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SYNTHETIC STUDIES DIRECTED TOWARD
POLYCAVERNOSIDE A AND TAXOL® (PACLITAXEL)

DISSERTATION

Presented in Partial Fulfillment of the Requirements
for the Degree Doctor of Philosophy in the
Graduate School of The Ohio State University

by

Jeffrey N. Johnston

The Ohio State University
1997

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SYNTHETIC STUDIES DIRECTED TOWARD
POLYCAVERNOSIDE A AND TAXOL® (PACLITAXEL)

By
Jeffrey N. Johnston, Ph.D.
The Ohio State University, 1997
Professor Leo A. Paquette, Adviser

A protected form of the disaccharide subunit found in polycavernoside A has been synthesized via a Mukaiyama-Nicolaou type coupling of an L-fucose-derived glycosyl fluoride and a D-xylose-derived thioglycoside. The fluorofucose derivative served as the glycosyl acceptor and could be accessed in a sequence of nine steps from commercially available L-fucose. Similarly, a D-xylose derivative in which the C(3) hydroxyl is singularly unprotected was made available in two steps from D-xylose, or from commercially available 1,2-O-isopropylidene-α-D-xylofuranose in seven steps.

Progress toward a total synthesis of the antitumor agent Taxol is also reported. Implementation of a phenylthio moiety as an oxygen surrogate is described with the report of a novel intermolecular sulfoxide displacement reaction which is a formal equivalent to the Mislow-Evans rearrangement. The resulting bridged cyclononene ring systems could be elaborated by an epoxidation/transannular epoxide ring opening strategy to give rise to products bearing
tetrahydrofuran, cyclopropane, and oxetane rings. This unique behavior is discussed in the context of the congested environment found in bridged ring systems of this type.

The use an aldol strategy to annulate the C-ring found in Taxol is also examined at length with a variety of B-ring saturated and unsaturated keto aldehydes. A summary of structural criteria necessary for successful C-ring closure is presented.

Finally, the design and implementation of a second-generation C-ring synthon that imposes fewer steric constraints upon the B-ring is discussed, emphasizing its adaptability to the incorporation of an oxygen at the C(2) position (Taxol numbering).
This work is dedicated to
my mother and father,
and my wife, Karen,
for their everlasting love, faith, and support.
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Dr. Kurt Loening and Dr. Robin Rogers are to be acknowledged for their assistance with nomenclature and X-ray crystallography, respectively. Additionally, I would like to express my appreciation to Dr. Dirk Friedrich for some last minute structural elucidation by NMR.

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PUBLICATIONS


FIELD OF STUDY

Major Field: Chemistry
Studies in Organic Chemistry
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>[α]</td>
<td>specific rotation</td>
</tr>
<tr>
<td>Ac</td>
<td>acetyl</td>
</tr>
<tr>
<td>Bn</td>
<td>benzyl</td>
</tr>
<tr>
<td>br</td>
<td>broad (spectral)</td>
</tr>
<tr>
<td>Bu</td>
<td>butyl</td>
</tr>
<tr>
<td>t-Bu</td>
<td>tert-butyl</td>
</tr>
<tr>
<td>ºC</td>
<td>degrees Celsius</td>
</tr>
<tr>
<td>calcd</td>
<td>calculated</td>
</tr>
<tr>
<td>δ</td>
<td>chemical shift in parts per million downfield from tetramethylsilane</td>
</tr>
<tr>
<td>d</td>
<td>day(s); doublet (spectral)</td>
</tr>
<tr>
<td>DAST</td>
<td>diethylaminosulfur trifluoride</td>
</tr>
<tr>
<td>DEPT</td>
<td>distortionless enhancement by polarization transfer</td>
</tr>
<tr>
<td>DMAP</td>
<td>4-(N,N-dimethylamino)pyridine</td>
</tr>
<tr>
<td>DMF</td>
<td>dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>El</td>
<td>electron ionization</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
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</table>
FAB  fast atom bombardment

g   gram(s)

h   hour(s)

Hz  hertz

IR  infrared

J   coupling constant (NMR)

L   liter(s)

m   milli; multiplet (spectral)

μ   micro

m-CPBA  m-chloroperbenzoic acid

Me  methyl

MHz  megahertz

min  minute(s)

mol  mole(s)

MOM  methoxymethyl

mp  melting point

MS  mass spectrometry

m/z  mass to charge ratio (mass spectrometry)

NBS  N-bromosuccinimide

NIS  N-iodosuccinimide
<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
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<tbody>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>NOE</td>
<td>nuclear Overhauser effect spectroscopy</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>PMB</td>
<td>p-methoxybenzyl</td>
</tr>
<tr>
<td>PMBz</td>
<td>p-methoxybenzoate</td>
</tr>
<tr>
<td>PMP</td>
<td>p-methoxyphenyl</td>
</tr>
<tr>
<td>ppm</td>
<td>parts per million (in NMR)</td>
</tr>
<tr>
<td>Pr</td>
<td>propyl</td>
</tr>
<tr>
<td>q</td>
<td>quartet (spectral)</td>
</tr>
<tr>
<td>rt</td>
<td>room temperature</td>
</tr>
<tr>
<td>s</td>
<td>singlet (spectral)</td>
</tr>
<tr>
<td>t</td>
<td>triplet (spectral)</td>
</tr>
<tr>
<td>TBAI</td>
<td>tetra-&lt;i&gt;n&lt;/i&gt;-butylammonium iodide</td>
</tr>
<tr>
<td>TBDMS</td>
<td>tert-butyldimethylsilyl</td>
</tr>
<tr>
<td>TfOH</td>
<td>trifluoromethanesulfonic acid</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethylsilyl</td>
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CHAPTER 1

Progress Towards a Total Synthesis of Polycavernoside A

1.1 Introduction

1.1.1 Polycavernoside A: Isolation and Structure

The discovery of the novel macrolide polycavernoside A (1, Figure 1) followed the illness of thirteen people caused by ingestion of the red alga *Polycavernosa tsudai* (formerly *Gracilaria edulis*) regularly collected and consumed on the beaches of Guam.\(^1\) Polycavernoside A was the first toxin identified, and the structure depicted in Figure 1 was proposed primarily on the basis of extensive NMR investigations.\(^2\) Shortly following the original report, a second publication appeared detailing the isolation and structural elucidation of four new structurally similar macrolides originating from the same alga produced annually for two years following the original appearance in 1991.\(^3\) Although the algal toxicity had declined in these two later years, the seasonal production allowed their isolation in vanishingly small quantities sufficient only for determination of their planar, nonconfigurational structures (Figure 1). The characteristic coupling patterns found in the monosaccharide components were relatively unchanged from those of 1, thereby allowing assignment of their relative configurational structures as shown with an acceptable degree of certainty. Although absolute stereochemistry was not determined, nor was an optical rotation reported, we have tentatively assigned the natural enantiomer as shown (*vide infra*).
Figure 1. Polycavemoside A and its congeners.
A detailed inspection of 1 and its congeners reveals significant structural deviation from known macrolides. The 3,5,7,13,15-pentahydroxy-9,10-dioxotricosanoic acid carbon backbone in 1 is unprecedented although the smaller trioxatridecane macrocycle is similar in principle to the trioxadodecane network found in aplysia toxins. The presence of an α-dicarbonyl moiety, as well as the lack of unsaturation within the macrolide ring are also atypical. The polyene tail that is conserved among all congeners (as a triene and diene in the A- and B-factors, respectively) may serve as a lipophilic "anchor" for attachment to a cell membrane. The relative relationships between substituents on the aglycon, and the presence and site of attachment of the sugar appendage are clearly reminiscent of the macrolide antibiotics. The algal origin of the
disaccharide, a unique molecular entity itself, is not surprising as judged by its high degree of methylation. It is reasonable to hypothesize that the variations in the disaccharide region of the polycavernosides contribute to the decreased toxicity of these algal constituents.

Our assignment of absolute stereochemistry is proposed on the basis of the Celmer model, a structural "road map" to macrolide stereostructure. The considerable structural homology between an "unravelled" view of polycavernoside A and the Celmer model (Figure 2) allows a tentative conclusion of the absolute configuration to be drawn. The assignment of
absolute stereochemistry for the monosaccharide subunits follows from the regularity of α-L and β-D glycosidic linkages in the macrolide antibiotics. It is worth mentioning that proponents of the Celmer model make no claim to its universal application, but the similarity between the model and the case at hand supports this "rational conjecture". The variations found in this case are not atypical and are therefore insufficient cause to abandon the method of comparison.

\[
\text{penicillin G}
\]

\[
\text{amphotericin B}
\]

**Figure 3.** Two structural classes of antibiotics and their representatives.

### 1.1.2 Antibiotics: Background and Significance

Antibiotics have found extensive use in the treatment of pneumonia, tuberculosis, dysentery, cholera, and other infectious mammalian ailments derived from bacteria and fungi. Since their practical introduction into medicine only a half-century ago, a respectable number of antibiotics have been formulated for clinical use. From a structural standpoint, antibiotics are represented by several different classes of organic molecules (Figure 3), including the penicillins.
Penicillin G and macrolides (amphotericin B). Whereas the penicillins have been thoroughly studied and synthetically modified to a point where they are easily produced, generally efficacious, and pose few adverse side effects, macrolide antibiotics are not as easily administered.

