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Total Synthesis of Herbicidin C and Aureonuclemycin: Impasses and New Avenues

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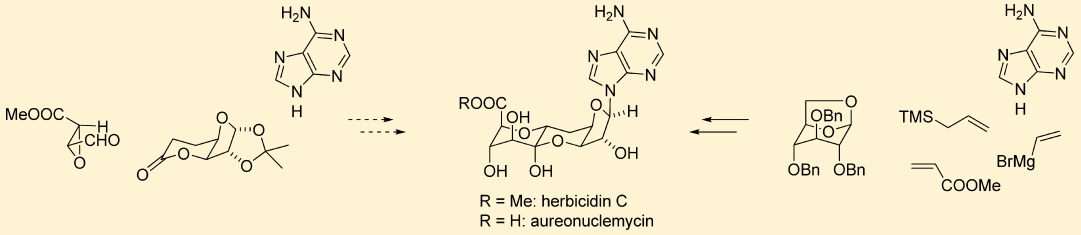
Supporting Information



ABSTRACT: The undecose nucleoside antibiotics herbicidin C and aureonuclemycin are biologically highly active and represent challenging targets for total synthesis. Herein, the gradual evolution of our synthetic strategy toward these natural products is described in detail. The initial route encompasses metalate addition chemistry but suffers from poor stereochemical control. In contrast, the ultimately successful strategy benefits from a variety of reagent-controlled stereoselective transformations, including a surprisingly facile and highly diastereoselective *N*-glycosylation process. The presented work also describes new building blocks that might find further application in carbohydrate chemistry.

INTRODUCTION

Nucleosides and nucleotides are not only the molecular building blocks of nucleic acids but also play a major role in many biosynthetic pathways. They function as energy currencies, secondary messengers, cofactors for a variety of enzymes, and post-translational modifiers, e.g., in methylation or glycosylation reactions. Thus, it is not surprising that the nucleoside motif can also be found in different classes of natural products.[1,2] Most of these bear the canonical purine and pyrimidine nucleobases but are highly diversified with respect to their carbohydrate moieties. The latter range from relatively simple ribose sugars to sophisticated higher-order mono- or polysaccharides. A case in point are the herbicidins (**1**–**9**), tunicamycins (**10**), and hikizimycin (**11**), all of which are examples of complex undecose nucleoside antibiotics (Figure 1). These contain linear 11-membered carbon chains folded into different heterocyclic scaffolds.

The herbicidins have been isolated from different *Streptomyces* strains and have attracted considerable attention because of their structural sophistication and remarkable biological activities.[3−11] Within the family, herbicidins A (**1**) and B (**2**) interfere with the growth of *Xanthomonas oryzae*, a bacterium that causes leaf blight infection in rice crops. In addition, they reduce the growth of algae and impede seed germination. However, the most promising feature of these compounds is their selective toxicity toward dicotyledons with practically no activity against animals.[3−6,9−11] Overall, the herbicidin compound class offers a framework for the discovery of potential lead structures in search of new herbicides and the development of novel biological tools.

The structures of the herbicidins exhibit a carbohydrate skeleton consisting of 11 carbons that are connected in a linear fashion. This chain, however, is incorporated into a tricyclic ring system to feature an unprecedented furano−pyrano−pyran moiety as well as nine stereogenic centers. The nucleobase adenine is glycosylated at the 1β-position, thus residing on the sterically more encumbered concave face. Furthermore, the pyrano−pyran system includes a hemiketal at the C-7 position that forces all substituents on the terminal pyran ring into the axial orientation. The individual members of the herbicidin family differ only in three positions, namely C-2, C-8, and C-11. While the substituent at C-2 is either a hydroxy or methoxy group and C-11 is the carbonyl carbon atom of a carboxylic acid or methyl ester, the side chain at C-8 can be either a hydroxy group or an ester derived from (*E*)-2-(hydroxymethyl)-2-butenoic acid, isobutyric acid, tiglic acid, or acetic acid.

Because of the potent bioactivity and the unusual structure, the herbicidins have been the focus of synthetic interest for some time. As a result, several approaches toward the herbicidins have been described in the literature,[12−25] and a selection of these investigations is summarized in Scheme 1.

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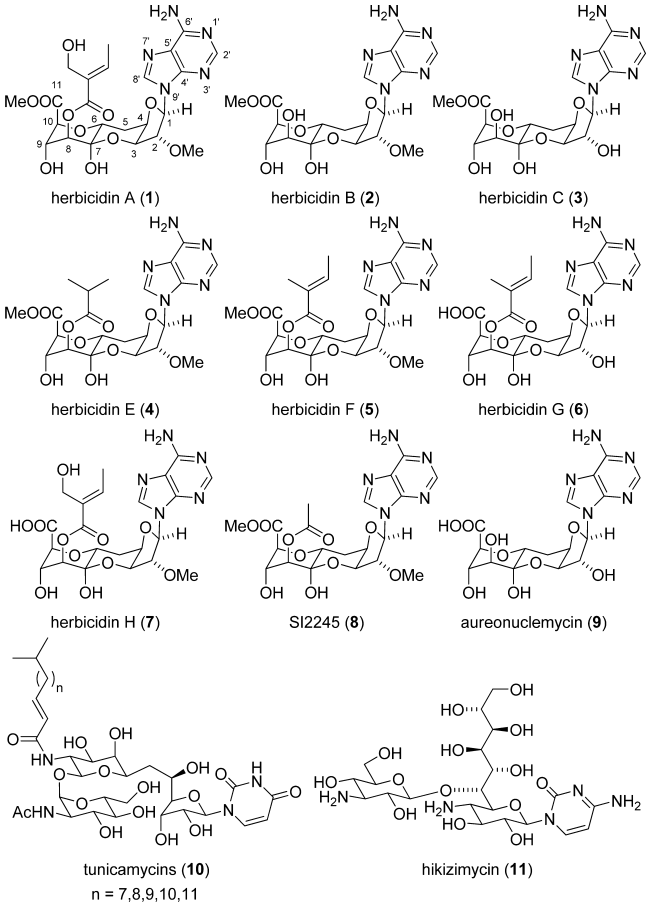


Figure 1. The herbicidin family (**1**–**9**) as well as the tunicamycins (**10**) and hikizimycin (**11**).

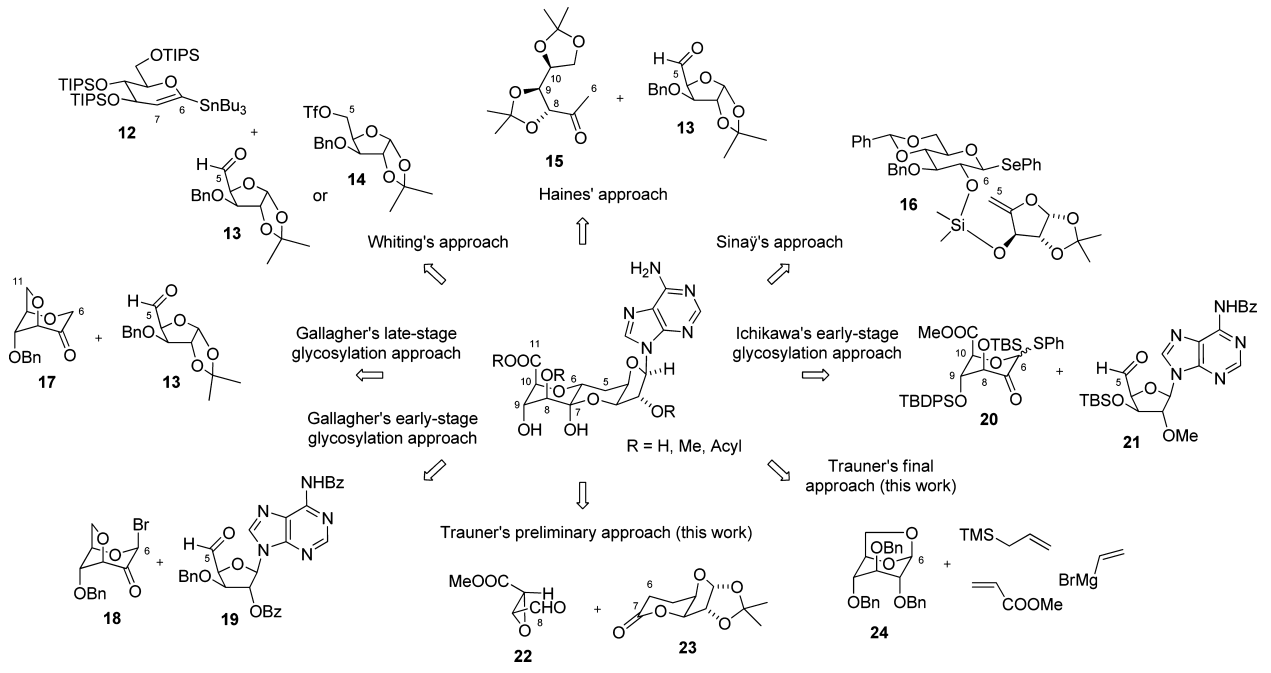
In general, two contrasting strategies regarding the *N*-glycosylation were envisioned: the nucleobase could be introduced either prior to or after the formation of the tricyclic carbohydrate moiety. Thus, these strategies are termed "early-stage" or "late-stage" glycosylation approaches, respectively.[17,26−28] The reported studies on herbicidins have mainly focused on the combination of C_6 and C_5 building blocks by means of *C*-glycosylation, a strategy that includes the most obvious and logical disconnection between C-5 and C-6 for the herbicidin undecose. For example, Whiting and co-workers employed an organolithium species accessed by transmetalation from stannane **12** in reaction with aldehyde **13** or triflate **14** (Scheme 1).[23,24] However, the installation of the ketone at C-7 (herbicidin nomenclature) was not successful.

Aldehyde **13** was later also used as a C_5 building block by Haines and co-workers.[25] Their aim was to combine ketone **15**, derived from L-rhamnose, with aldehyde **13** by means of an aldol reaction. Remarkably, this is the only example that made use of an open-chain C_6 carbohydrate building block to access the undecose moiety. Furthermore, the stereochemistry at C-8, C-9, and C-10 of compound **15** was opposite to that in the herbicidins. This was attributed to the availability of the starting materials: 1-deoxy-L-fructose derivative **15**, prepared from naturally occurring L-rhamnose, was more easily accessible than the respective 1-deoxy-D-fructose derivative, which would be needed for the assembly of the herbicidin undecose with the correct absolute configuration.

A molecular tethering approach followed by a radical cyclization was investigated by Sinaÿ and co-workers.[22] In this case, silaketal **16** was prepared by linking the respective D-glucose- and D-xylose-derived precursors. This intermediate eventually underwent radical 8-*endo*-*trig* cyclization to complete the 11-membered carbon chain. However, further studies toward the herbicidin framework have not been reported.

The investigations by the group of Gallagher date back to 1988,[16−21] encompassing two different strategies, namely, a late-stage and an early-stage approach. First, the same aldehyde **13** as was later used by Whiting and Haines was combined with an enolate derived from ketone **17** to link the C_5 and C_6 building blocks. Analogously, α-bromoketone **18**, prepared

Scheme 1. Selected Approaches toward the Herbicidin Framework, Including Our Strategies



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from D-glucose, was connected in a similar fashion to aldehyde **19**, wherein the nucleobase had already been installed. Although Gallagher and co-workers were able to assemble the glycosylated tricyclic framework, the C-11 position could not be adjusted to the right oxidation state.

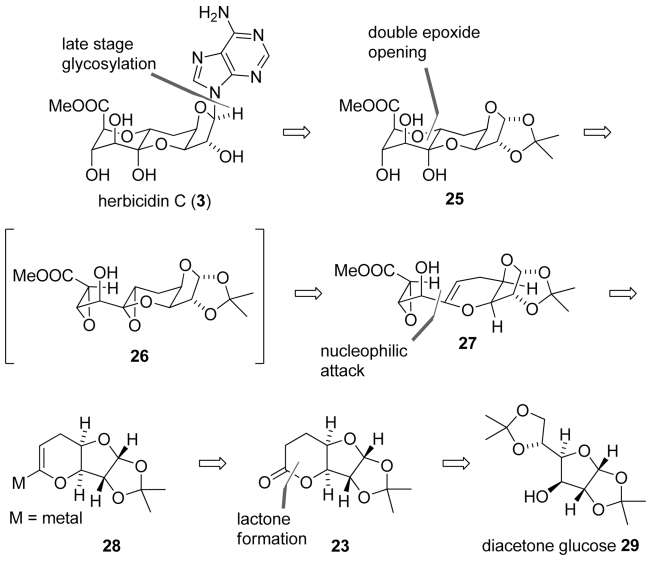
The first total synthesis of a member of the herbicidin family and the only synthesis of herbicidin B to date was developed by Ichikawa and co-workers in 1999.[13] A synthetic plan based on an early-stage glycosylation was envisioned and later successfully realized by a samarium diiodide-mediated aldol-type *C*-glycosylation between phenylthioulose **20** and aldehyde **21**. Further transformations finally afforded herbicidin B (**2**). This route required heavy optimization of the protecting groups in order to favor an all-axial conformation of the substituents at C-8, C-9, and C-10 in the C_6 building block **20**.

In this article, we report the total synthesis of herbicidin C (**3**) and its hydrolyzed congener aureonuclemycin (**9**) using a late-stage glycosylation approach. In particular, we describe two different approaches toward the undecose moiety. Initially, we sought to combine C_4 building block **22** with C_7 lactone **23**, but this approach stalled because of stereochemical issues. The more successful route involved C_6 carbohydrate **24**, which was readily elongated to afford the herbicidin undecose moiety. Synthetic challenges as well as stereochemical surprises of this strategy are included in the discussion. Finally, the stereoselective directed glycosylation of the C_{11} sugar is also described in detail.

RESULTS AND DISCUSSION

Initially, we expected that herbicidin C (**3**) should be accessible through a challenging late-state glycosylation on the sterically congested concave face of the herbicidin carbohydrate skeleton (Scheme 2). As a consequence, we envisioned the known

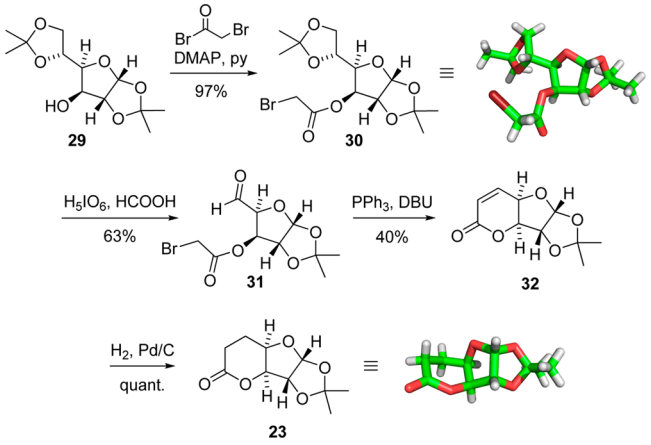
Scheme 2. Retrosynthetic Analysis of the Initial Approach toward Herbicidin C (3)



undecose sugar **25**[20] to be the desired precursor. In contrast to the combination of two separately prepared sugar units, as reported by Gallagher and co-workers,[20] we decided to assemble tetracycle **25** in a more straightforward fashion by a double epoxide-opening sequence from compound **27** via intermediate **26**. Alcohol **27** could stem from dihydropyran **28** and the respective α,β-epoxyaldehyde by a stereoselective addition of an organometallic species **28**. This compound would be prepared from lactone **23**, which could in turn be accessed from diacetone glucose **29**.

Initially, we aimed at preparing lactone **23** from commercially available diacetone glucose **29** (Scheme 3). It had already been

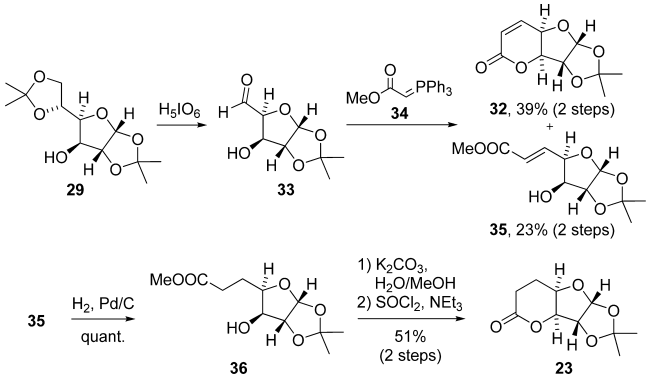
Scheme 3. Synthesis of Key Intermediate 23, Including an Intramolecular Wittig Reaction



reported that compound **29** can be esterified with 2-bromoacetyl bromide to yield ester **30**,[29] the structure of which was confirmed by X-ray crystallography. Subsequent regioselective acetonide deprotection with concomitant diol cleavage using periodic acid afforded aldehyde **31**, which underwent one-pot phosphonium salt formation/Wittig reaction to yield the known unsaturated lactone **32**.[29] The originally reported low yield of 22% was improved to 40% by using DBU as a hydrogen bromide scavenger instead of propylene oxide. Subsequent hydrogenation with hydrogen gas and palladium on charcoal gave key lactone **23** in quantitative yield. In addition, the identity of **23** was confirmed by X-ray analysis.

In order to improve the overall yield of lactone **23**, we also investigated an alternative approach wherein the succession of steps was altered (Scheme 4). Selective deprotection of the primary acetonide of diacetone glucose **29** followed by diol cleavage with periodic acid afforded aldehyde **33**. The intermolecular Wittig reaction of aldehyde **33** with ylide **34** resulted in the isolation of the (*Z*)-ester as the unsaturated

Scheme 4. Improved Route to Intermediate 23 through an Intermolecular Wittig Reaction



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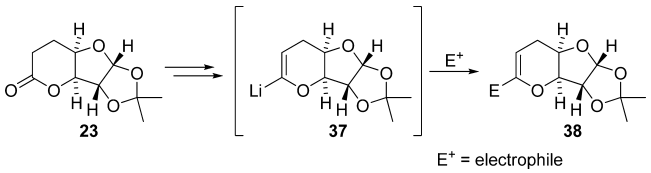
lactone **32** in 39% yield as well as (*E*)-ester **35** in 23% yield.[30] The former was reduced to **23** as shown above. The latter could be transformed into the desired lactone **23** by a short reduction/saponification/lactonization sequence. Thus, the overall yield from diacetone glucose **29** to lactone **23** was improved from 24% (intramolecular Wittig route) to 51% (intermolecular Wittig route).

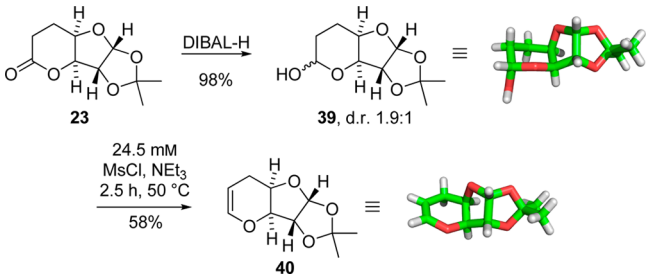
Next, we investigated the transformation of lactone **23** into a lithiated glycal species **37**, which could potentially be trapped with electrophiles to yield substituted dihydropyrans of type **38** (Scheme 5). Typically, the preparation of organometallic

Scheme 5. Conceptual Transformation of Lactone 23 to Dihydropyran 38



compounds of type **37** has been achieved by direct deprotonation of glycals.[31−33] Thus, lactone **23** was reduced with DIBAL-H to give the corresponding lactol **39** as a 1.9:1 mixture of diastereomers (Scheme 6). The major isomer could

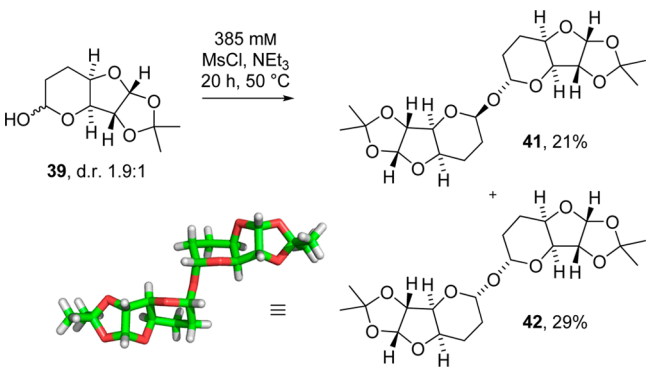
Scheme 6. Preparation of Dihydropyran 40 from Lactone 23



be identified by X-ray crystallography. After careful optimization of the reaction conditions, we found that dehydration of **38** could be achieved with mesyl chloride as the activating agent and triethylamine as the base to yield dihydropyran **40**.

