Total Synthesis of Everninomicin 13,384-1—Part 1: Retrosynthetic Analysis and Synthesis of the $A_1B(A)C$ Fragment

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Abstract: In this first of a series of four articles we introduce everninomicin 13,384-1 (**1**), a powerful antibiotic effective against drug resistant bacteria, as a target for total synthesis and discuss its retrosynthetic analysis. From the three defined fragments required for the synthesis (**2**: $A_1B(A)C$ fragment; **4**: DE fragment; **5**: $FGHA_2$ fragment), we describe herein two approaches to the $A_1B(A)C$ block. The first strategy relied on an olefin metathesis reaction to construct a common intermediate for rings B and C, but was faced with final protecting group problems. The second, and successful approach, involved a 1,2-phenylsulfeno migration and a sulfur directed glycosidation procedure to link rings B and C, as well as an acyl fluoride intermediate to install the sterically hindered aryl ester moiety (ring A_1). The final stages of the synthesis of the required 2-phenylseleno glycosyl fluoride **2** required introduction of a phenylseleno group at C-1 of ring C followed by a novel, DAST-promoted 1,2-migration to produce the desired 2-β-phenylseleno glycosyl fluoride moiety.

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

Introduction

The introduction of modern antibiotics in the 1940's for the treatment of infectious disease was heralded with enthusiasm as one of the greatest medical breakthroughs of the twentieth century and led many to believe that these deadly diseases would be defeated once and for all. Despite the saving of millions of lives, however, the widespread use, and sometimes misuse, of antibiotics led to drug resistance and the evolution of "superbugs", strains that threaten humanity once again with untreatable diseases and potential plagues of major proportions. Even vancomycin,[1] an antibiotic long considered to be effective as the last line of defense against drug resistant bacteria, has shown signs of weakness as vancomycin-resistant bacterial strains are reported around the world. Thus, there is a clear recognition for an urgent need to develop more effective antibiotics against such menacing bacteria or discover new ones based on novel mechanisms of action.[2] Everninomicin 13,384-1 (**1**, Figure 1), is a promising new weapon against drug resistant bacteria, including methicillin-resistant *Staphylococci* and vancomycin-resistant *Streptococci* and *Enterococci*.[3] The everninomicins, members of the orthosomycin class of oligosaccharide antibiotics,[4] were first isolated in the 1960's and showed strong activity against Gram-positive bacteria. Everninomicin component 13,384-1 (**1**) was isolated more recently as one of several active compounds found in the fermentation broth of *Micromonospora carbonacea var africana*, which was grown from a sample of soil collected from the banks of the Nyiro River in Kenya.[3] As a result of a better activity profile, a cyclodextrin-complex formulation[5] of 13,384-1 (**1**) which was proven safe in vivo, was developed and was undergoing advanced clinical trials under the tradename of Ziracin. In a number of studies, everninomicin 13,384-1 (**1**) demonstrated excellent in vitro activity against resistant strains of Gram-positive bacteria as compared to several reference antibiotics with MIC_{90} values that were similar to or two- to four-fold lower than those of vancomycin.[6] The mechanism of action of 13,384-1 (**1**) has not yet been fully determined. Given the structural similarity to the related orthosomycin antibiotic, avilamycin, it was however, suggested that 13,384-1 (**1**) also acts as an inhibitor of protein biosynthesis by targeting the 30S subunit of ribosomes.[7]

With the race for the development of new antibiotics against drug-resistant bacteria intensifying, we embarked

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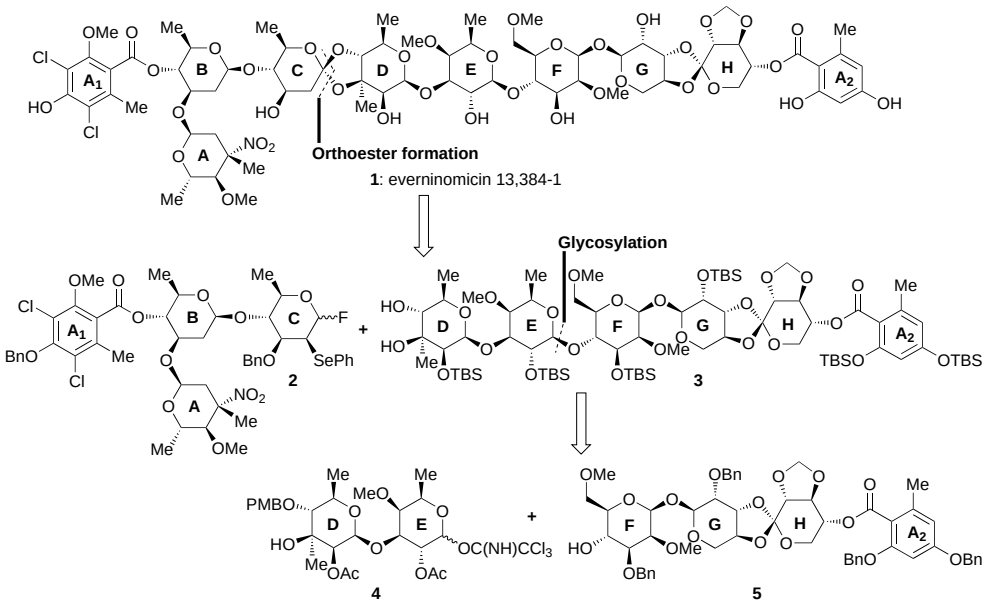

Figure 1. Retrosynthetic analysis of everninomicin 13,384-1 (**1**). Ac = acetyl; Bn = benzyl; PMB = *p*-methoxybenzyl; TBS = *tert*-butyldimethylsilyl.

upon a program directed towards the total synthesis[8] of everninomicin 13,384-1 (**1**) in search of chemical and biological knowledge that may help facilitate the drug discovery process in this area. Everninomicin 13,384-1 (**1**) possesses a novel, polyfunctional oligosaccharide structure focused around the unusual connectivity of two sensitive orthoester moieties. In addition, everninomicin 13,384-1 (**1**) contains within its structure a 1,1′-disaccharide bridge, a nitrosugar (evernitrose), two highly substituted aromatic esters, and two β-mannoside bonds. In total there are thirteen rings and thirty-five stereogenic centers within its structure.[9] The complex, yet sensitive nature of everninomicin 13,384-1 (**1**) constituted a formidable challenge for determination of its structure by Ganguly and co-workers[3] and more so for its present synthesis.[10] In this and the following three papers,[11–13] we describe the details of our investigations which culminated in the development of a number of new synthetic methods and strategies for the construction of structural motifs relevant to everninomicin 13,384-1 (**1**) and in its eventual total synthesis.

Abstract in Greek: Σ'αυτή την πρώτη από μια σειρά τεσσάρων εργασιών παρουσιάζουμε την Everninomicin 13,384-1 (**1**), ένα ισχυρό αντιβιοτικό δραστικό έναντι ανθεκτικών βακτηρίων, σαν στόχο για ολική σύνθεση και συζητάμε τη ρετρο-συνθετική της ανάλυση. Από τα τρία τμήματα που προσδιορίσαμε ότι απαιτούνται για την ολική σύνθεση (**2**: τμήμα $A_1B(A)C$; **4**: τμήμα DE; **5**: τμήμα $FGHA_2$), εδώ περιγράφουμε δύο διαφορετικές προσεγγίσεις για τη σύνθεση του κομματιού $A_1B(A)C$; Η πρώτη στρατηγική βασίστηκε σε μια αντίδραση μετάθεσης ολεφίνης για να δομηθεί ένα κοινό ενδιάμεσο για τους δακτυλίους B και C, που όμως αντιμετώπισε προβλήματα ομάδων προστασίας στα τελικά στάδια. Η δεύτερη και επιτυχημένη προσέγγιση περιελάμβανε μια αντίδραση 1,2-θειοφαινυλο-μετάθεσης και στη συνέχεια αντίδραση γλυκοσυλίωσης κατευθυνόμενη από το θείο για τη σύνδεση των δακτυλίων B και C, καθώς επίσης και μια αντίδραση εστεροποίησης χρησιμοποιώντας ακυλο-φθορίδιο για να ενσωματωθεί ο στερεοχημικά παρεμποδισμένος αρυλο-εστέρας (δακτύλιος A_1). Τα τελικά στάδια της σύνθεσης του ζητούμενου 2-σεληνιοφαινυλο-γλυκοσυλο-φθοριδίου **2** απαιτούσαν την εισαγωγή μιας σεληνιοφαινυλο-ομάδας στον C-1 του δακτυλίου C ακολουθούμενη στη συνέχεια από μια νέα αντίδραση 1,2-μετάθεσης, υποκινούμενης από το DAST, για να δώσει το επιθυμητό 2-β-σεληνιοφαινυλο-γλυκοσυλο-φθορίδιο.

Results and Discussion

Retrosynthetic analysis—Overall strategy: Figure 1 outlines, in retrosynthetic format, the strategy utilized in the present total synthesis. While the carbohydrate nature of everninomicin's structure presents several options for retrosynthetic simplification, the CD orthoester moiety was disassembled first, due to its extreme sensitivity to acidic conditions,[3] leading to 2-phenylseleno fluoride **2** [$A_1B(A)C$ fragment] and diol **3** [$DEFGHA_2$ fragment]. Examination of the larger fragment (**3**) revealed the EF glycosidic linkage as the most straightforward to construct, and this bond was, therefore, retrosynthetically disconnected, unraveling fragments **4** [DE] and **5** [$FGHA_2$] as potential key intermediates for its construction. By adopting the resulting approach, we ensured added flexibility for the later steps of the projected synthesis in that (following modification of the DE fragment) we could utilize either the $A_1B(A)CDE$ or the $DEFGHA_2$ fragment to couple with the respective remaining portion of the molecule. Herein, we describe the construction of the $A_1B(A)C$ fragment of the target molecule.

Initial approach to the $A_1B(A)C$ fragment: In our initial approach to the $A_1B(A)C$ fragment of everninomicin (**1**), we anticipated efficient constructions of rings B, C, and D from a small, common chiral starting material, and in order to confirm the viability of the overall approach, synthesized an $A_1B(A)C$ model system,[14] as depicted retrosynthetically, in Figure 2. The $A_1B(A)C$ portion of target molecule **1** contains

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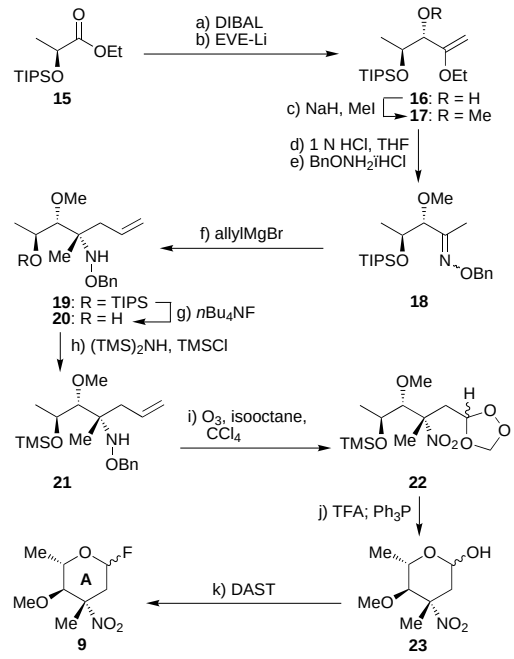
the nitrosugar A, a 2-deoxy-β-glycoside, and the fully substituted aromatic ring A_1, and has stimulated a number of synthetic studies. Notable among these studies are the formation of $A_1B(A)$ and A_1BC systems by Scharf[10b,c] and a BCDE model system by Sinaÿ.[10d] In our approach to this model system, a number of interesting strategies were featured, including; a) a ring closing olefin metathesis[15] based approach to a common precursor for carbohydrate systems B and C (**13** → **12**, Figure 2); b) control of the 2-deoxy-β-anomeric stereochemistry based on the 1,2-phenylsulfeno migration/sulfur-directed glycosidation procedure;[16] c) use of an acyl fluoride to effect formation of the sterically demanding ester bond between rings A_1 and B; and d) an efficient synthesis of the unusual nitrosugar, ring A.

Construction of the building blocks for the $A_1B(A)C$ fragment: While a key objective of our initial strategy toward the nitrogen-containing C-3-branched 2,6-dideoxy-L-sugars of the antibiotics vancomycin and everninomicin was the construction of an advanced common intermediate from which both targeted sugars could be generated,[17] the final route used herein for the construction of evernitrose donor **9** (Scheme 1) involved an improved sequence along the lines of our original synthesis. To achieve this goal, the C-3 functionality was projected to arise via nucleophilic chain extension of an oxime.[18] A stereocontrolled *anti*-addition[19] of an acyl anion equivalent to an aldehyde derived from L-lactate was envisioned as a means to install the C-4 stereocenter (carbohydrate numbering). Thus, the ethyl-L-lactate derived intermediate **15** (Scheme 1) was reduced with DIBAL and treated with EVE-Li at −100 °C in ether to afford enol ether **16** in 66% yield (for abbreviations of protecting groups and reagents, see legends in Schemes). The resulting alcohol **16** was methylated with NaH/MeI furnishing methoxy compound **17** in 96% yield, which was then hydrolyzed to the corresponding ketone with aqueous HCl and converted to oxime **18** by condensation with *O*-benzylhydroxylamine in pyridine (ca. 4:1 ratio of *E*:*Z* isomers, 91% yield for two steps). Addition of allylmagnesium bromide to **18** in ether at −35 °C afforded **19** (87%) which was subjected to silyl group removal (nBu$_4$NF, 92%) furnishing alcohol **20**. It was anticipated that exposure of **20** to ozone would generate simultaneously the required aldehyde and nitro groups.[20] However, ozonolysis of **20** (CH_2Cl_2, −78 °C), followed by Me_2S work-up and silica gel chromatography, afforded a remarkably stable intermediate ozonide (**22** without the TMS group) as a mixture of diastereoisomers (ca. 1:1 ratio). In contrast, Ph_3P work-up led smoothly to nitrosugar **23** in 63% overall yield from **20**. The yield of the latter transformation was significantly improved by reprotecting the alcohol as TMS ether **21** ($(TMS)_2NH$, TMSCl, 100%) and carrying out the ozonolysis in a 2:1 mixture of isooctane and CCl_4, furnishing, after in situ TMS removal with TFA and treatment with Ph_3P, the targeted nitrosugar **23** in 82% overall yield. Finally, exposure to



Scheme 1. Synthesis of nitrosugar A (**9**). a) 1.4 equiv DIBAL (1.0 M in CH_2Cl_2), Et_2O, −78 °C, 50 min; b) 3.0 equiv EVE-Li, THF, −100 °C, 5 min, 66% for two steps, 85% *de*; c) 1.1 equiv NaH, 2.7 equiv MeI, THF, 0 → 25 °C, 4 h, 96%; d) 1N aq HCl, THF/H_2O 4:1, 25 °C, 0.5 h, 100%; e) 1.1 equiv $BnONH_2 \cdot HCl$, py, 0 → 25 °C, 2 h, 91% (*E*:*Z* ca. 4:1); f) 2.5 equiv allyl-MgBr, Et_2O, −35 °C, 1 h, 87%; g) 1.1 equiv nBu$_4$NF, THF, 25 °C, 1 h, 92%; h) 5.0 equiv $(TMS)_2NH$, 0.03 equiv TMSCl, MeCN, 0 → 25 °C, 15 min, 100%; i) O_3, isooctane/CCl_4 2:1, −78 °C, 1 h; j) i) 2.0 equiv TFA, −78 → 25 °C, 1 h; ii) 2.0 equiv Ph_3P, −78 → 25 °C, 12 h, 82% over three steps, α:β ca. 1:1; k) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 20 min, 100%. TMS = trimethylsilyl; DAST = (diethylamino)sulfur trifluoride; TFA = trifluoroacetic acid; DIBAL = diisobutylaluminum hydride; EVE-Li = CH_2=C(OMe)Li.

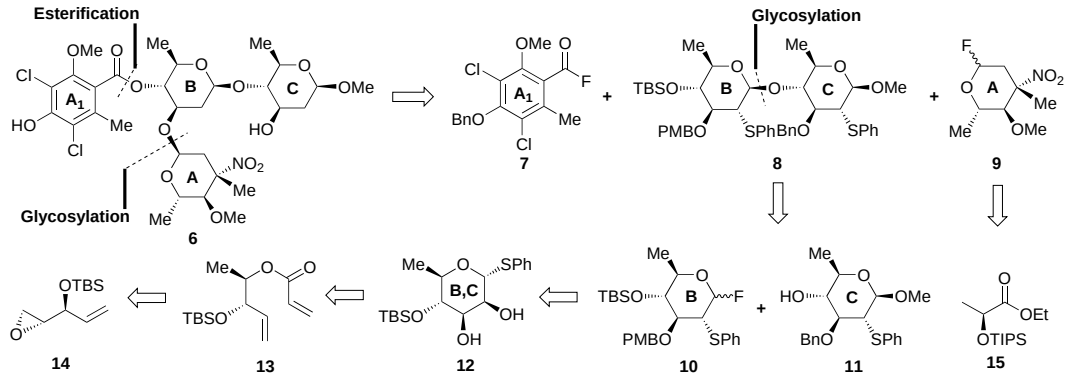
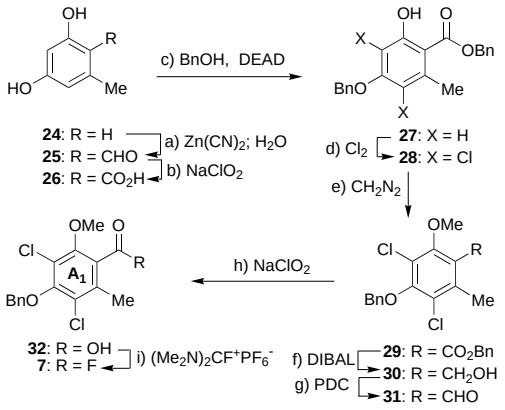


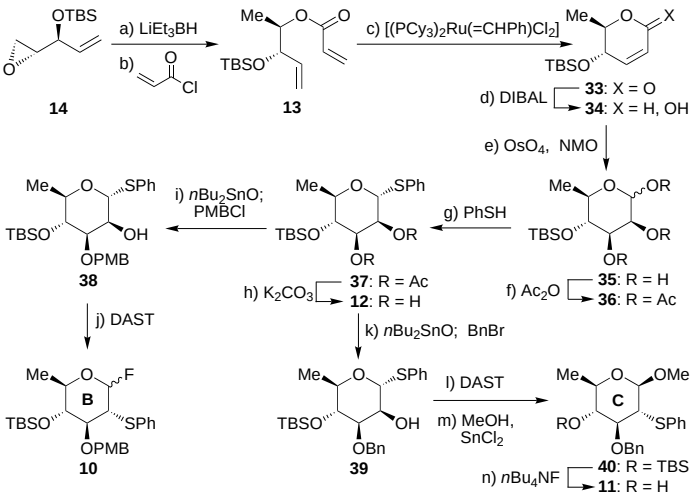
Figure 2. Retrosynthetic analysis of the $A_1B(A)C$ model system (**6**). TIPS = triisopropylsilyl.

DAST[21a] led to rapid conversion of **23** to a mixture of glycosyl fluorides[21b, c] **9** in quantitative yield (ca. 8:1 α:β anomers).

Previously reported difficulties[10b] in forming the ester bond between rings A_1 and B led us to evaluate the use of acyl fluoride **7** (Scheme 2) as a potential coupling partner. To this



Scheme 2. Synthesis of dichloroisoeverninic acyl fluoride **7**. a) i) 1.5 equiv $Zn(CN)_2$, 2.4 equiv $AlCl_3$, HCl (g), 0 °C, 3 h; ii) H_2O, 0 → 100 °C, 0.5 h, 92%; b) 2.4 equiv $NaClO_2$, 2.5 equiv NaH_2PO_4, H_2O/DMSO 1:2, 0 → 25 °C, 12 h, 80%; c) 2.0 equiv BnOH, 2.0 equiv DEAD, 2.0 equiv Ph_3P, THF, 0 °C, 4 h, 75%; d) 3.0 equiv Cl_2 (1.0 M in AcOH), 2.25 equiv NaOAc, AcOH, −50 → 0 °C, 3 h, 70%; e) CH_2N_2 (excess), Et_2O, dark, 0 °C, 12 h, 100%; f) 1.2 equiv DIBAL, CH_2Cl_2, −78 °C, 1 h, 90%; g) 3.0 equiv PDC, 3 Å MS, CH_2Cl_2, 25 °C, 3 h, 90%; h) 3.0 equiv $NaClO_2$, 3.0 equiv NaH_2PO_4, 4.0 equiv 2-methyl-2-butene (2.0 M in THF), *t*BuOH, H_2O, 25 °C, 3 h, 95%; i) 1.5 equiv $(Me_2N)_2CF^+PF_6^-$, 2.0 equiv *i*Pr_2NEt, CH_2Cl_2, 0 °C, 2 h, 97%. PDC = pyridinium dichromate, DMSO = dimethylsulfoxide, DEAD = diethylazodicarboxylate.



Scheme 3. Synthesis of intermediates **10** and **11**. a) 1.2 equiv $LiEt_3BH$ (1.0 M in THF), THF, −40 °C, 1 h, 91%; b) 1.2 equiv CH_2=CHC(O)Cl, 1.5 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 °C, 15 min, 95%; c) 0.15 equiv $(PCy_3)_2Ru(=CHPh)Cl_2$, CH_2Cl_2, 35 °C, 24 h, 90%; d) 3.1 equiv DIBAL, CH_2Cl_2, −78 °C, 1 h, 90%; e) 0.01 equiv OsO_4, 1.5 equiv NMO, acetone/H_2O 10:1, 25 °C, 12 h, 90%; f) 4.0 equiv Ac_2O, 6.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 → 25 °C, 1 h, 99%; g) 1.5 equiv PhSH, 0.2 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, −20 °C, 1 h, 69%; h) 0.2 equiv K_2CO_3, Et_2O/MeOH 1:1, 25 °C, 1 h, 97%; i) 1.1 equiv *n*Bu_2SnO, toluene, reflux, 3 h; 1.5 equiv PMBCl, 0.1 equiv *n*Bu_4NI, 25 → 110 °C, 2 h, 92%; j) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 0.5 h, 100%; k) 1.2 equiv *n*Bu_2SnO, toluene, reflux, 3 h; 1.5 equiv BnBr, 0.2 equiv *n*Bu_4NI, 25 → 110 °C, 2 h, 80%; l) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 0.5 h; m) 3.0 equiv MeOH, 1.8 equiv $SnCl_2$, 4 Å MS, Et_2O, −10 °C, 12 h, 100% for two steps, α:β ca. 1:10; n) 1.2 equiv *n*Bu_4NF, THF, 25 °C, 1 h, 94%. NMO = *N*-methylmorpholine-*N*-oxide; 4-DMAP = 4-dimethylaminopyridine; Tf = trifluoromethanesulfonyl; Cy = cyclohexyl; THF = tetrahydrofuran.

end, Gatterman formylation of orcinol (**24**) with $Zn(CN)_2$/$AlCl_3$ afforded aldehyde **25**[22] in 92% yield. Oxidation to carboxylic acid **26** ($NaClO_2$, 80%), followed by exposure to benzyl alcohol under Mitsunobu conditions led to the differentiated phenol derivative **27** (75%). Chlorination of **27** (Cl_2, buffered conditions,[10c] 70% yield) furnished **28**, and was followed by methylation of the remaining phenol affording ester **29** (CH_2N_2,[10c] 100%). The resistance of the benzyl ester in **29** towards saponification led us to develop a three-step protocol for its conversion to carboxylic acid **32**. The sequence involved the following steps: DIBAL reduction to alcohol **30** (90%); PDC oxidation to aldehyde **31** (90%); and finally $NaClO_2$ oxidation furnishing the acid in 95% yield. Exposure of **32** to $(Me_2N)_2CF^+PF_6^-$ [23] in the presence of diisopropylethylamine gave the targeted acyl fluoride **7**, which withstood admirably chromatographic purification.

An asymmetric synthesis of rings B and C from the common precursor **12** is shown in Scheme 3. Regioselective opening of epoxide **14**[24] with $LiEt_3BH$ (91%), followed by esterification with acryloyl chloride under basic conditions (Et_3N) provided diolefin **13** (95%). Ring closing metathesis was induced by the action of catalytic amounts of $[(PCy_3)_2Ru(=CHPh)Cl_2]$ and afforded lactone **33** in 90% yield. Contrary to expectations, dihydroxylation of **33** under a variety of conditions led to the undesired diol stereoisomer. Fortunately and remarkably, reduction of lactone **33** with DIBAL, followed by OsO_4-catalyzed dihydroxylation of the resulting lactol (**34**, mixture of anomers), led to exclusive formation of the desired triol **35** (90%). The latter compound was peracetylated to afford triacetate **36** (99%, mixture of anomers). Exposure of **36** to PhSH and $BF_3 \cdot Et_2O$, followed by deacetylation (K_2CO_3) gave thioglycoside **12** in 67% overall yield. Thioglycoside **12** was then converted to both glycosyl acceptor **11** and glycosyl donor **10** employing the 1,2-thiophenyl migration technology previously developed in these laboratories.[16] Thus, regioselective C-3 protection of **12** was effected by the use of tin-acetal chemistry[25] employing *n*Bu_2SnO/PMBCl for ring B and *n*Bu_2SnO/BnBr for ring C, leading to compounds **38** (92%) and **39** (80%), respectively. In both cases, the thioglycosides underwent smooth 1,2-migration on exposure to DAST, furnishing for ring B, glycosyl fluoride **10** (mixture of β:α anomers, ca. 17:1) and for ring C, the corresponding glycosyl fluoride which underwent glycosidation with MeOH in the presence of $SnCl_2$ in ether to afford predominantly β-methyl glycoside **40** (100%, ca. 10:1 ratio of anomers) as expected by virtue of the sulfur directing effect. Desilylation of **40** (*n*Bu_4NF) gave compound **11** in 94% yield.

