrofuranose **7** as the only product isolated in 74% yield. Oxidation of alcohol **7** with trifluoroacetic anhydride and dimethyl sulfoxide affords ketone **8** in 94% yield.

The successful rearrangement of **6** to **7** gave us the essential 1,6-anhydrofuranose core of the zaragozic acids, equipped with two bridgehead substituents, one destined to be converted into the C1 side chain and the other representing one of the three carboxy groups. It remained to add the other two one-carbon units, representing the other two carboxy groups of the zaragozic acids. A good deal of experimentation[9] eventually resulted in a protocol wherein ketone **8** is metalated by reaction with *tert*-butyllithium in THF and the resulting lithium enolate is treated with 1 equiv of paraformaldehyde. This procedure gives aldol **9** in 57% yield, along with 39% of recovered ketone **8**. Attempts to achieve higher conversion by using excess paraformaldehyde resulted in the formation of diol monoformate esters, resulting from intramolecular Tishchenko reduction.[10] The imperfect conversion is of little consequence, because **8** and **9** are

[⊗] Abstract published in *Advance ACS Abstracts,* December 1, 1996.

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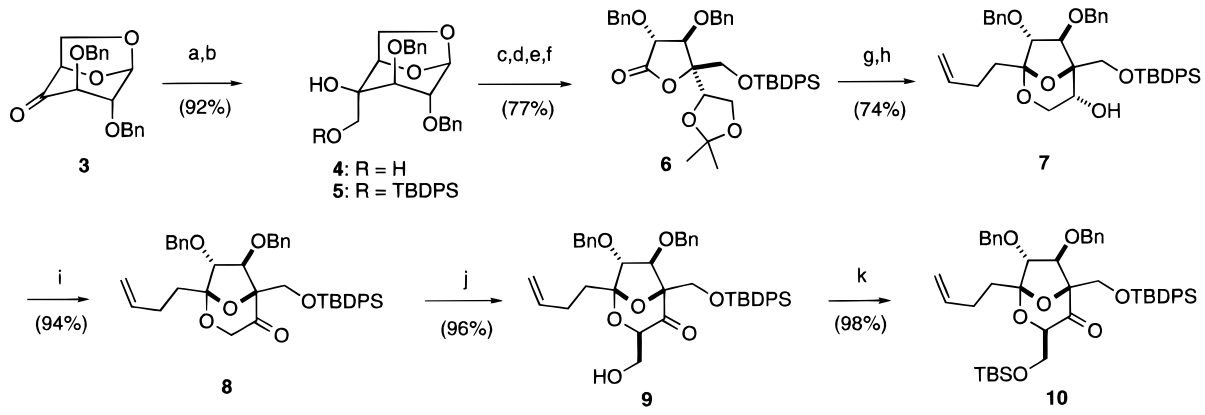
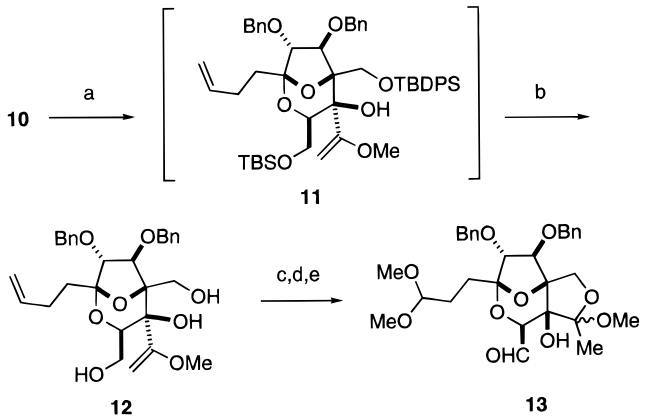
S0022-3263(96)01534-4 CCC: $12.00

Scheme 1[a]



[a] Reagents and conditions: (a) (i) $Me_2(i\text{-}PrO)SiCH_2MgCl$, THF, −78 °C; (ii) H_2O_2, MeOH, THF, $NaHCO_3$; (b) $t\text{-}BuPh_2SiCl$, imidazole, DMF; (c) TFA, Ac_2O; (d) NaOMe, MeOH; (e) acetone, H^+; (f) PDC, sieves, CH_2Cl_2; (g) $CH_2{=}CHCH_2CH_2CeCl_2$, THF, −78 °C; (h) HCl, H_2O, THF; (i) DMSO, TFAA, Et_3N, CH_2Cl_2; (j) *t*-BuLi, 1 equiv of CH_2O in THF; (k) $t\text{-}BuMe_2SiCl$, imidazole, DMF.

Scheme 2[a]



[a] Reagents and conditions: (a) $CH_2{=}C(Li)OMe$, THF; (b) TBAF, THF; (c) (i) O_3, CH_2Cl_2; (ii) Me_2S; (d) $(MeO)_3CH$, MeOH, PPTS; (e) Dess−Martin reagent.

very easy to separate by chromatography on silica gel. Silylation of the hydroxy group provided **10**.

For introduction of the final carbon, we had to add some acyl anion equivalent from the bottom face of the carbonyl group of ketone **10**. Our first candidate for a carboxy equivalent was lithiated methyl vinyl ether.[11,12] Addition proceeded smoothly to give an adduct, presumably **11** (Scheme 2). Some desilylation occurred, but the total product was desilylated by reaction with tetrabutylammonium fluoride to give **12**. Ozonolysis of this material gave a product that contained an aldehyde functionality, but clearly was not a methyl ester. Treatment of this material sequentially with trimethyl orthoformate in methanol in the presence of pyridinium *p*-toluenesulfonate and then with the Dess−Mardin periodinane[13] gave a product that was assigned structure **13** on the basis of its ^{1}H NMR spectrum. In particular, a sharp, one-proton singlet with δ = 4.72 ppm was attributed to the proton adjacent to the aldehyde. The aldehyde proton also appeared as a sharp singlet with δ = 9.65 ppm. In the alternative cyclic acetal, having the aldehyde at the bridgehead, the C3 proton would be a double doublet.

Because the addition to **10** appeared to be rather stereoselective, we sought other acyl anion equivalents that could be added as lithium reagents. The next species studied was 2-lithiofuran,[14] which adds to **10** in almost quantitative yield to give a single tertiary alcohol (Scheme 3). After desilylation, the resulting triol was treated sequentially with the Dess−Martin reagent[13] to obtain a dialdehyde that was oxidized to the diacid with sodium chlorite.[15] Treatment of the crude diacid with *O-tert*-butyl-*N*,*N*′-diisopropylisourea[16] provided **16** in 64% yield. However, ozonolysis of **16** gave a rather complex mixture of products. It was clear from the ^{1}H NMR spectrum of the crude product that both the terminal vinyl group and the furan ring had been oxidized, but we were unable to isolate a single product.

To improve our change of success in the ozonolysis step, 2-methylfuran was investigated as the acyl anion equivalent. It was hoped that ozonolysis of a more substituted and more electron-rich furan would be possible. The same reaction sequence used for **16** was repeated using 2-lithio-5-methylfuran (Scheme 3). The addition provided alcohol **17** in 87% yield. Desilylation led to triol **18** (83% yield), which was oxidized to the dialdehyde and thence to di-*tert*-butyl ester **19** in the modest but unoptimized yield of 30%. Upon reaction with ozone followed by reduction of the ozonides with triphenylphosphine, a new product was isolated in 88% yield. This material is believed to be enol acetate **20** because of its infrared and ^{1}H NMR spectra. The IR spectrum showed the two *tert*-butyl esters at 1725 cm^{-1}, the enol acetate carbonyl at 1759 cm^{-1}, and the enol acetate double bond at 1626 cm^{-1}. The ^{1}H NMR spectrum also showed the presence of the enol acetate with a resonance at 7.51 ppm which was coupled to the proton of the hemiacetal at 6.41 ppm with a coupling constant of 7.5 Hz. Moreover, it was determined that the product possessed three carboxylate groups from analysis of the ^{13}C NMR spectrum which had resonances at 164.69, 165.53, and 167.56 ppm. Compound **20** presumably arises from ozonolytic cleavage of the C2−C3 bond of the furan ring, which provides the

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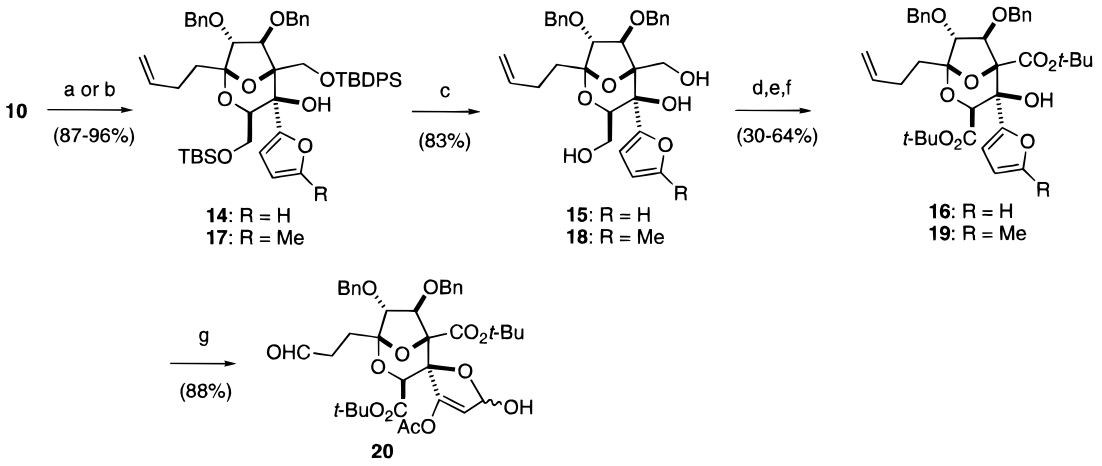
Scheme 3[a]



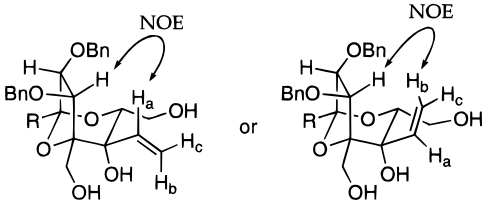
[a] Reagents and conditions: (a) 2-furyllithium, THF, −78 °C; (b) (5-methyl-2-furyl)lithium, THF, −78 °C; (c) TBAF, THF; (d) Dess−Martin periodinane, CH_2Cl_2; (e) $NaClO_2$; (f) (*t*-BuO)(*i*-PrNH)C=N(*i*-Pr); (g) O_3, MeOH, CH_2Cl_2.

observed enol acetate and leaves an α,β-unsurated aldehyde. Isomerization of the double bond from *Z* to *E*, followed by formation of the cyclic hemiacetal structure, gives **20**. Prolonged ozonolysis of **20** did not provide the desired carboxylic acid, and this approach was abandoned.