Penicillin antibiotics slow bacterial replication through inhibition of cell wall formation. The clinical success of the penicillins is largely due to their preference for bacterial cells over mammalian cells. Macrolide antibiotics, however, inhibit the cell's activities by disturbing the delicate equilibria of molecular transport into and out of the cell. A typical cell, which is comprised of an aqueous compartment isolated from an aqueous environment by a semipermeable hydrophobic membrane (Figure 4), maintains dynamic processes that are signs of its "life". The controlled shuttling of various molecules and ions across the hydrophobic membrane is a critical facet of healthy cells. Most cell toxins derive their adverse effects from their ability to disrupt one or more of these equilibria, resulting in a chemical imbalance and eventual cell death. It is believed that macrolide antibiotics fulfill this criterion by binding, for example, potassium ions (K^+) and transporting them across the hydrophobic membrane. This ability arises from their amphipathic nature; they exhibit hydrophilic regions that bind polar ions, in addition to lipophilic areas that

![Figure 4. A simplistic view of the cell and selected dynamic transmembrane processes.](image-url)
facilitate passage of the resulting complex through the hydrophobic membrane. Alternatively, channel-forming antibiotics (e.g., gramicidin D) actually span the length of the membrane, forming what is essentially an ion leak in the cell. For either mechanism, the net result is uncontrolled transport of substances between the cell interior and its environment, thereby resulting in cell death.9

1.1.3 Polycavernoside A: A New Benchmark for Antibiotic Research?

The high oral toxicity of 1 is actually quite unique among macrolide antibiotics. In fact, the minimal oral bioavailability of macrolide antibiotics (e.g., amphotericin B) is the factor perhaps most responsible for limiting their use in a clinical setting.10 It is conceivable that identification of the role of substituents in 1, particularly within the disaccharide, would shed light on those factors contributing to its efficacy. One cannot dismiss the valuable role that toxins have played in the past to elucidate events at the cellular level. The information from these studies oftentimes finds application to numerous areas of medical research, including oncology, neurology, and pharmacology. Unfortunately, polycavemoside A's utility as a probe of cellular events is currently limited by its scarcity.

From a synthetic standpoint, polycavemoside A contains a unique sugar constituted of two heretofore unreported monosaccharides. We are cognizant that the carbohydrate portion of many natural products is believed to be responsible for receptor interactions on the surface of the cell membrane. As suggested above, we expect to be eventually in a position to synthesize 1 and both known and unknown congeners for comparison of activity. Modifications in the disaccharide may elucidate the requirements for efficient and perhaps more bacterially selective receptor recognition.
The ultimate goal of this research is the synthetic acquisition of polycavernoside A and structurally important analogs, all of which are currently unavailable from any source. The ancillary desire is to confirm the proposed relative and absolute configuration of 1. These molecules, by virtue of the potent biological response they elicit, may be used initially to probe the mechanism of action of the polycavernoside class of molecules. Such an endeavor, of course, must begin with an efficient total synthesis. The evolution of our successful construction of the disaccharide subunit is the basis for the ensuing discussion.

1.1.4 Synthetic Approach to Polycavernoside A: The Disaccharide Component

Our approach\textsuperscript{11,12} to this unique macrolide begins with a typical, yet convergent disconnection at the aglycon-disaccharide bond linkage (Figure 5). Control of the xylopyranose anomeric configuration is to be achieved by implementation of either the Koenigs-Knorr
protocol\textsuperscript{13} or similar conditions designed to create a $\beta$-linkage to the aglycon. Anchimeric assistance is not an option here since it is our intent to attach a fully functionalized disaccharide, if possible. The second glycosidic linkage will be the next target for disconnection, thereby rapidly simplifying matters to the individual functionalized monosaccharides. The plethora of techniques reported to give the $\alpha$-configuration present at the (1$\rightarrow$4)-disaccharide linkage should render this bond formation routine. The xylose-derived component 3 should be accessible from commercially available 1,2-O-isopropylidene-$\alpha$-D-xylofuranose (5) or D-xylose (6) itself. The second monosaccharide is expected to be available from natural L-fucose (7) via a standard series of protection/deprotection steps.

1.2.1 Synthesis of Glycosyl Acceptors Derived From L-Fucose

An allyl functional group was chosen as the protection of choice for the anomeric center, owing to its reported ease of removal under numerous mild conditions. Hence, L-fucose was stirred in warm allyl alcohol in the presence of a catalytic amount of acid to give crystalline triol 8 (Scheme 1). Protection of the cis-vicinal diol at C(3) and C(4) as the isopropylidene\textsuperscript{14} gave carbinol 9 in which the singular hydroxyl could be methylated prior to acidic hydrolysis of the acetonide to give 11 in excellent overall conversion (93%, 3 steps). The stannylene acetal\textsuperscript{15} derived from 11 efficiently mediated regioselective protection of the equatorial hydroxyl to access 12, a proper candidate for alkaline protection of the remaining hydroxyl as a benzyl ether. The regioselection observed in the former step was evident from the $^1$H NMR spectrum of the $\beta$-anomer in which the sharp H(3) absorption (dd, $J = 10, 3$ Hz) and broad nature of H(4) supported the assignment accorded to 12. Additionally, the hydroxyl proton in the $\alpha$-anomer was readily visible and its common coupling ($J = 4$ Hz) with H(4) supported the configuration assigned to the 2,3-di-O-methyl isomer 12. The anomeric center was subsequently either deprotected and transformed to glycosyl acceptors 14a-d,\textsuperscript{16} or transformed directly to thioglycoside 14e\textsuperscript{17} and
Scheme 1. Synthesis of first-generation glycosyl acceptors derived from L-fucose. Reagents and Conditions: (a) CaSO₄, H₂SO₄, allyl alcohol, 80 °C (88%); (b) 2,2-dimethoxypropane, PTSA (cat), benzene; (c) NaH, CH₃I, DMF; (d) PTSA (cat), CH₃OH:H₂O (30:1) (93%, 3 steps); (e) (i) n-Bu₂SnO, CH₃OH; (ii) CsF, CH₃I, DMF (76%); (f) NaH, BnBr, TBAI (cat), DMF (99%); (g) 13, PdCl₂, NaOAc, 95% AcOH (aq), 60 °C (96%); (h) 14a, (COCl)₂, DMF; (i) 14a, Cl₂CCN, K₂CO₃, CH₂Cl₂ (96%); (j) 14a, n-BuLi, (PhO)₂POCl, THF; (k) 13, PhSSi(CH₃)₃, ZnCl₂, TBAI, (CH₂Cl)₂, 80 °C (67%); (l) 14e, DAST, NBS, CH₂Cl₂, 0 °C (100%).

then glycosyl fluoride 14f. Glycosyl acceptors 14a-f were each formed in good yield, although 14b and 14d were too hydrolytically unstable to characterize fully. Interestingly, trichloroacetimidate 14c was formed solely as the β-anomer.

1.2.2 Synthesis of Glycosyl Donors Derived from D-Xylose

Our starting point for the second monosaccharide initially took the form of commercially available 1,2-O-isopropylidene-α-D-xylofuranose (5) which was, through a series of classical
Scheme 2. Synthesis of glycosyl acceptors derived from D-xylose. Reagents and Conditions: (a) Ph₃CCl, TEA, DMAP (cat), DMF; (b) 15a, NaH, BnBr, TBAI, DMF; (c) 15b, PTSA, CH₃OH-Et₂O-H₂O (100:10:1) (81%, 3 steps); (d) (i) 15c, 60% AcOH (aq), 80 °C; (ii) CaSO₄, H₂SO₄ (cat), allyl alcohol, 80 °C; (e) NaH, CH₃I, DMF (49% from 15c); (f) Na, NH₃(l) (100%); (g) CaSO₄, H₂SO₄, (cat), allyl alcohol, 80 °C (41%).

protection/deprotection steps, transformed into primary carbinol 15c (Scheme 2). Sequential treatment of 15c with warm aqueous acetic acid and warm acidic allyl alcohol delivered diol 16 as a 1.7:1 mixture of α- and β-anomers. Our choice of an allyl group for protection of the anomeric position was motivated by those principles stated earlier. Care must be taken to monitor the equilibration process and subsequent glycosylation so as to achieve maximum production of the pyranose isomer. At least one H(5) proton in each anomer was sufficiently isolated at 300 MHz to be diagnostic of stereochemistry via its coupling constants (J₅eq (α) = 12, 5 Hz and J₅ax (β) = 12, 10 Hz), which showed no sign of broadening by a free hydroxyl. Bismethylation of diol 16 gave fully protected xylopyranose 17, which delivered reducing sugar 18 when subjected to the action of sodium in ammonia. The susceptibility of the allyl glycoside to cleavage during dissolving metal reduction proved deleterious to overall efficiency, and reprotection of the anomeric hydroxyl using the usual protocol gave glycosyl donor 3 in a total of seven steps (five steps from 15c, 20% yield).
For the sake of comparison and in an attempt to develop a more practical synthesis of 3, carbinol 15c was hydrolyzed and equilibrated to the xylopyranose form prior to glycosylation with methanolic hydrochloric acid (Scheme 3). The crude methyl glycoside was next exhaustively methylated and reductively debenzylated to afford carbinol 19 in which the free hydroxyl resides at the desired position of glycosylation as before. Carbinol 19 was warmed in acidic allyl alcohol to deliver carbinol 3 in a series of five steps (62% overall yield from 15c).

Scheme 3. Alternative synthesis of D-xylose-derived monosaccharide 3. Reagents and Conditions: (a) (i) H$_2$SO$_4$ (cat), 80% CH$_3$OH (aq), reflux; (ii) CH$_3$OH:HCl (19:1), reflux; (iii) NaH, CH$_3$I, DMF; (iv) H$_2$ (50 psi), 10% Pd/C (76%, 4 steps); (b) CaSO$_4$, H$_2$SO$_4$, (cat), allyl alcohol, 80 °C (81%).

1.2.3 Initial Studies of the Monosaccharide Coupling

Scheme 4. Initial attempts to couple L-fucose- and D-xylose-derived monosaccharides. Reagents and Conditions: (a) 14c or 14d, TMSOTf, CH$_2$Cl$_2$. 

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Despite the seemingly large and varied supply of glycosyl acceptors we had collected, their coupling to 3 was entirely unsuccessful (Scheme 4)\(^{20}\). In most cases, 3 could be recovered unchanged while the activated glycosides 14 merely decomposed. A clue to the problem at hand came in the form of the production of 13 in two circumstances and suggested that the anomeric allyl protecting group for the xylopyranose fragment was more labile than had previously been expected. To test this hypothesis, we attempted the glycosylation of 14e with a xylopyranose carrying a different group at the anomeric carbon.