When this reaction was carried out at higher concentrations (>24.5 mM), an undesired dimerization of lactol **39** was observed (Scheme 7). After 20 h at 50 °C and a concentration of 385 mM, two of three possible diastereomeric dimers were

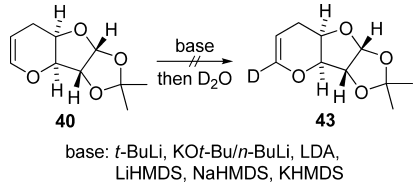
Scheme 7. Undesired Dimerization of Lactol 39 in Highly Concentrated Reaction Medium



isolated, namely, unsymmetrical dimer **41** and C_2-symmetric dimer **42**. As expected, the ^{1}H NMR spectrum of dimer **42** showed a reduced signal set compared with that of dimer **41**. The structure of the major product **42** was confirmed by X-ray crystallography. The second possible C_2-symmetric diastereomer was not observed. Presumably, **41** and **42** are formed through nucleophilic attack of **39** onto its mesylate or the corresponding oxonium ion.

With glycal **40** in hand, deprotonation with several bases was attempted (Scheme 8). Disappointingly, only protonated

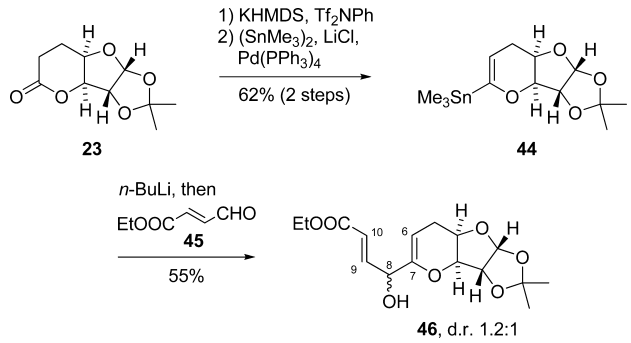
Scheme 8. Unsuccessful Attempts To Deprotonate Glycal 40



starting material **40** was recovered after treatment with *t*-BuLi, KO*t*-Bu/*n*-BuLi (Schlosser's base), LDA, or HMDS as the base and subsequent quenching with D_2O.

At this point, an alternative route to prepare organolithium species **37** from lactone **23** via stannane **44** was pursued (Scheme 9). Initial attempts to deprotonate tricycle **23** resulted

Scheme 9. Synthesis of Stannane 44 and Organolithium Addition to Aldehyde 45



in the opening of the lactone ring, and the respective carboxylic acid was isolated. However, trapping of the enolate with *N*-phenylbis(trifluoromethanesulfonimide) gave a sensitive triflyl ketene acetal that could be converted into stannane **44** without further purification. The trimethyltin group was then exchanged with lithium, and the organometallic species so obtained was reacted further with aldehyde **45** to afford alcohol **46** as a 1.2:1 mixture of diastereomers. Unfortunately, we were unable to carry out this reaction with the more highly functionalized known ethyl ester derivative of *α*,*β*-epoxyaldehyde **22**,[34−36] which was found to be extremely instable in our hands.

Compound **46** is an advanced intermediate that represents a significant portion of the herbicidins. Although all 11 carbon atoms of their undecose skeleton had been assembled and two of three rings had been installed, stereoselective functionalization of C-6, C-7, C-8, C-9, and C-10 in **46** still presented a formidable task. In addition, the preparation of large amounts of material, especially at the beginning of the sequence, was not practical, and the vinylstannane chemistry proved to be capricious. As a result, we decided to switch our synthetic strategy.

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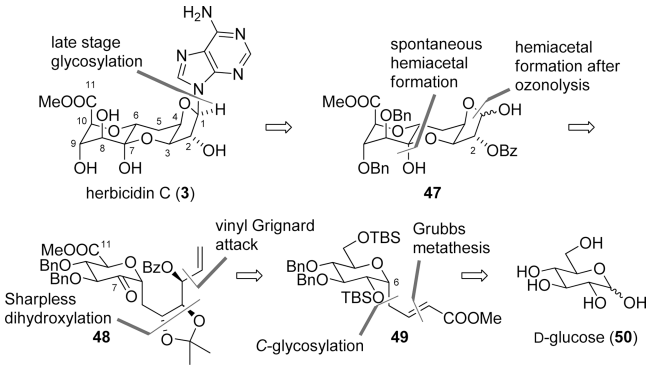
We reasoned that the stereochemistry at C-6, C-8, C-9, and C-10 should be set at an early stage of the synthesis since the functionalization of these carbons late in the game appeared to be more challenging than originally anticipated. In particular, we felt that early establishment of the stereocenter at C-6 would be beneficial. The problems encountered in Ichikawa's synthesis of herbicidin B at this junction reinforced us in our belief that this would be crucial for the success of the synthesis.

Similar to our first retrosynthetic strategy, a late-stage glycosylation would introduce the nucleobase in precursor **47**, whereby a neighboring benzoate at C-2 should control the stereochemistry of the reaction (Scheme 10).[12] Tricycle **47**

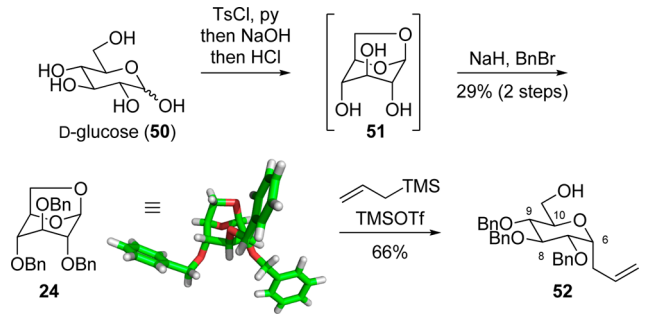
Scheme 10. Second-Generation Retrosynthetic Analysis toward Herbicidin C (3)



could be derived from terminal alkene **48**, which already possesses the right oxidation states at C-7 and C-11. This intermediate was expected to stem from unsaturated ester **49** through asymmetric dihydroxylation and vinyl Grignard addition, while compound **49** itself could be accessible from D-glucose (**50**) via axial *C*-glycosylation and Grubbs' olefin cross-metathesis.

In the event, **50** was converted to protected anhydro sugar **24** by a two-step protocol (Scheme 11).[12] Thus, dehydration of

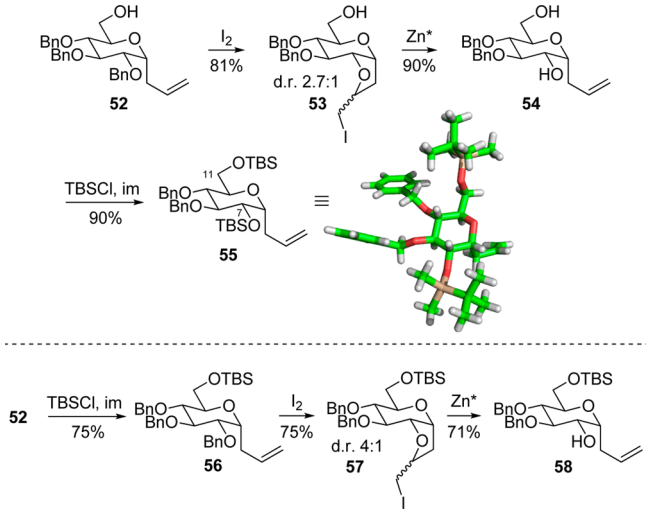
Scheme 11. Synthesis of *C*-Glycoside 52



50 provided anhydro glucose **51**,[37] which was directly tribenzylated to yield compound **24**.[38] Although this transformation was low-yielding, the reaction could be carried out on a large scale to efficiently furnish multigram quantities of bicycle **24**. The following Hosomi–Sakurai allylation afforded the known *C*-glycoside **52** in 66% yield,[38−43] wherein the stereochemical configuration of the C-6, C-8, C-9, and C-10 centers (herbicidin nomenclature) in **52** had been successfully controlled.

The next stage of the synthesis was the preparation of bis-silyl ether **55** in order to differentiate the C-7 and C-11 alcohols, the oxidation states of which would eventually be adjusted (Scheme 12). To this end, compound **52** was

Scheme 12. Preparation of Silyl Ether 55 and Carbohydrate Building Block 58

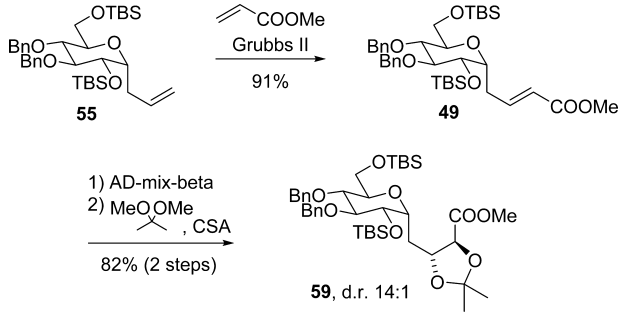


selectively debenzylated through a two-step protocol[44−46] involving the formation of iodo ether **53** and subsequent elimination to give diol **54**. After TBS protection, the desired intermediate **55** was obtained.

During these investigations, we found that permutation of the steps (TBS protection → **56** followed by the formation of iodo ether **57** and elimination) gives rise to carbohydrate building block **58** (Scheme 12), which could be, for example, protected as an acetate to have three out of four alcohols orthogonally protected. This building block might find further application in carbohydrate chemistry.

After modification of the pyran ring of the herbicidin backbone, we sought to establish the framework of the furan ring and the cyclic hemiacetal. Thus, the allyl side chain of intermediate **55** was elongated by Grubbs' cross-metathesis with methyl acrylate,[47,48] which afforded unsaturated ester **49** in excellent yield (Scheme 13). A subsequent highly diastereoselective Sharpless dihydroxylation[49] proved to be sluggish but was forced to completion by increasing the osmium tetroxide concentration. Subsequent acetonide formation yielded methyl ester **59** as an inseparable 14:1 mixture with its minor diastereomer. The diol protection under acidic

Scheme 13. Synthesis of Ester 59



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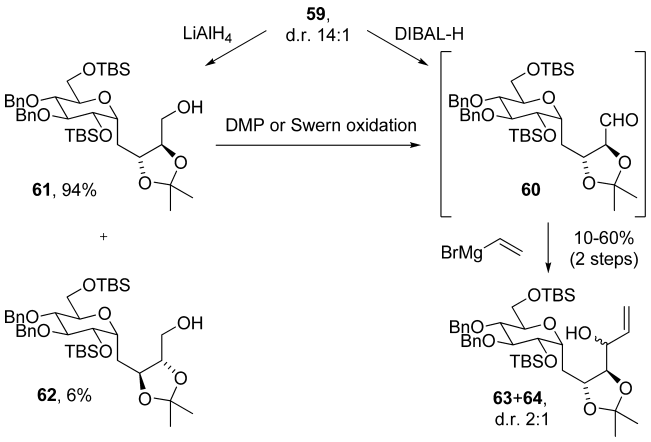
conditions had to be optimized because of the facile cleavage of the primary TBS ether in acidic media.

In order to attach the remaining carbon atoms and install an additional stereocenter, ester **59** was converted to aldehyde **60** using DIBAL-H (Scheme 14). As a side reaction, over-

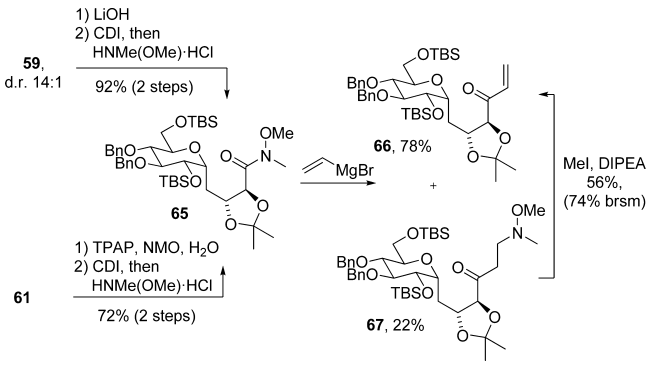
Scheme 14. Attempts To Synthesize Vinyl Alcohols 63 and 64



reduction with DIBAL-H was observed, necessitating the complete reduction of ester **59** with $LiAlH_4$. At this stage, it was possible to separate the diastereomeric alcohols **61** and **62**. The major isomer **61** could be readily oxidized using Dess–Martin periodinane (DMP) or via Swern oxidation. Although addition of vinylmagnesium bromide to the resulting aldehyde **60** did take place to afford a mixture of the two separable allyl alcohols **63** and **64**, the diastereomeric ratio was low and the yields were unreliable.

In search of a more efficient transformation of ester **59**, we found that the most practical method was the conversion of **59** to vinyl ketone **66**, which could then be stereoselectively reduced by reagent-controlled reactions, such as the Corey–Itsuno reduction (Scheme 15). The double bond in **66** was

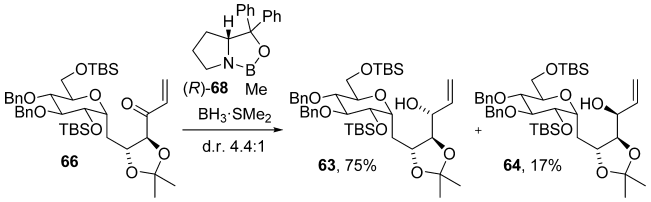
Scheme 15. Transformation of Ester 59 and Alcohol 61 into Vinyl Ketone 66



intended to serve as a carbonyl equivalent. Thus, saponification of the diastereomeric mixture of ester **59** provided the corresponding acid, which was immediately converted to Weinreb amide **65**. In order to access isomerically pure material for analysis, the diastereomers were separated after reduction of **59** with $LiAlH_4$ at the stage of alcohol **61**, as described above. Ley oxidation and subsequent formation of the Weinreb amide provided another practical route to **65**. The reaction of compound **65** with vinylmagnesium bromide then gave the desired vinyl ketone **66** and considerable amounts of ketone **67**. This side product, however, could be recycled to afford **66** by means of a Hofmann-type elimination, which gave a good overall yield of vinyl ketone **66**.

The seemingly straightforward Corey–Itsuno reduction of vinyl ketone **66** proved to be more challenging than anticipated.[12] Reduction of the carbonyl group in **66** with BH_3 and the *R*-configured reagent (*R*)-**68** gave a 4.4:1 mixture of compounds **63** and **64** in favor of the alcohol with the undesired stereochemistry (Scheme 16). This result was

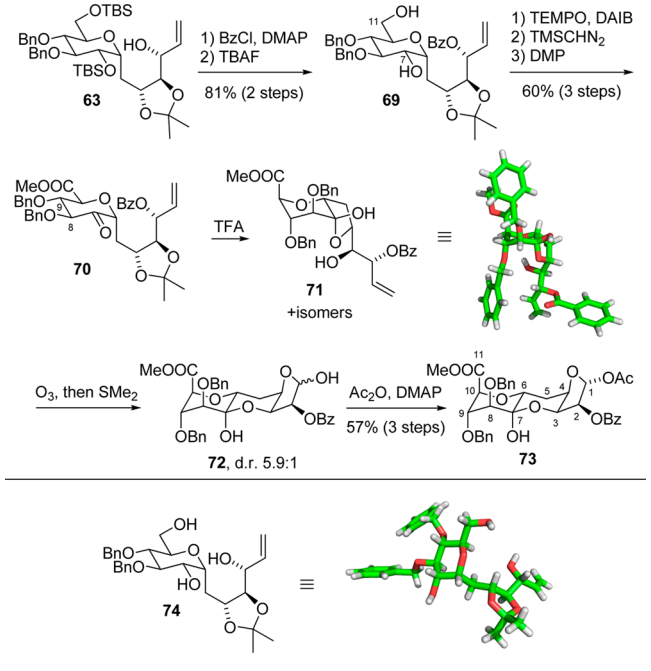
Scheme 16. Synthesis of the Undesired Diastereomer 63



unexpected because Corey–Itsuno reductions are typically reagent-controlled and the generally accepted transition-state model[50] with reagent (*R*)-**68** predicts the opposite outcome.

The undesired stereochemistry of alcohol **63** was revealed only after further synthetic transformations and the establishment of tricyclic compound **73** (Scheme 17, top). Protection of

Scheme 17. Establishment of the Tricyclic Core 73 (top) and X-ray Structure of Triol 74 (bottom)



the allylic alcohol in **63** and desilylation with TBAF afforded diol **69**. In order to oxidize C-7 and C-11, compound **69** was subjected to a variety of methods and reagents, such as DMP oxidation, Pinnick oxidation, pyridinium dichromate (PDC) oxidation, pyridinium chlorochromate (PCC), and Ley oxidation (TPAP, NMO). Most of these furnished intractable mixtures containing little or no desired product. Eventually, we

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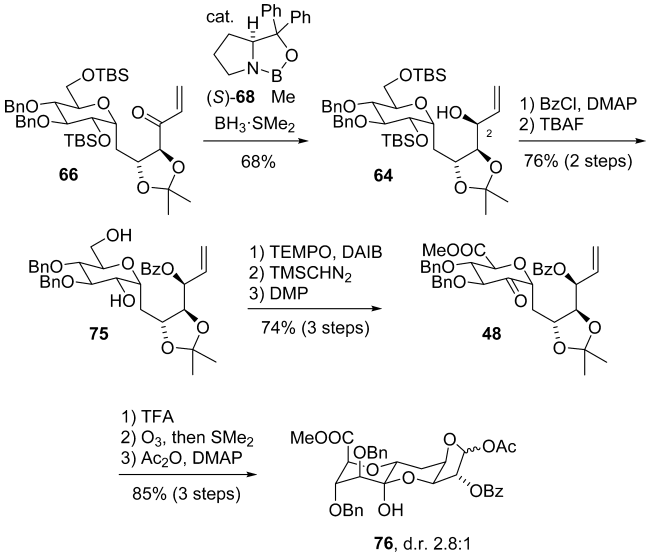
successfully performed the oxidation using 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and (diacetoxyiodo)benzene (DAIB) in the presence of water. Under these conditions, only the primary alcohol was oxidized to the corresponding dicarboxylic acid, whereas the secondary hydroxy group remained unaffected. Ketone **70** was then obtained after ester formation with (trimethylsilyl)diazomethane and subsequent DMP oxidation. Cleavage of the acetonide with trifluoroacetic acid (TFA) resulted in a mixture of isomeric hemiacetals with compound **71** as the major compound, which was identified by X-ray analysis. When this mixture was subjected to ozonolysis, the entire carbohydrate moiety rearranged to give the tricyclic core **72**, which was subsequently acylated at the sterically more accessible hemiacetal, yielding undecose **73** as a single diastereomer in 57% yield over three steps. The undesired stereochemistry at C-2 resulting from the Corey–Itsuno reduction could be deduced from the NOESY 2D NMR spectrum by the cross-peak of protons H-2 and H-4 in tricycle **73** and was later confirmed by the X-ray structure of the deprotected triol **74** (Scheme 17, bottom).

Detailed analysis of the NMR spectra showed that the six-membered chair in **70** had undergone ring inversion during the cyclization process to give **73**. Whereas the coupling constant of protons H-8 and H-9 in **70** was J = 7.1 Hz, the corresponding coupling in tricycle **73** showed a value of J = 3.4 Hz, an indication that both H-8 and H-9 now adopted equatorial positions.

In order to correct the stereochemistry at the C-2 position, we applied (*S*)-**68**, the enantiomer of the previously used oxazaborolidine, in catalytic amounts (10 mol %) (Scheme 18).

Scheme 18. Establishment of the Undecose Skeleton 76

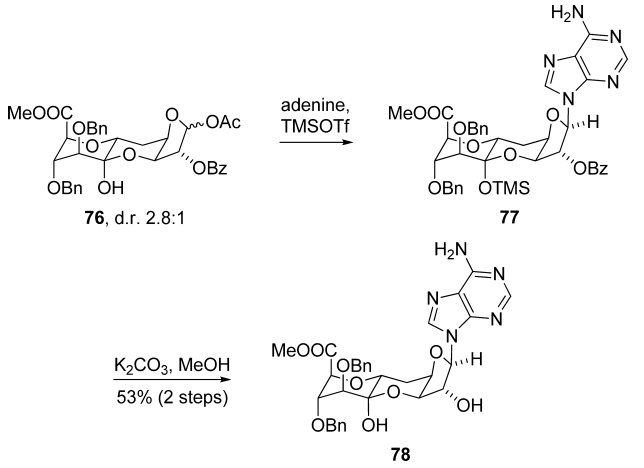


The resulting allylic alcohols **64** and **63** were obtained in a diastereomeric ratio of 14:1 (as determined by ^{1}H NMR spectroscopy of the crude product mixture), and the major isomer could be separated from the minor isomer by column chromatography, affording **64** in 68% isolated yield.