Assembly of the A_1B(A)C model system 6: The assembly of the A_1B(A)C ring system **6** from its monocyclic building blocks (**7**, **9**, **10**, and **11**) is shown in Scheme 4. Thus β-directed coupling[16] of **10** with **11** was promoted by $SnCl_2$ in ether to afford disaccharide **8** in 78% yield. Desulfurization of **8** with Raney Ni, followed by rebenzylation of the partially deprotected C_3-hydroxyl group of ring C and desilylation with

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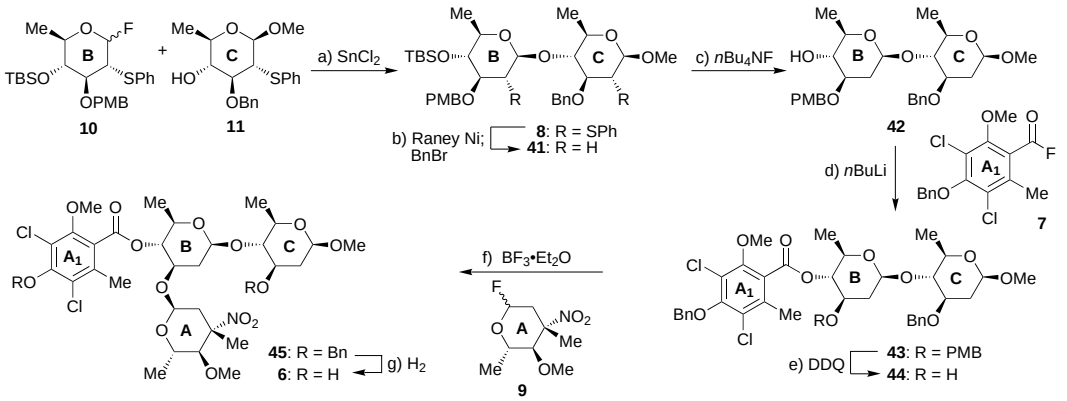


Scheme 4. Construction of $A_1B(A)C$ ring system **6**. a) 1.8 equiv **10**, 1.0 equiv **11**, 1.8 equiv $SnCl_2$, Et_2O, 4 Å MS, $-10\,^{\circ}C$, 12 h, 78%; b) i) Raney Ni (excess), MeOH, reflux, 2 h; ii) 1.3 equiv BnBr, 1.2 equiv NaH, 0.2 equiv nBu$_4$NI, DMF, $0 \rightarrow 25\,^{\circ}C$, 1 h; c) 1.2 equiv nBu$_4$NF, THF, $25\,^{\circ}C$, 1 h, 78% for three steps; d) i) **42**, 4 Å MS, THF, $25\,^{\circ}C$, 2 h; ii) 1.1 equiv nBuLi (1.6 M in hexanes), $25\,^{\circ}C$, 1 h; iii) 1.5 equiv **7**, THF, 24 h, 80%; e) 1.3 equiv DDQ, CH_2Cl_2/H_2O 10:1, $0 \rightarrow 25\,^{\circ}C$, 2 h, 80%; f) 2.1 equiv **9**, 0.6 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, 4 Å MS, $-35 \rightarrow 25\,^{\circ}C$, 12 h, 95%; g) H_2, 10% Pd/C, tBuOMe, $25\,^{\circ}C$, 2 h, 95%. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DMF = dimethylformamide.

nBu$_4$NF, furnished disaccharide **42** via **41** (78% yield for three steps). Activation of **42** with nBuLi facilitated its coupling with acyl fluoride **7**, leading to ester **43** in 80% yield. Finally, oxidative removal of the PMB group from **43** was achieved with aqueous DDQ, furnishing **44** in 80% yield. The coupling of alcohol **44** and glycosyl fluoride **9** in the presence of $BF_3 \cdot Et_2O$ proceeded smoothly and stereoselectively and in 95% yield to afford the desired α-glycoside **45**, from which the benzyl groups were selectively removed by hydrogenolysis (H_2, 10% Pd/C) to afford the targeted $A_1B(A)C$ model system **6** of everninomicin (**1**) in 95% yield.

The above-described construction demonstrated a number of novel synthetic strategies for the asymmetric synthesis of carbohydrate units and seemed suitable for applying to other portions of the target molecule (**1**). At the same time, however, we began to investigate potential methods for formation of the CD orthoester, and as will be described in much detail in Part 2 of this series,[11] we found that a revision of our overall strategy was, at this juncture, required.

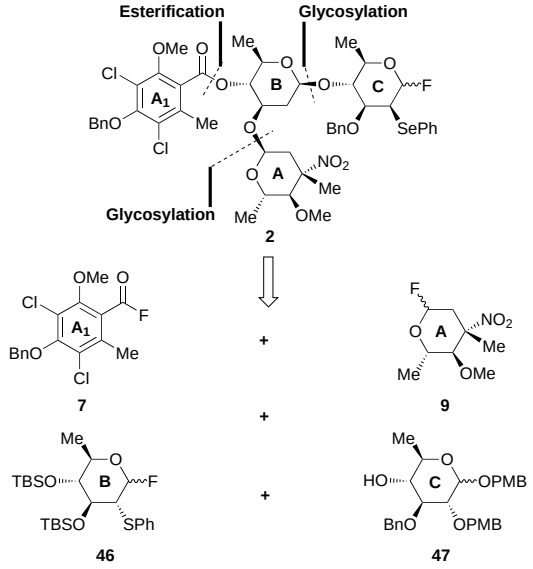
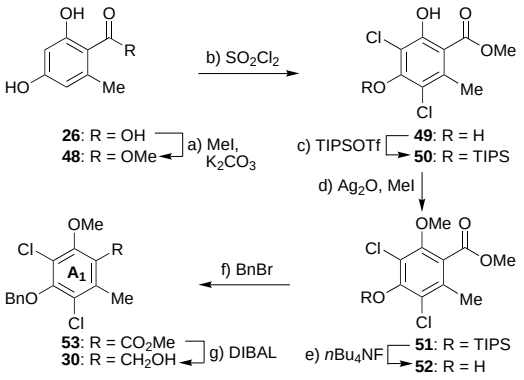


Figure 3. Retrosynthetic analysis of the $A_1B(A)C$ fragment (**2**).

Revised strategies: Crucial to a new plan were, 1,2-phenylseleno-[11] and 1,2-phenylthio migrations[16] on both rings B and C, setting the stage for the stereocontrolled constructions of the CD orthoester and the β-2-deoxy BC glycoside bond. Despite our success in the above model study[14] in constructing rings B and C from a common intermediate, we now required a more diverse array of protecting groups and glycosylation tactics for an eventual total synthesis. Furthermore, the revised routes for rings B and C required independent paths for their construction. After much experimentation (to be described in Part 2[11]), the method for construction of the orthoester was defined and a re-examination of the $A_1B(A)C$ fragment revealed that the functionalities depicted in compound **2** (Figure 3) would best suit our needs. Figure 3 depicts the revised retrosynthetic analysis of this fragment (**2**), whereby, disconnection at the indicated sites (two glycosidic and one ester bonds) defined building blocks **7**, **9**, **46**, and **47** as the requisite starting materials.

Construction of the building blocks 7, 9, 46, and 47: In order to facilitate production of the relatively large quantities of material required to complete a total synthesis of everninomicin (**1**), a revised synthesis for the aromatic fragment **7** was developed so as to avoid the large scale use of chlorine gas. This second-generation synthesis of **7** (to intermediate **30**) is summarized in Scheme 5 which depicts the efficient preparation of the previously utilized (see Scheme 2) intermediate **30**. Thus, carboxylic acid **26** was methylated (MeI/K_2CO_3) furnishing methyl ester **48** (90%), whose subsequent chlorination was easily carried out with SO_2Cl_2,[10c] providing dichloride **49** in 95% yield. Sequential protection of the two phenolic groups proceeded smoothly and regioselectively upon treatment with TIPSOTf/2,6-lutidine (90%), followed by Ag_2O/MeI (91%) leading to compound **51**. The TIPS group in **51** was then exchanged for a Bn group (nBu$_4$NF, 96%; K_2CO_3/BnBr, 92%) furnishing **53** via **52**. The inability to directly saponify this methyl ester, again led to a three-step-



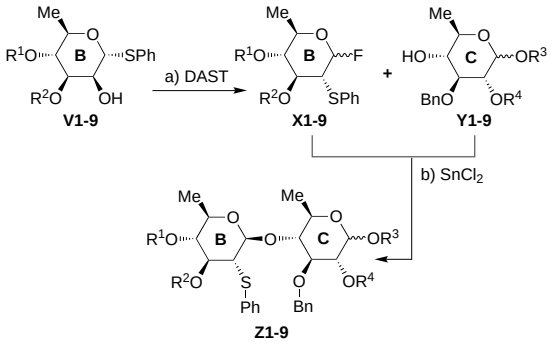
Scheme 5. Revised synthesis of intermediate **30**. a) 10.0 equiv MeI, 0.5 equiv K_2CO_3, Me_2CO, 25 °C, 24 h, 90 %; b) 2.5 equiv SO_2Cl_2, CH_2Cl_2, reflux, 3 h, 95 %; c) 1.0 equiv TIPSOTf, 1.4 equiv 2,6-lutidine, CH_2Cl_2, −78 °C, 0.5 h, 90 %; d) 4.0 equiv Ag_2O, 6.0 equiv MeI, Et_2O, reflux, 12 h, 91 %; e) 1.3 equiv nBu_4NF, THF, 25 °C, 2 h, 96 %; f) 1.2 equiv BnBr, 0.7 equiv K_2CO_3, Me_2CO, reflux, 8 h, 92 %; g) 1.2 equiv DIBAL, CH_2Cl_2, −78 °C, 1 h, 90 %.

protocol to transform it to the corresponding carboxylic acid, which was taken to **7** by the methods described in Scheme 2 (**53** → **30** → **31** → **32**).

In designing the new BC disaccharide, two issues had to be addressed. First, a 1-β-phenylseleno glycoside was required on ring C (in the final product) in order to facilitate construction of the CD orthoester; and second, we still desired to use the 1,2-thiophenyl migration/coupling strategy to construct the 2-deoxy-β-BC glycoside. We could overcome these issues by a sequential method of forming the BC glycoside, removing the thiophenyl group from ring B, followed by the introduction of the selenoglycoside in ring C. This linear sequence led to a third issue, the need for a more diverse ensemble of protecting groups. Table 1 describes the overall results from the design and experimentation with different combinations of protecting groups for rings B and C. We anticipated that the use of an ester at the C-4 position of ring B would provide the best results because it most closely resembles the functionality found in the subtarget **2**. However, treatment of requisite thioglycoside with DAST led to an unusual rearrangement of the starting material (Table 1, entries 1 and 2). After several other attempts, a winning combination was eventually discovered (Table 1, entry 9), revealing the need for building blocks **46** (see Scheme 6) and **47** (see Scheme 7), with TBS and PMB groups on rings B and C, respectively.

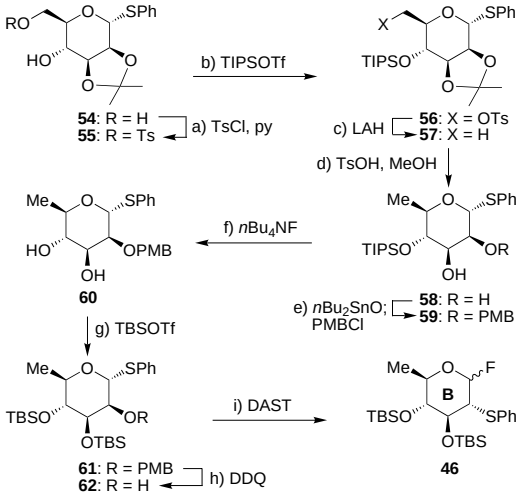
The synthesis of building block **46** is summarized in Scheme 6. Thus, the primary hydroxyl group of the known intermediate **54**[26] was tosylated with TsCl/py furnishing tosylate **55** which was silylated (**56**, TIPSOTf, 2,6-lutidine, 88 % over two steps) and reduced with LAH (90 %) to afford compound **57**. Acidic methanolysis (TsOH/MeOH) of the acetonide group in **57** provided diol **58** (80 %) whose selective protection at C-2 was achieved by exposure to nBu_2SnO followed by reacting the resulting tin-acetal with PMBCl/nBu_4NI, furnishing PMB ether **59** in 83 % yield. The C-2 regioselectivity in this case, was predicted due to the bulkiness of the TIPS group, as observed in the first synthesis of ring F, described in Part 2[11] of this series. For steric reasons, the TIPS group was then replaced with the slightly smaller TBS

Table 1. Attempted couplings of rings B and C.[a]



Entry	X[f]		Y[f]		Yield of Z
	R^1	R^2	R^3	R^4	[%]
1	Bz	PMB	TIPS	TIPS	NR[c, d]
2	Bz	PMB	TBS	TBS	NR[c, d]
3	Bz	PMB	Alloc	Alloc	Dec[e]
4	allyl	PMB	TBS	TBS	< 20 %
5	TES	PMB	TBS	TBS	< 20 %
6	TBS	PMB	TBS	TBS	NR[c]
7	Alloc	PMB	TBS	TBS	NR[c]
8	TBS	PMB	GI[b]	GI[b]	Dec[e]
9	TBS	TBS	PMB	TMB	71

[a] a) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 0.5 h; b) 1.2 equiv **X**, 1.0 equiv **Y**, 1.5 equiv $SnCl_2$, Et_2O, 0 → 25 °C, 3 h; [b] glycal **65** (Scheme 7) was used; [c] NR = no reaction; [d] rearrangement of ring B occurs; [e] decomposition of ring C occurs; [f] fluorides **X1 – 8** and alcohols **Y1 – 8** were prepared using standard carbohydrate chemistry, similar to that of **X9** and **Y9** shown in Schemes 6 and 7. Alloc = allyloxy carbonyl; Bz = benzoyl.



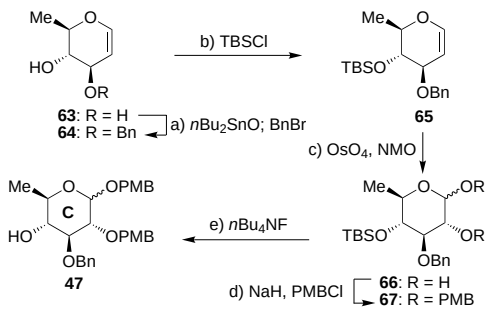
Scheme 6. Synthesis of carbohydrate building block B (**46**). a) 1.1 equiv TsCl, py, 0 → 25 °C, 12 h; b) 1.1 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 0.5 h, 88 % for two steps; c) 1.3 equiv LAH, THF, 0 → 45 °C, 6 h, 90 %; d) 0.2 equiv TsOH, 2.5 equiv $(CH_2OH)_2$, MeOH, 25 °C, 10 h, 80 %; e) 1.1 equiv nBu_2SnO, toluene, reflux, 3 h; 1.5 equiv PMBCl, 0.2 equiv nBu_4NI, 25 → 110 °C, 3 h, 83 %; f) 1.5 equiv nBu_4NF, THF, 25 °C, 2 h, 91 %; g) 2.2 equiv TBSOTf, 4.0 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 0.5 h, 93 %; h) 1.5 equiv DDQ, CH_2Cl_2/H_2O 10:1, 0 → 25 °C, 1 h, 91 %; i) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 0.5 h, 100 %, α:β ca. 10:1. Ts = *p*-toluenesulfonyl; LAH = lithium aluminumhydride; py = pyridine.

group. Thus, exposure of **59** to nBu_4NF led to diol **60** (91 %) whose treatment with TBSOTf and 2,6-lutidine furnished bis-TBS derivative **61** (93 %). Finally, the PMB ether at C-2 was oxidatively cleaved with DDQ, affording alcohol **62** (91 %)

0947-6539/00/0617-3100 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

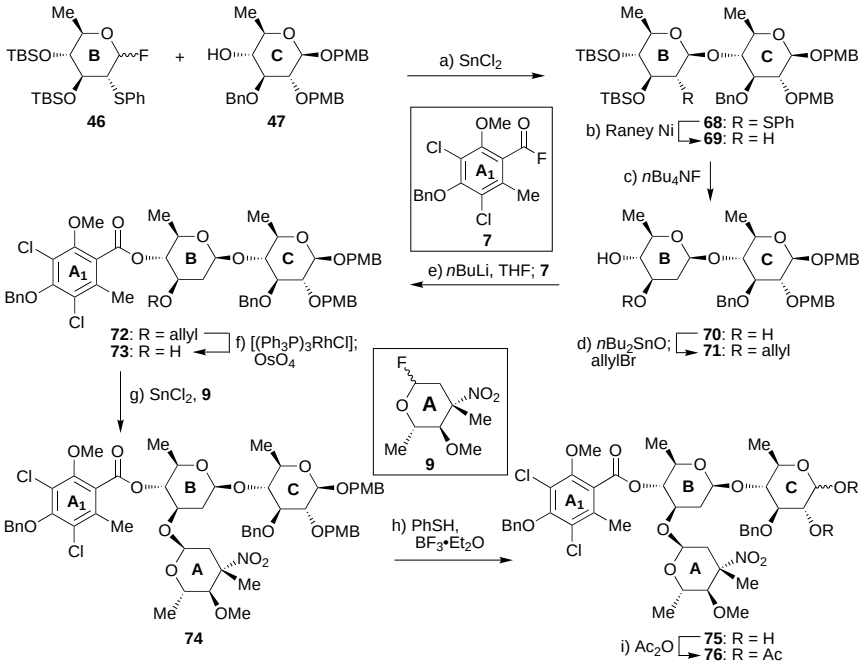
which was exposed to DAST causing the desired 1,2-migration of the thiophenyl group (with inversion of stereochemistry at C-2) and concomitant formation of the corresponding glycosyl fluoride **46** (100%, ca. 10:1 α:β mixture of anomers).

Ring C building block **47** was constructed in five steps from the readily available glucal **63**[27] as shown in Scheme 7. Regioselective tin-acetal mediated benzylation of **63** (nBu$_2$SnO; BnBr/nBu$_4$NI) afforded **64** with C-3 protection in 83% yield. Silylation of the C-4 alcohol with TBSCl/imidazole led to compound **65** (93%) whose exposure to OsO_4/NMO furnished diol **66** in 97% yield (ca. 1:1 mixture of anomers). Protection of both hydroxyl groups of **66** as PMB ethers (NaH, PMBCl, nBu$_4$NI, 95%) led to **67** (ca. 1:1 mixture of anomers). Exposure of the latter compound to nBu$_4$NF generated the desired building block **47** in 95% yield. The stereochemistry at C-1 (ca. 1:1) in **47** is inconsequential, as later on it will be destroyed.



Scheme 7. Synthesis of carbohydrate building block C (**47**). a) 1.1 equiv nBu$_2$SnO, toluene, reflux, 3 h; 1.5 equiv BnBr, 0.2 equiv nBu$_4$NI, 25 → 110 °C, 3 h, 83%; b) 1.5 equiv TBSCl, 2.5 equiv imidazole, CH_2Cl_2, 0 → 25 °C, 3 h, 93%; c) 1.1 equiv NMO, 0.05 equiv OsO_4, acetone/H_2O 10:1, 25 °C, 8 h, 97%; d) 2.4 equiv NaH, 3.0 equiv PMBCl, 0.2 equiv nBu$_4$NI, DMF, 0 → 25 °C, 3 h, 95%; e) 1.1 equiv nBu$_4$NF, THF, 25 °C, 1 h, 95%, α:β ca. 1:1.

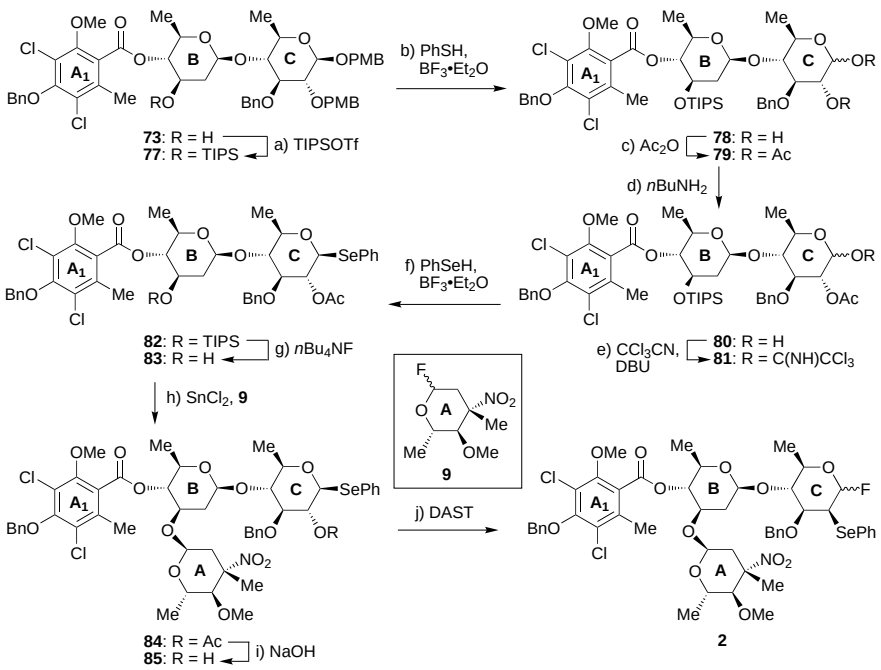
Assembly and completion of the A$_1$B(A)C fragment: With the requisite building blocks (**7**, **9**, **46**, and **47**) at hand, their stereoselective coupling to form the A$_1$B(A)C fragment **2** could now be attempted. Scheme 8 summarizes our initial results. Thus, $SnCl_2$ mediated coupling of glycosyl fluoride **46** with alcohol **47** in a 1:1:1 mixture of CH_2Cl_2/Et_2O/Me_2S (this solvent combination prevented loss of the PMB groups and also improved solubility of the reactants) at −10 °C,[16] gave disaccharide **68** in 71% yield and as a single stereoisomer. The 2-thiophenyl group, having completed its β-directing mission, was reductively cleaved with Raney Ni, this time without loss of the benzyl protecting group, furnishing 2-deoxy-β-disaccharide **69**. In preparation for its coupling with acyl fluoride **7**, bis-TBS ether **69** was exposed to excess nBu$_4$NF, facilitating bis-desilylation (78% for two steps) and formation of diol **70**. Subsequent regioselective tin-acetal mediated allylation with nBu$_2$SnO/allyl bromide furnished **71** in 93% yield. Coupling of acyl fluoride **7** with the activated form of hydroxy compound **71** (nBuLi, THF, −78 → 0 °C) led to the corresponding ester **72** in 99% yield. The allyl group was then removed from **72** by a two-step procedure involving Wilkinson's catalyst/DABCO and OsO_4/NMO, affording alcohol **73** (81%). At this juncture, two paths were available for adoption. The first option involved coupling with the ring A nitrosugar, followed by installation of a phenylseleno group on ring C; the second option involved the reverse sequence. Opting for the first scenario, alcohol **73** was coupled with **9** in the presence of $SnCl_2$, furnishing trisaccharide **74** in 77% yield as the desired α-anomer. The PMB groups on ring C were then removed by treatment with PhSH/$BF_3 \cdot Et_2O$ at −35 °C, affording diol **75** in 83% yield (prolonged exposure of **74** to DDQ resulted in decomposition). The resulting diol **75** was acetylated (Ac_2O, Et_3N, 97%) and then several attempts were made to introduce the phenylseleno group into diacetate **76** or its respective lactol. A variety of different activation methods (e.g., acetate, glycosyl fluoride, trichloroacetimidate, glycosyl bromide) failed to produce the desired



Scheme 8. Construction of A$_1$B(A)C fragment **76**. a) 1.0 equiv **46**, 0.9 equiv **47**, 1.8 equiv $SnCl_2$, 4 Å MS, CH_2Cl_2/Et_2O/Me_2S 1:1:1, −10 °C, 3 h, 71%; b) ca. 1.0 equiv Raney Ni (*w*/*w*), EtOH/THF 1:1, reflux, 8 h; c) 2.2 equiv nBu$_4$NF, THF, 25 °C, 2 h, 78% over two steps; d) 1.1 equiv nBu$_2$SnO, toluene, reflux, 3 h; 1.5 equiv allyl bromide, 0.2 equiv nBu$_4$NI, 25 → 110 °C, 3 h, 93%; e) 1.1 equiv nBuLi, THF, −78 → 0 °C, 1 h; 1.2 equiv **7**, THF, 0 → 25 °C, 4 h, 99%; f) i) 1.5 equiv DABCO, 0.05 equiv [$(Ph_3P)_3RhCl$], EtOH/H_2O 10:1, reflux, 2 h; ii) 1.1 equiv NMO, 0.05 equiv OsO_4, acetone/H_2O 10:1, 25 °C, 3 h, 81%; g) 1.7 equiv **9**, 1.6 equiv $SnCl_2$, CH_2Cl_2/Et_2O 1:1, 0 → 25 °C, 1 h, 77%; h) 8.0 equiv PhSH, 4.0 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, −35 °C, 2 h, 83%; i) 2.5 equiv Ac_2O, 4.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 → 25 °C, 1 h, 97%. DABCO = 1,4-diazabicyclo[2.2.2]octane.

compound, leading instead to decomposition of the trisaccharide. As a result, we returned to alcohol **73** and attempted the alternative pathway by which the phenylseleno group was to be introduced first. Scheme 9 summarizes this successful sequence.

Alcohol **73** was protected as a TIPS ether (TIPSOTf, 2,6-lutidine, 93%) affording compound **77**. The PMB groups were removed from the latter compound **77** by exposure to PhSH and $BF_3 \cdot Et_2O$ (83%) and acetate groups were installed in their place (Ac_2O, Et_3N, 4-DMAP, 98%), furnishing diacetate **79**. Exposure of diacetate **79** to nBuNH$_2$ led to selective cleavage of the C-1 acetate, liberating lactol **80** (91%) which was then converted to trichloroacetimidate[28] **81** by treatment with CCl_3CN in the presence of DBU. Addition of PhSeH[29] to **81** in the presence of $BF_3 \cdot Et_2O$ gave the desired β-phenylseleno glycoside **82** as expected from participation of the C-2 acetate (α:β ca. 1:9, 78% over two steps). The TIPS group was removed from **82** by exposure to nBu$_4$NF furnishing hydroxy phenylseleno glycoside **83** in 91% yield ready for the next coupling. Attachment of the evernitrose glycosyl fluoride **9** onto the A$_1$BC chain **83** proceeded smoothly under the influence of $SnCl_2$, and through a process in which the newly formed glycoside bond (B/A, α-anomer) was controlled by the anomeric effect, furnishing the desired A$_1$B(A)C assembly **84**, in 80% yield. The last two tasks included basic hydrolysis (NaOH/MeOH) of the acetate group from **84** furnishing the C-2 hydroxy compound **85** (91%) and treatment of the latter compound with DAST, leading to the targeted 2-phenylseleno glycosyl fluoride **2** in quantitative yield (100%). This last reaction proceeded with inversion of stereochemistry at C-2 of ring C (ca. 8:1 mixture of α:β anomers).



Scheme 9. Construction of A$_1$B(A)C fragment **2**. a) 1.2 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 1 h, 93%; b) 8.0 equiv PhSH, 4.0 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, −35 °C, 2 h, 83%; c) 2.5 equiv Ac_2O, 4.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 → 25 °C,1 h, 98%; d) 1.3 equiv nBuNH$_2$, THF, 25 °C, 5 h, 91%; e) 5.0 equiv CCl_3CN, 0.05 equiv DBU, CH_2Cl_2, 0 °C, 0.5 h; f) ca. 2.0 equiv PhSeH, 0.2 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, −78 °C, 1 h, 78% over two steps, α:β ca. 1:9; g) 1.2 equiv nBu$_4$NF, THF, 25 °C, 1 h, 91%; h) 2.0 equiv **9**, 1.2 equiv $SnCl_2$, CH_2Cl_2/Et_2O 1:1, 0 → 25 °C, 1 h, 80%; i) 0.3 equiv NaOH, MeOH/Et_2O 1:1, 25 °C, 1 h, 91%; j) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 20 min, 100%, α:β ca. 8:1. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

Conclusion

In this paper we described the design and synthesis of the A$_1$B(A)C fragment (**2**) of everninomicin 13,384-1 (**1**) in a suitably activated form for coupling with potential fragments for a possible total synthesis of the target molecule. Rings B and C were initially constructed from a common intermediate using an olefin metathesis reaction and the BC disaccharide unit was formed using a DAST promoted 1,2-thiophenyl migration and a subsequent coupling strategy. While formation of the aromatic ester and attachment of ring A were both successful, the anticipated CD orthoester formation dictated a need for a C-1 selenophenyl group, necessitating a revised strategy. Initial experiments indicated that the phenylselenium moiety had to be introduced before ring A, and the final sequence employed for the synthesis of **2** was both selective and efficient. In the following paper,[11] the development of strategies for orthoester construction and the assembly of the desired FGHA$_2$ fragment of everninomicin 13,384-1 (**1**) are described.