A more expeditious route to 14-20 took advantage of the selectivity with which D-xylose undergoes controlled acetylation (Scheme 5). Using the Utille and Gagnaire\(^{21}\) protocol, we were unable to improve the efficiency of this reaction (21%) in relation to that realized in the developmental stages. The inexpensive nature of D-xylose, however, and the ease with which

\[ \text{D-xylose (7)} \xrightarrow{a} \begin{array}{c} \text{AcO} \\ \text{HO} \\ \text{AcO} \\ \text{OAc} \end{array} \xrightarrow{b} \begin{array}{c} \text{AcO} \\ \text{HO} \\ \text{AcO} \\ \text{SPh} \end{array} \xrightarrow{c} \begin{array}{c} \text{AcO} \\ \text{BnO} \\ \text{OAc} \\ \text{OAc} \end{array} \xrightarrow{d} \begin{array}{c} \text{AcO} \\ \text{HO} \\ \text{AcO} \\ \text{SPh} \end{array} \]

Scheme 5. Two syntheses of glycosyl donor 21. Reagents and Conditions: (a) Ac\(_2\)O (3 eq), py, -35 °C (21%); (b) PhSSi(CH\(_3\))\(_3\), SnCl\(_4\), BF\(_3\)OEt\(_2\), benzene (66%); (c) (i) 50% aq AcOH, 100 °C; (ii) Ac\(_2\)O, py, DMAP (cat) (85%, 2 steps); (d) H\(_2\) (1200 psi), 10% Pd/C (cat), CH\(_3\)OH (96%).
the hydroxyl at C(3) was differentiated from the remaining equatorial hydroxyls were sufficient compensation for the low yield. Triacetate 20 was further manipulated to the more chemically versatile thioglycoside 21 without event. In order to demonstrate a more efficient approach to 20, 15c was hydrolyzed and equilibrated from the resulting xylofuranose to the reducing pyranose. Two additional steps were necessary to produce triacetate 20 as a mixture of anomers in 66% overall yield from 5.

When the α-anomer of triacetate 20 was stirred with 14e and N-iodosuccinimide, disaccharide 23 was retrieved in good yield (Scheme 6). This result appeared to confirm our previously described suspicion that the anomeric allyloxy group on the D-xylose fragment might be labile. We were also able to extend the success of this approach to thioglycoside 21. As such, fucopyranosyl fluoride 14f and glycosyl donor 21 were stirred with silver perchlorate and molecular sieves in dichloromethane for 15 minutes, after which the disaccharide 24 could be isolated from the resulting mixture in 87% yield.

Scheme 6. Synthesis of disaccharides 23 and 24. Reagents and Conditions: (a) NIS, 4 Å MS, CH₂Cl₂, TfOH (cat) (36%); (b) SnCl₂, AgClO₄, 4 Å MS, Et₂O (87%).
Figure 6. Final target monosaccharides.

1.3.1 A Second Generation Approach to Construct the Disaccharide

Clearly, we had several options to make the disaccharide linkage. As a result, our strategy was reevaluated based upon the chemistry described to this point, and a final generation of monosaccharides was targeted for synthesis and prepared for coupling (Figure 5). Thioglycoside 21, prepared in only two steps from D-xylose, remained the most promising candidate for incorporation into the disaccharide due to the latent versatility of the phenylthio functionality. Furthermore, a more efficient plan to exchange the acetates for methyls only after the 3-position had been "protected" as a glycoside was designed. Since our strategy was to incorporate 21 first into the disaccharide, saponify, and then methylate, the prospect for extension of this tactic to the fucose-derived monosaccharide seemed worthy of consideration. We were further enticed by the brevity with which we might access 25a-c relative to prefunctionalized glycosyl acceptor 26.

L-fucose (7) $\rightarrow$ a $\rightarrow$ H$_3$C O Ac TBSO OAc OAc H$_3$C O Ac TBSO OAc OAc b $\rightarrow$ H$_3$C O Ac TBSO OAc OAc H$_3$C O Ac TBSO OAc OAc c $\rightarrow$ H$_3$C O Ac TBSO OAc OAc

Scheme 7. Preparation of glycosyl acceptors 25a and 25c. Reagents and Conditions: (a) (i) Ac$_2$O, DMAP (cat), py; (ii) TBSOTf, imid, DMAP (cat), DMF, 60 °C (76%, 67% conversion); (b) PhSSi(CH$_3$)$_3$, BF$_3$*OEt$_2$, CH$_2$Cl$_2$ (86%); (c) DAST, BF$_3$*OEt$_2$, CH$_2$Cl$_2$ (91%).
The latter, although more laborious to access, was expected to be the most straightforward solution.

Glycosyl acceptors 25 were accessed relatively easily using standard chemistry as shown in Scheme 7. L-Fucose was treated with three equivalents of acetic anhydride to deliver a mixture of anomeric triacetates 27, contaminated with a small amount of peracetylated material. Treatment of the mixture with tert-butyl(dimethyl)silyl triflate in warm DMF gave anomerically homogeneous 25a in good yield. The regiochemistry of acetylation was undeniable after the chemical shift of H(4) (3.96 ppm) was compared with those of H(1), H(2), and H(3) (6.29, 5.44, 5.25 ppm, respectively). The transformation of 25a into thioglycoside 25b was effected with a mixture of (phenylthio)trimethylsilane and boron trifluoride etherate, and treatment of 25b with DAST/NBS in a separate step provided 25c as a mixture of anomeric fluorides.

The route to glycosyl fluoride 26 was somewhat more lengthy but followed our approach to 13 closely. L-Fucose was peracetylated and subsequently stirred with thiophenol and tin(IV) chloride to give triacetate 28 (Scheme 8). The C(1) isomers were separated at this point, and the...
β-anomer was individually advanced for reasons of practical simplicity. The acetates were saponified prior to protection of the vicinal diol, and methylation of the remaining hydroxyl at C(2) delivered 29. Preferential methylation of the hydroxyl at C(3) was mediated by the stannylene acetal, for which cesium fluoride served as the activating/cleaving agent of choice. Finally, silylation of the axial hydroxyl as before gave thioglycoside 31, which could be converted to a mixture of anomic fluorides in good yield (88%).

1.3.2 Coupling of the Second Generation Monosaccharides: Completion of the Disaccharide Component of Polycavernoside A

The expectation that 25a and 25c were effective glycosyl acceptors for 21 came to fruition when disaccharide 32 was successfully produced in both cases (Scheme 9). It was immediately obvious from inspection of the coupling constant for the fucosyl anomeric proton ($\Delta H(1) = 3.6$ Hz) that the disaccharide linkage consisted of the desired α-configuration. The diminished efficiency with which 32 is produced when using glycosyl fluoride 25c can be rationalized on the basis of the strength of the Lewis acid and the stability of the putative oxonium ion intermediate, which is highly electron deficient as a result of the acetates that adorn the fucose ring. The mechanistic details for both coupling processes are presumably similar, but the less

\[ \text{Scheme 9. Synthesis of protected tetra-O-acetyl disaccharide 32. Reagents and Conditions: (a) BF}_3\cdot\text{OEt}_2, 4 \text{ Å MS, CH}_2\text{Cl}_2, 0 \text{ °C (66%); (b) SnCl}_2, \text{AgClO}_4, 4 \text{ Å MS, CH}_2\text{Cl}_2 (87%).} \]
Lewis acidic activating agent (BF$_3$OEt$_2$) may enter into an equilibrium in which the oxonium ion is reversibly formed. Silver perchlorate, on the other hand, is more likely to abstract the fluoride irreversibly to produce the kinetically labile oxonium ion.

In the penultimate step, saponification of tetraacetate 32 led to a mixture of three major products as judged by thin layer chromatography. Although the separation of these three constituents was never attempted, it is reasonable to assume that they were isomers formed by a scrambling of the silyl ether at C(4) of the fucose ring with the hydroxyls at positions C(3) and C(2). This behavior could not be obviated in our hands despite efforts to employ numerous basic agents for the saponification.$^{28}$

We therefore turned our attention to the agency of pre-functionalized monosaccharide 26 to access the desired disaccharide. When an ethereal solution of glycosyl fluoride 26 was stirred with thioglycoside β-21 in the presence of molecular sieves, tin(II) chloride, and silver perchlorate, coupling product 34 was retrieved in good yield (Scheme 10). The coupling pattern for each of the hydrogens was consistent with structure 34, where the anomeric proton appeared at 4.88 ppm ($J = 3.4$ Hz) in the $^1$H NMR spectrum (C$_6$D$_6$). That acetate migration in the xylose ring had not transpired was confirmed by the chemical shift of H(2) and H(4) (5.27 and 5.02 ppm, respectively). The acetates of the xylose ring were then saponified, and the resulting free hydroxyls were methylated under basic conditions. A final confirmation of structure was achieved.

\[
\begin{align*}
26 + \beta-21 & \rightarrow a \quad 34 \\
            & \rightarrow b \quad 35
\end{align*}
\]

**Scheme 10.** Synthesis of fully protected tetra-O-methyl disaccharide 35. Reagents and Conditions: (a) SnCl$_2$, AgClO$_4$, Et$_2$O (57%); (b) (i) KOH, CH$_3$OH; (ii) NaH, CH$_3$I, DMF (84%).
using the semi-selective DEPT-45 experiment\textsuperscript{a} in which a clear $^3$J$_{HC}$ could be observed between methoxy carbons and both H(2) and H(4). Furthermore, irradiation of H(3) resulted in enhancement of the anomeric carbon C(1') of the fucose ring.

Simultaneous with the completion of our work, Murai and coworkers reported the coupling of a similar disaccharide (C(4') = OBn) carrying a thiophenyl group at C(1) with models of the aglycon pyran ring. According to their work, the $\beta$-configuration is formed preferentially in a single step (66%), despite the lack of any assistance from the substitution at C(2).\textsuperscript{30} Thus, our current focus is the completion of the aglycon of polycavemoside A.

1.4.1 Conclusion

We have developed a reasonably efficient synthesis of the disaccharide subunit of polycavemoside A. An attempt to couple two bisacetylated precursors was successful, but facile silyl group migration upon saponification of the esters obstructed the completion of what would have been a relatively expedient synthesis of the tetra-O-methyl protected disaccharide. The successful tactic employed a fucose phenylthioglycoside as a latent glycosyl acceptor. More importantly, the knowledge derived from the above chemistry will allow the synthesis of additional variants of the disaccharide for use in studies that elucidate the mechanistic role of the sugar. Such studies, however, await the completion of the aglycon and its coupling to the disaccharide in hand. These efforts will be reported in due course.\textsuperscript{31}
CHAPTER 2

Studies Toward a Total Synthesis of Taxol® (Paclitaxel) and Derivatives

2.1 Introduction

2.1.1 The Discovery and Identification of Taxol

As part of a NCI-sponsored search for antitumor natural products, Monroe E. Wall and M. C. Wani, working at the North Carolina Research Triangle Institute, isolated crude bark and wood extracts from the Pacific Yew (Taxus brevifolia) in 1963. Their interest was further magnified after
they discovered that these extracts were unusually general antitumor agents in various rodent assays. The incredibly low concentration (0.007%) of the active agent precluded its structural determination until these researchers and Andrew T. McPhail successfully crystallized a close derivative of the active component (10-desacetylbaccatin III), solved its X-ray crystallographic structure, and reported their results in 1971. They named the new chemical entity "taxol" (36a).

