Total Synthesis of Everninomicin 13,384-1—Part 2: Synthesis of the $FGHA_2$ Fragment

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

Abstract: The stereoselective synthesis of everninomicin's 13,384-1 (**1**) $FGHA_2$ fragment (**2**) in a suitable form for incorporation into the final target (**1**) is described. The construction of the FG 1,1′-disaccharide linkage relied on a new method based on tin-acetal chemistry, while for the GH orthoester bridge, a number of approaches were explored. Final success for the latter construction came when a novel 1,2-phenylseleno migration reaction was applied to couple rings G and H, followed by ketene acetal and orthoester formation.

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

Introduction

In the preceding paper,[1] we described studies that led to the construction of a fully substituted and activated $A_1B(A)C$ fragment (see structure **4**, Figure 1) designed for the total synthesis of everninomicin 13,384-1 (**1**). In this paper we detail our investigations which culminated in the synthesis of a suitable $FGHA_2$ fragment (see structure **2**, Figure 1) needed for the intended assembly of **1**.

Results and Discussion

First-generation approaches to the $FGHA_2$ fragment: According to the defined global retrosynthetic analysis outlined in Figure 1, the key advanced intermediates for the total synthesis of **1** were compounds **2**–**4**. Initial inspection of the $FGHA_2$ fragment **2**, revealed several options for further retrosynthetic simplification. Our first-generation analysis involved disassembly of this key intermediate through the indicated disconnections (1,1′-disaccharide and ester bonds) leading to acyl fluoride **5** (A_2 fragment), tin-acetal **6** (fragment F), and orthoester **7** (fragment GH). Further simplification of the GH orthoester **7** led to orthoester **8** which was then disconnected to reveal xylose lactone **9** and threitol derivative **10** as potential starting materials. Building blocks **5** and **6** were traced back to aromatic system **12** and carbohydrate unit **11**, respectively.

Aside from the orthoester moiety, one of the most serious challenges presented by the $FGHA_2$ fragment is its 1,1′-disaccharide linkage. Not only has one to construct this bridge between polyfunctional and sensitive substrates, but also one is faced with the problem of controlling its stereochemistry at the two glycoside bonds. In order to address this issue we considered the plan outlined in Figure 2, in which a trichloroacetimidate derivative of ring G carrying a directing group (acetate) at position 2 was envisioned as a means to ensure the α-stereochemistry of the ring G glycoside bond. The utilization of the lactol representative of ring F in which the α-anomer was expected to predominate was thought to be a sure entry into the α-glycoside (ring F) series, whereas the locking of the anomeric hydroxyl group into its β-configuration by forming a five-membered ring tin-acetal was proposed as an insurance for the generation of the desired β-glycoside bond (ring F). These ideas proved to be correct as shown in Scheme 1 in which the results of our initial studies along these lines are summarized. Thus, when acceptor **13** (R = Bn) was exposed to donor **14** in the presence of TMSOTf, the $1\alpha,1'\alpha$-disaccharide **15** was formed exclusively in 87% yield as expected (for abbreviations of protecting groups and reagents, see legends in schemes). On the other hand, conversion of **13** (R = H) to the tin-acetal **16** followed by in situ coupling with trichloroacetimidate **14** in the presence of TMSOTf led only to the desired $1\beta,1'\alpha$-disaccharide **17** in 66% yield. These initial findings were expanded to a general method[2] for the

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

  0947-6539/00/0617-3116 $ 17.50+.50/0

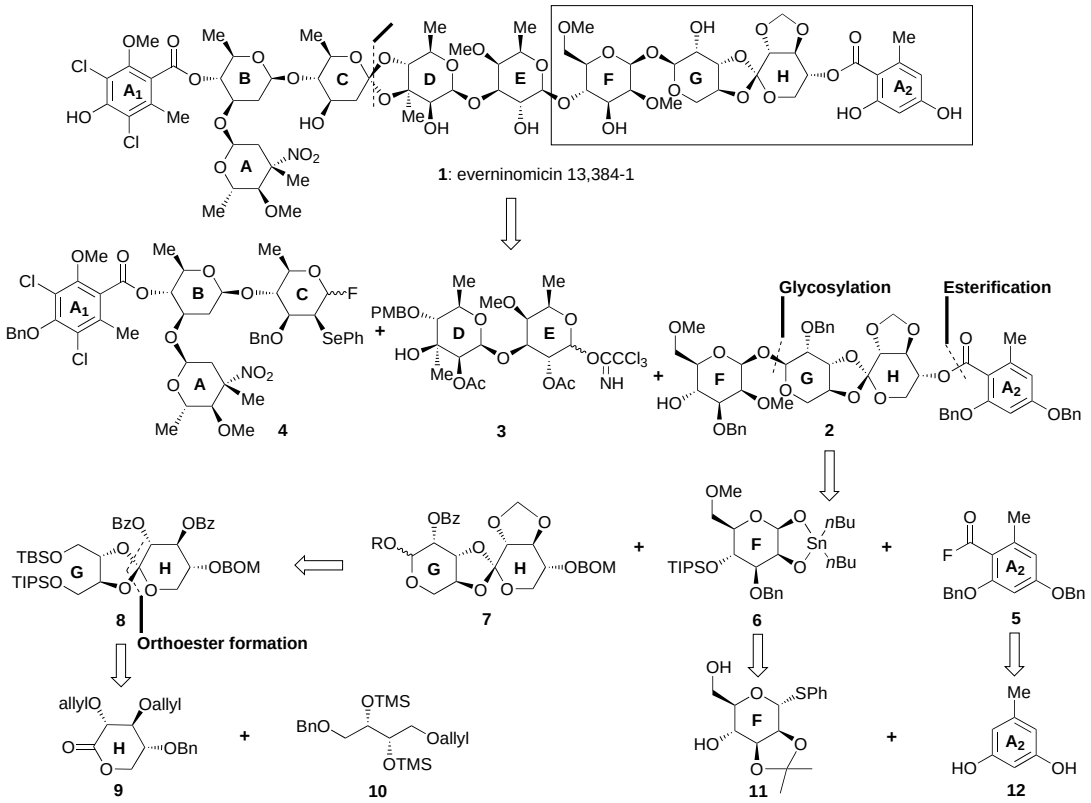


Figure 1. First-generation retrosynthetic analysis of $FGHA_2$ fragment **2**. Ac = acetyl; Bz = benzoyl; Bn = benzyl; PMB = *p*-methoxybenzyl; TBS = *t*butyldimethylsilyl; TIPS = triisopropylsilyl; TMS = trimethylsilyl; BOM = benzyloxy methoxy.

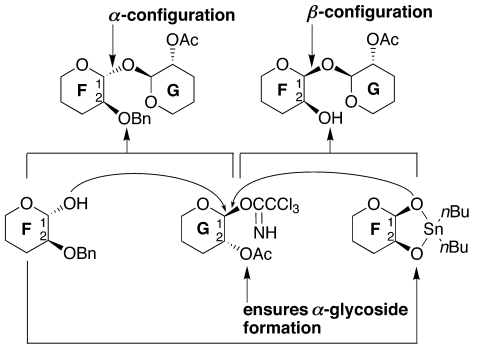
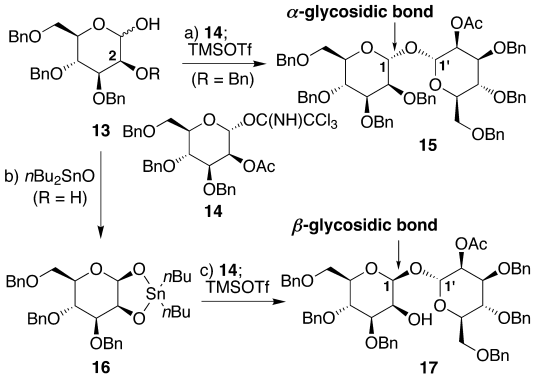


Figure 2. Devising stereocontrolled entries into 1,1′-disaccharides.

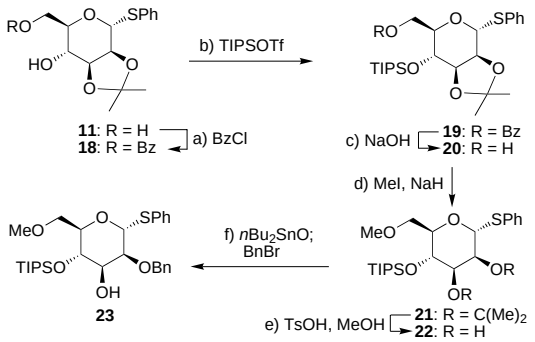


Scheme 1. Synthesis of model 1,1′-disaccharides **15** and **17**. a) 1.6 equiv **14**, 0.1 equiv TMSOTf, CH_2Cl_2, 0 → 25 °C, 20 min, 87 %; b) 1.1 equiv nBu_2SnO, MeOH, reflux, 3 h, 100 %; c) 1.6 equiv **14**, 0.5 equiv TMSOTf, Et_2O, 0 → 25 °C, 48 h, 66 %. Tf = trifluoromethanesulfonyl.

stereocontrolled construction of 1,1′-disaccharides and 1,1′:1″,2-trisaccharides as will be discussed in more detail in Part 4[3] of this series. It was also applied to the final ring FG system utilized in the total synthesis of **1** (vide infra).

Abstract in Greek: Περιγράφεται η στερεοεκλεκτική σύνθεση του τμήματος $FGHA_2$ της Everninomicin 13,384-1, σε κατάλληλη μορφή που θα οδηγήσει στον τελικό στόχο (**1**). Η δόμηση της FG 1,1′-δισακχαριτικής γέφυρας, βασίστηκε σε νέα μεθοδολογία που χρησιμοποιεί τη χημεία της κασσιτερικής ακετάλης, ενώ για τη γέφυρα του ορθοεστέρα GH εξερευνήθηκαν διάφοροι τρόποι προσέγγισης. Η επιτυχημένη σύνθεση της τελευταίας αυτής δομικής μονάδας έγινε τελικά εφαρμόζοντας τη νέα αντίδραση 1,2-σεληνιοφαινυλο-μετάθεσης για να συνδεθούν οι δακτύλιοι G και H, και ολοκληρώθηκε στη συνέχεια με τη δημιουργία της κετενοακετάλης και του ορθοεστέρα.

In our initial foray towards the $FGHA_2$ fragment we adopted tin-acetal **6** containing a TIPS ether at C-4 (see Figure 1). To prepare this compound, we embarked on the sequence shown in Scheme 2. Thus, selective monobenzoylation of mannose derivative **11**[4] (BzCl, Et_3N, 4-DMAP cat.) furnished primary benzoate **18** in 91 % yield whose silylation (TIPSOTf, 2,6-lutidine) gave **19** (99 %). Basic methanolysis (NaOH, MeOH, 94 % yield) followed by methylation (NaH, MeI, 92 % yield) gave **21** via **20**. Acidic hydrolysis of the acetonide from **21** (TsOH, MeOH) led to diol **22** (87 % yield based on 62 % conversion). At this stage, it was anticipated that the C-3 hydroxyl group (equatorial) would be



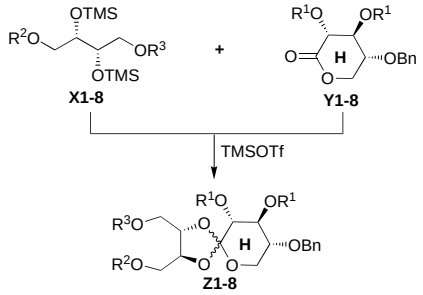
Scheme 2. Attempted synthesis of carbohydrate building block F (**6**). a) 1.0 equiv BzCl, 1.2 equiv Et_3N, 0.1 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 91 %; b) 1.2 equiv TIPSOTf, 1.4 equiv 2,6-lutidine, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 3 h, 99 %; c) 0.2 equiv NaOH, MeOH/Et_2O 1:1, $25\,^{\circ}C$, 1 h, 94 %, d) 1.2 equiv NaH, 1.6 equiv MeI, DMF, $0 \rightarrow 25\,^{\circ}C$, 2 h, 92 %; e) 0.03 equiv TsOH, 1.2 equiv $(CH_2OH)_2$, MeOH/Et_2O 10:1, $25\,^{\circ}C$, 8 h, 87 % based on 62 % conversion; f) 1.1 equiv nBu_2SnO, toluene, reflux, 3 h; 1.2 equiv BnBr, 0.2 equiv nBu_4NI, $25 \rightarrow 110\,^{\circ}C$, 5 h, 81 %. Ts = *p*-toluenesulfonyl; 4-DMAP = 4-dimethylaminopyridine; DMF = dimethylformamide.

preferentially benzylated over the C-2 hydroxyl (axial) in a tin-acetal mediated reaction.[5] In the event, however, benzylation of **22** (nBu_2SnO; BnBr, nBu_4NI) led to the undesired C-2 benzyl ether **23** in 81 % yield. After several unsuccessful attempts to reverse this outcome or further manipulate the product, we decided to re-examine the general strategy for the construction of the targeted $FGHA_2$ intermediate. In particular, the construction of the GH orthoester moiety was placed at higher priority, before returning to ring F.

Our first attempts to assemble the GH orthoester system were focused on the reaction of lactones with 1,2-diol derivatives. The condensation of bis-TMS protected diols with ketones or esters is a well documented process for the formation of simple cyclic ketals and orthoesters.[6] In this context, and while acyclic diols and *cis*-1,2-cyclohexane type diols work quite efficiently as partners, *trans*-1,2-cyclohexane diols are suspected to present difficulties, and indeed at least one such case is reported to give only marginal or no yield of product at all in such condensations.[6] One possible strategy that avoids the intrinsic strain asssociated with the *trans*-1,2-oxygenated polycyclic systems such as the one involved here, is to employ an open-chain equivalent of ring G which could later be elaborated to the desired polycyclic framework. Table 1 summarizes the results of an exploratory study of this strategy. Although fruitful, this strategy was plagued with protecting group problems (e.g. entry 2, Table 1) due to the acidic conditions (TMSOTf) required for the orthoester formation. However, benzyl and allyl protecting groups (e.g. entries 1, 3, 8, Table 1) served well and high yields of the orthoesters were obtained. Initial attempts to selectively elaborate the fully benzylated orthoester **Z1** (entry 1, Table 1) failed and the use of unsymmetrical diols (entries 4, 6, 8, Table 1) led to mixtures (ca. 1:1) of diastereoisomers. Fortunately, it was found that both diastereoisomers **Z8** (entry 8, Table 1) could be transformed into a single product by a series of protecting group exchanges, and therefore this compound was chosen for further study.

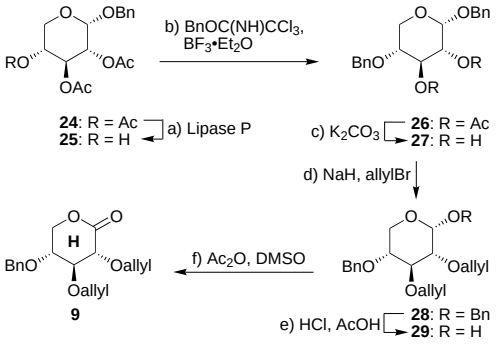
Lactone **Y8** was accessible from xylose benzyl glycoside **24**[7] by the sequence shown in Scheme 3. Thus, exposure of

Table 1. Synthesis of orthoesters related to the GH fragment.[a]



Entry	Y		X	Yield of Z
	R^1	R^2	R^3	[%]
1	Bn	Bn	Bn	92
2	PMB	Bn	Bn	[b]
3	allyl	Bn	Bn	97
4	allyl	Bn	TPS	31[d]
5	allyl	Bn	Bz	[c]
6	allyl	Bn	MMB	60[d]
7	allyl	allyl	SEM	[c]
8	allyl	allyl	Bn	97[d]

[a] 1.5 equiv **X**, 1.0 equiv **Y**, 0.3 equiv TMSOTf, CH_2Cl_2, $25\,^{\circ}C$, 12 h; [b] decomposition; [c] no reaction was observed; [d] $\approx$1:1 mixture of diastereoisomers at C-1. SEM = trimethylsilylethoxy methoxy; MMB = *m*-methoxybenzyl; TPS = *tert*-butyldiphenylsilyl.



Scheme 3. Synthesis of carbohydrate building block H (**9**). a) 2.0 equiv Lipase P (*w*/*w*), 2.0 equiv isoamyl alcohol, isooctane, $25\,^{\circ}C$, 96 h, 84 %; b) 0.1 equiv $BF_3 \cdot Et_2O$, 1.2 equiv $BnOC(NH)CCl_3$, CH_2Cl_2, $0\,^{\circ}C$, 3 h, 91 %; c) 0.2 equiv K_2CO_3, MeOH/Et_2O 1:1, $25\,^{\circ}C$, 1 h, 97 %; d) 2.2 equiv NaH, 3.2 equiv allyl bromide, DMF, $0 \rightarrow 25\,^{\circ}C$, 2 h, 92 %; e) 1N HCl in AcOH 1:40, $80\,^{\circ}C$, 5 h, 91 %; f) Ac_2O/DMSO (1:2), $25\,^{\circ}C$, 12 h, 96 %. DMSO = dimethyl sulfoxide.

triacetate **24** to Lipase P[8] in isooctane led to selective cleavage of the C-4 acetate furnishing **25** in 84 % yield. Compound **25** was then benzylated with $BnOC(NH)CCl_3$ in the presence of $BF_3 \cdot Et_2O$ leading to **26** (91 % yield) which was subjected to deacetylation (K_2CO_3, MeOH, 97 %) and bis-allylation of the resulting diol system (NaH, allyl bromide, 92 % yield), furnishing **28** via **27**. To reach **9**, the anomeric benzyl ether was cleaved (HCl, AcOH, $80\,^{\circ}C$) to afford lactol **29** (91 %), and the latter compound was oxidized with DMSO/Ac_2O (96 %). The other requisite fragment, bis-TMS ether **10** (see Scheme 4) was prepared from commercially available 2,3-*O*-isopropylidene-L-threitol by monoallylation (NaH, allyl bromide, 93 %), benzylation (NaH, BnBr, 97 %), acetonide cleavage (TsOH, MeOH, 96 %), and TMS ether formation (HMDS, TMSCl, 100 %).

0947-6539/00/0617-3118 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

The attempted construction of the GH orthoester system (e.g. compound **41**, Scheme 4) from building blocks **9** and **10** is shown in Scheme 4. Thus, mixing of **9** and **10** in the presence of TMSOTf, followed by cleavage of all three allyl ethers {[$(Ph_3P)_3RhCl$] cat.; OsO_4 cat./NMO} furnished triol orthoester **31** via **30** as a chromatographically separable mixture (ca. 1:1) of two diastereoisomers, and in 97% combined yield. The more polar stereoisomer of **31** was converted to the differentially protected derivative **35** by the following sequence: a) silylation (TBSOTf, 2,6-lutidine, $-78\,^{\circ}C$, 92% yield); b) benzoylation (BzCl, Et_3N, 4-DMAP cat., 97% yield; c) hydrogenolysis (H_2, 10% Pd/C, 95% yield); and d) silylation (TIPSOTf, 2,6-lutidine, 89% yield). The less polar isomer of **31** was also taken to **35** by implementing the reverse of the above sequence which proceeded with equal ease and in similar yields. The remaining secondary alcohol in **35** was protected as a BOM ether (BOMCl, iPr_2NEt, 89%) and the TBS group was selectively removed (PPTS, EtOH, 83%) from the resulting product to afford hydroxy compound **36** via **8**. The desired one-carbon homologation was then carried out by first oxidizing alcohol **36** to the corresponding aldehyde under Swern conditions[9] [$(COCl)_2$, DMSO, Et_3N] and then adding directly Dondoni's TMS/thiazole reagent[10] affording **37** (ca. 10:1 mixture of diastereoisomers) in 97% yield. The major diastereoisomer of **37** was converted to the TES derivative **38** by exposure to TESOTf and 2,6-lutidine (89% yield) and before unveiling the aldehyde moiety, several compounds were prepared and examined for their crystallinity as potential candidates for X-ray analysis. Thus, exposure of **38** to K_2CO_3 in MeOH led to the cleavage of both benzoate groups as well as the TES ether and the resulting triol was converted to the tri-*p*-bromobenzoate **39** (*p*-BrBzCl, Et_3N, 4-DMAP cat., 86% over two steps), which however, failed to crystallize.

Fortunately, exposure of **39** to nBu_4NF resulted in the removal of the TIPS group and one of the *p*-bromobenzoates (another migrated to the primary alcohol) leading to compound **40** whose crystalline form (m.p. 184 °C, CH_2Cl_2/hexanes) allowed its X-ray crystallographic analysis[11] (see ORTEP drawing, Figure 3). This analysis revealed that while the side chain hydroxyl group configuration was correct, the orthoester stereochemistry was not (see structure, Figure 3).

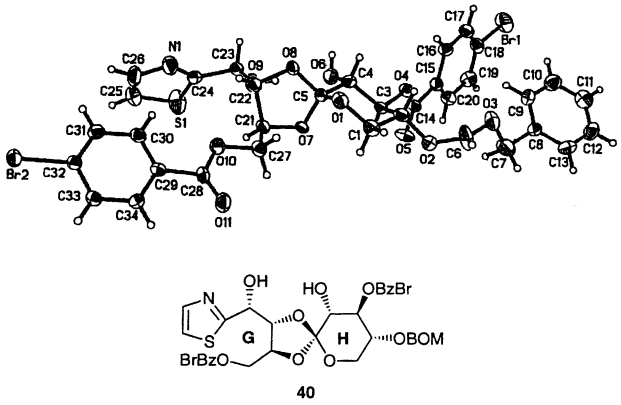
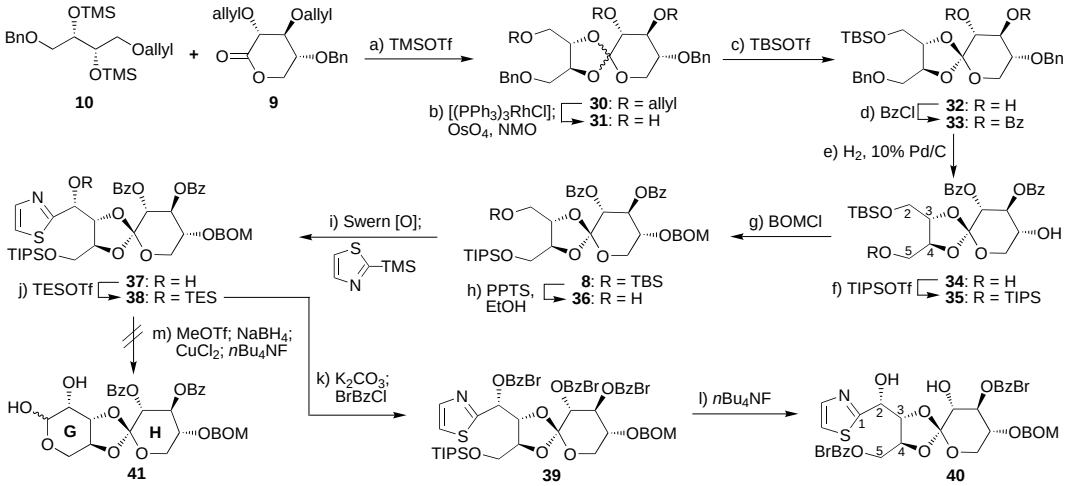


Figure 3. ORTEP drawing of orthoester **40** derived from an X-ray crystallographic analysis.[11]

Inversion of the orthoester stereochemistry could be easily obtained by simply reversing the TBS and TIPS protection steps described in the above sequence. In the end, however, our final drive towards the GH orthoester **41** did not succeed



Scheme 4. Attempted assembly of GH fragment **41**. a) 2.0 equiv **10**, 1.0 equiv **9**, 0.15 equiv TMSOTf, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 12 h, 97%, 1:1 mixture of diastereoisomers; b) i) 4.5 equiv DABCO, 0.07 equiv [$(Ph_3P)_3RhCl$], EtOH/H_2O 10:1, reflux, 2 h; ii) 4.5 equiv NMO, 0.2 equiv OsO_4, Me_2CO/H_2O 10:1, 25 °C, 8 h, 97% (two diastereoisomers ca. 1:1 ratio, more polar one shown here); c) 1.1 equiv TBSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, $-78\,^{\circ}C$, 0.5 h, 92%; d) 2.5 equiv BzCl, 4.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 97%; e) H_2, 10% Pd/C 0.1 equiv *w*/*w*, EtOAc, 25 °C, 2 h, 95%; f) 1.1 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, $-78\,^{\circ}C$, 0.5 h, 89%; g) 5.0 equiv BOMCl, 10.0 equiv iPr_2NEt, CH_2Cl_2, 50 °C, 4 h, 89%; h) 0.1 equiv PPTS, EtOH/THF (3:1), 50 °C, 6 h, 83%; i) i) 1.8 equiv $(COCl)_2$, 2.0 equiv DMSO, $-78\,^{\circ}C$, 2 h; ii) 4.0 equiv Et_3N, $-78 \rightarrow -40\,^{\circ}C$, 2 h; iii) 2.0 equiv TMS-thiazole, $-40 \rightarrow 25\,^{\circ}C$, 12 h; iv) 0.06 equiv PPTS, MeOH, 25 °C, 2 h, 97%, ca. 10:1 mixture of diastereoisomers; j) 1.1 equiv TESOTf, 1.2 equiv 2,6-lutidine, CH_2Cl_2, 0 °C, 0.5 h, 89%; k) 0.5 equiv K_2CO_3, MeOH, 25 °C, 1 h; 4.0 equiv BrBzCl, 5.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 86% over two steps; l) 1.3 equiv nBu_4NF, THF, 25 °C, 1 h, 88%; m) i) 1.2 equiv MeOTf, MeCN, 25 °C, 0.5 h; ii) 2.4 equiv $NaBH_4$, MeOH, $0 \rightarrow 25\,^{\circ}C$, 0.5 h; iii) 1.2 equiv $CuCl_2$, 8.0 equiv CuO, $MeCN/H_2O$ 5:1, 25 °C, 2 h; iv) 2.5 equiv nBu_4NF, THF, 25 °C, 2 h, decomposition. DABCO = 1,4-diazabicyclo[2. 2.2]octane; NMO = *N*-methylmorpholine *N*-oxide; PPTS = pyridinium *p*-toluenesulfonate; BrBz = *p*-bromobenzoyl, TES = triethylsilyl; THF = tetrahydrofuran.

in the face of the compounds' refusal to cyclize into the tricyclic framework. Thus, while the aldehyde moiety of **38** could be unmasked employing Dondoni's protocol (MeOTf; $NaBH_4$; $CuO/CuCl_2$),[10] subsequent attempts to remove the silicon groups with fluoride led to decomposition. Attempts to functionalize or trap in situ any incipient lactol **41** also failed and so did attempts to lactonize the corresponding carboxylic acid which was derived by oxidation of the aldehyde. With these failed attempts, evidence was accumulating supporting the notion that the strain caused by the orthoester moiety was insurmountable, even by this approach. A new plan had to be devised based on the belief that the FG 1,1′-disaccharide system would have to be constructed prior to the installation of the GH orthoester moiety.

As a prelude to embarking on our latest plan we wished to explore and evaluate further methods for orthoester formation. To this end a number of activated carbohydrate derivatives were considered and synthesized as potential precursors, however, all of them failed to produce orthoesters in their reactions with the diols. Faced with such a daunting problem exasperated by the special and sensitive structure of our target molecule, we then decided to use a literature orthoester synthesis. Sinaÿ and co-workers[12] had established a method for forming 2-deoxy carbohydrate orthoesters starting with glycals and PhSeCl. Noting that no method had been reported to be successful in constructing the GH orthoester system of everninomicin, and being mindful of our previous technology of 1,2-phenylsulfeno migrations in carbohydrates,[13] we decided to employ a 1,2-phenylseleno migration/selenoxide elimination/cyclization sequence to form the desired orthoester systems. The general Scheme embodying these concepts is shown in Figure 4. Thus, armed with the confidence derived from Sinaÿ's work and our own experience with the 1,2-migration reaction, we initiated a second-generation program towards the desired $FGHA_2$ fragment.

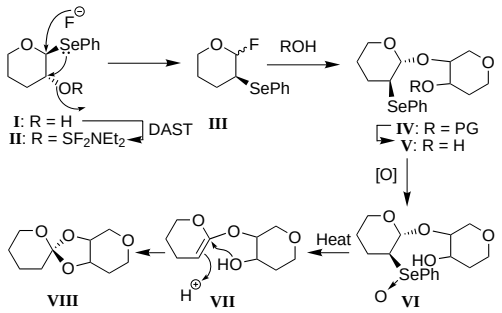


Figure 4. Orthoester formation via phenylseleno 1,2-migration followed by glycosylation (**I** → **II** → **III** → **IV**•) and ring closure after *syn*-elimination (**V** → **VI** → **VII** → **VIII**•). PG = protecting group.

Second-generation strategies towards the $FGHA_2$ fragment: Figure 5 outlines the second-generation retrosynthetic analysis of the targeted $FGHA_2$ fragment **2** based on the above findings and our new projections. Thus, disconnection of the indicated aromatic ester and orthoester bonds, revealed components **42** (FGH fragment) and **5** (A_2 fragment) as potential precursors. The FGH fragment **42** was further disconnected between rings G and H as shown, leading to FG diol **43** and 2-phenylseleno glycosyl fluoride **44** as key building blocks. A projected, selenium-assisted coupling of **44** and **43** was expected to furnish regio- and stereoselectively trisaccharide **42** whose functionality is poised for a Sinaÿ-type orthoester formation. Further disassembly of **43** by disconnection of its 1,1′-disaccharide bridge led to tin-acetal **45** and trichloroacetimidate **46** as desired building blocks. The stereoselective coupling of **45** with **46** was assured by our methodological studies on this chemistry as summarized above.

The constructions of the required building blocks **5**, **44**, **45**, and **46** are shown in Schemes 5 – 9. Returning to the ring F tin-acetal and recalling our difficulties with the TIPS group at C-4 (Scheme 2), which apparently thwarted our attempts to benzylate at C-3 due to its bulk, we now decided to use a much smaller protecting group at this position. This group had however, to be replaced later on in the synthesis. The successful synthesis of tin-acetal **45** is shown in Scheme 5. Thus, silylation of mannose-derived diol **11** (TBSOTf, 2,6-lutidine, −78 °C) furnished compound **47** (97 % yield) onto which the PMB group was installed by the action of NaH and PMBCl (95 % yield) affording, after desilylation (nBu_4NF, 95 % yield), primary alcohol **48**. Methylation of **48** (NaH, MeI, 95 % yield) then led to methyl ether **49** from which the acetonide group was removed by treatment with TsOH in MeOH to afford diol **50** (85 % yield). Pleasantly, this time the tin-acetal benzylation protocol (nBu_2SnO; BnBr, nBu_4NI

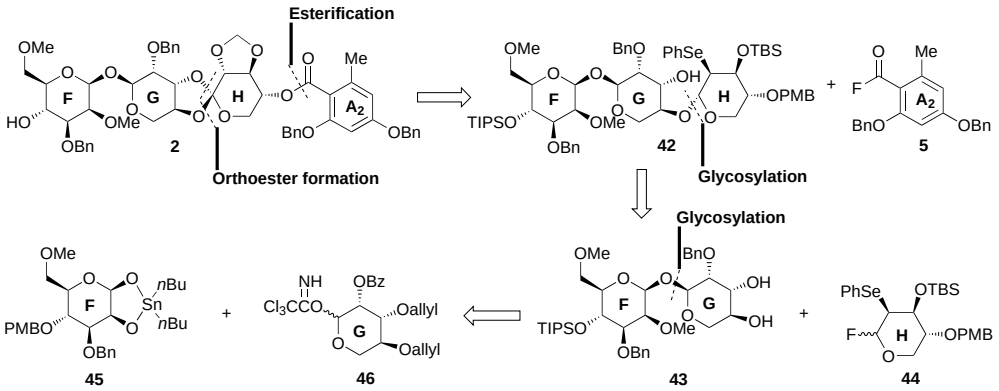
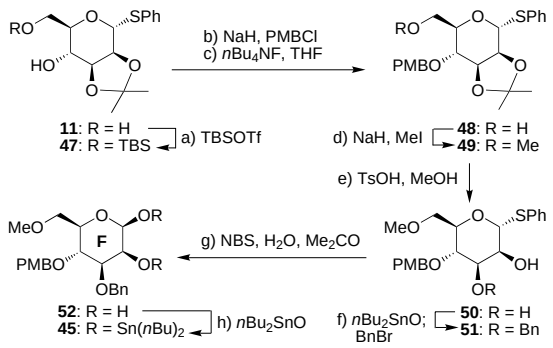


Figure 5. Revised retrosynthetic analysis of $FGHA_2$ fragment **2**.

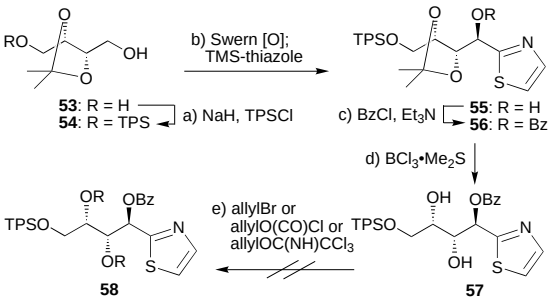
0947-6539/00/0617-3120 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17



Scheme 5. Synthesis of tin-acetal building block F (**45**). a) 1.1 equiv TBSOTf, 1.3 equiv 2,6-lutidine, CH_2Cl_2, $-78\,^{\circ}C$, 0.5 h, 97%; b) 1.1 equiv NaH, 1.3 equiv PMBCl, 0.2 equiv nBu_4NI, DMF/THF 1:1, $0 \rightarrow 25\,^{\circ}C$, 4 h, 95%; c) 1.2 equiv nBu_4NF, THF, $25\,^{\circ}C$, 1 h, 95%; d) 1.1 equiv NaH, 1.3 equiv MeI, DMF, $0 \rightarrow 25\,^{\circ}C$, 1 h, 95%; e) 0.2 equiv TsOH, 2.5 equiv $(CH_2OH)_2$, MeOH, $25\,^{\circ}C$, 5 h, 85%; f) 1.1 equiv nBu_2SnO, toluene, reflux, 3 h; 1.5 equiv BnBr, 0.2 equiv nBu_4NI, $25 \rightarrow 110\,^{\circ}C$, 5 h, 89%; g) 1.5 equiv NBS, Me_2CO/H_2O 10:1, $0 \rightarrow 25\,^{\circ}C$, 2 h, 97%; h) 1.1 equiv nBu_2SnO, MeOH, reflux, 3 h, 100%. NBS = *N*-bromosuccinimide.

cat.) provided the desired C-3 benzyl ether **51** in high yield (89%). Finally, the lactol was released from the phenylthioglycoside by the action of NBS/H_2O in acetone (97% yield) and the resulting diol **52** was engaged as the *cis*-1,2 tin-acetal **45** by treating with nBu_2SnO in refluxing MeOH. The quantitatively obtained *cis*-locked tin-acetal **45** was now ready for coupling with ring G.

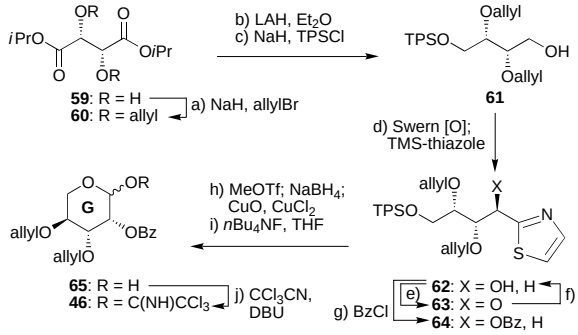
The next target was trichloroacetimidate[14] **46** for which two attempts were necessary before success. Our initial strategy towards this building block adopted Dondoni's TMS/thiazole chemistry and is shown in Scheme 6. Thus,



Scheme 6. Attempted synthesis of carbohydrate building block G (**58**). a) 1.0 equiv NaH, 1.0 equiv TPSCl, THF, $0 \rightarrow 25\,^{\circ}C$, 4 h, 90%; b) i) 2.0 equiv $(COCl)_2$, 2.5 equiv DMSO, CH_2Cl_2, $-78\,^{\circ}C$, 2 h; ii) 4.0 equiv Et_3N, $-78 \rightarrow 0\,^{\circ}C$, 2 h; iii) 2.0 equiv TMS-thiazole, $0 \rightarrow 25\,^{\circ}C$, 12 h; iv) 0.1 equiv PPTS, MeOH, $25\,^{\circ}C$, 2 h, 94%, ca. 10:1 mixture of diastereoisomers; c) 1.2 equiv BzCl, 1.5 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 96%; d) 2.0 equiv $BCl_3 \cdot Me_2S$, CH_2Cl_2, $0\,^{\circ}C$, 0.5 h, 91% based on 65% conversion.

monosilylation (NaH, TPSCl) of the commercially available diol **53** afforded TPS ether **54** (90% yield) setting the stage for a subsequent Swern oxidation [$(COCl)_2$/DMSO] and in situ reaction with TMS/thiazole leading, after acidic work-up to alcohol **55** (94% yield, ca. 10:1 ratio of diastereoisomers, **55** predominating). Benzoylation of **55** (BzCl, Et_3N, 4-DMAP cat., 96% yield) followed by acetonide cleavage led to diol **57**. Unfortunately, all attempts to obtain **58** from this diol through allyl protection (e.g. allyltrichloroacetimidate; allyl bromide; allyoxycarbonyl chloride) led either to decomposition or multiple inseparable products.

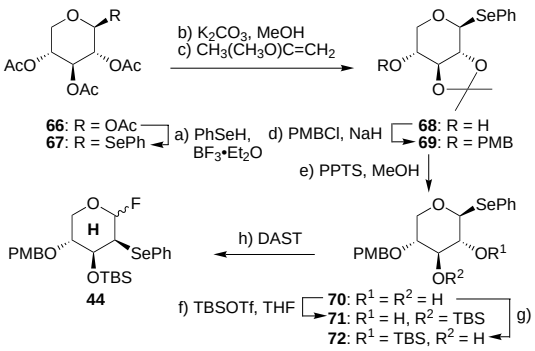
Faced with these difficulties, we opted for a second route which is shown in Scheme 7. Thus, bis-allylation of diisopropyl-L-tartrate (**59**) (NaH, allyl bromide) gave bis-allyl ether **60**



Scheme 7. Synthesis of carbohydrate building block G (**46**). a) 1.93 equiv NaH, 1.93 equiv allyl bromide, 0.02 equiv nBu_4NI, 0.005 equiv [18]crown-6, THF, $0 \rightarrow 25\,^{\circ}C$, 4 h, 97%; b) 1.7 equiv LAH, Et_2O, $0 \rightarrow 30\,^{\circ}C$, 3 h, 93%; c) 1.0 equiv NaH, 1.1 equiv TPSCl THF, $0 \rightarrow 25\,^{\circ}C$, 4 h, 90%; d) i) 2.0 equiv $(COCl)_2$, 2.5 equiv DMSO, CH_2Cl_2, $-78\,^{\circ}C$, 2 h; ii) 4.0 equiv Et_3N, $-78 \rightarrow 0\,^{\circ}C$, 2 h; iii) 2.0 equiv TMS-thiazole, $0 \rightarrow 25\,^{\circ}C$, 12 h; iv) 0.3 equiv PPTS, MeOH, $25\,^{\circ}C$, 2 h, 91%, 1:1 mixture of diastereoisomers; e) i) 2.0 equiv $(COCl)_2$, 3.0 equiv DMSO, $-78\,^{\circ}C$, 2 h; ii) 4.0 equiv Et_3N, $-78 \rightarrow 0\,^{\circ}C$, 2 h, 96%; f) 1.1 equiv LAH, Et_2O, $0\,^{\circ}C$, 2 h, 70%; g) 1.1 equiv BzCl, 1.5 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 98%; h) i) 1.2 equiv MeOTf, MeCN, $25\,^{\circ}C$, 15 min; ii) 2.4 equiv $NaBH_4$, MeOH, $0\,^{\circ}C$, 0.5 h; iii) 1.2 equiv $CuCl_2$, 8.0 equiv CuO, MeCN/H_2O 10:1, $25\,^{\circ}C$, 2 h; i) 1.5 equiv nBu_4NF, THF/AcOH 200:1, $25\,^{\circ}C$, 2 h, 81% over four steps; j) 5.0 equiv CCl_3CN, 0.05 equiv DBU, CH_2Cl_2, $0\,^{\circ}C$, 0.5 h, 85%, ca. 3:1 α:β mixture. LAH = lithium aluminumhydride; DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

(97% yield) whose LAH reduction (93% yield) followed by monosilylation (NaH, TPSCl, 90%) led to alcohol **61**, again setting the stage for a Dondoni one-carbon homologation. Swern oxidation [$(COCl)_2$/DMSO] followed by addition of TMS/thiazole afforded hydroxy compound **62** in 91% yield, but this time as a 1:1 mixture of diastereoisomers. While disappointed with the lack of selectivity, we were gratified with the finding that the wrong diastereoisomer could be recycled by oxidation [$(COCl)_2$/DMSO, 96% yield] followed by reduction of the resulting ketone **63**. The best ratio of products was obtained with LAH as the reducing agent (70% yield, ca. 2:1 ratio in favor of desired isomer **62**). Completion of the sequence included benzoylation of **62** to **64** (BzCl, Et_3N, 4-DMAP cat. 98% yield) followed by thiazole cleavage (MeOTf; $NaBH_4$; CuO/$CuCl_2$) and desilylation (nBu_4NF) to afford lactol **65** in 81% yield overall. Finally, exposure of lactol **65** to CCl_3CN and DBU furnished the desired trichloroacetimidate **46** in 85% yield as a mixture of anomers (α:β ca. 3:1).

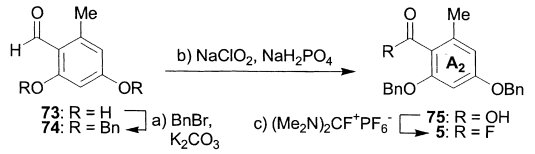
The required 2-phenylselenoglycosyl fluoride **44** representing ring H was synthesized from peracetylated xylose (**66**) as summarized in Scheme 8. Treatment of **66** with PhSeH[15] in the presence of $BF_3 \cdot Et_2O$ led to a mixture of β:α (ca. 5:1) selenoglycosides in 93% yield. The desired β-selenoglycoside **67** was subjected to basic methanolysis (K_2CO_3, MeOH) and



Scheme 8. Synthesis of carbohydrate building block H (**44**). a) ca. 2.0 equiv PhSeH, 0.95 equiv $BF_3 \cdot Et_2O$, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 12 h, 93%, α:β ca. 1:5; b) 0.1 equiv K_2CO_3, MeOH/THF 1:1, 25 °C, 12 h; c) 1.5 equiv $CH_3(CH_3O)C{=}CH_2$, 0.1 equiv TFA, DMF, 45 °C, 3 h, 74% over two steps; d) 1.1 equiv NaH, 1.3 equiv PMBCl, 0.2 equiv nBu_4NI, DMF, $0 \rightarrow 25\,^{\circ}C$, 2 h, 95%; e) 0.2 equiv PPTS, MeOH, 25 °C, 1 h, 96%; f) 1.1 equiv TBSOTf, 1.5 equiv 2,6-lutidine, THF, $-78\,^{\circ}C$, 0.5 h, 91%; g) 1.1 equiv TBSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, $-78\,^{\circ}C$, 0.5 h, 91%; h) 1.5 equiv DAST, CH_2Cl_2, 0 °C, 0.5 h, 100%. DAST = (diethylamino)sulfur trifluoride; TFA = trifluoroacetic acid.

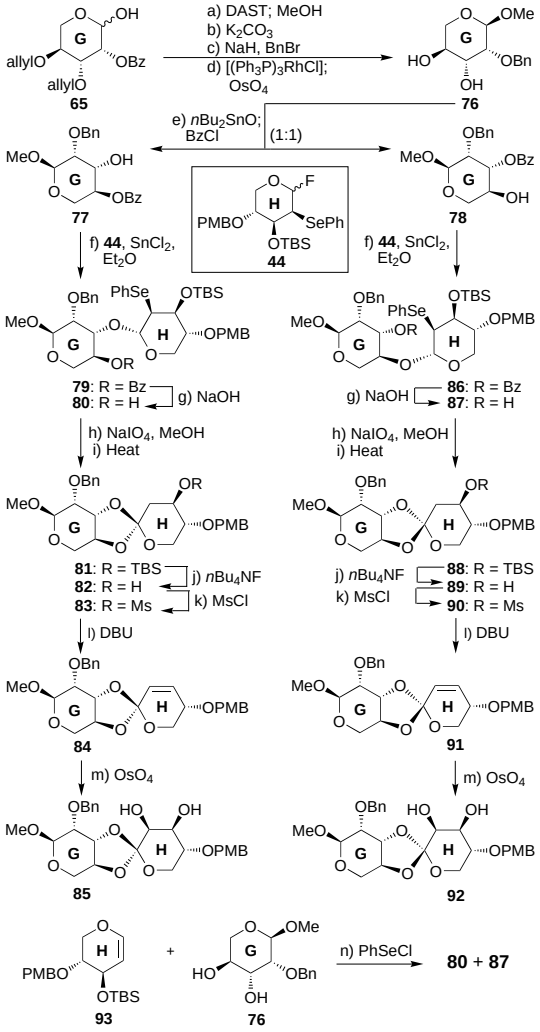
the resulting triol was engaged as the 2,3-acetonide **68** by reaction with 2-methoxypropene in the presence of TFA (74% yield for two steps). Protection of the remaining hydroxyl group in **68** (NaH, PMBCl, nBu_4NI cat., 95% yield) provided PMB ether **69** from which the acetonide was removed under acidic conditions (PPTS, MeOH, 96% yield) leading to diol **70**. After considerable experimentation it was discovered that treatment of **70** with TBSOTf-2,6-lutidine in THF at $-78\,^{\circ}C$ allowed selective protection at C-3 leading directly to silyl ether **71** in 91% yield. Remarkably this selectivity could be reversed by silylation under the same conditions but in CH_2Cl_2 solution rather than in THF (91% yield of **72**). Although this serendipitous discovery may be applicable to other suitable carbohydrate diols, a complete explanation for its manifestation is not available at present. In the final step of the sequence, substrate **71** was treated with DAST which induced a 1,2-migration furnishing 2-phenylselenoglycosyl fluoride **44** in quantitative yield.

