Total Synthesis of Calicheamicin γ_1^I. 1. Synthesis of the Oligosaccharide Fragment[1]

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Abstract: The first total synthesis of the calicheamicin γ_1^I oligosaccharide fragment in the form of its methyl glycoside (**62**) has been achieved. The synthetic challenge of the B-ring was recognized and studied initially, resulting in a novel and unique solution to the stereochemical problems posed involving a [3,3]-sigmatropic rearrangement of an allylic thionoimidazolide (**111**). This chemistry was initially worked out on a model for the ABC-ring system (**47**) and then successfully applied to the real system. The success of this synthesis has enabled the completion of the first synthesis of the natural product itself, calicheamicin γ_1^I (**1**), as will be described in the following papers in this issue.

Introduction

In 1987, the announcement of a new class of antitumor antibiotics, the enediynes, generated considerable excitement within the chemical community.[2] The first members, the calicheamicins[3] and esperamicins,[4] are typified by calicheamicin γ_1^I (**1**, Figure 1) and esperamicin A_1 (**2**, Figure 1), the first representatives of these two subclasses to be structurally characterized. Later, the previously identified neocarzinostatin chromophore (**3**, Figure 1) was included as an enediyne antibiotic due to the similarity of its mode of action,[5] and in 1989, the dynemicins,[6] represented by dynemicin A (**4**, Figure 1), were reported as a new series of enediynes. More recently, the structure of yet another naturally occurring enediyne, kedarcidin chromophore (**5**, Figure 1), has been disclosed by the Bristol Meyers Squibb group.[7] Not only do these compounds display extremely potent antitumor activity, with IC_{50} values in the nanogram/milliliter range, against a number of murine and human tumor cell lines but they also contain an array of structural features which were hitherto unseen.

At the heart of calicheamicin γ_1^I (**1**), the focus of this series of papers, is a rigid dihydroxylated bicyclic core, termed calicheamicinone by Danishefsky in accord with the naming of the anthracycline antibiotic aglycons. This aglycon core includes the mechanistically important 1,5-diyn-3-ene unit, an allylic methyl trisulfide, and an α,β-unsaturated ketone. The stereochemistry originally assigned to the propargylic hydroxyl group of the aglycon, to which the aryl tetrasaccharide is attached, has been corrected on the basis of an NMR analysis[8,3c] of calicheamicin derivatives and an X-ray crystal structure of a degradation product of the structurally related esperamicin.[4b] Calicheamicin γ_1^I (**1**) contains a single, highly unusual oligosaccharide appended at

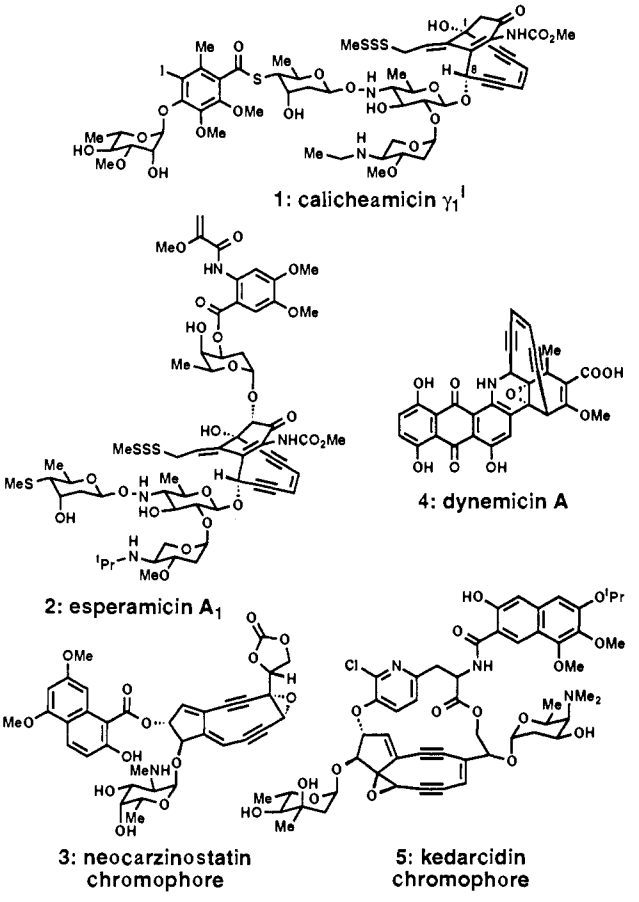

Figure 1. Structures of naturally occurring enediyne anticancer antibiotics.

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(1) Taken in part from the Ph.D. Thesis of Robert D. Groneberg, University of Pennsylvania, 1990. This work was partially carried out at the University of Pennsylvania.

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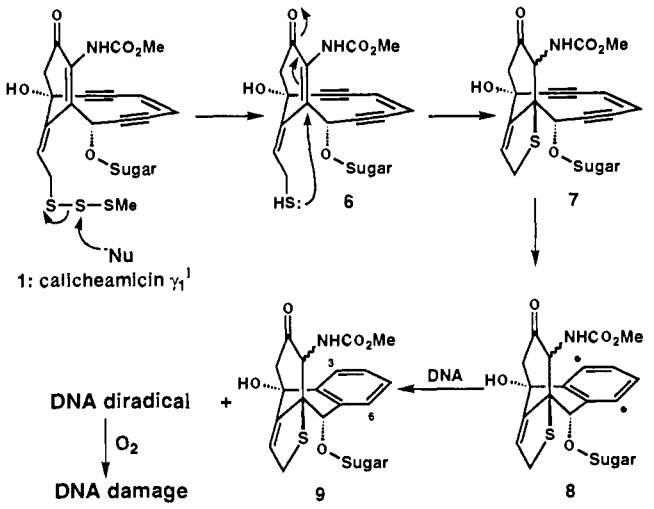
Scheme I. Proposed Mechanism of Action of Calicheamicin γ_1^1 (**1**)



C-8 which includes a hydroxylamine glycosidic linkage and an iodinated, hexasubstituted thiobenzoate.

The key to the biological activity of calicheamicin γ_1^1 (**1**) (and similarly esperamicin A_1 (**2**)) is believed to be a highly orchestrated series of events leading to DNA destruction in tumor cells. It is widely accepted that the oligosaccharide fragment serves as a recognition and delivery system, binding the molecule with remarkable specificity within the minor groove of duplex DNA at 5′-TCCT and 5′-TTTT and, to a lesser extent, at CTCT and ACCT sequences.[9] There is thought to be a significant hydrophobic interaction between the lipophilic oligosaccharide and the minor groove of duplex DNA,[10a] with binding being facilitated by substantial preorganization of the oligosaccharide in an extended conformation.[10b] Calculations by Schreiber *et al.* suggest that a significant proportion of the sequence selectivity for 5′-TCCT sites arises from a favorable interaction between the large and polarizable iodo substituent of the hexasubstituted aromatic ring and the N-2 amino substituents of the two guanines of the CC·GG tetrad.[11]

Before or after binding to the minor groove of DNA, a bionucleophile or reducing agent cleaves the trisulfide moiety of the aglycon, generating a thiolate species which adds in a 1,4-fashion to the adjacent enone functionality (**1** → **6** → **7**, Scheme I). The resulting change in hybridization from $sp^2 \rightarrow sp^3$ at the bridgehead position facilitates a cycloaromatization, commonly known as a Bergman cyclization, of the enediyne system, generating a reactive benzenoid diradical (**8**).[12] It has been demonstrated by atom-transfer experiments[13] that the calicheamicin diradical abstracts hydrogen atoms from duplex DNA at the C-5′ position of the cytidine in 5′-TCCT and at the C-4′ position of the nucleotide three base pairs removed on the 3′-side of the complimentary strand, leading to cleavage of both strands of DNA and, hence, cell death. These studies have also shown that the C-5′ nucleotide hydrogen is transferred to the C-6 position of the newly formed aromatic ring and the C-4′ nucleotide hydrogen is transferred to the C-3 position of that ring.

Whether or not the increased susceptibility of rapidly dividing tumor cells to DNA damage by calicheamicin γ_1^1 (**1**) and other enediyne antibiotics makes the natural products suitable drug candidates is questionable, since most exhibit unacceptable toxicity in animals. However, covalent attachment of derivatives to tumor-specific antibodies has shown exceptional promise,[14] and such hopes, combined with the synthetically challenging structures of the natural products, have led to a flurry of activity by synthetic chemists. Our own efforts, to date, have included studies of the Bergman reaction,[15] the synthesis and study of small molecules with DNA cleaving and antitumor activity inspired by the enediyne antibiotics,[16] the first synthesis of functioning model systems of dynemicin A, and the development of extremely potent and highly selective *in vivo* antitumor agents from these models.[17,18]

In this paper, we present full details of the first synthesis of the oligosaccharide fragment of calicheamicin γ_1^1 (**1**),[19,20] and in

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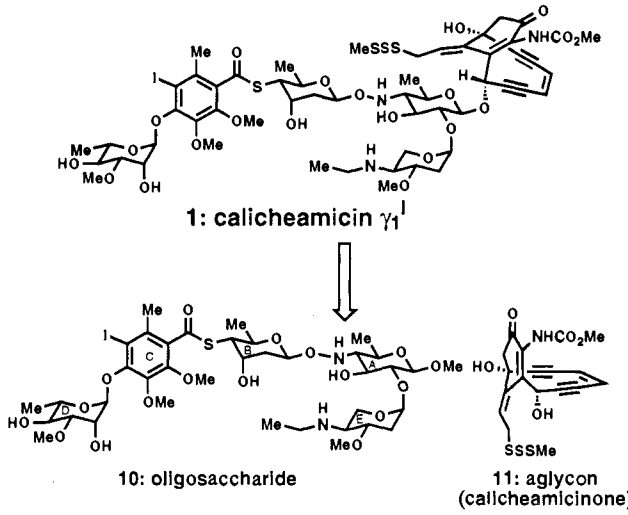
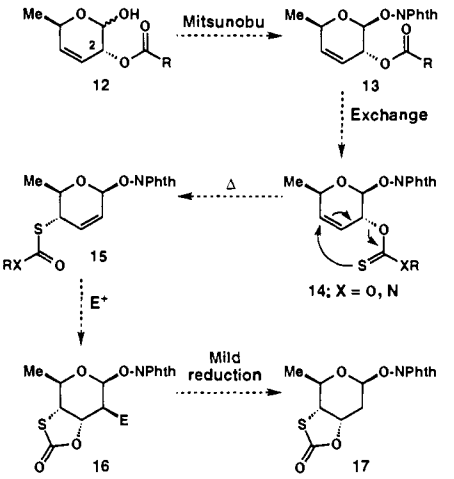
Scheme II. Retrosynthetic Analysis of Calicheamicin γ_1^I



Scheme III. Synthetic Design for Functionalization of the B-Ring Employing a [3,3]-Sigmatropic Rearrangement



the following papers, we describe details of the first enantioselective synthesis of (–)-calicheamicinone,[21,22] the coupling of the two pieces, and the appropriate elaboration for completing the first synthesis of calicheamicin γ_1^I (**1**).[23,24]

Results and Discussion

The overall synthetic strategy for calicheamicin γ_1^I (**1**) (Scheme II) relied upon the independent syntheses of the oligosaccharide fragment **10** and the aglycon fragment **11** and the coupling of appropriate forms of the two fragments in the latter stages of the synthesis. This paper details how we achieved the first of these goals, namely the synthesis of the oligosaccharide fragment **10**.

Synthetic Studies on the Oligosaccharide B-Ring. Our initial examination of the structure of **10** suggested that the most challenging portion of the molecule would probably be the synthesis of the central B-ring subunit. This subunit contains a highly unusual array of functionality, including the presence of the very unusual hydroxylamino glycosidic linkage to the A-ring, the sulfur atom in the 4-position, and the 2,6-dideoxy positions. By far, the most difficult synthetic challenge in this subunit is the 2-deoxy-β-glycosidic linkage. Standard methods which are used to generate β-glycosides employ a participating group (*i.e.*, an ester[25] or thiophenyl[26] substituent) in the 2-position, and any such approach would require the subsequent reductive removal of the 2-substituent in the presence of a hydroxylamino glycoside whose weak N–O bond would be sensitive toward reduction. Indeed, early investigations indicated that reductive removal of a 2-substituent would be troublesome. In addition, problems were encountered in the stereoselective introduction of the remaining sulfur and oxygen centers in the ring. In light of these observations, we designed an approach which would provide unique solutions to these problems.

The first stage of the operation would begin with the generation of an unsaturated lactol, **12** (Scheme III). The presence of the ester in the 2-position should allow the stereoselective incorporation of the β-hydroxylamino glycoside through a Mitsunobu reaction with *N*-hydroxyphthalimide.[27] With the β-glycoside safely installed, the remaining centers in the ring could be functionalized. Exchange of the ester protecting group for a thionocarbonate or thionocarbamate (**14**) would allow the simultaneous deoxygenation of the 2-position and stereospecific introduction of the sulfur at the 4-position to occur *via* a [3,3]-sigmatropic rearrangement to yield the thermodynamically more favorable allylic thiocarbonate or thiocarbamate **15**. Reaction of **15** with an electrophile would then allow oxygenation in the 3-position to be stereospecifically delivered in an intramolecular fashion, producing a cyclic thiocarbonate, **16**. Finally, reduction of the labile electrophilic element from the ring under mild conditions would lead to the targeted B-ring substituent **17**.

Examination of the literature revealed that there was precedent for the reactions outlined in Scheme III. Precedent for the crucial rearrangement was provided in the work of Ferrier, who had demonstrated the rearrangement of allylic xanthates.[28,29] Electrophilic cyclizations of the type **15** → **16** have been reported, although none include sulfur in the substrate. A variety of electrophilic cyclization reactions involving carbonates, carbamates, and phosphates have been reviewed by Bartlett.[30] Fraser-Reid reported the successful cyclization of an ethyl carbamate with iodonium dicollidine perchlorate.[31] Additional electrophiles which have been shown to efficiently induce cyclizations in benzylcarbonate systems include iodine and benzeneselenenyl chloride.[32]

Alcohol **20**, readily available from D-fucose (**18**), was used as a starting point (Scheme IV). Benzoylation and hydrogenolysis led to lactol **22** (accompanied by partial hydrolysis of the acetonide, which was readily reinstalled with dimethoxypropane). Mitsunobu coupling with *N*-hydroxyphthalimide[27] gave a 62% yield of the desired β-hydroxylamino glycoside **23**. Deprotection of the acetonide cleanly gave the corresponding diol which was transformed into the cyclic thionocarbonate **25** in 96% yield. Reduction with trimethyl phosphite under the Corey–Winter conditions[33] produced olefin **26** in 87% yield. Hydrolysis of the

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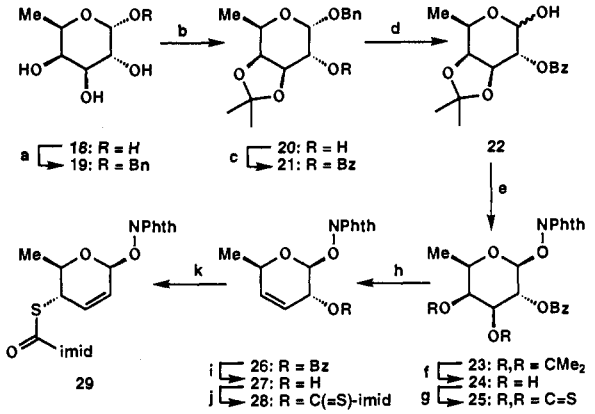
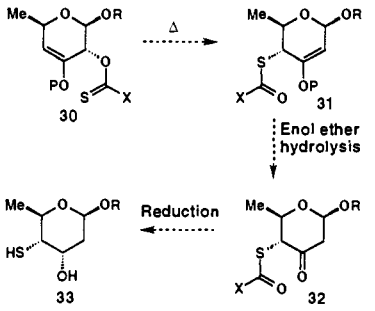
Scheme IV[a]



[a] Reagents and conditions: (a) BnOH, CSA, 85%; (b) 3 equiv of dimethoxypropane, TsOH (catalytic), Me_2CO, 25 °C, 1 h, 84%; (c) BzCl, Et_3N, DMAP, 98%; (d) H_2, $Pd(OH)_2$, MeOH, 97%; (e) HOMPhth, DIAD, PPh_3, THF, 62%; (f) HOAc, 0.2 M HCl, THF (10:1:10), 97%; (g) $(imid)_2C{=}S$, THF, 80 °C, 96%; (h) $P(OMe)_3$, 110 °C, 4.5 h, 87%; (i) NaOMe, MeOH, and then PhMe, 110 °C, 80–99%; (j) $(imid)_2C{=}S$, THF, 84%; (k) PhMe, 110 °C, 30 min, 100%.

Scheme V. A Novel [3,3]-Sigmatropic Rearrangement of an Allylic Thionocarbonate System Containing an Enol Ether



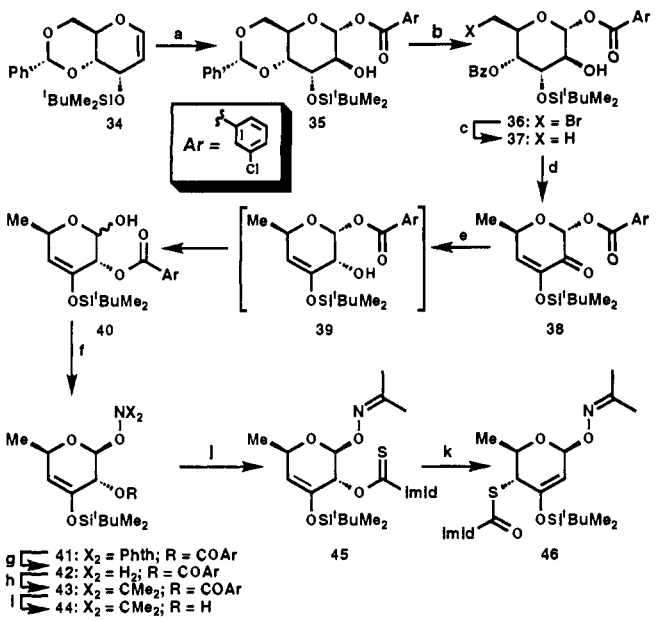
benzoate with sodium methoxide was complicated by methanolysis of the phthalimide ring; however, heating in refluxing toluene reclosed the phthalimide, yielding allylic alcohol **27**. Reaction with thiocarbonyldiimidazole produced thionoimidazole **28** which, gratifyingly, underwent the desired [3,3]-sigmatropic rearrangement upon heating in refluxing toluene to give a quantitative yield of thioimidazolide **29**. The stereochemistry of **29** was confirmed by X-ray crystallographic analysis, revealing a half-chair conformation driven by a very large anomeric effect.

The next step after the rearrangement reaction was the proposed electrophilic cyclization (**15** → **16**, Scheme III). However, under no circumstances could the desired cyclization product be obtained, despite trying a large number of substrates (thiocarbamates and thiocarbonates) and electrophilic reagents (*e.g.*, I_2, PhSeCl, NIS, NBS, and $I^+(collidine)_2ClO_4^-$).[34] Therefore, a slight modification of the sigmatropic rearrangement strategy was sought in order to install the desired oxygen at the 3-position.

In the modified strategy (Scheme V), the substrate (**3**) for the rearrangement would already contain an oxygen at the 3-position in the form of an enol ether. Such a modification would test the scope of the strategy, since the [3,3]-sigmatropic rearrangement of an allylic thionocarbonate system containing an enol ether had, to the best of our knowledge, not been previously reported in the literature.

The synthesis of a suitable substrate system for this modified strategy began with the known glycal **34**[35] (Scheme VI). Epoxidation with MCPBA[36] followed by ring opening with *in situ* generated 2-chlorobenzoic acid produced **35** as a single isomer. The yield of this reaction was significantly improved by treating the reaction mixture with small quantities of pure 2-chlorobenzoic acid. Benzylidene **35** was readily converted to the 4-benzoate-6-deoxy system **37** using the Hanessian ring opening[37] to give bromide **36** followed by tin hydride reduction. Swern oxidation[38] and *in situ* β-elimination proceeded cleanly, providing enone **38** in multigram quantities. A number of reagents were tested for the stereoselective reduction of the ketone in **38**. Luche reduction ($NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH)[39] directly transformed enone **38** to lactol **40**, in 69% yield, as a 1:1 mixture of anomers following chromatography. The intermediacy of the reduction product **39** was observable by TLC, although not isolable. Carrying out the Mitsunobu glycosidation with *N*-hydroxyphthalimide on the mixture of anomers resulted in a 92% yield of a 1:1 mixture of α-/β-glycosides. Conducting the same glycosidation on a crude mixture of lactols (*ca.* 3:1 α/β) produced a ratio of products corresponding to inversion of the anomeric center, implying that the intermediate phosphonium ion did not dissociate to form an oxonium ion prior to attack by the nucleophile, thereby not allowing for anchimeric assistance from the neighboring ester. The required lactol, therefore, was the initially formed α-stereoisomer. Unfortunately, the thermodynamically more stable lactol was the β-anomer which was obtained almost exclusively if the system was allowed to fully equilibrate. While not instantaneous, this equilibration was rapid enough to compete with the ester migration reaction (**39** → **40**) in the protic solvent used for the reduction. This led to the use of $Zn(BH_4)_2$ in diethyl ether as the reducing agent.[40] Using diethyl ether as the solvent preserved the stereochemistry of the anomeric center much better

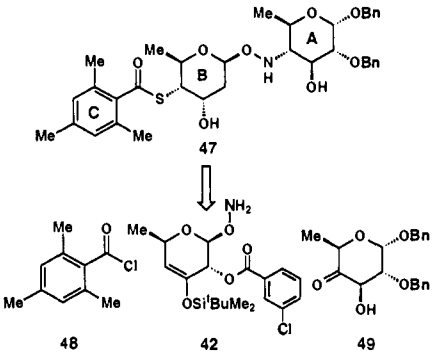
Scheme VI[a]



[a] Reagents and conditions: (a) 1.5 equiv of MCPBA, 0.17 equiv of 2-chlorobenzoic acid, CH_2Cl_2, 0 °C, 45 min, and then excess $Ca(OH)_2$, 0 °C, 20 min, ca. 80%; (b) 1.0 equiv of NBS, 0.6 equiv of $BaCO_3$, AIBN (catalytic), CCl_4, Δ, 45 min; (c) 1.1 equiv of *n*-Bu_3SnH, AIBN (catalytic), PhH, Δ, 1 h, 66% (over 2 steps); (d) 2.0 equiv of DMSO, 1.5 equiv of $(COCl)_2$, CH_2Cl_2, −78 °C, 1.5 h, and then 5.0 equiv of Et_3N, −78 → 25 °C, 80%; (e) 1.1 equiv of $Zn(BH_4)_2$, 0.5 equiv of NH_4Cl, Et_2O, 0 °C, 20 min; (f) 1.1 equiv of HONPhth, 1.2 equiv of Ph_3P, 1.2 equiv of DIAD, THF, 30 min, 53% (over 2 steps); (g) 1.6 equiv of $H_2NNH_2{\cdot}H_2O$, MeOH, 25 °C, 15 min, 100%; (h) Me_2CO, silica gel, 25 °C, 30 min, 94%; (i) 1.5 equiv of DIBAL, CH_2Cl_2, −78 °C, 90%; (j) $(imid)_2C{=}S$, THF; (k) PhMe, 110 °C.

(33) Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, *85*, 2677.
(34) Pauls, H. W.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1980**, *102*, 3956.
(35) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661.
(36) Wood, H. B., Jr.; Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 3234.
(37) Hanessian, S. *Carbohydr. Res.* **1966**, *2*, 86.
(38) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.
(39) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
(40) Gensler, W. J.; Johnson, F. A.; Sloan, A. D. B. *J. Am. Chem. Soc.* **1960**, *82*, 6074.

Scheme VII. Retrosynthetic Analysis of **47**, a Model for the ABC-Ring System of the Calicheamicin γ_1^1 Oligosaccharide



than methanol, while not inhibiting the migration reaction. The addition of NH_4Cl to the reaction mixture inhibited silyl-group migration. With the stereochemistry of the lactol well preserved (*ca.* 6–8:1 α/β), the ratio of β-glycoside **41** obtained in the Mitsunobu glycosidation was increased to between 5:1 and 7:1, with an overall yield of 53–56% from **38**.

Deprotection of the ester functionality in **41** proved to be troublesome. Attempted hydrolysis with NaOMe led to methanolysis of the phthalimide followed by decomposition upon extended reaction time. In order to test the rearrangement methodology, the phthalimide would first need to be removed. This was achieved by hydrazinolysis to liberate the free hydroxylamine **42**. For simplicity and potential future application, the free hydroxylamine was protected as its acetone oxime **43**. The ester was now readily removed using DIBAL, and subsequent treatment with thiocarbonyldiimidazole provided the rearrangement substrate **45**. The desired [3,3]-sigmatropic rearrangement then occurred in excellent yield to give thioimidazolide **46** upon heating in refluxing toluene.

Synthesis of a Model for the ABC-Ring System. Now that the viability of the strategy for functionalization of the B-ring had been demonstrated, the overall incorporation of the B-ring into the calicheamicin γ_1^1 oligosaccharide was examined. To this end, a model of the ABC-ring system was devised (**47**, Scheme VII). The B-ring of this model is identical to the natural sugar; however, the A- and C-rings were employed for convenience. The A-ring fragment would be available from ketone **49**, which was chosen for its similarity to the A-ring stereochemistry and its quick access from an available intermediate, **20** (Scheme IV). The C-ring fragment was modeled after a hindered benzoate ester and was available as acid chloride **48**.

Scheme VIII shows the synthesis of ketone **49** from the protected fucose derivative **20**. Benzylation of the free alcohol under standard conditions produced a near quantitative yield of fully protected fucose derivative **50**, which was hydrolyzed under acidic conditions to give diol **51**. The next step was a very effective method for carrying out the selective oxidation of a diol to the hydroxy ketone. Formation of the stannylene ketal and removal of the solvent followed by oxidation with stoichiometric amounts of bromine in benzene[41] led to the 4-keto sugar **49** in 76% yield and with a high degree of regioselectivity. The use of tributyltin methoxide was required to remove hydrogen bromide generated in the reaction.

