Synthesis of a C_{29}−C_{51} Subunit of Spongistatin 1 (Altohyrtin A) Starting from (*R*)-3-Benzyloxy-2-methylpropan-1-ol

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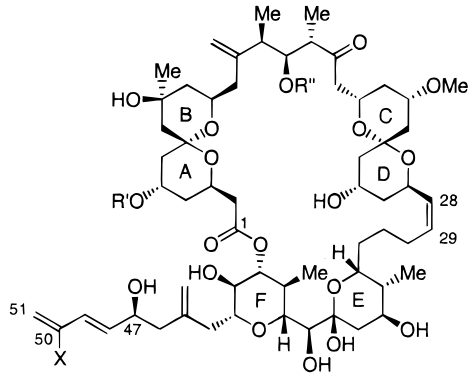
A protected C_{29}−C_{51} subunit ((+)-**38**) of spongistatin 1 has been obtained. Key steps involve the aldol condensation of (3*S*,4*R*)-3-methyl-7-[(*p*-methoxybenzyl)oxy]-4-[(triethylsilyl)oxy]octan-2-one ((−)-**6**) with (*tert*-butyl)dimethylsilyl 4-deoxy-2,3-di-*O*-(methoxymethyl)-4-methyl-6-*O*-(*tert*-butyl)-dimethylsilyl)-*β*-D-*glycero*-L-*gluco*-heptodialdo-1,5-pyranoside ((+)-**7**) and a C-glycosidation of (4*R*,7*R*&*S*,*E*)-7,8-dichloro-2-methylidene-1-(trimethylsilyl)oct-5-en-4-yl *p*-methoxybenzoate (**16**). Aldehyde (+)-**7** was derived from (*R*)-3-benzyloxy-2-methylpropan-1-ol ((+)-**10**) in 13 formal steps but requiring the isolation of five intermediate products only. The longest linear synthetic scheme converts (+)-**10** into (+)-**38** in 2% overall yield (isolation of 11 intermediate products).

The spongistatins[1,2] and altohyrtins[3,4] are cytotoxic macrolides isolated in minute amounts from marine organisms. They display especially powerful growth inhibitory activity in vitro against multidrug-resistant cancer cells, probably resulting from inhibition of tubulin polymerization.[2] A first total synthesis of spongistatin 1 (altohyrtin A), which is among the most potent congeners, has been reported by Kishi and co-workers,[5] a few weeks after the report of the group of Evans[6] on the total synthesis of spongistatin 2 (altohyrtin C).[7] Several other groups have already reported on the preparation of various fragments of this extremely important class of natural products.[8] In a preliminary report we converted (*R*)-(+)-3-benzyloxy-2-methylpropan-1-ol into a 4-deoxy-4-methyl-D-*threo*-L-*gluco*-heptanopyranose derivative and had studied its C-glycosidation, generating the C_{37}−C_{45} F-ring fragment of the spongistatins.[9] We show now that similar chemistry can be used to prepare a protected form of the C_{29}−C_{51} subunit of spongistatin 1, 3, 4, 5, and 9 (50-chloro-substituted congeners)[4] in which both rings E and F are formed.



spongistatin 1 X = Cl, R' = R'' = Ac
spongistatin 2 X = H, R' = R'' = Ac
spongistatin 3 X = Cl, R' = H, R'' = Ac
spongistatin 4 X = Cl, R' = Ac, R'' = H
spongistatin 6 X = H, R' = Ac, R'' = H

Retrosynthetic Plan. Our retrosynthetic analysis for the construction of spongistatin 1 (and other 50-chloro congeners) resembles that adopted by several groups.[4,5,8b,c,e] It implies the joining of a suitably protected C_{29}−C_{51} subunit **A** with a C_1−C_{28} fragment **B** via a Wittig olefination (Scheme 1), followed by a regioselective macrocyclization involving the diol at C-41, C-42.[5b] The subunit **A** will result from a *β*-C-glucosidation (stereocontrol by steric hindrance due to the protected alcoholic moiety at C-42) combining the synthetic intermediates **1** and **2** or analogues. Compound **1** is expected to be formed with high stereoselectivity through asymmetric allylation with **4**[10] using an enantiomerically pure Lewis acid as promoter.[11] The long-chain pyranoside **2** must bear orthogonal protective groups P at C-35, C-38, P′ at C-41, C-42, and P″ at C-29. Indeed, the terminal C-29 center of **A** should be deprotected selectively to allow its conversion into a phosphonium iodide while maintaining all other alcoholic moieties protected from the Wittig olefination. Furthermore, once **A** is combined with **B**, the diol at C-41, C-42 should be selectively liberated for the macrocyclization.

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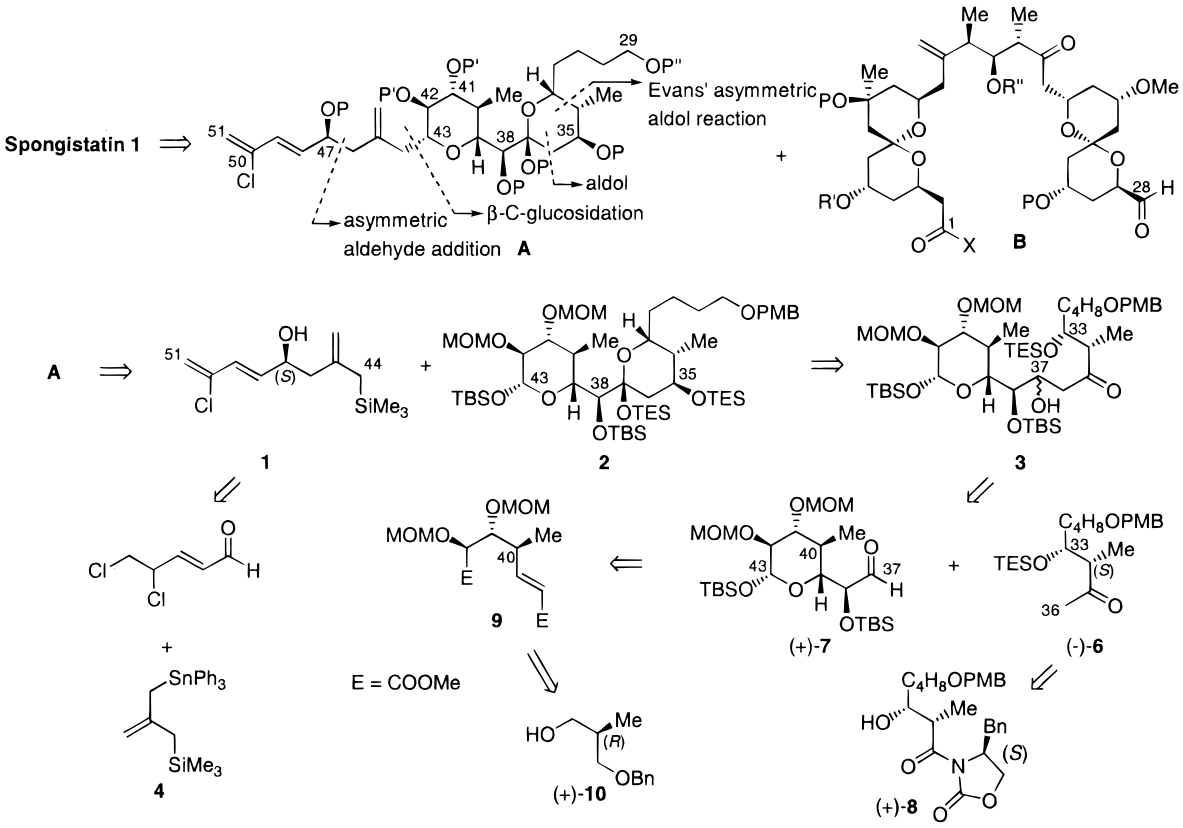
Scheme 1



We thus opted for a *p*-methoxybenzyl ether at C-29, methoxymethyl ethers at C-41, C-42, and silyl ethers at C-35, C-37, C-38, C-47. Synthetic intermediate **2** should result from a cross-aldolization between methyl ketone (−)-**6** and aldehyde (+)-**7**, giving aldols **3** that must be converted through appropriate protection, diastereoselective ketone reduction, and oxidation to a 37-keto derivative, precursor of **2**. Methyl ketone (−)-**6** will be prepared applying methods established by Evans and his group[12] via the *syn* α-methyl-*β*-hydroxyimide (+)-**8**. Aldehyde (+)-**7** will result from a diastereoselective dihydroxylation of the enediester **9**, followed by lactonization, reduction, and protection. Compound **9** will be derived from (+)-**10** following a procedure developed by us and presented earlier.[9]

Preparation of the $C_{44}-C_{51}$-Allylating Agent. Chlorination of methyl (*E*)-penta-2,4-dienoate (**11**)[13] in chloroform at 0 °C produced methyl (*E*)-4,5-dichloropent-2-enoate (**12**) in 76% yield. Reduction of **12** with $(i\text{-Bu})_2$AlH in CH_2Cl_2 gave the corresponding allylic alcohol **13** (80% yield), which was directly oxidized by Dess−Martin periodinane[14] to give enal **14** (81% yield). In the presence of 0.1 equiv of the enantiomerically pure titanium alcoholate derived from the mixing of (*S*)-BINOL (0.2 equiv) and Ti(O-*i*-Pr)$_4$ (0.1 equiv) in CH_2Cl_2, enal **14** added to {2-[(trimethylsilyl)methyl]prop-2-enyl}triphenylstannane (**4**),[10] giving alcohol **15** (60% yield). This relatively unstable compound was esterified without purification with *p*-MeO-C_6H_4COOCl in dry pyridine in the presence

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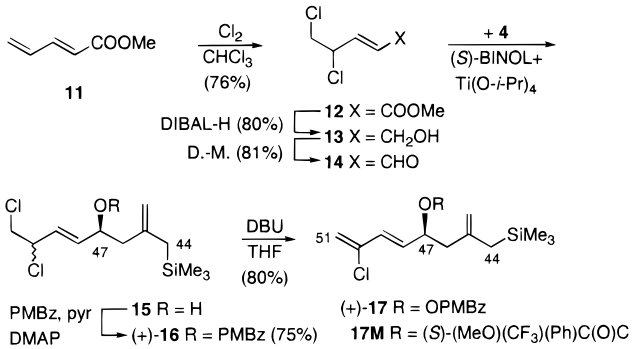
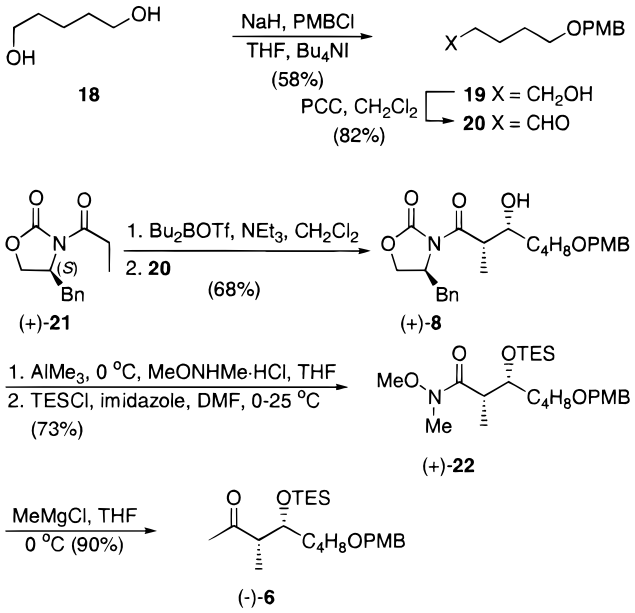
Scheme 2



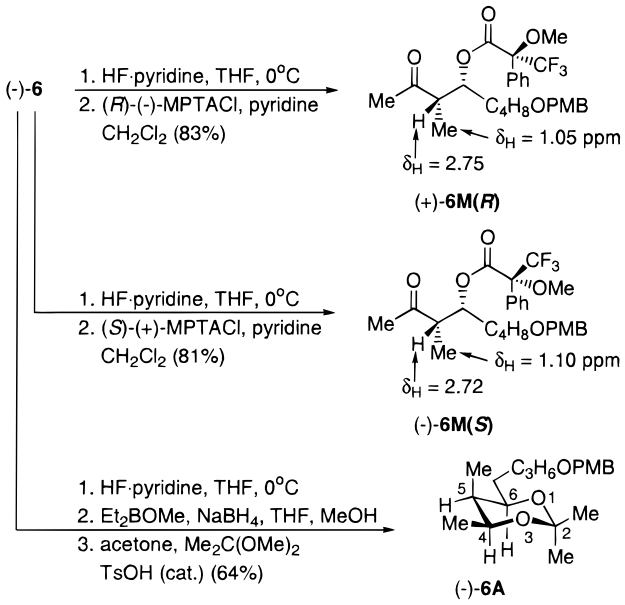
Scheme 3



of 4-(dimethylamino)pyridine (DMAP), affording ester (+)-**16** in 75% yield (based on **14**, 1:1 mixture of C(50) diastereomers that could not be separated). Treatment of (+)-**16** with DBU in THF (50 °C, 45 min) provided triene (+)-**17** in 80% yield (Scheme 2).