Experimental Section

General: All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran (THF), toluene and diethyl ether (ether) were distilled from sodium/benzophenone, and methylene chloride (CH_2Cl_2) from calcium hydride. Anhydrous solvents were also obtained by passing them through commercially available alumina columns. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at highest commercial quality and used without further purification unless otherwise stated. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel coated glass plates (60F-254) using UV light as visualizing agent and 7% ethanolic phosphomolybdic acid or p-anisaldehyde solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25, 0.50, or 1 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker DRX-600, AMX-500, AMX-400 or AC-250 instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to designate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin–Elmer

0947-6539/00/0617-3102 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

1600 series FT-IR spectrometer. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter. High resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions or an IonSpec mass spectrometer under matrix-assisted laser desorption/ionization fourier transform mass spectrometry (MALDI-FTMS) conditions with NBA or DHB as the matrix. Melting points (m.p.) are uncorrected and were recorded on a Thomas Hoover Unimelt capillary melting point apparatus.

Enol ether 16: Ethyl ester **15**[17] (11.20 g, 40.81 mmol) was dissolved in Et_2O (200 mL) and cooled to $-78\,^{\circ}C$. DIBAL (57.14 mL, 1.0 M solution in CH_2Cl_2, 57.14 mmol) was added dropwise via cannula while the temperature of the reaction mixture was maintained at $-78\,^{\circ}C$. After the addition was complete, the reaction mixture was stirred at $-78\,^{\circ}C$ for 50 min. Methanol (10 mL) was added at $-78\,^{\circ}C$ and was followed by addition of Et_2O (500 mL) and saturated aqueous sodium potassium tartrate solution (100 mL). The quenched reaction mixture was allowed to warm to 23 °C and stirred for 1 h. The organic layer was separated and the aqueous phase was extracted with Et_2O (3×100 mL). The combined organic phase was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude aldehyde was azotroped with benzene (2×10 mL) and then used crude. Ethyl vinyl ether (13.66 mL, 142.9 mmol, distilled from calcium hydride) was dissolved in THF (200 mL), cooled to $-78\,^{\circ}C$, and then *t*BuLi (72.0 mL, 122.40 mmol, 1.7 M in pentane) was added via cannula. The dark orange solution was allowed to warm to 0 °C over 1 h, at which time the solution was a pale yellow. The anion solution was cooled to $-100\,^{\circ}C$ and the crude aldehyde solution (dissolved in 100 mL THF and cooled to $-78\,^{\circ}C$) was added to the anion solution by fast addition via cannula. After stirring for 5 min, the reaction mixture was poured into saturated aqueous NH_4Cl (100 mL), diluted with ether (300 mL) and washed with H_2O (50 mL). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, $1\rightarrow10\%$ Et_2O in hexanes) yielded a 10:1 ratio of anti to *syn*-alcohols **16** (8.15 g, 66%) as colorless oils. **16**: $R_f=0.40$ (10% Et_2O in hexanes, 1% Et_3N); $[\alpha]_D^{22}=+11.6$ ($c=1.70$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3563$, 3482, 2942, 2867, 1665, 1625, 1382, 1294, 1226, 1147, 1095, 1066, 1017, 977, 938, 883, 813, 767, 679 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta=4.64$ (dd, $J=1.6$, 1.1 Hz, 1H, CH_2-*Z*), 4.31 (dq, $J=6.1$, 3.8 Hz, 1H, C*H*Me), 4.29 (br d, $J=1.9$ Hz, 1H, C*H*), 4.01 (d, $J=1.7$ Hz, 1H, CH_2-*E*), 3.43 (dq, $J=10.3$, 7.0 Hz, 2H, OCH_2), 2.51 (d, $J=2.8$ Hz, 1H, OH), 1.24 (d, $J=6.1$ Hz, 3H, Me), 1.05–0.99 (m, 24H, *i*Pr_3Si, OCH$_2$*Me*); ^{13}C NMR (125 MHz, C_6D_6): $\delta=161.5$, 81.7, 75.8, 70.2, 62.6, 18.2, 17.0, 14.4, 12.7; HRMS (FAB): calcd for $C_{16}H_{34}O_3Si$ $[M+H]^+$: 303.2355, found 303.2347.

Methyl ether 17: NaH (0.861 g, 21.53 mmol) was added to a solution of alcohol **16** (5.92 g, 19.57 mmol) in THF (200 mL) at 0 °C and the resulting mixture was stirred for 5 min. MeI (3.30 mL, 53.06 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 4 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (2.0 mL), diluted with Et_2O (1.0 L) and washed with saturated aqueous $NaHCO_3$ (2×50 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, $0\rightarrow20\%$ Et_2O in hexanes) to afford methyl ether **17** (5.94 g, 96%) as a colorless oil. **17**: $R_f=0.62$ (10% Et_2O in hexanes, 1% Et_3N); $[\alpha]_D^{22}=-7.1$ ($c=3.0$, $CHCl_3$); IR (thin film): $\tilde{\nu}=2941$, 2887, 1663, 1622, 1464, 1380, 1296, 1236, 1200, 1120, 1069, 1014, 883, 813, 764, 680 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta=4.32-4.31$ (m, 2H, CH_2-*Z*, C*H*Me), 4.00 (d, $J=1.4$ Hz, 1H, CH_2-*E*), 3.59 (d, $J=4.4$ Hz, 1H, C*H*), 3.43 (dq, $J=7.0$, 7.0 Hz, 2H, OCH_2), 3.29 (s, 3H, OMe), 1.38 (d, $J=6.2$ Hz, 3H, Me), 1.05–0.99 (m, 24H, *i*Pr_3Si, OCH$_2$*Me*); ^{13}C NMR (125 MHz, C_6D_6): $\delta=160.3$, 87.7, 83.4, 70.2, 62.8, 62.7, 57.7, 18.9, 18.5, 18.4, 18.3, 14.4, 13.0, 12.9, 12.8; HRMS (FAB): calcd for $C_{17}H_{37}O_3Si$ $[M+H]^+$: 317.2512, found 317.2527.

Oxime 18: 1 N aqueous HCl (25 mL) was added to solution of enol ether **17** (5.94 g, 18.79 mmol) in THF (100 mL) and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of Et_3N (30 mL), diluted with Et_2O (1.0 L) and washed with saturated aqueous $NaHCO_3$ (2×50 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, $0\rightarrow20\%$ Et_2O in hexanes) to afford the ketone (5.41 g, 100%) as a white foam. Ketone: $R_f=0.43$ (10% Et_2O in hexanes); $[\alpha]_D^{22}=-29.3$ ($c=5.8$, $CHCl_3$); IR (thin film): $\tilde{\nu}=2943$, 2867, 1717, 1464, 1380, 1352, 1248, 1200, 1144, 1105, 1065, 1022, 939, 883, 753, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=4.21$ (dq, $J=6.3$, 3.9 Hz, 1H, C*H*Me), 3.47 (d, $J=3.9$ Hz, 1H, C*H*), 3.40 (s, 3H, OMe), 2.16 (s, 3H, C(O)Me), 1.15 (d, $J=6.3$ Hz, 3H, Me), 1.03–0.99 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=210.4$, 91.8, 70.1, 58.9, 27.3, 19.4, 17.9, 12.4; HRMS (FAB): calcd for $C_{15}H_{33}O_3Si$ $[M+H]^+$: 289.2200, found 289.2207. $BnONH_2\cdot HCl$ (2.50 g, 15.63 mmol) was added to a solution of the ketone (4.10 g, 14.21 mmol) in pyridine (30 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of H_2O (10 mL), diluted with Et_2O (700 mL) and washed with saturated aqueous $NaHCO_3$ (70 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, $0\rightarrow20\%$ Et_2O in hexanes) to afford oximes **18** (5.09 g, 91%, *E*:*Z* ca. 4:1) as colorless oils. **18**: $R_f=0.56$ (10% Et_2O in hexanes); IR (thin film): $\tilde{\nu}=2942$, 2866, 1496, 1464, 1367, 1247, 1199, 1128, 1015, 938, 883, 755, 678 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, *E*:*Z* ca. 4:1): $\delta=7.39-7.28$ (m, 5H, ArH), 5.16, 5.13 (AB, $J=12.5$ Hz, 2H, CH$_2$Ar-*E*), 5.07, 5.04 (AB, $J=12.5$ Hz, 2H, CH$_2$Ar-*Z*), 4.56 (d, $J=3.8$ Hz, 1H, C*H*-*Z*), 4.20 (dq, $J=6.3$, 3.8 Hz, 1H, C*H*Me-*Z*), 4.08 (dq, $J=6.3$, 6.1 Hz, 1H, C*H*Me-*E*), 3.47 (d, $J=6.4$ Hz, 1H, C*H*-*E*), 3.35 (s, 3H, OMe-*Z*), 3.25 (s, 3H, OMe-*E*), 1.90 (s, 3H, C(N)Me-*Z*), 1.89 (s, 3H, C(N)Me-*E*), 1.25 (d, $J=6.1$ Hz, 3H, Me-*E*), 1.19 (d, $J=6.3$ Hz, 3H, Me-*Z*), 1.07–1.03 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=158.4$, 156.9, 138.1, 138.0, 128.2, 128.2, 127.9, 127.7, 127.5, 87.2, 80.9, 75.8, 75.6, 69.2, 68.8, 58.5, 56.8, 20.8, 19.2, 18.1, 18.0, 12.7, 12.4, 10.7; HRMS (FAB): calcd for $C_{22}H_{40}NO_3Si$ $[M+H]^+$: 394.2777, found 394.2789.

Olefin 19: Oxime **18** (4.20 g, 10.67 mmol) was dissolved in Et_2O (60 mL) and cooled to $-35\,^{\circ}C$. Allylmagnesium bromide (26.67 mL, 26.67 mmol, 1.0 M in Et_2O) was added dropwise and the reaction was stirred for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (300 mL) and washed with H_2O (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, $0\rightarrow20\%$ Et_2O in hexanes) to afford olefin **19** (4.04 g, 87%) as a colorless oil. **19**: $R_f=0.35$ (50% CH_2Cl_2 in hexanes); $[\alpha]_D^{22}=-2.0$ ($c=3.3$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3071$, 2943, 2866, 1639, 1464, 1383, 1366, 1246, 1138, 1107, 1061, 1003, 912, 883, 750, 681 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.35-7.27$ (m, 5H, ArH), 5.96–5.95 (m, 1H, A1), 5.85 (br s, 1H, NH), 5.10 (br d, $J=15.7$ Hz, 1H, CH_2-*Z*), 5.10 (br d, $J=11.9$ Hz, 1H, CH_2-*E*), 4.77, 4.72 (AB, $J=11.7$ Hz, 2H, CH$_2$Ar), 4.20 (dq, $J=6.2$, 1.3 Hz, 1H, A5), 3.59 (s, 3H, OMe), 3.53 (br d, $J=1.3$ Hz, 1H, A4), 2.53 (br dd, $J=13.8$, 6.5 Hz, 1H, A2), 2.23 (dd, $J=13.8$, 8.0 Hz, 1H, A2), 1.28 (d, $J=6.2$ Hz, 3H, A6), 1.10–1.09 (m, 21H, *i*Pr_3Si), 0.96 (s, 3H, Me(A3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=138.3$, 134.9, 128.2, 128.0, 127.5, 117.3, 87.4, 76.3, 70.0, 62.4, 61.0, 39.6, 19.4, 18.2, 18.2, 18.1, 12.5; HRMS (FAB): calcd for $C_{25}H_{46}NO_3Si$ $[M+H]^+$: 436.3325, found 436.3261.

Alcohol 20: *n*Bu_4NF (8.64 mL, 1 M in THF, 8.64 mmol) was added to a solution of olefin **19** (3.43 g, 7.85 mmol) in THF (40 mL) and the resulting mixture was stirred at 25 °C for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (300 mL) and washed with H_2O (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, $0\rightarrow50\%$ Et_2O in hexanes) to afford alcohol **20** (2.02 g, 92%) as a white foam. **20**: $R_f=0.16$ (30% Et_2O in hexanes); $[\alpha]_D^{22}=+73.3$ ($c=0.40$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3356$, 3070, 3030, 2977, 2933, 2831, 1639, 1496, 1454, 1368, 1317, 1276, 1191, 1108, 1001, 967, 912, 748, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.35-7.27$ (m, 5H, ArH), 5.86–5.78 (m, 1H, A1), 5.85 (br s, 2H, NH, OH), 5.08 (br d, $J=9.7$ Hz, 1H, CH_2-*E*), 5.06 (br d, $J=16.9$ Hz, 1H, CH_2-*Z*), 4.81, 4.67 (AB, $J=11.6$ Hz, 2H, CH$_2$Ar), 3.92 (dq, $J=7.9$, 6.2 Hz, 1H, A5), 3.47 (s, 3H, OMe), 3.07 (d, $J=7.9$ Hz, 1H, A4), 2.40 (br dd, $J=14.0$, 6.5 Hz, 1H, A2), 2.24 (dd, $J=14.0$, 8.4 Hz, 1H, A2), 1.29 (d, $J=6.2$ Hz, 3H, A6), 1.24 (s, 3H, Me (A3)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=137.0$, 133.4, 128.3, 128.2, 128.1, 127.8, 118.7, 86.4, 76.0, 68.7, 63.4, 61.3, 37.0, 21.0, 20.0; HRMS (FAB): calcd for $C_{16}H_{26}NO_3$ $[M+H]^+$: 280.1913, found 280.1918.

TMS ether 21: TMSCl (0.020 mL, 0.200 mmol) was added to a solution of alcohol **20** (2.00 g, 7.16 mmol) and $(TMS)_2NH$ (4.42 mL, 35.79 mmol) in MeCN (50 mL) at 0 °C and the resulting mixture was stirred for 15 min. The solvents were removed under reduced pressure and the residue was diluted with Et_2O (500 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure to afford crude TMS ether **21** (2.76 g, 100%) as a colorless oil. **21**: $R_f=0.63$

(20% Et_2O in hexanes); $[\alpha]_D^{22} = +6.8$ ($c = 1.70$, $CHCl_3$); IR (thin film): $\tilde{\nu} =$ 3070, 2954, 2833, 1638, 1496, 1453, 1366, 1251, 1109, 1057, 1003, 977, 841, 748, 697 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 7.32$ (d, $J = 7.0$ Hz, 2H, ArH), 7.18–7.15 (m, 2H, ArH), 7.09 (t, $J = 7.0$ Hz, 1H, ArH), 6.17–6.11 (m, 1H, A1), 6.05 (br s, 1H, NH), 5.19 (br d, $J = 17.5$ Hz, 1H, CH_2-*Z*), 5.11 (br d, $J = 10.5$ Hz, 1H, CH_2-*E*), 4.72, 4.67 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.06 (dq, $J = 6.5$, 4.0 Hz, 1H, A5), 3.44 (s, 3H, OMe), 3.41 (d, $J = 4.0$ Hz, 1H, A4), 2.64 (br dd, $J = 15.0$, 10.0 Hz, 1H, A2), 2.46 (br dd, $J = 15.0$, 10.0 Hz, 1H, A2), 1.28 (d, $J = 6.5$ Hz, 3H, A6), 1.07 (s, 3H, Me (A3)), 0.09 (s, 9H, Me_3Si); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 139.0$, 135.9, 128.5, 128.5, 128.3, 127.7, 116.8, 87.4, 76.8, 70.2, 63.1, 61.0, 39.7, 20.6, 18.3, 0.5; HRMS (FAB): calcd for $C_{19}H_{34}NO_3Si$ $[M+H]^+$: 352.2308, found 352.2319.

Ozonide 22: (Analytical sample) O_3 was bubbled through a solution of olefin **21** (0.028 g, 0.080 mmol) in isooctane/CCl_4 (2:1, 5 mL) at $-78\,^\circ C$ for 1 h. The solution and warmed to 25 °C, the solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 50% Et_2O in hexanes) to afford ozonide **22** as a white foam. **22**: $R_f = 0.24$ (10% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2956$, 2895, 2839, 1548, 1454, 1390, 1372, 1352, 1253, 1187, 1109, 1055, 1010, 966, 909, 844, 752 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 1:1 mixture of diastereoisomers): $\delta = 5.25$, 5.24 (t, $J = 6.0$ Hz, 1H, A1), 5.13, 5.05, 5.05, 5.05 (4 × s, 1H, OCH_2O), 3.77, 3.76 (2 × dq, $J = 6.0$, 3.0 Hz, 1H, A5), 3.53, 3.51 (2 × d, $J =$ 8.0 Hz, 1H, A4), 3.42, 3.40 (2 × s, 3H, OMe), 2.65, 2.60 (2 × dd, $J = 15.0$, 4.0 Hz, 1H, A2), 2.46, 2.44 (2 × dd, $J = 15.0$, 1.5 Hz, 1H, A2), 1.64, 1.61 (2 × s, 3H, Me (A3)), 1.26, 1.26 (2 × d, $J = 6.0$ Hz, 3H, A6), 0.11, 0.10 (2 × s, 9H, Me_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 100.5$, 94.0, 93.7, 90.9, 90.8, 89.5, 89.4, 69.4, 61.9, 61.9, 37.8, 37.2, 21.4, 19.0, 18.4, 0.4; HRMS (FAB): calcd for $C_{12}H_{25}NO_7SiNa$ $[M+Na]^+$: 346.1298, found 346.1313.

Lactol 23: O_3 was bubbled through a solution of olefin **21** (2.76 g, 7.85 mmol) in isooctane/CCl_4 (2:1, 150 mL) at $-78\,^\circ C$ for 1 h. TFA (2.0 mL, 15.70 mmol) was added and the solution was warmed to 25 °C and stirred for 1 h. The reaction mixture was recooled to $-78\,^\circ C$ and Ph_3P (4.12 g, 15.70 mmol) was added. The reaction mixture was warmed slowly to 25 °C and stirred for 12 h. 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 lactol **23** (1.32 g, 82% over three steps) as a white solid. **23**: $R_f = 0.25$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -31.5$ ($c =$ 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3381$, 2987, 2942, 2842, 1548, 1455, 1393, 1354, 1285, 1183, 1155, 1102, 1046, 988, 942, 913, 876, 857 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 1:1): $\delta = 5.32$ (d, $J = 4.0$ Hz, 1H, A1α), 4.88 (dd, $J = 7.3$, 4.0 Hz, 1H, A1β), 3.91 (dq, $J = 9.4$, 6.5 Hz, 1H, A5), 3.84 (br s, 1H, OH), 3.76 (d, $J = 9.5$ Hz, 1H, A4), 3.74 (d, $J = 9.5$ Hz, 1H, A4), 3.46 (dq, $J = 9.5$, 6.0 Hz, 1H, A5), 3.41 (s, 3H, OMe), 3.39 (s, 3H, OMe), 3.15 (br s, 1H, OH), 2.41 (dd, $J = 13.5$, 4.5 Hz, 1H, A2), 2.27–2.20 (m, 2H, A2), 2.17 (dd, $J = 13.5$, 1.5 Hz, 1H, A2), 1.81 (s, 3H, Me (A3)), 1.66 (s, 3H, Me (A3)), 1.36 (d, $J = 6.5$ Hz, 3H, A6), 1.31 (d, $J = 6.0$ Hz, 3H, A6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 92.4$, 90.6, 90.1, 89.6, 84.5, 84.2, 71.2, 66.1, 66.0, 66.0, 60.8, 60.8, 44.2, 40.8, 18.5, 18.4, 18.3, 16.6; HRMS (FAB): calcd for $C_8H_{15}NO_5Na$ $[M+Na]^+$: 228.0848, found 228.0848.

Ring A glycosyl fluoride 9: DAST (0.02 mL, 0.15 mmol) was added to a solution of lactol **23** (0.021 g, 0.10 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C. After stirring for 20 min, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL), diluted with CH_2Cl_2 (10 mL), and stirred for 5 min. The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (10 mL), and the combined organic layer was dried ($MgSO_4$), filtered and the solvents were removed under reduced pressure. The residue was azeotroped with benzene (2 mL), dried under vacuum for 1 h, and used crude in the next reaction.

Acid 26: $NaH_2PO_4 \cdot H_2O$ (9.86 g, 82.18 mmol, dissolved in 25 mL H_2O) was added to a solution of aldehyde **25**[22] (5.0 g, 32.86 mmol) in DMSO (100 mL) at 0 °C. $NaClO_2$ (7.13 g, 78.36 mmol, dissolved in 25 mL H_2O) was then added and the resulting mixture was warmed slowly to 25 °C and stirred for 12 h. The reaction mixture was diluted with saturated aqueous Na_2CO_3 (50 mL) and washed with EtOAc (20 mL). The aqueous layer was then acidified to pH 1 with aqueous HCl and stored at 0 °C for 12 h. The reaction mixture was filtered and the solid was washed with ice water to afford carboxylic acid **26** (4.39 g, 80%) as a white solid. **26**: $R_f = 0.16$ (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 3500-2500$, 1635, 1459, 1364, 1264, 1211, 1173 cm^{-1}; ^1H NMR (600 MHz, CD_3OD): $\delta = 6.19$ (s, 2H, ArH), 2.47 (s, 3H, Me); ^{13}C NMR (125 MHz, CD_3OD): $\delta = 173.7$, 165.1, 161.8, 144.3, 111.3, 100.4, 23.6; HRMS (FAB): calcd for $C_8H_9O_4$ $[M+H]^+$: 169.0501, found 169.0494.

Benzyl ester 27: DEAD (6.03 mL, 38.27 mmol) was added to a solution of acid **26** (3.14 g, 18.67 mmol), BnOH (3.96 mL, 38.27 mmol), and Ph_3P (10.06 g, 38.27 mmol) in THF (100 mL) at 0 °C and the resulting mixture was stirred for 4 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 60% Et_2O in hexanes) to afford benzyl ester **27** (4.87 g, 75%) as a colorless oil. **27**: $R_f = 0.60$ (60% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 3200$, 2933, 1649, 1610, 1578, 1455, 1324, 1280, 1211, 1170, 1027 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 11.68$ (s, 1H, OH), 7.45–7.35 (m, 10H, ArH), 6.41 (d, $J = 3.2$ Hz, 1H, ArH), 6.36 (d, $J = 3.2$ Hz, 1H, ArH), 5.39 (s, 2H, CH_2Ar), 5.06 (s, 2H, CH_2Ar), 2.49 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.5$, 143.3, 128.6, 128.4, 128.2, 127.5, 111.8, 99.7, 69.9, 67.0, 24.7; HRMS (MALDI): calcd for $C_{22}H_{21}O_4$ $[M+H]^+$: 349.1440, found 349.1433.

Bis-chlorobenzyl ester 28: Cl_2 (15.51 mL, 1M in AcOH, 15.51 mmol) was added to a solution of benzyl ester **27** (1.80 g, 5.17 mmol) and NaOAc (0.95, 11.61 mmol) in AcOH (25 mL) at $-50\,^\circ C$ and the resulting mixture was slowly warmed to 0 °C and stirred for 3 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (100 mL), diluted with CH_2Cl_2 (500 mL) and washed with saturated aqueous $NaHCO_3$ (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 → 50% Et_2O in hexanes) to afford bis-chlorobenzyl ester **28** (1.52 g, 70%) as a white solid. **28**: $R_f = 0.40$ (40% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2975$, 1752, 1670, 1543, 1380, 1301, 1223, 1099, 949 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): $\delta =$ 11.47 (s, 1H, OH), 7.59–7.26 (m, 10H, ArH), 5.44 (s, 2H, CH_2Ar), 5.06 (s, 2H, CH_2Ar), 2.61 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.3$, 157.5, 155.5, 137.9, 135.9, 134.4, 128.9, 128.8, 128.7, 128.6, 128.5, 122.0, 115.6, 111.2, 74.7, 68.2; HRMS (FAB): calcd for $C_{22}H_{19}Cl_2O_4$ $[M+H]^+$: 417.0660, found 417.0674.

Methyl ether 29: CH_2N_2 (excess, solution in Et_2O) was added to a solution of phenol **28** (1.50 g, 3.58 mmol) in Et_2O (25 mL) at 0 °C and the resulting mixture was stirred for 12 h in the dark. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 50% Et_2O in hexanes) to afford methyl ether **29** (1.55 g, 100%) as a white solid. **29**: $R_f = 0.48$ (20% EtOAc in hexanes); IR (thin film): $\tilde{\nu} = 2975$, 1723, 1456, 1369, 1267, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.58-7.37$ (m, 10H, ArH), 5.40 (s, 2H, CH_2Ar), 5.03 (s, 2H, CH_2Ar), 3.79 (s, 3H, OMe), 2.61 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 136.1$, 128.8, 128.7, 128.5, 74.9, 67.7, 62.2, 17.4; HRMS (FAB): calcd for $C_{23}H_{20}Cl_2O_4Na$ $[M+Na]^+$: 453.0636, found 453.0626.

Benzyl alcohol 30: DIBAL (4.15 mL, 1.0M in CH_2Cl_2, 4.15 mmol) was added to a solution of benzyl ester **29** (1.50 g, 3.46 mmol) in CH_2Cl_2 (20 mL) at $-78\,^\circ C$ and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (500 mL) and washed with saturated aqueous NH_4Cl (50 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 → 80% Et_2O in hexanes) to afford benzyl alcohol **30** (1.02 g, 90%) as a white solid. The same conditions were used with methyl ester **48**. **30**: $R_f = 0.56$ (50% EtOAc in hexanes); IR (thin film): $\tilde{\nu} = 3367$, 2940, 1561, 1450, 1397, 1374, 1326, 1199, 1102, 996, 950, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.59-7.37$ (m, 5H, ArH), 5.02 (s, 2H, CH_2Ar), 4.78 (d, $J = 6.0$ Hz, 2H, CH_2OH), 3.91 (s, 3H, OMe), 2.49 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 136.2$, 136.1, 130.2, 128.4, 74.6, 65.7, 62.0, 57.6, 16.3, 15.2; HRMS (FAB): calcd for $C_{16}H_{16}Cl_2O_3Na$ $[M+Na]^+$: 349.0374, found 349.0386.

Aldehyde 31: PDC (3.19 g, 8.47 mmol) was added to a solution of benzyl alcohol **30** (1.00 g, 2.82 mmol) and 3 Å MS in CH_2Cl_2 (15 mL) at 25 °C and the resulting mixture was stirred for 3 h. The reaction mixture was filtered 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 aldehyde **31** (0.82 g, 90%) as a white foam. **31**: $R_f = 0.63$ (20% EtOAc in hexanes); IR (thin film): $\tilde{\nu} = 2957$, 1698, 1559, 1542, 1448, 1365, 1312, 1188, 1093, 948 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 10.44$ (s, 1H, CHO), 7.56–7.38 (m, 5H, ArH), 5.09 (s, 2H, CH_2Ar), 3.96 (s, 3H, OMe), 2.66 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 190.1$, 156.0,

0947-6539/00/0617-3104 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

138.8, 135.8, 128.6, 128.5, 126.3, 75.0, 63.2, 16.8; HRMS (FAB): calcd for $C_{16}H_{15}Cl_2O_3$ $[M+H]^+$: 325.0398, found 325.0404.