Coupling of the unprotected keto alcohol **49** with hydroxylamine **42** proceeded smoothly under mildly acidic conditions to generate oxime **52**. Although only one geometrical isomer of the oxime was obtained, the geometry was not defined. It should be noted that attempts to couple the 3-*O*-*tert*-butyldimethylsilyl-protected ketone system failed under forcing conditions, presumably for steric reasons. The free alcohol was readily protected as *tert*-butyldimethylsilyl ether **53**, and the ester group was removed under reductive conditions (DIBAL) in order to avoid base-catalyzed silyl migration from the silyl enol ether onto the adjacent hydroxyl group. Treatment of alcohol **54** with thiocarbonyldiimidazole produced the required substrate **55** which smoothly underwent the [3,3]-sigmatropic rearrangement to give thioimidazole **56**. Sodium methoxide catalyzed hydrolysis of the thioimidazolide led to the corresponding thiol, although in modest yield (<50%). However, treatment of **56** with DIBAL was found to produce an intermediate which was not purified but treated directly with 2,4,6-trimethylbenzoyl chloride[42] in the presence of triethylamine and DMAP to yield the desired thioester **58**. The exact nature of the intermediate was later determined to be thioformate **57**, resulting from partial reduction of the thioimidazolide. *In situ*, base-induced formation and trapping of the labile thiol proved to be a highly efficient method (91%) for formation of the thioester.

Hydrolysis of the silyl enol ether with tetrabutylammonium fluoride (TBAF) in the presence of a proton source produced the labile ketone **59**. Upon extended reaction time, or attempted column chromatography, a greater proportion of an isomerized product was formed which was tentatively assigned as the epimer α to the ketone. Reduction with K-Selectride in DME produced the desired α-alcohol as the major isomer, in 68% overall yield, from **58**. The ratio of reduction products was greatly reduced from >8:1 for DME, to 3:1 for THF, to 1:1 for Et_2O as solvent for the reduction. The workup for the reaction included hydrolysis of an alkoxy–borane complex with methanolic silica gel. Reduction with sodium borohydride gave the epimeric β-alcohol as the only isomer. Difficulty associated with obtaining equatorial hydride attack during the reduction of 3-keto sugars has been reported.[43] Deprotection of the remaining silyl ether with TBAF proceeded in nearly quantitative yield to produce **61**. Finally, stereoselective reduction of the oxime ether was successfully achieved using excess $BH_3{\cdot}NH_3$ complex and pyridinium *p*-toluenesulfonate (PPTS) to give the targeted ABC-ring model **47**. The desired axial attack of the hydride was confirmed by observation of the large coupling constants (9.7, 9.7 Hz) for the protons adjacent to the newly formed nitrogen center (position 4) in the A-ring.

Synthesis of the Calicheamicin γ_1^1 Oligosaccharide. With an efficient synthesis of a model system for the B-ring completed, our attention now turned to the synthesis of the complete calicheamicin γ_1^1 oligosaccharide. The success of the tricyclic model system **47** revealed the synthetic utility of the central B-ring precursor **42**, which could be used as a cornerstone upon which to build the remaining subunits. The crude retrosynthesis outlined in Scheme II could now be refined and expanded to pave the way for a successful completion of the entire oligosaccharide (Scheme IX). Originally, methyl glycoside **62** was targeted for synthesis. A successful synthesis of the methyl glycoside would reveal any possible synthetic problems and facilitate the choice of a suitable labile protecting group for the A-ring anomeric position. As matters transpired, the corresponding *o*-nitrobenzyl glycoside series of compounds, synthesized by analogous chemistry, proved useful for coupling to the aglycon since this protecting group could be cleanly removed by photolysis.[23,44]

Retrosynthetic cleavage of the thioester of the oligosaccharide and functional group manipulation gave two main fragments, **63** and **64**. Aryl glycoside **64** would be obtained by glycosidation of a D-ring glycosyl donor and a hexasubstituted phenol. The remaining fragment **63** contains oxime, silyl enol ether, and thioimidazolide functionalities in addition to several protecting groups which were chosen for the ease by which they can be removed. The use of a triethylsilyl ether was preferable to that of a *tert*-butyldimethylsilyl ether since the latter required conditions which gave fluoride-induced C–D glycosidic bond cleavage. The 9-fluorenylmethyl carbamate (FMOC) protecting

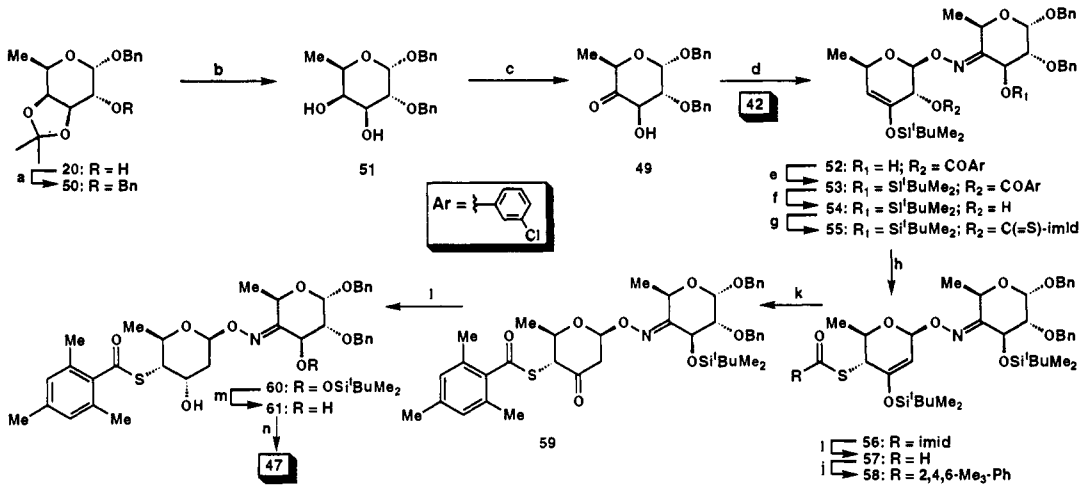
(41) David, S.; Thieffry, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1568.

(42) Gillespie, R. J.; Robinson, E. A. *J. Am. Chem. Soc.* **1965**, *87*, 2428.

(43) Danishefsky, S. J.; Langer, S. E. *J. Org. Chem.* **1985**, *50*, 3674.

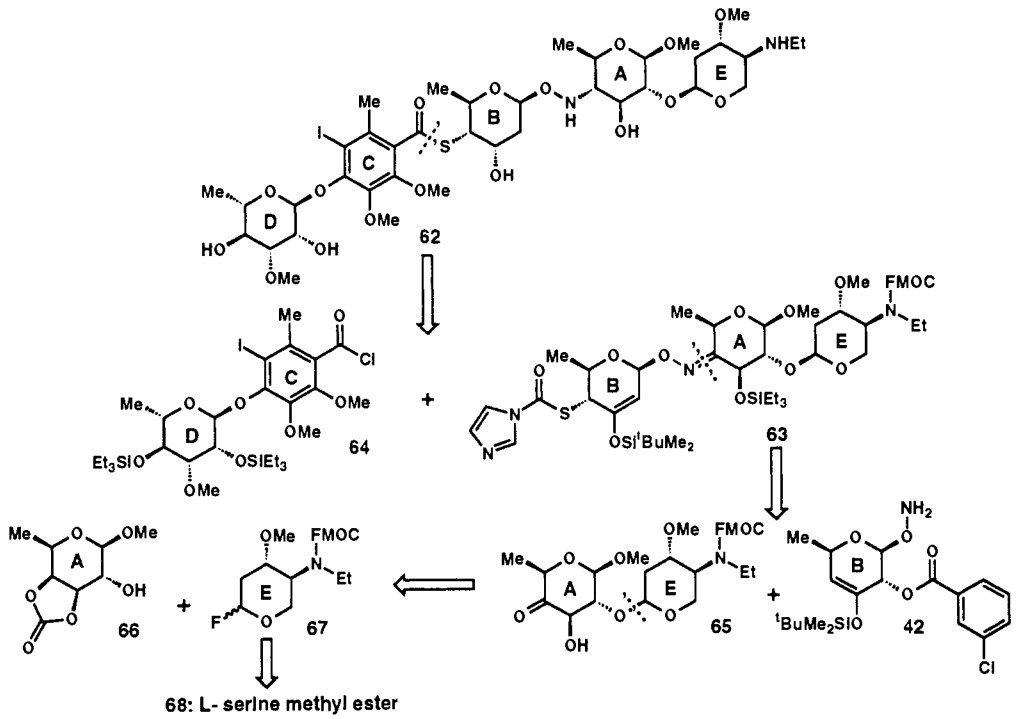
(44) Nicolaou, K. C.; Schreiner, E. P.; Iwabuchi, Y.; Suzuki, T. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 340.

Scheme VIII[a]



[a] Reagents and conditions: (a) 1.2 equiv of NaH, imidazole (catalytic), 1.5 equiv of BnBr, 0.2 equiv of *n*-Bu_4NI, THF, 25 °C, 45 min, 99%; (b) AcOH, 2 M HCl, THF, 25 °C, 6 h, 94%; (c) 1.1 equiv of *n*-Bu_2SnO, MeOH, Δ, 45 min, and then 0.9 equiv of Br_2, 1.1 equiv of *n*-Bu_3SnOMe, CH_2Cl_2, 25 °C, 5 min, 76%; (d) 1.0 equiv of **42**, 1.3 equiv of **49**, 0.1 equiv of PPTS, PhH, 25 °C, 3 h, 92%; (e) 1.5 equiv of $^tBuMe_2SiOTf$, 2.6 equiv of 2,6-lutidine, CH_2Cl_2, −25 → 0 °C, 30 min, 99%; (f) 2.5 equiv of DIBAL, CH_2Cl_2, −78 °C, 45 min, 90%; (g) 2.0 equiv of thiocarbonyldiimidazole, MeCN, 25 °C, 16 h; (h) PhMe, Δ, 1 h, 100%; (i) 6.0 equiv of DIBAL, CH_2Cl_2, −78 °C, 2 h; (j) 2.0 equiv of 2,4,6-trimethylbenzoyl chloride, 10.0 equiv of Et_3N, DMAP (catalytic), CH_2Cl_2, 25 °C, 12 h, 91%; (k) 1.0 equiv of TBAF, 1.6 equiv of AcOH, THF, H_2O, 0 °C, 15 min; (l) 3 equiv of K-Selectride, DME, −70 → −30 °C, 1 h, 68% (over 2 steps); (m) 1.4 equiv of TBAF, THF, 0 °C, 30 min, 98%; (n) excess BH_3·NH_3, *ca.* 2 equiv of PPTS, THF, 25 °C, 1 h, 81%.

Scheme IX. Retrosynthetic Analysis of the Calicheamicin γ_1^I Carbohydrate Fragment



group was selected for the E-ring amino substituent due to its ease of removal under mild conditions. Although it was potentially too labile, this concern was outweighed by the need for a group which could be easily removed in the final stages of the synthesis.

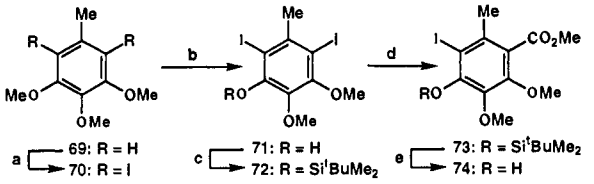
Disconnection of **63** gave the previously described hydroxylamine **42** and a disaccharide ketone, **65**. Further disconnection led to the D-fucose-derived A-ring **66** and an L-serine-derived E-ring, **67**. The use of L-serine as its methyl ester (**68**) as a starting material was, in part, dictated by the uncertainty of the absolute configuration of the ethylamino substituent at the time of conception of this work and the ready availability of both enantiomers.

Synthesis of the CD-Ring System. Synthesis of the CD-ring fragment started with an examination of the unusual hexasubstituted aromatic ring (Scheme X). In an improved synthesis of the aromatic ring over that originally published by us,[19d] 3,4,5-trimethoxytoluene (**69**) was diiodinated with periodic acid and I_2 in AcOH under the conditions of Suzuki[45] to afford diiodide **70** in 93% yield. Selective monodemethylation of **70** using boron trichloride led to phenol **71** in 53% yield plus 13% of a regioisomer. Apparently, BCl_3 complexes with the iodine of the benzene nucleus to selectively remove the methyl group at the C-3 or C-5 oxygen position. In the absence of the iodine atom, the C-4 oxygen methyl was removed first. Phenol **71** was silylated to give **72**. Selective lithiation with ^{t}BuLi and acylation with methyl chloroformate installed the ester functionality, and desilylation gave phenol **74**.

The synthesis of the D-ring fragment (Scheme XI) commenced with L-rhamnose (**75**) which was peracetylated (Ac_2O/Et_3N/

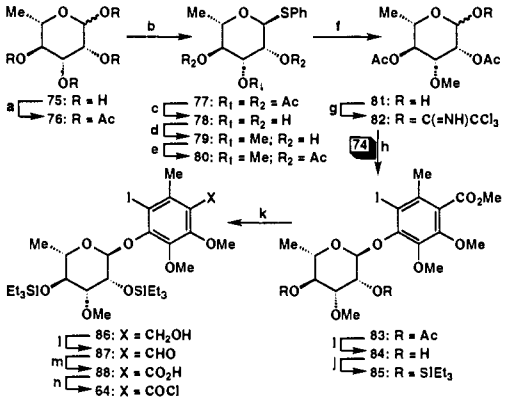
(45) Suzuki, H. *Org. Synth.* **1971**, *51*, 94.

Scheme X[a]



[a] Reagents and conditions: (a) 1.1 equiv of I_2, 0.55 equiv of $HIO_4 \cdot 2H_2O$, AcOH, 53 °C, 24 h, 93%; (b) 2.0 equiv of BCl_3, CH_2Cl_2, 25 °C, 48 h, 53%; (c) 2.0 equiv of ^{t}BuMe$_2$SiCl, 2.4 equiv of imidazole, DMF, 0 °C, 30 min, 96%; (d) 1.2 equiv of ^{t}BuLi, Et_2O, −108 °C, 1.5 h, and then 1.6 equiv of MeOCOCl, Et_2O, −78 → −40 °C, 2 h, 87%; (e) 1.6 equiv of AcOH, 1.2 equiv of TBAF, THF, 0 °C, 1.5 h, 95%.

Scheme XI[a]



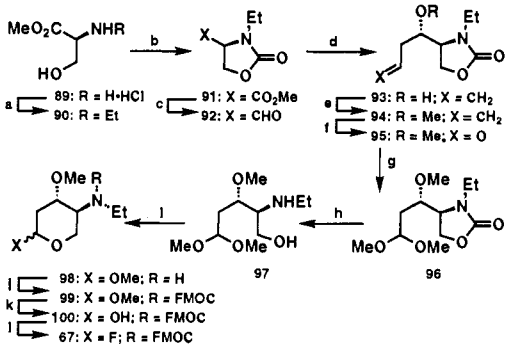
[a] Reagents and conditions: (a) 6.0 equiv of Ac_2O, 8.0 equiv of Et_3N, DMAP (catalytic), CH_2Cl_2, 0 → 25 °C, 12 h; (b) 1.1 equiv of PhSH, 0.7 equiv of $SnCl_4$, CH_2Cl_2, 0 °C, 4 h, 93%; (c) K_2CO_3 (catalytic), THF, MeOH, 25 °C, 10 h, 100%; (d) 1.1 equiv of *n*-Bu_2SnO, MeOH, Δ, and then 4.6 equiv of MeI, 1.0 equiv of CsF, DMF, 0 → 25 °C, 20 h, 77%; (e) 3.0 equiv of Ac_2O, 4.0 equiv of Et_3N, DMAP (catalytic), CH_2Cl_2, 25 °C, 2 h, 100%; (f) 2.0 equiv of NBS, Me_2CO, H_2O, 25 °C, 1 h, 70%; (g) excess Cl_3CCN, 0.9 equiv of NaH, CH_2Cl_2, 25 °C, 1 h; (h) 1.0 equiv of **74**, 1.3 equiv of **82**, 1.5 equiv of $BF_3 \cdot OEt_2$, 4-Å molecular sieves, CH_2Cl_2, −50 °C, 1 h, 95% (over 2 steps); (i) K_2CO_3 (catalytic), THF, MeOH, 25 °C, 2.5 h, 93%; (j) 3.0 equiv of Et_3SiOTf, 5.0 equiv of 2,6-lutidine, CH_2Cl_2, −20 → 0 °C, 1.5 h, 90%; (k) 2 equiv of DIBAL, CH_2Cl_2, −78 °C, 1.5 h, 83%; (f) 3.0 equiv of PDC, CH_2Cl_2, 25 °C, 1.5 h, 80%; (m) 2 equiv of $KMnO_4$, Me_2CO, H_2O, 25 °C, 2 h, 75%; (n) $(COCl)_2$, 25 °C, 1 h, *ca.* 100%.

DMAP). Treatment with PhSH in the presence of $SnCl_4$ gave α-phenyl glycoside **77** as a single anomer in 93% yield.[46] Deacylation and selective methylation[47] at the 3-hydroxy group with *n*-Bu_2SnO/CsF/MeI provided **79** as a single isomer in 77% yield. The selectivity of this reaction was confirmed by decoupling experiments and X-ray analysis of its diacetate. Diol **79** was then acetylated to give **80**, a derivative designed to undergo selective α-glycosidation due to neighboring-group participation. Oxidative removal of the thiophenyl glycoside and activation of the anomeric position as the trichloroacetimidate[48] then provided **82**, which was coupled with phenol **74** in the presence of $BF_3 \cdot OEt_2$ to give a 95% yield of **83** exclusively as the desired α-anomer. At this point of the synthesis, it was necessary to exchange hydroxyl protecting groups for compatibility with subsequent stages of the synthesis. Thus, deacetylation and silylation provided bis(silyl) ether **85**. The steric and/or electronic environment of methyl ester **85** made it resistant to hydrolysis, and so it was necessary to obtain the free acid **88** *via* reduction to alcohol **86** with DIBAL. Stepwise oxidation with PDC followed by potassium permanganate then gave carboxylic acid **88** which was converted to the desired CD-ring coupling fragment **64** by treatment with oxalyl chloride.

Synthesis of the E-Ring Subunit. Synthesis of the E-ring began

(46) Landge, A. B.; Ingle, T. R.; Bose, J. L. *Ind. J. Chem.* **1969**, *7*, 1200.
(47) Negashima, N.; Ohno, M. *Chem. Lett.* **1987**, 141.
(48) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

Scheme XII[a]



[a] Reagents and conditions: (a) 1.0 equiv of Et_3N, 1.0 equiv of MeCHO, MeOH, 0 °C, 2 h, and then 2.0 equiv of $NaBH_4$, 0 °C, 2 h, 64%; (b) 1.1 equiv of carbonyldiimidazole, MeCN, Δ, 2 h, 78%; (c) 1.1 equiv of DIBAL, CH_2Cl_2, −78 °C, 4 h; (d) 1.0 equiv of allyl-B(^{d}IPC)$_2$, THF, −78 °C, 6 h, 57% (over 2 steps); (e) 1.5 equiv of Ag_2O, 10.0 equiv of MeI, DMF, 40 °C, 36 h, 95%; (f) excess ozone, MeOH, −78 °C, and then 2.0 equiv of Me_2S, 91%; (g) Amberlyst 15 ion-exchange resin, MeOH, 25 °C, 6 h, 94%; (h) NaOH, MeOH, H_2O, Δ, 3 h, 96%; (i) 1.0 equiv of HCl, MeOH, Et_2O, 25 °C, 3 h, 95%; (j) 3.0 equiv of K_2CO_3, 1.5 equiv of FMOC-Cl, THF, H_2O, 0 °C, 50 min, 96%; (k) AcOH, H_2O, 95 °C, 6 h, 85%; (l) 4.0 equiv of DAST, 4-Å molecular sieves, THF, −78 → 0 °C, 2.5 h, 91%.

with the methyl ester of enantiomerically pure L-serine hydrochloride, **89** (Scheme XII). The primary amino group was first transformed into its monoethyl derivative **90** by reductive alkylation using acetaldehyde and sodium borohydride in 64% yield. A single protecting group was then used to protect both the amine and alcohol functionalities. Slow addition of carbonyldiimidazole (CDI) to a refluxing solution of the amino alcohol in acetonitrile produced oxazolidinone **91** in 78% yield. The enantiomeric purity of this material was determined to be ≥95% ee by ^{1}H NMR spectroscopy using the chiral shift reagent Pr(hfc)$_3$. Selective reduction of the ester to the corresponding aldehyde **92** was achieved in 76% yield with 1 equiv of DIBAL in dichloromethane.

The key reaction in this sequence was an asymmetric allyl addition reaction to aldehyde **92**. Brown's diisopinocamphenylborane, (−)-(IPC)$_2$B, was chosen as the chiral auxiliary for this reaction since it displays high diastereoselectivity in a variety of substrates, including α-substituted aldehydes, and the stereochemical outcome is also highly predictable.[49] Carrying out the reaction at −78 → 25 °C produced the corresponding alkoxyborane, which was hydrolyzed using Evans' buffered hydroperoxide–methanol protocol,[50] in an overall yield of 57% to give only the desired diastereomer **93**. Standard hydroperoxide workup of this reaction led to substantially reduced yields, presumably due to oxazolidinone ring opening. It should be noted that the use of achiral reagents displayed a lack of stereoselectivity in the reaction.

Treatment of **93** with silver oxide and methyl iodide methylated the hydroxyl group to give **94**. Ozonolysis of the terminal olefin followed by workup with either dimethyl sulfide or trimethyl phosphite produced the labile aldehyde **95** in 91% yield. This was protected as the dimethyl acetal in 94% yield with Amberlyst resin in methanol. Hydrolysis of oxazolidinone **96** under forcing conditions unmasked the polar amino alcohol **97**, which was readily cyclized to pentose **98** in acidic methanol, producing a nearly equimolar mixture of anomers. Separation of the isomers allowed verification of the stereochemistry of the stereocenter formed during the allylboration reaction by ^{1}H NMR spectroscopy. The equatorial orientation of all of the substituents in the β-anomer was evident by observation of large coupling constants between

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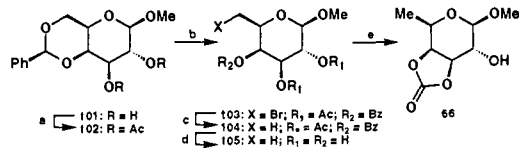
(50) Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099.

Scheme XIII[a]



[a] Reagents and conditions: (a) 2.5 equiv of Ac_2O, 3.0 equiv of Et_3N, DMAP (catalytic), CH_2Cl_2, 25 °C, 3 h, 100%; (b) 1.0 equiv of NBS, 0.6 equiv of $BaCO_3$, AIBN (catalytic), CCl_4, Δ, 10 min; (c) 1.1 equiv of n-Bu_3SnH, AIBN (catalytic), PhH, Δ, 20 min, 73% (over 2 steps); (d) NaOMe (catalytic), MeOH, 25 °C, 4 h, 99%; (e) 2.5 equiv of CDI, MeCN, Δ, 1 h, and then 2 M HCl, H_2O, Δ, 15 min, 76%.

the axially disposed protons on the pyran ring, proving that the allylboration reaction generated the desired stereochemistry at the newly formed center.

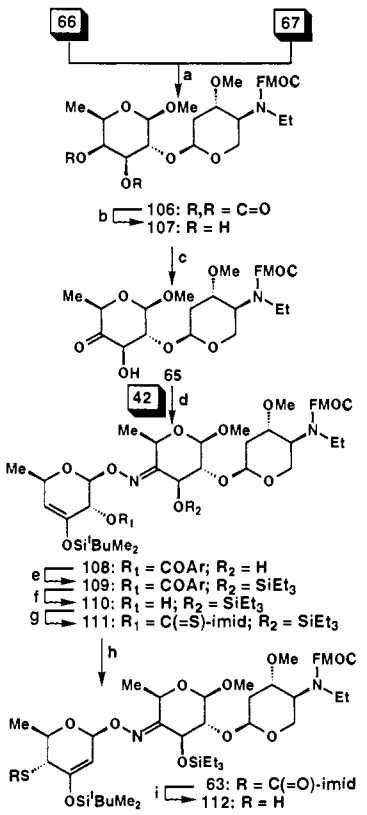
The free amine was protected as the base-labile FMOC derivative[51] using the corresponding chloroformate to give **99**. While the use of the FMOC protecting group proved to be a good choice, it had the drawback that slow rotation around the C–N bond resulted in a mixture of rotational isomers in the NMR spectra. The best spectra were obtained in DMSO-d_6 at temperatures around 340 K.[52]

Finally, a two-step procedure was used to generate the required glycosyl fluoride **67** from the methyl glycoside. The first step was generation of lactol **100** using aqueous acetic acid, producing a mixture of anomers in 85% yield along with a small amount of starting material. Conversion to the fluoride was accomplished with (diethylamino)sulfur trifluoride (DAST) in excellent yield.[53]

Synthesis and Glycosidation of the A-Ring Subunit. The next compound to be synthesized was the A-ring subunit, alcohol **66**, to be used as the glycosyl acceptor during glycosidation with the E-ring glycosyl fluoride. β-Methyl glycoside **105** (Scheme XIII)-was available directly from D-fucose; however, it was more conveniently prepared on large scale from the known galactose derivative **101**.[54] Although the next two steps would not be encumbered by the free hydroxyl groups, they were protected to facilitate product isolation. Thus, acetylation of diol **101** proceeded in quantitative yield, producing the fully protected β-methyl galactose derivative **102**. The previously employed two-step transposition of a benzylidene ring through the bromide to the deoxy system proceeded in good overall yield (73%) to give **104**. On large scale, to avoid removal of the tin byproduct by chromatography, the crude triester could be converted to the water-soluble triol **105** and the tin byproduct extracted into Et_2O without removal of the triol from the aqueous phase. Cyclic carbonate formation then proceeded by slow addition of excess carbonyldiimidazole to a refluxing solution of **105** in acetonitrile followed by acidic cleavage of the intermediate cyclic carbonate–imidazolide to give a 76% yield of **66**. With both alcohol **66** and glycosyl fluoride **67** available, the next step was to couple the two together.

