Total Synthesis of Everninomicin 13,384-1—Part 3: Synthesis of the DE Fragment and Completion of the Total Synthesis

K. C. Nicolaou,* Helen J. Mitchell, Rosa Maria Rodríguez, Konstantina C. Fylaktakidou, Hideo Suzuki, and Scott R. Conley[a]

Abstract: The stereoselective construction of the DE fragment (**2**) of everninomicin 13,384-1 (**1**) is reported. From the two possible ways of inserting the DE fragment between the $A_1B(A)C$ and $FGHA_2$ domains of the natural product, the sequence involving the $DEFGHA_2$ segment was found to be the most viable. This coupling was followed by attachment of a suitably protected and activated $A_1B(A)C$ fragment which led, after orthoester construction and final deprotection to the targeted everninomicin 13,384-1 (**1**), completing the total synthesis of this complex naturally occurring substance.

Keywords: carbohydrates · everninomicin · orthoester formation · phenylseleno glycoside · stereocontrolled glycosidation

Introduction

In the preceding two papers[1, 2] we described the evolution of the strategies for the construction of the $A_1B(A)C$ and $FGHA_2$ fragments of everninomicin 13,384-1 (**1**). These fragments were produced with appropriate activation and protecting groups for eventual insertion of the central DE fragment and with the flexibility of the initial coupling being carried out with either of the two larger fragments. In this article, we describe the construction of the remaining DE segment **2**, its union with fragments $A_1B(A)C$ and $FGHA_2$, and the completion of the total synthesis of **1**.

Results and Discussion

Retrosynthetic analysis and strategy: Figure 1 depicts the retrosynthetic analysis of everninomicin 13,384-1 (**1**) in which the excision of the appropriately protected and activated DE fragment **2** is highlighted. Thus, the trichloroacetimidate[3] group in conjunction with an acetate group at C-2 of ring E was chosen to ensure the stereoselective coupling of this fragment with the free hydroxy group of the $FGHA_2$ fragment. Functional group manipulation of **2**, followed by further disconnection of the resulting disaccharide **3**, led to carbohydrate units **4** and **5**. The protecting groups on **3** were carefully defined with optimum flexibility so as to allow for extension at either end in order to form the larger fragments $A_1B(A)CDE$ or $DEFGHA_2$, respectively. Eventually, it turned out that the ensemble illustrated by **2** was found to be the most viable form of the DE fragment for incorporation into the grand structure of the target molecule. Careful inspection of structure **3** reveals the following two challenging features: a) the β-mannoside linkage bridging sugars D and E; and b) the tertiary center on ring D. We chose the Kahne sulfoxide-based glycosidation reaction[4] as the procedure for coupling **4** and **5** and, in addition, incorporated a benzylidene ring in **4** in order to ensure the stereocontrolled formation of the β-mannoside bond, as reported by Crich.[5] Both the projected reaction conditions and use of a benzylidene ring suited our protecting group strategy and we, therefore, considered next the issue of introducing the branching to ring D. At this juncture it was postulated that the proper introduction of the methyl group at C-3 of ring D at the monosaccharide stage would be difficult[6] and, therefore, the planned nucleophilic attack on a carbonyl functionality was postponed until after the coupling so as to avoid any 1,3-diaxial interactions, as will be discussed further below.

Construction of building blocks: The construction of the ring D fragment, compound **4**, proceeded from known intermediate **6**[7] as shown in Scheme 1. Thus, regioselective tin-acetal[8] mediated protection of the C-3 hydroxyl group in

[a] Prof. Dr. K. C. Nicolaou, H. J. Mitchell, Dr. R. M. Rodríguez, Dr. K. C. Fylaktakidou, Dr. H. Suzuki, Dr. S. R. Conley
Department of Chemistry and The Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, California 92037 (USA)
and
Department of Chemistry and Biochemistry
University of California San Diego
9500 Gilman Drive, La Jolla, California 92093 (USA)
Fax: (+1) 858-784-2469
E-mail: kcn@scripps.edu

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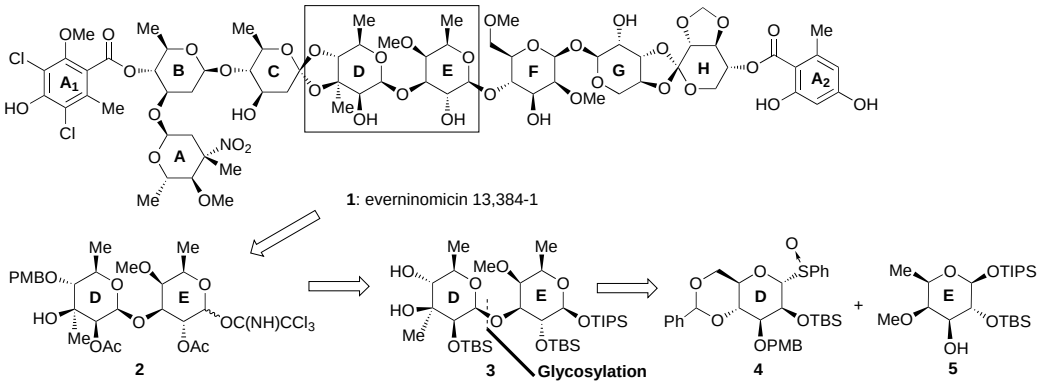
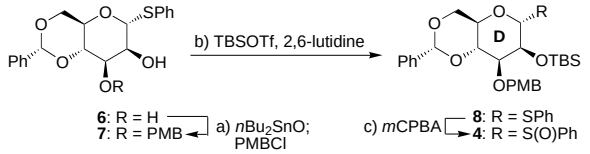


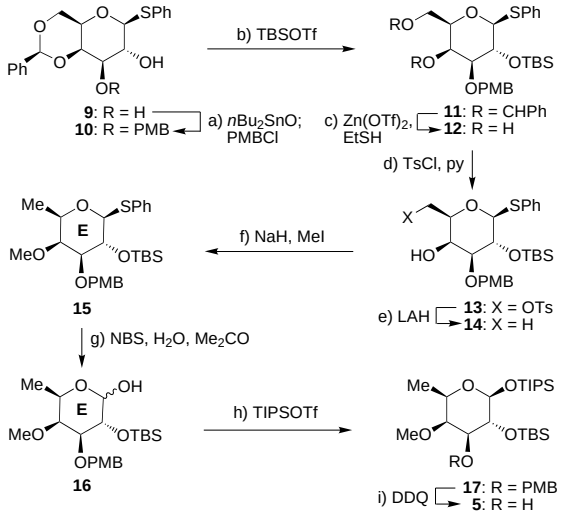
Figure 1. Retrosynthetic analysis of DE fragment **2**. Ac = acetyl; PMB = *p*-methoxybenzyl; TBS = *t*butyldimethylsilyl; TIPS = triisopropylsilyl.



Scheme 1. Synthesis of carbohydrate building block D (**4**). a) 1.1 equiv nBu$_2$SnO, toluene, reflux, 3 h; 1.5 equiv PMBCl, 0.2 equiv nBu$_4$NI, 25 → 110 °C, 2 h, 83 %; b) 1.2 equiv TBSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 0.5 h, 93 %; c) 1.1 equiv *m*CPBA, CH_2Cl_2, −20 → 0 °C, 2 h, 92 % (ca. 4:1 mixture of diastereoisomers). Tf = trifluoromethanesulfonyl; *m*CPBA = *m*-chloroperoxybenzoic acid.

6 as PMB ether **7** (nBu$_2$SnO; PMBCl, nBu$_4$NI, 83 % yield) followed by silylation at C-2 (TBSOTf, 2,6-lutidine, 93 % yield) to afford **8**, and oxidation of the sulfur moiety (*m*CPBA, 92 % yield) furnished the desired sulfoxide **4** (as a ca. 4:1 mixture of diastereoisomers).

Scheme 2 summarizes the synthesis of the required ring E acceptor fragment, compound **5**. This construction began with galactose diol **9**[9] whose monoprotection as a C-3 PMB ether proceeded smoothly under the tin-acetal technology, used successfully and so often in this project, (nBu$_2$SnO; PMBCl, nBu$_4$NI, 87 % yield). The protection of the C-2 hydroxyl group as a silyl ether (TBSOTf, 2,6-lutidine, 97 % yield) was followed by cleavage of the benzylidene group (Zn(OTf)$_2$/EtSH, 77 % yield) leading to diol **12** via **11**. The next objective was to deoxygenate at C-6, a task carried out successfully by first tosylating the primary alcohol (TsCl, py, 97 % yield) and then reducing the resulting tosylate (**13**) with LAH, leading to compound **14** (90 % yield). Methylation of the remaining hydroxyl group (at C-4) was effected with MeI in the presence of NaH to furnish methyl ether **15** in 94 % yield, and cleavage



Scheme 2. Synthesis of carbohydrate building block E (**5**). a) 1.1 equiv nBu$_2$SnO, toluene, reflux, 3 h; 1.5 equiv PMBCl, 0.2 equiv nBu$_4$NI, 25 → 110 °C, 2 h, 87 %; b) 1.2 equiv TBSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 1 h, 97 %; c) 2.5 equiv Zn(OTf)$_2$, 20 equiv EtSH, CH_2Cl_2, 0 °C, 2 h, 77 %; d) 1.1 equiv TsCl, py, 0 → 25 °C, 12 h, 97 %; e) 1.6 equiv LAH, THF, 0 → 45 °C, 3 h, 90 %; f) 1.1 equiv NaH, 1.3 equiv MeI, DMF, 0 → 25 °C, 1 h, 94 %; g) 1.5 equiv NBS, Me_2CO/H_2O 10:1, 0 → 25 °C, 2 h, 95 %; h) 1.2 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 6 h, 97 %, α:β ca. 1:2; i) 1.5 equiv DDQ, CH_2Cl_2/H_2O 10:1 0 → 25 °C, 1 h, 98 %. LAH = lithium aluminumhydride; Ts = *p*-toluenesulfonyl; DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; NBS = *N*-bromosuccinimide; py = pyridine.

of the thioglycoside with NBS in aqueous acetone led to lactol **16** (95 %). Silylation of the latter compound (**16**) (TIPSOTf, 2,6-lutidine) afforded compound **17** together with its α-anomer (97 % yield, β:α ca. 2:1, both anomers could be taken though the remainder of the sequence). The PMB group was removed from **17** by exposure to DDQ furnishing the targeted building block **5** in 98 % yield.

Scheme 3 outlines the coupling of building blocks **4** and **5** to form the advanced key intermediates **3** and **2**. Thus, union of **4** and **5** under the Kahne/Crich conditions (**4**, Tf_2O, DTBMP, −78 °C; followed by addition of **5**) produced smoothly, via the transient glycosyl triflate, the β-mannoside **18** in 71 % yield. It was then considered prudent to attempt the C-3 branching at this stage and before the required exchange of protecting groups. To this end, the PMB group was removed from ring D of compound **18** (DDQ, 95 % yield) and the resulting alcohol

Abstract in Greek: Αναφέρεται η στερεοεκλεκτική σύνθεση του τμήματος DE (**2**) της Everninomicin 13,384-1 (**1**). Από τους δύο πιθανούς τρόπους σύνδεσης του τμήματος DE με τα $A_1B(A)C$ και $FGHA_2$ υπόλοιπα του φυσικού προϊόντος, η ακολουθία που περιλαμβάνει το σχηματισμό του τμήματος $DEFGHA_2$ βρέθηκε να είναι η πιό βιώσιμη. Τη σύζευξη αυτή ακολούθησε η εισαγωγή του κατάλληλα προστατευμένου και ενεργοποιημένου τμήματος $A_1B(A)C$ που μετά από τη δόμηση και του ορθοεστέρα και τελικά την αποπροστασία όλων των ομάδων οδήγησε στο ζητούμενο μόριο, την Everninomicin 13,384-1 (**1**), ολοκληρώνοντας έτσι στην ολική σύνθεση του πολύπλοκου αυτού φυσικού προϊόντος.

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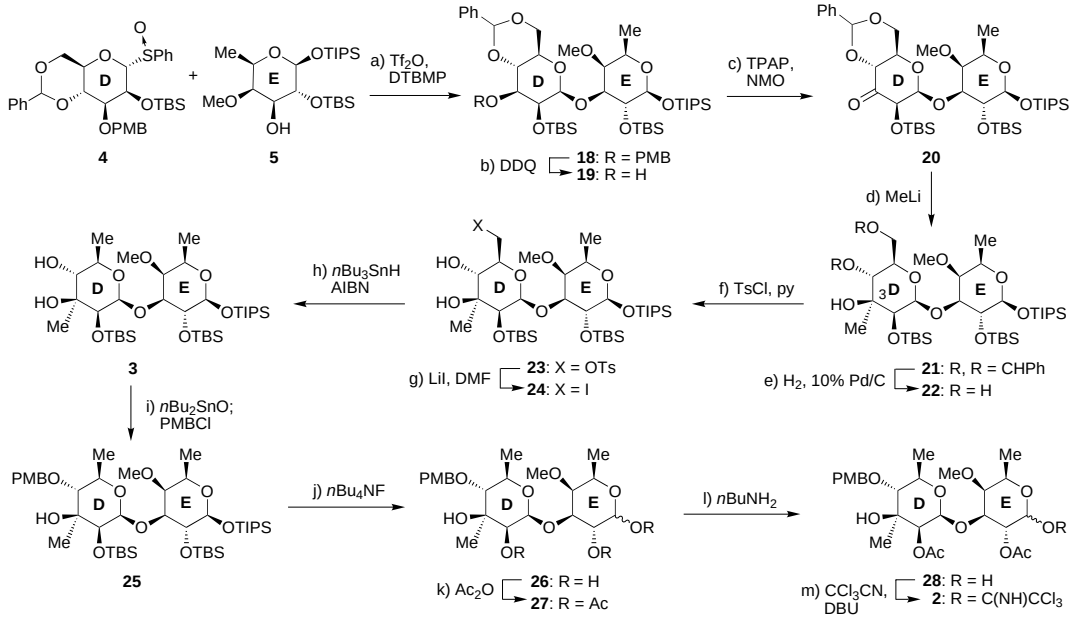


Scheme 3. Assembly of DE fragment **2**. a) 1.3 equiv **4**, 1.3 equiv Tf_2O, 2.2 equiv DTBMP, CH_2Cl_2, $-78\,^{\circ}C$; 1.0 equiv **5**, $-78 \rightarrow 0\,^{\circ}C$, 2 h, 71 %; b) 1.3 equiv DDQ, CH_2Cl_2/H_2O 10:1, $0 \rightarrow 25\,^{\circ}C$, 2 h, 95 %; c) 1.5 equiv NMO, 0.05 equiv TPAP, CH_2Cl_2, $25\,^{\circ}C$, 2 h; d) 1.4 equiv MeLi, Et_2O, $-78\,^{\circ}C$, 1 h, 88 % over two steps; e) H_2, 0.2 equiv 10 % Pd/C (*w*/*w*), EtOAc, $25\,^{\circ}C$, 2 h, 97 %; f) 1.2 equiv TsCl, py, $0 \rightarrow 25\,^{\circ}C$, 12 h, 87 %; g) 5.0 equiv LiI, DMF, $80 \rightarrow 100\,^{\circ}C$, 2 h, 86 %; h) 3.0 equiv $n$$Bu_3SnH$, 0.05 equiv AIBN, benzene, reflux, 0.5 h, 97 %; i) 1.1 equiv $n$$Bu_2SnO$, toluene, reflux, 5 h; 1.5 equiv PMBCl, 0.2 equiv $n$$Bu_4NI$, $25 \rightarrow 110\,^{\circ}C$, 8 h, 63 %; j) 4.0 equiv $n$$Bu_4NF$, THF, $25\,^{\circ}C$, 6 h; k) 2.5 equiv Ac_2O, 4.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$,1 h, 90 % for two steps; l) 1.2 equiv $n$$BuNH_2$, THF, $25\,^{\circ}C$, 5 h, 86 %; m) 5.0 equiv CCl_3CN, 0.05 equiv DBU, CH_2Cl_2, $0\,^{\circ}C$, 0.5 h, 89 %, α:β ca. 30:1. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene; DTBMP = di-*tert*-butyl-4-methylpyridine; AIBN = 2,2′-azobisisobutyronitrile; DMF = dimethylformamide.

(**19**) was oxidized with TPAP/NMO to afford ketone **20**. To our delight, reaction of this ketone (**20**) with MeLi in ether at $-78\,^{\circ}C$ produced the desired tertiary alcohol (**21**) in 88 % overall yield from **19**. The presumed trajectory leading to the observed product **21** along with the assumed conformation of ring D of **20** are depicted in Figure 2.

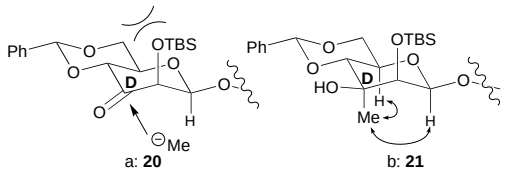
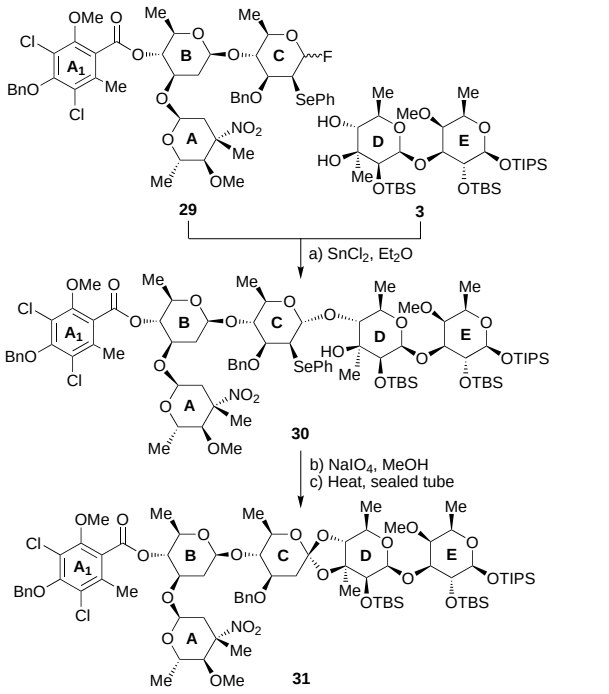


Figure 2. a) Illustration of preferential α-attack of MeLi on the C-3 carbonyl of ring D in ketone **20**. b) Illustration of NOEs used to confirm the structure of compound **21**.

Apparently, the equatorially orientated β-mannoside bond and the bulky, axially orientated TBS group at C-2 of compound **20** provided a decisively biased encounter for the incoming MeLi reagent, as opposed to the monosaccharide unit D carrying a 1α-substituent in which the reagent would have encountered opposing 1,2- and 1,3-interactions. Illustrated in Figure 2 are also the observed NOEs by ^{1}H-NMR studies and which served to assign the configuration of the newly generated stereocenter in **21**. The stereochemistry of the β-mannoside linkage was also confirmed by measuring the $^{13}C-^1H$ spin coupling constant[10] which was consistent with literature values (159.8 Hz). The resulting tertiary alcohol in **21** was found to be highly hindered and difficult to protect under standard conditions, leading to the conviction that it could remain unprotected throughout the remainder of the sequence without much interference—a prediction that was proven both correct and fortunate. The next task was to deoxygenate the C-6 position of ring D, and to this end, the benzylidene group of **21** was removed by mild hydrogenolysis (H_2, 10 % Pd/C, 97 % yield) to afford primary alcohol **22** which was converted to its tosylate **23** (TsCl, py, 87 % yield). Initial attempts to reduce this compound **23** resulted in decomposition, prompting us to exchange the tosylate group for an iodide (LiI, 86 % yield) furnishing derivative **24** whose reduction with $n$$Bu_3SnH$/AIBN cat. proceeded smoothly to afford the desired compound **3** in 97 % yield.

Testing of strategies: The availability of intermediate **3** gave us the early opportunity to test the first of the two approaches for the attachment of the DE fragment onto the growing backbone of the final target, namely the coupling of **3** to the $A_1B(A)C$ glycosyl fluoride **29**.[1] Scheme 4 summarizes the progress made following this strategy. Thus, coupling of donor **29** (see Part 1 in this series)[1] with diol acceptor **3** in Et_2O and in the presence of $SnCl_2$ afforded pentasaccharide **30** in 62 % yield. Although no product resulting from coupling at the tertiary alcohol on ring D was observed, a by-product with a double bond across the C-2/C-3 of ring C (i.e., loss of BnOSe-Ph) was formed on long reaction times and/or exposure to excessive amounts of Lewis acid catalyst. The next stage involved testing orthoester formation, and to this end, the selenium moiety in **30** was oxidized[11] [$NaIO_4$ in MeOH/CH_2Cl_2/H_2O 3:2:1] followed by heating in a sealed tube at $140\,^{\circ}C$ [toluene/vinyl acetate/diisopropylamine 2:2:1] whereby the resulting *syn*-elimination product was encouraged to cyclize. Pleasantly, this sequence afforded $A_1B(A)CDE$

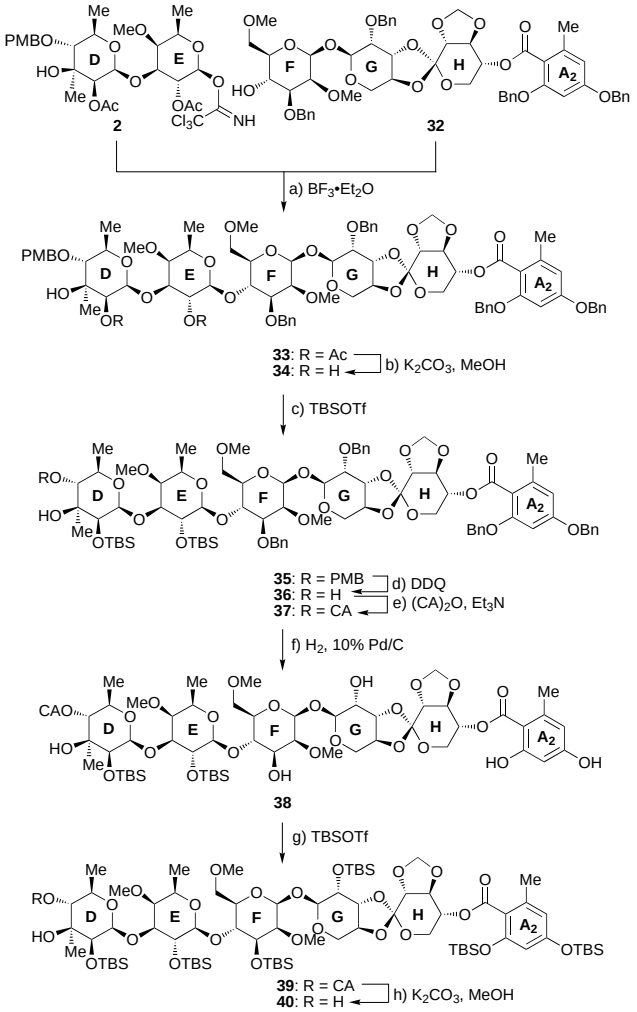


Scheme 4. Synthesis of the $A_1B(A)CDE$ system **31**. a) 1.1 equiv **3**, 1.0 equiv **29**, 1.3 equiv $SnCl_2$, Et_2O, $0 \rightarrow 25\,^{\circ}C$, 6 h, 62%; b) 10.0 equiv $NaIO_4$, 8.0 equiv $NaHCO_3$, $MeOH/CH_2Cl_2/H_2O$ 3:2:1, 25 °C, 4 h; c) vinyl acetate/toluene/diisopropylamine 2:2:1, sealed tube, 140 °C, 12 h, 60% over two steps. Bn = benzyl.

orthoester **31** in 60% overall yield and as a single stereoisomer. The original vision, however, of coupling either **31** or **30** with the $FGHA_2$ fragment was not realized because of difficulties encountered in attempting to further elaborate these intermediates. The successful arrival at compound **31**, however, was highly informative in that it confirmed that the diol system of ring D could indeed be used in the coupling reaction as a carbohydrate acceptor, and that an orthoester formation reaction with advanced intermediates was viable.

Recognizing the difficulties with the $A_1B(A)C+DE$ approach, we then focussed our attention to the alternative strategy of attaching a suitably activated DE fragment onto the $FGHA_2$ segment prior to the incorporation of the $A_1B(A)C$ fragment. To describe what followed, we have to return to Scheme 3 and compound **3**. Thus, in order to reach our second coupling partner, trichloroacetimidate **2**, we required suitable protection of the C-4 hydroxyl group of ring D and activation of the C-1 position of ring E. To this end, regioselective protection at C-4 of ring D was achieved with n-Bu_2SnO/PMBCl/n-Bu_4NI, providing PMB ether **25** (63% yield) which was fully desilylated (n-Bu_4NF) and peracetylated (Ac_2O, Et_3N, 4-DMAP cat.) to afford triacetate **27** (90% yield for two steps, α:β anomers ca. 1:1) via triol **26**. Exposure of the latter compound **27** to the mild action of n-$BuNH_2$ in THF led to the selective removal of the anomeric acetate furnishing lactol **28** (86% yield), whose conversion to trichloroacetimidate **2** required treatment with CCl_3CN in the presence of DBU (89% yield, ca. 30:1 α:β anomer ratio).