The enantiomeric excess of (+)-**17** was established as follows. Esterification of alcohol **15** with (*S*)-(−)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride,[15] followed by treatment with DBU/THF (50 °C), afforded the Mosher's ester **17M**, the ^{19}F NMR spectrum of which established an ee = 90% (δ_F −71.75 ppm (major), −71.96 ppm (minor)). The (47*S*) configuration of **15**−**17** was deduced from its mode of formation and the analogy with several related asymmetric allylations of aldehydes promoted by the Lewis acid used here.[16] It has been confirmed in the following way. Ozonolysis of **15** (O_3, Me_2S, CH_2Cl_2, −78 °C) gave a keto-aldehyde that was oxidized (H_2CrO_4/acetone) into the corresponding keto-carboxylic acid. Baeyer−Villiger oxidation of the latter with metachloroperbenzoic acid gave a diacid that was extracted with aqueous $NaHCO_3$. Acidification liberated L-(−)-malic acid ((*S*)-malic acid), $[\alpha]^{25}_D = -25.3$ ($c = 0.8$, pyridine), lit.[17] $[\alpha]^{20}_D = -28.7$ ($c = 5.5$, pyridine) thus proving the (47*S*) configuration of **15**.

Scheme 4



Preparation of the C_{29}−C_{36} Methyl Ketone. Treatment of pentane-1,5-diol (**18**) with 0.8 equiv of NaH, 0.9 equiv of paramethoxybenzyl chloride, and Bu_4NI (catalyst) provided the semiprotected diol **19** in 58% yield. Oxidation of **19** with pyridinium chlorochromate[18] gave aldehyde **20** (82% yield), which was reacted with the boron enolate derived from carboximide (+)-**21** and Bu_2BOTf.[19] The *syn*-α-methylaldol (+)-**8** was obtained in 68% yield, as a single diastereomer (Scheme 3). Formation of a Weinreb amide,[20b] followed by silylation of the secondary alcohol and reaction with methylmagnesium chloride, allowed efficient formation of methyl ketone (−)-**6**. The *syn* relative configuration has been confirmed by the ^{1}H NMR data of (−)-**6A** (see below). The absolute configuration of alcohol (+)-**8** was deduced from its mode of formation and in analogy with a large number of related cross-aldolizations using (+)-**21**.[12,20] We confirmed the absolute configuration of (−)-**6** by the ^{1}H NMR spectra of Mosher's esters (+)-**6M(*R*)** and (−)-**6M(*S*)** obtained as shown in Scheme 4 via esterification with (*R*)-(−)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride and the (*S*)-enantiomer, respectively.[21]

The *syn* relative configuration of (−)-**6** was confirmed by its conversion into acetonide (−)-**6A**, the ^{13}C NMR

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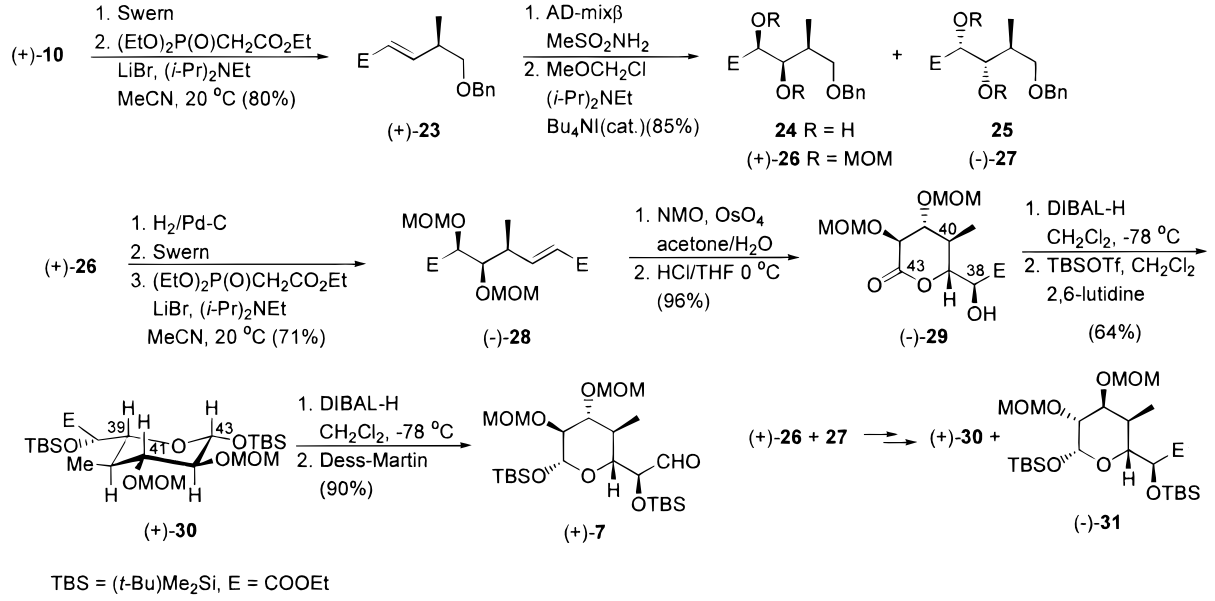
Scheme 5



TBS = (*t*-Bu)Me_2Si, E = COOEt

spectrum of which showed $\delta_C = 30.1$, 19.7 ppm for the methyl groups of the acetonide (chair conformation). Its ^{1}H NMR spectrum showed typical coupling constants ^3J(H-4,H-5) = 2.3 Hz and ^3J(H-5,H-6) = 2.2 Hz for vicinal equatorial/axial proton pairs. Furthermore, the 2D NOESY ^{1}H NMR spectrum of (−)-**6A** displayed cross-peaks for the signal pair at δ_H 4.12 (H-4) and 1.43 ppm (Me-C(2)), on one hand, and for the signal pair at δ_H 3.85 (H-6) and 1.43 ppm, on the other hand. Product (−)-**6A** was obtained in 64% overall yield by desilylation of (−)-**6** (HF−pyridine, THF, 0 °C), followed by *syn* selective aldol reduction (Et_2BOMe, $NaBH_4$, THF, MeOH)[22] and acetalization with acetone and 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid as catalyst.

Preparation of the $C_{37}-C_{43}$ Aldehyde. The starting (*R*)-(+)-3-benzyloxy-2-methylpropan-1-ol ((+)-**10**) was prepared by enzymatic resolution, as reported by Santaniello[23] with 90% ee. Alternatively, (+)-**10** (with ee >98%) was derived from the commercially available (+)-methyl L-β-hydroxyisobutyrate (ee >98%) by benzylation,[24] followed by reduction of the methyl ester with $LiAlH_4$.[25] After quantitative oxidation of the primary alcohol under Swern's condition,[26] a Wadworth−Horner−Emmons reaction with triethylphosphonoacetate[27] provided the α,β-unsaturated ester (+)-**23** in 80% yield. Treatment of (+)-**23** with enriched AD-mix-β[28] (*t*-BuOH/H_2O 1:1, $CH_3SO_2NH_2$, 12 h, 20 °C) led to a 4:1 mixture of diols **24** and **25** that could not be separated. Protected as bis(methoxymethyl)diethers **26** and **27**, the diastereoisomers were separated by flash chromatography (Scheme 5).[29] Hydrogenolysis of pure (+)-**26** (H_2/Pd−C, MeOH), followed by Swern oxidation and Wadworth−Horner−Emmons reaction with triethylphosphonoacetate,[27] gave pure diester (−)-**28** in 71% yield based on (+)-**26** (after flash chromatography on silica gel). Contrary to the dihydroxylation of (+)-**23** with *N*-methylmorpholine, catalyzed with OsO_4, which was not face selective, (−)-**28** was oxidized under these conditions,[30] giving a major diol, the treatment of which with concentrated HCl in tetrahydrofuran provided lactone (−)-**29** isolated as a single stereoisomer in 96% yield and with ee > 99% (^{19}F NMR of the corresponding Mosher's ester).

Chemoselective reduction of the lactone moiety of (−)-**29** was possible on exposure to 3 equiv of DIBAL-H in CH_2Cl_2 at −78 °C for 10 min and quenching with MeOH. The resulting crude lactol was directly silylated with (*t*-Bu)$Me_2SiOSO_2CF_3$/2,6-lutidine in CH_2Cl_2 (2 h, 0 °C), giving the uronic derivative (+)-**30** in 64% yield (2 steps). The ^{1}H NMR spectrum of (+)-**30** showed coupling constants for the vicinal proton pairs of the pyranoside (^3J(43,42) = 7.4 Hz, ^3J(42,41) = 9.2 Hz, ^3J(41,40) = 10.3 Hz, ^3J(40,39) = 10.4 Hz) typical for axial/axial proton pairs, thus proving the β-L-*gluco* configuration of the pyranoside. This assignment was confirmed by the 2D NOESY ^{1}H NMR spectrum of (+)-**30** that showed cross-peaks for signals at δ_H 4.47 (H-43), 3.23 (H-41), and 3.51 ppm (H-39). The relative configuration (D-*glycero*) of C-38 of (+)-**30** was deduced from that of C-39 (*cis* double hydroxylation of the (*E*)-enoate (−)-**28**) (Scheme 5).

When the 4:1 mixture of (+)-**26** and (−)-**27** was used instead of pure (+)-**26**, a 4:1 mixture of ethyl uronates (+)-**30** and (−)-**31** was obtained and could be readily separated by flash chromatography on silica gel. The β-L-*altro* configuration of the pyranoside moiety of (−)-**31** was confirmed by its ^{1}H NMR spectrum (^3J(43,42) = 1.0 Hz, ^3J(42,41) = 3.6 Hz, ^3J(41,40) = 3.3 Hz, ^3J(40,39) = 10.7 Hz).

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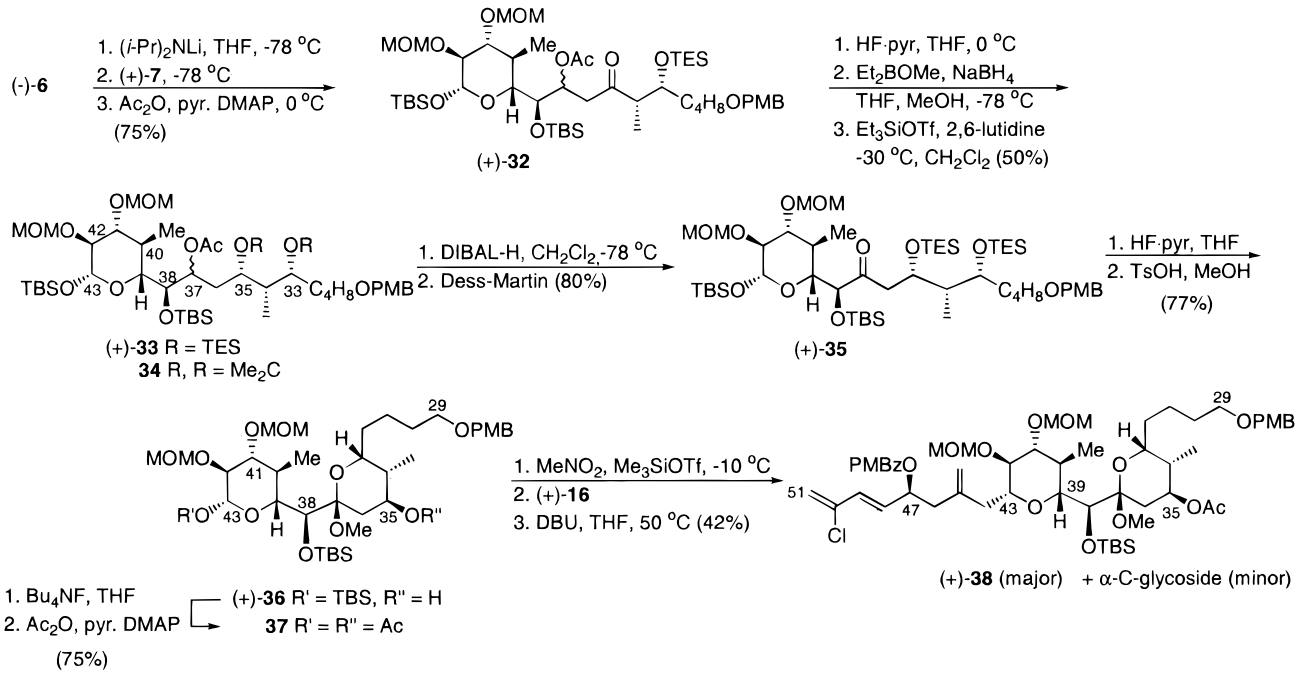
Scheme 6



Reduction of uronic ester (+)-**30** with DIBAL-H in CH_2Cl_2 (−78 °C, 30 min, quenching with MeOH) afforded the corresponding primary alcohol, which was not purified but directly oxidized into aldehyde (+)-**7** with Dess−Martin periodinane.[14] The overall yield for the conversion of (+)-**10** into (+)-**7** was 27% (13 formal steps, isolation of five intermediate products only!).