Coupling of the A- and E-ring subunits **66** and **67** (Scheme XIV) proceeded smoothly using standard conditions ($AgClO_4$, $SnCl_2$) developed for glycosyl fluorides.[55,56] THF was found to be essential as solvent for this reaction since the limited solubility of **66** in Et_2O resulted in variable yields. The coupled product **106** was obtained in 86% yield as a 4.5:1 mixture of α-/β-anomers in which the desired α-anomer predominated. Routinely, separation of the mixture of anomers was performed following the

Scheme XIV[a]



[a] Reagents and conditions: (a) 1.0 equiv of **67**, 1.5 equiv of **66**, 2.0 equiv of $AgClO_4$, 2.0 equiv of $SnCl_2$, 4-Å molecular sieves, THF, –78 → –20 °C, 7 h, 70%; (b) NaH (catalytic), THF–$(CH_2OH)_2$ (20:1), 0 °C, 1 h, 93%; (c) 1.1 equiv of n-Bu_2SnO, MeOH, Δ, 45 min, and then 1.0 equiv of Br_2, 1.1 equiv of n-Bu_3SnOMe, CH_2Cl_2, 25 °C, 5 min, 70%; (d) 1.0 equiv of **65**, 1.2 equiv of **42**, PPTS (catalytic), PhH, 25 °C, 1 h, 83%; (e) 1.5 equiv of 2,6-lutidine, 1.2 equiv of Et_3SiOTf, CH_2Cl_2, 0 °C, 30 min, 100%; (f) 3.0 equiv of DIBAL, CH_2Cl_2, –78 °C, 20 min, 91%; (g) 3.0 equiv of thiocarbonyldiimidazole, MeCN, 25 °C, 1.5 h, 87%; (h) PhMe, Δ, 30 min, 98%; (i) 1.0 equiv of NaSMe, 40 equiv of EtSH, CH_2Cl_2, 0 °C, 5 min, 96%.

next step for ease of separation. The axial orientation of the glycoside bond in **106** was readily identifiable by comparing its ^1H NMR spectrum to that of the axial methyl glycoside **99** (Scheme XII). Particularly revealing was the value of the coupling constant between the anomeric proton and the axial 2-position proton: $J_{1\text{–}2_{ax}}$ = 3.4 Hz for the methyl glycoside and 3.5 Hz for the disaccharide.

The next stage of the synthesis required functionalization of the A-ring to allow coupling of the B-ring subunit. The first requirement was deprotection of the cyclic carbonate in the presence of the FMOC protecting group to provide diol **107**. Initial attempts using sodium methoxide in methanol led to nearly equal rates of deprotection of the two protecting groups. It was observed by TLC analysis that when using low concentrations of sodium methoxide, the only products generated were the intermediate methyl carbonates as two regioisomers. Thus, the acyclic methyl carbonate was less reactive than the cyclic form and required a higher concentration of base for hydrolysis. This observation led to the use of ethylene glycol to promote the transesterification of the carbonate by facilitating the second stage of the hydrolysis through a proximity effect. This allowed for clean differentiation between the carbonate and FMOC, giving a 93% yield of the diol when the reaction was run in THF/ethylene glycol (20:1, 0.1 M) using a catalytic amount of sodium hydride to generate the alkoxide.

The remainder of the synthesis from diol **107** was analogous to the previous ABC-ring model system described above. Regiospecific oxidation of the diol to hydroxy ketone **65** proceeded

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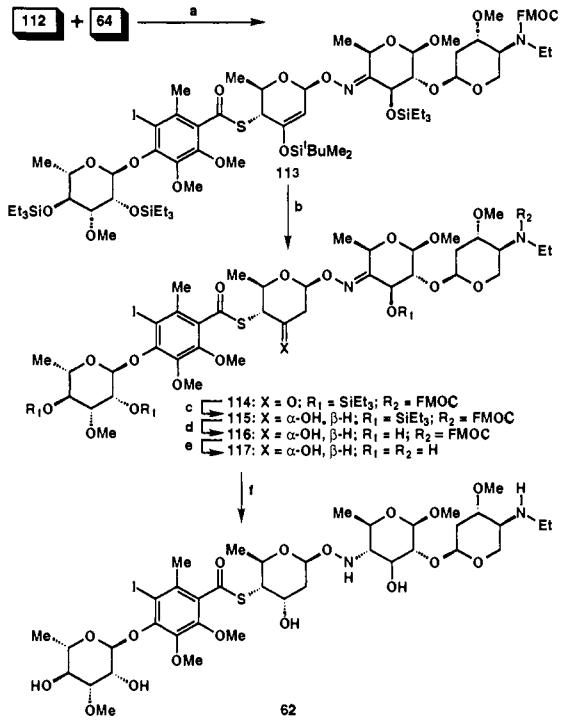
(52) Although elevated temperatures solved the problem of broad and/or multiple spectra due to FMOC rotamers in the ^1H NMR, high temperatures were not used in obtaining ^{13}C NMR spectra due to decomposition over the long experimental time required to obtain data. Therefore, some of the ^{13}C NMR spectra exhibit extra resonances, presumably due to rotational isomers.
(53) Card, P. J. *J. Carbohydr. Chem.* **1985**, *4*, 451.
(54) Bacon, J. S. D.; Bell, D. J.; Kosterlitz, H. W. *J. Chem. Soc.* **1939**, 1248.
(55) Mukaiyama, T.; Murai, Y.; Shoda, S. *Chem. Lett.* **1981**, 431.
(56) Nicolaou, K. C.; Dolle, R. E.; Papahatjis, D. P.; Randall, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 4189.

Scheme XV[a]



[a] Reagents and conditions: (a) 1.0 equiv of **112**, 1.2 equiv of **64**, 2.5 equiv of Et_3N, DMAP (catalytic), CH_2Cl_2, 0 °C, 1 h, 44%; (b) 1.0 equiv of TBAF, 5.0 equiv of AcOH in THF, –23 °C, 15 min; (c) 3.0 equiv of K-Selectride, DME, –78 °C, 2 h, 75% (over 2 steps); (d) HF·Py, CH_2Cl_2, THF, –20 → 0 °C, 1 h, 72%; (e) Et_2NH–THF (1:1), 25 °C, 2 h, 85%; (f) 30 equiv of $NaCNBH_3$, 13 equiv of BF_3·OEt_2, CH_2Cl_2, –60 → –40 °C, 1.5 h, 86% (6:1 mixture of isomers).

cleanly in 70% yield with 18% recovered starting material, using bromine oxidation of the stannylene acetal in the presence of tributyltin methoxide to absorb HBr. The unstable ketone was successfully coupled with hydroxylamine **42** using catalytic PPTS in benzene to give trisaccharide **108** in 83% yield. As in the model system, only one geometrical isomer about the oxime was obtained, although the stereochemistry was not assigned. Silylation and DIBAL deprotection of the ester cleanly provided alcohol **110** in 91% overall yield (*via* **109**) with no observable cleavage of the FMOC protecting group. Treatment with thiocarbonyldiimidazole gave the corresponding thionoimidazolide **111** in 87% yield. Thermolysis of **111** induced the [3,3]-sigmatropic rearrangement in nearly quantitative yield, providing multigram quantities of trisaccharide **63** for coupling with the aryl saccharide unit **64**.

Coupling of the trisaccharide subunit with the aryl subunit proved to be more difficult than the model system coupling reaction. The best procedure turned out to be cleavage of the thioimidazolide with sodium thiomethoxide in the presence of EtSH to give a near quantitative yield of thiol **112** (Scheme XIV). Coupling of the thiol with acid chloride **64** to give pentasaccharide **113** (Scheme XV) required more forcing conditions than those in the model system, and the yield was more modest (44%). This is, in part, explained by the low reactivity of acid chloride **64** due to the electron-rich nature of the aromatic ring which deactivates the carbonyl toward nucleophilic attack. Hydrolysis of the silyl enol ether then gave the unstable ketone **114**. Reduction of the crude mixture with K-Selectride in DME/THF (8:1) at –78 °C selectively gave the desired alcohol **115** in 75% overall yield. Deprotection of the silyl ethers was accomplished with HF·Py complex in good yield (72%) to reveal tetrol **116**. Removal of the FMOC protecting group proved straightforward using diethylamine in THF to produce the free amine **117** in 85% yield. As an alternative to the previous two steps, the transformation of **115** to **117** could be performed in one step using TBAF (10 equiv) in THF. With the oligosaccharide skeleton functionalized and fully deprotected, the only remaining step was reduction of the oxime functionality to the desired α-hydroxylamine **62**. This was best achieved with sodium cyanoborohydride in the presence of BF_3·OEt_2 at –40 °C, giving an 86% yield of an epimeric mixture of hydroxylamines in an α/β ratio of *ca* 6:1 in which the desired α-component predominated.

Conclusion

The first total synthesis of the oligosaccharide portion of calicheamicin γ_1^I (**1**) has been achieved in the form of its methyl glycoside (**62**). The synthesis utilized a [3,3]-sigmatropic rearrangement of an allylic thionoimidazolide to allow the formation of the correct β-glycosidic linkage of the B-ring and the stereoselective installation of the 3-hydroxy and 4-thio substituents of the B-ring. The completion of this synthesis paved the way for a synthesis of the entire natural product **1**[57,58] and allowed the preparation of several oligosaccharides for binding studies with DNA.[59]

Experimental Section

General Techniques. NMR spectra were recorded on Bruker AMX-500, AM-300, or AM-250 instruments. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad; obs, obscured. IR spectra were recorded on Nicolet 205 or Perkin-Elmer 1600 series FT-IR spectrophotometers. Melting points were obtained on a Thomas-Hoover Unimelt apparatus and are uncorrected. Optical rotations were recorded using a Perkin-Elmer 241 polarimeter. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions. Microanalyses were performed by Robertson Laboratory, Madison, NJ. X-ray crystallographic data were obtained by Pat Carroll at the University of Pennsylvania.

All reactions were monitored by thin-layer chromatography carried out on 0.25-mm E. Merck silica gel plates (60F-254) using UV light, 7% ethanolic phosphomolybdic acid, or *p*-anisaldehyde solution and heat as developing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Tetrahydrofuran (THF) and ethyl ether were distilled from sodium–benzophenone; methylene chloride, benzene, and toluene were distilled from calcium hydride.

All reactions were carried out under an argon atmosphere with anhydrous, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise stated.

1-*O*-(3-Chlorobenzyl)-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,6-*O*-(phenylmethylene)-α-D-altropyranose (35). MCPBA (102 g, 50–60% purity, *ca.* 330 mmol) was dissolved in CH_2Cl_2 (350 mL), washed with brine (200 mL), and dried ($MgSO_4$). 2-Chlorobenzoic acid (6 g, 38 mmol) was suspended in this solution and slowly added, *via* an addition funnel, to a solution of glycal **34**[35] (75.4 g, 218 mmol) in CH_2Cl_2 (1100 mL) at 0 °C over 45 min. After being stirred an additional 45 min, the reaction mixture was cooled to –78 °C and filtered. The filtrate was treated with $Ca(OH)_2$ (75 g) and cooled to 0 °C for 20 min. The mixture was refiltered and the filtrate washed with saturated aqueous $NaHCO_3$ (750 mL) and brine (500 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (20 → 50% Et_2O in petroleum ether) to give alcohol **35** (92 g, contaminated with a small amount of 2-chlorobenzoic acid) as a white solid. This compound was taken on without further purification. A sample of pure **35** exhibited the following data: mp = 51 °C; R_f = 0.18 (30% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +107° (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3500–3400, 3032, 3012, 2954, 2931, 2885, 2858, 1729, 1577 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1 H, aromatic), 8.01 (d, *J* = 7.8 Hz, 1 H, aromatic), 7.57 (m, 1 H, aromatic), 7.48 (m, 2 H, aromatic), 7.40–7.35 (m, 4 H, aromatic), 6.21 (s, 1 H, H-1), 5.63 (s, 1 H, benzylic), 4.52 (ddd, *J* = 10.4, 9.7, 5.4 Hz, 1 H, H-5), 4.35 (dd, *J* = 10.4, 5.4 Hz, 1 H, H-6), 4.26 (dd, *J* = 2.8, 2.7 Hz, 1 H, H-3), 4.07 (b s, 1 H, H-2), 4.02 (dd, *J* = 9.7, 2.8 Hz, 1 H, H-4), 3.79 (dd, *J* = 10.4, 10.4 Hz, 1 H, H-6′), 2.40 (b s, 1 H, O*H*), 0.82

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(58) Nicolaou, K. C.; Hummel, C. W.; Nakada, M.; Shibayama, K.; Pitsinos, E. N.; Saimoto, H.; Mizuno, Y.; Baldenius, K.-U.; Smith, A. L. *J. Am. Chem. Soc.*, third of three papers in this series.

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(s, 9H, ^{t}Bu), 0.11, 0.04 (2 × s, 6 H, 2 × CH_3Si); FAB HRMS (NBA) *m/e* 521.1766, M + H$^+$ calcd for $C_{26}H_{33}ClO_7Si$ 521.1762.

4-*O*-Benzoyl-1-*O*-(3-chlorobenzoyl)-6-deoxy-3-*O*-[(1,1-dimethylethyl)-dimethylsilyl]-α-D-altropyranose (37). *N*-Bromosuccinimide (6.4 g, 36 mmol), $BaCO_3$ (4.2 g, 22 mmol), and AIBN (175 mg, 1 mmol) were added to a solution of benzylidene **35** (18.5 g, 35.6 mmol) in dry CCl_4 (120 mL); the solution was deoxygenated and refluxed for 45 min. The reaction mixture was cooled and diluted with EtOAc (350 mL). The organic solution was washed with 1 M HCl (2 × 200 mL), saturated aqueous $NaHCO_3$ (2 × 200 mL), and brine (100 mL). The organic layer was dried ($MgSO_4$) and concentrated to give crude bromide **36** (21.4 g).

A solution of crude bromide **36** (21.4 g, 36 mmol) in benzene (125 mL) was treated with *n*-Bu_3SnH (11 mL, 40 mmol) and AIBN (300 mg, 1.8 mmol), deoxygenated, and refluxed for 1 h. The solution was cooled and concentrated, and the residue was purified by flash chromatography (40% Et_2O in petroleum ether) to give the pure 6-deoxy derivative **37** (12.3 g, 66%) as a white solid: R_f = 0.46 (25% EtOAc in PhH); $[\alpha]^{23}_D$ +84.2° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3500, 3030, 2956, 2931, 2859, 1721, 1602, 1577 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (m, 3 H, aromatic), 8.01 (m, 1 H, aromatic), 7.61–7.55 (m, 2 H, aromatic), 7.46 (m. 2 H, aromatic), 7.40 (m, 1 H, aromatic), 6.23 (d, *J* = 2.0 Hz, 1 H, H-1), 5.21 (dd, *J* = 8.9, 3.1 Hz, 1 H, H-4), 4.63 (dq, *J* = 8.9, 6.4 Hz, 1 H, H-5), 4.37 (dd, *J* = 4.0, 3.1 Hz, 1 H, H-3), 4.10 (dd, *J* = 4.0, 2.0 Hz, 1 H, H-2), 2.48 (b s, 1 H, O*H*), 1.34 (d, *J* = 6.4 Hz, 3 H, H-6), 0.77 (s, 9 H, ^{t}Bu), –0.01, –0.06 (2 × s, 6 H, 2 × CH_3Si); FAB HRMS (NBA/CsI) *m/e* 653.0750, M + Cs$^+$ calcd for $C_{26}H_{33}ClO_7Si$ 653.0738.

(2*R*)-*trans*-4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3,6-dihydro-6-methyl-3-oxo-2*H*-pyran-2-yl 3-Chlorobenzoate (38). DMSO (1.1 mL, 14 mmol) was added dropwise to a solution of oxalyl chloride (0.90 mL, 10 mmol) in CH_2Cl_2 (8 mL) at –78 °C. The solution was stirred for 15 min, and then a solution of alcohol **37** (3.57 g, 6.87 mmol) in CH_2Cl_2 (26 mL) was added dropwise and the solution stirred for 1.5 h. Triethylamine (4.8 mL, 34 mmol) was added, and the reaction mixture was allowed to slowly warm to 25 °C over 1 h. The reaction mixture was diluted with ether (250 mL) and washed with 0.5 M HCl (2 × 100 mL), saturated aqueous $NaHCO_3$ (2 × 100 mL), and brine (100 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (10% Et_2O in petroleum ether) to give enone **38** (2.2 g, 80%) as an oil: R_f = 0.47 (15% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –17.8° (*c* 0.54, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3032, 2956, 2932, 2860, 1739, 1711, 1633 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (b s, 1 H, aromatic), 7.91 (m, 1 H, aromatic), 7.56 (m, 1 H, aromatic), 7.39 (dd, *J* = 7.9, 7.9 Hz, 1 H, aromatic), 6.42 (s, 1 H, H-1), 6.19 (d, *J* = 2.0 Hz, 1 H, H-4), 4.94 (dq, *J* = 6.8, 2.0 Hz, 1 H, H-5), 1.40 (d, *J* = 6.8 Hz, 3 H, H-6), 0.98 (s, 9 H, ^{t}Bu), 0.22, 0.21 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.5, 163.6, 143.9, 134.7, 133.7, 133.2, 130.7, 129.9-(2), 129.8, 128.1, 91.7, 68.8, 67.1, 25.5, 21.2, 18.4, –4.7, –4.8; FAB HRMS (NBA) *m/e* 397.1238, M + H$^+$ calcd for $C_{19}H_{25}ClO_5Si$ 397.1238.

2-[[2-*O*-(3-Chlorobenzoyl)-4,6-dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]oxy]-1*H*-isoindole-1,3(2*H*)-dione (41). Ammonium chloride (55 mg, 1.0 mmol) and freshly prepared zinc borohydride (16 mL of a 0.15 M solution in Et_2O, 2.4 mmol)[40] were added to a solution of enone **38** (850 mg, 2.13 mmol) in Et_2O (5 mL) at 0 °C. The resulting mixture was stirred for 20 min, diluted with cold Et_2O (250 mL), and washed with cold saturated aqueous NH_4Cl (2 × 100 mL) and cold aqueous $NaHCO_3$ (100 mL). The organic layer was dried ($MgSO_4$) and concentrated at 0 °C to give crude lactol **40** which was used immediately in the next step.

Crude lactol **40** was dissolved in cold THF (11 mL), and *N*-hydroxyphthalimide (0.38 g, 2.3 mmol) and triphenylphosphine (0.67 g, 2.6 mmol) were added. Diisopropyl azodicarboxylate (0.51 mL, 2.6 mmol) was added dropwise over 5 min, and the resulting orange solution was allowed to stir for 30 min. The reaction mixture was diluted with CH_2Cl_2 (300 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 150 mL) and H_2O (2 × 150 mL). The organic phase was dried ($MgSO_4$) and the solution concentrated. The residue was purified by flash chromatography (CH_2Cl_2) to give pure β-glycoside **41** (0.617 g, 53%) as a crystalline solid: mp = 113 °C; R_f = 0.36 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –75.2° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3030, 2958, 2933, 2897, 2887, 2860, 1795, 1741, 1666, 1577 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, *J* = 1.5 Hz, 1 H, aromatic), 8.02 (dd, *J* = 7.8, 1.2 Hz, 1 H, aromatic), 7.85–7.83 (m, 2 H, phth), 7.76–7.73 (m, 2 H, phth), 7.55–7.53 (m, 1 H, aromatic), 7.41 (dd, *J* = 7.8, 7.8, 1 H, aromatic), 5.86 (ddd, *J* = 5.9, 2.0, 1.0 Hz, 1 H, H-2), 5.44 (d, *J* = 5.9 Hz, 1 H, H-1), 5.03 (dd, *J* = 1.8, 1.0 Hz, 1 H, H-4), 4.52 (ddd, *J* = 6.6, 2.0, 1.7 Hz, 1 H, H-5), 1.40 (d, *J* = 6.6 Hz, 3 H, H-6), 0.81 (s, 9 H, ^{t}Bu), 0.19, 0.12 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.0, 144.0, 134.5, 134.4, 133.1, 130.0, 129.7, 128.9, 128.0, 123.7, 110.3, 105.3, 69.7, 68.0, 25.4, 22.4, 17.9, –4.6, –4.7; FAB HRMS (NBA) *m/e* 544.1530, M + H$^+$ calcd for $C_{27}H_{30}ClNO_7Si$ 544.1558. Anal. Calcd for $C_{27}H_{30}ClNO_7Si$: C, 59.61; H, 5.56; N, 2.57. Found: C, 59.64; H, 5.51; N, 2.52.

Phenylmethyl 6-Deoxy-3,4-*O*-(1-methylethylidene)-α-D-galactopyranoside (20). The known triol **19**[60] (13.6 g, 53.4 mmol) in acetone (150 mL) was treated with dimethoxypropane (20 mL, 160 mmol) and TsOH (1 g, 5 mmol) at 0 °C. The reaction mixture was brought to 25 °C and stirred for 1 h. Triethylamine (1.1 mL, 8 mmol) was added, and the reaction mixture was concentrated and purified by flash chromatography (50% Et_2O in petroleum ether) to give acetonide **20** (13.2 g, 84%) as a colorless oil: R_f = 0.34 (65% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +138° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3568, 3013, 2992, 2938, 2914 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.31 (m, 5 H, aromatic), 4.94 (d, *J* = 3.9 Hz, 1 H, H-1), 4.78 (d, *J* = 11.8 Hz, 1 H, benzylic), 4.57 (d, *J* = 11.8 Hz, 1 H, benzylic), 4.22 (dd, *J* = 6.5, 6.0 Hz, 1 H, H-3), 4.15 (dq, *J* = 6.6, 2.2 Hz, 1 H, H-5), 4.06 (dd, *J* = 6.0, 2.2 Hz, 1 H, H-4), 3.81 (dd, *J* = 6.5, 3.9 Hz, 1 H, H-2), 2.18 (b s, 1 H, O*H*), 1.51, 1.35 (2 × s, 6 H, 2 × CH_3), 1.31 (d, *J* = 6.6 Hz, 3 H, H-6); FAB HRMS (NBA/CsI) *m/e* 427.0530, M + Cs$^+$ calcd for $C_{16}H_{22}O_5$ 427.0526.

Phenylmethyl 6-Deoxy-3,4-*O*-(1-methylethylidene)-2-*O*-(phenylmethyl)-α-D-galactopyranoside (50). A solution of alcohol **20** (4.14 g, 14.0 mmol) in THF (35 mL) was treated with sodium hydride (0.84 g, 60% w/w in mineral oil, 17 mmol) at 0 °C. Imidazole (2 mg, catalytic) was added, and the reaction mixture was stirred at 0 °C for 5 min and then at 25 °C for 45 min. Benzyl bromide (2.5 mL, 21 mmol) and *n*-Bu_4NI (1.0 g, 2.8 mmol) were added, and the reaction mixture was stirred for 3 h. The reaction was quenched with AcOH (2 mL) and the mixture diluted with EtOAc (300 mL). The organic phase was washed with 0.5 M HCl (2 × 100 mL), water (100 mL), saturated aqueous sodium thiosulfate (100 mL), saturated $NaHCO_3$ (2 × 100 mL), and brine (100 mL). The organic solution was dried ($MgSO_4$), concentrated, and purified by flash chromatography (30% Et_2O in petroleum ether) to give benzyl ether **50** (5.33 g, 99%) as a colorless oil: R_f = 0.40 (35% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +151° (*c* 6.8, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3012, 2993, 2938, 2910, 2876, 1497 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.24 (m, 10 H, aromatic), 4.83 (d, *J* = 3.6 Hz, 1 H, H-1), 4.71 (d, *J* = 12.5 Hz, 1 H, benzylic), 4.70 (d, *J* = 12.3 Hz, 1 H, benzylic), 4.64 (d, *J* = 12.5 Hz, 1 H, benzylic), 4.54 (d, *J* = 12.3 Hz, 1 H, benzylic), 4.37 (dd, *J* = 7.9, 5.5 Hz, 1 H, H-3), 4.13 (dq, *J* = 6.7, 2.5 Hz, 1 H, H-5), 4.05 (dd, *J* = 5.5, 2.5 Hz, 1 H, H-4), 3.52 (dd, *J* = 7.9, 3.6 Hz, 1 H, H-2), 1.41, 1.35 (2 × s, 6 H, 2 × CH_3), 1.30 (d, *J* = 6.7 Hz, 3 H, H-6); FAB HRMS (NBA/CsI) *m/e* 517.1001, M + Cs$^+$ calcd for $C_{23}H_{28}O_5$ 517.0991.

Phenylmethyl 6-Deoxy-2-*O*-(phenylmethyl)-α-D-galactopyranoside (51). A solution of acetonide **50** (5.25 g, 13.7 mmol) in THF (20 mL) was treated with AcOH (15 mL) and 2 M HCl (5 mL). The reaction mixture was stirred for 6 h at 25 °C and carefully poured into a mixture of EtOAc (1 L) and saturated aqueous K_2CO_3 (300 mL), and the solution was stirred until neutral. The layers were separated, and the organic phase was dried ($MgSO_4$), concentrated, and filtered through a short plug of silica (5% MeOH in CH_2Cl_2) to give diol **51** (4.45 g, 94%) as a white solid: mp = 97 °C; R_f = 0.33 (Et_2O); $[\alpha]^{23}_D$ +160° (*c* 2.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3587, 3013, 2912, 1456 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.27 (m, 10 H, aromatic), 4.91 (d, *J* = 3.6 Hz, 1 H, H-1), 4.68 (d, *J* = 12.2 Hz, 1 H, benzylic), 4.56–4.49 (m, 3 H, benzylic), 4.06 (dd, *J* = 9.8, 3.4 Hz, 1 H, H-3), 3.98 (dq, *J* = 6.6, 1.0 Hz, 1 H, H-5), 3.82 (dd, *J* = 3.4, 1.0 Hz, 1 H, H-4), 3.70 (dd, *J* = 9.8, 3.6 Hz, 1 H, H-2), 2.8–1.5 (b s, 2 H, 2 × O*H*), 1.30 (d, *J* = 6.6 Hz, 3 H, H-6); FAB HRMS (NBA/CsI) *m/e* 477.0683, M + Cs$^+$ calcd for $C_{20}H_{24}O_5$ 477.0678. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.38; H, 6.98.

Phenylmethyl 6-Deoxy-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose (49). A solution of diol **51** (812 mg, 2.36 mmol) in MeOH (16 mL) was treated with dibutyltin oxide (0.62 g, 2.5 mmol) and refluxed for 45 min. The resulting clear solution was cooled, concentrated, and azeotroped with benzene to remove traces of MeOH. The crude stannylene acetal was dissolved in CH_2Cl_2 (16 mL), and *n*-Bu_3SnOMe (0.77 mL, 2.7 mmol) was added. The mixture was titrated with a 1.0 M solution of bromine in CCl_4 (2.2 mL, 2.2 mmol). The yellow solution was diluted with EtOAc (150 mL), washed with saturated aqueous $NaHCO_3$ (80 mL) and brine (2 × 100 mL), and dried ($MgSO_4$). The solution was filtered through Celite and washed with EtOAc, and the filtrate was concentrated and purified by flash chromatography (50% Et_2O in petroleum ether) to give pure ketone **49** (611 mg, 76%) as a white solid: R_f = 0.27 (70% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +129° (*c* 2.0, $CHCl_3$);

(60) Flowers, H. M. *Adv. Carbohydr. Chem. Biochem.* **1981**, *39*, 293.