Having established the undecose framework of herbicidin with the desired configuration at C-2, we proceeded with the oxidation state adjustment and the formation of the heterotricyclic ring system (Scheme 18). At this point, a benzoyl group was introduced at C-2 to later control the stereochemical outcome of the *N*-glycosylation. Desilylation using TBAF yielded diol **75**, after which the previously established oxidation/esterification sequence (TEMPO/DAIB, $TMSCHN_2$, DMP) furnished ketone **48**. Application of our previously optimized cyclization conditions (TFA; O_3; Ac_2O) gave the desired tricycle **76** with the correct stereochemistry at C-2 as a 2.8:1 mixture of anomeric acetates.

With undecose **76** in hand, we accomplished the crucial late-stage *N*-glycosylation by using a modified silyl-Hilbert–Johnson (also Vorbrüggen) protocol. Under these conditions, glycosylamine **77** was readily obtained, and the protected herbicidin C precursor **78** was isolated in 53% yield over two steps (Scheme 19).

Scheme 19. Glycosylation of Compound 78



In order to complete the total synthesis of herbicidin C (**3**), the benzyl protecting groups of **77** or **78** had to be cleaved. However, this transformation was more problematic than originally anticipated. First, compound **77** was subjected to a variety of debenzylation conditions [e.g., H_2 (6 bar), Pd/C, MeOH; H_2 (8 bar), $Pd(OH)_2$/C, MeOH; H_2 (8 bar), $Pd(OH)_2$/C, AcOH; $HCOONH_4$, $Pd(OH)_2$/C, MeOH; H_2, Raney Ni; $FeCl_3$; BBr_3; DDQ; Li, NH_3], all of which proved unsuccessful. Attempts to deprotect compound **78** under reductive conditions (H_2, Pd/C, MeOH; H_2, Pd/C, EtOAc; H_2, PtO_2, MeOH) also failed. When lithium 4,4′-di-*tert*-butyldiphenyl (LDBB) was applied to benzyl ether **78**, a monobenzylated product was isolated in 20% yield (as indicated by ^{1}H NMR spectroscopy and mass spectrometry).

Since final debenzylation could not be effected during the final stretch of the synthesis, we decided to change the order of debenzylation and glycosylation (Scheme 20). To this end, the benzyl groups in **76** were cleaved via hydrogenolysis. Subsequent acetylation then gave pentaester **79** in 74% yield over two steps. Notably, the hemiacetal hydroxy group at the pyran ring juncture remained unaffected under these conditions.

To our relief, Vorbrüggen glycosylation under the previously established conditions also worked with substrate **79**, yielding adenyl nucleotide **80** as the only isolable diastereomer in 55% yield. Global deprotection using NaOMe/MeOH gave herbicidin C (**3**), whose structure was confirmed by detailed spectroscopic analysis, including NMR titration experiments with an authentic sample of the natural product. Further saponification of the base-labile natural product **3** under mild

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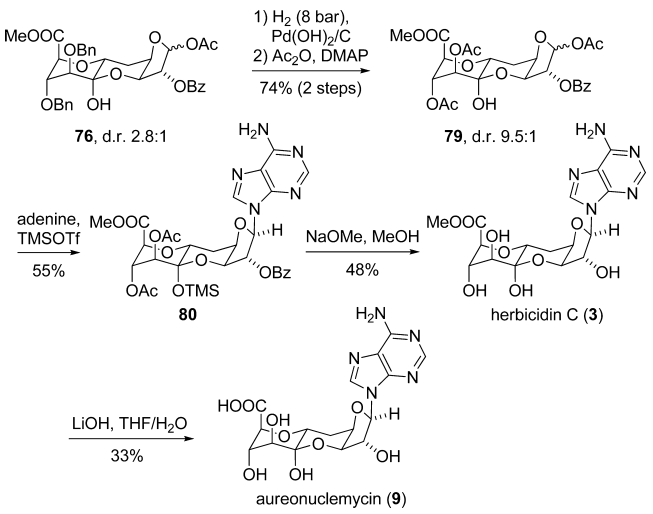
Scheme 20. Total Synthesis of Herbicidin C (3) and Aureonuclemycin (9)



conditions finally yielded aureonuclemycin (**9**), another member of the herbicidin family.

CONCLUSION

In summary, we have presented two different strategies toward the herbicidins, both of which are based on a late-stage glycosylation as the key step. Our initial strategy yielded lactone **23**, which already includes seven carbon atoms of the undecose chain, from inexpensive carbohydrate starting materials. However, this approach suffered from weak stereocontrol and the need to employ toxic organotin reagents. By contrast, the second route turned out to be more robust, and large quantities of the undecose chain could be procured. Although we had to overcome unexpected stereochemical problems, we eventually established the correct absolute configuration of the undecose moiety by a stereoselective *C*-glycosylation and several reagent-controlled transformations. One further synthetic obstacle regarding the protecting group chemistry needed to be solved before the highly diastereoselective *N*-glycosylation completed the total synthesis of the natural products herbicidin C (**3**) and aureonuclemycin (**9**). The realization of a late-stage glycosylation strategy provides flexibility and new pathways for the fast preparation of herbicidin derivatives, e.g., for structure–activity relationship studies.

EXPERIMENTAL SECTION

(3a*R*,5*R*,6*S*,6a*R*)-5-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-6-yl 2-Bromoacetate (30).[29] A stirred solution of diacetone-D-glucose **29** (15.0 g, 57.6 mmol, 1.0 equiv), DMAP (70.4 mg, 0.576 mmol, 10 mol %), and pyridine (6.96 mL, 86.4 mmol, 1.5 equiv) in CH_2Cl_2 (125 mL) was cooled to 0 °C, and 2-bromoacetyl bromide was added dropwise. The reaction mixture was stirred for 40 min at 0 °C, after which the reaction was quenched at 0 °C with water (1.2 mL) and the mixture was allowed to warm to room temperature. After stirring for an additional 15 min at room temperature, the resulting solution was diluted with EtOAc (200 mL). The organic phase was washed with water (2 × 30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [CH_2Cl_2:acetone 99:1] provided bromo ester **30** (21.3 g, 56.0 mmol, 97%) as a white solid: R_f 0.39 [petroleum ether:EtOAc 4:1]; $[\alpha]_D^{21}$ −39.6 (*c* = 0.93, MeOH); mp 51–53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90 (d, *J* = 3.7 Hz, 1H), 5.32 (d, *J* = 2.8 Hz, 1H), 4.51 (d, *J* = 3.7 Hz, 1H), 4.27–4.19 (m, 2H), 4.11 (dd, *J* = 8.8, 5.6 Hz, 1H), 4.01 (dd, *J* = 8.7, 4.5 Hz, 1H), 3.87 (d, *J* = 12.3 Hz, 1H), 3.84 (d, *J* = 12.3 Hz, 1H), 1.52 (s, 3H), 1.41 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 112.6, 109.7, 105.2, 83.2, 80.0, 77.8, 72.4, 67.6, 27.0, 26.9, 26.4, 25.4, 25.4; IR (ATR) $\tilde{\nu}$ 2983, 1769, 1741, 1383, 1268, 1205, 1135, 1069, 1018, 841 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{25}BrNO_7^+$ 398.0809, found 398.0806 [M + NH_4]$^+$.

(3a*R*,5*S*,6*S*,6a*R*)-5-Formyl-2,2-dimethyltetrahydro-2*H*-furo-[2,3-*d*][1,3]dioxol-6-yl 2-Bromoacetate (31).[29] A solution of bromo ester **30** (6.71 g, 17.6 mmol, 1.0 equiv) in Et_2O:MeOH (9:1, 50 mL) was cooled to 0 °C, and formic acid (25 mL) followed by periodic acid (4.81 g, 21.2 mmol, 1.2 equiv) was added. The reaction mixture was stirred at 0 °C for 10 min, allowed to warm to room temperature, and stirred for an additional 30 min until complete consumption of the starting material (as indicated by TLC analysis). The mixture was diluted with EtOAc (100 mL), and the organic phase was washed with water (2 × 20 mL), aq. $NaHCO_3$ (3 × 30 mL of a saturated solution), and aq. $Na_2S_2O_3$ (3 × 10 mL of a saturated solution), dried ($MgSO_4$), and concentrated in vacuo to provide aldehyde **31** (3.44 g, 11.1 mmol, 63%) as a white solid: R_f 0.24 [PE:EtOAc 1:1] (streaking); $[\alpha]_D^{21}$ −17.3 (*c* = 1.0, MeOH); mp 66–67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 6.09 (d, *J* = 3.5 Hz, 1H), 5.53 (dd, *J* = 3.4, 0.3 Hz, 1H), 4.74 (dd, *J* = 3.4, 0.8 Hz, 1H), 4.59 (d, *J* = 3.5 Hz, 1H), 3.78 (d, *J* = 12.5 Hz, 1H), 3.76 (d, *J* = 12.9 Hz, 1H), 1.51 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 166.1, 113.3, 105.6, 83.2, 82.8, 78.6, 26.9, 26.4, 24.7; IR (ATR) $\tilde{\nu}$ 3456, 2987, 1742, 1376, 1263, 1160, 1013, 851 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{17}BrNO_6^+$ 326.0234, found 326.0234 [M + NH_4]$^+$.

(1*S*,2*R*,6*R*,8*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodec-9-en-11-one (32). A solution of aldehyde **31** (200 mg, 0.647 mmol, 1.0 equiv) and PPh_3 (170 mg, 0.647 mmol, 1.0 equiv) in MeCN (2 mL) was stirred at room temperature for 9 h. 1,8-Diazabicyclo[5.4.0]undec-7-ene (98.5 mg, 0.647 mmol, 1.0 equiv) was added, and the mixture was stirred at room temperature for an additional 24 h before being diluted with Et_2O (30 mL). The organic phase was washed with water (2 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [CH_2Cl_2:acetone 99:1] afforded unsaturated lactone **32** (55.5 mg, 0.262 mmol, 40%) as a white solid: R_f 0.59 [PE:EtOAc 1:1]; $[\alpha]_D^{21}$ +28.9 (*c* = 0.56, MeOH); mp 70 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.96 (dd, *J* = 9.8, 5.7 Hz, 1H), 6.23 (d, *J* = 9.8 Hz, 1H), 6.02 (d, *J* = 3.7 Hz, 1H), 4.82 (d, *J* = 3.8 Hz, 1H), 4.81 (d, *J* = 3.2 Hz, 1H), 4.62 (dd, *J* = 5.7, 3.1 Hz, 1H), 1.53 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.9, 138.8, 125.5, 112.7, 105.4, 84.1, 82.6, 67.7, 26.9, 26.3; IR (ATR) $\tilde{\nu}$ 2924, 1729, 1384, 1212, 1068, 1017, 888, 826 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{16}NO_5^+$ 230.1023, found 230.1022 [M + NH_4]$^+$.

(1*S*,2*R*,6*R*,8*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodecan-11-one (23). To a solution of unsaturated lactone **32** (246 mg, 1.16 mmol) in EtOAc (5 mL) was added palladium on charcoal (10 wt %, 47.0 mg), and the flask was purged with hydrogen gas five times. The mixture was then stirred under a hydrogen atmosphere at room temperature for 15 h. The catalyst was removed by filtration through a pad of Celite, and the Celite was washed with EtOAc (20 mL). After concentration of the filtrate in vacuo, flash column chromatography [PE:EtOAc 4:1 → 3:1] afforded lactone **23** (238 mg, 1.11 mmol, 96%) as a white solid: R_f 0.46 [PE:EtOAc 1:1]; $[\alpha]_D^{21}$ +32.4 (*c* = 0.67, MeOH); mp 53–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (d, *J* = 3.8 Hz, 1H), 4.69 (m, 2H), 4.54 (ddd, *J* = 3.6, 3.6, 3.6 Hz, 1H), 2.65 (ddd, *J* = 17.6, 11.0, 6.6 Hz, 1H), 2.45 (ddd, *J* = 17.5, 6.1, 4.4 Hz, 1H), 2.27–2.06 (m, 2H), 1.50 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 112.4, 105.0, 84.2, 83.9, 71.5, 26.7, 26.3, 25.1, 21.8; IR (ATR) $\tilde{\nu}$ 2982, 2946, 1738, 1389, 1183, 1040, 918 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{15}O_5^+$ 215.0914, found 215.0927 [M + H]$^+$.

(1*S*,2*R*,6*R*,8*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodec-9-en-11-one (32) and Methyl (2*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-6-Hydroxy-2,2-dimethyltetrahydro-2*H*-furo-[2,3-*d*][1,3] dioxol-5-yl]prop-2-enoate (35).[30] To a solution of diacetone-D-glucose **29** (3.00 g, 11.5 mmol, 1.0 equiv) in EtOAc (215 mL) was added periodic acid (2.89 g, 12.7 mmol, 1.1 equiv), and the

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resulting solution was stirred at room temperature for 2.5 h. During the reaction a white solid precipitated, which was removed by filtration through a pad of Celite. The Celite was washed with EtOAc (100 mL), and the filtrate was concentrated in vacuo. The crude sugar was then dried by azeotropic distillation with benzene (50 mL). A phosphonium ylide was prepared in a separate flask by adding dropwise a solution of *n*-BuLi in hexanes (2.5 M, 5.52 mL, 13.8 mmol, 1.2 equiv) to a solution of (methoxycarbonylmethyl)triphenylphosphonium bromide (5.73 g, 13.8 mmol, 1.2 equiv) in THF (180 mL) at 0 °C. This mixture was stirred at 0 °C for 30 min, and then a solution of the previously obtained crude sugar in THF (30 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred at this temperature for 18 h. Water (50 mL) was added, and the mixture was extracted with EtOAc (3 × 60 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated in vacuo. Flash column chromatography [PE:EtOAc 4:1 → 3:1 → 2:1 → 1:1] afforded unsaturated lactone **32** (959 mg, 4.52 mmol, 39%) as a white solid as well as *trans*-ester **35** (632 mg, 2.59 mmol, 23%) as a colorless oil. Unsaturated lactone **32**: the analytical data were identical to those of the material obtained earlier. *trans*-Ester **35**: R_f 0.38 [PE:EtOAc 1:1]; $[\alpha]_D^{18}$ −48.9° (*c* = 0.34, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.92 (dd, *J* = 15.7, 4.3 Hz, 1H), 6.24 (d, *J* = 15.7 Hz, 1H), 5.97 (d, *J* = 3.7 Hz, 1H), 4.85−4.82 (m, 1H), 4.56 (d, *J* = 3.7 Hz, 1H), 4.23 (d, *J* = 2.8 Hz, 1H), 3.73 (s, 3H), 2.29 (br s, 1H), 1.49 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.7, 141.2, 123.8, 112.2, 104.8, 85.1, 79.8, 76.1, 51.9, 26.9, 26.3; IR (ATR) $\tilde{\nu}$ 3432, 2957, 1707, 1311, 1215, 1072, 1009, 79 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{20}NO_6^+$ 262.1285, found 262.1284 $[M + NH_4]^+$.

Methyl 3-[(3a*R*,5*R*,6*S*,6a*R*)-6-Hydroxy-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl]propanoate (36). To a solution of unsaturated ester **35** (2.44 g, 10.0 mmol) in MeOH (40 mL) was added palladium on charcoal (10 wt %, 203 mg), and the flask was purged with hydrogen gas five times. The mixture was then stirred under a hydrogen atmosphere at room temperature for 22 h. The catalyst was removed by filtration through a pad of Celite, and the Celite was washed with MeOH (60 mL). The filtrate was then concentrated in vacuo to afford ester **36** (2.47 g, 10.0 mmol, quant.) as a white solid: R_f 0.31 [PE:EtOAc 1:1]; $[\alpha]_D^{21}$ −24.7 (*c* = 0.34, MeOH); mp 80−81 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 5.83 (d, *J* = 3.8 Hz, 1H), 4.46 (d, *J* = 3.8 Hz, 1H), 4.12−4.06 (m, 1H), 3.95 (d, *J* = 2.7 Hz, 1H), 3.67 (s, 3H), 2.49−2.42 (m, 2H), 1.99−1.88 (m, 2H), 1.43 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.5, 112.4, 105.8, 86.9, 81.0, 75.9, 52.1, 31.4, 27.0, 26.4, 24.6; IR (ATR) $\tilde{\nu}$ 3372, 2991, 1735, 1372, 1164, 1082, 788 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{18}NaO_6^+$ 269.0996, found 269.0994 $[M + Na]^+$.

3-[(3a*R*,5*R*,6*S*,6a*R*)-6-Hydroxy-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl]propanoic Acid (S1). A solution of ester **36** (2.47 g, 10.0 mmol, 1.0 equiv) and potassium carbonate (2.76 g, 20.0 mmol, 2.0 equiv) in a mixture of MeOH and water (4:1, 50 mL) was stirred at room temperature for 22 h. The reaction mixture was concentrated under reduced pressure to a total volume of ca. 20 mL and then diluted with water (50 mL). After extraction of the mixture with EtOAc (50 mL), the aqueous layer was acidified to pH 1 with aq. HCl (1 N, ca. 45 mL). The acidic aqueous layer was further extracted with EtOAc (6 × 100 mL). The combined organic fractions were then dried ($MgSO_4$) and concentrated in vacuo to afford carboxylic acid **S1** (2.30 g, 9.90 mmol, 99%) as a white solid: R_f 0.71 [EtOAc:MeOH (0.5% formic acid) 9:1]; $[\alpha]_D^{21}$ −22.9 (*c* = 0.44, MeOH); mp 96−97 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 5.83 (d, *J* = 3.8 Hz, 1H), 4.47 (d, *J* = 3.8 Hz, 1H), 4.14−4.08 (m, 1H), 3.96 (d, *J* = 2.7 Hz, 1H), 2.46−2.39 (m, 2H), 1.98−1.86 (m, 2H), 1.43 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 177.1, 112.4, 105.8, 86.9, 81.1, 75.9, 31.5, 27.0, 26.4, 24.6; IR (ATR) $\tilde{\nu}$ 3361, 2988, 1715, 1382, 1195, 997, 866 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{15}O_6^-$ 231.0874, found 231.0872 $[M - H]^-$.

(1*S*,2*R*,6*R*,8*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodecan-11-one (23). A solution of carboxylic acid **S1** (2.28 g, 9.82 mmol, 1.0 equiv) and triethylamine (2.72 mL, 19.6 mmol, 2.0 equiv) in CH_2Cl_2 (200 mL) was cooled to 0 °C, and thionyl chloride (1.42 mL, 19.6 mmol, 2.0 equiv) was added dropwise. The mixture was allowed to warm to room temperature and stirred at this temperature for 20 min. The reaction was then quenched with aq. NH_4Cl (100 mL of a saturated solution), and the mixture was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic fractions were washed with water (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 4:1 → 3:1 → 2:1] afforded lactone **23** (1.09 g, 5.09 mmol, 52%) as a white solid. The analytical data were identical to those of the material obtained earlier.

(1*S*,2*R*,6*R*,8*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodecan-11-ol (39). A solution of lactone **23** (380 mg, 1.77 mmol, 1.0 equiv) in CH_2Cl_2 (6 mL) was cooled to −78 °C, and a solution of diisobutylaluminum hydride in CH_2Cl_2 (1.0 M, 1.95 mL, 1.95 mmol, 1.1 equiv) was added dropwise. After the mixture was stirred at −78 °C for 20 min, the reaction was quenched at −78 °C by addition of aq. Rochelle salt (1.5 mL of a saturated solution) and water (1 mL). The mixture was allowed to warm to room temperature, stirred at this temperature for an additional 3 h, and then extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were dried ($MgSO_4$) and concentrated in vacuo to afford lactol **39** (374 mg, 1.73 mmol, 98%) as a white solid consisting of two diastereomers (d.r. 1.9:1 as determined by ^{1}H NMR spectroscopy) as an inseparable mixture: R_f 0.41 [PE:EtOAc 1:1]; ^{1}H NMR (600 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 5.90 (d, *J* = 3.8 Hz, 1H), 5.23−5.21 (m, 1H), 4.47 (d, *J* = 3.8 Hz, 1H), 4.23 (br s, 2H), 2.88 (br s, 1H), 2.17−2.09 (m, 1H), 1.93−1.86 (m, 2H), 1.55−1.50 (m, 1H), 1.49 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 111.5, 105.3, 91.3, 84.9, 73.4, 72.6, 26.8, 26.3, 23.7, 18.0; IR (ATR) $\tilde{\nu}$ 3429, 2931, 1374, 1208, 1079, 820 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{15}O_5^-$ 215.0925, found 215.0931 $[M - H]^-$.