Synthesis of the $DEFGHA_2$ fragment: With trichloroacetimidate **2** in hand, we were now ready to proceed with the second strategy of incorporation, which called for coupling **2** with the $FGHA_2$ fragment **32** (see Scheme 5). Thus, reaction of **2** with **32** in CH_2Cl_2 and in the presence of $BF_3 \cdot Et_2O$ at $-20\,^{\circ}C$ furnished oligosaccharide **33** with the desired β-glycoside bond (between rings E and F) and in 55% yield. This reaction also produced a small amount of the corresponding α-glycoside (between rings E and F, 5% yield) and



Scheme 5. Completion of the synthesis of the $DEFGHA_2$ fragment (**40**). a) 1.7 equiv **2**, 0.5 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, $-20\,^{\circ}C$; 2 h, 55% yield of desired β-anomer, 18% of unknown compound (β-anomer) and 5% yield of α-anomer, α:β ca. 1:10; b) 0.5 equiv K_2CO_3, MeOH/THF 1:1, 25 °C, 1 h, 93%; c) 2.5 equiv TBSOTf, 4.0 equiv 2,6-lutidine, CH_2Cl_2, $-10 \rightarrow 0\,^{\circ}C$, 1 h, 92%; d) 1.5 equiv DDQ, CH_2Cl_2/H_2O 10:1, $0 \rightarrow 25\,^{\circ}C$, 1 h, 98%; e) 1.5 equiv $(CA)_2O$, 2.0 equiv Et_3N, 0.1 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 1 h, 99%; f) H_2, 0.2 equiv 10% Pd/C (*w*/*w*), EtOAc, 25 °C, 3 h, 94%; g) 6.0 equiv TBSOTf, 8.0 equiv lutidine, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 92%; h) 0.2 equiv K_2CO_3, THF/MeOH 2:1, 25 °C, 15 min, 85%. CA = chloroacetyl.

another compound whose complete structure remains unassigned but which appears to be isomeric to **33** and possesses the E/F β-glycoside stereochemistry (18% yield). The lack of complete structural information of this by-product created the need to confirm unambiguously the structure of the major isomer **33**, and it was decided that this could be done through degradation studies with everninomicin 13,384-1 (**1**). Specif-

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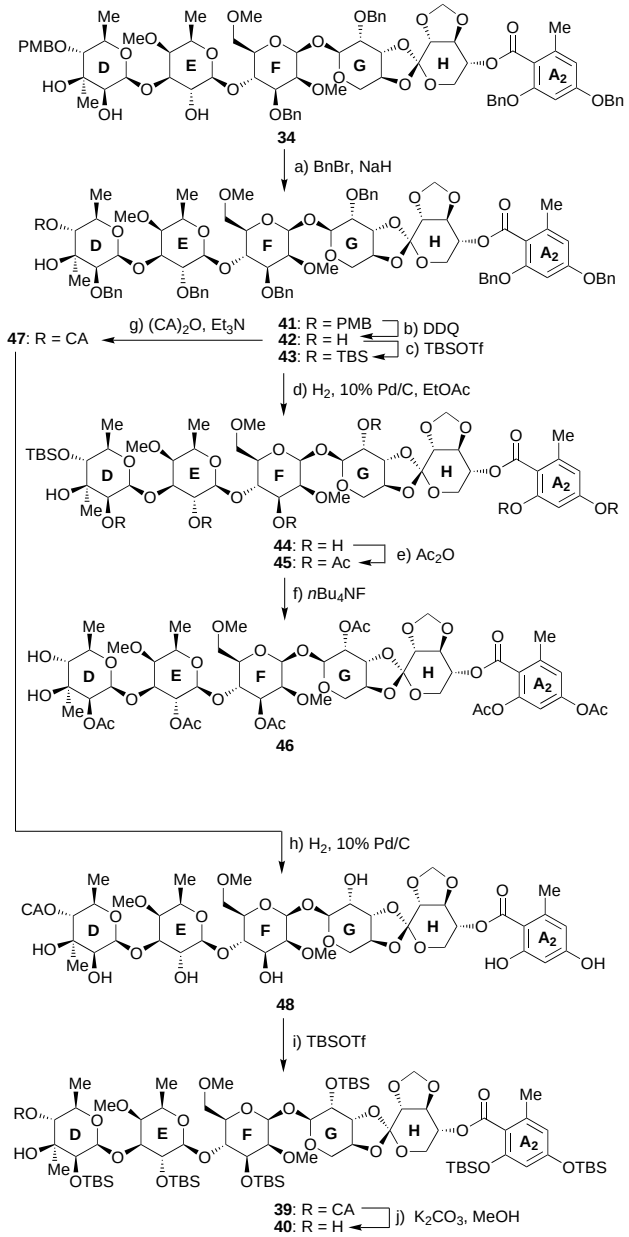
ically, we set out to prepare a common intermediate (i.e., compound **41**, Scheme 6) from **33** (Scheme 5) and from **1** (see Scheme 7), for spectroscopic comparison. Therefore, pentasaccharide **33** was deacetylated (Scheme 5) with K_2CO_3 in MeOH to afford triol **34** (93% yield) which was then cleanly dibenzylated (see Scheme 6) with NaH/BnBr (95% yield) leading to hexabenzyl ether **41** in which the tertiary alcohol on ring D remained free. Hexa-benzyl ether **41** could also be

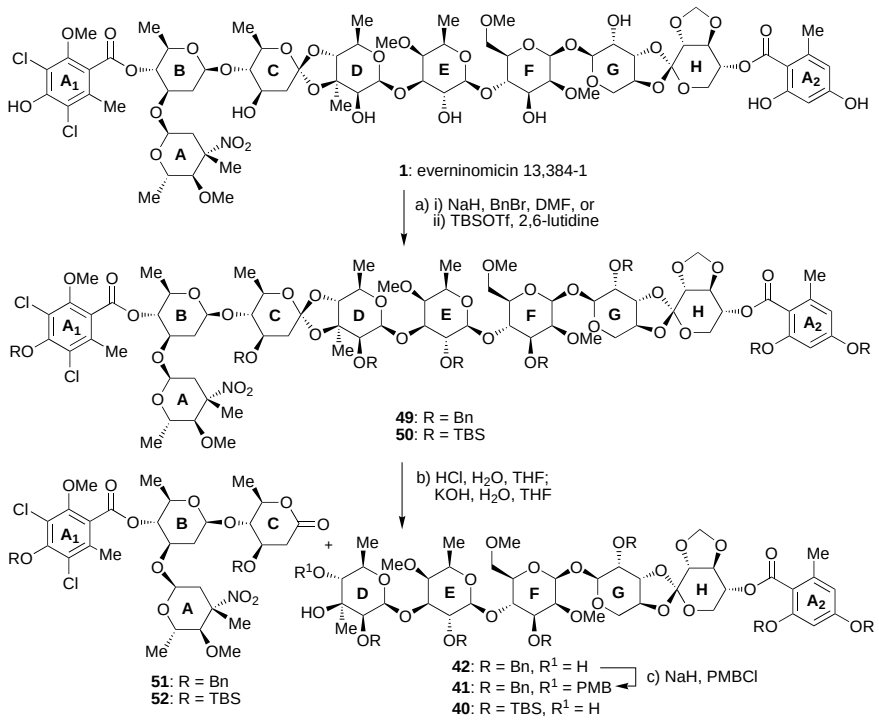


Scheme 6. Synthesis of $DEFGHA_2$ fragments **40**, **42**, and **46**, initial strategies. a) 3.0 equiv NaH, 2.5 equiv BnBr, 0.2 equiv nBu_4NI, DMF, $0 \rightarrow 25\,^{\circ}C$, 2 h, 95%; b) 1.5 equiv DDQ, CH_2Cl_2/H_2O 10:1, $0 \rightarrow 25\,^{\circ}C$, 2 h, 95%; c) 1.5 equiv TBSOTf, 3.0 equiv lutidine, CH_2Cl_2, $-10 \rightarrow 0\,^{\circ}C$, 1 h, 96%; d) 0.5 equiv 10% Pd/C (*w*/*w*), EtOAc, 25 °C, 6 h; e) 10.0 equiv Ac_2O, 20 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 88% over two steps; f) 1.5 equiv nBu_4NF, 1.5 equiv AcOH, THF, $0 \rightarrow 25\,^{\circ}C$, 2 h, 90%; g) 1.5 equiv $(CA)_2O$, 3.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 1 h, 98%; h) 0.5 equiv 10% Pd/C (*w*/*w*), EtOAc, 25 °C, 4 h; i) 8.0 equiv TBSOTf, 20 equiv 2,6-di-*tert*-butylpyridine, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 8 h, 65% over two steps; j) 0.2 equiv K_2CO_3, MeOH, 25 °C,15 min, 85%.

derived from the natural product (**1**) by degradation as illustrated in Scheme 7. Thus, everninomicin 13,384-1 (**1**)[12] was benzylated by treatment with excess NaH/BnBr in DMF affording the fully benzylated everninomicin **49** in 93% yield. The CD orthoester bridge was then selectively ruptured with dilute aqueous HCl in THF[13] affording the corresponding open-chain dihydroxy ester which was treated in situ with aqueous KOH causing cyclization to δ-lactone **51** and release of diol **42**. The C-4 position of ring D in compound **42** was selectively protected as the PMB ether (NaH/PMBCl, 93% yield) affording the targeted **41**. The latter compound was found to be identical to that derived from synthetic material, thus confirming the latter's structural identity. The next task was to devise and test the best forward scenario involving coupling of the $A_1B(A)C$ and $DEFGHA_2$ fragments and final drive for completion of the synthesis. Compatibility of protecting groups during coupling and their ability to promote such coupling as well as deprotection issues had to be resolved before a path to the end was found. In all, three sets of protecting groups on fragment $DEFGHA_2$ were tested before the final path was opened.

We had initially targeted the hexa-benzyl diol **42** (Scheme 6) as a potential partner in the projected final coupling with the $A_1B(A)C$ fragment, therefore, the PMB group was oxidatively removed (DDQ, 95% yield) from **41** to give hexabenzyl diol **42**. This plan was, however, thwarted by low glycosidation yields and rupture of the sensitive CD orthoester moiety upon attempted debenzylation of the expected coupling product (**49**, Scheme 7). We then turned our attention to the hexa-acetyl counterpart of **42** and proceeded as summarized in Scheme 6. Thus, treatment of hexabenzyl diol **42** with TBSOTf/2,6-lutidine allowed selective protection at C-4 of ring D (**43**, 96% yield) while hydrogenolysis of the resulting product followed by acetylation (Ac_2O, Et_3N, 4-DMAP cat.) furnished hexa-acetate **45** via compound **44** in 88% overall yield. Removal of the TBS group from ring D of **45** (nBu_4NF) afforded diol **46** which, however, upon attempted glycosidation with glycosyl donor **29** [$A_1B(A)C$ fragment] revealed its own glycosidation problems (e.g. sluggish reactivity and low coupling yields).

Our third and final strategy involved the adoption of the hexa-TBS derivative **40** (Scheme 6) as the $DEFGHA_2$ coupling partner. Our initial synthesis of this compound began with **42** and proceeded as shown in Scheme 6. Thus, selective formation of the chloroacetate moiety on ring D of **42** [$(CA)_2O$, Et_3N, 4-DMAP cat., 98% yield] led to **47** which was subjected to hydrogenolysis (H_2, 10% Pd/C) affording heptaol **48**. Six TBS groups were then installed on **48** by exposure to excess TBSOTf in the presence of 2,6-di-*tert*-butylpyridine providing the TBS derivative **39** (65% yield over two steps) whose tertiary hydroxy group (ring D) remained free. The chloroacetate (CA) group was then removed from the latter compound (K_2CO_3, MeOH) furnishing the targeted diol **40** in 85% yield. Upon realizing, from preliminary results, the promising potential of diol **40** as a coupling partner, we returned to compound **34** (Scheme 5) for a more efficient route to this compound (**40**). Thus, triol **34** was silylated with TBSOTf/2,6-lutidine leading to bis-TBS derivative **35** (92% yield) from which the PMB group was



Scheme 7. Degradation studies with everninomicin 13,384-1 (**1**). a) i) 15 equiv NaH, 20 equiv BnBr, 0.1 equiv nBu$_4$NI, DMF, 0→25 °C, 2 h, 93%; ii) 15 equiv TBSOTf, 30 equiv lutidine, CH_2Cl_2, 0→25 °C, 3 h, 64%; b) i) R = Bn: 5% aq HCl, THF, 25 °C; then 1N aq KOH, THF, 25 °C, 85% of **51**, 90% of **42;** ii) R = TBS: 5% aq HCl, THF, 25 °C; then 1N aq KOH, THF, 25 °C, 83% of **52**, 91% of **40;** c) 1.2 equiv NaH, 1.5 equiv PMBCl, 0.1 equiv nBu$_4$NI, DMF, 0→25 °C, 1 h, 93%.

removed (DDQ, 98% yield) and replaced with a chloroacetate protecting group [$(CA)_2O$, Et_3N, 4-DMAP cat., 99% yield] to afford chloroacetate **37** via diol **36**. In a subsequent sequence, the four benzyl groups were removed from **37** (H_2, 10% Pd/C, 94% yield) furnishing pentaol **38** onto which four TBS groups were installed (TBSOTf, 2,6-lutidine, 92% yield) to afford **39**, and finally the chloroacetate was cleaved from the latter compound (K_2CO_3, MeOH, 85% yield) leading to the desired hexa-TBS diol system **40**. The overall yield for the conversion of **40** from **34** (as depicted in Scheme 5) was 66% over six steps; in comparison, the six-step conversion of **34** to **40** as shown in Scheme 6, proceeded in 49% overall yield.

Final stages of the total synthesis of everninomicin 13,384-1: The final stages of the total synthesis of everninomicin 13,384-1 (**1**) beginning with the union of the two advanced intermediates described above is shown in Scheme 8. Thus, coupling of the $A_1B(A)C$ glycosyl fluoride donor **29** with the $DEFGHA_2$ hexa-TBS diol acceptor **40** in the presence of $SnCl_2$ in Et_2O proceeded smoothly and with complete stereocontrol leading to the 2-phenylseleno glycoside **53** in 70% yield. No problems arising from elimination of the BnO and PhSe groups were in evidence this time, as was for the case in our initial attempts to bring about the union of **29** and **3** (vide supra). Formation of the remaining orthoester site was then accomplished with equal facility upon exposure of **53** to the Sinaÿ conditions [$NaIO_4$ oxidation to the selenoxide in $MeOH/CH_2Cl_2/H_2O$ 3:2:1 followed by heating in a sealed tube at 140 °C in toluene/vinyl acetate/diisopropylamine 2:2:1] to afford the fully protected everninomicin 13,384-1 derivative **54** in 65% yield and as a single stereoisomer. The remaining task for the generation of everninomicin from **54** was the removal of the protecting groups which was accomplished by the following two-step sequence. Upon extensive experimentation with different catalysts, solvents and buffer systems, it was discovered that the optimum conditions for removal of the two benzyl ethers—without damaging the chlorine, nitro or orthoester sites—required exposure to H_2 in the presence of 10% Pd/C and $NaHCO_3$ in tBuOMe. The resulting hexa-TBS derivative was then fully deprotected through the action of nBu$_4$NF in THF furnishing the targeted molecule (**1**) in 75% overall yield from **54**. Synthetic everninomicin 13,384-1 (**1**) was identical by the usual criteria (TLC, ^{1}H NMR, ^{13}C NMR, IR, MS, [α]) with an authentic sample.[12]

Later on, and after the completion of the described synthesis of **1**, we found that hexa-TBS derivative **40** could also be obtained via a degradative route from the natural product (**1**) following an analogous sequence as that employed for the generation of the benzylated derivative **42** (Scheme 7). Thus, exposure of everninomicin (**1**) to TBSOTf in the presence of 2,6-lutidine furnished the fully silylated everninomicin **50** in 64% yield. Treatment of **50** with dilute aq HCl followed by subsequent addition of aq KOH furnished the bis-silylated δ-lactone **52** (83%) and the targeted hexa-silylated diol **40** (91% yield). This degradative route provides ample quantities of the rather complex $DEFGHA_2$ fragment **40**, which could potentially be useful for the semisynthesis of analogs and libraries thereof.

Conclusion

The described program culminating in the total synthesis of everninomicin 13,384-1 (**1**) served as an opportunity to develop a number of novel synthetic reactions and strategies, explore their scope and generality, and apply them to complex situations. Some of these explorations will be described in more detail in the following article.[14] Furthermore, the reported total synthesis constituted an adventure in which the power of new synthetic reactions both from our own and from other laboratories was demonstrated. Most notable of these methods are the stereocontrolled construction of 1,1′-disaccharides,[14–15] the 1,2-phenylthio-[16] and the 1,2-phenylseleno-[2, 14] migrations on carbohydrate templates and their use in

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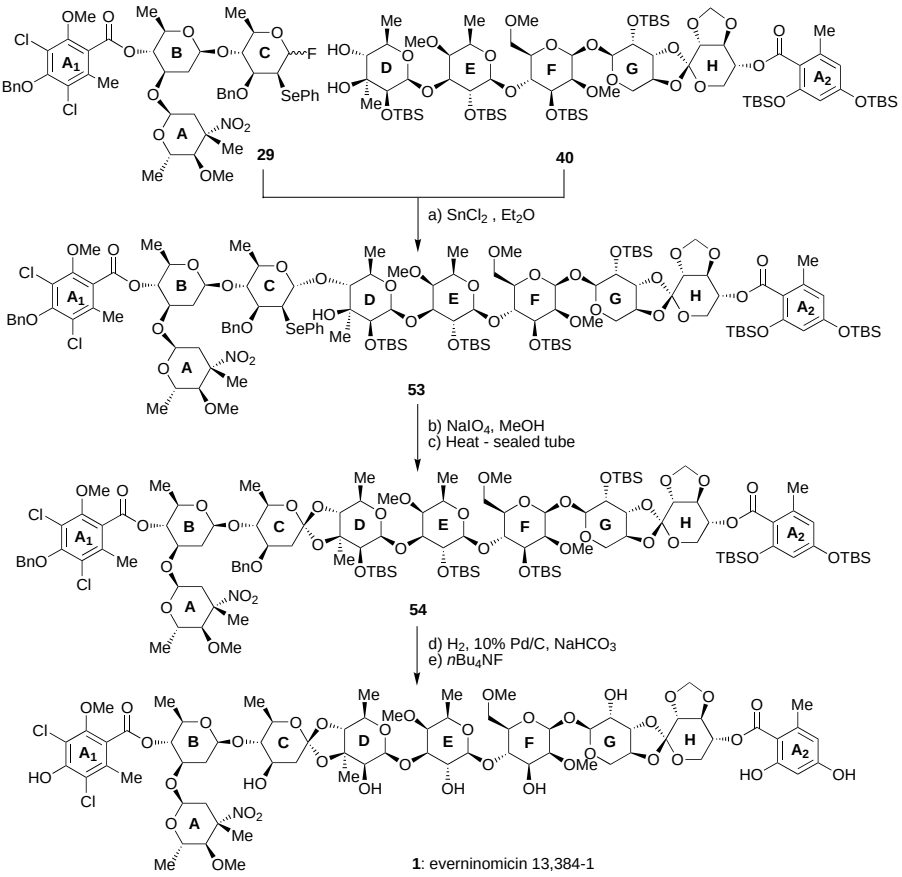

Scheme 8. Final stages of the total synthesis of everninomicin 13,384-1 (**1**). a) 2.4 equiv **29**, 2.0 equiv $SnCl_2$, Et_2O, $0 \rightarrow 25\,^{\circ}C$, 6 h, 70%; b) 10.0 equiv $NaIO_4$, 8.0 equiv $NaHCO_3$, MeOH/CH_2Cl_2/H_2O 3:2:1, 25 °C, 4 h; c) vinyl acetate/toluene/diisopropylamine 2:2:1, sealed tube, 140 °C, 12 h, 65% over two steps; d) H_2, 0.2 equiv 10% Pd/C (*w*/*w*), 4.0 equiv $NaHCO_3$, *t*BuOMe, 25 °C, 1 h; e) 10.0 equiv nBu_4NF, THF, 25 °C, 10 h, 75% for two steps.

stereocontrolled glycosidation reactions. Other processes explored and championed in these investigations include the selective silylation of carbohydrate diols in different solvents, the use of acyl fluorides for the formation of sterically hindered esters, the Sinaÿ orthoester formation protocol,[11] the Kahne sulfoxide β-mannoside forming glycosidation,[4, 5] the Schmidt trichloroacetimidate glycosidation method,[3] the Mukaiyama glycosyl fluoride methodology,[17] and the tin-acetal technology[8] for differentiating 1,2-diols. In addition, a considerable body of knowledge regarding selectivity in protective group chemistry was accumulated, and light was shed on conformational effects on selective functionalization of carbohydrate substrates. Significantly, the stage is now set for further studies in the field, including semisynthesis of designed analogues of everninomicin 13,384-1 (**1**), solid-phase synthesis, combinatorial chemistry, and chemical biology studies.

Experimental Section

General: For general procedures and techniques, see Part 1[1] in this series.

PMB ether 7: nBu_2SnO (7.44 g, 29.9 mmol) was added to a solution of mannose diol **6**[7] (9.80 g, 27.2 mmol) in toluene (130 mL) and the resulting mixture was refluxed with removal of H_2O using a Dean Stark apparatus for 3 h. The reaction mixture was cooled to 25 °C and PMBCl (5.53 mL, 40.8 mmol) and nBu_4NI (2.01 g, 5.4 mmol) were added. The reaction mixture was refluxed again for 2 h, and then the reaction mixture was quenched by the addition of H_2O (2 mL). The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, $0 \rightarrow 80\%$ Et_2O in hexanes) to afford PMB ether **7** (10.85 g, 83%) as a white solid. **7**: $R_f = 0.30$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = +186.6$ ($c = 2.89$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3434$, 3060, 2950, 1511, 1248, 1090, 1028, 786, 747, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta =$ 7.54–7.27 (m, 12H, ArH), 6.90 (d, $J = 8.6$ Hz, 2H, PMB), 5.63 (s, 1H, CHAr), 5.59 (s, 1H, D1), 4.83, 4.68 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.34 (ddd, $J = 9.8$, 9.8, 4.9 Hz, 1H, D5), 4.23 (t, $J = 1.8$ Hz, 1H, D2), 4.22 (dd, $J =$ 10.3, 4.9 Hz, 1H, D6), 4.17 (t, $J =$ 9.5 Hz, 1H, D4), 3.95 (dd, $J = 9.6$, 3.3 Hz, 1H, D3), 3.86 (t, $J = 10.3$ Hz, 1H, D6), 3.82 (s, 3H, OMe), 2.97 (d, $J = 1.3$ Hz, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.5$, 137.4, 133.3, 131.6, 129.7, 129.6, 129.2, 128.9, 128.2, 127.6, 126.0, 113.9, 101.5, 87.8, 78.9, 75.3, 72.9, 71.3, 68.5, 64.6, 55.2; HRMS (MALDI): calcd for $C_{27}H_{28}O_6SNa$ $[M+Na]^+$: 503.1504, found 503.1505.

TBS ether 8: TBSOTf (5.73 mL, 25.0 mmol) was added to a solution of PMB ether **7** (10.00 g, 20.8 mmol) and 2,6-lutidine (3.64 mL, 31.0 mmol) in CH_2Cl_2 (110 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 0.5 h. The reaction mixture was diluted with CH_2Cl_2 (800 mL) and washed with saturated aqueous $NaHCO_3$ (80 mL) and brine (80 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, $0 \rightarrow 80\%$ Et_2O in hexanes) to afford TBS ether **8** (11.51 g, 93%) as a white foam. **8**: $R_f = 0.76$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +142.9$ ($c = 0.41$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2930$, 2857, 1613, 1515, 1471, 1372, 1250, 1101, 1034, 837, 780, 741, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta =$ 7.53–7.28 (m, 12H, ArH), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 5.64 (s, 1H, CHAr), 5.33 (d, $J = 0.9$ Hz, 1H, D1), 4.76, 4.66 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.29 (ddd, $J = 9.7$, 9.7, 4.8 Hz, 1H, D5), 4.23 (br s, 1H, D2), 4.21 (dd, $J = 10.2$, 4.5 Hz, 1H, D6), 4.20 (t, $J = 9.3$ Hz, 1H, D4), 3.87 (dd, $J = 9.7$, 2.8 Hz, 1H, D3), 3.86 (t, $J = 10.4$ Hz, 1H, D6), 3.82 (s, 3H, OMe), 0.90 (s, 9H, *t*BuSi), 0.09 (s, 3H, MeSi), 0.05 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.1$, 137.7, 133.8, 131.9, 130.5, 129.5, 129.1, 128.8, 128.1, 127.6, 126.1, 113.6, 101.5, 90.3, 79.2, 75.5, 72.7, 72.6, 68.6, 65.5, 55.2, 25.8, 18.2, −4.4, −5.0; HRMS (MALDI): calcd for $C_{33}H_{42}O_6SSiNa$ $[M+Na]^+$: 617.2369, found 617.2358.