IR ($CHCl_3$) ν_{max} 3510, 3068, 3032, 3013, 2941, 2877, 1729 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44–7.27 (m, 10 H, aromatic), 4.94 (d, J = 3.5 Hz, 1 H, H-1), 4.84 (d, J = 12.2 Hz, 1 H, benzylic), 4.77 (d, J = 12.3 Hz, 1 H, benzylic), 4.70 (d, J = 10.0 Hz, 1 H, H-3), 4.67–4.62 (m, 2 H, benzylic), 4.31 (q, J = 6.5 Hz, 1 H, H-5), 3.58 (dd, J = 10.0, 3.6 Hz, 1 H, H-2), 3.40 (b s, 1 H, O*H*), 1.26 (d, J = 6.5 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6, 137.9, 136.8, 128.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 96.1, 82.0, 75.8, 73.1, 70.3, 68.3, 13.5; FAB HRMS (NBA/ CsI) m/e 475.0527, M + Cs^+ calcd for $C_{20}H_{22}O_5$ 475.0522.

Phenylmethyl 6-Deoxy-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[2-*O*-(3-Chlorobenzoyl)-4,6-dideoxy-3-*O*-[(1,1-dimethylethyl)-dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]oxime (52). A suspension of phthalimide **41** (694 mg, 1.27 mmol) in MeOH (6.3 mL) was stirred rapidly and treated with 55% hydrazine hydrate (0.06 mL, 2 mmol). After 15 min, the reaction mixture was diluted with Et_2O (40 mL) and filtered through Celite. The Celite was washed with Et_2O (2 × 10 mL), and the filtrate was concentrated. The residual milky oil was again dissolved in Et_2O (20 mL) and filtered through Celite, washed with Et_2O (2 × 5 mL), and concentrated to give hydroxylamine **42** (0.53 g) as a clear oil.

Crude hydroxylamine **42** (0.53 g, 1.3 mmol) and ketone **49** (0.521 g, 1.52 mmol) were combined and azeotroped with benzene. Benzene (2.5 mL) and PPTS (32 mg, 0.13 mmol) were added, and the mixture was stirred for 3 h at 25 °C, diluted with EtOAc (100 mL), washed with saturated aqueous $NaHCO_3$ (2 × 75 mL), and dried ($MgSO_4$). The organic layer was concentrated and purified by flash chromatography (50% Et_2O in petroleum ether) to give oxime **52** (0.865 g, 92% from **41**) as a white foam: R_f = 0.39 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –31.5° (c 1.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600, 3012, 2933, 2861, 1729, 1667, 1580, 1500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01 (b s, 1 H, aromatic), 7.92 (d, J = 7.8 Hz, 1 H, aromatic), 7.52 (d, J = 7.5 Hz, 1 H, aromatic), 7.39–7.28 (m, 11 H, aromatic), 5.64 (dd, J = 5.5, 1.7 Hz, 1 H, B-2), 5.42 (d, J = 5.5 Hz, 1 H, B-1), 5.05 (d, J = 1.4 Hz, 1 H, B-4), 4.91 (d, J = 3.2 Hz, 1 H, A-1), 4.76 (q, J = 6.8 Hz, 1 H, A-5), 4.73 (d, J = 12.3 Hz, 2 H, 2 × benzylic), 4.62 (m, 2 H, A-3, benzylic), 4.57 (ddq, J = 6.6, 1.7, 1.4 Hz, 1 H, B-5), 4.52 (d, J = 12.4 Hz, 1 H, benzylic), 3.67 (dd, J = 6.2, 3.2 Hz, 1 H, A-2), 2.61 (b s, 1 H, O*H*), 1.39 (d, J = 6.8 Hz, 3 H, A-6), 1.28 (d, J = 6.5 Hz, 3 H, B-6), 0.79 (s, 9 H, ^{t}Bu), 0.17, 0.12 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 159.8, 144.1, 138.1, 137.2, 134.5, 133.2, 131.5, 129.8, 129.7, 128.4, 128.3, 127.9, 127.8, 127.8, 127.7, 127.7, 110.8, 102.3, 94.7, 79.4, 72.3, 70.4, 69.7, 68.7, 68.3, 64.8, 25.3, 22.4, 18.7, 17.8, –4.6, –4.7; FAB HRMS (NBA) m/e 738.2844, M + H^+ calcd for $C_{39}H_{48}ClNO_9Si$ 738.2865.

Phenylmethyl 6-Deoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[2-*O*-(3-Chlorobenzoyl)-4,6-dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]oxime (53). A solution of alcohol **52** (549 mg, 0.743 mmol) in CH_2Cl_2 (3 mL) was treated at –25 °C with 2,6-lutidine (0.22 mL, 1.9 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.27 mL, 1.1 mmol). After 15 min, the reaction mixture was warmed to 0 °C and stirred a further 10 min. The reaction mixture was diluted with Et_2O (50 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 30 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (15% Et_2O in petroleum ether) to give silyl ether **53** (625 mg, 99%) as a white foam: R_f = 0.50 (25% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –34.2° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3011, 2957, 2931, 2860, 1729, 1667, 1578 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 (b d, 1 H, aromatic), 7.92 (d, J = 7.8 Hz, 1 H, aromatic), 7.52 (d, J = 8.0 Hz, 1 H, aromatic), 7.38–7.25 (m, 11 H, aromatic), 5.63 (dd, J = 5.4, 1.9 Hz, 1 H, B-2), 5.44 (d, J = 5.4 Hz, 1 H, B-1), 5.09 (q, J = 6.9 Hz, 1 H, A-5), 5.05 (d, J = 1.6 Hz, 1 H, B-4), 5.03 (d, J = 2.2 Hz, 1 H, A-1), 4.86 (d, J = 12.3 Hz, 1 H, benzylic), 4.68 (d, J = 12.4 Hz, 1 H, benzylic), 4.64 (d, J = 12.4 Hz, 1 H, benzylic), 4.57 (m, 1 H, B-5), 4.54 (d, J = 12.3 Hz, 1 H, benzylic), 4.38 (d, J = 3.4 Hz, 1 H, A-3), 3.56 (dd, J = 3.4, 2.2 Hz, 1 H, A-2), 1.30 (d, J = 6.9 Hz, 3 H, A-6), 1.30 (d, J = 6.6 Hz, 3 H, B-6), 0.81, 0.71 (2 × s, 18 H, 2 × ^{t}Bu), 0.18, 0.12, –0.03, –0.12 (4 × s, 12 H, 4 × CH_3Si); FAB HRMS (NBA/CsI) m/e 984.2706, M + Cs^+ calcd for $C_{45}H_{62}ClNO_9Si_2$ 984.2706.

Phenylmethyl 6-Deoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[4,6-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]-oxime (54). DIBAL (1.8 mL of a 1.0 M solution in CH_2Cl_2, 1.8 mmol) was added dropwise to a solution of ester **53** (604 mg, 0.708 mmol) in CH_2Cl_2 (2.5 mL) at –78 °C. The solution was stirred for 45 min and the reaction quenched by the addition of EtOAc (75 mL). The mixture was washed with saturated aqueous Rochelle salt (3 × 75 mL), saturated aqueous NH_4Cl (40 mL), and brine (40 mL) and dried ($MgSO_4$). The solution was concentrated and purified by flash chromatography (9% EtOAc in PhH) to give alcohol **54** (456 mg, 90%) as a white foam: R_f = 0.26 (30% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +12.6° (c 0.7, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3581, 3011, 2957, 2932, 2860, 1673 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.24 (m, 10 H, aromatic), 5.27 (d, J = 4.9 Hz, 1 H, B-1), 5.14 (q, J = 7.0 Hz, 1 H, A-5), 5.09 (d, J = 2.1 Hz, 1 H, A-1), 4.89 (d, J ≈ 1.9 Hz, 1 H, B-4), 4.88 (d, J = 12.4 Hz, 1 H, benzylic), 4.71 (d, J = 12.3 Hz, 1 H, benzylic), 4.66 (d, J = 12.3 Hz, 1 H, benzylic), 4.56 (d, J = 12.4 Hz, 1 H, benzylic), 4.48 (ddq, J = 6.7, 2.0, 1.9 Hz, 1 H, B-5), 4.42 (d, J = 3.5 Hz, 1 H, A-3), 4.01 (dd, J = 4.9, 1.9 Hz, 1 H, B-2), 3.59 (dd, J = 3.5, 2.1 Hz, 1 H, A-2), 2.19 (b s, 1 H, O*H*), 1.45 (d, J = 7.0 Hz, 3 H, A-6), 1.23 (d, J = 6.7 Hz, 3 H, B-6), 0.95, 0.78 (2 × s, 18 H, 2 × ^{t}Bu), 0.21, 0.01, 0.01, 0.00 (4 × s, 12 H, 4 × CH_3Si); FAB HRMS (NBA) m/e 714.3842, M + H^+ calcd for $C_{38}H_{59}NO_8Si_2$ 714.3856.

Phenylmethyl 6-Deoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[4,6-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(1*H*-imidazol-1-ylthioxomethyl)-β-D-*erythro*-hex-3-enopyranosyl]oxime (55). A solution of alcohol **54** (285 mg, 0.40 mmol) in acetonitrile (1.3 mL) was treated with thiocarbonyldiimidazole (140 mg, 0.80 mmol) and stirred at 25 °C for 16 h. The reaction mixture was diluted with Et_2O (80 mL) and washed with water (4 × 40 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give a mixture of **55** and **56** (280 mg, 85%). A sample of **55** was isolated for characterization as a white foam: R_f = 0.42 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –30.6° (c 3.2, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2957, 2933, 2860, 1666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.36, 7.64 (2 × s, 2 H, imidazole), 7.36–7.26 (m, 10 H, aromatic), 7.04 (s, 1 H, imidazole), 6.15 (dd, J = 4.7, 1.9 Hz, 1 H, B-2), 5.54 (d, J = 4.7 Hz, 1 H, B-1), 5.11 (d, J = 1.1 Hz, 1 H, B-4), 5.08 (q, J = 7.0 Hz, 1 H, A-5), 5.05 (d, J = 2.2 Hz, 1 H, A-1), 4.86 (d, J = 12.3 Hz, 1 H, benzylic), 4.69 (d, J = 12.4 Hz, 1 H, benzylic), 4.65 (d, J = 12.4 Hz, 1 H, benzylic), 4.59 (qdd, J = 6.7, 1.9 Hz, 1 H, B-5), 4.55 (d, J = 12.3 Hz, 1 H, benzylic), 4.38 (d, J = 3.4 Hz, 1 H, A-3), 3.58 (dd, J = 3.4, 2.2 Hz, 1 H, A-2), 1.36 (d, J = 7.0 Hz, 3 H, A-6), 1.30 (d, J = 6.7 Hz, 3 H, B-6), 0.82, 0.74 (2 × s, 18 H, 2 × ^{t}Bu), 0.19, 0.13, –0.03, –0.11 (4 × s, 12 H, 4 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 183.6, 158.9, 142.6, 138.0, 137.4, 136.8, 130.4, 128.3, 128.3, 127.9, 127.8, 127.6, 118.1, 111.8, 101.3, 93.1, 78.8, 75.9, 72.4, 70.9, 70.1, 68.8, 65.6, 25.5, 25.3, 22.6, 18.0, 17.8, 17.8, –4.5, –4.6, –5.4; FAB HRMS (NBA/CsI) m/e 956.2743, M + Cs^+ calcd for $C_{42}H_{61}N_3O_8SSi_2$ 956.2772.

Phenylmethyl 6-Deoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4-*S*-(1*H*-imidazol-1-ylcarbonyl)-4-thio-β-D-*erythro*-hex-2-enopyranosyl]oxime (56). A mixture of **55** and **56** (250 mg, 0.30 mmol) was dissolved in toluene (7 mL) and refluxed for 1 h. The reaction mixture was cooled and the solution concentrated to give pure thioimidazolide **56** (250 mg, 100%) as a white foam: R_f = 0.34 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +87.7° (c 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3017, 2957, 2932, 2860, 1697, 1672 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (b s, 1 H, imidazole), 7.48 (b s, 1 H, imidazole), 7.36–7.25 (m, 10 H, aromatic), 7.13 (b s, 1 H, imidazole), 5.83 (d, J = 2.8 Hz, 1 H, B-1), 5.12–5.07 (m, 3 H, A-1, A-5, B-2), 5.88 (d, J = 12.3 Hz, 1 H, benzylic), 4.70 (d, J = 12.3 Hz, 1 H, benzylic), 4.67 (d, J = 12.3 Hz, 1 H, benzylic), 4.57 (d, J = 12.3 Hz, 1 H, benzylic), 4.42 (d, J = 3.3 Hz, 1 H, A-3), 4.28 (dq, J = 6.8, 1.9 Hz, 1 H, B-5), 4.05 (d, J = 1.7 Hz, 1 H, B-4), 3.59 (dd, J = 3.3, 2.2 Hz, 1 H, A-2), 1.47 (d, J = 6.8 Hz, 3 H, B-6), 1.42 (d, J = 7.0 Hz, 3 H, A-6), 0.91, 0.79 (2 × s, 18 H, 2 × ^{t}Bu), 0.25, 0.21, 0.01, 0.00 (4 × s, 12 H, 4 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 157.5, 148.3, 138.1, 137.4, 131.1, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 103.4, 97.7, 93.0, 78.5, 74.1, 72.3, 70.9, 65.7, 48.5, 25.6, 25.4, 20.8, 17.9, –4.3, –4.6, –4.9, –5.4; FAB HRMS (NBA) m/e 824.3836, M + H^+ calcd for $C_{42}H_{61}O_8N_3SSi_2$ 824.3796.

Phenylmethyl 6-Deoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4-*S*-(2,4,6-trimethylbenzoyl)-4-thio-β-D-*erythro*-hex-2-enopyranosyl]oxime (58). A solution of thioimidazolide **56** (86 mg, 0.10 mmol) in CH_2Cl_2 (1 mL) was treated with DIBAL (0.60 mL of a 1.0 M solution in CH_2Cl_2, 0.6 mmol) at –78 °C. The reaction mixture was stirred for 2 h, the reaction was quenched with EtOAc (40 mL), and the mixture was washed successively with saturated aqueous Rochelle salt (3 × 30 mL), saturated aqueous NH_4Cl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$), concentrated, and azeotroped with benzene. The crude

product **57** was dissolved in CH_2Cl_2 (1 mL), and triethylamine (0.14 mL, 1.0 mmol), distilled 2,4,6-trimethylbenzoyl chloride (0.03 mL, 0.2 mmol), and DMAP (4.5 mg, 0.04 mmol) were added. The solution was stirred at 25 °C for 12 h, diluted with Et_2O (50 mL), and washed with saturated aqueous NH_4Cl (3 × 20 mL), saturated aqueous $NaHCO_3$ (3 × 20 mL), and brine (20 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (15% Et_2O in petroleum ether) to give thioester **58** (80 mg, 91%) as a white foam: R_f = 0.24 (15% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +110° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3011, 2957, 2931, 2898, 2886, 2859, 1669, 1655 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.26 (m, 10 H, aromatic), 6.83 (s, 2 H, aromatic), 5.81 (d, *J* = 2.8 Hz, 1 H, B-1), 5.12 (q, *J* = 7.0 Hz, 1 H, A-5), 5.10 (d, *J* = 2.8 Hz, 1 H, A-1), 5.03 (d, *J* = 2.8 Hz, 1 H, B-2), 4.89 (d, *J* = 12.4 Hz, 1 H, benzylic), 4.70 (s, 2 H, 2 × benzylic), 4.57 (d, *J* = 12.4 Hz, 1 H, benzylic), 4.44 (d, *J* = 3.3 Hz, 1 H, A-3), 4.23 (q, *J* = 6.8 Hz, 1 H, B-5), 4.04 (s, 1 H, B-4), 3.58 (dd, *J* = 3.3, 2.8 Hz, 1 H, A-2), 2.28 (s, 9 H, 3 × ArCH_3), 1.50 (d, *J* = 6.8 Hz, 3 H, B-6), 1.43 (d, *J* = 7.0 Hz, 3 H, A-6), 0.95, 0.78 (2 × s, 18 H, 2 × ^{t}Bu), 0.26, 0.20, 0.00, –0.01 (4 × s, 12 H, 4 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 157.2, 149.4, 139.4, 138.2, 137.5, 136.9, 133.8, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 102.8, 97.9, 93.1, 78.4, 74.7, 72.2, 70.9, 70.0, 65.8, 47.2, 25.6, 25.5, 21.1, 20.9, 19.0, 18.0, 17.9, 17.8, –4.2, –4.5, –4.8, –5.4; FAB HRMS (NBA) *m/e* 876.4396, M + H^+ calcd for $C_{48}H_{69}NO_8SSi_2$ 876.4360.

Phenylmethyl 6-Deoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-4-*S*-(2,4,6-trimethylbenzoyl)-4-thio-β-D-*ribo*-hexopyranosyl]oxime (60). Silyl enol ether **58** (62.1 mg, 70.9 μmol) was dissolved in THF (0.75 mL), water (0.19 mL), and AcOH (7 μL, 120 μmol) and cooled to 0 °C. A solution of TBAF (71 μL of a 1.0 M solution in THF, 71 μmol) was added, and the solution was stirred for 15 min. The reaction mixture was diluted with Et_2O (40 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 20 mL) and water (20 mL). The organic layer was dried ($MgSO_4$) and concentrated to give crude ketone **59** which was used directly in the next step.

A solution of K-Selectride (0.21 mL of a 1.0 M solution in THF, 0.21 mmol) was added dropwise to a solution of ketone **59** (51 mg, 67 μmol) in DME (3.3 mL) at –70 °C. The reaction temperature was held for 45 min and then raised to –30 °C for 15 min. Saturated aqueous NH_4Cl (10 mL) was added, and the mixture was poured into Et_2O (40 mL) and extracted. The layers were separated, and the organic layer was washed successively with saturated aqueous NH_4Cl (2 × 10 mL), saturated aqueous $NaHCO_3$ (3 × 10 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$) and concentrated, and the residue was dissolved in 5% MeOH in CH_2Cl_2 (30 mL) and stirred with silica gel (1 g) for 2 h. The mixture was filtered and concentrated, and the crude alcohol was purified by flash chromatography (35% Et_2O in petroleum ether) to give pure **60** (36.8 mg, 68%) as a colorless oil: R_f = 0.45 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +56.6° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3610, 3032, 3012, 2956, 2931, 1674, 1610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.24 (m, 10 H, aromatic), 6.85 (s, 2 H, aromatic), 5.50 (dd, *J* = 9.2, 2.3 Hz, 1 H, B-1), 5.15 (q, *J* = 6.9 Hz, A-5), 5.07 (d, *J* = 2.2 Hz, 1 H, A-1), 4.89, 4.70, 4.66, 4.57 (4 × d, *J* = 12.3 Hz, 4 H, 4 × benzylic), 4.39 (d, *J* = 3.4 Hz, 1 H, A-3), 4.36 (b s, 1 H, B-3), 4.12 (dq, *J* = 10.2, 6.3 Hz, 1 H, B-5), 3.79 (dd, *J* = 10.1, 2.6 Hz, 1 H, B-4), 3.59 (dd, *J* = 3.6, 2.3 Hz, 1 H, A-2), 2.28 (s, 9 H, 3 × ArCH_3), 2.16 (ddd, *J* = 13.3, 3.8, 2.3 Hz, 1 H, B-2_{eq}), 2.08 (b s, 1 H, O*H*), 2.03 (ddd, *J* = 13.3, 9.6, 3.0 Hz, 1 H, B-2_{ax}), 1.42 (d, *J* = 6.9 Hz, 3 H, A-6), 1.40 (d, *J* = 6.3 Hz, 3 H, B-6), 0.79 (s, 9 H, ^{t}Bu), 0.00, 0.00 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.0, 158.0, 139.6, 138.1, 137.6, 137.1, 133.5, 128.5, 128.3, 128.2, 127.9, 127.6, 127.6, 99.4, 93.2, 78.9, 72.4, 71.0, 70.0, 69.3, 68.3, 65.5, 51.7, 36.7, 29.7, 25.6, 21.2, 19.7, 19.1, 18.0, 17.9, –4.5, –5.4; FAB HRMS (NBA) *m/e* 764.3637, M + H^+ calcd for $C_{42}H_{57}NO_8SSi$ 764.3652.

Phenylmethyl 6-Deoxy-2-*O*-(phenylmethyl)-α-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-4-*S*-[2,4,6-trimethylbenzoyl)-4-thio-β-D-*ribo*-hexopyranosyl]oxime (61). A solution of silyl ether **60** (16 mg, 21 μmol) in THF (1 mL) was treated with TBAF (30 μL of a 1.0 M solution in THF, 30 μmol) at 0 °C. After 30 min, the solution was diluted with Et_2O (30 mL) and washed with saturated aqueous NH_4Cl (15 mL), saturated aqueous $NaHCO_3$ (2 × 15 mL), and brine (15 mL). The solution was dried ($MgSO_4$), concentrated, and purified by flash chromatography (2% MeOH in CH_2Cl_2) to give diol **61** (13 mg, 98%) as a colorless oil: R_f = 0.40 (80% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +70 °C (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3687, 3601, 3018, 2928, 2856, 1728, 1674, 1609 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.26 (m, 10 H, aromatic), 6.85 (s, 2 H, aromatic), 5.50 (dd, *J* = 9.7, 2.3 Hz, 1 H, B-1), 4.92 (d, *J* = 3.3 Hz, 1 H, A-1), 4.79–4.71 (m, 2 H, A-5, benzylic), 4.67 (s, 2 H, 2 × benzylic), 4.63 (d, *J* = 5.4 Hz, 1 H, A-3), 4.55 (d, *J* = 12.3 Hz, 1 H, benzylic), 4.34 (b d, *J* = 2.6 Hz, 1 H, B-3), 4.12 (m, 1 H, B-5), 3.78 (dd, *J* = 10.5, 2.6 Hz, 1 H, B-4), 3.68 (dd, *J* = 9.9, 3.3 Hz, 1 H, A-2), 2.72 (b s, 1 H, O*H*), 2.28 (s, 9 H, 3 × ArCH_3), 2.13 (m, 1 H, B-2_{eq}), 3.08 (b s, 1 H, O*H*), 2.00 (m, 1 H, B-2_{ax}), 1.50 (d, *J* = 6.8 Hz, 3 H, A-6), 1.42 (d, *J* = 6.4 Hz, 1 H, B-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 158.8, 139.7, 137.3, 133.4, 128.5, 128.4, 128.3, 127.9, 127.8, 127.7, 127.7, 99.8, 95.0, 79.7, 72.4, 70.5, 69.8, 69.4, 68.5, 64.7, 51.5, 36.7, 29.7, 21.1, 19.6, 19.0; FAB HRMS (NBA) *m/e* 650.2750, M + H^+ calcd for $C_{36}H_{43}NO_8S$ 650.2787.

Phenylmethyl 4,6-Dideoxy-4-[[[(2,6-dideoxy-4-*S*-(2,4,6-trimethylbenzoyl)-4-thio-β-D-*ribo*-hexopyranosyl]oxy]amino]-2-*O*-(phenylmethyl)-α-D-glucopyranoside (47). A solution of oxime **61** (12 mg, 18 μmol) in THF (1 mL) was treated with a $BH_3{\cdot}NH_3$ complex (2 mg, 0.06 mmol) and PPTS (3 mg, 0.01 mmol). Subsequent additions (2–3) were made of each reagent at 1-h intervals until the reaction was complete. The reaction mixture was diluted with Et_2O (50 mL) and washed with saturated aqueous $NaHCO_3$ (30 mL), saturated aqueous NH_4Cl (2 × 30 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL), and brine (20 mL). The solution was dried ($MgSO_4$), concentrated, and purified by flash chromatography (80% Et_2O in petroleum ether) to give hydroxylamine **47** (9.4 mg, 81%) as a colorless oil and a single isomer: R_f = 0.30 (80% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +46.4° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3604, 3494, 3031, 3011, 2958, 2928, 2874, 2858, 1726, 1675, 1610 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41–7.26 (m, 10 H, aromatic), 6.85 (s, 2 H, aromatic), 5.04 (dd, *J* = 10.0, 1.8 Hz, 1 H, B-1), 4.82 (d, *J* = 3.6 Hz, 1 H, A-1), 4.71 (d, *J* = 12.4 Hz, 1 H, benzylic), 4.65 (d, *J* = 12.0 Hz, 1 H, benzylic), 4.58 (d, *J* = 12.0 Hz, 1 H, benzylic), 4.52 (d, *J* = 12.4 Hz, 1 H, benzylic), 4.40 (dd, *J* = 9.7, 9.7 Hz, 1 H, A-3), 4.27 (b d, 1 H, B-3), 4.08–3.98 (m, 2 H, A-5, B-5), 3.72 (dd, *J* = 10.7, 2.5 Hz, 1 H, B-4), 3.40 (dd, *J* = 9.7, 3.6 Hz, 1 H, A-2), 3.05 (b s, 1 H, O*H*), 2.38 (dd, *J* = 9.7, 0.7 Hz, 1 H, A-4), 2.28 (s, 3 H, ArCH_3), 2.27 (s, 6 H, 2 × ArCH_3), 2.05 (b s, 1 H, O*H*), 1.98 (m, 1 H, B-2_{eq}), 1.80 (m, 1 H, B-2_{ax}), 1.41 (d, *J* = 6.3 Hz, 1 H, A-6 or B-6), 1.29 (d, *J* = 6.3 Hz, A-6 or B-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.7, 139.6, 138.2, 137.6, 137.1, 133.4, 128.5, 128.4, 128.4, 128.1, 127.9, 127.7, 127.7, 99.8, 95.3, 80.1, 72.5, 68.8, 68.7, 68.6, 68.0, 66.5, 64.5, 51.7, 36.7, 21.1, 19.4, 19.0, 18.2; FAB HRMS (NBA) *m/e* 652.2936, M + H^+ calcd for $C_{36}H_{45}NO_8S$ 652.2944.