The last requisite fragment for our purposes was acyl fluoride **5** whose construction is briefly described in Scheme 9. Thus, benzylation of bis-phenol **73**[1] (K_2CO_3, BnBr, 92% yield) followed by oxidation of the resulting aldehyde **74** to carboxylic acid **75** (80% yield) followed by exposure to $(Me_2N)_2CF^+PF_6^-$[16] in the presence of diisopropylethylamine yielded chromatographically (silica gel) stable acyl fluoride **5** in 80% yield.



Scheme 9. Synthesis of acyl fluoride **5**. a) 2.5 equiv BnBr, 4.0 equiv K_2CO_3, Me_2CO, reflux, 8 h, 92%; b) 2.2 equiv $NaClO_2$, 2.4 equiv NaH_2PO_4, DMSO, $0 \rightarrow 25\,^{\circ}C$, 12 h, 80%; c) 1.5 equiv $(Me_2N)_2CF^+PF_6^-$, 2.0 equiv iPr_2NEt, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 80%.

Orthoester formation—The GH model system: Before assembling the FGH fragment, we wanted to explore the stereochemical outcome of the orthoester formation, and therefore assembled a simple GH model system, as illustrated in Scheme 10. Diol **76** was prepared from ring G lactol **65** as follows: a) methyl glycoside formation (DAST; MeOH, $SnCl_2$, 62% and α:β ca. 4:1); b) debenzoylation (K_2CO_3, MeOH, 95%); c) benzylation (NaH, BnBr, 98%); and d) allyl deprotection ([$(Ph_3P)_3RhCl$]; OsO_4/NMO, 95% over



Scheme 10. Assembly of GH model systems **85** and **92**. a) i) 2.0 equiv DAST, CH_2Cl_2, 0 °C, 0.5 h; ii) 5.0 equiv MeOH, 1.8 equiv $SnCl_2$, $0 \rightarrow 25\,^{\circ}C$, Et_2O, 12 h, 62%, α:β ca. 4:1; b) 1.0 equiv K_2CO_3, MeOH, 25 °C, 12 h, 95%; c) 1.3 equiv NaH, 1.5 equiv BnBr, 0.3 equiv nBu_4NI, DMF, $0 \rightarrow 25\,^{\circ}C$, 2.5 h, 98%; d) i) 2.5 equiv DABCO, 0.05 equiv [$(Ph_3P)_3RhCl$], EtOH/H_2O 10:1, reflux, 2 h; ii) 2.5 equiv NMO, 0.05 equiv OsO_4, Me_2CO/H_2O 10:1, 25 °C, 8 h, 95% over two steps; e) 1.1 equiv nBu_2SnO, toluene, reflux, 3 h; 1.1 equiv BzCl, $0 \rightarrow 25\,^{\circ}C$, 1 h, 92%, 1:1 mixture of regioisomers; f) 1.5 equiv **44**, 1.3 equiv $SnCl_2$, $0 \rightarrow 25\,^{\circ}C$, Et_2O, 3 h, 69% of **79**, 70% of **86**; g) 1.2 equiv NaOH, MeOH, 25 °C, 1 h, 99% of **80**, 99% of **87**; h) 10.0 equiv $NaIO_4$, 8.0 equiv $NaHCO_3$, MeOH/CH_2Cl_2/H_2O 3:2:1, 25 °C, 2 h; i) vinyl acetate/toluene/diisopropylamine 2:2:1, sealed tube, 140 °C, 16 h, 70% of **81**, 75% of **88**; j) 1.2 equiv nBu_4NF, THF, 25 °C, 1 h, 98% of **82**, 97% of **89**; k) 1.2 equiv MsCl, 2.0 equiv Et_3N, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 2 h, 97% of **83**, 95% of **90**; l) 10.0 equiv DBU, toluene, reflux, 24 h, 87% of **84**, 87% of **91**; m) 1.2 equiv NMO, 0.05 equiv OsO_4, Me_2CO/H_2O 10:1, 25 °C, 24 h, 71% of **85**, 72% of **92**; n) i) 1.0 equiv **93**, 1.2 equiv PhSeCl, MeCN, 25 °C, 5 min; ii) 1.5 equiv collidine, 1.2 equiv **76**, 25 °C, 12 h, 54% of **80** and **87** combined. Ms = methanesulfonyl.

0947-6539/00/0617-3122 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

two steps). Direct coupling of diol **76** with 2-phenylselenoglycosyl fluoride **44** led to a moderate yield (65%) of the disaccharides as a 1:1 mixture of C-3 and C-4 regioisomers. In comparison, coupling of glycal **93** with **76** afforded only a 54% yield of a 1:1 mixture of C-3 and C-4 regioisomers (**80** and **87**) as well as some β-coupled products. The ring G monobenzoates were prepared by exposure of diol **76** to nBu$_2$SnO, followed by BzCl at 0 °C furnishing a 1:1 mixture of C-4 and C-3 benzoates **77** and **78** (92% combined yield). Each benzoate was then coupled with 2-phenylselenoglycosyl fluoride **44** in the presence of $SnCl_2$ to afford the glycosides **79** and **86** in 69 and 70% yield, respectively. Basic methanolysis of **79** and **86** (NaOH, MeOH) removed the benzoate esters, furnishing alcohols **80** and **87** in high yield. Each alcohol was then subjected to Sinaÿ's orthoester protocol[12] [oxidation: $NaIO_4$ in MeOH/CH_2Cl_2/H_2O 3:2:1; followed by heating at 140 °C for 12 h in vinyl acetate/toluene/diisopropylamine 2:2:1] providing orthoesters **81** and **88** in 70 and 75% yield, respectively (ca. 8:1 ratio of diastereoisomers in each case). With the orthoester formation secured, our attention was turned to the installation of the C-2 hydroxyl group found on ring H. While, it was presumed that orthoester **88** had the correct stereochemistry based on the influence of the anomeric effect[17] (see Figure 6 for reaction intermediates), both orthoesters were carried through the sequence to test compatibility to reaction conditions.

The TBS groups were removed from **81** and **88** (nBu$_4$NF) furnishing alcohols **82** and **89**, respectively. Several attempts to implement an α-hydroxylation reaction led to decomposition, therefore, we decided that elimination to the double bond followed by epoxidation/opening or dihydroxylation/inversion would be better alternatives. The alcohols (**82** and **89**) were mesylated (MsCl/Et$_3$N) to afford **83** and **90**, followed by heating in the presence of DBU to facilitate elimination to olefins **84** and **91** in 83 and 80% overall yields for the three

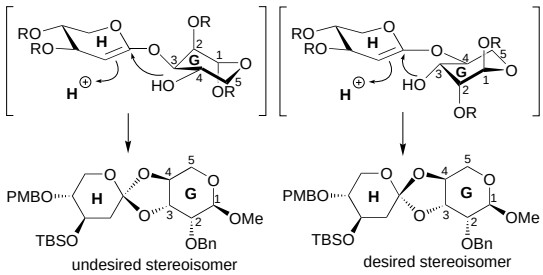
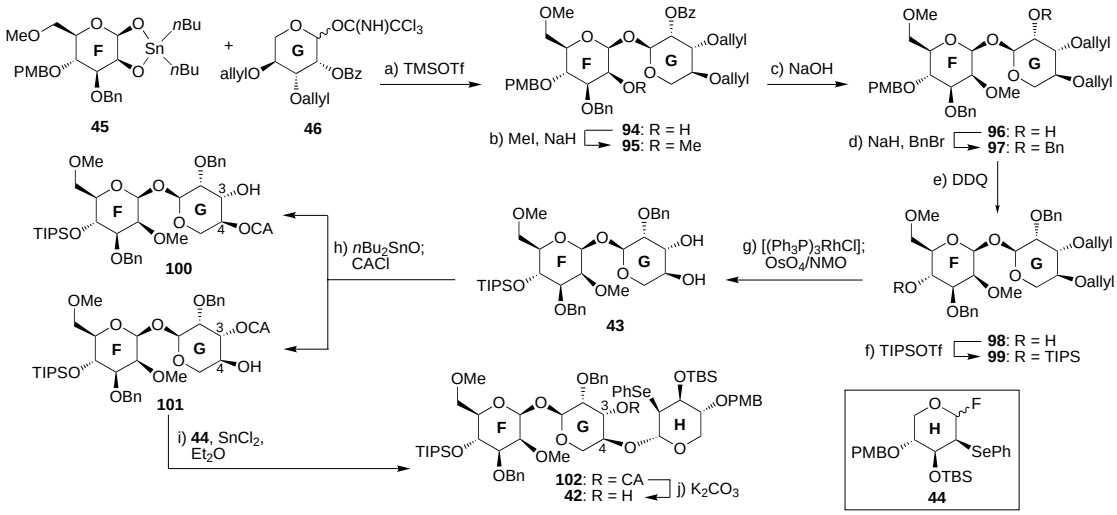


Figure 6. Transition states illustrating stereoselective GH orthoester formation. Joining rings G and H with the C-4 oxygen followed by ring closure was crucial for the formation of the desired orthoester stereoisomer. A C-3 linked disaccharide leads predominantly to the undesired orthoester stereoisomer.

steps, respectively. Attempts to epoxidize the olefin (mCPBA, mCPBA/NaHCO$_3$, (CF$_3$)MeC(O)$_2$ led to decomposition or no reaction. However, exposure of the olefins to OsO$_4$/NMO/quinuclidine for 24 h facilitated smooth dihydroxylation providing diols **85** and **92** in 71 and 72% yield, respectively.

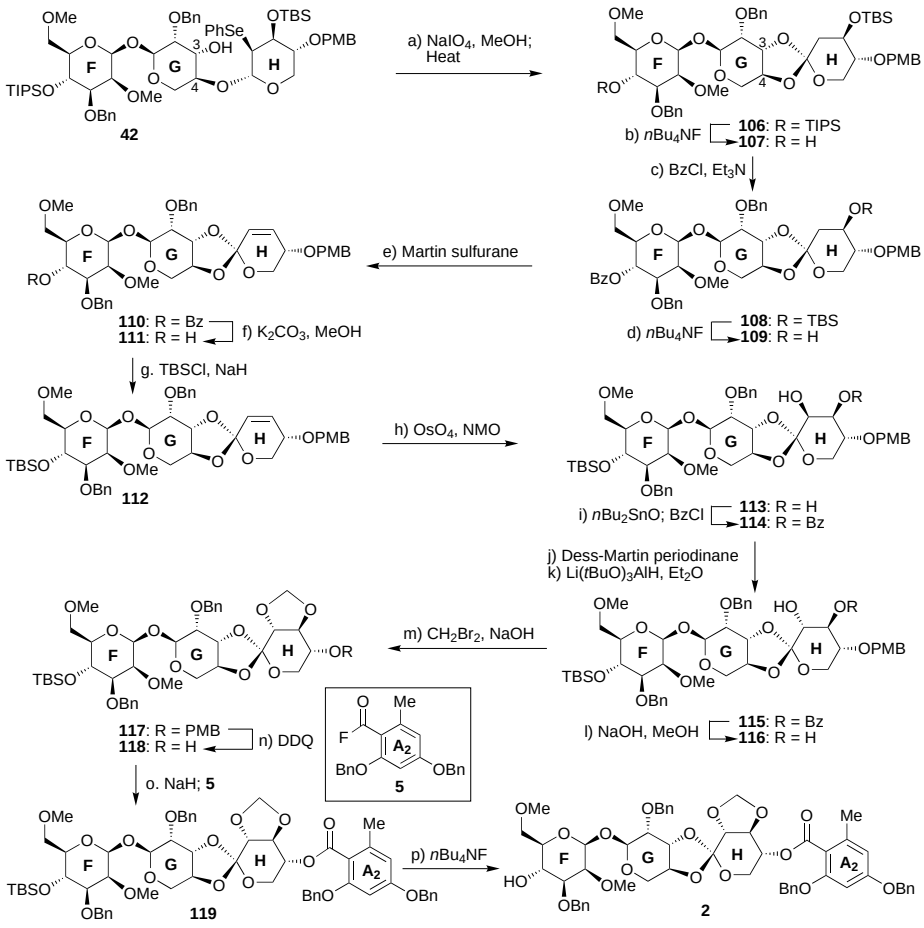
Assembly of the FGHA$_2$ fragment: With all building blocks needed at hand and the model studies for the orthoester formation completed, the assembly of the entire FGHA$_2$ fragment of everninomicin was initiated as shown in Scheme 11. Thus, coupling of tin-acetal **45** with trichloroacetimidate **46** in the presence of TMSOTf followed by acidic work-up afforded the desired β-mannoside containing 1,1′-disaccharide **94** in 74% yield. Careful methylation of **94** (NaH, MeI, 87% yield) afforded **95** whose debenzoylation (NaOH, MeOH, 95% yield) was followed by benzylation (NaH, BnBr, 90% yield) to afford benzyl ether **97** via **96**. The PMB ether was then exchanged for a TIPS group by deprotection (DDQ, 91% yield of **98**) followed by exposure to TIPSOTf and 2,6-lutidine furnishing **99** in 97% yield. In preparation for coupling with the next sugar unit (ring H), the



Scheme 11. Assembly of FGH fragment **42**. a) i) 2.1 equiv **45**, 1.0 equiv **46**, 0.5 equiv TMSOTf, CH_2Cl_2, 0 → 25 °C, 12 h; ii) 0.3 equiv PPTS, MeOH, 25 °C, 1 h, 74% over two steps; b) 1.1 equiv NaH, 3.0 equiv MeI, DMF, 0 → 25 °C, 1 h, 87%; c) 0.3 equiv NaOH, MeOH/Et$_2$O 1:1, 25 °C, 1 h, 95%; d) 1.1 equiv NaH, 1.3 equiv BnBr, 0.2 equiv nBu$_4$NI, DMF, 0 → 25 °C, 4 h, 90%; e) 1.5 equiv DDQ, CH_2Cl_2/H_2O 10:1 0 → 25 °C, 1 h, 91%; f) 1.2 equiv TIPSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, 0 → 25 °C, 1 h, 97%; g) i) 2.5 equiv DABCO, 0.1 equiv [(Ph$_3$P)$_3$RhCl], EtOH/H_2O 10:1, reflux, 2 h; ii) 2.2 equiv NMO, 0.05 equiv OsO$_4$, Me$_2$CO/H_2O 10:1, 25 °C, 8 h, 81% over two steps; h) 1.1 equiv nBu$_2$SnO, toluene, reflux, 3 h; 1.05 equiv CACl, 0 → 25 °C, 1 h, 97%, 1:1 mixture of regioisomers; i) 2.0 equiv **44**, 1.8 equiv $SnCl_2$, 0 → 25 °C, Et$_2$O, 3 h, 92%; j) 0.2 equiv K_2CO_3, MeOH/Et$_2$O 1:1, 25 °C, 1 h, 98%. CA = chloroacetyl; DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

  0947-6539/00/0617-3123 $ 17.50+.50/0

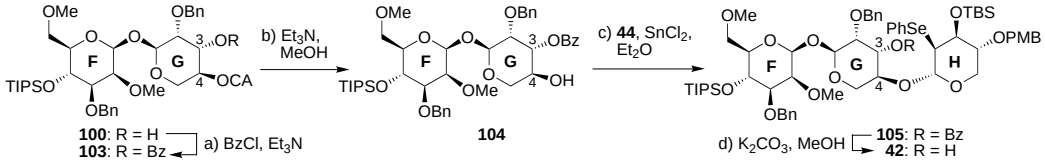
allyl groups were removed by sequential treatment with $[(Ph_3P)_3RhCl]$ and OsO_4/NMO furnishing diol **43** (81% yield). At this stage, and based on the model studies described above, we postulated that the C-4 glycoside (i.e., **42**, Scheme 11) would provide the correct orthoester stereoisomer. An appropriately C-3 protected derivative of **43** was therefore sought for further advancement. Despite many attempts to achieve selective C-3 protection using tin-acetal chemistry and other means, the best result was only a 1:1 mixture of regioisomers **100** and **101**, albeit in 97% combined yield, when the tin-acetal derived from **43** (nBu$_2$SnO) was reacted with chloroacetylchloride (CACl). The two isomers were chromatographically separated and the correct hydroxy ester **101** was reacted with 2-phenylselenoglycosyl fluoride **44** in ether and in the presence of $SnCl_2$ to afford trisaccharide **102** in 92% yield and as a single anomer. The stereo-directing effect of the selenium in such coupling reactions was discussed and rationalized previously.[18] The chloroacetate was then removed from **102** by exposure to K_2CO_3 in MeOH furnishing the desired hydroxy selenide **42** in 98% yield.



Scheme 13. Completion of the synthesis of the FGHA$_2$ fragment **2**. a) i) 10.0 equiv $NaIO_4$, 8.0 equiv $NaHCO_3$, MeOH/CH_2Cl_2/H_2O 3:2:1, 25 °C, 2 h; ii) vinyl acetate/toluene/diisopropylamine 2:2:1, sealed tube, 140 °C, 12 h, 81% over two steps; b) 1.1 equiv nBu$_4$NF, THF, 0 °C, 0.5 h, 95%; c) 1.2 equiv BzCl, 1.8 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 → 25 °C, 2 h, 97%; d) 1.5 equiv nBu$_4$NF, 0.2 equiv AcOH, THF, 25 °C, 1 h, 95%; e) 4.0 equiv Martin sulfurane, 0.05 equiv Et_3N, $CHCl_3$, 50 °C, 2 h, 85%; f) 0.5 equiv K_2CO_3, MeOH, 25 °C, 6 h, 90%; g) 6.0 equiv NaH, 12 equiv TBSCl, 1.0 equiv [18]crown-6, THF, 0 °C, 2 h, 80%; h) 5.0 equiv NMO, 0.5 equiv OsO_4, 1.0 equiv quinuclidine, Me_2CO/H_2O 10:1, 25 °C, 36 h, 70%, 8:1 mixture of diastereoisomers; i) 1.1 equiv nBu$_2$SnO, MeOH, reflux, 3 h; 1.5 equiv BzCl, 1,4-dioxane, 15 °C, 0.5 h, 97%, 5:1 mixture of regioisomers; j) 2.0 equiv Dess–Martin periodinane, 20 equiv $NaHCO_3$, CH_2Cl_2, 25 °C,1 h; k) 1.1 equiv Li(tBuO)$_3$AlH, Et_2O, −10 °C, 1 h, 80% over two steps; l) 0.5 equiv NaOH, MeOH, 25 °C, 1 h, 98%; m) 3.0 equiv nBu$_4$NBr, CH_2Br_2:50% aqueous NaOH 1:1, 65 °C, 2 h, 90%; n) 1.5 equiv DDQ, CH_2Cl_2/H_2O 10:1 (pH 7) 0 → 25 °C, 1 h, 85%; o) 1.2 equiv NaH, THF, 0 °C; then 1.5 equiv **5**, 0 → 25 °C, 2 h, 96%; p) 1.2 equiv nBu$_4$NF, THF, 25 °C, 1 h, 91%.

The sequence was made more efficient by the development of a route for funneling the C-4 chloroacetate derivative **100** back into the main path as shown in Scheme 12. Thus, benzoylation of **100** (BzCl, Et_3N, 4-DMAP cat., 96%) followed by selective removal of the chloroacetate with Et_3N in MeOH furnished the C-3 benzoate **104** (96% yield). Subsequent coupling of **104** with 2-phenylselenoglycosyl fluoride **44** in ether and in the presence of $SnCl_2$ led stereoselectively to **105** in 92% yield. The benzoate group was then removed from **105** (K_2CO_3, MeOH) affording the same alcohol **42** (98% yield) as before.

Our initial attempts to construct the orthoester moiety with the desired framework are illustrated in Scheme 13. Thus, exposure of alcohol **42** to the orthoester formation protocol



Scheme 12. Recycling of FG fragment **100** and synthesis of FGH fragment **42**. a) 1.2 equiv BzCl, 2.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 → 25 °C, 2 h, 96%; b) 2.0 equiv Et_3N, MeOH/CH_2Cl_2 1:1, 40 °C, 6 h, 96%; c) 2.0 equiv **44**, 1.8 equiv $SnCl_2$, 0 → 25 °C, Et_2O, 3 h, 92%; d) 0.2 equiv K_2CO_3, MeOH/Et_2O 1:1, 25 °C, 12 h, 98%.

0947-6539/00/0617-3124 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

[$NaIO_4$/$NaHCO_3$ in MeOH/CH_2Cl_2/H_2O 3:2:1; vinyl acetate/toluene/diisopropylamine 2:2:1, 140 °C, 12 h] furnished 2-deoxyorthoester **106** in 81 % overall yield and as a ca. 8:1 mixture of diastereoisomers (**106** predominating). The next task was to remove the TBS group from ring H, but unfortunately and unexpectedly, treatment of **106** with nBu$_4$NF in THF at 0 °C induced exclusive removal of the ring F TIPS group. Hoping to avoid the extra steps imposed by this finding, we opted at this stage to test another route involving removal of the TBS group from ring H prior to orthoester formation. We shall return to Scheme 13 shortly.

Thus, returning to **42** and proceeding to Scheme 14, we found that its treatment with nBu$_4$NF in THF at 0 °C, indeed caused cleavage of the TBS group furnishing diol **120** (Scheme 14) in 82 % yield (based on 85 % conversion). Furthermore, when diol **120** was subjected to the above described orthoester formation conditions the orthoester proceeded well (74 % yield) but this time was accompanied by a Ferrier-type rearrangement leading to what was assumed (on the basis of our model studies described above) to be the desired orthoester, that is to say the one with the opposite stereochemistry to that shown in structure **121**. We were initially excited about this route, in that, it was three steps shorter and led directly to the allylic orthoester, which was set for a dihydroxylation reaction. As it turned out, however, this assumption was wrong, the shown stereochemistry being proven by X-ray crystallographic analysis of a subsequent intermediate (vide infra). With the assumption of the correct stereochemistry, we proceeded to elaborate orthoester **121** to compound **124** as shown in Scheme 14. Thus, exposure of **121** to dihydroxylation conditions (OsO_4 cat./NMO) led to *cis*-diol **122** in 65 % yield and ca. 8:1 ratio of diastereoisomers. Following unsuccessful attempts to monoprotect this diol for oxidation/reduction purposes (in order to invert the C-2 stereochemistry of ring H), a different approach was undertaken. Exposure of **122** to $SOCl_2$ and Et_3N, followed by $NaIO_4$ oxidation furnished the cyclic sulfate **123** in 97 % overall yield. Opening of this cyclic sulfate with KOBz in DMF at 120 °C furnished monobenzoate **124**, whose ^{1}H-NMR spectrum revealed a *trans* relationship at C-2/C-3 but also the wrong position for the benzoate.

At this stage, an X-ray crystallographic analysis was deemed important, and fortunately, the *p*-bromobenzoate derivative **125** (*p*-BrBzCl, Et_3N, 4-DMAP cat., 100 % yield) crystallized nicely for this purpose (m.p. 156 °C, CH_2Cl_2/hexanes). The X-ray structure[11] of **125** (see ORTEP drawing in Figure 7) proved the wrong stereochemistry for the orthoester moiety indicating that the crucial cyclization (**120** → **121**) during orthoester formation had occurred from the undesired face of the olefin involved.

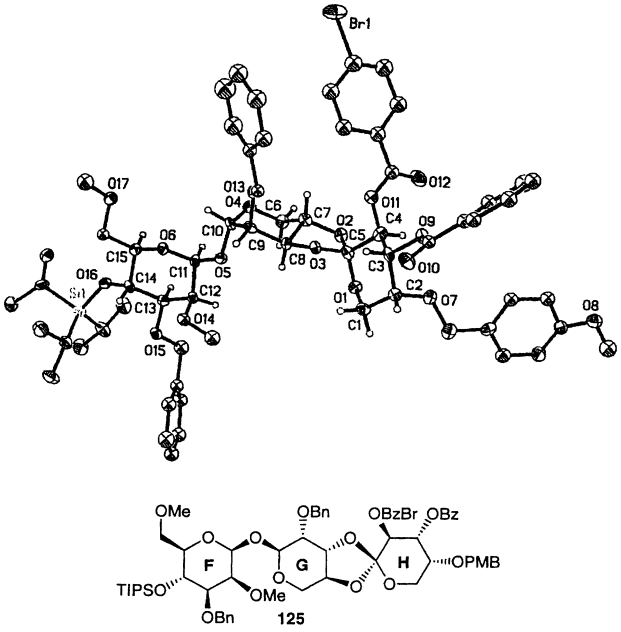
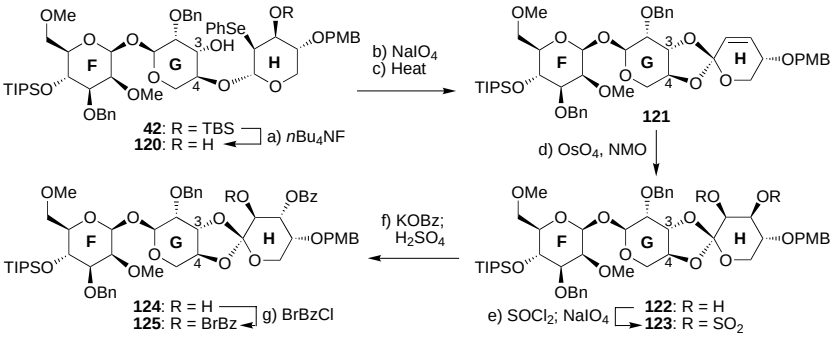
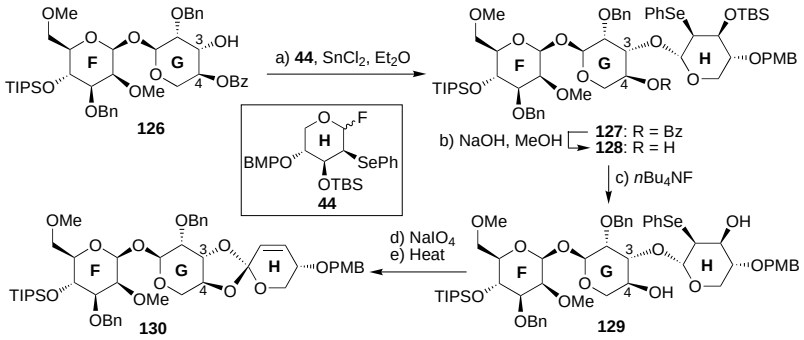


Figure 7. ORTEP drawing of orthoester **125** derived from an X-ray crystallographic analysis.[11]

Hoping to reverse the stereochemical outcome and recalling our model studies, we adopted a plan to construct the allylic orthoester directly starting from the C-3 coupled disaccharide as shown in Scheme 15. Thus, monobenzoate **126** was coupled with 2-phenylselenoglycosyl fluoride **44** in the presence of $SnCl_2$ in ether furnishing C-3 linked trisaccharide **127** in 60 % yield. The benzoate group was then removed from **127** (NaOH, MeOH, 93 %) leading to **128** from which the TBS group was cleaved by the action of nBu$_4$NF to give diol **129** in 81 % yield. Treatment of **129** to slightly modified orthoester formation conditions ($NaIO_4$/$NaHCO_3$ in MeOH/CH_2Cl_2/H_2O 12:7:1; followed by heating at 140 °C for 12 h in vinyl acetate/toluene/diisopropylamine 1:1:2) facilitated the expected *syn*-elimination and cyclization and led to allylic orthoester **130**, unfortunately in only 45 % yield and as a 4:1 inseparable mixture of stereo-



Scheme 14. Synthesis of FGH intermediates **124** and **125**. a) 1.05 equiv nBu$_4$NF, THF, 0 °C, 15 min, 82 % based on 85 % conversion; b) 10.0 equiv $NaIO_4$, 8.0 equiv $NaHCO_3$, MeOH/CH_2Cl_2/H_2O 3:2:1, 25 °C, 4 h; c) vinyl acetate/toluene/diisopropylamine 2:2:1, sealed tube, 140 °C, 12 h, 74 % over two steps; d) 2.5 equiv NMO, 0.5 equiv OsO_4, 1.0 equiv quinuclidine, Me_2CO/H_2O 10:1, 25 °C, 24 h, 65 %; e) 1.5 equiv $SOCl_2$, 3.0 equiv Et_3N, CH_2Cl_2, 0 °C, 5 min; 20 equiv $NaIO_4$, 18 equiv $NaHCO_3$, CCl_4/MeCN/H_2O 1:1:1.5, 0 → 25 °C, 1 h, 97 % over two steps; f) 3.0 equiv BzOK, 1.0 equiv [18]crown-6, DMF, 120 °C, 1 h; then 0.5 N H_2SO_4 and 0.5 N H_2O in THF, THF, 0 °C, 0.5 h, 76 %; g) 1.4 equiv BrBzCl, 4.0 equiv Et_3N, 0.2 equiv 4-DMAP, CH_2Cl_2, 0 → 25 °C, 12 h, 100 %.

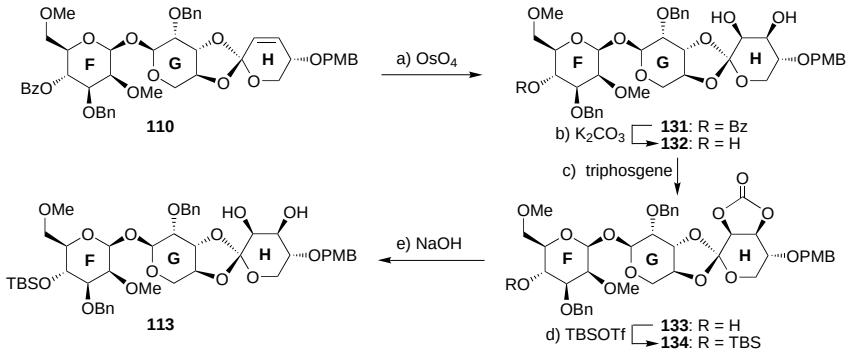


Scheme 15. Synthesis of FGH fragment **130**. a) 2.0 equiv **44**, 2.0 equiv $SnCl_2$, $0 \rightarrow 25\,^{\circ}C$, Et_2O, 12 h, 60%; b) 0.1 equiv NaOH, MeOH, 25 °C, 1 h, 93%; c) 1.0 equiv nBu$_4$NF, THF, 25 °C, 1 h, 81%; d) 10.0 equiv $NaIO_4$, 8.0 equiv $NaHCO_3$, MeOH/CH_2Cl_2/H_2O 12:7:1, 25 °C, 4 h; e) vinyl acetate/toluene/diisopropylamine 1:1:2, sealed tube, 140 °C, 12 h, 45% over two steps.

isomers. Unsatisfied with these results, the more efficient sequence of Scheme 13 was reactivated.

As already mentioned above, the orthoester **106** (Scheme 13) was efficiently (81% yield) obtained from hydroxy selenide **42**. Its stereochemistry was established by comparison of the ^{1}H-NMR spectrum of the allylic orthoester **110** generated from it, and the corresponding spectra of allylic orthoesters **121** (Scheme 14) and **130** (Scheme 15) whose structures were unambiguously secured through X-ray crystallographic analysis of crystalline derivative **125** (see Figure 7). Due to previously obtained results, it was necessary to adopt a round-about sequence for the procurement of the desired hydroxy compound **109** (Scheme 13). Thus, alcohol **107** obtained already as described above (nBu$_4$NF, 95% yield) was benzoylated (BzCl, Et_3N, 4-DMAP cat., 97% yield) and the resulting compound **108** was desilylated (nBu$_4$NF, AcOH, THF, 95% yield) to afford alcohol **109** which was dehydrated by exposure to Martin sulfurane[19] furnishing olefin **110** (85% yield). The stage was now set for a dihydroxylation of ring H, but before that, it was found necessary to exchange the benzoate group on ring F with a TBS group in order to ensure the success of subsequent steps. To this end, benzoate **110** was exposed to K_2CO_3 in MeOH furnishing hydroxy compound **111** (90% yield) whose treatment with TBSCl in the presence of NaH and [18]crown-6 led to silyl ether **112** (80% yield). Reaction of the highly sensitive olefinic orthoester **112** with OsO_4 cat./NMO in the presence of quinuclidine led to 1,2-diol **113** as the major product (70% yield, ca. 8:1 mixture of β:α diastereoisomers). Due to the extreme sensitivity of orthoesters **110**–**112**, an alternative approach to compound **113** was sought and secured as shown in Scheme 16. Thus, olefin **110** was treated directly under the dihydroxylation conditions (OsO_4 cat./NMO) affording diol **131** in 97% yield based on 70% conversion and ca. 10:1 ratio of diastereoisomers. The benzoate was then removed (K_2CO_3, MeOH, 98% yield) providing triol **132** from which the hydroxy carbonate **133** was derived upon exposure to triphosgene in pyridine (96% yield). The TBS group was then installed in **133** with ease (TBSOTf, 2,6-lutidine, 93% yield) leading to the corresponding silyl ether (**134**) from which the diol **113** was liberated by cleavage of the carbonate group (NaOH, MeOH, 95% yield). The coupling constants (J) for the H-2 and H-3 protons in **134** and other related derivatives confirmed the configuration of the ring H diol system in this series of compounds.

Going back to Scheme 13, diol **113** was regioselectively converted to the monobenzoate **114** by treatment with nBu$_2$SnO/BzCl[20] (97% yield, ca. 5:1 ratio with its regioisomer, chromatographically separated). The plan was now to oxidize the remained hydroxy group and then stereoselectively reduce it in order to arrive at the desired *trans* diol system on ring H. To this end, several oxidizing agents (e.g. Dess–Martin periodinane, Swern, TPAP/NMO, nBu$_2$SnO/Br_2) and reducing agents (e.g. LAH, Li(tBuO)$_3$AlH, Selectrides, $LiEt_3BH$, $NaBH_4$, Na(AcO)$_3$BH) were investigated. The best combination involved oxidation with Dess–Martin periodinane[21] followed by reduction with Li(tBuO)$_3$AlH to afford, via the corresponding ketone, the desired alcohol **115** (80% overall for two steps). The benzoate group was then removed from **115** (NaOH, MeOH) to furnish diol **116** (98% yield) and setting the stage for formation of the methylene acetal moiety. The latter goal was achieved by slow addition of **116** to a mixture of aqueous NaOH, CH_2Br_2, and nBu$_4$NBr, at 65 °C[22] leading to the desired compound **117** in 90% yield. The remaining sequence for the completion of the synthesis of the FGHA$_2$ fragment (**2**) involved DDQ-mediated removal of the PMB group from **117** to afford **118** in 85% yield, followed by esterification with acyl fluoride **5** in the presence of NaH



Scheme 16. Alternative synthesis of FGH fragment **113**. a) 5.0 equiv NMO, 0.5 equiv OsO_4, 1.0 equiv quinuclidine, Me_2CO/H_2O 10:1, 25 °C, 24 h, 97% based on 70% conversion, 10:1 mixture of diastereoisomers; b) 0.2 equiv K_2CO_3, MeOH, 25 °C, 4 h, 98%; c) 2.0 equiv triphosgene, 20 equiv py, CH_2Cl_2, $-78 \rightarrow 25\,^{\circ}C$, 1 h, 96%; d) 1.2 equiv TBSOTf, 1.5 equiv 2,6-lutidine, CH_2Cl_2, $0 \rightarrow 25\,^{\circ}C$, 1 h, 93%; e) 0.5 equiv NaOH, MeOH/Et_2O 1:1, 25 °C, 1 h, 95%. py = pyridine.

0947-6539/00/0617-3126 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

furnishing **119** in 96% yield (again proving the utility of the acyl fluoride moiety[1]), and finally, desilylation of **119** with nBu$_4$NF affording target **2** in 91% yield.

Conclusion

In this article, methods were described for the stereoselective construction of the 1,1′-disaccharide and orthoester linkages of everninomicin, bridging rings F to G and G to H, respectively. The first method[2] relied on a cyclic tin-acetal intermediate to lock the anomeric stereochemistry of ring F, while the anomeric stereochemistry of ring G was secured through an acetoxy participating group at C-2. The orthoester formation method combined a newly developed 1,2-phenylseleno migration in carbohydrate chemistry with elements of the Sinaÿ sequence for orthoester formation and proved stereoselective depending on the point (C-3 or C-4) of linkage of the disaccharide unit involved. While both methods performed admirably in the final strategy for the construction of the FGHA$_2$ fragment **2** required for the total synthesis of the targeted everninomicin (**1**), a closer examination of these methods is described in Part 4[3] of this series. The following paper[23] describes the construction of the DE fragment and its insertion between segments A$_1$B(A)C and FGHA$_2$, as well as the completion of the total synthesis of everninomicin 13,384-1 (**1**).

Experimental Section

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

Disaccharide 15: For a general procedure for the preparation of disaccharides **15** and **17**, refer to paper 4[3] in this series. **15**: $R_f = 0.38$ (60% ether in hexanes); $[\alpha]_D^{22} = +31.6$ ($c = 0.9$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3030$, 2920, 1732, 1453, 1366, 1234, 1099, 1025, 826, 741, 698 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.38-7.20$ (m, 30H, ArH), 5.26 (dd, $J = 3.2$, 1.9 Hz, 1H, H2′), 5.19 (d, $J = 1.7$ Hz, 1H, H1), 5.14 (d, $J = 1.5$ Hz, 1H, H1′), 4.91–4.49 (m, 12H, CH_2Ar), 4.09 (dd, $J = 9.9$, 9.8 Hz, 1H, H4′), 3.88 (dd, $J = 9.9$, 9.8 Hz, 1H, H4), 3.86–3.83 (m, 2H, H6, H6′), 3.80 (dd, $J = 9.3$, 3.2 Hz, 1H, H3′), 3.78 (ddd, $J = 10.0$, 4.1, 1.6 Hz, 1H, H5′), 3.73–3.71 (m, 2H, H6, H6′), 3.62 (dd, $J = 2.3$, 1.6 Hz, 1H, H2), 3.59 (dd, $J = 10.7$, 1.6 Hz, 1H, H3), 3.55 (ddd, $J = 10.0$, 4.4, 1.5 Hz, 1H, H5), 2.13 (s, 3H, OAc); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.2$, 138.3, 138.2, 138.2, 138.1, 138.0, 137.9, 137.7, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 128.0, 127.8, 127.8, 127.8, 127.7, 127.7, 127.5, 93.2, 93.1, 79.4, 77.7, 75.3, 75.2, 74.4, 74.0, 74.0, 73.5, 73.3, 72.5, 72.3, 72.1, 71.8, 68.6, 68.5, 68.2, 21.0; ^{13}C NMR (150 MHz, $CDCl_3$; proton coupled): $\delta = 93.2$ ($J_{C,H} = 174.1$ Hz), 93.1 ($J_{C,H} = 175.1$ Hz); HRMS (FAB): calcd for $C_{63}H_{66}O_{12}Cs$ [M+Cs]$^+$: 1147.3609, found 1147.3678.

Disaccharide 17: $R_f = 0.15$ (60% ether in hexanes); $[\alpha]_D^{22} = +29.4$ ($c = 0.49$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3467$, 3030, 2918, 2864, 1742, 1496, 1453, 1368, 1237, 1103, 1051, 911, 738, 698 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.38-7.17$ (m, 30H, ArH), 5.40 (dd, $J = 3.1$, 1.8 Hz, 1H, H2′), 5.17 (d, $J = 1.6$ Hz, 1H, H1′), 4.89–4.32 (m, 12H, CH_2Ar), 4.68 (s, 1H, H1), 4.14 (br d, $J = 10.3$ Hz, 1H, H5′), 4.12 (d, $J = 3.0$ Hz, 1H, H2), 4.07 (dd, $J = 9.7$, 3.2 Hz, 1H, H3′), 3.98 (dd, $J = 9.9$, 9.8 Hz, 1H, H4′), 3.87 (dd, $J = 9.8$, 9.4 Hz, 1H, H4), 3.70 (dd, $J = 10.9$, 3.0 Hz, 1H, H6′), 3.65 (d, $J = 2.6$ Hz, 2H, H6), 3.60 (dd, $J = 11.0$, 2.5 Hz, 1H, H6′), 3.56 (dd, $J = 9.3$, 2.9 Hz, 1H, H3), 3.42 (dt, $J = 9.8$, 2.7 Hz, 1H, H5), 2.15 (s, 3H, OAc); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.5$, 138.6, 138.2, 138.1, 137.9, 137.6, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.7, 127.6, 127.5, 127.4, 99.2, 98.0, 81.3, 77.8, 75.5, 75.1, 74.9, 74.0, 73.7, 73.3, 73.2, 72.2, 72.1, 71.5, 68.9, 68.6, 68.2, 21.1; ^{13}C NMR (150 MHz, $CDCl_3$; proton coupled): $\delta = 99.2$ ($J_{C,H} = 156.9$ Hz), 98.0 ($J_{C,H} = 171.3$ Hz); HRMS (FAB): calcd for $C_{56}H_{60}O_{12}Cs$ [M+Cs]$^+$: 1057.3139, found 1057.3111.

Benzoate 18: BzCl (0.83 mL, 7.27 mmol) was added to a solution of mannose diol **11**[4] (2.27 g, 7.27 mmol), Et_3N (1.22 mL, 8.73 mmol), and 4-DMAP (0.09 g, 0.73 mmol) in CH_2Cl_2 (100 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (10 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 → 60% Et_2O in hexanes) to afford benzoate **18** (2.74 g, 91%) as a white foam. **18**: $R_f = 0.27$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +87.8$ ($c = 0.67$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3442$, 3062, 2984, 1743, 1454, 1381, 1274, 1220, 1066, 867, 714 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.95$ (d, $J = 8.0$ Hz, 2H, ArH), 7.55 (t, $J = 7.5$ Hz, 1H, ArH), 7.49–7.47 (m, 2H, ArH), 7.39 (d, $J = 7.5$ Hz, 2H, ArH), 7.22–7.19 (m, 3H, ArH), 5.85 (s, 1H, F1), 4.68 (dd, $J = 12.0$, 5.5 Hz, 1H, F6), 4.47 (dd, $J = 12.0$, 2.0 Hz, 1H, F6), 4.38 (d, $J = 5.5$ Hz, 1H, F2), 4.37–4.34 (m, 1H, F4), 4.22 (dd, $J = 7.4$, 6.0 Hz, 1H, F3), 3.73–3.69 (m, 1H, F5), 3.14 (d, $J = 4.5$ Hz, 1H, OH), 1.49 (s, 3H, Me), 1.37 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.7$, 133.2, 133.0, 131.5, 129.8, 129.5, 129.0, 128.3, 127.5, 109.9, 83.8, 78.0, 76.1, 69.8, 69.5, 63.9, 28.0, 26.3; HRMS (MALDI): calcd for $C_{22}H_{24}O_6SNa$ [M+Na]$^+$: 439.1191, found 439.1205.

TIPS ether 19: TIPSOTf (4.24 mL, 15.78 mmol) was added to a solution of alcohol **18** (5.48 g, 13.15 mmol) and 2,6-lutidine (2.15 mL, 18.41 mmol) in CH_2Cl_2 (200 mL) at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (250 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60% Et_2O in hexanes) to afford TIPS ether **19** (7.46 g, 99%) as a white foam. **19**: $R_f = 0.62$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +214.3$ ($c = 0.21$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2943$, 2867, 1724, 1457, 1381, 1273, 1219, 1162, 1109, 1069, 1027, 881, 751, 711, 686 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.90$ (dd, $J = 8.0$, 1.0 Hz, 2H, ArH), 7.54–7.46 (m, 3H, ArH), 7.36 (t, $J = 7.5$ Hz, 3H, ArH), 7.16–7.11 (m, 2H, ArH), 5.80 (s, 1H, F1), 4.65 (dd, $J = 12.0$, 2.5 Hz, 1H, F6), 4.45 (dd, $J = 12.0$, 7.0 Hz, 1H, F6), 4.39 (dd, $J = 4.0$, 2.0 Hz, 1H, F2), 4.37 (dd, $J = 6.0$, 2.0 Hz, 1H, F3), 4.18 (t, $J = 6.5$ Hz, 1H, F4), 3.97 (dd, $J = 9.5$, 7.0 Hz, 1H, F5), 1.54 (s, 3H, Me), 1.38 (s, 3H, Me), 1.22–1.06 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.2$, 133.4, 132.8, 131.0, 129.9, 129.7, 128.9, 128.2, 127.2, 109.4, 83.8, 78.8, 76.2, 71.5, 70.5, 64.3, 27.9, 26.3, 18.2, 18.1, 12.6; HRMS (MALDI): calcd for $C_{31}H_{44}O_6SSiNa$ [M+Na]$^+$: 595.2525, found 595.2519.

Alcohol 20: NaOH (50 mg, 1.19 mmol) was added to a solution of **19** (3.42 g, 5.97 mmol) in MeOH/Et_2O (1:1, 30 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 (200 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes) to afford alcohol **20** (2.63 g, 94%) as a white foam. **20**: $R_f = 0.54$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +156.4$ ($c = 1.07$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3498$, 2942, 2866, 1460, 1381, 1243, 1217, 1163, 1104, 1065, 1019, 874, 753, 685 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.50$ (d, $J = 7.2$ Hz, 2H, ArH), 7.34–7.26 (m, 3H, ArH), 5.76 (s, 1H, F1), 4.34 (dd, $J = 5.8$, 0.6 Hz, 1H, F2), 4.15 (t, $J = 6.3$ Hz, 1H, F4), 4.04 (ddd, $J = 9.0$, 5.8, 2.8 Hz, 1H, F5), 3.86 (dd, $J = 9.5$, 6.6 Hz, 1H, F3), 3.80 (dd, $J = 11.6$, 2.8 Hz, 1H, F6), 3.70 (dd, $J = 11.6$, 5.8 Hz, 1H, F6), 1.50 (s, 3H, Me), 1.36 (s, 3H, Me), 1.21–1.10 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 132.3$, 129.1, 127.8, 109.3, 84.0, 78.9, 76.1, 72.1, 71.2, 62.3, 27.8, 26.3, 18.2, 12.6; HRMS (MALDI): calcd for $C_{24}H_{40}O_5SSiNa$ [M+Na]$^+$: 491.2263, found 491.2244.