Coupling of the Various Fragments into a C_{29}−C_{51} Subunit. The lithium enolate of methyl ketone (−)-**6** obtained on treatment with $(i\text{-Pr})_2$NLi in THF at −78 °C reacted with aldehyde (+)-**7** (−78 °C, 20 min) to yield a major aldol product that was not isolated but acetylated with Ac_2O/pyridine/DMAP (0 °C, 40 min) to give the corresponding acetate (+)-**32** with a diastereomeric ratio >95:5 and 75% yield. The relative configuration of the acetate was not established, as it will be transformed later into a ketone (Scheme 6). Selective desilylation of the triethylsilyl ether of (+)-**32** with HF−pyridine in THF (0 °C) followed by *syn*-selective reduction of the intermediate β-hydroxyketone under Narasaka conditions (Et_2BOMe, $NaBH_4$)[22] gave a diol that was protected by silylation with Et_3SiOTf/2,6-lutidine in CH_2Cl_2 at −30 °C, furnishing (+)-**33**. The *syn* relative configuration at C-9 and C-11 of (+)-**33** was confirmed in the following way. Protection of the intermediate 1,3-diol arising from the Narasaka reduction as an acetonide ($Me_2C(OMe)_2$, acetone, TsOH) gave **34**, the ^{13}C NMR spectrum of which displayed two different signals at δ_C 19.4 and 29.6 ppm typical for the *syn* relative configuration.[31] All our attempts to hydrolyze (K_2CO_3, MeOH; NaOMe, MeOH; NH_3, MeOH) the acetate moiety of (+)-**33** failed to give the expected alcohol. Finally the acetate was reduced with $(i\text{-Bu})_2$AlH in CH_2Cl_2 at −78 °C, and the intermediate alcohol was oxidized with Dess−Martin periodinane,[14] providing the desired ketone (+)-**35** (80%). Chemoselective desilylation (TES vs TBS) of (+)-**35** with HF−pyridine, followed by Fischer glycosidation in methanol (TsOH as catalyst, 20 °C)[32] gave methyl α-pyranuloside (+)-**36** in 77% yield, the structure of which was confirmed by its 2D NOESY ^{1}H NMR spectrum in C_6D_6. In particular, the relative configuration of C-37, C-35, and C-34 was confirmed by the observation of cross-peaks for signals at δ_H 3.38 (MeO−C(37)) and 5.39 ppm (HO−C(35), ^3J(OH,H-35) = 5.1 Hz, vanishes on adding D_2O), on one hand, and for signals at δ_H = 0.78 (Me−C(34)) and 4.15 ppm (H-35), on the other hand.

Selective desilylation of the β-L-glucopyranoside without cleavage of the silyl ether at C-6 was possible by treating (+)-**36** with 1.1 equiv of Bu_4NF in THF at −30 °C. The resulting pyranose was directly acetylated with Ac_2O/pyridine and DMAP (catalyst) at 0 °C to produce diacetate **37** (75%), an unstable compound that was directly used in the C-glycosidation of silane **16**. The latter reaction[33] was run in nitromethane, a solvent known to favor β-allylation,[34] requiring an excess of **16** and of the Lewis acid promoter $Me_3SiOSO_2CF_3$. A mixture of compounds was obtained that was not purified but heated in THF (50 °C) in the presence of 3 equiv of DBU to induce the HCl elimination, providing a 4:1 mixture (42%) of β-C-glycoside (+)-**38** and its α-anomer.[35] Pure (+)-**38** was obtained after a second column chromatography on silica gel, in 30% yield. The β-L-glucopyranoside configuration of fragment C-9−C-13 of (+)-**38** was confirmed by its ^{1}H NMR data (^3J(H-43,H-42) =

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(35) Under similar conditions, the C-glycosidation of triene (+)-**17** failed and led to decomposition only.

10.0 Hz, ^3J(H-42,H-41) = 9.1 Hz, ^3J(H-41,H-40) = 9.0 Hz, ^3J(H-40,H-39) = 11.1 Hz).

Conclusion

A convergent approach to the synthesis of a protected form of the $C_{29}-C_{51}$ fragment of spongistatin 1 (altohyrtin A) has been presented. The allylsilane **16** ($C_{44}-C_{51}$ fragment) used in the C-glycosidation of the F-ring 4-deoxy-4-methyl-L-glucopyranoside moiety was derived from methyl (*E*)-penta-2,4-dienoate in four steps and 37% overall yield. The methyl ketone (−)-**6** ($C_{29}-C_{36}$ fragment) was derived from pentane-1,5-diol in five steps and 21% overall yield. Aldehyde (+)-**7** ($C_{37}-C_{43}$ fragment) was derived from (*R*)-(+)-3-benzyloxy-2-methylpropan-1-ol ((+)-**10**) in 12 steps and 27% overall yield. In fact the method required the isolation of only five intermediate products during the conversion of (+)-**10** into (+)-**7**. Thus (+)-**10** was converted into (+)-**38** in 20 steps and 2% overall yield, the longest linear synthetic scheme requiring the isolation of only 11 intermediate products. Our approach can be compared with that of Kishi and co-workers[5] in which their $C_{29}-C_{51}$ fragment was derived from 2-[tris(isopropyl)silyloxy]ethanol in 26 steps and 0.8% overall yield. Compound (+)-**38** bears six different alcoholic protective groups that have been chosen in such a way that (+)-**38** should be useful in its condensation with suitable C_1-C_{28} fragments to generate spongistatin 1 and derivatives.

Experimental Section

General Remarks. See ref 36. ^{1}H NMR spectrum signal assignments were confirmed by 2D COSY and 2D NOESY ^{1}H NMR spectra.

Methyl (*E*)-4,5-Dichloropent-2-enoate (12). Cl_2 was bubbled through a solution of methyl (*E*)-penta-2,4-dienoate (**11**, Fluka, 5 mL, 43 mmol) in $CHCl_3$ (60 mL) stirred at 0 °C for 30 min. Excess Cl_2 was removed by bubbling Ar for 5 min. After solvent evaporation the residue was distilled under vacuum (Vigreux column) to give a pale yellow oil (6.0 g, 76%). Bp: 74 °C (0.07 Torr). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.91 (dd, 1H), 6.16 (dd, 1H), 4.65−4.59 (m, 1H), 3.86 (dd, 1H), 3.79 (s, 3H), 3.71 (dd, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.6, 142.2, 125.0, 57.6, 52.0, 46.5. Anal. Calcd for $C_6H_8O_2Cl_2$ (183.03): C, 39.34; H, 4.37; Cl, 38.80. Found: C, 39.48; H, 4.52; Cl, 38.62.

(*E*)-4,5-Dichloropent-2-enol (13). One molar $(i\text{-Bu})_2$AH in CH_2Cl_2 (41 mL, 0.41 mmol) was added over 30 min to a stirred solution of **12** (2.5 g, 0.135 mmol) in anhydrous CH_2Cl_2 (70 mL) cooled to −78 °C. After stirring at −78 °C for 1 h, the cooling bath was removed and the mixture stirred for 1 h. Methanol (10 mL) was added under vigorous stirring and the mixture poured into 1 M aqueous HCl (120 mL). The aqueous layer was extracted with $CHCl_3$. The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated. The residual oil was purified by flash chromatography on silica gel (1:3 EtOAc/light petroleum ether), affording a colorless oil (1.7 g, 80%), R_f (1:4 EtOAc/light petroleum ether) = 0.24. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.03 (dtd, J = 15.3, 4.8, 0.7 Hz, 1H), 5.82 (ddt, J = 15.3, 8.4, 1.7 Hz, 1H), 4.55 (m, 1H), 4.24 (m, 2H), 3.81 (dd, J = 11.9, 5.4 Hz, 1H), 3.69 (dd, J = 11.9, 8.0 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 134.9, 127.6, 62.2, 59.9, 47.6. Anal. Calcd for $C_5H_8OCl_2$ (155.02): C, 38.70; H, 5.16; Cl, 45.16. Found: C, 38.85; H, 5.15; Cl, 44.98.

(*E*)-4,5-Dichloropent-2-enal (14). A mixture of **13** (1.35 g, 8.7 mmol), anhydrous CH_2Cl_2 (50 mL), and Dess−Martin periodinane (1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one, 7.4 g, 17.4 mmol) was stirred at 20 °C for 1.5 h. Diethyl ether (40 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL), and $Na_2S_2O_3$ (28 g) were added. After vigorous shaking for 5 min, the aqueous layer was extracted with Et_2O. The combined etheral extracts were washed with a saturated aqueous solution of $NaHCO_3$, then with brine, and dried ($MgSO_4$). Solvent evaporation in vacuo afforded a pale yellow oil (1.08 g, 81%) that was not purified further. R_f (1:4 EtOAc/light petroleum ether) = 0.46. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.64 (d, J = 7.4 Hz, 1H), 6.78 (dd, J = 15.5, 7.4 Hz, 1H), 6.38 (ddd, J = 15.5, 7.4, 1.1 Hz, 1H), 4.73 (m, 1H), 3.90 (dd, J = 11.4, 5.0 Hz, 1H), 3.75 (dd, J = 11.4, 8.4 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 192.0, 149.4, 134.6, 57.2, 46.2.

1:1 Mixture of (4*S*,7*R*,*E*) and (4*S*,7*S*,*E*)-7,8-Dichloro-2-methylidene-1-(trimethlysilyl)oct-5-en-4-yl *p*-Methoxybenzoate (16). A 1 M solution of freshly distilled $Ti(O\text{-}i\text{-}Pr)_4$ in anhydrous CH_2Cl_2 (196 μL, 0.196 mmol) was added to a stirred solution of (*S*)-BINOL ((*S*)-(−)-2,2′-dihydroxy-1,1′-dinaphthyl, Fluka, 112 mg, 0.392 mmol) in anhydrous CH_2Cl_2 (7.5 mL) at 25 °C for 45 min. The dark red solution was cooled to 0 °C under an Ar atmosphere, and **14** (0.3 g, 1.96 mmol) in solution in anhydrous CH_2Cl_2 (2 mL) was added, followed by the addition of {2-[(trimethylsilyl)methyl]prop-2-enyl}triphenylstannane[10] (**4**) (1.22 g, 2.55 mmol). After stirring at 0 °C for 3 h, EtOAc (10 mL) and a saturated aqueous solution of $NaHCO_3$ (2 mL) were added under vigorous stirring. After stirring for 1 h at 20 °C, the layers were separated and the aqueous phase extracted with CH_2Cl_2 (5 mL, twice). The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (1:8 EtOAc/light petroleum ether), affording a pale yellow oil (330 mg, 60%). Because of its instability, this oil could not be purified further and was dissolved in anhydrous pyridine (11 mL), and the solution was cooled to 0 °C. *p*-Methoxybenzoyl chloride (0.49 mL, 0.638 mmol) and 4-(dimethylamino)pyridine (15 mg) were added. After stirring at 0 °C for 1 h, EtOAc (25 mL) and H_2O (25 mL) were added, and the mixture was shaken vigorously at 20 °C for 1 h. The layers were separated, and the aqueous phase was extracted with EtOAc. The combined organic extracts were washed first with 1 N aqueous HCl, then with saturated aqueous solution of $NaHCO_3$, and finally with brine. After drying ($MgSO_4$), solvent evaporation, and flash chromatography on silica gel (1:10 EtOAc/light petroleum ether), **16** was obtained as a colorless oil (363 mg, 75%). R_f (1:10 EtOAc/light petroleum ether) = 0.44. $[\alpha]^{25}_D$ = 11 (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03, 6.95 (2d, J = 8.8 Hz, 4H), 5.99 (dd, J = 15.3, 5.8 Hz, 1H), 5.84 (dm, J = 15.3 Hz, 1H), 5.72 (m, 1H), 4.72, 4.65 (2 br s, 2H), 4.56−4.50 (m, 1H), 3.89 (s, 3H), 3.78, 3.67 (2m, 2H), 2.51 (dd, J = 14.1, 7.6 Hz, 1H), 2.35 (dd, J = 14.1, 6.1 Hz, 1H), 1.60 (br s, 1H), 0.05 (s, 9H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.3, 163.4, 142.1, 134.1, 131.7, 128.5, 122.6, 113.6, 111.1, 71.43, 59.9, 55.5, 47.6, 43.3, 16.7, −1.4. Anal. Calcd for $C_{20}H_{28}O_3SiCl_2$ (415.43): C, 57.82; H, 6.79. Found: C, 57.80; H, 6.68.