2,6-Diiodo-3,4,5-trimethoxytoluene (70). Iodine (15.32 g, 60.4 mmol) and $HIO_4{\cdot}2H_2O$ (6.9 g, 30.4 mmol) were added to a solution of 3,4,5-trimethoxytoluene (**69**; 10 g, 54.8 mmol) in glacial acetic acid (120 mL), and the mixture was heated to 53 °C for 24 h. The mixture was diluted with EtOAc (120 mL) and Et_2O (200 mL), washed with H_2O (100 mL), brine (2 × 150 mL), and saturated aqueous $NaHCO_3$ (200 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (10% Et_2O in petroleum ether) to give diiodide **70** (22.3 g, *ca.* 93%). This was rediluted with Et_2O (400 mL), washed with 5% $Na_2S_2O_3$ (2 × 150 mL) to remove the remaining I_2, dried ($MgSO_4$), concentrated, and recrystallized from MeOH to give **70** as colorless crystals: mp = 74 °C (from MeOH); R_f = 0.78 (50% ether in *n*-hexane); IR (CH_2Cl_2) ν_{max} 3015, 2980, 2940, 1463, 1407, 1364, 1320, 1090, 1046, 1005, 950 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.90 (s, 3 H, CH_3O), 3.89 (s, 6 H, 2 × CH_3O), 2.81 (s, 3 H, ArCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 142.5, 138.8, 92.0, 60.9, 60.5, 35.2; CI HRMS *m/e* 451.9213, M + NH_4^+ calcd for $C_{10}H_{12}I_2O_3$ 451.9220.

5-Hydroxy-2,6-diiodo-3,4-dimethoxytoluene (71). BCl_3 (102.2 mL of a 1.0 M solution in CH_2Cl_2, 102.2 mmol) was added to a solution of diiodide **70** (22.3 g, 51.1 mmol) in CH_2Cl_2 (255 mL) at 25 °C, and the reaction mixture was stirred for 2 days, diluted with Et_2O (300 mL), and washed with H_2O (150 mL), saturated aqueous $NaHCO_3$ (150 mL), and brine (50 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (15 → 20% Et_2O in petroleum ether) to give phenol **71** (11.4 g, 53%) along with 2.8 g (13%) of a regioisomer, 2.6 g (12%) of a dihydroxy compound, and 0.1 g (5%) of starting material. Allowing the reaction to proceed to completion increased the production of undesired byproducts. Phenol **71** was obtained as a white solid: mp = 80.5 °C (from Et_2O–petroleum ether); R_f = 0.40 (50% Et_2O in *n*-hexane); IR (CH_2Cl_2) ν_{max} 3465, 2980, 2940, 2880, 1460, 1415, 1332, 1285, 1222, 1203, 1159, 1090, 995, 947, 810 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.30 (s, 1 H, O*H*), 3.94 (s, 3 H, CH_3O), 3.87 (s, 3 H, CH_3O), 2.80 (s, 3 H, ArCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.4, 149.1, 138.4, 135.6, 86.4, 81.9, 61.0, 60.9, 34.7; EI HRMS *m/e* 419.874, M^+ calcd for $C_9H_{10}I_2O_3$ 419.871.

5-[(*tert*-Butyldimethylsilyl)oxy]-2,6-diiodo-3,4-dimethoxytoluene (72). A solution of phenol **71** (18.9 g, 44.9 mmol) in DMF (100 mL) was

treated at 0 °C with imidazole (7.4 g, 107.7 mmol) and *tert*-butyldimethylsilyl chloride (8.2 g, 89.8 mmol). After 30 min, the reaction was diluted with petroleum ether (400 mL) and washed with H_2O (2 × 200 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (2% Et_2O in petroleum ether) to give silyl ether **72** (23.10 g, 96%) as a colorless oil: R_f = 0.62 (5% Et_2O in petroleum ether); IR (neat) ν_{max} 2931, 2856, 1533, 1455, 1411, 1368, 1328, 1251, 1212, 1166, 1102, 1039 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3 H, CH_3O), 3.74 (s, 3 H, CH_3O), 2.80 (s, 3 H, $ArCH_3$), 1.03 (s, 9 H, *'Bu*), 0.27 (s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.0, 149.6, 139.8, 138.5, 91.3, 88.2, 60.4, 60.1, 35.8, 26.2, 18.8, −3.4; EI HRMS *m/e* 532.9522, M − H^+ calcd for $C_{15}H_{24}I_2O_3Si$ 532.9506.

Methyl 4-[(*tert*-Butyldimethylsilyl)oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoate (73). A solution of diiodide **72** (20.1 g, 37.6 mmol) in Et_2O (600 mL) was treated at −108 °C (EtOH–liquid N_2) with *tert*-butyllithium (27 mL of a 1.7 M solution in pentane, 45.2 mmol). The reaction mixture was allowed to warm to −78 °C over a period of 1.5 h and treated with a precooled solution of methyl chloroformate (4.7 mL, 60.2 mmol) in Et_2O (50 mL). The reaction mixture was allowed to warm to −40 °C over a period of 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$ (100 mL), and the mixture was extracted with Et_2O. The organic layer was washed with brine (200 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (2 → 5% Et_2O in petroleum ether) to give **73** (15.2 g, 87%) as a colorless oil: IR (neat) ν_{max} 2936, 2857, 1732, 1576, 1551, 1461, 1422, 1398, 1342, 1267, 1206, 1164, 1106, 1069, 1009 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 3 H, CH_3O), 3.80 (s, 3 H, CH_3O), 3.69 (s, 3 H, CH_3O), 2.29 (s, 3 H, $ArCH_3$), 0.99 (s, 9 H, *'Bu*), 0.22 (s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 150.6, 140.6, 133.6, 122.5, 93.1, 61.1, 52.1, 26.0, 18.8, −3.6; FAB HRMS (NBA/CsI) *m/e* 598.9727, M + Cs^+ calcd for $C_{17}H_{27}IO_5Si$ 598.9727.

Methyl 4-Hydroxy-5-iodo-2,3-dimethoxy-6-methylbenzoate (74). A solution of silyl ether **73** (39.5 g, 84.7 mmol) in THF (500 mL) was treated at 0 °C with AcOH (7.6 mL, 135 mmol) and TBAF (102 mL of a 1.0 M solution in THF, 102 mmol). The reaction mixture was stirred for 1.5 h, diluted with Et_2O (500 mL), and washed with H_2O (2 × 200 mL) and brine (200 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give **74** (28.3 g 95%) as pale purple prisms: mp = 134–135 °C (from $CHCl_3$–petroleum ether); R_f = 0.24 (34% Et_2O in *n*-hexane); UV (MeOH) λ_{max} 214 nm; IR ($CHCl_3$) ν_{max} 3519, 3040, 3020, 2960, 1730, 1575, 1465, 1428, 1364, 1270, 1234, 1099, 1070, 1001 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.42 (s, 1 H, O*H*), 3.88 (s, 3 H, CH_3O), 3.87 (s, 3 H, CH_3O), 3.84 (s, 3 H, CH_3O), 2.32 (s, 3 H, $ArCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 150.4, 149.6, 136.5, 134.0, 121.8, 84.0, 61.3, 61.0, 52.4, 25.2; FAB HRMS (NBA) *m/e* 352.984, M + H^+ calcd for $C_{11}H_{13}IO_5$ 352.988.

Acetyl 2,3,4-Tri-*O*-acetyl-α-L-rhamnopyranoside (76). L-Rhamnose monohydrate (100 g, 549 mmol) suspended in CH_2Cl_2 (500 mL) was treated at 0 °C with Et_3N (612 mL, 4.4 mol), DMAP (6.7 g, 55 mmol), and Ac_2O (311 mL, 3.3 mol). The reaction mixture was stirred at 25 °C for 12 h and treated with MeOH (10 mL). After concentration, the residue was dissolved in EtOAc (500 mL) and washed with brine (2 × 300 mL). The aqueous layers were extracted with EtOAc (3 × 100 mL), and the organic layers were combined and washed with 5% HCl (200 mL), saturated aqueous $NaHCO_3$ (washed until aqueous layer was pH > 7), and brine (200 mL). This solution was dried ($MgSO_4$) and concentrated to afford crude tetraacetate **76** (182 g). This product was taken on without further purification.

Phenyl 2,3,4-Tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (77). Thiophenol (6.92 g, 62.8 mmol) and $SnCl_4$ (10.4 g, 40 mmol) were added to a solution of L-rhamnose tetraacetate **76** (20 g, 57.1 mmol) in CH_2Cl_2 (285 mL) at 0 °C. The mixture was stirred at 0 °C for 4 h, diluted with Et_2O (1200 mL), washed with 2% HCl (150 mL), H_2O (2 × 200 mL), saturated aqueous $NaHCO_3$ (2 × 200 mL), and brine (100 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give only the α-anomer of thioglycoside **77** (21.3 g, 93%) as a white solid: mp = 118 °C (from ethyl acetate); R_f = 0.37 (50% ether in petroleum ether); $[\alpha]^{25}_D$ −107.0° (*c* 2.4, $CHCl_3$); IR (CH_2Cl_2) ν_{max} 3005, 2980, 2960, 2880, 1750, 1540, 1420, 1380, 1260, 1240, 1220, 1110, 1060 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.47 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.51 (m, 1 H, H-2), 5.42 (d, *J* = 1.4 Hz, H-1), 5.30 (m, 1 H, H-3), 5.16 (dd, *J* = 9.9, 9.9 Hz, 1 H, H-4), 4.37 (m, 1 H, H-5), 2.15 (s, 3 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 1.25 (d, *J* = 6.2 Hz, 3 H, H-6); EI HRMS *m/e* 382.107, M^+ calcd for $C_{18}H_{22}O_7S$ 382.108.

Phenyl 1-Thio-α-L-rhamnopyranoside (78). A catalytic amount of K_2CO_3 (1.46 g, 10.6 mmol) was added to a solution of thioglycoside **77** (21.3 g, 53.2 mmol) in THF:MeOH (266 mL, 1:1) at 25 °C, and the reaction mixture was stirred for 10 h. The mixture was filtered through a pad of silica gel, concentrated, and purified by flash chromatography (10% methanol in CH_2Cl_2) to give triol **78** (14.6 g, 100%) as a white solid: mp = 99 °C (from MeOH); R_f = 0.29 (10% MeOH in CH_2Cl_2); $[\alpha]^{25}_D$ −274.7° (*c* 0.7, $CHCl_3$); IR (CH_2Cl_2) ν_{max} 3405, 3400, 1583, 1478, 1451, 1065, 974 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.38 (m, 2 H, aromatic), 7.18 (m, 3 H, aromatic), 5.49 (s, 1 H, H-1), 4.98 (b s, 1 H), 4.60 (b s, 2 H), 4.24 (b s, 1 H), 4.17 (m, 1 H, H-4), 3.81 (m, 1 H), 3.59 (m, 1 H), 1.31 (d, *J* = 5.9 Hz, 3 H, H-6); EI HRMS *m/e* 256.024, M^+ calcd for $C_{12}H_{16}O_4S$ 256.026.

Phenyl 3-*O*-Methyl-1-thio-α-L-rhamnopyranoside (79). *n*-Bu_2SnO (23.1 g, 92.81 mmol) was added to a solution of triol **78** (21.6 g, 84.4 mmol) in MeOH (526 mL). The reaction mixture was refluxed until all the dibutyltin oxide had dissolved and the solution became clear. The solution was cooled to room temperature, concentrated, azeotroped with benzene (500 mL), and dried *in vacuo* over P_2O_5 for 5 h. The remaining oily residue was dissolved in DMF (526 mL), and MeI (55.86 g, 390 mmol) was added followed by CsF (13.2 g, 86.8 mmol). The reaction mixture was stirred at 25 °C for 20 h, concentrated, and purified by flash chromatography (100% petroleum ether then 7% MeOH in CH_2Cl_2) to give diol **79** (17.0 g, 77%) as a colorless oil: R_f = 0.42 (10% MeOH in CH_2Cl_2); $[\alpha]^{25}_D$ −195.4° (*c* 1.7, $CHCl_3$); IR (CH_2Cl_2) ν_{max} 3586, 3567, 3554, 3546, 3447, 3080, 3012, 2978, 2910, 1480, 1464, 1455, 1100 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, 2 H, aromatic), 7.44 (m, 3 H, aromatic), 5.56 (d, *J* = 1.1 Hz, 1 H, H-1), 4.33 (dd, *J* = 3.0, 1.3 Hz, 1 H, H-2), 4.16 (dq, *J* = 9.3, 6.2 Hz, 1 H, H-5), 3.60 (dd, *J* = 9.4, 9.4 Hz, 1 H, H-4), 3.49 (s, 3 H, CH_3O), 3.41 (dd, *J* = 9.3, 3.1 Hz, 1 H, H-3), 2.69 (b s, 1 H, O*H*), 1.31 (d, *J* = 6.2 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.0, 131.0, 128.8, 127.1, 87.3, 81.5, 71.2, 69.0, 68.5, 56.9, 17.4; EI HRMS *m/e* 270.093, M^+ calcd for $C_{13}H_{18}O_4S$ 270.092.

Phenyl 2,4-Di-*O*-acetyl-3-*O*-methyl-1-thio-α-L-rhamnopyranoside (80). Et_3N (23.8 g, 235.6 mmol), Ac_2O (18.0 g, 176.7 mmol), and a catalytic amount of DMAP (1.44 g, 11.8 mmol) were added to a solution of diol **79** (17.0 g, 58.9 mmol) in CH_2Cl_2 (295 mL). The mixture was stirred at 25 °C for 2 h, diluted with Et_2O (900 mL), and washed with 2% aqueous HCl (200 mL), H_2O (200 mL), saturated aqueous $NaHCO_3$ (2 × 150 mL), and H_2O again (300 mL). The solution was washed with brine (100 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (50% Et_2O in petroleum ether) to give diacetate **80** (20.9 g, 100%) as a white solid: mp = 112 °C (from EtOAc); R_f = 0.26 (40% Et_2O in petroleum ether); $[\alpha]^{25}_D$ −100.2° (*c* 0.7, $CHCl_3$); IR (CH_2Cl_2) ν_{max} 3028, 3000, 2980, 2910, 1740, 1440, 1124, 1104 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 (m, 2 H, aromatic), 7.30 (m, 3 H, aromatic), 5.57 (dd, *J* = 3.3, 1.5 Hz, 1 H, H-2), 5.44 (d, *J* = 1.5 Hz, 1 H, H-1), 5.05 (dd, *J* = 9.7, 9.7 Hz, 1 H, H-4), 4.28 (dq, *J* = 9.7, 6.3 Hz, 1 H, H-5), 3.57 (dd, *J* = 9.7, 3.2 Hz, 1 H, H-3), 3.37 (s, 3 H, CH_3O), 2.13 (s, 3 H, CH_3CO), 2.11 (s, 3 H, CH_3CO), 1.22 (d, *J* = 6.3 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 169.7, 133.3, 131.3, 128.9, 127.5, 85.7, 77.2, 72.2, 69.2, 67.4, 57.3, 20.6, 17.0; EI HRMS *m/e* 354.114, M^+ calcd for $C_{17}H_{22}O_6S$ 354.113.

2,4-Di-*O*-acetyl-3-*O*-methyl-L-rhamnopyranose (81). A solution of thioglycoside **80** (40.9 g, 115.5 mmol) in acetone (200 mL) was treated at 0 °C with NBS (42.0 g, 231 mmol) and H_2O (10 mL). The reaction mixture was allowed to warm to 25 °C and stirred for 1 h. Acetone was removed *in vacuo*, and the residue was taken up in EtOAc (500 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 200 mL) and brine (200 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give lactol **81** (21.2 g, 70%) as a 10:1 anomeric mixture: IR ($CHCl_3$) ν_{max} 3435, 2983, 2937, 1747, 1732, 1435, 1373, 1230, 1099, 1047 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.42 (b d, *J* = 2.7 Hz, 0.09 H, H_β-2), 5.24 (dd, *J* = 3.1, 2.0 Hz, 0.91 H, H_α-2), 5.06 (dd, *J* = 3.7, 1.4 Hz, 0.91 H, H_α-1), 4.87 (dd, *J* = 9.8, 9.8 Hz, 0.91 H, H_α-4), 4.80 (dd, *J* = 9.8, 9.8 Hz, 0.09 H, H_β-4), 4.78 (b d, *J* = 8.3 Hz, 0.09 H, H_β-1), 4.39 (d, *J* = 8.3 Hz, 0.09 H, O*H*), 4.26 (b d, *J* = 3.9 Hz, 0.91 H, O*H*), 3.95 (m, 1 H, H-5), 3.60 (dd, *J* = 9.8, 3.3 Hz, 0.91 H, H_α-3), 3.27 (s, 3 H, CH_3O), 2.12 (s, 0.27 H, CH_3CO), 2.07 (s, 2.73 H, CH_3CO), 2.02 (s, 3 H, CH_3CO), 1.16 (d, *J* = 6.2 Hz, 0.27 H, H_β-6), 1.10 (d, *J* = 6.2 Hz, 2.73 H, H_α-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 170.4, 92.9, 92.0, 79.5, 76.4, 72.5, 71.8, 70.4, 68.5, 66.1, 57.5, 20.8, 17.3; FAB HRMS (NBA/CsI) *m/e* 395.0099, M + Cs^+ calcd for $C_{11}H_{18}O_7$ 395.0107.

Methyl 4-[[2,4-Di-*O*-acetyl-3-*O*-methyl-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoate (83). A solution of lactol **81** (21.3 g, 81.3 mmol) in CH_2Cl_2 (650 mL) and trichloroacetonitrile (65.2 mL,

650 mmol) was treated with NaH (2.92 g of a 60% dispersion in oil, 73.2 mmol) at 0 °C, and the mixture was stirred at 25 °C for 1 h. The reaction mixture was filtered through a pad of Celite and concentrated to give crude trichloroacetimidate **82**. This was used directly for the next coupling reaction.

A mixture of the crude **82** and phenol **74** (22 g, 62.5 mmol) was azeotroped with freshly distilled benzene (200 mL) and toluene (2 × 200 mL) and taken up in CH_2Cl_2 (400 mL). Flame-dried powdered 4-Å molecular sieves (40 g) were added, and the mixture was cooled to −65 °C and treated with $BF_3{\cdot}OEt_2$ (5.0 mL, 40.7 mmol). The reaction mixture was allowed to warm to −50 °C over a period of 1 h, and solid $NaHCO_3$ (16 g, 200 mmol) was added. After 1 h, H_2O (200 mL) was added and the mixture was filtered through Celite. The filtrate was washed with saturated aqueous $NaHCO_3$ (200 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give **83** (35.3 g, 95%) as a colorless oil: R_f = 0.10 (40% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ −18.7° (*c* 1.15, $CHCl_3$); IR (neat) ν_{max} 3120, 3110, 3100, 1770, 1480, 1440, 1420, 1400, 1300, 1240, 1180, 1100, 1080, 1000 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.73 (dd, *J* = 3.5, 2.1 Hz, 1 H, H-2), 5.61 (d, *J* = 1.7 Hz, 1 H, H-1), 5.07 (dd, *J* = 9.9, 9.9 Hz, 1 H, H-4), 4.29 (m, 1 H, H-5), 4.02 (dd, *J* = 9.8, 3.5 Hz, 1 H, H-3), 3.89 (s, 3 H, C*H*$_3$O), 3.84 (s, 3 H, C*H*$_3$O), 3.81 (s, 3 H, C*H*$_3$O), 3.41 (s, 3 H, C*H*$_3$O), 2.34 (s, 3 H, ArC*H*$_3$), 2.14 (s, 3 H, C*H*$_3$CO), 2.10 (s, 3 H, C*H*$_3$CO), 1.16 (d, *J* = 6.2 Hz, 3 H, H-6); FAB HRMS (NBA/CsI) *m/e* 728.982, M + Cs$^+$ calcd for $C_{22}H_{29}IO_{11}$ 728.980.

Methyl 4-[[3-*O*-Methyl-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoate (84). K_2CO_3 (0.24 g, 1.68 mmol) was added to a solution of diacetate **83** (5.0 g, 8.4 mmol) in THF:MeOH (42 mL, 1:1). The reaction mixture was stirred at 25 °C for 2.5 h, filtered through a pad of Celite, concentrated, and purified by flash chromatography (Et_2O) to give diol **84** (4.0 g, 93%) as a white solid: mp = 137 °C (from Et_2O); R_f = 0.20 (70% ethyl acetate in petroleum ether); $[\alpha]^{25}_D$ −47.4° (*c* 0.5, $CHCl_3$); IR (neat) ν_{max} 3600, 3010, 3000, 2950, 1750, 1460, 1410, 1400, 1380, 1280 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.72 (s, 1 H, H-1), 4.45 (s, 1 H, H-2), 4.16 (m, 1 H, H-5), 3.90 (s, 3 H, C*H*$_3$O), 3.85 (s, 3 H, C*H*$_3$O), 3.82 (m, 4 H, C*H*$_3$O, H-3), 3.61 (dd, *J* = 9.5, 9.5 Hz, H-4), 3.54 (s, 3 H, C*H*$_3$O), 2.44 (s, 1 H, O*H*), 2.34 (s, 3 H, ArC*H*$_3$), 1.60 (b s, 1 H, O*H*), 1.27 (d, *J* = 6.2 Hz, 3 H, H-6); CI HRMS *m/e* 530.083, M + NH_4^+ calcd for $C_{18}H_{25}IO_9$ 530.088.

Methyl 4-[[3-*O*-Methyl-2,4-bis-*O*-(triethylsilyl)-α-L-rhamnopyranosyl]-oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoate (85). 2,6-Lutidine (4.18 g, 39 mmol) and triethylsilyl trifluoromethanesulfonate (6.18 g, 23.4 mmol) were added to a solution of diol **84** (4.0 g, 7.8 mmol) in CH_2Cl_2 (39 mL) at −20 °C. The mixture was allowed to warm to 0 °C over a period of 1.5 h, diluted with Et_2O (150 mL), washed with H_2O (2 × 150 mL), saturated aqueous $NaHCO_3$ (100 mL), and brine (100 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (10 → 20% Et_2O in petroleum ether) to give bis(silyl) ether **85** (5.2 g, 90%) as a colorless oil: R_f 0.17 (10% Et_2O in petroleum ether); $[\alpha]^{25}_D$ −37.7° (*c* 0.95, $CHCl_3$); IR (neat) ν_{max} 2890, 2880, 2850, 2830, 1760, 1540, 1550, 1460, 1410, 1400, 1340, 1320, 1270, 1210, 1150, 1080, 1000, 960, 940 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.38 (d, *J* = 2.0 Hz, 1 H, H-1), 4.41 (dd, *J* = 2.3, 2.0 Hz, 1 H, H-2), 4.08 (m, 1 H, H-5), 3.89 (s, 3 H, C*H*$_3$O), 3.85 (s, 3 H, C*H*$_3$O), 3.78 (s, 3 H, C*H*$_3$O), 3.71 (dd, *J* = 9.1, 9.1 Hz, 1 H, H-4), 3.55 (dd, *J* = 9.2, 2.3 Hz, 1 H, H-3), 3.40 (s, 3 H, C*H*$_3$O), 2.34 (s, 3 H, ArC*H*$_3$), 1.21 (d, *J* = 6.3 Hz, 3 H, H-6), 0.95 (m, 18 H, 2 × Si(CH$_2$C*H*$_3$)$_3$), 0.62 (m, 12 H, 2 × Si(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.5, 151.9, 151.1, 143.0, 134.0, 125.2, 104.5, 93.5, 81.3, 72.2, 68.5, 61.3, 60.6, 60.3 57.0, 52.3, 25.8, 17.9, 6.9, 6.3, 5.1, 4.7; FAB HRMS (NBA/CsI) *m/e* 873.133, M + Cs$^+$ calcd for $C_{30}H_{53}IO_9Si_2$ 873.132.

4-[[3-*O*-Methyl-2,4-bis-*O*-(triethylsilyl)-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzyl Alcohol (86). DIBAL (15.4 mL of a 1.0 M solution in hexanes, 15.4 mmol) was added dropwise to a solution of methyl ester **85** (5.2 g, 7.0 mmol) in CH_2Cl_2 (52 mL) at −78 °C. The reaction mixture was allowed to warm to −40 °C over a period of 1.5 h, diluted with EtOAc (200 mL), and washed with saturated aqueous Rochelle salt (3 × 100 mL), H_2O (100 mL), and brine (100 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give benzyl alcohol **86** (4.16 g, 83%) as a yellow oil: R_f 0.25 (40% Et_2O in petroleum ether); $[\alpha]^{25}_D$ −35.4° (*c* 0.5, $CHCl_3$); IR (neat) ν_{max} 3390, 2980, 2970, 2940, 2820, 2780, 1550, 1450, 1400, 1300, 1240, 1150, 1130, 1000, 950, 910, 880, 800 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.31 (d, *J* = 2.0 Hz, 1 H, H-1), 4.72 (s, 2 H, PhC*H*$_2$O), 4.44 (dd, *J* = 2.6, 2.0 Hz, 1 H, H-2), 4.12 (m, 1 H, H-5), 3.86 (s, 3 H, C*H*$_3$O), 3.77 (s, 3 H, C*H*$_3$O), 3.71 (s, 3 H, C*H*$_3$O), 3.71 (dd, *J* = 9.2, 9.2 Hz, 1 H, H-4), 3.54 (dd, *J* = 9.2, 2.6 Hz, 1 H, H-3), 3.40 (s, 3 H, C*H*$_3$O), 2.52 (s, 3 H, ArC*H*$_3$), 1.85 (b s, 1 H, O*H*), 1.21 (d, *J* = 6.3 Hz, 3 H, H-6), 0.93 (m, 18 H, 2 × Si(CH$_2$C*H*$_3$)$_3$), 0.61 (m, 12 H, 2 × Si(C*H*$_2$CH$_3$)$_3$); FAB HRMS (NBA/CsI) *m/e* 845.139, M + Cs$^+$ calcd for $C_{29}H_{53}IO_8Si_2$ 845.137.

4-[[3-*O*-Methyl-2,4-bis-*O*-(triethylsilyl)-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzaldehyde (87). PDC (0.124 g, 0.33 mmol) was added to a solution of benzyl alcohol **86** (0.158 g, 0.22 mmol) in CH_2Cl_2 (2.2 mL). After 1 h, more PDC (0.124 g, 0.33 mmol) was added and the mixture was stirred for an additional 0.5 h, diluted with Et_2O (10 mL), washed with water (2 mL) and brine (2 mL), dried ($MgSO_4$), and purified by flash chromatography (10% Et_2O in petroleum ether) to give benzaldehyde **87** (0.126 g, 80%) as a colorless oil: R_f = 0.26 (10% Et_2O in petroleum ether); $[\alpha]^{25}_D$ −34° (*c* 1.4, $CHCl_3$); IR (neat) ν_{max} 2980, 2960, 2880, 2840, 1680, 1570, 1525, 1460, 1420, 1380, 1300, 1230, 1175, 1100, 1000, 920, 900, 800 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.28 (s, 1 H, C(O)*H*), 5.58 (d, *J* = 2.0 Hz, H-1), 4.40 (t, *J* = 2.3 Hz, 1 H, H-2), 4.00 (m, 1 H, H-5), 3.94 (s, 3 H, C*H*$_3$O), 3.81 (s, 3 H, C*H*$_3$O), 3.71 (t, *J* = 9.1 Hz, 1 H, H-4), 3.60 (dd, *J* = 9.0, 2.6 Hz, 1 H, H-3), 3.40 (s, 3 H, C*H*$_3$O), 2.70 (s, 3 H, ArC*H*$_3$), 1.19 (d, *J* = 6.2 Hz, 3 H, H-6), 0.93 (m, 18 H, 2 × Si(CH$_2$C*H*$_3$)$_3$), 0.60 (m, 12 H, 2 × Si(C*H*$_2$CH$_3$)$_3$); FAB HRMS *m/e* 843.115, M + Cs$^+$ calcd for $C_{29}H_{51}IO_8Si_2$ 843.122.