Methyl ether 21: NaH (0.237 g, 5.91 mmol) was added to a solution of alcohol **20** (2.31 g, 4.93 mmol) in DMF (25 mL) at 0 °C and the resulting mixture was stirred for 15 min. MeI (0.50 mL, 7.89 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with Et_2O (200 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 70% Et_2O in hexanes) to afford methyl ether **21** (2.20 g, 92%) as a white solid. **21**: $R_f = 0.61$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +197.5$ ($c = 0.40$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2942$, 2866, 1459, 1380, 1243, 1219, 1163, 1107,

1071, 879, 752, 685 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.53$ (d, $J =$ 7.5 Hz, 2H, ArH), 7.32 – 7.24 (m, 3H, ArH), 5.74 (s, 1H, F1), 4.33 (dd, $J = 6.0$, 1.0 Hz, 1H, F2), 4.13 (t, $J = 6.5$ Hz, 1H, F4), 4.07 (ddd, $J = 9.5$, 5.0, 2.5 Hz, 1H, F5), 3.96 (dd, $J = 9.5$, 6.5 Hz, 1H, F3), 3.65 (dd, $J = 10.0$, 4.5 Hz, 1H, F6), 3.53 (dd, $J = 10.0$, 2.0 Hz, 1H, F6), 3.29 (s, 3H, OMe), 1.49 (s, 3H, Me), 1.34 (s, 3H, Me), 1.22 – 1.08 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 133.8$, 131.6, 128.9, 127.4, 109.3, 84.3, 79.1, 76.3, 71.7, 71.2, 70.7, 58.9, 27.8, 26.3, 18.2, 12.6; HRMS (MALDI): calcd for $C_{25}H_{42}O_5SSiNa$ $[M+Na]^+$: 505.2420, found 505.2487.

Diol 22: TsOH (17.0 mg, 0.091 mmol) was added to a solution of methyl ether **21** (1.46 g, 3.02 mmol) and ethylene glycol (1.20 mL, 3.63 mmol) in MeOH/Et_2O (10:1, 22 mL) at 25 °C and the resulting mixture was stirred for 8 h. The reaction mixture was quenched by the addition of Et_3N (10 mL) and the solvents were removed under reduced pressure. The residue was 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 % EtOAc in hexanes) to afford diol **22** (0.72 g, 54 %) as a white foam, and recovered starting material (0.56 g, 38 %). **22**: $R_f = 0.20$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = +194.5$ ($c = 1.0$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3372$, 2941, 2865, 1461, 1101, 1024, 883, 778, 688 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.47 – 7.21 (m, 5H, ArH), 5.50 (s, 1H, F1), 4.16 (dd, $J = 3.3$, 1.9 Hz, 1H, F2), 4.02 (ddd, $J = 9.6$, 3.7, 2.2 Hz, 1H, F5), 3.96 (dd, $J = 11.4$, 4.1 Hz, 1H, F6), 3.91 (dd, $J = 11.4$, 1.9 Hz, 1H, F6), 3.89 (dt, $J = 9.2$, 3.3 Hz, 1H, F3), 3.59 (s, 3H, OMe), 3.55 (t, $J = 9.6$ Hz, 1H, F4), 2.86 (br s, 2H, OH), 1.22 – 1.08 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 134.4$, 131.0, 128.9, 127.1, 87.5, 77.4, 73.4, 72.4, 72.1, 62.6, 60.6, 17.9, 17.9, 11.9; HRMS (MALDI): calcd for $C_{22}H_{38}O_5SSiNa$ $[M+Na]^+$: 465.2101, found 465.2115.

Benzyl ether 23: nBu$_2$SnO (0.322 g, 1.29 mmol) was added to a solution of diol **22** (0.52 g, 1.18 mmol) in toluene (10 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 (0.17 mL, 1.41 mmol) and nBu$_4$NI (0.087 g, 0.235 mmol) were added. The reaction mixture was refluxed again for 5 h, and then 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 → 80 % Et_2O in hexanes) to afford benzyl ether **23** (0.51 g, 81 %) as a white foam. **23**: $R_f =$ 0.58 (70 % Et_2O in hexanes); $[\alpha]_D^{22} = +67.9$ ($c = 0.95$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3551$, 2941, 2865, 1458, 1391, 1104, 1020, 884, 740, 680 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.51 - 7.27$ (m, 10H, ArH), 5.61 (d, $J =$ 1.9 Hz, 1H, F1), 4.76, 4.47 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.11 (ddd, $J = 8.8$, 5.1, 2.2 Hz, 1H, F5), 4.00 (t, $J = 8.8$ Hz, 1H, F4), 3.94 (dd, $J = 3.7$, 1.9 Hz, 1H, F2), 3.73 (dd, $J = 7.4$, 3.7 Hz, 1H, F3), 3.72 (dd, $J = 10.6$, 5.1 Hz, 1H, F6), 3.63 (dd, $J = 10.3$, 1.9 Hz, 1H, F6), 3.35 (s, 3H, OMe), 2.30 (br s, 1H, OH), 1.22 – 1.08 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 137.3$, 134.2, 131.8, 129.0, 128.6, 128.1, 127.9, 127.4, 84.9, 79.2, 73.5, 72.3, 72.1, 71.4, 70.7, 59.0, 18.3, 13.0; HRMS (MALDI): calcd for $C_{29}H_{44}O_5SSiNa$ $[M+Na]^+$: 555.2571, found 555.2583.

Alcohol 25: Lipase P (13.0 g, Amano) was added to a solution of triacetate **24**[7] (6.50 g, 17.74 mmol) and isoamyl alcohol (3.86 mL, 35.48 mmol) in isooctane (600 mL) at 25 °C and the resulting mixture was shaken for 96 h. The reaction mixture was filtered and the enzyme pad was washed with hexanes (250 mL) and CH_2Cl_2 (250 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 alcohol **25** (4.83 g, 84 %) as a white foam. **25**: $R_f = 0.16$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = +120.1$ ($c = 3.09$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3460$, 3032, 2939, 2885, 1750, 1736, 1369, 1241, 1046, 940, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.37 - 7.30$ (m, 5H, ArH), 5.25 (t, $J = 10.0$ Hz, 1H, H3), 5.01 (d, $J = 3.5$ Hz, 1H, H1), 4.81 (dd, $J = 10.0$, 3.5 Hz, 1H, H2), 4.76, 4.50 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 3.82 – 3.65 (m, 3H, H4, H5, H5), 2.66 (d, $J = 5.0$ Hz, 1H, OH), 2.10 (s, 3H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.5$, 170.5, 136.5, 128.4, 128.0, 127.8, 94.7, 74.0, 70.5, 69.6, 69.3, 61.8, 20.9, 20.7; HRMS (MALDI): calcd for $C_{16}H_{20}O_7Na$ $[M+Na]^+$: 347.1107, found 347.1112.

Benzyl ether 26: $BF_3 \cdot Et_2O$ (0.21 mL, 1.67 mmol) was added to a solution of alcohol **25** (5.40 g, 16.65 mmol) and benzyltrichloroacetimidate (3.71 mL, 19.97 mmol) in CH_2Cl_2 (200 mL) at 0 °C and the resulting mixture was stirred for 3 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (10 mL), diluted with CH_2Cl_2 (250 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 → 100 % Et_2O in hexanes) to afford the desired benzyl ether **26** (6.28 g, 91 %) as a white foam. **26**: $R_f = 0.31$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = +76.8$ ($c = 0.59$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3032$, 2939, 2882, 1751, 1455, 1369, 1242, 1056, 735, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.38 - 7.18$ (m, 10H, ArH), 5.53 (t, $J = 9.5$ Hz, 1H, H3), 5.00 (d, $J = 3.5$ Hz, 1H, H1), 4.76 (dd, $J = 10.0$, 3.5 Hz, 1H, H2), 4.74, 4.48 (AB, $J =$ 12.5 Hz, 2H, CH_2Ar), 4.61, 4.56 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 3.72 (d, $J =$ 7.5 Hz, 1H, H5), 3.71 (d, $J = 9.5$ Hz, 1H, H5), 3.62 (ddd, $J = 9.0$, 9.0, 7.0 Hz, 1H, H4), 2.02 (s, 6H, OAc); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.3$, 169.9, 137.8, 136.9, 128.4, 127.9, 127.7, 127.6, 94.8, 75.7, 72.9, 71.3, 71.1, 69.2, 59.7, 20.9, 20.6; HRMS (MALDI): calcd for $C_{23}H_{26}O_7Na$ $[M+Na]^+$: 437.1576, found 437.1588.

Diol 27: K_2CO_3 (0.410 g, 2.96 mmol) was added to a solution of benzyl ether **26** (6.14 g, 14.81 mmol) in MeOH/Et_2O (1:1, 80 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 (200 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O in hexanes) to afford diol **27** (4.75 g, 97 %) as a white foam. **27**: $R_f =$ 0.21 (100 % Et_2O); $[\alpha]_D^{22} = +96.9$ ($c = 0.29$, $CHCl_3$); IR (thin film): $\tilde{\nu} =$ 3435, 3031, 2932, 1496, 1454, 1370, 1211, 1134, 1062, 943, 734, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.36 - 7.28$ (m, 10H, ArH), 4.90 (d, $J =$ 4.0 Hz, 1H, H1), 4.75, 4.48 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.72, 4.64 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 3.83 (t, $J = 9.0$ Hz, 1H, H3), 3.68 (dd, $J = 10.5$, 5.0 Hz, 1H, H5), 3.57 (t, $J = 10.5$ Hz, 1H, H5), 3.51 (dd, $J = 9.5$, 4.0 Hz, 1H, H2), 3.51 – 3.45 (m, 1H, H4); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.0$, 136.9, 128.5, 128.0, 97.3, 77.4, 74.2, 73.1, 72.4, 69.5, 60.0, 15.2; HRMS (MALDI): calcd for $C_{19}H_{22}O_5Na$ $[M+Na]^+$: 353.1359, found 353.1346.

Bis-allyl ether 28: NaH (1.21 g, 30.17 mmol) was added to a solution of diol **27** (4.53 g, 13.71 mmol) in DMF (75 mL) at 0 °C and the resulting mixture was stirred for 15 min. Allyl bromide (3.85 mL, 44.43 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (15 mL), diluted with Et_2O (200 mL) and washed with brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 50 % Et_2O in hexanes) to afford bis-allyl ether **28** (5.59 g, 92 %) as a white solid. **28**: $R_f = 0.30$ (30 % Et_2O in hexanes); $[\alpha]_D^{22} =$ $+103.9$ ($c = 0.54$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3064$, 3030, 2917, 1648, 1605, 1495, 1455, 1351, 1074, 932, 734, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.43 – 7.31 (m, 10H, ArH), 6.07 – 5.99 (m, 1H, C*H*=CH$_2$), 5.93 – 5.85 (m, 1H, C*H*=CH$_2$), 5.35 (d, $J = 17.5$ Hz, 1H, CH_2-*E*), 5.27 (d, $J = 17.5$ Hz, 1H, CH_2-*E*), 5.18 (d, $J = 10.0$ Hz, 1H, CH_2-*Z*), 5.16 (d, $J = 10.0$ Hz, 1H, CH_2-*Z*), 4.87 (d, $J = 3.5$ Hz, 1H, H1), 4.81, 4.58 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.77, 4.66 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.45 – 4.35 (m, 2H, OCH_2), 4.17 – 4.05 (m, 2H, OCH_2), 3.81 (t, $J = 9.0$ Hz, 1H, H3), 3.66 – 3.51 (m, 3H, H4, H5, H5), 3.37 (dd, $J = 9.5$, 3.5 Hz, 1H, H2); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 135.4$, 134.8, 128.3, 128.3, 128.0, 127.7, 117.1, 116.3, 95.4, 81.0, 79.4, 77.8, 74.3, 73.5, 72.1, 68.6, 60.6; HRMS (MALDI): calcd for $C_{25}H_{30}O_5Na$ $[M+Na]^+$: 433.1985, found 433.1965.

Lactol 29: HCl (2.0 mL, 1N aq solution) was added to a solution of bis-allyl ether **28** (3.85 g, 9.38 mmol) in AcOH (80 mL) at 25 °C and the resulting mixture was heated to 80 °C and stirred for 5 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 $NaHCO_3$ (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 → 100 % Et_2O in hexanes) to afford lactol **29** (2.73 g, 91 %) as a white foam. **29**: $R_f = 0.19$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +14.8$ ($c = 1.47$, $CHCl_3$); IR (thin film): $\tilde{\nu} =$ 3394, 3080, 2871, 1649, 1456, 1351, 1074, 994, 927, 738, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, ca. 1:1 mixture of anomers): $\delta = 7.35 - 7.26$ (m, 10H, ArH), 6.01 – 5.88 (m, 4H, C*H*=CH$_2$), 5.50 (d, $J = 17.5$ Hz, 4H, CH_2-*E*), 5.21 – 5.16 (m, 4H, CH_2-*Z*), 4.74, 4.64 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.73, 4.62 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.58 (dd, $J = 7.0$, 5.5 Hz, 1H, H1), 4.36 – 4.15 (m, 9H, OCH_2, H-1), 3.91 (dd, $J = 11.5$, 5.0 Hz, 1H, H5), 3.77 (t, $J = 10.5$ Hz, 1H, H-3), 3.69 (t, $J = 9.0$ Hz, 1H, H3), 3.65 (dd, $J = 11.0$,

0947-6539/00/0617-3128 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

5.5 Hz, 1H, H5), 3.56–3.46 (m, 2H, H4), 3.42 (t, J = 9.0 Hz, 1H, H-2), 3.36 (dd, J = 9.0, 3.5 Hz, 1H, H2), 3.33 (d, J = 6.0 Hz, 1H, OH), 3.23 (dd, J = 11.5, 9.5 Hz, 1H, H5), 3.14 (dd, J = 8.5, 7.0 Hz, 1H, H5), 2.99 (d, J = 3.0 Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.5, 137.2, 135.2, 135.1, 135.0, 134.5, 128.4, 127.8, 127.7, 117.7, 117.1, 116.8, 116.7, 97.5, 91.5, 83.0, 81.9, 80.2, 79.2, 77.3, 74.2, 73.6, 73.3, 72.5, 63.8, 60.3; HRMS (MALDI): calcd for $C_{18}H_{24}O_5Na$ $[M+Na]^+$: 343.1521, found 343.1513.

Lactone 9: Ac_2O (4.0 mL) was added to a solution of lactol **29** (2.70 g, 8.43 mmol) in DMSO (8.0 mL) at 25 °C and the resulting mixture was stirred for 12 h. The reaction mixture was quenched by the addition of ice (100 mL), 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. The residue was purified by flash column chromatography (silica gel, 0 → 60 % Et_2O in hexanes) to afford lactone **9** (2.58 g, 96 %) as a white foam. **9**: R_f = 0.21 (50 % Et_2O in hexanes); $[\alpha]_D^{22}$ = +98.6 (c = 0.14, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3063, 3031, 2917, 1751, 1495, 1455, 1258, 1142, 1075, 873, 739, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.28 (m, 5H, ArH), 5.97–5.84 (m, 2H, C*H*=CH$_2$), 5.34 (ddt, J = 17.0, 1.5, 1.5 Hz, 1H, CH$_2$-*E*), 5.28 (ddt, J = 17.0, 1.5, 1.5 Hz, 1H, CH$_2$-*E*), 5.21 (ddt, J = 11.0, 1.5, 1.5 Hz, 1H, CH$_2$-*Z*), 5.20 (ddt, J = 11.0, 1.5, 1.5 Hz, 1H, CH$_2$-*Z*), 4.60, 4.56 (AB, J = 12.0 Hz, 2H, CH$_2$Ar), 4.46–4.42 (m, 1H, OC*H*$_2$), 4.39 (dd, J = 12.0, 3.0 Hz, 1H, H5), 4.28 (dd, J = 12.0, 2.0 Hz, 1H, H5), 4.18–4.05 (m, 3H, OC*H*$_2$), 4.04 (d, J = 6.5 Hz, 1H, H2), 3.76 (dt, J = 7.0, 2.0 Hz, 1H, H3), 3.73 (dt, J = 3.5, 2.0 Hz, 1H, H4); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.9, 136.9, 133.8, 133.6, 128.4, 128.0, 127.7, 118.1, 117.6, 81.1, 81.0, 77.9, 74.9, 72.3, 71.4, 70.4, 65.5; HRMS (MALDI): calcd for $C_{18}H_{22}O_5Na$ $[M+Na]^+$: 341.1365, found 341.1363.

Bis-TMS ether 10: NaH (0.90 g, 22.67 mmol) was added to a solution of the 2,3-*O*-isopropylidene-L-threitol (3.50 g, 21.58 mmol) in DMF (50 mL) at 0 °C and the resulting mixture was stirred for 15 min. BnBr (2.34 mL, 23.74 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (20 mL), 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. The residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford the alcohol (5.00 g, 92 %) as a colorless oil. alcohol: R_f = 0.27 (70 % Et_2O in hexanes); $[\alpha]_D^{22}$ = +7.50 (c = 1.22, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3479, 3032, 2987, 2873, 1454, 1376, 1214, 1167, 1075, 990, 847, 738, 700 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 5H, ArH), 4.56 (brs, 2H, CH_2Ar), 4.03 (dt, J = 6.9, 4.4 Hz, 1H, C*H*O), 3.92 (dt, J = 7.2, 3.7 Hz, 1H, C*H*O), 3.73 (dd, J = 9.8, 3.5 Hz, 1H, CH_2), 3.65 (dd, J = 4.2, 3.7 Hz, 1H, CH_2), 3.64 (t, J = 3.7 Hz, 1H, CH_2), 3.54 (dd, J = 8.4, 4.6 Hz, 1H, CH_2), 2.62 (brs, 1H, OH), 1.40 (s, 6H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.5, 128.3, 127.7, 127.6, 109.2, 79.4, 76.1, 73.5, 62.2, 26.8; HRMS (MALDI): calcd for $C_{14}H_{20}O_4Na$ $[M+Na]^+$: 275.1259, found 275.1256. NaH (0.90 g, 22.67 mmol) was added to a solution of the above alcohol (5.00 g, 20.00 mmol) in DMF (50 mL) at 0 °C and the resulting mixture was stirred for 15 min. Allyl bromide (2.05 mL, 23.74 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (15 mL), 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. The residue was dissolved in MeOH (30 mL) and 1N aqueous HCl (3 mL) was added. The reaction mixture was stirred for 1 h, Et_3N (5 mL) was added, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O) to afford the diol (4.90 g, 98 %) as a white solid. diol: R_f = 0.16 (70 % Et_2O in hexanes); $[\alpha]_D^{22}$ = −3.9 (c = 0.97, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3420, 3052, 2938, 2873, 1454, 1317, 1275, 1115, 1072, 933 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.28 (m, 5H, ArH), 5.92–5.85 (m, 1H, C*H*=CH$_2$), 5.26 (ddd, J = 17.0, 1.5, 1.5 Hz, 1H, CH$_2$-*E*), 5.19 (ddd, J = 10.5, 1.5, 1.5 Hz, 1H, CH$_2$-*Z*), 4.57, 4.54 (AB, J = 12.0 Hz, 2H, CH$_2$Ar), 4.04–3.98 (m, 2H, OC*H*$_2$), 3.88–3.84 (m, 2H, C*H*OH, C*H*OH), 3.65–3.48 (m, 4H, CH_2O, CH_2O), 2.90 (d, J = 7.0 Hz, 1H, OH), 2.89 (d, J = 7.0 Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.7, 134.2, 128.5, 127.8, 117.4, 73.5, 72.4, 71.9, 71.9, 70.5, 70.5; HRMS (MALDI): calcd for $C_{14}H_{20}O_4Na$ $[M+Na]^+$: 275.1259, found 275.1257. TMSCl (0.020 mL, 0.200 mmol) was added to a solution of the above diol (5.00 g, 19.82 mmol) and HMDS (41.80 mL, 198.2 mmol) in MeCN (100 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.

GH orthoester 30: Lactone **9** (2.52 g, 7.93 mmol) and the crude bis-TMS ether **10** were azeotroped with benzene (3 × 10 mL) and then dried under high vacuum for 1 h. The residue was dissolved in CH_2Cl_2 (50 mL) and cooled to 0 °C. TMSOTf (2.38 mL, 0.5 M solution in CH_2Cl_2, 1.19 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL), diluted with CH_2Cl_2, (500 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford GH orthoester **30** (3.97 g, 97 %, 1:1 mixture of inseparable diastereoisomers) as a white foam. **30**: R_f = 0.58 (50 % Et_2O in hexanes); IR (thin film): $\tilde{\nu}$ = 3065, 3030, 2864, 1455, 1365, 1234, 1077, 1000, 923, 727, 699 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 20H, ArH), 6.00–5.79 (m, 6H, C*H*=CH$_2$), 5.30–5.03 (m, 12H, CH_2), 4.76, 4.61 (AB, J = 11.6 Hz, 2H, CH$_2$Ar), 4.75, 4.60 (AB, J = 11.6 Hz, 2H, CH$_2$Ar), 4.56 (brs, 4H, CH$_2$Ar), 4.44–4.18 (m, 12H, OC*H*$_2$), 4.03–3.97 (m, 4H), 3.77–3.51 (m, 16H), 3.46 (t, J = 10.6 Hz, 1H), 3.41 (dd, J = 9.4, 1.7 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.3, 137.8, 135.3, 135.0, 135.0, 134.4, 128.4, 127.7, 127.7, 127.6, 127.1, 120.5, 117.3, 117.1, 117.0, 116.6, 82.8, 78.9, 78.9, 78.7, 78.6, 78.4, 78.3, 77.5, 74.5, 74.3, 73.6, 73.5, 73.4, 72.3, 71.2, 70.0, 62.2; HRMS (MALDI): calcd for $C_{32}H_{40}O_8Na$ $[M+Na]^+$: 575.2621, found 575.2631.

GH triol 31 (bottom diastereoisomer): $[(Ph_3P)_3RhCl]$ (0.20 g, 0.21 mmol) was added to a solution of GH orthoester **30** (1.48 g, 2.86 mmol) and DABCO (1.45 g, 12.89 mmol) in EtOH/H_2O (10:1, 25 mL, degassed 1 h) at 25 °C. The resulting mixture was refluxed for 2 h and then cooled. 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, 25 mL). NMO (1.51 g, 12.89 mmol) and OsO_4 (0.30 mL, 2.5 % solution in *t*BuOH) were added and the reaction mixture was stirred for 8 h at 25 °C. The reaction mixture was diluted with CH_2Cl_2 (300 mL) and washed with saturated aqueous $NaHCO_3$ (30 mL) and brine (30 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 → 10 % MeOH in CH_2Cl_2) to afford GH triol **31** (0.58 g of each diastereoisomer, 97 % overall yield) as a white foam. More polar diastereoisomer: **31**: R_f = 0.11 (100 % EtOAc); $[\alpha]_D^{22}$ = +25.2 (c = 0.21, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3415, 3032, 2892, 1454, 1368, 1233, 1073, 910, 736, 700 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 10H, ArH), 4.75, 4.59 (AB, J = 11.8 Hz, 2H, CH$_2$Ar), 4.57–4.48 (m, 5H, CH$_2$Ar, G4, G5, G5), 4.21 (ddd, J = 4.6, 4.6, 2.3 Hz, 1H, G3), 3.88 (dd, J = 12.8, 2.0 Hz, 1H, G2), 3.87 (t, J = 9.4 Hz, 1H, H3), 3.68 (d, J = 9.7 Hz, 1H, H2), 3.67–3.62 (m, 1H, H5), 3.54 (dd, J = 12.6, 2.5 Hz, 1H, G2), 3.53–3.46 (m, 2H, H4, OH), 3.44 (t, J = 10.6 Hz, 1H, H5), 2.08 (s, 2H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.3, 137.6, 128.4, 128.3, 127.6, 127.5, 120.2, 81.2, 80.0, 77.2, 76.9, 74.7, 73.2, 73.1, 71.9, 71.3, 62.3, 61.9; HRMS (FAB): calcd for $C_{23}H_{28}O_8Na$ $[M+Na]^+$: 455.1682, found 455.1687.

GH TBS ether 32: TBSOTf (0.93 mL, 4.05 mmol) was added to a solution of GH triol (bottom diastereoisomer) **31** (1.54 g, 3.68 mmol) and 2,6-lutidine (0.64 mL, 5.52 mmol) in CH_2Cl_2 (20 mL) at −78 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of MeOH (1.0 mL), diluted with CH_2Cl_2 (250 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60 % EtOAc in hexanes) to afford GH TBS ether **32** (1.85 g, 92 %) as a white foam. **32**: R_f = 0.28 (40 % EtOAc in hexanes); $[\alpha]_D^{22}$ = +25.4 (c = 0.95, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3445, 3032, 2930, 2858, 1457, 1364, 1255, 1072, 1003, 839, 780, 699 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.25 (m, 10H, ArH), 4.75, 4.62 (AB, J = 11.8 Hz, 2H, CH$_2$Ar), 4.55 (brs, 2H, CH$_2$Ar), 4.20 (ddd, J = 6.0, 6.0, 6.0 Hz, 1H, G4), 4.20 (dt, J = 6.2, 3.7 Hz, 1H, G3), 3.92 (dd, J = 11.0, 4.3 Hz, 1H, G2), 3.85 (dd, J = 11.0, 3.5 Hz, 1H, G2), 3.83 (brt, J = 8.9 Hz, 1H, H3), 3.71 (dt, J = 2.3, 2.3 Hz, 1H, H5), 3.67 (dd, J = 9.9, 6.4 Hz, 1H, G5), 3.61 (brd, J = 9.2 Hz, 1H, H2), 3.58 (dd, J = 9.9, 5.7 Hz, 1H, G5), 3.53–3.48 (m, 2H, H4, H5), 3.00 (brs, 1H, OH), 2.89 (s, 1H, OH), 0.89 (s, 9H, *t*BuSi), 0.08 (s, 6H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.1, 137.7, 128.4, 128.4, 127.8,

127.7, 127.6, 120.2, 79.4, 78.5, 76.8, 75.1 73.4, 73.0, 72.2, 71.5, 63.2, 62.4, 60.3, 25.8, 18.3, 14.1, −5.5; HRMS (FAB): calcd for $C_{29}H_{42}O_8SiNa$ $[M+Na]^+$: 569.2547, found 569.2556.

GH dibenzoate 33: BzCl (1.0 mL, 8.23 mmol) was added to a solution of GH diol **32** (1.80 g, 3.29 mmol), Et_3N (1.84 mL, 13.17 mmol) and 4-DMAP (0.08 g, 0.66 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (1.0 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 → 70 % Et_2O in hexanes) to afford GH dibenzoate **33** (2.41 g, 97 %) as a white foam. **33**: $R_f = 0.41$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +63.0$ ($c = 0.44$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3032$, 2931, 2858, 1733, 1604, 1454, 1366, 1272, 1106, 1026, 912, 840, 780, 735, 708 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.01$ (d, $J = 8.0$ Hz, 2H, ArH), 7.96 (d, $J = 7.5$ Hz, 2H, ArH), 7.50 – 7.17 (m, 16H, ArH), 5.90 (dd, $J = 10.3$, 8.6 Hz, 1H, H3), 5.55 (d, $J = 10.3$ Hz, 1H, H2), 4.64 (brs, 2H, CH_2Ar), 4.60, 4.56 (AB, $J = 12.2$ Hz, 2H, CH_2Ar), 4.34 (ddd, $J = 6.4$, 6.4, 4.7 Hz, 1H, G3), 4.21 – 4.17 (m, 1H, G4), 3.94 – 3.85 (m, 2H, H4, H5), 3.82 (t, $J = 2.3$ Hz, 1H, H5), 3.73 (dd, $J = 10.2$, 6.8 Hz, 1H, G2), 3.66 (dd, $J = 10.2$, 5.2 Hz, 1H, G2), 3.57 (dd, $J = 10.4$, 5.2 Hz, 1H, G5), 3.34 (dd, $J = 10.4$, 7.1 Hz, 1H, G5), 0.74 (s, 9H, *t*BuSi), −0.16 (s, 3H, MeSi), −0.21 (s, 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.5$, 165.1, 137.8, 137.6, 133.0, 132.9, 129.7, 129.6, 128.3, 128.2, 127.6, 127.6, 119.1, 80.2, 78.9, 75.2, 73.5, 73.3, 72.7, 71.3, 69.6, 64.4, 63.2, 62.3, 31.5, 27.0, 25.5, 15.2, −5.8, −6.0; HRMS (MALDI): calcd for $C_{43}H_{50}O_{10}SiNa$ $[M+Na]^+$: 777.3071, found 777.3084.

GH diol 34: 10 % Pd/C (200 mg) was added to a solution of GH di-benzoate **33** (2.20 g, 2.91 mmol) in EtOAc (10 mL) and the resulting mixture was stirred under 1 atm of H_2 (balloon) at 25 °C for 2 h. The reaction mixture was diluted with EtOAc (150 mL) and filtered through a short pad of Celite and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O in hexanes) to afford GH diol **34** (1.59 g, 95 %) as a white foam. **34**: $R_f = 0.18$ (40 % EtOAc in hexanes); $[\alpha]_D^{22} = +21.3$ ($c = 0.23$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3425$, 2931, 2858, 1734, 1454, 1260, 1117, 1029, 839, 711 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.00$ (d, $J = 8.1$ Hz, 2H, ArH), 7.93 (d, $J = 8.1$ Hz, 2H, ArH), 7.52 – 7.44 (m, 2H, ArH), 7.38 (t, $J = 8.0$ Hz, 2H, ArH), 7.33 (t, $J = 8.0$ Hz, 2H, ArH), 5.61 (d, $J = 10.1$ Hz, 1H, H2), 5.54 (dd, $J = 10.0$, 8.9 Hz, 1H, H3), 4.28 – 4.22 (m, 2H, G3, G4), 4.12 – 4.08 (m, 1H, H5), 4.05 (dd, $J = 11.1$, 5.8 Hz, 1H, H4), 3.84 (t, $J = 10.7$ Hz, 1H, H5), 3.83 (dd, $J = 12.0$, 3.5 Hz, 1H, G2), 3.77 (dd, $J = 12.0$, 5.1 Hz, 1H, G2), 3.64 (dd, $J = 10.1$, 4.8 Hz, 1H, G5), 3.25 (dd, $J = 10.1$, 7.8 Hz, 1H, G5), 3.02 (brs, 1H, OH), 0.73 (s, 9H, *t*BuSi), −0.15, −0.19 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 167.3$, 165.2, 133.5, 133.4, 129.9, 129.7, 129.0, 128.8, 128.5, 128.4, 119.0, 83.1, 78.0, 76.2, 69.2, 69.1, 64.5, 63.7, 63.2, 25.6, 18.0, 14.1, −5.8, −5.9; HRMS (MALDI): calcd for $C_{29}H_{38}O_{10}SiNa$ $[M+Na]^+$: 597.2126, found 597.2117.

GH TIPS ether 35: TIPSOTf (0.53 mL, 1.95 mmol) was added to a solution of GH diol **34** (1.02 g, 1.77 mmol) and 2,6-lutidine (0.31 mL, 2.66 mmol) in CH_2Cl_2 (20 mL) at −78 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of MeOH (1.0 mL), diluted with CH_2Cl_2 (250 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60 % Et_2O in hexanes) to afford GH TIPS ether **35** (1.15 g, 89 %) as a white foam. **35**: $R_f = 0.41$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +105.5$ ($c = 0.11$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3491$, 3068, 2866, 2847, 1734, 1603, 1456, 1316, 1256, 1114, 1070, 1028, 839, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.01$ (d, $J = 8.1$ Hz, 2H, ArH), 7.94 (d, $J = 8.1$ Hz, 2H, ArH), 7.52 – 7.33 (m, 6H, ArH), 5.61 (d, $J = 10.1$ Hz, 1H, H2), 5.49 (t, $J = 10.1$ Hz, 1H, H3), 4.28 (dd, $J = 6.3$, 6.3 Hz, 1H, G4), 4.17 (dd, $J = 5.6$, 5.6 Hz, 1H, G3), 4.08 (ddd, $J = 10.0$, 10.0, 6.0 Hz, 1H, H4), 3.98 (dd, $J = 11.5$, 5.9 Hz, 1H, H5), 3.94 (dd, $J = 10.4$, 5.5 Hz, 1H, G2), 3.90 (dd, $J = 10.4$, 5.5 Hz, 1H, G2), 3.82 (t, $J = 11.1$ Hz, 1H, H5), 3.55 (dd, $J = 10.4$, 5.3 Hz, 1H, G5), 3.38 (dd, $J = 10.4$, 6.6 Hz, 1H, G5), 3.26 (s, 1H, OH), 1.14 – 1.07 (m, 21H, *i*Pr_3Si), 0.71 (s, 9H, *t*BuSi), −0.18, −0.22 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 167.6$, 165.2, 133.5, 133.3, 129.9, 129.8, 129.2, 128.8, 128.4, 128.4, 118.9, 81.8, 79.0, 69.5, 66.2, 64.3, 63.5, 25.7, 18.1, 11.9, −5.8, −5.9; HRMS (MALDI): calcd for $C_{38}H_{58}O_{10}Si_2Na$ $[M+Na]^+$: 753.3461, found 753.3462.

GH BOM ether 8: BOMCl (0.79 mL, 5.68 mmol) was added to a solution of GH alcohol **35** (0.83 g, 1.14 mmol) and diisopropylethylamine (2.0 mL, 11.35 mmol) in CH_2Cl_2 (1 mL) and the resulting mixture was heated at 50 °C and stirred for 4 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL), diluted with CH_2Cl_2 (250 mL), and washed with 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 GH BOM ether **8** (0.86 g, 89 %) as a white foam. **8**: $R_f = 0.32$ (30 % Et_2O in hexanes); $[\alpha]_D^{22} = +84.7$ ($c = 0.45$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3033$, 2947, 2865, 1736, 1456, 1266, 1112, 1047, 838, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.00$ (d, $J = 7.3$ Hz, 2H, ArH), 7.95 (d, $J = 7.3$ Hz, 2H, ArH), 7.55 – 7.17 (m, 11H, ArH), 5.84 (t, $J = 9.9$ Hz, 1H, H3), 5.59 (d, $J = 10.0$ Hz, 1H, H2), 4.77, 4.74 (AB, $J = 7.1$ Hz, 2H, OCH_2O), 4.52, 4.42 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.29 (ddd, $J = 6.2$, 6.2, 6.2 Hz, 1H, G4), 4.19 (ddd, $J = 5.5$, 5.5, 5.5 Hz, 1H, G3), 4.12 (ddd, $J = 10.4$, 10.4, 5.8 Hz, 1H, H4), 4.06 (dd, $J = 11.1$, 5.8 Hz, 1H, H5), 3.95 (dd, $J = 10.5$, 5.4 Hz, 1H, G2), 3.91 (dd, $J = 10.5$, 5.4 Hz, 1H, G2), 3.88 (t, $J = 10.9$ Hz, 1H, H5), 3.55 (dd, $J = 10.2$, 5.2 Hz, 1H, G5), 3.36 (dd, $J = 10.2$, 6.8 Hz, 1H, G5), 1.16 – 1.07 (m, 21H, *i*Pr_3Si), 0.72 (s, 9H, *t*BuSi), −0.18, −0.23 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.6$, 165.1, 137.2, 133.1, 133.0, 129.8, 129.7, 129.4, 129.2, 128.3, 128.3, 127.8, 127.6, 127.5, 118.9, 94.5, 81.7, 78.9, 74.5, 73.3, 69.8, 69.5, 64.2, 63.4, 62.8, 25.6, 17.9, 11.8, −5.8, −6.0; HRMS (MALDI): calcd for $C_{46}H_{66}O_{11}Si_2Na$ $[M+Na]^+$: 873.4041, found 873.4032.

GH alcohol 36: PPTS (30 mg, 0.088 mmol) was added to a solution of GH TBS ether **8** (0.75 g, 0.88 mmol) in EtOH/THF (3:1, 2 mL) and the resulting mixture was heated to 50 °C and stirred for 6 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL), diluted with CH_2Cl_2 (250 mL) and washed with 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 → 70 % Et_2O in hexanes) to afford GH alcohol **36** (0.69 g, 83 %) as a white foam. **36**: $R_f = 0.26$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +90.9$ ($c = 0.11$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3517$, 3034, 2944, 2867, 1732, 1604, 1454, 1267, 1112, 1045, 914, 884, 735, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.99$ (d, $J = 8.0$ Hz, 2H, ArH), 7.96 (d, $J = 8.1$ Hz, 2H, ArH), 7.51 – 7.25 (m, 9H, ArH), 7.17 (d, $J = 8.2$ Hz, 2H, ArH), 5.84 (t, $J = 9.9$ Hz, 1H, H3), 5.58 (d, $J = 10.1$ Hz, 1H, H2), 4.78, 4.75 (AB, $J = 7.2$ Hz, 2H, OCH_2O), 4.52, 4.44 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.40 (dt, $J = 7.7$, 4.0 Hz, 1H, G4), 4.21 (dd, $J = 7.3$, 4.5 Hz, 1H, G3), 4.14 (ddd, $J = 10.5$, 10.5, 5.8 Hz, 1H, H4), 4.02 (dd, $J = 11.2$, 5.4 Hz, 1H, H5), 4.02 (dd, $J = 9.9$, 5.3 Hz, 1H, G2), 3.86 (dd, $J = 10.0$, 7.5 Hz, 1H, G2), 3.81 (t, $J = 11.0$ Hz, 1H, H5), 3.68 (dd, $J = 12.3$, 3.6 Hz, 1H, G5), 3.46 (dd, $J = 12.3$, 4.4 Hz, 1H, G5), 1.91 (brs, 1H, OH), 1.17 – 1.08 (m, 21H, *i*Pr_3Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.6$, 165.5, 137.1, 133.4, 133.1, 129.7, 129.7, 129.3, 128.8, 128.4, 128.3, 127.7, 127.5, 119.6, 94.5, 80.5, 79.4, 74.3, 73.1, 70.1, 69.5, 63.8, 62.7, 61.9, 17.9, 11.8; HRMS (MALDI): calcd for $C_{40}H_{52}O_{11}SiNa$ $[M+Na]^+$: 759.3176, found 759.3165.

GH thiazole 37: DMSO (94 μL, 1.06 mmol) was added dropwise to a solution of oxalyl chloride (92 μL, 0.95 mmol) in CH_2Cl_2 (5 mL) at −78 °C and the resulting mixture was stirred for 10 min. GH alcohol **36** (0.39 g, 0.53 mmol) was dissolved in CH_2Cl_2 (5 mL) and added to the reaction mixture via cannula over 15 min. The reaction mixture was stirred at −78 °C for 2 h, and then Et_3N (0.30 mL, 2.17 mmol) was added and the reaction mixture was allowed to warm to −40 °C over 2 h. TMS-thiazole (0.17 g, 1.06 mmol) was added and the reaction mixture was allowed to warm to 25 °C over 12 h. The reaction mixture was 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 dissolved in MeOH (10 mL) and PPTS (0.02 g, 0.03 mmol) was added. The resulting mixture was stirred for 2 h at 25 °C and then Et_3N (2 mL) was added. 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 GH thiazole **37** (0.43 g, 97 %) as a white foam. **37**: $R_f = 0.25$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +47.7$ ($c = 0.13$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3748$, 2940, 2864, 1735, 1265, 1117, 1029, 710 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.00 – 7.15$ (m, 17H, ArH), 5.84 (t, $J = 9.9$ Hz, 1H, H3), 5.60 (d, $J = 10.3$ Hz, 1H, H2), 4.93 (brs, 1H), 4.75, 4.73 (AB, $J = 7.2$ Hz, 2H, OCH_2O), 4.63 (brs, 1H), 4.52 (brs, 1H), 4.46, 4.41 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.10 (ddd, $J = 10.5$, 10.5, 5.8 Hz, 1H, H4),

0947-6539/00/0617-3130 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

4.05 (dd, $J = 11.3$, 5.7 Hz, 1H, H5), 3.89 (t, $J = 10.9$ Hz, 1H, H5), 3.88–3.82 (m, 2H), 3.77 (s, 1H), 1.17–1.08 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.5$, 165.5, 137.2, 133.6, 133.1, 129.8, 129.7, 129.3, 128.6, 128.4, 128.3, 128.1, 127.7, 127.6, 119.1, 94.7, 74.5, 73.3, 70.0, 69.6, 63.9, 63.0, 29.7, 17.9, 11.9; HRMS (MALDI): calcd for $C_{43}H_{53}NO_{11}SSiNa$ $[M+Na]^+$: 842.3006, found 842.2993.

GH TES ether 38: TESOTf (62 µL, 0.27 mmol) was added to a solution of GH alcohol **37** (0.201 g, 0.25 mmol) and 2,6-lutidine (30 µL, 0.27 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 MeOH (0.1 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 → 60 % Et_2O in hexanes) to afford GH TES ether **38** (0.213 g, 89 %) as a white foam. **38**: $R_f = 0.53$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = -17.5$ ($c = 0.08$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2940$, 2873, 1736, 1454, 1266, 1094, 1070, 709 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.94$ (d, $J = 7.9$ Hz, 2H, ArH), 7.90 (d, $J = 7.9$ Hz, 2H, ArH), 7.50–7.14 (m, 12H, ArH), 6.90 (d, $J = 3.0$ Hz, 1H, CH-TH), 5.75 (t, $J = 9.4$ Hz, 1H, H3), 5.56 (d, $J = 10.0$ Hz, 1H, H2), 4.91 (d, $J = 5.4$ Hz, 1H, G2), 4.73, 4.71 (AB, $J = 7.1$ Hz, 2H, OCH_2O), 4.58 (t, $J = 5.8$ Hz, 1H, G3), 4.49, 4.39 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.45–4.42 (m, 1H, G4), 4.04 (ddd, $J = 9.6$, 9.6, 5.7 Hz, 1H, H4), 4.01 (dd, $J = 11.3$, 5.7 Hz, 1H, H5), 3.89–3.82 (m, 3H, G5, G5, H5), 1.17–1.08 (m, 21H, iPr$_3$Si), 0.74 (t, $J =$ 8.0 Hz, 9H, $SiCH_2CH_3$), 0.35 (q, $J = 8.0$ Hz, 6H, $SiCH_2$); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.6$, 164.9, 141.7, 137.3, 133.0, 132.9, 130.0, 129.7, 129.6, 129.5, 128.3, 128.2, 127.7, 127.6, 119.4, 118.7, 94.6, 80.9, 74.5, 73.7, 71.8, 69.5, 69.5, 63.9, 62.7, 18.0, 11.9, 6.5, 4.4; HRMS (MALDI): calcd for $C_{49}H_{68}NO_{11}SSi_2$ $[M+H]^+$: 934.4046, found 934.4011.

GH tribenzoate 39: K_2CO_3 (9.0 mg, 0.062 mmol) was added to a solution of GH TES ether **38** (0.115 g, 0.123 mmol) in MeOH (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 → 100 % Et_2O in hexanes) to afford the triol (0.068 g) as a white foam. BrBzCl (0.097 g, 0.44 mmol) was added to a solution of the above triol (0.068 g, 0.111 mmol), Et_3N (0.077 mL, 0.55 mmol) and 4-DMAP (0.003 g, 0.022 mmol) in CH_2Cl_2 (1 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (0.5 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 → 70 % Et_2O in hexanes) to afford GH tribenzoate **39** (0.122 g, 86 % over two steps) as a white foam. **39**: $R_f = 0.64$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +21.4$ ($c = 0.31$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2944$, 2866, 1736, 1590, 1486, 1397, 1267, 1098, 1012, 909, 846, 751, 733, 683 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.74$ (d, $J = 6.8$ Hz, 2H, ArH), 7.68 (d, $J = 6.8$ Hz, 2H, ArH), 7.57 (d, $J = 6.8$ Hz, 2H, ArH), 7.48 (d, $J = 2.9$ Hz, 1H, CH-TH), 7.45 (d, $J = 6.8$ Hz, 2H, ArH), 7.40 (d, $J = 6.8$ Hz, 2H, ArH), 7.35 (d, $J =$ 6.8 Hz, 2H, ArH), 7.29–7.13 (m, 5H, ArH), 6.93 (d, $J = 2.9$ Hz, 1H, CH-TH), 6.47 (d, $J = 3.4$ Hz, 1H, G2), 5.72 (t, $J = 10.1$ Hz, 1H, H3), 5.51 (d, $J =$ 10.1 Hz, 1H, H2), 4.94 (dd, $J = 6.8$, 3.4 Hz, 1H, G3), 4.73, 4.70 (AB, $J =$ 7.2 Hz, 2H, OCH_2O), 4.62 (dt, $J = 5.2$, 5.2 Hz, 1H, G4), 4.47, 4.40 (AB, $J =$ 11.9 Hz, 2H, CH_2Ar), 4.07–4.02 (m, 2H, H4, H5), 3.92 (d, $J = 5.1$ Hz, 2H, G5, G5), 3.87–3.81 (m, 1H, H5), 1.16–0.86 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 164.8$, 164.2, 163.8, 142.6, 137.0, 131.7, 131.7, 131.5, 131.2, 131.2, 131.1, 128.9, 128.5, 128.4, 127.9, 127.7, 127.6, 127.5, 127.4, 119.9, 118.5, 94.7, 79.6, 78.7, 74.4, 73.6, 71.4, 69.6, 69.4, 63.9, 62.7, 17.9, 11.9; HRMS (MALDI): calcd for $C_{50}H_{54}Br_3NO_{12}SSiNa$ $[M+Na]^+$: 1182.0558, found 1182.0603.

GH diol 40: nBu$_4$NF (0.135 mL, 0.135 mmol) was added to a solution of GH tribenzoate **39** (0.12 g, 0.104 mmol) in THF (1 mL) and the resulting mixture was stirred at 25 °C for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (0.5 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 → 100 % Et_2O in hexanes) to afford the GH diol **40** (0.075 g, 88 %) as a white solid. **40**: $R_f = 0.11$ (70 % Et_2O in hexanes); m.p. 184 °C, CH_2Cl_2/hexanes; $[\alpha]_D^{22} = +23.8$ ($c = 0.17$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3387$, 2952, 1727, 1590, 1454, 1397, 1270, 1040, 911, 848, 752 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.88$ (d, $J = 8.5$ Hz, 2H, ArH), 7.86 (d, $J = 8.5$ Hz, 2H, ArH), 7.66 (d, $J = 3.5$ Hz, 1H, CH-TH), 7.57 (d, $J =$ 8.5 Hz, 2H, ArH), 7.52 (d, $J = 8.5$ Hz, 2H, ArH), 7.31–7.14 (m, 6H, ArH, CH-TH), 5.38 (br s, 1H, G2), 5.37 (t, $J = 9.6$ Hz, 1H, H3), 4.96 (br s, 1H, G3), 4.81 (br s, 1H, OH), 4.78 (dt, $J = 4.8$, 4.8 Hz, 1H, G4), 4.74, 4.72 (AB, $J = 8.8$ Hz, 2H, OCH_2O), 4.47, 4.42 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.41 (dd, $J = 11.8$, 7.7 Hz, 1H, G5), 4.27 (dd, $J = 11.8$, 5.9 Hz, 1H, G5), 3.98 (ddd, $J =$ 10.3, 10.3, 5.9 Hz, 1H, H4), 3.92 (d, $J = 10.1$ Hz, 1H, H2), 3.89 (dd, $J = 11.7$, 5.9 Hz, 2H, H5), 3.63 (t, $J = 11.8$ Hz, 1H, H5); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.8$, 165.3, 137.0, 131.9, 131.7, 131.3, 128.8, 128.5, 128.4, 128.0, 127.8, 127.5, 121.1, 119.6, 94.7, 81.9, 76.7, 76.4, 73.4, 72.0, 72.0, 69.8, 65.1, 63.0; HRMS (MALDI): calcd for $C_{34}H_{32}Br_2NO_{11}S$ $[M+H]^+$: 820.0064, found 820.0029.