(1*S*,2*R*,6*R*,8*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodec-10-ene (40). A solution of lactol **39** (79.5 mg, 0.368 mmol, 1.0 equiv) and triethylamine (816 μL, 5.89 mmol, 16 equiv) in CH_2Cl_2 (15 mL) was cooled to 0 °C, and methanesulfonyl chloride (37.1 μL, 0.478 mmol, 1.3 equiv) was added dropwise. The mixture was heated to 50 °C, stirred at this temperature for 2.5 h, and then cooled to room temperature. The volatile material was removed in vacuo, and the residue was subjected to gravity column chromatography [CH_2Cl_2] to afford dihydropyran **40** (42.2 mg, 0.213 mmol, 58%) as a white solid: R_f 0.79 [PE:EtOAc 2:1]; $[\alpha]_D^{21}$ +98.7 (*c* = 0.79, MeOH); mp 39−40 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.31−6.28 (m, 1H), 5.94 (d, *J* = 3.8 Hz, 1H), 4.69−4.65 (m, 1H), 4.60 (d, *J* = 3.8 Hz, 1H), 4.52−4.48 (m, 1H), 4.13 (br s, 1H), 2.40−2.33 (m, 1H), 4.60 (dd, *J* = 18.7, 4.4 Hz, 1H), 1.52 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 111.9, 105.0, 97.2, 84.3, 75.9, 72.5, 26.7, 26.3, 20.7; IR (ATR) $\tilde{\nu}$ 2936, 1662, 1376, 1208, 1076, 829 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{14}O_4^+$ 198.0887, found 198.0886 $[M]^+$.

(2*R*,6*R*)-11-{[(2*R*,6*R*,11*S*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo[6.4.0.0^{2,6}]dodecan-11-yl]oxy}-4,4-dimethyl-3,5,7,12-tetraoxatricyclo[6.4.0.0^{2,6}]dodecane (41) and (2*R*,6*R*)-11-{[(2*R*,6*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo[6.4.0.0^{2,6}]-dodecan-11-yl]oxy}-4,4-dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodecane (42). A solution of lactol **39** (333 mg, 1.54 mmol, 1.0 equiv) and triethylamine (500 μL, 3.61 mmol, 2.3 equiv) in CH_2Cl_2 (4 mL) was cooled to 0 °C, and methanesulfonyl chloride (164 μL, 2.00 mmol, 1.3 equiv) was added dropwise. The mixture was heated to 50 °C, stirred at this temperature for 20 h, and cooled to room temperature. The volatile material was removed in vacuo, and the residue was subjected to gravity column chromatography [CH_2Cl_2] to afford dimer **41** (68.5 mg, 0.165 mmol, 21%) as a colorless oil and C_2-symmetric dimer **42** (91.9 mg, 0.222 mmol, 29%) as a white solid. Dimer **41**: R_f 0.40 [PE:EtOAc 2:1]; $[\alpha]_D^{21}$ +15.4 (*c* = 0.36, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.95 (d, *J* = 3.8 Hz, 1H), 5.89 (d, *J* = 3.8 Hz, 1H), 4.99 (br s, 1H), 4.59−4.56 (m, 1H), 4.55 (d, *J* = 3.8 Hz, 1H), 4.47 (d, *J* = 3.7 Hz, 1H), 4.33 (d, *J* = 2.1 Hz, 1H), 4.24−4.42 (m, 1H), 4.12−4.09 (m, 1H), 4.06 (d, *J* = 1.9 Hz, 1H), 2.23−2.19 (m, 1H), 2.14−2.06 (m, 1H), 1.93−1.85 (m, 2H), 1.83−1.73 (m, 2H), 1.62−1.55 (m, 1H), 1.55−1.48 (m, 1H), 1.50 (s, 3H), 1.49 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 111.5, 111.5, 105.5, 105.3, 100.5, 96.7, 84.9, 84.6, 79.7, 73.4, 73.3, 72.3, 26.9, 26.8, 26.4, 26.3, 25.6, 24.1, 23.7, 18.6; IR (ATR) $\tilde{\nu}$ 2934, 1445, 1372, 1213, 1164, 1068, 1010, 947, 902, 825, 756 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{34}NO_9^+$ 432.2228, found 432.2227 $[M + NH_4]^+$. C_2-symmetric dimer **42**: R_f 0.34 [PE:EtOAc 4:1]; $[\alpha]_D^{20}$ +208.2 (c = 1.0, MeOH); mp 149−153 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.91 (d, J = 3.8 Hz, 2H), 5.10 (br s, 2H), 4.48 (d, J = 3.8 Hz, 2H), 4.23−4.21 (m, 2H), 3.97 (d, J = 2.1 Hz, 2H), 2.10−2.04 (m, 2H), 1.99−1.89 (m, 4H), 1.49 (s, 6H), 1.52−1.44 (m, 2H), 1.31 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 111.5 (2C), 105.3 (2C), 91.8 (2C), 84.7 (2C), 73.3 (2C), 73.0 (2C), 26.8 (2C), 26.3 (2C), 23.3 (2C), 18.5 (2C); IR (ATR) $\tilde{\nu}$ 2936, 1443, 1376, 1214, 1134, 1077, 1016, 982, 902, 827, 745 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{34}NO_9^+$ 432.2228, found 432.2228 $[M + NH_4]^+$.

[(2*R*,6*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo[6.4.0.0^{2,6}]-dodec-10-en-11-yl]trimethylstannane (44). A solution of lactone **23** (50.0 mg, 1.77 mmol, 1.0 equiv) and *N*-phenylbis-(trifluoromethanesulfonimide) (91.6 mg, 0.256 mmol, 1.1 equiv) in THF (3 mL) was added slowly (over 45 min) with the aid of a syringe pump to a cold (−78 °C) solution of potassium hexamethyldisilazide (0.5 M in toluene, 606 μL, 0.303 mmol, 1.3 equiv) in THF (1 mL). After complete addition, the reaction mixture was stirred for an additional 10 min at −78 °C and then allowed to warm to room temperature. Volatile material was removed in vacuo, and the residue was subjected to flash column chromatography [PE:Et_2O 4:1 (+0.5% NEt_3)] to afford the respective enol triflate. This sensitive compound was immediately dissolved in THF (6 mL), and hexamethyldistannane (72.5 μL, 0.350 mmol, 1.5 equiv) and lithium chloride (98.8 mg, 2.33 mmol, 10 equiv) followed by tetrakis(triphenylphosphine)-palladium(0) (13.5 mg, 11.7 μmol, 5 mol %) were added. The mixture was stirred at room temperature for 24 h, and then the volatile material was removed in vacuo. The residue was subjected to column chromatography [PE:Et_2O 9:1] to afford stannane **44** (52.4 mg, 0.145 mmol, 62% over two steps) as a colorless oil: R_f 0.22 [PE:Et_2O 9:1]; $[\alpha]_D^{19}$ +41.4 (c = 0.24, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.92 (d, J = 3.8, 1H), 4.79−4.71 (m, 1H), 4.58 (d, J = 3.8 Hz, 1H), 4.52−4.49 (m, 1H), 4.05 (br s, 1H), 2.40−2.32 (m, 1H), 2.28−2.21 (m, 1H), 1.52 (s, 3H), 1.33 (s, 3H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 111.8, 107.8, 105.1, 84.6, 75.6, 72.8, 26.7, 26.3, 21.5, −9.7; IR (ATR) $\tilde{\nu}$ 2924, 1623, 1373, 1077, 1016, 767 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{22}O_4Sn^+$ 362.0535, found 362.0541 $[M]^+$.

Ethyl (2*E*)-4-[(2*R*,6*R*)-4,4-Dimethyl-3,5,7,12-tetraoxatricyclo-[6.4.0.0^{2,6}]dodec-10-en-11-yl]-4-hydroxybut-2-enoate (46). A solution of stannane **44** (46.5 mg, 0.129 mmol, 1.0 equiv) in THF (5 mL) was cooled to −78 °C, and a solution of *n*-butyllithium in hexanes (2.4 M, 64.6 μL, 0.155 mmol, 1.2 equiv) was added dropwise. After the mixture was stirred at −78 °C for 15 min, aldehyde **45** (18.7 μL, 0.155 mmol, 1.2 equiv) was added, and the resulting solution was stirred at −78 °C for an additional 15 min. The reaction was quenched with aq. NH_4Cl (4 mL of a saturated solution), and the mixture was extracted with Et_2O (3 × 25 mL). The combined organic fractions were washed with brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 4:1 → 3:1] afforded alcohol **46** (23.1 mg, 70.8 μmol, 55%) as a colorless oil consisting of two diastereomers in a ratio of 1.2:1 (as determined by ^{1}H NMR spectroscopy) as an inseparable mixture along with protodemetalated product **40** (7.40 mg, 37.3 μmol, 29%) as a white solid. Alcohol **46**: R_f 0.52 [PE:EtOAc 1:1]; ^{1}H NMR (600 MHz, $CDCl_3$) (mixture of isomers, both isomers quoted) δ 6.96−6.89 (m, 2H), 6.14−6.06 (m, 2H), 5.92−5.88 (m, 2H), 4.86−4.83 (m, 1H), 4.81−4.78 (m, 1H), 4.67−4.60 (m, 4H), 4.50−4.47 (m, 2H), 4.23−4.17 (m, 6H), 2.43−2.33 (m, 4H), 1.52 (br s, 6H), 1.33 (br s, 6H), 1.30−1.27 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) (mixture of isomers, both isomers quoted) δ 166.6, 166.5, 150.6, 150.5, 146.2, 145.7, 122.0, 121.6, 112.1, 112.1, 104.9, 104.9, 95.3, 94.7, 84.1, 84.0, 77.4, 77.4, 72.1, 72.0, 71.4, 71.3, 60.7, 60.7, 26.6 (2C), 26.2, 26.2, 21.5, 21.5, 14.3 (2C); IR (ATR) $\tilde{\nu}$ 3420, 2962, 1703, 1374, 1081, 1016, 865 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{26}NO_7^+$ 344.1704, found 344.1704 $[M + NH_4]^+$. Protodemetalated product **40**: the analytical data were identical to those of the material obtained earlier.

1,6-Anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose (24)..[12,37,38] A stirred solution of D-(+)-glucose monohydrate **50** (100 g, 505 mmol, 1.0 equiv) in pyridine (1 L, dried over KOH pellets) was cooled to 16 °C (internal temperature), and a solution of *p*-toluenesulfonyl chloride (144 g, 757 mmol, 1.5 equiv) in pyridine (300 mL, dried over KOH pellets) was added dropwise, keeping the internal temperature of the reaction mixture between 15 and 20 °C with the aid of a water−ice bath. After complete addition, stirring was continued for an additional 90 min at 20 °C. The mixture was brought to pH 9 by addition of aq. NaOH (10 wt %, ca. 600 mL) and then stirred for 60 min at room temperature. The pH was lowered to 7 by careful addition of conc. aq. HCl (ca. 20 mL), and the solvents were evaporated in vacuo. Azeotropic removal of pyridine and water residues with toluene (3 × 500 mL) gave a solid that was suspended in EtOH (500 mL) and filtered through a pad of florisil (14 cm × 5 cm, 100−200 mesh). Washing with ethanol (3.5 L) was continued until the filtrate was free of sugar derivatives (as indicated by TLC), and subsequent removal of the solvent in vacuo (15 h in a rotary evaporator at 10 mbar followed by 3 days under high vacuum at 10^{-2} mbar) provided a brown oil. The crude 1,6-anhydro glucose **51** was dissolved in DMF (500 mL), and the solution was carefully added to a stirred, cooled suspension (water−ice bath) of sodium hydride (60 wt % in mineral oil, 202 g, 5.05 mol, 10 equiv) in DMF (500 mL). After 25 min, benzyl bromide (360 mL, 3.03 mol, 6.0 equiv) was added dropwise with the aid of a dropping funnel (*Caution*: exothermic reaction!), and the reaction mixture was allowed to warm slowly to room temperature over 15 h. The reaction was then quenched carefully by dropwise addition of MeOH (300 mL) over a period of 3 h (dropping funnel) followed by the addition of water (500 mL). The mixture was divided into four aliquots, and each aliquot was diluted with EtOAc (1 L) and water (500 mL), which was followed by separation of the phases. Each aqueous phase was extracted with EtOAc (2 × 500 mL), and all of the organic extracts were combined. The resulting organic fraction (ca. 8 L) was again divided into eight parts, and every part (ca. 1 L) was washed successively with water (2 × 500 mL), aq. $NaHCO_3$ (2 × 500 mL of a saturated solution), aq. $KHSO_4$ (500 mL of a saturated solution), and brine (500 mL) and then dried ($MgSO_4$). Removal of the solvent in vacuo gave a brown oil that was purified by flash column chromatography [PE:EtOAc 9:1 → 4:1] to provide the crude tribenzylated anhydro sugar **24**, which was crystallized from EtOH (150 mL) to afford pure product **24** (56.3 g, 130 mmol, 26%) as white needles. Concentration of the mother liquors and flash column chromatography [PE:EtOAc 9:1 → 4:1] followed by recrystallization afforded additional material of **24** (7.15 g, 16.5 mmol), raising the total yield to 29%. Anhydro sugar **24**: R_f 0.46 [PE:EtOAc 3:1]; $[\alpha]_D^{21}$ −30.4 (c = 1.0, $CHCl_3$); mp 89 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.27 (m, 13H), 7.26−7.24 (m, 2H), 5.48 (s, 1H), 4.64−4.54 (m, 5H), 4.47 (d, J = 12.1 Hz, 1H), 4.42 (d, J = 12.1 Hz, 1H), 3.92 (dd, J = 7.2, 1.0 Hz, 1H), 3.69 (dd, J = 7.1, 5.9 Hz, 1H), 3.62−3.60 (m, 1H), 3.38−3.35 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.1, 138.0, 138.0, 128.6 (2C), 128.6 (2C), 128.6 (2C), 128.1 (2C), 128.0, 128.0 (2C), 128.0, 128.0, 127.9 (2C), 100.8, 77.0, 76.3, 76.2, 74.5, 72.2, 71.9, 71.3, 65.6; IR (ATR) $\tilde{\nu}$ 2961, 2902, 1454, 1090, 1022, 748 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{28}NaO_5^+$ 455.1829, found 455.1825 $[M + Na]^+$.

[(2*R*,3*R*,4*R*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-6-(prop-2-en-1-yl)-oxan-2-yl]methanol (52)..[12,38,40] A solution of tribenzylated anhydro glucose **24** (50.1 g, 116 mmol, 1.0 equiv) and allyltrimethylsilane (55.2 mL, 348 mmol, 3.0 equiv) in MeCN (500 mL) was cooled to 0 °C, and trimethylsilyl trifluoromethanesulfonate (21.0 mL, 116 mmol, 1.0 equiv) was added dropwise. After the reaction mixture was stirred at room temperature for 22 h, the reaction was quenched with aq. $NaHCO_3$ (550 mL of a saturated solution). The mixture was diluted with water (300 mL) and extracted with CH_2Cl_2 (3 × 400 mL), and the combined organic fractions were washed with brine (1 L), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 6:1 → 5:1 → 4:1 → 3:1 → 1:1 → 1:2] afforded alkene **52** (36.4 g, 76.7 mmol, 66%) as a white solid: R_f 0.21 [PE:EtOAc 3:1]; $[\alpha]_D^{21}$ +44.4 (c = 0.69, CH_2Cl_2); mp 78−79 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36−7.27 (m, 15H),

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5.77 (dddd, J = 17.3, 10.2, 6.9, 6.9 Hz, 1H), 5.14−5.07 (m, 2H), 4.94 (d, J = 10.9 Hz, 1H), 4.87 (d, J = 10.9 Hz, 1H), 4.83 (d, J = 10.9 Hz, 1H), 4.71 (d, J = 11.6 Hz, 1H), 4.63 (d, J = 11.6 Hz, 2H), 4.04−4.07 (m, 1H), 3.82 (dd, J = 9.1, 8.7 Hz, 1H), 3.78−3.75 (m, 1H), 3.71 (dd, J = 9.4, 5.8 Hz, 1H), 3.66−3.63 (m, 1H), 3.56−3.53 (m, 1H), 3.50 (dd, J = 9.8, 8.4 Hz, 1H), 2.55−2.46 (m, 2H), 1.79 (dd, J = 6.4, 6.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 138.3, 138.2, 134.6, 128.7 (2C), 128.6 (2C), 128.6 (2C), 128.2 (2C), 128.1, 128.0 (2C), 128.0, 128.0 (2C), 127.8, 117.4, 82.4, 80.3, 78.2, 75.6, 75.3, 73.8, 73.3, 71.7, 62.5, 30.1; IR (ATR) $\tilde{\nu}$ 3344, 3032, 2900, 2336, 1453, 1094, 1026, 693 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{38}NO_5^+$ 492.2744, found 492.2742 $[M + NH_4]^+$.

[(3a*R*,5*R*,6*R*,7*S*,7a*S*)-6,7-Bis(benzyloxy)-2-(iodomethyl)-hexahydro-2*H*-furo[3,2-*b*]pyran-5-yl]methanol (53).[12] A solution of **52** (23.7 g, 49.9 mmol, 1.0 equiv) in CH_2Cl_2 (170 mL) was cooled to 0 °C, and iodine (13.9 g, 54.9 mmol, 1.1 equiv) was added in one portion. The mixture was stirred at 0 °C for 55 min until complete consumption of the starting material (as indicated by TLC analysis). The reaction was quenched with aq. $Na_2S_2O_3$ (150 mL of a saturated solution), and the biphasic system was stirred vigorously at room temperature for 30 min. The organic phase was separated, and the aqueous layer was extracted further with CH_2Cl_2 (2 × 200 mL). The combined organic fractions were washed with water (200 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 4:1 → 2:1] afforded iodides **53** (20.6 g, 40.4 mmol, 81%) as a colorless oil consisting of two diastereomers in a ratio of 2.7:1 (as determined by ^{1}H NMR spectroscopy) as an inseparable mixture: R_f 0.46 [PE:EtOAc 1:1]; ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 7.44−7.27 (m, 10H), 4.91 (d, J = 11.7 Hz, 1H), 4.88 (d, J = 11.3 Hz, 1H), 4.75 (d, J = 11.8 Hz, 1H), 4.60 (d, J = 11.1 Hz, 1H), 4.16−4.08 (m, 1H), 4.06 (dd, J = 5.6, 5.6 Hz, 1H), 3.88 (dd, J = 8.7, 5.5 Hz, 1H), 3.75−3.65 (m, 3H), 3.51−5.45 (m, 1H), 3.35 (dd, J = 9.9, 5.4 Hz, 1H), 3.31−3.26 (m, 1H), 2.31−2.23 (m, 1H), 2.01−1.93 (m, 1H), 1.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 138.4, 138.1, 128.6 (2C), 128.5 (2C), 128.2 (2C), 128.0 (2C), 128.0, 127.8, 83.1, 82.6, 78.3, 75.2, 75.1, 74.6, 74.4, 73.0, 62.2, 36.9, 9.8; IR (ATR) $\tilde{\nu}$ 3448, 2874, 1453, 1363, 1026, 1094, 695 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{27}INaO_5^+$ 533.0795, found 533.0794 $[M + Na]^+$.

(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-(hydroxymethyl)-2-(prop-2-en-1-yl)oxan-3-ol (54).[12] A suspension of zinc dust (26.4 g, 404 mmol, 10 equiv) in THF (100 mL) containing 1,2-dibromoethane (348 μL, 4.04 mmol, 0.1 equiv) was heated to 70 °C for 1 min. After the mixture was cooled to room temperature, chlorotrimethylsilane (516 μL, 4.04 mmol, 0.1 equiv) was added, and the suspension was stirred for 15 min until gas evolution had ceased.[51] A solution of the diastereomeric mixture of iodides **53** (20.6 g, 40.4 mmol, 1.0 equiv) in THF (150 mL) was added, followed by water (50 mL), and the reaction mixture was stirred for 1 h at room temperature. The solid was removed by filtering the suspension through a pad of Celite, and the residue was washed with Et_2O (300 mL). The filtrate was washed with aq. HCl (1 N, 200 mL), and the phases were separated. The aqueous layer was extracted further with Et_2O (2 × 300 mL). The combined organic fractions were washed with aq. $NaHCO_3$ (500 mL of a saturated solution) and brine (500 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 4:1 → 3:1 → 2:1 → 1:1] afforded diol **54** (14.0 g, 36.4 mmol, 90%) as a white solid: R_f 0.52 [PE:EtOAc 1:1]; $[\alpha]_D^{20}$ +32.8 (c = 0.63, $CHCl_3$); mp 89−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.28 (m, 10H), 5.82 (dddd, J = 17.1, 10.2, 7.0, 7.0 Hz, 1H), 5.17−5.12 (m, 1H), 5.12−5.07 (m, 1H), 4.74 (d, J = 11.6 Hz, 1H), 4.69 (d, J = 11.4 Hz, 1H), 4.65 (d, J = 11.6 Hz, 1H), 4.63 (d, J = 11.4 Hz, 1H), 4.00 (ddd, J = 9.0, 5.0, 3.7 Hz, 1H), 3.93 (dd, J = 11.4, 7.0 Hz, 1H), 3.89−3.84 (m, 1H), 3.75 (dd, J = 6.1, 6.1 Hz, 1H), 3.69 (dd, J = 6.3, 3.6 Hz, 1H), 3.63 (dd, J = 11.4, 3.3 Hz, 1H), 3.48 (dd, J = 5.6, 5.6 Hz, 1H), 2.50−2.34 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.0, 137.5, 134.6, 128.8 (2C), 128.7 (2C), 128.2, 128.2, 128.1 (2C), 127.8 (2C), 117.5, 78.6, 76.0, 74.4, 74.0, 73.5, 71.7, 69.9, 61.1, 32.5; IR (ATR) $\tilde{\nu}$ 3375, 2915, 2362, 1453, 1088, 990, 694 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{28}NaO_5^+$ 407.1829, found 407.1832 $[M + Na]^+$.