(4*S*)-7-Chloro-2-methylidene-1-(trimethylsilyl)octa-5,7-dien-4-yl *p*-Methoxybenzoate ((+)-17). A mixture of (+)-**16** (30 mg, 0.072 mmol), anhydrous THF (1.5 mL), and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, Fluka, 33 μL, 0.21 mmol) was warmed to 50 °C for 45 min. The solution was poured into H_2O (8 mL) and extracted with Et_2O (10 mL, 3 times). The combined ethereal extracts were washed successively with 1 N aqueous HCl, a saturated aqueous solution of $NaHCO_3$, and brine. After drying ($MgSO_4$) and solvent evaporation in vacuo, the residue was purified by flash chromatography on silica gel (1:15 EtOAc/light petroleum ether), affording a colorless oil (22 mg, 80%). R_f (1:10 EtOAc/light petroleum ether) = 0.53. $[\alpha]^{25}_D$ = 62 (c = 0.3, CH_2Cl_2). ^{1}H NMR (400 MHz, C_6D_6): δ 8.23, 6.68 (2d, J = 9.0 Hz, 4 H), 6.47 (dd, J = 15.0, 5.7 Hz, 1H), 6.41 (d, J = 15.0 Hz, 1H), 6.10 (m, 1H), 5.16, 4.91 (2d, J = 1.1 Hz, 2H), 4.87, 4.72 (2br s, 2H), 3.17 (s, 3H), 2.57 (dd, J = 14.2, 8.7 Hz, 1 H), 2.35 (dd, J = 14.2, 5.8 Hz, 1H), 1.63, 1.59 (2d, J = 13.7 Hz, 2H), 0.04 (s, 9H). ^{13}C NMR (100.6 MHz, C_6D_6): δ 165.1, 163.4, 142.4, 137.9, 133.3, 131.8, 128.8, 123.1, 116.4, 113.7, 111.0, 71.7, 54.5, 43.6, 26.5, −1.7.

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5-[(*p*-Methoxybenzyl)oxy]pentan-1-ol (19). A mixture of pentane-1,5-diol (2.56 g, 24.6 mmol, Fluka), anhydrous THF (75 mL), and 55% NaH in oil (858 mg, 19.6 mmol) was stirred at 0 °C for 10 min under an Ar atmosphere. *p*-Methoxybenzyl chloride (3 mL, 22 mmol) and Bu_4NI (0.2 g) were added. The mixture was stirred at 0 °C for 1 h, then at 20 °C for 2 h, and was left overnight at 45 °C. The mixture was poured into a vigorously stirred saturated aqueous solution of $NaHCO_3$ (250 mL). The aqueous layer was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated in vacuo. The residue was purified by flash chromatography on silica gel (1:1 EtOAc/light petroleum ether), affording a pale yellow oil (3.18 g, 58%). R_f (1:4 EtOAc/light petroleum ether) = 0.15. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 5.7 Hz, 2H), 6.88 (d, J = 5.7 Hz, 2 H), 4.22 (s, 2H), 3.81 (s, 3H), 3.64 (t, J = 6.5 Hz, 2H), 3.46 (t, J = 6.5 Hz, 2H), 1.66−1.55, 1.48−1.46 (2m, 6H), 1.54 (br s, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 159.1, 130.6, 129.2, 113.7, 72.5, 69.9, 62.8, 55.2, 32.5, 29.4, 22.4. Anal. Calcd for $C_{13}H_{20}O_3$ (224.30): C, 69.61; H, 8.99. Found: C, 69.52; H, 9.01.

5-[(*p*-Methoxybenzyl)oxy]pentanal (20). A mixture of **19** (3.12 g, 13.3 mmol), anhydrous CH_2Cl_2 (90 mL), and pyridinium chlorochromate (4.81 g, 22.3 mmol, Fluka) was stirred at 20 °C for 3 h. The black precipitate was taken off by filtration on a pad of silica gel (elution with 800 mL of Et_2O). Solvent evaporation and flash chromatography on silica gel (1:4 EtOAc/light petroleum ether) afforded a colorless oil (2.42 g, 82%). R_f (1:4 EtOAc/light petroleum ether) = 0.34. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.75 (t, J = 1.7 Hz, 1H), 7.25 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 4.42 (s, 2H), 3.80 (s, 3H), 3.46 (t, J = 6.5 Hz, 2H), 2.44 (td, ^3J = 7.0, 1.7 Hz, 2H), 1.75−1.61 (m, 4H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 202.5, 159.1, 130.5, 129.2, 113.7, 72.5, 69.4, 55.2, 43.5, 29.1, 18.9. Anal. Calcd for $C_{13}H_{18}O_3$ (222.28): C, 69.64; H, 8.93. Found: C, 69.72; H, 8.88.

(2′*S*,3′*R*,5*S*)-5-Benzyl-*N*-{7-[(*p*-methoxybenzyl)oxy]-3-hydroxy-2-methylheptoyl}-2-oxazolidinone ((+)-8). In a Schlenk tube (100 mL, flame dried) (5*S*)-5-benzyl-2-oxazolidinone ((+)-**21**, 1.5 g, 6.44 mmol, prepared according to ref 12a) was dissolved in anhydrous CH_2Cl_2 (32 mL) under an Ar atmosphere. After cooling to 0 °C, Bu_2BOTf[19] (2.12 g, 7.72 mmol) dissolved in anhydrous CH_2Cl_2 (3 mL) was added. Et_3N (1.25 mL, 9 mmol) was then added dropwise at 0 °C. After stirring at 0 °C for 45 min the solution was cooled to −78 °C, and **20** (1.57 g, 7.08 mmol) in solution in anhydrous CH_2Cl_2 (3 mL) was added slowly. The mixture was stirred at −78 °C for 1 h, then at −20 °C for 1 h, and at 0 °C for 1 h. Phosphate buffer (pH 7, 20 mL) was added, followed by MeOH (50 mL). The resulting mixture was then added dropwise into a stirred solution of MeOH (80 mL) and 35% H_2O_2 (7 mL) and cooled to 0 °C. After stirring at 0 °C for 1 h, H_2O (120 mL) was added. The aqueous layer was extracted with $CHCl_3$ (130 mL, three times). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$, then with brine, and dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:1 EtOAc/light petroleum ether) afforded pure (+)-**8** (single stereoisomer) as a colorless oil (1.99 g, 68%). R_f (1:2 EtOAc/light petroleum ether) = 0.13. $[\alpha]^{25}_D$ = 47 (c = 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.27 (m, 5 H), 7.26 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 4.70 (dddd, J = 9.4, 7.5, 3.3, 3.2 Hz, 1H), 4.43 (s, 2H), 4.23 (dd, J = 16.6, 7.5 Hz, 1H), 4.19 (dd, J = 16.6, 3.2 Hz, 1H), 3.97−3.93 (m, 1H), 3.80 (s, 3H), 3.76 (qd, J = 7.1, 2.7 Hz, 1H), 3.46 (t, J = 6.4 Hz, 2H), 3.25 (dd, J = 13.4, 3.3 Hz, 1H), 2.80 (dd, J = 13.4, 9.4 Hz, 1H), 1.67−1.62 (m, 2H), 1.58−1.54, 1.47−1.41 (2m, 4H), 1.26 (d, J = 7.1 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 177.5, 159.1, 153.0, 135.0, 130.7, 129.4, 129.2, 128.9, 127.4, 113.7, 72.5, 71.3, 69.9, 66.1, 55.2, 55.1, 42.1, 37.8, 33.6, 22.7, 29.5, 10.4. Anal. Calcd for $C_{26}H_{33}NO_6$: C, 68.57; H, 7.25; N, 3.08. Found: C, 68.45; H, 7.29; N, 3.09.

(2*S*,3*R*)-*N*-Methoxy-*N*-2-dimethyl-7-[(*p*-methoxybenzyl)oxy]-3-[(triethylsilyl)oxy]heptanamide ((+)-22). (MeO)-MeNH−HCl (746 mg, 7.65 mmol) was suspended in anhydrous THF (14 mL) in a Schlenk tube under an Ar atmosphere. After cooling to 0 °C, a 2 M solution of $AlMe_3$ in heptane (3.82 mL, 7.65 mmol) was added slowly. After the end of gas evolution, the solution was stirred at 20 °C for 30 min. The solution was cooled to 0 °C, and (+)-**8** (870 mg, 1.91 mmol) in solution in anhydrous THF (4 mL) was added. After stirring at 0 °C for 25 min, the mixture was poured into a vigorously stirred mixture of CH_2Cl_2 (110 mL) and 0.5 M HCl (70 mL) and cooled to 0 °C. The aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine and dried ($MgSO_4$), and the solvent was evaporated. The pale yellow residue was dissolved in anhydrous DMF (10 mL) and the solution cooled to 0 °C. Imidazole (260 mg, 3.82 mmol) and Et_3SiCl (385 μL, 2.29 mmol) were added successively. After stirring at 0 °C for 1 h, the mixture was allowed to stand at 20 °C for 2 h. It was poured into H_2O (50 mL). The aqueous layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated. Flash chromatography on silica gel (1:4 EtOAc/light petroleum ether) afforded a colorless oil (636 mg, 73%). R_f (1:2 EtOAc/light petroleum ether) = 0.70. $[\alpha]^{25}_D$ = 6 (c = 1.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25, 6.87 (2d, J = 8.7 Hz, 4H), 4.42 (s, 2H), 3.95−3.91 (m, 1H), 3.80 (s, 3H), 3.65 (s, 3H), 3.43 (t, J = 6.6 Hz, 2H), 3.16 (br s, 3H), 2.96 (br s, 1H), 1.64−1.49, 1.47−1.39 (2m, 6H), 1.16 (d, J = 6.9 Hz, 3H), 0.97 (t, J = 7.8 Hz, 9H), 0.63 (q, J = 7.8 Hz, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 176.6, 159.0, 130.8, 129.1, 113.6, 73.8, 72.4, 70.1, 61.3, 55.2, 40.9, 35.8, 32.1, 30.0, 21.3, 14.5, 7.0, 5.1. Anal. Calcd for $C_{24}H_{43}NO_5Si$ (453.70): C, 63.58; H, 9.49; N, 3.09. Found: C, 63.51; H, 9.32; N, 3.10.