Ring D sulfoxide 4: *m*CPBA (3.19 g, 18.5 mmol) was added to a solution of TBS ether **8** (10.00 g, 16.8 mmol) in CH_2Cl_2 (85 mL) at −20 °C and the resulting mixture was warmed to 0 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL), diluted with CH_2Cl_2 (800 mL), and washed with brine (80 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, $0 \rightarrow 50\%$ Et_2O in hexanes) to afford ring D sulfoxide **4** (9.52 g, 92%, ca. 4:1 mixture of diastereoisomers) as a white foam. **4**: $R_f =$ 0.19 (30% Et_2O in hexanes); $[\alpha]_D^{22} = -41.8$ ($c = 3.03$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3060$, 2931, 2857, 1613, 1586, 1515, 1467, 1381, 1251, 1119, 1030, 834, 752 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.62 - 7.36$ (m, 10H, ArH), 7.35 (d, $J = 8.6$ Hz, 2H, PMB), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 5.65 (s, 1H, CHAr), 4.82, 4.72 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.68 (d, $J = 1.0$ Hz, 1H,

D1), 4.23 (d, $J = 0.8$ Hz, 1H, D2), 4.24–4.21 (m, 1H, D3), 4.23 (t, $J = 7.2$ Hz, 1H, D4), 4.21 (dd, $J = 10.3$, 4.8 Hz, 1H, D6), 4.12–4.08 (m, 1H, D5), 3.82 (s, 3H, OMe), 3.75 (t, $J = 10.1$ Hz, 1H, D6), 0.84 (s, 9H, *t*BuSi), 0.04 (s, 3H, MeSi), −0.08 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 160.1$, 142.3, 138.2, 134.0, 132.6, 131.3, 131.0, 130.7, 130.3, 129.8, 129.1, 127.0, 125.4, 114.5, 102.5, 101.4, 79.0, 76.5, 73.8, 71.2, 69.1, 68.2, 56.1, 26.6, 19.0, −3.6, −4.5; HRMS (MALDI): calcd for $C_{33}H_{42}O_7SSiNa$ $[M+Na]^+$: 633.2318, found 633.2327.

PMB ether 10: nBu$_2$SnO (11.45 g, 46.0 mmol) was added to a solution of galactose diol **9**[9] (15.00 g, 41.6 mmol) in toluene (500 mL) and the resulting mixture was refluxed with removal of H_2O using a Dean Stark apparatus for 3 h. The reaction mixture was cooled to 25 °C and PMBCl (8.46 mL, 62.4 mmol) and nBu$_4$NI (3.07 g, 8.3 mmol) were added. The reaction mixture was refluxed again for 2 h, and then the reaction mixture was quenched by the addition of H_2O (5 mL). The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford PMB ether **10** (17.41 g, 87 %) as a white solid. **10**: $R_f = 0.31$ (100 % Et_2O); $[\alpha]_D^{22} = +32.9$ ($c = 0.85$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3440$, 3071, 2928, 2873, 1612, 1513, 1248, 1173, 1102, 1078, 1030, 996, 817, 747, 697 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.69$ (d, $J = 7.0$ Hz, 2H, ArH), 7.43–7.23 (m, 10H, ArH), 6.85 (d, $J = 8.5$ Hz, 2H, PMB), 5.44 (s, 1H, CHAr), 4.68, 4.63 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.52 (d, $J = 9.5$ Hz, 1H, E1), 4.35 (d, $J = 12.0$, Hz, 1H, E6), 4.12 (d, $J = 3.5$ Hz, 1H, E4), 3.97 (d, $J = 12.0$, Hz, 1H, E6), 3.93 (t, $J = 9.5$ Hz, 1H, E2), 3.78 (s, 3H, OMe), 3.49 (dd, $J = 9.9$, 3.5 Hz, 1H, E3), 3.42 (s, 1H, E5), 2.55 (s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.6$, 137.8, 133.6, 129.4, 128.9, 128.8, 128.0, 127.9, 126.5, 113.8, 101.0, 87.0, 79.9, 73.2, 71.1, 70.0, 69.3, 67.1, 55.2; HRMS (MALDI): calcd for $C_{27}H_{28}O_6SNa$ $[M+Na]^+$: 503.1504, found 503.1491.

TBS ether 11: TBSOTf (9.75 mL, 42.4 mmol) was added to a solution of PMB ether **10** (17.00 g, 35.4 mmol) and 2,6-lutidine (6.18 mL, 53.1 mmol) in CH_2Cl_2 (175 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (800 mL) and washed with saturated aqueous $NaHCO_3$ (80 mL) and brine (80 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford TBS ether **11** (20.41 g, 97 %) as a white foam. **11**: $R_f = 0.61$ (50 % Et_2O); $[\alpha]_D^{22} = +57.2$ ($c = 0.32$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2954$, 2856, 1613, 1585, 1514, 1471, 1363, 1249, 1172, 1100, 1048, 1001, 909, 865, 838, 818, 735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.63$–7.19 (m, 10H, ArH), 7.32 (d, $J = 8.6$ Hz, 2H, PMB), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 5.39 (s, 1H, CHAr), 4.61, 4.58 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.59 (d, $J = 9.5$ Hz, 1H, E1), 4.33 (dd, $J = 12.0$, 1.5 Hz, 1H, E6), 4.09 (d, $J = 2.5$ Hz, 1H, E4), 4.08 (t, $J = 9.0$ Hz, 1H, E2), 3.95 (dd, $J = 12.0$, 1.5 Hz, 1H, E6), 3.81 (s, 3H, OMe), 3.43 (dd, $J = 8.5$, 3.5 Hz, 1H, E3), 3.37 (br s, 1H, E5), 0.96 (s, 9H, *t*BuSi), 0.06 (s, 3H, MeSi), 0.05 (s, 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.1$, 138.1, 134.4, 131.1, 130.4, 129.3, 128.8, 128.6, 128.0, 126.6, 126.4, 113.5, 101.0, 88.9, 81.9, 72.8, 70.6, 69.7, 69.4, 68.9, 55.2, 26.1, 18.4, −3.7, −4.7; HRMS (MALDI): calcd for $C_{33}H_{42}O_6SSiNa$ $[M+Na]^+$: 617.2369, found 617.2395.

Diol 12: $Zn(OTf)_2$ (22.90 g, 63.0 mmol) was added to a solution of TBS ether **11** (15.00 g, 25.2 mmol) and EtSH (40.00 mL, 500 mmol) in CH_2Cl_2 (150 mL) at 0 °C and the resulting mixture was stirred at 0 °C for 2 h. The reaction mixture was quenched by the careful addition of saturated aqueous $NaHCO_3$ (200 mL), diluted with CH_2Cl_2 (800 mL) and washed with brine (100 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O in hexanes) to afford diol **12** (9.86 g, 77 %) as a white solid. **12**: $R_f = 0.41$ (100 % Et_2O); $[\alpha]_D^{22} = -39.2$ ($c = 1.07$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3418$, 2929, 2855, 1514, 1472, 1244, 1132, 1084, 1035, 872, 779 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.47$ (d, $J = 8.3$ Hz, 2H, ArH), 7.31–7.19 (m, 5H, ArH), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 4.58, 4.53 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.57 (d, $J = 9.5$ Hz, 1H, E1), 3.95 (d, $J = 3.0$ Hz, 1H, E4), 3.93 (dd, $J = 11.8$, 7.1 Hz, 1H, E6), 3.85 (t, $J = 9.0$ Hz, 1H, E2), 3.80 (s, 3H, OMe), 3.73 (dd, $J = 11.8$, 4.3 Hz, 1H, E6), 3.47 (dd, $J = 7.6$, 4.1 Hz, 1H, E5), 3.38 (dd, $J = 8.5$, 3.3 Hz, 1H, E3), 2.33 (br s, 2H, OH), 0.94 (s, 9H, *t*BuSi), 0.15 (s, 3H, MeSi), 0.10 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.4$, 134.8, 130.9, 129.5, 128.8, 126.9, 113.9, 89.5, 83.0, 77.9, 71.1, 70.0, 66.3, 62.4, 55.2, 30.0, 26.0, 18.3, −3.7, −4.3; HRMS (MALDI): calcd for $C_{26}H_{38}O_6SSiNa$ $[M+Na]^+$: 529.2056, found 529.2062.

Tosylate 13: Recrystallized TsCl (5.20 g, 27.3 mmol) was added to a solution of diol **12** (12.60 g, 24.8 mmol) in pyridine (55 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2 (500 mL) and washed with saturated aqueous NH_4Cl (100 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O in hexanes) to afford tosylate **13** (15.92 g, 97 %) as a white foam. **13**: $R_f = 0.53$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -50.3$ ($c = 0.29$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3433$, 2928, 2855, 1612, 1513, 1363, 1250, 1176, 1130, 1095, 1034, 983 837 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.74$ (d, $J = 8.2$ Hz, 2H, ArH), 7.49–7.24 (m, 9H, ArH), 6.89 (d, $J = 8.6$ Hz, 2H, PMB), 4.59, 4.48 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.52 (d, $J = 9.6$ Hz, 1H, E1), 4.21 (dd, $J = 10.4$, 5.1 Hz, 1H, E6), 4.17 (dd, $J = 10.4$, 7.2 Hz, 1H, E6), 3.88 (dd, $J = 3.0$, 0.8 Hz, 1H, E4), 3.82 (s, 3H, OMe), 3.75 (dd, $J = 9.3$, 8.5 Hz, 1H, E2), 3.70–3.68 (m, 1H, E5), 3.36 (dd, $J = 8.4$, 3.3 Hz, 1H, E3), 2.41 (s, 3H, OMe), 1.43 (s, 1H, OH), 0.93 (s, 9H, *t*BuSi), 0.14 (s, 3H, MeSi), 0.08 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.5$, 144.9, 134.5, 132.4, 131.1, 129.8, 129.6, 129.3, 128.8, 128.0, 127.2, 114.0, 89.6, 82.7, 75.2, 71.6, 69.8, 68.6, 65.6, 55.2, 30.3, 26.1, 21.6, 18.3, −3.7, −4.3; HRMS (ESI): calcd for $C_{33}H_{44}O_8S_2SiNa$ $[M+Na]^+$: 683, found 683.

Alcohol 14: LAH (0.50 g, 13.1 mmol) was added slowly to a solution of tosylate **13** (5.41 g, 8.2 mmol) in THF (40 mL) at 0 °C. The resulting mixture was heated to 45 °C and stirred for 3 h. The reaction mixture was cooled to 0 °C and carefully quenched by the addition of saturated aqueous NH_4Cl (10 mL), diluted with Et_2O (500 mL), and stirred for 1 h. The mixture was diluted with Et_2O (200 mL) and washed with brine (80 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford alcohol **14** (3.61 g, 90 %) as a white foam. **14**: $R_f = 0.37$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = -6.2$ ($c = 0.86$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3495$, 2931, 2856, 1613, 1585, 1515, 1469, 1366, 1250, 1130, 1089, 1042, 998, 872, 789, 779, 744 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.50$ (d, $J = 7.1$ Hz, 2H, ArH), 7.29–7.20 (m, 5H, ArH), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 4.57, 4.54 (AB, $J = 11.2$ Hz, 2H, CH_2Ar), 4.53 (d, $J = 9.6$ Hz, 1H, E1), 3.81 (s, 3H, OMe), 3.79 (t, $J = 9.4$ Hz, 1H, E2), 3.76 (d, $J = 3.2$ Hz, 1H, E4), 3.55 (br q, $J = 6.5$ Hz, 1H, E5), 3.37 (dd, $J = 8.5$, 3.3 Hz, 1H, E3), 2.00 (s, 1H, OH), 1.34 (d, $J = 6.5$ Hz, 3H, E6), 0.93 (s, 9H, *t*BuSi), 0.15 (s, 3H, MeSi), 0.08 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.4$, 135.1, 131.1, 129.6, 128.7, 126.9, 113.9, 89.7, 83.4, 73.9, 71.1, 69.8, 68.6, 55.2, 30.3, 26.1, 18.3, 16.8, −3.6, −4.3; HRMS (MALDI): calcd for $C_{26}H_{38}O_5SSiNa$ $[M+Na]^+$: 513.2107, found 513.2129.

Methyl ether 15: NaH (0.29 g, 7.2 mmol) was added to a solution of alcohol **14** (3.22 g, 6.5 mmol) in DMF (30 mL) at 0 °C and the resulting mixture was stirred for 5 min. MeI (0.53 mL, 8.5 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (250 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 70 % Et_2O in hexanes) to afford methyl ether **15** (3.12 g, 94 %) as a white foam. **15**: $R_f = 0.47$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = -19.2$ ($c = 0.63$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931$, 2855, 1612, 1514, 1463, 1365, 1249, 1130, 1056, 1038, 837, 779 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.51$–7.16 (m, 7H, ArH), 6.87 (d, $J = 8.6$ Hz, 2H, PMB), 4.62, 4.57 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.50 (d, $J = 9.5$ Hz, 1H, E1), 3.91 (dd, $J = 9.4$, 8.2 Hz, 1H, E2), 3.81 (s, 3H, OMe), 3.57 (s, 3H, OMe), 3.48 (br q, $J = 6.3$ Hz, 1H, E5), 3.31 (dd, $J = 8.1$, 2.9 Hz, 1H, E3), 3.30 (br s, 1H, E4), 1.29 (d, $J = 6.3$ Hz, 3H, E6), 0.91 (s, 9H, *t*BuSi), 0.17 (s, 3H, MeSi), 0.06 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.1$, 135.7, 131.1, 130.2, 129.3, 129.1, 128.6, 126.7, 113.7, 91.9, 84.5, 78.7, 74.4, 71.7, 70.3, 61.7, 55.2, 26.2, 18.3, 17.0, −3.6, −4.2; HRMS (MALDI): calcd for $C_{27}H_{40}O_5SSiNa$ $[M+Na]^+$: 527.2263, found 527.2284.

Lactol 16: NBS (1.70 g, 9.5 mmol) was added to a solution of methyl ether **15** (3.21 g, 6.4 mmol) in acetone/H_2O (10:1, 33 mL) at 0 °C and the resulting mixture warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL), diluted with CH_2Cl_2 (250 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O in hexanes) to afford the lactol **16** (2.49 g, 95 %) as a white foam. **16**: $R_f = 0.26$, 0.41 (70 % Et_2O in hexanes); $[\alpha]_D^{22} = +22.9$ ($c =$

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0.17, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3416, 2931, 2862, 1612, 1513, 1465, 1250, 1088, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ (ca. 3:1 α:β ratio)): δ = 7.29 (d, J = 8.6 Hz, 2.6 H, PMB), 6.87 (d, J = 8.6 Hz, 2.6 H, PMB), 5.12 (d, J = 3.8 Hz, 1 H, E1), 4.68–4.57 (m, 2.6 H, CH_2Ar), 4.43 (t, J = 7.3 Hz, 0.3 H, E1), 4.09 (br q, J = 6.5 Hz, 1 H, E5), 4.04 (dd, J = 9.5, 3.8 Hz, 1 H, E2), 3.81 (s, 4 H, OMe), 3.67 (dd, J = 9.4, 7.3 Hz, 0.3 H, E2), 3.60–3.55 (m, 5 H, E3, OMe), 3.52 (br q, J = 6.5 Hz, 0.3 H, E5), 3.31 (d, J = 2.1 Hz, 1 H, E4), 3.24 (dd, J = 9.4, 2.9 Hz, 0.3 H, E3), 3.21 (d, J = 2.6 Hz, 0.3 H, E-4), 3.07 (br s, 1 H, OH), 2.87 (d, J = 7.3 Hz, 0.3 H, OH), 1.27 (d, J = 6.5 Hz, 1 H, E6), 1.24 (d, J = 6.5 Hz, 3 H, E6), 0.90 (s, 10 H, *t*BuSi), 0.10 (s, 1 H, MeSi), 0.09 (s, 3 H, MeSi), 0.08 (s, 3 H, MeSi), 0.05 (s, 1 H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.1, 130.5, 129.3, 129.1, 113.7, 98.0, 93.5, 82.6, 79.8, 79.2, 78.9, 73.7, 72.3, 72.2, 70.7, 70.1, 66.7, 61.7, 55.2, 25.9, 25.8, 18.2, 18.0, 16.7, 16.5, −4.3, −4.4, −4.5, −4.9; HRMS (MALDI): calcd for $C_{21}H_{36}O_6SiNa$ $[M+Na]^+$: 435.2179, found 435.2168.

TIPS ether 17: TIPSOTf (1.77 mL, 6.57 mmol) was added to a solution of lactol **16** (2.26 g, 5.48 mmol) and 2,6-lutidine (0.96 mL, 8.22 mmol) in CH_2Cl_2 (27 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 6 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 40 % Et_2O in hexanes) to afford TIPS ether **17** (3.02 g, 97 %) as a white foam. **17**: R_f = 0.56 (15 % Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 2937, 2865, 1514, 1466, 1250, 1106, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ (1:2.3 α:β ratio)): δ = 7.28 (d, J = 8.6 Hz, 3 H, PMB), 6.87 (d, J = 8.6 Hz, 3 H, PMB), 5.17 (d, J = 3.5 Hz, 1 H, E1), 4.63–4.55 (m, 6 H, CH_2Ar), 4.49 (d, J = 7.5 Hz, 2 H, E1), 4.06 (dd, J = 9.5, 3.0 Hz, 1 H, E2), 4.01 (br q, J = 6.5 Hz, 1 H, E5), 3.81 (s, 10 H, OMe), 3.73 (dd, J = 10.0, 2.5 Hz, 2 H, E3), 3.67 (dd, J = 9.0, 7.0 Hz, 2 H, E2), 3.58 (s, 3 H, OMe), 3.54 (s, 6 H, OMe), 3.45 (br q, J = 6.5 Hz, 2 H, E5), 3.27 (br s, 1 H, E4), 3.24 (dd, J = 9.0, 3.0 Hz, 2 H, E3), 3.22 (dd, J = 3.0, 0.5 Hz, 2 H, E4), 1.23 (d, J = 6.5 Hz, 6 H, E6), 1.17 (d, J = 6.5 Hz, 3 H, E6), 1.10–1.05 (m, 63 H, *i*Pr_3Si), 0.89 (s, 9 H, *t*BuSi), 0.87 (s, 18 H, *t*BuSi), 0.09 (s, 6 H, MeSi), 0.07 (s, 3 H, MeSi), 0.06 (s, 9 H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 130.6, 129.2, 113.6, 98.9, 94.5, 83.4, 80.7, 79.1, 78.1, 73.5, 72.2, 70.6, 70.4, 66.3, 61.6, 61.4, 55.2, 26.1, 18.2, 18.1, 16.5, 16.3, 12.7, 12.3, −3.9, −4.2, −4.3, −4.5; HRMS (MALDI): calcd for $C_{30}H_{56}O_6Si_2Na$ $[M+Na]^+$: 591.3513, found 591.3535.

Ring E alcohol 5: DDQ (1.65 g, 7.3 mmol) was added to a solution of TIPS ether **17** (2.75 g, 4.8 mmol) in CH_2Cl_2/H_2O (10:1, 33 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (250 mL) and washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford ring E alcohol **5** (2.13 g, 98 %) as a white foam. **5**: R_f = 0.49 (15 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −1.15 (c = 0.33, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3488, 2943, 2865, 1465, 1252, 1090, 1046, 886, 837, 778, 684 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$ (β only)): δ = 4.44 (d, J = 6.7 Hz, 1 H, E1), 3.56 (s, 3 H, OMe), 3.52 (br q, J = 6.6 Hz, 1 H, E5), 3.43 (ddd, J = 7.0, 7.0, 3.4 Hz, 1 H, E3), 3.40 (t, J = 6.8 Hz, 1 H, E2), 3.25 (d, J = 3.4 Hz, 1 H, E4), 2.13 (d, J = 7.7 Hz, 1 H, OH), 1.27 (d, J = 6.6 Hz, 3 H, E6), 1.10–0.99 (m, 21 H, *i*Pr_3Si), 0.88 (s, 9 H, *t*BuSi), 0.10 (s, 3 H, MeSi), 0.08 (s, 3 H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 98.2, 82.2, 75.6, 75.3, 70.6, 62.3, 25.9, 17.9, 16.5, 12.5, −3.9, −4.5; HRMS (MALDI): calcd for $C_{22}H_{48}O_5Si_2Na$ $[M+Na]^+$: 471.2938, found 471.2940.

DE disaccharide 18: Ring D sulfoxide **4** (2.23 g, 3.65 mmol) and di-*tert*-butyl-4-methylpyridine (1.27 g, 6.18 mmol) were azeotroped with benzene, dissolved in CH_2Cl_2 (7 mL) and cooled to −78 °C. 4 Å MS (0.3 g) were added and the reaction mixture was stirred for 5 min. Tf_2O (0.614 mL, 3.65 mmol) was added dropwise and the reaction mixture was stirred for 5 min. Ring E alcohol **5** (1.26 g, 2.81 mmol) was dissolved in CH_2Cl_2 (4 mL) and added to the reaction mixture by cannula. The flask was rinsed with CH_2Cl_2 (2 × 2 mL) and this was also transferred to the reaction mixture. The reaction mixture was stirred at −78 °C for 30 min, followed by gradual warming to 0 °C over 2 h. The reaction mixture was then quenched by the addition of saturated aqueous $NaHCO_3$ (50 mL), diluted with CH_2Cl_2 (500 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford β-DE disaccharide **18** (1.86 g, 71 %) as a white foam. **18**: R_f = 0.45 (10 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −17.7 (c = 0.90, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2960, 2855, 1613, 1515, 1469, 1383, 1303, 1252, 1072, 777, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.52–7.35 (m, 5 H, ArH), 7.27 (d, J = 8.6 Hz, 2 H, PMB), 6.85 (d, J = 8.6 Hz, 2 H, PMB), 5.60 (s, 1 H, CHAr), 4.70, 4.64 (AB, J = 12.0 Hz, 2 H, CH_2Ar), 4.49 (s, 1 H, D1), 4.46 (d, J = 7.5 Hz, 1 H, E1), 4.25 (dd, J = 10.0, 4.5 Hz, 1 H, D6), 4.22 (d, J = 2.5 Hz, 1 H, D2), 4.04 (t, J = 9.0 Hz, 1 H, D4), 3.83 (t, J = 10.0 Hz, 1 H, D6), 3.81 (s, 3 H, OMe), 3.61 (dd, J = 9.5, 7.5 Hz, 1 H, E2), 3.54 (s, 3 H, OMe), 3.51 (br q, J = 6.5 Hz, 1 H, E5), 3.42 (dd, J = 10.0, 3.0 Hz, 1 H, D3), 3.37 (dd, J = 9.5, 3.5 Hz, 1 H, E3), 3.29 (d, J = 3.5 Hz, 1 H, E4), 3.28 (ddd, J = 10.0, 10.0, 4.5 Hz, 1 H, D5), 1.25 (d, J = 6.5 Hz, 3 H, E6), 1.09–1.04 (m, 21 H, *i*Pr_3Si), 0.92 (s, 9 H, *t*BuSi), 0.84 (s, 9 H, *t*BuSi), 0.16 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi), 0.12 (s, 6 H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.0, 137.6, 130.3, 129.6, 129.1, 128.8, 128.1, 128.0, 126.4, 126.1, 113.5, 104.3, 101.5, 98.8, 84.7, 82.4, 79.2, 76.7, 74.8, 73.3, 72.3, 71.4, 70.4, 68.9, 67.6, 62.3, 55.0, 26.0, 18.0, 17.8, 16.1, 12.7, −3.2, −3.9, −4.1, −4.3; HRMS (FAB): calcd for $C_{49}H_{84}O_{11}Si_3Cs$ $[M+Cs]^+$: 1065.4376, found 1065.4326.