It was eventually decided to use a simple vinyl group as a synthon for the third carboxylic acid. We had previously tried to avoid the use of an unsubstituted vinyl group for several reasons. First, we thought the alkene of the C1 side chain and the vinyl group at C4 would have to be differentiated, resulting in a longer synthesis. Second, the use of a simple vinyl group would necessitate an additional oxidation because ozonolysis of the double bond would leave us one oxidation state lower than desired; this would also add an additional step to the synthesis. However, during the course of our work we became aware of the experience of Carreira and Dubois in their synthesis of zaragozic acid C.[17] These workers introduced the carboxy group in question by successful ozonolysis of a vinyl group, which had been obtained by addition of an acetylene anion followed by partial reduction of the alkyne to the alkene. Because of the relative difficulty we had with ozonolysis of the furyl groups, we thought there was a good chance the two vinyl groups would cleave at sufficiently different rates to make this approach viable.

Because of the level of stereocontrol achieved with lithiated vinyl ethers and furans, addition of vinyllithium to ketone **10** was investigated first. Vinyllithium was generated by addition of methyllithium to tetravinylstannane[18] and added to ketone **10**. Although the reaction provided the desired allylic alcohol as a single diastereoisomer, the product could not be separated from residual tin derivatives. Addition of vinylmagnesium bromide was next attempted, but the reaction was extremely slow. However, transmetalation of vinylmagnesium bromide to the cerium reagent prior to addition to ketone **10** provided the desired product, which appeared to be slightly unstable on silica gel. The crude addition product was treated with tetrabutylammonium fluoride to provide triol **21** in 88% overall yield from ketone **10** (Scheme 4).

The high level and sense of diastereoselection achieved in this addition was somewhat surprising, as Carreirra had reported that addition of nucleophiles to a similar substrate leads to diastereoisomeric mixtures, usually favoring the undesired product.[19] Therefore the relative configuration of the newly created C4 stereocenter was verified using several NMR experiments. A combination of 2D NMR experiments allowed the assignment of all carbon and hydrogen atoms of the molecule. COSY[20] and HMBC[21] experiments conclusively located the different protons of the vinyl group and the two methine protons adjacent to the benzyloxy groups. A NOESY[22] experiment showed a definite correlation between one of the two benzyloxy methines and one of the vinyl hydrogens, either H_a or H_b, which have almost the same chemical shift. Regardless of which vinyl hydrogen correlates with the benzyloxy methine, the relative configuration at C4 must be that desired for conversion into zaragozic acid:



21

With the final carbon in place, all that remained was the elaboration of the three *tert*-butyl esters, ozonolysis of the C1 side chain, cleavage of the two benzyl ethers, and formation of the dimethyl acetal. As shown in Scheme 4, the two primary hydroxy groups of triol **21** were oxidized to dialdehyde **22**. As reported by Meyer and Schreiber, addition of a catalytic amount of water to the solution containing triol **21** and the Dess−Martin periodinane increased the rate of the reaction.[23] Oxidation to the dicarboxylic acid **22** was accomplished with sodium chlorite,[15] and this oxidation was followed by bis-

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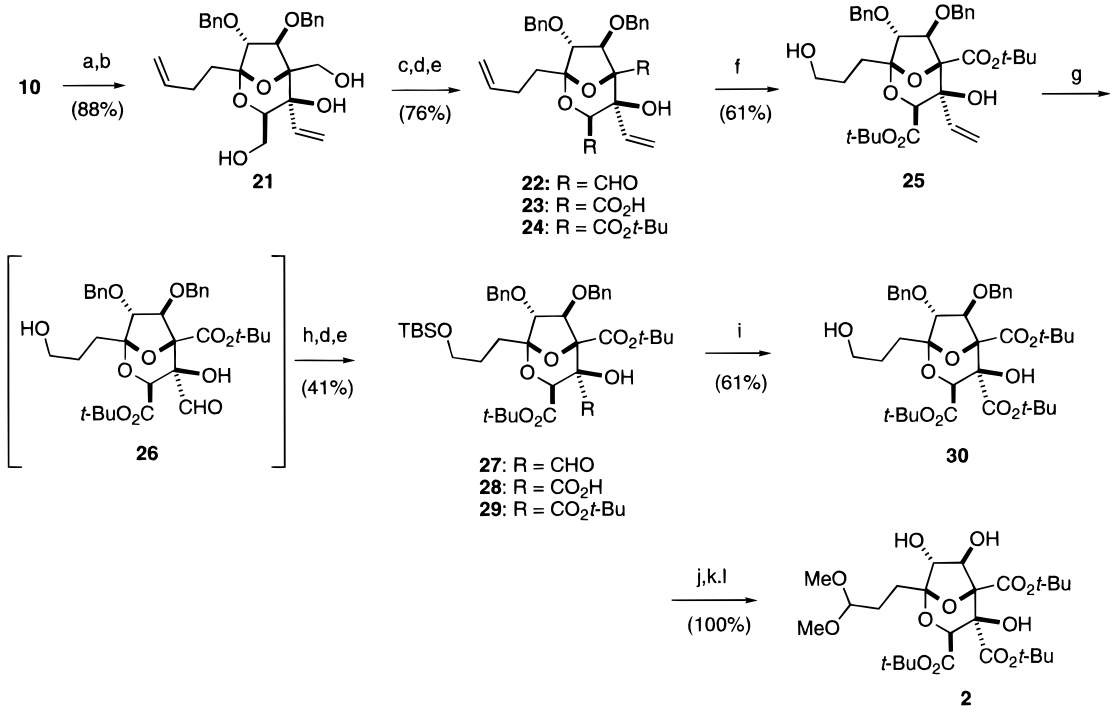
(23) Meyer, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549.

Scheme 4[a]



[a] Reagents and conditions: (a) CH_2=CHMgBr, $CeCl_3$; (b) TBAF, THF; (c) Dess−Martin, CH_2Cl_2; (d) $NaClO_2$; (e) (*t*-BuO)(*i*-PrNH)C=N(*i*-Pr); (f) (i) O_3; (ii) $NaBH_4$; (g) O_3; (h) *t*-$BuMe_2SiCl$, imidazole, DMF; (i) TBAF, THF; (j) Dess−Martin; (k) $(MeO)_3CH$, MeOH, PPTS; (l) H_2, $Pd(OH)_2$, MeOH.

esterification using *O-tert*-butyl-*N*,*N*′-diisopropylisourea[16] to provide diester **24** in 76% overall yield from triol **21**. Monoozonolysis of the alkene of the C1 side chain of **24** was achieved by carefully adding a saturated solution of ozone in methylene chloride. Reduction of the ozonide with sodium borohydride afforded the desired primary alcohol **25** in 61% yield.

We first attempted to complete the preparation of the relay compound **2** without protection of the primary hydroxy group of the C1 side chain. Allylic alcohol **25** was ozonized without incident to provide an aldehyde that was further oxidized to a carboxylic acid. However, conversion to the tri-*tert*-butyl ester **30** was complicated by concomitant formation of the *tert*-butyl ether of the primary alcohol. The solution to this problem was obviously to protect the primary alcohol. Therefore, after the ozonolysis of the more reactive double bond of **25**, the primary alcohol **26** was protected as a *tert*-butyldimethylsilyl ether (**27**) and the aldehyde was converted to the *tert*-butyl ester by sodium chlorite oxidation and esterification of the resulting acid **28** with *O-tert*-butyl-*N*,*N*′-diisopropylisourea. Compound **29** was obtained in 41% yield from **25**. The silyl ether was cleaved using tetrabutylammonium fluoride to provide diol **30** in 61% yield. The primary hydroxyl group was oxidized with the Dess−Martin periodinane to afford an aldehyde which was allowed to react with trimethyl orthoformate in acidic methanol prior to hydrogenolysis of the two benzyl protecting groups. This reaction sequence provided the relay compound **2** in quantitative yield (Scheme 4).

The synthetic material was identical in almost all respects to the material prepared by degradation of zaragozic acid A/squalestatin S1 (**1**).[1] The only difference observed was the chemical shift of the two hydroxyl groups at C6 and C7 in the ^1H NMR spectrum. The successful synthesis of **2** from **3** completes a total synthesis of zaragozic acid A (**1**), since **2** has been converted into the natural product.[1]

Experimental Section

General. Unless otherwise noted, starting materials were obtained from commercial suppliers and used without further purification. Diethyl ether and THF were distilled from Na/benzophenone ketyl. Benzene, CH_2Cl_2, Et_3N, *i*-Pr_2NH, *t*-BuOH, and toluene were distilled from CaH_2. Furan and 2-methylfuran were distilled from Na immediately prior to use. Acetic anhydride (Ac_2O) and trifluoroacetic anhydride (TFAA) were distilled from P_2O_5. All reactions involving oxygen or moisture sensitive compounds were performed under a dry N_2 atmosphere. Alkyllithiums were titrated with diphenylacetic acid[24] and Grignard reagents were titrated with a 1.0 M solution of 2-butanol in xylene using 1,10-phenanthroline as an indicator.[25] Organic extracts were dried with $MgSO_4$ and concentrated with a rotary evaporator under reduced pressure (aspirator). Silica gel chromatography was carried out with ICI SiliTech 32-63 D A silica gel according to Still's procedure.[26] Thin layer chromatography (TLC) was performed with Merck F-254 TLC plates. Melting points were measured in open capillary tubes. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$. IR spectra were measured as thin films on NaCl plates unless otherwise indicated. Optical rotations were measured at rt.