{[(2*R*,3*R*,4*S*,5*S*,6*R*)-3,4-Bis(benzyloxy)-5-[(*tert*-butyldimethylsilyl)oxy]-6-(prop-2-en-1-yl)oxan-2-yl]methoxy}-*tert*-butyldimethylsilane (55).[12] To a solution of diol **54** (14.0 g, 36.4 mmol, 1.0 equiv) and imidazole (12.4 g, 182 mmol, 5.0 equiv) in DMF (30 mL) was added *tert*-butyldimethylsilyl chloride (16.5 g, 109 mmol, 3.0 equiv), and the resulting mixture was stirred at room temperature for 42 h. Upon completion of the reaction as monitored by TLC, the mixture was diluted with water (200 mL) and extracted with EtOAc (3 × 300 mL). The combined organic fractions were washed with aq. LiCl (10 wt %, 3 × 300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 99:1 → 49:1 → 24:1] afforded bis-silyl ether **55** (20.0 g, 32.6 mmol, 90%) as a white solid: R_f 0.62 [PE:EtOAc 9:1]; $[\alpha]_D^{18}$ +31.3 (c = 1.3, $CHCl_3$); mp 55−57 °C; ^{1} H NMR (400 MHz, $CDCl_3$) δ 7.39−7.21 (m, 10H), 5.84 (dddd, J = 17.1, 10.2, 6.9, 6.9 Hz, 1H), 5.15−5.02 (m, 2H), 4.91 (d, J = 11.3 Hz, 1H), 4.82 (d, J = 10.8 Hz, 1H), 4.81 (d, J = 11.3 Hz, 1H), 4.63 (d, J = 10.8 Hz, 1H), 3.96−3.89 (m, 1H), 3.84 (dd, J = 9.1, 5.9 Hz, 1H), 3.81−3.74 (m, 2H), 3.69−3.63 (m, 1H), 3.54−3.46 (m, 2H), 2.55−2.40 (m, 2H), 0.92 (s, 9H), 0.90 (s, 9H), 0.09 (s, 6H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.6, 135.3, 128.5 (2C), 128.4 (2C), 128.1 (2C), 127.8, 127.7 (2C), 127.5, 116.7, 83.4, 78.6, 76.3, 75.6, 75.2, 73.6, 72.7, 63.0, 29.3, 26.1 (3C), 26.1 (3C), 18.5, 18.1, −4.4, −4.5, −4.9, −5.2; IR (ATR) $\tilde{\nu}$ 2928, 1462, 1252, 1088, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{60}NO_5Si_2^+$ 630.4005, found 630.4010 $[M + NH_4]^+$.

***tert*-Butyldimethyl{[(2*R*,3*R*,4*R*,5*S*,6*R*)-3,4,5-tris(benzyloxy)-6-(prop-2-en-1-yl)oxan-2-yl]methoxy}silane (56).** To a solution of alcohol **52** (388 mg, 0.818 mmol, 1.0 equiv) and imidazole (140 mg, 2.05 mmol, 2.5 equiv) in DMF (1.5 mL) was added *tert*-butyldimethylsilyl chloride (148 mg, 0.982 mmol, 1.2 equiv), and the resulting mixture was stirred at room temperature for 72 h. The mixture was diluted with water (10 mL) and extracted with EtOAc (3 × 25 mL). The combined organic fractions were washed with aq. LiCl (10 wt %, 3 × 25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 99:1 → 49:1 → 19:1] afforded silyl ether **56** (360 mg, 0.611 mmol, 75%) as a colorless oil: R_f 0.52 [PE:EtOAc 9:1]; $[\alpha]_D^{20}$ +33.9 (c = 1.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.28 (m, 15H), 5.84 (dddd, J = 17.1, 10.2, 6.8, 6.8 Hz, 1H), 5.14−5.09 (m, 1H), 5.09−5.05 (m, 1H), 4.93 (d, J = 10.9 Hz, 1H), 4.88 (d, J = 10.9 Hz, 1H), 4.82 (d, J = 10.9 Hz, 1H), 4.71 (d, J = 11.6 Hz, 1H), 4.68 (d, J = 10.9 Hz, 1H), 4.65 (d, J = 11.6 Hz, 1H), 4.13−4.07 (m, 1H), 3.82 (dd, J = 8.9, 8.9 Hz, 1H), 3.82−3.78 (m, 2H), 3.71 (dd, J = 9.2, 5.7 Hz, 1H), 3.58 (dd, J = 9.6, 8.8 Hz, 1H), 3.53−3.50 (m, 1H), 2.56−2.48 (m, 1H), 2.48−2.42 (m, 1H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.6, 138.5, 135.0, 128.6 (2C), 128.6 (2C), 128.5 (2C), 128.1 (2C), 128.1 (2C), 127.9 (2C), 127.9, 127.8, 116.8, 82.6, 80.5, 78.2, 75.6, 75.1, 73.5, 73.2, 72.7, 62.9, 30.1, 26.1 (3C), 18.5, −4.9, −5.2; IR (ATR) $\tilde{\nu}$ 3066, 3031, 2927, 2856, 1454, 1360, 1252, 1090, 1028, 912, 836, 697 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{52}NO_5Si^+$ 606.3609, found 606.3614 $[M + NH_4]^+$.

{[(3a*R*,5*R*,6*R*,7*S*,7a*S*)-6,7-Bis(benzyloxy)-2-(iodomethyl)-hexahydro-2*H*-furo[3,2-*b*]pyran-5-yl]methoxy}-*tert*-butyldimethylsilane (57). A solution of alkene **56** (188 mg, 0.319 mmol, 1.0 equiv) in THF (1 mL) was cooled to 0 °C, and iodine (502 mg, 1.98 mmol, 6.2 equiv) was added in one portion. The mixture was stirred at 0 °C for 60 min until complete consumption of the starting material (as indicated by TLC analysis). The reaction was quenched with aq. $Na_2S_2O_3$ (2 mL of a saturated solution), and the biphasic system was stirred vigorously at room temperature for 30 min. The mixture was diluted with water (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with water (20 mL) and brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 19:1 → 9:1] afforded iodides **57** (149 mg, 0.238 mmol, 75%) as a colorless oil consisting of two diastereomers (d.r. 4:1 as determined by ^{1}H NMR spectroscopy) as an inseparable mixture: R_f 0.34 [PE:EtOAc 9:1]; ^{1}H NMR (400 MHz,

$CDCl_3$) (mixture of isomers, major isomer quoted) δ 7.43−7.28 (m, 10H), 4.96−4.87 (m, 2H), 4.78−4.74 (m, 1H), 4.71−4.66 (m, 1H), 4.60 (d, J = 11.2 Hz, 1H), 4.24−4.12 (m, 1H), 4.02 (dd, J = 5.1, 5.1 Hz, 1H), 3.86 (dd, J = 9.7, 5.3 Hz, 1H), 3.84−3.74 (m, 3H), 3.68−3.62 (m, 1H), 3.36 (dd, J = 9.7, 5.7 Hz, 1H), 3.32−3.26 (m, 1H), 2.31−2.22 (m, 1H), 1.95 (ddd, J = 13.7, 5.7, 3.7 Hz, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 138.7, 138.7, 128.5 (2C), 128.5 (2C), 128.1 (2C), 128.0 (2C), 127.8, 127.7, 85.5, 83.7, 79.0, 77.0, 75.5, 74.7, 74.4, 73.0, 63.6, 37.6, 26.1 (3C), 18.4, 10.0, −5.2, −5.7; IR (ATR) $\tilde{\nu}$ 2928, 2856, 1454, 1361, 1252, 1086, 905, 834, 776, 696 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{45}INO_5Si^+$ 642.2106, found 642.2111 $[M + NH_4]^+$.

(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}-2-(prop-2-en-1-yl)oxan-3-ol (58). A suspension of zinc dust (137 mg, 2.10 mmol, 10 equiv) in THF (1 mL) containing 1,2-dibromoethane (9.05 μL, 0.105 mmol, 0.5 equiv) was heated to 70 °C for 1 min. After the mixture was cooled to room temperature, chlorotrimethylsilane (13.4 μL, 0.105 mmol, 0.5 equiv) was added, and the suspension was stirred for 15 min until gas evolution had ceased. A solution of the diastereomeric mixture of iodides **57** (131 mg, 0.210 mmol, 1.0 equiv) in THF (4 mL) was added, followed by water (1 mL), and the reaction mixture was stirred for 1 h at room temperature. The solid was removed by filtering the suspension through a pad of Celite, and the residue was washed with Et_2O (50 mL). The filtrate was diluted with water (10 mL), and the phases were separated. The aqueous layer was extracted further with Et_2O (2 × 20 mL). The combined organic fractions were washed with aq. $NaHCO_3$ (30 mL of a saturated solution) and brine (30 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 19:1 → 9:1] afforded alcohol **58** (74.0 mg, 0.148 mmol, 71%) as a colorless oil: R_f 0.15 [PE:EtOAc 9:1]; $[\alpha]_D^{20}$ +19.1 (c = 0.87, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.26 (m, 10H), 5.84 (dddd, J = 17.1, 10.2, 6.9, 6.9 Hz, 1H), 5.16−5.11 (m, 1H), 5.08−5.04 (m, 1H), 4.69−4.54 (m, 4H), 3.95−3.83 (m, 4H), 3.79 (dd, J = 4.7, 4.7 Hz, 1H), 3.71−3.68 (m, 1H), 3.62 (br s, 1H), 3.02 (br s, 1H), 2.47−2.33 (m, 2H), 0.88 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.1, 137.7, 135.0, 128.7 (2C), 128.1, 128.0, 128.0 (2C), 127.8 (2C), 117.0, 77.0, 75.6, 73.8, 73.1, 72.6, 70.8, 69.0, 61.4, 34.0, 26.0 (3C), 18.4, −5.2, −5.2; IR (ATR) $\tilde{\nu}$ 3490, 2928, 2857, 1455, 1253, 1081, 834, 778, 698 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{42}NaO_5Si^+$ 521.2694, found 521.2696 $[M + Na]^+$.

Methyl (2*E*)-4-[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}oxan-2-yl]but-2-enoate (49).[12] Second-generation Grubbs' catalyst (172 mg, 0.203 mmol, 7 mol %) was added in one portion to a solution of alkene **55** (1.78 g, 2.90 mmol, 1.0 equiv) and methyl acrylate (1.31 mL, 14.5 mmol, 5.0 equiv) in toluene (15 mL), and the reaction mixture was stirred for 22 h at 60 °C and then cooled to room temperature. The volatile material was removed in vacuo, and the residue was subjected to flash column chromatography [PE:EtOAc 100:0 → 49:1 → 19:1] to afford *trans*-ester **49** (1.77 g, 2.64 mmol, 91%) as a colorless oil: R_f 0.32 [PE:EtOAc 9:1]; $[\alpha]_D^{18}$ +48.2 (c = 0.51, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37−7.20 (m, 10H), 6.98 (ddd, J = 15.6, 7.5, 7.4 Hz, 1H) 5.92 (dd, J = 15.7, 0.7 Hz, 1H), 4.88 (d, J = 11.3 Hz, 1H), 4.80 (d, J = 11.3 Hz, 1H), 4.80 (d, J = 10.8 Hz, 1H), 4.62 (d, J = 10.8 Hz, 1H), 3.99 (ddd, J = 10.2, 5.2, 5.2 Hz, 1H), 3.83 (dd, J = 9.1, 5.9 Hz, 1H), 3.79−3.74 (m, 2H), 3.73 (s, 3H), 3.62 (dd, J = 8.9, 8.9 Hz, 1H), 3.52−3.44 (m, 2H), 2.67−2.56 (m, 2H), 0.90 (s, 9H), 0.89 (s, 9H), 0.08 (s, 6H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9, 146.1, 138.9, 138.5, 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.6 (2C), 127.6, 123.0, 83.2, 78.3, 75.7, 75.6, 75.2, 73.2, 73.1, 62.9, 51.5, 27.9, 26.1 (3C), 26.0 (3C), 18.5, 18.1, −4.4, −4.5, −5.0, −5.2; IR (ATR) $\tilde{\nu}$ 2928, 1726, 1471, 1252, 1089, 835, 697 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{62}NO_7Si_2^+$ 688.4059, found 688.4065 $[M + NH_4]^+$.

Methyl (4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolane-4-carboxylate (59).[12] A solution of $K_3Fe(CN)_6$ (7.38 g, 22.4 mmol, 3.0 equiv), K_2CO_3 (3.10 g, 22.4 mmol, 3.0 equiv), $MeSO_2NH_2$ (709 mg, 7.45 mmol, 1.0 equiv), and $(DHQD)_2PHAL$ (2.32 g, 2.98 mmol, 0.4 equiv) in water (37 mL) was added to a solution of unsaturated ester **49** (5.00 g, 7.45 mmol, 1.0 equiv) in *t*-BuOH (37 mL). To the biphasic system was added a solution of OsO_4 in *t*-BuOH (2.5 wt %, 1.49 mL, 0.119 mmol, 1.6 mol %), and the mixture was stirred vigorously at room temperature for 19 h. An excess of solid Na_2SO_3 (23 g) was added in one portion, and the mixture was stirred for an additional 30 min. Water (100 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 150 mL). The combined organic fractions were washed successively with aq. HCl (1 N, 150 mL) and brine (150 mL), dried ($MgSO_4$), and concentrated in vacuo to afford crude diols as a mixture of two diastereomers (d.r. 14:1 as determined by ^{1}H NMR spectroscopy). The crude product was dissolved in CH_2Cl_2 (150 mL), and 2,2-dimethoxypropane (8.70 mL, 70.6 mmol, 10 equiv) and (1*R*)-(−)-10-camphorsulfonic acid (164 mg, 0.706 mmol, 10 mol %) were added in succession. The reaction mixture was stirred at room temperature for 60 min, and then the reaction was quenched with aq. $NaHCO_3$ (150 mL of a saturated solution). The biphasic system was extracted with EtOAc (250 mL, 2 × 150 mL), and the combined organic fractions were washed with brine (250 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 49:1 → 19:1 → 9:1 → 4:1] afforded acetonides **59** (4.56 g, 6.12 mmol, 82% over two steps) as a colorless oil consisting of two diastereomers (d.r. 14:1 as determined by ^{1}H NMR spectroscopy) as an inseparable mixture. An analytical sample of the mixture was purified by HPLC [Dynamax Microsorb 60-8 C18 (250 mm × 21.4 mm) with a water (A)/MeOH (B) gradient of 0 min 85% B, 50 min 85% B, 70 min 90% B, 85 min 90% B, 100 min 92% B, and 180 min 92% B at a flow rate of 21 mL/min with detection at 205 nm: t_R(major) = 137.1 min, t_R(minor) = 149.3 min] for full characterization of the major isomer of acetonide **59**: R_f 0.25 [PE:EtOAc 9:1]; $[\alpha]_D^{21}$ +36.9 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.21 (m, 10H), 4.90 (d, J = 11.2 Hz, 1H), 4.81 (d, J = 10.8 Hz, 1H), 4.79 (d, J = 11.3 Hz, 1H), 4.58 (d, J = 10.8 Hz, 1H), 4.27 (ddd, J = 10.3, 7.9, 2.5 Hz, 1H), 4.21−4.15 (m, 1H), 4.19 (d, J = 7.9 Hz, 1H), 3.84 (dd, J = 9.3, 6.1 Hz, 1H), 3.81−3.77 (m, 1H), 3.77 (s, 3H), 3.70 (dd, J = 11.1, 4.8 Hz, 1H), 3.60 (dd, J = 8.9, 8.9 Hz, 1H), 3.50−3.45 (m, 1H), 3.42 (dd, J = 9.8, 8.5 Hz, 1H), 2.20 (ddd, J = 14.6, 12.2, 2.4 Hz, 1H), 1.97 (ddd, J = 14.7, 10.2, 2.1 Hz, 1H), 1.43 (s, 6H), 0.91 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 139.0, 138.4, 128.6 (2C), 128.4 (2C), 128.1 (2C), 127.9, 127.6 (2C), 127.5, 111.1, 83.3, 79.3, 78.6, 75.6, 75.3, 75.2, 73.2, 73.2, 73.1, 63.2, 52.5, 28.7, 27.3, 26.1 (3C), 26.1 (3C), 25.9, 18.5, 18.2, −4.5, −4.5, −5.0, −5.2; IR (ATR) $\tilde{\nu}$ 2928, 1765, 1497, 1252, 1087, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{40}H_{68}NO_9Si_2^+$ 762.4427, found 762.4437 $[M + NH_4]^+$.

[(4*R*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]methanol (61) and [(4*S*,5*S*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-l]methanol (62). A suspension of lithium aluminum hydride (167 mg, 4.39 mmol, 1.0 equiv) in Et_2O (8 mL) was cooled to 0 °C, and a solution of the diastereomeric mixture of ester **59** (188 mg, 0.319 mmol, 1.0 equiv) in Et_2O (35 mL) was added via cannula. The resulting mixture was stirred at 0 °C for 10 min, and then the reaction was quenched carefully with aq. Rochelle salt (50 mL of a saturated solution). The mixture was allowed to warm to room temperature and stirred at this temperature for an additional 4 h. The resulting solution was then extracted with Et_2O (3 × 100 mL), and the combined organic fractions were washed with (brine), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 49:1 → 19:1 → 9:1 → 6:1 → 4:1 → 2:1] afforded major alcohol **61** (3.00 g, 4.18 mmol, 94%) and minor alcohol **62** (210 mg, 0.293 mmol, 6%), both as a colorless oils. Major alcohol **61**: R_f 0.47 [PE:EtOAc 3:1]; $[\alpha]_D^{19}$ +35.4 (c = 0.98, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37−7.34 (m, 2H), 7.33−7.25 (m, 6H), 7.23−7.20 (m, 2H), 4.89 (d, J = 11.3 Hz, 1H), 4.80 (d, J = 11.0 Hz, 1H), 4.78 (d, J = 11.5, 1H), 4.57

(d, J = 10.8 Hz, 1H), 4.15−4.09 (m, 1H), 4.01 (ddd, J = 8.5, 8.5, 4.3 Hz, 1H), 3.85−3.81 (m, 2H), 3.79 (dd, J = 11.1, 1.7 Hz, 1H), 3.75 (br dd, J = 11.7, 3.5 Hz, 1H), 3.72−3.66 (m, 2H), 3.57 (dd, J = 9.0, 9.0 Hz, 1H), 3.50−3.46 (m, 1H), 3.44−3.39 (m, 1H), 2.05−1.90 (m, 3H), 1.40 (s, 3H), 1.39 (s, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 138.4, 128.6 (2C), 128.4 (2C), 128.1 (2C), 127.9, 127.7 (2C), 127.6, 108.9, 83.2, 81.7, 78.5, 75.6, 75.2, 74.6, 73.5, 73.2, 73.1, 63.3, 62.7, 28.2, 27.4, 27.2, 26.1 (3C), 26.1 (3C), 18.6, 18.2, −4.4, −4.5, −5.0, −5.2; IR (ATR) $\tilde{\nu}$ 3476, 2929, 2857, 1462, 1379, 1252, 1081, 834, 776, 733, 696 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{68}NO_8Si_2^+$ 734.4478, found 734.4478 $[M + NH_4]^+$. Minor alcohol **62**: R_f 0.55 [PE:EtOAc 3:1]; $[\alpha]_D^{19}$ +20.6 (c = 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.24 (m, 8H), 7.23−7.18 (m, 2H), 4.89 (d, J = 11.3 Hz, 1H), 4.79 (d, J = 11.1 Hz, 1H), 4.78 (d, J = 11.4 Hz, 1H), 4.54 (d, J = 11.1 Hz, 1H), 4.11−4.02 (m, 2H), 3.98−3.92 (m, 1H), 3.85−3.54 (m, 7H), 3.30 (dd, J = 9.2, 9.2 Hz, 1H), 2.72−2.64 (m, 1H), 2.25 (ddd, J = 16.1, 11.9, 4.2 Hz, 1H), 1.99 (ddd, J = 15.0, 7.3, 2.9 Hz, 1H), 1.39 (s, 3H), 1.38 (s, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 138.3, 128.6 (2C), 128.4 (2C), 128.1 (2C), 127.9, 127.7 (2C), 127.6, 108.2, 83.2, 80.1, 78.6, 75.8, 75.6, 75.1, 73.2, 73.1, 72.9, 63.8, 63.2, 27.2, 27.2, 27.1, 26.2 (3C), 26.0 (3C), 18.7, 18.1, −4.4, −4.5, −5.1, −5.3; IR (ATR) $\tilde{\nu}$ 3479, 2929, 2857, 1462, 1379, 1252, 1089, 834, 776, 753, 696 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{68}NO_8Si_2^+$ 734.4478, found 734.4480 $[M + NH_4]^+$.