Aromatic acid 32: $NaClO_2$ (0.67 g, 7.41 mmol) was added to a solution of aldehyde **31** (0.80 g, 2.47 mmol), $NaH_2PO_4 \cdot H_2O$ (0.89 g, 7.41 mmol), and 2-methyl-2-butene (4.94 mL, 2 M in CH_2Cl_2, 9.88 mmol) in *t*BuOH/H_2O (1:1, 15 mL) at 25 °C and the resulting mixture was stirred for 3 h. The reaction mixture was diluted with saturated aqueous Na_2CO_3 (50 mL) and washed with EtOAc (20 mL). The aqueous layer was then acidified to pH 1 with 5 % aqueous HCl and extracted with EtOAc (300 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 acid **32**[10c] (0.80 g, 95 %) as a white solid. **32**: $R_f = 0.18$ (50 % EtOAc in hexanes); IR (thin film): $\tilde{\nu} = 3397, 2947, 1701, 1657, 1284, 1098\ cm^{-1}$; ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.57-7.40$ (m, 5H, ArH), 5.06 (s, 2H, CH_2Ar), 3.97 (s, 3H, OMe), 2.47 (s, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.2, 153.6, 153.4, 136.0, 133.9, 128.5, 126.4, 125.9, 121.8, 74.9, 62.5, 17.7$; HRMS (ESI): calcd for $C_{16}H_{14}Cl_2O_4$ $[M+Na]^+$: 363, found 363.

Acyl fluoride 7: $(Me_2N)_2CF^+PF_6^-$ (0.411 g, 1.56 mmol) was added to a solution of acid **32** (0.354 g, 1.04 mmol) and diisopropylethylamine (0.36 mL, 2.08 mmol) in CH_2Cl_2 (5 mL) at 0 °C and the resulting mixture was stirred for 2 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford acyl fluoride **7** (0.345 g, 97 %) as a white solid. **7**: $R_f = 0.92$ (50 % Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2957, 1813, 1559, 1457, 1390, 1370, 1327, 1225, 1101, 936, 902\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.57-7.41$ (m, 5H, ArH), 5.08 (s, 2H, CH_2Ar), 3.97 (s, 3H, OMe), 2.46 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 156.9, 154.8, 154.1, 135.7, 135.4, 128.7, 128.5, 128.5, 126.6, 122.2, 121.5, 121.1, 75.1, 62.5, 17.9$; HRMS (FAB): calcd for $C_{16}H_{13}Cl_2FO_3Na$ $[M+Na]^+$: 365.0124, found 365.0118.

Di-olefin 13: $LiEt_3BH$ (7.28 mL, 1.0 M solution in THF, 7.28 mmol) was added dropwise to a solution of epoxide **14**[24] (1.30 g, 6.07 mmol) in THF (50 mL) at −40 °C and the reaction mixture was stirred for 1 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (50 mL), diluted Et_2O (100 mL), and washed with brine (30 mL). The organic layer was dried ($MgSO_4$) 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 the alcohol (1.2 g, 91 %) as a colorless oil. alcohol: $R_f = 0.37$ (25 % Et_2O in hexanes); $[\alpha]_D^{22} = +12.0$ ($c = 0.08$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3447, 2956, 2929, 2857, 1473, 1253, 1080, 1026, 925, 835, 776\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.80$ (ddd, $J = 17.2, 10.5, 6.7$ Hz, 1H, H2), 5.21 (m, 2H, H1), 3.99 (m, 1H, H3), 3.72 (dq, $J = 6.5, 3.2$ Hz, 1H, H4), 2.17 (d, $J = 4.5$ Hz, 1H, OH), 1.10 (d, $J = 6.5$ Hz, 3H, H5), 0.89 (s, 9H, *t*BuSi), 0.07, 0.04 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 137.0, 117.1, 78.0, 70.6, 25.8, 18.1, 17.4, -4.3, -5.0$; HRMS (MALDI): calcd for $C_{11}H_{24}O_2SiNa$ $[M+Na]^+$: 239, found 239. Acryloyl chloride (0.53 mL, 6.49 mmol) was added dropwise to a solution of the above alcohol (1.17 g, 5.41 mmol), Et_3N (1.13 mL, 8.11 mmol) and 4-DMAP (0.132 g, 1.08 mmol) in CH_2Cl_2 (30 mL) at 0 °C over 15 min. The resulting mixture was stirred for 15 min and then the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), diluted with CH_2Cl_2 (200 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 → 50 % Et_2O in hexanes) to afford di-olefin **13** (1.39 g, 95 %) as a colorless oil. **13**: $R_f = 0.74$ (25 % Et_2O in hexanes); $[\alpha]_D^{22} = +33.7$ ($c = 0.86$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2986, 2957, 2858, 1724, 1638, 1620, 1471, 1405, 1296, 1254, 1197, 1034, 988, 929, 836\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.39$ (dd, $J = 17.2$, 1.6 Hz, 1H, H8), 6.09 (dd, $J = 17.2$, 10.4 Hz, 1H, H7), 5.82–5.74 (m, 2H, H2, H8), 5.28 (ddd, $J = 17.2$, 1.7, 1.6 Hz, 1H, H1), 5.15 (ddd, $J = 10.4$, 1.6, 1.6 Hz, 1H, H1), 4.92 (dq, $J = 6.4$, 3.5 Hz, 1H, H4), 4.25 (m, 1H, H3), 1.20 (d, $J = 6.4$ Hz, 3H, H5), 0.89 (s, 9H, *t*BuSi), 0.04, 0.01 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.7, 137.5, 130.5, 128.9, 91.7, 75.0, 73.5, 25.7, 18.2, 13.7, -4.6, -4.9$; HRMS (ESI): calcd for $C_{14}H_{27}O_3SiNa$ $[M+Na]^+$: 271, found 271.

Lactone 33: Grubb's catalyst (0.143 g, 0.17 mmol) was added to a solution of ester **13** (0.94 g, 3.48 mmol) in degassed CH_2Cl_2 (120 mL) at 25 °C. The resulting mixture was heated to 35 °C and stirred for 10 h. Another portion of catalyst was added and stirring continued for a total of 24 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 30 % Et_2O in hexanes) to afford the lactone **33** (0.76 g, 90 %) as a colorless oil. **33**: $R_f = 0.26$ (20 % Et_2O in hexanes); $[\alpha]_D^{22} = +35.5$ ($c = 0.47$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2955, 2858, 1736, 1469, 1385, 1284, 1239, 1133, 1028, 966, 941, 881, 841\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.70$ (br dd, $J = 10.0$, 2.1 Hz, 1H, H2), 5.92 (br dd, $J = 10.0$, 2.1 Hz, 1H, H3), 4.28 (dq, $J = 9.5$, 6.4 Hz, 1H, H5), 4.21 (ddd, $J = 9.5$, 2.0, 2.0 Hz, 1H, H4), 1.41 (d, $J = 6.5$ Hz, 3H, H6), 0.91 (s, 9H, *t*BuSi), 0.12, 0.11 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 163.3, 150.3, 119.8, 79.1, 68.8, 25.5, 18.1, -4.4, -4.9$; HRMS (FAB): calcd for $C_{12}H_{22}O_3SiNa$ $[M+Na]^+$: 265.1236, found 265.1230.

Lactol 34: DIBAL (0.77 mL, 1.0 M in CH_2Cl_2, 0.77 mmol) was added to a solution of lactone **33** (0.069 g, 0.247 mmol) in CH_2Cl_2 (3 mL) at −78 °C and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by the addition of MeOH (2 mL), diluted with CH_2Cl_2 (100 mL) and washed with saturated aqueous NH_4Cl (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 → 80 % Et_2O in hexanes) to afford lactol **34** (0.062 g, 90 %) as a white solid. **34**: $R_f = 0.42$ (40 % Et_2O in hexanes); $[\alpha]_D^{22} = +39.1$ ($c = 0.43$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3384, 2956, 2939, 2857, 1467, 1384, 1256\ 1096, 1007, 941, 881, 836\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 3:1): $\delta =$ 5.86 (br d, $J = 10.5$ Hz, 1H, H2), 5.83 (br dd, $J = 10.5$, 8.5 Hz, 1H, H2), 5.72 (ddd, $J = 10.5$, 1.5, 1.5 Hz, 1H, H3), 5.72 (ddd, $J = 10.5$, 1.5, 1.5 Hz, 1H, H3), 5.38 (d, $J = 8.5$ Hz, 1H, H1), 5.33 (br s, 1H, H1), 3.96 (dddd, $J = 8.5$, 2.0, 2.0, 2.0 Hz, 1H, H4), 3.86 (dddd, $J = 8.5$, 2.0, 2.0, 2.0 Hz, 1H, H4), 3.81 (dq, $J =$ 8.5, 6.0 Hz, 1H, H5), 3.56 (dq, $J = 8.5$, 6.0 Hz, 1H, H5), 1.30 (d, $J = 6.0$ Hz, 3H, H6), 1.25 (d, $J = 6.0$ Hz, 3H, H6), 0.89 (s, 18H, *t*BuSi), 0.10, 0.09 (2 × s, 2 × 6H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 134.8, 134.2, 128.6, 126.1, 92.1, 88.9, 74.8, 69.9, 69.6, 67.7, 25.7, 18.2, -4.3, -4.7$; HRMS (FAB): calcd for $C_{12}H_{24}O_3SiNa$ $[M+Na]^+$: 267.1392, found 267.1384.

Triol 35: OsO_4 (0.10 mL, 2.5 % solution in *t*BuOH) was added to a solution of lactol **34** (0.055 g, 0.22 mmol) and NMO (0.039 g, 0.33 mmol) in acetone/H_2O (10:1, 3 mL) and the reaction mixture was stirred for 12 h at 25 °C. 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), 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 triol **35** (0.056 g, 90 %) as a white foam. **35**: $R_f = 0.31$ (80 % Et_2O in hexanes); $[\alpha]_D^{22} = +26.7$ ($c = 1.16$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3388, 2954, 2931, 2857, 1253, 1111, 1064, 979, 873, 837\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 3:1): $\delta = 5.18$ (s, 1H, H1), 4.75 (s, 1H, H1), 3.95 (br s, 2H, H2), 3.87 (dq, $J = 8.5$, 6.0 Hz, 1H, H5), 3.77 (dd, $J = 8.7$, 3.3 Hz, 1H, H3), 3.49–3.45 (m, 2H, H3, H4), 3.37 (dd, $J =$ 9.0, 8.5 Hz, 1H, H4), 3.30 (dq, $J = 9.0$, 6.0 Hz, 1H, H5), 1.28 (d, $J = 6.0$ Hz, 3H, H6), 1.24 (d, $J = 6.0$ Hz, 3H, H6), 0.89 (s, 18H, *t*BuSi), 0.13, 0.10 (2 × s, 2 × 6H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 94.0, 93.9, 74.6, 74.3, 72.6, 71.6, 71.6, 71.4, 68.6, 65.9, 25.9, 18.2, -3.7, -4.4$; HRMS (FAB): calcd for $C_{12}H_{26}O_5SiNa$ $[M+Na]^+$: 301.1447, found 301.1440.

Triacetate 36: Ac_2O (0.175 mL, 1.73 mmol) was added to a solution of triol **35** (0.120 g, 0.43 mmol), Et_3N (0.36 mL, 2.59 mmol), and 4-DMAP (0.011 g, 0.09 mmol) in CH_2Cl_2 (2 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of MeOH (1 mL), diluted with CH_2Cl_2 (200 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 → 80 % Et_2O in hexanes) to afford triacetate **36** (0.173 g, 99 %) as a white foam. **36**: $R_f = 0.47$ (50 % Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2933, 2858, 1751, 1471, 1368, 1226, 1109, 972, 922, 838, 779\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 1.4:1): $\delta = 5.96$ (d, $J = 2.0$ Hz, 1H, H1), 5.83 (d, $J = 1.0$ Hz, 1H, H1), 5.46 (br d, $J = 3.0$ Hz, 1H, H2), 5.25 (dd, $J = 3.0$, 2.0 Hz, 1H, H2), 5.08 (dd, $J = 9.5$, 3.0 Hz, 1H, H3), 4.85 (dd, $J = 9.5$, 3.0 Hz, 1H, H3), 3.80 (dq, $J = 9.5$, 6.0 Hz, 1H, H5), 3.69 (t, $J = 9.0$ Hz, 1H, H4), 3.65 (t, $J = 9.0$ Hz, 1H, H4), 3.51 (dq, $J = 9.5$, 6.0 Hz, 1H, H5), 2.18 (s, 3H, OAc), 2.16 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 6H, OAc), 1.35 (d, $J = 6.5$ Hz, 3H, H6), 1.30 (d, $J = 6.5$ Hz, 3H, H6), 0.87, 0.86 (2 × s, 2 × 9H, *t*BuSi), 0.11, 0.10, 0.07, 0.06 (4 × s, 4 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.3, 170.0, 169.9, 169.8, 168.7, 168.4, 90.8, 90.2, 74.0, 73.8, 71.9, 71.3, 70.9, 70.8, 68.9, 31.5, 25.6, 21.0, 20.9, 20.9, 20.7, 18.2, 18.0, 14.0, -4.2, -4.4$; HRMS (FAB): calcd for $C_{18}H_{32}O_8SiNa$ $[M+Na]^+$: 427.1764, found 427.1776.

  0947-6539/00/0617-3105 $ 17.50+.50/0

Thioglycoside 37: $BF_3 \cdot Et_2O$ (0.010 mL, 0.084 mmol) was added to a solution of triacetate **36** (0.170 g, 0.42 mmol) and PhSH (0.065 mL, 0.63 mmol) in CH_2Cl_2 (2 mL) at $-20\,^{\circ}C$ and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by the addition of Et_3N (2 mL), 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, $0 \rightarrow 5\%$ Et_2O in hexanes) to afford thioglycoside **37** (0.134 g, 69%) as a white foam. **37**: $R_f = 0.51$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +66.5$ ($c = 0.90$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2932, 2857, 1751, 1369, 1235, 1106, 838, 778, 739\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.48-7.25$ (m, 5H, ArH), 5.51 (dd, $J = 3.0$, 1.5 Hz, 1H, H2), 5.34 (d, $J = 1.5$ Hz, 1H, H1), 5.06 (dd, $J = 9.5$, 3.0 Hz, 1H, H3), 4.21 (dq, $J = 9.5$, 6.5 Hz, 1H, H5), 3.71 (t, $J = 9.5$ Hz, 1H, H4), 2.11 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.31 (d, $J = 6.5$ Hz, 3H, H6), 0.87 (s, 9H, *t*BuSi), 0.11, 0.08 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.0$, 169.9, 133.7, 132.0, 131.8, 129.1, 127.7, 86.0, 85.6, 72.7, 71.6, 71.5, 70.3, 26.0, 21.0, 18.2, -4.1, -4.4; HRMS (FAB): calcd for $C_{22}H_{34}O_6SSiNa$ $[M+Na]^+$: 477.1743, found 477.1725.

Diol 12: K_2CO_3 (8 mg, 0.06 mmol) was added to a solution of bis-acetate **37** (0.13 g, 0.29 mmol) in MeOH/Et_2O (1:1, 1 mL) at 25 °C and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (1 mL), diluted with Et_2O (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, $0 \rightarrow 70\%$ Et_2O in hexanes) to afford diol **12** (0.103 g, 97%) as a white foam. **12**: $R_f = 0.24$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +224.0$ ($c = 0.92$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3420, 2930, 2856, 1582, 1474, 1384, 1283, 1104, 976, 882, 839\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.48-7.25$ (m, 5H, ArH), 5.47 (d, $J =$ 1.5 Hz, 1H, H1), 4.19 (br s, 1H, H2), 4.10 (dq, $J = 9.0$, 6.0 Hz, 1H, H5), 3.75 (ddd, $J = 9.0$, 5.5, 3.5 Hz, 1H, H3), 3.54 (t, $J = 9.0$ Hz, 1H, H4), 2.62 (d, $J =$ 3.5 Hz, 1H, OH), 2.32 (d, $J = 6.0$ Hz, 1H, OH), 1.27 (d, $J = 6.0$ Hz, 3H, H6), 0.92 (s, 9H, *t*BuSi), 0.16, 0.12 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 134.1$, 131.4, 131.4, 129.0, 129.0, 127.0, 87.5, 74.9, 72.6, 69.8, 25.9, 18.2, 17.9, -3.8, -4.5; HRMS (FAB): calcd for $C_{18}H_{30}O_4SSiNa$ $[M+Na]^+$: 393.1532, found 393.1541.

PMB ether 38: nBu_2SnO (0.27 g, 1.08 mmol) was added to a solution of diol **12** (0.365 g, 0.98 mmol) in toluene (30 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 (0.20 mL, 1.48 mmol) and nBu_4NI (0.036 g, 0.10 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 (1 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 ring B alcohol **38** (0.445 g, 92%) as a white foam. **38**: $R_f = 0.38$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +174.6$ ($c = 1.5$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3475, 2955, 2931, 2856, 1612, 1584, 1514, 1461, 1442, 1382, 1303, 1251, 1104, 982, 881, 839\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.48-7.25$ (m, 5H, ArH), 6.90 (d, $J = 8.5$ Hz, 2H, PMB), 5.50 (d, $J = 1.5$ Hz, 1H, B1), 4.64, 4.51 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.12–4.11 (m, 2H, B2, B5), 3.82 (s, 3H, OMe), 3.61–3.60 (m, 2H, B3, B4), 2.63 (d, $J =$ 1.5 Hz, 1H, OH), 1.27 (d, $J = 6.5$ Hz, 3H, B6), 0.92 (s, 9H, *t*BuSi), 0.09, 0.08 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.0$, 134.2, 131.4, 131.4, 129.7, 129.7, 129.6, 129.6, 129.0, 129.0, 127.2, 114.0, 86.9, 80.1, 72.8, 71.6, 70.1, 69.7, 55.2, 25.9, 18.1, -3.7, -4.5; HRMS (FAB): calcd for $C_{26}H_{38}O_5SSiNa$ $[M+Na]^+$: 513.2107, found 513.2122.

Benzyl ether 39: nBu_2SnO (0.208 g, 0.83 mmol) was added to a solution of diol **12** (0.258 g, 0.69 mmol) in toluene (30 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 BnBr (0.124 mL, 1.04 mmol) and nBu_4NI (0.051 g, 0.14 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 (1 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 ring C alcohol **39** (0.256 g, 80%) as a white foam. **39**: $R_f = 0.29$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +199.3$ ($c = 1.2$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3463, 3062, 2930, 2899, 2857, 1583, 1475, 1458, 1383, 1253, 1107, 981, 883, 839, 778, 698\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.47-7.26$ (m, 10H, ArH), 5.52 (d, $J = 1.5$ Hz, 1H, C1), 4.69, 4.59 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.17–4.16 (m, 1H, C2), 4.12 (dq, $J =$ 8.5, 6.0 Hz, 1H, C5), 3.65 (t, $J = 8.5$ Hz, 1H, C4), 3.64–3.62 (m, 1H, C3), 2.63 (d, $J = 2.0$ Hz, 1H, OH), 1.28 (d, $J = 6.0$ Hz, 3H, C6), 0.92 (s, 9H, *t*BuSi), 0.09 (s, 6H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 137.5$, 134.1, 131.4, 129.0, 128.6, 128.0, 127.3, 86.9, 80.4, 72.8, 71.9, 70.1, 69.7, 25.9, 18.1, -3.8, -4.5; HRMS (FAB): calcd for $C_{25}H_{36}O_4SSiCs$ $[M+Cs]^+$: 593.1158, found 593.1141.

Ring C methyl glycoside 40: DAST (0.094 mL, 0.71 mmol) was added to a solution of ring C alcohol **39** (0.225 g, 0.47 mmol) in CH_2Cl_2 (2 mL) at 0 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL), 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 used crude. The crude glycosyl fluoride (0.225 g, 0.47 mmol) was azeotroped with benzene (3×2 mL) and then dried under high vacuum for 1 h. The residue was dissolved in Et_2O (2 mL), 4 Å MS and MeOH (0.057 mL, 1.42 mmol) were added, and the mixture was stirred for 5 min. The reaction mixture was cooled to $-10\,^{\circ}C$ and $SnCl_2$ (0.16 g, 0.85 mmol) was added in one portion. The resulting mixture was stirred at $-10\,^{\circ}C$ for 12 h. The reaction mixture was quenched by the addition of Et_3N (5 mL), 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, $0 \rightarrow 50\%$ Et_2O in hexanes) to afford ring C methyl glycoside **40** (0.220 g, 100%) as a white foam. **40**: $R_f = 0.87$ (40% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 3062, 2930, 2855, 1728, 1472, 1256, 1010, 871, 838, 778\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 1:10): $\delta = 7.54-7.12$ (m, 10H, ArH), 5.08, 4.80 (AB, $J =$ 10.5 Hz, 2H, CH_2Ar), 4.26 (d, $J = 8.5$ Hz, 1H, C1), 4.21 (dq, $J = 9.0$, 6.5 Hz, 1H, C5), 3.47 (s, 3H, OMe), 3.51–3.27 (m, 2H, C2, C3), 3.13 (t, $J = 10.0$ Hz, 1H, C4), 1.27 (d, $J = 6.5$ Hz, 3H, C6), 0.93 (s, 9H, *t*BuSi), 0.05, -0.01 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.4$, 132.0, 130.8, 128.6, 128.0, 127.4, 127.2, 126.8, 104.3, 83.3, 77.2, 75.7, 72.3, 68.1, 57.0, 56.7, 30.3, 26.0, 18.3, 10.9, -3.7, -4.0; HRMS (FAB): calcd for $C_{26}H_{38}O_4SSiNa$ $[M+Na]^+$: 497.2158, found 497.2140.

Ring C alcohol 11: nBu_4NF (0.55 mL, 0.55 mmol) was added to a solution of methyl glycoside **40** (0.22 g, 0.46 mmol) in THF (2 mL) and the resulting mixture was stirred at 25 °C for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (100 mL), and washed with H_2O (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, $0 \rightarrow 80\%$ Et_2O in hexanes) to afford ring C alcohol **11** (0.16 g, 94%) as a white foam. **11**: $R_f = 0.28$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -32.5$ ($c = 0.66$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3458, 2934, 1582, 1497, 1476, 1454, 1382, 1068\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.57-7.20$ (m, 10H, ArH), 5.06, 4.75 (AB, $J =$ 11.0 Hz, 2H, CH_2Ar), 4.24 (d, $J = 8.5$ Hz, 1H, C1), 3.48 (s, 3H, OMe), 3.34–3.23 (m, 3H, C3, C4, C5), 3.10 (dd, $J = 10.5$, 8.5 Hz, 1H, C2), 2.12 (s, 1H, OH), 1.28 (d, $J = 6.0$ Hz, 3H, C6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 138.2, 134.6, 132.2, 132.2, 128.7, 128.7, 128.2, 128.1, 128.1, 127.1, 104.0, 83.3, 76.2, 75.2, 71.1, 57.1, 55.6, 17.6; HRMS (FAB): calcd for $C_{20}H_{24}O_4SNa$ $[M+Na]^+$: 383.1293, found 383.1283.

Ring B glycosyl fluoride 10: DAST (0.077 mL, 0.58 mmol) was added to a solution of ring B alcohol **38** (0.190 g, 0.39 mmol) in CH_2Cl_2 (2 mL) at 0 °C and the resulting mixture stirred for 0.5 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL), 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 used crude in the next reaction.

BC disaccharide 8: The crude glycosyl fluoride **10** (0.225 g, 0.47 mmol) and ring C alcohol **11** (0.093 g, 0.26 mmol) were azeotroped with benzene ($3 \times$ 2 mL) and then dried under high vacuum for 1 h. The residue was dissolved in Et_2O (2 mL), 4 Å MS were added and the mixture was stirred for 5 min. The reaction mixture was cooled to $-10\,^{\circ}C$ and $SnCl_2$ (0.09 g, 0.46 mmol) was added in one portion. The resulting mixture was stirred at $-10\,^{\circ}C$ for 12 h. The reaction mixture was quenched by the addition of Et_3N (5 mL), 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, $0 \rightarrow 50\%$ Et_2O in

0947-6539/00/0617-3106 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

hexanes) to afford BC disaccharide **8** (0.168 g, 78%, β:α ca. 10:1) as a white foam. **8**: $R_f = 0.42$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -45.3$ ($c = 0.97$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2930$, 2855, 1514, 1472, 1438, 1248, 1102, 1024, 871, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.51-7.22$ (m, 17H, ArH), 6.79 (d, $J = 8.5$ Hz, 2H, PMB), 4.92, 4.72 (AB, $J = 10.0$ Hz, 2H, CH_2Ar), 4.85, 4.67 (AB, $J = 10.0$ Hz, 2H, CH_2Ar), 4.68 (d, $J = 9.0$ Hz, 1H, B1), 4.07 (d, $J = 8.5$ Hz, 1H, C1), 3.77 (s, 3H, OMe), 3.56 (dd, $J = 9.5$, 9.0 Hz, 1H, C4), 3.44 (s, 3H, OMe), 3.33–3.28 (m, 4H, C5 or B5, C3, B3, B4), 3.10 (dd, $J =$ 10.5, 8.5 Hz, 1H, C2), 3.05 (dq, $J = 9.5$, 6.0 Hz, 1H, B5 or C5), 3.00 (dd, $J =$ 11.0, 9.0 Hz, 1H, B2), 1.45 (d, $J = 6.5$ Hz, 3H, C6 or B6), 1.12 (d, $J = 6.0$ Hz, 3H, B6 or C6), 0.92 (s, 9H, *t*BuSi), 0.06, 0.05 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.2$, 159.1, 138.8, 136.8, 134.5, 133.0, 130.6, 129.6, 129.1, 128.9, 128.5, 127.9, 127.4, 127.1, 126.2, 113.5, 103.9, 102.9, 82.9, 81.7, 80.8, 76.8, 75.7, 75.1, 74.6, 74.4, 72.5, 71.1, 70.7, 57.6, 56.9, 55.6, 55.2, 26.0, 18.7, 18.3, 18.0, −3.4, −3.9; HRMS (FAB): calcd for $C_{46}H_{60}O_8S_2SiCs$ $[M+Cs]^+$: 965.2553, found 965.2515.