TBS ether 47: TBSOTf (24.80 mL, 108.0 mmol) was added to a solution of mannose diol **11**[4] (30.66 g, 98.15 mmol) and 2,6-lutidine (14.86 mL, 127.60 mmol) in CH_2Cl_2 (500 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 (750 mL) 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 → 40 % Et_2O in hexanes) to afford TBS ether **47** (40.50 g, 97 %) as a white foam. **47**: $R_f = 0.45$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +146.8$ ($c = 0.63$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3456$, 2931, 2854, 1474, 1381, 1248, 1220, 1160, 1065, 870, 835, 779, 744 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.48–7.46$ (m, 2H, ArH), 7.30–7.25 (m, 3H, ArH), 5.75 (s, 1H, F1), 4.33 (dd, $J = 5.7$, 1.1 Hz, 1H, F2), 4.18 (dd, $J = 7.4$, 5.9 Hz, 1H, F3), 3.99 (ddd, $J = 10.0$, 4.9, 4.9 Hz, 1H, F5), 3.86–3.83 (m, 2H, F4, F6), 3.74 (dd, $J = 10.6$, 5.7 Hz, 1H, F6), 3.00 (br s, 1H, OH), 1.54 (s, 3H, Me), 1.38 (s, 3H, Me), 0.89 (s, 9H, tBuSi), 0.05 (s, 6H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 132.4$, 131.7, 129.0, 127.5, 109.8, 83.7, 78.0, 75.9, 72.0, 69.7, 64.3, 28.0, 26.3, 25.8, 19.6, −5.5; HRMS (MALDI): calcd for $C_{21}H_{34}O_5SSiNa$ $[M+Na]^+$: 449.1794, found 449.1808.

Alcohol 48: NaH (4.18 g, 104.42 mmol) was added to a solution of alcohol **47** (40.50 g, 94.92 mmol) in DMF/THF (1:1, 400 mL) at 0 °C and the resulting mixture was stirred for 15 min. PMBCl (16.73 mL, 123.41 mmol) and nBu$_4$NI (7.01 g, 19.00 mmol) were 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 (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 the PMB ether (49.31 g, 95 %) as a white foam. PMB ether: $R_f = 0.75$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +158.8$ ($c = 0.83$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2987$, 2931, 2884, 1613, 1515, 1460, 1380, 1248, 1219, 1163, 1104, 1073, 872, 835, 779 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.51–7.48$ (m, 2H, ArH), 7.31–7.23 (m, 5H, ArH), 6.88 (d, $J = 8.5$ Hz, 2H, PMB), 5.76 (s, 1H, F1), 4.83, 4.58 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.35 (t, $J = 5.5$ Hz, 1H, F3), 4.34 (s, 1H, F2), 4.02 (ddd, $J = 10.0$, 4.0, 2.0 Hz, 1H, F5), 3.84 (dd, $J = 11.5$, 4.0 Hz, 1H, F6), 3.80 (s, 3H, OMe), 3.73 (dd, $J = 11.5$, 2.0 Hz, 1H, F6), 3.70 (dd, $J = 10.0$, 7.0 Hz, 1H, F4), 1.51 (s, 3H, Me), 1.39 (s, 3H, Me), 0.88 (s, 9H, tBuSi), 0.02, 0.01 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.2$, 133.7, 131.5, 130.5, 129.6, 128.8, 127.3, 113.7, 109.4, 83.9, 78.6, 76.4, 75.2, 72.8, 71.2, 62.3, 55.2, 27.9, 26.5, 25.9, 18.3, −5.2, −5.3; HRMS (MALDI): calcd for $C_{29}H_{42}O_6SSiNa$ $[M+Na]^+$: 569.2369, found 569.2391. nBu$_4$NF (98.80 mL, 98.76 mmol) was added to a solution of the above PMB ether (45.00 g, 82.30 mmol) in THF (400 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 → 60 % Et_2O in hexanes) to afford alcohol **48** (33.82 g, 95 %) as a white solid. **48**: $R_f = 0.26$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +182.4$ ($c = 0.55$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3416$, 2982, 2934, 1613, 1515, 1379, 1304, 1246, 1219, 1162, 1086, 1080, 870, 816, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.48–7.46$ (m, 2H, ArH), 7.34–7.27 (m, 5H, ArH), 6.88 (d, $J = 8.5$ Hz, 2H, PMB), 5.80 (s, 1H, F1), 4.84, 4.57 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.37 (dd, $J = 7.4$, 5.9 Hz, 1H, F3), 4.36 (s, 1H, F2), 4.10 (ddd, $J = 10.0$, 4.5, 3.0 Hz, 1H, F5), 3.81 (s, 3H, OMe), 3.74 (ddd, $J = 12.0$, 6.5, 4.0 Hz, 1H, F6), 3.59 (ddd, $J = 12.0$, 7.5, 5.0 Hz, 1H, F6), 3.59 (dd, $J = 10.0$,

6.5 Hz, 1H, F4), 1.64 (t, $J = 6.5$ Hz, 1H, OH), 1.52 (s, 3H, Me), 1.40 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.0$, 132.3, 129.7, 129.1, 127.9, 113.8, 109.5, 83.8, 78.5, 76.3, 75.9, 72.7, 70.0, 62.3, 55.3, 28.0, 26.4; HRMS (MALDI): calcd for $C_{23}H_{28}O_6SNa$ $[M+Na]^+$: 455.1499, found 455.1503.

Methyl ether 49: NaH (3.42 g, 85.53 mmol) was added to a solution of alcohol **48** (33.63 g, 77.75 mmol) in DMF (200 mL) at 0 °C and the resulting mixture was stirred for 15 min. MeI (6.29 mL, 101.08 mmol) was added and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (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, $0 \rightarrow 70\%$ Et_2O in hexanes) to afford methyl ether **49** (33.00 g, 95%) as a white solid. **49**: $R_f = 0.43$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = +170.5$ ($c = 2.23$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2983$, 2933, 1612, 1585, 1517, 1466, 1379, 1304, 1244, 1072, 910, 871, 823, 753, 717, 693 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.52 - 7.50$ (m, 2H, ArH), 7.32 – 7.24 (m, 5H, ArH), 6.89 (d, $J = 8.5$ Hz, 2H, PMB), 5.82 (s, 1H, F1), 4.84, 4.58 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.37 (s, 1H, F2), 4.35 (t, $J = 7.0$ Hz, 1H, F4), 4.17 (ddd, $J =$ 10.0, 4.0, 2.0 Hz, 1H, F5), 3.79 (s, 3H, OMe), 3.73 – 3.68 (m, 1H, F3), 3.62 (dd, $J = 10.5$, 4.0 Hz, 1H, F6), 3.52 (dd, $J = 10.5$, 2.0 Hz, 1H, F6), 3.31 (s, 3H, OMe), 1.53 (s, 3H, Me), 1.39 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.1$, 133.3, 131.6, 131.5, 130.2, 129.4, 129.2, 128.7, 127.3, 113.6, 109.3, 84.0, 78.5, 76.3, 75.2, 74.1, 72.7, 71.0, 69.5, 59.0, 57.6, 55.0, 27.8, 26.3; HRMS (MALDI): calcd for $C_{24}H_{30}O_6SNa$ $[M+Na]^+$: 469.1655, found 469.1672.

Diol 50: TsOH (2.78 g, 14.63 mmol) was added to a solution of methyl ether **49** (32.68 g, 73.18 mmol) and ethylene glycol (9.70 mL, 183.00 mmol) in MeOH (500 mL) at 25 °C and the resulting mixture was stirred for 5 h. The reaction mixture was quenched by the addition of Et_3N (100 mL) and the solvents were removed under reduced pressure. The residue was diluted with CH_2Cl_2 (1.0 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, $0 \rightarrow 100\%$ EtOAc in hexanes) to afford diol **50** (25.29 g, 85%) as a white foam. **50**: $R_f = 0.21$ (100% Et_2O); $[\alpha]_D^{22} =$ $+197.2$ ($c = 0.72$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3339$, 2905, 1617, 1517, 1459, 1250, 1098, 823, 749 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.46 - 7.44$ (m, 2H, ArH), 7.31 – 7.23 (m, 5H, ArH), 6.90 (d, $J = 8.6$ Hz, 2H, PMB), 5.56 (d, $J = 1.3$ Hz, 1H, F1), 4.71, 4.64 (AB, $J = 11.1$ Hz, 2H, CH_2Ar), 4.19 (ddd, $J =$ 9.6, 3.5, 2.0 Hz, 1H, F5), 4.15 (dd, $J = 3.3$, 1.6 Hz, 1H, F2), 3.91 (ddd, $J = 9.2$, 6.0, 3.3 Hz, 1H, F3), 3.83 (t, $J = 9.6$ Hz, 1H, F4), 3.80 (s, 3H, OMe), 3.71 (dd, $J = 10.7$, 3.5 Hz, 1H, F6), 3.57 (dd, $J = 10.7$, 2.0 Hz, 1H, F6), 3.37 (s, 3H, OMe), 2.86 (br s, 2H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3$, 137.7, 131.3, 130.4, 129.6, 129.0, 128.0, 127.8, 127.3, 113.8, 87.3, 80.1, 74.9, 73.9, 72.0, 71.0, 69.9, 59.1, 55.3; HRMS (MALDI): calcd for $C_{21}H_{26}O_6SNa$ $[M+Na]^+$: 429.1348, found 429.1338.

Benzyl ether 51: nBu$_2$SnO (22.00 g, 88.33 mmol) was added to a solution of diol **50** (32.64 g, 80.30 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 (14.33 mL, 120.45 mmol) and nBu$_4$NI (5.93 g, 16.06 mmol) were added. The reaction mixture was refluxed again for 5 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, $0 \rightarrow 80\%$ Et_2O in hexanes) to afford benzyl ether **51** (35.50 g, 89%) as a white foam. **51**: $R_f = 0.18$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = +176.6$ ($c = 0.94$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3418$, 3060, 2889, 2836, 1612, 1584, 1515, 1458, 1303, 1249, 1096, 1034, 851, 795, 769, 741, 698 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.47 - 7.25$ (m, 12H, ArH), 6.89 (d, $J = 8.5$ Hz, 2H, PMB), 5.61 (s, 1H, F1), 4.81, 4.57 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.74 (s, 2H, CH_2Ar), 4.25 – 4.24 (m, 1H, F2), 4.20 (ddd, $J = 9.7$, 3.6, 1.6 Hz, 1H, F5), 3.87 (t, $J = 9.4$ Hz, 1H, F4), 3.87 (dd, $J = 9.2$, 3.1 Hz, 1H, F3), 3.81 (s, 3H, OMe), 3.68 (dd, $J = 10.8$, 4.1 Hz, 1H, F6), 3.55 (dd, $J =$ 10.8, 1.7 Hz, 1H, F6), 3.35 (s, 3H, OMe), 2.75 (br s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3$, 133.9, 131.2, 130.3, 129.6, 129.0, 127.3, 113.9, 87.8, 75.2, 74.4, 72.2, 71.6, 71.0, 59.1, 55.2; HRMS (MALDI): calcd for $C_{28}H_{32}O_6SNa$ $[M+Na]^+$: 519.1817, found 519.1832.

Ring F lactol 52: NBS (17.92 g, 100.67 mmol) was added to a solution of alcohol **51** (33.33 g, 67.11 mmol) in acetone/H_2O (10:1, 440 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 saturated aqueous $NaHCO_3$ (100 mL), diluted with CH_2Cl_2 (1.5 L) 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, $0 \rightarrow 100\%$ EtOAc in hexanes) to afford ring F lactol **52** (26.33 g, 97%) as a white foam. **52**: $R_f = 0.10$ (100% Et_2O); $[\alpha]_D^{22} = +9.0$ ($c = 0.50$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3391$, 2931, 1712, 1613, 1515, 1455, 1367, 1250, 1178, 1093, 821 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.37 -$ 7.22 (m, 7H, ArH), 6.86 (d, $J = 8.5$ Hz, 2H, PMB), 5.25 (br s, 1H, F1), 4.80, 4.50 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.71, 4.68 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.06 (br s, 1H, F2), 4.03 – 4.00 (m, 1H, F5), 3.94 (dd, $J = 9.0$, 3.0 Hz, 1H, F3), 3.80 (s, 3H, OMe), 3.68 (t, $J = 9.5$ Hz, 1H, F4), 3.61 – 3.53 (m, 2H, F6, F6), 3.34 (s, 3H, OMe), 2.85 (d, $J = 2.5$ Hz, 1H, OH), 2.30 (br s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.2$, 137.9, 130.4, 129.6, 128.4, 127.8, 113.7, 93.8, 79.6, 74.7, 74.2, 71.9, 70.2, 68.5, 58.9, 55.2, 29.5; HRMS (MALDI): calcd for $C_{22}H_{28}O_7Na$ $[M+Na]^+$: 427.1733, found 427.1724.

Ring F tin-acetal 45: nBu$_2$SnO (6.59 g, 26.50 mmol) was added to a solution of ring F diol **52** (9.74 g, 25.47 mmol) in MeOH (150 mL) and the resulting mixture was refluxed for 3 h. The solvents were removed under reduced pressure and the residue was azeotroped with benzene (25 mL) and used crude in the next reaction.

Alcohol 54: NaH (3.82 g, 95.4 mmol) was dissolved in THF (100 mL) in a 500 mL, three-neck flask, (with two 250 mL dropping funnels attached) and cooled to 0 °C. 2,3-*O*-Isopropylidene-L-threitol **53** (15.48 g, 95.4 mmol) was placed in one of the addition funnels and diluted with THF (100 mL). The diol solution was added dropwise to the NaH solution over 45 min and then the resulting mixture was warmed to 25 °C and stirred for 1 h. TPSCl (24.82 mL, 95.4 mmol) was placed in the second dropping funnel and diluted with THF (100 mL). The reaction mixture was cooled to 0 °C and then the TPSCl solution was added dropwise to the reaction mixture over 45 min with vigorous stirring. 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 (100 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, $0 \rightarrow 80\%$ Et_2O in hexanes) to afford alcohol **54** (34.41 g, 90%) as a colorless oil. **54**: $R_f = 0.34$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -8.5$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3445$, 2930, 2840, 1639, 1462, 1429, 1385, 1231, 1116, 1072 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.69 - 7.66$ (m, 4H, ArH), 7.46 – 7.38 (m, 6H, ArH), 4.08 (dt, $J =$ 8.0, 4.0 Hz, 1H), 3.97 (ddd, $J = 8.0$, 6.0, 4.0 Hz, 1H), 3.84 – 3.80 (m, 2H), 3.75 (dd, $J = 10.5$, 6.0 Hz, 1H), 3.66 (ddd, $J = 12.5$, 8.0, 4.5 Hz, 1H), 2.17 (dd, $J = 8.0$, 5.0 Hz, 1H, OH), 1.42 (s, 3H, Me), 1.40 (s, 3H, Me), 1.07 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 135.6$, 132.8, 129.9, 127.8, 109.2, 79.5, 64.1, 62.5, 27.1, 26.8, 19.2; HRMS (MALDI): calcd for $C_{23}H_{32}O_4SiNa$ $[M+Na]^+$: 423.1967, found 423.1982.

Thiazole 55: DMSO (3.77 mL, 53.07 mmol) was added dropwise to a solution of oxalyl chloride (3.70 mL, 42.45 mmol) in CH_2Cl_2 (100 mL) at -78 °C and the resulting mixture was stirred for 10 min. Alcohol **54** (8.50 g, 21.23 mmol) was dissolved in CH_2Cl_2 (100 mL) and added to the reaction mixture via cannula over 15 min. The reaction mixture was stirred at -78 °C for 2 h, and then Et_3N (11.83 mL, 84.91 mmol) was added and the reaction mixture was allowed to warm to 0 °C over 2 h. TMS-thiazole (6.70 g, 42.45 mmol) was added and the reaction mixture was allowed to warm to 25 °C over 12 h. The reaction mixture was diluted with CH_2Cl_2 (1.0 L) and washed with H_2O (150 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was dissolved in MeOH (200 mL) and PPTS (0.100 g, 0.32 mmol) was added. The resulting mixture was stirred for 2 h at 25 °C and then Et_3N (5 mL) was added. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, $0 \rightarrow$ 40% Et_2O in hexanes) to afford thiazole **55** (9.65 g, 94%) as a white foam. **55**: $R_f = 0.22$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -23.7$ ($c = 0.83$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3379$, 3071, 2917, 2862, 1501, 1473, 1424, 1380, 1248, 1204, 1110, 1083, 989, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.73$ (d, $J =$ 3.5 Hz, 1H, CH-TH), 7.68 – 7.62 (m, 4H, ArH), 7.44 – 7.36 (m, 6H, ArH), 7.29 (d, $J = 3.5$ Hz, 1H, CH-TH), 5.20 (dd, $J = 5.5$, 3.0 Hz, 1H, G2), 4.44 (dd, $J = 7.5$, 5.5 Hz, 1H, G3), 4.22 (ddd, $J = 7.5$, 7.5, 4.0 Hz, 1H, G4), 3.67 (br d, $J = 3.0$ Hz, 1H, OH), 3.63 (dd, $J = 11.0$, 4.0 Hz, 1H, G5), 3.36 (dd, $J =$ 11.0, 4.0 Hz, 1H, G5), 1.44 (br s, 6H, Me), 1.04 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.9$, 142.3, 135.7, 132.9, 129.7, 127.7, 119.4, 109.8,

0947-6539/00/0617-3132 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

79.6, 78.0, 71.8, 63.8, 27.1, 26.7, 19.2; HRMS (MALDI): calcd for $C_{26}H_{33}NO_4SSiNa$ $[M+Na]^+$: 506.1797, found 506.1810.

Benzoate 56: BzCl (2.78 mL, 23.94 mmol) was added to a solution of alcohol **55** (9.65 g, 19.95 mmol), Et_3N (4.20 mL, 30.00 mmol) and 4-DMAP (0.48 g, 3.99 mmol) in CH_2Cl_2 (100 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (350 mL) and washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60 % Et_2O in hexanes) to afford benzoate **56** (11.23 g, 96 %) as a white foam. **56**: $R_f = 0.41$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = -49.5$ ($c = 0.76$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3070$, 2931, 2857, 1730, 1427, 1261, 1110, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.10$ (d, $J = 8.0$ Hz, 2H, ArH), 7.78 (d, $J = 3.0$ Hz, 1H, CH-TH), 7.70–7.34 (m, 13H, ArH), 7.31 (d, $J = 3.0$ Hz, 1H, CH-TH), 6.60 (d, $J = 4.5$ Hz, 1H, G2), 4.81 (dd, $J = 8.0$, 4.5 Hz, 1H, G3), 4.39 (ddd, $J = 7.5$, 7.5, 3.5 Hz, 1H, G4), 3.78 (dd, $J = 11.5$, 3.5 Hz, 1H, G5), 3.58 (dd, $J = 11.5$, 3.5 Hz, 1H, G5), 1.45 (s, 3H, Me), 1.25 (s, 3H, Me), 1.05 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.7$, 165.0, 142.7, 135.7, 133.5, 133.1, 130.0, 129.7, 128.5, 127.6, 119.7, 110.4, 78.4, 78.4, 72.9, 63.5, 27.4, 26.8, 19.2; HRMS (MALDI): calcd for $C_{33}H_{37}NO_5SSiNa$ $[M+Na]^+$: 610.2059, found 610.2053.

Ring G diol 57: $BCl_3 \cdot Me_2S$ (3.80 mL, 7.62 mmol) was added to a solution of acetonide **56** (2.24 g, 3.81 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 careful addition of saturated aqueous $NaHCO_3$ (10 mL), diluted with CH_2Cl_2 (250 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 ring G diol **57** (1.24 g, 59 %) as a white foam and recovered starting material (0.78 g, 35 %). **57**: $R_f = 0.18$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -7.8$ ($c = 0.46$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3439$, 3070, 2931, 2857, 1727, 1427, 1267, 1110, 824, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.13$ (d, $J = 8.1$ Hz, 2H, ArH), 7.82 (d, $J = 2.7$ Hz, 1H, CH-TH), 7.70–7.26 (m, 14H, ArH), 6.46 (d, $J = 6.5$ Hz, 1H, G2), 4.47 (dd, $J = 6.1$, 1.4 Hz, 1H, G3), 3.99 (ddd, $J = 6.1$, 6.1, 1.4 Hz, 1H, G4), 3.81 (d, $J = 6.1$ Hz, 2H, G5, G5), 3.51 (s, 2H, OH), 1.07 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.4$, 165.2, 141.8, 139.8, 135.5, 133.7 133.0, 130.1, 129.8, 129.0, 128.7, 128.6, 127.8, 120.2, 72.8, 71.9, 69.9, 64.9, 26.8, 19.2; HRMS (MALDI): calcd for $C_{30}H_{33}NO_5SSiNa$ $[M+Na]^+$: 570.1746, found 570.1762.

Bis-allyl ether 60: NaH (58.74 g, 1.469 mol) was dissolved in THF (2 L) in a 5 L, three-neck flask, (with two 500 mL dropping funnels attached) and cooled to 0 °C. Diisopropyl-L-tartrate (**59**) (160.0 mL, 0.761 mol) was placed in one of addition funnels and diluted with THF (300 mL). The tartrate solution was added dropwise to the NaH solution over 45 min and then the resulting mixture was warmed to 25 °C and stirred for 1 h. nBu_4NI (5.62 g, 15.22 mmol) and [18]crown-6 (1.01 g, 3.86 mmol) were added and the resulting mixture was cooled to 0 °C. Allyl bromide (127.08 mL, 1.469 mol) was placed in the second dropping funnel and added dropwise to the reaction mixture over 45 min with vigorous stirring. 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 (150 mL), diluted with Et_2O (2.0 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 → 30 % Et_2O in hexanes) to afford bis-allyl ether **60** (211.0 g, 97 %) as a colorless oil. **60**: $R_f = 0.56$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +55.8$ ($c = 0.66$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2982$, 2937, 1753, 1726, 1458, 1375, 1273, 1205, 1162, 1104, 996, 993 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.88–5.80$ (m, 2H, C*H*=CH_2), 5.21 (ddd, $J = 17.0$, 3.0, 1.5 Hz, 2H, CH_2-*E*), 5.14 (dm, $J = 10.5$ Hz, 2H, CH_2-*Z*), 5.11 (sept, $J = 6.0$ Hz, 2H, C*H*(Me)$_2$), 4.33 (s, 2H, CH), 4.30–4.23 (m, 2H, OCH_2), 3.94–3.89 (m, 2H, OCH_2), 1.27 (d, $J = 6.0$ Hz, 6H, CH(Me)$_2$), 1.26 (d, $J = 6.0$ Hz, 6H, CH(Me)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.8$, 133.8, 118.0, 78.6, 72.6, 68.9, 21.8; HRMS (MALDI): calcd for $C_{16}H_{26}O_6Na$ $[M+Na]^+$: 337.1622, found 337.1615.

Alcohol 61: LAH (22.25 g, 0.586 mol) was suspended in Et_2O (2 L) in a 5 L, three-neck flask, (with one 500 mL dropping funnel, and one large condenser attached). The resulting mixture was refluxed for 30 min and then removed from the heat. Bis-allyl ether **60** (108.37 g, 0.345 mol) was added to the addition funnel and diluted with Et_2O (300 mL). The allyl ether solution was then added dropwise to the LAH solution over 45 min. The resulting mixture was refluxed for 3 h and then cooled to 0 °C. The reaction was quenched by the careful addition of H_2O (25 mL) and a 4 N aqueous NaOH solution (25 mL). The reaction mixture was diluted with Et_2O (1.0 L) and stirred for 12 h. The reaction mixture was filtered and the solvents were removed under reduced pressure to afford the crude diol (64.85 g, 93 %) as a colorless oil. diol: $R_f = 0.18$ (100 % Et_2O); $[\alpha]_D^{22} = -2.5$ ($c = 0.28$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3410$, 2924, 1458, 1426, 1052, 996, 927 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.92–5.84$ (m, 2H, C*H*=CH_2), 5.24 (ddd, $J = 17.5$, 3.5, 1.5 Hz, 2H, CH_2-*E*), 5.15 (ddd, $J = 10.5$, 2.5, 1.0 Hz, 2H, CH_2-*Z*), 4.10 (dddd, $J = 12.5$, 5.5, 1.0, 1.0 Hz, 4H, CH_2OH), 3.75–3.70 (m, 2H, OCH_2), 3.65–3.61 (m, 2H, OCH_2), 3.56–3.53 (m, 2H, CH), 3.03 (t, $J = 6.0$ Hz, 2H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 134.6$, 117.3, 78.9, 71.5, 60.6; HRMS (MALDI): calcd for $C_{10}H_{18}O_4Na$ $[M+Na]^+$: 225.1103, found 225.1111. NaH (14.55 g, 0.364 mol) was suspended in THF (1.0 L) in a 5 L, three-neck flask, (with two 500 mL dropping funnels attached) and cooled to 0 °C. The above crude diol (73.58 g, 0.364 mol) was placed in one of the addition funnels and diluted with THF (300 mL). The diol solution was added dropwise to the NaH solution over 45 min and then the resulting mixture was warmed to 25 °C and stirred for 1 h. TPSCl (104.06 mL, 0.400 mol) was placed in the second dropping funnel and diluted with THF (200 mL). The reaction mixture was cooled to 0 °C and then the TPSCl solution was added dropwise to the reaction mixture over 45 min with vigorous stirring. 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 (150 mL), diluted with Et_2O (2.0 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 → 80 % Et_2O in hexanes) to afford alcohol **61** (144.28 g, 90 %) as a colorless oil. **61**: $R_f = 0.50$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +1.60$ ($c = 2.31$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3453$, 3072, 2932, 2857, 1470, 1110, 996, 925, 824, 741, 705, 613, 506 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.74–7.71$ (m, 4H, ArH), 7.45–7.40 (m, 6H, ArH), 5.97–5.85 (m, 2H, C*H*=CH_2), 5.28 (ddd, $J = 17.0$, 3.0, 1.5 Hz, 1H, CH_2-*E*), 5.23 (ddd, $J = 17.0$, 3.0, 1.5 Hz, 1H, CH_2-*E*), 5.18 (ddd, $J = 10.0$, 3.0, 1.5 Hz, 1H, CH_2-*Z*), 5.16 (ddd, $J = 10.0$, 3.0, 1.5 Hz, 1H, CH_2-*Z*), 4.17 (s, 1H, CH), 4.16 (s, 1H, CH), 4.14–4.10 (m, 1H, OCH_2), 3.88–3.78 (m, 3H, OCH_2, CH_2), 3.73–3.67 (m, 3H, OCH_2, CH_2OH), 3.61–3.58 (m, 1H, CH_2OH), 2.58–2.55 (m, 1H, OH), 1.09 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 135.6$, 135.5, 134.9, 134.8, 133.1, 129.7 127.7, 117.0, 80.0, 78.8, 72.0, 71.9, 62.6, 61.8, 26.7, 19.1; HRMS (MALDI): calcd for $C_{26}H_{36}O_4SiNa$ $[M+Na]^+$: 463.2275, found 463.2286.

Thiazole 62: DMSO (29.03 mL, 0.328 mol) was added dropwise to a solution of oxalyl chloride (18.31 mL, 0.262 mol) in CH_2Cl_2 (800 mL) at −78 °C and the resulting mixture was stirred for 10 min. Alcohol **61** (71.11 g, 0.131 mol) was dissolved in CH_2Cl_2 (800 mL) and added to the reaction mixture via cannula over 15 min. The reaction mixture was stirred at −78 °C for 2 h, and then Et_3N (73.11 mL, 0.524 mol) was added and the reaction mixture was allowed to warm to 0 °C over 2 h. TMS-thiazole (41.25 g, 0.262 mol) was added and the reaction mixture was allowed to warm to 25 °C over 12 h. The reaction mixture was diluted with CH_2Cl_2 (1.0 L) and washed with H_2O (150 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was dissolved in MeOH (500 mL) and PPTS (1.05, 0.032 mol) was added. The resulting mixture was stirred for 2 h at 25 °C and then Et_3N (50.00 mL) was added. The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, 0 → 40 % Et_2O in hexanes) to afford the desired ring G alcohol **62** (38.50 g, 46 %) and the undesired ring G alcohol (38.00 g, 45 %) as white foams. Desired **60**: $R_f = 0.28$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +10.4$ ($c = 0.23$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3417$, 3072, 2931, 2857, 1469, 1427, 1111, 928, 923, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.81$ (d, $J = 3.5$ Hz, 1H, TH-CH), 7.64 (br d, $J = 8.0$ Hz, 2H, ArH), 7.58 (br d, $J = 6.5$ Hz, 2H, ArH), 7.45–7.32 (m, 7H, ArH, TH-CH), 5.91–5.74 (m, 2H, C*H*=CH_2), 5.34 (dd, $J = 6.5$, 5.0 Hz, 1H, G2), 5.28 (dd, $J = 17.0$, 1.0 Hz, 1H, CH_2-*E*), 5.15 (dd, $J = 10.5$, 1.0 Hz, 1H, CH_2-*Z*), 5.09 (dd, $J = 17.0$, 1.0 Hz, 1H, CH_2-*E*), 5.07 (dd, $J = 10.0$, 1.0 Hz, 1H, CH_2-*Z*), 4.72 (d, $J = 6.5$ Hz, 1H, OH), 4.16 (dd, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 4.12 (dd, $J = 5.0$, 2.5 Hz, 1H, G3), 4.07 (dd, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 3.95 (dd, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 3.95 (dd, $J = 10.5$, 7.0 Hz, 1H, G5), 3.70 (dd, $J = 10.5$, 5.5 Hz, 1H, G5), 3.70 (dd, $J = 12.5$, 6.0 Hz, 1H, OCH_2), 3.52–3.50 (m, 1H, G4), 1.03 (s, 9H, *t*BuSi);

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 142.8, 135.6, 135.5, 134.3, 134.0, 133.0, 129.8, 127.7, 119.0, 118.0, 117.9, 79.7, 78.6, 72.3, 72.0, 61.8, 26.8, 19.1; HRMS (MALDI): calcd for $C_{29}H_{37}NO_4SSiNa$ $[M+Na]^+$: 546.2110, found 546.2118. Undesired ring G alcohol: R_f = 0.37 (50% Et_2O in hexanes); $[\alpha]_D^{22}$ = +4.30 (c = 2.21, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3383, 3072, 2932, 2858, 1470, 1427, 1111, 996, 927, 824, 741, 705 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.79 (d, J = 3.0 Hz, 1H, CH-TH), 7.68 (d, J = 7.5 Hz, 2H, ArH), 7.63 (d, J = 8.0 Hz, 2H, ArH), 7.45 – 7.34 (m, 6H, ArH), 7.31 (d, J = 3.0 Hz, 1H, CH-TH), 5.92 – 5.77 (m, 2H, C*H*=CH$_2$), 5.37 (d, J = 5.0 Hz, 1H, G2), 5.26 (dd, J = 17.5, 1.5 Hz, 1H, CH$_2$-*E*), 5.15 (br d, J = 10.0 Hz, 1H, CH$_2$-*Z*), 5.13 (dd, J = 17.5, 1.5 Hz, 1H, CH$_2$-*E*), 5.08 (br d, J = 10.0 Hz, 1H, CH$_2$-*Z*), 4.91 (br s, 1H, OH), 4.19 – 4.15 (m, 3H, G3, OC*H*$_2$), 4.09 (dd, J = 12.5, 6.0 Hz, 1H, OC*H*$_2$), 3.99 (dd, J = 12.0, 6.0 Hz, 1H, OC*H*$_2$), 3.90 (dd, J = 10.0, 6.5 Hz, 1H, G5), 3.82 (dd, J = 10.5, 5.5 Hz, 1H, G5), 3.76 (dd, J = 12.0, 6.0 Hz, 1H, OC*H*$_2$), 3.61 – 3.58 (m, 1H, G4), 1.08 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 142.5, 135.4, 134.2, 133.9, 132.9, 129.9, 127.6, 118.9, 117.5, 79.4, 78.8, 71.8, 71.8, 61.7, 26.6, 18.9; HRMS (MALDI): calcd for $C_{29}H_{38}NO_4SSi$ $[M+H]^+$: 524.2291, found 524.2305.

Ketone 63: DMSO (13.92 mL, 0.196 mol) was added dropwise to a solution of oxalyl chloride (11.43 mL, 0.130 mol) in CH_2Cl_2 (200 mL) at −78 °C and the resulting mixture was stirred for 10 min. Undesired ring G alcohol **62** (34.25 g, 0.065 mol) was dissolved in CH_2Cl_2 (200 mL) and added to the reaction mixture via cannula over 15 min. The reaction mixture was stirred at −78 °C for 2 h, and then Et_3N (36.46 mL, 0.261 mol) was added and the reaction mixture was allowed to warm to 0 °C over 2 h. The reaction mixture was diluted with CH_2Cl_2 (1.0 L) and washed with H_2O (150 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 → 40% Et_2O in hexanes) to afford ketone **63** (32.75 g, 96%) as a white foam. **63**: R_f = 0.49 (50% Et_2O in hexanes); $[\alpha]_D^{22}$ = +8.94 (c = 1.51, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3073, 2932, 2857, 1697, 1474, 1427, 1389, 1111, 996, 931, 823, 705, 613, 505 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04 (d, J = 3.0 Hz, 1H, CH-TH), 7.78 – 7.70 (m, 5H, ArH, CH-TH), 7.41 – 7.38 (m, 6H, ArH), 5.98 – 5.91 (m, 1H, C*H*=CH$_2$), 5.54 – 5.46 (m, 1H, C*H*=CH$_2$), 5.43 (d, J = 3.2 Hz, 1H, G3), 5.25 (dd, J = 17.2, 1.4 Hz, 1H, CH$_2$-*E*), 5.15 (dd, J = 10.4, 1.1 Hz, 1H, CH$_2$-*Z*), 4.87 (dd, J = 17.2, 1.4 Hz, 1H, CH$_2$-*E*), 4.82 (dd, J = 10.4, 1.0 Hz, 1H, CH$_2$-*Z*), 4.32 – 4.26 (m, 2H, G4, OC*H*$_2$), 4.04 – 4.00 (m, 2H, G5, OC*H*$_2$), 3.88 (dd, J = 12.8, 5.5 Hz, 1H, OC*H*$_2$), 3.80 (dd, J = 10.2, 5.5 Hz, 1H, G5), 3.67 (dd, J = 12.8, 5.5 Hz, 1H, OC*H*$_2$), 1.09 (s, 9H, *t*BuSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.8, 165.4, 144.5, 135.6, 135.4, 134.3, 133.2, 129.6, 127.6, 126.2, 117.8, 117.2, 80.8, 79.2, 72.3, 71.9, 65.7, 62.0, 26.7, 19.0, 15.2; HRMS (MALDI): calcd for $C_{29}H_{35}NO_4SSiNa$ $[M+Na]^+$: 544.1948, found 544.1948.

Reduction of Ketone 63: LAH (3.4 g, 108.0 mmol) was added to a solution of ketone **61** (12.00 g, 98.15 mmol) in Et_2O (200 mL) at 0 °C and the resulting mixture was stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (20 mL), diluted with CH_2Cl_2 (750 mL) 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 → 40% Et_2O in hexanes) to afford the ring G alcohols **62** (8.4 g, 70%, 2:1 mixture of desired:undesired) as white foams.

Benzoate 64: BzCl (5.00 mL, 43.05 mmol) was added to a solution of desired alcohol **62** (20.50 g, 39.14 mmol), Et_3N (8.18 mL, 58.70 mmol), and 4-DMAP (0.96 g, 7.80 mmol) in CH_2Cl_2 (200 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (750 mL) 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 → 60% Et_2O in hexanes) to afford benzoate **64** (24.08 g, 98%) as a white foam. **64**: R_f = 0.49 (50% Et_2O in hexanes); $[\alpha]_D^{22}$ = −6.83 (c = 2.08, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3071, 2931, 2857, 1726, 1453, 1427, 1266, 1110, 997, 928, 746, 707, 613, 506 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.09 (d, J = 8.3 Hz, 2H, ArH), 7.81 (d, J = 3.2 Hz, 1H, TH-CH), 7.71 – 7.69 (m, 4H, ArH), 7.60 (t, J = 7.5 Hz, 1H, ArH), 7.48 – 7.36 (m, 8H, ArH), 7.35 (d, J = 3.2 Hz, 1H, TH-CH), 6.50 (d, J = 7.0 Hz, 1H, G2), 5.74 – 5.65 (m, 2H, C*H*=CH$_2$), 5.09 (dd, J = 17.0, 1.5 Hz, 1H, CH$_2$-*E*), 5.03 (dd, J = 10.1, 1.0 Hz, 1H, CH$_2$-*Z*), 4.94 (dd, J = 17.2, 1.5 Hz, 1H, CH$_2$-*E*), 4.87 (dd, J = 10.0, 1.0 Hz, 1H, CH$_2$-*Z*), 4.44 (dd, J = 7.0, 3.2 Hz, 1H, G3), 4.01 (dd, J = 12.3, 6.2 Hz, 1H, OC*H*$_2$), 3.93 (dd, J = 12.4, 5.7 Hz, 1H, OC*H*$_2$), 3.90 – 3.84 (m, 3H, G5, OC*H*$_2$), 3.72 (dd, J = 12.4, 6.4 Hz, 1H, OC*H*$_2$), 3.70 – 3.67 (m, 1H, G4), 1.10 (s, 9H, *t*BuSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.7, 166.3, 142.3, 135.6, 135.5, 134.6, 134.4, 129.8, 129.7, 128.4, 127.7, 120.2, 117.6, 117.3, 79.2, 78.6, 74.2, 72.2, 71.4, 62.0, 26.8, 19.2; HRMS (MALDI): calcd for $C_{36}H_{41}NO_5SSiNa$ $[M+Na]^+$: 650.2367, found 650.2339.

Ring G lactol 65: MeOTf (5.96 mL, 48.62 mmol) was added to a solution of benzoate **64** (25.44 g, 40.52 mmol) and 4 Å MS in MeCN (200 mL) at 25 °C and the resulting mixture was stirred for 15 min. The solvents were removed under reduced pressure, and the residue was dissolved in MeOH (200 mL) and cooled to 0 °C. $NaBH_4$ (3.68 g, 97.24 mmol) was added portionwise and the resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of acetone (10 mL), filtered through a pad of Celite, and the solvents were removed under reduced pressure. The residue was dissolved in MeCN/sH_2O (10:1, 220 mL) and CuO (25.78 g, 0.324 mol) was added. $CuCl_2$ (7.27 g, 48.62 mmol) was added portionwise followed by vigorous stirring for 2 h at 25 °C. The reaction mixture was diluted with Et_2O (500 mL), filtered through a pad of Celite, and the solvents were removed under reduced pressure. The residue was dissolved in THF (200 mL) and nBu$_4$NF (60.78 mL, 60.78 mmol) and AcOH (1.0 mL) were added. The resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was diluted with CH_2Cl_2 (750 mL) 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% Et_2O in hexanes) to afford ring G lactol **65** (10.97 g, 81% over four steps) as a white foam. **65**: R_f = 0.42 (70% Et_2O in hexanes); $[\alpha]_D^{22}$ = +36.7 (c = 0.70, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3411, 3074, 2934, 1723, 1453, 1356, 1273, 1117, 929, 712 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, J = 8.5 Hz, 2H, ArH), 7.60 – 7.56 (m, 1H, ArH), 7.48 – 7.44 (m, 2H, ArH), 5.96 – 5.84 (m, 2H, C*H*=CH$_2$), 5.40 (d, J = 3.5 Hz, 1H, G2), 5.31 (dd, J = 17.5, 1.5 Hz, 1H, CH$_2$-*E*), 5.27 (dm, J = 17.0 Hz, 1H, CH$_2$-*E*), 5.21 – 5.18 (m, 2H, G1, CH$_2$-*Z*), 5.14 (dm, J = 9.0 Hz, 1H, CH$_2$-*Z*), 4.22 – 4.10 (m, 4H, OC*H*$_2$), 3.95 (dd, J = 7.5, 3.0 Hz, 1H, G5), 3.92 – 3.84 (m, 2H, G3, G4), 3.76 (dd, J = 7.5, 5.0 Hz, 1H, G5), 2.87 (d, J = 5.5 Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.0, 134.7, 134.5, 133.3, 133.1, 129.7, 128.4, 128.3, 118.5, 117.6, 117.0, 92.7, 82.1, 76.0, 74.1, 72.7, 71.8, 71.2, 70.6, 69.5, 66.0, 61.6; HRMS (MALDI): calcd for $C_{18}H_{22}O_6Na$ $[M+Na]^+$: 357.1309, found 357.1295.

Ring G trichloroacetimidate 46: DBU (0.22 mL, 0.020 mmol) was added to a solution of ring G lactol **65** (12.05 g, 36.04 mmol) and Cl_3CCN (18.07 mL, 180.20 mmol) in CH_2Cl_2 (200 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 → 100% EtOAc in hexanes) to afford ring G trichloroacetimdiate **46** (14.67 g, 85%) as a white foam. **46**: R_f = 0.80 (70% Et_2O in hexanes); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.70 (s, 1H, NH), 8.08 (d, J = 8.3 Hz, 2H, ArH), 7.59 (t, J = 8.5 Hz, 1H, ArH), 7.47 (t, J = 7.8 Hz, 2H, ArH), 6.28 (d, J = 2.5 Hz, 1H, G1), 5.96 – 5.85 (m, 2H, C*H*=CH$_2$), 5.65 (t, J = 2.7 Hz, 1H, G2), 5.31 (dd, J = 17.2, 1.5 Hz, 1H, CH$_2$-*E*), 5.27 (dd, J = 17.1, 1.5 Hz, 1H, CH$_2$-*E*), 5.20 (dd, J = 10.3, 1.0 Hz, 1H, CH$_2$-*Z*), 5.14 (dd, J = 10.3, 1.0 Hz, 1H, CH$_2$-*Z*), 4.28 (dd, J = 12.7, 5.2 Hz, 1H, OC*H*$_2$), 4.22 – 4.11 (m, 3H, OC*H*$_2$), 4.04 (dd, J = 11.4, 5.1 Hz, 1H, G5), 3.96 (dd, J = 8.9, 3.2 Hz, 1H, G3), 3.93 (ddd, J = 9.1, 9.1, 4.1 Hz, 1H, G4), 3.78 (dd, J = 11.4, 9.8 Hz, 1H, G5); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.5, 160.3, 134.7, 134.3, 133.4, 129.9, 129.5, 128.4, 117.5, 117.3, 95.3, 76.4, 76.1, 73.4, 72.7, 71.2, 68.4, 63.6.

Seleno-glycoside 67: $BF_3 \cdot Et_2O$ (32.2 mL, 0.253 mol) was added to a solution of peracetylated xylose **66** (84.76 g, 0.266 mol) and PhSeH (120 mL, 5.0 M solution in CH_2Cl_2, 0.532 mmol) in CH_2Cl_2 (1.0 L) at 0 °C. The reaction mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was quenched by the addition of Et_3N (50 mL), diluted with CH_2Cl_2 (800 mL) 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% Et_2O in hexanes) to afford seleno-glycoside **67** (103.13 g, 93%, α:β ca. 1:5) as a white foam. **67**: R_f = 0.33 (70% Et_2O in hexanes); $[\alpha]_D^{22}$ = −83.2 (c = 6.51, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3056, 2976, 2868, 1752, 1578, 1477, 1438, 1370, 1245, 1222, 1061, 742 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 (br d, J = 7.5 Hz, 2H, ArH), 7.29 – 7.24 (m, 3H, ArH), 5.16 (d, J = 6.5 Hz, 1H, H1), 5.10 (t, J = 6.5 Hz, 1H, H2), 5.01 (t, J = 6.5 Hz, 1H, H3), 4.84 (ddd, J = 7.0, 7.0, 4.0 Hz, 1H, H4), 4.33 (dd, J = 12.5, 4.5 Hz, 1H, H5), 3.51 (dd, J = 12.5, 7.0 Hz, 1H, H5), 2.06 (s, 6H, OAc), 2.03 (s, 3H, OAc); ^{13}C NMR (125 MHz,

0947-6539/00/0617-3134 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

$CDCl_3$): $\delta = 169.6, 169.3, 169.2, 134.2, 129.0, 128.3, 128.1, 82.1, 70.2, 70.0, 67.8, 64.7, 20.7, 20.6$; HRMS (FAB): calcd for $C_{17}H_{20}O_7SeCs$ $[M+Cs]^+$: 548.9429, found 548.9412.

Alcohol 68: K_2CO_3 (2.94 g, 0.021 mol) was added to a solution of selenoglycoside **67** (88.70 g, 0.213 mol) in MeOH/THF (1:1, 1.0 L) and the mixture was stirred for 12 h at 25 °C. The reaction mixture was quenched by the addition of Amberlyst (5.0 g), diluted with CH_2Cl_2 (800 mL) and filtered. The solvents were removed under reduced pressure and the residue was azeotroped with toluene (2×100 mL). The residue was dissolved in DMF (400 mL) and heated to 45 °C. 2-Methoxypropene (30.61 mL, 0.320 mol) and TFA (0.10 mL, 0.021 mol) were added and the reaction mixture was stirred for 3 h. The reaction was quenched with Et_3N (50 mL), the solvents were removed under reduced pressure, and the residue was purified by flash column chromatography (silica gel, $0 \rightarrow 100\%$ Et_2O in hexanes) to afford alcohol **68** (51.92 g, 74% over two steps) as a white foam. **68**: $R_f = 0.24$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -47.0$ ($c = 1.63$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3430, 2984, 2889, 1477, 1438, 1382, 1372, 1228, 1148, 1048, 836, 741\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.68-7.66$ (m, 2H, ArH), 7.35–7.25 (m, 3H, ArH), 4.99 (d, $J = 9.5$ Hz, 1H, H1), 4.11 (dd, $J = 11.5$, 5.5 Hz, 1H, H5), 3.96–3.91 (m, 1H, H4), 3.49 (t, $J = 9.0$ Hz, 1H, H3), 3.22 (t, $J = 9.5$ Hz, 1H, H2), 3.20 (dd, $J = 11.5$, 5.0 Hz, 1H, H5), 2.51 (d, $J = 4.0$ Hz, 1H, OH), 1.48 (s, 3H, Me), 1.40 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 135.4, 128.9, 128.4, 110.9, 82.8, 80.5, 75.8, 70.6, 69.0, 26.5$; HRMS (FAB): calcd for $C_{14}H_{19}O_4Se$ $[M+H]^+$: 331.0449, found 331.0461.