DE alcohol 19: DDQ (0.26 g, 1.13 mmol) was added to a solution of DE disaccharide **18** (0.81 g, 0.87 mmol) in CH_2Cl_2/H_2O (10:1, 5.2 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was diluted with CH_2Cl_2 (250 mL) and washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 30 % Et_2O in hexanes) to afford DE alcohol **19** (0.67 g, 95 %) as a white foam. **19**: R_f = 0.54 (20 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −39.9 (c = 6.53, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3472, 2932, 2862, 1467, 1384, 1253, 1181, 1095, 1018, 837, 779 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.51–7.35 (m, 5 H, ArH), 5.55 (s, 1 H, CHAr), 4.62 (s, 1 H, D1), 4.48 (d, J = 7.5 Hz, 1 H, E1), 4.27 (dd, J = 10.5, 5.0 Hz, 1 H, D6), 4.25 (d, J = 3.5 Hz, 1 H, D2), 3.81 (t, J = 10.0 Hz, 1 H, D6), 3.78 (t, J = 9.0 Hz, 1 H, D4), 3.70 (ddd, J = 10.0, 7.0, 3.0 Hz, 1 H, D3), 3.63 (dd, J = 9.5, 7.0 Hz, 1 H, E2), 3.54 (s, 3 H, OMe), 3.52 (q, J = 6.5 Hz, 1 H, E5), 3.43 (dd, J = 9.5, 3.5 Hz, 1 H, E3), 3.35 (ddd, J = 9.5, 9.5, 5.0 Hz, 1 H, D5), 3.30 (d, J = 3.0 Hz, 1 H, E4), 2.15 (d, J = 6.5 Hz, 1 H, OH), 1.25 (d, J = 6.5 Hz, 3 H, E6), 1.14–1.06 (m, 21 H, *i*Pr_3Si), 0.95 (s, 9 H, *t*BuSi), 0.89 (s, 9 H, *t*BuSi), 0.25 (s, 3 H, MeSi), 0.17 (s, 3 H, MeSi), 0.14 (s, 3 H, MeSi), 0.13 (s, 3 H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.2, 129.2, 128.3, 126.3, 103.9, 102.2, 98.9, 84.6, 79.2, 73.5, 72.0, 71.7, 70.4, 68.8, 67.2, 62.3, 26.1, 26.0, 18.2, 18.0, 16.2, 12.8, −3.4, −3.8, −4.6; HRMS (FAB): calcd for $C_{41}H_{76}O_{10}Si_3Cs$ $[M+Cs]^+$: 945.3801, found 945.3825.

DE ketone 20: DE alcohol **19** (0.49 g, 0.61 mmol), NMO (0.11 g, 0.91 mmol), and 4 Å MS (0.1 g) were dissolved in CH_2Cl_2 (4 mL) and the reaction mixture was stirred for 5 min. TPAP (11 mg, 0.03 mmol) was added and the reaction mixture was stirred at 25 °C for 2 h. The reaction mixture was diluted with Et_2O (30 mL), filtered through a short pad of silica gel, and then the solvents were removed under reduced pressure to afford ketone **20** (ca. 0.46 g) as a white foam. **20**: R_f = 0.32 (10 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −33.8 (c = 3.69, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2930, 2864, 1750, 1472, 1384, 1254, 1180, 1096, 1017, 838, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.36 (m, 5 H, ArH), 5.60 (s, 1 H, CHAr), 4.82 (d, J = 10.0 Hz, 1 H, D4), 4.76 (s, 1 H, D1), 4.49 (d, J = 7.1 Hz, 1 H, E1), 4.42 (dd, J = 10.3, 4.6 Hz, 1 H, D6), 4.34 (s, 1 H, D2), 3.96 (t, J = 10.0 Hz, 1 H, D6), 3.66 (dd, J = 9.4, 7.1 Hz, 1 H, E2), 3.61 (s, 3 H, OMe), 3.55 (dd, J = 9.2, 3.0 Hz, 1 H, E3), 3.51–3.34 (m, 2 H, D5, E5), 3.33 (d, J = 2.9 Hz, 1 H, E4), 1.26 (d, J = 6.5 Hz, 3 H, E6), 1.16–1.03 (m, 21 H, *i*Pr_3Si), 0.90 (s, 9 H, *t*BuSi), 0.87 (s, 9 H, *t*BuSi), 0.16 (s, 3 H, MeSi), 0.12 (s, 3 H, MeSi), 0.11 (s, 3 H, MeSi), 0.10 (s, 3 H, MeSi); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.5, 136.4, 129.4, 128.3, 126.4, 104.7, 102.2, 98.8, 84.5, 82.4, 80.7, 78.2, 73.3, 70.3, 69.3, 67.4, 65.8, 62.1, 26.1, 25.7, 18.2, 18.0, 16.1, 12.8, −3.5, −3.8, −4.6, −5.0; HRMS (FAB): calcd for $C_{41}H_{74}O_{10}Si_3Cs$ $[M+Cs]^+$: 943.3644, found 943.3677.

DE alcohol 21: Crude DE ketone **20** (ca. 0.46 g, 0.61 mmol) was dissolved in Et_2O (4 mL) and cooled to −78 °C. MeLi (0.61 mL, 0.85 mmol, 1.8 M solution in Et_2O) was added dropwise and the reaction mixture was stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (10 mL), diluted with Et_2O (150 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford DE alcohol **21** (0.44 g, 88 % over two steps) as a white foam. **21**: R_f = 0.56 (10 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −54.6 (c = 0.33, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3500,

2929, 2864, 1463, 1383, 1253, 1183, 1092, 1017, 835, 779 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.51-7.31$ (m, 5H, ArH), 5.56 (s, 1H, CHAr), 4.80 (s, 1H, D1), 4.48 (d, $J = 7.1$ Hz, 1H, E1), 4.26 (dd, $J = 10.2$, 4.9 Hz, 1H, D6), 3.87 (s, 1H, D2), 3.75 (t, $J = 10.1$ Hz, 1H, D6), 3.71 (d, $J = 9.5$ Hz, 1H, D4), 3.62 (dd, $J = 9.3$, 7.1 Hz, 1H, E2), 3.53–3.51 (m, 1H, E5), 3.52 (s, 3H, OMe), 3.43 (ddd, $J = 9.8$, 9.8, 5.0 Hz, 1H, D5), 3.42 (dd, $J = 9.4$, 3.4 Hz, 1H, E3), 3.31 (d, $J = 3.3$ Hz, 1H, E4), 2.48 (s, 1H, OH), 1.32 (s, 3H, Me (D3)), 1.26 (d, $J = 6.4$ Hz, 3H, E6), 1.16–1.03 (m, 21H, iPr$_3$Si), 0.96 (s, 9H, tBuSi), 0.91 (s, 9H, tBuSi), 0.30 (s, 3H, MeSi), 0.17 (s, 3H, MeSi), 0.15 (s, 3H, MeSi), 0.14 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 137.5$, 129.0, 128.2, 126.3, 125.5, 102.7 ($J_{C1,H1} = 159.8$ Hz), 102.2 ($J_{C1,H1} = 157.5$ Hz), 99.1, 85.3, 82.7, 82.2, 76.8, 73.6, 72.3, 70.5, 69.2, 66.3, 62.3, 30.3, 26.2, 26.2, 18.2, 18.1, 16.2, 13.0, −3.3, −3.4, −3.9, −4.7; HRMS (FAB): calcd for $C_{42}H_{78}O_{10}Si_3Cs$ $[M+Cs]^+$: 959.3957, found 959.3997.

DE triol 22: 10% Pd/C (40 mg) was added to a solution of DE benzylidene **21** (0.22 g, 0.26 mmol) in EtOAc (3.0 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 2 h. The reaction mixture was diluted with EtOAc (50 mL) and filtered through a short pad of Celite and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DE triol **22** (0.19 g, 97%) as a white foam. **22**: $R_f = 0.27$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -70.7$ ($c = 0.44$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3422$, 2928, 2864, 1463, 1382, 1254, 1178, 1090, 836, 779 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 4.79$ (s, 1H, D1), 4.47 (d, $J = 7.1$ Hz, 1H, E1), 3.85 (dd, $J = 11.6$, 3.9 Hz, 1H, D6), 3.84 (d, $J = 3.3$ Hz, 1H, D2), 3.78 (dd, $J = 11.4$, 3.9 Hz, 1H, D6), 3.77 (d, $J = 9.7$ Hz, 1H, D4), 3.60 (dd, $J = 9.3$, 7.1 Hz, 1H, E2), 3.51 (s, 3H, OMe), 3.50 (q, $J = 6.5$ Hz, 1H, E5), 3.40 (dd, $J = 9.3$, 3.5 Hz, 1H, E3), 3.34 (ddd, $J = 9.6$, 9.6, 3.9 Hz, 1H, D5), 3.31 (d, $J = 3.4$ Hz, 1H, E4), 2.33 (s, 1H, OH), 2.02 (s, 1H, OH), 1.43 (s, 3H, Me (D3)), 1.24 (d, $J = 6.4$ Hz, 3H, E6), 1.17–1.04 (m, 21H, iPr$_3$Si), 0.92 (s, 9H, tBuSi), 0.90 (s, 9H, tBuSi), 0.29 (s, 3H, MeSi), 0.15 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.13 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 102.0$, 99.1, 85.3, 83.0, 76.1, 74.2, 74.1, 73.6, 71.8, 70.4, 63.2, 62.3, 31.5, 26.2, 26.0, 18.2, 17.2, 16.2, 13.0, −3.4, −3.4, −3.9, −4.9; HRMS (FAB): calcd for $C_{35}H_{74}O_{10}Si_3Cs$ $[M+Cs]^+$: 871.3644, found 871.3610.

Tosylate 23: Recrystallized TsCl (0.06 g, 0.31 mmol) was added to a solution of DE triol **22** (0.19 g, 0.26 mmol) in pyridine (1.0 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DE tosylate **23** (0.20 g, 87%) as a white foam. **23**: $R_f = 0.42$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -25.9$ ($c = 0.27$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3542$, 3436, 2931, 2851, 1595, 1461, 1361, 1249, 1179, 1085, 985, 838, 779, 720 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.77$ (d, $J = 8.3$ Hz, 2H, ArH), 7.34 (d, $J = 8.3$ Hz, 2H, ArH), 4.71 (s, 1H, D1), 4.46 (d, $J = 7.1$ Hz, 1H, E1), 4.29 (dd, $J = 10.6$, 1.4 Hz, 1H, D6), 4.22 (dd, $J = 10.6$, 6.2 Hz, 1H, D6), 3.81 (s, 1H, D2), 3.59 (dd, $J = 9.3$, 7.1 Hz, 1H, E2), 3.57 (d, $J = 3.9$ Hz, 1H, E4), 3.53–3.48 (m, 3H, D4, D5, E5), 3.50 (s, 3H, OMe), 3.40 (dd, $J = 9.4$, 3.6 Hz, 1H, E3), 2.43 (s, 3H, ArMe), 2.27 (s, 1H, OH), 2.02 (d, $J = 1.9$ Hz, 1H, OH), 1.26 (d, $J = 6.2$ Hz, 3H, E6), 1.25 (s, 3H, Me (D3)), 1.13–1.05 (m, 21H, iPr$_3$Si), 0.91 (s, 9H, tBuSi), 0.88 (s, 9H, tBuSi), 0.30 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.12 (s, 3H, MeSi), 0.11 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 144.7$, 133.3, 129.8, 127.6, 101.7, 99.0, 85.5, 82.1, 75.8, 74.1, 73.5, 72.5, 71.0, 70.5, 70.1, 62.1, 26.2, 26.0, 21.6, 18.4, 18.1, 18.0, 16.9, 16.0, 12.8, −3.4, −3.5, −4.0, −4.9; HRMS (FAB): calcd for $C_{42}H_{80}O_{12}SSi_3Cs$ $[M+Cs]^+$: 1025.3733, found 1025.3783.

DE iodide 24: LiI (0.15 g, 1.12 mmol) was added to a solution of DE tosylate **23** (0.20 g, 0.22 mmol) in DMF (2.0 mL) at 25 °C and the resulting mixture was heated from 80 °C to 100 °C over 2 h. The reaction mixture was cooled, diluted with Et_2O (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes) to afford DE iodide **24** (0.16 g, 86%) as a white foam. **24**: $R_f = 0.46$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -10.5$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3554$, 3460, 2931, 1861, 1467, 1373, 1302, 1255, 1178, 1085, 861, 826, 773, 732 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 4.75$ (s, 1H, D1), 4.47 (d, $J = 7.1$ Hz, 1H, E1), 3.82 (s, 1H, D2), 3.73 (d, $J = 3.5$ Hz, 1H, E4), 3.62–3.60 (m, 2H, E2, D4), 3.55 (s, 3H, OMe), 3.53–3.50 (m, 2H, D6, E5), 3.41 (dd, $J = 9.4$, 3.6 Hz, 1H, E3), 3.25–3.19 (m, 2H, D5, D6), 2.50 (s, 1H, OH), 2.12 (d, $J = 2.4$ Hz, 1H, OH), 1.26 (d, $J = 6.5$ Hz, 3H, E6), 1.16 (s, 3H, Me (D3)), 1.15–1.06 (m, 21H, iPr$_3$Si), 0.93 (s, 9H, tBuSi), 0.89 (s, 9H, tBuSi), 0.31 (s, 3H, MeSi), 0.14 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.12 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 102.0$, 99.1, 85.5, 82.3, 76.2, 75.2, 74.8, 74.2, 74.1, 73.5, 70.5, 62.4, 26.2, 26.0, 18.2, 18.1, 17.2, 16.1, 15.3, 12.9, 7.6, −3.3, −3.5, −4.0, −5.0; HRMS (FAB): calcd for $C_{35}H_{73}IO_9Si_3Cs$ $[M+Cs]^+$: 981.2662, found 981.2645.

DE diol 3: AIBN (5.0 mg, 0.01 mmol) was added to a solution of DE iodide **24** (0.16 g, 0.19 mmol) and nBu$_3$SnH (0.16 mL, 0.60 mmol) in benzene (3.0 mL) at 25 °C and the resulting mixture was immediately refluxed for 0.5 h. The reaction mixture was cooled and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes) to afford DE diol **3** (0.13 g, 97%) as a white foam. **3**: $R_f = 0.45$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -21.2$ ($c = 0.43$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3432$, 2931, 2857, 1463, 1301, 1248, 1175, 1073, 818 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 4.70$ (s, 1H, D1), 4.46 (d, $J = 6.5$ Hz, 1H, E1), 3.80 (s, 1H, D2), 3.58 (d, $J = 8.5$ Hz, 1H, E2), 3.52 (s, 3H, OMe), 3.50 (q, $J = 6.5$ Hz, 1H, E5), 3.41–3.31 (m, 4H, D4, D5, E3, E4), 2.00 (s, 1H, OH), 1.43 (d, $J = 0.5$ Hz, 1H, OH), 1.28 (d, $J = 5.5$ Hz, 3H, D6), 1.24 (d, $J = 5.5$ Hz, 3H, E6), 1.16 (s, 3H, Me (D3)), 1.14–1.06 (m, 21H, iPr$_3$Si), 0.92 (s, 9H, tBuSi), 0.89 (s, 9H, tBuSi), 0.30 (s, 3H, MeSi), 0.14 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.12 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 119.0$, 101.6, 99.1, 85.1, 82.5, 76.6, 76.3, 74.0, 73.6, 70.5, 63.3, 26.2, 26.0, 18.4, 18.2, 17.1, 16.2, 12.9, −3.4, −3.6, −4.1, −4.8; HRMS (MALDI): calcd for $C_{35}H_{74}O_9Si_3Na$ $[M+Na]^+$: 745.4538, found 745.4520.

DE PMB ether 25: nBu$_2$SnO (45.0 mg, 0.18 mmol) was added to a solution of DE diol **3** (0.12 g, 0.17 mmol) in toluene (10 mL) and the resulting mixture was refluxed with removal of H_2O using a Dean Stark apparatus for 5 h. The reaction mixture was cooled to 25 °C and PMBCl (34.0 μL, 0.25 mmol) and nBu$_4$NI (12 mg, 0.03 mmol) were added. The reaction mixture was refluxed again for 8 h, and then the reaction mixture was quenched by the addition of H_2O (0.5 mL). The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes) to afford DE PMB ether **25** (88 mg, 63%) as a white foam. **25**: $R_f = 0.62$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -10.0$ ($c = 0.11$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3450$, 2932, 2861, 1519, 1249, 1185, 1091, 844, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.28$ (d, $J = 8.5$ Hz, 2H, PMB), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 4.84, 4.55 (AB, $J = 10.9$ Hz, 2H, CH_2Ar), 4.64 (s, 1H, D1), 4.47 (d, $J = 7.1$ Hz, 1H, E1), 3.80 (s, 3H, OMe), 3.74 (s, 1H, D2), 3.58 (dd, $J = 9.2$, 7.2 Hz, 1H, E2), 3.51 (s, 3H, OMe), 3.48 (q, $J = 7.3$ Hz, 1H, E5), 3.40 (d, $J = 3.3$ Hz, 1H, E4), 3.34 (dd, $J = 9.4$, 3.5 Hz, 1H, E3), 3.29 (dd, $J = 9.4$, 6.0 Hz, 1H, D5), 3.18 (d, $J = 9.4$ Hz, 1H, D4), 2.55 (s, 1H, OH), 1.25 (d, $J = 6.9$ Hz, 6H, D6, E6), 1.21 (s, 3H, Me (D3)), 1.14–1.04 (m, 21H, iPr$_3$Si), 0.93 (s, 9H, tBuSi), 0.89 (s, 9H, tBuSi), 0.29 (s, 3H, MeSi), 0.14 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.11 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.2$, 130.6, 129.9, 113.7, 101.6, 99.1, 85.1, 83.6, 82.5, 75.0, 74.8, 73.5, 70.6, 70.4, 62.3, 55.3, 29.7, 26.2, 26.1, 18.8, 18.5, 18.2, 18.1, 18.1, 16.2, 12.9, −3.3, −3.5, −3.9, −4.9; HRMS (MALDI): calcd for $C_{43}H_{82}O_{10}Si_3Na$ $[M+Na]^+$: 865.5113, found 865.5104.

DE triacetate 27: nBu$_4$NF (0.81 mL, 0.81 mmol) was added to a solution of DE alcohol **25** (0.17 g, 0.20 mmol) in THF (1.0 mL) and the resulting mixture was stirred at 25 °C for 6 h. The reaction mixture was diluted with CH_2Cl_2 (1.0 mL) and Et_3N (0.112 mL, 0.81 mmol) and 4-DMAP (5.0 mg, 0.01 mmol) were added. The resulting mixture was cooled to 0 °C and Ac_2O (51.0 μL, 0.50 mmol) was added. The reaction mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford DE triacetate **27** (0.106 g, 90% over two steps) as a white foam. **27**: $R_f = 0.30$ (100% Et_2O); IR (thin film): $\tilde{\nu} = 3452$, 2934, 1754, 1613, 1513, 1371, 1245, 1091, 919, 732 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, ca. 1:1 mixture of anomers): $\delta = 7.28$ (d, $J = 8.6$ Hz, 2H, PMB), 7.27 (d, $J = 8.6$ Hz, 2H, PMB), 6.87 (d, $J = 8.6$ Hz, 4H, PMB), 6.26 (d, $J = 3.7$ Hz, 1H, E1), 5.53 (d, $J = 8.3$ Hz, 1H, E1), 5.29 (dd, $J = 10.3$, 8.3 Hz, 1H, E2), 5.26 (dd, $J = 10.3$, 3.7 Hz, 1H, E2), 4.96 (s, 1H, D1), 4.93 (s, 1H, D1), 4.81, 4.55 (AB, $J = 10.8$ Hz, 4H, CH_2Ar), 4.79 (s, 1H, D2), 4.72 (s, 1H, D2), 4.03 (br q, $J = 6.3$ Hz, 1H, E5), 3.99 (dd, $J = 10.6$, 2.8 Hz, 1H, E3), 3.80 (s, 6H, OMe), 3.75 (dd, $J = 10.2$, 2.8 Hz, 1H, E3), 3.68 (br q, $J = 6.4$ Hz, 1H, E5), 3.52 (d, $J = 2.0$ Hz, 1H, E4), 3.45 (d, $J = 2.7$ Hz,

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1H, E4), 3.44–3.23 (m, 4H, D4, D4, D5, D5), 2.14 (s, 3H, OAc), 2.13 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.03 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.37 (s, 6H, Me (D3)), 1.36 (d, J = 6.1 Hz, 3H, D6), 1.34 (d, J = 6.1 Hz, 3H, D6), 1.30 (d, J = 6.1 Hz, 3H, E6), 1.23 (d, J = 6.1 Hz, 3H, E6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.9, 170.8, 169.6, 169.6, 169.2, 168.8, 159.3, 135.7, 130.4, 129.6, 125.5, 113.8, 99.0, 98.8, 92.4, 90.4, 82.6, 82.5, 81.3, 80.8, 80.4, 75.9, 75.9, 75.0, 73.8, 71.6, 70.9, 70.9, 69.7, 69.0, 68.5, 61.4, 61.3, 55.2, 30.3, 29.3, 21.0, 20.9, 20.9, 20.8, 20.7, 20.6, 19.9, 18.6, 18.5, 16.2; HRMS (MALDI): calcd for $C_{28}H_{40}O_{13}Na$ [M+Na]$^+$: 607.2367, found 607.2352.

DE lactol 28: nBuNH$_2$ (15.0 μL, 0.21 mmol) was added to a solution of DE triacetate **27** (100 mg, 0.17 mmol) in THF (1.0 mL) and the resulting mixture was stirred at 25 °C for 5 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford DE lactol **28** (80 mg, 86%) as a white foam. **28**: R_f = 0.30 (100% EtOAc); IR (thin film): $\tilde{\nu}$ = 3366, 2931, 2872, 1737, 1649, 1549, 1515, 1372, 1247, 1088 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$ (α:β ca. 10:1)): δ = 7.26 (d, J = 8.5 Hz, 2H, PMB), 6.86 (d, J = 8.5 Hz, 2H, PMB), 5.38 (d, J = 3.6 Hz, 1H, E1), 5.04 (dd, J = 10.6, 3.7 Hz, 1H, E2), 4.93 (s, 1H, D1), 4.80 (s, 1H, D2), 4.78, 4.53 (AB, J = 10.8 Hz, 2H, CH_2Ar), 4.15 (br q, J = 6.4 Hz, 1H, E5), 4.11 (dd, J = 10.6, 2.8 Hz, 1H, E3), 3.78 (s, 3H, OMe), 3.55 (s, 3H, OMe), 3.45 (d, J = 2.1 Hz, 1H, E4), 3.38 (dq, J = 9.5, 6.4 Hz, 1H, D5), 3.30 (d, J = 9.5 Hz, 1H, D4), 2.10 (s, 3H, OAc), 2.07 (s, 3H, OAc), 1.33 (s, 3H, Me (D3)), 1.31 (d, J = 6.4 Hz, 3H, E6), 1.19 (d, J = 6.4 Hz, 3H, D6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.9, 170.1, 159.2, 130.4, 129.6, 113.7, 98.9, 95.9, 90.4, 82.6, 81.9, 76.2, 75.9, 74.9, 73.7, 71.0, 70.7, 65.9, 60.3, 55.2, 39.3, 31.5, 21.1, 19.9, 19.6, 18.5, 16.1; HRMS (MALDI): calcd for $C_{26}H_{38}O_{12}Na$ [M+Na]$^+$: 565.2261, found 565.2282.

DE trichloroacetimidate 2: DBU (1 drop) was added to a solution of DE lactol **28** (86 mg, 0.16 mmol) and Cl_3CCN (0.10 mL, 0.80 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C and the resulting mixture was stirred for 0.5 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford DE trichloroacetimdiate **2** (97 mg, 89%, α:β ca. 30:1) as a white foam. **2**: R_f = 0.60 (80% EtOAc in hexanes); IR (thin film): $\tilde{\nu}$ = 3495, 3331, 2978, 2951, 2884, 1743, 1678, 1614, 1508, 1455, 1373, 1243, 1091, 1049, 844, 791 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.54 (s, 1H, NH), 7.27 (d, J = 8.5 Hz, 2H, PMB), 6.87 (d, J = 8.5 Hz, 2H, PMB), 6.47 (d, J = 3.7 Hz, 1H, E1), 5.28 (dd, J = 10.6, 3.7 Hz, 1H, E2), 4.99 (s, 1H, D2), 4.81, 4.56 (AB, J = 11.0 Hz, 2H, CH_2Ar), 4.16–4.12 (m, 2H, E3, E5), 3.79 (s, 3H, OMe), 3.59 (s, 3H, OMe), 3.57 (br s, 1H, E4), 3.42 (dq, J = 9.6, 5.9 Hz, 1H, D5), 3.32 (d, J = 9.6 Hz, 1H, D4), 2.14 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.37 (s, 3H, Me (D3)), 1.35 (d, J = 6.0 Hz, 3H, D6), 1.26 (d, J = 6.6 Hz, 3H, E6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 170.0, 161.1, 159.0, 130.5, 129.8, 114.4, 98.5, 94.3, 91.6, 82.5, 81.7, 76.1, 75.0, 74.3, 71.0, 69.4, 65.5, 61.5, 55.5, 30.2, 21.2, 21.0, 20.3, 18.2, 16.3.