Following a period of eight years during which taxol research was plagued by supply and formulation complications, Susan B. Horwitz and co-workers reported that taxol acts in a mechanistically unique manner to disable tumor cells. Their results spawned renewed excitement about the natural product and stimulated the search for an alternative source. The quest for a purely synthetic source was joined by a massive number of researchers in both the United States and abroad, and by 1988, a total synthesis of taxusin (37), a structurally similar natural product, was reported by Holton and associates.

Our aesthetic appreciation for this unique molecular framework was spawned by the level of steric congestion present in the natural product and even partially deprotected derivatives (e.g. Figure 7. Stereoview of a partially deprotected taxol molecule illustrating the resident steric congestion.)
Holton et al., 1994, ca. 38 steps

Nicolaou et al., 1994, ca. 40 steps

Danishefsky et al., 1996, ca. 47 steps

Wender et al., 1997, ca. 38 steps

Figure 8. Starting materials and general strategies for successful total syntheses of Taxol.

A, Figure 6). The steric crowding that results from the high degree of oxygenation is further compounded by the bridged nature of the ring system, which effectively pulls the backbone
carbons and functionality with which they are adorned even closer. Steric congestion is therefore an unavoidable issue that must be addressed by any synthetic approach, particularly as intermediates increasingly resemble 36a.

The call to complete a total synthesis of taxol went unanswered until recently when four research groups over a period of three years published their successful efforts (Figure 7). These synthetic feats are indeed respectable accomplishments since the natural product poses challenges synthetically heretofore unseen in a single molecule. But each route fails to answer the call for an efficient, practical source of the natural product particularly due to their excessive length. Aside from an overall exhausting synthetic process, additional complications can be found in these approaches that limit their overall practicality, such as the need for a late-stage resolution in the Nicolaou synthesis.

The research described herein attempts to address the deficiencies of those reported syntheses of 36a, particularly the issue of length, while also offering a viable route to currently inaccessible but medicinally important analogs of 36a. 1-Deoxytaxol (36b) and the isomer of 36a where the oxetane is stereochemically inverted (38) are representative of the latter. Interest in these two congeners was stimulated by the discovery that Taxol's biological effects are very sensitive to changes along its southern "rim". Conversely, its activity was generally tolerant to modifications along the northern edge. The importance of the C(1) hydroxyl and C(2) benzoate for hydrogen bonding to microtubule subunits has been proposed on the basis of X-ray crystallographic data for 36a but remains to be confirmed by experiment. Although we make no claim to a total synthesis of 36a at the present time, the most pressing problem encountered to-date in the Paquette approach has been addressed while optimizing several aspects that would have unnecessarily protracted our efforts.

2.1.2 Previous Work

The pursuit of taxusin, taxol, and select derivatives thereof in this group has existed for approximately ten years. Over this period of time, numerous papers have been published by the team that document the general viability of the oxy-Cope/pinacol rearrangement as a strategy to construct the taxane backbone. Additionally, the ability to install various functionality about the backbone has been demonstrated, albeit in a typically modular fashion. It was not until recently that these tactics have been converged in an attempt to produce the fully functionalized taxane framework.

One significant change in strategy was recently made and has physically modified the playing field for the construction of the taxane congeners via the Paquette approach. In 1995, postdoctoral associates Simon Bailey, Francis Montgomery, and T. Z. Wang developed an aldol approach for the annulation of ring C (Scheme 11). This work detailed an enantioselective eleven-step synthesis of C-ring synthon 40 from D-mannitol and a method for its amalgamation
with the camphor building block. Beyond this point, they demonstrated a relatively expedient manner in which this adduct could be transformed into the taxol backbone where greater than 70% of the oxygenation is present after a total of 21 steps. They were unable, however, to install the C(2) oxygen at any point during the synthesis.

Our efforts to retain the newly developed oxy-Cope / aldol C-ring annulation / α-ketol bridge migration strategy while incorporating all of the necessary oxygenation prior to the bridge migration are described in the following pages. Perhaps most importantly, one should recognize the importance of understanding the topologies found in the various intermediates en route to
the target molecule, as well as the definitive role that steric congestion plays. It is only through the indirect elucidation of these factors that we have come to understand the chemistry applicable to these intermediates, and have recently begun to make rapid advances toward what we expect will be an efficient and expedient synthesis of taxol and its biologically important congeners.

2.1.3 Incorporation of C(2) Oxygenation Prior to the Sigmatropic Rearrangement

Paquette, Huber, and Thompson reported the first study of the ramifications of C(2) oxygen incorporation prior to the anionic oxy-Cope rearrangement as a part of their approach (Figure 8). Their findings demonstrated the sensitivity of the sigmatropic rearrangement kinetics to the relationship between the stereochemistry of both the enol ether double bond and the sp3-hybridized carbon destined to become C(4). These results were interpreted on the basis of the transition state conformations necessary for the sigmatropic rearrangement to transpire. Specifically, those arrangements in which the methoxymethyl ether could be projected away from the center of the six-membered chair transition state (viz. 44a and 44b) were shown to be effected under relatively mild conditions, whereas their epimeric counterparts 46a and 46b required either elevated temperature (46a) or a prolonged reaction time (46b) in order to coerce [3,3] sigmatropy.

Despite this earlier work, we remained cautiously optimistic that carbinols 49 (Scheme 12) would undergo the prescribed rearrangement once the appropriate conditions were developed. Notable differences between this candidate and those reviewed above include the more highly substituted nature of C(4) and the conformationally less restricted character of the C-ring synthon. The aforementioned vinyllithium 40 was formed in situ by combining the precursor vinyl iodide with ketones 48 individually and treated as such with n-butyllithium. Each adduct was next subjected to various basic conditions intended to promote sigmatropic rearrangement, but only triene 50 in which the acetonide had been eliminated could be recovered from 49a.44 Only.
when KHMDS was rapidly added to a chilled solution of 49b and 18-crown-6 could products 51a and 51b, both the result of sigmatropic rearrangement, be isolated. Unfortunately, elimination of the acetonide could not be circumvented, and it appears that this event precedes the desired oxy-Cope rearrangement. The lability of the acetonide was entirely unexpected in light of the stability of 41 and 42 to the presence of excess base. It was our conclusion that the steric compression generated as C(2) and C(3) begin to enter into a bond-forming process (A, Figure 9) is sufficient to slow the rearrangement to the extent that the elimination process dominates. It is

\[
\begin{align*}
\text{H}_3\text{C} & \quad - \quad \text{CH}_3 \\
\text{OMOM} & \quad \text{OPMP} & \quad \text{OPMP} & \quad \text{OMOM} \\
48\text{a}, (Z)-\text{OPMP} & \quad 48\text{b}, (E)-\text{OPMP} & \quad 49\text{a}, (Z)-\text{OPMP} & \quad 49\text{b}, (E)-\text{OPMP} \\
\end{align*}
\]

Scheme 12. Effect of C(2) oxygen on sigmatropic rearrangement with C-ring synthon 40. Reagents and Conditions: (a) 40, Et_2O, -78 °C (49a, 34%, 49b, 29%); (b) 49a, KHMDS (3 eq), 18-crown-6, THF, -78 °C, then CH_3I (52%); (c) 49b, KHMDS (5 eq), 18-crown-6, THF, 0 °C (51a, 55%, 51b, 14%).

only after C(4) is transformed from a tetrahedral sp^3 to a planar sp^2 geometry (B, Figure 9) that rearrangement becomes a thermodynamically favorable process. It remains unclear, however,
why the side chain undergoes elimination so easily prior to rearrangement, but appears to be less prone to this destructive manifold thereafter. Perhaps the hydrogen being abstracted lies close to the alkoxide derived from 49 as a direct result of the side chain conformation. This situation may give rise to an *intramolecular* elimination manifold otherwise unavailable following rearrangement.

### 2.2.1 Oxygen Surrogates for the Anionic Oxy-Cope Rearrangement

Our need for an oxygen protecting group that is sufficiently stable to incorporation into the camphor substructure yet reasonably labile to cleavage once the adjacent carbon has been effectively reduced to the alcohol oxidation state remained unaddressed. We therefore turned to alternative tactics that were less direct in their approach, but decompressed the area between C(2) and C(4) relative to the situation existing in 49. Although various methods exist to convert keto aldehyde 52 to allene 53a (Scheme 13), and allenés have been shown to participate in the desired [3,3] sigmatropy, it was predicted that the resulting triene would lack sufficient orthogonality to allow chemoselective transformation of the exo-alkene into a carbonyl. We therefore turned our attention to the sterically less demanding methoxy and methylthio substituents in the S,O-ketene acetal 53b, which could be formed in an unoptimized 33% yield from 52. The coupling of vinyl lithium 40 with 53b delivered camphor derivative 54a, the
Scheme 13. Synthesis of possible precursors to a C(2) oxygenated intermediate. Reagents and Conditions: (a) \((\text{EtO})_2\text{P(O)CH(OCH}_3\text{SCH}_3\), tert-BuLi, THF (33%); (b) \(\text{Ph}_3\text{PCH}_2\text{SPh}, \text{KHMDS}, \text{THF}, 0 \, ^\circ\text{C} \) (Z-53c, 63%, E-53c, 21%); (c) 40, 53b, Et\(_2\)O; (d) 40, 53c, Et\(_2\)O (85%); (e) KHMDS, 18-cr-6, THF, -78 \, ^\circ\text{C}, then CH\(_3\)I (80%).

Theoretical precursor to rearrangement bicycle 55a in which the S,0-acetal could be unmasked to a carbonyl under a variety of conditions. Despite the lability of 53b, ketone 54a was obtained as a mixture of stereoisomers contaminated with its co-polar precursor. Although several attempts were made to effect the rearrangement, the desired product was never isolated in a pure state.