Disaccharide 42: Raney Ni (0.2 g, added portionwise at 0.1 g h^{-1}) was added to a solution of BC disaccharide **8** (0.23 g, 0.28 mmol) in MeOH (30 mL) at 25 °C and the resulting mixture was refluxed for 2 h. The reaction mixture was filtered and the solvents were removed under reduced pressure. NaH (0.013 g, 0.33 mmol) was added to a solution of the crude residue (ca. 0.28 mmol) in DMF (1 mL) at 0 °C and the resulting mixture was stirred for 5 min. BnBr (0.043 mL, 0.36 mmol) and nBu$_4$NI (0.020 g, 0.06 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 (1 mL), diluted with Et_2O (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 dissolved in THF (2 mL), nBu$_4$NF (0.33 mL, 0.33 mmol) was added and the resulting mixture was stirred at 25 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (2 mL), diluted with Et_2O (100 mL) and washed with H_2O (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 BC alcohol **42** (0.11 g, 78% over three steps) as a white foam. **42**: $R_f = 0.12$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -20.5$ ($c = 0.40$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3476$, 2931, 1612, 1514, 1452, 1366, 1249, 1068, 993, 909, 823, 734 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.37-7.24$ (m, 7H, ArH), 6.89 (d, $J =$ 8.5 Hz, 2H, PMB), 4.75 (dd, $J = 9.5$, 2.0 Hz, 1H, B1), 4.68, 4.64 (AB, $J =$ 11.5 Hz, 2H, CH_2Ar), 4.60, 4.39 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.33 (dd, $J = 9.5$, 2.0 Hz, 1H, C1), 3.80 (s, 3H, OMe), 3.61–3.46 (m, 1H, B3), 3.48 (s, 3H, OMe), 3.36–3.15 (m, 5H, B4, B5, C3, C4, C5), 2.50 (br s, 1H, OH), 2.35–2.27 (m, 2H, B2, C2), 1.58 (ddd, $J = 12.0$, 10.0, 10.0 Hz, 1H, B2), 1.50 (ddd, $J = 12.0$, 10.0, 10.0 Hz, 1H, C2), 1.34 (d, $J = 6.0$ Hz, 3H, B6), 1.28 (d, $J = 6.0$ Hz, 3H, C6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.4$, 138.6, 130.3, 129.4, 128.3, 127.5, 114.0, 100.5, 100.0, 82.5, 78.5, 77.8, 75.5, 71.8, 71.0, 70.6, 56.5, 55.3, 36.9, 36.3, 30.2, 18.3, 18.0; HRMS (FAB): calcd for $C_{28}H_{38}O_8Cs$ $[M+Cs]^+$: 635.1621, found 635.1600.

Ester 43: 4 Å MS (0.10 g) were added to a solution of BC alcohol **42** (0.10 g, 0.20 mmol) in THF (1 mL) at 25 °C and the resulting mixture was stirred for 2 h. The solution was transferred to another flask via cannula and nBuLi (0.14 mL, 1.6 M in hexanes, 0.22 mmol) was added at 25 °C and the reaction mixture was stirred for 1 h. Acyl fluoride **7** (0.10 g, 0.30 mmol) was dissolved in THF (0.5 mL) and added to the reaction mixture by cannula and the resulting mixture was stirred for 24 h. The reaction was quenched with saturated aqueous NH_4Cl (1 mL), diluted with Et_2O (100 mL), and washed with H_2O (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 ester **43** (0.13 g, 80%) as a white foam. **43**: $R_f = 0.36$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -10.6$ ($c = 0.70$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2961$, 2928, 2851, 1738, 1513, 1455, 1258, 1095, 800, 741 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.57$ (d, $J = 7.0$ Hz, 2H, ArH), 7.44–7.25 (m, 8H, ArH), 7.21 (d, $J = 8.5$ Hz, 2H, PMB), 6.83 (d, $J = 8.5$ Hz, 2H, PMB), 5.02 (s, 2H, CH_2Ar), 5.00 (t, $J = 9.5$ Hz, 1H, B4), 4.74 (dd, $J = 9.5$, 1.0 Hz, 1H, B1), 4.70, 4.66 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.54, 4.42 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.33 (dd, $J = 9.5$, 2.0 Hz, 1H, C1), 3.81 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.63–3.57 (m, 2H, B3, C3), 3.48 (s, 3H, OMe), 3.38, 3.35 (dq, $J = 9.5$, 6.0 Hz, 2H, B5, C5), 3.27 (t, $J = 9.0$ Hz, 1H, C4), 2.37–2.29 (m, 2H, B2, C2), 2.22 (s, 3H, ArMe), 1.66, 1.58 (ddd, $J = 12.0$, 10.0 10.0 Hz, 2H, B2, C2), 1.34, 1.31 (d, $J = 6.0$ Hz, 6H, B6, C6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 165.8, 159.2, 152.8, 152.1, 138.6, 136.1, 133.6, 129.9, 129.1, 128.5, 128.5, 128.3, 128.3, 127.6, 127.5, 127.4, 127.4, 126.1, 121.4, 113.7, 100.6, 100.2, 83.0, 77.7, 75.8, 74.9, 71.8, 71.0, 70.4, 62.2, 56.6, 55.3, 37.0, 30.3, 29.7, 17.7, 17.4; HRMS (FAB): calcd for $C_{44}H_{50}Cl_2O_{11}Cs$ $[M+Cs]^+$: 957.1785, found 957.1820.

Alcohol 44: DDQ (0.047 g, 0.20 mmol) was added to a solution of ester **43** (0.13 g, 0.16 mmol) in CH_2Cl_2/H_2O (10:1, 1 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 (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 → 80% Et_2O in hexanes) to afford alcohol **44** (0.09 g, 80%) as a white foam. **44**: $R_f = 0.29$ (60% Et_2O in hexanes); $[\alpha]_D^{22} = -6.43$ ($c = 0.53$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3500$, 2925, 1736, 1651, 1558, 1456, 1392, 1258, 1095, 1068, 1034 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.60$ (br d, $J = 8.0$ Hz, 2H, ArH), 7.44–7.32 (m, 8H, ArH), 5.03 (s, 2H, CH_2Ar), 4.82 (dd, $J = 9.0$, 8.5 Hz, 1H, B4), 4.80 (br d, $J = 9.0$ Hz, 1H, B1), 4.71, 4.67 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.34 (dd, $J = 10.0$, 2.0 Hz, 1H, C1), 3.88 (s, 3H, OMe), 3.79 (br ddd, $J = 9.5$, 9.0, 4.0 Hz, 1H, B3), 3.59 (ddd, $J = 11.5$, 8.5, 5.5 Hz, 1H, C3), 3.48 (s, 3H, OMe), 3.38 (m, 2H, B5, C5), 3.29 (dd, $J = 9.5$, 8.5 Hz, 1H, C4), 2.68 (d, $J = 4.0$ Hz, 1H, OH), 2.36 (s, 3H, ArMe), 2.32–2.26 (m, 1H, B2), 2.3 (ddd, $J = 12.5$, 5.5, 2.0 Hz, 1H, C2), 1.74 (ddd, $J = 12.5$, 9.5, 9.0 Hz, 1H, B2), 1.59 (ddd, $J =$ 12.5, 11.5, 10.0 Hz, 1H, C2), 1.34 (d, $J = 5.5$ Hz, 3H, B6), 1.30 (d, $J = 6.0$ Hz, 3H, C6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 166.4$, 153.0, 151.9, 138.6, 135.9, 133.2, 128.6, 128.5, 127.5, 127.4, 127.0, 125.5, 121.4, 100.5, 100.4, 83.2, 79.9, 77.6, 74.9, 71.8, 70.9, 69.7, 62.4, 56.5, 39.4, 37.0, 30.3, 18.2, 17.7, 17.4; HRMS (FAB): calcd for $C_{36}H_{42}O_{10}Cl_2Na$ $[M+Na]^+$: 727.2053, found 727.2029.

A_1B(A)C fragment 45: A ring glycosyl fluoride **9** (0.014 g, 0.07 mmol) and alcohol **44** (0.023 g, 0.033 mmol) were azeotroped with benzene (1 mL) and then dried under high vacuum for 1 h. The residue was dissolved in CH_2Cl_2 (0.2 mL), 4 Å MS were added, and the mixture was cooled to −35 °C and stirred for 5 min. $BF_3 \cdot Et_2O$ (0.096 mL, 0.38 M solution in CH_2Cl_2, 0.04 mmol) was added to the reaction mixture in one portion and the resulting mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was quenched by the addition of Et_3N (1 mL), 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 $A_1B(A)C$ model system **45** (0.028 g, 95%) as a white foam. **45**: $R_f = 0.28$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -53.6$ ($c = 0.61$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2936$, 1736, 1543 1455, 1391, 1251, 1128, 1033, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.58-7.28$ (m, 10H, ArH), 5.05, 5.02 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.96 (dd, $J = 5.0$, 1.7 Hz, 1H, A1), 4.88 (t, $J = 9.5$ Hz, 1H, B4), 4.76 (dd, $J =$ 9.5, 1.5 Hz, 1H, B1), 4.68 (s, 2H, CH_2Ar), 4.34 (dd, $J = 9.5$, 1.5 Hz, 1H, C1), 3.89–3.83 (m, 1H, B5), 3.83 (s, 3H, OMe), 3.65 (d, $J = 9.5$ Hz, 1H, A4), 3.64–3.58 (m, 1H, B3), 3.51–3.47 (m, 1H, A5), 3.48 (s, 3H, OMe), 3.39–3.30 (m, 2H, C3, C5), 3.36 (s, 3H, OMe), 3.27 (t, $J = 9.0$ Hz, 1H, C4), 2.43 (dd, $J = 13.0$, 4.0 Hz, 1H, A2), 2.38 (s, 3H, ArMe), 2.37–2.27 (m, 2H, B2, C2), 2.02 (dd, $J = 13.0$, 0.5 Hz, 1H, A2), 1.69 (s, 3H, Me (A3)), 1.68–1.60 (m, 2H, B2, C2), 1.35–1.33 (m, 6H, B6, C6), 0.83 (d, $J = 6.0$ Hz, 3H, A6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.6$, 153.3, 153.2, 138.6, 135.9, 134.8, 128.6, 128.5, 128.3, 127.5, 127.4, 127.3, 126.4, 126.0, 125.5, 121.7, 100.5, 100.0, 92.4, 90.0, 84.3, 83.0, 77.7, 76.2, 74.9, 72.5, 71.6, 71.0, 66.2, 62.0, 60.8, 56.5, 40.1, 36.9, 36.5, 34.2, 30.3, 29.7, 19.4, 18.4, 17.6; HRMS (FAB): calcd for $C_{44}H_{55}Cl_2NO_{14}Na$ $[M+Na]^+$: 914.2897, found 914.2931.

A_1B(A)C diol 6: 10% Pd/C (2.0 mg) was added to a solution of the $A_1B(A)C$ model system **45** (25 mg, 0.03 mmol) in *t*BuOMe (1.5 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 2 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. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford $A_1B(A)C$ diol **6** (0.019 g, 95%) as a white foam. **6**: $R_f = 0.36$ (90% Et_2O in hexanes); $[\alpha]_D^{22} = -45.2$ ($c = 0.54$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3456$, 2926, 2854, 1725, 1544, 1449, 1389, 1299, 1250, 1127, 1037 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 6.98$ (s, 1H, OH), 4.98 (dd, $J = 4.5$, 1.5 Hz, 1H, A1), 4.94 (t, $J = 9.0$ Hz, 1H, B4), 4.53 (dd, $J = 9.5$, 1.5 Hz, 1H, B1), 4.40 (dd, $J = 9.5$, 1.5 Hz, 1H, C1), 4.21 (ddd, $J = 11.5$, 9.5, 5.5 Hz, 1H, B3), 3.92 (dq, $J = 9.0$, 6.5 Hz, 1H, C5), 3.88 (s, 3H, OMe), 3.65 (d, $J = 9.0$ Hz, 1H, A4), 3.64 (dq, $J = 9.0$,

6.5 Hz, 1H, A5), 3.63 (m, 1H, C3), 3.49 (s, 3H, OMe), 3.48–3.37 (m, 1H, B5), 3.35 (s, 3H, OMe), 2.99 (dd, J = 9.0, 8.5 Hz, 1H, C4), 2.47 (dd, J = 14.0, 5.0 Hz, 1H, A2), 2.38 (s, 3H, ArMe), 2.37–2.28 (m, 2H, B2, C2), 2.03 (dd, J = 14.0, 2.0 Hz, 1H, A2), 1.76–1.58 (m, 2H, B2, C2), 1.67 (s, 3H, Me (A3)), 1.44 (d, J = 6.5 Hz, 3H, B6 or C6), 1.29 (d, J = 6.0 Hz, 3H, B6 or C6), 0.86 (d, J = 6.0 Hz, 3H, A6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 153.5, 150.2, 134.7, 125.5, 121.6, 117.6, 100.7, 92.5, 89.9, 89.0, 84.3, 82.8, 75.5, 72.0, 70.2, 69.5, 66.4, 62.1, 60.8, 56.7, 40.0, 38.1, 36.0, 34.3, 29.7, 19.5, 18.1, 17.8, 17.7; HRMS (FAB): calcd for $C_{30}H_{43}Cl_2NO_{14}Na$ $[M+Na]^+$: 734.1958, found 734.1938.

Methyl ester 48: K_2CO_3 (4.52 g, 37.70 mmol) was added to a solution of acid **26** (11.00 g, 65.40 mmol) in acetone (300 mL) at 25 °C and the resulting mixture was stirred for 2 h. MeI (41.00 mL, 655.0 mmol) was added and the resulting mixture was stirred for 24 h at 25 °C. The reaction mixture was filtered 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 methyl ester **48** (10.72 g, 90%) as a white foam. **48**: R_f = 0.38 (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3401, 2940, 1612, 1502, 1450, 1381, 1327, 1264, 1210, 1187, 1107, 1062, 996, 951, 834, 800 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.82 (s, 1H, OH), 6.28 (d, J = 2.5 Hz, 1H, ArH), 6.23 (d, J = 2.5 Hz, 1H, ArH), 5.69 (s, 1H, OH), 3.92 (s, 3H, OMe), 2.48 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1, 160.3, 144.0, 111.4, 101.2, 51.9, 24.2; HRMS (MALDI): calcd for $C_8H_9O_4$ $[M+H]^+$: 169.0501, found 169.0502.

Bis-chloromethyl ester 49: SO_2Cl_2 (6.10 mL, 75.47 mmol) was added to a solution of methyl ester **48** (5.50 g, 30.19 mmol) in CH_2Cl_2 (200 mL) at 25 °C and the resulting mixture was refluxed for 3 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 60% Et_2O in hexanes) to afford the bis-chloromethyl ester **49** (7.20 g, 95%) as a white foam. **49**: R_f = 0.57 (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3606, 3526, 2962, 1718, 1649, 1590, 1544, 1413, 1331, 1262, 1217, 960, 803, 764 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.48 (br s, 1H, OH), 3.98 (s, 3H, OMe), 2.61 (s, 3H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.4, 158.1, 152.4, 137.9, 113.9, 107.2, 106.6, 53.0, 21.4; HRMS (MALDI): calcd for $C_9H_9Cl_2O_4$ $[M+H]^+$: 250.9883, found 250.9876.

TIPS ether 50: TIPSOTf (7.65 mL, 28.46 mmol) was added to a solution of methyl ester **49** (6.50 g, 28.46 mmol) and 2,6-lutidine (4.36 mL, 38.81 mmol) in CH_2Cl_2 (150 mL) at −78 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (500 mL) and washed with saturated aqueous $NaHCO_3$ (70 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 → 20% Et_2O in hexanes) to afford TIPS ether **50** (9.49 g, 90%) as a white foam. **50**: R_f = 0.57 (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 2943, 2869, 1736, 1665, 1542, 1458, 1379, 1317, 1283, 1244, 1123, 972, 886, 781, 684 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.87 (s, 1H, OH), 3.97 (s, 3H, CO_2Me), 2.60 (s, 3H, Me), 1.49–1.46 (m, 3H, iPr$_3$Si), 1.13 (d, J = 7.5 Hz, 18H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.4, 164.3, 158.1, 152.3, 137.8, 113.9, 107.2, 64.5, 52.7, 19.7, 17.2; HRMS (MALDI): calcd for $C_{18}H_{29}Cl_2O_4Si$ $[M+H]^+$: 407.1212, found 407.1222.

Methyl ether 51: MeI (6.79 mL, 109.0 mmol) was added to a solution of phenol **50** (7.40 g, 18.17 mmol) and Ag_2O (16.84 g, 72.67 mmol) in Et_2O (300 mL) at 25 °C and the resulting mixture was refluxed for 12 h. The reaction mixture was filtered and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 20% Et_2O in hexanes) to afford the methyl ether **51** (6.97 g, 91%) as a white foam. **51**: R_f = 0.68 (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 2945, 2867, 1732, 1574, 1556, 1458, 1392, 1352, 1258, 1192, 1127, 1065, 1005, 960, 884, 768, 686, 658 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.90 (s, 3H, CO_2Me), 3.83 (s, 3H, OMe), 2.60 (s, 3H, Me), 1.45–1.43 (m, 3H, iPr$_3$Si), 1.11 (d, J = 7.5 Hz, 18H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.2, 152.4, 151.2, 132.9, 123.6, 122.8, 118.3, 61.9, 52.4, 31.5, 22.6, 17.7, 14.0; HRMS (MALDI): calcd for $C_{19}H_{30}Cl_2O_4SiNa$ $[M+Na]^+$: 443.1188, found 443.1185.

Phenol 52: nBu$_4$NF (23.76 mL, 23.76 mmol) was added to a solution of TIPS ether **51** (7.70 g, 18.28 mmol) in THF (100 mL) and the resulting mixture was stirred at 25 °C for 2 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 50% Et_2O in hexanes) to afford phenol **52** (4.65 g, 96%) as a white solid. **52**: R_f = 0.53 (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3520, 2943, 2872, 1725, 1572, 1461, 1355, 1251, 1202, 1132, 1096, 955, 885, 803 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.08 (s, 1H, OH), 3.91 (s, 3H, CO_2Me), 3.86 (s, 3H, OMe), 2.28 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.0, 152.4, 149.7, 133.1, 122.8, 117.2, 112.9, 62.1, 52.6, 17.3; HRMS (MALDI): calcd for $C_{10}H_{10}Cl_2O_4Na$ $[M+Na]^+$: 286.9855, found 286.9831.

Benzyl ether 53: K_2CO_3 (1.35 g, 9.77 mmol) was added to a solution of phenol **52** (3.70 g, 13.95 mmol) and BnBr (1.99 mL, 16.74 mmol) in acetone (100 mL) at 25 °C and the resulting mixture was refluxed for 8 h. The reaction mixture was filtered 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 methyl ester **53** (4.56 g, 92%) as a white foam. **53**: R_f = 0.65 (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3020, 2944, 2866, 1734, 1560, 1462, 1376, 1330, 1265, 1130, 1098, 972, 834, 744 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.58 (d, J = 7.0 Hz, 2H, ArH), 7.42–7.36 (m, 3H, ArH), 5.03 (s, 2H, CH_2Ar), 3.95 (s, 3H, CO_2Me), 3.89 (s, 3H, OMe), 2.33 (s, 3H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.8, 152.7, 152.3, 135.9, 133.3, 128.3, 127.0, 125.9, 121.4, 74.7, 62.0, 52.5, 17.5, 17.3, 12.2; HRMS (MALDI): calcd for $C_{17}H_{16}Cl_2O_4Na$ $[M+Na]^+$: 377.0323, found 377.0337.

Ring B V1, 2, 3: R_f = 0.40 (50% Et_2O in hexanes); $[\alpha]_D^{22}$ = +108.6 (c = 2.10, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3479, 2931, 1724, 1513, 1258, 1200, 1117, 1068, 711 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00 (d, J = 7.7 Hz, 2H, ArH), 7.60 (d, J = 7.0 Hz, 1H, ArH), 7.50–7.25 (m, 7H, ArH), 7.10 (d, J = 8.5 Hz, 2H, PMB), 6.70 (d, J = 8.5 Hz, 2H, PMB), 5.61 (s, 1H, B1), 5.37 (t, J = 10.0 Hz, 1H, B4), 4.58, 4.47 (AB, J = 11.8 Hz, 2H, CH_2Ar), 4.35 (dq, J = 10.0, 5.9 Hz, 1H, B5), 4.28 (dd, J = 3.3, 1.8 Hz, 1H, B2), 3.87 (dd, J = 9.2, 3.0 Hz, 1H, B3), 3.74 (s, 3H, OMe), 2.80 (br s, 1H, OH), 1.23 (d, J = 6.0 Hz, 3H, B6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.1, 159.9, 134.2, 133.6, 131.8, 130.3, 130.2, 129.6, 129.5, 128.8, 127.9, 87.3, 76.6, 73.5, 71.8, 70.2, 68.2, 55.7, 17.8; HRMS (MALDI): calcd for $C_{27}H_{28}O_6SNa$ $[M+Na]^+$: 503.1504, found 503.1509.

Ring B V4: R_f = 0.45 (50% Et_2O in hexanes); $[\alpha]_D^{22}$ = +154.6 (c = 1.05, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3442, 2932, 1612, 1514, 1249, 1102, 845, 767 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.44–7.24 (m, 7H, ArH), 6.90 (d, J = 8.8 Hz, 2H, PMB), 5.97–5.90 (m, 1H, C*H*CH$_2$), 5.49 (d, J = 1.1 Hz, 1H, B1), 5.27 (dm, J = 17.3 Hz, 1H, C*H*$_2$-*E*), 5.18 (dm, J = 10.7 Hz, 1H, C*H*$_2$-*Z*), 4.64, 4.61 (AB, J = 11.4 Hz, 2H, CH_2Ar), 4.36–4.32 (m, 1H, OC*H*$_2$), 4.18–4.11 (m, 3H, OC*H*$_2$, B2, B5), 3.81 (s, 3H, OMe), 3.76 (dd, J = 9.2, 3.3 Hz, 1H, B3), 3.37 (t, J = 9.6 Hz, 1H, B4), 2.67 (br s, 1H, OH), 1.29 (d, J = 6.3 Hz, 3H, B6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.0, 135.3, 134.6, 131.8, 130.2, 130.0, 129.4, 127.7, 117.4, 114.4, 87.4, 80.3, 80.0, 74.6, 72.4, 70.6, 69.2, 55.7, 18.2; HRMS (MALDI): calcd for $C_{23}H_{28}O_5SNa$ $[M+Na]^+$: 439.1555, found 439.1560.

Ring B V5: R_f = 0.60 (30% Et_2O in hexanes); $[\alpha]_D^{22}$ = +169.4 (c = 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3502, 2954, 2875, 1612, 1514, 1458, 1249, 1105, 840, 741 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.22 (m, 7H, ArH), 6.89 (d, J = 8.7 Hz, 2H, PMB), 5.49 (d, J = 1.4 Hz, 1H, B1), 4.60, 4.51 (AB, J = 11.2 Hz, 2H, CH_2Ar), 4.12 (dd, J = 2.8, 1.4 Hz, 1H, B2), 4.09 (dq, J = 8.3, 6.3 Hz, 1H, B5), 3.81 (s, 3H, OMe), 3.62 (t, J = 8.8 Hz, 1H, B4), 3.60 (dd, J = 8.7, 3.1 Hz, 1H, B3), 2.60 (br s, 1H, OH), 1.26 (d, J = 6.3 Hz, 3H, B6), 0.96 (t, J = 8.0 Hz, 9H, *Me*CH$_2$Si), 0.66–0.55 (m, 6H, CH_2Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.5, 134.2, 131.4, 129.8, 129.5, 129.0, 127.5, 114.0, 86.9, 80.3, 73.0, 71.6, 70.1, 69.6, 55.3, 17.9, 7.0, 5.2; HRMS (MALDI): calcd for $C_{26}H_{38}O_5SSiNa$ $[M+Na]^+$: 513.2107, found 513.2108.

Ring B V7: R_f = 0.36 (50% Et_2O in hexanes); $[\alpha]_D^{22}$ = +152.2 (c = 1.0, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3476, 3058, 2982, 2935, 2897, 2836, 1752, 1612, 1514, 1370, 1256, 1102, 988, 771 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43–7.22 (m, 7H, ArH), 6.88 (d, J = 8.5 Hz, 2H, PMB), 5.98–5.91 (m, 1H, C*H*CH$_2$), 5.53 (d, J = 1.1 Hz, 1H, B1), 5.38 (dd, J = 17.3, 1.5 Hz, 1H, C*H*$_2$-*E*), 5.28 (dd, J = 10.6, 1.5 Hz, 1H, C*H*$_2$-*Z*), 4.89 (t, J = 9.6 Hz, 1H, B4), 4.60–4.61 (m, 2H, OC*H*$_2$), 4.60, 4.56 (AB, J = 11.8 Hz, 2H, CH_2Ar), 4.26 (dq, J = 9.5, 6.2 Hz, 1H, B5), 4.19 (dd, J = 3.3, 1.9 Hz, 1H, B2), 3.80 (s, 3H, OMe), 3.79 (dd, J = 7.7, 4.4 Hz, 1H, B3), 2.80 (br s, 1H, OH), 1.24 (d, J = 6.2 Hz, 3H, B6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.5, 154.6, 133.7, 131.4, 131.3, 129.4, 129.0, 127.4, 119.0, 113.9, 86.7, 71.9, 70.0, 68.7, 67.2, 55.2, 17.2; HRMS (MALDI): calcd for $C_{24}H_{28}O_7SNa$ $[M+Na]^+$: 483.1448, found 483.1456.

0947-6539/00/0617-3108 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

Ring C Y1: $R_f = 0.68$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -37.8$ ($c = 1.07$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3456, 2943, 2856, 1463, 1383, 1066, 884, 791, 685\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, β only): $\delta = 7.36-7.27$ (m, 5H, ArH), 4.93, 4.69 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.65 (d, $J = 7.0$ Hz, 1H, C1), 3.63 (t, $J = 8.1$ Hz, 1H, C2), 3.29 (dq, $J = 9.2$, 6.3 Hz, 1H, C5), 3.26 (t, $J = 8.4$ Hz, 1H, C3), 3.21 (t, $J = 8.8$ Hz, 1H, C4), 1.80 (br s, 1H, OH), 1.23 (d, $J = 6.0$ Hz, 3H, C6), 1.20–1.05 (m, 42H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 139.1, 128.6, 127.7, 127.5, 98.7, 86.7, 77.6, 75.6, 74.9, 71.2, 18.3, 18.1, 13.6, 13.2$; HRMS (MALDI): calcd for $C_{31}H_{58}O_5Si_2Na$ $[M+Na]^+$: 589.3720, found 589.3738.

Ring C Y2, 4, 5, 6, 7: $R_f = 0.68$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -57.3$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3456, 2945, 2930, 2856, 1471, 1253, 1069, 838, 780\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$, β only): $\delta = 7.27-7.10$ (m, 5H, ArH), 4.86, 4.51 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.39 (d, $J = 6.1$ Hz, 1H, C1), 3.33 (t, $J = 8.4$ Hz, 1H, C2), 3.16 (dq, $J = 9.0$, 6.1 Hz, 1H, C5), 3.12 (t, $J = 8.7$ Hz, 1H, C3), 3.07 (t, $J = 8.9$ Hz, 1H, C4), 1.60 (br s, 1H, OH), 1.14 (d, $J = 6.0$ Hz, 3H, C6), 0.84, 0.81 (2 × s, 2 × 9H, tBuSi), 0.03, 0.02 (2 × s, 2 × 3H, MeSi), 0.02 (s, 6H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.7, 128.8, 128.0, 98.1, 86.1, 75.9, 75.3, 71.3, 26.1, 18.4, 18.1, 17.7, -3.6, -3.8, -4.2, -4.7$; HRMS (MALDI): calcd for $C_{25}H_{46}O_5Si_2Na$ $[M+Na]^+$: 505.2781, found 505.2776.