4-[[3-*O*-Methyl-2,4-bis-*O*-(triethylsilyl)-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoic Acid (88). Water (1 mL) and $KMnO_4$ (0.026 g, 0.168 mmol) were added to a solution of benzaldehyde **87** (0.12 g, 0.168 mmol) in acetone (2.6 mL), and the mixture was stirred at 25 °C for 1 h. Further $KMnO_4$ (0.026 g, 0.168 mmol) was added, and the reaction mixture was stirred for another 1 h, filtered through a short plug of silica gel, and purified by flash chromatography (10% MeOH in CH_2Cl_2) to give free acid **88** (91 mg, 75%) as a colorless oil: R_f = 0.20 (10% MeOH in CH_2Cl_2); $[\alpha]^{25}_D$ −29.1° (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 2960, 2940, 2920, 2850, 1750, 1700, 1450, 1400, 1340, 1300, 1280, 1260, 1150, 1100, 1080, 1000, 920, 900, 800 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.43 (d, *J* = 1.8 Hz, H-1), 4.44 (dd, *J* = 2.6, 1.8 Hz, 1 H, H-2), 4.11 (m, 1 H, H-5), 3.93 (s, 3 H, C*H*$_3$O), 3.82 (s, 3 H, C*H*$_3$O), 3.74 (dd, *J* = 9.2, 9.2 Hz, 1 H, H-4), 3.58 (dd, *J* = 9.1, 2.6 Hz, 1 H, H-3), 3.43 (s, 3 H, C*H*$_3$O), 2.49 (s, 3 H, ArC*H*$_3$), 1.24 (d, *J* = 6.2 Hz, 3 H, H-6), 0.98 (m, 18 H, 2 × Si(CH$_2$C*H*$_3$)$_3$), 0.64 (m, 12 H, 2 × Si(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 152.2, 151.2, 143.1, 134.1, 104.5, 93.8, 81.2, 72.3, 72.3, 68.5, 61.5, 60.7, 57.1, 26.0, 17.9, 6.8, 6.6, 5.1, 4.8; FAB HRMS (NBA/CsI) *m/e* 991.0099, M − H$^+$ + 2Cs$^+$ calcd for $C_{29}H_{50}IO_9Si_2$ 991.0147.

***N*-Ethyl-L-serine, Methyl Ester (90).** Et_3N (22.4 mL, 0.161 mol) and acetaldehyde (9.0 mL, 0.161 mol) were added to a solution of L-serine methyl ester hydrochloride (**89**; 25.0 g, 0.161 mol) in MeOH (125 mL), and the mixture was stirred for 2 h at 0 °C. Sodium borohydride (12.1 g, 0.322 mol) was then added portionwise over 2 h while the temperature was maintained below 5 °C. The mixture was carefully partitioned between 20% aqueous HCl (200 mL) and Et_2O (125 mL). The phases were separated, and the organic phase was extracted twice with 20% HCl and then discarded. The combined aqueous layers were carefully neutralized with solid $KHCO_3$ and then extracted with EtOAc (7 × 500 mL). The combined organic extracts were dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (15% MeOH in CH_2Cl_2) to give ethylamine **90** (15.2 g, 64%) as a colorless oil: R_f = 0.45 (15% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ −27.0° (*c* 3.3, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3420–3320, 3200, 3010, 2971, 2874, 1737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (dd, *J* = 10.9, 4.3 Hz, 1 H, C*H*$_2$O), 3.72 (s, 3 H, C*H*$_3$O), 3.61 (dd, *J* = 10.9, 6.0 Hz, 1 H, C*H*$_2$O), 3.36 (dd, *J* = 6.0, 4.3 Hz, 1 H, C*H*N), 2.98 (b s, 1 H, O*H*), 2.74–2.67 (m, 1 H, C*H*$_2$N), 2.59–2.52 (m, 1 H, C*H*$_2$N), 1.09 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 62.5, 62.3, 52.1, 42.5, 15.0; FAB HRMS (NBA) *m/e* 148.0988, M + H$^+$ calcd for $C_6H_{13}NO_3$ 148.0973.

(*S*)-Methyl 3-Ethyl-2-oxo-4-oxazolidinecarboxylate (91). A solution of carbonyldiimidazole (18.3 g, 0.113 mol) in MeCN (500 mL) was added dropwise over 2 h to a refluxing solution of amino alcohol **90** (15.2 g, 0.103 mmol) in MeCN (300 mL). The reaction mixture was cooled and concentrated and the residue dissolved in EtOAc (500 mL) and washed with 2 M HCl (2 × 200 mL). The aqueous layer was extracted with EtOAc (200 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (300 mL) until neutral. The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (Et_2O) to give oxazolidinone **91** (13.9 g, 78%) as a white solid: mp = 34 °C (from Et_2O); R_f = 0.36 (Et_2O); $[\alpha]^{23}_D$ −39.2° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3495, 3025, 2984, 2958, 1773–1737 (b) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.45 (dd, *J* = 8.7, 8.7 Hz, 1 H, C*H*$_2$O), 4.38–4.31 (m, 2 H, C*H*$_2$O, C*H*N), 3.81 (s, 3 H, C*H*$_3$O), 3.62 (dq, *J* = 14.4, 7.2

Hz, 1 H, CH_2N), 3.20 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 1.16 (t, J = 7.2 Hz, 3 H, CH_3); FAB HRMS (NBA/CsI) m/e 305.9745, M + Cs^+ calcd for $C_7H_{11}NO_4$ 305.9742.

[*S*-(*R,*R**)]-3-Ethyl-4-(1-hydroxy-3-butenyl)-2-oxazolidinone (93).** DIBAL (66 mL of a 1.0 M solution in CH_2Cl_2, 66 mmol) was added over 4 h to a solution of oxazolidinone **91** (10.8 g, 62.4 mmol) in CH_2Cl_2 (350 mL) at −78 °C. After an additional 0.5 h at −78 °C, the reaction was quenched with MeOH (5 mL) and the mixture poured into a vigorously stirred mixture of saturated aqueous Rochelle salt (70 mL) and EtOAc (350 mL). After 20 min, the phases were separated and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to give crude aldehyde **92** (6.8 g, 76% crude) which was used in the next step without further purification.

Allylmagnesium bromide (48 mL of a 1.0 M solution in Et_2O, 48 mmol) was added dropwise to a stirred solution of (−)-*B*-methoxydiisopinocampheylborane (15.2 g, 48 mmol) in THF (60 mL) at −78 °C. The temperature was maintained at −78 °C for 15 min, and then the reaction mixture was allowed to warm to 25 °C over 1 h. After the mixture was cooled to −78 °C, a solution of crude aldehyde **92** (6.8 g, 48 mmol) in THF (50 mL) was added slowly over 20 min. The temperature was maintained at −78 °C for 6 h and then allowed to slowly warm to 25 °C. The reaction was quenched by the addition of pH 7 buffer (30 mL) and the mixture extracted with EtOAc (4 × 75 mL). The combined extracts were concentrated, and the residue was dissolved in MeOH (145 mL). The solution was cooled to 0 °C, and 30% H_2O_2 (48 mL) was added dropwise. The solution was stirred 20 min, water (240 mL) was added, and the mixture was concentrated to remove the MeOH. The mixture was extracted with EtOAc (5 × 200 mL), and the combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash chromatography (1 → 5% MeOH in CH_2Cl_2) to give **93** (6.6 g, 57% from **91**) as a white, amorphous solid: R_f = 0.27 (5% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ −4.7° (c 3.2, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3580, 3440, 3012, 2982, 2938, 1744, 1642 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84–5.76 (m, 1 H, CH=CH_2), 5.22–5.17 (m, 2 H, CH_2=CH), 4.26 (dd, J = 9.1, 9.0 Hz, 1 H, CH_2O), 4.16 (dd, J = 9.1, 5.3 Hz, 1 H, CH_2O), 3.92–3.88 (m, 1 H, CHN), 3.82 (b m, 1 H, CHO), 3.55 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 3.25 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 2.55 (b s, 1 H, OH), 2.29–2.24 (m, 1 H, CH_2), 2.14–2.08 (m, 1 H, CH_2), 1.17 (t, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 133.1, 119.6, 70.7, 63.6, 57.7, 38.3, 36.2, 12.7; FAB HRMS (NBA) m/e 186.1130, M + H^+ calcd for $C_9H_{15}NO_3$ 186.1130. Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.28; H, 8.05; N, 7.21

[*S*-(*R,*R**)]-3-Ethyl-4-(1-methoxy-3-butenyl)-2-oxazolidinone (94).** Alcohol **93** (6.3 g, 34.0 mmol) was rapidly stirred in the dark with Ag_2O (11.8 g, 51 mmol), MeI (21 mL, 0.34 mol), and DMF (100 mL) at 40 °C for 36 h. Following careful removal of MeI *in vacuo*, the reaction mixture was diluted with EtOAc (400 mL) and filtered through a pad of Celite. The filtrate was washed with brine (2 × 100 mL) and water (3 × 100 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (50% EtOAc in petroleum ether) to give pure methyl ether **94** (6.4 g, 95%) as a colorless oil: R_f = 0.25 (40% EtOAc in petroleum ether); $[\alpha]^{23}_D$ +13.9° (c 4.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3480, 3015, 2984, 2937, 2830, 1744, 1642 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.87–5.78 (m, 1 H, CH=CH_2), 5.14–5.10 (m, 2 H, CH_2=CH), 4.24 (dd, J = 9.1, 9.1 Hz, 1 H, CH_2O), 4.09 (dd, J = 9.1, 5.5 Hz, 1 H, CH_2O), 3.95–3.91 (m, 1 H, CHN), 3.56 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 3.41–3.38 (m, 1 H, CHO), 3.40 (s, 3 H, CH_3O), 3.18 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 2.38–2.32 (m, 1 H, CH_2), 2.20–2.14 (m, 1 H, CH_2), 1.17 (t, J = 7.2 Hz, 3 H, CH_3); FAB HRMS (NBA) m/e 200.1295, M + H^+ calcd for $C_{10}H_{17}NO_3$ 200.1287.

[*S*-(*R,*R**)]-3-Ethyl-β-methoxy-2-oxo-4-oxazolidinepropanal (95).** A solution of **94** (6.4 g, 32 mmol) in MeOH (200 mL) was cooled to −78 °C, and ozone was introduced *via* a bubbler until the color of the solution was slightly blue. Excess ozone was displaced with a stream of argon (5 min), and Me_2S (4.7 mL, 64 mmol) was added dropwise to the solution at −78 °C. After 5 min, the bath was removed and the reaction mixture was allowed to stir at 25 °C for 12 h. Concentration of the reaction mixture and purification of the residue by flash chromatography (80% EtOAc in petroleum ether) gave aldehyde **95** (5.9 g, 91%) as a colorless oil: R_f = 0.32 (80% EtOAc in petroleum ether); $[\alpha]^{23}_D$ −6.1° (c 0.56, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3025, 3012, 2986, 2936, 2834, 1748, 1728 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.85 (t, J = 1.6 Hz, 1 H, C(O)H), 4.27 (dd, J = 9.3, 9.3 Hz, 1 H, CH_2O), 4.17 (dd, J = 9.3, 4.0 Hz, 1 H, CH_2O), 4.09–4.05 (m, 2 H, CHN, CHO), 3.52 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 3.06 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 2.69 (ddd, J = 17.5, 7.7, 1.6 Hz, 1 H, CH_2), 2.58 (dd, J = 17.5, 3.1 Hz, 1 H, CH_2), 1.18 (t, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.1, 158.3, 74.7, 63.3, 58.3, 54.7, 42.8, 37.8, 12.8; FAB HRMS (NBA) m/e 202.1077, M + H^+ calcd for $C_9H_{15}NO_4$ 202.1079.

[*S*-(*R,*R**)]-3-Ethyl-4-(1,3,3-trimethoxypropyl)-2-oxazolidinone (96).** Amberlyst 15 ion-exchange resin (6 g) was washed with MeOH (3 × 50 mL) and added to a solution of aldehyde **95** (5.9 g, 29 mmol) in MeOH (200 mL). The reaction mixture was stirred for 6 h at 25 °C, filtered, concentrated, and purified by flash chromatography (80% EtOAc in petroleum ether) to give acetal **96** (6.7 g, 94%) as a colorless oil: R_f = 0.35 (80% EtOAc in petroleum ether); $[\alpha]^{23}_D$ −21.2° (c 5.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3480, 3014, 2937, 2834, 1744 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.55 (dd, J = 7.1, 4.1 Hz, 1 H, $CH(OMe)_2$), 4.24 (dd, J = 9.2, 9.2 Hz, 1 H, CH_2O), 4.12 (dd, J = 9.2, 5.0 Hz, 1 H, CH_2O), 4.01–3.97 (m, 1 H, CHN), 3.57 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 3.52–3.49 (m, 1 H, CHO), 3.39, 3.33, 3.32 (3 × s, 9 H, 3 × CH_3O), 3.12 (dq, J = 14.4, 7.2 Hz, 1 H, CH_2N), 1.75 (ddd, J = 14.4, 7.1, 3.0 Hz, 1 H, CH_2), 1.66 (ddd, J = 14.4, 8.5, 4.1 Hz, 1 H, CH_2), 1.18 (t, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2, 101.7, 77.6, 63.5, 58.3, 54.9, 53.3, 53.1, 37.2, 32.2, 12.6; FAB HRMS (NBA) m/e 248.1488, M + H^+ calcd for $C_{11}H_{21}NO_5$ 248.1498. Anal. Calcd for $C_{11}H_{21}NO_5$: C, 53.43; H, 8.56; N, 5.66. Found: C, 53.01; H, 8.65; N, 5.68.

2,4-Dideoxy-4-(ethylamino)-3-*O*-methyl-L-*threo*-pentose Dimethyl Acetal (97). A solution of **96** (6.7 g, 27 mmol) in MeOH (15 mL) was treated with 50% aqueous NaOH (15 mL) and refluxed for 3 h. The solution was cooled, concentrated to remove the MeOH, and extracted with EtOAc (10 × 50 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash chromatography through a short column of silica (10 → 30% MeOH in CH_2Cl_2) to give **97** (5.7 g, 96%) as a colorless oil: R_f = 0.20 (20% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ −3.2° (c 3.7, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3470, 3012, 2966, 2938, 2834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.53 (dd, J = 6.7, 4.7 Hz, 1 H, $CH(OMe)_2$), 3.65 (dd, J = 11.0, 4.6 Hz, 1 H, CH_2O), 3.44 (dd, J = 11.0, 4.7 Hz, 1 H, CH_2O), 3.41–3.37 (m, 1 H, CHO), 3.37, 3.32, 3.31 (3 × s, 9 H, 3 × CH_3O), 2.71–2.61 (m, 3 H, CH_2N, CHN), 2.32 (b s, 2 H, OH, NH), 1.91 (ddd, J = 14.3, 6.7, 4.1 Hz, 1 H, CH_2), 1.77 (ddd, J = 14.3, 7.6, 4.7 Hz, 1 H, CH_2), 1.10 (t, J = 7.1 Hz, 3 H, CH_3); FAB HRMS (NBA) m/e 222.1685, M + H^+ calcd for $C_{10}H_{23}NO_4$ 222.1705. Anal. Calcd for $C_{10}H_{23}NO_4$: C, 54.28; H, 10.48; N, 6.33. Found: C, 54.03; H, 10.23; N, 6.24.

Methyl 2,4-Dideoxy-4-(ethylamino)-3-*O*-methyl-L-*threo*-pentopyranoside (98). A 1.0 M solution of HCl in Et_2O (26 mL, 26 mmol) was added to a solution of amino alcohol **97** (5.68 g, 25.7 mmol) in MeOH (50 mL), and the mixture was stirred for 3 h. The solution was cooled to 0 °C, Et_3N (3.6 mL, 26 mmol) was added slowly, and the mixture was concentrated. The residue was purified by flash chromatography (10% MeOH in EtOAc) to give an equimolar mixture of α-/β-anomers **98** (4.63 g, 95%). The two anomers were separated for characterization purposes. α-**98**: oil; R_f = 0.27 (10% MeOH in EtOAc); $[\alpha]^{23}_D$ −56.7° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3315, 3012, 2969, 2937, 2911, 2834 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 4.66 (dd, J = 3.6, 2.2 Hz, 1 H, H-1), 3.79 (dd, J = 11.0, 4.7 Hz, 1 H, H-5_{eq}), 3.61–3.51 (m, 2 H, H-3, H-5_{ax}), 3.15 (s, 3 H, CH_3O), 3.03 (s, 3 H, CH_3O), 2.74 (ddd, J = 9.7, 9.0, 4.7 Hz, 1 H, H-4), 2.52–2.38 (m, 2 H, CH_2N), 2.11 (ddd, J = 12.7, 4.5, 2.2 Hz, 1 H, H-2_{eq}), 1.47 (ddd, J = 12.7, 10.5, 3.6 Hz, 1 H, H-2_{ax}), 1.30 (b s, 1 H, NH), 0.91 (t, J = 7.1 Hz, 3 H, CH_3); EI HRMS m/e 189.1363, M^+ calcd for $C_9H_{19}NO_3$ 189.1365. β-**98**: colorless needles; mp = 123 °C (from EtOAc); R_f = 0.18 (10% MeOH in EtOAc); $[\alpha]^{23}_D$ +99.7° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 2971, 2836, 2700 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 4.14–4.07 (m, 2 H, H-1, H-5_{eq}), 3.37 (s, 3 H, CH_3O), 3.07 (dd, J = 9.6, 9.0 Hz, 1 H, H-5_{ax}), 3.07–3.00 (m, 4 H, H-3, CH_3O), 2.66 (ddd, J = 9.0, 9.0, 4.5 Hz, 1 H, H-4), 2.46–2.33 (m, 2 H, CH_2N), 2.13 (ddd, J = 12.4, 4.5, 2.4 Hz, 1 H, H-2_{eq}), 1.96 (b s, 1 H, NH), 1.59 (ddd, J = 12.4, 10.5, 8.9 Hz, 1 H, H-2_{ax}), 0.89 (t, J = 7.1 Hz, 3 H, CH_3); EI HRMS m/e 189.1366, M^+ calcd for $C_9H_{19}NO_3$ 189.1365.

Methyl 2,4-Dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-L-*threo*-pentopyranoside (99). K_2CO_3 (10.1 g, 73 mmol) was added to a solution of amine **98** (4.60 g, 24.3 mmol, mixture of α-/β-anomers) in THF (50 mL) and H_2O (20 mL) at 0 °C followed by the portionwise addition of FMOC-Cl (9.43 g, 36.5 mmol) over 20 min. Stirring was continued for 30 min, and then the layers were separated. The aqueous phase was extracted with Et_2O (2 × 100 mL), and the combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash chromatography (30 → 80% Et_2O in petroleum ether) to give carbamate **99** (9.60 g, 96%) as a mixture of anomers. α-**99**: oil; R_f = 0.30 (65% Et_2O in petroleum ether); $[\alpha]^{23}_D$ −56.0° (c 2.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3018, 2976, 2937, 2898, 1692 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.85 (d, J = 7.5 Hz, 2 H, aromatic), 7.63 (d, J =

7.5 Hz, 2 H, aromatic), 7.40 (dd, J = 7.5, 7.5 Hz, 2 H, aromatic), 7.31 (ddd, J = 7.5, 7.5, 1.0 Hz, 2 H, aromatic), 4.73 (dd, J = 3.5, 1.6 Hz, 1 H, H-1), 4.48–4.42 (m, 2 H, CH_2(FMOC)), 4.27 (t, J = 5.9 Hz, 1 H, benzylic-FMOC), 3.76 (b m, 1 H, CHO), 3.60 (b s, 2 H, 2 × CHO), 3.32 (b d, 5.8 Hz, 1 H, H-4), 3.23 (s, 3 H, CH_3O), 3.15 (s, 3 H, CH_3O), 3.05 (b s, 2 H, CH_2N), 2.21 (ddd, J = 14.2, 4.7, 1.6 Hz, 1 H, H-2_{eq}), 1.37 (ddd, J = 14.2, 10.7, 3.5 Hz, 1 H, H-2_{ax}), 0.89 (b s, 3 H, CH_3CH_2N); ^{13}C NMR (see ref 52) (125 MHz, $CDCl_3$) δ 155.9, 144.3, 144.1, 143.9, 141.4, 141.3, 127.6, 127.0, 125.3, 125.1, 124.8, 119.9, 98.9, 72.3, 72.0, 67.4, 66.8, 59.9, 59.4, 58.9, 57.6, 56.0, 55.8, 54.9, 54.8, 47.4, 47.3, 40.6, 35.2, 14.8, 14.7; EI HRMS m/e 411.2048, M^+ calcd for $C_{24}H_{29}O_5N$ 411.2046. **β-98**: white, amorphous solid; R_f = 0.25 (65% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +69.8° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3500, 3012, 2964, 2936, 1692 cm^{-1}; EI HRMS m/e 411.2047, M^+ calcd for $C_{24}H_{29}NO_5$ 411.2046.

2,4-Dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-L-*threo*-pentopyranosyl Fluoride (67). A solution of an anomeric mixture of **99** (8.32 g, 20.2 mmol) in AcOH (100 mL) and water (20 mL) was heated to 95 °C for 6 h. Upon cooling, toluene (100 mL) was added and the darkened mixture was concentrated. Azeotropic removal of AcOH was repeated three to four times. Purification of the residue by flash chromatography (80 → 100% Et_2O in petroleum ether) gave an inseparable mixture of lactol anomers **100** (6.86 g, 85%) and some recovered **99** (330 mg, 4%).

Powdered 4-Å molecular sieves (7 g) were added to a stirred solution of lactol **100** (7.25 g, 18.2 mmol) in THF (90 mL). The mixture was cooled to −78 °C, and DAST (9.6 mL, 73 mmol) was added dropwise over 15 min. The temperature was allowed to slowly rise to −30 °C over 2 h and then held at 0 °C for 15 min. The reaction mixture was diluted with Et_2O (400 mL) and quickly filtered through a pad of Celite followed by washing with Et_2O (2 × 50 mL). The filtrate was extensively washed with cold saturated aqueous $NaHCO_3$ (8 × 100 mL), dried ($MgSO_4$), and concentrated. The residue was quickly filtered through a short plug of silica (50% Et_2O in petroleum ether) to give glycosyl fluoride **67** (6.35 g, 91%) as a mixture of anomers: oil; R_f = 0.26 (α), 0.16 (β) (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ −1.2° (*ca.* 10:1 α/β; c 0.68; $CHCl_3$); IR ($CHCl_3$) ν_{max} 3012, 2969, 2933, 1693 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 65 °C) the α-anomeric signal was identified at δ 5.39 (d, J = 52 Hz); FAB HRMS (NBA/CsI) m/e 532.0888, M + Cs^+ calcd for $C_{23}H_{26}FNO_4$ 532.0900.

Methyl 2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-β-D-galactopyranoside (102). Et_3N (30 mL, 0.22 mol), Ac_2O (17 mL, 0.18 mol), and DMAP (0.89 g, 7.3 mmol) were added to a solution of diol **101**[54] (20.6 g, 73 mmol) in CH_2Cl_2 (200 mL) at 0 °C. The reaction mixture was warmed to 25 °C, stirred for 3 h, diluted with CH_2Cl_2 (200 mL), and washed with 2 M HCl (2 × 200 mL), water (200 mL), saturated aqueous $NaHCO_3$ (2 × 200 mL), and brine (200 mL). The organic phase was dried ($MgSO_4$) and concentrated to give pure diester **102** (26.7 g, 100%) as a white solid: mp = 155 °C; R_f = 0.41 (2% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ +79.3° (c 2.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3028, 3014, 2871, 2844, 1742 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.50 (m, 2 H, aromatic), 7.38–7.35 (m, 3 H, aromatic), 5.38 (dd, J = 10.4, 8.0 Hz, 1 H, H-2), 4.96 (dd, J = 10.4, 3.6 Hz, 1 H, H-3), 4.43 (d, J = 8.0 Hz, 1 H, H-1), 4.37 (b d, J = 3.5 Hz, 1 H, H-4), 4.34 (dd, J = 12.4, 1.5 Hz, 1 H, H-6), 4.07 (dd, J = 12.4, 1.7 Hz, 1 H, H-6′), 3.52 (s, 3 H, CH_3O), 3.52 (obs, 1 H, H-5), 2.07 (s, 6 H, 2 × CH_3CO); FAB HRMS (NBA/CsI) m/e 499.0370, M + Cs^+ calcd for $C_{18}H_{22}O_8$ 499.0369. Anal. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 58.80; H, 6.01.

Methyl 2,3-Di-*O*-acetyl-4-*O*-benzoyl-6-deoxy-β-D-galactopyranoside (104). A solution of benzylidene **102** (26.2 g, 71.6 mmol) in CCl_4 (240 mL) was treated with NBS (12.7 g, 72 mmol), $BaCO_3$ (8.4 g, 43 mmol), and AIBN (350 mg, 2 mmol), deoxygenated under vacuum, and refluxed for 10 min. The mixture was cooled, diluted with EtOAc (200 mL), and washed with 1 M HCl (2 × 200 mL), water (200 mL), saturated aqueous $NaHCO_3$ (2 × 200 mL), and brine (200 mL). The organic layer was dried ($MgSO_4$) and concentrated to give crude bromide **103** (32.2 g), which was used without purification.