1,6-Anhydro-2,3-di-*O*-benzyl-4-(hydroxymethyl)-*β*-D-galactopyranose (4). To a solution of ketone **3**[3] (9.60 g, 28.2 mmol) in THF (100 mL) at −78 °C was added [(dimethylisopropoxysilyl)methyl]magnesium chloride (45.0 mL of a 0.70 M solution in THF, 31.5 mmol). The solution was stirred at −78 °C for 30 min, allowed to warm to −15 °C over 2 h, poured into cold saturated NH_4Cl (200 mL), and extracted with ether (2 × 200 mL). The organic extracts were washed with cold H_2O (150 mL) and cold brine (150 mL), dried, filtered, and

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concentrated at 0 °C. The crude oil was dissolved in THF (75 mL) and MeOH (75 mL), to which $NaHCO_3$ (2.38 g, 28.3 mmol) and H_2O_2 (30% in H_2O, 27 mL) were added. The suspension was heated to reflux for 12 h and cooled to 0 °C, and $Na_2S_2O_3$ (15 g) was very slowly added. $MgSO_4$ was added, and the mixture was filtered through a plug of Celite. The filter cake was washed thoroughly with ether (500 mL), and the combined filtrate was concentrated. The resulting crude oil was purified by flash chromatography on silica gel (EtOAc/hexanes, 60/40) to give diol **4** as a colorless oil (9.55 g, 91%). TLC: R_f 0.24 (EtOAc/hexanes, 50/50). $[\alpha]_D$: −69.4 (*c* 0.48, $CHCl_3$). IR: 3473 cm^{-1}. ^1H NMR (500 MHz): δ 2.04 (br s, 1), 3.55 (s, 1), 3.57 (br s, 1), 3.66 (dd, 1, J = 7.4, 5.3), 3.68 (d, 1, J = 1.3), 3.80 (d, 1, J = 11.5), 3.84 (d, 1, J = 11.5), 4.19 (d, 1, J = 7.8), 4.20 (d, 1, J = 6.3), 4.35 (d, 1, J = 11.5), 4.51 (d, 1, J = 12.1), 4.56 (d, 1, J = 11.5), 4.57 (d, 1, J = 12.1), 5.41 (s, 1), 7.26−7.38 (m, 10). ^{13}C NMR (100 MHz): δ 63.82, 65.59, 69.66, 72.07, 74.66, 75.33, 75.52, 100.22, 127.84, 127.93, 128.11, 128.28, 128.58, 128.67, 136.86, 137.34. Anal. Calcd for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.66; H, 6.56.

1,6-Anhydro-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-β-D-galactopyranose (5). To a solution of diol **4** (0.682 g, 1.66 mmol) in DMF were added imidazole (0.310 g, 4.55 mmol) and *tert*-butyl-diphenylsilyl chloride (0.550 mL, 2.12 mmol). The reaction mixture was stirred at rt overnight, poured into H_2O (15 mL), and extracted with ether (2 × 40 mL). The organic extracts were washed with H_2O (40 mL) and brine (25 mL), dried, filtered, and concentrated. The crude product was purified by flash chromatography on silica gel (EtOAc/hexanes, 25/75) to give **5** as a colorless oil (1.118 g, 100%). TLC: R_f 0.44 (EtOAc/hexanes, 30/70). $[\alpha]_D$: −24.4 (*c* 0.34, $CHCl_3$). IR: 3525 cm^{-1}. ^1H NMR (400 MHz): δ 1.07 (s, 9), 3.45 (s, 1), 3.52 (s, 1), 3.67 (dd, 1, J = 7.3, 5.5, 3.72 (d, 1, J = 1.1), 3.88 (d, 1, J = 10.4), 3.99 (d, 1, J = 10.4), 4.30 (m, 2), 4.41 (d, 1, J = 12.1), 4.47 (d, 1, J = 12.1), 4.48 (d, 1, J = 11.8), 4.58 (d, 1, J = 11.8), 5.42 (s, 1), 7.19−7.42 (m, 16), 7.69−7.76 (m, 4). ^{13}C NMR (100 MHz): δ 19.42, 26.82, 63.85, 66.78, 70.36, 71.89, 73.29, 74.89, 75.75, 100.24, 127.64, 127.81, 127.85, 128.06, 128.45, 128.58, 128.58, 129.57, 129.61, 133.24, 133.49, 135.62, 135.74, 137.30, 137.53. Anal. Calcd for $C_{37}H_{42}O_6Si$: C, 72.76; H, 6.93. Found: C, 72.98; H, 6.77.

2,3-Di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-5,6-*O*-isopropylidene-D-galacto-1,4-lactone (6). To a solution of alcohol **5** (14.26 g, 23.35 mmol) in Ac_2O (80.0 mL) was added TFA (4.1 mL). The solution was stirred at 68 °C for 90 min, cooled to rt, and concentrated. The crude product was dissolved in MeOH (100 mL), and a 25 wt % solution of MeONa in MeOH (2.0 mL) was added dropwise. The solution was stirred at rt for 2 h, filtered through a plug of silica gel, and washed thoroughly with EtOAc. The filtrate was concentrated to afford a crude foam which was dissolved in acetone (300 mL) containing *p*-TsOH (2.21 g). The reaction mixture was stirred for 90 min, and $NaHCO_3$ (8.0 g) was added. The mixture was filtered and concentrated. The crude product was dissolved in CH_2Cl_2 (400 mL) with Celite (10.5 g), 4 Å molecular sieves (15.0 g), and PDC (14.5 g). The resulting suspension was stirred at rt for 3 h, filtered through a plug of silica gel, and washed thoroughly with ether (500 mL). The filtrate was concentrated and the crude product purified by chromatography on silica gel (EtOAC/hexanes, 20/80) to provide lactone **5** as a colorless oil (11.93 g, 77%). TLC: R_f 0.54 (EtOAc/hexanes, 30/70). $[\alpha]_D$: +34.5 (*c* 0.31, $CHCl_3$). IR: 1790 cm^{-1}. ^1H NMR (400 MHz): δ 0.93 (s, 9), 1.28 (s, 3), 1.33 (s, 3), 3.41 (d, 1, J = 10.9), 3.78−3.96 (m, 4), 4.56 (d, 1, J = 7.9), 4.63 (d, 1, J = 11.3), 4.72 (d, 1, J = 11.3), 4.84 (d, 1, J = 11.7), 4.87 (d, 1, J = 7.9), 5.13 (d, 1, J = 11.7), 7.15 (t, 2, J = 7.6), 7.25−7.42 (m, 14), 7.57−7.65 (m, 4). ^{13}C NMR (100 MHz): δ 18.90, 25.32, 25.88, 26.51, 62.48, 64.45, 72.51, 73.37, 75.06, 78.93, 81.05, 84.62, 109.78, 127.07, 127.92, 127.96, 128.12, 128.43, 128.55, 129.74, 129.95, 131.78, 132.23, 135.53, 135.60, 137.08, 137.53, 172.69. Anal. Calcd for $C_{40}H_{46}O_7Si$: C, 72.04; H, 6.95. Found: C, 72.34; H, 6.96.

1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-β-D-galactofuranose (7). To a suspension of dried $CeCl_3$ (3.33 g, 13.5 mmol) in THF (45 mL) at −78 °C was added 3-butenylmagnesium bromide (18.0 mL of a 0.75 M solution in ether). The resulting suspension was stirred for 30 min prior to addition of lactone **6** (2.999 g, 4.497 mmol) in THF (10 mL, 2 × 2 mL rinse) and was allowed to warm to −50 °C over 6 h. The mixture was poured into saturated NH_4Cl (200 mL) and extracted with ether (2 × 200 mL). The organic extracts were washed with H_2O (200 mL) and brine (150 mL), dried, filtered, and concentrated. The crude product was dissolved in THF (85 mL) and 2 N HCl (5 mL), and the solution was heated to reflux for 3 h, cooled to rt, and poured into H_2O (150 mL). The product was extracted with ether (2 × 200 mL), and the organic extracts were washed wtih H_2O (150 mL) and brine (100 mL), dried, filtered, and concentrated. The product was purified by chromatography on silica gel (EtOAc/hexanes, 20/80) to provide **7** as a colorless oil (2.221 g, 74%). TLC: R_f 0.29 (EtOAc/hexanes, 20/80). $[\alpha]_D$: +12.6 (*c* 0.73, $CHCl_3$). IR: 3493 cm^{-1}. ^1H NMR (500 MHz): δ 1.08 (s, 9), 1.70 (ddd, 1, J = 14.0, 11.6, 5.2), 1.85 (ddd, 1, J = 14.0, 11.5, 5.0), 2.04−2.22 (m, 2), 3.47 (br s, 1), 3.82 (d, 1, J = 10.8), 3.85 (d, 1, J = 11.1), 3.89 (d, 1, J = 2.4), 4.04 (dd, 1, J = 11.3, 6.7), 4.15 (d, 1, J = 10.8), 4.27 (dd, 1, J = 10.6, 6.8), 4.35 (d, 1, J = 2.5), 4.50−4.63 (m, 4), 4.89−4.98 (m, 2), 5.73−5.81 (m, 1), 7.11−7.46 (m, 16), 7.62−7.67 (m, 4). ^{13}C NMR (100 MHz): δ 19.12, 26.90, 27.47, 35.61, 64.03, 64.85, 65.65, 72.44, 72.51, 82.75, 83.59, 89.12, 103.42, 114.39, 127.70, 127.79, 127.85, 127.87, 128.37, 130.01, 132.12, 135.65, 137.50, 137.70, 138.26. Anal. Calcd for $C_{41}H_{48}O_6Si$: C, 74.06; H, 7.27. Found: C, 73.99; H, 7.22.