PMB ether 69: NaH (2.16 g, 53.89 mmol) was added to a solution of alcohol **68** (16.13 g, 49.00 mmol) in DMF (150 mL) at 0 °C and the resulting mixture was stirred for 5 min. PMBCl (8.64 mL, 63.69 mmol) and nBu_4NI (3.62 g, 9.79 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (50 mL), diluted with Et_2O (800 mL) and washed with brine (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, $0 \rightarrow 100\%$ Et_2O in hexanes) to afford PMB ether **69** (20.92 g, 95%) as a white foam. **69**: $R_f = 0.42$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -4.0$ ($c = 4.53$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3058, 2985, 2888, 1614, 1580, 1518, 1455, 1382, 1303, 1249, 1150, 1038, 969, 837, 787, 742, 692, 510\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.67$ (d, $J = 8.2$ Hz, 2H, ArH), 7.37–7.25 (m, 5H, ArH), 6.87 (d, $J = 8.6$ Hz, 2H, PMB), 5.01 (d, $J = 9.6$ Hz, 1H, H1), 4.73, 4.50 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.07 (dd, $J = 11.8$, 5.1 Hz, 1H, H5), 3.79 (s, 3H, OMe), 3.72 (ddd, $J = 8.9$, 8.9, 5.2 Hz, 1H, H4), 3.61 (t, $J = 9.0$ Hz, 1H, H5), 3.24–3.21 (m, 2H, H2, H3), 1.50 (s, 3H, Me), 1.43 (s, 3H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3, 135.2, 130.0, 129.5, 128.9, 128.3, 126.8, 113.7, 110.8, 82.3, 80.5, 76.0, 75.1, 71.6, 69.1, 55.2, 26.7, 26.6$; HRMS (FAB): calcd for $C_{22}H_{26}O_5SeCs$ $[M+Cs]^+$: 583.0001, found 583.0014.

Diol 70: PPTS (2.09 g, 8.31 mmol) was added to a solution of acetonide **69** (18.74 g, 41.56 mmol) dissolved in MeOH (500 mL). The reaction mixture was stirred at 25 °C for 1 h and then the reaction was quenched by the addition of Et_3N (50 mL). The solvents were removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, $0 \rightarrow 100\%$ Et_2O in hexanes) to afford diol **70** (16.36 g, 96%) as a white foam. **70**: $R_f = 0.43$ (100% Et_2O); $[\alpha]_D^{22} = -84.7$ ($c = 1.03$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3426, 3056, 2909, 1612, 1513, 1249, 1053, 821, 740\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.63-7.61$ (m, 2H, ArH), 7.32–7.24 (m, 5H, ArH), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 4.91 (d, $J = 8.0$ Hz, 1H, H1), 4.58 (br s, 2H, CH_2Ar), 4.13 (dd, $J = 11.5$, 4.0 Hz, 1H, H5), 3.80 (s, 3H, OMe), 3.70 (dd, $J = 8.0$, 8.0, 2.5 Hz, 1H, H3), 3.51–3.45 (m, 1H, H4), 3.44 (dd, $J = 7.5$, 4.0 Hz, 1H, H2), 3.34 (dd, $J = 12.0$, 9.0 Hz, 1H, H5), 3.06 (d, $J = 4.0$ Hz, 1H, OH), 2.82 (d, $J = 3.0$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.5, 134.6, 129.7, 129.5, 129.1, 128.1, 114.1, 85.7, 76.3, 74.6, 72.5, 72.5, 66.6, 55.3$; HRMS (FAB): calcd for $C_{19}H_{22}O_5SeNa$ $[M+Na]^+$: 433.0530, found 433.0515.

H-3 TBS ether 71: TBSOTf (9.72 mL, 42.32 mmol) was added to a solution of diol **70** (15.75 g, 38.48 mmol) and 2,6-lutidine (6.72 mL, 57.72 mmol) in THF (200 mL) at −78 °C. 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 (800 mL), 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, $0 \rightarrow 50\%$ Et_2O in hexanes) to afford H-3 TBS ether **71** (18.40 g, 91%) as a white foam. **71**: $R_f = 0.76$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -185.3$ ($c = 1.92$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3490, 3048, 2951, 1843, 1607, 1581, 1516, 1467, 1440, 1252, 1095, 1042, 842, 783, 740\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.62-7.60$ (m, 2H, ArH), 7.29–7.24 (m, 5H, ArH), 6.90 (d, $J = 8.5$ Hz, 2H, PMB), 5.65 (br s, 1H, H1), 4.67, 4.52 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.14 (br d, $J = 11.0$ Hz, 1H, H5), 3.96 (br s, 1H, H3), 3.89 (br d, $J = 11.0$ Hz, 1H, H5), 3.81 (s, 3H, OMe), 3.81–3.79 (m, 1H, H2), 3.35 (s, 1H, H4), 0.95 (s, 9H, *t*BuSi), 0.13, 0.06 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.5, 133.8, 132.7, 129.5, 128.8, 127.5, 126.9, 113.9, 86.8, 75.4, 72.9, 71.0, 67.2, 59.4, 55.2, 25.8, 18.1, -5.0, -5.3$; HRMS (FAB): calcd for $C_{25}H_{36}O_5SeSiCs$ $[M+Cs]^+$: 657.0553, found 657.0575.

H-2 TBS ether 72: TBSOTf (0.97 mL, 4.23 mmol) was added to a solution of diol **70** (1.58 g, 38.48 mmol) and 2,6-lutidine (0.67 mL, 5.77 mmol) in CH_2Cl_2 (20.0 mL) at −78 °C. The resulting mixture was stirred for 0.5 h. The reaction mixture was quenched by the addition of MeOH (1.0 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 H-2 TBS ether **72** (1.84 g, 91%) as a white foam. **72**: $R_f = 0.76$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -132.3$ ($c = 0.85$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3480, 3057, 2955, 2856, 1612, 1582, 1514, 1473, 1251, 1076, 839, 779, 739\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.62-7.60$ (m, 2H, ArH), 7.29–7.26 (m, 3H, ArH), 7.24 (d, $J = 8.5$ Hz, 2H, PMB), 6.88 (d, $J = 8.5$ Hz, 2H, PMB), 4.79 (d, $J = 9.5$ Hz, 1H, H1), 4.57, 4.53 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.02 (dd, $J = 11.5$, 5.0 Hz, 1H, H5), 3.79 (s, 3H, OMe), 3.58 (dd, $J = 9.5$, 8.0 Hz, 1H, H2), 3.51 (dt, $J = 9.0$, 3.0 Hz, 1H, H3), 3.45 (ddd, $J = 9.0$, 9.0, 5.0 Hz, 1H, H4), 3.15 (dd, $J = 11.5$, 10.0 Hz, 1H, H5), 2.72 (d, $J = 3.0$ Hz, 1H, OH), 0.97 (s, 9H, *t*BuSi), 0.20, 0.17 ($2 \times$ s, 2×3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.5, 133.7, 129.9, 129.7, 129.4, 128.8, 127.4, 113.9, 86.3, 77.3, 74.6, 72.5, 72.5, 68.1, 55.1, 26.1, -3.8, -4.4$; HRMS (FAB): calcd for $C_{25}H_{36}O_5SeSiCs$ $[M+Cs]^+$: 657.0553, found 657.0575.

Bis-benzyl ether 74: K_2CO_3 (6.36 g, 46.0 mmol) was added to a solution of aldehyde **73**[1] (1.75 g, 11.5 mmol) and BnBr (3.42 mL, 28.8 mmol) in acetone (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. The residue was purified by flash column chromatography (silica gel, $0 \rightarrow 60\%$ Et_2O in hexanes) to afford bis-benzyl ether **74** (3.52 g, 92%) as a white foam. **74**: $R_f = 0.40$ (60% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 3033, 2925, 2871, 2783, 1679, 1603, 1498, 1450, 1378, 1319, 1155, 1092, 1044, 910, 834, 738, 698\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 10.60$ (s, 1H, CHO), 7.43–7.40 (m, 10H, ArH), 6.50 (s, 1H, ArH (A_2)), 6.44 (s, 1H, ArH (A_2)), 5.10 (s, 2H, CH_2Ar), 5.09 (s, 2H, CH_2Ar), 2.62 (s, 3H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 190.3, 164.1, 163.3, 144.6, 136.0, 135.9, 128.6, 128.6, 128.2, 128.1, 127.5, 127.2, 117.7, 109.7, 97.7, 70.4, 70.0, 22.3$; HRMS (MALDI): calcd for $C_{22}H_{20}O_3Na$ $[M+Na]^+$: 355.1310, found 355.1331.

Aromatic acid 75: $NaH_2PO_4 \cdot H_2O$ (1.20 g, 8.66 mmol, dissolved in 1 mL H_2O) was added to a solution of aldehyde **74** (1.20 g, 3.61 mmol) in DMSO (20 mL) at 0 °C. $NaClO_2$ (0.75 g, 8.30 mmol, dissolved in 1.0 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 $NaHCO_3$ (50 mL) and washed with EtOAc (20 mL). The aqueous layer was then acidified to pH 1 with aqueous HCl and washed with EtOAc (200 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 aromatic acid **75** (1.01 g, 80%) as a white solid. **75**: $R_f = 0.30$ (70% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 3436-2872, 1690, 1590, 1449, 1384, 1320, 1167, 1102, 832, 750, 697\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.42-7.26$ (m, 10H, ArH), 6.53 (d, $J = 1.9$ Hz, 1H, ArH (A_2)), 6.52 (d, $J = 1.9$ Hz, 1H, ArH (A_2)), 5.14 (s, 2H, CH_2Ar), 5.06 (s, 2H, CH_2Ar), 2.55 (s, 3H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 168.4, 161.2, 158.5, 143.8, 136.1, 135.3, 128.8, 128.7, 128.5, 128.3, 127.5, 113.1, 110.3, 98.7, 71.6, 70.1, 22.5$; HRMS (MALDI): calcd for $C_{22}H_{20}O_4Na$ $[M+Na]^+$: 371.1259, found 371.1275.

Aromatic A_2 acyl fluoride 5: $(Me_2N)_2CF^+PF_6^-$ (0.318 g, 1.21 mmol) was added to a solution of aromatic acid **75** (0.280 g, 0.804 mmol) and diisopropylethyamine (0.280 mL, 1.61 mmol) in CH_2Cl_2 (4 mL) at 0 °C and the resulting mixture was warmed to 25 °C and 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 aromatic A_2 acyl fluoride **5** (0.225 g, 80%) as a white solid. **5**: $R_f = 0.79$ (80% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2925, 1790, 1590, 1443, 1320, 1220, 1155, 1085, 997, 736, 696\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.43-7.26$ (m, 10H, ArH), 6.48 (s, 1H, ArH (A_2)), 6.47 (s, 1H, ArH (A_2)), 5.11 (s, 2H, CH_2Ar), 5.06 (s, 2H, CH_2Ar), 2.46 (s, 3H, Me); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 162.7, 143.7, 136.0, 135.9, 128.7, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.5, 127.2, 126.9, 109.2, 98.5, 70.6, 70.2, 21.6$; HRMS (MALDI): calcd for $C_{22}H_{19}FO_3Na$ $[M+Na]^+$: 373.1216, found 373.1226.

Diol 76: DAST (1.7 mL, 12.87 mmol) was added to a solution of lactol **65** (2.15 g, 6.44 mmol) in CH_2Cl_2 (43 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 $NaHCO_3$ (100 mL), diluted with CH_2Cl_2 (500 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 crude glycosyl fluoride was azeotroped with benzene (3 × 10 mL) and then dried under high vacuum for 1 h. Et_2O (43 mL) and 4 Å MS were added and the mixture was cooled to 0 °C and stirred for 5 min. MeOH (1.3 mL, 32.18 mmol) and $SnCl_2$ (2.20 g, 11.59 mmol) were added 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 (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), 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 ring G methyl glycoside (1.39 g, 62%, $\alpha:\beta$ ca. 4:1, separable) as white foams. Methyl glycoside: $R_f = 0.44$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = +31.84$ ($c = 7.65$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3076, 2979, 2886, 1724, 1648, 1603, 1452, 1362, 1320, 1270, 1116, 1026, 928, 896, 857\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.06$ (dd, $J = 8.0$, 1.0 Hz, 2H, ArH), 7.54 (t, $J = 7.3$ Hz, 1H, ArH), 7.43 (t, $J = 8.0$ Hz, 2H, ArH), 5.94–5.80 (m, 2H, C*H*=CH_2), 5.45 (t, $J = 2.2$ Hz, 1H, G2), 5.28 (ddm, $J = 18.2$, 2.0 Hz, 1H, CH_2-*E*), 5.24 (ddm, $J = 18.2$, 2.0 Hz, 1H, CH_2-*E*), 5.15 (ddm, $J = 10.2$, 1.7 Hz, 1H, CH_2-*Z*), 5.09 (ddm, $J = 10.2$, 1.7 Hz, 1H, CH_2-*Z*), 4.73 (d, $J = 2.5$ Hz, 1H, G1), 4.25 (ddt, $J = 14.0$, 5.5, 1.7 Hz, 1H, OCH_2), 4.18–4.05 (m, 2H, OCH_2), 4.08 (ddt, $J = 14.0$, 5.5, 1.7 Hz, 1H, OCH_2), 3.85–3.78 (m, 3H, G3, G5, G5), 3.58–3.53 (m, 1H, G4), 3.37 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.6, 134.9, 134.6, 133.0, 129.7, 128.3, 116.7, 116.6, 98.9, 76.7, 73.9, 72.3, 70.7, 69.7, 60.9, 54.9$; HRMS (FAB): calcd for $C_{19}H_{24}O_6Na$ $[M+Na]^+$: 371.1471, found 371.1482. Ring G alcohol: K_2CO_3 (440 mg, 3.19 mmol) was added to a solution of the above ring G α-methyl glycoside (1.11 g, 3.19 mmol) in MeOH (30 mL) at 25 °C and the resulting mixture was stirred for 12 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (50 mL), diluted with Et_2O (500 mL) and washed with brine (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 → 100% Et_2O in hexanes) to afford the ring G alcohol (0.74 g, 95%) as a white foam. Ring G alcohol: $R_f = 0.19$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -55.63$ ($c = 0.76$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3457, 2932, 1647, 1459, 1423, 1357, 1134, 1061, 1022, 926, 857, 769\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 5.82-5.70$ (m, 2H, C*H*=CH_2), 5.16 (ddm, $J = 17.5$, 1.5 Hz 1H, CH_2-*E*), 5.13 (ddm, $J = 17.5$, 1.5 Hz, 1H, CH_2-*E*), 5.03 (ddm $J = 10.2$, 1.5 Hz, 1H, CH_2-*Z*), 5.00 (ddm, $J = 10.2$, 1.5 Hz, 1H, CH_2-*Z*), 4.83 (d, $J = 2.5$ Hz, 1H, G1), 4.05–4.02 (m, 2H, OCH_2), 4.01 (ddt, $J = 14.0$, 5.5, 1.5 Hz, 1H, OCH_2), 3.95 (ddt, $J = 14.0$, 5.5, 1.5 Hz, 1H, OCH_2), 3.77 (dd, $J = 5.7$, 3.2 Hz, 1H, G2), 3.60–3.54 (m, 2H, G5, G5), 3.46 (dd, $J = 8.3$, 3.2 Hz, 1H, G3), 3.34–3.28 (m, 1H, G4), 3.21 (s, 3H, OMe), 2.98 (d, $J = 3.0$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 134.6, 134.4, 116.6, 116.3, 100.3, 77.8, 73.4, 71.4, 71.4, 68.4, 60.3, 54.6$; HRMS (FAB): calcd for $C_{12}H_{20}O_5Na$ $[M+Na]^+$: 267.1208, found 267.1207. Ring G benzyl ether: NaH (0.16 g, 3.95 mmol) was added to a solution of the above ring G alcohol (0.74 g, 3.03 mmol) in DMF (15 mL) at 0 °C and the resulting mixture was stirred for 5 min. BnBr (0.54 mL, 4.55 mmol) and nBu_4NI (336 mg, 0.91 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 2.5 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (50 mL), diluted with Et_2O (200 mL) and washed with brine (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 → 40% Et_2O in hexanes) to afford the ring G benzyl ether (994 mg, 98%) as a white foam. Ring G benzyl ether: $R_f = 0.50$ (30% Et_2O in hexanes); $[\alpha]_D^{22} = -28.42$ ($c = 0.38$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2910, 1495, 1455, 1358, 1312, 1198, 1135, 1065, 995, 965, 924, 779\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.39-7.26$ (m, 5H, ArH), 5.95–5.86 (m, 2H, C*H*=CH_2), 5.31 (ddm, $J = 15.2$, 2.0 Hz, 1H, CH_2-*E*), 5.27 (ddm, $J = 15.2$, 2.0 Hz, 1H, CH_2-*E*), 5.20–5.14 (m, 2H, CH_2-*Z*), 4.77, 4.72 (AB, $J = 12.2$ Hz, 2H, CH_2Ar), 4.61 (d, $J = 3.0$ Hz, 1H, G1), 4.20–4.08 (m, 4H, OCH_2), 3.83–3.75 (m, 2H, G5, G5), 3.70 (t, $J = 3.0$ Hz, 1H, G2), 3.65 (dd, $J = 8.2$, 3.2 Hz, 1H, G3), 3.46 (ddd, $J = 9.5$, 9.5, 2.0 Hz, 1H, G4), 3.34 (s, 3H, OMe); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 135.1, 135.1, 128.3, 127.9, 127.6, 116.5, 116.4, 100.0, 78.5, 75.4, 74.5, 73.2, 71.8, 71.6, 61.3, 55.0$; HRMS (FAB): calcd for $C_{19}H_{26}O_5Na$ $[M+Na]^+$: 357.1678, found 357.1672. $[(Ph_3P)_3RhCl]$ (138 mg, 0.15 mmol) was added to a solution of the above ring G benzyl ether (994 mg, 2.98 mmol) and DABCO (835 mg, 7.44 mmol) in EtOH/H_2O (10:1, 22 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 (874 mg, 7.44 mmol) and OsO_4 (0.5 mL, 2.5% solution in *t*BuOH) were added and the reaction mixture was stirred for 8 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 → 100% EtOAc in hexanes) to afford diol **76** (719 mg, 95% over two steps) as a white foam. **76**: $R_f = 0.13$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -9.19$ ($c = 10.45$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3417, 2932, 1612, 1495, 1456, 1379, 1310, 1249, 1196, 1135, 1065, 996, 968, 911, 886\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.43-7.26$ (m, 5H, ArH), 4.67, 4.60 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.62 (d, $J = 2.0$ Hz, 1H, G1), 3.86 (ddd, $J = 8.5$, 8.5, 5.0 Hz, 1H, G4), 3.76 (dd, $J = 8.5$, 3.5 Hz, 1H, G3), 3.70 (dd, $J = 11.5$, 5.0 Hz, 1H, G5), 3.65 (t, $J = 3.0$ Hz, 1H, G2), 3.41 (dd, $J = 11.0$, 9.5 Hz, 1H, G5), 3.32 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 137.7, 132.0, 128.5, 128.4, 128.3, 127.8, 99.0, 77.7, 73.1, 71.5, 67.8, 62.3, 55.0$; HRMS (FAB): calcd for $C_{13}H_{18}O_5Na$ $[M+Na]^+$: 277.1052, found 277.048.

Benzoates 77 and 78: nBu_2SnO (1.20 g, 4.80 mmol) was added to a solution of ring G diol **76** (1.11 g, 4.37 mmol) in toluene (50 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 0 °C and BzCl (0.55 mL, 4.80 mmol) was added. The reaction mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with EtOAc (200 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% Et_2O in hexanes) to afford ring G benzoates **77** and **78** (1.44 g, 92%, 1:1 mixture of G3 and G4 regioisomers) as white foams. **77**: $R_f = 0.44$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = +36.59$ ($c = 0.85$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3460, 2919, 1721, 1604, 1513, 1454, 1386, 1319, 1270, 1116, 1030, 962, 887, 712\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.04$ (dd, $J = 8.5$, 1.0 Hz, 2H, ArH), 7.56 (t, $J = 7.3$ Hz, 1H, ArH), 7.43 (t, $J = 8.0$ Hz, 2H, ArH), 7.39–7.26 (m, 5H, ArH), 5.27 (ddd, $J = 8.0$, 8.0, 4.5 Hz, 1H, G4), 4.80, 4.65 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.73 (d, $J = 3.0$ Hz, 1H, G1), 4.08 (dt, $J = 8.0$, 3.5 Hz, 1H, G3), 3.94 (dd, $J = 11.5$, 4.5 Hz, 1H, G5), 3.74 (t, $J = 3.5$ Hz, 1H, G2), 3.71 (dd, $J = 11.5$, 8.2 Hz, 1H, G5), 3.44 (s, 3H, OMe), 2.51 (d, $J = 8.0$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 166.5, 138.5, 133.2, 129.8, 128.6, 128.3, 128.0, 127.9, 99.3, 77.6, 73.4, 70.9, 69.1, 60.4, 55.7$; HRMS (FAB): calcd for $C_{20}H_{22}O_6Na$ $[M+Na]^+$: 381.1314, found 381.1324. **78**: $R_f = 0.26$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -6.34$ ($c = 1.42$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3470, 2929, 1720, 1453, 1274, 1121, 1063, 837, 713\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.03$ (d, $J = 8.3$ Hz, 2H, ArH), 7.57 (t, $J = 7.4$ Hz, 1H, ArH), 7.43 (t, $J = 8.0$ Hz, 2H, ArH), 7.35–7.19 (m, 5H, ArH), 5.30 (dd, $J = 9.2$, 3.3 Hz, 1H, G3), 4.70 (d, $J = 3.0$ Hz, 1H, G1), 4.65 (s, 2H, CH_2Ar), 4.28 (ddd, $J = 9.4$, 9.4, 5.2 Hz, 1H, G4), 3.91 (t, $J = 2.9$ Hz, 1H, G2), 3.86 (dd, $J = 11.2$, 5.2 Hz, 1H, G5), 3.59 (t, $J = 10.9$ Hz, 1H, G5), 3.39 (s, 3H, OMe), 2.30 (d, $J = 5.5$ Hz, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.6, 137.6, 133.2, 129.8, 129.6, 128.4, 128.3, 127.7, 99.4, 75.7, 74.7, 73.2, 65.9, 62.9, 55.1$; HRMS (FAB): calcd for $C_{20}H_{22}O_6Na$ $[M+Na]^+$: 381.1314, found 381.1322.

Disaccharides 79 and 86: DAST (0.39 mL, 2.70 mmol) was added to a solution of ring H alcohol **71** (0.95 g, 1.80 mmol) in CH_2Cl_2 (8.0 mL) at 0 °C and the resulting mixture was stirred for 0.5 h. The reaction mixture was

0947-6539/00/0617-3136 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

quenched by the addition of saturated aqueous $NaHCO_3$ (10 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 crude ring H glycosyl fluoride **44** (0.95 g, 1.80 mmol) and ring G alcohol **77** (0.43 g, 1.20 mmol) were azeotroped with benzene (3 × 10 mL) and then dried under high vacuum for 1 h. Et_2O (6.0 mL) and 4 Å MS were added, the mixture was cooled to 0 °C and stirred for 5 min. $SnCl_2$ (0.30 g, 1.60 mmol) was added in one portion and the resulting mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was quenched by the addition of Et_3N (5 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, 50 % Et_2O in hexanes) to afford GH disaccharide **79** (0.71 g, 69 %) as a white foam. **79**: $R_f = 0.54$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +17.38$ ($c = 0.65$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931, 1719, 1607, 1507, 1455, 1367, 1255, 1108, 1067, 1032, 832, 779, 708\ cm^{-1}$; ^1H NMR (600 MHz, C_6D_6, 340 K): $\delta = 8.09$ (d, $J = 8.4$ Hz, 2H, ArH), 7.64 (d, $J = 7.9$ Hz, 2H, ArH), 7.32 (d, $J = 7.3$ Hz, 2H, ArH), 7.24–7.12 (m, 2H, ArH), 7.10–7.04 (m, 6H, ArH), 6.95–6.88 (m, 3H, ArH), 6.74 (d, $J = 8.6$ Hz, 2H, PMB), 5.77–5.68 (m, 1H, G4), 5.37 (d, $J = 5.0$ Hz, 1H, H1), 4.60 (d, $J = 4.3$ Hz, 1H, G1), 4.55, 4.49 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.48 (dd, $J = 7.4$, 3.2 Hz, 1H, G3), 4.46 (dd, $J = 6.2$, 3.8 Hz, 1H, H2), 4.32 (s, 2H, CH_2Ar), 3.99 (dd, $J = 5.0$, 3.9 Hz, 1H, H2), 3.91 (dd, $J = 11.6$, 4.2 Hz, 1H, G5), 3.85–3.75 (m, 3H, G2, H5, H5), 3.70 (dd, $J = 11.6$, 7.0 Hz, 1H, G5), 3.53–3.50 (m, 1H, H4), 3.36 (s, 3H, OMe), 3.14 (s, 3H, OMe), 0.97 (s, 9H, *t*BuSi), 0.15, 0.01 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, C_6D_6, 340 K): $\delta = 165.5, 160.0, 139.3, 133.9, 132.7, 131.3, 131.0, 130.2, 129.5, 129.2, 128.5, 128.4, 128.3, 127.6, 127.1, 114.3, 100.9, 78.3, 76.5, 76.3, 74.8, 73.7, 73.1, 71.9, 70.4, 62.7, 61.7, 55.1, 54.9, 51.5, 26.2, 18.4, −4.3, −4.5$; HRMS (FAB): calcd for $C_{45}H_{56}O_{10}SeSiCs$ $[M+Cs]^+$: 997.1863, found 997.1880. Alcohol **78** was coupled in a similar fashion to afford GH disaccharide **86** (70 %) as a white foam. **86**: $R_f = 0.61$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = +13.98$ ($c = 1.13$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931, 2860, 1719, 1608, 1584, 1507, 1455, 1355, 1249, 1114, 1067, 1038, 831, 773, 708\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.08$ (d, $J = 7.0$ Hz, 2H, ArH), 7.55–7.50 (m, 3H, ArH), 7.40 (d, $J = 7.7$ Hz, 2H, ArH), 7.24–7.14 (m, 8H, ArH), 7.09 (d, $J = 8.8$ Hz, 2H, PMB), 6.79 (d, $J = 8.8$ Hz, 2H, PMB), 5.38 (dd, $J = 8.9$, 3.3 Hz, 1H, G3), 4.80 (d, $J = 7.0$ Hz, 1H, H1), 4.60 (d, $J = 2.6$ Hz, 1H, G1), 4.58, 4.55 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.40, 4.31 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.24 (ddd, $J = 9.1$, 9.1, 5.1 Hz, 1H, G4), 4.14 (t, $J = 4.0$ Hz, 1H, H3), 3.86 (t, $J = 3.1$ Hz, 1H, G2), 3.77 (s, 3H, OMe), 3.62 (dd, $J = 11.4$, 5.3 Hz, 1H, G5), 3.55–3.48 (m, 3H, H2, H5, H5), 3.41 (dd, $J = 11.0$, 9.6 Hz, 1H, G5), 3.31 (s, 3H, OMe), 3.18–3.12 (brs, 1H, H4), 0.86 (s, 9H, *t*BuSi), 0.06, −0.13 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$,): $\delta = 165.5, 159.2, 137.8, 132.8, 132.6, 130.3, 130.2, 129.9, 129.2, 128.8, 128.3, 128.2, 127.7, 127.6, 126.6, 113.7, 99.4, 75.6, 75.0, 73.2, 72.6, 72.4, 70.9, 62.2, 60.4, 55.3, 55.1, 50.0, 25.8, 18.0, −4.5, −4.8$; HRMS (MALDI): calcd for $C_{45}H_{56}O_{10}SeSiNa$ $[M+Na]^+$: 887.2705, found 887.2730.

Alcohols 80 and 87: NaOH (0.014 g, 0.35 mmol) was added to a solution of GH disaccharide **79** (0.25 g, 0.29 mmol) in MeOH (1.5 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 (200 mL) and washed with brine (2 × 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 GH alcohol **80** (0.220 g, 99 %) as a white foam. **80**: $R_f = 0.55$ (100 % Et_2O); $[\alpha]_D^{22} = +20.77$ ($c = 0.98$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3436, 2931, 1608, 1578, 1507, 1461, 1354, 1296, 1249, 1132, 1067, 1032, 832, 773, 738, 697\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.56$ (dd, $J = 7.8$, 1.9 Hz, 2H, ArH), 7.35–7.06 (m, 10H, ArH), 6.83 (d, $J = 6.7$ Hz, 2H, PMB), 4.79 (d, $J = 8.9$ Hz, 1H, H1), 4.58, 4.44 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.49 (s, 1H, G1), 4.36, 4.28 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.26 (brs, 1H, H3), 4.10 (m, 1H, G4), 3.97 (d, $J = 12.3$ Hz, 1H, H5), 3.92 (d, $J = 12.3$ Hz, 1H, H5), 3.82 (dd, $J = 11.0$, 5.7 Hz, 1H, G5), 3.77 (s, 3H, OMe), 3.74–3.70 (m, 2H, G2, G3), 3.64 (dd, $J = 8.9$, 2.7 Hz, 1H, H2), 3.38 (t, $J = 10.7$ Hz, 1H, G5), 3.28 (s, 3H, OMe), 3.22 (brs, 1H, H4), 1.25 (brs, 1H, OH), 0.88 (s, 9H, *t*BuSi), 0.13, −0.09 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.4, 138.6, 131.6, 131.3, 129.7, 129.4, 128.9, 128.1, 127.4, 127.2, 126.4, 113.9, 102.3, 99.7, 83.3, 76.8, 74.7, 73.2, 73.1, 71.0, 65.6, 63.6, 62.4, 55.3, 54.7, 49.2, 25.9, 18.1, −4.5, −4.6$; HRMS (MALDI): calcd for $C_{38}H_{52}O_9SeSiNa$ $[M+Na]^+$: 783.2443, found 783.2411. GH disaccharide **86** was treated in a similar fashion to afford GH alcohol **87** (99 %) as a white foam. **87**: $R_f = 0.17$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +17.27$ ($c = 0.22$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3435, 2930, 2856, 1612, 1581, 1513, 1461, 1358, 1302, 1250, 1132, 1067, 1033, 834, 777, 738\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.50$ (d, $J = 8.3$ Hz, 2H, ArH), 7.35–7.12 (m, 10H, ArH), 6.83 (d, $J = 8.7$ Hz, 2H, PMB), 4.83, 4.63 (AB, $J = 12.3$ Hz, 2H, CH_2Ar), 4.75 (d, $J = 9.2$ Hz, 1H, H1), 4.58, 4.44 (AB, $J = 12.3$ Hz, 2H, CH_2Ar), 4.49 (s, 1H, G1), 4.25 (brs, 1H, H3), 3.94 (d, $J = 12.2$ Hz, 1H, H5), 3.89 (d, $J = 12.2$ Hz, 1H, H5), 3.87 (ddd, $J = 9.2$, 9.2, 5.3 Hz, 1H, G4), 3.76 (s, 3H, OMe), 3.74 (dd, $J = 9.2$, 3.5 Hz, 1H, G3), 3.70 (brs, 1H, G2), 3.59 (dd, $J = 11.4$, 5.3 Hz, 1H, G5), 3.53 (dd, $J = 8.8$, 3.0 Hz, 1H, H2), 3.20 (s, 3H, OMe), 3.18 (brs, 1H, H4), 3.12 (t, $J = 11.0$ Hz, 1H, G5), 1.72 (brs, 1H, OH), 0.85 (s, 9H, *t*BuSi), 0.09, −0.11 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.4, 138.5, 132.1, 131.2, 129.7, 129.4, 128.7, 128.3, 127.7, 127.5, 126.4, 113.9, 102.8, 99.6, 79.0, 77.4, 74.7, 73.7, 72.9, 70.9, 70.4, 63.4, 59.8, 55.2, 54.9, 48.9, 25.8, 25.8, 18.0, −4.4, −4.7$; HRMS (FAB): calcd for $C_{38}H_{52}O_9SeSiCs$ $[M+Cs]^+$: 893.1600, found 893.1632.

Orthoesters 81 and 88: $NaIO_4$ (0.60 g, 2.70 mmol) and $NaHCO_3$ (0.19 g, 2.20 mmol) were added to a solution of GH alcohol **80** (0.210 g, 0.28 mmol) in $MeOH/CH_2Cl_2/H_2O$ (3:2:1, 2.1 mL) and the resulting mixture was stirred at 25 °C for 4 h. The reaction mixture was diluted with CH_2Cl_2 (250 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The crude selenoxide was dissolved in toluene (2 mL) and transferred by cannula to a sealed tube. The flask was washed with toluene (2 × 2 mL) and the organics were transferred to the sealed tube. Diisopropylamine (3 mL) and vinyl acetate (6 mL) were added, and the tube was sealed and heated to 140 °C for 12 h. After cooling, the reaction mixture was concentrated and the residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford the GH orthoester **81** (0.120 g, 70 % over two steps) as a white foam. **81**: $R_f = 0.27$ (30 % Et_2O in hexanes); $[\alpha]_D^{22} = -12.8$ ($c = 14.7$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931, 1612, 1586, 1514, 1385, 1359, 1319, 1250, 1210, 1175, 1113, 1040, 983, 955, 920, 866, 837, 778\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.25–7.15$ (m, 7H, ArH), 6.76 (d, $J = 8.6$ Hz, 2H, PMB), 4.71, 4.51 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.58 (s, 1H, G1), 4.53, 4.43 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.00–3.92 (m, 4H, G2, G3, G5, G4), 3.87 (ddd, $J = 9.4$, 7.5, 4.9 Hz, 1H, H3), 3.72–3.68 (m, 4H, H5, OMe), 3.62 (t, $J = 9.9$ Hz, 1H, G5), 3.45 (dd, $J = 11.6$, 8.8 Hz, 1H, H5), 3.25–3.20 (m, 4H, H4, OMe), 2.03 (dd, $J = 13.1$, 4.9 Hz, 1H, H2), 1.83 (dd, $J = 13.1$, 9.5 Hz, 1H, H2), 0.80 (s, 9H, *t*BuSi), −0.02 (s, 6H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.1, 137.8, 130.5, 129.4, 129.2, 128.3, 127.6, 119.3, 113.6, 100.3, 77.8, 77.3, 75.5, 72.9, 72.4, 70.7, 70.2, 63.3, 62.8, 55.2, 55.1, 40.2, 25.7, 17.9, 11.0, −4.7, −4.8$; HRMS (FAB): calcd for $C_{32}H_{46}O_9SiCs$ $[M+Cs]^+$: 735.1965, found 735.1940. GH alcohol **87** was treated in similar manner to afford GH orthoester **88** (75 %) as a white foam. **88**: $R_f = 0.59$ (60 % Et_2O in hexanes); $[\alpha]_D^{22} = -7.78$ ($c = 0.27$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931, 1725, 1608, 1514, 1461, 1378, 1249, 1108, 1032, 950, 908, 826, 779\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.35–7.21$ (m, 7H, ArH), 6.84 (d, $J = 8.6$ Hz, 2H, PMB), 4.88, 4.58 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.69 (brs, 1H, G1), 4.65, 4.49 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.36 (ddd, $J = 10.4$, 10.4, 4.6 Hz, 1H, G4), 4.05 (t, $J = 1.9$ Hz, 1H, G2), 4.04 (dd, $J = 10.0$, 4.6 Hz, 1H, G5), 3.97 (ddd, $J = 10.5$, 8.2, 5.2 Hz, 1H, H3), 3.80 (dd, $J = 9.9$, 2.5 Hz, 1H, G3), 3.78 (s, 3H, OMe), 3.77 (dd, $J = 9.4$, 5.1 Hz, 1H, H5), 3.69 (t, $J = 10.2$ Hz, 1H, G5), 3.52 (t, $J = 10.7$ Hz, 1H, H5), 3.35 (ddd, $J = 9.8$, 8.3, 5.1 Hz, 1H, H4), 3.32 (s, 3H, OMe), 2.06 (dd, $J = 12.9$, 5.2 Hz, 1H, H2), 1.88 (dd, $J = 12.9$, 10.7 Hz, 1H, H2), 0.89 (s, 9H, *t*BuSi), 0.09, 0.08 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.2, 138.0, 130.4, 129.4, 128.3, 127.7, 127.6, 119.6, 113.7, 100.7, 79.9, 77.9, 75.6, 73.1, 73.0, 70.8, 69.4, 63.0, 62.8, 55.3, 55.2, 40.9, 29.7, 25.8, 18.0, −4.5, −4.7$; HRMS (FAB): calcd for $C_{32}H_{46}O_9SiCs$ $[M+Cs]^+$: 735.1965, found 735.1940.

Alcohols 82 and 89: *n*Bu_4NF (0.22 mL, 1.0 M solution in THF, 0.22 mmol) was added quickly to a solution of GH orthoester **81** (0.11 g, 0.18 mmol) in THF (1.0 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 (2 mL), diluted with CH_2Cl_2 (100 mL) and washed with brine (2 × 5 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. 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 GH alcohol **82** (0.087 g, 98 %) as a white foam. **82**: $R_f = 0.32$ (80 % Et_2O in hexanes);

$[\alpha]_D^{22} = -38.2$ ($c = 0.48$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3372$, 2938, 1720, 1611, 1509, 1454, 1364, 1303, 1243, 1207, 1170, 1116, 1080, 1032, 983, 911, 808, 742, 693 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.25-7.15$ (m, 7H, ArH), 6.79 (d, $J = 8.6$ Hz, 2H, PMB), 4.67, 4.54 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.62 (d, $J = 1.1$ Hz, 1H, G1), 4.50, 4.43 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.03–3.98 (m, 3H, G2, G3, G5), 3.96–3.93 (m, 1H, G4), 3.91 (br s, 1H, H3), 3.86 (dd, $J = 11.9$, 3.8 Hz, 1H, H5), 3.71 (s, 3H, OMe), 3.65 (t, $J = 9.6$ Hz, 1H, G5), 3.59 (dd, $J = 11.8$, 7.2 Hz, 1H, H5), 3.29 (dt, $J = 7.0$, 3.9 Hz, 1H, H4), 3.25 (s, 3H, OMe), 2.64 (d, $J = 3.2$ Hz, 1H, OH), 2.25 (dd, $J = 13.3$, 4.6 Hz, 1H, H2), 1.86 (dd, $J = 13.3$, 8.4 Hz, 1H, H2); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 159.4, 137.7, 130.0, 129.4, 128.4, 127.8, 127.7, 119.4, 113.9, 100.2, 77.7, 76.5, 75.5, 72.9, 71.7, 70.9, 68.7, 63.2, 62.4, 55.2, 55.2, 37.5; HRMS (FAB): calcd for $C_{26}H_{33}O_9$ $[M+H]^+$: 489.2124, found 489.2290. GH orthoestser **88** was treated in a similar manner to afford alcohol **89** (97%) as a white foam. **89**: $R_f = 0.19$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -35.54$ ($c = 0.65$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3507$, 2931, 1608, 1508, 1455, 1355, 1308, 1243, 1208, 1108, 1079, 1032, 949, 908, 814, 767, 697 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta =$ 7.29–7.14 (m, 7H, ArH), 6.78 (d, $J = 8.6$ Hz, 2H, PMB), 4.80, 4.52 (AB, $J =$ 11.9 Hz, 2H, CH_2Ar), 4.60 (d, $J = 1.0$ Hz, 1H, G1), 4.50, 4.43 (AB, $J =$ 11.5 Hz, 2H, CH_2Ar), 4.30 (ddd, $J = 10.4$, 10.4, 4.6 Hz, 1H, G4), 3.98 (dd, $J = 11.0$, 4.7 Hz, 1H, G5), 3.96 (br s, 1H, G2), 3.92 (ddd, $J = 9.2$, 7.4, 4.7 Hz, 1H, H3), 3.88 (dd, $J = 11.6$, 4.2 Hz, 1H, H5), 3.75 (dd, $J = 10.0$, 2.4 Hz, 1H, G3), 3.70 (s, 3H, OMe), 3.63 (t, $J = 10.2$ Hz, 1H, G5), 3.57 (dd, $J = 11.7$, 8.0 Hz, 1H, H5), 3.30 (dt, $J = 7.6$, 4.1 Hz, 1H, H4), 3.24 (s, 3H, OMe), 3.00 (br s, 1H, OH), 2.20 (dd, $J = 13.0$, 4.7 Hz, 1H, H2), 1.82 (dd, $J = 13.1$, 9.2 Hz, 1H, H2); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3$, 137.9, 130.0, 129.4, 128.2, 127.7, 127.6, 119.6, 113.9, 100.5, 79.9, 75.4, 72.9, 72.0, 69.3, 68.9, 62.6, 55.2, 55.1, 46.1, 38.1, 30.2, 11.4; HRMS (FAB): calcd for $C_{26}H_{32}O_9Na$ $[M+Na]^+$: 511.1944, found 511.1957.

Mesylates 83 and 90: MsCl (0.016 mL, 0.21 mmol) was added to a solution of GH alcohol **82** (0.085 g, 0.17 mmol) and Et_3N (0.050 mL, 0.35 mmol) in CH_2Cl_2 (1.0 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (1.0 mL), diluted with CH_2Cl_2 (350 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 → 80% Et_2O in hexanes) to afford GH mesylate **83** (0.095 g, 97%) as a white foam. **83**: $R_f = 0.13$ (60% Et_2O in hexanes); $[\alpha]_D^{22} = -21.3$ ($c = 0.35$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2919$, 1608, 1513, 1455, 1355, 1320, 1249, 1208, 1173, 1114, 1079, 1032, 961, 926, 855 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.33-7.25$ (m, 5H, ArH), 7.22 (d, $J = 8.6$ Hz, 2H, PMB), 6.85 (d, $J = 8.6$ Hz, 2H, PMB), 4.80 (ddd, $J = 10.0$, 7.8, 5.4 Hz, 1H, H3), 4.74, 4.60 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.67 (d, $J = 1.1$ Hz, 1H, G1), 4.54 (s, 2H, CH_2Ar), 4.09 (ddd, $J = 10.1$, 10.1, 4.5 Hz, 1H, G4), 4.06 (t, $J = 1.3$ Hz, 1H, G2), 4.04 (dd, $J = 9.9$, 2.4 Hz, 1H, G3), 4.01 (dd, $J = 9.5$, 4.4 Hz, 1H, G5), 3.92–3.86 (m, 1H, H5), 3.78 (s, 3H, OMe), 3.69 (t, $J = 10.0$ Hz, 1H, G5), 3.63–3.58 (m, 2H, H4, H5), 3.31 (s, 3H, OMe), 2.93 (s, 3H, Me), 2.45 (dd, $J = 13.1$, 5.2 Hz, 1H, H2), 2.17 (dd, $J = 13.1$, 10.2 Hz, 1H, H2); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 159.5, 137.7, 129.5, 129.4, 128.4, 127.8, 127.7, 118.5, 113.9, 100.2, 79.0, 78.2, 75.4, 74.3, 72.9, 72.5, 71.1, 63.1, 62.4, 55.3, 55.2, 38.2, 30.3, 29.7; HRMS (MALDI): calcd for $C_{27}H_{34}O_{11}SNa$ $[M+Na]^+$: 589.1719, found 589.1722. Alcohol **89** was treated in a similar fashion to afford mesylate **90** (95%) as a white foam. **90**: $R_f = 0.19$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -6.5$ ($c = 0.74$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931$, 1608, 1508, 1455, 1408, 1355, 1325, 1249, 1208, 1173, 1108, 1038, 961, 914, 849, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.24-7.14$ (m, 5H, ArH), 7.12 (d, $J = 8.6$ Hz, 2H, PMB), 6.76 (d, $J = 8.6$ Hz, 2H, PMB), 4.74, 4.49 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.73 (ddd, $J = 11.0$, 8.5, 5.4 Hz, 1H, H3), 4.59 (d, $J = 0.9$ Hz, 1H, G1), 4.46, 4.44 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.25 (ddd, $J = 10.4$, 10.4, 4.6 Hz, 1H, G4), 3.96 (br s, 1H, G2), 3.94 (dd, $J = 9.5$, 4.6 Hz, 1H, G5), 3.81 (dd, $J = 10.7$, 4.6 Hz, 1H, H5), 3.75 (dd, $J = 10.0$, 2.4 Hz, 1H, G3), 3.69 (s, 3H, OMe), 3.60 (t, $J = 10.0$ Hz, 1H, G5), 3.53 (dt, $J = 9.9$, 4.9 Hz, 1H, H4), 3.50 (t, $J =$ 10.4 Hz, 1H, H5), 3.22 (s, 3H, OMe), 2.87 (s, 3H, Me), 2.32 (dd, $J = 12.8$, 5.4 Hz, 1H, H2), 2.04 (dd, $J = 12.8$, 11.0 Hz, 1H, H2); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.6$, 137.8, 129.6, 129.3, 128.4, 127.7, 127.6, 118.8, 113.9, 100.4, 80.1, 79.4, 75.6, 74.6, 73.1, 72.7, 69.8, 62.5, 55.3, 55.2, 38.7, 38.2; HRMS (MALDI): calcd for $C_{27}H_{34}O_{11}SNa$ $[M+Na]^+$: 589.1719, found 589.1722.