A solution of crude bromide **103** (32.2 g, 72 mmol) in benzene (250 mL) was treated with n-Bu_3SnH (21 mL, 79 mmol) and AIBN (590 mg, 3.6 mmol), deoxygenated, and refluxed for 20 min. The reaction mixture was cooled, concentrated, and purified by flash chromatography (30% Et_2O in petroleum ether) to give pure triester **104** (19.5 g, 73%) as an amorphous solid: R_f = 0.31 (10% EtOAc in PhH); $[\alpha]^{23}_D$ +76.1° (c 3.3, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3030, 3011, 2993, 2941, 2846, 1750, 1722, 1603 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13–8.11 (m, 2 H, aromatic), 7.62–7.58 (m, 1 H, aromatic), 7.49–7.46 (m, 2 H, aromatic), 5.49 (dd, J = 3.4, 1.0 Hz, 1 H, H-4), 5.27 (dd, J = 10.4, 7.9 Hz, 1 H, H-2), 5.12 (dd, J = 10.4, 3.4 Hz, 1 H, H-3), 4.43 (d, J = 7.9 Hz, 1 H, H-1), 3.92 (dq, J = 6.4, 1.0 Hz, 1 H, H-5), 3.56 (s, 3 H, CH_3O), 2.06, 1.94 (2 × s, 6 H, 2 × CH_3CO), 1.28 (d, J = 6.4 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 169.6, 166.1, 133.5, 130.0, 129.2, 128.5, 102.0, 71.5, 70.8, 69.4, 69.0, 56.9, 20.8, 20.6, 16.2; FAB HRMS (NBA) m/e 367.1398, M + H^+ calcd for $C_{18}H_{22}O_8$ 367.1393.

Methyl 6-Deoxy-β-D-galactopyranoside (105). A solution of triester **104** (19.3 g, 52.7 mmol) in MeOH (200 mL) was treated with NaOMe (1.0 g, 18 mmol) and stirred for 4 h at 25 °C. Amberlyst 15 ion-exchange resin (2 g) was added, and the mixture was stirred until neutral. The reaction mixture was filtered through Celite followed by washing with methanol (3 × 75 mL). The filtrate was concentrated and purified by flash chromatography (15% MeOH in CH_2Cl_2) to give triol **105** (9.3 g, 99%) as colorless needles: mp = 121 °C (from EtOAc); R_f = 0.16 (10% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ −23.0° (c 1.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600, 3430, 3011, 2939, 2875, 1449 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.14 (d, J = 7.2 Hz, 1 H, H-1), 3.73 (b d, J = 1.6 Hz, 1 H, H-4), 3.65–3.58 (m, 3 H, H-2, H-3, H-5), 3.54 (s, 3 H, CH_3O), 1.33 (d, J = 6.5 Hz, 3 H, H-6); FAB HRMS (NBA/CsI) m/e 310.9888, M + Cs^+ calcd for $C_7H_{14}O_5$ 310.9896.

Methyl 6-Deoxy-β-D-galactopyranoside Cyclic 3,4-Carbonate (66). A solution of triol **105** (47.8 mmol) in acetonitrile (200 mL) was added dropwise to a refluxing solution of carbonyldiimidazole (21.3 g, 120 mmol) in acetonitrile (250 mL) over 1 h. The solution was refluxed for an additional 15 min, and 2 M HCl (180 mL) was added with continued heating for another 15 min. The mixture was cooled and neutralized with solid K_2CO_3, and the aqueous layer was separated and extracted with EtOAc (2 × 200 mL). The combined organic layers were dried ($MgSO_4$), concentrated, and purified by flash chromatography (5% MeOH in CH_2Cl_2) to give carbonate **66** (7.43 g, 76%) as a white solid: mp = 146 °C (from Et_2O–CH_2Cl_2); R_f = 0.36 (5% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ −27.2° (c 0.76, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3596, 3400, 3029, 2941, 1824, 1804, 1449 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.66 (dd, J = 7.1, 7.1 Hz, 1 H, H-3), 4.58 (dd, J = 7.1, 2.1 Hz, 1 H, H-4), 4.23 (d, J = 7.4 Hz, 1 H, H-1), 3.91 (dq, J = 6.6, 2.1 Hz, 1 H, H-5), 3.69 (ddd, J = 7.4, 7.1, 2.9 Hz, 1 H, H-2), 3.54 (s, 3 H, CH_3O), 2.73 (d, J = 2.9 Hz, 1 H, OH), 1.46 (d, J = 6.6 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.0, 101.9, 78.7, 76.8, 71.9, 68.1, 56.9, 16.2; FAB HRMS (NBA/CsI) m/e 336.9701, M + Cs^+ calcd for $C_8H_{12}O_6$ 336.9688. Anal. Calcd for $C_8H_{12}O_6$: C, 47.06; H, 5.92. Found: C, 46.82; H, 5.87.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-galactopyranoside Cyclic 3,4-Carbonate (106). A suspension of anhydrous silver perchlorate (0.97 g, 4.7 mmol) and stannous chloride (0.88 g, 4.7 mmol), dried by azeotropic removal of benzene (2 × 10 mL), and powdered, activated 4-Å molecular sieves (1 g) in THF (20 mL) was stirred in the dark at 25 °C for 15 min and then cooled to −78 °C. A solution of fluoride **67** (936 mg, 2.34 mmol) and alcohol **66** (720 mg, 3.53 mmol) in THF (20 mL) was added slowly to this solution and the solution stirred at −78 °C for 3 h. The reaction mixture was allowed to warm slowly to −20 °C over 4 h, diluted with Et_2O (150 mL), and filtered through Celite. The resulting solution was washed with saturated aqueous sodium bicarbonate (7 × 200 mL) and brine (200 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (50 → 100% EtOAc in petroleum ether) to give pure α-glycoside **106** (958 mg, 70% based on **67**) and the corresponding β-glycoside (217 mg, 16%). α-Glycoside **106** was obtained as an oil: R_f = 0.27 (60% EtOAc in petroleum ether); $[\alpha]^{23}_D$ −61.8° (c 1.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3031, 3012, 2968, 2938, 1807, 1691, 1479 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.85 (d, J = 7.5 Hz, 2 H, aromatic), 7.63 (d, J = 7.5 Hz, 2 H, aromatic), 7.40 (dd, J = 7.5, 7.5 Hz, 2 H, aromatic), 7.34 (dd, J = 7.5, 7.5 Hz, 2 H, aromatic), 5.13 (b s, 1 H, E-1), 4.94 (dd, J = 7.7, 4.7 Hz, 1 H, A-3), 4.81 (dd, J = 7.7, 1.9 Hz, 1 H, A-4), 4.53 (d, J = 5.8 Hz, 1 H, A-1), 4.44 (b s, 2 H, CH_2-FMOC), 4.28 (t, J = 6.0 Hz, 1 H, benzylic-FMOC), 4.02 (dq, J = 6.6, 1.9 Hz, 1 H, A-5), 3.81–3.65 (b m, 3 H, E-3, E-5, E-5′), 3.57 (dd, J = 5.8, 4.7 Hz, 1 H, A-2), 3.37 (s, 3 H, CH_3O), 3.33 (dd, J = 10.7, 4.8 Hz, 1 H, E-4), 3.17 (s, 3 H, CH_3O), 2.99 (b m, 2 H, CH_2N), 2.27 (b d, J = 12.8 Hz, 1 H, E-2_{eq}), 1.45 (ddd, J = 12.8, 10.5, 3.4 Hz, 1 H, E-2_{ax}), 1.27 (d, J = 6.6 Hz, 3 H, A-6), 0.89 (b s, 3 H, CH_3CH_2N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 155.6, 153.9, 153.6, 144.2, 144.0, 143.8, 141.3, 141.3, 127.6, 127.0, 125.2, 125.1, 124.8, 119.9, 100.4, 100.1, 97.9, 97.0, 78.1, 76.7, 73.2, 71.7, 71.5, 67.5, 67.4, 66.8, 66.6, 60.3, 59.9, 59.5, 56.2, 56.1, 56.0, 55.7, 47.3, 47.3, 35.4, 34.9, 16.7, 16.5, 14.8, 14.7; FAB HRMS (NBA/CsI) m/z 716.1465, M + Cs^+ calcd for $C_{31}H_{37}NO_{10}$ 716.1471. Anal. Calcd for $C_{31}H_{37}NO_{10}$: C, 63.80; H, 6.39. Found: C, 63.92; H, 6.20.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-galactopyranoside (107). Cyclic carbonate **106** (1.22 g, 2.10 mmol) was dissolved in a rapidly stirring solution of THF (20 mL) and ethylene glycol (1.0 mL) at 0 °C. Catalytic sodium hydride (1–2 mg of a 60% suspension in mineral oil) was added, and the reaction mixture was stirred while the progress of the reaction was carefully monitored by TLC (60% EtOAc in petroleum ether) for a period of 0.5–1 h until complete. The mixture was diluted with EtOAc (300 mL) and washed with saturated aqueous NH_4Cl (2 × 200 mL), saturated aqueous sodium bicarbonate (2 × 200 mL), and brine (200 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (80% EtOAc in petroleum ether) to give diol **107** (1.10 g, 93%) as a white foam: R_f = 0.30 (80% EtOAc in petroleum ether); $[\alpha]^{23}_D$ –61.4° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3554, 3448, 3036, 3013, 2938, 1690 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.85 (d, *J* = 7.5 Hz, 2 H, aromatic), 7.64 (d, *J* = 7.5 Hz, 2 H, aromatic), 7.40 (dd, *J* = 7.5, 7.5 Hz, 2 H, aromatic), 7.31 (dd, *J* = 7.5, 7.5 Hz, 2 H, aromatic), 5.33 (b s, 1 H, E-1), 4.53 (d, *J* = 6.7 Hz, 1 H, O*H*), 4.43 (b s, 2 H, CH_2-FMOC), 4.29–4.25 (m, 2 H, O*H*, benzylic-FMOC), 4.12 (d, *J* = 7.4 Hz, 1 H, A-1), 3.97 (dd, *J* = 11.1, 11.1 Hz, 1 H, E-5_{ax}), 3.73 (b m, 2 H, E-3, E-5_{eq}), 3.53 (q, *J* = 6.4 Hz, 1 H, A-5), 3.51–3.40 (m, 3 H, A-2, A-3, A-4), 3.35 (s, 3 H, CH_3O-A ring), 3.21–3.19 (m, 1 H, E-4), 3.17 (s, 3 H, CH_3O-E ring), 3.00 (b m, 2 H, CH_2N), 2.31–2.29 (b d, 1 H, E-2_{eq}), 1.35–1.30 (b t, 1 H, E-2_{ax}), 1.15 (d, *J* = 6.4 Hz, 3 H, A-6), 0.89 (b s, 3 H, CH_3CH$_2$N); FAB HRMS (NBA/CsI) *m/e* 690.1693, M + Cs^+ calcd for $C_{30}H_{39}NO_9$ 690.1679.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-*xylo*-hexopyranosid-4-ulose (65). A solution of diol **107** (943 mg, 1.69 mmol) in dry MeOH (11 mL) and dibutyltin oxide (444 mg, 1.77 mmol) was heated at reflux for 45 min. The resulting clear solution was cooled, concentrated, and azeotroped with dry benzene to remove trace MeOH. The resulting crude stannylene acetal was dissolved in dry CH_2Cl_2 (11 mL), and tributyltin methoxide (0.55 mL, 1.9 mmol) was added. The reaction was titrated with a solution of bromine in carbon tetrachloride (1.7 mL, 1.0 M Br_2 in CCl_4, 1.7 mmol), allowing for slow addition near the end. The yellow reaction mixture was diluted with EtOAc (200 mL), washed with saturated aqueous bicarbonate (150 mL) and brine (2 × 150 mL), and dried ($MgSO_4$). The solution was filtered through Celite (removing insoluble tin byproducts), and the Celite was washed with EtOAc. The filtrate was concentrated and purified by flash chromatography (80% EtOAc in petroleum ether) to give ketone **65** (655 mg, 70%) as a white foam and recovered diol **107** (170 mg, 18%). **65**: R_f = 0.29 (60% EtOAc in petroleum ether); $[\alpha]^{23}_D$ –71.6° (*c* 0.67, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3510, 3012, 2963, 2935, 2874, 1735, 1691, 1451, 1424, 1277, 1141, 1097, 1060, 998, 761 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.85 (d, *J* = 7.6 Hz, 2 H, aromatic), 7.64 (d, *J* = 7.4 Hz, 2 H, aromatic), 7.40 (dd, *J* = 7.4, 7.4 Hz, 2 H, aromatic), 7.31 (dd, *J* = 7.4, 7.4 Hz, 2 H, aromatic), 5.37 (d, *J* = 5.9 Hz, 1 H, O*H*), 5.31 (b s, 1 H, E-1), 4.70 (d, *J* = 7.1 Hz, 1 H, A-1), 4.44 (b s, 2 H, CH_2-FMOC), 4.31 (dd, *J* = 9.3, 5.9 Hz, 1 H, A-3), 4.28 (t, *J* = 6.8 Hz, 1 H, benzylic-FMOC), 4.22 (q, *J* = 6.6 Hz, 1 H, A-5), 3.92 (dd, *J* = 11.3, 10.7 Hz, 1 H, E-5_{ax}), 3.77 (b m, 2 H, E-3, E-5_{eq}), 3.51 (dd, *J* = 9.3, 7.1 Hz, 1H, A-2), 3.43 (s, 3 H, CH_3O), 3.27 (dd, *J* = 10.7, 4.7 Hz, 1 H, E-4), 3.18 (s, 3 H, CH_3O), 3.00 (b m, 2 H, CH_2N), 2.30 (b d, 1 H, E-2_{eq}), 1.38 (m, 1 H, E-2_{ax}), 1.20 (d, *J* = 6.6 Hz, 3 H, A-6), 0.88 (b s, 3 H, CH_3CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.9, 204.4, 156.1, 144.3, 144.2, 143.9, 141.4, 127.6, 127.0, 125.4, 125.2, 124.9, 119.9, 102.4, 102.1, 97.5, 97.2, 79.4, 78.9, 78.2, 78.1, 73.2, 71.8, 71.6, 67.6, 66.9, 60.2, 59.7, 56.8, 56.7, 55.9, 55.7, 47.4, 47.3, 35.0, 34.8, 29.7, 27.1, 26.8, 17.5, 14.9, 14.8, 14.5, 13.6; FAB HRMS (NBA/CsI) *m/e* 688.1523, M + Cs^+ calcd for $C_{30}H_{37}NO_9$ 688.1530.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2-*O*-(3-Chlorobenzoyl)-4,6-dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]oxime (108). A solution of ketone **65** (650 mg, 1.17 mmol) and hydroxylamine **42** (0.58 g, 1.4 mmol) in benzene (3.5 mL) was treated with PPTS (15 mg, 0.06 mmol) and stirred for 1 h at 25 °C. The reaction mixture was diluted with EtOAc (100 mL), washed with saturated aqueous sodium bicarbonate (2 × 50 mL) and brine (50 mL), and dried ($MgSO_4$). The solution was concentrated and the residue purified by flash chromatography (7% acetone in CH_2Cl_2) to give oxime **108** (968 mg, 83%) as a white foam: R_f = 0.30 (7% acetone in CH_2Cl_2); $[\alpha]^{23}_D$ –111° (*c* 1.9, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600–3400, 3020, 3011, 2958, 2934, 2899, 2860, 1729, 1690 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.90 (m, 2 H, aromatic), 7.84 (d, *J* = 7.5 Hz, 2 H, FMOC), 7.72 (d, *J* = 9.0 Hz, 1 H, aromatic), 7.63 (d, *J* = 7.4 Hz, 2 H, FMOC), 7.57 (dd, *J* = 8.1, 8.1 Hz, 1 H, aromatic), 7.39 (dd, *J* = 7.4, 7.4 Hz, 2 H, FMOC), 7.31 (dd, *J* = 7.4, 7.4 Hz, 2 H, FMOC), 5.51 (dd, *J* = 5.6, 2.1 Hz, 1 H, B-2), 5.41 (d, *J* = 5.6 Hz, 1 H, B-1), 5.38 (d, *J* = 4.8 Hz, 1 H, O*H*), 5.18 (d, *J* = 1.7 Hz, 1 H, B-4), 5.09 (b s, 1 H, E-1), 4.67 (q, *J* = 6.7 Hz, 1 H, A-5), 4.56 (ddq, *J* = 6.6, 2.1, 1.7 Hz, 1 H, B-5), 4.43 (b m, 2 H, CH_2-FMOC), 4.27 (t, *J* = 6.0 Hz, 1 H, benzylic-FMOC), 4.18 (d, *J* = 6.3 Hz, 1 H, A-1), 4.07 (dd, *J* = 4.8, 2.3 Hz, 1 H, A-3), 3.73 (b m, 3 H, E-3, E-5, E-5′), 3.71 (dd, *J* = 6.3, 2.3 Hz, 1 H, A-2), 3.34 (s, 3 H, CH_3O), 3.29 (b d, *J* = 5.9 Hz, 1 H, E-4), 3.05 (s, 3 H, CH_3O), 3.01–2.90 (b m, 2 H, CH_2N), 2.21 (b d, *J* = 11.8 Hz, 1 H, E-2_{eq}), 1.41 (m, 1 H, E-2_{ax}), 1.31 (d, *J* = 6.7 Hz, 3 H, A-6), 1.25 (d, *J* = 6.6 Hz, 3 H, B-6), 0.91–0.85 (b m, 3 H, CH_3CH$_2$N), 0.78 (s, 9 H, ^{t}Bu), 0.17, 0.11 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 160.8, 156.0, 155.9, 144.4, 144.2, 144.1, 144.1, 143.9, 141.3, 141.2, 134.5, 133.2, 131.4, 129.7, 129.7, 128.3, 128.2, 127.8, 127.6, 127.0, 125.3, 125.2, 124.8, 119.9, 110.4, 103.6, 103.4, 102.3, 102.3, 96.7, 75.9, 75.8, 71.7, 71.6, 69.9, 69.8, 68.9, 68.8, 68.7, 68.1, 67.5, 66.8, 60.2, 59.6, 57.0, 56.1, 55.9, 55.7, 47.3, 47.2, 34.9, 34.7, 25.3, 22.3, 19.0, 17.8, 14.9, 14.9, –4.7, –4.8; FAB HRMS (NBA/CsI) *m/e* 1083.2846, M + Cs^+ calcd for $C_{49}H_{63}ClN_2O_{13}Si$ 1083.2839. Anal. Calcd for $C_{49}H_{63}ClN_2O_{13}Si$: C, 61.85; H, 6.67; N, 2.99. Found: C, 61.62; H, 6.57; N, 2.86.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-3-*O*-(triethylsilyl)-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2-*O*-(3-Chlorobenzoyl)-4,6-dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]oxime (109). A solution of alcohol **108** (950 mg, 0.0998 mmol) in CH_2Cl_2 (10 mL) was treated at 0 °C with 2,6-lutidine (0.17 mL, 1.5 mmol) and triethylsilyl trifluoromethanesulfonate (0.27 mL, 1.2 mmol) and stirred for 30 min. The reaction mixture was diluted with EtOAc (100 mL) and washed with 0.1 M HCl (2 × 50 mL), water (50 mL), saturated aqueous sodium bicarbonate (3 × 50 mL), and brine (50 mL). The organic layer was dried ($MgSO_4$) and concentrated to give pure silyl ether **109** (1.25 g, 100%) as a white foam: R_f = 0.38 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –85.6° (*c* 2.8, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3010, 2958, 2936, 2878, 1730, 1690 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.89–7.83 (m, 4 H, aromatic), 7.74 (b d, *J* = 8.2 Hz, 1 H, aromatic), 7.64 (d, *J* = 7.4 Hz, 2 H, FMOC), 7.56 (dd, *J* = 7.8 Hz, 1 H, aromatic), 7.39 (dd, *J* = 7.4, 7.4 Hz, 2 H, FMOC), 7.31 (ddd, *J* = 7.4, 7.4, 0.9 Hz, 2 H, FMOC), 5.52 (ddd, *J* = 6.1, 1.5, 0.8 Hz, 1 H, B-2), 5.39 (d, *J* = 6.1 Hz, 1 H, B-1), 5.17 (m, 1 H, B-4), 5.04 (b s, 1 H, E-1), 4.68 (q, *J* = 6.7 Hz, 1 H, A-5), 4.56 (ddq, *J* = 6.6, 2.0, 1.6 Hz, 1 H, B-5), 4.43 (b s, 2 H, CH_2-FMOC), 4.27 (t, *J* = 6.0 Hz, 1 H, benzylic-FMOC), 4.20 (d, *J* = 6.3 Hz, 1 H, A-1), 4.16 (s, 1 H, A-3), 3.72 (b s, 3 H, E-3, E-5, E-5′), 3.67 (b d, *J* = 6.3 Hz, 1 H, A-2), 3.35 (s, 3 H, CH_3O), 3.28 (m, 1 H, E-4), 3.16 (s, 3 H, CH_3O), 3.00 (b s, 2 H, CH_2N), 2.22 (b d, 1 H, E-2_{eq}), 1.43 (b t, 1 H, E-2_{ax}), 1.28 (d, *J* = 6.7 Hz, 3 H, A-6), 1.25 (d, *J* = 6.6 Hz, 3 H, B-6), 0.9–0.7 (b s, 3 H, CH_3CH$_2$N), 0.82 (t, *J* = 7.9 Hz, 9 H, Si(CH$_2$CH_3)$_3$), 0.77 (s, 9 H, ^{t}Bu), 0.52 (q, *J* = 7.9 Hz, 6 H, Si(CH_2CH$_3$)$_3$), 0.17, 0.11 (2 × s, 6 H, 2 × CH_3Si); FAB HRMS (NBA/CsI) *m/e* 1198.3840, M + Cs^+ calcd for $^{13}CC_{54}H_{77}ClN_2O_{13}Si_2$ 1198.3741.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-3-*O*-(triethylsilyl)-β-D-*xylo*-hexopyranosid-4-ulose *O*-[4,6-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-β-D-*erythro*-hex-3-enopyranosyl]oxime (110). A solution of ester **109** (970 mg, 0.910 mmol) in CH_2Cl_2 (10 mL) at –78 °C was treated with DIBAL (2.7 mL of a 1.0 M solution in CH_2Cl_2, 2.7 mmol) and stirred for 20 min, and the reaction was quenched with EtOAc (250 mL). The solution was washed with saturated aqueous Rochelle salt (4 × 100 mL), saturated aqueous NH_4Cl (75 mL), saturated aqueous $NaHCO_3$ (2 × 75 mL), and brine (75 mL). The organic layer was dried ($MgSO_4$), concentrated, and purified by flash chromatography (60% Et_2O in petroleum ether) to give alcohol **110** (766 mg, 91%) as a white foam: R_f = 0.23 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –58.5° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600, 3500, 3012, 2958, 2935, 2879, 1690 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.84 (d, *J* = 7.5 Hz, 2 H, FMOC), 7.63 (d, *J* = 7.5 Hz, 2 H, FMOC), 7.39 (dd, *J* = 7.5, 7.5 Hz, 2 H, FMOC), 7.31 (dd, *J* = 7.5, 7.5 Hz, 2 H, FMOC), 5.12 (d, *J* = 4.3 Hz, 1 H, B-1), 5.07 (b s, 1 H, E-1), 5.05 (d, *J* = 6.5 Hz, 1 H, O*H*), 4.90 (d, *J* = 2.1 Hz, 1 H, B-4), 4.68 (q, *J* = 6.7 Hz, 1 H, A-5), 4.44 (b s, 2 H, CH_2-FMOC), 4.38 (ddq, *J* = 6.6, 2.1, 1.6 Hz, 1 H, B-5), 4.27 (t, *J* = 5.9 Hz, 1 H, benzylic-FMOC), 4.22–4.21 (m, 2 H, A-1, A-3), 3.76 (ddd, *J* = 6.5, 4.3, 1.6 Hz, 1 H, B-2), 3.75 (b m, 3 H, E-3, E-5, E-5′), 3.71 (dd, *J* = 5.9, 2.1 Hz, 1 H, A-2), 3.36 (s, 3 H, CH_3O), 3.30 (b d, *J* = 6.0 Hz, 1 H, E-4), 3.16 (s, 3 H, CH_3O), 3.00 (b s, 2 H, CH_2N), 2.21 (b d, 1 H, E-2_{eq}), 1.45 (d, *J* = 6.7 Hz, 3 H, A-6), 1.44 (b s, 1 H, E-2_{ax}),

1.15 (d, J = 6.6 Hz, 3 H, B-6), 0.93 (t, J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$), 0.93 (s, 9 H, ^{t}Bu), 0.88 (b s, 3 H, CH_3CH_2N), 0.62 (q, J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$), 0.17, 0.16 (2 × s, 6 H, 2 × CH_3Si); FAB HRMS (NBA/CsI) m/e 1059.3800, M + Cs$^+$ calcd for $C_{48}H_{74}N_2O_{12}Si_2$ 1059.3835.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-3-*O*-(triethylsilyl)-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4-*S*-(1*H*-imidazol-1-ylcarbonyl)-4-thio-β-D-*erythro*-hex-2-enopyranosyl]oxime (63). Thiocarbonyldiimidazole (400 mg, 2.27 mmol) was added to a rapidly stirring solution of alcohol **110** (700 mg, 0.755 mmol) in acetonitrile (2.5 mL). The reaction mixture was stirred for 1.5 h at 25 °C, diluted with Et_2O (60 mL), and washed with water (5 × 40 mL) and brine (40 mL). The solution was dried ($MgSO_4$), concentrated, and purified by flash chromatography (15% EtOAc in CH_2Cl_2) to give the thermally unstable thionoimidazolide **111** (680 mg, 87%).