The highly substituted nature of the bonding carbons in 49 and 54a, and the resulting generation of steric strain in the anionic oxy-Cope transition state, was deemed the significant factor preventing rearrangement. As a result, we hypothesized that the increased sulfur-carbon bond length relative to that between oxygen and carbon may lessen the congestion between groups associated with C(2) and C(4). And with the accessibility of thiophenyl enol ether 53c, our investigation into the use of sulfur as an oxygen surrogate was launched. To this end, keto
aldehyde 52 was chemoselectively alkylidenated with triphenylphosphonium phenylthiomethylide under basic conditions. The resulting Z-enol ether that was produced preferentially \((Z:E = 3:1)\) could be efficiently coupled with vinylolithium 40 to provide 54b. This adduct, when subjected to the action of base at low temperature and then methyl iodide, routinely delivered the desired rearrangement product 55b in high yield (80%). The configuration of the methyl at C(4)\(^47\) was assigned on the basis of NOE enhancements of later derivatives. The ease with which 54b undergoes [3,3] sigmatropic rearrangement is notable, and is attributable to the aforementioned increase in carbon-sulfur bond length or a potential stereoelectronic contribution from sulfur. Our experience suggests that a combination of these factors is responsible, although the latter may impose slightly more influence (vide infra). With ketone 55b in hand, the stage was set to explore tactics to effect ipso substitution of the phenylthio moiety with oxygen. At the outset, the thiophenyl functional group appeared particularly well-suited for this goal, since there exists a plethora of techniques for substituting oxygen for sulfur, both directly and indirectly. Various strategies may be envisioned for the other sulfur oxidation states as well.

2.2.2 Exploration of the Chemistry Surrounding the 6-(Phenylthio)bicyclo[6.2.1]undec-7-en-3-one Ring System

Allylic alcohol 56 was delineated as an immediate synthetic target (Scheme 14), since dihydroxylation of the endocyclic alkene would deliver a triol in which the hydroxyl functional groups could be suitably protected. An intermediate of this type would then be prepared for advancement as before to the bridge-migration product analogous to 43 where C(2) would now be oxygenated. Theoretically, the sulfoxide 57, made available by treatment of 55b with a single equivalent of \(m\)-CPBA, could undergo Mislow-Evans rearrangement\(^48\) to give 56 in a single step. Unfortunately, sulfoxide 57 readily underwent unimolecular elimination to triene 58, presumably due to the eclipsed alignment between the thiophenylsulfinyl moiety and the adjacent tertiary
Scheme 14. The chemistry of C(2) phenylthio rearrangement product 55b. Reagents and Conditions: (a) m-CPBA (1 eq), NaHCO₃, CH₂Cl₂ (96%); (b) Δ, CH₂Cl₂ (62%); (c) 55b, m-CPBA (2 eq), NaHCO₃, CH₂Cl₂ (67%); (d) OsO₄, py, then Na₂S₂O₄; (e) 55b, m-CPBA (3 eq), NaHCO₃, CH₂Cl₂ (78%).
hydrogen. This facile manifold of decomposition preempted all attempts to effect either Mislow-
Evans or Pummerer-type rearrangements aimed at an internal transfer of oxidation state from
sulfur to the adjacent carbon; such a process would access derivatives akin to 55a.

We then turned to the sulfone oxidation state where the sulfur would be "protected" from
the oxidizing nature of osmium tetroxide, the prime factor obviating all attempts to dihydroxylate
55b. While the sulfur was indeed generally inert to the action of osmium(IV), the nascent diol
appeared to undergo transannular hemiketalization to form pyranose 60. All attempts to prevent
this process by immediate treatment of the crude diol with tert-butyldimethylsilyl chloride were
unsuccessful in returning the desired protected carbinol. Additionally, evidence was uncovered
that suggested competing oxidation at the less-hindered terminal alkene contributed to the
complexity of the reaction mixtures.

The allylic nature of phenylsulfone 59 presented a third parallel level of oxidation state.
As such, epoxy sulfone 61 was produced efficiently via treatment of 55b with three equivalents
of m-CPBA. The resulting ketone was entirely inert and did not respond to various attempts to
effect either reductive elimination of the epoxy sulfone to give 56, or base-induced β-elimination
of the epoxide to give a vinyl sulfone that could potentially be reduced to the same compound.

The possibility that the carbonyl could be conflicting with either or both of these strategies
was briefly entertained, and ketone 55b was accordingly reduced with lithium aluminum hydride,
with addition occurring predominantly (11:1) to the α-face of the carbonyl (Scheme 15).
Relevantly, all compounds discussed here behave as if the major B-ring conformation oriented
the carbonyl "up". Interestingly, the resulting hydroxyl is sterically shielded to the extent that
when vigorous conditions were applied to effect its protection in one case, pentacycle 63 could
be isolated in modest yield. This presumably acid-promoted reaction manifold illustrates a
complication that occasionally surfaced when forcing conditions were applied to the phenylthio-
containing compounds. Allylic sulfide 62a was therefore oxidized directly to 64 and stirred in the
presence of amalgamated sodium. These conditions, designed to promote reductive elimination, simply deprotonated the alcohol instead, thereby heightening its nucleophilic character sufficiently to promote transannular epoxide ring opening. We were confident that an ether linkage had formed due to the three-bond coupling observed from H(7) to C(3) and H(3) to C(7). It was also apparent that a tertiary hydroxyl had been formed at the expense of the secondary hydroxyl and epoxide. Molecular models clearly show the close proximity of the ether linkage.
hydroxyl to the epoxide in 64. That this process was simply base-promoted was verified by
treatment of the carbinol with KHMS in dry tetrahydrofuran to give a product identical to that
observed above. The preservation of C(6) stereochemistry from 64 to 66 also suggests that the
hydroxyl is in fact opening the epoxide and not adding to vinyl sulfone 65a that could result from
initial base-promoted β-elimination of the epoxide. Treatment of pyran 66 with various stronger
bases to encourage such a process returned either unchanged starting material or products of
decomposition.

Although these strategies failed to access any intermediates that lay closer to a C(2)
 oxygenated substrate, they did indirectly reveal reactivity motifs that appear to be characteristic of
this ring system. First, the topology of 55b was such that the hydrogen situated on the same
carbon as the thiophenyl moiety was chemically inaccessible. Of particular note is the
observation, albeit only circumstantially via thin layer chromatography, that a diastereomERICally
pure sulfoxide 57 could be partially epimerized to a mixture of the diastereomERIC sulfoxides when
treated with trifluoroacetic anhydride and pyridine. The inference that may be drawn is that
although the sulfoxide oxygen and sulfur are accessible to electrophiles and nucleophiles,
respectively, the hydrogen adjacent to sulfur is shielded from intermolecular attack.

A second important observation is that the medium-sized bicyclic ring displays a
pronounced tendency toward transannular bond formation. Such a process is typically
interpreted as a means to relieve strain derived from non-bonded interactions by forming a
diatomic bond. In the present situation, this behavior is manifested in the tendency of oxygen on
either the northern or southern B-ring rim to behave as a nucleophile in conjunction with an
electrophilic site on the opposite edge (recall the formation of 60 and 65). This behavior is well
documented in more rigid ring systems of this type, but appears to occur with equal facility here.
With an awareness of these two characteristics, we sought to modify our approach to the problem
at hand.
2.2.3 A Novel Intermolecular Displacement of Activated Allylic Sulfoxides With Weakly Nucleophilic Species

It was decided that the sulfoxide chemistry should be revisited, despite its penchant for thermal elimination. The motivation was the idea that the Pummerer oxidation-reduction strategy might succeed if the base necessary to abstract H(6) was situated within the molecule (see 64→66). That is, although the topology of the medium ring sterically prevented intermolecular deprotonation, intramolecular deprotonation may still be feasible. Furthermore, our system seemed well suited to this strategy since carbinol 67 contained a Lewis basic hydroxyl function that appeared quite near H(6) when models were inspected (Figure 11). Finally, the hydroxyl could potentially add to the intermediate sulfenium ion once formed to give transannularly O,S-acetal 68. The latter was predicated on the propensity of this hydroxyl to bond as in 64. We were not unaware that the success of this process would be tempered by the degree of strain present in 68 which was difficult to predict accurately from the outset.

In the event, when sulfide 62a was treated with buffered peroxyacid, the sulfoxide 67a was produced in good yield, with a single unidentified by-product constituting 20% of the crude
mixture (Scheme 16). This mixture of sulfoxides, which was equally prone to thermal elimination as before, was then subjected to the action of trifluoroacetic anhydride and pyridine. Upon

Scheme 16. Uncovering the sulfoxide displacement reaction. Reagents and Conditions: (a) m-CPBA (1 eq), NaHCO₃, CH₂Cl₂; (b) (CF₃CO)₂O, CH₂Cl₂ (62a→69a, 53%); (c) (CF₃CO)₂O, py, CH₂Cl₂ (62a→70a, 55%); (d) DDQ, H₂O, CH₂Cl₂ (79%); (e) Dess-Martin periodinane, CH₂Cl₂ (100%); (f) K₂CO₃, CH₃OH (62a→72a, 35%; 62b→72b, 23%); (g) CH₃COCls (xs), CH₂Cl₂ (11% from 62a).
workup, a product (70a) could be isolated whose spectral characteristics clearly revealed that the thiophenyl moiety had been excised, leaving a pair of alkene carbons in its wake. The coupling for the protons attached to these two carbons suggested that they were situated adjacent to one another and together formed a Z-alkene ($J_{HH} = 12.1$ Hz). Furthermore, one proton of the pair was flanked by a quaternary carbon, but the other was coupled to a tertiary proton. More extensive decoupling experiments revealed that the remaining portion of the molecule was unchanged. Interestingly, it appeared that the quaternary carbon adjacent to C(7) carried an oxygen atom, as evidenced by the presence of an absorption at 96.6 ppm (CDCl$_3$) in the $^{13}$C NMR spectrum.

Despite these reasonable assignments, there remained a few uncertainties associated with chemical shifts in the $^1$H NMR spectrum. Namely, the deshielded nature of H(3) (5.29 ppm, CDCl$_3$) could not be unambiguously assigned to the presence of a trifluoroacetate on the attached oxygen since the carbons associated with the fluorinated ester could not be clearly identified in the $^{13}$C NMR spectrum, presumably due to extensive coupling to fluorine. Furthermore, the lack of any hydroxyl absorption in the IR spectrum led us to question what group might be attached to the bridgehead oxygen. These ambiguities led us to single-crystal X-ray diffractometry for corroboration.