(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide (65). To a solution of alcohol **61** (2.06 g, 2.87 mmol, 1.0 equiv), tetra-*n*-propylammonium perruthenate (202 mg, 0.574 mmol, 20 mol %), and *N*-methylmorpholine-*N*-oxide (1.35 g, 11.5 mmol, 4.0 equiv) in MeCN (100 mL) was added water (1 mL), and the resulting solution was stirred at room temperature for 30 min. The solvent was evaporated in vacuo, and azeotropic removal of water residues with toluene (1 × 20 mL) provided the crude product, which was subjected to flash column chromatography [PE:EtOAc 9:1 → 3:1 → 3:1 + 1% AcOH]. The obtained carboxylic acid was subsequently dissolved in CH_2Cl_2 (300 mL), and 1,1′-carbonyldiimidazole (1.16 g, 7.18 mmol, 2.5 equiv) was added successively in 10 equal portions; the mixture was stirred at room temperature for 10 min after each addition. Complete consumption of the carboxylic acid was monitored by TLC analysis ("mini-workup" with MeOH). Thereafter, *N*,*O*-dimethylhydroxylamine hydrochloride (700 mg, 7.18 mmol, 2.5 equiv) was added in one portion, and the mixture was stirred for an additional 4 h. The reaction was quenched with water (100 mL), and the organic phase was separated. The aqueous layer was extracted further with EtOAc (3 × 250 mL). The combined organic fractions were washed with brine (250 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 4:1] afforded Weinreb amide **65** (1.61 g, 2.08 mmol, 72% over two steps) as a colorless oil: R_f 0.47 [PE:EtOAc 3:1]; $[\alpha]_D^{19}$ +27.2 (c = 0.92, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36−7.22 (m, 10H), 4.88 (d, J = 11.3 Hz, 1H), 4.80 (d, J = 10.8 Hz, 1H), 4.78 (d, J = 11.3 Hz, 1H), 4.63 (d, J = 10.8 Hz, 1H), 4.54−4.40 (m, 2H), 4.15 (ddd, J = 11.7, 6.0, 2.3 Hz, 1H), 3.85−3.78 (m, 3H), 3.74 (s, 3H), 3.59−3.53 (m, 2H), 3.49−3.42 (m, 1H), 3.22 (br s, 3H), 2.08−2.01 (m, 1H), 1.99−1.93 (m, 1H), 1.45 (s, 3H), 1.44 (s, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4, 139.0, 138.6, 128.5 (2C), 128.4 (2C), 128.1 (2C), 127.8, 127.7 (2C), 127.5, 110.6, 83.2, 78.2, 77.6, 75.5, 75.1, 75.1, 73.2, 73.1, 72.9, 62.7, 61.8, 32.5, 28.1, 27.6, 26.4, 26.1 (3C), 26.1 (3C), 18.5, 18.2, −4.5, −4.5, −4.9, −5.3; IR (ATR) $\tilde{\nu}$ 2930, 1669, 1252, 1086, 833, 697 cm^{-1}; HRMS (ESI) calcd for $C_{41}H_{71}N_2O_9Si_2^+$ 791.4693, found 791.4694 $[M + NH_4]^+$.

(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-*N*-methoxy-*N*,2,2-trimethyl-1,3-dioxolane-4-carboxamide (65).[12] To a solution of the diastereomeric mixture of ester **59** (13.1 g, 17.5 mmol, 1.0 equiv) in a mixture of THF and water (3:1, 300 mL) was added lithium hydroxide monohydrate (2.20 g, 52.5 mmol, 3.0 equiv), and the resulting solution was stirred at room temperature for 35 min. The mixture was diluted with water (100 mL) and extracted with EtOAc (3 × 300 mL). The combined organic fractions were washed with brine (300 mL), dried ($MgSO_4$), and concentrated in vacuo to provide the crude carboxylic acid. Further azeotropic removal of solvent residues (toluene, 2 × 150 mL) provided the dry acid, which was subsequently dissolved in CH_2Cl_2 (300 mL). 1,1′-Carbonyldiimidazole (8.52 g, 52.5 mmol, 3.0 equiv) was added in six equal portions, and the mixture was stirred at room temperature for 10 min after each addition. Complete consumption of carboxylic acid was monitored by TLC analysis ("mini-workup" with MeOH), after which *N*,*O*-dimethylhydroxylamine hydrochloride (5.12 g, 52.5 mmol, 3.0 equiv) was added in one portion and the mixture was stirred for an additional 4 h. The reaction was quenched with water (200 mL), and the organic phase was separated. The aqueous layer was extracted further with Et_2O (3 × 300 mL). The combined organic fractions were washed with brine (300 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 4:1 → 1:1] afforded Weinreb amide **65** (12.5 g, 16.1 mmol, 92% over two steps) as a colorless oil. The ^{1}H NMR spectrum indicated traces of the second diastereomer resulting from the Sharpless dihydroxylation.

1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-one (66)[12] and 1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-3-[methoxy(methyl)amino]propan-1-one (67). A solution of Weinreb amide **65** (6.70 g, 8.65 mmol, 1.0 equiv) in THF (300 mL) was cooled to −10 °C, and a solution of vinylmagnesium bromide in THF (1.0 M, 7.80 mL, 7.75 mmol, 1.2 equiv) was added dropwise. After stirring for 30 min at −10 °C, the mixture was allowed to warm to room temperature and stirred for an additional 10 min. The reaction was quenched with water (300 mL), and the aqueous layer was extracted with Et_2O (3 × 400 mL). The combined organic fractions were washed with brine (400 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 19:1 → 9:1 → 4:1] afforded vinyl ketone **66** (3.72 g, 5.02 mmol, 78%) and ketone **67** (1.14 g, 1.42 mmol, 22%), both as colorless oils. Vinyl ketone **66**: R_f 0.39 [PE:EtOAc 9:1]; $[\alpha]_D^{19}$ +26.9 (c = 1.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37−7.23 (m, 10H), 6.88 (dd, J = 17.4, 10.6 Hz, 1H), 6.45 (dd, J = 17.4, 1.7 Hz, 1H), 5.82 (dd, J = 10.6, 1.8 Hz, 1H), 4.90 (d, J = 11.2 Hz, 1H), 4.82 (d, J = 11.1 Hz, 1H), 4.79 (d, J = 11.3 Hz, 1H), 4.59 (d, J = 11.0 Hz, 1H), 4.22−4.17 (m, 3H), 3.84 (dd, J = 9.4, 6.1 Hz, 1H), 3.77 (dd, J = 11.2, 1.8 Hz, 1H), 3.70 (dd, J = 11.1, 5.0 Hz, 1H), 3.61 (dd, J = 9.1, 9.1 Hz, 1H), 3.48 (ddd, J = 9.8, 5.0, 1.8 Hz, 1H), 3.42 (dd, J = 9.8, 8.9 Hz, 1H), 2.18−2.12 (m, 1H), 2.02−1.95 (m, 1H), 1.45 (s, 3H), 1.42 (s, 3H), 0.93 (s, 9H), 0.87 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.1, 139.0, 138.5, 131.2, 130.6, 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.8, 127.7 (2C), 127.5, 110.6, 84.7, 83.3, 78.6, 75.6, 75.1, 74.5, 73.1, 73.1, 73.0, 63.2, 28.6, 27.3, 26.4, 26.1 (3C), 26.1 (3C), 18.5, 18.2, −4.5, −4.5, −5.0, −5.3; IR (ATR) $\tilde{\nu}$ 2929, 1698, 1252, 1086, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{41}H_{68}NO_8Si_2^+$ 758.4478, found 758.4480 $[M + NH_4]^+$. Ketone **67**: R_f 0.59 [PE:EtOAc 3:1]; $[\alpha]_D^{20}$ +23.9 (c = 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.22 (m, 10H), 4.88 (d, J = 11.2 Hz, 1H), 4.81 (d, J = 11.0 Hz, 1H), 4.78 (d, J = 11.2 Hz, 1H), 4.60 (d, J = 11.0 Hz, 1H), 4.17 (ddd, J = 12.2, 6.1, 2.0 Hz, 1H), 4.12 (ddd, J = 10.5, 8.2, 2.2 Hz, 1H), 4.04 (d, J = 8.2 Hz, 1H), 3.83 (dd, J = 9.4, 6.1 Hz, 1H), 3.76 (dd, J = 11.2, 1.7 Hz, 1H), 3.73 (dd, J = 11.2, 4.1 Hz, 1H), 3.59 (dd, J = 8.8, 8.8 Hz, 1H), 3.51 (br s, 3H), 3.50−3.42 (m, 2H), 3.03−2.84 (m, 4H), 2.60 (s, 3H), 2.16 (ddd, J = 14.5, 12.3, 2.2 Hz, 1H), 1.93 (ddd, J = 14.8, 10.5, 2.1 Hz, 1H), 1.42 (s, 3H), 1.42 (s, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.9, 139.0, 138.6, 128.5 (2C), 128.4 (2C), 127.9 (2C), 127.7, 127.7 (2C), 127.5, 110.4, 85.3, 83.3, 78.5, 75.6, 75.1, 74.2, 73.1, 73.1, 72.9,

63.1, 60.1, 54.5, 45.1, 36.8, 28.8, 27.3, 26.5, 26.1 (3C), 26.1 (3C), 18.5, 18.2, −4.5, −4.5, −4.9, −5.3; IR (ATR) $\tilde{\nu}$ 2930, 1715, 1252, 1086, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{43}H_{72}NO_9Si_2^+$ 802.4740, found 802.4743 $[M + H]^+$.

1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-one (66). To a solution of ketone **67** (200 mg, 0.249 mmol, 1.0 equiv) in THF (15 mL) was added *N*,*N*-diisopropylethylamine (84.7 μL, 0.498 mmol, 2.0 equiv) followed by methyl iodide (0.23 mL, 3.74 mmol, 15 equiv), and the resulting mixture was heated to 50 °C for 7 days. The reaction was quenched with aq. $NaHCO_3$ (20 mL of a saturated solution), and the mixture was extracted with Et_2O (3 × 25 mL). The combined organic fractions were washed with brine (40 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 19:1 → 9:1] afforded vinyl ketone **66** (103 mg, 0.139 mmol, 56%) and starting material **67** (48.1 mg, 60.0 μmol, 24%), both as colorless oils. The analytical data were identical to those of the material obtained earlier.

(1*R*)-1-[(4*R*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-ol (63) and (1*S*)-1-[(4*R*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-en-1-ol (64).[12] Toluene was removed from a solution of (*R*)-(−)-2-methyloxazaborolidine [(*R*)-**68**] in toluene (1.0 M, 4.24 mL, 4.24 mmol, 2.0 equiv), and the residue was dried in vacuo. The oxazaborolidine reagent was redissolved in THF (50 mL), and the resulting solution was added via cannula to a stirred solution of vinyl ketone **66** (1.57 g, 2.12 mmol, 1.0 equiv) in THF (110 mL) that had been precooled to −30 °C. A solution of borane dimethyl sulfide complex in THF (2.0 M, 1.17 mL, 2.33 mmol, 1.1 equiv) was then added dropwise, and the mixture was stirred at −30 °C for 1.5 h. The reaction was quenched at −30 °C with MeOH (10 mL), and the mixture was allowed to warm to room temperature. A mixture (2:1, 120 mL) of aq. NaOH (10 wt %) and aq. $NaHCO_3$ (saturated solution) was added, and the resulting solution was extracted with Et_2O (3 × 200 mL). The combined organic fractions were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo to afford crude alcohols **63** and **64** as a mixture of two diastereomers (d.r. 4.4:1 as determined by ^1H NMR spectroscopy). Flash column chromatography [PE:EtOAc 19:1 → 9:1 → 4:1] afforded allylic alcohol **63** (1.19 g, 1.60 mmol, 75%) and the minor diastereomer **64** (267 mg, 0.359 mmol, 17%), both as colorless oils. Allylic alcohol **63**: R_f 0.73 [PE:EtOAc 3:1]; $[\alpha]_D^{20}$ = +32.2 (*c* = 1.1, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.36−7.21 (m, 10H), 5.93 (ddd, *J* = 17.3, 10.6, 5.3 Hz, 1H), 5.39 (ddd, *J* = 17.3, 1.6, 1.6 Hz, 1H), 5.25 (ddd, *J* = 10.6, 1.5, 1.5 Hz, 1H), 4.89 (d, *J* = 11.3 Hz, 1H), 4.79 (d, *J* = 10.7 Hz, 1H), 4.78 (d, *J* = 11.0 Hz, 1H), 4.60 (d, *J* = 10.9 Hz, 1H), 4.28−4.25 (m, 1H), 4.18−4.13 (m, 2H), 3.83 (dd, *J* = 9.3, 6.1 Hz, 1H), 3.80−3.75 (m, 1H), 3.75−3.69 (m, 2H), 3.55 (dd, *J* = 8.9, 8.9 Hz, 1H), 3.47−3.41 (m, 2H), 2.33 (br s, 1H), 1.99 (ddd, *J* = 14.7, 12.1, 2.6 Hz, 1H), 1.89 (ddd, *J* = 14.8, 10.0, 2.2 Hz, 1H), 1.40 (s, 3H), 1.38 (s, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.0, 138.5, 136.6, 128.5 (2C), 128.4 (2C), 128.1 (2C), 127.8, 127.6 (2C), 127.5, 116.5, 109.1, 83.4, 83.2, 78.6, 75.6, 74.2, 74.1, 73.6, 73.2, 72.0, 72.6, 63.2, 29.3, 27.5, 27.2, 26.2 (3C), 26.1 (3C), 18.6, 18.2, −4.4, −4.5, −5.0, −5.2; IR (ATR) $\tilde{\nu}$ 3460, 2929, 1462, 1252, 1077, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{41}H_{70}NO_8Si_2^+$ 760.4634, found 760.4636 $[M + NH_4]^+$. Allylic alcohol **64**: R_f 0.67 [PE:EtOAc 3:1]; $[\alpha]_D^{20}$ +57.5 (*c* = 0.41, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.36−7.21 (m, 10H), 5.85 (ddd, *J* = 17.1, 10.5, 6.2 Hz, 1H), 5.40 (ddd, *J* = 17.2, 1.7, 1.7 Hz, 1H), 5.27 (ddd, *J* = 10.5, 1.3, 1.3 Hz, 1H), 4.89 (d, *J* = 11.3 Hz, 1H), 4.79 (d, *J* = 10.7 Hz, 1H), 4.78 (d, *J* = 11.1 Hz, 1H), 4.59 (d, *J* = 10.8 Hz, 1H), 4.17−4.13 (m, 1H), 4.13−4.09 (m, 1H), 4.09−4.04 (m, 1H), 3.82 (dd, *J* = 9.3, 6.1 Hz, 1H), 3.77 (dd, *J* = 11.1, 1.8 Hz, 1H), 3.73 (dd, *J* = 11.1, 4.6 Hz, 1H), 3.68 (dd, *J* = 7.8, 5.4 Hz, 1H), 3.54 (dd, *J* = 9.0, 9.0 Hz, 1H), 3.45 (dd, *J* = 9.3, 9.3 Hz, 1H), 3.39 (ddd, *J* = 9.8, 4.6, 1.8 Hz, 1H), 2.35 (br d, *J* = 4.8 Hz, 1H), 1.93−1.87 (m, 2H), 1.41 (s, 3H), 1.39 (s, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.0, 138.5, 136.8, 128.6 (2C), 128.4 (2C), 128.1 (2C), 127.9, 127.6 (2C), 127.5, 117.7, 109.3, 83.9, 83.3, 78.5, 75.6, 75.2, 74.0, 73.5, 73.4, 73.2, 73.1, 63.1, 28.6, 27.6, 27.3, 26.2 (3C), 26.1 (3C), 18.5, 18.2, −4.4, −4.5, −5.0, −5.2; IR (ATR) $\tilde{\nu}$ 3458, 2929, 1462, 1252, 1083, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{41}H_{70}NO_8Si_2^+$ 760.4634, found 760.4635 $[M + NH_4]^+$.

(1*R*)-1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-yl Benzoate (S2).[12] A solution of allylic alcohol **63** (120 mg, 0.161 mmol, 1.0 equiv), 4-(dimethylamino)pyridine (2.00 mg, 16.1 μmol, 10 mol %), and triethylamine (134 μL, 0.966 mmol, 6.0 equiv) in CH_2Cl_2 (3 mL) was cooled to 0 °C, and benzoyl chloride (37.4 μL, 0.322 mmol, 2.0 equiv) was added dropwise. The solution was stirred at 0 °C for 10 min and then at room temperature for a further 20 h. The reaction was quenched with aq. $NaHCO_3$ (5 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 49:1 → 29:1 → 9:1] afforded benzoate ester **S2** (132 mg, 0.156 mmol, 97%) as a colorless oil: R_f 0.47 [PE:EtOAc 9:1]; $[\alpha]_D^{20}$ +42.9 (*c* = 0.63, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 8.08−8.05 (m, 2H), 7.44−7.40 (m, 1H), 7.37−7.24 (m, 10H), 7.19−7.16 (m, 2H), 6.00 (ddd, *J* = 17.2, 10.6, 6.0 Hz, 1H), 5.64−5.60 (m, 1H), 5.40 (ddd, *J* = 17.3, 1.3, 1.3 Hz, 1H), 5.33 (ddd, *J* = 10.6, 1.2, 1.2 Hz, 1H), 4.84 (d, *J* = 11.2 Hz, 1H), 4.74 (d, *J* = 10.9 Hz, 1H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.54 (d, *J* = 10.9 Hz, 1H), 4.21−4.13 (m, 2H), 3.96 (dd, *J* = 7.7, 5.5 Hz, 1H), 3.81−3.77 (m, 1H), 3.59−3.54 (m, 2H), 3.46−3.40 (m, 2H), 3.17−3.13 (m, 1H), 2.03−1.89 (m, 2H), 1.40 (s, 3H), 1.36 (s, 3H), 0.91 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.4, 139.0, 138.8, 133.4, 133.1, 129.9, 129.8 (2C), 128.7 (2C), 128.4 (2C), 128.4 (2C), 128.0 (2C), 127.7 (3C), 127.5, 118.7, 109.8, 83.4, 82.0, 78.2, 75.6, 74.9, 74.9, 74.5, 73.3, 73.1, 72.9, 62.6, 29.1, 27.7, 27.1, 26.2 (3C), 26.1 (3C), 18.5, 18.2, −4.5, −4.5, −4.9, −5.3; IR (ATR) $\tilde{\nu}$ 2930, 1726, 1252, 1085, 834, 697 cm^{-1}; HRMS (ESI) calcd for $C_{48}H_{74}NO_9Si_2^+$ 864.4897, found 864.4896 $[M + NH_4]^+$.