(3*S*,4*R*)-3-Methyl-7-[(*p*-methoxybenzyl)oxy]-4-[(trimethylsily)oxy]octan-2-one ((−)-6). A 3 M solution of MeMgCl in anhydrous THF (2.65 mL, 7.94 mmol) was added dropwise to a solution of (+)-**22** (0.6 g, 1.32 mmol) in anhydrous THF (10 mL) stirred at 0 °C under an Ar atmosphere. After stirring at 0 °C for 3 h the mixture was poured into a vigorously stirred saturated aqueous solution of NH_4Cl (50 mL). H_2O (5 mL) was added to dissolve the precipitate, and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:8 EtOAc/light petroleum ether) afforded a colorless oil (488 mg, 90%). R_f (1:4 EtOAc/light petroleum ether) = 0.73. $[\alpha]^{25}_D$ = −32 (c = 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26, 6.88 (2d, J = 8.7 Hz, 4H), 4.43 (s, 2H), 3.93 (m, 1H), 3.81 (s, 3H), 3.43 (t, J = 6.5 Hz, 2H), 2.63 (qd, J = 7.0, 4.7 Hz, 1H), 2.18 (s, 3H), 1.65−1.56 (m, 2H), 1.49−1.30 (m, 4H), 1.06 (d, J = 7.0 Hz, 3 H), 0.96 (t, J = 8.0 Hz, 9H), 0.60 (q, J = 8.0 Hz, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 211.7, 159.0, 130.1, 129.2, 113.7, 73.6, 72.5, 69.8, 55.2, 52.0, 34.5, 30.0, 29.8, 22.3, 11.4, 6.9, 5.1. Anal. Calcd for $C_{23}H_{40}O_4Si$ (408.65): C, 67.65; H, 9.80; Si, 6.86. Found: C, 67.68; H, 9.91; Si, 6.97.

(α*R*,3*S*,4*R*)-3-Methyl-8-[(*p*-methoxybenzyl)oxy]-4-[α-methoxy-α-(trifluoromethyl)-α-phenylacetoxy]octan-2-one ((+)-6M(R). A mixture of (−)-**6** (50 mg, 0.123 mmol), anhydrous THF (6 mL), and HF−pyridine (0.32 μL) was stirred at 0 °C for 1 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (15 mL) and extracted with EtOAc. The combined organic extracts were washed with H_2O and dried ($MgSO_4$). Solvent evaporation in vacuo gave a pale yellow oil (36 mg, 100%, (3*S*,4*R*)-4-hydroxy-3-methyl-7-[(*p*-methoxybenzyl)oxy]octan-2-one), from which 20 mg (0.06 mmol) was dissolved in anhydrous CH_2Cl_2 (1 mL) and cooled to 0 °C. Pyridine (16 μL, 0.2 mmol) and (*R*)-(−)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride (19 μL, 0.1 mmol) were added. After stirring at 0 °C for 15 min, the mixture was stirred at 20 °C for 4 h. After the addition of EtOAc (10 mL), the solution was washed successively with 1 N aqueous HCl (2 mL), $NaHCO_3$ (2 mL), and H_2O (2 mL). After drying ($MgSO_4$), the solvent was evaporated. Flash chromatography on silica gel (1:4 EtOAc/light petroleum ether) afforded a colorless oil (29 mg, 83%). R_f (1:4 EtOAc/light petroleum ether) = 0.37. $[\alpha]^{25}_D$ = 5 (c = 0.3, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55−7.52, 7.39−7.38 (2m, 5H), 7.25, 6.88 (2d, J = 8.7 Hz, 4H), 5.44 (m, 1H), 4.42 (s, 2H), 3.81 (s, 3H), 3.53 (s, 3H), 3.41 (t, J = 6.3 Hz, 2H), 2.75 (dd, J = 7.0, 4.7 Hz, 1H), 2.06 (s, 3H), 1.71−1.56, 1.43−1.36 (2m, 6H), 1.05 (d, J = 7.1

Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 207.8, 166.3, 159.4, 132.2, 130.6, 129.6, 129.3, 128.4, 127.3, 122.1, 113.8, 76.7, 72.6, 69.5, 55.5, 55.3, 49.5, 31.6, 29.3, 29.0, 22.3, 11.1. Anal. Calcd for $C_{27}H_{33}O_6F_3$ (510.55): C, 63.52; H, 6.51. Found: C, 63.66; H, 6.63.

(α*S*,3*S*,4*R*)-3-Methyl-8-[(*p*-methoxybenzyl)oxy]-4-[α-methoxy-α-(trifluoromethyl)-α-phenylacetoxy]octan-2-one ((−)-6M(*S*)). The same procedure as for the preparation of (+)-**6M(*R*)** was adopted, starting with 16 mg of (3*S*,4*R*)-3−4-hydroxymethyl-7-[(paramethoxybenzyl)oxy]-octan-2-one and using (*S*)-(+)-α-methoxy-α-(trifluoromethyl)-α-phenylacetyl chloride (Fluka). (−)-**6M(*S*)** was obtained as a colorless oil (22.6 g, 81%). R_f (1:4 EtOAc/light petroleum ether) = 0.36. $[\alpha]^{25}_D$ = −132 (c = 0.4, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.51, 7.38 (2m, 5H), 7.24, 6.88 (2d, J = 8.7 Hz, 4H), 5.48, 5.44 (m, 1H), 4.40 (s, 2H), 3.81 (s, 3H), 3.50 (s, 3H), 3.37 (t, J = 6.4 Hz, 2H), 2.72 (qd, J = 7.0, 4.5 Hz, 1H), 2.17 (s, 3H), 1.68−1.50, 1.31−1.25 (2m, 6H), 1.10 (d, J = 7.1 Hz, 3 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 208.8, 166.2, 159.2, 132.0, 130.6, 129.6, 128.4, 127.5, 113.8, 76.4, 72.6, 69.5, 55.4, 55.3, 49.6, 31.6, 29.3, 29.0, 22.1, 10.8. Anal. Calcd for $C_{27}H_{33}O_6F_3$ (510.55): C, 63.52; H, 6.51. Found: C, 63.65; H, 6.58.

(4*S*,5*R*,6*S*)-2,2,4,5-Tetramethyl-6-{4[(*p*-methoxybenzyl)oxy]butyl}-1,3-dioxane ((−)-6A). A mixture of (−)-**6** (165 mg, 0.41 mmol), anhydrous THF (15 mL), and HF−pyridine (1 mL) was stirred at 0 °C for 1 h. It was then poured into a saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The combined organic extracts were washed with H_2O and dried ($MgSO_4$), and the solvent was evaporated in vacuo. The residue was dissolved in THF (2 mL) and MeOH (0.5 mL) and cooled to −78 °C. One molar Et_2BOMe in THF (0.6 mL, 0.6 mmol) was added. The mixture was stirred at −78 °C for 15 min, and $NaBH_4$ (23 mg, 0.61 mmol) was added. After stirring at −78 °C for 45 min, AcOH (20 μL) was added and the mixture was poured into a saturated aqueous solution of $NaHCO_3$ (10 mL) and extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$). The solvent was evaporated in vacuo and the residue dissolved in MeOH (3 mL). The solvent was evaporated in vacuo. The same operation was repeated once more. The resulting colorless oil was dissolved in a mixture of acetone (1 mL) and 2,2-dimethoxypropane (1 mL), containing *p*-toluenesulfonic acid (6 mg). After stirring at 20 °C for 90 min the solvent was evaporated and the residue purified by flash chromatography on silica gel (1:8 EtOAc/light petroleum ether), affording a pale yellow oil (88 mg, 64%). R_f (1:8 EtOAc/light petroleum ether) = 0.40. $[\alpha]^{25}_D$ = −103 (c = 0.2, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.27, 6.88 (2d, J = 8.7 Hz, 4H), 4.44 (s, 2H), 4.12 (qd, J = 6.9, 2.3 Hz, 1H), 3.85 (ddd, J = 8.8, 5.0, 2.2 Hz, 1H), 3.81 (s, 3H), 3.45 (t, J = 6.6 Hz, 2H), 1.66−1.60, 1.38−1.27 (2m, 7H), 1.43, 1.40 (2s, 6H), 1.13 (d, J = 6.4 Hz, 3H), 0.84 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 159.1, 130.7, 129.2, 113.8, 98.7, 73.2, 72.5, 69.9, 69.0, 55.3, 35.9, 32.6, 30.1, 29.7, 22.3, 19.7, 19.0, 4.3. Anal. Calcd for $C_{20}H_{32}O_4$ (336.47): C, 71.39; H, 9.59. Found: C, 71.45; H, 9.56.

(4*S*,*E*)-Ethyl 5-Benzyloxy-4-methylpent-2-enoate ((+)-23). DMSO (6.2 mL, 87 mmol) was added to a stirred solution of oxalyl chloride (3.57 mL, 41.5 mmol) in anhydrous CH_2Cl_2 (175 mL) cooled to −78 °C. After stirring at −78 °C for 20 min, (+)-**10** (prepared according ref 24 and 25; 6.5 g, 36.1 mmol) in solution in anhydrous CH_2Cl_2 (75 mL) was added dropwise. After stirring at −78 °C for 20 min, Et_3N (25 mL) was added and the mixture stirred at −30 °C for 30 min. The mixture was poured into H_2O (300 mL) and extracted with Et_2O (400 mL, three times). The combined organic extracts were washed with brine (250 mL), dried ($MgSO_4$), and concentrated in vacuo to afford a pale yellow oil ((*R*)-3-benzyloxy-2-methylpropanal). A mixture of LiBr (4.5 g, 52 mmol), MeCN (110 mL), and triethyl phosphonoacetate (7.8 mL, 39.1 mmol) was stirred at 20 °C for 5 min. EtN(*i*-Pr)$_2$ (8.4 mL, 48.8 mmol) was added portionwise, and stirring was continued for an additional 10 min. A solution of the crude (*R*)-3-benzyloxy-2-methylpropanal (5.8 g, 32.5 mmol) in MeCN (20 mL) was added, and the mixture was stirred at 20 °C for 11 h. The mixture was then poured into 1 M aqueous HCl (250 mL) under vigorous stirring. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography on silica gel (1:6 EtOAc/light petroleum ether) afforded a colorless oil (7.16 g, 80%). R_f (1:10 EtOAc/light petroleum ether) = 0.35. $[\alpha]^{25}_D$ = 6 (c = 1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.29 (m, 5H), 6.96 (dd, J = 15.8, 7.1 Hz, 1 H), 5.87 (dd, J = 15.8, 1.4 Hz, 1H), 4.53 (s, 2H), 4.20 (q, J = 7.1 Hz, 2H), 3.43 (dd, J = 9.2, 6.8 Hz, 1H), 3.39 (dd, J = 9.2, 6.3 Hz, 1H), 2.69−2.66 (m, 1H), 1.30 (t, J = 7.1 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 166.7, 151.1, 138.2, 128.4, 127.6, 121.0, 73.9, 73.1, 60.2, 36.8, 16.0, 14.2. Anal. Calcd for $C_{15}H_{20}O_3$ (248.32): C, 72.58; H, 8.06. Found: C, 72.64; H, 8.14.

(2*S*,3*R*,4*S*)-Ethyl5-Benzyloxy-4-methyl-2,3-bis[(methoxymethyl)oxy]pentanoate ((+)-26) and (2*R*,3*S*,4*S*)-Ethyl 5-Benzyloxy-4-methyl-2,3-bis[(methoxymethyl)oxy]pentanoate ((−)-27). A mixture of (+)-**23** (11.4 g, 46.1 mmol), *t*-BuOH (90 mL), H_2O (90 mL), methanesulfonamide (4.38 g, 46 mmol), and enriched AD-mix-β (70 g, $K_3Fe(CN)_6$, 47.7 g; K_2CO_3, 20.05 g; $(DHQD)_2PHAL$, 1.88 g, $K_2OsO_2(OH)_4$, 370 mg) was stirred at 20 °C for 12 h. EtOAc (200 mL) and anhydrous Na_2SO_3 (55 g) were added, and the mixture was stirred at 20 °C for 45 min. The precipitate was filtered off and the solution diluted with H_2O (200 mL) and extracted with EtOAc. The combined organic extracts were washed with 1 M aqueous HCl, then with brine, and dried ($MgSO_4$). Solvent evaporation afforded a 4:1 mixture of diols **24** and **25** as a pale yellow oil, which was dissolved (13 g, 46.1 mmol) in anhydrous CH_2Cl_2 (300 mL). After cooling to 0 °C, EtN(*i*-Pr)$_2$ (95 mL, 0.553 mmol) and $MeOCH_2Cl$ (28 mL, 0.369 mol) were added dropwise. Bu_4NI (50 mg) was then added, and the mixture was stirred at 20 °C for 12 h. The solution was poured into vigorously stirred 1 M aqueous HCl (500 mL). The aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:6 EtOAc/light petroleum ether) afforded a 4:1 mixture of (+)-**26** and (−)-**27** (14.6 g, 85%), which can be separated at this stage by a second flash chromatography to obtain an analytical sample. For preparative purposes, the mixture of (+)-**26** and (−)-**27** can be used as such in the following steps (see below: mixture of (+)-**30** and (−)-**31**).