A solution of thionoimidazolide **111** (674 mg, 0.649 mmol) in toluene (15 mL) was refluxed for 30 min, cooled, concentrated, and purified by flash chromatography (20% EtOAc in CH_2Cl_2) to give the rearrangement product **63** (663 mg, 98%) as a white foam: R_f = 0.22 (20% EtOAc in PhH); $[\alpha]^{23}_D$ +8.9° (c 2.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3008, 2959, 2935, 2879, 1692 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 8.35 (s, 1 H, imidazole), 7.84 (d, J = 7.5 Hz, 2 H, FMOC), 7.68 (dd, J = 1.5, 1.5 Hz, 1 H, imidazole), 7.63 (d, J = 7.5 Hz, 2 H, FMOC), 7.39 (dd, J = 7.5, 7.5 Hz, 2 H, FMOC), 7.31 (dd, J = 7.5, 7.5 Hz, 2 H, FMOC), 7.12 (dd, J = 1.5, 0.7 Hz, 1 H, imidazole), 5.78 (d, J = 2.5 Hz, 1 H, B-1), 5.15 (d, J = 2.5, 1 H, B-2), 5.06 (b s, 1 H, E-1), 4.68 (q, J = 6.7 Hz, 1 H, A-5), 4.44 (b s, 2 H, CH_2-FMOC), 4.28–4.24 (m, 2 H, benzylic-FMOC, B-5), 4.23 (d, J = 6.1 Hz, 1 H, A-1), 4.20 (d, J = 1.9 Hz, 1 H, A-3), 4.05 (d, J = 3.7 Hz, 1 H, B-4), 3.78–3.70 (b m, 3 H, E-3, E-5, E-5′), 3.72 (dd, J = 6.1, 1.9 Hz, 1 H, A-2), 3.37 (s, 3 H, CH_3O), 3.30 (b m, 1 H, E-4), 3.15 (s, 3 H, CH_3O), 2.98 (b m, 2 H, CH_2N), 2.20 (b d, 1 H, E-2$_{eq}$), 1.47–1.42 (m, 7 H, E-2$_{ax}$, A-6, B-6), 0.94 (t, J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$), 0.91–0.87 (b m, 3 H, CH_3CH_2N), 0.87 (s, 9 H, ^{t}Bu), 0.62 (q, J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$), 0.22, 0.19 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 159.8, 156.0, 155.8, 148.4, 148.3, 144.2, 144.1, 144.1, 143.8, 141.3, 141.2, 141.2, 135.6, 131.1, 128.2, 127.5, 126.9, 125.3, 125.2, 124.8, 119.8, 116.0, 104.1, 103.8, 103.4, 103.4, 98.4, 98.3, 95.2, 94.9, 78.5, 73.7, 71.7, 71.6, 71.6, 69.7, 69.6, 67.5, 66.8, 60.0, 59.5, 56.9, 56.6, 56.5, 55.9, 55.6, 48.6, 47.4, 47.2, 34.9, 34.7, 31.9, 30.2, 29.6, 25.3, 22.6, 20.7, 18.4, 17.9, 14.9, 14.9, 6.7, 4.6, –4.5, –4.9; FAB HRMS (NBA/CsI) m/e 1170.3817, M + Cs$^+$ calcd for ^{13}-$CC_{51}H_{76}N_4O_{12}SSi_2$ 1170.3807.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-3-*O*-(triethylsilyl)-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-4-*S*-[4-[[3-*O*-methyl-2,4-bis-*O*-(triethylsilyl)-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6methylbenzoyl]-3-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4-thio-β-D-*erythro*-hex-2-enopyranosyl]oxime (113). Preparation of thiol **112**. A solution of thioimidazole **63** (104 mg, 0.10 mmol) in CH_2Cl_2 (3 mL) was treated with EtSH (0.3 mL, 4 mmol) and NaSMe (7 mg, 0.10 mmol) at 0 °C. After being stirred vigorously for 5 min, the reaction mixture was poured into ice-cold saturated aqueous NH_4Cl (20 mL) and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (2 × 20 mL), dried ($MgSO_4$), concentrated, and purified by flash chromatography (40% Et_2O in petroleum ether) to give the labile thiol **112** (91 mg, 96%) which was used immediately.

Acid **88** (118 mg, 0.16 mmol) was stirred in oxalyl chloride (1 mL) at 25 °C for 1 h. The mixture was concentrated, dissolved in CH_2Cl_2 (1 mL), and cooled to 0 °C. Et_3N (33 μL, 0.24 mmol) was added followed by a solution of thiol **112** (122 mg, 0.13 mmol) in CH_2Cl_2 (3 mL). The reaction mixture was stirred for 30 min, catalytic DMAP (1–2 mg) was added, and the mixture was stirred for an additional 30 min. The solution was diluted with CH_2Cl_2 (30 mL) and washed successively with saturated aqueous NH_4Cl (2 × 20 mL) and brine (2 × 20 mL). The organic extract was dried ($MgSO_4$), concentrated, and purified by flash chromatography (35% Et_2O in petroleum ether) to give thioester **113** (95 mg, 44%) as a white foam: R_f = 0.36 (40% Et_2O in petroleum ether); $[\alpha]^{23}_D$ +7.0° (c 1.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3008, 2958, 2937, 2878, 1685, 1674 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.84 (d, J = 7.5 Hz, 2 H, aromatic), 7.63 (d, J = 7.5 Hz, 2 H, aromatic), 7.39 (dd, J = 7.5, 7.5 Hz, 2 H, aromatic), 7.31 (dd, J = 7.5, 7.5 Hz, 2 H, aromatic), 5.74 (d, J = 2.3 Hz, 1 H, B-1), 5.38 (d, J = 2.0 Hz, 1 H, D-1), 5.12 (d, J = 2.3 Hz, 1 H, B-2), 5.06 (b s, 1 H, E-1), 4.67 (q, J = 6.7 Hz, 1 H, A-5), 4.43 (m, 3 H, CH_2-FMOC, D-2), 4.28 (t, J = 6.8 Hz, 1 H, benzylic-FMOC), 4.22 (d, J = 6.1 Hz, 1 H, A-1), 4.19 (d, J = 1.7 Hz, 1 H, A-3), 4.14 (m, 1 H, B-5 or D-5), 4.06 (m, 1 H, B-5 or D-5), 4.01 (d, J = 3.9 Hz, 1 H, B-4), 3.82 (s, 3 H, CH_3O), 3.77 (s, 3 H, CH_3O), 3.77–3.68 (m, 5 H, A-2, D-4, E-3, E-5, E-5′), 3.55 (dd, J = 8.9, 2.6 Hz, 1 H, D-3), 3.39 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 3.30 (m, 1 H, E-4), 3.16 (b s, 3 H, CH_3O), 3.00 (b m, 2 H, CH_2N), 2.31 (s, 3 H, ArCH_3), 2.21 (m, 1 H, E-2$_{eq}$), 1.45 (d, J = 6.7 Hz, 3 H, A-6), 1.44 (d, J = 6.6 Hz, B-6), 1.44 (b s, 1 H, E-2$_{ax}$), 1.16 (d, J = 6.2 Hz, 3 H, D-6), 0.96 (t, J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$), 0.94 (s, 9 H, ^{t}Bu), 0.86 (b t, 3 H, CH_3CH_2N), 0.62 (q, J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$), 0.24, 0.22 (2 × s, 6 H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.5, 159.5, 156.1, 152.4, 150.7, 149.4, 149.3, 144.3, 144.2, 144.1, 143.9, 143.1, 141.3, 141.2, 133.5, 129.8, 127.6, 127.0, 125.4, 125.2, 124.8, 119.9, 110.5, 104.7, 104.1, 103.8, 103.1, 103.0, 98.5, 98.4, 95.0, 94.7, 93.8, 91.3, 78.7, 74.4, 72.4, 72.3, 71.8, 71.6, 69.8, 69.7, 68.6, 67.6, 66.8, 61.6, 60.8, 60.0, 59.5, 57.2, 56.7, 56.6, 55.9, 55.7, 47.5, 47.3, 47.2, 40.1, 34.8, 34.7, 31.9, 29.7, 29.3, 25.6, 25.6, 25.5, 25.4, 24.0, 22.7, 21.9, 20.8, 18.4, 18.0, 15.0, 14.9, 14.1, 6.9, 6.7, 6.7, 5.1, 4.8, 4.6, –4.4, –4.7; FAB HRMS (NBA/CsI) m/e 1784.5711, M + Cs$^+$ calcd for $^{13}CC_{76}H_{123}IN_2O_{19}SSi_4$ 1784.5657.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-3-*O*-(triethylsilyl)-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-4-*S*-[4-[[3-*O*-methyl-2,4-bis-*O*-(triethylsilyl)-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoyl]-4-thio-β-D-*ribo*-hexopyranosyl]oxime (115). A solution of silyl enol ether **113** (115 mg, 69.6 μmol) in THF (7.0 mL) containing AcOH (0.02 mL, 0.35 mmol) at –23 °C was treated with TBAF (0.70 mL of a 0.10 M solution in THF, 70 μmol). The reaction mixture was stirred for 15 min, diluted with Et_2O (100 mL), and washed with saturated aqueous $NaHCO_3$ (3 × 60 mL), water (60 mL), and brine (60 mL). The organic extract was dried ($MgSO_4$) and concentrated to give crude ketone **114** as an unstable foam. Ketone **114** was dissolved in DME (6.3 mL) and THF (0.7 mL), cooled to –78 °C, and treated with K-Selectride (0.21 mL of a 1.0 M solution in THF, 0.21 mmol). The mixture was stirred for 2 h at –78 °C, the reaction was quenched with saturated aqueous NH_4Cl (40 mL), and the mixture was diluted with Et_2O (125 mL) and extracted. The aqueous layer was extracted with additional Et_2O (50 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated. Hydrolysis of the residual alkoxyborane was accomplished by dissolving the residue in 10% MeOH in CH_2Cl_2 (15 mL) and stirring with silica gel (1.5 g) for 1 h. The mixture was filtered and concentrated and the residue purified by flash chromatography (50% Et_2O in petroleum ether) to give pure α-alcohol **115** (81 mg, 75% from **113**) as a white foam: R_f = 0.28 (50% Et_2O in petroleum ether); $[\alpha]^{23}_D$ –32.8° (c 0.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3010, 2958, 2938, 2914, 2878, 1687 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.84 (d, J = 7.5 Hz, 2 H, FMOC), 7.63 (d, J = 7.5 Hz, 2 H, FMOC), 7.39 (dd, J = 7.5, 7.5 Hz, 2 H, FMOC), 7.31 (dd, J = 7.5, 7.5 Hz, 2 H, FMOC), 5.40 (b s, 1 H, B-1), 5.38 (d, J = 1.9 Hz, 1 H, D-1), 5.35 (d, J = 4.3 Hz, 1 H, OH), 5.08 (b s, 1 H, E-1), 4.75 (q, J = 6.7 Hz, 1 H, A-5), 4.44 (m, 3 H, D-2, CH_2-FMOC), 4.28 (d, J = 6.1 Hz, 1 H, A-1), 4.28 (b s, 1 H, benzylic-FMOC), 4.23 (d, J = 2.2 Hz, 1 H, A-3), 4.18 (m, 1 H, B-3), 4.09 (m, 1 H, D-5), 4.03–3.98 (m, 1 H, B-5), 3.82 (s, 3 H, CH_3O), 3.78 (s, 3 H, CH_3O), 3.77–3.69 (m, 5 H, A-2, D-4, E-3, E-5, E-5′), 3.63 (dd, J = 10.3, 2.5 Hz, 1 H, B-4), 3.55 (dd, J = 9.0, 2.6 Hz, 1 H, D-3), 3.40, 3.38 (2 × s, 6 H, 2 × CH_3O), 3.30 (m, 1 H, E-4), 3.17 (b s, 3 H, CH_3O), 3.00 (b s, 2 H, CH_2N), 2.32 (s, 3 h, ArCH_3), 2.23 (m, 1 H, E-2$_{eq}$), 2.00 (m, 1 H, B-2$_{eq}$), 1.88 (m, 1 H, B-2$_{ax}$), 1.44 (d, J = 6.7 Hz, 3 H, A-6), 1.27 (d, J = 6.3 Hz, 3 H, B-6), 1.16 (d, J = 6.2 Hz, 3 H, D-6), 0.95 (t, J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$), 0.89 (b m, 3 H, CH_3CH_2N), 0.62 (q, J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 160.7, 156.1, 152.5, 150.6, 144.2, 144.1, 143.9, 143.2, 141.4, 141.3, 133.4, 130.1, 127.6, 127.0, 125.4, 125.2, 124.9, 119.9, 104.7, 104.1, 103.9, 99.6, 95.5, 95.2, 94.0, 93.6, 81.4, 78.5, 72.4, 72.3, 71.9, 71.7, 71.5, 69.5, 69.3, 68.6, 68.2, 67.6, 66.9, 61.7, 60.9, 60.1, 59.6, 57.3, 56.6, 56.6, 55.9, 51.8, 47.4, 47.3, 43.9, 38.5, 37.0, 35.8, 29.7, 25.4, 19.3, 18.6, 18.0, 14.9, 7.0, 6.8, 6.7, 5.6, 5.2, 4.9, 4.6; FAB HRMS (NBA/CsI) m/e 1671.5001, M + Cs$^+$ calcd for $C_{71}H_{111}IN_2O_{19}SSi_3$ 1671.4909.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-[ethyl[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino]-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-4-*S*-[4-[[3-*O*-methyl-α-L-rhamnopyranosyl]oxy]-5-iodo-2,3-dimethoxy-6-methylbenzoyl]-4-thio-β-D-*ribo*-hexopyranosyl]oxime (116). A solution of tris(silyl)ether **115** (62.5 mg, 40.6 μmol) in CH_2Cl_2 (3.5 mL) and THF (0.5 mL) was cooled to –20 °C, and HF·Py complex (0.30 mL, 7 mL/mmol of compound) was added dropwise. The reaction mixture was stirred for 20 min and the temperature raised to 0 °C for 45 min. The mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ (3 × 20 mL) and brine (20 mL), concentrated, and purified by flash chromatography (5 → 10% MeOH

in CH_2Cl_2) to give tetraol **116** (35 mg, 72%) as a white foam: R_f = 0.34 (10% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ –44.4° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3580, 3500, 3012, 2939, 1688 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.85 (d, *J* = 7.5 Hz, 2 H, FMOC), 7.63 (d, *J* = 7.5 Hz, 2 H, FMOC), 7.40 (dd, *J* = 7.5, 7.5 Hz, 2 H, FMOC), 7.32 (dd, *J* = 7.5, 7.5 Hz, 2 H, FMOC), 5.46 (d, *J* = 2.0 Hz, 1 H, D-1), 5.41 (dd, *J* = 9.9, 2.1 Hz, 1 H, B-1), 5.34 (b m, 1 H, O*H*), 5.12 (b s, 1 H, E-1), 4.76–4.72 (m, 3 H, 2 × O*H*, A-5), 4.44 (b m, 2 H, CH_2-FMOC), 4.30–4.25 (m, 2 H, D-2, benzylic-FMOC), 4.26 (d, *J* = 6.2 Hz, 1 H, A-1), 4.18 (b s, 1 H, B-3), 4.10 (m, 1 H, A-3), 4.05–3.98 (m, 2 H, B-5, D-5), 3.83 (s, 3 H, CH_3O), 3.78 (s, 3 H, CH_3O), 3.78–3.72 (m, 3 H, O*H*, 2 × C*H*O), 3.74 (dd, *J* = 6.2, 2.4 Hz, 1 H, A-2), 3.64 (dd, *J* = 9.4, 2.8 Hz, 1 H, B-4), 3.59 (dd, *J* = 9.1, 3.2 Hz, 1 H, D-3), 3.50–3.46 (m, 1 H, D-4), 3.44 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 3.30 (m, 1 H, E-4), 3.17 (s, 3 H, CH_3O), 3.00 (b s, 2 H, CH_2N), 2.31 (s, 3 H, ArCH_3), 2.22 (m, 1 H, E-2$_{eq}$), 2.00 (m, 1 H, B-2$_{eq}$), 1.87 (m, 1 H, B-2$_{ax}$), 1.44 (d, *J* = 6.7 Hz, 3 H, A-6), 1.43 (m, 1 H, E-2$_{ax}$), 1.28 (d, *J* = 6.3 Hz, 3 H, B-6), 1.16 (d, *J* = 6.2 Hz, 3 H, D-6), 0.89 (b s, 3 H, CH_3CH$_2$N); FAB HRMS (NBA/CsI) *m/e* 1329.2331, M + Cs^+ calcd for $C_{53}H_{69}IN_2O_{19}S$ 1329.2314.

Methyl 6-Deoxy-2-*O*-[2,4-dideoxy-4-(ethylamino)-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-*xylo*-hexopyranosid-4-ulose *O*-[2,6-Dideoxy-4-*S*-[4-[[3-*O*-methyl-α-L-rhamnopyranosyl]oxy]-5-Iodo-2,3-dimethoxy-6-methylbenzoyl]-4-thio-β-D-*ribo*-hexopyranosyl]oxime (117). A solution of FMOC-amine **116** (26 mg, 22 μmol) in THF (1 mL) and diethylamine (1 mL) was stirred at 25 °C for 2 h, concentrated, and azeotroped with benzene (5 mL). The residue was purified by flash chromatography (5 → 30% MeOH in CH_2Cl_2) to give the free amine **117** (18 mg, 85%) as a white solid: R_f 0.60 (20% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ –36.7° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600–3550, 3550–3200, 2980, 2938, 2855, 1683, 1677 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.73 (d, *J* = 1.7 Hz, 1 H, D-1), 5.56 (dd, *J* = 10.0, 2.0 Hz, 1 H, B-1), 5.20 (s, 1 H, E-1), 4.91 (q, *J* = 7.0 Hz, 1 H, A-5), 4.61 (d, *J* = 4.6 Hz, 1 H, A-1), 4.48 (dd, *J* = 3.1, 1.7 Hz, 1 H, D-2), 4.38 (b d, *J* = 2.7 Hz, 1 H, B-3), 4.32 (d, *J* = 6.0 Hz, 1 H, A-3), 4.20 (m, 1 H, D-5), 4.14 (m, 1 H, B-5), 3.92 (dd, *J* = 5.6, 4.8 Hz, 1 H, A-2), 3.89 (s, 3 H, CH_3O), 3.84 (s, 3 H, CH_3O), 3.84 (m, 1 H, D-3), 3.79 (dd, *J* = 10.6, 2.6 Hz, 1 H, B-4), 3.79 (b s, 1 H, 1 H, C*H*O), 3.65 (dd, *J* = 9.5, 9.5 Hz, 1 H, D-4), 3.65–3.49 (b s, 2 H, C*H*O), 3.57 (s, 3 H, CH_3O), 3.52 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 2.81–2.65 (b m, 3 H, CH_2N, E-4), 2.36 (s, 3 H, ArCH_3), 2.35 (m, 1 H, E-2$_{eq}$), 2.17 (m, 1 H, E-2$_{eq}$), 2.17 (m, 1 H, B-2$_{eq}$), 1.99 (m, 1 H, B-2$_{ax}$), 1.56 (d, *J* = 7.0 Hz, 3 H, A-6), 1.52 (m, 1 H, E-2$_{ax}$), 1.42 (d, *J* = 6.3 Hz, 3 H, B-6), 1.31 (d, *J* = 6.2 Hz, 3 H, D-6), 1.24 (m, 3 H, CH_3CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.1, 160.1, 151.5, 150.6, 143.0, 133.4, 130.2, 103.4, 102.6, 99.8, 97.0, 93.5, 80.8, 76.5, 75.8, 71.0, 70.4, 69.6, 69.4, 69.5, 68.1, 67.0, 61.6, 60.9, 58.9, 57.2, 56.2, 56.1, 51.5, 41.9, 37.0, 33.7, 29.6, 25.3, 19.3, 19.2, 17.6, 14.8, 14.1; FAB HRMS (NBA/CsI) *m/e* 1107.1634, M + Cs^+ calcd for $C_{38}H_{59}IN_2O_{17}S$ 1107.1634.

As an alternative to the previous two steps, the transformation of **115** to **117** could be performed in one step using TBAF (10 equiv) in THF.

Methyl 4,6-Dideoxy-4-[[[2,6-dideoxy-4-*S*-[4-[[3-*O*-methyl-α-L-rhamnopyranosyl]oxy]-5-Iodo-2,3-dimethoxy-6-methylbenzoyl]-4-thio-β-D-*ribo*-hexopyranosyl]oxy]amino]-2-*O*-[2,4-dideoxy-4-(ethylamino)-3-*O*-methyl-α-L-*threo*-pentopyranosyl]-β-D-glucopyranoside (62). A solution of oxime **117** (9.6 mg, 9.9 μmol) in CH_2Cl_2 (0.3 mL) at –60 °C was sequentially and dropwise treated with BF_3·OEt_2 (0.13 mL of a 1.0 M solution in Et_2O, 0.13 mmol) and $NaCNBH_3$ (0.30 mL of a 1.0 M solution in THF, 0.30 mmol). The reaction mixture was warmed to –40 °C and stirred for 1.5 h. The reaction was quenched with solid $NaHCO_3$ (50 mg), and the solution was diluted with $CHCl_3$ (5 mL) and saturated aqueous $NaHCO_3$ (5 mL) and then allowed to warm to 25 °C. The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$ (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated, and the crude product was purified by preparative TLC (direct application, silica, chloroform:ethyl acetate:methanol = 5:2:1.5) to give a mixture of **62** and its A-4 β-epimer (86%, α/β = 6:1). This mixture was further purified by flash chromatography (10 → 15% MeOH in CH_2Cl_2) using deactivated silica (6% water) to give pure product **62** as a white solid.

62 as the free base: R_f = 0.28 (15% MeOH in CH_2Cl_2); $[\alpha]^{23}_D$ –40° (*c* 0.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600–3200, 3050–2940, 2932, 1678, 1457, 1416, 1393, 1322, 1238, 1094, 1066, 1003, 960 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.33 (b s, 1 H, ON*H*), 5.73 (d, *J* = 1.7 Hz, 1 H, D-1), 5.43 (m, 1 H, E-1), 5.05 (dd, *J* = 10.2, 2.0 Hz, 1 H, B-1), 4.48 (dd, *J* = 3.2, 1.7 Hz, 1 H, D-2), 4.32 (m, 1 H, B-3), 4.23 (d, *J* = 7.7 Hz, 1 H, A-1), 4.20 (dq, *J* = 9.6, 6.1 Hz, 1 H, D-5), 4.08 (dq, *J* = 10.8, 6.2 Hz, 1 H, B-5), 4.01 (dd, *J* = 9.7, 9.7 Hz, 1 H, A-3), 3.89 (s, 3 H, CH_3O-aromatic), 3.84 (s, 3 H, CH_3O-aromatic), 3.84 (dd, *J* = 9.5, 3.0 Hz, 1 H, B-4), 3.80–3.71 (m, 3 H, D-3, E-5$_{ax}$, E-5$_{eq}$), 3.66 (obs, 1 H, A-5), 3.65 (dd, *J* = 9.5, 9.5 Hz, 1 H, D-4), 3.55–3.46 (m, 2 H, A-2, E-3), 3.53 (s, 3 H, CH_3O), 3.38 (s, 3 H, CH_3O), 2.74–2.66 (m, 2 H, CH_2N), 2.62 (m, 1 H, E-4), 2.36 (s, 3 H, ArCH_3), 2.34 (dd, *J* = 9.6, 9.6 Hz, 1 H, A-4), 2.31 (m, 1 H, E-2$_{eq}$), 2.03 (m, 1 H, B-2$_{eq}$), 1.78 (m, 1 H, B-2$_{ax}$), 1.54 (m, 1 H, E-2$_{ax}$), 1.42 (d, *J* = 6.2 Hz, 3 H, B-6), 1.35 (d, *J* = 6.2 Hz, 3 H, A-6), 1.31 (d, *J* = 6.2 Hz, 3 H, D-6), 1.13 (t, *J* = 7.1 Hz, 3 H, CH_3CH$_2$N); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 151.5, 150.6, 143.0, 133.4, 130.2, 102.7, 102.6, 99.7, 98.4, 93.5, 80.8, 78.1, 71.1, 70.4, 69.0, 68.3, 68.2, 67.0, 65.9, 62.0, 61.7, 60.9, 59.3, 57.2, 56.8, 56.1, 51.7, 41.9, 36.8, 33.8, 29.7, 25.3, 18.9, 17.7, 17.6, 15.5; FAB HRMS (NBA/CsI) *m/e* 1109.1702, M + Cs^+ calcd for $C_{38}H_{61}IN_2O_{17}S$ 1109.1790.

62 as the HCl salt: $[\alpha]^{23}_D$ –31° (*c* 0.32, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600–3550, 3550–3200, 3030–2940, 2937, 2855, 1725, 1683, 1676 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.35 (b s, 1 H, ON*H*), 5.73 (d, *J* = 1.7 Hz, 1 H, D-1), 5.44 (dd, *J* = 3.3, 1.9 Hz, 1 H, E-1), 5.05 (dd, *J* = 10.2, 2.0 Hz, 1 H, B-1), 4.48 (dd, *J* = 3.2, 1.7 Hz, 1 H, D-2), 4.32 (m, 1 H, B-3), 4.25 (d, *J* = 7.7 Hz, 1 H, A-1), 4.25 (b s, 1 H, E-5$_{eq}$), 4.20 (m, 1 H, D-5), 4.07 (m, 1 H, B-5), 4.02 (b s, 1 H, E-3), 4.01 (dd, *J* = 9.7, 9.7 Hz, 1 H, A-3), 3.89 (s, 3 H, CH_3O-aromatic), 3.89 (b s, 1 H, E-5$_{ax}$), 3.84 (s, 3 H, CH_3O-aromatic), 3.84 (dd, *J* = 9.5, 3.2 Hz, 1 H, D-3), 3.76 (dd, *J* = 10.8, 2.7 Hz, 1 H, B-4), 3.65 (dd, *J* = 9.5, 9.5 Hz, 1 H, D-4), 3.65 (obs, 1 H, A-5), 3.57 (s, 6 H, CH_3O-A ring, CH_3O-D ring), 3.43 (s, 3 H, CH_3O-E ring), 3.43 (obs, 1 H, A-2), 3.13, 3.01 (b m, 2 H, CH_2N), 2.95 (b m, 1 H, E-4), 2.46 (ddd, *J* = 12.9, 4.7, 1.9 Hz, 1 H, E-2$_{eq}$), 2.35 (s, 3 H, ArCH_3), 2.34 (dd, *J* = 9.7, 9.7 Hz, 1 H, A-4), 2.04 (ddd, *J* = 13.6, 3.4, 2.0 Hz, 1 H, B-2$_{eq}$), 1.79 (ddd, *J* = 13.6, 10.2, 3.0 Hz, 1 H, B-2$_{ax}$), 1.50 (ddd, *J* = 12.9, 10.5, 3.3 Hz, 1 H, E-2$_{ax}$), 1.41 (d, *J* = 6.2 Hz, 3 H, B-6), 1.40 (b s, 3 H, CH_3CH$_2$N), 1.35 (d, *J* = 6.2 Hz, 3 H, A-6), 1.30 (d, *J* = 6.2 Hz, 3 H, D-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 151.5, 150.6, 143.0, 133.4, 130.3, 102.6, 102.6, 99.8, 97.6, 93.5, 80.8, 78.4, 71.1, 70.9, 70.4, 69.1, 68.5, 68.3, 68.1, 67.0, 61.7, 60.9, 58.0, 57.2, 57.1, 56.1, 51.6, 41.9, 36.9, 33.7, 25.3, 19.0, 17.8, 17.6, 12.0; FAB HRMS (NBA/CsI) *m/e* 1109.1772, M + Cs^+ calcd for $C_{38}H_{61}IN_2O_{17}S$ 1109.1790.

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