Ring C Y3: $R_f = 0.19$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -5.3$ ($c = 1.20$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3518, 3031, 2938, 1767, 1453, 1366, 1238, 1077, 1016, 972, 786, 701\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.37-7.30$ (m, 5H, ArH), 5.95–5.86 (m, 2H, CHCH$_2$), 5.50 (d, $J = 8.3$ Hz, 1H, C1), 5.35 (d, $J = 17.1$ Hz, 1H, CH_2-*E*), 5.34 (d, $J = 17.1$ Hz, 1H, CH_2-*E*), 5.27 (d, $J = 10.5$ Hz, 1H, CH_2-*Z*), 5.24 (d, $J = 10.5$ Hz, 1H, CH_2-*Z*), 4.91 (dd, $J = 9.4$, 8.3 Hz, 1H, C2), 4.79, 4.67 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.65–4.63 (m, 4H, OCH_2), 3.55 (t, $J = 9.3$ Hz, 1H, C3), 3.50 (dq, $J = 9.4$, 6.1 Hz, 1H, C5), 3.35 (t, $J = 9.4$ Hz, 1H, C4), 2.33 (s, 1H, OH), 1.33 (d, $J = 6.1$ Hz, 3H, C6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 153.9, 153.4, 137.7, 131.2, 131.0, 128.7, 128.0, 127.9, 119.3, 119.2, 95.2, 82.3, 76.2, 74.9, 74.6, 72.7, 69.0, 69.0, 17.4$; HRMS (MALDI): calcd for $C_{21}H_{26}O_9Na$ $[M+Na]^+$: 445.1474, found 445.1455.

Tosylate 56: TsCl (14.10 g, 73.95 mmol) was added to a solution of diol **54**[26] (21.0 g, 67.22 mmol) in pyridine (130 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was quenched by the addition of H_2O (10 mL), diluted with Et_2O (1.0 L) and washed with saturated aqueous $NaHCO_3$ (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 dissolved in CH_2Cl_2 (300 mL) and 2,6-lutidine (11.75 mL, 100.8 mmol) was added. The reaction mixture was cooled to 0 °C and TIPSOTf (19.20 mL, 73.95 mmol) was added. The resulting mixture was warmed to 25 °C and stirred for 0.5 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (1 L), and washed with saturated aqueous $NaHCO_3$ (100 mL) and 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 → 50% Et_2O in hexanes) to afford tosylate **56** (36.85 g, 88% over two steps) as a white foam. **56**: $R_f = 0.66$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = +120.5$ ($c = 1.03$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3061, 2942, 2867, 1598, 1459, 1366, 1243, 1216, 1184, 1107, 972, 879, 811, 752, 670\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.66$ (d, $J = 8.2$ Hz, 2H, ArH), 7.51–7.24 (m, 7H, ArH), 5.56 (s, 1H, B1), 4.31–4.28 (m, 2H, B2, B3), 4.22–4.18 (m, 1H, B5), 4.10 (dd, $J = 10.2$, 6.7 Hz, 1H, B6), 4.07 (t, $J = 6.2$ Hz, 1H, B4), 3.73 (dd, $J = 9.4$, 6.7 Hz, 1H, B6), 2.42 (s, 3H, ArMe), 1.44 (s, 3H, Me), 1.32 (s, 3H, Me), 1.13–1.01 (m, 21H, iPr$_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 144.6, 133.0, 132.7, 132.3, 129.6, 129.1, 128.0, 127.8, 78.6, 76.1, 70.9, 70.1, 69.2, 27.8, 26.2, 21.6, 18.2, 17.7, 12.5$; HRMS (MALDI): calcd for $C_{31}H_{46}O_7S_2SiNa$ $[M+Na]^+$: 645.2352, found 645.2358.

TIPS ether 57: LAH (2.72 g, 71.68 mmol) was added to a solution of tosylate **56** (34.35 g, 55.14 mmol) in THF (300 mL) at 0 °C and the resulting mixture was heated to 45 °C and stirred for 6 h. The reaction mixture was cooled to 0 °C, quenched by the addition of saturated aqueous NH_4Cl (50 mL) and stirred for 1 h. The reaction mixture was diluted with Et_2O (1 L) and washed with saturated aqueous NH_4Cl (100 mL) and 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 → 50% Et_2O in hexanes) to afford TIPS ether **57** (21.47 g, 90%) as a white foam. **57**: $R_f = 0.41$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = +158.2$ ($c = 1.01$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3060, 2941, 2867, 1583, 1459, 1381, 1243, 1218, 1164, 1110, 1072, 1019, 865, 751, 685\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.50-7.24$ (m, 5H, ArH), 5.56 (d, $J = 0.6$ Hz, 1H, B1), 4.32 (dd, $J = 5.9$, 1.5 Hz, 1H, B2), 4.08 (t, $J = 6.2$ Hz, 1H, B3), 4.02 (dq, $J = 8.8$, 6.2 Hz, 1H, B5), 3.62 (dd, $J = 9.1$, 6.5 Hz, 1H, B4), 1.50 (s, 3H, Me), 1.34 (s, 3H, Me), 1.25 (d, $J = 6.5$ Hz, 3H, B6), 1.22–1.08 (m, 21H, iPr$_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 133.8, 131.7, 129.0, 109.1, 83.9, 78.9, 76.5, 76.3, 27.9, 26.4, 18.3, 18.2, 17.7$; HRMS (MALDI): calcd for $C_{24}H_{40}O_4SSiNa$ $[M+Na]^+$: 475.2314, found 475.2322.

Diol 58: TsOH (1.85 g, 9.71 mmol) was added to a solution of TIPS ether **57** (21.00 g, 48.55 mmol) and ethylene glycol (6.43 mL, 121.37 mmol) in MeOH (200 mL) at 25 °C and the resulting mixture was stirred for 10 h. The reaction mixture was quenched by the addition of Et_3N (50 mL) and the solvents were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (1 L) and washed with saturated aqueous $NaHCO_3$ (100 mL) and 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% EtOAc in hexanes) to afford diol **58** (16.03 g, 80%) as a white foam. **58**: $R_f = 0.35$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +214.3$ ($c = 1.01$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3382, 2940, 2864, 1586, 1462, 1350, 1250, 1167, 1128, 1074, 1020, 972, 884, 842, 789, 735, 684\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.50-7.26$ (m, 5H, ArH), 5.56 (s, 1H, B1), 4.15–4.12 (m, 1H, B3), 4.10 (dq, $J = 8.2$, 6.2 Hz, 1H, B5), 3.78 (ddd, $J = 8.2$, 6.2, 3.2 Hz, 1H, B2), 3.72 (t, $J = 8.2$ Hz, 1H, B4), 2.63 (d, $J = 4.4$ Hz, 1H, OH), 2.40 (d, $J = 5.9$ Hz, 1H, OH), 1.34 (d, $J = 6.2$ Hz, 3H, B6), 1.21–1.09 (m, 21H, iPr$_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 134.0, 131.5, 129.0, 127.4, 87.0, 75.4, 72.8, 72.3, 70.5, 18.3, 17.8, 13.0$; HRMS (MALDI): calcd for $C_{21}H_{36}O_4SSiNa$ $[M+Na]^+$: 435.2001, found 435.2004.

Alcohol 59: nBu$_2$SnO (10.62 g, 42.65 mmol) was added to a solution of diol **58** (16.00 g, 38.77 mmol) in toluene (200 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 (7.89 mL, 58.16 mmol) and nBu$_4$NI (2.86 g, 7.75 mmol) were added. The reaction mixture was refluxed again for 3 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 alcohol **59** (17.15 g, 83%) as a white solid. **59**: $R_f = 0.50$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +53.2$ ($c = 1.05$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3559, 3059, 2942, 1613, 1585, 1517, 1461, 1249, 1110, 883, 739, 683\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.45-7.23$ (m, 5H, ArH), 7.22 (d, $J = 8.5$ Hz, 2H, PMB), 6.86 (d, $J = 8.5$ Hz, 2H, PMB), 5.48 (d, $J = 1.5$ Hz, 1H, B1), 4.68, 4.44 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.02 (dq, $J = 8.2$, 6.4 Hz, 1H, B5), 3.92 (dd, $J = 3.2$, 1.5 Hz, 1H, B2), 3.80 (s, 3H, OMe), 3.68 (ddd, $J = 9.7$, 8.5, 3.2 Hz, 1H, B3), 3.65 (t, $J = 8.5$ Hz, 1H, B4), 2.24 (d, $J = 9.7$ Hz, 1H, OH), 1.33 (d, $J = 6.4$ Hz, 3H, B6), 1.26–1.07 (m, 21H, iPr$_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.5, 134.5, 131.5, 129.6, 129.3, 129.0, 127.3, 114.0, 84.9, 79.1, 76.1, 72.1, 72.0, 70.4, 55.2, 18.3, 13.0$; HRMS (MALDI): calcd for $C_{29}H_{44}O_5SSiNa$ $[M+Na]^+$: 555.2576, found 555.2596.

Diol 60: nBu$_4$NF (48.14 mL, 48.14 mmol) was added to a solution of alcohol **59** (17.10 g, 32.09 mmol) in THF (200 mL) and the resulting mixture was stirred at 25 °C for 2 h. 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 diol **60** (11.00 g, 91%) as a white solid. **60**: $R_f = 0.10$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +63.6$ ($c = 1.01$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3416, 3058, 2933, 1612, 1584, 1515, 1458, 1249, 1176, 1061, 842, 743\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.44-7.25$ (m, 5H, ArH), 7.23 (d, $J = 8.8$ Hz, 2H, PMB), 6.86 (d, $J = 8.8$ Hz, 2H, PMB), 5.53 (s, 1H, B1), 4.65, 4.42 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.10 (dq, $J = 9.4$, 6.2 Hz, 1H, B5), 3.96 (dd, $J = 3.8$, 1.4 Hz, 1H, B2), 3.78 (s, 3H, OMe), 3.73–3.71 (m, 1H, B3), 3.49 (t, $J = 9.4$ Hz, 1H, B4), 1.32 (d, $J = 6.2$ Hz, 3H, B6); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.6, 134.3, 129.7, 129.2, 129.0, 127.5, 114.0, 85.1, 79.2, 74.2, 72.0, 69.1, 55.3, 17.5$; HRMS (MALDI): calcd for $C_{20}H_{24}O_5SNa$ $[M+Na]^+$: 399.1242, found 399.1239.

Bis-TBS ether 61: TBSOTf (14.76 mL, 64.28 mmol) was added to a solution of diol **60** (11.00 g, 29.22 mmol) and 2,6-lutidine (13.61 mL, 116.88 mmol) in CH_2Cl_2 (150 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 0.5 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (1 L), and washed with saturated aqueous $NaHCO_3$ (100 mL) and 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 →

30% Et_2O in hexanes) to afford bis-TBS ether **61** (16.44 g, 93%) as a white foam. **61**: $R_f = 0.60$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = +76.9$ ($c = 1.01$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3037, 2943, 2872, 1614, 1514, 1455, 1255, 1067, 879, 779\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.44-7.21$ (m, 7H, ArH), 6.84 (d, $J = 8.6$ Hz, 2H, PMB), 5.38 (br s, 1H, B1), 4.60, 4.56 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 3.95 (br s, 1H, B2), 3.86 (dq, $J = 9.1$, 6.8 Hz, 1H, B5), 3.83 (br s, 1H, B3), 3.79 (s, 3H, OMe), 3.70 (s, 1H, B4), 1.28 (d, $J = 6.8$ Hz, 3H, B6), 0.93, 0.90 ($2 \times$ s, 2×9H, *t*BuSi), 0.13, 0.08 ($2 \times$ s, 2×3H, MeSi), 0.11 (s, 6H, MeSi); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 159.1, 135.1, 131.2, 130.3, 128.8, 126.9, 113.6, 77.3, 73.8, 72.3, 55.2, 26.3, 26.0, 18.4, 18.3, 18.0, -4.1$; HRMS (MALDI): calcd for $C_{32}H_{52}O_5SSi_2Na$ $[M+Na]^+$: 627.2972, found 627.2958.

Ring B alcohol 62: DDQ (9.20 g, 40.54 mmol) was added to a solution of PMB ether **61** (16.35 g, 27.03 mmol) in CH_2Cl_2/H_2O (10:1, 150 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 (1 L) and washed with saturated aqueous $NaHCO_3$ (100 mL) and 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 → 50% Et_2O in hexanes) to afford ring B alcohol **62** (11.92 g, 91%) as a colorless oil. **62**: $R_f = 0.39$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = +129.6$ ($c = 1.10$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3568, 2930, 2895, 2857, 1473, 1258, 1100, 838, 776\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.48$ (d, $J = 8.1$ Hz, 2H, ArH), 7.30–7.24 (m, 3H, ArH), 5.43 (d, $J = 2.5$ Hz, 1H, B1), 4.05 (q, $J = 6.5$ Hz, 1H, B5), 4.05–4.03 (m, 1H, B2), 3.89 (dd, $J = 7.8$, 3.0 Hz, 1H, B3), 3.63 (t, $J = 7.8$ Hz, 1H, B4), 2.60 (s, 1H, OH), 1.28 (d, $J = 6.5$ Hz, 3H, B6), 0.94, 0.91 ($2 \times$ s, 2×9H, *t*BuSi), 0.17 ($2 \times$ s, 2×3H, MeSi), 0.10, 0.09 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 134.0, 131.5, 128.9, 128.8, 127.7, 86.0, 74.0, 73.7, 72.5, 71.2, 26.2, 26.0, 18.2, 18.0, -3.0, -3.7, -4.0, -4.5$; HRMS (MALDI): calcd for $C_{24}H_{44}O_4SSi_2Na$ $[M+Na]^+$: 507.2396, found 507.2403.

Ring B glycosyl fluoride 46: DAST (1.15 mL, 7.13 mmol) was added to a solution of ring B alcohol **62** (2.80 g, 4.76 mmol) in CH_2Cl_2 (20 mL) at 0 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL), diluted with CH_2Cl_2 (200 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 used crude in the next reaction.

Alcohol 64: nBu_2SnO (25.25 g, 101.43 mmol) was added to a solution of diol **63**[27] (12.00 g, 92.21 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 BnBr (16.45 mL, 138.31 mmol) and nBu_4NI (6.81 g, 18.44 mmol) were added. The reaction mixture was refluxed again for 3 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 alcohol **64** (16.86 g, 83%) as a white solid. **64**: $R_f = 0.32$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -108.5$ ($c = 0.59$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3433, 3053, 2977, 2874, 1648, 1452, 1386, 1237, 1111, 1054, 737, 699\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.46-7.28$ (m, 5H, ArH), 6.34 (dd, $J = 6.0$, 0.6 Hz, 1H, C1), 4.84 (dd, $J = 6.0$, 2.1 Hz, 1H, C2), 4.68, 4.54 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.05 (br d, $J = 5.6$ Hz, 1H, C3), 3.88 (dq, $J = 9.3$, 6.3 Hz, 1H, C5), 3.60 (dd, $J = 9.3$, 7.1 Hz, 1H, C4), 2.74 (s, 1H, OH), 1.33 (d, $J = 6.3$ Hz, 3H, C6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 144.9, 138.1, 128.4, 127.9, 99.6, 76.5, 74.4, 72.5, 70.3, 17.1$; HRMS (MALDI): calcd for $C_{13}H_{16}O_3Na$ $[M+Na]^+$: 243.0997, found 243.0998.

TBS ether 65: TBSCl (17.16 g, 113.86 mmol) was added to a solution of alcohol **64** (16.72 g, 75.91 mmol) and imidazole (12.92 g, 189.77 mmol) in CH_2Cl_2 (400 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 (1 L) and washed with saturated aqueous $NaHCO_3$ (100 mL) and 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 → 50% Et_2O in hexanes) to afford TBS ether **65** (23.62 g, 93%) as a white foam. **65**: $R_f = 0.65$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -52.7$ ($c = 2.41$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2952, 2931, 2857, 1650, 1457, 1251, 1122, 1057, 884, 837, 778\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.42-7.28$ (m, 5H, ArH), 6.37 (d, $J = 6.1$ Hz, 1H, C1), 4.84 (dd, $J = 6.1$, 2.2 Hz, 1H, C2), 4.63, 4.54 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.02 (br d, $J = 6.6$ Hz, 1H, C3), 3.85 (dq, $J = 9.1$, 6.4 Hz, 1H, C5), 3.66 (dd, $J = 9.1$, 6.6 Hz, 1H, C4), 1.37 (d, $J = 6.4$ Hz, 3H, C6), 0.93 (s, 9H, *t*BuSi), 0.13 (s, 6H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 144.8, 138.4, 128.4, 127.7, 127.4, 99.9, 77.8, 75.5, 73.6, 70.3, 25.9, 18.1, 17.9, -4.0, -4.7$; HRMS (MALDI): calcd for $C_{19}H_{30}O_3SiNa$ $[M+Na]^+$: 357.1862, found 357.1856.

Diol 66: OsO_4 (0.50 mL, 2.5% solution in *t*BuOH) was added to a solution of TBS ether **65** (23.57 g, 70.46 mmol) and NMO (9.08 g, 77.50 mmol) in acetone/H_2O (10:1, 350 mL) and the reaction mixture was stirred for 8 h at 25 °C. The reaction mixture was diluted with CH_2Cl_2 (1.5 L) and washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The organic layer was dried (Na_2SO_4), 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 diol **66** (22.83 g, 97%) as a white foam. **66**: $R_f = 0.43$ (100% Et_2O); IR (thin film): $\tilde{\nu} = 3394, 2931, 2857, 1456, 1359, 1254, 1121, 1089, 860, 837, 778\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$, $\alpha:\beta$ ca. 1.7:1 ratio): $\delta = 7.38-7.25$ (m, 15H, ArH), 5.44 (br s, 1.7H, C1), 4.93, 4.73 (AB, $J = 11.4$ Hz, 3.4H, CH_2Ar), 4.85, 4.75 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.51 (br s, 1.7H, C1), 3.92 (dq, $J = 8.6$, 6.5 Hz, 1H, C5), 3.69 (d, $J = 3.7$ Hz, 1.7H, OH), 3.60 (ddd, $J = 7.4$, 7.4, 3.5 Hz, 1H, C2), 3.58 (t, $J = 8.7$ Hz, 1H, C3), 3.43 (dt, $J = 8.4$, 2.9 Hz, 1H, OH), 3.36–3.22 (m, 6.8H, C2, C3, C4, C5), 2.97 (d, $J = 7.4$ Hz, 1H, OH), 2.70 (s, 1.7H, OH), 1.25 (d, $J = 6.0$ Hz, 5.1H, C6), 1.23 (d, $J = 6.0$ Hz, 3H, C6), 0.92 (s, 9H, *t*BuSi), 0.91 (s, 15.3H, *t*BuSi), 0.06 (s, 3H, MeSi), 0.05 (s, 5.1H, MeSi), 0.03 (s, 3H, MeSi), 0.02 (s, 5.1H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 138.7, 138.7, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 96.3, 91.8, 84.3, 82.0, 75.9, 75.7, 74.9, 74.9, 72.9, 68.7, 25.9, 18.3, 18.0, 17.9, -3.7, -3.8, -4.3$; HRMS (MALDI): calcd for $C_{19}H_{32}O_5SiNa$ $[M+Na]^+$: 391.1917, found 391.1904.

Bis-PMB ether 67: NaH (6.19 g, 154.71 mmol) was added to a solution of diol **66** (21.53 g, 64.46 mmol) in DMF (250 mL) at 0 °C and the resulting mixture was stirred for 15 min. PMBCl (26.22 mL, 193.39 mmol) and nBu_4NI (4.76 g, 12.89 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (50 mL), diluted with Et_2O (1.0 L), and washed with brine (2×100 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 → 70% Et_2O in hexanes) to afford bis-PMB ether **67** (37.29 g, 95%, ca. 1:1 mixture of separable isomers) as a white foam. **67**: $R_f = 0.59$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +14.1$ ($c = 0.64$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2953, 2855, 1613, 1514, 1360, 1249, 1172, 1074, 836, 778\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$, β anomer only): $\delta = 7.45-7.26$ (m, 7H, ArH), 7.14 (d, $J = 8.4$ Hz, 2H, PMB), 6.93 (d, $J = 8.6$ Hz, 2H, PMB), 6.80 (d, $J = 8.6$ Hz, 2H, PMB), 5.07, 4.76 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.95, 4.65 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.91, 4.62 (AB, $J = 10.4$ Hz, 2H, CH_2Ar), 4.56 (d, $J = 7.8$ Hz, 1H, C1), 3.83 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.54 (t, $J = 7.9$ Hz, 1H, C2), 3.44 (t, $J = 7.9$ Hz, 1H, C3), 3.42–3.37 (m, 2H, C4, C5), 1.39 (d, $J = 5.4$ Hz, 3H, C6), 0.96 (s, 9H, *t*BuSi), 0.14, 0.06 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.2, 159.0, 139.0, 130.5, 129.6, 129.5, 128.4, 127.0, 126.9, 113.7, 113.5, 102.1, 84.3, 82.5, 76.0, 74.8, 74.1, 72.3, 71.3, 70.6, 64.7, 55.1, 55.0, 25.9, 18.4, 18.0, -3.8, -4.4$; HRMS (MALDI): calcd for $C_{35}H_{48}O_7SiNa$ $[M+Na]^+$: 631.3067, found 631.3050.

Ring C alcohol 47: nBu_4NF (63.79 mL, 63.79 mmol) was added to a solution of bis-PMB ether **67** (35.31 g, 58.00 mmol) in THF (300 mL) and the resulting mixture was stirred at 25 °C for 1 h. 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 ring C alcohol **47** (27.03 g, 95%) as a white solid (while both anomers could be taken through the following sequence, data is given for the β-anomer only). **47**: $R_f = 0.16$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -60.5$ ($c = 1.06$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3296, 2908, 2856, 1610, 1520, 1360, 1304, 1246, 1167, 1072, 1040, 982, 829, 739\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$, β-only): $\delta = 7.37-7.28$ (m, 7H, ArH), 7.21 (d, $J = 8.6$ Hz, 2H, PMB), 6.89 (d, $J = 8.6$ Hz, 2H, PMB), 6.84 (d, $J = 8.6$ Hz, 2H, PMB), 4.96, 4.64 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.87, 4.63 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.85, 4.60 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.49 (d, $J = 7.8$ Hz, 1H, C1), 3.82 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.46 (dd, $J = 9.1$, 7.7 Hz, 1H, C2), 3.36 (t, $J = 9.0$ Hz, 1H, C3), 3.32 (dq, $J = 9.4$, 6.0 Hz, 1H, C5), 3.24 (t, $J = 9.1$ Hz, 1H, C4), 2.14 (br s, 1H, OH), 1.34 (d, $J = 6.0$ Hz, 3H, C6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.2, 159.1, 138.5, 130.5, 129.8, 129.6, 129.4, 128.5, 127.8, 113.8, 113.6, 102.2, 83.9, 81.7, 75.0, 74.8, 74.2, 71.1, 70.8, 55.2, 30.2, 17.7$; HRMS (MALDI): calcd for $C_{29}H_{34}O_7Na$ $[M+Na]^+$: 517.2202, found 517.2204.

0947-6539/00/0617-3110 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

BC disaccharide 68: The crude glycosyl fluoride **46** (2.80 g, 4.76 mmol) and ring C alcohol **47** (1.98 g, 4.04 mmol) were azeotroped with benzene (3 × 20 mL) and then dried under high vacuum for 1 h. The residue was dissolved in $Et_2O/CH_2Cl_2/Me_2S$ (1:1:1, 30 mL), 4 Å MS were added, and the mixture was stirred for 5 min. The reaction mixture was cooled to −10 °C and $SnCl_2$ (1.62 g, 8.56 mmol) was added in one portion. The resulting mixture was stirred at −10 °C for 3 h. The reaction mixture was quenched by the addition of Et_3N (20 mL), diluted with CH_2Cl_2 (500 mL) and washed with saturated aqueous $NaHCO_3$ (50 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 → 50 % Et_2O in hexanes) to afford BC disaccharide **68** (2.75 g, 71 %) as a white foam. **68**: $R_f = 0.41$ (50 % Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3049, 2940, 2870, 1614, 1589, 1514, 1464, 1245, 1116, 832 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 1:10): δ = 7.49–7.12 (m, 14H, ArH), 6.89 (d, J = 8.6 Hz, 2H, PMB), 6.83 (d, J = 8.6 Hz, 2H, PMB), 5.12 (d, J = 7.9 Hz, 1H, B1), 5.07, 4.73 (AB, J = 10.5 Hz, 2H, CH_2Ar), 4.86, 4.56 (AB, J = 11.3 Hz, 2H, CH_2Ar), 4.81, 4.65 (AB, J = 10.3 Hz, 2H, CH_2Ar), 4.40 (d, J = 7.4 Hz, 1H, C1), 4.10 (br d, J = 1.7 Hz, 1H, B3), 3.81 (s, 3H, OMe), 3.80 (s, 3H, OMe), 3.80–3.78 (m, 1H, B5), 3.57–3.53 (m, 1H, B4), 3.54 (t, J = 9.0 Hz, 1H, C3), 3.46–3.41 (m, 2H, C2, C4), 3.24 (dd, J = 7.8, 1.7 Hz, 1H, B2), 3.14 (dq, J = 9.4, 6.2 Hz, 1H, C5), 1.47 (d, J = 6.2 Hz, 3H, C6), 1.35 (d, J = 6.0 Hz, 3H, B6), 0.96, 0.87 (2 × s, 2 × 9H, *t*BuSi), 0.11, 0.08, 0.05, −0.02 (4 × s, 4 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.2, 159.1, 139.1, 137.5, 131.9, 130.8, 130.8, 129.9, 129.7, 129.5, 129.1, 128.5, 128.3, 127.9, 127.2, 126.0, 113.7, 113.6, 102.0, 82.9, 81.8, 81.7, 78.5, 77.9, 75.4, 74.7, 74.6, 71.3, 70.7, 55.7, 55.2, 30.3, 25.8, 25.7, 20.2, 18.5, −4.5, −4.6, −4.7, −4.8; HRMS (FAB): calcd for $C_{53}H_{76}O_{10}SSi_2Cs$ $[M+Cs]^+$: 1093.3752, found 1093.3794.

2-Deoxy disaccharide 69: Raney Ni (2.0 g, added portionwise at 0.5 g h^{-1}) was added to a solution of BC disaccharide **68** (2.74 g, 2.85 mmol) in EtOH/THF (1:1, 60 mL) at 25 °C and the resulting mixture was refluxed for 8 h. The reaction mixture was filtered and the solvents were removed under reduced pressure. An analytical sample was purifed by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford BC disaccharide **69**. **69**: $R_f = 0.41$ (50 % Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 2931, 2837, 1614, 1513, 1472, 1361, 1249, 1085, 838, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, α:β ca. 1:10): δ = 7.42–7.25 (m, 7H, ArH), 7.16 (d, J = 8.5 Hz, 2H, PMB), 6.87 (d, J = 8.5 Hz, 2H, PMB), 6.80 (d, J = 8.5 Hz, 2H, PMB), 4.94, 4.76 (AB, J = 12.6 Hz, 2H, CH_2Ar), 4.87, 4.58 (AB, J = 13.2 Hz, 2H, CH_2Ar), 4.80, 4.57 (AB, J = 12.6 Hz, 2H, CH_2Ar), 4.66–4.61 (m, 1H, B1), 4.45 (d, J = 7.5 Hz, 1H, C1), 3.80 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.58–3.55 (m, 1H, B5), 3.51 (t, J = 9.0 Hz, 1H, B4), 3.51–3.44 (m, 1H, B3), 3.42 (t, J = 9.0 Hz, 1H, C3), 3.41–3.36 (m, 1H, C4), 3.13–3.11 (m, 2H, C2, C5), 2.17 (dd, J = 12.2, 6.5 Hz, 1H, B2), 1.54 (dd, J = 12.2, 9.5 Hz, 1H, B2), 1.32 (d, J = 6.0 Hz, 3H, C6), 1.20 (d, J = 6.2 Hz, 3H, B6), 0.90, 0.88 (2 × s, 2 × 9H, *t*BuSi), 0.09, 0.08 (2 × s, 2 × 3H, MeSi), 0.08 (s, 6H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 159.0, 138.9, 130.6, 129.8, 129.5, 129.4, 128.0, 127.9, 127.8, 127.2, 113.7, 113.0, 102.1, 99.8, 83.0, 81.9, 81.8, 77.8, 75.4, 74.5, 72.9, 72.8, 70.8, 70.8, 55.1, 41.3, 26.1, 25.5, 18.6, 18.2, 17.9, −2.8, −3.1, −4.3, −4.8; HRMS (FAB): calcd for $C_{47}H_{72}O_{10}Si_2Cs$ $[M+Cs]^+$: 985.3718, found 985.3748.