A$_1$B(A)CDE pentasaccharide 30: A$_1$B(A)C glycosyl fluoride **29**[1] (30 mg, 0.028 mmol) and DE diol **3** (22 mg, 0.030 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. Et_2O (0.15 mL) and 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 15 min. $SnCl_2$ (6.6 mg, 0.035 mmol) was added in one portion and the resulting mixture was warmed to 25 °C and stirred for 6 h. The reaction mixture was diluted with EtOAc (100 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 50% Et_2O in hexanes) to afford A$_1$B(A)CDE pentasaccharide **30** (33 mg, 62%) as a white foam. **30**: R_f = 0.21 (30% Et_2O in hexanes); $[\alpha]_D^{22}$ = −11.1 (c = 0.10, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2934, 2864, 1738, 1548, 1455, 1392, 1252, 1092, 836, 778, 736 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.60–7.17 (m, 15H, ArH), 5.21 (d, J = 1.8 Hz, 1H, C1), 5.05, 5.02 (AB, J = 10.1 Hz, 2H, CH_2Ar), 4.94 (br d, J = 3.2 Hz, 1H, A1), 4.87 (t, J = 9.4 Hz, 1H, B4), 4.80 (br d, J = 8.7 Hz, 1H, B1), 4.66, 4.53 (AB, J = 11.2 Hz, 2H, CH_2Ar), 4.60 (s, 1H, D1), 4.46 (d, J = 7.1 Hz, 1H, E1), 4.15 (dd, J = 7.8, 4.4 Hz, 1H, C3), 4.01 (br s, 1H, C2), 3.93–3.88 (m, 1H, C5), 3.86–3.84 (m, 1H, B3), 3.82 (s, 3H, OMe), 3.69 (s, 1H, D2), 3.64 (d, J = 9.5 Hz, 1H, A4), 3.57 (dd, J = 9.0, 7.6 Hz, 1H, E2), 3.56 (t, J = 7.1 Hz, 1H, C4), 3.53–3.46 (m, 2H, A5, D5), 3.49 (s, 3H, OMe), 3.39–3.30 (m, 3H, B5, D4, E3), 3.35 (s, 3H, OMe), 3.23–3.20 (m, 2H, E4, E5), 2.45 (dd, J = 13.7, 4.9 Hz, 1H, A2), 2.38 (s, 3H, Me), 2.30 (ddd, J = 12.3, 4.8, 1.9 Hz, 1H, B2), 2.03 (dd, J = 13.7, 1.7 Hz, 1H, A2), 1.69 (s, 3H, Me (A3)), 1.63 (dt, J = 12.2, 12.2 Hz, 1H, B2), 1.33 (d, J = 6.2 Hz, 3H, B6), 1.31 (d, J = 6.2 Hz, 3H, C6), 1.25 (s, 3H, Me (D3)), 1.24 (d, J = 6.4 Hz, 3H, D6), 1.24 (d, J = 5.4 Hz, 3H, E6), 1.14–1.04 (m, 21H, iPr$_3$Si), 0.88 (s, 9H, tBuSi), 0.86 (s, 9H, tBuSi), 0.83 (d, J = 6.2 Hz, 3H, A6), 0.26 (s, 3H, MeSi), 0.11 (s, 6H, MeSi), 0.09 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.6, 153.3, 153.2, 138.2, 135.9, 134.8, 134.5, 129.0, 128.6, 128.5, 128.2, 127.6, 127.5, 126.4, 126.0, 121.7, 102.3, 101.5, 100.1, 99.1, 92.4, 89.9, 85.1, 84.2, 82.5, 80.0, 78.0, 76.1, 74.9, 74.5, 73.5, 72.3, 71.1, 71.0, 70.5, 70.0, 67.6, 66.2, 65.8, 62.2, 62.0, 60.8, 48.5, 40.1, 36.3, 29.7, 26.2, 26.1, 25.1, 19.4, 19.3, 18.5, 18.4, 18.1, 18.0, 17.8, 16.2, 15.3, 12.8, −3.4, −3.5, −3.9, −4.9; HRMS (FAB): calcd for $C_{84}H_{129}Cl_2NO_{22}SeSi_3Cs$ [M+Cs]$^+$: 1870.5911, found 1870.6012.

A$_1$B(A)CDE orthoester 31: $NaIO_4$ (41 mg, 0.19 mmol) and $NaHCO_3$ (13 mg, 0.15 mmol) were added to a solution of A$_1$B(A)CDE pentasaccharide **30** (33 mg, 0.019 mmol) in MeOH/CH_2Cl_2/H_2O (3:2:1, 1.0 mL) and the resulting mixture was stirred at 25 °C for 4 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The crude selenoxide was dissolved in toluene (1 mL) and transferred by cannula to a sealed tube. The flask was washed with toluene (2 × 0.5 mL) and the organics were transferred to the sealed tube. Diisopropylamine (1 mL) and vinyl acetate (2 mL) were added, and the tube was sealed and heated to 140 °C for 12 h. After cooling, the reaction mixture was concentrated and the residue was purified by preparative TLC (silica gel, 50% Et_2O in hexanes) to afford A$_1$B(A)CDE orthoester **31** (18 mg, 60% over two steps) as a white foam. **31**: R_f = 0.21 (30% Et_2O in hexanes); $[\alpha]_D^{22}$ = −8.0 (c = 0.64, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2934, 2863, 1737, 1543, 1457, 1388, 1251, 1128, 1095, 1043, 907, 840, 778, 735 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.3 Hz, 2H, ArH), 7.43–7.27 (m, 8H, ArH), 5.05, 5.02 (AB, J = 10.1 Hz, 2H, CH_2Ar), 4.94 (br d, J = 3.2 Hz, 1H, A1), 4.88 (t, J = 9.4 Hz, 1H, B4), 4.87 (s, 1H, D1), 4.75 (dd, J = 9.8, 1.6 Hz, 1H, B1), 4.68, 4.55 (AB, J = 11.0 Hz, 2H, CH_2Ar), 4.45 (d, J = 7.1 Hz, 1H, E1), 4.11 (s, 1H, D2), 3.94–3.79 (m, 6H, B3, C3, C4, C5, D4, E5), 3.82 (s, 3H, OMe), 3.73 (dq, J = 10.0, 6.4 Hz, 1H, D5), 3.64 (d, J = 9.4 Hz, 1H, A4), 3.59 (dd, J = 9.2, 7.2 Hz, 1H, E2), 3.54 (s, 3H, OMe), 3.53–3.46 (m, 1H, A5), 3.43 (dd, J = 9.4, 3.4 Hz, 1H, E3), 3.35 (s, 3H, OMe), 3.34–3.31 (m, 2H, B5, E4), 2.51 (dd, J = 12.8, 5.1 Hz, 1H, C2), 2.44 (dd, J = 13.8, 5.0 Hz, 1H, A2), 2.38 (s, 3H, Me (A$_1$)), 2.29 (dd, J = 10.7, 3.3 Hz, 1H, B2), 2.01 (dd, J = 13.7, 1.8 Hz, 1H, A2), 1.90 (t, J = 12.1 Hz, 1H, C2), 1.69 (dt, J = 12.2, 12.2 Hz, 1H, B2), 1.69 (s, 3H, Me (A3)), 1.34 (s, 3H, Me (D3)), 1.32 (d, J = 6.2 Hz, 3H, C6), 1.30 (d, J = 6.0 Hz, 3H, B6), 1.27 (d, J = 6.3 Hz, 3H, D6), 1.23 (d, J = 6.4 Hz, 3H, E6), 1.19–1.06 (m, 21H, iPr$_3$Si), 0.94 (s, 9H, tBuSi), 0.89 (s, 9H, tBuSi), 0.82 (d, J = 6.2 Hz, 3H, A6), 0.20 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.13 (s, 3H, MeSi), 0.12 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.6, 153.3, 153.2, 151.5, 138.7, 135.9, 134.8, 128.7, 128.6, 128.2, 127.5, 127.3, 126.4, 126.0, 121.7, 120.1, 102.4, 100.2, 99.2, 92.4, 90.0, 84.7, 84.3, 82.9, 82.5, 81.6, 79.1, 77.2, 76.2, 74.9, 74.1, 73.9, 72.5, 71.8, 71.1, 70.4, 70.1, 68.3, 66.2, 65.9, 62.3, 62.0, 60.8, 45.5, 40.1, 38.9, 36.4, 29.7, 26.3, 24.0, 21.0, 20.6, 19.4, 19.2, 18.4, 18.3, 18.1, 17.6, 16.2, 15.3, 13.0, −3.5, −3.8, −3.9, −4.5; HRMS (ESI): calcd for $C_{78}H_{125}Cl_2NO_{23}Si_3Na$ [M+H$_2$O+Na]$^+$: 1620, found 1620.

DEFGHA$_2$ β-pentasaccharide 33: DE trichloroacetimidate **2** (82 mg, 0.12 mmol) and FGHA$_2$ alcohol **32**[2] (73 mg, 0.07 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (0.35 mL) and 4 Å MS were added, and the mixture was stirred for 15 min. The resulting mixture was cooled to −20 °C and $BF_3 \cdot Et_2O$ (74 μL, 0.5 M solution in CH_2Cl_2, 0.037 mmol) was added dropwise. The reaction mixture was stirred at −20 °C for 2 h. The reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 10% acetone in CH_2Cl_2) to afford DEFGHA$_2$ β-pentasaccharide **33** (61 mg, 55%) as a white foam, DEFGHA$_2$ α-pentasaccharide (6.0 mg, 5%) (α:β ca. 1:10) and a rearranged DEFGHA$_2$ β-pentasaccharide (20 mg, 18%). **33**: R_f = 0.15 (100% Et_2O); $[\alpha]_D^{22}$ = −14.0 (c = 0.10, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3422, 2971, 2939, 2895, 1743, 1732, 1600, 1517, 1451, 1369, 1242, 1154, 1088, 1044 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.44–7.22 (m, 22H, ArH, PMB), 6.87 (d, J = 8.6 Hz, 2H, PMB), 6.41 (s, 2H, ArH (A$_2$)), 5.41 (dd, J = 9.8, 9.8, 5.6 Hz, 1H, H4), 5.27 (s, 1H, G1), 5.14 (s, 1H, OCH_2O), 5.13 (dd, J = 10.2, 8.0 Hz, 1H, E2), 5.01 (s,

2H, CH_2Ar), 4.99 (s, 1H, OCH_2O), 4.99 (s, 2H, CH_2Ar), 4.90 (s, 1H, D1), 4.81, 4.55 (AB, $J = 10.8$ Hz, 2H, CH_2Ar), 4.77, 4.69 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.74, 4.69 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, D2), 4.63 (s, 1H, F1), 4.61 (d, $J = 7.8$ Hz, 1H, E1), 4.50 (ddd, $J = 10.6$, 10.6, 4.6 Hz, 1H, G4), 4.24 (br s, 1H, G2), 4.14 – 4.12 (m, 1H, G5), 4.10 (dd, $J = 11.6$, 5.5 Hz, 1H, H5), 4.00 (dd, $J = 10.2$, 2.3 Hz, 1H, G3), 3.91 (t, $J = 9.8$ Hz, 1H, H3), 3.90 (t, $J = 8.7$ Hz, 1H, F4), 3.80 (s, 3H, OMe), 3.78 (t, $J = 10.3$ Hz, 1H, G5), 3.59 – 3.47 (m, 7H, E3, E4, F2, F6, F6, H2, H5), 3.55 (s, 3H, OMe), 3.51 (s, 3H, OMe), 3.38 (dq, $J = 9.4$, 6.1 Hz, 1H, D5), 3.37 – 3.30 (m, 4H, D4, E5, F3, F5), 3.30 (s, 3H, OMe), 2.31 (s, 3H, Me (A_2)), 2.13 (s, 3H, OAc), 2.05 (s, 3H, OAc), 1.75 (br s, 1H, OH), 1.35 (s, 3H, Me (D3)), 1.31 (d, $J = 6.0$ Hz, 3H, D6), 1.17 (d, $J = 6.2$ Hz, 3H, E6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 170.9, 168.9, 166.8, 160.7, 159.3, 157.3, 138.7, 138.6, 137.6, 136.4, 136.3, 130.4, 129.7, 128.6, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.5, 127.4, 127.2, 127.1, 119.1, 115.9, 113.8, 108.1, 100.8, 98.8, 98.2, 96.7, 96.0, 95.8, 82.6, 81.5, 81.0, 80.7, 80.5, 77.6, 77.5, 76.0, 75.6, 75.0, 74.9, 74.4, 73.8, 73.1, 72.1, 71.5, 70.8, 70.8, 70.4, 70.3, 70.2, 70.0, 69.7, 65.8, 63.4, 63.3, 61.6, 61.2, 59.1, 55.2, 45.8, 21.0, 20.8, 20.0, 18.5, 16.4, 15.2, 14.2, 8.6; HRMS (MALDI): calcd for $C_{81}H_{96}O_{28}Na$ $[M+Na]^+$: 1539.5986, found 1539.6047. Rearranged DEFGHA$_2$ β-pentasaccharide: $R_f = 0.16$ (100% Et_2O); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.43 - 7.62$ (m, 22H, ArH, PMB), 6.87 (d, $J = 8.6$ Hz, 2H, PMB), 6.42 (s, 2H, ArH (A_2)), 5.37 (ddd, $J = 9.4$, 9.4, 5.5 Hz, 1H, H4), 5.28 (d, $J = 0.8$ Hz, 1H, G1), 5.20 (s, 1H, OCH_2O), 5.12 (dd, $J = 10.2$, 8.0 Hz, 1H, E2), 5.09 (s, 1H, OCH_2O), 5.02 (s, 4H, CH_2Ar), 4.90 (br s, 1H, D1), 4.87, 4.60 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.80, 4.55 (AB, $J = 10.8$ Hz, 2H, CH_2Ar), 4.75, 4.68 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.66 (d, $J = 0.7$ Hz, 1H, D2), 4.63 (s, 1H, F1), 4.59 (d, $J = 7.7$ Hz, 1H, E1), 4.35 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.28 (br s, 1H, G2), 4.12 – 4.08 (m, 3H, G3, G5, H5), 3.91 (t, $J = 8.8$ Hz, 1H, F4), 3.89 (t, $J = 9.8$ Hz, 1H, H3), 3.80 (s, 3H, OMe), 3.73 (t, $J = 10.4$ Hz, 1H, G5), 3.63 (d, $J = 9.6$ Hz, 1H, H2), 3.59 – 3.47 (m, 6H, E3, E4, F2, F6, F6, H5), 3.55 (s, 3H, OMe), 3.52 (s, 3H, OMe), 3.37 (dq, $J =$ 9.4, 6.0 Hz, 1H, D5), 3.35 – 3.31 (m, 4H, D4, E5, F3, F5), 3.30 (s, 3H, OMe), 2.32 (s, 3H, Me (A_2)), 2.12 (s, 3H, OAc), 2.05 (s, 3H, OAc), 1.33 (s, 3H, Me (D3)), 1.31 (d, $J = 6.0$ Hz, 3H, D6), 1.17 (d, $J = 6.3$ Hz, 3H, E6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.9$, 169.0, 167.0, 160.7, 159.3, 157.5, 138.9, 138.7, 137.7, 136.4, 136.4, 130.4, 129.7, 128.6, 128.5, 128.3, 128.1, 128.0, 127.8, 127.7, 127.5, 127.4, 127.2, 127.1, 123.9, 119.1, 115.9, 113.8, 108.1, 100.9, 98.8, 98.3, 96.8, 95.8, 94.4, 82.6, 81.5, 80.7, 78.5, 77.6, 76.0, 75.3, 75.2, 75.1, 75.0, 74.4, 73.8, 73.2, 72.2, 72.2, 71.5, 70.9, 70.8, 70.4, 70.1, 65.8, 63.8, 63.5, 61.7, 61.2, 60.4, 59.2, 55.3, 45.8, 29.7, 21.0, 21.0, 20.1, 16.4, 15.3, 14.2, 8.6; HRMS (MALDI): calcd for $C_{81}H_{96}O_{28}Na$ $[M+Na]^+$: 1539.5986, found 1539.6047.

DEFGHA$_2$ triol 34: K_2CO_3 (3 mg, 0.02 mmol) was added to a solution of DEFGHA$_2$ diacetate **33** (34 mg, 0.02 mmol) in THF/MeOH (2:1, 0.3 mL) and the resulting mixture was stirred at 25 °C for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 100% EtOAc) to afford DEFGHA$_2$ triol **34** (30 mg, 93%) as a white foam. **34**: $R_f = 0.21$ (100% EtOAc); $[\alpha]_D^{22} = -20.5$ ($c = 0.22$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3420$, 2931, 2884, 1732, 1600, 1512, 1451, 1374, 1253, 1160, 1083, 918, 736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.41 - 7.24$ (m, 22H, ArH, PMB), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 6.41 (s, 2H, ArH (A_2)), 5.42 (ddd, $J = 9.7$, 9.7, 5.6 Hz, 1H, H4), 5.25 (s, 1H, G1), 5.16 (s, 1H, OCH_2O), 5.02 (s, 1H, OCH_2O), 5.02 (s, 2H, CH_2Ar), 4.99 (s, 2H, CH_2Ar), 4.90 (s, 1H, D1), 4.79, 4.59 (AB, $J =$ 10.7 Hz, 2H, CH_2Ar), 4.79, 4.58 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.72 (s, 2H, CH_2Ar), 4.60 (s, 1H, F1), 4.58 (d, $J = 7.7$ Hz, 1H, E1), 4.51 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.25 (br s, 1H, G2), 4.14 (dd, $J = 9.2$, 4.4 Hz, 1H, G5), 4.13 (t, $J = 8.3$ Hz, 1H, F4), 4.10 (dd, $J = 11.4$, 5.2 Hz, 1H, H5), 4.00 (dd, $J =$ 10.2, 2.2 Hz, 1H, G3), 3.92 (t, $J = 9.8$ Hz, 1H, H3), 3.80 (s, 3H, OMe), 3.77 (t, $J = 10.3$ Hz, 1H, G5), 3.71 – 3.67 (m, 3H, D2, E2, H2), 3.62 – 3.52 (m, 7H, D4, E3, E4, F2, F6, F6, H5), 3.54 (s, 3H, OMe), 3.52 (s, 3H, OMe), 3.46 (d, $J = 2.6$ Hz, 1H, OH), 3.41 – 3.31 (m, 4H, D5, E5, F3, F5), 3.39 (s, 3H, OMe), 3.28 (d, $J = 2.5$ Hz, 1H, OH), 2.31 (s, 3H, Me (A_2)), 1.35 (s, 3H, Me (D3)), 1.28 (d, $J = 5.2$ Hz, 3H, D6), 1.17 (d, $J = 6.3$ Hz, 3H, E6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 166.8$, 160.7, 159.2, 157.3, 138.7, 138.0, 137.6, 136.4, 136.4, 130.7, 129.7, 128.6, 128.4, 128.3, 128.1, 127.9, 127.8, 127.5, 127.4, 127.3, 127.1, 119.1, 115.9, 113.7, 108.2, 104.3, 99.2, 98.3, 96.7, 96.2, 96.1, 83.3, 81.8, 80.9, 80.5, 77.6, 77.5, 75.6, 75.3, 75.0, 74.7, 74.4, 74.2, 74.2, 74.2, 72.1, 71.8, 70.9, 70.7, 70.4, 70.2, 70.1, 69.7, 63.5, 61.9, 61.8, 60.3, 59.4, 55.2, 21.0, 20.0, 18.5, 18.3, 16.3, 14.2; HRMS (MALDI): calcd for $C_{77}H_{92}O_{26}Na$ $[M+Na]^+$: 1455.5774, found 1455.5704.

DEFGHA$_2$ bis-TBS ether 35: TBSOTf (14.0 μL, 0.05 mmol) was added to a solution of DEFGHA$_2$ diol **34** (30 mg, 0.02 mmol) and 2,6-lutidine (10.0 μL, 0.08 mmol) in CH_2Cl_2 (0.3 mL) at −10 °C and the resulting mixture was warmed to 0 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60% EtOAc in hexanes) to afford DEFGHA$_2$ bis-TBS ether **35** (32 mg, 92%) as a white foam. **35**: $R_f = 0.43$ (40% EtOAc in hexanes); $[\alpha]_D^{22} = -30.0$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3403$, 2929, 2873, 1732, 1605, 1451, 1374, 1248, 1094, 1050, 841 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.42 - 7.22$ (m, 22H, ArH, PMB), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 6.41 (s, 2H, ArH (A_2)), 5.42 (ddd, $J = 9.7$, 9.7, 5.5 Hz, 1H, H4), 5.28 (d, $J = 1.1$ Hz, 1H, G1), 5.12 (s, 1H, OCH_2O), 5.02 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.93 (s, 1H, OCH_2O), 4.88, 4.48 (AB, $J = 10.6$ Hz, 2H, CH_2Ar), 4.79 (s, 1H, D1), 4.78, 4.71 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.78, 4.61 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.78 (d, $J = 7.6$ Hz, 1H, E1), 4.66 (s, 1H, F1), 4.51 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.20 (br s, 1H, G2), 4.14 – 4.09 (m, 4H, D2, F4, G5, H3), 4.07 (dd, $J =$ 10.3, 2.4 Hz, 1H, G3), 3.91 (t, $J = 9.7$ Hz, 2H, H5, G5), 3.80 (s, 3H, OMe), 3.67 (dd, $J = 9.3$, 7.6 Hz, 1H, E2), 3.61 – 3.40 (m, 11H, D4, E3, E4, E5, F2, F6, F6, F3, F5, H2, H5), 3.60 (s, 3H, OMe), 3.47 (s, 3H, OMe), 3.29 (dq, $J =$ 9.3, 7.6 Hz, 1H, D5), 3.26 (s, 3H, OMe), 2.31 (s, 3H, Me (A_2)), 1.37 (s, 3H, Me (D3)), 1.27 (d, $J = 7.1$ Hz, 3H, D6), 1.17 (d, $J = 6.4$ Hz, 3H, E6), 0.95 (s, 9H, *t*BuSi), 0.89 (s, 9H, *t*BuSi), 0.22 (s, 3H, MeSi), 0.19 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.03 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.9$, 160.7, 159.2, 157.4, 138.7, 137.8, 136.4, 130.9, 129.4, 128.6, 128.5, 128.3, 128.1, 128.1 127.9, 127.7, 127.5, 127.4, 127.2, 127.1, 119.1, 116.0, 108.2, 102.6, 100.9, 98.3, 95.7, 84.4, 83.6, 82.3, 81.2, 78.1, 75.7, 75.4, 75.3, 75.0, 73.3, 73.0, 72.7, 71.3, 70.5, 70.4, 70.3, 70.1, 69.9, 65.8, 61.9, 58.8, 55.3, 29.7, 26.1, 20.0, 18.6, 18.4, 18.0, 16.4, 15.3, 14.2, −1.7, −2.3, −3.5, −4.5; HRMS (MALDI): calcd for $C_{89}H_{120}O_{26}Si_2Na$ $[M+Na]^+$: 1683.7504, found 1683.7512.

DEFGHA$_2$ diol 36: DDQ (4.0 mg, 0.03 mmol) was added to a solution of DEFGHA$_2$ bis-TBS ether **35** (32 mg, 0.02 mmol) in CH_2Cl_2/H_2O (10:1, 0.3 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60% EtOAc in hexanes) to afford DEFGHA$_2$ diol **36** (29 mg, 98%) as a white foam. **36**: $R_f = 0.39$ (50% EtOAc in hexanes); $[\alpha]_D^{22} =$ −12.9 ($c = 0.21$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3420$, 2930, 2895, 2862, 1732, 1605, 1457, 1374, 1154, 1105, 1044, 841 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.42 - 7.22$ (m, 20H, ArH), 6.41 (s, 2H, ArH (A_2)), 5.42 (ddd, $J = 9.7$, 9.7, 5.4 Hz, 1H, H4), 5.28 (s, 1H, G1), 5.12 (s, 1H, OCH_2O), 5.02 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.93 (s, 1H, OCH_2O), 4.79 (s, 1H, D1), 4.78, 4.71 (AB, $J = 12.2$ Hz, 2H, CH_2Ar), 4.78, 4.62 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.72 (s, 1H, F1), 4.51 (ddd, $J = 10.6$, 10.6, 4.6 Hz, 1H, G4), 4.20 (br s, 1H, G2), 4.14 – 4.08 (m, 5H, E1, F4, G5, H2, H3), 4.07 (dd, $J = 10.4$, 2.4 Hz, 1H, G3), 3.91 (t, $J = 9.5$ Hz, 2H, H5, G5), 3.80 (s, 1H, D2), 3.67 (dd, $J = 9.3$, 7.6 Hz, 1H, E2), 3.60 – 3.44 (m, 9H, D4, E3, E4, E5, F3, F5, F6, F6, H5), 3.59 (s, 3H, OMe), 3.51 (s, 3H, OMe), 3.40 (d, $J = 3.0$ Hz, 1H, F2), 3.37 (dq, $J = 9.6$, 6.0 Hz, 1H, D5), 3.27 (s, 3H, OMe), 2.31 (s, 3H, Me (A_2)), 1.81 (d, $J = 2.4$ Hz, 1H, OH), 1.30 (d, $J = 6.4$ Hz, 3H, D6), 1.24 (d, $J = 6.4$ Hz, 3H, E6), 1.22 (s, 3H, Me (D3)), 0.90 (s, 9H, *t*BuSi), 0.89 (s, 9H, *t*BuSi), 0.18 (s, 3H, MeSi), 0.15 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.03 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.9$, 160.7, 157.4, 139.2, 139.0, 138.7, 137.8, 136.4, 136.4, 132.0, 128.7, 128.6, 128.6, 128.5, 128.3, 128.1, 128.1, 127.9, 127.8, 127.7, 127.5, 127.4, 127.1, 126.9, 119.1, 116.0, 114.3, 108.2, 101.0, 98.4, 96.7, 95.7, 95.0, 84.3, 82.3, 81.1, 75.7, 75.6, 74.9, 73.4, 73.0, 72.8, 71.3, 71.2, 70.4, 70.4, 70.3, 70.1, 69.9, 65.8, 63.5, 63.2, 61.9, 60.6, 58.8, 26.1, 19.3, 18.4, 18.3, 18.0, 16.4, 15.3, −2.3, −2.7, −3.5, −4.5; HRMS (MALDI): calcd for $C_{81}H_{112}O_{25}Si_2Na$ $[M+Na]^+$: 1563.6929, found 1563.6920.