Data for (+)-26: R_f (1:4 EtOAc/light petroleum ether) = 0.35. $[\alpha]^{25}_D$ = 20 (c = 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.28 (m, 5H), 4.71, 4.68 (2s, 4H), 4.53 (d, J = 11.6 Hz, 1H), 4.48 (d, J = 11.6 Hz, 1H), 4.27−4.17 (m, 3H), 4.03 (dd, J = 4.8 Hz, 1H), 3.51 (dd, J = 9.2, 6.3 Hz, 1H), 3.40 (dd, J = 9.2, 6.2 Hz, 1H), 3.69, 3.35 (2s, 6H), 2.10−2.06 (m, 1H), 1.30 (t, ^3J = 7.1 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3 H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.8, 138.4, 128.3, 127.6, 127.5, 98.2, 96.8, 79.7, 78.0, 73.0, 72.3, 61.0, 56.4, 56.2, 35.5, 14.1, 12.5. Anal. Calcd for $C_{19}H_{30}O_7$ (370.44): C, 61.62; H, 8.11. Found: C, 61.65; H, 8.14.

Data for (−)-27: R_f (1:4 EtOAc/light petroleum ether) = 0.24. $[\alpha]^{25}_D$ = −66 (c = 0.3, CH_2Cl_2).

(4*S*,5*R*,6*S*,*E*)-Diethyl 5,6-Bis[(methoxymethyl)oxy]-4-methylhept-2-ene-dioate ((−)-28). A mixture of (+)-**26** (10 g, 27 mmol), MeOH (400 mL), and 5% Pd on charcoal (0.6 g) was degassed and then pressurized with H_2 (1 atm). After shaking at 20 °C for 12 h the catalyst was filtered off on a pad of silica gel (eluting with EtOAc). Solvent evaporation afforded (2*R*,3*R*,4*S*)-ethyl 5-hydroxy-2,3-bis[(methoxymethyl)oxy]-4-methylpentanoate as a colorless oil (7.4 g, 98%). DMSO (4.5 mL, 63.6 mmol) was added to a stirred solution of oxalyl chloride (2.6 mL, 30.4 mmol) in anhydrous CH_2Cl_2 (150 mL) cooled to −78 °C. After stirring at −78 °C for 15 min, the crude (2*S*,3*R*,4*S*)-ethyl 5-hydroxy-4-methyl-2,3-bis[(methoxymethyl)-oxy]pentanoate in solution in anhydrous CH_2Cl_2 (75 mL) was added dropwise under stirring. After stirring at −78 °C for 30 min, Et_3N (20 mL) was added and stirring was continued at −30 °C for 30 min. The mixture was poured into H_2O and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to afford (2*S*,3*R*,4*S*)-ethyl 2,3-bis[(methoxymethyl)oxy]-4-methyl-5-oxopentanoate as a pale yellow oil (7.12 g, 97%). A mixture of LiBr (7.8 g, 89.6 mmol), MeCN (150 mL), and

triethyl phosphonoacetate (13.3 mL, 66.6 mmol) was stirred at 20 °C under an Ar atmosphere for 5 min. EtN(*i*-Pr)$_2$ (14.4 mL, 84.5 mmol) was added, and the mixture stirred for an additional 10 min. The crude aldehyde obtained above dissolved in MeCN (10 mL) was added, and the mixture was stirred at 20 °C overnight. It was then poured into 1 M aqueous HCl under vigorous stirring. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:4 EtOAc/light petroleum ether) afforded a colorless oil (6.6 g, 71%). R_f (1:2 EtOAc/light petroleum ether) = 0.47. $[\alpha]^{25}_D = -25$ (c = 0.4, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (dd, J = 15.8, 7.8 Hz, 1H), 5.87 (dd, J = 15.8, 1.2 Hz, 1H), 4.73, 4.69 (2d, J = 7.0 Hz, 2 H), 4.68, 4.66 (2d, J = 6.9 Hz, 2H), 4.25−4.16 (m, 5H), 3.90 (dd, J = 6.9, 3.3 Hz, 1H), 3.42, 33.5 (2s, 6H), 2.79−2.76 (m, 1H), 1.32−1.27 (m, 6H), 1.18 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.6, 166.4, 149.9, 121.7, 97.8, 96.9, 81.6, 76.6, 61.2, 60.3, 56.7, 56.4, 38.4, 15.3, 14.2, 14.1. Anal. Calcd for $C_{16}H_{28}O_8$ (348.39): C, 61.62; H, 8.11. Found: C, 61.65; H, 8.14.

Ethyl 4-Deoxy-5,6-di-*O*-(methoxymethyl)-4-methyl-D-*glycero*-L-*galacto*-heptar-1-ate-7,3-lactone ((−)-29). A 0.1 M solution of OsO_4 in CCl_4 (5.4 mL, 0.54 mmol, 7% mol) was added dropwise to a stirred solution of (−)-**28** (2.7 g, 7.7 mmol) and *N*-methylmorpholine-*N*-oxide (2.64 g, 19.4 mmol) in acetone (40 mL) and H_2O (5 mL). The mixture was stirred at 20 °C for 12 h. After dilution with EtOAc (150 mL) and cooling to 0 °C, $Na_2S_2O_5$ (9.5 g) was added portionwise and the mixture stirred at 0 °C for 45 min. The precipitate was filtered off, and EtOAc (200 mL) was added. The solution was washed with 1 M aqueous HCl, then with brine. The aqueous layers were extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated in vacuo. The resulting pale yellow oil was dissolved in THF (60 mL), and concentrated aqueous HCl (15 drops) was added at 0 °C. After stirring at 0 °C for 1 h, $NaHCO_3$ was added portionwise and the mixture stirred at 20 °C for 10 min. The precipitate was filtered off, and the solvent was evaporated to afford (−)-**29** as a pale yellow oil pure enough for the next steps (2.5 g, 96%). An analytical sample of (−)-**29** was obtained by flash chromatography (2:3 EtOAc/light petroleum ether), giving a white solid. Mp: 85−87 °C. R_f (2:3 EtOAc/light petroleum ether) = 0.24. $[\alpha]^{25}_D = -22$ (c = 0.4, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.97, 4.77 (2d, J = 6.7 Hz, 2H), 4.91, 4.70 (2d, J = 7.0 Hz, 2H), 4.45 (dd, J = 10.5, 1.5 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 4.21 (d, J = 7.1 Hz, 1H), 3.70 (dd, J = 8.9, 7.1 Hz, 1H), 3.44, 3.43 (2s, 6H), 3.16 (br s, 1H), 2.41−2.34 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H), 1.23 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 171.4, 169.4, 97.4, 96.9, 81.7, 78.2, 76.0, 69.5, 62.6, 56.3, 35.4, 14.2, 14.1. Anal. Calcd for $C_{14}H_{24}O_9$ (336.33): C, 50.00; H, 7.14. Found: C, 50.03; H, 7.19.

Ethyl [(*tert*-Butyl)dimethylsilyl 4-Deoxy-2,3-di-*O*-(methoxymethyl)-4-methyl-6-*O*-(*tert*-butyl)dimethylsilyl-β-D-*glycero*-L-*gluco*-heptapyranosid]uronate ((+)-30). One molar (*i*-Bu)$_2$AlH in CH_2Cl_2 (55 mL, 55 mmol) was added dropwise to a stirred solution of (−)-**29** (6.2 g, 18.4 mmol) in anhydrous CH_2Cl_2 (140 mL) cooled to −78 °C. After stirring at −78 °C for 10 min, MeOH (10 mL) was added and the mixture was poured into vigorously stirred 1 M aqueous HCl (300 mL). The aqueous layer was extracted with $CHCl_3$. The combined organic extracts were dried ($MgSO_4$), and the solvent was evaporated in vacuo, affording a pale yellow oil (4.74 g, 76% of pyranose), which was dissolved in anhydrous CH_2Cl_2 (120 mL) and cooled to 0 °C. 2,6-Lutidine (8.1 mL, 70 mmol) and (*t*-Bu)Me$_2$SiOSO$_2$CF$_3$ (9 mL, 39 mmol) were added. After stirring at 0 °C for 2 h, the mixture was poured into 2 M aqueous NaOH. The aqueous layer was extracted with $CHCl_3$. The combined organic extracts were washed with 1 M aqueous HCl, then with brine, and dried ($MgSO_4$). The solvent was evaporated and the residue purified by flash chromatography on silica gel (1:15 EtOAc/light petroleum ether), affording a colorless oil (6.7 g, 64%). R_f (1:4 EtOAc/light petroleum ether) = 0.68. $[\alpha]^{25}_D = +8$ (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.01, 4.74 (2d, J = 6.8 Hz, 2H), 4.98, 4.73 (2d, J = 5.7 Hz, 2H), 4.47 (d, J = 7.4 Hz, 1H), 4.37 (d, J = 1.9 Hz, 1H), 4.22−4.19 (m, 2H), 3.51 (dd, J = 10.4, 1.9 Hz, 1H), 3.45, 3.43 (2s, 6H), 3.31 (dd, J = 9.2, 7.4 Hz, 1 H), 3.23 (dd, J = 10.3, 10.2 Hz, 1H), 1.99−1.93 (m, 1H), 1.29 (t, J = 7.1 Hz, 1H), 1.03 (d, J = 6.6 Hz, 1H), 0.93, 0.87 (2s, 18H), 0.13, 0.07, 0.05, 0.03 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 172.1, 98.7, 98.3, 97.7, 82.0, 81.9, 78.9, 71.7, 61.1, 56.4, 56.3, 36.5, 25.8, 25.6, 18.4, 17.7, 14.0, 13.0, −4.0, −4.4, −5.1, −5.6. Anal. Calcd for $C_{26}H_{54}O_9Si_2$ (566.88): C, 55.12; H, 9.54; Si, 9.89. Found: C, 55.24; H, 9.58; Si, 9.72.

Ethyl [(*tert*-Butyl)dimethylsilyl 4-Deoxy-2,3-di-*O*-(methoxymethyl)-4-methyl-6-*O*-(*tert*-butyl)dimethylsilyl-β-D-*glycero*-L-*altro*-heptopyranosid]uronate ((−)-31). When the synthesis started with a 4:1 mixture of (+)-**26** and (−)-**27**, (−)-**31** was isolated in the above flash chromatography. R_f (1:4 EtOAc/light petroleum ether) = 0.71. $[\alpha]^{25}_D = -23$ (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.99 (d, J = 1.0 Hz, 1H), 4.84, 4.64 (2d, J = 6.4 Hz, 2H), 4.75, 4.70 (2d, J = 6.8 Hz, 2H), 4.30 (d, J = 2.1 Hz, 1H), 4.24−4.13 (m, 2H), 3.88 (dd, J = 10.7, 3.1 Hz, 1H), 3.74 (dd, J = 3.6, 3.3 Hz, 1H), 3.58 (dd, J = 3.6, 1.0 Hz, 1H), 3.41, 3.38 (2s, 6H), 2.34−2.32 (m, 1H), 1.30 (t, J = 7.2 Hz, 3 H), 0.94 (d, J = 8.3 Hz, 3 H), 0.94, 0.87 (2s, 18H), 0.16, 0.10, 0.07, 0.04 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 172.3, 97.3, 97.0, 94.3, 79.7, 77.6, 73.7, 72.5, 60.8, 55.8, 55.4, 29.5, 25.9, 25.8, 18.4, 17.9, 14.1, 12.4, −3.9, −4.1, −5.1, −5.5. Anal. Calcd for $C_{26}H_{54}O_9Si_2$ (566.88): C, 55.12; H, 9.54; Si, 9.89. Found: C, 55.22; H, 9.42; Si, 9.91.