The oily nature of 70a prevented direct examination, but its treatment with DDQ effected removal of the p-methoxybenzyl protecting group to give secondary carbinol 70b as a crystalline solid. The NMR spectra of 70b suggested that no additional chemical events had transpired beyond removal of the benzyl ether. Fortunately, crystals of 70b could be grown from ethanol that were suitable for crystallography, the result of which is the three-dimensional diagram shown in Figure 11.
Figure 12. Computer generated drawing of the final X-ray model of 70b.
2.2.4 Examination of the Crystal Structure of 70b: Structural and Conformational Aspects

The X-ray crystal structure provided information well beyond simple structural identification; many of the structural and stereochemical assignments made previously on the basis of NMR data could be unambiguously confirmed at this point. The immediate information garnered was that the bridgehead carbon had indeed been oxygenated, and that both B-ring hydroxyls were protected as trifluoroacetate esters. The Z-geometry of the endocyclic olefin was also clearly in evidence. The configurations of the hydroxyl at C(3) and the methyl at C(4) substantiate earlier assignments that were based upon NOE enhancements.

The conformation adopted by the B-ring results in an exo projection of the endocyclic olefin; the α-face is therefore that open to attack since the northern rim of the B-ring effectively shields the β-face. This fortuitous circumstance would allow setting of the C(6) oxygen stereochemistry in the correct (taxol) configuration via dihydroxylation of the alkene.

A final aspect worthy of comment is the conformation of the side chain in the solid-state. The three-dimensional structure reveals that the side chain, which projects from the β-face of the B-ring, actually curls around to orient the terminal alkene below the plane of the B-ring, proximal to the α-face of C(4) where the C-ring will be closed in an intramolecular aldol reaction. Although any conclusions drawn regarding this somewhat flexible alicyclic chain are mitigated by the lack of a protecting group at the side chain oxygen and the uncertain extent to which crystal packing forces change the chain conformation relative to that in solution, NOE data for several intermediates support such a conformation.

2.2.5 The Allylic Sulfoxide / Allylic Trifluoroacetate Transformation: A Brief Inspection of Mechanism

Scrutiny of the sulfoxide/TFAA/pyridine reaction revealed that 69a could be isolated as the major product when pyridine was omitted from the reaction sequence, thereby suggesting that the aromatic amine's role was limited to assistance with protection of the hydroxyl at C(3). The
ready accessibility to this hydroxyl, which was somewhat unexpected due to resistance exhibited by 62a toward protection, was further demonstrated by oxidation to ketone 71 using the Dess-Martin periodinane\textsuperscript{51}. While attempting to optimize the reaction sequence, it was found that benzene, dichloromethane, and chloroform are the solvents of choice, whereas THF, ether, and acetonitrile give little or no 69a. When using dichloromethane, the reaction was instantaneous at -78 °C, although elevated temperatures (0 °C) gave similar results.

In order to explore indirectly whether the allylic trifluoroacetate was formed via an intramolecular or intermolecular mechanism, the sulfoxide was treated with trichloroacetic anhydride and trichloroacetyl chloride in two separate experiments. Both reactions led to major products that lacked a thiophenyl group while displaying the characteristic B-ring olefin absorptions in their respective \textsuperscript{1}H NMR spectrum. These two products, however, displayed slightly different spectra from 69a, suggesting that the allylic bridgehead carbons were differently substituted. The situation was further clarified by isolation and full characterization of 73\textsuperscript{52} albeit in low yield, after extended treatment of 67a with acetyl chloride; removal of the methoxymethyl ether protecting group was not typically observed during these reactions. The conclusion that may be drawn is that the sulfoxide, after activation by acylation of the sulfoxide oxygen, is displaced in an \textit{S_{N}'} manner by a weakly nucleophilic counterion (trifluoroacetate, trichloroacetate, or chloride). The resulting Z-alkene geometry would suggest a concerted \textit{S_{N}'} displacement based on the conformation of the B-ring and the orientation of the phenyl sulfoxide, but the intermediacy of a tight ion pair cannot be discounted. To our knowledge, the only parallel to this reaction in the literature was reported recently where both activation and displacement events occurred \textit{intramolecularly} (Figure 12).\textsuperscript{53} It is important to note that subjecting the sulfoxide to Mislow-Evans rearrangement conditions ((MeO)\textsubscript{3}P, MeOH, Δ) resulted only in sulfoxide elimination; apparently, little or no equilibrium exists between the allylic sulfoxide and sulfenate ester. The
C(3) hydroxyl, which is projected toward the interior of the B-ring, was in some way initially believed to be responsible for the success of the reaction, since identical conditions failed to return any trace of the displacement products when applied to ketone 57. To test this hypothesis, carbinol 61b, obtained in limited amounts as the minor product from reduction of 55b, was subjected to the reaction sequence. Although the mono-trifluoroacetate 68b contained a persistent co-polar contaminant, saponification provided homogenous diol 71b, for which NOE studies confirmed the relative stereochemistry as shown. It is tempting to suggest that the carbonyl exerts a transannular electronic effect upon the allylic sulfoxide, thereby attenuating its propensity toward displacement, but the subtle conformational changes associated with a change in hybridization at C(3) from sp2 to sp3 could just as easily play a relevant role.

Ultimately, a one-pot process was developed for effecting the transformation. As such, the sulfoxide is chilled in dichloromethane and treated first with m-CPBA/NaHCO3 for one hour, followed by excess trifluoroacetic anhydride for 15 min and finally pyridine for a minimum of 15 min. The pyridine addition is not necessary for the success of the sulfoxide displacement reaction, but simply aids in purification and prevents any loss of material resulting from premature bis-acylation prior to introduction of the amine base. In our hands, the bistrifluoroacetate was
routinely saponified in a suspension of potassium carbonate in methanol. In this manner, diol 71a was consistently retrieved in an overall yield of 35% from sulfide 61a.

2.2.6 Attempts to Functionalize the Bicyclo[6.2.1]undec-2-ene-1,6-diol Ring System

With diol 72a in hand, the stage was set to apply our predetermined strategy for functionalization of the southern B-ring rim to the 1,2,3-triol by its treatment with osmium tetraoxide. We soon discovered that the terminal alkene was preferentially dihydroxylated, thereby necessitating prior conversion to 74 (Scheme 17). This triol was most expediently accessed directly from 70a. Unfortunately, triol 74 was found to be completely inert to even the most forcing dihydroxylation conditions (OsO₄, pyridine, reflux or permanganate-based oxidants), typically returning unchanged triol. After inspection of the stereoview for 70b (Figure 14), it is immediately obvious that an acetonide methyl is projected directly over the face of the B-ring olefin. This arrangement may reasonably explain the unreactivity of the endocyclic alkene. We had no reason to doubt that 70b was an accurate model for the conformation adopted by 74. One may further conclude that the β-face of the alkene is shielded by the northern rim of the B-

Figure 14. Stereoview of 70b drawn from X-ray diffraction coordinates.
Scheme 17. Functionalization of the olefinic bonds in 70a. Reagents and Conditions: (a) BH$_3$-THF, then NaOOH (54%); (b) m-CPBA (4 eq), NaHCO$_3$, CH$_2$Cl$_2$ (40%).

ring, the π-cloud being positioned essentially perpendicular to the plane of the ring. The net result is inaccessibility of the olefin to a large reagent such as osmium tetroxide. Although the mechanistic details of olefin osmylation remain in dispute, it is generally considered to involve either a [2+2] or [3+2] pathway, both of which require two atoms to bond simultaneously with, and therefore occupy the space immediately above, the olefin.

The obvious solution to this impasse, removal of the acetonide, was even less straightforward. Unfortunately, this protecting group was found to be stable to acidic conditions, resulting in the preemptive decomposition of 72a and most precursors tested. In only a single case (55b) was the acetonide removed successfully, but only after a cascade of electrophilic species had joined in bond formation (Scheme 18; cf. 62a→63). The β-configuration of the tertiary hydroxyl follows from observation of an NOE (4.9%, 5.6%) between H(5) and both endo hydrogens, H(9) and H(10). This assignment is also consistent with transannular attack of the bridgehead alkene on the "carbonyl-up" conformer.

Despite the lack of success in attempts to dihydroxylate 74, we hypothesized that a smaller reagent might successfully gain access to the olefin. In contrast to its inertness toward osmium tetroxide, the disubstituted alkene, when treated with m-CPBA, gave a triol whose spectrum was consistent with 75. Once again, the tendency for the medium-ring carbinol to
undergo transannular bond formation appeared to have resurfaced. Inspection of molecular models support the notion that the putative B-ring epoxide is conformationally predisposed toward opening by the relatively close C(3) hydroxyl, which is ideally situated for an \( S_N2 \) attack at C(6), analogous to the circumstances in 64. These events spawned a study of the feasibility to implement transannular epoxide ring opening as a means to functionalize the southern rim of the bicyclo[6.2.1]undec-2-ene ring system. The practical application of this strategy to a total synthesis of taxol would come to fruition late in the synthesis when the tetrahydrofuranyl ether bridge would be cleaved from a back-side carbonyl \( \alpha \) to the ether using samarium(II) iodide.\(^5^4\) Molecular models conclusively show that the plane of the carbonyl would be orthogonal to the C-O bond, as required for C-O fragmentation via a ketyl radical anion.

### 2.2.7 Transannular Bond Forming Processes Within the Bicyclo[6.2.1]undec-2-ene Framework

The two issues that we intended to address in planning this study included: (a) Could a free hydroxyl at C(2), C(3), and C(4) individually open the epoxide transannularly with comparable
facility? and (b) if so, how would the regiochemistry of the event vary as a function of hydroxyl position, if at all? Molecular models must surrender to preparative chemistry at this point, particularly due to the conformationally uncertain nature of the carbinols in question; the Curtin-Hammett principle was not to be overlooked. To this end, diol 72a was treated with excess m-CPBA (buffered) in dichloromethane at rt for several hours (Scheme 19). In this case, transannular epoxide ring opening occurred in situ to deliver 77a directly without the need for separate base treatment. The only additional products observed were the result of overoxidation at the terminal olefin. The behavior of 72a parallels and somewhat substantiates that observed with 74, since the latter was not fully characterized. Decoupling experiments clearly traced a path from the secondary hydroxyl proton to H(5) and along the northern edge to H(2). On the basis of these coupling motifs, it was clear that the ether bridge had formed at C(6) and the hydroxyl resided at C(7). The presence of the oxygen bridge between C(3) and C(6) was further substantiated by observation of a $^3J_{HC}$ from H(3) to C(6) and H(6) to C(3), using the long-range INEPT experiment.