DEFGHA$_2$ chloroacetate 37: Chloroacetic anhydride (CA_2O) (4.5 mg, 0.03 mmol) was added to a solution of DEFGHA$_2$ diol **36** (29 mg, 0.02 mmol), Et_3N (5.2 μL, 0.04 mmol) and 4-DMAP (0.2 mg, 0.002 mmol) in CH_2Cl_2 (0.3 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL).

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The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60% EtOAc in hexanes) to afford DEFGHA$_2$ chloroacetate **37** (30 mg, 99%) as a white foam. **37**: $R_f = 0.45$ (50% EtOAc in hexanes); $[\alpha]_D^{22} = -35.0$ ($c = 0.14$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3500, 2928, 2855, 1733, 1604, 1458, 1380, 1257, 1150, 1100, 1039, 841\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.42-7.22$ (m, 20H, ArH), 6.41 (s, 2H, ArH (A_2)), 5.42 (ddd, $J = 9.8, 9.8, 5.5$ Hz, 1H, H4), 5.28 (s, 1H, G1), 5.15 (d, $J = 10.1$ Hz, 1H, D4), 5.12 (s, 1H, OCH_2O), 5.02 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.93 (s, 1H, OCH_2O), 4.79 (s, 1H, D1), 4.78, 4.61 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.77, 4.71 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.76 (s, 1H, F1), 4.51 (ddd, $J = 10.6, 10.6, 4.6$ Hz, 1H, G4), 4.20 (brs, 1H, G2), 4.13 (t, $J = 7.5$ Hz, 1H, F4), 4.12–4.10 (m, 3H, E1, G5, H3), 4.09 (dd, $J = 10.8, 2.5$ Hz, 1H, G3), 4.06 (s, 2H, CH_2Cl), 3.91 (t, $J = 10.0$ Hz, 2H, H5, G5), 3.80 (s, 1H, D2), 3.68 (dd, $J = 8.0, 7.7$ Hz, 1H, E2), 3.63–3.44 (m, 10H, D5, E3, E4, E5, F3, F5, F6, F6, H2, H5), 3.60 (s, 3H, OMe), 3.51 (s, 3H, OMe), 3.38 (d, $J = 3.0$ Hz, 1H, F2), 3.27 (s, 3H, OMe), 2.31 (s, 3H, Me (A_2)), 1.30 (s, 3H, Me (D3)), 1.24 (d, $J = 6.4$ Hz, 3H, E6), 1.20 (d, $J = 6.4$ Hz, 3H, D6), 0.89 (s, 9H, *t*BuSi), 0.84 (s, 9H, *t*BuSi), 0.17 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.04 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.9, 166.2, 160.7, 157.3, 155.7, 154.5, 139.1, 138.7, 137.7, 136.4, 128.8, 128.6, 128.6, 128.5, 128.3, 128.1, 128.1, 127.9, 127.7, 127.5, 127.4, 127.2, 127.1, 126.9, 119.1, 116.0, 108.2, 102.5, 100.9, 98.3, 97.8, 96.7, 95.7, 95.0, 84.5, 82.3, 81.1, 77.7, 77.5, 75.7, 75.5, 75.3, 73.3, 73.0, 72.7, 71.3, 70.4, 70.4, 70.3, 70.1, 69.8, 68.9, 63.5, 63.2, 62.0, 60.6, 58.8, 40.8, 29.7, 26.0, 25.7, 20.0, 19.9, 18.0, 18.0, 16.3, −2.2, −2.8, −3.5, −4.5$; HRMS (MALDI): calcd for $C_{83}H_{113}ClO_{26}Si_2Na$ $[M+Na]^+$: 1639.6645, found 1639.6676.

DEFGHA$_2$ pentaol 38: 10% Pd/C (5 mg) was added to a solution of DEFGHA$_2$ alcohol **37** (30 mg, 0.02 mmol) in EtOAc (1.0 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 3 h. The reaction mixture was diluted with EtOAc (50 mL) and filtered through a short pad of Celite and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford DEFGHA$_2$ pentaol **38** (22 mg, 94%) as a white foam. **38**: $R_f = 0.14$ (70% EtOAc in hexanes); $[\alpha]_D^{22} = -10.0$ ($c = 0.21$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3463, 2929, 1740, 1651, 1458, 1256, 1043, 840, 779\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 6.28$ (d, $J = 2.5$ Hz, 1H, ArH (A_2)), 6.24 (d, $J = 2.5$ Hz, 1H, ArH (A_2)), 5.41 (ddd, $J = 9.2, 9.2, 5.5$ Hz, 1H, H4), 5.30 (s, 1H, G1), 5.21 (s, 1H, OCH_2O), 5.17 (s, 1H, OCH_2O), 5.15 (d, $J = 10.0$ Hz, 1H, D4), 4.75 (d, $J = 8.6$ Hz, 2H, CH_2Cl), 4.51 (brs, 1H, G2), 4.40 (ddd, $J = 10.5, 10.5, 4.6$ Hz, 1H, G4), 4.27 (dd, $J = 11.7, 5.6$ Hz, 1H, H5), 4.17 (brs, 1H, D1), 4.15 (dd, $J = 9.6, 4.5$ Hz, 1H, G5), 4.10 (d, $J = 7.6$ Hz, 1H, E1), 4.06 (s, 1H, F1), 4.03 (t, $J = 9.8$ Hz, 1H, H3), 4.00 (dd, $J = 10.1, 2.6$ Hz, 1H, G3), 3.91 (t, $J = 10.2$ Hz, 1H, G5), 3.76 (s, 1H, D2), 3.74–3.60 (m, 9H, E2, E3, E4, E5, F4, F6, F6, H2, H5), 3.61 (s, 6H, OMe), 3.52–3.46 (m, 3H, D5, F2, F3), 3.42–3.39 (m, 1H, F5), 3.36 (s, 3H, OMe), 2.49 (s, 3H, Me (A_2)), 2.24 (s, 1H, OH), 1.31 (d, $J = 6.4$ Hz, 3H, E6), 1.25 (s, 3H, Me (D3)), 1.21 (d, $J = 7.0$ Hz, 3H, D6), 0.91 (s, 9H, *t*BuSi), 0.84 (s, 9H, *t*BuSi), 0.16 (s, 3H, MeSi), 0.11 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.03 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.2, 165.8, 161.1, 144.1, 119.1, 111.8, 104.7, 103.3, 101.4, 101.0, 97.0, 97.0, 95.8, 84.3, 81.9, 80.7, 79.4, 75.5, 75.3, 75.1, 75.0, 72.7, 71.0, 71.0, 70.6, 70.3, 69.1, 69.0, 65.9, 63.8, 63.2, 62.0, 59.2, 40.8, 29.7, 26.1, 25.7, 24.6, 19.8, 18.2, 18.0, 17.9, 16.0, 15.2, 14.1, −2.2, −2.8, −3.4, −4.7$; HRMS (MALDI): calcd for $C_{55}H_{89}ClO_{26}Si_2Na$ $[M+Na]^+$: 1279.4767, found 1279.4761.

DEFGHA$_2$ hexa-TBS chloroacetate 39: TBSOTf (4.8 μL, 0.108 mmol) was added to a solution of DEFGHA$_2$ pentaol **38** (22 mg, 0.018 mmol) and 2,6-lutidine (16.0 μL, 0.144 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-TBS chloroacetate **39**: (28 mg, 92%) as a white foam. **39**: $R_f = 0.54$ (100% Et_2O); $[\alpha]_D^{22} = -30.7$ ($c = 0.30$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3421, 3031, 2857, 1737, 1601, 1472, 1256, 1172, 1102, 1048, 836, 780\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 6.28$ (d, $J = 2.0$ Hz, 1H, ArH (A_2)), 6.16 (d, $J = 2.0$ Hz, 1H, ArH (A_2)), 5.34 (ddd, $J = 10.0, 10.0, 5.6$ Hz, 1H, H4), 5.17 (s, 1H, G1), 5.14 (d, $J = 10.0$ Hz, 1H, D4), 5.06 (s, 1H, OCH_2O), 5.01 (s, 1H, OCH_2O), 4.99 (brs, 1H, F1), 4.75 (s, 1H, D1), 4.38 (ddd, $J = 10.5, 10.5, 6.0$ Hz, 1H, G4), 4.26 (brs, 1H, G2), 4.17 (dd, $J = 11.1, 5.4$ Hz, 1H, H5), 4.09 (d, $J = 7.5$ Hz, 1H, E1), 4.07–4.02 (m, 1H, G5), 4.05 (s, 2H, CH_2Cl), 3.99 (dd, $J = 10.1, 2.3$ Hz, 1H, G3), 3.94 (t, $J = 9.4$ Hz, 1H, H3), 3.93 (t, $J = 9.8$ Hz, 1H, G5), 3.85–3.83 (m, 2H, F4, E3), 3.79 (s, 1H, D2), 3.67 (dd, $J = 9.2, 7.8$ Hz, 1H, E2), 3.59 (s, 3H, OMe), 3.53–3.40 (m, 9H, D5, E4, E5, F3, F5, F6, F6, H2, H5), 3.43 (s, 3H, OMe), 3.38 (d, $J = 3.0$ Hz, 1H, F2), 3.31 (s, 3H, OMe), 2.23 (s, 3H, Me (A_2)), 1.41 (s, 3H, Me (D3)), 1.26 (d, $J = 6.4$ Hz, 3H, D6), 1.19 (d, $J = 6.8$ Hz, 3H, E6), 0.97 (s, 9H, *t*BuSi), 0.96 (s, 9H, *t*BuSi), 0.90 (s, 18H, *t*BuSi), 0.89 (s, 9H, *t*BuSi), 0.84 (s, 9H, *t*BuSi), 0.21 (s, 6H, MeSi), 0.18 (s, 6H, MeSi), 0.16 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.09 (s, 6H, MeSi), 0.08 (s, 3H, MeSi), 0.07 (s, 6H, MeSi), 0.06 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 167.1, 166.2, 157.3, 153.9, 138.0, 135.8, 128.3, 127.7, 125.5, 119.1, 119.0, 114.9, 108.5, 103.3, 100.9, 97.3, 96.5, 84.4, 82.3, 80.9, 77.8, 77.5, 75.6, 75.3, 75.1, 70.9, 70.6, 70.5, 70.4, 69.5, 68.9, 65.8, 63.4, 63.1, 62.0, 58.5, 40.8, 34.2, 30.3, 29.7, 19.9, 19.8, 18.7, 18.6, 18.1, 18.0, 17.9, 16.3, 15.3, −2.2, −2.8, −3.8, −4.2, −4.3, −4.4, −4.5, −4.6, −4.9, −4.9, −5.0$; HRMS (MALDI): calcd for $C_{79}H_{145}ClO_{26}Si_6Na$ $[M+Na]^+$: 1735.8225, found 1735.8271.

DEFGHA$_2$ hexa-TBS diol 40: K_2CO_3 (0.6 mg, 0.004 mmol) was added to a solution of DEFGHA$_2$ hexa-TBS chloroacetate **39** (35 mg, 0.02 mmol) in THF/MeOH (2:1, 0.3 mL) and the resulting mixture was stirred at 25 °C for 15 min. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-TBS diol **40** (28 mg, 85%) as a white foam. **40**: $R_f = 0.27$ (40% Et_2O in hexanes); $[\alpha]_D^{22} = -29.1$ ($c = 0.10$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3495, 2955, 2919, 2861, 1737, 1602, 1467, 1361, 1255, 1073, 838, 779\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 6.29$ (d, $J = 1.7$ Hz, 1H, ArH (A_2)), 6.16 (d, $J = 1.8$ Hz, 1H, ArH (A_2)), 5.33 (ddd, $J = 10.1, 10.1, 5.6$ Hz, 1H, H4), 5.18 (s, 1H, OCH_2O), 5.06 (s, 1H, OCH_2O), 5.05 (brs, 1H, F1), 5.01 (s, 1H, G1), 4.68 (s, 1H, D1), 4.39 (ddd, $J = 10.3, 10.3, 2.5$ Hz, 1H, G4), 4.24 (brs, 1H, G2), 4.17 (dd, $J = 11.1, 5.4$ Hz, 1H, H5), 4.12 (brs, 1H, F3), 4.08 (d, $J = 7.4$ Hz, 1H, E1), 4.05 (dd, $J = 9.4, 4.8$ Hz, 1H, G5), 4.00 (dd, $J = 10.1, 2.2$ Hz, 1H, G3), 3.96 (t, $J = 9.4$ Hz, 1H, G5), 3.95 (t, $J = 9.4$ Hz, 1H, H3), 3.89 (t, $J = 8.3$ Hz, 1H, F4), 3.77 (s, 1H, D2), 3.64 (dd, $J = 8.0, 8.0$ Hz, 1H, E2), 3.59 (t, $J = 10.0$ Hz, 1H, H5), 3.58 (d, $J = 9.5$ Hz, 1H, H2), 3.53 (s, 3H, OMe), 3.52–3.51 (m, 1H, D5 or E5), 3.49–3.37 (m, 7H, D4, E3, E4, F2, F5, F6. F6), 3.40 (s, 3H, OMe), 3.33–3.29 (m, 1H, D5 or E5), 3.30 (s, 3H, OMe), 2.44 (s, 1H, OH), 2.24 (s, 3H, Me (A_2)), 1.93 (brs, 1H, OH), 1.29 (d, $J = 5.9$ Hz, 3H, D6 or E6), 1.27 (d, $J = 6.5$ Hz, 3H, D6 or E6), 1.16 (s, 3H, Me (D3)), 0.96 (s, 9H, *t*BuSi), 0.95 (s, 9H, *t*BuSi), 0.92 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.89 (s, 9H, *t*BuSi), 0.28 (s, 3H, MeSi), 0.21 (s, 3H, MeSi), 0.18 (s, 3H, MeSi), 0.18 (s, 3H, MeSi), 0.14 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.10 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.07 (s, 3H, MeSi), 0.07 (s, 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 167.4, 157.3, 153.9, 137.9, 119.0, 118.9, 114.9, 108.4, 103.5, 101.6, 97.2, 96.4, 84.8, 82.4, 81.1, 77.3, 76.7, 76.4, 75.1, 73.9, 72.7, 71.3, 70.6, 70.5, 70.0, 69.5, 65.8, 63.3, 63.0, 62.4, 58.4, 29.3, 28.0, 25.8, 25.6, 19.8, 18.4, 18.2, 18.1, 18.0, 17.1, 16.3, 15.3, −3.4, −3.7, −3.9, −4.2, −4.3, −4.4, −4.6, −4.9, −4.9, −5.0, −5.2$; HRMS (FAB): calcd for $C_{77}H_{144}O_{25}Si_6Na$ $[M+Na]^+$: 1659.8509, found 1659.8452.

DEFGHA$_2$ hexa-benzyl PMB ether 41: NaH (4.0 mg, 0.09 mmol) was added to a solution of DEFGHA$_2$ triol **34** (40 mg, 0.03 mmol) in DMF (0.5 mL) at 0 °C and the resulting mixture was stirred for 5 min. BnBr (7.4 μL, 0.075 mmol) and nBu_4NI (2.0 mg, 0.006 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (3 mL), diluted with Et_2O (150 mL), and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-benzyl PMB ether **41** (43 mg, 95%) as a white foam. **41**: $R_f = 0.69$ (100% Et_2O); $[\alpha]_D^{22} = -37.5$ ($c = 0.12$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3526, 3026, 2928, 2884, 1732, 1605, 1517, 1451, 1369, 1253, 1094, 912, 736\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.51-7.20$ (m, 32H, ArH, PMB), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 6.42 (s, 2H, ArH (A_2)), 5.42 (ddd, $J = 9.8, 9.8, 5.5$ Hz, 1H, H4), 5.29 (s, 1H, G1), 5.15 (s, 1H, OCH_2O), 5.12, 4.57 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 5.02 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.98 (s, 1H, OCH_2O), 4.86, 4.62 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.84, 4.47 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.83, 4.62 (AB, $J = 11.1$ Hz, 2H, CH_2Ar), 4.81, 4.74 (AB, $J = 12.1$ Hz, 2H,

CH_2Ar), 4.80 (s, 1H, D1), 4.74 (s, 1H, F1), 4.52 (ddd, $J=10.4$, 10.4, 6.1 Hz, 1H, G4), 4.44 (d, $J=8.3$ Hz, 1H, E1), 4.24 (s, 1H, G2), 4.13 (dd, $J=10.9$, 4.6 Hz, 1H, H5), 4.11 (dd, $J=11.4$, 5.6 Hz, 1H, G5), 4.05 (dd, $J=11.0$, 2.5 Hz, 1H, G3), 4.04 (t, $J=8.3$ Hz, 1H, F4), 3.92 (t, $J=9.7$ Hz, 1H, H3), 3.85 (t, $J=10.0$ Hz, 1H, G5), 3.79 (s, 3H, OMe), 3.68–3.41 (m, 12H, D2, D4, E2, E3, E4, E5, F3, F5, F6, F6, H2, H5), 3.59 (s, 3H, OMe), 3.53 (s, 3H, OMe), 3.37 (d, $J=2.9$ Hz, 1H, F2), 3.24 (dq, $J=9.5$, 7.0 Hz, 1H, D5), 3.18 (s, 3H, OMe), 3.00 (br s, 1H, OH), 2.32 (s, 3H, Me (A_2)), 1.28 (d, $J=5.8$ Hz, 3H, E6), 1.27 (s, 3H, Me (D3)), 1.22 (d, $J=6.3$ Hz, 3H, D6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=166.9$, 160.7, 159.2, 157.4, 139.0, 138.7, 138.5, 138.2, 137.7, 137.7, 136.4, 136.4, 130.8, 129.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4, 127.4, 127.3, 127.1, 119.1, 116.0, 113.7, 108.2, 103.2, 102.1, 98.3, 95.9, 95.4, 84.0, 83.4, 82.8, 81.9, 79.4, 79.2, 77.5, 77.3, 75.7, 75.5, 75.4, 75.2, 75.1, 74.8, 74.0, 73.1, 72.5, 71.1, 70.8, 70.4, 70.3, 70.3, 70.1, 69.8, 63.2, 61.8, 61.2, 58.9, 55.2, 31.5, 20.0, 18.5, 18.2, 16.3, 14.1; HRMS (MALDI): calcd for $C_{91}H_{104}O_{26}Na$ $[M+Na]^+$: 1635.6713, found 1635.6692.

DEFGHA$_2$ hexa-benzyl diol 42: DDQ (4.0 mg, 0.033 mmol) was added to a solution of DEFGHA$_2$ hexa-benzyl PMB ether **41** (35 mg, 0.022 mmol) in CH_2Cl_2/H_2O (10:1, 0.5 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80% EtOAc in hexanes) to afford DEFGHA$_2$ hexa-benzyl diol **42** (31 mg, 95%) as a as a white foam. **42**: $R_f=0.38$ (75% EtOAc in hexanes); $[\alpha]_D^{22}=-24.8$ ($c=1.82$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3565$, 2891, 1732, 1456, 1070, 734, 698 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.46-7.11$ (m, 30H, ArH), 6.42 (s, 2H, ArH (A_2)), 5.44 (ddd, $J=9.7$, 9.7, 5.5 Hz, 1H, H4), 5.31 (s, 1H, G1), 5.15 (s, 1H, OCH_2O), 5.12, 4.52 (AB, $J=11.7$ Hz, 2H, CH_2Ar), 5.02 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.99 (s, 1H, OCH_2O), 4.87, 4.61 (AB, $J=11.4$ Hz, 2H, CH_2Ar), 4.85 (s, 1H, D1), 4.83, 4.76 (AB, $J=12.2$ Hz, 2H, CH_2Ar), 4.79, 4.61 (AB, $J=11.8$ Hz, 2H, CH_2Ar), 4.75 (s, 1H, F1), 4.55 (ddd, $J=10.4$, 10.4, 6.1 Hz, 1H, G4), 4.47 (d, $J=7.6$ Hz, 1H, E1), 4.25 (s, 1H, G2), 4.14 (dd, $J=9.6$, 4.6 Hz, 1H, H5), 4.12 (dd, $J=10.8$, 8.0 Hz, 1H, G5), 4.07–4.04 (m, 2H, F4, G3), 3.93 (t, $J=9.7$ Hz, 1H, H3), 3.86 (t, $J=10.1$ Hz, 1H, G5), 3.68–3.43 (m, 11H, D2, E2, E3, E4, E5, F3, F5, F6, F6, H2, H5), 3.58 (s, 3H, OMe), 3.54 (s, 3H, OMe), 3.38 (d, $J=2.4$ Hz, 1H, F2), 3.36 (d, $J=9.6$ Hz, 1H, D4), 3.33 (s, 1H, OH), 3.28 (dq, $J=9.6$, 5.8 Hz, 1H, D5), 3.20 (s, 3H, OMe), 2.89 (s, 1H, OH), 2.32 (s, 3H, Me (A_2)), 1.30 (d, $J=5.8$ Hz, 3H, D6), 1.24 (d, $J=7.2$ Hz, 3H, E6), 1.22 (s, 3H, Me (D3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=166.8$, 160.6, 157.3, 138.9, 138.7, 138.5, 138.0, 137.6, 136.3, 136.3, 128.5, 128.4, 128.4, 128.4, 128.2, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.0, 127.0, 119.0, 115.8, 108.0, 103.1, 102.0, 98.2, 96.6, 95.8, 95.3, 82.6, 81.7, 81.0, 79.7, 79.1, 77.8, 77.4, 76.5, 75.6, 75.3, 75.2, 75.0, 74.9, 73.0, 72.9, 72.4, 71.0, 70.5, 70.3, 70.2, 70.0, 69.7, 65.7, 63.4, 63.2, 61.8, 61.2, 58.8, 19.9, 18.1, 17.0, 16.3, 15.2; HRMS (MALDI): calcd for $C_{83}H_{96}O_{25}Cs$ $[M+Cs]^+$: 1625.5295, found 1625.5366.