Olefins 84 and 91: DBU (0.21 mL, 1.67 mmol) was added to a solution of GH mesylate **83** (0.095 g, 0.17 mmol) in toluene (3 mL) at 25 °C. The resulting mixture was refluxed for 24 h. The reaction mixture was cooled and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 60% Et_2O in hexanes) to afford GH olefin **84** (0.070 g, 87%) as a white foam. **84**: $R_f =$ 0.48 (70% Et_2O in hexanes); $[\alpha]_D^{22} = +14.8$ ($c = 0.70$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2922$, 1744, 1612, 1513, 1452, 1366, 1248, 1165, 1116, 1070, 1036, 984, 953 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.34-7.24$ (m, 5H, ArH), 7.31–7.24 (m, 2H, ArH), 6.86 (d, $J = 8.7$ Hz, 2H, PMB), 6.17 (dd, $J = 10.1$, 4.7 Hz, 1H, H3), 5.82 (d, $J = 10.1$ Hz, 1H, H2), 4.81, 4.61 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.71 (d, $J = 1.1$ Hz, 1H, G1), 4.55, 4.54 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.16–4.02 (m, 6H, G2, G4, G3, G5, H5, H5), 3.89–3.85 (m, 1H, H4), 3.82–3.78 (m, 4H, G5, OMe), 3.33 (s, 3H, OMe); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3$, 137.9, 130.3, 129.3, 128.5, 128.4, 127.7, 127.6, 125.8, 115.7, 113.8, 100.3, 77.1, 75.9, 72.9, 71.2, 70.0, 66.9, 65.9, 63.3, 55.3, 55.2, 30.3; HRMS (FAB): calcd for $C_{26}H_{30}O_8Cs$ $[M+Cs]^+$: 603.0995, found 603.0975. Mesylate **90** was treated in a similar manner to afford olefin **91** (87%) as a white foam. **91**: $R_f = 0.47$ (70% Et_2O in hexanes); $[\alpha]_D^{22} = -3.03$ ($c = 2.05$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2924$, 1612, 1513, 1456, 1410, 1323, 1303, 1249, 1164, 1116, 1066, 1036, 983, 952 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.41-7.25$ (m, 7H, ArH), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 6.17 (dd, $J = 10.0$, 4.0 Hz, 1H, H3), 4.78 (d, $J = 10.0$ Hz, 1H, H2), 4.97, 4.65 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.71 (s, 1H, G1), 4.56 (s, 2H, CH_2Ar), 4.39 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.16–4.06 (m, 4H, G2, G5, H5, H5), 3.90 (m, 1H, H4), 3.87 (dd, $J = 10.0$, 2.5 Hz, 1H, G3), 3.80 (s, 3H, OMe), 3.74 (t, $J = 10.0$ Hz, 1H, G5), 3.34 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 159.5, 137.9, 130.6, 129.3, 128.3, 128.1, 127.9, 127.6, 113.8, 100.7, 80.2, 75.4, 72.3, 70.3, 68.7, 67.1, 65.7, 62.9, 55.2, 55.2, 30.3; HRMS (FAB): calcd for $C_{26}H_{30}O_8Cs$ $[M+Cs]^+$: 603.0995, found 603.1009.

Diols 85 and 92: OsO_4 (0.05 mL, 2.5% solution in *t*BuOH) was added to a solution of GH olefin **84** (0.065 g, 0.14 mmol) and NMO (0.019 mg, 0.16 mmol) in acetone/H_2O (10:1, 1 mL), and the reaction mixture was stirred for 24 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 GH *cis*-diol **85** (0.050 g, 71%) as a white foam. **85**: $R_f = 0.20$ (100% Et_2O); $[\alpha]_D^{22} =$ -11.43 ($c = 0.7$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3435$, 2924, 1628, 1611, 1567, 1496, 1248, 1172, 1115, 1071, 1034, 991, 814 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.36-7.21$ (m, 7H, ArH), 6.87 (d, $J = 8.6$ Hz, 2H, PMB), 4.74 (d, $J = 1.5$ Hz, 1H, G1), 4.71 (s, 2H, CH_2Ar), 4.59, 4.52 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.20 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.13 (br s, 1H, H2), 4.10–4.02 (m, 4H, G2, G5, H3, H5), 4.96 (dd, $J = 12.5$, 2.5 Hz, 1H, G3), 3.80 (s, 3H, OMe), 3.76 (dd, $J = 7.0$, 5.1 Hz, 1H, H5), 3.75 (t, $J = 10.2$ Hz, 1H, G5), 3.64–3.61 (m, 1H, H4), 3.35 (s, 3H, OMe), 2.54 (d, $J = 7.0$ Hz, 1H, OH), 2.32 (d, $J = 7.0$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 129.3$, 128.5, 127.9, 127.6, 113.9, 100.0, 77.7, 76.1, 75.0, 73.1, 72.1, 71.4, 71.4, 69.2, 63.3, 62.1, 55.3, 30.3; HRMS (FAB): calcd for $C_{26}H_{32}O_{10}Cs$ $[M+Cs]^+$: 637.1050, found 637.1073. Olefin **91** was treated in a similar manner to afford diol **92** (72%) as a white foam. **92**: $R_f = 0.11$ (100% Et_2O); $[\alpha]_D^{22} =$ -37.58 ($c = 0.62$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3389$, 2931, 1608, 1508, 1461, 1396, 1361, 1246, 1168, 1111, 1064, 1033, 973, 808 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.35-7.20$ (m, 7H, ArH), 6.85 (d, $J = 8.5$ Hz, 2H, PMB), 4.88, 4.59 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, G1), 4.57, 4.54 (AB, $J =$ 11.6 Hz, 2H, CH_2Ar), 4.37 (ddd, $J = 10.4$, 10.4, 4.6 Hz, 1H, G4), 4.08 (dd, $J = 9.6$, 4.6 Hz, 1H, G5), 4.06–4.03 (m, 3H, G2, H2, H3), 3.97 (dd, $J = 12.3$, 3.2 Hz, 1H, H5), 3.91 (dd, $J = 10.1$, 2.3 Hz, 1H, G3), 3.77 (s, 3H, OMe), 3.74 (t, $J = 9.6$ Hz, 1H, G5), 3.72 (t, $J = 6.0$ Hz, 1H, H5), 3.66–3.63 (m, 1H, H4), 3.30 (s, 3H, OMe), 2.75 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 159.2, 137.8, 129.3, 128.2, 127.7, 127.6, 119.4, 113.8, 100.4, 80.8, 75.3, 74.8, 72.9, 71.6, 71.4, 69.5, 69.4, 62.5, 62.2, 55.2, 55.1; HRMS (MALDI): calcd for $C_{26}H_{32}O_{10}Na$ $[M+Na]^+$: 527.1893, found 527.1897.

Ring H glycal 93: $R_f = 0.68$ (50% Et_2O in hexanes); $[\alpha]_D^{22} = -16.6$ ($c = 0.29$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2930$, 2857, 1648, 1615, 1515, 1469, 1301, 1246, 1175, 1092, 917, 836, 778 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.27$ (d, $J =$ 8.7 Hz, 2H, PMB), 6.88 (d, $J = 8.7$ Hz, 2H, PMB), 6.44 (d, $J = 6.2$ Hz, 1H, H1), 4.77 (ddd, $J = 5.9$, 4.5, 1.1 Hz, 1H, H2), 4.60, 4.57 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.02–4.01 (m, 1H, H3), 4.00 (dd, $J = 11.7$, 4.5 Hz, 1H, H5), 3.91 (dd, $J = 11.7$, 2.1 Hz, 1H, H5), 3.80 (s, 3H, OMe), 3.47–3.45 (m, 1H, H4), 0.89 (s, 9H, *t*BuSi), 0.10 (s, 6H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.3$, 145.3, 130.2, 129.3, 113.8, 102.2, 75.0, 71.0, 63.5, 55.2, 25.8, 18.0,

0947-6539/00/0617-3138 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

– 4.4, – 4.7; HRMS (MALDI): calcd for $C_{19}H_{30}O_4SiNa$ $[M+Na]^+$: 373.1811, found 373.1829.

FG alcohol 94: Ring G trichloroacetimidate **46** (9.80 g, 12.73 mmol) and ring F tin-acetal **45** (17.25 g, 26.50 mmol) were azeotroped with benzene (3 × 30 mL) and then dried under high vacuum for 1 h. CH_2Cl_2 (100 mL) was added, the resulting mixture was cooled to 0 °C and TMSOTf (1.23 mL, 6.14 mmol) was added dropwise. The reaction mixture was warmed to 25 °C and stirred 12 h. The reaction mixture was quenched by the addition of Et_3N (20 mL), diluted with CH_2Cl_2 (800 mL) 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 dissolved in MeOH (100 mL) and PPTS (1.0 g, 3.82 mmol) was added. The reaction mixture was stirred at 25 °C for 1 h and then the reaction mixture was quenched by the addition of Et_3N (20 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 FG alcohol **94** (10.82 g, 74 % over two steps) as a white foam. **94**: $R_f = 0.26$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -14.2$ ($c = 3.11$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3458, 3066, 3009, 2886, 1726, 1611, 1514, 1452, 1365, 1269, 1104, 1033, 1000, 931, 754, 713\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 8.0$ Hz, 2H, ArH), 7.57 (t, $J = 7.5$ Hz, 1H, ArH), 7.46 – 7.32 (m, 7H, ArH), 7.25 (d, $J = 8.5$ Hz, 2H, PMB), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 5.90 – 5.82 (m, 2H, C*H*=CH_2), 5.64 (t, $J = 2.5$ Hz, 1H, G2), 5.30 (d, $J = 2.5$ Hz, 1H, G1), 5.29 (dd, $J = 17.5$, 1.8 Hz, 1H, CH_2-*E*), 5.25 (dd, $J =$ 17.5, 1.8 Hz, 1H, CH_2-*E*), 5.19 (dd, $J = 10.5$, 1.1 Hz, 1H, CH_2-*Z*), 5.11 (dd, $J = 10.5$, 1.1 Hz, 1H, CH_2-*Z*), 4.84, 4.56 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.79, 4.70 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.71 (s, 1H, F1), 4.25, 4.18, 4.12, 4.03 (4 × dd, $J = 12.9$, 5.9 Hz, 4H, OCH_2), 4.08 (d, $J = 2.9$ Hz, 1H, F2), 3.92 (t, $J = 9.5$ Hz, 1H, F4), 3.90 – 3.82 (m, 3H, G3, G4, G5), 3.80 (s, 3H, OMe), 3.64 – 3.54 (m, 4H, F3, F6, F6, G5), 3.38 – 3.54 (m, 1H, F5), 3.36 (s, 3H, OMe), 2.41 (d, $J = 2.5$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 165.2, 159.3, 137.7, 134.8, 134.5, 133.1, 130.4, 129.9, 129.8, 129.7, 128.5, 128.3, 127.9, 127.8, 117.0, 116.8, 113.8, 95.0, 94.7, 81.2, 76.6, 75.3, 74.8, 73.6, 73.4, 72.6, 71.4, 71.1, 70.7, 68.9, 68.2, 61.8, 59.3, 55.2; HRMS (FAB): calcd for $C_{40}H_{48}O_{12}Cs$ $[M+Cs]^+$: 853.2200, found 853.2231.

FG methyl ether 95: NaH (0.497 g, 12.43 mmol) was added to a solution of FG alcohol **94** (8.13 g, 11.29 mmol) and MeI (2.10 mL, 33.88 mmol) in DMF (60 mL) at 0 °C. 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 (50 mL), diluted with Et_2O (500 mL), and washed with brine (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 → 80 % Et_2O in hexanes) to afford FG methyl ether **95** (7.21 g, 87 %) as a white foam. **95**: $R_f = 0.35$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -14.1$ ($c = 2.02$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3067, 2978, 2885, 1728, 1610, 1514, 1451, 1352, 1286, 1104, 932, 856, 824, 767, 714\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 8.4$ Hz, 2H, ArH), 7.58 – 7.31 (m, 8H, ArH), 7.23 (d, $J = 8.6$ Hz, 2H, PMB), 6.86 (d, $J =$ 8.6 Hz, 2H, PMB), 5.94 – 5.82 (m, 2H, C*H*=CH_2), 5.65 (t, $J = 2.5$ Hz, 1H, G2), 5.29 (dm, $J = 15.8$ Hz, 1H, CH_2-*E*), 5.26 (d, $J = 2.5$ Hz, 1H, G1), 5.23 (dm, $J = 15.8$ Hz, 1H, CH_2-*E*), 5.19 (dm, $J = 10.0$ Hz, 1H, CH_2-*Z*), 5.11 (dm, $J = 10.0$ Hz, 1H, CH_2-*Z*), 4.84, 4.53 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.76, 4.72 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.30 – 4.03 (m, 4H, OCH_2), 3.89 – 3.79 (m, 7H, G3, G4, G5, F4, OMe), 3.66 (s, 3H, OMe), 3.63 – 3.52 (m, 5H, F2, F3, F6, F6, G5), 3.35 (s, 3H, OMe), 3.35 – 3.31 (m, 1H, F5); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.1, 159.3, 138.0, 134.8, 134.6, 133.0, 130.5, 129.9, 129.9, 129.7, 128.5, 128.3, 127.8, 127.7, 117.1, 113.8, 95.8, 95.0, 81.8, 78.0, 76.5, 75.8, 74.9, 74.3, 73.7, 72.8, 72.0, 71.4, 70.6, 69.0, 61.9, 59.3, 55.3$; HRMS (FAB): calcd for $C_{41}H_{50}O_{12}Cs$ $[M+Cs]^+$: 867.2357, found 867.2329.

FG alcohol 96: NaOH (0.23 g, 5.76 mmol) was added to a solution of FG benzoate **95** (14.10 g, 19.19 mmol) in MeOH/Et_2O (1:1, 140 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 (50 mL), diluted with Et_2O (500 mL) and washed with brine (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 → 100 % Et_2O in hexanes) to afford FG alcohol **96** (11.50 g, 95 %) as a white foam. **96**: $R_f = 0.20$ (100 % Et_2O); $[\alpha]_D^{22} = -49.8$ ($c = 1.24$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3469, 3067, 2883, 1612, 1514, 1457, 1372, 1249, 1100, 1035, 1002, 930, 735\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.40 – 7.29$ (m, 5H, ArH), 7.23 (d, $J = 8.5$ Hz, 2H, PMB), 6.86 (d, $J = 8.5$ Hz, 2H, PMB), 5.95 – 5.86 (m, 2H, C*H*=CH_2), 5.28 (dm, $J = 17.5$ Hz, 2H, CH_2-*E*), 5.20 – 5.17 (m, 3H, G1, CH_2-*Z*), 4.83, 4.52 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.74, 4.71 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.65 (s, 1H, F1), 4.21 – 4.09 (m, 4H, OCH_2), 4.08 (dd, $J = 5.0$, 2.5 Hz, 1H, G2), 3.82 – 3.73 (m, 6H, G4, G5, F4, OMe), 3.64 – 3.55 (m, 7H, F2, F6, F6, G3, OMe), 3.51 (dd, $J = 9.5$, 3.0 Hz, 1H, F3), 3.46 (dd, $J = 9.5$, 9.5 Hz, 1H, G5), 3.36 – 3.31 (m, 1H, F5), 3.35 (s, 3H, OMe), 2.52 (d, $J = 2.0$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.0$, 138.2, 134.7, 134.6, 131.3, 129.7, 128.5, 127.8, 127.7, 117.3, 113.8, 96.5, 96.1, 81.9, 78.1, 77.7, 75.5, 74.9, 74.3, 73.6, 72.3, 72.1, 71.4, 71.2, 68.4, 61.9, 61.6, 59.2, 55.3; HRMS (FAB): calcd for $C_{34}H_{46}O_{11}Cs$ $[M+Cs]^+$: 763.2094, found 763.2073.

FG benzyl ether 97: NaH (0.89 g, 22.15 mmol) was added to a solution of FG alcohol **96** (12.70 g, 20.14 mmol) in DMF (100 mL) at 0 °C and the resulting mixture was stirred for 5 min. BnBr (2.57 mL, 26.18 mmol) and nBu_4NI (1.48 g, 4.03 mmol) were 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 (50 mL), diluted with Et_2O (800 mL) and washed with brine (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 → 100 % Et_2O in hexanes) to afford FG benzyl ether **97** (13.06 g, 90 %) as a white foam. **97**: $R_f = 0.18$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -31.6$ ($c = 1.73$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3064, 3031, 2882, 1612, 1514, 1456, 1368, 1304, 1249, 1102, 1055, 1005, 927, 737\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.40 – 7.30 (m, 10H, ArH), 7.24 (d, $J = 8.5$ Hz, 2H, PMB), 6.87 (d, $J = 8.5$ Hz, 2H, PMB), 5.96 – 5.85 (m, 2H, C*H*=CH_2), 5.29 (dd, $J = 17.5$, 2.0 Hz, 1H, CH_2-*E*), 5.27 (dd, $J = 17.5$, 2.0 Hz, 1H, CH_2-*E*), 5.20 (d, $J = 2.0$ Hz, 1H, G1), 5.18 (dd, $J = 10.5$, 1.0 Hz, 1H, CH_2-*Z*), 5.14 (dd, $J = 10.5$, 1.0 Hz, 1H, CH_2-*Z*), 4.84, 4.52 (AB, $J = 10.5$ Hz, 2H, CH_2Ar), 4.78, 4.68 (AB, $J = 12.5$ Hz, 2H, CH_2Ar), 4.74, 4.71 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.62 (s, 1H, F1), 4.27 (dd, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 4.14 (dd, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 4.11 – 4.05 (m, 2H, OCH_2), 3.91 (t, $J = 2.0$ Hz, 1H, G2), 3.90 (ddd, $J = 10.0$, 10.0, 5.5 Hz, 1H, G4), 3.83 – 3.78 (m, 5H, G5, F4, OMe), 3.65 (dd, $J = 9.5$, 3.0 Hz, 1H, G3), 3.63 (s, 3H, OMe), 3.60 (d, $J = 1.5$ Hz, 1H, F2), 3.57 – 3.54 (m, 2H, F6, F6), 3.51 (dd, $J = 9.5$, 3.0 Hz, 1H, F3), 3.40 (t, $J = 9.5$ Hz, 1H, G5), 3.34 (s, 3H, OMe), 3.33 – 3.30 (m, 1H, F5); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.3, 138.3, 138.0, 134.9, 130.5, 129.7, 128.5, 128.2, 127.8, 127.7, 127.5, 117.0, 116.7, 113.8, 95.8, 95.3, 81.8, 78.3, 78.1, 75.5, 75.1, 74.9, 74.2, 74.1, 73.2, 72.6, 72.0, 71.3, 71.1, 62.0, 59.2, 55.2$; HRMS (FAB): calcd for $C_{41}H_{52}O_{11}Cs$ $[M+Cs]^+$: 853.2564, found 853.2587.

FG alcohol 98: DDQ (3.87 g, 17.06 mmol) was added to a solution of FG PMB ether **97** (8.20 g, 11.38 mmol) in CH_2Cl_2/H_2O (10:1, 110 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 (500 mL) and washed with saturated aqueous $NaHCO_3$ (80 mL) and brine (80 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100 % Et_2O) to afford FG alcohol **98** (6.22 g, 91 %) as a white foam. **98**: $R_f = 0.29$ (100 % Et_2O); $[\alpha]_D^{22} = -74.8$ ($c = 0.93$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3456, 3064, 2882, 1453, 1374, 1199, 1106, 999, 928, 737, 701\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.38 – 7.27$ (m, 10H, ArH), 5.96 – 5.85 (m, 2H, C*H*=CH_2), 5.29 (dm, $J = 17.5$ Hz, 1H, CH_2-*E*), 5.25 (dm, $J = 17.5$ Hz, 1H, CH_2-*E*), 5.20 (d, $J = 2.5$ Hz, 1H, G1), 5.18 (dm, $J = 10.5$ Hz, 1H, CH_2-*Z*), 5.14 (dm, $J = 10.5$ Hz, 1H, CH_2-*Z*), 4.76, 4.68 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.75, 4.63 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.68 (s, 1H, F1), 4.26 (ddm, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 4.13 (ddm, $J = 12.5$, 5.5 Hz, 1H, OCH_2), 4.10 – 4.07 (m, 2H, OCH_2), 3.91 – 3.88 (m, 1H, G4), 3.90 (t, $J = 2.5$ Hz, 1H, G2), 3.86 (dt, $J = 8.5$, 2.0 Hz, 1H, F4), 3.82 (dd, $J = 11.0$, 5.5 Hz, 1H, G5), 3.70 (dd, $J = 10.5$, 4.0 Hz, 1H, F6), 3.65 (dd, $J = 9.0$, 3.0 Hz, 1H, G3), 3.61 (dd, $J = 10.5$, 5.5 Hz, 1H, F6), 3.58 (s, 3H, OMe), 3.57 (d, $J = 3.0$ Hz, 1H, F2), 3.40 (t, $J = 10.5$ Hz, 1H, G5), 3.37 (s, 3H, OMe), 3.36 – 3.32 (m, 2H, F3, F5); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.2$, 137.7, 134.9, 128.6, 128.2, 128.0, 127.8, 127.7, 127.6, 117.1, 116.7, 95.8, 95.4, 81.3, 78.3, 77.3, 75.0, 74.9, 74.1, 73.2, 72.7, 71.8, 71.1, 68.1, 62.1, 61.9, 59.4; HRMS (FAB): calcd for $C_{33}H_{44}O_{10}Cs$ $[M+Cs]^+$: 733.1989, found 733.2010.

FG TIPS ether 99: TIPSOTf (5.34 mL, 19.98 mmol) was added to a solution of FG alcohol **98** (10.00 g, 16.64 mmol) and 2,6-lutidine (2.91 mL, 24.97 mmol) in CH_2Cl_2 (85 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched by the addition of MeOH (10 mL), diluted with CH_2Cl_2 (800 mL) 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 → 80 % Et_2O in hexanes) to afford FG TIPS ether **99** (12.22 g, 97 %) as a white foam. **99**: $R_f = 0.67$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -43.9$ ($c = 5.50$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3031, 2941, 2866, 1457, 1364, 1311, 1256, 1200, 1105, 997, 885, 830, 738, 700, 679\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.38-7.24$ (m, 10H, ArH), 5.90–5.84 (m, 2H, C*H*=CH_2), 5.29 (dm, $J = 17.5$ Hz, 1H, CH_2-*E*), 5.25 (dm, $J = 17.5$ Hz, 1H, CH_2-*E*), 5.24 (d, $J = 2.5$ Hz, 1H, G1), 5.17 (dm, $J = 10.0$ Hz, 1H, CH_2-*Z*), 5.12 (dm, $J = 10.0$ Hz, 1H, CH_2-*Z*), 4.77, 4.70 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.76 (s, 1H, F1), 4.70, 4.41 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.28–4.25 (m, 1H, OCH_2), 4.16–4.12 (m, 1H, OCH_2), 4.08–4.03 (m, 2H, OCH_2), 4.01 (t, $J = 8.5$ Hz, 1H, F4), 3.91 (ddd, $J = 10.5, 10.5, 5.0$ Hz, 1H, G4), 3.90 (t, $J = 2.5$ Hz, 1H, G2), 3.82 (dd, $J = 11.0, 5.5$ Hz, 1H, G5), 3.72 (dd, $J = 10.5, 2.0$ Hz, 1H, F6), 3.66 (d, $J = 3.0$ Hz, 1H, F2), 3.64 (dd, $J = 9.0, 3.0$ Hz, 1H, G3), 3.58 (dd, $J = 10.5, 6.0$ Hz, 1H, F6), 3.51 (s, 3H, OMe), 3.45 (t, $J = 10.5$ Hz, 1H, G5), 3.38–3.35 (m, 2H, F3, F5), 3.33 (s, 3H, OMe), 1.05–0.97 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.2, 138.0, 134.9, 128.2, 128.0, 127.7, 127.4, 116.9, 116.5, 95.5, 95.2, 82.4, 78.3, 76.7, 76.3, 75.0, 74.1, 73.0, 72.6, 71.8, 71.0, 70.6, 68.0, 61.9, 61.4, 58.9, 18.2, 18.0, 13.0$; HRMS (FAB): calcd for $C_{42}H_{64}O_{10}SiCs$ $[M+Cs]^+$: 889.3323, found 889.3355.

FG diol 43: $[(Ph_3P)_3RhCl]$ (1.57 g, 1.70 mmol) was added to a solution of FG bis-allyl ether **99** (12.80 g, 16.91 mmol) and DABCO (4.74 g, 42.27 mmol) in EtOH/H_2O (10:1, 150 mL, degassed 1 h) at 25 °C. The resulting mixture was refluxed for 2 h. The reaction mixture was diluted with CH_2Cl_2 (800 mL) and washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL). The solvents were removed under reduced pressure and then the residue was dissolved in acetone/H_2O (10:1, 150 mL). NMO (4.38 g, 37.19 mmol) and OsO_4 (1.0 mL, 2.5 % solution in *t*BuOH) were added and the reaction mixture was stirred for 8 h at 25 °C. The reaction mixture was diluted with CH_2Cl_2 (800 mL) 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 FG diol **43** (9.27 g, 81 % over two steps) as a white foam. **43**: $R_f = 0.24$ (100 % Et_2O); $[\alpha]_D^{22} = -42.9$ ($c = 0.80$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3441, 2943, 2866, 1465, 1373, 1313, 1253, 1201, 1119, 1052, 995, 885, 773, 690, 678\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.37-7.28$ (m, 10H, ArH), 5.37 (d, $J = 1.5$ Hz, 1H, G1), 4.80 (s, 1H, F1), 4.76, 4.52 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.71, 4.42 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.02 (t, $J = 9.0$ Hz, 1H, F4), 3.92–3.87 (m, 1H, G4), 3.86 (dd, $J = 3.5, 2.0$ Hz, 1H, G2), 3.79 (dd, $J = 11.0, 5.5$ Hz, 1H, G5), 3.73–3.68 (m, 3H, F2, F6, G3), 3.64 (dd, $J = 10.5, 6.0$ Hz, 1H, F6), 3.51 (s, 3H, OMe), 3.47 (t, $J = 10.5$ Hz, 1H, G5), 3.42–3.37 (m, 1H, F5), 3.38 (dd, $J = 8.5, 3.0$ Hz, 1H, F3), 3.34 (s, 3H, OMe), 2.64 (d, $J = 2.5$ Hz, 1H, OH), 2.41 (d, $J = 9.5$ Hz, 1H, OH), 1.06–0.97 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.0, 137.3, 128.6, 128.2, 128.0, 127.9, 127.5, 127.5, 95.5, 94.1, 82.3, 77.7, 77.3, 76.3, 73.0, 72.0, 71.5, 70.8, 68.1, 62.6, 61.4, 58.9, 30.3, 18.2, 18.1, 13.0$; HRMS (FAB): calcd for $C_{36}H_{56}O_{10}SiCs$ $[M+Cs]^+$: 809.2697, found 809.2730.

FG chloroacetates 100 and 101: *n*Bu_2SnO (3.87 g, 15.56 mmol) was added to a solution of FG diol **43** (9.52 g, 14.06 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 0 °C and chloroacetyl chloride (CACl) (1.18 mL, 14.77 mmol) was added. The reaction mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with EtOAc (500 mL) and washed with saturated aqueous $NaHCO_3$ (80 mL) and brine (80 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 % Et_2O in hexanes) to afford FG chloroacetates **100** and **101** (10.34 g, 97 %, 1:1 mixture of G3 and G4 regioisomers) as a white foam. G-3 chloroacetate **101**: $R_f = 0.21$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -30.7$ ($c = 0.30$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3434, 2945, 2863, 1760, 1500, 1423, 1114\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.37-7.27$ (m, 10H, ArH), 5.32 (d, $J = 2.0$ Hz, 1H, G1), 5.05 (dd, $J = 9.8, 3.2$ Hz, 1H, G3), 4.81 (s, 1H, F1), 4.72, 4.54 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.70, 4.44 (AB, $J = 11.2$ Hz, 2H, CH_2Ar), 4.27–4.23 (m, 1H, G4), 4.03 (t, $J = 8.4$ Hz, 1H, F4), 3.99 (dd, $J = 3.1, 2.4$ Hz, 1H, G2), 3.98, 3.87 (AB, $J = 14.9$ Hz, 2H, CH_2Cl), 3.86 (dd, $J = 11.7, 6.0$ Hz, 1H, G5), 3.71 (dd, $J = 10.4, 5.9$ Hz, 1H, F6), 3.70 (s, 1H, F2), 3.64 (dd, $J = 10.4, 5.9$ Hz, 1H, F6), 3.54 (s, 3H, OMe), 3.53 (dd, $J = 11.6, 5.7$ Hz, 1H, G5), 3.42–3.38 (m, 2H, F3, F5), 3.34 (s, 3H, OMe), 2.21 (br s, 1H, OH), 1.10–0.95 (m, 21H, *i*Pr_3Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.7, 138.0, 137.5, 128.4, 128.2, 128.0, 127.9, 127.5, 95.4, 94.4, 82.0, 77.3, 76.3, 75.9, 75.5, 73.3, 72.0, 70.9, 68.1, 65.3, 63.2, 61.3, 58.9, 40.6, 30.1, 18.3, 18.1, 13.0$; HRMS (FAB): calcd for $C_{38}H_{57}ClO_{11}SiCs$ $[M+Cs]^+$: 885.2413, found 885.2443. G-4 chloroacetate **100**: $R_f = 0.30$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -30.2$ ($c = 0.33$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3493, 2942, 2865, 1738, 1454, 1384, 1261, 1200, 1113, 1057, 1029, 1007, 884, 748\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.37-7.27$ (m, 10H, ArH), 5.35 (d, $J = 2.0$ Hz, 1H, G1), 5.15 (ddd, $J = 10.0, 10.0, 4.0$ Hz, 1H, G4), 4.81 (s, 1H, F1), 4.80, 4.57 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.73, 4.44 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.11, 4.07 (AB, $J = 15.0$ Hz, 2H, CH_2Cl), 4.05 (t, $J = 8.5$ Hz, 1H, F4), 3.91 (dd, $J = 9.5, 3.5$ Hz, 1H, G3), 3.89–3.86 (m, 1H, G2), 3.85 (dd, $J = 11.0, 5.5$ Hz, 1H, G5), 3.73–3.70 (m, 2H, F2, F6), 3.65 (dd, $J = 10.5, 6.0$ Hz, 1H, F6), 3.57 (t, $J = 10.0$ Hz, 1H, G5), 3.54 (s, 3H, OMe), 3.44–3.39 (m, 2H, F3, F5), 3.34 (s, 3H, OMe), 2.35 (d, $J = 10.0$ Hz, 1H, OH), 1.06–0.90 (m, 21H, *i*Pr_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 166.9, 138.0, 137.3, 128.6, 128.1, 128.1, 127.9, 127.5, 127.4, 95.7, 94.0, 82.1, 77.7, 77.4, 76.3, 73.1, 72.0, 71.9, 70.8, 68.6, 68.1, 61.2, 59.9, 58.9, 40.7, 18.2, 18.0, 13.0$; HRMS (FAB): calcd for $C_{38}H_{57}ClO_{11}SiCs$ $[M+Cs]^+$: 885.2413, found 885.2444.

FGH trisaccharide 102: DAST (0.85 mL, 6.45 mmol) was added to a solution of ring H alcohol **71** (2.26 g, 4.30 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 $NaHCO_3$ (10 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 crude ring H glycosyl fluoride **44** (2.30 g, 4.30 mmol) and FG alcohol **101** (1.62 g, 2.15 mmol) were azeotroped with benzene (3 × 10 mL) and then dried under high vacuum for 1 h. Et_2O (12.0 mL) and 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 5 min. $SnCl_2$ (0.734 g, 3.87 mmol) was added in one portion and the resulting mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was quenched by the addition of Et_3N (10 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, 50 % Et_2O in hexanes) to afford FGH trisaccharide **102** (2.49 g, 92 %) as a white foam. **102**: $R_f = 0.32$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = +2.26$ ($c = 1.37$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2995, 2865, 1770, 1732, 1614, 1580, 1514, 1470, 1384, 1254, 1114, 834, 753, 697\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 7.1$ Hz, 2H, ArH), 7.36–7.27 (m, 10H, ArH), 7.23 (d, $J = 8.5$ Hz, 2H, ArH), 7.16 (t, $J = 7.5$ Hz, 2H, ArH), 7.06 (t, $J = 7.3$ Hz, 1H, ArH), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 5.24 (d, $J = 2.3$ Hz, 1H, G1), 5.23 (dd, $J = 9.9, 3.3$ Hz, 1H, G3), 4.74 (d, $J = 7.9$ Hz, 1H, H1), 4.67 (s, 1H, F1), 4.66, 4.61 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.64, 4.35 (AB, $J = 11.1$ Hz, 2H, CH_2Ar), 4.57, 4.47 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.23 (br s, 1H, H3), 4.20 (ddd, $J = 10.0, 10.0, 5.6$ Hz, 1H, G4), 4.08, 3.96 (AB, $J = 15.2$ Hz, 2H, CH_2Cl), 3.97 (t, $J = 8.6$ Hz, 1H, F4), 3.92 (t, $J = 2.4$ Hz, 1H, G2), 3.84–3.78 (m, 6H, OMe, F2, G5, H5), 3.69 (dd, $J = 10.5, 1.9$ Hz, 1H, F6), 3.59 (dd, $J = 10.5, 6.1$ Hz, 1H, F6), 3.51–3.49 (m, 2H, H2, H5), 3.47 (s, 3H, OMe), 3.33–3.28 (m, 6H, F3, F5, G5, OMe), 3.23 (br s, 1H, H4), 1.08–0.95 (m, 21H, *i*Pr_3Si), 0.90 (s, 9H, *t*BuSi), 0.12, −0.06 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 166.5, 159.3, 138.0, 137.8, 131.6, 130.0, 129.3, 128.7, 128.4, 128.1, 128.0, 127.8, 127.5, 126.1, 113.9, 101.4, 95.3, 94.3, 82.1, 77.4, 76.2, 75.9, 75.0, 73.4, 72.8, 71.9, 71.0, 70.4, 68.0, 62.8, 61.8, 60.9, 59.0, 55.3, 41.0, 25.8, 18.2, 18.0, 13.0, −4.4, −4.8$; HRMS (FAB): calcd for $C_{63}H_{91}ClO_{15}Se$-Si_2Cs $[M+Cs]^+$: 1391.3805, found 1391.3720.

FGH alcohol 42: K_2CO_3 (0.10 g, 0.72 mmol) was added to a solution of FGH trisaccharide **102** (or **105**) (4.52 g, 3.60 mmol) in MeOH/Et_2O (1:1, 18 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 (50 mL), diluted with Et_2O (500 mL), and washed with brine (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 → 100 % Et_2O in hexanes) to afford FGH alcohol **42** (4.16 g, 98 %) as a white foam. **42**: $R_f = 0.18$ (50 % EtOAc in hexanes); $[\alpha]_D^{22} = -22.7$ ($c = 2.7$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3451, 3051, 2930, 2863, 1612, 1582, 1513, 1463, 1383, 1357, 1304, 1251, 1110, 1031, 942, 885, 883\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.55$ (d, $J = 7.1$ Hz, 2H, ArH),

0947-6539/00/0617-3140 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

7.39–7.25 (m, 14H, ArH), 7.15 (t, $J=7.8$ Hz, 2H, ArH), 7.06 (t, $J=7.3$ Hz, 1H, ArH), 6.82 (d, $J=8.6$ Hz, 2H, PMB), 5.16 (d, $J=1.7$ Hz, 1H, G1), 4.87, 4.69 (AB, $J=12.2$ Hz, 2H, CH_2Ar), 4.80 (d, $J=9.1$ Hz, 1H, H1), 4.69, 4.40 (AB, $J=11.1$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.61, 4.47 (AB, $J=12.1$ Hz, 2H, CH_2Ar), 4.30 (brs, 1H, H3), 4.01–3.92 (m, 5H, F4, H5, H5, G4, G2), 3.83–3.79 (m, 1H, G3), 3.80 (s, 3H, OMe), 3.71–3.68 (m, 2H, G5, F6), 3.61 (dd, $J=9.1$, 2.7 Hz, 1H, H2), 3.56 (dd, $J=10.5$, 6.1 Hz, 1H, F6), 3.51 (d, $J=2.6$ Hz, 1H, F2), 3.47 (s, 3H, OMe), 3.33–3.31 (m, 2H, F3, F5), 3.32 (s, 3H, OMe), 3.22 (brs, 1H, H4), 3.15 (t, $J=10.9$ Hz, 1H, G5), 1.02–0.96 (m, 21H, iPr$_3$Si), 0.90 (s, 9H, tBuSi), 0.14, −0.07 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=159.4$, 138.4, 138.0, 131.6, 129.6, 129.4, 128.5, 128.4, 128.2, 128.1, 127.6, 127.5, 127.4, 127.4, 127.2, 126.0, 113.9, 102.8, 95.6, 95.2, 82.2, 78.9, 77.4, 76.8, 76.3, 74.4, 73.6, 72.9, 71.9, 70.8, 70.5, 70.1, 68.0, 63.4, 61.5, 60.3, 59.0, 55.2, 48.4, 25.7, 18.2, 18.0, 18.0, 18.0, 13.2, 13.0, −4.4, −4.8; HRMS (FAB): calcd for $C_{61}H_{90}O_{14}SeSi_2Cs$ $[M+Cs]^+$: 1315.4089, found 1315.4022.

FG benzoate 103: BzCl (1.20 mL, 8.19 mmol) was added to a solution of FG alcohol **100** (5.14 g, 6.82 mmol), Et_3N (1.50 mL, 13.23 mmol) and 4-DMAP (0.20 g, 1.36 mmol) in CH_2Cl_2 (35 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (1.0 mL), diluted with CH_2Cl_2 (350 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 → 60% Et_2O in hexanes) to afford FG benzoate **103** (5.62 g, 96%) as a white foam. **103**: $R_f=0.41$ (50% Et_2O in hexanes); $[\alpha]_D^{22}=-111.0$ ($c=0.47$, $CHCl_3$); IR (thin film): $\tilde{\nu}=2942$, 2865, 1728, 1452, 1269, 1112, 883, 751 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.99$ (brd, $J=7.9$ Hz, 2H, ArH), 7.58 (t, $J=7.4$ Hz, 1H, ArH), 7.44 (t, $J=8.0$ Hz, 2H, ArH), 7.40 (brd, $J=7.2$ Hz, 2H, ArH), 7.35 (t, $J=7.1$ Hz, 2H, ArH), 7.30–7.26 (m, 3H, ArH), 7.21–7.17 (m, 3H, ArH), 5.66 (ddd, $J=10.1$, 10.1, 5.5 Hz, 1H, G4), 5.51 (dd, $J=10.0$, 3.3 Hz, 1H, G3), 5.39 (d, $J=2.1$ Hz, 1H, G1), 4.86 (s, 1H, F1), 4.76, 4.47 (AB, $J=11.3$ Hz, 2H, CH_2Ar), 4.68, 4.63 (AB, $J=12.0$ Hz, 2H, CH_2Ar), 4.14 (t, $J=2.8$ Hz, 1H, G2), 4.07 (t, $J=8.3$ Hz, 1H, F4), 4.00 (dd, $J=10.9$, 5.6 Hz, 1H, G5), 3.96, 3.93 (AB, $J=10.1$ Hz, 2H, CH_2Cl), 3.75–3.68 (m, 3H, F2, F6, G5), 3.66 (dd, $J=10.5$, 5.9 Hz, 1H, F6), 3.62 (s, 3H, OMe), 3.46–3.42 (m, 2H, F3, F5), 3.34 (s, 3H, OMe), 1.27–0.99 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=166.5$, 165.3, 138.0, 137.4, 133.3, 129.8, 129.3, 128.4, 128.3, 128.1, 127.7, 127.5, 95.5, 94.5, 81.9, 77.4, 76.2, 75.7, 73.4, 71.9, 70.9, 70.8, 68.7, 68.0, 61.4, 60.5, 58.9, 40.5, 18.2, 18.1, 12.9; HRMS (FAB): calcd for $C_{45}H_{61}ClO_{12}SiCs$ $[M+Cs]^+$: 989.2675, found 989.2710.

FG alcohol 104: Et_3N (1.50 mL, 13.23 mmol) was added to a solution of FG benzoate **103** (5.14 g, 6.82 mmol) in CH_2Cl_2/MeOH (1:1, 40 mL) at 25 °C. The resulting mixture was warmed to 40 °C and stirred for 6 h. The reaction mixture was diluted with CH_2Cl_2 (350 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes) to afford FG alcohol **104** (5.62 g, 96%) as a white foam. **104**: $R_f=0.35$ (70% Et_2O in hexanes); $[\alpha]_D^{22}=-50.2$ ($c=1.06$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3443$, 2943, 2865, 1725, 1453, 1381, 1315, 1275, 1200, 1116, 996, 908, 884, 829, 781, 734, 716 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=8.01$ (d, $J=8.2$ Hz, 2H, ArH), 7.59 (t, $J=7.5$ Hz, 1H, ArH), 7.44 (t, $J=7.6$ Hz, 2H, ArH), 7.38 (d, $J=7.1$ Hz, 2H, ArH), 7.35–7.32 (m, 3H, ArH), 7.29–7.22 (m, 5H, ArH), 5.37 (d, $J=2.0$ Hz, 1H, G1), 5.30 (dd, $J=9.7$, 3.3 Hz, 1H, G3), 4.85 (s, 1H, F1), 4.73, 4.45 (AB, $J=11.3$ Hz, 2H, CH_2Ar), 4.71, 4.65 (AB, $J=11.9$ Hz, 2H, CH_2Ar), 4.38 (ddd, $J=10.0$, 10.0, 5.5 Hz, 1H, G4), 4.08 (t, $J=2.3$ Hz, 1H, G2), 4.06 (t, $J=8.5$ Hz, 1H, F4), 3.93 (dd, $J=11.1$, 5.5 Hz, 1H, G5), 3.74–3.72 (m, 2H, F2, F6), 3.64 (dd, $J=10.2$, 6.1 Hz, 1H, F6), 3.62 (t, $J=10.2$ Hz, 1H, G5), 3.59 (s, 3H, OMe), 3.44–3.40 (m, 2H, F3, F5), 3.34 (s, 3H, OMe), 2.45 (brs, 1H, OH), 1.08–0.97 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=167.2$, 137.7, 137.6, 133.3, 129.8, 129.7, 128.4, 128.3, 128.2, 127.7, 127.5, 95.5, 94.6, 82.6, 77.4, 76.3, 76.1, 74.8, 73.4, 72.0, 70.8, 68.1, 65.9, 63.4, 61.5, 59.0, 18.2, 18.1, 13.0; HRMS (FAB): calcd for $C_{43}H_{60}O_{11}SiCs$ $[M+Cs]^+$: 913.2959, found 913.2989.

FGH trisaccharide 105 (Bz): DAST (0.64 mL, 4.83 mmol) was added to a solution of ring H alcohol **71** (1.69 g, 3.22 mmol) in CH_2Cl_2 (16 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 $NaHCO_3$ (10 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 crude ring H glycosyl fluoride **44** (1.80 g, 3.22 mmol) and FG alcohol **104** (1.26 g, 1.61 mmol) were azeotroped with benzene (3 × 10 mL) and then dried under high vacuum for 1 h. Et_2O (8 mL) and 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 5 min. $SnCl_2$ (0.55 g, 2.90 mmol) was added in one portion and the resulting mixture was warmed to 25 °C and stirred for 3 h. The reaction mixture was quenched by the addition of Et_3N (10 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 FGH trisaccharide (Bz) **105** (1.91 g, 92%) as a white foam. **105**: $R_f=0.28$ (30% Et_2O in hexanes); $[\alpha]_D^{22}=-55.8$ ($c=3.12$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3065$, 2931, 2862, 1726, 1611, 1582, 1513, 1458, 1356, 1250, 1109, 1040, 908, 835, 736 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=8.08$ (d, $J=8.3$ Hz, 2H, ArH), 7.54 (d, $J=7.2$ Hz, 4H, ArH), 7.42–7.08 (m, 16H, ArH), 6.80 (d, $J=8.6$ Hz, 2H, PMB), 5.41 (dd, $J=9.6$, 3.3 Hz, 1H, G3), 5.29 (d, $J=2.0$ Hz, 1H, G1), 4.82 (d, $J=7.8$ Hz, 1H, H1), 4.72 (s, 1H, F1), 4.69, 4.60 (AB, $J=12.0$ Hz, 2H, CH_2Ar), 4.64, 4.60 (AB, $J=12.0$ Hz, 2H, CH_2Ar), 4.40, 4.26 (AB, $J=11.9$ Hz, 2H, CH_2Ar), 4.37 (ddd, $J=10.0$, 10.0, 5.6 Hz, 1H, G4), 4.17 (t, $J=3.5$ Hz, 1H, H3), 4.05 (t, $J=2.4$ Hz, 1H, G2), 3.99 (t, $J=8.8$ Hz, 1H, F4), 3.78 (s, 3H, OMe), 3.72 (d, $J=1.7$ Hz, 1H, F2), 3.71–3.78 (m, 1H, F6), 3.61 (dd, $J=10.8$, 6.1 Hz, 1H, F6), 3.55 (s, 3H, OMe), 3.52 (dd, $J=7.8$, 3.1 Hz, 1H, H2), 3.36–3.46 (m, 3H, F3, F5, G5), 3.32 (s, 3H, OMe), 3.23 (s, 1H, H4), 1.09–0.96 (m, 21H, iPr$_3$Si), 0.89 (s, 9H, tBuSi), 0.09, −0.12 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=165.3$, 159.3, 138.1, 137.8, 132.6, 131.9, 129.9, 129.2, 128.7, 128.2, 128.1, 128.0, 127.7, 127.6, 127.5, 126.2, 113.7, 101.4, 95.3, 94.4, 82.2, 77.5, 76.2, 74.9, 73.4, 72.9, 72.1, 72.0, 70.5, 68.2, 62.2, 61.0, 59.0, 55.2, 49.0, 25.8, 18.2, 18.1, 13.0, −4.5, −4.8; HRMS (FAB): calcd for $C_{68}H_{94}O_{15}SeSi_2Cs$ $[M+Cs]^+$: 1419.4351, found 1419.4434.