Vicinal diol 77a was advanced toward the bridge migration step by oxidation using the Parikh-Doering protocol to give α-ketol 77b, which itself could be quantitatively converted to an isomeric acyloin upon treatment with aluminum tri(tert-butoxide). The thermodynamically-controlled α-ketol rearrangement can potentially result in two products (78a or 79) whose identity is determined by the adjacent bond that migrates (a or b, respectively). These two possibilities (only one produced here) are typically differentiated by $^3J_{HC}$ observed when a single geminal methyl at the bridgehead carbon is irradiated. In the present case, the product acyloin exhibited a heightened degree of kinetic anisotropy in the $^{13}$C NMR spectrum about the carbons of interest that prohibited detection of the necessary three-bond coupling. The carbonyl was therefore reduced to diol 78b which responded to the INEPT experiment; upon irradiation of a
Scheme 19. Transannular reactions of the bicyclo[6.2.1]undec-2-ene framework with an hydroxyl at C(3). Reagents and Conditions: (a) m-CPBA (3 eq), NaHCO₃, CH₂Cl₂ (75%); (b) SO₃-py, Et₃N, DMSO (84%); (c) Al(O-t-Bu)₃, benzene, 60 °C (100%); (d) LiAlH₄, Et₂O (70%).

geminal methyl at 1.21 ppm (CDCl₃), enhancement of a tertiary (not quaternary) carbon at 85.5 ppm was observed, a response characteristic only of 78b. Thus, the undesired bridge-migration product 78a had been produced to the exclusion of 79. Acyloin 77b was then subjected to the action of aluminum tri(tetra-butoxide) in benzene at room temperature to determine whether 78a was the kinetic migration product as well. Although the reaction was much slower, 78a was produced exclusively once again, thereby suggesting that it was both the kinetic and thermodynamic product.

Following the success of transannular epoxide ring opening with 72a, we sought the analogous system in which a free hydroxyl resided at C(2). It seemed less likely that the epoxide would be opened with ether formation at C(6). If the desired pyran would be formed by opening
of the epoxide at C(7), the resulting hydroxyl at C(6) would bear the correct configuration as in taxol, and protection could be easily effected. This arrangement also carried the advantage that the C-O transannular bond at C(2) was already adjacent to a carbonyl, thereby allowing an early test of the ease with which the samarium(II) C-O scission strategy would transpire. In the event, 72a was oxidized with the aid of the Dess-Martin periodinane, the methoxymethyl ether was cleaved with PPTS/t-BuOH, and the alkene was epoxidized as before (Scheme 20). In this case, transannular bond formation was not spontaneous under the epoxidation conditions, and when epoxy alcohol 81 was treated with potassium hydroxide in dimethyl sulfoxide, a completely unexpected cascade of events was set in motion. In preference to oxygen attack onto the epoxide the carbonyl was enolized, and the resulting carbanion opened the epoxide with complete regioselectivity to form the cyclopropane 82 (H(9), H(10) = 1.51, 1.83 ppm). The resulting C(7) hydroxyl lay in close proximity to the C(3) carbonyl, resulting in hemiketal formation as the final step of the process, as evidenced by the absence of the carbonyl absorption and appearance of a quaternary carbon at 105.8 ppm. Long-range INEPT experiments further supported the formation of the proposed transannular bonds. An attempt to effect the desired transformation with boron trifluoride etherate resulted only in deprotection of the p-methoxybenzyl ether. Inspection of molecular models shows that the line of attack necessary for the C(2) hydroxyl to close onto the epoxide may be blocked by the endo bridgehead methyl.

So as not to be diswayed by this anomalous behavior, we quickly proceeded to our final target for this study by oxygenating the C(4) carbon. Hydroxy ketone 80a and 18-crown-6 were stirred in chilled tetrahydrofuran while dry oxygen was bubbled through the solution (Scheme 21). Once the solvent was sufficiently oxygenated, potassium hexamethyldisilazide was added without disturbing the oxygenation process. Finally, the intermediate hydroperoxide had to be decomposed to the acyloin in situ by the addition of triphenylphosphine. The product mixture actually contained two primary products of α-oxygenation, diol 83a and its derivative in which the
Scheme 20. Transannular reactions of the bicyclo[6.2.1]undec-2-ene framework with an hydroxyl at C(2). Reagents and Conditions: (a) Dess-Martin periodinane, CH₂Cl₂ (91%); (b) PPTS, t-BuOH, 80 °C (70%); (c) m-CPBA (4 eq), NaHCO₃, CH₂Cl₂ (77%); KOH, DMSO (93%).

Bridgehead hydroxyl had been silylated (83b). The latter, which was the major constituent when the solvent mixture was not pre-saturated with oxygen, could be recycled in high yield to the desired diol with tetra-n-butylammonium fluoride. Failure to add the crown ether, or a lowering of the temperature beyond 0 °C were both detrimental to the production of 83a. The stereochemistry of hydroxylation was assigned on the basis of NOE experiments that included a 1.4% enhancement from H(6) to H(14). This configuration is also that expected on the basis of the E geometry of the intermediate enolate and its exo orientation, whereby attack of the α-face is possible as predicted by molecular models. The diol was then epoxidized using the usual conditions to furnish 84 in 96% yield.

Despite the fact that the hydroxyl was configured opposite to that which we desired, it was treated with potassium hydroxide in warm (50 °C) dimethylsulfoxide to return a more polar product in which the epoxide had indeed been opened. Decoupling experiments revealed a string of
couplings identical to that expected for a product in which the epoxide had been opened by an oxygen with the same regiochemistry as in the two previous cases (72a and 81). The remainder of the hydrogens in the molecule were found to be unchanged, with the exception of a highly deshielded methyl singlet, thereby suggesting its attachment to a carbonyl carbon. These observations are consistent with structure 85, the result of a ring-contracting pinacol-type rearrangement. Unfortunately, a trace of three-bond H,C couplings does not definitively confirm the formation of an oxetane as in 85, since the 3,4H,C through oxygen has a symmetrical
counterpart through carbon. Attempts to coerce this oil to crystallize were met with a general lack of success, and attempts to generate crystalline derivatives of 85 were similarly fruitless. Hydroboration of the terminal olefin, followed by an oxidative work-up, delivered two products (86 and 87) whose structures differed markedly. These two compounds were subjected to extensive NMR analysis, which conclusively affirmed the structural depictions as shown.\textsuperscript{58}

Despite the inability to develop 72a into a suitable taxol precursor, we have illustrated the atypical behavior of these medium-ring bicyclic systems. The successful incorporation of these intermediates into a total synthesis of any kind is limited by the facile transannular processes that typify their chemistry. Importantly, their application to a Taxol total synthesis requires the presence of oxygenation on both rims of the nine-membered ring, and these aberrant reaction manifolds may be circumvented only until an appropriate nucleophile-electrophile pair is revealed on opposing ring edges. The degree to which the bicyclic nature of 72a and its progeny contributes to the facility of these transannular processes remains unclear.

2.3.1 Examination of the Aldol C-Ring Annulation Strategy: Scope and Limitations

The chemistry described above provided a variety of intermediates that could be elaborated to the keto aldehyde necessary for C-ring closure via an aldol carbon-carbon bond-forming process. The first opportunity arose with the production of phenyl sulfide 55b. Treatment of the terminal olefin with disiamylborane, formed from borane-dimethyl sulfide and 2-methyl-2-butene, led to successful hydroboration of the alicyclic alkene to produce primary carbinol 88a (Scheme 22). A second entity, 89a, was produced as a minor product in which the boron species had subsequently added to the bridgehead alkene and eliminated via a four-center transition state in which a boron-sulfur bond was formed with the thiophenyl group. The formation of this compound could be encouraged to predominate with some variation in the reaction conditions.\textsuperscript{59} These two carbinols were successfully oxidized under Swem conditions to the
Scheme 22. Preparation of aldol annulation precursor ketoaldehydes. Reagents and Conditions: (a) disiamyl borane, THF, then NaOOH (88a, 64%; 89a, 5%); (b) Dess-Martin periodinane, CH$_2$Cl$_2$ (88b, 91%; 89b, 71%; 90, 77%).
keto aldehydes 88b and 89b. The latter keto aldehyde was believed to be a suitable model for
the behavior of its bridgehead-oxygenated analog 90 which was unavailable at the time. Some
time after acquisition of 88b and 89b, keto aldehyde 90 was successfully accessed as shown in
Scheme 22.

The first successful aldol annulation was achieved by Montgomery and Wang using keto
aldehyde 91 in which rotation about σ-bonds in the B-ring was restricted only by gauche and
transannular non-bonded interactions. Our intermediates were designed to test whether
unsaturation in ring-B could be tolerated. Keto aldehydes 88b, 89b, and 90 were subjected to
basic conditions at low temperature (0 °C) until consumption of the keto aldehyde was complete.
In the case of bridgehead olefin 88b, the product of oxoaldehyde β-elimination (93) was
efficiently produced without detection of any desired annulation product. The geometry of the
conjugated olefin was clearly E, as judged by the coupling between the vinyl protons (J = 15.7
Hz). As the olefin is moved from the bridgehead to a position of presumably diminished ring strain
as in 89b, the process of β-elimination still predominates, but two important differences are
observed. First, all product that results from β-elimination is funneled through a Z-α,β-unsaturated
aldehyde that allows the aldol process to occur. Secondly, the desired aldol annulation is now
competitive with the β-elimination manifold. The depressed yield of 94 was expected to be
remedied by optimization, which would be tackled later as a separate issue. Importantly, the
behavior of 89b was believed to be a harbinger for that of 90, a congener in which the
bridgehead hydrogen had been replaced with a free hydroxyl. These positive results
couraged us to retain the aldol methodology.