DEFGHA$_2$ hexa-benzyl TBS ether 43: TBSOTf (12.0 μL, 0.05 mmol) was added to a solution of DEFGHA$_2$ hexa-benzyl diol **42** (52 mg, 0.034 mmol) and 2,6-lutidine (12.0 μL, 0.10 mmol) in CH_2Cl_2 (0.5 mL) at −10 °C and the resulting mixture was warmed to 0 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-benzyl TBS ether **43** (53 mg, 96%) as a white foam. **43**: $R_f=0.24$ (70% Et_2O in hexanes); $[\alpha]_D^{22}=-13.0$ ($c=0.10$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3550$, 2931, 1735, 1602, 1259, 1075, 912, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.53-7.31$ (m, 30H, ArH), 6.51 (s, 2H, ArH (A_2)), 5.51 (ddd, $J=9.7$, 9.7, 4.2 Hz, 1H, H4), 5.38 (d, $J=1.1$ Hz, 1H, G1), 5.23 (s, 1H, OCH_2O), 5.17, 4.67 (AB, $J=11.8$ Hz, 2H, CH_2Ar), 5.10 (s, 2H, CH_2Ar), 5.08 (s, 2H, CH_2Ar), 5.07 (s, 1H, OCH_2O), 4.94, 4.87 (AB, $J=11.2$ Hz, 2H, CH_2Ar), 4.91, 4.67 (AB, $J=10.9$ Hz, 2H, CH_2Ar), 4.89 (s, 1H, D1), 4.85, 4.69 (AB, $J=11.5$ Hz, 2H, CH_2Ar), 4.81 (s, 1H, F1), 4.61 (ddd, $J=10.6$, 10.6, 4.0 Hz, 1H, G4), 4.54 (d, $J=7.6$ Hz, 1H, E1), 4.33 (br s, 1H, G2), 4.23 (dd, $J=10.0$, 4.0 Hz, 1H, G5), 4.21 (dd, $J=10.0$, 5.6 Hz, 1H, H5), 4.14 (dd, $J=10.0$, 2.6 Hz, 1H, G3), 4.13 (t, $J=7.8$ Hz, 1H, F4), 4.01 (t, $J=9.8$ Hz, 1H, H3), 3.95 (t, $J=9.8$ Hz, 1H, G5), 3.75 (br s, 1H, D2), 3.75–3.57 (m, 10H, E2, E3, E4, E5, F3, F5, F6, F6, H2, H5), 3.67 (s, 3H, OMe), 3.62 (s, 3H, OMe), 3.46 (d, $J=2.8$ Hz, 1H, F2), 3.40 (d, $J=9.3$ Hz, 1H, D4), 3.28 (s, 3H, OMe), 3.27 (dq, $J=9.3$, 6.1 Hz, 1H, D5), 2.87 (br s, 1H, OH), 2.40 (s, 3H, Me (A_2)), 1.35 (s, 3H, Me (D3)), 1.33 (d, $J=5.8$ Hz, 3H, D6), 1.30 (d, $J=7.2$ Hz, 3H, E6), 0.95 (s, 9H, *t*BuSi), 0.19 (s, 3H, MeSi), 0.13 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=166.8$, 160.7, 157.3, 138.9, 138.1, 137.6, 136.4, 136.3, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.0, 119.1, 115.9, 108.1, 103.2, 102.1, 98.2, 96.7, 95.3, 95.2, 83.0, 82.6, 81.8, 81.0, 79.8, 78.0, 77.9, 77.4, 75.6, 75.4, 75.3, 75.2, 75.1, 75.0, 73.1, 73.0, 72.5, 71.8, 71.0, 70.3, 70.2, 70.0, 69.8, 67.9, 63.4, 63.2, 61.8, 61.2, 58.8, 53.4, 30.3, 29.5, 26.0, 20.0, 18.7, 18.3, 17.6, 16.3, 15.2, −3.8, −4.8; HRMS (FAB): calcd for $C_{89}H_{110}O_{25}SiCs$ $[M+Cs]^+$: 1739.6160, found 1739.6267.

DEFGHA$_2$ heptaol 44: 10% Pd/C (20 mg) was added to a solution of DEFGHA$_2$ hexa-benzyl TBS ether **43** (50 mg, 0.03 mmol) in EtOAc (1.0 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 6 h. The reaction mixture was diluted with EtOAc (50 mL) and filtered through a short pad of Celite and the solvents were removed under reduced pressure to afford crude DEFGHA$_2$ heptaol **44** as a white foam; HRMS (FAB): calcd for $C_{47}H_{74}O_{25}SiCs$ $[M+Cs]^+$: 1199.3393, found 1199.3396.

DEFGHA$_2$ hexa-acetyl TBS ether 45: Ac_2O (31.0 μL, 0.30 mmol) was added to a solution of the above crude DEFGHA$_2$ heptaol **44** (45 mg), Et_3N (84.0 μL, 0.60 mmol) and 4-DMAP (1.0 mg, 0.006 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford DEFGHA$_2$ hexa-acetyl TBS ether **45** (36 mg, 88% over two steps) as a white foam. **45**: $R_f=0.33$ (100% EtOAc); $[\alpha]_D^{22}=-26.0$ ($c=0.05$, $CHCl_3$); IR (thin film): $\tilde{\nu}=2955$, 2885, 1749, 1362, 1226, 1132, 1049 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=6.88$ (d, $J=1.8$ Hz, 1H, ArH (A_2)), 6.81 (d, $J=1.8$ Hz, 1H, ArH (A_2)), 5.50 (br s, 1H, G2), 5.34 (ddd, $J=9.5$, 9.5, 5.6 Hz, 1H, H4), 5.22 (s, 1H, G1), 5.17 (s, 1H, OCH_2O), 5.08 (s, 1H, OCH_2O), 5.06 (dd, $J=10.2$, 8.0 Hz, 1H, E2), 4.93 (dd, $J=8.9$, 3.3 Hz, 1H, F3), 4.91 (s, 1H, D2), 4.75 (s, 1H, D1), 4.69 (s, 1H, F1), 4.34 (d, $J=7.9$ Hz, 1H, E1), 4.29 (ddd, $J=10.6$, 10.6, 4.5 Hz, 1H, G4), 4.17 (dd, $J=11.4$, 5.5 Hz, 1H, H5), 4.14 (dd, $J=9.6$, 4.3 Hz, 1H, G5), 4.03 (dd, $J=10.2$, 2.7 Hz, 1H, G3), 3.95 (t, $J=8.7$ Hz, 1H, F4), 3.93 (t, $J=9.7$ Hz, 1H, H3), 3.85 (t, $J=10.3$ Hz, 1H, G5), 3.65–3.33 (m, 10H, D4, E3, E4, E5, F2, F5, F6, F6, H2, H5), 3.61 (s, 3H, OMe), 3.48 (s, 3H, OMe), 3.36 (s, 3H, OMe), 3.30 (dq, $J=9.0$, 6.1 Hz, 1H, D5), 2.40 (s, 3H, Me (A_2)), 2.27 (s, 3H, OAc), 2.25 (s, 3H, OAc), 2.09 (s, 9H, OAc), 2.04 (s, 3H, OAc), 1.42 (s, 3H, Me (D3)), 1.27 (d, $J=6.0$ Hz, 3H, D6), 1.26 (d, $J=6.2$ Hz, 3H, E6), 0.89 (s, 9H, *t*BuSi), 0.10 (s, 3H, MeSi), 0.07 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=170.7$, 170.0, 169.2, 168.7, 168.7, 168.5, 164.8, 152.0, 149.3, 139.8, 125.5, 122.6, 119.0, 114.2, 101.0, 98.8, 96.8, 95.1, 94.7, 81.2, 80.7, 78.5, 76.6, 75.6, 75.5, 75.1, 74.8, 73.0, 72.8, 72.0, 71.0, 70.7, 70.5, 69.8, 69.6, 63.2, 63.2, 61.3, 61.3, 59.3, 30.3, 26.0, 21.0, 21.0, 20.8, 20.8, 20.6, 20.0, 19.4, 18.8, 18.3, 16.4, −3.9, −4.5; HRMS (FAB): calcd for $C_{59}H_{86}O_{31}SiCs$ $[M+Cs]^+$: 1451.3977, found 1451.3911.

DEFGHA$_2$ hexa-acetyl diol 46: nBu$_4$NF (31.0 μL, 0.03 mmol) was added to a solution of DEFGHA$_2$ hexa-acetyl TBS ether **45** (22 mg, 0.02 mmol) and AcOH (1.0 μL, 0.03 mmol) in THF (0.3 mL) and the resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 10% MeOH in EtOAc) to afford DEFGHA$_2$ hexa-acetyl diol **46** (18 mg, 90%) as a white foam. **46**: $R_f=0.11$ (100% EtOAc); $[\alpha]_D^{22}=-10.0$ ($c=0.04$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3390$, 2926, 1749, 1650, 1446, 1385, 1319, 1259, 1072 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=6.56$ (d, $J=1.7$ Hz, 1H, ArH (A_2)), 6.41 (d, $J=1.7$ Hz, 1H, ArH (A_2)), 5.50 (br s, 1H, G2), 5.30 (ddd, $J=9.5$, 9.5, 5.6 Hz, 1H, H4), 5.22 (s, 1H, G1), 5.16 (s, 1H, OCH_2O), 5.08 (s, 1H, OCH_2O), 5.06 (dd, $J=10.0$, 8.1 Hz, 1H, E2), 4.92 (dd, $J=8.9$, 3.2 Hz, 1H, F3), 4.92 (s, 1H, D2), 4.75 (s, 1H, D1), 4.71 (s, 1H, F1), 4.34 (d, $J=8.0$ Hz, 1H, E1), 4.28 (ddd, $J=10.6$, 10.6, 4.5 Hz, 1H, G4), 4.16 (dd, $J=11.4$, 5.5 Hz, 1H, H5), 4.14 (dd, $J=9.6$, 3.7 Hz, 1H, G5), 4.01 (dd, $J=10.1$, 2.5 Hz, 1H, G3), 3.95 (t, $J=8.7$ Hz, 1H, F4), 3.93 (t, $J=9.7$ Hz, 1H, H3), 3.85 (t, $J=10.1$ Hz, 1H, G5), 3.65–3.37 (m, 11H, D4, D5, E3, E4, E5, F2, F5, F6, F6, H2, H5), 3.54

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(s, 3H, OMe), 3.48 (s, 3H, OMe), 3.36 (s, 3H, OMe), 2.71 (s, 1H, OH), 2.36 (s, 3H, Me (A_2)), 2.25 (s, 3H, OAc), 2.09 (s, 6H, OAc), 2.08 (s, 3H, OAc), 2.04 (s, 6H, OAc), 1.42 (s, 3H, Me (D3)), 1.33 (d, J = 5.9 Hz, 3H, D6), 1.26 (d, J = 6.4 Hz, 3H, E6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.9, 170.1, 169.4, 168.9, 165.2, 159.2, 154.4, 150.8, 141.2, 119.1, 115.9, 108.2, 101.0, 98.8, 96.8, 95.1, 94.8, 81.4, 80.7, 75.5, 75.2, 75.1, 74.8, 73.0, 72.7, 71.1, 70.8, 70.5, 70.4, 69.6, 65.8, 63.4, 63.1, 61.4, 61.3, 59.3, 30.3, 21.2, 21.0, 20.9, 20.8, 20.7, 20.6, 20.4, 18.7, 18.2, 16.4, 15.2, 13.7; HRMS (MALDI): calcd for $C_{53}H_{72}O_{31}SiNa$ $[M+Na]^+$: 1227.3955, found 1227.3943.

DEFGHA$_2$ hexa-benzyl chloroacetate 47: Chloroacetic anhydride (CA_2O) (4.0 mg, 0.022 mmol) was added to a solution of DEFGHA$_2$ hexa-benzyl diol **42** (22 mg, 0.015 mmol), Et_3N (4.4 μL, 0.044 mmol) and 4-DMAP (0.4 mg, 0.003 mmol) in CH_2Cl_2 (0.3 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-benzyl chloroacetate **47** (23 mg, 98%) as a white foam. **47**: R_f = 0.16 (70% Et_2O in hexanes); $[\alpha]_D^{22} = -30.0$ (c = 0.11, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2924, 2861, 1731, 1655, 1449, 1361, 1261, 1155, 1072, 1038, 744, 697 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.48–7.27 (m, 30H, ArH), 6.43 (s, 2H, ArH (A_2)), 5.44 (ddd, J = 9.7, 9.7, 5.6 Hz, 1H, H4), 5.33 (s, 1H, G1), 5.17 (s, 1H, OCH_2O), 5.12, 4.61 (AB, J = 11.6 Hz, 2H, CH_2Ar), 5.03 (s, 2H, CH_2Ar), 5.01 (s, 2H, CH_2Ar), 5.00 (s, 1H, OCH_2O), 4.92 (d, J = 9.8 Hz, 1H, D4), 4.91, 4.61 (AB, J = 11.4 Hz, 2H, CH_2Ar), 4.87 (s, 1H, D1), 4.84, 4.77 (AB, J = 12.0 Hz, 2H, CH_2Ar), 4.80, 4.62 (AB, J = 11.8 Hz, 2H, CH_2Ar), 4.77 (s, 1H, F1), 4.54 (ddd, J = 9.7, 9.7, 4.9 Hz, 1H, G4), 4.49 (d, J = 7.6 Hz, 1H, E1), 4.26 (brs, 1H, G2), 4.16 (dd, J = 9.6, 4.6 Hz, 1H, G5), 4.14 (dd, J = 11.5, 5.6 Hz, 1H, H5), 4.08 (dd, J = 9.7, 2.0 Hz, 1H, G3), 4.07 (s, 2H, CH_2Cl), 3.95 (t, J = 9.7 Hz, 1H, H3), 3.88 (t, J = 10.1 Hz, 1H, G5), 3.71–3.47 (m, 11H, D2, E2, E3, E4, F3, F4, F5, F6, F6, H2, H5), 3.60 (s, 3H, OMe), 3.56 (s, 3H, OMe), 3.46–3.41 (m, 2H, D5, E5), 3.38 (d, J = 2.9 Hz, 1H, F2), 3.32 (s, 1H, OH), 3.22 (s, 3H, OMe), 2.33 (s, 3H, Me (A_2)), 1.29 (s, 3H, Me (D3)), 1.25 (d, J = 6.3 Hz, 3H, D6), 1.21 (d, J = 6.1 Hz, 3H, E6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.8, 160.6, 157.2, 138.8, 138.6, 138.4, 137.7, 137.6, 136.3, 136.3, 128.5, 128.4, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 127.0, 125.4, 119.0, 115.8, 108.1, 103.1, 101.9, 98.2, 96.6, 95.7, 95.2, 82.5, 82.5, 81.7, 79.7, 79.1, 78.3, 77.8, 77.4, 75.5, 75.3, 75.3, 75.1, 75.0, 74.9, 73.0, 72.4, 72.0, 71.0, 70.2, 70.1, 69.9, 69.7, 68.9, 63.4, 63.1, 61.8, 58.8, 40.7, 30.2, 29.6, 19.9, 17.7, 17.5, 16.2; HRMS (FAB): calcd for $C_{85}H_{97}ClO_{26}Cs$ $[M+Cs]^+$: 1701.5011, found 1701.5107.

DEFGHA$_2$ hexa-TBS chloroacetate 39 from 47: 10% Pd/C (20 mg) was added to a solution of DEFGHA$_2$ hexa-benzyl chloroacetate **47** (70 mg, 0.045 mmol) in EtOAc (3.0 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 4 h. The reaction mixture was filtered through a pad of Celite, the pad was washed with EtOAc (150 mL), and the solvents were removed under reduced pressure to afford the crude CA-DEFGHA$_2$ heptaol **48** as a white foam. The crude heptaol was then dissolved in CH_2Cl_2 (1.0 mL), 2,6-di-*tert*-butylpyridine (0.20 mL, 0.89 mmol) was added and the reaction mixture was cooled to 0 °C. TBSOTf (820 μL, 0.36 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 8 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-TBS chloroacetate **39** (50 mg, 65% over two steps) as a white foam, identical to that above.

Fully benzylated everninomicin 49: NaH (18.4 mg, 0.46 mmol) was added to a solution of everninomicin 13,384-1 (**1**)[12] (50 mg, 0.031 mmol) in DMF (0.5 mL) at 0 °C and the resulting mixture was stirred for 5 min. BnBr (72.9 μL, 0.61 mmol) and nBu$_4$NI (1.1 mg, 0.003 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (3 mL), diluted with Et_2O (150 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford fully benzylated everninomicin **49** (73 mg, 93%) as a white foam. **49**: R_f = 0.37 (50% EtOAc in hexanes); $[\alpha]_D^{22} = -22.0$ (c = 3.89, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2935, 1736, 1603, 1542, 1454, 1370, 1330, 1253, 1102 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58–7.06 (m, 40H, ArH), 6.42 (s, 2H, ArH (A_2)), 5.43 (ddd, J = 9.7, 9.7, 5.5 Hz, 1H, H4), 5.31 (s, 1H, OCH_2O), 5.15 (s, 1H, OCH_2O), 5.07–4.97 (m, 8H, 3 × CH_2Ar, D1, G1), 4.92 (t, J = 9.3 Hz, 1H, B4), 4.86–4.59 (m, 13H, 4.5 × CH_2Ar, A1, B1, D2, F1), 4.53 (ddd, J = 10.4, 10.4, 4.5 Hz, 1H, G4), 4.45 (brd, J = 7.6 Hz, 1H, E1), 4.33 (d, J = 11.6 Hz, 1H, CH_2Ar), 4.25 (brs, 1H, G2), 4.15–4.07 (m, 2H, G5, H5), 4.06–4.03 (m, 3H, F4, G3, G5), 3.95 (d, J = 10.0 Hz, 1H, H2), 3.93 (t, J = 9.9 Hz, 1H, H3), 3.90–3.83 (m, 4H, B3, C3, C4, C5 or D5 or E5), 3.83 (s, 3H, OMe), 3.71–3.49 (m, 12H, A4, A5, D4, E2, E3, E4, F3, F5, F6, F6, H5, C5 or D5 or E5), 3.64 (s, 3H, OMe), 3.53 (s, 3H, OMe), 3.47–3.36 (m, 3H, B5, F2, C5 or D5 or E5), 3.37 (s, 3H, OMe), 3.19 (s, 3H, OMe), 2.49–2.43 (m, 2H, A2, C2), 2.40 (s, 3H, Me (A_1)), 2.35–2.29 (m, 4H, B2, Me), 2.05–2.02 (m, 1H, A2), 1.82 (t, J = 12.0 Hz, 1H, C2), 1.72 (dt, J = 12.1, 12.1 Hz, 1H, B2), 1.71 (s, 3H, Me (A_2)), 1.36 (d, J = 6.1 Hz, 3H, B6), 1.34 (s, 3H, Me (D3)), 1.31 (d, J = 6.0 Hz, 6H, C6 or D6 or E6), 1.24 (d, J = 5.2 Hz, 3H, C6 or D6 or E6), 1.02 (s, 3H, Me (A3)), 0.84 (d, J = 6.2 Hz, 3H, A6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 166.7, 165.5, 160.6, 157.2, 153.2, 153.0, 138.8, 138.6, 138.4, 137.5, 136.3, 136.2, 135.7, 134.7, 128.0, 127.8, 127.6, 127.4, 127.4, 127.3, 127.2, 127.1, 127.0, 126.2, 125.9, 121.6, 119.8, 119.0, 115.8, 108.0, 103.1, 101.4, 99.8, 98.1, 95.8, 95.6, 95.2, 92.3, 89.8, 84.1, 82.6, 82.5, 81.5, 81.0, 80.8, 79.9, 79.6, 79.2, 77.6, 76.5, 76.0, 75.5, 75.2, 75.0, 74.9, 73.8, 73.0, 72.3, 71.3, 71.0, 70.4, 70.2, 70.2, 69.9, 69.7, 68.1, 66.1, 63.4, 63.1, 61.8, 61.7, 61.0, 60.6, 60.2, 58.7, 40.0, 38.3, 36.4, 20.9, 20.0, 19.2, 18.6, 18.2, 18.1, 17.9, 17.5, 16.2, 14.1; HRMS (FAB): calcd for $C_{126}H_{145}Cl_2NO_{38}Cs$ $[M+Cs]^+$: 2485, found 2485.

A$_1$B(A)C lactone (benzylated) 51: A solution of 5% aqueous HCl (20.0 μL) was added to a solution of the fully benzylated everninomicin **49** (63 mg, 0.027 mmol) in THF (3.0 mL) and the reaction mixture was stirred at 25 °C until TLC analysis showed that no starting material remained, and a more polar spot appeared by TLC. A solution of 1N aqueous KOH (0.1–0.5 mL) was then added while stirring rapidly, until TLC indicated the formation of two new spots, one above and one below the spot from the acidic reaction. The reaction mixture was then quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL), diluted with CH_2Cl_2 (150 mL), and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford the A$_1$B(A)C lactone **51** (20 mg, 85%) and hexa-benzyl DEFGHA$_2$ diol **42** (36 mg, 90%) both as white foams. **51**: R_f = 0.53 (75% EtOAc in hexanes); $[\alpha]_D^{22} = -43.4$ (c = 0.59, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 2978, 2931, 1872, 1760, 1725, 1537, 1449, 1384, 1249, 1090, 903, 732 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.0 Hz, 2H, ArH), 7.43–7.31 (m, 8H, ArH), 5.07, 5.03 (AB, J = 10.1 Hz, 2H, CH_2Ar), 4.98 (dd, J = 4.7, 1.7 Hz, 1H, A1), 4.90 (t, J = 9.4 Hz, 1H, B4), 4.64, 4.57 (AB, J = 11.8 Hz, 2H, CH_2Ar), 4.64 (dd, J = 9.5, 1.3 Hz, 1H, B1), 4.23–4.18 (m, 2H, C3, C5), 3.92–3.87 (m, 1H, B3), 3.89 (s, 3H, OMe), 3.70 (brd, J = 6.7 Hz, 1H, C4), 3.64 (d, J = 10.4 Hz, 1H, A4), 3.48 (dq, J = 9.2, 6.2 Hz, 1H, A5), 3.45 (dq, J = 9.3, 6.3 Hz, 1H, B5), 3.36 (s, 3H, OMe), 2.82 (dd, J = 16.1, 2.8 Hz, 1H, C2), 2.77 (dd, J = 16.1, 4.1 Hz, 1H, C2), 2.47 (dd, J = 13.9, 5.0 Hz, 1H, A2), 2.40 (s, 3H, Me (A_1)), 2.32 (dd, J = 11.1, 4.7 Hz, 1H, B2), 2.02 (dd, J = 13.9, 1.9 Hz, 1H, A2), 1.70 (dt, J = 12.2, 12.2 Hz, 1H, B2), 1.69 (s, 3H, Me (A3)), 1.46 (d, J = 6.4 Hz, 3H, C6), 1.37 (d, J = 6.2 Hz, 3H, B6), 0.86 (d, J = 6.2 Hz, 3H, A6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.0, 165.6, 153.3, 153.1, 137.5, 135.8, 134.7, 128.6, 128.5, 128.4, 127.8, 127.5, 127.4, 126.4, 125.9, 121.7, 100.6, 92.5, 89.8, 84.2, 81.6, 76.0, 75.8, 75.6, 74.9, 72.1, 71.1, 66.3, 62.0, 60.8, 53.4, 39.8, 36.3, 33.2, 19.4, 18.9, 18.2, 18.0, 17.7; HRMS (FAB): calcd for $C_{43}H_{53}Cl_2NO_{15}Cs$ $[M+H_2O+Cs]^+$: 1026.1847, found 1026.1857.

DEFGHA$_2$ hexa-benzyl PMB ether 41 from hexa-benzyl DEFGHA$_2$ diol 42: NaH (0.3 mg, 0.08 mmol) was added to a solution of DEFGHA$_2$ diol **42** (10 mg, 0.067 mmol) in DMF (0.5 mL) at 0 °C and the resulting mixture was stirred for 5 min. PMBCl (1.5 μL, 0.010 mmol) and nBu$_4$NI (0.2 mg, 0.006 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (3 mL), diluted with Et_2O (150 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford DEFGHA$_2$ hexa-benzyl PMB ether **41** (10 mg, 93%) as a white foam, which was identical to that described above.