1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-D-galactofuranos-5-ulose (8). To a solution of DMSO (2.50 mL, 35.2 mmol) in CH_2Cl_2 (100 mL) at −78 °C was added TFAA (2.50 mL, 17.7 mmol). The solution was stirred for 15 min, and alcohol **7** (7.70 g, 11.6 mmol) in CH_2Cl_2 (10 mL, 2 × 5 mL rinse) was added. After 45 min Et_3N (7.00 mL, 50.3 mmol) was added, and the solution was allowed to warm to rt over 30 min. The mixture was poured into H_2O (200 mL), extracted with ether (2 × 200 mL), and washed with H_2O (150 mL) and brine (100 mL). The organic extracts were dried, filtered, and concentrated, and the crude product was purified by chromatography on silica gel (EtOAc/hexanes, 20/80) to provide **8** as a colorless oil (7.24 g, 94%). TLC: R_f 0.52 (EtOAc/hexanes, 20/80). $[\alpha]_D$: −20.9 (*c* 3.2, $CHCl_3$). IR: 1745 cm^{-1}. ^1H NMR (500 MHz): δ 0.99 (s, 9), 1.89 (ddd, 1, J = 14.0, 10.8, 5.5), 2.06 (ddd, 1, J = 14.0, 10.7, 5.5), 2.26−2.36 (m, 2), 3.81 (d, 1, J = 1.8), 3.84 (d, 1, J = 1.8), 3.96 (d, 1, J = 11.2), 4.27 (d, 1, J = 11.2), 4.29 (d, 1, J = 11.6), 4.31 (d, 1, J = 16.6), 4.32 (d, 1, J = 11.7), 4.44 (d, 1, J = 16.6), 4.47 (d, 1, J = 11.8), 4.57 (d, 1, J = 11.8), 4.96−4.98 (m, 1), 5.02−5.06 (m, 1), 5.84−5.92 (m, 1), 7.03−7.05 (m, 2), 7.20−7.46 (m, 14), 7.66−7.72 (m, 4). ^{13}C NMR (100 MHz): δ 19.27, 26.57, 27.26, 36.43, 61.66, 69.93, 72.54, 72.63, 85.85, 88.14, 93.16, 105.01, 114.68, 127.56, 127.64, 127.67, 127.84, 127.99, 128.02, 128.43, 128.49, 129.57, 129.62, 133.13, 133.27, 135.63, 135.74, 136.86, 137.21, 138.07, 205.77. Anal. Calcd for $C_{41}H_{46}O_6Si$: C, 74.29; H, 6.99. Found: C, 74.02; H, 7.00.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-6-(hydroxymethyl)-D-galactofuranos-5-ulose (9). To a solution of ketone **8** (0.855 g, 1.29 mmol) in THF (6.0 mL) at −78 °C was added *tert*-butyllithium (1.00 mL of a 1.4 M solution in pentane). The solution was stirred for 10 min, and a solution of formaldehyde in THF[27] (10 mL) was added. The resulting solution was stirred at −78 °C for 1 h, poured into saturated NH_4Cl (100 mL), and extracted with ether (2 × 100 mL). The organic extracts were washed with H_2O (100 mL) and brine (75 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel to provide recovered ketone **8** (0.333 g, 39%) and hydroxy ketone **9** (0.507 g, 57%) as a colorless oil. TLC: R_f 0.47 (EtOAc/hexanes, 30/70). $[\alpha]_D$: +2.1 (*c* 2.1, $CHCl_3$). IR: 3463, 1738 cm^{-1}. ^1H NMR (500 MHz): δ 1.00 (s, 9), 1.96 (ddd, 1, J = 14.2, 10.3, 5.6), 2.11 (ddd, 1, J = 14.2, 10.2, 5.8), 2.30−2.39 (m, 2), 3.72 (d, 1, J = 0.9), 3.84 (dd, 1, J = 11.5, 4.7), 3.89 (d, 1, J = 0.9), 3.91 (d, 1, J = 11.2), 3.96 (dd, 1, J = 11.5, 6.0), 4.20 (d, 1, J = 11.2), 4.26 (d,

(27) Schlosser, M.; Jenny, T.; Guggisberg, Y. *Synlett* **1990**, 704.