(1*R*)-1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-hydroxy-6-(hydroxymethyl)oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-en-1-yl Benzoate (69).[12] To a solution of bis-silyl ether **S2** (936 mg, 1.10 mmol, 1.0 equiv) in THF (50 mL) was added a solution of tetrabutylammonium fluoride in THF (1.0 M, 3.30 mL, 3.30 mmol, 3.0 equiv), and the resulting mixture was stirred at room temperature for 20 h. The reaction was quenched with aq. $NaHCO_3$ (70 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 100 mL). The combined organic fractions were washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 3:1] afforded diol **69** (569 mg, 0.920 mmol, 84%) as a white sticky foam: R_f 0.51 [PE:EtOAc 1:1]; $[\alpha]_D^{22}$ +34.5 (*c* = 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 8.09−8.06 (m, 2H), 7.54−7.51 (m, 1H), 7.44−7.40 (m, 2H), 7.37−7.29 (m, 6H), 7.28−7.24 (m, 4H) 5.98 (ddd, *J* = 17.1, 10.6, 6.3 Hz, 1H), 5.69−5.65 (m, 1H), 5.43 (ddd, *J* = 17.3, 1.2, 1.2 Hz, 1H), 5.35 (ddd, *J* = 10.6, 1.2, 1.2 Hz, 1H), 4.61−4.52 (m, 4H), 4.32 (ddd, *J* = 10.9, 8.0, 3.3 Hz, 1H), 4.21 (ddd, *J* = 11.2, 2.9, 2.9 Hz, 1H), 4.17 (dd, *J* = 12.3, 9.4 Hz, 1H), 3.96 (dd, *J* = 8.0, 4.8 Hz, 1H), 3.95−3.90 (m, 1H), 3.73−3.70 (m, 1H), 3.59−3.55 (m, 1H), 3.38 (dd, *J* = 12.3, 3.9 Hz, 1H), 3.35−3.31 (m, 1H), 2.95 (br s, 1H), 2.24 (ddd, *J* = 14.3, 11.2, 3.3 Hz, 1H), 1.65 (ddd, *J* = 13.9, 10.5, 3.3 Hz, 1H), 1.43 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 137.8, 137.3, 133.3, 132.5, 130.0, 129.9 (2C), 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.2, 128.2, 128.0 (2C), 127.8 (2C), 119.3, 109.5, 82.6, 76.5, 75.6, 74.6, 74.4, 74.1, 73.3, 72.6, 69.3, 66.2, 59.5, 33.2, 27.6, 26.9; IR (ATR) $\tilde{\nu}$ 3473, 2880, 1721, 1267, 1070, 856, 751 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{46}NO_9^+$ 636.3167, found 636.3169 $[M + NH_4]^+$.

Methyl (2*S*,3*S*,4*R*,5*S*,6*R*)-6-{[(4*R*,5*S*)-5-[(1*R*)-1-(Benzoyloxy)-prop-2-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl]methyl}-3,4-

bis(benzyloxy)-5-hydroxyoxane-2-carboxylate (S3).[12] To a solution of diol **69** (110 mg, 0.178 mmol, 1.0 equiv) in a mixture of CH_2Cl_2 and water (2:1, 9 mL) were added 2,2,6,6-tetramethylpiperidine-1-oxyl (27.8 mg, 0.178 mmol, 1.0 equiv) and (diacetoxyiodo)benzene (287 mg, 0.890 mmol, 5.0 equiv), and the resulting biphasic system was stirred vigorously at room temperature for 5 h. A second equivalent of 2,2,6,6-tetramethylpiperidine-1-oxyl (27.8 mg, 0.178 mmol, 1.0 equiv) was added, and the mixture was stirred at room temperature for an additional 2 h. The reaction was quenched with aq. $Na_2S_2O_3$ (10 mL of a half-saturated solution), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo to provide the crude carboxylic acid, which was immediately redissolved in toluene:MeOH (7:1, 8 mL). To this mixture was carefully added dropwise a solution of (trimethylsilyl)diazomethane in hexanes (2.0 M, 107 μL, 0.214 mmol, 1.2 equiv), and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched with acetic acid (100 μL), and the mixture was diluted with water (15 mL) and extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 19:1 → 9:1 → 4:1] afforded ester **S3** (78.4 mg, 0.121 mmol, 68% over two steps) as a colorless oil: R_f 0.50 [PE:EtOAc 3:1]; $[\alpha]_D^{20}$ +39.1 (c = 0.89, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09−8.07 (m, 2H), 7.49−7.54 (m, 1H), 7.40−7.27 (m, 10H), 7.22−7.19 (m, 2H), 5.74 (ddd, J = 17.2, 10.6, 6.6 Hz, 1H), 5.76−5.72 (m, 1H), 5.46 (ddd, J = 17.3, 1.3, 1.3 Hz, 1H), 5.35 (ddd, J = 10.6, 1.2, 1.2 Hz, 1H), 4.62 (d, J = 11.7 Hz, 1H), 4.53 (d, J = 11.7 Hz, 1H), 4.50−4.50 (m, 3H), 4.40 (d, J = 11.8 Hz, 1H), 4.34 (ddd, J = 8.0, 8.0, 3.4 Hz, 1H), 4.17−4.14 (m, 1H), 4.00 (dd, J = 7.9, 4.5 Hz, 1H), 3.77 (dd, J = 3.2, 3.2 Hz, 1H), 3.60 (s, 3H), 3.54−3.50 (m, 1H), 3.28 (br d, J = 11.4 Hz, 1H), 2.23 (ddd, J = 14.5, 10.1, 3.4 Hz, 1H), 1.77 (ddd, J = 14.6, 8.1, 2.8 Hz, 1H), 1.44 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3, 165.6, 137.5, 136.9, 133.1, 132.8, 130.4, 130.0 (2C), 128.8 (2C), 128.5 (2C), 128.4 (2C), 128.4, 128.0 (2C), 128.0, 127.7 (2C), 119.4, 109.4, 82.5, 75.8, 75.1, 74.2, 73.3, 72.9, 72.3, 71.9, 69.3, 69.1, 52.0, 36.4, 27.7, 27.0; IR (ATR) $\tilde{\nu}$ 3513, 2932, 1754, 1720, 1453, 1266, 1095, 920, 711 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{42}ClO_{10}^-$ 681.2472; found 681.2471 $[M + Cl]^-$.

Methyl (2*S*,3*S*,4*S*,6*R*)-6-{[(4*R*,5*S*)-5-[(1*R*)-1-(Benzoyloxy)prop-2-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl]methyl}-3,4-bis(benzyloxy)-5-oxooxane-2-carboxylate (70).[12] To a solution of alcohol **S3** (78.4 mg, 0.121 mmol, 1.0 equiv) in CH_2Cl_2 (7 mL) was added $NaHCO_3$ (153 mg, 1.82 mmol, 15 equiv) followed by Dess−Martin periodinane (128 mg, 0.303 mmol, 2.5 equiv) in one portion, and the resulting suspension was stirred at room temperature for 40 min. The reaction was quenched with a mixture (1:1, 14 mL) of aq. $NaHCO_3$ (saturated solution) and aq. $Na_2S_2O_3$ (saturated solution), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 4:1] afforded ketone **70** (68.5 mg, 0.106 mmol, 88%) as a colorless oil: R_f 0.53 [PE:EtOAc 3:1]; $[\alpha]_D^{20}$ +54.6 (c = 0.95, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08−8.05 (m, 2H), 7.54−7.50 (m, 1H), 7.42−7.39 (m, 2H), 7.36−7.26 (m, 10H), 6.00 (ddd, J = 17.2, 10.6, 6.5 Hz, 1H), 5.72−5.68 (m, 1H), 5.44 (ddd, J = 17.3, 1.3, 1.3 Hz, 1H), 5.34 (ddd, J = 10.6, 1.2, 1.2 Hz, 1H), 4.75−4.68 (m, 3H), 4.64 (d, J = 10.4 Hz, 1H), 4.53−4.49 (m, 2H), 4.27−4.23 (m, 2H), 4.19 (d, J = 7.1 Hz, 1H), 3.98 (dd, J = 7.8, 4.5 Hz, 1H), 3.66 (s, 3H), 2.17 (ddd, J = 14.5, 8.8, 3.0 Hz, 1H), 1.97 (ddd, J = 14.4, 10.1, 3.3 Hz, 1H), 1.41 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.3, 170.1, 165.5, 137.5, 137.1, 133.2, 132.5, 130.2, 129.9 (2C), 128.6 (2C), 128.6 (2C), 128.5 (2C), 128.2, 128.1 (2C), 128.1, 128.1 (2C), 119.5, 109.8, 82.1, 81.6, 79.2, 75.9, 75.3, 74.6, 74.3, 73.4, 73.4, 52.4, 34.7, 27.6, 27.1; IR (ATR) $\tilde{\nu}$ 2934, 1722, 1453, 1268, 1069, 711 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{44}NO_{10}^+$ 662.2960, found 662.2958 $[M + NH_4]^+$.

Methyl (1*R*,3*S*,4*S*,5*R*,7*R*,9*R*,11*S*,12*S*,13*S*)-5-(Acetyloxy)-4-(benzoyloxy)-12,13-bis(benzyl-oxy)-1-hydroxy-2,6,10-trioxatricyclo[7.4.0.0^{3,7}]tridecane-11-carboxylate (73).[12] A solution of ketone **70** (64.0 mg, 99.3 μmol, 1.0 equiv) in a TFA:CH_2Cl_2:H_2O (9:1:1, 4 mL) mixture was stirred at room temperature for 15 min. The solvent was removed by azeotropic distillation with toluene (3 × 8 mL), after which the resulting residue was taken up in EtOAc (20 mL) and aq. $NaHCO_3$ (15 mL of a saturated solution) was added. The organic phase was separated, and the aqueous layer was extracted further with EtOAc (2 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was dissolved in CH_2Cl_2 (6 mL), and the resulting solution was cooled to −78 °C. Ozone was bubbled through the reaction mixture until a slight blue color persisted. Excess ozone was discharged by bubbling argon through the mixture, and dimethyl sulfide (0.29 mL, 3.97 mmol, 40 equiv) was added at −78 °C. The solution was allowed to warm to room temperature and stirred at this temperature for 3 h. Water (15 mL) was added, and the mixture was extracted with EtOAc (2 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo to provide the crude hemiacetal, which was subsequently dissolved in CH_2Cl_2 (5 mL). To this solution were added 4-(dimethylamino)pyridine (2.43 mg, 19.9 μmol, 20 mol %), triethylamine (20.7 μL, 0.149 mmol, 1.5 equiv), and acetic anhydride (11.2 μL, 0.119 mmol, 1.2 equiv), and the mixture was stirred at room temperature for 1 h. The reaction was quenched with aq. NH_4Cl (15 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 4:1 → 3:1 → 1:1] afforded the tricyclic compound **73** (36.5 mg, 56.3 μmol, 57% over three steps) as a colorless oil and as a single diastereomer: R_f 0.55 [PE:EtOAc 1:1]; $[\alpha]_D^{22}$ +68.4 (c = 0.98, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01−7.98 (m, 2H), 7.57−7.53 (m, 1H), 7.39−7.35 (m, 2H), 7.34−7.21 (m, 8H), 7.10−7.04 (m, 2H), 6.46 (d, J = 3.8 Hz, 1H), 5.45 (dd, J = 4.9, 3.8 Hz, 1H), 4.84 (dd, J = 4.9, 2.0 Hz, 1H), 4.80 (d, J = 11.8 Hz, 1H), 4.73 (dd, J = 11.6, 5.1 Hz, 1H), 4.60−4.51 (m, 4H), 4.47 (s, 1H), 4.35 (d, J = 11.8 Hz, 1H), 4.25 (dd, J = 3.4, 1.2 Hz, 1H), 3.59 (s, 3H), 3.50 (d, J = 3.4 Hz, 1H), 2.32 (ddd, J = 13.6, 5.1, 2.5 Hz, 1H), 2.19−2.12 (m, 1H), 2.12 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.4, 169.6, 165.3, 138.1, 136.2, 133.5, 130.0 (2C), 129.2, 128.8 (2C), 128.6 (2C), 128.5, 128.4 (2C), 128.0 (2C), 127.7, 127.3 (2C), 99.9, 93.8, 80.0, 78.3, 78.0, 74.1, 73.8, 73.7, 72.4, 70.1, 65.4, 52.4, 25.9, 21.3; IR (ATR) $\tilde{\nu}$ 3443, 2952, 1726, 1453, 1276, 1096, 1006, 698 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{40}O_{12}N^+$ 666.2545, found 666.2541 $[M + NH_4]^+$.

(1*S*)-1-[(4*R*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-ol (64).[12] Toluene was removed from a solution of (*S*)-(−)-2-methyloxazaborolidine [(*S*)-**68**] in toluene (1.0 M, 675 μL, 0.675 mmol, 10 mol %), and the residue was dried in vacuo. The oxazaborolidine reagent was redissolved in THF (30 mL), and the resulting solution was added via cannula to a stirred solution of vinyl ketone **66** (5.00 g, 6.75 mmol, 1.0 equiv) in THF (170 mL) that had been precooled to −25 °C. A solution of borane dimethyl sulfide complex in THF (2.0 M, 3.71 mL, 7.42 mmol, 1.1 equiv) was added dropwise. The mixture was allowed to warm to 0 °C over 2 h and stirred at this temperature for an additional 30 min. The reaction was quenched with MeOH (10 mL), and the solution was diluted with a mixture (2:1, 120 mL) of aq. NaOH (10 wt %) and aq. $NaHCO_3$ (saturated solution). The resulting solution was extracted with Et_2O (3 × 250 mL), and the combined organic fractions were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo to provide crude alcohols **64** and **63** as a mixture of two diastereomers (d.r. 14:1 as determined by ^{1}H NMR spectroscopy). Flash column chromatography [PE:EtOAc 19:1 → 9:1 → 4:1] afforded allylic alcohol **64** (3.43 g, 4.62 mmol, 68%) as a colorless oil. The analytical data were identical to those of the material obtained earlier.

(1*S*)-1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*S*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-6-{[(*tert*-butyldimethylsilyl)oxy]-methyl}oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]-prop-2-en-1-yl Benzoate (S4).[12] A solution of allylic alcohol **64**

(3.43 g, 4.62 mmol, 1.0 equiv), 4-(dimethylamino)pyridine (56.4 mg, 0.462 mmol, 10 mol %), and triethylamine (3.86 mL, 27.7 mmol, 6.0 equiv) in CH_2Cl_2 (80 mL) was cooled to 0 °C, and benzoyl chloride (1.07 mL, 9.24 mmol, 2.0 equiv) was added dropwise. The mixture was stirred at 0 °C for 10 min and then allowed to warm to room temperature and stirred at this temperature for 10 h. The reaction was quenched with aq. $NaHCO_3$ (150 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 200 mL). The combined organic fractions were washed with brine (250 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 49:1 → 29:1 → 9:1] afforded benzoyl-protected alcohol **S4** (3.89 g, 4.59 mmol, 99%) as a colorless oil: R_f 0.47 [PE:EtOAc 9:1]; $[\alpha]_D^{20}$ +16.0 (c = 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10−8.07 (m, 2H), 7.52−7.49 (m, 1H), 7.42−7.38 (m, 2H), 7.36−7.24 (m, 10H), 5.98 (ddd, J = 17.1, 10.6, 6.4 Hz, 1H), 5.73−5.70 (m, 1H), 5.45 (ddd, J = 17.3, 1.3, 1.3 Hz, 1H), 5.35 (ddd, J = 10.6, 1.2, 1.2 Hz, 1H), 4.86 (d, J = 11.2 Hz, 1H), 4.82 (d, J = 10.8 Hz, 1H), 4.76 (d, J = 11.2 Hz, 1H), 4.65 (d, J = 10.8 Hz, 1H), 4.16 (ddd, J = 12.0, 6.1, 2.1 Hz, 1H), 4.09 (ddd, J = 10.4, 8.1, 2.2 Hz, 1H), 3.94 (dd, J = 8.1, 4.9 Hz, 1H), 3.84−3.79 (m, 2H), 3.68 (dd, J = 11.3, 1.7 Hz, 1H), 3.55−3.51 (m, 2H), 3.47−3.42 (m, 1H), 2.01 (ddd, J = 14.3, 12.1, 2.2 Hz, 1H), 1.91 (ddd, J = 14.7, 10.4, 2.1 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 139.0, 138.7, 133.3, 132.8, 130.1, 129.9 (2C), 128.7 (2C), 128.5 (2C), 128.4 (2C), 128.1 (2C), 127.7, 127.7 (2C), 127.5, 119.2, 109.5, 83.5, 81.8, 78.2, 75.6, 75.1, 74.1, 73.3, 73.2, 73.1, 73.0, 62.8, 28.3, 27.6, 27.0, 26.2 (3C), 26.1 (3C), 18.5, 18.2, −4.5, −4.5, −5.0, −5.3; IR (ATR) $\tilde{\nu}$ 2929, 1723, 1251, 1086, 834, 696 cm^{-1}; HRMS (ESI) calcd for $C_{48}H_{74}NO_9Si_2^+$ 864.4897, found 864.4899 $[M + NH_4]^+$.

(1*S*)-1-[(4*S*,5*R*)-5-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-Bis(benzyloxy)-3-hydroxy-6-(hydroxymethyl)oxan-2-yl]methyl}-2,2-dimethyl-1,3-dioxolan-4-yl]prop-2-en-1-yl Benzoate (75).[12] To a solution of benzoyl-protected alcohol **S4** (254 mg, 0.300 mmol, 1.0 equiv) in THF (12 mL) was added a solution of tetrabutylammonium fluoride in THF (1.0 M, 900 μL, 0.900 mmol, 3.0 equiv), and the resulting mixture was stirred at room temperature for 16 h. The reaction was quenched with aq. $NaHCO_3$ (20 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 25 mL). The combined organic fractions were washed with brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 3:1] afforded diol **75** (143 mg, 0.231 mmol, 77%) as a white sticky foam: R_f 0.51 [PE:EtOAc 1:1]; $[\alpha]_D^{22}$ +8.1 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11−8.07 (m, 2H), 7.58−7.53 (m, 1H), 7.46−7.41 (m, 2H), 7.38−7.26 (m, 10H), 5.97 (ddd, J = 17.2, 10.6, 6.3 Hz, 1H), 5.74−5.69 (m, 1H), 5.46 (ddd, J = 17.3, 1.3, 1.3 Hz, 1H), 5.36 (ddd, J = 10.6, 1.2, 1.2 Hz, 1H), 4.66−4.56 (m, 4H), 4.27−4.15 (m, 3H), 4.02−3.95 (m, 2H), 3.75 (dd, J = 4.5, 4.5 Hz, 1H), 3.61−3.55 (br m, 1H), 3.42 (dd, J = 12.3, 3.6 Hz, 1H), 3.38 (dd, J = 4.0, 4.0 Hz, 1H), 3.02 (br d, J = 8.4 Hz, 1H), 2.79 (br s, 1H), 2.24 (ddd, J = 14.5, 11.3, 3.5 Hz, 1H), 1.65 (ddd, J = 13.6, 10.1, 3.2 Hz, 1H), 1.45 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 137.8, 137.3, 133.3, 132.5, 130.0, 130.0 (2C), 128.7 (2C), 128.7 (2C), 128.6 (2C), 128.2, 128.2, 128.0 (2C), 127.8 (2C), 119.3, 109.4, 82.3, 76.7, 75.5, 74.3, 73.8 (2C), 73.4, 72.7, 69.4, 66.5, 59.6, 32.6, 27.6, 26.9; IR (ATR) $\tilde{\nu}$ 3449, 2932, 1719, 1266, 1068, 851, 696 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{46}NO_9^+$ 636.3167, found 636.3164 $[M + NH_4]^+$.

Methyl (2*S*,3*S*,4*R*,5*S*,6*R*)-6-{[(4*R*,5*S*)-5-[(1*S*)-1-(Benzoyloxy)prop-2-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl]methyl}-3,4-bis(benzyloxy)-5-hydroxyoxane-2-carboxylate (S5).[12] To a solution of diol **75** (1.87 g, 3.02 mmol, 1.0 equiv) in a mixture of CH_2Cl_2 and water (2:1, 135 mL) were added 2,2,6,6-tetramethylpiperidine-1-oxyl (472 mg, 3.02 mmol, 1.0 equiv) and (diacetoxyiodo)-benzene (4.86 g, 15.1 mmol, 5.0 equiv), and the resulting biphasic system was stirred vigorously at room temperature for 2 h. A second equivalent of 2,2,6,6-tetramethylpiperidine-1-oxyl (472 mg, 3.02 mmol, 1.0 equiv) was added, and the mixture was stirred for an additional 3.5 h. The reaction was quenched with aq. $Na_2S_2O_3$ (100 mL of a half-saturated solution), and the aqueous layer was extracted with EtOAc (3 × 150 mL). The combined organic fractions were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo to provide the crude carboxylic acid, which was immediately redissolved in toluene:MeOH (7:1, 120 mL). To this mixture, a solution of (trimethylsilyl)diazomethane in hexanes (2.0 M, 1.81 mL, 3.63 mmol, 1.2 equiv) was added dropwise, and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched with acetic acid (1.4 mL), and the mixture was diluted with water (100 mL) and extracted with EtOAc (3 × 150 mL). The combined organic fractions were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 9:1 → 4:1] afforded ester **S5** (1.54 g, 2.38 mmol, 79% over two steps) as a white sticky foam: R_f 0.28 [PE:EtOAc 3:1]; $[\alpha]_D^{23}$ +5.4 (c = 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12−8.09 (m, 2H), 7.54−7.51 (m, 1H), 7.42−7.26 (m, 10H), 7.21−7.19 (m, 2H), 5.99 (ddd, J = 17.2, 8.4, 4.2 Hz, 1H), 5.75−5.72 (m, 1H), 5.42 (ddd, J = 17.3, 1.3, 1.3 Hz, 1H), 5.32 (ddd, J = 10.6, 1.3, 1.3 Hz, 1H), 4.71 (d, J = 11.6 Hz, 1H), 4.61 (d, J = 11.6 Hz, 1H), 4.55 (s, 1H), 4.50−4.44 (m, 2H), 4.40 (d, J = 11.7 Hz, 1H), 4.37 (ddd, J = 7.7, 7.7, 3.7 Hz, 1H), 4.19 (ddd, J = 3.0, 1.4, 1.4 Hz, 1H), 3.96 (dd, J = 7.8, 4.3 Hz, 1H), 3.80 (dd, J = 3.3, 3.3 Hz, 1H), 3.55−3.51 (m, 1H), 3.48 (s, 3H), 3.38 (d, J = 11.6 Hz, 1H), 2.19 (ddd, J = 14.4, 10.0, 3.7 Hz, 1H), 1.77 (ddd, J = 14.4, 10.0, 3.7 Hz, 1H), 1.50 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.1, 165.6, 137.4, 136.8, 133.2, 133.0, 130.4, 129.9 (2C), 128.8 (2C), 128.5 (2C), 128.5 (2C), 128.4, 128.1 (2C), 128.0, 127.7 (2C), 118.6, 109.1, 82.5, 74.7, 74.3, 73.8, 73.3, 72.9, 72.4, 71.9, 69.3, 69.2, 51.9, 35.7, 27.7, 27.0; IR (ATR) $\tilde{\nu}$ 3507, 2931, 1755, 1720, 1452, 1267, 1069, 921, 711 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{46}NO_{10}^+$ 664.3116; found 664.3114 $[M + NH_4]^+$.