BC diol 70: The above crude **69** was dissolved in THF (30 mL) and nBu$_4$NF (6.27 mL, 1 M in THF, 6.27 mmol) was added. The resulting mixture was stirred at 25 °C for 2 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 BC diol **70** (1.39 g, 78 % over two steps) as a white solid. **70**: $R_f = 0.13$ (100 % Et_2O); IR (thin film): $\tilde{\nu}$ = 3378, 2943, 2893, 2861, 1607, 1502, 1455, 1238, 1173, 1073, 908, 820, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α:β ca. 1:10): δ = 7.40–7.26 (m, 7H, ArH, PMB), 7.17 (d, J = 8.6 Hz, 2H, PMB), 6.88 (d, J = 8.6 Hz, 2H, PMB), 6.80 (d, J = 8.6 Hz, 2H, PMB), 4.93, 4.81 (AB, J = 10.9 Hz, 2H, CH_2Ar), 4.90, 4.61 (AB, J = 11.5 Hz, 2H, CH_2Ar), 4.81, 4.59 (AB, J = 11.6 Hz, 2H, CH_2Ar), 4.70 (dd, J = 9.6, 1.6 Hz, 1H, B1), 4.47 (d, J = 7.8 Hz, 1H, C1), 3.81 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.54 (br t, J = 9.1 Hz, 1H, B4), 3.48 (dd, J = 9.0, 7.1 Hz, 1H, C2), 3.43 (t, J = 9.1 Hz, 1H, C3), 3.41–3.32 (m, 1H, C5), 3.15–3.08 (m, 2H, B5, C4), 3.00 (ddd, J = 8.8, 8.8, 4.1 Hz, 1H, B3), 2.20 (ddd, J = 12.4, 4.8, 1.8 Hz, 1H, B2), 2.09 (s, 2H, OH), 1.53 (dd, J = 12.4, 8.8 Hz, 1H, B2), 1.33 (d, J = 5.2 Hz, 3H, C6), 1.21 (d, J = 6.0 Hz, 3H, B6); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2, 159.1, 139.0, 130.5, 130.1, 129.8, 129.5, 129.4, 128.1, 127.6, 127.3, 113.7, 113.6, 102.1, 100.2, 83.1, 82.0, 81.8, 77.3, 75.2, 74.5, 71.8, 71.3, 70.9, 70.8, 55.2, 39.2, 18.0, 17.6; HRMS (FAB): calcd for $C_{35}H_{44}O_{10}Cs$ $[M+Cs]^+$: 757.1989, found 757.1970.

BC allyl ether 71: nBu$_2$SnO (0.61 g, 2.45 mmol) was added to a solution of BC diol **70** (1.39 g, 2.22 mmol) in toluene (20 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 allyl bromide (0.29 mL, 3.34 mmol) and nBu$_4$NI (0.16 g, 0.44 mmol) were added. The reaction mixture was refluxed again for 3 h, and then the reaction mixture was quenched by the addition of H_2O (1 mL). The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O in hexanes) to afford BC allyl ether **71** (1.38 g, 93 %) as a white foam. **71**: $R_f = 0.25$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -23.4$ (c = 0.80, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3387, 2955, 2908, 2861, 1608, 1584, 1455, 1355, 1302, 1249, 1173, 1091, 1044, 926, 814, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.24 (m, 7H, ArH, PMB), 7.17 (d, J = 8.5 Hz, 2H, PMB), 6.88 (d, J = 8.5 Hz, 2H, PMB), 6.79 (d, J = 8.5 Hz, 2H, PMB), 5.90 (dddd, J = 17.0, 10.5, 6.0, 5.5 Hz, 1H, C*H*=CH_2), 5.28 (dd, J = 17.0, 1.5 Hz, 1H, CH_2-*E*), 5.19 (dd, J = 10.5, 1.0 Hz, 1H, CH_2-*Z*), 4.92, 4.83 (AB, J = 11.0 Hz, 2H, CH_2Ar), 4.88, 4.59 (AB, J = 11.5 Hz, 2H, CH_2Ar), 4.81, 4.61(AB, J = 10.5 Hz, 2H, CH_2Ar), 4.70 (dd, J = 9.5, 2.0 Hz, 1H, B1), 4.47 (d, J = 8.0 Hz, 1H, C1), 4.11 (dd, J = 12.5, 5.5 Hz, 1H, OCH_2), 3.94 (dd, J = 12.5, 6.0 Hz, 1H, OCH_2), 3.80 (s, 3H, OMe), 3.77 (s, 3H, OMe), 3.54 (t, J = 8.5 Hz, 1H, C3), 3.44 (t, J = 8.5 Hz, 1H, C2), 3.41–3.35 (m, 2H, C4, C5), 3.30–3.22 (m, 1H, B3), 3.21–3.10 (m, 2H, B4, B5), 2.64 (d, J = 2.0 Hz, 1H, OH), 2.30 (ddd, J = 12.5, 4.5, 2.0 Hz, 1H, B2), 1.46 (dt, J = 12.5, 9.5 Hz, 1H, B2), 1.35 (d, J = 5.0 Hz, 3H, C6), 1.24 (d, J = 5.5 Hz, 3H, B6); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 159.0, 138.9, 134.5, 130.5, 130.0, 129.7, 129.7, 129.5, 129.5, 129.4, 128.1, 127.5, 127.2, 117.3, 113.7, 113.5, 102.1, 100.0, 94.8, 83.1, 82.0, 81.8, 81.6, 78.5, 75.4, 75.2, 74.7, 71.8, 70.8, 69.8, 55.1, 36.2, 18.0, 17.8; HRMS (FAB): calcd for $C_{38}H_{48}O_{10}Cs$ $[M+Cs]^+$: 797.2302, found 797.2287.

A_1BC ester 72: nBuLi (1.30 mL, 1.6 M in THF, 2.13 mmol) was added to a solution of BC alcohol **71** (1.25 g, 1.94 mmol) in THF (10 mL) at −78 °C and the resulting mixture was warmed slowly to 0 °C and stirred for 1 h. Acyl fluoride **7** (0.80 g, 2.33 mmol) was dissolved in THF (5 mL) and added to the reaction mixture by cannula and the resulting mixture was warmed to 25 °C and stirred for 4 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (200 mL) and washed with H_2O (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 % Et_2O in hexanes) to afford A_1BC ester **72** (1.90 g, 99 %) as a white foam. **72**: $R_f = 0.38$ (70 % Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3030, 2931, 2872, 1737, 1614, 1519, 1455, 1255, 1091, 903, 738 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 1:10): δ = 7.58 (d, J = 7.2 Hz, 2H, ArH), 7.44–7.26 (m, 10H, ArH, PMB), 7.18 (d, J = 8.5 Hz, 2H, PMB), 6.89 (d, J = 8.5 Hz, 2H, PMB), 6.80 (d, J = 8.5 Hz, 2H, PMB), 5.90–5.83 (m, 1H, C*H*=CH_2), 5.26 (d, J = 17.2 Hz, 1H, CH_2-*E*), 5.17 (d, J = 10.2 Hz, 1H, CH_2-*Z*), 5.03 (s, 2H, CH_2Ar), 4.96, 4.93 (AB, J = 9.4 Hz, 2H, CH_2Ar), 4.93 (t, J = 9.4 Hz, 1H, B4), 4.93, 4.86 (AB, J = 10.4 Hz, 2H, CH_2Ar), 4.89, 4.62 (AB, J = 11.0 Hz, 2H, CH_2Ar), 4.72 (dd, J = 9.6, 1.3 Hz, 1H, B1), 4.49 (d, J = 7.8 Hz, 1H, C1), 4.09 (dd, J = 12.3, 5.3 Hz, 1H, OCH_2), 3.93 (dd, J = 12.3, 5.8 Hz, 1H, OCH_2), 3.86 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.57–3.50 (m, 3H, B3, C3, C4), 3.48–3.41 (m, 2H, C2, C5), 3.35 (dq, J = 9.7, 6.2 Hz, 1H, B5), 2.41 (dd, J = 12.3, 4.9 Hz, 1H, B2), 2.36 (s, 3H, Me (A_1)), 1.72 (dt, J = 11.9, 11.9 Hz, 1H, B2), 1.36 (d, J = 5.1 Hz, 3H, C6), 1.29 (d, J = 6.1 Hz, 3H, B6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.6, 159.2, 159.0, 152.7, 152.0, 138.9, 135.9, 134.3, 133.4, 130.4, 130.0, 129.7, 129.5, 129.4, 128.4, 128.3, 128.0, 127.4, 127.4, 127.3, 127.2, 126.0, 121.3, 117.1, 113.7, 113.5, 102.1, 99.9, 83.0, 82.0, 81.8, 76.4, 75.5, 75.2, 74.7, 74.4, 70.8, 70.7, 70.3, 69.3, 62.1, 55.1, 36.5, 18.0, 17.5, 17.4; HRMS (FAB): calcd for $C_{54}H_{60}Cl_2O_{13}Cs$ $[M+Cs]^+$: 1119.2465, found 1119.2421.

A_1BC alcohol 73: $[(Ph_3P)_3RhCl]$ (0.07 g, 0.076 mmol) was added to a solution of BC allyl ether **72** (1.50 g, 1.52 mmol) and DABCO (0.257 g, 2.28 mmol) in EtOH/H_2O (10:1, 10 mL, degassed 1 h) at 25 °C. The resulting mixture was refluxed for 2 h. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The solvents were removed under reduced pressure and then the residue was dissolved in acetone/H_2O (10:1, 20 mL). NMO (0.20 g, 1.67 mmol) and OsO_4 (0.10 mL, 2.5 % solution in *t*BuOH) were added and the reaction mixture was stirred for 3 h at 25 °C. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with

saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), 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 A_1BC alcohol **73** (1.17 g, 81%) as a white foam. **73**: $R_f = 0.24$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = +12.0$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3425, 2931, 2884, 1731, 1614, 1544, 1438, 1326, 1302, 1249, 1120, 1073, 938, 820, 749\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.57$ (d, $J = 6.9$ Hz, 2H, ArH), 7.43–7.28 (m, 10H, ArH, PMB), 7.16 (d, $J = 8.6$ Hz, 2H, PMB), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 6.79 (d, $J = 8.6$ Hz, 2H, PMB), 5.03 (br s, 2H, CH_2Ar), 4.93, 4.83 (AB, $J = 10.9$ Hz, 2H, CH_2Ar), 4.88, 4.59 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.81, 4.59 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.78 (t, $J = 9.4$ Hz, 1H, B4), 4.74 (dd, $J = 9.7$, 1.8 Hz, 1H, B1), 4.47 (d, $J = 7.9$ Hz, 1H, C1), 3.87 (s, 3H, OMe), 3.85–3.72 (m, 1H, B3), 3.81 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.55 (br t, $J = 9.0$ Hz, 1H, C3), 3.43 (dd, $J = 9.0$, 7.9 Hz, 1H, C2), 3.41–3.36 (m, 2H, C4, C5), 3.33 (dq, $J = 9.4$, 6.2 Hz, 1H, B5), 2.66 (d, $J = 4.4$ Hz, 1H, OH), 2.36 (s, 3H, Me (A_1)), 2.40–2.30 (m, 1H, B2), 1.72 (dt, $J = 12.2$, 9.7 Hz, 1H, B2), 1.35 (d, $J = 5.3$ Hz, 3H, C6), 1.23 (d, $J = 6.2$ Hz, 3H, B6); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 166.4$, 159.3, 159.1, 153.0, 151.8, 139.0, 138.9, 133.2, 130.5, 130.1, 129.8, 129.7, 129.6, 129.5, 129.2, 128.5, 128.2, 127.5, 127.3, 126.4, 125.5, 121.4, 113.8, 113.6, 102.2, 100.3, 84.2, 82.9, 81.9, 79.5, 75.3, 74.9, 74.5, 70.9, 70.8, 69.8, 69.6, 65.8, 62.4, 55.2, 39.3, 34.2, 30.3, 29.5, 21.1, 18.0, 17.6, 17.4, 15.2; HRMS (FAB): calcd for $C_{51}H_{56}Cl_2O_{13}Na$ $[M+Na]^+$: 969.2995, found 969.2998.

$A_1B(A)C$ trisaccharide 74: Ring A glycosyl fluoride **9** (0.025 g, 0.11 mmol) and A_1BC alcohol **73** (0.060 g, 0.063 mmol) were azeotroped with benzene (1 mL) and then dried under high vacuum for 1 h. The residue was dissolved in Et_2O/CH_2Cl_2 (1:1, 1 mL), 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 5 min. $SnCl_2$ (0.019 g, 0.10 mmol) was added to the reaction mixture in one portion and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of Et_3N (1 mL), 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, $0 \rightarrow 100\%$ Et_2O in hexanes) to afford $A_1B(A)C$ trisaccharide **74** (0.055 g, 77%) as a white foam. **74**: $R_f = 0.12$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -20.7$ ($c = 0.28$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931, 2872, 1731, 1549, 1455, 1390, 1237, 1090, 744\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.58$ (d, $J = 7.0$ Hz, 2H, ArH), 7.44–7.28 (m, 10H, ArH, PMB), 7.17 (d, $J = 8.6$ Hz, 2H, PMB), 6.89 (d, $J = 8.6$ Hz, 2H, PMB), 6.80 (d, $J = 8.6$ Hz, 2H, PMB), 5.05, 5.02 (AB, $J = 8.1$ Hz, 2H, CH_2Ar), 5.03, 4.90 (AB, $J = 9.7$ Hz, 2H, CH_2Ar), 4.93 (br d, $J = 5.1$ Hz, 1H, A1), 4.89, 4.63 (AB, $J = 10.6$ Hz, 2H, CH_2Ar), 4.87 (t, $J = 9.1$ Hz, 1H, B4), 4.83, 4.60 (AB, $J = 10.4$ Hz, 2H, CH_2Ar), 4.70 (br d, $J = 9.6$ Hz, 1H, B1), 4.48 (d, $J = 7.7$ Hz, 1H, C1), 3.92–3.75 (m, 2H, B3, C3), 3.84 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.65 (d, $J = 9.4$ Hz, 1H, A4), 3.57–3.29 (m, 5H, A5, B5, C2, C4, C5), 3.36 (s, 3H, OMe), 2.45 (dd, $J = 13.7$, 5.0 Hz, 1H, A2), 2.39 (s, 3H, Me (A_1)), 2.29–2.28 (m, 1H, B2), 2.01 (dd, $J = 13.7$, 1.6 Hz, 1H, A2), 1.69–1.64 (m, 1H, B2), 1.44 (s, 3H, Me (A3)), 1.36 (d, $J = 5.3$ Hz, 3H, C6), 1.29 (d, $J = 6.2$ Hz, 3H, B6), 0.84 (d, $J = 6.2$ Hz, 3H, A6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.5$, 159.3, 159.1, 153.2, 153.1, 139.0, 138.8, 134.8, 130.5, 130.2, 130.1, 129.8, 129.6, 129.5, 129.4, 128.6, 128.5, 128.1, 127.5, 127.4, 126.3, 126.0, 125.5, 121.7, 113.8, 113.6, 102.2, 99.8, 92.4, 89.9, 84.2, 83.1, 82.1, 81.9, 76.1, 75.1, 74.9, 74.5, 72.4, 71.1, 70.9, 70.8, 68.6, 66.2, 61.9, 60.7, 55.2, 40.1, 36.4, 31.5, 30.3, 29.7, 22.6, 19.3, 18.2, 18.1, 18.0, 17.6; HRMS (FAB): calcd for $C_{59}H_{69}Cl_2NO_{17}Cs$ $[M+Cs]^+$: 1266.2997, found 1266.3051.

$A_1B(A)C$ diol 75: $BF_3 \cdot Et_2O$ (0.024 mL, 0.194 mmol) was added to a solution of $A_1B(A)C$ trisaccharide **74** (0.055 g, 0.048 mmol) and PhSH (0.040 mL, 0.39 mmol) in CH_2Cl_2 (1 mL) at -35 °C and the resulting mixture was stirred for 2 h. The reaction mixture was quenched by the addition of Et_3N (1 mL), 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, $0 \rightarrow 100\%$ EtOAc in hexanes) to afford $A_1B(A)C$ diol **75** (0.036 g, 83%) as a white foam. **75**: $R_f = 0.17$ (100% Et_2O); IR (thin film): $\tilde{\nu} = 3416, 2978, 2931, 2872, 1731, 1537, 1449, 1384, 1249, 1090, 1032, 908, 738\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 1:1): $\delta = 7.57$ (d, $J = 7.1$ Hz, 2H, ArH), 7.43–7.29 (m, 8H, ArH), 5.21 (br s, 1H, C1α), 5.05, 5.02 (AB, $J = 11.8$ Hz, 4H, CH_2Ar), 5.02, 4.78 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 5.02, 4.74 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.97 (br s, 2H, A1), 4.91, 4.89 (t, $J = 9.4$ Hz, 2H, B4), 4.67, 4.66 (br d, $J = 8.4$ Hz, 2H, B1), 4.62–4.59 (m, 1H, C1β), 4.02 (dq, $J = 6.0$ Hz, 1H, C5), 3.90–3.82 (m, 4H, B3, B3, C3, C3), 3.87 (s, 3H, OMe), 3.85 (s, 3H, OMe), 3.75–3.73 (m, 3H, B5, C2, C2), 3.72 (t, $J = 8.8$ Hz, 1H, C4), 3.65 (d, $J = 9.3$ Hz, 2H, A4), 3.51–3.35 (m, 5H, A5, A5, B5, C4, C5), 3.36 (s, 3H, OMe), 3.07 (br s, 1H, OH), 2.87 (br s, 1H, OH), 2.47 (dd, $J = 13.9$, 4.7 Hz, 2H, A2), 2.39, 2.38 (s, 3H, Me (A_1)), 2.35–2.30 (m, 2H, B2), 2.02 (dd, $J = 13.7$, 2.1 Hz, 2H, A2), 1.72–1.67 (m, 2H, B2), 1.43 (s, 6H, Me (A3)), 1.32 (d, $J = 5.9$ Hz, 6H, C6), 1.27 (d, $J = 6.2$ Hz, 6H, B6), 0.84 (d, $J = 6.2$ Hz, 6H, A6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.6$, 153.3, 153.2, 138.7, 135.8, 134.7, 128.6, 128.5, 128.5, 128.4, 127.8, 127.8, 127.7, 127.7, 126.4, 126.0, 126.0, 125.5, 99.8, 96.3, 92.5, 91.8, 89.9, 84.2, 82.6, 82.1, 82.0, 80.3, 76.2, 76.1, 75.3, 75.0, 74.9, 74.9, 72.4, 72.4, 72.2, 71.4, 71.4, 67.1, 66.2, 62.0, 60.8, 60.4, 40.0, 36.4, 30.3, 19.4, 18.3, 18.0, 17.9, 17.6, 14.2; HRMS (FAB): calcd for $C_{43}H_{53}Cl_2NO_{15}Cs$ $[M+Cs]^+$: 1026.1847, found 1026.1809.

$A_1B(A)C$ bis-acetate 76: Ac_2O (0.010 mL, 0.10 mmol) was added to a solution of $A_1B(A)C$ diol **75** (0.036 g, 0.040 mmol), Et_3N (0.022 mL, 0.16 mmol), and 4-DMAP (1 mg, 0.01 mmol) in CH_2Cl_2 (0.5 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 (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, $0 \rightarrow 100\%$ Et_2O in hexanes) to afford $A_1B(A)C$ bis-acetate **76** (0.038 g, 97%) as a white foam. **76**: $R_f = 0.61$ (100% Et_2O); IR (thin film): $\tilde{\nu} = 2938, 1750, 1542, 1456, 1371, 1247, 1129, 1036, 737\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 1:1): $\delta = 7.57–7.21$ (m, 20H, ArH), 6.19 (d, $J = 3.6$ Hz, 1H, C1α), 5.59 (d, $J = 8.3$ Hz, 1H, C1β), 5.06 (t, $J = 9.2$ Hz, 1H, C2β), 5.04, 5.02 (AB, $J = 9.9$ Hz, 4H, CH_2Ar), 4.99 (dd, $J = 10.0$, 3.6 Hz, 1H, C2α), 4.97, 4.71 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.93, 4.63 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.95–4.94 (m, 2H, A1), 4.89 (t, $J = 9.4$ Hz, 2H, B4), 4.70, 4.67 (dd, $J = 10.1$, 1.9 Hz, 2H, B1), 3.93–3.81 (m, 4H, B3, B3, C3, C4), 3.85, 3.84 (2 × s, 3H, OMe), 3.65 (d, $J = 9.5$ Hz, 2H, A4), 3.61 (t, $J = 10.0$ Hz, 1H, C3), 3.53–3.32 (m, 7H, A5, A5, B5, B5, C4, C5, C5), 3.37 (s, 6H, OMe), 2.46 (dd, $J = 13.8$, 4.8 Hz, 2H, A2), 2.38, 2.27 (s, 3H, Me (A_1)), 2.31–2.28 (m, 2H, B2), 2.13 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.01 (dd, $J = 13.8$, 1.5 Hz, 2H, A2), 1.72–1.67 (m, 2H, B2), 1.95 (s, 3H, OAc), 1.91 (s, 3H, OAc), 1.43 (s, 6H, Me (A3)), 1.29–1.22 (m, 12H, B6, C6), 0.84 (d, $J = 6.2$ Hz, 6H, A6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 169.9, 169.2, 165.6, 153.3, 153.1, 138.7, 135.9, 134.8, 129.5, 128.6, 128.5, 128.3, 128.2, 127.7, 127.6, 127.2, 125.9, 125.5, 121.7, 113.8, 100.3, 92.5, 92.0, 89.9, 89.5, 84.2, 82.3, 80.9, 78.3, 75.1, 74.8, 72.1, 71.6, 71.1, 69.1, 66.3, 62.0, 60.8, 40.0, 36.5, 30.2, 29.7, 20.9, 20.7, 19.4, 18.2, 18.0, 17.6$; HRMS (FAB): calcd for $C_{47}H_{57}Cl_2NO_{17}Cs$ $[M+Cs]^+$: 1110.2058, found 1110.2017.

A_1BC TIPS ether 77: TIPSOTf (0.37 mL, 1.39 mmol) was added to a solution of A_1BC alcohol **73** (1.10 g, 1.16 mmol) and 2,6-lutidine (0.20 mL, 1.74 mmol) in CH_2Cl_2 (6 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of MeOH (1 mL), diluted with CH_2Cl_2 (200 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, $0 \rightarrow 80\%$ Et_2O in hexanes) to afford A_1BC TIPS ether **77** (1.19 g, 93%) as a white foam. **77**: $R_f = 0.60$ (50% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2943, 2872, 1731, 1614, 1508, 1461, 1384, 1249, 1094, 1061, 908, 744\ cm^{-1}$; ^1H NMR (400 MHz, $CDCl_3$, α:β ca. 1:10): $\delta = 7.57$ (d, $J = 7.1$ Hz, 2H, ArH), 7.44–7.27 (m, 10H, ArH, PMB), 7.18 (d, $J = 8.6$ Hz, 2H, PMB), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 6.80 (d, $J = 8.6$ Hz, 2H, PMB), 5.05 (br s, 2H, CH_2Ar), 4.93, 4.89 (AB, $J = 10.8$ Hz, 2H, CH_2Ar), 4.88 (t, $J = 8.9$ Hz, 1H, B4), 4.88, 4.63 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.81, 4.58 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.69 (br d, $J = 8.2$ Hz, 1H, B1), 4.48 (d, $J = 7.7$ Hz, 1H, C1), 3.95–3.86 (m, 1H, B3), 3.83 (s, 3H, OMe), 3.82 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.56 (br t, $J = 8.8$ Hz, 1H, C3), 3.51–3.28 (m, 4H, C2, C4, C5, B5), 2.37 (s, 3H, Me (A_1)), 2.33 (dd, $J = 12.2$, 6.0 Hz, 1H, B2), 1.74 (dt, $J = 11.7$, 11.7 Hz, 1H, B2), 1.34 (d, $J = 6.0$ Hz, 3H, B6), 1.32 (d, $J = 5.8$ Hz, 3H, C6), 1.01 (s, 21H, iPr$_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 165.7, 159.3, 159.1, 152.9, 152.7, 139.2, 138.9, 135.9, 134.3, 130.5, 130.0, 129.9, 129.6, 129.5, 129.4, 128.5, 128.1, 127.7, 126.7, 126.1, 121.5, 113.7, 113.6, 102.2, 99.8, 94.7, 83.1, 82.2, 81.8, 80.3, 79.3, 70.0, 68.6, 66.2, 61.9, 55.2, 41.0, 18.0, 17.8, 12.8$; HRMS (FAB): calcd for $C_{60}H_{76}Cl_2O_{13}SiCs$ $[M+Cs]^+$: 1235.3489, found 1235.3427.

A_1BC diol 78: $BF_3 \cdot Et_2O$ (0.46 mL, 3.62 mmol) was added to a solution of A_1BC TIPS ether **77** (1.00 g, 0.91 mmol) and PhSH (0.74 mL, 7.24 mmol) in

0947-6539/00/0617-3112 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

CH_2Cl_2 (10 mL) at −35 °C and the resulting mixture was stirred for 2 h. The reaction mixture was quenched by the addition of Et_3N (5 mL), diluted with CH_2Cl_2 (300 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 A_1BC diol **78** (0.65 g, 83 %) as a white foam. **78**: R_f = 0.21 (100 % Et_2O); IR (thin film): $\tilde{\nu}$ = 3405, 2942, 2866, 1739, 1567, 1454, 1390, 1328, 1254, 1127, 1059 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 1:1): δ = 7.57 (d, J = 7.2 Hz, 4H, ArH), 7.44–7.29 (m, 16H, ArH), 5.20 (br s, 1H), 5.10 (t, J = 10.8 Hz, 1H), 5.09–5.10 (m, 4H), 4.90 (dt, J = 9.2, 4.1 Hz, 4H), 4.76, 4.72 (AB, J = 11.1 Hz, 2H, CH_2Ar), 4.66 (dt, J = 9.2, 9.2 Hz, 1H), 4.60 (br d, J = 7.6 Hz, 1H), 4.06–3.98 (m, 4H), 3.81 (s, 6H, OMe), 3.74 (t, J = 8.9 Hz, 1H), 3.69–3.63 (m, 2H), 3.25–3.22 (m, 2H), 2.62 (s, 1H), 2.48 (d, J = 5.3 Hz, 1H), 2.37 (s, 6H, Me), 2.37–2.28 (m, 3H), 1.80 (dt, J = 9.9, 9.9 Hz, 1H, B2), 1.78 (dt, J = 9.9, 9.9 Hz, 1H, B2), 1.38 (d, J = 5.9 Hz, 3H), 1.37 (d, J = 5.9 Hz, 3H), 1.31 (d, J = 5.9 Hz, 3H), 1.27 (d, J = 5.9 Hz, 3H), 1.08–0.89 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.8, 152.9, 152.8, 138.7, 138.6, 136.0, 135.7, 134.3, 128.7, 128.5, 128.4, 128.0, 127.7, 126.7, 126.2, 125.5, 121.6, 99.8, 96.3, 91.8, 82.5, 82.3, 80.2, 79.3, 75.2, 75.1, 75.0, 72.1, 71.5, 70.8, 70.0, 67.2, 62.0, 41.0, 34.2, 30.3, 29.7, 18.0, 17.8, 12.8; HRMS (FAB): calcd for $C_{44}H_{60}Cl_2O_{11}SiCs$ $[M+Cs]^+$: 995.2336, found 995.2377.