1, J = 11.9), 4.32 (d, 1, J = 11.8), 4.44 (d, 1, J = 11.7), 4.78 (dd, 1, J = 5.9, 4.8), 4.60 (d, 1, J = 11.9), 4.98−5.01 (m, 1), 5.05−5.09 (m, 1), 5.86−5.93 (m, 1), 7.00−7.02 (m, 2), 7.19−7.44 (m, 14), 7.67−7.72 (m, 4). ^{13}C NMR (100 MHz): δ 19.16, 26.57, 27.48, 37.20, 61.55, 64.38, 72.24, 72.50, 81.12, 85.99, 88.06, 93.39, 105.78, 114.81, 127.60, 127.68, 127.73, 128.01, 128.08, 128.44, 128.53, 129.62, 129.68, 133.01, 133.07, 135.69, 135.75, 136.81, 137.07, 138.11, 205.45. Anal. Calcd for $C_{42}H_{48}O_7Si$: C, 72.80; H, 6.98. Found: C, 72.53; H, 6.96.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-D-galactofuranos-5-ulose (10). To a solution of hydroxy ketone **9** (2.07 g, 2.99 mmol) in DMF (15.0 mL) were added imidazole (0.500 g, 7.34 mmol) and TBSCl (0.500 g, 2.32 mmol). The solution was stirred at rt for 45 min, poured into H_2O (100 mL), and extracted with ether (2 × 150 mL). The organic extracts were washed with H_2O (100 mL) and brine (100 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 20/80) to provide **10** as a colorless oil (2.37 g, 98%). TLC: R_f 0.62 (EtOAc/hexanes, 30.70). $[\alpha]_D$: −2.1 (c 1.0, $CHCl_3$). IR: 1738 cm^{-1}. ^{1}H NMR (500 MHz): δ 0.05 (s, 3), 0.06 (s, 3), 0.89 (s, 9), 1.01 (s, 9), 1.93 (ddd, 1, J = 13.9, 11.3, 5.1), 2.09 (ddd, 1, J = 13.9, 11.3, 4.9), 2.31−2.37 (m, 1), 2.41−2.47 (m, 1), 3.75 (d, 1, J = 1.1), 3.86 (d, 1, J = 1.2), 3.89 (d, 1, J = 11.1), 3.90 (m, 1), 4.02 (dd, 1, J = 10.7, 7.8), 4.19 (d, 1, J = 11.1), 4.26 (d, 1, J = 11.8), 4.32 (d, 1, J = 11.7), 4.45−4.46 (m, 1), 4.46 (d, 1, J = 11.7), 4.62 (d, 1, J = 11.8), 4.98 (dd, 1, J = 10.2, 1.8), 5.06 (ddd, 1, J = 17.1, 3.3, 1.6), 5.86−5.95 (m, 1), 7.00−7.03 (m, 2), 7.19−7.45 (m, 14), 7.67−7.75 (m, 4). ^{13}C NMR (100 MHz): δ −5.42, −5.36, 18.29, 19.30, 25.91, 26.86, 27.59, 35.83, 63.35, 65.27, 66.80, 72.40, 72.51, 73.09, 83.74, 84.07, 89.34, 103.65, 114.21, 127.62, 127.67, 127.75, 128.30, 128.34, 129.64, 129.68, 133.02, 133.18, 135.70, 135.76, 137.75, 137.79, 138.62. Anal. Calcd for $C_{48}H_{64}O_7Si_2$: C, 71.25; H, 7.97. Found: C, 71.13; H, 7.96.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-5-(2-furyl)-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-L-altrofuranose (14). To a solution of ketone **10** (0.125 g, 0.155 mmol) in THF (2.0 mL) at −78 °C was added dropwise 2-furyllithium (0.40 mL of a 0.54 M solution in THF prepared from furan and *n*-butyllithium at −20 °C for 3 h, 0.43 mmol). The solution was stirred at −78 °C for 1 h, poured into H_2O (15 mL), and extracted with ether (2 × 25 mL). The organic extracts were washed with brine (20 mL), dried, filtered, and concentrated. The ^{1}H NMR spectrum indicated a diastereoselection of ∼10:1. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 20/80) to provide alcohol **14** as a colorless oil (0.130 g, 96%). TLC: R_f 0.57 (EtOAc/hexanes, 30/70). $[\alpha]_D$: −10.0 (c 1.2, $CHCl_3$). IR: 3441 cm^{-1}. ^{1}H NMR (500 MHz): δ −0.01 (s, 3), 0.02 (s, 3), 0.84 (s, 9), 1.07 (s, 9), 1.91 (ddd, 1, J = 13.9, 11.5, 5.3), 2.15 (ddd, 1, J = 13.9, 11.4, 4.9), 2.30−2.36 (m, 1), 2.44−2.48 (m, 1), 3.69 (d, 1, J = 11.8), 3.74 (dd, 1, J = 11.5, 2.7), 3.86 (dd, 1, J = 11.5, 6.7), 3.91 (d, 1, J = 2.7), 3.97 (d, 1, J = 11.7), 4.10 (d, 1, J = 11.8), 4.27 (d, 1, J = 11.8), 4.53−4.55 (m, 1), 4.56 (d, 1, J = 11.8), 4.63 (d, 1, J = 2.7), 4.71 (d, 1, J = 11.8), 4.99 (ddd, 1, J = 9.0, 3.1, 1.9), 5.07 (ddd, 1, J = 17.2, 3.5, 1.6), 5.64 (d, 1, J = 1.6), 5.92−5.97 (m, 1), 6.39 (dd, 1, J = 3.3, 1.9), 6.67 (dd, 1, J = 3.3, 0.8), 6.87−6.89 (m, 2), 7.14−7.52 (m, 15), 7.62 (dd, 2, J = 8.1, 1.4), 7.78 (dd, 2, J = 8.0, 1.4). ^{13}C NMR (100 MHz): δ −5.13, 18.38, 19.11, 25.96, 26.75, 27.75, 36.00, 63.31, 66.05, 72.02, 72.46, 73.84, 84.83, 85.14, 88.64, 104.58, 109.07, 110.41, 114.31, 127.58, 127.65, 127.69, 127.73, 128.24, 128.32, 129.80, 129.86, 132.02, 132.32, 135.66, 135.79, 135.86, 137.47, 138.01, 138.71, 141.99, 154.84. Anal. Calcd for $C_{52}H_{66}O_8Si_2$: C, 71.36; H, 7.60. Found: C, 71.39; H, 7.78.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4,6-bis-(hydroxymethyl)-5-(2-furyl)-L-altrofuranose (15). To a solution of silyl ether **14** (0.145 g, 0.166 mmol) in THF (2.0 mL) at −78 °C was added TBAF (0.80 mL of a 1.0 M solution in THF, 0.80 mmol). The solution was stirred for 2 h, poured into H_2O (15 mL), and extracted with ether (2 × 20 mL). The organic extracts were washed with H_2O (15 mL) and brine (15 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 40/60) to provide triol **15** as a colorless oil, which crystallized upon standing (71.8 mg, 83%). TLC: R_f 0.44 (EtOAc/hexanes, 50/50). $[\alpha]_D$: −7.0 (c 0.76, $CHCl_3$). IR: 3381 cm^{-1}. ^{1}H NMR (400 MHz): δ 1.91 (ddd, 1, J = 14.1, 10.8, 5.7), 2.02 (dd, 1, J = 8.4, 4.6), 2.08 (dd, 1, J = 14.1, 10.5, 5.4), 2.23−2.42 (m, 2), 2.72 (dd, 1, J = 8.9, 4.6), 3.54 (ddd, 1, J = 12.0, 8.4, 3.3), 3.66 (dd, 1, J = 12.6, 4.6), 3.69 (dd, 1, J = 12.1, 4.6), 3.82 (dd, 1, J = 12.6, 8.9), 3.98 (s, 1), 4.05 (d, 1, J = 2.7), 4.44 (d, 1, J = 11.7), 4.49 (dd, 1, J = 5.6, 3.3), 4.52 (d, 1, J = 11.8), 4.62 (dd, 1, J = 11.7), 4.66 (d, 1, J = 11.7), 4.74 (d, 1, J = 2.7), 4.94−4.98 (m, 1), 5.03 (dd, 1, J = 17.2, 3.4, 1.6), 5.79−5.89 (m, 1), 6.36 (dd, 1, J = 3.3, 1.8), 6.45 (dd, 1, J = 3.3, 0.8), 7.22−7.26 (m, 2), 7.28 (dd, 1, J = 1.8, 0.9), 7.28−7.40 (m, 8). ^{13}C NMR (100 MHz): δ 27.55, 35.55, 60.97, 62.04, 72.42, 72.73, 72.79, 74.86, 85.23, 86.55, 88.59, 104.87, 108.98, 110.64, 114.64, 127.78, 128.08, 128.18, 128.52, 128.59, 136.75, 137.37, 138.21, 142.55, 151.31. Anal. Calcd for $C_{30}H_{34}O_8$: C, 68.95; H, 6.56. Found: C, 68.61; H, 6.62.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4,6-bis-(*tert*-butoxycarbonyl)-5-(2-furyl)-L-altrofuranose (16). To a solution of triol **15** (30.4 mg, 58.2 μmol) in CH_2Cl_2 (2.0 mL) was added the Dess−Martin reagent (95.5 mg, 0.225 mmol). The suspension was stirred at rt overnight, poured into saturated $Na_2S_2O_3$ (10 mL), and extracted with ether (2 × 10 mL). The organic extracts were washed with saturated $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (10 mL), dried, filtered, and concentrated to provide 29.8 mg of dialdehyde as a colorless oil that showed the following NMR data. ^{1}H NMR (500 MHz): δ 2.01 (ddd, 1, J = 14.2, 10.6, 5.9), 2.16 (ddd, 1, J = 14.2, 10.3, 5.3), 2.31−2.48 (m, 2), 3.68 (s, 1), 4.08 (d, 1, J = 2.1), 4.39 (d, 1, J = 11.9), 4.65 (d, 1, J = 11.9), 4.55 (d, 1, J = 11.7), 4.62 (d, 1, J = 11.7), 4.93 (d, 1, J = 2.1), 4.94 (s, 1), 5.00 (ddd, 1, J = 10.1, 2.9, 1.3), 5.08 (ddd, 1, J = 10.8, 3.3, 1.7), 5.83−5.93 (m, 1), 6.46 (dd, 1, J = 3.4, 1.8), 6.48 (dd, 1, J = 3.4, 0.9), 7.19−7.41 (m, 10), 7.41 (dd, 1, J = 1.8, 0.9), 9.21 (s, 1), 9.30 (d, 1, J = 0.4). ^{13}C NMR (125 MHz): δ 27.41, 35.22, 71.82, 72.20, 73.07, 79.36, 83.23, 87.89, 91.64, 105.71, 110.54, 111.16, 115.00, 127.95, 128.15, 128.25, 128.34, 128.58, 128.62, 136.46, 136.73, 137.80, 143.12, 148.27, 193.78, 196.10.

To a solution of the foregoing crude dialdehyde (41.2 mg, 80.6 μmol) in *t*-BuOH (2.0 mL) and 2-methyl-2-butene (0.8 mL) was added dropwise a solution of NaH_2PO_4 (0.100 g, 0.724 μmol) and $NaClO_2$ (0.100 g, 0.885 μmol) in H_2O (0.50 mL). The biphasic mixture was stirred at rt for 30 min, poured into 2 N HCl (10 mL), and extracted with H_2O (10 mL). The organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried, filtered, and concentrated. The crude diacid was dissolved in CH_2Cl_2 (2.0 mL) and *i*-PrNHC(O-Bu)N-*i*-Pr (0.300 g, 1.5 mmol), and the solution was stirred at rt for 4 h. The reaction mixture was poured into 1 N HCl (10 mL) and extracted with ether (2 × 10 mL). The organic extracts were washed with brine (10 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 25/75) to provide diester **16** as a colorless oil (32.4 mg, 64% from **15**). TLC: R_f 0.43 (EtOAc/hexanes, 30/70). ^{1}H NMR (500 MHz): δ 1.21 (s, 9), 1.27 (s, 9), 1.94 (ddd, 1, J = 14.1, 11.2, 5.4), 2.12 (ddd, 1, J = 14.1, 11.1, 5.0), 2.33−2.38 (m, 2), 3.69 (s, 1), 4.05 (d, 1, J = 2.1), 4.43 (d, 1, J = 11.9), 4.50 (d, 1, J = 11.8), 4.55 (d, 1, J = 12.4), 4.58 (d, 1, J = 12.3), 4.90 (d, 1, J = 2.1), 4.95 (ddd, 1, J = 10.2, 3.2, 1.3), 4.98 (s, 1), 5.04 (ddd, 1, J = 17.1, 3.5, 1.6), 5.81−5.88 (m, 1), 6.39 (dd, 1, J = 3.2, 0.9), 6.42 (dd, 1, J = 3.2, 1.8), 7.21−7.37 (m, 10), 7.42 (dd, 1, J = 1.8, 0.9). ^{13}C NMR (100 MHz): δ 27.39, 27.71, 27.76, 35.66, 72.17, 72.65, 72.72, 75.73, 81.78, 82.29, 83.20, 88.27, 91.48, 104.56, 108.85, 110.68, 114.67, 127.88, 127.91, 128.06, 128.37, 128.43, 137.18, 137.35, 138.07, 141.40, 151.76, 163.95, 165.58.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-5-(5-methyl-2-furyl)-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-L-altrofuranose (17). To a solution of 2-methylfuran (0.20 mL, 2.2 mmol) in THF at −78 °C was added *n*-butyllithium (0.78 mL of a 2.16 M solution in hexanes, 1.68 mmol). The solution was warmed to −30 °C over 2 h, and the solution was added to a −78 °C solution of ketone **10** (57.5 mmol, 71.2 μmol) in THF (2.0 mL).