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Fully silylated everninomicin 50: TBSOTf (55.0 μL, 0.24 mmol) was added to a solution of everninomicin 13,384-1 (**1**)[12] (26 mg, 0.016 mmol) and 2,6-lutidine (56.0 μL, 0.48 mmol) in CH_2Cl_2 (0.2 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 50% Et_2O in hexanes) to afford fully silylated everninomicin **50** (26 mg, 64%) as a white foam. **50**: $R_f = 0.46$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -34.3$ ($c = 0.70$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2932, 2861, 1731, 1602, 1549, 1461, 1390, 1355, 1255, 1060, 832, 779, 738\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 6.28$ (d, $J = 2.0$ Hz, 1H, ArH (A_2)), 6.16 (d, $J = 2.0$ Hz, 1H, ArH (A_2)), 5.35 (ddd, $J = 10.0, 10.0, 5.6$ Hz, 1H, H4), 5.17 (s, 1H, OCH_2O), 5.07 (br s, 1H, F1), 5.05 (s, 1H, OCH_2O), 5.00 (s, 1H, G1), 4.97 (dd, $J = 4.6, 1.5$ Hz, 1H, A1), 4.88 (t, $J = 9.4$ Hz, 1H, B4), 4.85 (s, 1H, D1), 4.66 (d, $J = 9.5$ Hz, 1H, B1), 4.38 (ddd, $J = 10.4, 10.4, 4.6$ Hz, 1H, G4), 4.23 (br s, 1H, G2), 4.17 (dd, $J = 11.1, 5.5$ Hz, 1H, H5), 4.10 (s, 1H, D2), 4.06 (d, $J = 7.5$ Hz, 1H, E1), 4.04 (dd, $J = 9.4, 4.4$ Hz, 1H, G5), 4.00 (dd, $J = 10.1, 2.3$ Hz, 1H, G3), 3.96 (t, $J = 10.1$ Hz, 2H, F4, G5), 3.93 (t, $J = 9.7$ Hz, 1H, H3), 3.93–3.80 (m, 3H, B3, C3, F3), 3.86 (s, 6H, OMe), 3.80 (d, $J = 10.0$ Hz, 1H, D4), 3.77 (d, $J = 6.3$ Hz, 1H, E4), 3.69 (dq, $J = 9.8, 6.0$ Hz, 1H, D5), 3.65 (dd, $J = 9.1, 7.5$ Hz, 1H, E2), 3.64 (d, $J = 9.4$ Hz, 1H, A4), 3.58 (d, $J = 9.4$ Hz, 1H, H2), 3.58 (t, $J = 10.0$ Hz, 1H, H5), 3.54–3.41 (m, 8H, A5, B5, C5, E3, E5, F5, F6, F6), 3.39 (s, 3H, OMe), 3.35 (s, 3H, OMe), 3.31 (t, $J = 4.2$ Hz, 1H, F2), 3.29 (s, 3H, OMe), 3.26 (dd, $J = 9.4, 8.2$ Hz, 1H, C4), 2.46 (dd, $J = 13.6, 4.7$ Hz, 1H, A2), 2.37 (s, 3H, Me (A_1)), 2.29 (dd, $J = 11.9, 4.2$ Hz, 1H, B2), 2.24 (s, 3H, Me (A_2)), 2.24–2.21 (m, 1H, C2), 2.04 (dd, $J = 13.6, 1.7$ Hz, 1H, A2), 1.92 (dd, $J = 13.0, 1.1$ Hz, 1H, C2), 1.64 (dt, $J = 12.4, 12.4$ Hz, 1H, B2), 1.43 (s, 3H, Me (D3)), 1.40 (d, $J = 6.2$ Hz, 3H, B6), 1.38 (s, 3H, Me (A3)), 1.26–1.24 (m, 9H, C6, D6, E6), 1.05 (s, 9H, *t*BuSi), 0.96 (s, 9H, *t*BuSi), 0.95 (s, 9H, *t*BuSi), 0.93 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.89 (s, 9H, *t*BuSi), 0.88 (s, 9H, *t*BuSi), 0.88 (s, 9H, *t*BuSi), 0.85 (d, $J = 6.2$ Hz, 3H, A6), 0.30 (s, 3H, MeSi), 0.29 (s, 3H, MeSi), 0.21 (s, 3H, MeSi), 0.21 (s, 3H, MeSi), 0.18 (s, 6H, MeSi), 0.14 (s, 3H, MeSi), 0.14 (s, 3H, MeSi), 0.12 (s, 3H, MeSi), 0.11 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.07 (s, 3H, MeSi), 0.07 (s, 3H, MeSi), 0.06 (s, 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 167.0, 165.8, 157.2, 153.8, 153.2, 150.8, 137.8, 134.4, 125.4, 123.5, 122.8, 120.1, 119.0, 118.9, 118.8, 114.9, 108.3, 103.5, 102.3, 98.7, 97.0, 96.3, 92.4\ 89.8, 84.2, 84.1, 82.4, 82.3, 81.5, 81.0, 78.8, 76.0, 75.0, 74.2, 73.3, 72.8, 72.4, 71.5, 71.1, 70.5, 70.3, 69.9, 62.4, 61.7, 60.6, 58.2, 42.2, 40.1, 36.2, 34.5, 31.5, 30.2, 29.6, 26.3, 26.0, 25.9, 25.7, 25.5, 25.2, 22.5, 21.1, 20.6, 19.7, 19.3, 19.2, 18.8, 18.4, 18.3, 18.3, 18.2, 18.2, 18.2, 18.0, 18.0, 17.9, 17.5, 16.2, 15.2, 14.0, −3.1, −3.1, −3.8, −3.9, −4.1, −4.2, −4.2, −4.3, −4.4, −4.5, −4.6, −5.0, −5.1, −5.3$; HRMS (FAB): calcd for $C_{118}H_{209}Cl_2NO_{38}Si_8Na$ $[M+Na]^+$: 2565, found 2533.

A_1B(A)C lactone (silylated) 52: A solution of 5% aqueous HCl (10.0 μL) was added to a solution of the fully silylated everninomicin **50** (30 mg, 0.03 mmol) in THF (1.0 mL) and the reaction mixture was stirred at 25 °C until TLC analysis showed that no starting material remained, and a more polar spot appeared by TLC. A solution of 1N aqueous KOH (0.1–0.5 mL) was then added while stirring rapidly, until TLC indicated the formation of two new spots, one above and one below the spot from the acidic reaction. The reaction mixture was then quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL), diluted with CH_2Cl_2 (100 mL), and washed with brine (10 mL). The organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford A_1B(A)C lactone **52** (9.0 mg, 83%) and hexa-TBS DEFGHA_2 diol **40** (10 mg, 91%) both as white foams. **52**: $R_f = 0.23$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -35.7$ ($c = 0.23$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2935, 2859, 1736, 1544, 1453, 1388, 1252, 1092, 914, 832, 782, 735\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 4.96$ (br d, $J = 4.5$ Hz, 1H, A1), 4.90 (t, $J = 9.7$ Hz, 1H, B4), 4.61 (dd, $J = 9.6, 1.7$ Hz, 1H, B1), 4.37 (dt, $J = 3.5, 3.1$ Hz, 1H, C3), 4.29 (dq, $J = 6.5, 5.2$ Hz, 1H, C5), 3.91–3.85 (m, 1H, B3), 3.85 (s, 3H, OMe), 3.64 (d, $J = 9.2$ Hz, 1H, A4), 3.57–3.55 (m, 1H, C4), 3.52–3.48 (m, 2H, A5, B5), 3.34 (s, 3H, OMe), 2.80 (dd, $J = 16.2, 3.5$ Hz, 1H, C2), 2.54 (dd, $J = 16.2, 2.6$ Hz, 1H, C2), 2.46 (dd, $J = 13.6, 4.8$ Hz, 1H, A2), 2.36 (s, 3H, Me (A_1)), 2.30 (dd, $J = 12.7, 4.9$ Hz, 1H, B2), 2.02 (dd, $J = 13.6, 1.7$ Hz, 1H, A2), 1.70–1.65 (m, 1H, B2), 1.67 (s, 3H, Me (A3)), 1.48 (d, $J = 6.5$ Hz, 3H, C6), 1.41 (d, $J = 6.5$ Hz, 3H, B6), 1.04 (s, 9H, *t*BuSi), 0.87 (s, 9H, *t*BuSi), 0.85 (d, $J = 6.1$ Hz, 3H, A6), 0.29 (s, 3H, MeSi), 0.28 (s, 3H, MeSi), 0.09 (s, 6H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 169.7, 165.9, 153.2, 151.0, 134.5, 125.5, 123.7, 122.7, 118.8, 100.0, 92.5, 89.9, 84.2, 81.1, 77.5, 75.7, 72.1, 71.2, 69.2, 66.2, 61.8, 60.7, 39.9, 36.3, 35.9, 30.3, 25.8, 25.5, 20.2, 19.4, 18.9, 18.2, 17.9, 17.7, 15.2, −3.0, −4.8, −5.0$; HRMS (FAB): calcd for $C_{41}H_{67}Cl_2NO_{14}Si_2Na$ $[M+Na]^+$: 946.3375, found 946.3391.

A_1B(A)CDEFGHA_2 2-phenylselenide 53: A_1B(A)C glycosyl fluoride **29**[1] (56 mg, 0.054 mmol) and DEFGHA_2 hexa-TBS diol **40** (36 mg, 0.022 mmol) were azeotroped with benzene (3 × 3 mL) and then dried under high vacuum for 1 h. Et_2O (0.15 mL) and 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 15 min. $SnCl_2$ (8.3 mg, 0.043 mmol) was added in one portion and the resulting mixture was warmed to 25 °C and stirred for 6 h. The reaction mixture was diluted with EtOAc (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by preparative TLC (silica gel, 50% Et_2O in hexanes) to afford A_1B(A)C-DEFGHA_2 2-phenylselenide **53** (41 mg, 70%) as a white foam. **53**: $R_f = 0.43$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -13.1$ ($c = 0.32$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2930, 2857, 1736, 1599, 1474, 1389, 1253, 1173, 1104, 982, 837, 779, 734\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.60$ (d, $J = 7.6$ Hz, 2H, ArH), 7.57 (d, $J = 7.1$ Hz, 2H, ArH), 7.43–7.20 (m, 11H, ArH), 6.29 (d, $J = 1.9$ Hz, 1H, ArH (A_2)), 6.16 (d, $J = 1.9$ Hz, 1H, ArH (A_2)), 5.35 (ddd, $J = 9.9, 9.9, 5.6$ Hz, 1H, H4), 5.21 (d, $J = 1.4$ Hz, 1H, C1), 5.06 (s, 2H, OCH_2O, G1), 5.05, 5.02 (AB, $J = 10.2$ Hz, 2H, CH_2Ar), 5.01 (s, 2H, F1, OCH_2O), 4.94 (dd, $J = 4.7, 1.5$ Hz, 1H, A1), 4.87 (t, $J = 9.3$ Hz, 1H, B4), 4.79 (br d, $J = 9.5$ Hz, 1H, B1), 4.64, 4.52 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.59 (s, 1H, D1), 4.39 (ddd, $J = 10.4, 10.4, 4.4$ Hz, 1H, G4), 4.24 (br s, 1H, G2), 4.17 (dd, $J = 11.1, 5.5$ Hz, 1H, H5), 4.15 (dd, $J = 8.1, 4.5$ Hz, 1H, C3), 4.11 (br s, 1H, F3), 4.08 (d, $J = 7.5$ Hz, 1H, E1), 4.04 (dd, $J = 9.5, 4.7$ Hz, 1H, G5), 4.02–3.97 (m, 2H, C2, G3), 3.96 (t, $J = 8.1$ Hz, 1H, F4), 3.93 (t, $J = 9.8$ Hz, 1H, H3), 3.90–3.76 (m, 2H, B3, G5), 3.82 (s, 3H, OMe), 3.67 (s, 1H, D2), 3.64 (d, $J = 9.4$ Hz, 1H, A4), 3.61 (t, $J = 8.8$ Hz, 1H, E2), 3.59 (d, $J = 10.4$ Hz, 1H, H2), 3.57 (t, $J = 8.9$ Hz, 1H, H5), 3.53–3.46 (m, 8H, A5, C4, C5, D4, D5, F5, F6, F6), 3.50 (s, 3H, OMe), 3.43 (d, $J = 3.1$ Hz, 1H, F2), 3.40 (s, 3H, OMe), 3.38–3.28 (m, 2H, B5, E3), 3.35 (s, 3H, OMe), 3.30 (s, 3H, OMe), 3.29–3.18 (m, 2H, E4, E5), 2.45 (dd, $J = 13.7, 5.0$ Hz, 1H, A2), 2.38 (s, 3H, Me (A_2)), 2.29 (dd, $J = 12.3, 6.1$ Hz, 1H, B2), 2.26 (s, 3H, Me (A_1)), 2.02 (dd, $J = 13.7, 1.6$ Hz, 1H, A2), 2.02 (dt, $J = 11.9, 11.9$ Hz, 1H, B2), 1.68 (s, 3H, Me (A3)), 1.33 (d, $J = 6.2$ Hz, 3H, B6), 1.31 (d, $J = 6.2$ Hz, 3H, C6), 1.27 (d, $J = 6.4$ Hz, 3H, D6), 1.25 (s, 3H, Me (D3)), 1.22 (d, $J = 5.4$ Hz, 3H, E6), 0.97 (s, 9H, *t*BuSi), 0.96 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.87 (s, 9H, *t*BuSi), 0.86 (s, 9H, *t*BuSi), 0.83 (d, $J = 6.2$ Hz, 3H, A6), 0.25 (s, 3H, MeSi), 0.22 (s, 3H, MeSi), 0.18 (s, 6H, MeSi), 0.11 (s, 3H, MeSi), 0.09 (s, 6H, MeSi), 0.08 (s, 6H, MeSi), 0.08 (s, 3H, MeSi), 0.07 (s, 3H, MeSi), 0.07 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 167.1, 165.6, 157.3, 153.9, 153.3, 153.2, 138.2, 137.9, 135.9, 134.8, 134.4, 129.0, 128.6, 128.5, 128.5, 128.2, 127.6, 127.5, 126.4, 126.0, 121.7, 119.0, 114.9, 108.4, 103.4, 102.3, 101.5, 100.1, 97.2, 96.4, 92.4, 89.9, 89.9, 84.2, 82.3, 81.1, 80.0, 78.0, 77.3, 76.1, 75.1, 74.9, 74.5, 72.7, 72.3, 71.3, 71.1, 71.0, 70.9, 70.6, 70.5, 70.3, 70.0, 69.5, 67.6, 66.2, 65.8, 63.3, 63.0, 62.4, 62.0, 60.8, 58.4, 48.5, 40.1, 36.3, 29.6, 26.1, 26.0, 25.8, 25.6, 25.3, 19.8, 19.3, 18.7, 18.4, 18.2, 18.1, 18.0, 18.0, 17.6, 16.3, −3.5, −3.7, −4.0, −4.2, −4.3, −4.4, −4.6, −4.9, −4.9, −5.0, −5.2$; HRMS (ESI): calcd for $C_{126}H_{199}Cl_2NO_{38}SeSi_6Na$ $[M+Na]^+$: 2670/2684, found 2677/2678 $[M+Na]^+$.

Fully protected everninomicin 54: $NaIO_4$ (31 mg, 0.14 mmol) and $NaHCO_3$ (10 mg, 0.11 mmol) were added to a solution of A_1B(A)CDEFGHA_2 2-phenylselenide **53** (38 mg, 0.014 mmol) in MeOH/CH_2Cl_2/H_2O (3:2:1, 1.0 mL) and the resulting mixture was stirred at 25 °C for 4 h. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The crude selenoxide was dissolved in toluene (1 mL) and transferred by cannula to a sealed tube. The flask was washed with toluene (2 × 0.5 mL) and the organics were transferred to the tube. Diisopropylamine (1 mL) and vinyl acetate (2 mL) were added, and the tube was sealed and heated to 140 °C for 12 h. After cooling, the reaction mixture was concentrated and the residue was purified by preparative TLC (silica gel, 50% Et_2O in hexanes) to afford the fully protected everninomicin **54** (23 mg, 65% over two steps) as a white foam. Fully protected everninomicin **54**: $R_f = 0.32$ (60% Et_2O in hexanes); $[\alpha]_D^{22} = -19.5$ ($c = 0.20$, $CHCl_3$); IR (thin film):

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$\tilde{\nu}$ = 2955, 2919, 2861, 1737, 1602, 1543, 1455, 1384, 1255, 1108, 1067, 1038, 838, 779 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57 (d, J = 7.1 Hz, 2H, ArH), 7.43–7.31 (m, 8H, ArH), 6.29 (d, J = 1.8 Hz, 1H, ArH (A_2)), 6.16 (d, J = 1.8 Hz, 1H, ArH (A_2)), 5.35 (ddd, J = 9.9, 9.9, 5.5 Hz, 1H, H4), 5.18 (s, 1H, OCH_2O), 5.07 (br s, 1H, F1), 5.06 (s, 1H, OCH_2O), 5.05, 5.02 (AB, J = 10.2 Hz, 2H, CH_2Ar), 5.00 (s, 1H, G1), 4.95 (dd, J = 4.6, 1.4 Hz, 1H, A1), 4.88 (t, J = 9.4 Hz, 1H, B4), 4.86 (s, 1H, D1), 4.75 (br d, J = 9.8 Hz, 1H, B1), 4.68, 4.57 (AB, J = 11.0 Hz, 2H, CH_2Ar), 4.39 (ddd, J = 10.5, 10.5, 4.8 Hz, 1H, G4), 4.23 (br s, 1H, G2), 4.17 (dd, J = 11.4, 5.7 Hz, 1H, H5), 4.14 (br s, 1H, F3), 4.09 (s, 1H, D2), 4.07 (d, J = 7.4 Hz, 1H, E1), 4.04 (dd, J = 9.2, 4.4 Hz, 1H, G5), 4.01 (dd, J = 10.1, 2.6 Hz, 1H, G3), 3.97 (dd, J = 10.1, 9.2 Hz, 1H, G5), 3.93 (t, J = 9.6 Hz, 1H, H3), 3.89 (br t, J = 8.3 Hz, 1H, C4), 3.86–3.80 (m, 5H, B3, C3, D4, E5, F4), 3.82 (s, 3H, OMe), 3.72 (dq, J = 6.2, 4.0 Hz, 1H, D5), 3.65 (dd, J = 9.2, 7.4 Hz, 1H, E2), 3.64 (d, J = 9.7 Hz, 1H, A4), 3.59 (t, J = 11.0 Hz, 1H, H5), 3.59 (d, J = 9.2 Hz, 1H, H2), 3.56 (s, 3H, OMe), 3.53–3.50 (m, 4H, C5, E4, F6, F6), 3.48–3.46 (m, 1H, A5), 3.47 (dd, J = 9.2, 3.1 Hz, 1H, E3), 3.43 (t, J = 3.5 Hz, 1H, F2), 3.39 (s, 3H, OMe), 3.35 (s, 3H, OMe), 3.34–3.33 (m, 2H, B5, F5), 3.30 (s, 3H, OMe), 2.51 (dd, J = 12.5, 8.5 Hz, 1H, C2), 2.45 (dd, J = 13.7, 4.9 Hz, 1H, A2), 2.38 (s, 3H, Me (A_1)), 2.29 (br dd, J = 12.4, 8.6 Hz, 1H, B2), 2.26 (s, 3H, Me (A_2)), 2.01 (dd, J = 13.7, 1.6 Hz, 1H, A2), 1.90 (t, J = 12.1 Hz, 1H, C2), 1.70–1.66 (m, 1H, B2), 1.68 (s, 3H, Me (A3)), 1.34 (s, 3H, Me (D3)), 1.32 (d, J = 6.4 Hz, 3H, B6), 1.31 (d, J = 6.2 Hz, 3H, D6), 1.28 (d, J = 6.6 Hz, 3H, E6), 1.26 (d, J = 6.8 Hz, 3H, C6), 0.96 (s, 9H, *t*BuSi), 0.95 (s, 9H, *t*BuSi), 0.94 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.89 (s, 18H, *t*BuSi), 0.83 (d, J = 6.2 Hz, 3H, A6), 0.21 (s, 6H, MeSi), 0.19 (s, 3H, MeSi), 0.18 (s, 6H, MeSi), 0.14 (s, 3H, MeSi), 0.10 (s, 6H, MeSi), 0.10 (s, 3H, MeSi), 0.09 (s, 3H, MeSi), 0.07 (s, 3H, MeSi), 0.06 (s, 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.1, 165.6, 157.3, 153.9, 153.2, 152.3, 138.7, 137.9, 135.9, 134.8, 128.6, 128.6, 128.5, 127.5, 127.2, 126.4, 126.0, 121.7, 120.1, 119.0, 119.0, 114.9, 108.5, 103.5, 102.3, 100.2, 97.2, 96.4, 92.6, 89.9, 84.3, 82.8, 82.4, 81.5, 81.1, 79.0, 77.3, 76.1, 75.1, 74.9, 74.1, 73.5, 72.8, 72.4, 71.8, 71.6, 71.1, 70.5, 70.4, 70.0, 69.1, 68.3, 66.2, 63.3, 63.0, 62.5, 62.0, 60.8, 58.4, 46.2, 40.1, 38.8, 36.4, 29.7, 26.2, 26.0, 25.8, 25.6, 25.6, 19.8, 19.3, 19.2, 18.4, 18.3, 18.3, 18.1, 18.1, 18.0, 18.0, 17.6, 16.2, 11.6, −3.7, −3.8, −3.9, −4.2, −4.3, −4.4, −4.4, −4.5, −4.5, −4.9, −5.0, −5.2; HRMS (FAB): calcd for $C_{120}H_{193}Cl_2NO_{38}Si_6Na$ $[M+Na]^+$: 2496/2497, found 2498/2499.

Everninomicin 13,384-1 (1): 10% Pd/C (2.0 mg) was added to a solution of the fully protected everninomicin **54** (10 mg, 0.004 mmol) and $NaHCO_3$ (1.3 mg, 0.016 mmol) in *t*BuOMe (1.0 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 1 h. The reaction mixture was filtered through a pad of Celite, the pad was washed with EtOAc (50 mL), and the solvents were removed under reduced pressure to afford the crude $A_1B(A)CDEFGHA_2$ diol as a white foam. The crude diol was then dissolved in THF (0.1 mL), nBu$_4$NF (40.01 μL, 0.04 mmol) was added, and the resulting mixture was stirred at 25 °C for 10 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 10% MeOH in EtOAc (1% Et_3N)), followed by preparative TLC (silica gel, 5% MeOH in EtOAc (1% Et_3N)) to afford everninomicin 13,384-1 (**1**) (5.0 mg, 75% over two steps) as a white solid. **1**: R_f = 0.26 (5% MeOH in EtOAc); $[\alpha]_D^{22}$ = (syn.) −38.8 (c = 0.08, $CHCl_3$), (nat.) −45.0 (c = 0.10, $CHCl_3$); IR (KBr pellet) $\tilde{\nu}$ = 3487, 2979, 2939, 1736, 1721, 1652, 1621, 1543, 1457, 1382, 1257, 1200, 1050, 994, 600 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$/CD_3OD 20:1): δ = 6.16 (br s, 2H, ArH (A_2)), 5.32 (ddd, J = 9.4, 9.4, 5.6 Hz, 1H, H4), 5.14 (s, 1H, G1), 5.12 (s, 1H, OCH_2O), 5.07 (s, 1H, OCH_2O), 4.93 (s, 1H, D1), 4.90 (br d, J = 4.6 Hz, 1H, A1), 4.85 (t, J = 9.4 Hz, 1H, B4), 4.68 (s, 1H, F1), 4.48 (br d, J = 9.7 Hz, 1H, B1), 4.36 (br s, 1H, G2), 4.35 (ddd, J = 10.5, 10.5, 4.6 Hz, 1H, G4), 4.17 (dd, J = 11.7, 5.5 Hz, 1H, H5), 4.12 (d, J = 7.6 Hz, 1H, E1), 4.08 (dd, J = 9.6, 4.5 Hz, 1H, G5), 3.99 (s, 1H, D2), 3.96 (t, J = 9.8 Hz, 1H, H3), 3.88 (dd, J = 10.2, 2.5 Hz, 1H, G3), 3.86 (t, J = 10.6 Hz, 1H, C3), 3.86–3.83 (m, 3H, B3, C5, D4), 3.79 (s, 3H, OMe), 3.78–3.72 (m, 4H, D5, E5, F6, G5), 3.67 (dd, J = 9.5, 8.3 Hz, 1H, H5), 3.61–3.50 (m, 7H, A4, E2, E5, F3, F4, F6, H2), 3.54 (s, 3H, OMe), 3.52 (s, 3H, OMe), 3.50–3.36 (m, 6H, A5, B5, E3, E4, F2, F5), 3.30 (s, 3H, OMe), 3.27 (s, 3H, OMe), 2.99 (t, J = 9.0 Hz, 1H, C4), 2.39–2.37 (m, 1H, A2), 2.32 (dd, J = 12.0, 5.1 Hz, 1H, B2), 2.29 (s, 3H, Me (A_1)), 2.29–2.26 (m, 1H, C2), 2.26 (s, 3H, Me (A_2)), 1.96 (dd, J = 13.7, 1.4 Hz, 1H, A2), 1.73 (t, J = 12.3 Hz, 1H, C2), 1.66 (dt, J = 12.3, 12.3 Hz, 1H, B2), 1.59 (s, 3H, Me (A3)), 1.35 (d, J = 6.2 Hz, 3H, B6), 1.30 (s, 3H, Me (D3)), 1.26 (d, J = 5.9 Hz, 3H, D6), 1.24 (d, J = 5.9 Hz, 3H, E6), 1.24 (d, J = 6.2 Hz, 3H, C6), 0.77 (d, J = 6.2 Hz, 3H, A6); ^{13}C NMR (150 MHz, $CDCl_3$/CD_3OD 20:1): δ = 170.5, 165.8, 165.2, 162.6, 153.2, 151.3, 143.7, 134.4, 120.6, 120.1, 118.8, 118.3, 113.6, 112.1, 104.0, 103.4, 101.0, 100.8, 100.4, 97.5, 96.7, 96.0, 92.3, 89.8, 87.8, 84.1, 82.7, 80.8, 80.7, 80.3, 80.0, 79.3, 78.2, 77.3, 75.2, 75.0, 73.8, 72.6, 72.4, 71.8, 71.8, 71.0, 70.9, 70.6, 69.8, 69.7, 68.9, 68.5, 68.5, 67.9, 66.2, 65.7, 63.6, 63.2, 61.9, 61.8, 61.7, 60.6, 58.9, 39.8, 39.5, 35.8, 24.3, 19.1, 18.5, 18.2, 17.8, 17.7, 17.5, 17.3, 15.9, 14.9; HRMS (ESI): calcd for $C_{70}H_{97}Cl_2NO_{38}Na$ $[M+Na]^+$: 1653, found 1653.

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