(*tert*-Butyl)dimethylsilyl 4-Deoxy-2,3-di-*O*-(methoxymethyl)-4-methyl-6-*O*-(*tert*-butyl)dimethylsilyl)-β-D-*glycero*-L-*gluco*-heptodialdo-1,5-pyranoside ((+)-7). One molar (*i*-Bu)$_2$AlH in CH_2Cl_2 (9.3 mL, 93 mmol) was slowly added to a stirred solution of (+)-**30** (2.1 g, 37 mmol) in anhydrous CH_2Cl_2 (30 mL) cooled to −78 °C. After stirring at −78 °C for 30 min, MeOH (5 mL) was added and the mixture poured into 1 M aqueous HCl (60 mL). The aqueous layer was extracted with $CHCl_3$. The combined organic extracts were dried ($MgSO_4$). After solvent evaporation in vacuo the residue was dissolved in anhydrous CH_2Cl_2 (18 mL), and Dess−Martin periodinane (1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one, 2.8 g, 65 mmol) was added. After stirring at 20 °C for 90 min, Et_2O (30 mL), a saturated aqueous solution of $NaHCO_3$ (40 mL), and anhydrous $Na_2S_2O_3$ (12 g) were added. After vigorous stirring for 5 min, the aqueous layer was extracted with Et_2O (50 mL, twice). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$, then with HCl, and dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:4 EtOAc/light petroleum ether) afforded a colorless oil (1.74 g, 90%). R_f (1:4 EtOAc/light petroleum ether) = 0.69. $[\alpha]^{25}_D = +51$ (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, J = 1.0 Hz, 1H), 5.01, 4.74 (2d, J = 6.8 Hz, 2H), 4.97, 4.72 (2d, J = 6.3 Hz, 2H), 4.44 (d, J = 7.5 Hz, 1H), 4.11−4.09 (m, 2H), 3.45, 3.43 (2s, 6H), 3.44 (masked dd, 1H), 3.33 (dd, J = 9.1, 7.5 Hz, 1H), 3.22 (dd, J = 10.3, 9.1 Hz, 1H), 2.03−1.96 (m, 1H), 1.00 (d, J = 6.5 Hz, 3H), 0.95, 0.88 (2s, 18H), 0.11, 0.09, 0.05, 0.04 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 205.1, 98.7, 98.2, 97.6, 81.7, 81.6, 79.1, 76.7, 56.4, 56.3, 36.4, 25.7, 25.6, 17.7, 12.7, −4.2, −4.3, −5.0, −5.3. Anal. Calcd for $C_{24}H_{50}O_8Si_2$ (522.83): C, 55.14; H, 9.64. Found: C, 55.58; H, 9.62.

(*tert*-Butyl)dimethylsilyl 7-*O*-Acetyl-4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-*O*-(*tert*-butyl)dimethylsilyl]-11-*O*-(triethylsilyl)-β-D-*galacto*-L-*gluco* or β-D-*gulo*-L-*gluco*-pentadecopyranosid-9-ulose ((+)-32). In a Schlenk tube (flame dried), 1.4 M *n*-BuLi in hexanes (1.3 mL, 1.83 mmol) was added to a stirred solution of (*i*-Pr)$_2$NH (0.3 mL, 2.1 mmol) in anhydrous THF (18 mL) cooled to −60 °C. After stirring at −60 °C for 15 min, the mixture was cooled to −78 °C, and (−)-**6** (588 mg, 1.44 mmol) in solution in anhydrous THF (1.5 mL) was added. After stirring at −78 °C for 15 min (+)-**7** (683 mg, 1.31 mmol) was added in solution in anhydrous THF (2 mL). After stirring for 15 min at −78 °C, the mixture was poured into half-saturated aqueous solution of NH_4Cl (50 mL) cooled to 0 °C. The aqueous layer was extracted with EtOAc. The combined extracts were washed with brine and dried ($MgSO_4$).

After solvent evaporation, the residue was dissolved at 0 °C in a mixture of pyridine (7 mL) and Ac_2O (7 mL), containing 4-(dimethylamino)pyridine (20 mg). After stirring at 0 °C for 40 min, the solvents were evaporated in vacuo to dryness and the residue was purified by flash chromatography on silica gel (1:2 EtOAc/light petroleum ether), affording a colorless oil (1.05 g, 75%). R_f (1:4 EtOAc/light petroleum ether) = 0.48. $[\alpha]^{25}_D$ = 15 (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 5.35 (dt, J = 10.0, 2.8 Hz, 1H), 4.98, 4.73 (2d, J = 6.8 Hz, 2H), 4.94, 4.70 (2d, J = 6.3 Hz, 2H), 4.42 (s, 2H), 4.41 (d, J = 7.5 Hz, 1H), 4.02 (t, J = 2.8 Hz, 1H), 3.99 (m, 1H), 3.81 (s, 3H), 3.43, 3.42 (2s, 6H), 3.42 (t, ^3J = 6.8 Hz, 2H), 3.27 (dd, J = 9.1, 7.5 Hz, 1H), 3.22 (dd, J = 10.6, 2.8 Hz, 1H), 3.16 (dd, J = 10.0, 9.1 Hz, 1H), 3.02 (dd, J = 17.8, 10.0 Hz, 1H), 2.91 (dd, J = 17.8, 2.8 Hz, 1H), 2.50−2.46 (m, 1H), 1.98 (s, 3H), 1.93−1.86 (m, 1H), 1.60−1.53 (m, 2H), 1.45−1.37 (m, 4H), 1.12 (d, J = 7.1 Hz, 3H), 1.01 (d, J = 6.5 Hz, 3H), 0.95 (t, J = 8.0 Hz, 9H), 0.94, 0.88 (2s, 18H), 0.60 (q, J = 8.0 Hz, 6H), 0.13, 0.09, 0.07, 0.06 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 210.2, 196.0, 159.0, 130.7, 129.1, 113.7, 98.6, 98.2, 97.9, 82.4, 82.8, 81.8, 78.9, 73.4, 73.0, 72.6, 72.5, 70.0, 56.3, 56.2, 55.2, 52.4, 41.6, 37.1, 35.4, 29.9, 26.0, 25.6, 21.8, 21.0, 18.4, 17.8, 13.4, 12.0, 7.0, 5.2, −4.0, −4.4, −4.8, −5.3. Anal. Calcd for $C_{49}H_{92}O_{13}Si_3$ (973.52): C, 60.49; H, 9.47; Si, 8.45. Found: C, 60.08; H, 9.47; Si, 8.64.

(*tert*-Butyl)dimethylsilyl 7-*O*-Acetyl-4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-*O*-[(*tert*-butyl)dimethylsilyl]-9,11-*O*-bis(triethylsilyl)-β-D-*glycero*-L-*ido* or l-*talo*-L-*gluco*-pentadecopyranoside ((+)-33). HF−pyridine (1.5 mL) was added to a stirred solution of (+)-**32** (620 mg, 0.637 mmol) in anhydrous THF (30 mL) cooled to −20 °C under an Ar atmosphere. The mixture was stirred at −20 °C for 15 min and at 0 °C for 1 h. It was poured into a saturated aqueous solution of $NaHCO_3$ (40 mL). The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$). Solvent evaporation in vacuo afforded a pale yellow oil (547 mg, 100% (*tert*-butyl)dimethylsilyl 7-*O*-acetyl-4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-*O*-[(*tert*-butyl)dimethylsilyl]-β-D-*galacto*-L-*gluco*- or β-D-*gulo*-L-*gluco*-pentadecopyranosid-9-ulose), which was dissolved in THF (4 mL) and MeOH (1 mL). After cooling to −78 °C 1 M Et_2BOMe[22] in THF (0.83 mL, 0.83 mmol) was added. After stirring at −78 °C for 15 min, $NaBH_4$ (34 mg, 0.89 mmol) was added and the stirring continued for 1 h at −78 °C. AcOH (10 drops) was added and the mixture poured into a saturated aqueous solution of $NaHCO_3$ (20 mL) under vigorous stirring. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine and dried ($MgSO_4$). The solvent was evaporated in vacuo. The residue was taken up in MeOH (4 mL) and the solvent evaporated in vacuo. This operation was repeated once to afford a pale yellow oil (427 mg, 78%, of (*tert*-butyl)dimethylsilyl 7-*O*-acetyl-4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-*O*-[(*tert*-butyl)dimethylsilyl]-β-D-*glycero*-L-*ido* or l-*talo*-L-*gluco*-pentadecopyranoside), which was dissolved in dry DMF (4 mL). After cooling to 0 °C, imidazole (169 mg, 2.48 mmol) and Et_3SiCl (267 μL, 1.59 mmol) were added and the mixture stirred at 20 °C for 3 h. The mixture was then poured into H_2O (20 mL), and the aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine and dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:7 EtOAc/light petroleum ether) afforded a colorless oil (346 mg, 50%). $[\alpha]^{25}_D$ = 13 (c = 0.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27, 6.88 (2d, J = 8.3 Hz, 4H), 4.95 (d, J = 6.8 Hz, 1H), 4.90 (d, J = 6.4 Hz, 1H), 4.90 (ddd, J = 10.1, 4.8, 4.7 Hz, 1H), 4.74−4.72 (m, 2H), 4.43 (s, 2H), 4.43 (d, J = 7.2 Hz, 1H), 3.88 (dd, J = 4.8, 1.6 Hz, 1H), 3.81 (s, 3H), 3.78 (m, 1H), 3.68−3.66 (m, 1H), 3.45 (t, J = 6.3 Hz, 2H), 3.45, 3.42 (2s, 6H), 3.24 (dd, J = 9.0, 7.2 Hz, 1H), 3.12 (dd, J = 9.0, 8.9 Hz, 1H), 2.98 (dd, J = 10.8, 1.6 Hz, 1H), 2.07−1.98 (m, 1H), 1.96 (s, 3H), 1.92−1.85 (m, 3H), 1.68−1.63 (m, 1H), 1.62−1.33 (m, 6H), 1.07 (d, J = 6.4 Hz, 3H), 0.96 (t, J = 8.0 Hz, 18H), 0.91, 0.90 (2s, 18H), 0.87 (d, J = 7.1 Hz, 3H), 0.60 (q, J = 8.0 Hz, 12H), 0.14, 0.12, 0.08, 0.07 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.0, 159.0, 130.8, 129.1, 113.7, 98.6, 98.2, 97.7, 82.5, 82.0, 77.1, 73.6, 73.5, 72.5, 70.3, 68.7, 56.35, 56.3, 55.2, 40.0, 38.0, 35.5, 34.3, 30.5, 25.8, 25.7, 21.1, 18.1, 17.9, 13.4, 9.2, 7.0, 6.95, 5.4, 5.2, −4.0, −4.4, −4.7, −5.2. Anal. Calcd for $C_{55}H_{108}O_{13}Si_4$ (1089.45): C, 60.66; H, 9.93; Si, 10.29. Found: C, 60.52; H, 9.97; Si, 10.13.

(*tert*-Butyl)dimethylsilyl 7-*O*-Acetyl-4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-O-[(*tert*-butyl)dimethylsilyl]-9,11-*O*-isopropyliden-β-D-*glycero*-L-*ido* or l-*talo*-L-*gluco*-pentadecopyranoside (34). Crude (*tert*-butyl)dimethylsilyl 7-*O*-acetyl-4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-*O*-[(*tert*-butyl)dimethylsilyl]-β-D-*glycero*-L-*ido* or l-*talo*-L-*gluco*-pentadecopyranoside obtained as above (50 mg, 0.058 mmol) was dissolved in acetone (1.2 mL) and 2,2-dimethoxypropane (1.2 mL) containing paratoluenesulfonic acid (5 mg). After stirring at 20 °C for 6 h, the solvents were evaporated and the residue was chromatographied on silica gel (1:8 EtOAc/light petroleum ether) to afford a colorless oil (42 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26, 6.88 (2d, J = 6.7 Hz, 4H), 4.99, 4.70 (2d, J = 6.8 Hz, 2H), 4.94, 4.73 (2d, J = 6.9 Hz, 2H), 4.50, 4.48 (m, 1H), 4.43 (s, 2H), 4.38 (d, J = 7.5 Hz, 1H), 4.20 (d, J = 1.8 Hz, 1H), 3.91, 3.89 (m, 1H), 3.81 (s, 3H), 3.44 (t, J = 8.1 Hz, 2H), 3.44, 3.42 (2s, 6H), 3.42 (dd, J = 9.9, 1.8 H, 1H), 3.29 (dd, J = 9.2, 7.5 Hz, 1H), 3.19 (dd, J = 9.7, 9.2 Hz, 1H), 3.12 (dd, J = 18.1, 8.8 Hz, 1H), 2.30 (dd, J = 18.1, 3.5 Hz, 1H), 1.94−1.91 (m, 1H), 1.66, 1.59 (m, 2H), 1.43, 1.32 (2s, 6H), 1.43, 1.22 (m, 7H), 1.02 (d, J = 6.4 Hz, 3H), 0.96, 0.87 (2s, 18H), 0.83 (d, J = 6.8 Hz, 3H), 0.13, 0.05, 0.04, 0.03 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 209.9, 159.1, 130.7, 129.2, 113.7, 98.8, 98.6, 97.8, 96.1, 82.1, 81.7, 79.7, 78.0, 73.0, 72.5, 69.9, 68.3, 56.3, 55.2, 42.3, 36.4, 34.4, 32.6, 29.8, 29.6, 25.9, 25.6, 22.0, 19.4, 18.3, 17.8, 13.3, 5.2, −4.3, −4.4, −4.7, −5.3. Anal. Calcd for $C_{44}H_{80}O_{12}Si_2$ (857.28): C, 61.65; H, 9.41. Found: C, 61.42; H, 9.35.