The resulting solution was stirred for 1 h, poured into H_2O, and extracted with ether (2 × 20 mL). The organic extracts were washed with brine (20 mL), dried, filtered, and concentrated. Analysis of the ^{1}H NMR spectrum of the crude product indicated a diastereoselection of ≥10:1. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 25/75) to provide alcohol **17** as a colorless oil (55.2 mg, 87%). TLC: R_f 0.63 (EtOAc/hexanes, 30/70). $[\alpha]_D$: −3.6 (*c* 0.88, $CHCl_3$). IR: 3453, 1471, 1428 cm^{-1}. ^{1}H NMR (500 MHz): δ 0.02 (s, 3), 0.04 (s, 3), 0.86 (s, 9), 1.07 (s, 9), 1.90 (ddd, 1, J = 13.8, 11.6, 5.2), 2.14 (ddd, 1, J = 13.8, 11.5, 4.8), 2.26 (s, 3), 2.28−2.47 (m, 2), 3.78 (d, 1, J = 11.7), 3.81 (dd, 1, J = 11.6, 2.5), 3.87 (dd, 1, J = 11.6, 6.7), 3.90 (d, 1, J = 2.7), 3.97 (d, 1, J = 11.7), 4.08 (d, 1, J = 11.6), 4.23 (d, 1, J = 11.6), 4.50−4.51 (m, 1), 4.55 (d, 1, J = 11.9), 4.56 (d, 1, J = 2.7), 4.71 (d, 1, J = 11.8), 4.99 (dd, 1, J = 10.1, 1.4), 5.08 (dd, 1, J = 17.1, 1.6), 5.59 (d, 1, J = 1.3), 5.90−5.96 (m, 1), 5.98 (d, 1, J = 2.8), 6.40 (d, 1, J = 3.1), 6.86 (d, 2, J = 6.9), 7.14−7.44 (m, 14), 7.64−7.66 (m, 2), 7.77−7.79 (m, 2). ^{13}C NMR (100 MHz): δ −5.19, −5.09, 13.73, 18.38, 19.11, 25.96, 26.74, 27.74, 35.93, 63.50, 66.11, 72.26, 72.47, 73.70, 77.16, 104.45, 106.53, 109.80, 114.30, 125.99, 127.40, 127.58, 127.64, 127.67, 127.70, 128.24, 128.33, 129.77, 129.85, 132.04, 132.35, 135.68, 135.79, 137.51, 138.06, 138.71, 151.63, 152.57. Anal. Calcd for $C_{53}H_{68}O_8Si_2$: C, 71.58; H, 7.71. Found: C, 71.29; H, 7.68.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4,6-bis-(hydroxymethyl)-5-(5-methyl-2-furyl)-L-altrofuranose (18). To a solution of **17** (54.0 mg, 60.7 μmol) in THF (2.0 mL) at 0 °C was added TBAF (0.20 mL of a 1.0 M solution, 0.20 mmol). The solution was stirred for 90 min, poured into H_2O (10 mL), and extracted with ether (2 × 20 mL). The organic extracts were washed with brine (20 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 45/55) to provide triol **18** as a colorless oil which crystallized upon standing (27.0 mg, 83%). TLC: R_f 0.35 (EtOAc/hexanes, 50/50). $[\alpha]_D$: +0.41 (*c* 0.73, $CHCl_3$). IR: 3390 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.91 (ddd, 1, J = 14.1, 10.9, 5.5), 2.03−2.11 (m, 1), 2.19−2.40 (m, 2), 2.27 (s, 3), 2.83 (brs, 1), 3.61 (dd, 1, J = 12.2, 3.2), 3.71−3.75 (m, 2), 3.84 (brd, 1), 4.03 (d, 1, J = 2.7), 4.08 (s, 1), 4.45 (s, 2), 4.47 (dd, 1, J = 5.8, 3.4), 4.60 (d, 1, J = 11.8), 4.69 (d, 1, J = 11.7), 4.70 (d, 1, J = 2.7), 4.96 (dd, 1, J = 10.2, 1.5), 5.04 (dd, 1, J = 17.1, 1.7), 5.80−5.88 (m, 1), 5.94 (dd, 1, J = 3.1, 0.9), 6.32 (d, 1, J = 3.1), 7.23−7.41 (m, 10). ^{13}C NMR (100 MHz): δ 13.64, 27.55, 35.52, 61.01, 62.11, 72.61, 72.69, 72.86, 75.02, 85.74, 86.69, 88.72, 104.77, 106.70, 109.80, 114.61, 127.80, 127.93, 128.05, 128.19, 128.53, 128.54, 136.95, 137.47, 138.25, 149.25, 152.37. Anal. Calcd for $C_{31}H_{36}O_8$: C, 69.39; H, 6.76. Found: C, 69.38; H, 6.77.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4,6-bis-(*tert*-butoxycarbonyl)-5-(5-methyl-2-furyl)-L-altrofuranose (19). To a solution of triol **18** (27.0 mg, 50.3 μmol) in CH_2Cl_2 (1.0 mL) was added the Dess−Martin reagent (60.1 mg, 0.142 mmol). The suspension was stirred at rt overnight, poured into saturated $Na_2S_2O_3$ (15 mL), and extracted with ether (2 × 15 mL). The organic extracts were washed with saturated $NaHCO_3$ (15 mL) and brine (15 mL), dried, filtered, and concentrated to provide the dialdehyde as an oil that showed the following IR and NMR data. ^{1}H NMR (500 MHz): δ 1.91−2.36 (m, 4), 2.28 (s, 3), 2.74 (s, 1), 4.06 (d, 1, J = 2.1), 4.37 (d, 1, J = 11.8), 4.41 (d, 1, J = 11.8), 4.55 (d, 1, J = 12.0), 4.63 (d, 1, J = 11.8), 4.88 (d, 1, J = 2.1), 4.92 (s, 1), 4.96−5.02 (m, 1), 5.04−5.08 (m, 1), 5.81−5.90 (m, 1), 6.03 (d, 1, J = 3.0), 6.35 (d, 1, J = 3.1), 7.16−7.39 (m, 10), 9.27 (s, 1), 9.33 (s, 1).

To the foregoing crude dialdehyde (27.0 mg, 50.3 μmol) in *t*-BuOH (2.0 mL) and 2-methyl-2-butene (0.8 mL) was added dropwise a solution of NaH_2PO_4 (0.100 g, 0.724 μmol) and $NaClO_2$ (0.100 g, 0.885 μmol) in H_2O (0.50 mL). The biphasic mixture was stirred at rt for 30 min, poured into 2 N HCl (10 mL), and extracted with H_2O (10 mL). The organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried, filtered, and concentrated. The crude diacid was dissolved in CH_2Cl_2 (2.0 mL) and *i*-PrNHC(C-*t*-Bu)N-*i*-Pr (0.100 g, 0.5 mmol), and the solution was stirred at rt overnight. The reaction mixture was poured into 1 N HCl (10 mL) and extracted with ether (2 × 10 mL). The organic extracts were washed with brine (10 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 25/75) to provide diester **19** as a colorless oil (10.2 mg, 30% unoptimized). TLC: R_f 0.44 (EtOAc/hexanes, 30/70). ^{1}H NMR (500 MHz): δ 1.22 (s, 9), 1.23 (s, 9), 1.90−1.09 (m, 2), 2.31 (s, 3), 2.32−2.45 (m, 2), 3.64 (s, 1), 4.04 (d, 1, J = 2.0), 4.40 (1, d, J = 11.8), 4.48 (d, 1, J = 11.8), 4.56 (d, 1, J = 12.3), 4.59 (d, 1, J = 12.3), 4.87 (d, 1, J = 2.1), 4.92−5.07 (m, 2), 4.94 (s, 1), 5.80−5.89 (m, 1), 6.00 (dd, 1, J = 3.1, 1.0), 6.23 (d, 1, J = 3.1), 7.26−7.41 (m, 10).

(1*S*,4*R*-(3α,5α,6α,7*β*))-1-(3-Oxopropyl)-6,7-bis(benzyloxy)-2,8-dioxabicyclo[3.2.1]octane 3,5-Bis(1,1-dimethylethyl) Ester 4-Spiro 2-Hydroxy-4-acetoxy-3,4-dihydrofuran 20. To a solution of diester **19** (5.0 mg, 7.4 μmol) in CH_2Cl_2 (1.0 mL) and MeOH (3.0 mL) at −78 °C was bubbled ozone for 25 min (2.0 L/min). To the resulting blue solution was added PPh_3 (20 mg), and the reaction mixture was allowed to warm to rt over 1.5 h and concentrated. The crude product was purified by chromatography on silica gel (EtOAC/hexanes, 50/50) to provide hemiacetal **20** (4.6 mg, 88%) as a colorless oil. TLC: R_f 0.45 (EtOAc/hexanes, 50/50). IR: 3455, 1759, 1725, 1626 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.37 (s, 9), 1.38 (s, 9), 2.09 (ddd, 1, J = 14.6, 8.3, 6.2), 2.29−2.35 (m, 1), 2.32 (s, 3), 2.64−2.79 (m, 2), 3.52 (brs, 1), 3.93 (d, 1, J = 2.1), 4.31 (d, 1, J = 11.9), 4.38 (d, 1, J = 11.9), 4.48 (d, 1, J = 11.7), 4.59 (d, 1, J = 4.59), 5.05 (s, 1), 5.13 (d, 1, J = 1.9), 6.41 (d, 1, J = 7.5), 7.19−7.33 (m, 10), 7.51 (d, 1, J = 7.5), 9.76 (t, 1, J = 1.4). ^{13}C NMR (100 MHz): δ 20.78, 27.77, 27.89, 29.03, 37.82, 72.59, 73.33, 76.68, 82.95, 83.25, 84.02, 87.85, 87.92, 91.69, 104.19, 106.40, 110.49, 127.88, 127.98, 128.03, 128.30, 128.39, 128.42, 136.85, 137.27, 142.85, 164.69, 165.53, 167.56, 201.42.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4,6-bis-(hydroxymethyl)-5-vinyl-6-L-altrofuranose (21). To a slurry of anhydrous $CeCl_3$ (3.56 g, 14.4 mmol) in THF (30 mL, stirred overnight at rt) at −78 °C was added vinylmagnesium bromide (14.0 mL of a 1.0 M solution in THF). The resulting suspension was stirred for 30 min, and ketone **10** (2.33 g, 2.89 mmol) in THF (10 mL, 2 × 4.0 mL rinse) was added. The reaction mixture was allowed to warm to −50 °C over 3 h, poured into 1 N HCl (100 mL), and extracted with ether (2 × 200 mL). The organic extracts were washed with H_2O (100 mL) and brine (100 mL), dried, filtered, and concentrated. Analysis of the ^{1}H NMR spectrum of the crude reaction mixture indicated a diastereoselection >15:1, and the material showed the following IR and NMR data. IR: 3465, 1472, 1429 cm^{-1}. ^{1}H NMR (500 MHz): δ 0.046 (s, 3), 0.049 (s, 3), 0.86 (s, 9), 1.04 (s, 9), 1.85 (ddd, 1, J = 13.9, 11.4, 5.2), 2.10 (ddd, 1, J = 13.9, 11.4, 4.7), 2.29−2.45 (m, 2), 3.79 (dd, 1, J = 11.6, 6.7), 3.84 (dd, 1, J = 11.6, 2.4), 3.88 (d, 1, J = 10.8), 3.93 (d, 1, J = 11.6), 3.99 (d, 1, J = 2.6), 4.10 (dd, 1, J = 6.9, 1.8), 4.23 (d, 1, J = 11.8), 4.36 (d, 1, J = 11.8), 4.51 (d, 1, J = 11.6), 4.71 (d, 1, J = 11.6), 4.87 (s, 1), 4.97 (dd, 1, J = 10.2, 1.8), 5.05 (ddd, 1, J = 17.1, 3.3, 1.6), 5.36 (dd, 1, J = 9.8, 2.9), 5.75 (d, 1, J = 2.9), 5.77 (d, 1, J = 9.8), 5.80−5.94 (m, 1), 6.92−6.94 (m, 2), 7.17−7.45 (m, 14), 7.75 (dd, 4, J = 7.9, 1.2). ^{13}C NMR (100 MHz): δ −5.10, −4.94, 18.38, 19.08, 25.96, 26.77, 27.74, 36.22, 63.11, 65.51, 71.83, 72.46, 74.86, 77.41, 84.58, 85.32, 88.44, 104.33, 114.35, 118.19, 127.50, 127.64, 127.66, 127.69, 127.73, 128.08, 129.30, 128.34, 129.75, 129.88, 132.08, 132.37, 135.69, 135.80, 136.42, 137.26, 137.84.