Methyl (2*S*,3*S*,4*S*,6*R*)-6-{[(4*R*,5*S*)-5-[(1*S*)-1-(Benzoyloxy)prop-2-en-1-yl]-2,2-dimethyl-1,3-dioxolan-4-yl]methyl}-3,4-bis(benzyloxy)-5-oxooxane-2-carboxylate (48).[12] To a solution of alcohol **S5** (1.54 g, 2.38 mmol, 1.0 equiv) in CH_2Cl_2 (120 mL) were added $NaHCO_3$ (3.00 g, 35.7 mmol, 15 equiv) and Dess−Martin periodinane (2.52 g, 5.95 mmol, 2.5 equiv) in one portion, and the resulting suspension was stirred at room temperature for 1 h. The reaction was quenched with a mixture (1:1, 100 mL) of aq. $NaHCO_3$ (saturated solution) and aq. $Na_2S_2O_3$ (saturated solution), and the mixture was diluted with water (100 mL) and extracted with EtOAc (3 × 150 mL). The combined organic fractions were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 5:1] afforded ketone **48** (1.45 g, 2.25 mmol, 94%) as a colorless oil: R_f 0.40 [PE:EtOAc 3:1]; $[\alpha]_D^{22}$ +25.2 (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10−8.06 (m, 2H), 7.58−7.52 (m, 1H), 7.46−7.40 (m, 2H), 7.38−7.27 (m, 10H), 5.95 (ddd, J = 17.2, 10.6, 6.2 Hz, 1H), 5.72−5.65 (m, 1H), 5.43 (ddd, J = 17.3, 1.3, 1.3 Hz, 1H), 5.33 (ddd, J = 10.6, 1.2, 1.2 Hz, 1H), 4.76−4.70 (m, 3H), 4.68 (d, J = 11.5 Hz, 1H), 4.57 (d, J = 4.2 Hz, 1H), 4.51 (d, J = 11.4 Hz, 1H), 4.28 (dd, J = 7.1, 4.2 Hz, 1H), 4.26−4.19 (m, 2H), 3.96 (dd, J = 7.7, 4.7 Hz, 1H), 3.60 (s, 3H), 2.14 (ddd, J = 14.5, 8.5, 2.9 Hz, 1H), 1.95 (ddd, J = 13.7, 10.0, 3.4 Hz, 1H), 1.45 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 170.0, 166.0, 137.4, 137.1, 133.2, 132.7, 130.2, 129.9 (2C), 128.6 (2C), 128.6 (2C), 128.2, 128.1, 128.1 (4C), 119.1, 109.6, 81.9, 81.5, 79.3, 75.9, 75.2, 73.8, 73.4, 73.4, 73.4, 52.4, 34.1, 27.6, 27.1; IR (ATR) $\tilde{\nu}$ 2934, 1720, 1452, 1267, 1066, 711 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{44}NO_{10}^+$ 662.2960, found 662.2960 $[M + NH_4]^+$.

Methyl (1*R*,3*S*,4*R*,7*R*,9*R*,11*S*,12*S*,13*S*)-5-(Acetyloxy)-4-(benzoyloxy)-12,13-bis(benzyloxy)-1-hydroxy-2,6,10-trioxatricyclo-[7.4.0.0^{3,7}]tridecane-11-carboxylate (76).[12] A solution of ketone **48** (880 mg, 1.36 mmol, 1.0 equiv) in a TFA:CH_2Cl_2:H_2O (9:1:1, 600 mL) mixture was stirred at room temperature for 15 min. After the solvent was removed by azeotropic distillation with toluene (3 × 50 mL), the resulting residue was taken up in EtOAc (50 mL), and aq. $NaHCO_3$ (50 mL of a saturated solution) was added. The organic phase was separated, and the aqueous layer was extracted further with EtOAc (2 × 50 mL). The combined organic fractions were washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was dissolved in CH_2Cl_2 (70 mL), and the resulting solution was cooled to −78 °C. Ozone was bubbled through the reaction mixture until a slight blue color persisted. Excess ozone was

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discharged by bubbling argon through the mixture, and dimethyl sulfide (4.02 mL, 54.4 mmol, 40 equiv) was added at −78 °C. The solution was allowed to warm to room temperature and stirred at this temperature for 2.5 h. Water (80 mL) was added, and the mixture was extracted with EtOAc (3 × 150 mL). The combined organic fractions were washed with brine (150 mL), dried ($MgSO_4$), and concentrated in vacuo to provide the crude hemiacetal, which was subsequently dissolved in CH_2Cl_2 (60 mL). To this solution were added 4-(dimethylamino)pyridine (33.2 mg, 0.272 mmol, 20 mol %), triethylamine (377 μL, 2.72 mmol, 2.0 equiv), and acetic anhydride (193 μL, 2.04 mmol, 1.5 equiv), and the mixture was stirred at room temperature for 3 h. The reaction was quenched with aq. NH_4Cl (100 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 150 mL). The combined organic fractions were washed with brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 4:1 → 3:1 → 2:1 → 1:1] afforded tricyclic compound **76** (750 mg, 1.16 mmol, 85% over three steps) as a white solid consisting of two diastereomers (d.r. 2.8:1 as determined by ^{1}H NMR spectroscopy) as an inseparable mixture: R_f 0.15 [PE:EtOAc 3:1]; ^{1}H NMR (600 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 8.05−8.02 (m, 2H), 7.61−7.58 (m, 1H), 7.48−7.44 (m, 2H), 7.38−7.25 (m, 10H), 6.51 (d, *J* = 4.7 Hz, 1H), 5.47 (d, *J* = 4.7 Hz, 1H), 4.74 (d, *J* = 11.8 Hz, 1H), 4.68−4.62 (m, 4H), 4.62−4.58 (m, 1H), 4.55−4.53 (m, 1H), 4.49 (br s, 1H), 4.34−4.32 (m, 1H), 3.60 (d, *J* = 4.7 Hz, 1H), 3.59 (s, 3H), 2.40−2.32 (m, 1H), 2.21−2.13 (m, 1H), 1.91 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 169.5, 169.5, 165.1, 137.8, 136.2, 133.6, 129.8 (2C), 129.3, 128.9 (2C), 128.7 (2C), 128.6, 128.5 (2C), 128.2 (2C), 127.9, 127.6 (2C), 95.4, 93.7, 78.0, 77.9, 77.0, 75.3, 74.2, 74.1, 73.7, 72.6, 65.2, 52.4, 25.4, 20.9; IR (ATR) $\tilde{\nu}$ 3442, 2948, 1752, 1726, 1452, 1270, 1107, 1011, 713 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{36}ClO_{12}^-$ 683.1901, found 683.1894 [M + Cl]$^-$.

Methyl (1*R*,3*S*,4*R*,5*R*,7*R*,9*R*,11*S*,12*S*,13*S*)-5-(6-Amino-9*H*-purin-9-yl)-4-(benzoyloxy)-12,13-bis(benzyloxy)-1-hydroxy-2,6,10-trioxatricyclo[7.4.0.0^{3,7}]tridecane-11-carboxylate (78). To a suspension of acetate **76** (77.6 mg, 0.120 mmol, 1.0 equiv) and adenine (24.2 mg, 0.179 mmol, 1.5 equiv) in MeCN (5.5 mL) was added dropwise trimethylsilyl trifluoromethanesulfonate (130 μL, 0.720 mmol, 6.0 equiv). The resulting solution was stirred at room temperature for 15 min and then diluted with aq. $NaHCO_3$ (10 mL of a saturated solution). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was redissolved in a mixture of MeOH and CH_2Cl_2 (2:1, 6 mL), and K_2CO_3 (16.6 mg, 0.120 mmol, 1.0 equiv) was added in one portion. The reaction mixture was stirred at room temperature for 50 min, and the reaction was quenched with aq. $NaHCO_3$ (10 mL of a saturated solution). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [CH_2Cl_2:MeOH 49:1 → 24:1] afforded glycoside **78** (39.1 mg, 63.1 μmol, 53% over two steps) as a white solid as a single diastereomer: R_f 0.47 [CH_2Cl_2:MeOH 9:1]; $[\alpha]_D^{20}$ −20.4 (*c* = 1.29, $CHCl_3$); mp 128 °C (decomposition); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.26 (s, 1H), 7.33−7.28 (m, 3H), 7.21−7.14 (m, 5H), 7.05−7.01 (m, 2H), 6.18 (s, 2H), 6.14 (s, 1H), 4.91 (s, 1H), 4.73 (dd, *J* = 11.6, 5.2 Hz, 1H), 4.60 (d, *J* = 2.3 Hz, 1H), 4.50−4.41 (m, 6H), 4.27 (d, *J* = 12.7 Hz, 1H), 4.12−4.09 (m, 1H), 3.73 (s, 3H), 3.46 (d, *J* = 3.1 Hz, 1H), 2.76 (br s, 1H), 2.46−2.38 (m, 1H), 2.26−2.19 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.6, 155.6, 152.6, 149.0, 139.7, 136.7, 136.2, 128.8 (2C), 128.6, 128.5 (2C), 128.4 (2C), 128.2 (3C), 119.5, 93.2, 91.7, 81.5, 78.6, 76.7, 76.3, 74.1, 73.3, 73.1, 72.4, 65.6, 52.5, 25.7; IR (ATR) $\tilde{\nu}$ 3338, 3130, 2941, 1751, 1638, 1598, 1416, 1291, 1206, 1053, 964, 856, 741, 698 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{34}O_9N_5^+$ 620.2351, found 620.2352 [M + H]$^+$.

Methyl (1*R*,3*S*,4*R*,7*R*,9*R*,11*S*,12*S*,13*S*)-5,12,13-Tris(acetyloxy)-4-(benzoyloxy)-1-hydroxy-2,6,10-trioxatricyclo[7.4.0.0^{3,7}]tridecane-11-carboxylate (79).[12] An autoclave apparatus was charged with a solution of tricyclic compound **76** (282 mg, 0.435 mmol, 1.0 equiv) in EtOAc (28 mL), and $Pd(OH)_2/C$ (20 wt %, 196 mg) was added. The autoclave apparatus was purged with hydrogen gas five times, and the resulting suspension was stirred under a hydrogen atmosphere (8 bar) at room temperature for 20 h. The catalyst was removed by filtration through a pad of Celite, and the Celite was washed with EtOAc (40 mL) and the filtrate concentrated in vacuo. Flash column chromatography [PE:EtOAc 2:1 → 1:1] afforded the respective triol (172 mg, 0.367 mmol, 84%) as a white solid representing a complex mixture of structurally unknown isomers. The mixture was used immediately in the next step. To a solution of the triol (127 mg, 0.271 mmol, 1.0 equiv) in CH_2Cl_2 (7 mL) were added 4-(dimethylamino)pyridine (6.62 mg, 54.2 μmol, 20 mol %), triethylamine (94.0 μL, 0.678 mmol, 2.5 equiv), and acetic anhydride (56.3 μL, 0.596 mmol, 2.2 equiv), and the mixture was stirred at room temperature for 8 min. The reaction was quenched with aq. NH_4Cl (10 mL of a saturated solution), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic fractions were washed with brine (20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [PE:EtOAc 3:1 → 1:1 → 1:2] afforded triacetate **79** (112 mg, 0.239 mmol, 88%) as a white solid consisting of two diastereomers (d.r. 9.5:1 as determined by ^{1}H NMR spectroscopy) as an inseparable mixture: R_f 0.47 [PE:EtOAc 1:2]; ^{1}H NMR (600 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 8.03−8.00 (m, 2H), 7.61−7.57 (m, 1H), 7.47−7.44 (m, 2H), 6.48 (d, *J* = 4.6 Hz, 1H), 5.53−5.52 (m, 1H), 5.39 (d, *J* = 4.6 Hz, 1H), 4.97 (d, *J* = 2.9 Hz, 1H), 4.62−4.58 (m, 2H), 4.49 (s, 1H), 4.40 (dd, *J* = 11.6, 5.3 Hz, 1H), 3.84 (s, 3H), 3.39 (s, 1H), 2.42−2.38 (m, 1H), 2.18 (s, 3H), 2.19−2.15 (m, 1H), 2.06 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) (mixture of isomers, major isomer quoted) δ 169.5, 168.9, 168.5, 168.4, 165.1, 133.7, 129.8 (2C), 129.2, 128.7 (2C), 95.2, 91.3, 77.7, 76.5, 75.3, 74.7, 70.4, 68.4, 65.4, 52.9, 25.2, 21.2, 21.0, 20.8; IR (ATR) $\tilde{\nu}$ 3446, 2947, 1730, 1370, 1222, 1012, 713 cm^{-1}; HRMS (ESI) calcd for $C_{25}H_{28}ClO_{14}^-$ 587.1173, found 587.1178 [M + Cl]$^-$.

Methyl (1*S*,3*S*,4*R*,5*R*,7*R*,9*R*,11*S*,12*S*,13*S*)-12,13-Bis(acetyloxy)-5-(6-amino-9*H*-purin-9-yl)-4-(benzoyloxy)-1-[(trimethylsilyl)oxy]-2,6,10-trioxatricyclo[7.4.0.0^{3,7}]tridecane-11-carboxylate (80).[12] To a suspension of triacetate **79** (112 mg, 0.239 mmol, 1.0 equiv) and adenine (48.5 mg, 0.359 mmol, 1.5 equiv) in MeCN (11 mL) was added dropwise trimethylsilyl trifluoromethanesulfonate (260 μL, 1.43 mmol, 6.0 equiv). The resulting solution was stirred at room temperature for 5 min and then diluted with aq. $NaHCO_3$ (20 mL of a saturated solution). The mixture was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic fractions were washed with brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash column chromatography [CH_2Cl_2:MeOH 99:1 → 49:1 → 29:1] afforded glycoside **80** (92.3 mg, 0.132 mmol, 55%) as a white solid as a single diastereomer: R_f 0.39 [EtOAc]; $[\alpha]_D^{23}$ −18.8 (*c* = 0.88, $CHCl_3$); mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.28 (s, 1H), 8.07−8.02 (m, 2H), 7.65−7.59 (m, 1H), 7.50−7.45 (m, 2H), 6.45 (d, *J* = 1.5 Hz, 1H), 5.83 (s, 2H), 5.52−5.50 (m, 2H), 5.13 (d, *J* = 2.5 Hz, 1H), 4.58−4.55 (m, 1H), 4.51 (s, 1H), 4.44−4.37 (m, 2H), 3.78 (s, 3H), 2.42−2.35 (m, 1H), 2.30 (s, 3H), 2.29−2.21 (m, 1H), 2.19 (s, 3H), 0.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.3, 169.0, 165.0, 155.5, 153.4, 150.0, 139.3, 134.1, 130.0 (2C), 128.8 (2C), 128.6, 119.3, 93.9, 86.9, 83.1, 77.8, 75.5, 74.8, 70.4, 69.6, 66.5, 52.9, 25.3, 21.7, 21.2, 2.50 (3C); IR (ATR) $\tilde{\nu}$ 3374, 2953, 1733, 1634, 1594, 1253, 1045, 843 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{38}O_{12}N_5Si^+$ 700.2281, found 700.2287 [M + H]$^+$.

Herbicidin C (3).[12] To a solution of glycoside **80** (10.6 mg, 15.1 μmol, 1.0 equiv) in MeOH (1 mL) was added sodium methoxide (3.27 mg, 60.6 μmol, 4.0 equiv), and the resulting mixture was stirred at room temperature for 90 min. The reaction was quenched with aq. HCl (1 N, 1 mL), and the mixture was concentrated in vacuo. RP-18 flash column chromatography [H_2O:MeOH 100:0 → 9:1 → 4:1 → 2:1 → 1:1] afforded herbicidin C (**3**) (3.10 mg, 7.06 μmol, 48%) as a white solid: R_f 0.22 [CH_2Cl_2:MeOH 6:1]; $[\alpha]_D^{21}$ +26.9 (*c* = 0.70, MeOH); mp 152 °C (decomposition); ^{1}H NMR (600 MHz, CD_3OD) δ 8.70 (s, 1H), 8.21 (s, 1H), 6.11 (d, *J* = 1.0 Hz, 1H), 4.66 (dd, *J* = 10.6, 6.3 Hz, 1H), 4.53 (ddd, *J* = 2.8, 2.8, 2.7 Hz, 1H), 4.36 (br s, 1H), 4.34 (dd, *J* = 3.5, 1.5 Hz, 1H), 4.32 (s, 1H), 4.31 (d, *J* = 2.3 Hz, 1H), 3.71 (s, 3H), 3.70 (d, *J* = 3.5 Hz, 1H), 2.25−2.21 (m, 2H); ^{13}C NMR

(150 MHz, CD_3OD) δ 171.8, 157.2, 153.9, 150.4, 142.6, 119.4, 94.5, 91.6, 82.8, 79.7, 78.0, 77.3, 73.8, 71.2, 65.6, 52.3, 26.5; IR (ATR) $\tilde{\nu}$ 3212, 2924, 1732, 1623, 1220, 1049 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{22}N_5O_9^+$ 440.1412, found 440.1418 $[M + H]^+$.

Aureonuclemycin (9).[12] A solution of herbicidin C (**3**) (4.70 mg, 10.7 μmol, 1.0 equiv) and lithium hydroxide (0.38 mg, 16.0 μmol, 1.5 equiv) in a mixture of THF and water (3:1, 1 mL) was stirred at room temperature for 15 min. The reaction was quenched with one drop of acetic acid, and the mixture was concentrated in vacuo. RP-18 flash column chromatography [H_2O:MeCN 100:0 → 99:1 → 9:1 → 4:1] afforded aureonuclemycin (**9**) (1.50 mg, 3.53 μmol, 33%) as a white solid: R_f 0.52 [RP, H_2O]; $[\alpha]_D^{21}$ +32.0 (c = 0.08, MeOH); mp 195 °C (decomposition); ^{1}H NMR (600 MHz, CD_3OD) δ 8.78 (s, 1H), 8.20 (s, 1H), 6.09 (d, J = 0.9 Hz, 1H), 4.60 (dd, J = 11.7, 5.2 Hz, 1H), 4.53−4.50 (m, 1H), 4.41 (d, J = 3.1 Hz, 1H), 4.32 (s, 1H), 4.30 (d, J = 2.2 Hz, 1H), 4.25 (br s, 1H), 3.70 (d, J = 3.2 Hz, 1H), 2.31−2.26 (m, 1H), 2.22−2.16 (m, 1H); ^{13}C NMR (150 MHz, CD_3OD) δ 175.2 (inferred from HMBC), 157.2, 153.8, 150.4, 142.9, 119.4, 94.8, 91.4, 82.9, 80.0 (br), 79.6, 77.2, 73.3, 72.0, 65.2, 26.5; IR (ATR) $\tilde{\nu}$ 3198, 1603, 1418, 1080 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{20}N_5O_9^+$ 426.1256, found 426.1257 $[M + H]^+$.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra as well as X-ray data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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