FGH orthoester 106: $NaIO_4$ (1.103 g, 5.16 mmol) and $NaHCO_3$ (0.350 g, 4.13 mmol) were added to a solution of FGH alcohol **42** (0.610 g, 0.516 mmol) in MeOH/CH_2Cl_2/H_2O (3:2:1, 12 mL) and the resulting mixture was stirred at 25 °C for 2 h. The reaction mixture was 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 crude selenoxide was dissolved in toluene (12 mL) and transferred by cannula to six sealed tubes (2 mL each, 20 mL size). The flask was washed with toluene (2 × 12 mL) and the organics were transferred to the tubes (4 mL to each tube). Diisopropylamine (3 mL) and vinyl acetate (6 mL) were added to each tube, and the tubes were sealed and heated to 140 °C for 12 h. After cooling, the reaction mixture was concentrated and the residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes, 1% Et_3N) to afford FGH orthoester **106** (430 mg, 81% over two steps) as a white foam. **106**: $R_f=0.47$ (40% EtOAc in hexanes); IR (thin film): $\tilde{\nu}=3037$, 2943, 2861, 1614, 1514, 1463, 1250, 1110, 918, 836, 780, 733 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.36–7.21$ (m, 12H, ArH), 6.86 (d, $J=8.5$ Hz, 2H, PMB), 5.30 (s, 1H, G1), 4.87, 4.61 (AB, $J=11.7$ Hz, 2H, CH_2Ar), 4.78 (s, 1H, F1), 4.72, 4.43 (AB, $J=11.2$ Hz, 2H, CH_2Ar), 4.66, 4.51 (AB, $J=11.4$ Hz, 2H, CH_2Ar), 4.45 (ddd, $J=9.4$, 9.4, 4.5 Hz, 1H, G4), 4.24 (s, 1H, G2), 4.11 (dd, $J=9.6$, 4.6 Hz, 1H, G5), 4.04 (t, $J=8.5$ Hz, 1H, F4), 4.03–3.97 (m, 1H, H3), 3.83 (dd, $J=10.1$, 2.1 Hz, 1H, G3), 3.80–3.76 (m, 1H, H5), 3.78 (s, 3H, OMe), 3.77 (t, $J=10.1$ Hz, 1H, G5), 3.69 (dd, $J=10.6$, 2.4 Hz, 1H, F6), 3.67 (d, $J=2.4$ Hz, 1H, F2), 3.59 (dd, $J=10.6$, 5.9 Hz, 1H, F6), 3.54 (t, $J=10.3$ Hz, 1H, H5), 3.52 (s, 3H, OMe), 3.40–3.36 (m, 3H, F3, F5, H4), 3.32 (s, 3H, OMe), 2.07 (dd, $J=13.0$, 5.1 Hz, 1H, H2), 1.90 (dd, $J=13.0$, 10.6 Hz, 1H, H2), 1.06–0.97 (m, 21H, iPr$_3$Si), 0.90 (s, 9H, tBuSi), 0.10, 0.08 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=159.2$, 138.0, 137.9, 130.4, 129.3, 128.3, 128.1, 127.7, 127.5, 127.3, 119.6, 113.7, 96.4, 95.9, 82.2, 79.6, 77.8, 77.3, 76.3, 75.8, 73.2, 72.9, 72.4, 70.9, 70.7, 69.2, 67.9, 63.5, 63.0, 61.2, 58.9, 55.2, 40.2, 30.2, 29.6, 25.7, 18.2, 18.0, 12.0, −4.5, −4.8; HRMS (FAB): calcd for $C_{55}H_{84}O_{14}Si_2Cs$ $[M+Cs]^+$: 1157.4454, found 1157.4402.

FGH alcohol 107: nBu$_4$NF (1.18 mL, 1.0 M solution in THF, 1.18 mmol) was added to a solution of FGH orthoester **106** (1.10 g, 1.07 mmol) in THF (6 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 NH_4Cl (5 mL), diluted with CH_2Cl_2 (250 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced

pressure. The residue was purified by flash column chromatography (silica gel, 0 → 70% Et_2O in hexanes) to afford FGH alcohol **107** (0.886 g, 95%) as a white foam. **107**: $R_f = 0.58$ (100% Et_2O); $[\alpha]_D^{22} = -24.0$ ($c = 0.47$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3478, 2930, 2873, 1608, 1508, 1461, 1379, 1314, 1250, 1109, 1050, 916, 826, 785, 738\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta =$ 7.36–7.22 (m, 12H, ArH), 6.84 (d, $J = 8.6$ Hz, 2H, PMB), 5.25 (d, $J =$ 0.9 Hz, 1H, G1), 4.85, 4.57 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.74, 4.62 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.65 (s, 1H, F1), 4.64, 4.50 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.41 (ddd, $J = 10.6$, 10.6, 4.6 Hz, 1H, G4), 4.23 (s, 1H, G2), 4.10 (dd, $J = 9.6$, 4.6 Hz, 1H, G5), 3.97 (ddd, $J = 10.6$, 8.2, 5.3 Hz, 1H, H3), 3.86 (t, $J = 9.5$ Hz, 1H, F4), 3.80–3.72 (m, 2H, G3, H5), 3.77 (s, 3H, OMe), 3.70 (t, $J = 10.5$ Hz, 1H, G5), 3.67 (dd, $J = 10.7$, 3.8 Hz, 1H, F6), 3.60 (dd, $J =$ 10.6, 5.5 Hz, 1H, F6), 3.59 (s, 3H, OMe), 3.58–3.48 (br s, 1H, F2), 3.52 (t, $J = 11.2$ Hz, 1H, H5), 3.38–3.20 (m, 3H, H4, F3, F5), 3.26 (s, 3H, OMe), 2.67 (s, 1H, OH), 2.06 (dd, $J = 13.0$, 5.2 Hz, 1H, H2), 1.89 (dd, $J = 13.0$, 10.6 Hz, 1H, H2), 0.89 (s, 9H, *t*BuSi), −0.01, −0.02 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.2$, 137.8, 137.7, 130.3, 129.3, 128.5, 128.2, 128.0, 127.7, 127.6, 127.6, 125.4, 119.7, 113.7, 96.6, 96.3, 81.4, 79.6, 77.8, 77.4, 75.7, 74.9, 73.2, 72.9, 72.5, 71.9, 70.7, 69.2, 67.9, 63.7, 63.0, 61.7, 59.4, 55.2, 40.8, 30.2, 25.7, 17.9, −4.5, −4.8; HRMS (FAB): calcd for $C_{46}H_{64}O_{14}SiCs$ $[M+Cs]^+$: 1001.3120, found 1001.3167.

FGH benzoate 108: BzCl (75.0 μL, 0.648 mmol) was added to a solution of FGH alcohol **107** (0.469 g, 0.540 mmol), Et_3N (135 μL, 0.971 mmol) and 4-DMAP (13 mg, 0.108 mmol) in CH_2Cl_2 (3.0 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of MeOH (0.5 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 → 100% Et_2O in hexanes) to afford FGH benzoate **108** (0.510 g, 97%) as a white foam. **108**: $R_f = 0.44$ (60% Et_2O in hexanes); $[\alpha]_D^{22} = -45.5$ ($c = 0.32$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2931, 2896, 1725, 1614, 1508, 1455, 1255, 1102, 1037, 914, 832, 779, 732\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.07$ (d, $J = 7.1$ Hz, 2H, ArH), 7.68 (t, $J = 7.4$ Hz, 1H, ArH), 7.53 (t, $J = 7.6$ Hz, 2H, ArH), 7.46–7.20 (m, 12H, ArH), 6.93 (d, $J = 8.6$ Hz, 2H, PMB), 5.55 (t, $J = 9.3$ Hz, 1H, F4), 5.39 (d, $J = 1.2$ Hz, 1H, G1), 4.97, 4.68 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.84 (s, 1H, F1), 4.75, 4.62 (AB, $J = 12.7$ Hz, 2H, CH_2Ar), 4.75, 4.59 (AB, $J = 11.0$ Hz, 2H, CH_2Ar), 4.53 (ddd, $J = 10.4$, 10.4, 6.0 Hz, 1H, G4), 4.36 (br s, 1H, G2), 4.21 (dd, $J =$ 9.5, 4.6 Hz, 1H, G5), 4.09 (ddd, $J = 10.5$, 8.2, 5.1 Hz, 1H, H3), 3.92 (dd, $J =$ 10.0, 2.3 Hz, 1H, G3), 3.90–3.85 (m, 1H, H5), 3.87 (s, 3H, OMe), 3.83 (t, $J = 10.3$ Hz, 1H, G5), 3.74 (s, 3H, OMe), 3.73–3.56 (m, 6H, F2, F3, F5, F6, F6, H5), 3.46 (ddd, $J = 9.8$, 8.4, 4.7 Hz, 1H, H4), 3.33 (s, 3H, OMe), 2.15 (dd, $J = 13.0$, 5.2 Hz, 1H, H2), 2.00 (dd, $J = 13.0$, 10.7 Hz, 1H, H2), 0.99 (s, 9H, *t*BuSi), 0.19, 0.18 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.3, 159.2, 156.3, 137.8, 137.4, 133.1, 130.4, 129.7, 129.7, 129.4, 128.4, 128.3, 128.3, 127.8, 127.6, 127.6, 125.4, 119.7, 113.7, 96.7, 96.0, 80.0, 78.7, 78.0, 77.5, 75.7, 74.4, 73.3, 72.9, 71.9, 71.6, 70.7, 69.2, 68.9, 63.7, 63.0, 61.8, 59.3, 55.2, 40.8, 30.2, 25.7, 18.0, −4.5, −4.8$; HRMS (FAB): calcd for $C_{53}H_{68}O_{15}SiCs$ $[M+Cs]^+$: 1105.3382, found 1105.3333.

FGH alcohol 109: nBu$_4$NF (1.08 mL, 1.0 M solution in THF, 1.08 mmol) was added to a solution of FGH benzoate **108** (0.700 g, 0.719 mmol) and AcOH (8.0 μL, 0.144 mmol) in THF (4 mL) at 25 °C and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL), diluted with CH_2Cl_2 (250 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford FGH alcohol **109** (0.587 g, 95%) as a white foam. **109**: $R_f = 0.46$ (100% Et_2O); $[\alpha]_D^{22} = -46.3$ ($c = 0.30$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2908, 1725, 1602, 1514, 1361, 1265, 1096, 1043, 808, 712\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.99$ (d, $J = 7.2$ Hz, 2H, ArH), 7.59 (t, $J = 7.4$ Hz, 1H, ArH), 7.45 (t, $J = 7.7$ Hz, 2H, ArH), 7.36–7.16 (m, 12H, ArH), 6.88 (d, $J = 8.6$ Hz, 2H, PMB), 5.46 (t, $J = 9.5$ Hz, 1H, F4), 5.33 (s, 1H, G1), 4.88, 4.60 (AB, $J =$ 11.6 Hz, 2H, CH_2Ar), 4.76 (s, 1H, F1), 4.67, 4.54 (AB, $J = 12.4$ Hz, 2H, CH_2Ar), 4.62, 4.53 (AB, $J = 11.2$ Hz, 2H, CH_2Ar), 4.46 (ddd, $J = 10.5$, 10.5, 4.6 Hz, 1H, G4), 4.27 (br s, 1H, G2), 4.14 (dd, $J = 9.5$, 4.6 Hz, 1H, G5), 4.02 (ddd, $J = 12.3$, 8.8, 4.3 Hz, 1H, H3), 3.98 (dd, $J = 11.8$, 4.2 Hz, 1H, H5), 3.84 (dd, $J = 10.0$, 2.4 Hz, 1H, G3), 3.80 (s, 3H, OMe), 3.76 (t, $J = 10.4$ Hz, 1H, G5), 3.66–3.62 (m, 3H, F2, F3, F5), 3.64 (s, 3H, OMe), 3.61 (ddd, $J = 9.4$, 6.0, 3.7 Hz, 1H, H5), 3.54–3.51 (m, 2H, F6, F6), 3.41 (ddd, $J = 7.8$, 7.8, 4.2 Hz, 1H, H4), 3.25 (s, 3H, OMe), 2.64 (d, $J = 4.2$ Hz, 1H, OH), 2.30 (dd, $J = 13.1$, 4.8 Hz, 1H, H2), 1.94 (dd, $J = 13.1$, 9.4 Hz, 1H, H2); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.4, 159.5, 137.8, 137.4, 133.2, 129.9, 129.7, 129.7, 128.6, 127.8, 127.6, 119.8, 114.0, 96.2, 95.6, 79.7, 78.6, 77.5, 75.5, 74.4, 73.2, 72.0$ 71.9, 71.6 69.2, 69.0, 68.9, 65.8, 63.6, 62.7, 61.9, 59.3, 55.3, 37.9; HRMS (FAB): calcd for $C_{47}H_{54}O_{15}Cs$ $[M+Cs]^+$: 991.2517, found 991.2551.

FGH olefin 110: Martin sulfurane dehydrating agent (0.77 g, 1.14 mmol) was added to a solution of FGH alcohol **109** (0.245 g, 0.285 mmol) and Et_3N (2.0 μL, 0.014 mmol) in $CHCl_3$ (1.5 mL) at 25 °C and the resulting mixture was heated to 50 °C and stirred for 2 h. 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 FGH olefin **110** (0.204 g, 85%) as a white foam. **110**: $R_f = 0.27$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -40.3$ ($c = 1.02$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2924, 1727, 1265, 1113, 1044, 710\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 8.0$ Hz, 2H, ArH), 7.66 (t, $J = 7.3$ Hz, 1H, ArH), 7.53 (t, $J = 7.6$ Hz, 2H, ArH), 7.46–7.25 (m, 12H, ArH), 6.95 (d, $J = 8.6$ Hz, 2H, PMB), 6.27 (dd, $J = 10.0$, 3.6 Hz, 1H, H3), 5.87 (dd, $J = 10.0$, 1.1 Hz, 1H, H2), 5.54 (t, $J = 9.0$ Hz, 1H, F4), 5.41 (s, 1H, G1), 5.03, 4.72 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.84 (s, 1H, F1), 4.74, 4.61 (AB, $J = 12.5$ Hz, 2H, CH_2Ar), 4.64 (s, 2H, CH_2Ar), 4.54 (ddd, $J = 10.4$, 10.4, 4.6 Hz, 1H, G4), 4.36 (br s, 1H, G2), 4.32–4.14 (m, 2H, G5, H5), 4.00 (ddd, $J = 6.9$, 6.9, 2.9 Hz, 1H, H4), 3.96 (dd, $J = 9.9$, 2.2 Hz, 1H, G3), 3.87 (s, 3H, OMe), 3.84 (t, $J = 10.3$ Hz, 1H, G5), 3.74–3.67 (m, 4H, F2, F3, F5, H5), 3.71 (s, 3H, OMe), 3.61–3.58 (m, 2H, F6), 3.33 (s, 3H, OMe); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 165.3, 159.3, 137.8, 137.4, 133.1, 131.2, 130.1, 129.7, 129.4, 128.4, 128.3, 127.9, 127.7, 127.6, 127.5, 116.0, 113.8, 96.4, 95.6, 79.9, 78.6, 77.5, 75.4, 74.4, 73.2, 71.9, 71.6, 70.3, 68.9, 68.5, 67.0, 65.8, 61.8, 59.3, 55.2, 15.2$; HRMS (FAB): calcd for $C_{47}H_{52}O_{14}Cs$ $[M+Cs]^+$: 973.2411, found 973.2445.

FGH alcohol 111: K_2CO_3 (9.0 mg, 0.065 mmol) was added to a solution of FGH benzoate **110** (0.110 g, 0.131 mmol) in MeOH (1.0 mL) at 25 °C and the resulting mixture was stirred for 6 h. 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 FGH alcohol **111** (87 mg, 90%) as a white foam. **111**: $R_f = 0.43$ (100% Et_2O); $[\alpha]_D^{22} = -42.3$ ($c = 0.13$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3448, 2924, 1610, 1513, 1452, 1249, 1167, 1102, 1050\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.38–7.27$ (m, 12H, ArH), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 6.18 (dd, $J = 10.0$, 3.7 Hz, 1H, H3), 5.78 (dd, $J = 10.0$, 1.0 Hz, 1H, H2), 5.29 (d, $J = 1.1$ Hz, 1H, G1), 5.01 (s, 1H, F1), 4.94, 4.62 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.77, 4.66 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.68 (s, 2H, CH_2Ar), 4.45 (ddd, $J = 10.5$, 10.5, 4.6 Hz, 1H, G4), 4.26 (br s, 1H, G2), 4.16–4.06 (m, 3H, G5, H5, H5), 3.92 (ddd, $J = 3.9$, 3.9, 3.9 Hz, 1H, H4), 3.88 (t, $J = 9.4$ Hz, 1H, F4), 3.84 (dd, $J = 10.0$, 2.4 Hz, 1H, G3), 3.80 (s, 3H, OMe), 3.73 (t, $J = 10.2$ Hz, 1H, G5), 3.69 (dd, $J = 10.0$, 4.0 Hz, 1H, F6), 3.62 (dd, $J = 10.0$, 5.5 Hz, 1H, F6), 3.58 (s, 3H, OMe), 3.56 (d, $J = 2.9$ Hz, 1H, F2), 3.37 (s, 3H, OMe), 3.36–3.33 (m, 2H, F3, F5), 2.68 (s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 137.9, 131.3, 130.2, 129.4, 128.6, 128.4, 128.0, 127.8, 127.7, 113.9, 96.4, 95.9, 81.5, 79.4, 75.6, 74.9, 73.2, 72.7, 70.4, 68.6, 68.2, 68.0, 67.1, 65.8, 64.4, 61.8, 59.5, 55.3, 46.5$; HRMS (FAB): calcd for $C_{40}H_{48}O_{13}Cs$ $[M+Cs]^+$: 869.2149, found 869.2118.

FGH TBS ether 112: NaH (28 mg, 0.709 mmol) was added to a solution of FGH alcohol **111** (87 mg, 0.118 mmol) and [18]crown-6 (50 mg, 0.118 mmol) in THF (0.6 mL) at 0 °C and the resulting mixture was stirred for 15 min. TBSCl (38 mg, 0.236 mmol) was added at 10 min intervals (6 ×) and the resulting mixture was stirred for 1 h. The reaction mixture was quenched by slow addition of saturated aqueous $NaHCO_3$ (1 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 → 70% Et_2O in hexanes) to afford FGH TBS ether **112** (81 mg, 80%) as a white foam. **112**: $R_f = 0.59$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -24.6$ ($c =$ 0.23, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2926, 1611, 1513, 1462, 1250, 1110, 1032, 837, 779\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.37–7.25$ (m, 12H, ArH), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 6.16 (dd, $J = 9.8$, 3.2 Hz, 1H, H3), 5.76 (dd, $J = 10.1$, 1.0 Hz, 1H, H2), 5.32 (s, 1H, G1), 4.92, 4.63 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.78 (s, 1H, F1), 4.65, 4.61 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.54 (s, 2H, CH_2Ar), 4.42 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.24 (br s, 1H, G2), 4.12–4.03 (m, 3H, G5, H5, H5), 3.91 (br t, $J = 3.8$ Hz, 1H, H4), 3.86 (t, $J =$ 8.9 Hz, 1H, F4), 3.82 (dd, $J = 10.0$, 2.4 Hz, 1H, G3), 3.79 (s, 3H, OMe), 3.69 (t, $J = 10.5$ Hz, 1H, G5), 3.60 (br d, $J = 10.3$ Hz, 1H, F6), 3.54–3.47 (m, 2H, F2, F6), 3.51 (s, 3H, OMe), 3.31 (s, 3H, OMe), 3.30–3.25 (m, 2H, F3, F5),

0947-6539/00/0617-3142 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

0.88 (s, 9H, *t*BuSi), 0.04, 0.03 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.9, 137.5, 131.2, 129.4, 128.3, 128.3, 127.9, 127.8, 127.7, 127.6, 113.8, 96.2, 95.9, 82.1, 80.0, 75.3, 73.2, 71.6, 71.3, 70.3, 68.6, 67.5, 67.0, 63.6, 59.1, 55.3, 38.7, 29.7, 25.9, 18.1, −3.7, −5.2; HRMS (FAB): calcd for $C_{46}H_{62}O_{13}SiCs$ $[M+Cs]^+$: 983.3014, found 983.3036.

FGH *cis*-diol 113 from 112: OsO_4 (0.10 mL, 2.5% solution in *t*BuOH) was added to a solution of FGH olefin **112** (201 mg, 0.106 mmol), NMO (59.0 mg, 0.526 mmol), and quinuclidine (27.0 mg, 0.106 mmol) in acetone/H_2O (10:1, 1 mL) and the reaction mixture was stirred for 36 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 FGH diol **113** (144 mg, 70%, ca. 8:1 mixture of diastereoisomers) as a white foam, identical to that described below.

FGH *cis*-diol 113 from 134: NaOH (4.0 mg, 0.089 mmol) was added to a solution of FGH TBS ether **134** (163 mg, 0.179 mmol) in MeOH/Et_2O (1:1, 1.0 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 → 100% Et_2O in hexanes) to afford FGH *cis*-diol **113** (150 mg, 95%) as a white foam. **113**: R_f = 0.32 (70% EtOAc in hexanes); $[\alpha]_D^{22} = -24.0$ (c = 0.12, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3453, 2929, 1612, 1514, 1464, 1382, 1250, 1108, 838, 781, 737 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.39–7.24 (m, 12H, ArH), 6.88 (d, J = 8.4 Hz, 2H, PMB), 5.30 (s, 1H, G1), 4.88, 4.61 (AB, J = 11.8 Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.64, 4.58 (AB, J = 11.8 Hz, 2H, CH_2Ar), 4.58, 4.54 (AB, J = 10.1 Hz, 2H, CH_2Ar), 4.44 (ddd, J = 10.5, 10.5, 4.6 Hz, 1H, G4), 4.26 (br s, 1H, G2), 4.13 (dd, J = 9.5, 4.6 Hz, 1H, G5), 4.06–4.03 (m, 2H, H2, H3), 3.97 (dd, J = 12.0, 3.2 Hz, 1H, H5), 3.89 (dd, J = 10.2, 2.2 Hz, 1H, G3), 3.73 (dd, J = 12.5, 5.8 Hz, 1H, H5), 3.86 (t, J = 9.0 Hz, 1H, F4), 3.80 (s, 3H, OMe), 3.74 (t, J = 10.5 Hz, 1H, G5), 3.68–3.66 (m, 1H, H4), 3.61 (dd, J = 10.6, 1.8 Hz, 1H, F6), 3.51 (s, 3H, OMe), 3.53 (dd, J = 10.5, 5.6 Hz, 1H, F6), 3.51 (br s, 1H, F2), 3.33 (s, 3H, OMe), 3.33–3.25 (m, 2H, F3, F5), 2.71 (d, J = 6.5 Hz, 1H, OH), 2.56 (d, J = 5.4 Hz, 1H, OH), 0.86 (s, 9H, *t*BuSi), 0.04, 0.03 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.4, 157.7, 137.8, 129.8, 129.4, 128.3, 128.3, 127.7, 127.7, 119.5, 113.9, 95.9, 82.9, 80.7, 77.1, 77.1, 75.6, 74.7, 73.2, 71.8, 71.5, 71.3, 69.6, 69.3, 63.3, 62.3, 61.7, 59.0, 55.2, 30.2, 25.9, 18.1, −3.8, −5.2; HRMS (MALDI): calcd for $C_{46}H_{64}O_{15}SiCs$ $[M+Cs]^+$: 1017.3069, found 1017.3030.

FGH benzoate 114: nBu$_2$SnO (47 mg, 0.189 mmol) was added to a solution of FGH diol **113** (152 mg, 0.172 mmol) in MeOH (3.0 mL) and the resulting mixture was refluxed for 3 h. The reaction mixture was cooled and the solvents were removed under reduced pressure. The residue was azeotroped with 1,4-dioxane (2 × 2 mL) and then pumped under high vacuum for 1 h. The residue was dissolved in 1,4-dioxane (1.0 mL) and cooled to 15 °C. BzCl (31 μL, 0.257 mmol) was added and the reaction mixture was stirred for 0.5 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), 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 FGH benzoate **114** (135 mg of H3 and 30 mg of H2, 97%, 5:1 mixture of H3:H2 regioisomers) as a white foam. **114**: R_f = 0.24 (40% EtOAc in hexanes); $[\alpha]_D^{22} = -17.2$ (c = 0.17, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3438, 2929, 2896, 1719, 1608, 1514, 1455, 1373, 1261, 1096, 1043, 838, 785, 720 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.08 (d, J = 7.2 Hz, 2H, ArH), 7.61 (t, J = 7.4 Hz, 1H, ArH), 7.47 (t, J = 7.9 Hz, 2H, ArH), 7.41–7.25 (m, 12H, ArH), 6.83 (d, J = 8.7 Hz, 2H, PMB), 5.55 (dd, J = 5.8, 3.8 Hz, 1H, H3), 5.31 (d, J = 0.7 Hz, 1H, G1), 4.93, 4.63 (AB, J = 11.7 Hz, 2H, CH_2Ar), 4.68 (s, 1H, F1), 4.63, 4.56 (AB, J = 11.7 Hz, 2H, CH_2Ar), 4.62 (s, 2H, CH_2Ar), 4.51 (ddd, J = 10.6, 10.6, 4.6 Hz, 1H, G4), 4.29 (br s, 2H, G2, H2), 4.17 (dd, J = 9.5, 4.6 Hz, 1H, G5), 4.05 (dd, J = 12.1, 3.1 Hz, 1H, H5), 3.92 (dd, J = 10.2, 2.3 Hz, 1H, G3), 3.86 (t, J = 9.1 Hz, 1H, F4), 3.86–3.84 (m, 1H, H4), 3.81 (dd, J = 12.1, 5.4 Hz, 1H, H5), 3.78 (s, 3H, OMe), 3.75 (t, J = 10.3 Hz, 1H, G5), 3.62 (dd, J = 10.6, 1.8 Hz, 1H, F6), 3.54 (dd, J = 10.6, 5.4 Hz, 1H, F6), 3.52 (s, 3H, OMe), 3.50 (d, J = 2.6 Hz, 1H, F2), 3.33 (s, 3H, OMe), 3.30–3.27 (m, 2H, F3, F5), 2.36 (s, 1H, OH), 0.86 (s, 9H, *t*BuSi), 0.04, 0.02 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.6, 159.4, 137.9, 137.8, 133.4, 130.2, 129.8, 129.6, 129.6, 129.5, 129.4, 128.5, 128.4, 128.3, 127.8, 127.6, 127.6, 126.9, 119.2, 113.8, 95.8, 95.7, 82.2, 80.9, 75.6, 73.3, 72.7, 71.8, 71.8, 71.3, 71.2, 69.4, 68.5, 67.5, 65.8, 63.4, 63.0, 61.8, 59.1, 55.2, 25.9, 18.1, 15.2, −3.7, −5.1; HRMS (MALDI): calcd for $C_{53}H_{68}O_{16}SiNa$ $[M+Na]^+$: 1011.4174, found 1011.4205.

FGH inverted alcohol 115: Dess–Martin periodinane (73 mg, 0.172 mmol) was added to a solution of FGH alcohol **114** (85 mg, 0.086 mmol) and $NaHCO_3$ (144 mg, 1.719 mmol) in CH_2Cl_2 (0.5 mL) at 25 °C and the resulting mixture was 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 to afford the crude FGH ketone (85 mg) as a white foam. Crude ketone: R_f = 0.35 (60% EtOAc in hexanes); IR (thin film): $\tilde{\nu}$ = 2926, 2872, 1766, 1719, 1608, 1514, 1467, 1367, 1249, 1102, 1038, 838 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.06 (d, J = 7.4 Hz, 2H, ArH), 7.61 (t, J = 7.4 Hz, 1H, ArH), 7.48 (t, J = 7.9 Hz, 2H, ArH), 7.41–7.25 (m, 10H, ArH), 7.17 (d, J = 8.5 Hz, 2H, PMB), 6.80 (d, J = 8.5 Hz, 2H, PMB), 5.97 (d, J = 9.6 Hz, 1H, H3), 5.36 (s, 1H, G1), 4.84, 4.64 (AB, J = 11.6 Hz, 2H, CH_2Ar), 4.68 (s, 1H, F1), 4.62–4.57 (m, 4H, CH_2Ar), 4.49 (ddd, J = 10.5, 10.5, 4.6 Hz, 1H, G4), 4.29 (br s, 2H, G2), 4.14 (dd, J = 9.8, 4.8 Hz, 1H, G5), 4.11 (dd, J = 9.7, 6.0 Hz, 1H, H5), 4.07–4.03 (m, 1H, H4), 3.88 (dd, J = 10.3, 2.4 Hz, 1H, G3), 3.86 (t, J = 9.1 Hz, 1H, F4), 3.81–3.75 (m, 2H, G5, H5), 3.77 (s, 3H, OMe), 3.61 (dd, J = 10.5, 1.8 Hz, 1H, F6), 3.55 (dd, J = 10.5, 5.5 Hz, 1H, F6), 3.51 (s, 3H, OMe), 3.46 (d, J = 3.1 Hz, 1H, F2), 3.32 (s, 3H, OMe), 3.31–3.26 (m, 2H, F3, F5), 0.86 (s, 9H, *t*BuSi), 0.04 (s, 6H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 188.8, 165.1, 159.6, 137.8, 137.6, 133.0, 130.0, 129.6, 129.1, 129.0, 128.5, 128.4, 128.3, 127.8, 127.7, 127.5, 113.9, 95.6, 95.3, 82.1, 80.4, 78.6, 76.5, 75.9, 73.4, 73.2, 71.5, 71.3, 70.6, 67.5, 63.1, 62.7, 62.0, 59.0, 55.2, 53.4, 30.3, 29.7, 25.9, 18.1, −3.7, −5.1; HRMS (FAB): calcd for $C_{53}H_{66}O_{16}SiCs$ $[M+Cs]^+$: 1119.3174, found 1119.3133. The above crude ketone was azeotroped with benzene (2 × 2 mL) and then pumped under high vacuum for 1 h. The residue was dissolved in Et_2O (1.0 mL) and cooled to −10 °C. Li(*t*BuO)$_3$AlH (95 μL, 1.0 M solution in THF, 0.095 mmol) was added and the reaction mixture was stirred for 1 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (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), 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 FGH inverted alcohol **115** (68 mg, 80% over two steps) as a white foam. **115**: R_f = 0.34 (50% EtOAc in hexanes); $[\alpha]_D^{22} = -19.2$ (c = 0.12, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3448, 2943, 2861, 1725, 1614, 1514, 1455, 1372, 1308, 1255, 1108, 1079, 1032, 843, 779 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04 (d, J = 7.1 Hz, 2H, ArH), 7.61 (t, J = 7.4 Hz, 1H, ArH), 7.47 (t, J = 7.9 Hz, 2H, ArH), 7.37–7.29 (m, 10H, ArH), 7.12 (d, J = 8.6 Hz, 2H, PMB), 6.75 (d, J = 8.6 Hz, 2H, PMB), 5.43 (t, J = 9.2 Hz, 1H, H3), 5.34 (s, 1H, G1), 4.87, 4.66 (AB, J = 11.6 Hz, 2H, CH_2Ar), 4.67 (s, 1H, F1), 4.63, 4.56 (AB, J = 11.5 Hz, 2H, CH_2Ar), 4.53, 4.50 (AB, J = 11.0 Hz, 2H, CH_2Ar), 4.48 (ddd, J = 10.5, 10.5, 6.1 Hz, 1H, G4), 4.30 (br s, 1H, G2), 4.11 (dd, J = 9.6, 4.5 Hz, 1H, G5), 4.00 (dd, J = 10.2, 2.3 Hz, 1H, G3), 3.90 (dd, J = 11.4, 5.4 Hz, 1H, H5), 3.87 (t, J = 9.0 Hz, 1H, F4), 3.82–3.76 (m, 3H, G5, H2, H4), 3.76 (s, 3H, OMe), 3.69 (t, J = 11.0 Hz, 1H, H5), 3.62 (dd, J = 10.4, 1.8 Hz, 1H, F6), 3.55 (dd, J = 10.8, 5.3 Hz, 1H, F6), 3.52 (s, 3H, OMe), 3.49 (br s, 1H, F2), 3.33 (s, 3H, OMe), 3.29–3.27 (m, 2H, F3, F5), 2.49 (d, J = 8.3 Hz, 1H, OH), 0.86 (s, 9H, *t*BuSi), 0.04, 0.03 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.1, 159.4, 137.9, 137.8, 133.4, 129.9, 129.5, 129.5, 128.4, 128.3, 127.8, 127.7, 127.7, 127.6, 119.3, 113.8, 95.7, 82.0, 81.7, 77.1, 76.7, 75.8, 73.6, 73.4, 72.7, 71.9, 71.4, 71.4, 69.7, 67.5, 63.3, 62.5, 61.8, 59.0, 55.2, 29.7, 25.9, 18.1, −3.7, −5.1; HRMS (FAB): calcd for $C_{53}H_{68}O_{16}SiNa$ $[M+Na]^+$: 1011.4174, found 1011.4202.

FGH *trans*-diol 116: NaOH (2.0 mg, 0.061 mmol) was added to a solution of FGH benzoate **115** (120 mg, 0.121 mmol) in MeOH (1.0 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 (2 mL), diluted with CH_2Cl_2 (100 mL) and washed with brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford FGH *trans*-diol **116** (105 mg, 98%) as a white foam. **116**: R_f = 0.34 (60% EtOAc in hexanes); $[\alpha]_D^{22} = -22.0$ (c = 0.24, $CHCl_3$); IR (thin film): $\tilde{\nu}$ = 3460, 2931, 2884, 1519, 1455, 1373, 1249, 1085, 832, 785, 732 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.38–7.25 (m,

12H, ArH), 6.88 (d, $J=8.6$ Hz, 2H, PMB), 5.31 (d, $J=0.7$ Hz, 1H, G1), 4.84, 4.63 (AB, $J=11.6$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.63, 4.58 (AB, $J=11.8$ Hz, 2H, CH_2Ar), 4.61, 4.56 (AB, $J=10.2$ Hz, 2H, CH_2Ar), 4.46 (ddd, $J=10.6$, 10.6, 4.6 Hz, 1H, G4), 4.27 (br s, 1H, G2), 4.12 (dd, $J=9.5$, 4.6 Hz, 1H, G5), 3.98 (dd, $J=10.2$, 2.4 Hz, 1H, G3), 3.86 (t, $J=9.0$ Hz, 1H, F4), 3.84–3.78 (m, 2H, H3, H5), 3.80 (s, 3H, OMe), 3.79 (t, $J=10.3$ Hz, 1H, G5), 3.76 (dd, $J=9.0$, 5.5 Hz, 1H, H2), 3.60 (dd, $J=10.0$, 1.9 Hz, 1H, F6), 3.55 (t, $J=10.4$ Hz, 1H, H5), 3.54–3.51 (m, 3H, F2, F6, H4), 3.51 (s, 3H, OMe), 3.32 (s, 3H, OMe), 3.30–3.28 (m, 2H, F3, F5), 2.67 (d, $J=$ 2.6 Hz, 1H, OH), 2.34 (d, $J=5.6$ Hz, 1H, OH), 0.82 (s, 9H, *t*BuSi), 0.04, 0.00 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=159.5$, 137.9, 137.8, 130.5, 129.8, 129.6, 128.3, 128.3, 127.7, 127.7, 127.7, 127.7, 127.6, 119.2, 114.0, 95.8, 82.1, 81.4, 77.2 76.4, 75.6, 74.8, 73.3, 72.5, 72.3, 71.5, 71.3, 69.5, 67.5, 63.3, 62.5, 61.8, 59.0, 55.2, 29.7, 25.9, 18.1, −3.7, −5.2; HRMS (MALDI): calcd for $C_{46}H_{64}O_{15}SiNa$ $[M+Na]^+$: 907.3912, found 907.3891.

FGH methylene acetal 117: *n*Bu_4NBr (11 mg, 0.033 mmol) was added to a 1:1 mixture of CH_2Br_2 and 50% aqueous NaOH (4 mL) and the resulting mixture was heated to 65 °C and stirred vigorously. A solution of FGH diol **116** (10 mg, 0.011 mmol) in CH_2Br_2 (1.0 mL) was added very slowly, dropwise to the CH_2Br_2/NaOH mixture with vigorous stirring, over 1 h. After completion of the addition, the resulting mixture was stirred for 1 h and then the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% EtOAc in hexanes) to afford FGH methylene acetal **117** (9.1 mg, 90%) as a white foam. **117**: $R_f=0.59$ (silica gel, 60% Et_2O in hexanes); $[\alpha]_D^{22}=-79.2$ ($c=0.27$, $CHCl_3$); IR (thin film): $\tilde{\nu}=2919$, 2861, 1461, 1361, 1255, 1091, 1044, 838, 779 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.41-7.25$ (m, 12H, ArH), 6.88 (d, $J=$ 8.6 Hz, 2H, PMB), 5.32 (d, $J=1.0$ Hz, 1H, G1), 5.12 (s, 1H, OCH_2O), 5.10 (s, 1H, OCH_2O), 4.83, 4.58 (AB, $J=11.6$ Hz, 2H, CH_2Ar), 4.78, 4.56 (AB, $J=11.3$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.64, 4.62 (AB, $J=11.1$ Hz, 2H, CH_2Ar), 4.50 (ddd, $J=10.5$, 10.5, 4.5 Hz, 1H, G4), 4.27 (br s, 1H, G2), 4.12 (dd, $J=9.6$, 4.6 Hz, 1H, G5), 4.01 (dd, $J=10.2$, 2.4 Hz, 1H, G3), 3.96 (dd, $J=11.3$, 5.2 Hz, 1H, H5), 3.91 (t, $J=9.3$ Hz, 1H, H3), 3.91–3.89 (m, 1H, H4), 3.88 (t, $J=10.7$ Hz, 1H, F4), 3.80 (s, 3H, OMe), 3.78 (t, $J=10.1$ Hz, 1H, G5), 3.61 (dd, $J=10.6$, 1.9 Hz, 1H, F6), 3.55 (dd, $J=10.6$, 5.5 Hz, 1H, F6), 3.53 (s, 3H, OMe), 3.53–3.48 (m, 2H, F2, H5), 3.45 (d, $J=9.3$ Hz, 1H, H2), 3.32 (s, 3H, OMe), 3.31–3.26 (m, 2H, F3, F5), 0.86 (s, 9H, *t*BuSi), 0.05, 0.04 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=159.4$, 137.9, 137.7, 129.7, 129.5, 128.3, 127.8, 127.7, 127.7, 127.6, 119.0, 113.9, 96.6, 96.0, 96.0, 82.1, 81.1, 80.2, 77.1, 77.1, 75.7, 75.0, 74.9, 73.3, 72.0, 71.5, 71.3, 69.7, 67.5, 65.8, 64.8, 63.3, 61.8, 59.0, 55.2, 29.7, 25.9, 18.1, 15.2, −3.7, −5.7; HRMS (MALDI): calcd for $C_{47}H_{64}O_{15}SiNa$ $[M+Na]^+$: 919.3912, found 919.3912.

FGH alcohol 118: DDQ (30 mg, 0.134 mmol) was added to a solution of FGH PMB ether **117** (80 mg, 0.089 mmol) in CH_2Cl_2/buffer solution (pH 7) (10:1, 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 → 100% Et_2O in hexanes) to afford FGH alcohol **118** (59 mg, 85%) as a white foam. **118**: $R_f=0.29$ (silica gel, 80% Et_2O in hexanes); $[\alpha]_D^{22}=-11.0$ ($c=0.01$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3475$, 2928, 2884, 1455, 1373, 1320, 1255, 1108, 1044, 838, 773 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.39-7.26$ (m, 10H, ArH), 5.33 (s, 1H, G1), 5.15 (s, 1H, OCH_2O), 5.10 (s, 1H, OCH_2O), 4.84, 4.65 (AB, $J=11.6$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.63, 4.58 (AB, $J=11.8$ Hz, 2H, CH_2Ar), 4.52 (ddd, $J=$ 10.6, 10.6, 4.6 Hz, 1H, G4), 4.30 (br s, 1H, G2), 4.15–4.10 (m, 2H, G5, H3), 4.01 (dd, $J=10.2$, 2.3 Hz, 1H, G3), 3.98 (dd, $J=11.4$, 5.5 Hz, 1H, H5), 3.87 (t, $J=9.1$ Hz, 1H, F4), 3.79 (d, $J=10.1$ Hz, 1H, H2), 3.74 (t, $J=9.6$ Hz, 1H, G5), 3.61 (dd, $J=10.3$, 1.3 Hz, 1H, F6), 3.55 (dd, $J=10.3$, 5.4 Hz, 1H, F6), 3.53 (s, 3H, OMe), 3.52–3.37 (m, 2H, F2, H4), 3.45 (t, $J=9.6$ Hz, 1H, H5), 3.33 (s, 3H, OMe), 3.32–3.27 (m, 2H, F3, F5), 2.73 (br s, 1H, OH), 0.86 (s, 9H, *t*BuSi), 0.05, 0.04 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=137.8$, 137.7, 128.3, 127.7, 127.7, 127.5, 119.1, 96.5, 96.0, 95.9, 82.0, 81.0, 80.2, 77.0, 75.7, 74.6, 73.2, 71.4, 71.3, 69.7, 69.0, 67.4, 66.2, 63.3, 61.7, 59.0, 30.2, 29.6, 25.9, 18.1, −3.7, −5.2; HRMS (MALDI): calcd for $C_{39}H_{56}O_{14}SiNa$ $[M+Na]^+$: 799.3337, found 799.3426.

$FGHA_2$ ester 119: NaH (4.0 mg, 0.094 mmol) was added to a solution of FGH alcohol **118** (61 mg, 0.079 mmol) in THF (0.2 mL) at 0 °C. The resulting mixture was stirred for 5 min and then A_2 aromatic acyl fluoride **5** (41 mg, 0.118 mmol, dissolved in THF (0.2 mL)), was added dropwise. The resulting reaction mixture was warmed to 25 °C and stirred for 2 h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (1 mL), diluted with CH_2Cl_2 (100 mL), and washed with brine (10 mL). The organic layer was dried (Na_2SO_4), and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 0 → 100% Et_2O in hexanes) to afford $FGHA_2$ ester **119** (83 mg, 96%) as a white foam. **119**: $R_f=0.58$ (80% Et_2O in hexanes); $[\alpha]_D^{22}=-17.6$ ($c=0.25$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3025$, 2926, 2872, 1731, 1602, 1449, 1261, 1149, 1102, 1043, 832, 779, 738, 697 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.41-7.24$ (m, 20H, ArH), 6.43 (s, 2H, ArH (A_2)), 5.44 (ddd, $J=9.8$, 9.8, 5.5 Hz, 1H, H4), 5.35 (s, 1H, G1), 5.18 (s, 1H, OCH_2O), 5.05 (s, 1H, OCH_2O), 5.03 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.80, 4.62 (AB, $J=11.7$ Hz, 2H, CH_2Ar), 4.69 (s, 1H, F1), 4.66, 4.61 (AB, $J=11.8$ Hz, 2H, CH_2Ar), 4.55 (ddd, $J=10.6$, 10.6, 4.6 Hz, 1H, G4), 4.30 (br s, 1H, G2), 4.16 (dd, $J=9.6$, 4.6 Hz, 1H, G5), 4.13 (dd, $J=$ 11.5, 5.6 Hz, 1H, H5), 4.05 (dd, $J=10.2$, 2.4 Hz, 1H, G3), 3.95 (t, $J=9.8$ Hz, 1H, H3), 3.90 (t, $J=9.1$ Hz, 1H, F4), 3.81 (t, $J=10.3$ Hz, 1H, G5), 3.63 (dd, $J=9.1$, 1.8 Hz, 1H, F6), 3.62 (d, $J=9.4$ Hz, 1H, H2), 3.59–3.52 (m, 3H, F2, F6, H5), 3.56 (s, 3H, OMe), 3.34 (s, 3H, OMe), 3.33–3.29 (m, 2H, F3, F5), 2.34 (s, 3H, Me (A_2)), 0.89 (s, 9H, *t*BuSi), 0.07 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=166.8$, 160.6, 157.3, 138.7, 137.8, 137.6, 136.3, 136.3, 128.6, 128.4, 128.3, 128.3, 128.1, 127.8, 127.7, 127.7, 127.4, 127.4, 127.0, 119.0, 115.8, 108.1, 98.2, 96.7, 96.1, 95.9, 82.0, 81.0, 77.4, 77.0, 75.7, 74.9, 73.1, 71.4, 71.3, 70.3, 70.1, 70.0, 69.7, 67.4, 63.4, 63.2, 61.7, 59.0, 31.5, 29.6, 25.9, 22.6, 20.0, 18.1, 14.1, −3.7, −5.2; HRMS (FAB): calcd for $C_{61}H_{74}O_{17}SiNa$ $[M+Na]^+$: 1129.4695, found 1129.4632.

$FGHA_2$ alcohol 2: *n*Bu_4NF (96 μL, 1.0 M solution in THF, 0.096 mmol) was added to a solution of FGH TBS ether **119** (89 mg, 0.080 mmol) in THF (0.5 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 (2 mL), diluted with CH_2Cl_2 (150 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 → 80% EtOAc in hexanes) to afford $FGHA_2$ alcohol **2** (72 mg, 91%) as a white foam. **2**: $R_f=0.21$ (60% EtOAc in hexanes); $[\alpha]_D^{22}=-5.7$ ($c=$ 0.14, $CHCl_3$); IR (thin film): $\tilde{\nu}=3448$, 2955, 2919, 2872, 1725, 1602, 1449, 1378, 1255, 1155, 1108, 1049, 932, 738 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.39-7.23$ (m, 20H, ArH), 6.43 (s, 2H, ArH (A_2)), 5.44 (ddd, $J=9.7$, 9.7, 5.5 Hz, 1H, H4), 5.33 (d, $J=0.8$ Hz, 1H, G1), 5.18 (s, 1H, OCH_2O), 5.05 (s, 1H, OCH_2O), 5.02 (s, 2H, CH_2Ar), 5.00 (s, 2H, CH_2Ar), 4.77, 4.61 (AB, $J=$ 11.7 Hz, 2H, CH_2Ar), 4.75, 4.66 (AB, $J=11.9$ Hz, 2H, CH_2Ar), 4.69 (s, 1H, F1), 4.54 (ddd, $J=10.5$, 10.5, 4.5 Hz, 1H, G4), 4.29 (br s, 1H, G2), 4.18 (dd, $J=9.7$, 5.1 Hz, 1H, G5), 4.12 (dd, $J=11.3$, 5.4 Hz, 1H, H5), 4.05 (dd, $J=$ 10.2, 5.4 Hz, 1H, G3), 3.94 (t, $J=9.8$ Hz, 1H, H3), 3.88 (t, $J=9.5$ Hz, 1H, F4), 3.82 (dd, $J=10.6$, 10.6 Hz, 1H, G5), 3.70 (dd, $J=10.5$, 3.7 Hz, 1H, F6), 3.63 (dd, $J=10.5$, 5.1 Hz, 1H, F6), 3.61–3.59 (m, 2H, F2, H2), 3.60 (s, 3H, OMe), 3.56 (dd, $J=11.3$, 9.7 Hz, 1H, H5), 3.37 (s, 3H, OMe), 3.36–3.34 (m, 2H, F3, F5), 2.32 (s, 3H, Me (A_2)), 2.12 (br s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=166.8$, 160.6, 157.3, 138.7, 137.7, 137.5, 136.3, 136.3, 128.6, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.5, 127.4, 127.0, 119.1, 115.8, 108.1, 98.2, 96.7, 96.0, 96.0, 81.3, 81.0, 77.4, 75.6, 74.9, 73.2, 72.4, 71.8, 70.3, 70.1, 70.1, 69.6, 67.8, 63.4, 63.4, 61.8, 59.3, 53.8, 29.6, 29.6, 20.0, 14.1, 14.0; HRMS (FAB): calcd for $C_{55}H_{60}O_{17}Na$ $[M+Na]^+$: 1015.3728, found 1015.3735.