For removal of the silyl protecting group, the foregoing crude product was dissolved in THF (8.0 mL), and TBAF (8.6 mL of a 1.0 M solution in THF) was added at 0 °C. The solution was stirred for 1 h, poured into 1 N HCl (75 mL), and extracted with ether (2 × 150 mL). The organic extracts were washed with brine (75 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 50/50) to provide triol **21** as a colorless oil which crystallized upon standing (1.23 g, 88% from **10**), mp 65−66 °C. TLC: R_f 0.29 (EtOAc/hexanes, 50/50). $[\alpha]_D$: −6.6 (*c* 0.98, $CHCl_3$). IR: 3388 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.88 (ddd, 1, J = 14.1, 10.8, 5.6), 2.06 (ddd, 1, J = 14.1, 10.7, 5.3), 2.24−2.39 (m, 2), 3.70 (dd, 1, J = 12.2, 3.5), 3.75 (dd, 1, J = 12.2, 5.6), 3.83 (s, 2), 4.03 (d, 1, J = 2.6), 4.06 (dd, 1, J = 5.6, 3.5), 4.10 (d, 1, J = 2.6), 4.48 (d, 1, J = 11.6), 4.58 (d, 1, J = 11.5), 4.60 (d, 1, J = 11.6), 4.71 (d, 1, J = 11.6), 4.96 (dd, 1, J

= 10.2, 1.9), 5.02 (ddd, 1, J = 17.1, 3.3, 1.6), 5.34 (dd, 1, J = 9.6, 3.0), 5.54−5.60 (m, 2), 5.79−5.87 (m, 1), 7.20−7.39 (m, 10). ^{13}C NMR (100 MHz): δ 27.45, 35.71, 60.89, 61.64, 72.28, 72.80, 73.73, 75.13, 85.55, 86.11, 88.42, 104.56, 114.61, 118.98, 127.77, 127.94, 128.08, 128.26, 128.51, 128.61, 132.77, 136.55, 137.22, 138.13. Anal. Calcd for $C_{28}H_{34}O_7$: C, 69.69; H, 7.10. Found: C, 69.75; H, 7.12.

(6*S*)-1,6-Anhydro-1-(but-3-enyl)-2,3-di-*O*-benzyl-4,6-bis(*tert*-butoxycarbonyl)-5-vinyl-L-altrofuranose (24). To a solution of triol **21** (23.0 mg, 47.7 μmol) in CH_2Cl_2 (1.5 mL) was added the Dess−Martin periodinane (0.100 g, 0.236 mmol), and the reaction mixture was stirred at rt overnight. The mixture was poured into saturated $Na_2S_2O_3$ (10 mL) and extracted with ether (2 × 15 mL). The organic extracts were washed with saturated $NaHCO_3$ (20 mL) and brine (10 mL), dried, filtered, and concentrated to provide dialdehyde **22** as a colorless oil that showed the following IR and NMR data. IR: 3458, 1740, 1596 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.97 (ddd, 1, J = 14.2, 10.7, 5.7), 2.14 (ddd, 1, J = 14.2, 10.5, 5.3), 2.29−2.44 (m, 2), 3.53 (d, 1, J = 1.7), 4.05 (d, 1, J = 2.1), 4.27 (d, 1, J = 2.1), 4.44 (d, 1, J = 11.8), 4.47 (s, 1), 4.48 (d, 1, J = 12.8), 4.51 (d, 1, J = 11.8), 4.61 (d, 1, J = 11.6), 4.99 (ddd, 1, J = 10.2, 2.8, 1.2), 5.06 (ddd, 1, J = 17.1, 3.3, 1.6), 5.52 (dd, 1, J = 11.1, 1.0), 5.60 (dd, 1, J = 17.1, 1.0), 5.82−5.90 (m, 1), 5.97 (ddd, 1, J = 17.1, 11.1, 1.6), 7.18−7.42 (m, 10), 9.40 (s, 1), 9.42 (d, 1, J = 0.8). ^{13}C NMR (100 MHz): δ 27.31, 35.37, 72.17, 73.10, 73.18, 79.38, 87.78, 91.25, 105.32, 114.96, 121.07, 127.93, 127.99, 128.34, 128.37, 128.62, 130.06, 136.24, 136.58, 137.72, 194.41, 196.44.

To a solution of the foregoing crude dialdehyde in *t*-BuOH (1.0 mL) and 2-methyl-2-butene (0.6 mL) was added over 30 min a solution of $NaClO_2$ (0.101 g of a 80% mixture, 18.7 mmol) and NaH_2PO_4 (0.100 g, 15.2 mmol) in H_2O (1.0 mL). The reaction mixture was stirred for 30 min, poured into 1 N HCl (10 mL), and extracted with ether (2 × 10 mL). The organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried, filtered, and concentrated. The crude product was dissolved in CH_2Cl_2 (1.0 mL), and *i*-PrNHC(O-*t*-Bu)N-*i*-Pr (0.104 g, 0.519 mmol) was added. The solution was stirred at rt overnight, poured into 1 N HCl (10 mL), and extracted with ether (2 × 10 mL). The organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 25/75) to provide diester **24** as a colorless oil (20.7 mg, 70% from **21**). TLC: R_f 0.48 (EtOAc/hexanes, 30/70). IR: 3507, 1748 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.39 (s, 9), 1.42 (s, 9), 1.91 (ddd, 1, J = 14.1, 11.0, 5.5), 2.08 (ddd, 1, J = 14.1, 10.8, 5.1), 2.32−2.45 (m, 2), 3.56 (d, 1, J = 1.8), 4.02 (d, 1, J = 2.0), 4.12 (d, 1, J = 2.0), 4.44 (d, 1, J = 11.7), 4.54 (d, 1, J = 11.9), 4.55 (d, 1, J = 11.7), 4.57 (s, 1), 4.61 (d, 1, J = 11.9), 4.93−4.96 (m, 1), 5.03 (ddd, 1, J = 17.2, 3.4, 1.6), 5.35 (dd, 1, J = 11.0, 1.7), 5.51 (dd, 1, J = 16.9, 1.7), 5.81−5.87 (m, 1), 5.88 (ddd, 1, J = 16.9, 11.0, 1.8), 7.22−7.34 (m, 10). ^{13}C NMR (100 MHz): δ 27.34, 28.00, 28.10, 35.81, 72.66, 72.78, 73.02, 75.97, 82.45, 82.88, 83.89, 88.13, 91.30, 104.19, 114.61, 117.02, 127.91, 128.11, 128.37, 128.46, 133.50, 137.01, 138.12, 164.17, 165.71. Anal. Calcd for $C_{36}H_{46}O_9$: C, 69.43; H, 7.45. Found: C, 67.68; H, 7.65. Several attempts to obtain elemental analysis on this compound provided neatly identical results, and we were unable to eliminate what appears to be 1 equiv of water from this viscous oil.