A_1BC bis-acetate 79: Ac_2O (0.19 mL, 1.88 mmol) was added to a solution of A_1BC diol **78** (0.65 g, 0.75 mmol), Et_3N (0.43 mL, 3.00 mmol), and 4-DMAP (0.018 g, 0.15 mmol) in CH_2Cl_2 (6 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of MeOH (1 mL), diluted with CH_2Cl_2 (200 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 A_1BC bis-acetate **79** (0.700 g, 98 %) as a white foam. **79**: R_f = 0.42 (70 % Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 2943, 2867, 1749, 1566, 1454, 1372, 1248, 1062, 911, 736 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, α:β ca. 1:1): δ = 7.56 (d, J = 7.1 Hz, 4H, ArH), 7.44–7.25 (m, 16H, ArH), 6.20 (d, J = 3.7 Hz, 1H, C1α), 5.60 (d, J = 8.3 Hz, 1H, C1β), 5.07 (t, J = 9.1 Hz, 1H, C2β), 5.04 (br s, 4H, CH_2Ar), 5.00 (dd, J = 10.0, 3.7 Hz, 1H, C2α), 5.00, 4.70 (AB, J = 11.4 Hz, 2H, CH_2Ar), 4.97, 4.64 (AB, J = 11.5 Hz, 2H, CH_2Ar), 4.90, 4.89 (t, J = 9.2 Hz, 2H, B4), 4.70 (dd, J = 9.7, 1.6 Hz, 1H, B1), 4.70 (dd, J = 10.0, 1.4 Hz, 1H, B1), 4.00 (ddd, J = 11.6, 8.9, 5.0 Hz, 2H, B3), 3.92 (t, J = 9.3 Hz, 1H, C3), 3.91–3.88 (m, 1H, C5), 3.85 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.65 (t, J = 9.1 Hz, 1H, C3), 3.59 (dq, J = 9.5, 6.1 Hz, 1H, C5), 3.40 (t, J = 9.1 Hz, 1H, C4), 3.47 (t, J = 9.0 Hz, 1H, C4), 3.39, 3.37 (2 × dq, J = 9.7, 6.2 Hz, 2H, B5), 2.37 (s, 6H, Me (A_1)), 2.37–2.35 (m, 2H, B2), 2.13 (s, 3H, OAc), 2.08 (s, 3H, OAc), 1.96 (s, 3H, OAc), 1.92 (s, 3H, OAc), 1.79 (dt, J = 11.9, 11.9 Hz, 2H, B2), 1.33 (d, J = 6.2 Hz, 9H, B6, C6), 1.30 (d, J = 6.2 Hz, 3H, C6), 1.08–0.98 (m, 42H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.8, 169.3, 169.3, 169.1, 165.7, 152.9, 152.7, 138.7, 138.4, 135.9, 134.2, 128.4, 128.2, 128.2, 127.7, 127.5, 127.4, 127.3, 126.6, 126.6, 126.1, 121.5, 100.1, 100.0, 91.9, 89.4, 82.5, 82.2, 80.8, 79.2, 78.0, 75.0, 74.8, 72.1, 71.7, 71.5, 70.7, 69.9, 69.0, 61.9, 41.0, 41.0, 20.9, 20.6, 20.6, 18.1, 17.9, 17.7, 12.8; HRMS (FAB): calcd for $C_{48}H_{64}Cl_2O_{13}SiNa$ $[M+Na]^+$: 969.3391, found 969.3367.

A_1BC lactol 80: nBuNH$_2$ (0.082 mL, 0.824 mmol) was added to a solution of A_1BC bis-acetate **79** (0.60 g, 0.63 mmol) in THF (3 mL) at 25 °C and the resulting mixture was stirred for 5 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (10 mL), diluted with CH_2Cl_2 (200 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_1BC lactol **80** (0.532 g, 91 %) as a white foam. **80**: R_f = 0.21 (70 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −0.67 (c = 0.75, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3410, 2944, 2868, 1740, 1570, 1454, 1373, 1251, 1066, 911, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, α:β ca. 1:1): δ = 7.56 (d, J = 7.2 Hz, 4H, ArH), 7.43–7.24 (m, 16H, ArH), 5.31 (d, J = 3.8 Hz, 1H, C1α), 5.04 (br s, 4H, CH_2Ar), 5.00, 4.70 (AB, J = 11.5 Hz, 2H, CH_2Ar), 4.98, 4.68 (AB, J = 11.4 Hz, 2H, CH_2Ar), 4.89 (t, J = 9.2 Hz, 2H, B4), 4.82 (dd, J = 9.9, 3.7 Hz, 1H, C2α), 4.77 (dd, J = 9.3, 8.4 Hz, 1H, C2β), 4.70–4.62 (m, 2H, B1), 4.58–4.51 (m, 1H, C1β), 4.09–3.89 (m, 4H, B3, C3, C5), 3.84 (s, 6H, OMe), 3.65–3.61 (m, 1H, C5), 3.50–3.34 (m, 6H, B5, B5, C3, C_4, C_4), 3.28 (s, 1H, OH), 2.37 (s, 6H, Me (A_1)), 2.37–2.34 (m, 2H, B2), 2.02 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.79 (dt, J = 11.8, 11.8 Hz, 2H, B2), 1.33 (d, J = 6.0 Hz, 9H, B6, C6), 1.26 (d, J = 6.2 Hz, 3H, C6), 1.07–0.97 (m, 42H, iPr$_3$Si); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 170.3, 165.8, 152.9, 152.8, 138.8, 138.5, 135.9, 134.2, 129.2, 128.5, 128.3, 128.2, 127.7, 127.5, 127.4, 127.3, 126.7, 126.6, 126.1, 100.1, 95.5, 90.0, 83.0, 82.8, 80.5, 79.3, 79.3, 77.9, 75.7, 75.2, 75.0, 74.8, 73.4, 71.3, 70.7, 70.0, 70.0, 66.4, 62.0, 41.0, 30.2, 20.9, 18.0, 17.8, 12.8; HRMS (FAB): calcd for $C_{46}H_{62}Cl_2O_{12}SiCs$ $[M+Cs]^+$: 1037.2442, found 1037.2492.

Trichloroacetimidate 81: DBU (0.02 mL, 0.002 mmol) was added to a solution of A_1BC lactol **80** (0.53 g, 0.59 mmol) and Cl_3CCN (0.30 mL, 2.93 mmol) in CH_2Cl_2 (3 mL) at 0 °C and the resulting mixture was stirred 0.5 h. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford A_1BC trichloroacetimdiate **81** (0.55 g) as a white foam.

A_1BC seleno-glycoside 82: PhSeH (2.3 mL, 0.5 M solution in CH_2Cl_2, 1.17 mmol) was added to a solution of A_1BC trichloroacetimdiate **81** (0.55 g) and 4 Å MS in CH_2Cl_2 (2 mL), and the resulting mixture was stirred for 5 min. The reaction mixture was cooled to −78 °C, $BF_3 \cdot Et_2O$ (0.015 mL, 0.12 mmol) was added dropwise, and the reaction mixture was stirred for 1 h. The reaction mixture was quenched by the addition of Et_3N (2 mL), diluted with CH_2Cl_2 (200 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 → 50 % Et_2O in hexanes) to afford A_1BC seleno-glycoside **82** (0.477 g, 78 % over two steps, α:β ca. 1:9) as a white foam. **82**: R_f = 0.16 (30 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −8.1 (c = 1.36, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3033, 2952, 2871, 1739, 1566, 1451, 1376, 1249, 1134, 1065, 903, 731 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.59 (d, J = 6.8 Hz, 2H, ArH), 7.50 (d, J = 7.3 Hz, 2H, ArH), 7.42–7.25 (m, 11H, ArH), 5.05, 5.03 (AB, J = 10.4 Hz, 2H, CH_2Ar), 5.03 (dt, J = 8.8, 0.9 Hz, 1H, C2), 4.94, 4.64 (AB, J = 11.4 Hz, 2H, CH_2Ar), 4.88 (t, J = 8.9 Hz, 1H, B4), 4.81 (dd, J = 10.2, 0.9 Hz, 1H, C1), 4.67 (d, J = 9.7 Hz, 1H, B1), 3.98 (ddd, J = 12.9, 11.3, 4.9 Hz, 1H, B3), 3.84 (s, 3H, OMe), 3.61 (br t, J = 7.0 Hz, 1H, C3), 3.47–3.41 (m, 2H, C4, C5), 3.37 (dq, J = 9.4, 6.0 Hz, 1H, B5), 2.37 (s, 3H, Me (A_1)), 2.34 (dd, J = 12.4, 4.9 Hz, 1H, B2), 1.97 (s, 3H, OAc), 1.76 (dt, J = 11.6, 11.6 Hz, 1H, B2), 1.35 (d, J = 4.6 Hz, 3H, C6), 1.32 (d, J = 6.2 Hz, 3H, B6), 1.05–0.99 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.5, 165.7, 152.9, 152.7, 138.5, 135.9, 134.5, 134.2, 129.0, 128.5, 128.4, 128.2, 128.1, 128.0, 127.7, 127.5, 126.6, 126.1, 121.6, 100.0, 82.4, 82.3, 81.8, 79.3, 76.5, 74.8, 74.8, 72.5, 70.7, 69.9, 61.9, 41.0, 20.9, 18.1, 17.9, 17.9, 12.8; HRMS (FAB): calcd for $C_{52}H_{66}Cl_2O_{11}SeSiCs$ $[M+Cs]^+$: 1177.1971, found 1177.1919.

A_1BC alcohol 83: nBu$_4$NF (0.55 mL, 0.55 mmol) was added to a solution of A_1BC seleno-glycoside **82** (0.475 g, 0.45 mmol) in THF (2 mL) and the resulting mixture was stirred at 25 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), diluted with CH_2Cl_2 (200 mL) and washed with H_2O (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 → 70 % Et_2O in hexanes) to afford A_1BC alcohol **83** (0.37 g, 91 %) as a white foam. **83**: R_f = 0.18 (50 % Et_2O in hexanes); $[\alpha]_D^{22}$ = +7.8 (c = 0.27, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3425, 3050, 2943, 2872, 1737, 1449, 1373, 1255, 1126, 1061, 1026, 908, 744, 697 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.59–7.24 (m, 15H, ArH), 5.02 (s, 2H, CH_2Ar), 5.00 (t, J = 9.6 Hz, 1H, C2), 4.93, 4.63 (AB, J = 11.6 Hz, 2H, CH_2Ar), 4.79 (d, J = 10.3 Hz, 1H, C1), 4.78 (t, J = 10.4 Hz, 1H, B4), 4.69 (dd, J = 9.7, 1.9 Hz, 1H, B1), 3.87 (s, 3H, OMe), 3.78 (br s, 1H, B3), 3.57 (br t, J = 8.7 Hz, 1H, C3), 3.45 (t, J = 9.4 Hz, 1H, C4), 3.43 (dq, J = 9.4, 5.7 Hz, 1H, C5), 3.36 (dq, J = 9.5, 6.2 Hz, 1H, B5), 2.73 (br d, J = 2.3 Hz, 1H, OH), 2.35 (s, 3H, Me (A_1)), 2.35–2.32 (m, 1H, B2), 1.95 (s, 3H, OAc), 1.73 (dt, J = 12.2, 9.8 Hz, 1H, B2), 1.34 (d, J = 5.7 Hz, 3H, C6), 1.23 (d, J = 6.2 Hz, 3H, B6); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.5, 166.4, 153.0, 151.8, 138.6, 135.9, 134.6, 133.2, 128.9, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.6, 127.4, 126.9, 126.4, 100.5, 82.5, 82.4, 81.8, 79.8, 76.6, 74.9, 74.9, 72.5, 69.8, 69.6, 62.4, 39.3, 21.0, 18.1, 17.6, 17.4; HRMS (FAB): calcd for $C_{43}H_{46}Cl_2O_{11}SeCs$ $[M+Cs]^+$: 1021.0637, found 1021.0677.

A_1B(A)C trisaccharide 84: Ring A glycosyl fluoride **9** (0.110 g, 0.50 mmol) and A_1BC alcohol **83** (0.22 g, 0.25 mmol) were azeotroped with benzene (2 × 2 mL) and then dried under high vacuum for 1 h. The residue was dissolved in Et_2O/CH_2Cl_2 (1:1, 1.5 mL), 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 5 min. $SnCl_2$ (0.056 g, 0.29 mmol) was added to the reaction mixture in one portion and the resulting mixture

was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of Et_3N (2 mL), diluted with CH_2Cl_2 (200 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 $A_1B(A)C$ trisaccharide **84** (0.211 g, 80%) as a white foam. **84**: $R_f = 0.11$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -30.0$ ($c = 0.21$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3002, 2966, 2931, 2861, 1737, 1543, 1455, 1384, 1243, 1132, 1085, 1031, 908, 738, 697\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.60-7.25$ (m, 15H, ArH), 5.05, 5.02 (AB, $J = 10.1$ Hz, 2H, CH_2Ar), 5.01 (t, $J = 10.1$ Hz, 1H, C2), 4.94 (dd, $J = 4.8$, 1.6 Hz, 1H, A1), 4.91, 4.64 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.87 (t, $J = 9.4$ Hz, 1H, B4), 4.80 (d, $J = 10.2$ Hz, 1H, C1), 4.67 (dd, $J = 9.9$, 1.7 Hz, 1H, B1), 3.85 (s, 3H, OMe), 3.85–3.81 (m, 1H, B3), 3.64 (d, $J = 9.4$ Hz, 1H, A4), 3.57 (t, $J = 8.8$ Hz, 1H, C3), 3.50–3.39 (m, 4H, A5, B5, C4, C5), 3.35 (s, 3H, OMe), 2.45 (dd, $J = 13.8$, 5.1 Hz, 1H, A2), 2.38 (s, 3H, Me (A_1)), 2.29 (ddd, $J = 12.6$, 4.9, 1.5 Hz, 1H, B2), 2.01 (dd, $J = 13.8$, 1.8 Hz, 1H, A2), 1.96 (s, 3H, OAc), 1.71–1.67 (m, 1H, B2), 1.56 (s, 3H, Me (A3)), 1.34 (d, $J = 5.9$ Hz, 3H, C6), 1.29 (d, $J = 6.2$ Hz, 3H, B6), 0.84 (d, $J = 6.2$ Hz, 3H, A6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 169.5, 165.5, 153.3, 153.2, 138.5, 135.8, 134.7, 134.6, 129.0, 128.9, 128.6, 128.5, 128.2, 128.0, 128.0, 127.5, 127.5, 127.3, 121.6, 100.0, 92.4, 89.9, 84.2, 82.4, 82.1, 81.8, 76.6, 76.0, 74.9, 74.8, 72.6, 72.3, 71.0, 66.2, 65.8, 62.0, 60.7, 40.0, 36.4, 30.3, 21.0, 19.3, 18.2, 18.0, 17.6, 15.2$; HRMS (FAB): calcd for $C_{51}H_{59}Cl_2NO_{15}SeCs$ $[M+Cs]^+$: 1207.2426, found 1207.2421.

$A_1B(A)C$ alcohol 85: NaOH (2 mg, 0.06 mmol) was added to a solution of $A_1B(A)C$ trisaccharide **84** (0.21 g, 0.20 mmol) in MeOH/Et_2O (1:1, 1 mL) at 25 °C and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (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 → 70% Et_2O in hexanes) to afford $A_1B(A)C$ alcohol **85** (0.185 g, 91%) as a white foam. **85**: $R_f = 0.20$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -36.1$ ($c = 0.40$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3476, 2939, 1732, 1542, 1453, 1391, 1251, 1128, 1032, 911, 736\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.64$ (d, $J = 7.0$ Hz, 2H, ArH), 7.57 (d, $J = 7.0$ Hz, 2H, ArH), 7.45–7.27 (m, 11H, ArH), 5.06, 5.03 (AB, $J = 10.2$ Hz, 2H, CH_2Ar), 4.98, 4.83 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.94 (dd, $J = 5.0$, 1.8 Hz, 1H, A1), 4.89 (t, $J = 9.4$ Hz, 1H, B4), 4.72 (d, $J = 9.6$ Hz, 1H, C1), 4.67 (dd, $J = 9.7$, 1.8 Hz, 1H, B1), 3.89–3.83 (m, 1H, B3), 3.86 (s, 3H, OMe), 3.65 (d, $J = 9.4$ Hz, 1H, A4), 3.53–3.32 (m, 6H, A5, B5, C2, C3, C4, C5), 3.36 (s, 3H, OMe), 2.49 (br s, 1H, OH), 2.46 (dd, $J =$ 13.8, 5.0 Hz, 1H, A2), 2.39 (s, 3H, Me (A_1)), 2.29 (ddd, $J = 12.9$, 5.1, 1.8 Hz, 1H, B2), 2.02 (dd, $J = 13.8$, 1.8 Hz, 1H, A2), 1.72–1.65 (m, 1H, B2), 1.68 (s, 3H, Me (A3)), 1.34 (d, $J = 5.9$ Hz, 3H, B6 or C6), 1.33 (d, $J = 6.2$ Hz, 3H, B6 or C6), 0.84 (d, $J = 6.2$ Hz, 3H, A6); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 165.5, 153.2, 153.1, 138.7, 135.8, 135.1, 134.7, 129.0, 128.6, 128.5, 128.3, 128.2, 127.6, 127.5, 126.3, 125.9, 125.4, 99.7, 92.4, 89.9, 84.3, 84.2, 83.0, 81.7, 77.0, 76.1, 75.0, 74.9, 73.1, 72.3, 71.0, 66.2, 61.9, 60.7, 40.0, 36.4, 30.2, 19.3, 18.3, 18.2, 18.0, 17.6; HRMS (FAB): calcd for $C_{49}H_{57}Cl_2NO_{14}SeCs$ $[M+Cs]^+$: 1166.1378, found 1166.1319.

$A_1B(A)C$ 2-phenylseleno-1-fluoro donor 2: DAST (0.013 mL, 0.090 mmol) was added to a solution of $A_1B(A)C$ alcohol **85** (0.062 g, 0.060 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (2 mL), 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 to afford the crude fluoride **2** (ca. 100%, α:β ca. 8:1) which was used crude in the next reaction.

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[1] For a review on the chemistry and biology of vancomycin and other glycopeptide antibiotics, see: K. C. Nicolaou, C. N. C. Boddy, S. Bräse, N. Winssinger, *Angew. Chem.* **1999**, *109*, 1518–1519; *Angew. Chem. Int. Ed.* **1999**, *38*, 2096–2152.

[2] H. Breithaupt, *Nat. Biotechnol.* **1999**, *17*, 1165–1169.

[3] a) A. K. Ganguly, B. Pramanik, T. C. Chan, O. Sarre, Y.-T. Liu, J. Morton, V. M. Girijavallabhan, *Heterocycles* **1989**, *28*, 83–88; b) A. K. Ganguly in *Topics in Antibiotic Chemistry*, *Vol. 2* (*Part B*) (Ed.: P. G. Sammes), Wiley, New York, **1978**, pp. 61–96; c) A. K. Ganguly, V. M. Girijavallabhan, O. Sarre, International Patent **1987**, WO87/02366 [*Chem. Abstr.* **1987**, *107*, 97061]; d) J. Waltz, M. Patel, J. Marquez, M. Kalyanpur, A. Horan, United States Patent **1986**, 4597968 A [*Chem. Abstr.* **1986**, *105*, 170628]; e) A. K. Ganguly, J. L. McCormick, L. Jinping, A. K. Saksena, P. R. Das, R. Pradip, T. M. Chan, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1209–1214.

[4] D. E. Wright, *Tetrahedron* **1979**, *35*, 1207–1237.

[5] a) M. Patel, V. Gullo, R. Hare, D. Loebenberg, H. Kwon, G. Miller, European Patent **1993**, EP0538011A1 [*Chem. Abstr.* **1993**, *119*, 103331]; b) M. Patel, V. Gullo, R. Hare, D. Loebenberg, H. Kwon, G. Miller, United States Patent **1998**, US5624914 [*Chem. Abstr.* **1997**, *129*, 86048].

[6] a) J. A. Maertens, *Curr. Opin. Anti-Infect. Invest. Drugs* **1999**, *1*, 49–56; b) J. A. Maertens, *IDrugs* **1999**, *2*, 446–453.

[7] H. Wolf, *FEBS Letters* **1973**, *36*, 181–186.

[8] a) K. C. Nicolaou, H. J. Mitchell, H. Suzuki, R. M. Rodriguez, O. Baudoin, K. C. Fylaktakidou, *Angew. Chem.* **1999**, *111*, 3523–3528; *Angew. Chem. Int. Ed.* **1999**, *38*, 3334–3339; b) K. C. Nicolaou, R. M. Rodriguez, K. C. Fylaktakidou, H. Suzuki, H. J. Mitchell, *Angew. Chem.* **1999**, *111*, 3529–3534; *Angew. Chem. Int. Ed.* **1999**, *38*, 3340–3345; c) K. C. Nicolaou, H. J. Mitchell, R. M. Rodriguez, K. C. Fylaktakidou, H. Suzuki, *Angew. Chem.* **1999**, *111*, 3535–3540; *Angew. Chem. Int. Ed.* **1999**, *38*, 3345–3350.

[9] a) A. K. Ganguly, J. L. McCormick, T. M. Chan, A. K. Saksena, P. R. Das, *Tetrahedron Lett.* **1997**, *38*, 7989–7991; b) T. M. Chan, R. M. Osterman, J. B. Morton, A. K. Ganguly, *Magn. Reson. Chem.* **1997**, *35*, 529–532.

[10] For synthetic studies within the orthosomicin class, see: a) (review) P. Juetten, C. Zagar, H. D. Scharf, *Recent Prog. Chem. Synth. Antibiot. Relat. Microb. Prod.* **1993**, 475–549 and references therein; b) P. Juetten, H. D. Scharf, G. Raabe, *J. Org. Chem.* **1991**, *56*, 7144–7149; c) J. Dornhagen, H. D. Scharf, *Tetrahedron* **1985**, *41*, 173–175; d) M. Trumtel, P. Tavecchia, A. Veyrières, P. Sinaÿ, *Carbohydr. Res.* **1990**, *202*, 257–275.

[11] K. C. Nicolaou, H. J. Mitchell, K. C. Fylaktakidou, R. M. Rodríguez, H. Suzuki, *Chem. Eur. J.* **2000**, *6*, ■■, Part 2 in this series of four papers.

[12] K. C. Nicolaou, H. J. Mitchell, R. M. Rodríguez, K. C. Fylaktakidou, H. Suzuki, S. R. Conley, *Chem. Eur. J.* **2000**, *6*, ■■, Part 3 in this series of four papers.

[13] K. C. Nicolaou, K. C. Fylaktakidou, H. J. Mitchell, F. van Delft, R. M. Rodríguez, S. R. Conley, Z. Jin, *Chem. Eur. J.* **2000**, *6*, ■■, Part 4 in this series of four papers.

[14] K. C. Nicolaou, R. M. Rodríguez, H. J. Mitchell, F. L. van Delft, *Angew. Chem.* **1998**, *110*, 1975–1977; *Angew. Chem. Int. Ed.* **1998**, *37*, 1874–1876.

[15] For a recent review, see: M. Schuster, S. Blechert, *Angew. Chem.* **1997**, *109*, 2124–2145; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2036–2056.

[16] K. C. Nicolaou, T. Ladduwahetty, J. L. Randall, A. Chucholowski, *J. Am. Chem. Soc.* **1986**, *108*, 2466–2467.

[17] a) K. C. Nicolaou, H. J. Mitchell, F. L. van Delft, F. Rübsam, R. M. Rodríguez, *Angew. Chem.* **1998**, *110*, 1972–1974; *Angew. Chem. Int. Ed.* **1998**, *37*, 1871–1874; b) K. C. Nicolaou, H. J. Mitchell, N. F. Jain, N. Winssinger, R. Hughes, T. Bando, *Angew. Chem.* **1999**, *111*, 253–257; *Angew. Chem. Int. Ed.* **1999**, *38*, 240–244; c) K. C. Nicolaou, H. J. Mitchell, N. F. Jain, T. Bando, R. Hughes, N. Winssinger, S. Natarajan, A. E. Koumbis, *Chem. Eur. J.* **1999**, *5*, 2648–2667.

  0947-6539/00/0617-3114 $ 17.50+.50/0

[18] J. A. Marco, M. Cards, J. Murga, F. González, E. Falomir, *Tetrahedron Lett*. **1997**, *38*, 1841–1844.
[19] M. Hirama, I. Nishizaki, T. Shigemoto, S. Itô, *J. Chem. Soc. Chem. Commun*. **1986**, 393–394.
[20] P. S. Bailey, J. E. Keller, *J. Org. Chem*. **1968**, *33*, 2680–2684.
[21] a) W. Rosenbrook, Jr., D. A. Riley, P. A. Lartey, *Tetrahedron Lett*. **1985**, *26*, 3–4; b) G. H. Posner, S. R. Haines, *Tetrahedron Lett*. **1985**, *26*, 5–8; c) T. Mukaiyama, Y. Murai, S. Shoda, *Chem. Lett*. **1981**, 431–433.
[22] G. Solladie, A. Rubio, M. Carreno, J. Ruano, *Tetrahedron: Asymmetry* **1990**, *1*, 187–198.
[23] L. A. Carpino, A. El-Faham, *J. Am. Chem. Soc*. **1995**, *117*, 5401–5402.
[24] S. Hatakeyama, K. Sakurai, S. Takano, *Tetrahedron Lett*. **1986**, *27*, 4485–4488.
[25] For a review on the chemistry of tin-containing intermediates in carbohydrate chemistry, see: T. B. Grindley, *Adv. Carbohydr. Chem. Biochem*. **1998**, *53*, 17–142.
[26] A. Y. Chemyak, K. V. Antonov, N. K. Kochetkov, *Biorg. Khim*. **1989**, *15*, 1113–1127.
[27] S. Czernecki, K. Vijayakumaran, G. Ville, *J. Org. Chem*. **1986**, *51*, 5472–5474.
[28] R. R. Schmidt, J. Michel, *Angew. Chem*. **1980**, *92*, 763–765; *Angew. Chem. Int. Ed. Engl*. **1980**, *19*, 731–733.
[29] S. Mehta, B. M. Pinto, *J. Org. Chem*. **1993**, *58*, 3269–3276.

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  0947-6539/00/0617-3115 $ 17.50+.50/0