FGH diol 120: *n*Bu_4NF (0.38 mL, 1.0 M solution in THF, 0.38 mmol) was added quickly to a solution of FGH alcohol **42** (0.43 g, 0.36 mmol) and 4 Å MS in THF (2.5 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 15 min. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (5 mL), diluted with CH_2Cl_2 (100 mL) and washed with brine (2 × 5 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 FGH diol **120** (0.27 g, 70%) as a white foam, and recovered starting material (0.06 g, 15%). **120**: $R_f=0.14$ (70% Et_2O in hexanes); $[\alpha]_D^{22}=$ −24.6 ($c=2.31$, $CHCl_3$); IR (thin film): $\tilde{\nu}=3456$, 2938, 2865, 1613, 1514, 1454, 1249, 1112, 1036, 742 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.59-$ 7.57 (m, 2H, ArH), 7.37–7.23 (m, 13H, ArH), 7.21 (d, $J=8.6$ Hz, 2H, PMB), 6.85 (d, $J=8.6$ Hz, 2H, PMB), 5.24 (d, $J=2.0$ Hz, 1H, G1), 4.91 (d, $J=6.7$ Hz, 1H, H1), 4.79, 4.71 (AB, $J=12.0$ Hz, 2H, CH_2Ar), 4.72 (s, 1H,

0947-6539/00/0617-3144 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

F1), 4.71, 4.41 (AB, $J = 11.1$ Hz, 2H, CH_2Ar), 4.55, 4.47 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.07 (brs, 1H, H3), 4.00 (t, $J = 8.7$ Hz, 1H, F4), 3.95 (ddd, $J =$ 9.5, 9.5, 5.3 Hz, 1H, G4), 3.93–3.91 (m, 1H, G2), 3.90 (dd, $J = 10.5$, 2.8 Hz, 1H, H5), 3.87–3.85 (m, 1H, G3), 3.79 (s, 3H, OMe), 3.73 (dd, $J = 11.3$, 5.5 Hz, 1H, G5), 3.70 (dd, $J = 11.3$, 2.7 Hz, 1H, F6), 3.68 (dd, $J = 6.7$, 3.4 Hz, 1H, H2), 3.63 (d, $J = 2.7$ Hz, 1H, OH), 3.59 (dd, $J = 10.5$, 6.1 Hz, 1H, F6), 3.56 (brd, $J = 3.2$ Hz, 1H, H5), 3.50 (s, 3H, OMe), 3.43 (ddd, $J = 7.7$, 7.7, 4.5 Hz, 1H, H4), 3.38 (t, $J = 10.7$ Hz, 1H, G5), 3.38–3.34 (m, 2H, F3, F5), 3.32 (s, 3H, OMe), 2.28 (brs, 1H, OH), 1.03–0.96 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3$, 138.2, 138.0, 133.6, 129.8, 129.3, 129.2, 128.7, 128.3, 128.1, 127.7, 127.6, 127.5, 127.5, 127.4, 113.9, 100.8, 95.5, 94.8, 82.3, 77.4, 77.3, 76.3, 73.6, 71.9, 71.4, 70.6, 70.0, 69.4, 68.1, 65.8, 62.9, 61.5, 60.6, 59.0, 55.2, 50.5, 30.3, 18.2, 18.1, 13.0; HRMS (FAB): calcd for $C_{55}H_{76}O_{14}SeSiCs$ $[M+Cs]^+$: 1201.3224, found 1201.3164.

FGH allylic orthoester 121: $NaIO_4$ (308 mg, 1.44 mmol) and $NaHCO_3$ (97 mg, 1.15 mmol) were added to a solution of FGH diol **120** (154 mg, 0.14 mmol) in MeOH/CH_2Cl_2/H_2O (3:2:1, 2.1 mL) and the resulting mixture was stirred at 25 °C for 4 h. The reaction mixture was diluted with CH_2Cl_2 (250 mL) and washed with saturated aqueous NH_4Cl (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4) and the solvents were removed under reduced pressure. The crude selenoxide was dissolved in toluene (2 mL) and transferred by cannula to a sealed tube. The flask was washed with toluene (2 × 2 mL) and the organics were transferred to the sealed tube. Diisopropylamine (3 mL) and vinyl acetate (6 mL) were added, and the tube was sealed and heated to 140 °C for 12 h. After cooling, the reaction mixture was concentrated and the residue was purified by flash column chromatography (silica gel, 0 → 80 % Et_2O in hexanes) to afford the FGH allylic orthoester **121** (95 mg, 74 % over two steps) as a white foam. **121**: $R_f = 0.76$ (50 % Et_2O in hexanes); $[\alpha]_D^{22} = -26.2$ ($c = 0.53$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3020$, 2927, 1618, 1519, 1456, 1245, 1100 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.37–7.25$ (m, 12H, ArH), 6.86 (d, $J =$ 8.5 Hz, 2H, PMB), 6.17 (dd, $J = 11.0$, 4.5 Hz, 1H, H3), 5.81 (dd, $J = 10.0$, 1.0 Hz, 1H, H2), 5.34 (d, $J = 1.5$ Hz, 1H, G1), 4.78, 4.63 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.78 (s, 1H, F1), 4.72, 4.43 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.55, 4.53 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.27 (t, $J = 2.0$ Hz, 1H, G2), 4.15 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.11–4.04 (m, 4H, G3, G5, H5, H5), 4.02 (t, $J = 8.5$ Hz, 1H, F4), 3.86 (d, $J = 3.5$ Hz, 1H, H4), 3.85 (t, $J = 10.5$ Hz, 1H, G5), 3.79 (s, 3H, OMe), 3.69 (dd, $J = 10.5$, 2.5 Hz, 1H, F6), 3.66 (d, $J =$ 2.5 Hz, 1H, F2), 3.60 (dd, $J = 10.5$, 6.0 Hz, 1H, F6), 3.51 (s, 3H, OMe), 3.40–3.36 (m, 2H, F3, F5), 3.31 (s, 3H, OMe), 1.02–0.97 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.3$, 138.2, 138.0, 130.3, 130.2, 129.3, 128.4, 128.3, 127.5, 125.5, 113.9, 95.9, 95.6, 82.2, 73.1, 72.0, 71.0, 69.3, 68.9, 66.1, 64.0, 58.9, 55.3, 46.3, 30.3, 18.2, 13.0; HRMS (FAB): calcd for $C_{49}H_{68}O_{13}SiCs$ $[M+Cs]^+$: 1025.3484, found 1025.3447.

FGH *cis*-diol 122: OsO_4 (0.30 mL, 2.5 % solution in tBuOH) was added to a solution of FGH allylic orthoester **121** (95 mg, 0.106 mmol), NMO (31 mg, 0.266 mmol), and quinuclidine (12 mg, 0.106 mmol) in acetone/H_2O (10:1, 1 mL) and the reaction mixture was stirred for 24 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 FGH *cis*-diol **122** (64 mg, 65 %) as a white foam. **122**: $R_f = 0.38$ (100 % Et_2O); $[\alpha]_D^{22} = -38.6$ ($c = 0.78$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3360$, 2927, 1614, 1514, 1454, 1250, 1105 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.36–7.26$ (m, 10H, ArH), 7.25 (d, $J = 8.6$ Hz, 2H, PMB), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 5.36 (d, $J = 1.1$ Hz, 1H, G1), 4.78 (s, 1H, F1), 4.71, 4.68 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.71, 4.44 (AB, $J =$ 11.3 Hz, 2H, CH_2Ar), 4.57, 4.51 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.30 (brs, 1H, G2), 4.26 (ddd, $J = 10.6$, 10.6, 4.5 Hz, 1H, G4), 4.10 (dd, $J = 9.6$, 4.6 Hz, 1H, G5), 4.06 (dd, $J = 10.0$, 2.6 Hz, 1H, G3), 4.04–4.02 (m, 3H, F4, H2, H3), 3.94 (dd, $J = 12.6$, 2.6 Hz, 1H, H5), 3.79 (s, 3H, OMe), 3.78 (t, $J =$ 10.6 Hz, 1H, G5), 3.74 (dd, $J = 12.5$, 4.1 Hz, 1H, H5), 3.69 (dd, $J = 10.5$, 2.5 Hz, 1H, F6), 3.67 (d, $J = 2.1$ Hz, 1H, F2), 3.62 (dd, $J = 10.5$, 5.9 Hz, 1H, F6), 3.61–3.58 (m, 1H, H4), 3.50 (s, 3H, OMe), 3.41–3.38 (m, 2H, F3, F5), 3.33 (s, 3H, OMe), 2.63 (brs, 1H, OH), 2.40 (brs, 1H, OH), 1.07–0.95 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 138.0$, 137.8, 133.8, 129.9, 129.3, 128.5, 128.2, 127.9, 127.5, 127.5, 127.4, 125.5, 119.6, 113.9, 95.7, 95.5, 82.3, 77.4 76.3, 75.0, 73.1, 71.9, 71.3, 70.9, 69.1, 68.1, 64.0, 62.1, 61.3, 58.9, 55.3, 49.2, 30.3, 29.7, 21.2, 18.2, 18.1, 13.0, 11.5; HRMS (FAB): calcd for $C_{49}H_{70}O_{15}SiCs$ $[M+Cs]^+$: 1059.3538, found 1059.3578.

FGH cyclic sulfate 123: $SOCl_2$ (7.0 μL, 0.097 mmol) was added to a solution of FGH diol **122** (60 mg, 0.065 mmol) and Et_3N (27.0 μL, 0.194 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C and the reaction mixture was stirred for 5 min. The reaction mixture was 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 CCl_4/MeCN/H_2O (1:1:1.5, 2.0 mL) and cooled to 0 °C. $NaHCO_3$ (97 mg, 1.15 mmol) and $NaIO_4$ (308 mg, 1.44 mmol) were added and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was diluted with Et_2O (150 mL) and washed with saturated aqueous NH_4Cl (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 → 100 % EtOAc in hexanes) to afford FGH cyclic sulfate **123** (62 mg, 97 % over two steps) as a white foam. **123**: $R_f = 0.65$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -10.7$ ($c = 0.41$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2929$, 1618, 1520, 1458, 1400, 1252, 1215, 1116 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.40–7.25$ (m, 10H, ArH), 7.26 (d, $J = 8.5$ Hz, 2H, PMB), 6.90 (d, $J = 8.6$ Hz, 2H, PMB), 5.33 (d, $J =$ 1.1 Hz, 1H, G1), 5.04 (t, $J = 5.8$ Hz, 1H, H3), 4.91 (d, $J = 5.4$ Hz, 1H, H2), 4.83, 4.64 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.80 (s, 1H, F1), 4.73, 4.44 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.67, 4.58 (AB, $J = 11.4$ Hz, 2H, CH_2Ar), 4.32 (brs, 1H, G2), 4.23 (ddd, $J = 10.4$, 10.4, 4.5 Hz, 1H, G4), 4.14 (dd, $J =$ 10.1, 2.4 Hz, 1H, G3), 4.12–4.08 (m, 2H, G5, H4), 4.05 (t, $J = 8.1$ Hz, 1H, F4), 3.94 (dd, $J = 12.3$, 4.8 Hz, 1H, H5), 3.82 (t, $J = 10.7$ Hz, 1H, G5), 3.81 (s, 3H, OMe), 3.71 (dd, $J = 12.3$, 8.0 Hz, 1H, F6), 3.70–3.68 (m, 2H, F2, H5), 3.59 (dd, $J = 10.3$, 5.7 Hz, 1H, F6), 3.50 (s, 3H, OMe), 3.43–3.40 (m, 2H, F3, F5), 3.31 (s, 3H, OMe), 1.11–0.98 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.7$, 138.0, 137.5, 129.7, 128.7, 128.4, 128.2, 127.9, 127.8, 127.7, 127.5, 127.3, 125.5, 115.6, 114.0, 96.0, 95.6, 82.9, 81.9, 79.0, 78.7, 77.4, 76.2, 75.6, 73.4, 72.6, 72.1, 71.9, 71.0, 70.6, 68.0, 63.5, 61.6, 61.1, 58.9, 55.3, 30.3, 29.6, 18.2, 18.0, 12.9; HRMS (ESI): calcd for $C_{49}H_{68}O_{17}SSiNa$ $[M+Na]^+$: 1011, found 1011.

FGH benzoate 124: BzOK (30 mg, 0.188 mmol) was added to a solution of FGH cyclic sulfate **123** (62 mg, 0.063 mmol) and [18]crown-6 (17 mg, 0.063 mmol) in DMF (0.5 mL) and the resulting mixture was heated to 120 °C and was stirred for 1 h. The solvents were removed under reduced pressure and the residue was dissolved in THF (2.0 mL) and cooled to 0 °C. A 0.5 N solution of H_2O and H_2SO_4 in THF were added in 25 μL increments until TLC analysis indicated that no baseline material remained. The reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried (Na_2SO_4), 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 FGH benzoate **124** (49 mg, 76 %) as a white foam. **124**: $R_f = 0.33$ (70 % Et_2O in hexanes); $[\alpha]_D^{22} = -22.3$ ($c =$ 0.27, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3476$, 2944, 2866, 1716, 1613, 1514, 1454, 1275, 1070, 883, 712 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.09$ (d, $J =$ 7.1 Hz, 2H, ArH), 7.60 (t, $J = 7.4$ Hz, 1H, ArH), 7.47 (t, $J = 7.9$ Hz, 2H, ArH), 7.37–7.21 (m, 10H, ArH), 7.17 (d, $J = 8.6$ Hz, 2H, PMB), 6.71 (d, $J =$ 8.6 Hz, 2H, PMB), 5.35 (d, $J = 0.7$ Hz, 1H, G1), 5.16 (dd, $J = 10.5$, 3.1 Hz, 1H, H3), 4.80 (s, 1H, F1), 4.74, 4.72 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.74, 4.45 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.59, 4.48 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.39 (d, $J = 7.4$ Hz, 1H, H2), 4.33 (ddd, $J = 10.5$, 10.5, 4.4 Hz, 1H, G4), 4.31 (brs, 1H, G2), 4.12 (dd, $J = 9.5$, 4.6 Hz, 1H, G5), 4.06 (dd, $J =$ 10.9, 2.6 Hz, 1H, G3), 4.05 (t, $J = 8.5$ Hz, 1H, F4), 3.93 (d, $J = 2.5$ Hz, 1H, H4), 3.92 (dd, $J = 11.7$, 2.5 Hz, 1H, H5), 3.82 (t, $J = 10.9$ Hz, 1H, G5), 3.81 (dd, $J = 12.1$, 4.0 Hz, 1H, H5), 3.73 (s, 3H, OMe), 3.71 (dd, $J = 10.3$, 2.1 Hz, 1H, F6), 3.69 (d, $J = 2.0$ Hz, 1H, F2), 3.64 (dd, $J = 10.3$, 5.9 Hz, 1H, F6), 3.52 (s, 3H, OMe), 3.43–3.40 (m, 2H, F3, F5), 3.34 (s, 3H, OMe), 1.91 (brs, 1H, OH), 1.08–0.97 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 166.4, 159.2, 138.1, 137.7, 133.2, 129.9, 129.8, 129.8, 129.2, 128.5, 128.4, 128.2, 127.9, 127.7, 127.5, 125.5, 120.1, 113.7, 95.9, 95.8, 82.3, 77.3, 76.8, 76.4, 76.4, 74.8, 73.2, 73.2, 72.3, 71.9, 71.4, 71.0, 69.8, 68.1, 64.0, 63.5, 61.2, 58.9, 55.1, 46.2, 30.3, 18.2, 18.1, 13.0; HRMS (FAB): calcd for $C_{56}H_{74}O_{16}SiCs$ $[M+Cs]^+$: 1163.3800, found 1163.3854.

FGH bromobenzoate 125: BrBzCl (5.6 mg, 0.026 mmol) was added to a solution of FGH alcohol **124** (20 mg, 0.019 mmol), Et_3N (10.5 μL, 0.076 mmol) and 4-DMAP (1.2 mg, 0.004 mmol) in CH_2Cl_2 (0.20 mL) at 0 °C. The resulting mixture was warmed to 25 °C and stirred for 12 h. The reaction mixture was quenched by the addition of MeOH (1.0 mL), diluted with CH_2Cl_2 (50 mL) and washed with saturated aqueous $NaHCO_3$ (5 mL)

and brine (5 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 FGH bromobenzoate **125** (23 mg, 100%) as a white solid. **125**: $R_f = 0.53$ (60% Et_2O in hexanes); m.p. 156 °C, CH_2Cl_2/hexanes; $[\alpha]_D^{22} = -66.7$ ($c = 0.75$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2932, 2872, 1728, 1631, 1458, 1274, 1099, 830, 711\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.96$ (d, $J = 8.6$ Hz, 2H, ArH), 7.73 (d, $J = 8.5$ Hz, 2H, ArH), 7.53 (d, $J = 8.6$ Hz, 2H, ArH), 7.40–7.24 (m, 11H, ArH), 7.15 (d, $J = 8.6$ Hz, 2H, PMB), 6.93 (d, $J = 8.6$ Hz, 2H, ArH), 6.64 (d, $J = 8.6$ Hz, 2H, PMB), 6.14 (d, $J = 10.8$ Hz, 1H, H2), 5.49 (dd, $J = 10.8$, 3.3 Hz, 1H, H3), 5.35 (s, 1H, G1), 4.90, 4.76 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.77 (s, 1H, F1), 4.73, 4.43 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.59, 4.48 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.49–4.48 (m, 1H, G4), 4.33 (br s, 1H, G2), 4.11–4.03 (m, 3H, G3, G5, H4), 4.03 (t, $J = 8.6$ Hz, 1H, F4), 3.97–3.93 (m, 2H, H5, H5), 3.78 (t, $J = 9.6$ Hz, 1H, G5), 3.71 (s, 3H, OMe), 3.70–3.67 (m, 2H, F2, F6), 3.61 (dd, $J = 10.4$, 5.9 Hz, 1H, F6), 3.51 (s, 3H, OMe), 3.41–3.38 (m, 2H, F3, F5), 3.31 (s, 3H, OMe), 1.05–0.93 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.2, 165.8, 164.8, 159.1, 138.0, 137.6, 136.0, 133.3, 131.6, 131.2, 129.8, 129.6, 129.3, 129.2, 128.5, 128.4, 128.2, 128.2, 128.0, 127.5, 127.4, 123.3, 123.3, 119.0, 113.6, 95.9, 95.7, 73.2, 72.8, 72.7, 71.8, 71.5, 69.1, 68.0, 63.9, 61.3, 58.9, 55.1, 29.7, 18.2, 18.1, 13.0$; HRMS (FAB): calcd for $C_{63}H_{77}BrO_{17}SiNa$ $[M+Na]^+$: 1235.4011, found 1235.4020.

FGH trisaccharide (G-3 linked) 127: DAST (0.026 mL, 0.195 mmol) was added to a solution of ring H alcohol **71** (0.069 g, 0.130 mmol) in CH_2Cl_2 (0.70 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 $NaHCO_3$ (10 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 crude ring H glycosyl fluoride **44** (0.069 g, 0.130 mmol) and FG alcohol **126** (0.051 g, 0.066 mmol) were azeotroped with benzene (3 × 2 mL) and then dried under high vacuum for 1 h. Et_2O (0.40 mL) and 4 Å MS were added, and the mixture was cooled to 0 °C and stirred for 5 min. $SnCl_2$ (0.025 g, 0.013 mmol) was added 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 → 60% Et_2O in hexanes) to afford FGH trisaccharide (G-3 linked) **127** (0.051 g, 60%) as a white foam. **127**: $R_f = 0.79$ (60% Et_2O in hexanes); $[\alpha]_D^{22} = +1.8$ ($c = 0.33$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2928, 2862, 1725, 1512, 1457, 1251, 1108, 1033, 834\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.03$ (d, $J = 7.6$ Hz, 2H, ArH), 7.53 (d, $J = 7.7$ Hz, 2H, ArH), 7.49 (t, $J = 7.7$ Hz, 1H, ArH), 7.40–7.08 (m, 17H, ArH), 6.81 (d, $J = 8.6$ Hz, 2H, PMB), 5.46 (br s, 1H, G4), 5.22 (br s, 1H, G1), 4.97 (br s, 1H, H1), 4.81 (br s, 1H, F1), 4.72, 4.43 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.49–4.38 (m, 4H, CH_2Ar), 4.26 (br d, $J = 8.6$ Hz, 1H, G3), 4.19 (br t, $J = 4.2$ Hz, 1H, H3), 4.05 (t, $J = 8.6$ Hz, 1H, F4), 3.90 (br s, 1H, G2), 3.88 (br s, 1H, H2), 3.78 (s, 3H, OMe), 3.69–3.53 (m, 6H, F2, F6, F6, G5, G5, H5), 3.57 (s, 3H, OMe), 3.37–3.30 (m, 4H, F3, F5, H4, H5), 3.34 (s, 3H, OMe), 1.06–0.98 (m, 21H, iPr$_3$Si), 0.90 (s, 9H, tBuSi), 0.08, 0.06 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.1, 138.3, 132.9, 130.0, 129.8, 129.4, 129.2, 128.3, 127.4, 113.7, 99.6, 82.6, 80.0, 76.5, 75.4, 74.8, 73.2, 71.7, 70.6, 67.9, 61.6, 59.0, 55.3, 25.8, 18.2, 18.1, 13.1, −4.5, −4.8$; HRMS (MALDI): calcd for $C_{68}H_{94}O_{15}SeSi_2Na$ $[M+Na]^+$: 1309.5192, found 1309.5229.

FGH alcohol 128: NaOH (0.1 mg, 0.002 mmol) was added to a solution of FGH benzoate **127** (20 mg, 0.016 mmol) in MeOH (0.1 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 CH_2Cl_2 (100 mL) and washed with brine (5 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 → 90% Et_2O in hexanes) to afford FGH alcohol **128** (17 mg, 93%) as a white foam. **128**: $R_f = 0.58$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -7.0$ ($c = 0.37$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2928, 2849, 1514, 1455, 1367, 1243, 1107, 1032, 826, 738\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.57–7.07$ (m, 17H, ArH), 6.84 (d, $J = 8.5$ Hz, 2H, PMB), 5.18 (s, 1H, G1), 4.77 (s, 1H, F1), 4.75 (d, $J = 9.0$ Hz, 1H, H1), 4.70, 4.40 (AB, $J = 11.2$ Hz, 2H, CH_2Ar), 4.60, 4.46 (AB, $J = 12.1$ Hz, 2H, CH_2Ar), 4.35, 4.28 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.27 (br s, 1H, H3), 4.20–4.17 (m, 2H, G2, G4), 4.01 (t, $J = 9.0$ Hz, 1H, F4), 3.97 (br s, 2H, H5, H5), 3.93–3.89 (m, 1H, G5), 3.78 (s, 3H, OMe), 3.73 (dd, $J = 9.6$, 2.7 Hz, 1H, G3), 3.68–3.64 (m, 3H, F2, F6, H2), 3.56 (dd, $J = 10.4$, 5.7 Hz, 1H, F6), 3.53 (s, 3H, OMe), 3.44 (t, $J = 10.9$ Hz, 1H, G5), 3.34–3.30 (m, 2H, F3, F5), 3.30 (s, 3H, OMe), 3.22 (br s, 1H, H4), 1.63 (br s, 1H, OH), 1.08–0.98 (m, 21H, iPr$_3$Si), 0.89 (s, 9H, tBuSi), 0.13, −0.10 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.4, 138.0, 131.6, 129.7, 129.4, 128.9, 128.2, 128.0, 127.6, 127.5, 127.5, 127.2, 127.1, 126.4, 113.9, 103.1, 95.6, 95.2, 84.0, 82.8, 79.2, 77.4, 76.5, 74.7, 73.1, 73.0, 71.7, 71.7, 70.6, 67.9, 65.4, 63.9, 63.2, 61.6, 59.0, 55.3, 48.9, 30.2, 25.7, 18.2, 18.0, 13.1, −4.3, −4.8$; HRMS (MALDI): calcd for $C_{61}H_{90}O_{14}SeSi_2Na$ $[M+Na]^+$: 1205.4931, found 1205.4918.

FGH diol 129: nBu$_4$NF (9.3 μL, 1.0 M solution in THF, 0.0093 mmol) was added quickly to a solution of FGH alcohol **128** (11 mg, 0.0093 mmol) in THF (0.1 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 CH_2Cl_2 (100 mL) and washed with brine (5 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 FGH diol **129** (8 mg, 81%) as a white foam. **129**: $R_f = 0.21$ (80% Et_2O in hexanes); $[\alpha]_D^{22} = -13.3$ ($c = 0.23$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3465, 2924, 2864, 1510, 1460, 1248, 1112, 1028, 742\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.57–7.18$ (m, 17H, ArH), 6.84 (d, $J = 8.5$ Hz, 2H, PMB), 5.20 (d, $J = 1.8$ Hz, 1H, G1), 4.83 (d, $J = 6.9$ Hz, 1H, H1), 4.74 (s, 1H, F1), 4.71, 4.60 (AB, $J = 11.9$ Hz, 2H, CH_2Ar), 4.70, 4.60 (AB, $J = 11.2$ Hz, 2H, CH_2Ar), 4.51, 4.47 (AB, $J = 12.0$ Hz, 2H, CH_2Ar), 4.15 (ddd, $J = 9.5$, 9.5, 4.2 Hz, 1H, G4), 4.02 (t, $J = 9.0$ Hz, 1H, F4), 3.98 (br s, 1H, G2), 3.94–3.86 (m, 5H, G5, H3, H4, H5, H5), 3.80 (s, 3H, OMe), 3.75 (dd, $J = 6.8$, 3.2 Hz, 1H, H2), 3.71–3.68 (m, 2H, F6, G3), 3.58 (dd, $J = 10.2$, 6.4 Hz, 1H, F6), 3.53 (s, 3H, OMe), 3.51–3.48 (br s, 1H, F2), 3.44 (t, $J = 10.4$ Hz, 1H, G5), 3.36–3.31 (m, 2H, F3, F5), 3.32 (s, 3H, OMe), 2.60 (br s, 2H, OH), 1.05–0.96 (m, 21H, iPr$_3$Si); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 138.4, 134.3, 129.4, 129.4, 128.3, 128.2, 128.0, 127.7, 127.5, 127.4, 113.9, 100.7, 95.9, 95.9, 82.7, 77.7, 76.5, 74.7, 73.8, 71.9, 71.6, 70.8, 68.8, 68.0, 65.6, 63.3, 63.0, 61.6, 60.0, 55.3, 51.9, 51.0, 49.0, 29.7, 18.2, 18.0, 13.0$; HRMS (FAB): calcd for $C_{55}H_{76}O_{14}SeSiNa$ $[M+Na]^+$: 1091.4066, found 1091.4114.

FGH allylic orthoester 130: $NaIO_4$ (16 mg, 0.07 mmol) and $NaHCO_3$ (5 mg, 0.056 mmol) were added to a solution of FGH diol **129** (7.4 mg, 0.007 mmol) in MeOH/CH_2Cl_2/H_2O (12:7:1, 0.7 mL) and the resulting mixture was stirred at 25 °C for 4 h. The reaction mixture was 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 crude selenoxide was dissolved in toluene (2 mL) and transferred by cannula to a sealed tube. The flask was washed with toluene (1 × 2 mL) and the organics were transferred to the sealed tube. Diisopropylamine (8 mL) and vinyl acetate (4 mL) were added, and the tube was sealed and heated to 140 °C for 12 h. After cooling, the reaction mixture was concentrated and the residue was purified by flash column chromatography (silica gel, 0 → 80% Et_2O in hexanes) to afford FGH allylic orthoester **130** (2.8 mg, 45% over two steps, ca. 4:1 mixture) as a white foam. **130**: $R_f = 0.54$ (60% Et_2O in hexanes); IR (thin film): $\tilde{\nu} = 2919, 2861, 1514, 1455, 1367, 1237, 1102\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.34–7.24$ (m, 12H, ArH), 6.86 (d, $J = 8.6$ Hz, 2H, PMB), 6.16 (dd, $J = 9.8$, 3.7 Hz, 1H, H3), 5.72 (d, $J = 9.0$ Hz, 1H, H2), 5.32 (s, 1H, G1), 4.93, 4.54 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.79 (s, 1H, F1), 4.71, 4.42 (AB, $J = 11.3$ Hz, 2H, CH_2Ar), 4.63, 4.42 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.45–4.40 (m, 1H, G4), 4.22 (s, 1H, G2), 4.13–4.08 (m, 3H, G5, H5, H5), 4.02 (t, $J = 8.3$ Hz, 1H, F4), 3.91–3.89 (m, 1H, H4), 3.85 (dd, $J = 9.8$, 2.3 Hz, 1H, G3), 3.80 (s, 3H, OMe), 3.69–3.65 (m, 2H, F6, G5), 3.59–3.57 (m, 2H, F2, F6), 3.49 (s, 3H, OMe), 3.41–3.39 (m, 2H, F3, F5), 3.29 (s, 3H, OMe), 1.03–0.98 (m, 21H, iPr$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 159.3, 144.8, 138.0, 131.1, 130.0, 129.5, 129.4, 128.6, 128.3, 128.2, 127.9, 127.6, 127.5, 127.5, 127.3, 114.1, 96.2, 95.3, 80.0, 77.7, 76.3, 75.5, 73.1, 71.9, 70.9, 70.3, 69.2, 68.7, 68.0, 67.1, 65.7, 63.5, 59.0, 55.3, 53.0, 46.1, 29.7, 18.3, 18.0, 13.0$; HRMS (FAB): calcd for $C_{49}H_{68}O_{13}SiCs$ $[M+Cs]^+$: 1025.3484, found 1025.3447.

FGH *cis*-diol 131: OsO_4 (0.10 mL, 2.5% solution in tBuOH) was added to a solution of FGH olefin **110** (201 mg, 0.106 mmol), NMO (59.0 mg, 0.526 mmol), and quinuclidine (27.0 mg, 0.106 mmol) in acetone/H_2O (10:1, 1 mL) and the reaction mixture was stirred for 24 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

0947-6539/00/0617-3146 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 17

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 FGH *cis*-diol **131** (143 mg, 68 %, ca. 10:1 mixture of diastereoisomers) as a white foam, and recovered starting material (60 mg, 30 %). **131**: $R_f = 0.40$ (80 % EtOAc in hexanes); $[\alpha]_D^{22} = -1.43$ ($c = 0.20$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3495, 3066, 2926, 1728, 1610, 1515, 1452, 1267, 1072, 912, 739\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 7.8$ Hz, 2H, ArH), 7.68 (t, $J = 7.4$ Hz, 1H, ArH), 7.54 (t, $J = 7.7$ Hz, 2H, ArH), 7.45–7.29 (m, 12H, ArH), 6.96 (d, $J = 8.5$ Hz, 2H, PMB), 5.54 (t, $J = 9.5$ Hz, 1H, F4), 5.41 (s, 1H, G1), 4.98, 4.71 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.85 (s, 1H, F1), 4.67, 4.63 (AB, $J = 12.4$ Hz, 2H, CH_2Ar), 4.67, 4.63 (AB, $J = 11.5$ Hz, 2H, CH_2Ar), 4.55 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, G4), 4.37 (br s, 1H, G2), 4.26 (dd, $J = 9.6$, 4.6 Hz, 1H, G5), 4.16 (br s, 2H, H2, H3), 4.08 (dd, $J = 12.2$, 3.2 Hz, 1H, H5), 4.03 (dd, $J = 10.1$, 2.1 Hz, 1H, G3), 3.91 (t, $J = 9.6$ Hz, 1H, G5), 3.87 (s, 3H, OMe), 3.82 (dd, $J = 12.4$, 6.0 Hz, 1H, H5), 3.77–3.70 (m, 3H, F2, F3, H4), 3.68 (ddd, $J = 9.5$, 6.3, 3.0 Hz, 1H, F5), 3.64 (s, 3H, OMe), 3.62–3.55 (m, 2H, F6), 3.34 (s, 3H, OMe), 2.98 (d, $J = 6.0$ Hz, 1H, OH), 2.93 (d, $J = 4.8$ Hz, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.3, 159.3, 137.7, 137.3, 133.2, 129.8, 129.7, 129.6, 129.4, 128.4, 128.3, 128.3, 127.8, 127.7, 127.7, 127.6, 125.4, 119.5, 113.6, 96.0, 95.5, 80.6, 78.5, 77.3, 75.4, 74.7, 74.2, 73.2, 71.7, 71.6, 71.5, 71.4, 69.5, 69.2, 68.7, 65.8, 63.5, 62.2, 61.8, 59.2, 55.1, 43.1, 30.2, 15.2$; HRMS (MALDI): calcd for $C_{47}H_{54}O_{16}Na$ $[M+Na]^+$: 897.3309, found 897.3351.

FGH triol 132: K_2CO_3 (5.0 mg, 0.034 mmol) was added to a solution of FGH diol **131** (150 mg, 0.171 mmol) in MeOH (1.0 mL) at 25 °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 → 20 % MeOH in CH_2Cl_2) to afford FGH triol **132** (130 mg, 98 %) as a white foam. **132**: $R_f = 0.37$ (80 % EtOAc in hexanes); $[\alpha]_D^{22} = -33.3$ ($c = 0.18$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3421, 2924, 2854, 1460, 1260, 1072, 802\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.37–7.25$ (m, 12H, ArH), 6.86 (d, $J = 8.4$ Hz, 2H, PMB), 5.20 (br s, 1H, G1), 4.87, 4.60 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.74, 4.62 (AB, $J = 11.6$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.58, 4.53 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.44 (ddd, $J = 10.4$, 10.4, 4.5 Hz, 1H, G4), 4.25 (br s, 1H, G2), 4.15 (dd, $J = 9.5$, 4.6 Hz, 1H, G5), 4.04 (br s, 2H, H2, H3), 3.97 (dd, $J = 12.1$, 2.9 Hz, 1H, H5), 3.90 (dd, $J = 10.1$, 1.6 Hz, 1H, G3), 3.84 (t, $J = 9.7$ Hz, 1H, F4), 3.78 (s, 3H, OMe), 3.77 (t, $J = 10.4$ Hz, 1H, G5), 3.72 (dd, $J = 12.0$, 5.6 Hz, 1H, H5), 3.67 (dd, $J = 10.5$, 3.4 Hz, 1H, F6), 3.67–3.64 (m, 1H, H4), 3.61 (dd, $J = 10.5$, 5.4 Hz, 1H, F6), 3.56 (s, 3H, OMe), 3.35 (s, 3H, OMe), 3.35–3.31 (m, 3H, F2, F3, F5), 2.90 (br s, 1H, OH), 2.84 (br s, 1H, OH), 2.78 (br s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.3, 137.7, 137.6, 129.8, 129.7, 129.6, 129.4, 128.6, 128.4, 128.3, 128.0, 127.8, 127.7, 119.5, 113.9, 95.9, 95.5, 81.4, 80.6, 75.5, 75.0, 74.7, 73.2, 72.3, 71.8, 71.7, 71.4, 69.5, 69.2, 67.6, 63.5, 62.2, 61.8, 60.4, 59.3, 55.2, 45.8, 43.2, 29.6$; HRMS (MALDI): calcd for $C_{40}H_{50}O_{15}Na$ $[M+Na]^+$: 793.3047, found 793.3057.

FGH carbonate 133: Triphosgene (113 mg, 0.382 mmol) was added to a solution of FGH triol **132** (147 mg, 0.191 mmol) and pyridine (332 μL, 3.817 mmol) in CH_2Cl_2 (1.0 mL) at −78 °C. The resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was 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 % EtOAc in hexanes) to afford FGH carbonate **133** (146 mg, 96 %) as a white foam. **133**: $R_f = 0.39$ (80 % EtOAc in hexanes); $[\alpha]_D^{22} = -39.0$ ($c = 0.10$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 3440, 2925, 1727, 1611, 1514, 1453, 1267, 1105, 707\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.41–7.26$ (m, 12H, ArH), 6.89 (d, $J = 8.6$ Hz, 2H, PMB), 5.31 (d, $J = 1.3$ Hz, 1H, G1), 4.85, 4.61 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.83–4.78 (m, 2H, H2, H3), 4.80, 4.63 (AB, $J = 11.8$ Hz, 2H, CH_2Ar), 4.62 (s, 1H, F1), 4.60 (s, 2H, CH_2Ar), 4.43 (ddd, $J = 10.5$, 10.5, 4.6 Hz, 1H, G4), 4.27 (t, $J = 1.5$ Hz, 1H, G2), 4.14–4.11 (m, 2H, G5, H5), 4.01 (dd, $J = 10.1$, 2.5 Hz, 1H, G3), 3.98–3.97 (m, 1H, H4), 3.93 (dd, $J = 12.2$, 5.4 Hz, 1H, H5), 3.86 (t, $J = 9.5$ Hz, 1H, F4), 3.81 (s, 3H, OMe), 3.76 (t, $J = 10.1$ Hz, 1H, G5), 3.76 (dd, $J = 10.5$, 3.6 Hz, 1H, F6), 3.66 (d, $J = 2.7$ Hz, 1H, F2), 3.62 (s, 3H, OMe), 3.61 (dd, $J = 10.2$, 5.4 Hz, 1H, F6), 3.36 (s, 3H, OMe), 3.36–3.32 (m, 2H, F3, F5), 2.63 (s, 1H, OH); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.6, 153.8, 137.6, 137.5, 129.5, 128.7, 128.6, 128.3, 128.0, 127.8, 127.7, 117.0, 114.0, 95.9, 95.7, 81.3, 80.8, 77.9, 77.0, 75.3, 75.0, 73.8, 73.1, 72.4, 71.9, 71.7, 70.4, 69.5, 67.6, 63.4, 62.3, 61.9, 59.4, 55.2, 30.2, 14.1$; HRMS (MALDI): calcd for $C_{41}H_{48}O_{16}Na$ $[M+Na]^+$: 819.2840, found 819.2869.

FGH TBS ether 134: TBSOTf (54.0 μL, 108.0 mmol) was added to a solution of FGH alcohol **133** (157 mg, 0.197 mmol) and 2,6-lutidine (34.0 μL, 0.296 mmol) in CH_2Cl_2 (1.0 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 (0.2 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 → 80 % EtOAc in hexanes) to afford FGH TBS ether **134** (167 mg, 93 %) as a white foam. **134**: $R_f = 0.65$ (60 % EtOAc in hexanes); $[\alpha]_D^{22} = -18.0$ ($c = 0.05$, $CHCl_3$); IR (thin film): $\tilde{\nu} = 2927, 1730, 1516, 1454, 1270, 1099\ cm^{-1}$; ^1H NMR (600 MHz, $CDCl_3$): $\delta = 7.41–7.26$ (m, 12H, ArH), 6.89 (d, $J = 8.5$ Hz, 2H, PMB), 5.31 (s, 1H, G1), 4.86, 4.61 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.81 (dd, $J = 7.0$, 4.2 Hz, 1H, H3), 4.80 (d, $J = 4.2$ Hz, 1H, H2), 4.69, 4.59 (AB, $J = 11.7$ Hz, 2H, CH_2Ar), 4.66 (s, 1H, F1), 4.57 (s, 2H, CH_2Ar), 4.42 (ddd, $J = 10.5$, 10.5, 4.6 Hz, 1H, G4), 4.26 (br s, 1H, G2), 4.12 (dd, $J = 10.0$, 3.4 Hz, 1H, G5), 4.10 (dd, $J = 9.0$, 4.6 Hz, 1H, H5), 3.99 (dd, $J = 10.2$, 2.3 Hz, 1H, G3), 3.98–3.96 (m, 1H, H4), 3.92 (dd, $J = 12.2$, 5.6 Hz, 1H, H5), 3.86 (t, $J = 9.1$ Hz, 1H, F4), 3.81 (s, 3H, OMe), 3.74 (t, $J = 10.3$ Hz, 1H, G5), 3.61 (dd, $J = 10.6$, 1.5 Hz, 1H, F6), 3.60 (d, $J = 3.0$ Hz, 1H, F2), 3.56 (s, 3H, OMe), 3.53 (dd, $J = 10.9$, 5.3 Hz, 1H, F6), 3.32 (s, 3H, OMe), 3.32–3.25 (m, 2H, F3, F5), 0.86 (s, 9H, *t*BuSi), 0.04, 0.03 (2 × s, 2 × 3H, MeSi); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 159.6, 157.6, 153.7, 137.8, 137.6, 129.5, 128.7, 128.3, 127.8, 127.7, 127.7, 127.6, 125.5, 120.1, 117.0, 114.0, 95.9, 95.6, 81.9, 80.8, 78.0, 77.1, 76.8, 75.4, 73.8, 73.0, 71.7, 71.4, 71.3, 70.5, 69.6, 67.4, 63.3, 62.3, 61.8, 59.0, 55.2, 30.2, 29.6, 25.9, 24.4, 18.1, −3.7, −5.2$; HRMS (MALDI): calcd for $C_{47}H_{62}O_{16}SiNa$ $[M+Na]^+$: 933.3705, found 933.3743.

Acknowledgements

We thank Dr. A. K. Ganguly for helpful discussions and a generous gift of everninomicin 13,384-1 and Drs. D. H. Huang, G. Siuzdak, and R. Chadha for NMR spectroscopic, mass spectroscopic and X-ray crystallographic assistance, respectively. This work was financially supported by the National Institutes of Health (USA), the Skaggs Institute for Chemical Biology, postdoctoral fellowships from M.E.C., Spain (R.M.R., Fullbright), the Japan Society for the Promotion of Science (H.S.) and the George Hewitt Foundation (K.C.F.), and grants from Schering–Plough, Pfizer, Glaxo–Wellcome, Merck, Hoffmann–LaRoche, DuPont, Bayer, Boehringer Ingelheim, and Abbott Laboratories.

[1] K. C. Nicolaou, R. M. Rodríguez, H. J. Mitchell, H. Suzuki, K. C. Fylaktakidou, O. Baudoin, F. L. van Delft, *Chem. Eur. J.* **2000**, *6*, ■■, Part 1 in this series of four papers.

[2] K. C. Nicolaou, F. L. van Delft, S. C. Conley, H. J. Mitchell, J. Jin, M. Rodríguez, *J. Am. Chem. Soc.* **1997**, *119*, 9057–9058.

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

[4] A. Y. Chemyak, K. V. Antonov, N. K. Kochetkov, *Biorg. Khim.* **1989**, *15*, 1113–1127.

[5] For a review of the chemistry of tin-containing intermediates in carbohydrate chemistry, see: T. B. Grindley, *Adv. Carbohydr. Chem. Biochem.* **1998**, *53*, 17–142.

[6] a) J. Yoshimura, M. Tamaru, *Carbohydr. Res.* **1979**, *72*, C9–C11; b) S. Horito, K. Asano, K. Umemura, H. Hashimoto, J. Yoshimura, *Carbohydr. Res.* **1983**, *121*, 175–185.

[7] E. Lee, J. P. O'Reilly, J. P. O'Callaghan, A. Bruzzi, *Proc. R. Ir. Acad. Sect. B* **1984**, *84*, 35–41.

[8] R. Lopez, C. Perez, A. F. Mayoralas, S. Conde, *J. Carbohydr. Chem.* **1993**, *12*, 165–171.

[9] a) R. E. Ireland, D. W. Norbeck, *J. Org. Chem.* **1985**, *50*, 2198–2200; b) A. J. Mancuso, D. Swern, *Synthesis* **1981**, 165–185.

[10] a) A. Dondoni, G. Fantink, M. Fogagnolo, A. Medici, P. Pedrini, *J. Org. Chem.* **1988**, *53*, 1748–1761; b) A. Dondoni, A. Marra, D. Perrone, *J. Org. Chem.* **1993**, *58*, 275–277.

[11] Crystallographic data (excluding structure factors) for the structures **40** and **125** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-139034 (**40**) and CCDC-134793 (**125**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk)..
[12] a) G. Jaurand, J.-M. Beau, P. Sinaÿ, *J. Chem. Soc. Chem. Commun.* **1982**, 701–703; b) J.-M. Beau, G. Jaurand, J. Esnault, P. Sinaÿ, *Tetrahedron Lett.* **1987**, *28*, 1105–1108; c) M. Trumtel, P. Tavecchia, A. Veyrières, P. Sinaÿ, *Carbohydr. Res.* **1990**, *202*, 257–275.
[13] K. C. Nicolaou, T. Ladduwahetty, J. L. Randall, A. Chucholowski, *J. Am. Chem. Soc.* **1986**, *108*, 2466–2467.
[14] R. R. Schmidt, J. Michel, *Angew. Chem.* **1980**, *92*, 763–765; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 731–733.
[15] S. Mehta, B. M. Pinto, *J. Org. Chem.* **1993**, *58*, 3269–3276.
[16] L. A. Carpino, A. El-Faham, *J. Am. Chem. Soc.* **1995**, *117*, 5401–5402.
[17] a) P. Deslongschamps, R. Chênevert, R. J. Taillefer, C. Moreau, J. K. Saunders, *Can. J. Chem.* **1975**, *53*, 1601–1615; b) P. Deslongschamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, New York, **1983**.
[18] K. C. Nicolaou, H. J. Mitchell, K. C. Fylaktakidou, H. Suzuki, R. M. Rodríguez, *Angew. Chem.* **2000**, *112*, 1131–1135; *Angew. Chem. Int. Ed.* **2000**, *39*, 1089–1093.
[19] J. C. Martin, R. J. Arhart, *J. Am. Chem. Soc.* **1971**, *93*, 4327–4329.
[20] X. Wu, F. Kong, *Carbohydrate Res.* **1987**, *162*, 166–169.
[21] a) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155–4157; b) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277–7279; c) S. D. Meyer, S. L. Schrieber, *J. Org. Chem.* **1994**, *59*, 7549–7552.
[22] K. S. Kim, W. A. Szarek, *Synthesis* **1978**, 48–50.
[23] 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.

Received: February 11, 2000 [F2295]

  0947-6539/00/0617-3148 $ 17.50+.50/0