(6*S*)-1,6-Anhydro-1-(3-hydroxybutyl)-2,3-di-*O*-benzyl-4,6-bis(*tert*-butoxycarbonyl)-5-vinyl-L-altrofuranose (25). To a solution of diester **24** (97.0 mg, 0.156 mmol) in CH_2Cl_2 (3.6 mL) and MeOH (0.4 mL) at −78 °C was added a saturated solution of ozone in CH_2Cl_2 until TLC analysis showed disappearance of the starting material. $NaBH_4$ (0.100 g) was then added in small portions, and the reaction mixture was warmed to rt, stirred 30 min, poured into saturated NH_4Cl (25 mL), and extracted with ether (2 × 50 mL). The organic extracts were washed with brine (20 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes, 50/50) to afford alcohol **25** as a colorless oil (59.2 mg, 61%). TLC: R_f 0.28 (EtOAc/hexanes, 50/50). $[\alpha]_D$: +12.7 (*c* 0.44, $CHCl_3$). IR: 3492, 1738 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.38 (s, 9), 1.41 (s, 9), 1.82−2.12 (m, 4), 3.73−3.75 (m, 2), 3.84 (brs, 1), 4.02 (d, 1, J = 2.0), 4.13 (d, 1, J = 2.0), 4.45 (d, 1, J = 11.8), 4.53 (d, 1, J = 12.0), 4.55 (d, 1, J = 12.0), 4.58 (s, 1), 4.60 (d, 1, J = 11.8), 5.36 (dd, 1, J = 11.0, 1.7), 5.51 (ddd, 1, J = 16.9, 1.7), 5.88 (dd, 1, J = 16.9, 10.9), 7.21−7.35 (m, 10). ^{13}C NMR (100 MHz): δ 26.74, 27.98, 28.08, 34.04, 62.58, 72.74, 72.83, 73.00, 76.02, 82.86, 83.00, 83.92, 91.33, 104.22, 117.21, 127.94, 128.16, 128.25, 128.38, 128.49, 133.37, 136.96, 137.06, 164.07, 166.02. Anal. Calcd for $C_{35}H_{46}O_{10}$: C, 67.07; H, 7.40. Found: C, 67.29; H, 7.54.

(1*S*-(1α,3α,4*β*,5α,6α,7*β*))-1-(3-[[(1,1-Dimethylethyl)silyl]oxy]propyl)-4-hydroxy-6,7-bis(benzyloxy)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic Acid 3,4,5-Tris(1,1-dimethylethyl) Ester (29). Into a solution of allylic alcohol **25** (72.5 mg, 116 μmol) in CH_2Cl_2 (10.0 mL) and MeOH (2.0 mL) at −78 °C was passed a stream of ozone (0.8 L/min) for 30 min. Dimethyl sulfide (2.0 mL) was added, and the solution was stirred at rt for 1 h. The reaction mixture was concentrated, and the resulting crude aldehyde **26** was used without further purification. The crude product was dissolved in DMF (0.80 mL), and imidazole (45.5 mg, 0.668 mmol) and TBSCl (46.5 mg, 0.185 mmol) were added. The resulting solution was stirred at rt for 30 min, poured into H_2O (20 mL), and extracted with ether (2 × 30 mL). The organic extracts were washed with H_2O (20 mL) and brine (20 mL), dried, filtered, and concentrated to give a silyl ether (**27**). The crude product was dissolved in a solution of *t*-BuOH (15.0 mL) and β-isoamylene (3.0 mL) to which was added $NaClO_2$ (0.169 g, 1.49 mmol) and NaH_2PO_4 (0.104 g, 0.754 mmol) in H_2O (1.4 mL). The reaction mixture was stirred at rt for 8 h, poured into pH 3 NaH_2PO_4/HCl (20 mL), and extracted with CH_2Cl_2 (2 × 30 mL). The organic extracts were dried, filtered, and concentrated to yield a carboxylic acid (**28**). The crude acid was dissolved in CH_2Cl_2 (5.0 mL) to which was added *i*-PrNHC(O-*t*-Bu)N-*i*-Pr (0.340 g, 1.70 mmol). The reaction mixture was stirred at rt for 18 h, filtered through Celite, and washed thoroughly with ether. The filtrate was concentrated, and the crude product was purified by chromatography on silica gel (EtOAc/hexanes, 20/80) to provide triester **29** as a colorless oil (38.8 mg, 41%). TLC: R_f 0.30 (EtOAc/hexanes, 20/80). $[\alpha]_D$: +4.3 (*c* 0.44, $CHCl_3$). IR: 3449, 1759, 1731 cm^{-1}. ^{1}H NMR (500 MHz): δ 0.03 (s, 6), 0.88 (s, 9), 1.42 (s, 9), 1.43 (s, 9), 1.52 (s, 9), 1.73−1.90 (m, 2), 1.94−2.09 (m, 2), 3.66 (dt, 2, J = 2.4, 6.3), 3.92 (brs, 1), 4.00 (d, t, J = 1.6), 4.49 (d, 1, J = 11.9), 4.50 (d, 1, J = 11.9), 4.53 (d, 1, J = 11.9), 4.60 (d, 1, J = 11.9), 4.92 (d, 1, J = 1.5), 4.95 (s, 1), 7.26−7.34 (m, 10). ^{13}C NMR (100 MHz): δ −5.26, 18.33, 26.01, 26.45, 27.93, 28.07, 28.17, 33.20, 63.14, 72.53, 72.73, 74.32, 75.44, 82.86, 83.12, 84.00, 84.61, 87.63, 91.17, 104.66, 127.61, 127.84, 127.88, 127.96, 128.35, 128.41, 137.46, 137.50, 165.42, 166.18, 169.02. Anal. Calcd for $C_{44}H_{66}O_{12}$: C, 64.84; H, 8.16. Found: C, 64.62; H, 8.10.

(1*S*-(1α,3α,4*β*,5α,6α,7*β*))-1-(3-Hydroxypropyl)-4-hydroxy-6,7-bis(benzyloxy)-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic Acid 3,4,5-Tris(1,1-dimethylethyl) Ester (30). To a solution of silyl ether **29** (30.0 mg, 36.8 μmol) in THF (0.45 mL) was added TBAF (0.300 mL of a 1.0 M solution in THF). The solution was stirred at rt for 2.5 h, poured into H_2O (10 mL), and extracted with ether (2 × 20 mL). The organic extracts were washed with brine (10 mL), dried, filtered, and concentrated. The crude product was purified by chromatography on silica gel to provide diol **30** as a colorless oil (15.8 mg, 61%). TLC: R_f 0.16 (EtOAc/hexanes, 50/50). $[\alpha]_D$: +2.6 (*c* 0.38, $CHCl_3$). IR: 3461, 1731 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.42 (s, 9), 1.44 (s, 9), 1.53 (s, 9), 1.80−1.86 (m, 2), 1.99−2.05 (m, 1), 2.13−2.17 (m, 1), 3.74−3.77 (m, 2), 4.00 (d, 1, J = 1.6), 4.50−4.53 (m, 1), 4.50 (d, 1, J = 11.8), 4.53 (d, 1, J = 11.8), 4.60 (d, 1, J = 12.0), 4.92 (d, 1, J = 1.6), 4.96 (s, 1), 7.27−7.35 (m, 10). ^{13}C NMR (100 MHz): δ 26.50, 27.91, 28.06, 28.15, 33.09, 61.95, 72.62, 72.75, 74.16, 75.45, 83.43, 83.46, 84.00, 84.91, 88.04, 91.17, 104.55, 127.70, 127.92, 127.98, 128.01, 128.40, 128.47, 137.24, 137.33, 165.22, 166.13, 168.90. Elemental analysis was not obtained because an insufficient amount of material was available.

(1*S*-(1α,3α,4*β*,5α,6α,7*β*))-1-(3,3-Dimethoxypropyl)-4,6,7-trihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic Acid 3,4,5-Tris(1,1-dimethylethyl) Ester (2). To so-

lution of diol **30** (9.0 mg, 13 μmol) in CH_2Cl_2 (2.0 mL) was added the Dess−Martin periodinane (30.0 mg, 70.7 μmol), and the reaction mixture was stirred at rt for 30 min after which it was poured into saturated $Na_2S_2O_3$ (10 mL) and extracted with ether (2 × 20 mL). The organic extracts were washed with saturated $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried, filtered, and concentrated to afford a crude aldehyde which was used without further purification. The crude product was dissolved in a solution of trimethyl orthoformate (0.50 mL) and MeOH (0.50 mL), containing a catalytic amount of PPTS (0.5 mg). The solution was stirred at rt for 10 min, and $Pd(OH)_2$ (38.0 mg) was added. The reaction mixture was stirred under an atmosphere of H_2 for 6 h. The black suspension was filtered through Celite, washed thoroughly with ether, and concentrated. The crude product was purified by chromatography on silica gel (EtOAc/hexanes/Et_3N, 70/29/1) to afford triol **2** as a white solid (7.3 mg, 100%), mp 139−140 °C. TLC: R_f 0.18 (EtOAc/hexanes, 75/25). $[\alpha]_D$: +1.8 (*c* 0.40, CH_2Cl_2). IR: (KBr) 3493, 1739, 1734 cm^{-1}. ^1H NMR (500 MHz): δ 1.44 (s, 9), 1.48 (s, 9), 1.58 (s, 9), 1.88−1.92 (m, 1), 1.94−2.01 (m, 2), 2.05−2.09 (m, 1), 2.42 (d, 1, J = 4.8), 3.05−3.07 (m, 1), 3.337 (s, 3), 3.338 (s, 3), 3.90 (s, 1), 4.09 (dd, 1, J = 3.3, 2.1), 4.47 (t, 1, J = 5.1), 4.95 (s, 1), 5.03 (dd, 1, J = 4.6, 1.9). ^{13}C NMR (100 MHz): δ 26.47, 27.99, 28.08, 28.18, 31.05, 53.21, 74.35, 75.11, 78.92, 82.57, 83.09, 84.17, 84.94, 91.15, 104.76, 104.88, 165.92, 166.39, 168.59. Anal. Calcd for $C_{26}H_{44}O_{13}$: C, 55.31; H, 7.85. Found: C, 54.92; H, 7.96. This material was identical in all respects to a sample obtained by degradation of zaragozic acid A/squalestatin S1 (**1**).

Acknowledgment. We thank the National Science Foundation for a research grant and FCAR and Pfizer for awarding graduate fellowships to S.C.

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JO961534E