(*tert*-Butyl)dimethylsilyl 4,8,10,12,13,14-Hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-O-[(*tert*-butyl)dimethylsilyl]-9,11-(bis(triethylsilyl)-β-D-*gulo*-L-*gluco*-pentadecopyranosid-7-ulose ((+)-35). A mixture of (+)-**33** (300 mg, 0.276 mmol), anhydrous CH_2Cl_2 (3 mL), and 1 M (i-Bu)$_2$Al in CH_2Cl_2 (827 μL, 0.827 mmol) was stirred at −78 °C for 10 min under an Ar atmosphere. MeOH (0.5 mL) was added and the mixture poured into 1 M aqueous HCl (15 mL) cooled to 0 °C. The aqueous layer was extracted with $CHCl_3$. The combined organic extracts were dried ($MgSO_4$). After solvent evaporation, the residue (260 mg, 0.248 mmol) was dissolved in anhydrous CH_2Cl_2 (3 mL), and 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one (158 mg, 0.372 mmol) was added. After stirring at 20 °C for 30 min, Et_2O (15 mL), a saturated aqueous solution of $NaHCO_3$ (15 mL), and $Na_2S_2O_3$ (0.5 g) were added. The mixture was stirred at 20 °C for 10 min and extracted with Et_2O. The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$, then with brine, and dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:5 EtOAc/light petroleum ether) afforded a colorless oil (231 mg, 80%). $[\alpha]^{25}_D$ = 38 (c = 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27, 6.88 (2d, J = 8.7 Hz, 4H), 5.00, 4.73 (2d, J = 6.8 Hz, 2H), 4.95, 4.71 (2d, J = 6.3 Hz, 2H), 4.44 (s, 2H), 4.43 (d, J = 7.1 Hz, 1H), 4.28−4.26 (m, 1H), 4.24 (d, J = 1.7 Hz, 1H), 3.81 (s, 3H), 3.74−3.71 (m, 1H), 3.51 (dd, ^3J = 10.4, 1.7 Hz, 1H), 3.46 (t, J = 6.8 Hz, 2H), 3.45, 3.42 (2s, 6H), 3.26 (dd, J = 9.1, 7.1 Hz, 1H), 3.20 (t, J = 9.1 Hz, 1H), 2.78 (dd, J = 17.0, 6.3 Hz, 1H), 2.64 (dd, J = 17.0, 5.0 Hz, 1H), 1.91−1.87 (m, 1H), 1.65−1.49, 1.43−1.41 (m, 7H), 1.04 (d, J = 6.5 Hz, 3H), 0.97 (d, J = 7.6 Hz, 3H), 0.95−0.93 (m, 18H), 0.87 (s, 18H), 0.59 (q, J = 7.8 Hz, 12 H), 0.13, 0.04, 0.01 (3s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 208.4, 159.0, 130.8, 129.1, 113.7, 98.6, 98.2, 97.7, 82.0, 81.9, 78.8, 78.7, 73.1, 72.5, 70.3, 69.0, 56.3, 55.2, 44.8, 42.3, 36.8, 34.9, 30.2, 25.9, 25.7, 21.0, 18.4, 17.8, 13.3, 10.2, 7.0, 5.3, 5.2, −3.9, −4.0, −4.6, −5.3. Anal. Calcd for $C_{55}H_{104}O_{12}Si_4$ (1045.75): C, 60.92; H, 9.96. Found: C, 60.64; H, 9.75.

Methyl [(*tert*-Butyl)dimethylsilyl 4,8,10,12,13,14-Hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-*O*-[(*tert*-butyl)dimethylsilyl]-*β*-D-*gulo*-L-*gluco*-pentadecopyranosid]-7-ulo-7,11-pyranoside ((+)-36). HF−pyridine (0.23 mL) was added to a stirred solution of (+)-**35** (116 mg, 0.11 mmol) in anhydrous THF (2.4 mL) cooled to 0 °C. After stirring at 0 °C for 30 min, the mixture was poured into a saturated aqueous solution of $NaHCO_3$ (15 mL) and then extracted with EtOAc. The solvent was evaporated in vacuo, and the crude oil (7-ulo-7,1-pyranose) was dissolved in MeOH (1.5 mL). After the addition of *p*-toluenesulfonic acid (4 mg), the mixture was stirred at 20 °C for 2 h. $NaHCO_3$ (15 mg) was added. After stirring at 20 °C for 5 min the precipitate was filtered off. Solvent evaporation and flash chromatography on silica gel (1:6 EtOAc/light petroleum ether) afforded a colorless oil (71 mg, 77%). R_f (1:4 EtOAc/light petroleum ether) = 0.57. $[\alpha]^{25}_D = 9$ ($c = 0.5$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33, 6.91 (2d, 4H), 5.39 (br.d, $J = 5.1$ Hz, 1H), 5.25, 4.86 (2d, $J = 6.1$ Hz, 2H), 5.24, 4.77 (2d, $J = 6.7$ Hz, 2H), 4.62 (d, $J = 7.6$ Hz, 1H), 4.44 (s, 2H), 4.41 (br s, 1H), 4.15 (m, 1H), 3.68 (dd, $J = 9.2$, 7.6 Hz, 1H), 3.45 (t, $J = 6.0$ Hz, 2H), 3.39−3.26 (m, 3H), 3.38 (s, 3H), 3.34, 3.31 (2s, 6H), 3.27 (s, 3H), 2.21−2.14 (m, 1H), 1.86−1.57 (m, 9H), 1.31 (d, $J = 6.5$ Hz, 3H), 1.07, 1.06 (2s, 18H), 0.78 (d, $J = 7.2$ Hz, 3H), 0.38, 0.30, 0.17, 0.13 (4s, 12H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 156.7, 132.0, 129.8, 114.5, 99.4, 99.35, 98.3, 96.4, 83.2, 82.7, 79.4, 77.2, 75.4, 73.2, 72.9, 70.6, 56.5, 55.5, 55.2, 38.5, 35.8, 32.6, 32.6, 30.7, 23.7, 26.6, 18.9, 18.7, 14.4, 10.6, −2.9, −3.8, −4.4, −4.5. Anal. Calcd for $C_{42}H_{78}O_{12}Si_2$ (831.24): C, 60.69; H, 9.46. Found: C, 60.84; H, 9.31.

(4*S*,*E*)-7-Chloro-1-{methyl 4,8,10,12,13,14-hexadeoxy-2,3-*O*-bis(methoxymethyl)-4,10-dimethyl-15-*O*-(*p*-methoxybenzyl)-6-[(*tert*-butyl)dimethylsilyl]-*β*-D-*gulo*-L-*gluco*-pentadecos-7-ulo-α-7,11-pyranosid-5,1-pyranosid}-2-methylidene-4-[(*p*-methoxybenzoyl)oxy]octa-5,7-diene ((+)-38). A mixture of (+)-**36** (30 mg, 0.036 mmol), anhydrous THF (1.1 mL), and 1 M Bu_4NF in THF (39 μL, 0.039 mmol) was stirred at −30 °C for 1.5 h. Solvent evaporation, filtration through a pad of silica gel (3:1 EtOAc/light petroleum ether), and solvent evaporation afforded a colorless oil, which was dissolved at 0 °C in pyridine (0.4 mL) and Ac_2O (0.4 mL). After addition of 4-(dimethylamino)pyridine (3 mg), the mixture was stirred at 0 °C for 1 h. Solvents were evaporated under high vacuum (10^{-2} Torr). The residue was dissolved in CH_2Cl_2 (8 mL). The solution was washed with 1 M aqueous HCl (2 mL), then with saturated aqueous solution of $NaHCO_3$ (2 mL) and finally with H_2O (2 mL). After drying ($MgSO_4$), the solvent was evaporated, affording unstable diacetate **37** as a pale yellow oil (22 mg, 75%). The crude diacetate **37** (20 mg, 0.025 mmol) was dissolved in CD_3NO_2 (5 mm NMR tube) and cooled to −10 °C. **16** (83 mg, 0.2 mmol) and $Me_3SiOSO_2CF_3$ (31 μL, 0.2 mmol) were added, and the reaction was followed by ^{1}H NMR at −10 °C. After 3 h at −10 °C the mixture was poured into a saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with EtOAc (8 mL, four times). The combined organic extracts were washed with brine and dried ($MgSO_4$). After solvent evaporation in vacuo the residue was dissolved in anhydrous THF (1.5 mL), and DBU (60 μL) was added. After stirring at 50 °C for 30 min, the mixture was poured into H_2O (5 mL) and extracted with Et_2O. The combined organic extracts were washed successively with 1 M aqueous HCl, a saturated aqueous solution of $NaHCO_3$ and brine and then dried ($MgSO_4$). Solvent evaporation and flash chromatography on silica gel (1:8 to 1:4 EtOAc/light petroleum ether) afforded a colorless oil (11 mg, 42%) containing a 4:1 mixture of β/α C-glycosides. A second flash chromatography on silica gel afforded pure (+)-**38** (8 mg, 30%). R_f (1:16 EtOAc/light petroleum ether) = 0.13. $[\alpha]^{25}_D = 65$ ($c = 0.3$, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02, 6.93 (2d, $J = 9.0$ Hz, 4H), 7.26, 6.88 (2d, $J = 8.7$ Hz, 4H), 6.38 (dd, $J = 15.0$, 0.9 Hz, 1H), 6.19 (dd, $J = 15.0$, 6.2 Hz, 1H), 5.38, 5.31 (2s, 2H), 4.95 (d, $J = 6.8$ Hz, 1H), 4.79−4.77 (m, 1H), 4.76, 4.64 (2br s, 2H), 4.73−4.67 (m, 3H), 4.44 (s, 2H), 3.93−3.90 (m, 1H), 3.87, 3.81 (2s, 6H), 3.80 (br s, 1H), 3.70 (d, $J = 11.1$ Hz, 1H), 3.55 (dm, $J = 10.0$, 1H), 3.47 (t, $J = 7.1$ Hz, 2H), 3.45, 3.33 (2s, 6H), 3.38 (dd, $J = 9.1$, 9.0 Hz, 1H), 3.24 (dd, $J = 10.0$, 9.1 Hz, 1H), 3.12 (s, 3H), 2.52 (dd, $J = 14.3$, 8.0 Hz, 1H), 2.36 (dd, $J = 14.3$, 5.8 Hz, 1H), 2.11 (s, 3H), 2.10−2.06 (m, 2H), 1.86−1.80 (m, 1H), 1.79−1.56, 1.45−1.28 (2m, 9H), 1.06 (d, $J = 6.5$ Hz, 3H), 0.90 (s, 9H), 0.89 (d, $J = 7.1$ Hz, 3H), 0.10, 0.07 (2s, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.4, 165.4, 163.4, 159.1, 142.2, 137.7, 133.0, 131.7, 130.7, 129.2, 128.5, 122.7, 116.5, 113.7, 113.6, 110.9, 100.8, 98.4, 97.1, 83.6, 79.6, 79.1, 78.3, 72.7, 72.6, 71.8, 70.4, 69.9, 67.6, 56.4, 55.7, 55.4, 55.3, 47.0, 43.4, 37.4, 36.7, 34.5, 32.2, 29.9, 25.9, 22.8, 20.9, 18.4, 13.7, 10.2, −3.1, −4.4. Anal. Calcd for $C_{55}H_{85}O_{15}SiCl$ (1049.80): C, 62.93; H, 8.16. Found: C, 62.72; H, 8.05.

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Supporting Information Available: Data for (−)-**6**, (−)-**6A**, (−)-**6M(*S*)**, (+)-**6M(*R*)**, (+)-**7**, (+)-**8**, **12**-**14**, **16**, (+)-**17**, **19**, **20**, (+)-**22**, (+)-**23**, (+)-**26**, (−)-**28**, (−)-**29**, (+)-**30**, (−)-**31**, (+)-**32**, (+)-**33**, (+)-**35**, (+)-**36**, (+)-**38**. This material is available free of charge via the Internet at http://pubs.acs.org.

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