Once keto aldehyde 90 was in hand, it was subjected to the usual conditions of sodium
hydroxide in methanol, but β-elimination product 96 was surprisingly the sole product. Variations
of the conditions (base, temperature) failed to return any aldol product. The aldol reaction was
Scheme 23. The effect of B-ring structure on the aldol annulation of ring C. Reagents and Conditions: (a) NaOH (3 eq), CH$_3$OH-THF, 0 °C (90, 85%; 91, 77%; 92, 34%; 93, 26%).
also attempted with the aid of a Lewis acid (Sn(OTf)2, N-ethyl pyrrolidine, CH2Cl2), only to return a product in which the acetonide had been removed in good yield. The contrasting behavior of 89b and 90 underscores the sensitivity of the aldol process to subtle changes in B-ring structure. The likelihood that C-ring annulation can be effected while maintaining unsaturation in ring B appears to be marginal at best. The two processes that appear to be competing here are the rate of formation of the B-ring enol/enolate versus that of the side chain. It seems reasonable to assume that, once formed, the B-ring enolate will quickly close onto the aldehyde to form ring C. As such, our prime consideration for the aldol strategy was the relief of B-ring unsaturation that would slow enolization of the C(3) carbonyl. In order to address this limitation, a new strategy that might allow functionalization of the B-ring alkene was developed.

2.4.1 Development of a Second-Generation C-Ring Synthon Derived From D-Mannitol

We had become convinced that an acetonide methyl was preventing access to the B-ring alkene by any useful bis-oxygenating reagents. Since this protecting group was inert toward conditions designed for its removal, we sought to modify the protecting scheme. It was deemed undesirable to rework the entire side chain synthesis if a simple change of protecting groups could be exercised at some point along the synthetic route.

A second point of concern was the extensive deprotection/protection scheme necessary to transform the present trioxygen side chain array into the desired oxetane as a part of the total synthesis. The procedure used by Mr. Qingbei Zeng on an advanced intermediate is demonstrative (97→98) and entailed seven steps (Scheme 24). It was immediately obvious that the most straightforward protecting group arrangement would agree with general template 99. This array would require only two steps for oxetane formation and has been described elsewhere by this group. Our desire to streamline this process was motivated by our intention to develop a
Scheme 24. Installation of the oxetane ring using the current side chain. Reagents and conditions: (a) 80% AcOH-H2O; (b) Bz2O, (DMAP), CH2Cl2; (c) SEMCl, i-Pr2NEt, CH2Cl2; (d) DDQ, H2O, CH2Cl2; (e) 1% NaOH, CH3OH; (f) MsCl, Et3N, CH2Cl2; (g) 3N NaOH (aq), (n-Bu)4NHSO4, CH2Cl2.

short total synthesis of taxol. With these considerations in mind, we sought to examine protecting group manipulations associated with intermediates en route to 40.

2.4.2 Reengineering of the Oxetane Precursors

The presence of a p-methoxybenzyl group in the side chain was immediately considered a boon to our efforts since it behaves as a chemically orthogonal yet readily removable protecting group and also displays a chameleon-like character through its latent oxidation states easily accessible with mild oxidants. In order to use this property to advantage, we sought to test whether the diol 100 would cyclize onto the incipient benzylic cation to form a five- or six-membered dioxolane ring (Scheme 25), preferably the latter. Hence, oxidation of the benzylic
position from the ether to acetal oxidation state concomitantly protects a second hydroxyl while preserving the relative inertness of the protecting group. We could not predict, however, whether the steric bulk that accompanied the tertiary hydroxyl would be sufficient to steer cyclization toward the primary carbinol as we desired. The configuration at the nascent acetal carbon was of particular concern since it was unclear what effect this stereocenter might exert during the aldol C-ring annulation (vide infra). Notwithstanding, when 100 was treated with DDQ under anhydrous conditions, 101 was formed as a 1.6:1 mixture of anomers. The (major) $\alpha$-epimer was treated with acetic anhydride in pyridine to facilitate structural elucidation. Inspection of the 300 MHz $^1$H NMR spectrum for 102 clearly indicated that the methylene protons of the terminal alcohol were deshielded to 4.86 and 4.72 ppm, consistent with acylation of the resident primary alcohol. Further corroborating evidence was derived from NOE enhancements and long-range INEPT enhancements observed from the benzylic acetal proton to $\text{C}(3)$ and $\text{C}(4)$, all of which confirm formation of a dioxolane ring instead of the dioxane isomer. Thus, the cyclization appears to be a kinetically controlled process.
Scheme 25. Initial Study of PMB-oxidative cyclization. *Reagents and Conditions:* (a) DDQ, 3 Å MS, CH₂Cl₂; (b) Ac₂O, (DMAP), py (54%, 2 steps); (c) DDQ, 3 Å MS, CH₂Cl₂, then DDQ, H₂O (76%).

Although this strategy failed to provide direct access to the desired 1,3-protected diol, 101 could be further oxidized with DDQ/water to produce a 1.2:1 mixture of 1,3- and 1,2-diols 103a and 103b, respectively. This process could be performed in a one-pot sequence from 100, and the desired 1,3 diol predominated. Unfortunately, the level of regioselection was impractical for large-scale production of 103a.
We then looked to a later intermediate in which the PMB-protected oxygen and the primary hydroxyl that we wished to protect were locked in a cis fashion so as to allow efficient “tying” of these two moieties together. The disadvantage of this approach arose from our inability to control which p-methoxybenzylidene acetal anomer would be formed. In the event, 105 was first generated from 100 by a hydrolysis/equilibration process, then treated with DDQ in anhydrous dichloromethane (Scheme 26). The desired p-methoxybenzylidene acetal was formed stereoselectively, the aromatic ring being consistently situated in an equatorial orientation within both tetrahydrofuran anomers. The success of this tactic carried further with transformation of the primary carbinol to an iodide (107),© and protection of the tertiary hydroxyl as its trimethylsilyl ethoxymethyl ether 108 under basic conditions.© The fully protected furanose was then fragmented using the Bemet-Vasella protocol© to deliver enal 109 in good yield. The aldehyde was alkylidenated as before© to deliver vinyl iodide 110 in 72% yield, with addition of only a single step relative to the production of vinyl lithium 40.
2.4.3 Implementation of the Second Generation C-Ring Synthon: Reconsidering the Use of a Thiophenyl Group as an Oxygen Surrogate

Now that the protecting groups associated with the side chain had been effectively "tied-back" from the southern rim of the B-ring, it was first necessary to find whether the original chemistry that was attempted at C(6) would now work in a less encumbered environment. Secondly, we wished to determine the viability of the sulfoxide activation/displacement chemistry in the present context. To this end, vinyl iodide 110 was transmetalated and coupled with ketone 53c to arrive at tertiary carbinol 111, which underwent charge-accelerated [3,3] sigmatropic

Scheme 27. Deployment of C-ring synthon 110 when C(6) is substituted with a phenylthio moiety. Reagents and Conditions: (a) 110, n-BuLi, Et₂O (72%); (b) KHMDS, 18-crown-6, THF, then CH₃I (94%); (c) m-CPBA, NaHCO₃, CH₂Cl₂ (96%); (d) NaOAc, Ac₂O, 120 °C (76%); (e) LiAlH₄, Et₂O, 0 °C (70%).
rearrangement and methylation to deliver 112 (Scheme 27). The sulfoxides generated from 112 and its reduced form 115 were notably more stable toward thermal elimination, presumably due to the lessened steric congestion that served to facilitate elimination in 57, and could be stored without decomposition for extended periods of time. However, extended heating facilitated the elimination process (→114) and prevented the use of more forcing conditions to effect either Pummerer or Mislow-Evans rearrangement. Furthermore, we failed to detect any of the desired displacement product expected upon treatment of sulfoxides 113 or those derived from 115 with trifluoroacetic anhydride. We appear to have demarcated a line between the steric congestion necessary to expel the activated sulfoxide and the steric openness needed to access H(6) chemically.

Additional chemistry related to sulfide 112 and its various oxidation states was similarly unsuccessful. But the salient features of the functional group array in 112 were not to be overlooked. The use of 110 in similar oxy-Cope products where C(6) was unsubstituted may once again prove successful as the C(6) position is expected to be more sterically available to direct oxygenation. Secondly, in contrast to the first generation side chain where free rotation about the C(3)-C(4) bond allowed anti-elimination of the elements of acetone, we have effectively prevented this decomposition pathway by fixing the oxygen leaving group (OSEM) syn to the hydrogen that must be removed. Efforts along these two fronts form the basis of the discussion that follows.

2.4.4 Implementation of the Second Generation C-Ring Synthon: Coupling With 39 and Subsequent Elaboration

The vinyllithium derived from 110 was generated once again and added to ketone 39 (Scheme 28). The resulting carbinol 112 was found to undergo charge-accelerated sigmatropic rearrangement efficiently to produce 113, although when the methylation step was employed,
Scheme 28. Deployment of C-ring synthon 110 when C(6) is unsubstituted. Reagents and Conditions: (a) 110, n-BuLi, Et₂O (76%); (b) KHMDS, 18-cr-6, THF, (85%); (c) KHMDS, 18-cr-6, THF, then CH₃I (53%); (d) OsO₄, py, 0 °C (41%); (e) TBSCI, imid. (DMAP), DMF (92%); (f) thexylborane, THF, then KOOH (41%); (g) Dess-Martin periodinane, CH₂Cl₂ (100%); (h) NaOH, CH₃OH-THF, 0 °C.
varing degrees of success in producing 114 were encountered. This anomalous behavior is not completely understood at the present time, but may be related to premature protonation of the nascent enolate prior to addition of methyl iodide. Although this problem stands in stark contrast to the behavior of 54b and 107, additional cases are known in which the efficiency of the methylation step is capricious. Notwithstanding, the bridgehead alkene could be dihydroxylated in a modest (unoptimized) yield. In contrast to the analogous intermediate where the first-generation side chain was present, 115a could be isolated after silica gel chromatography in the open form, without any sign of transannular hemiketalization. The explanation for this behavior may also be found in the less sterically imposing nature of the protecting groups now associated with the side chain.

The diol could be monoprotected as the secondary TBS ether prior to hydroboration/oxidation of the terminal olefin and formation of 116a. The Dess-Martin periodinane was used to gain access to keto aldehyde 116b, which served as a fundamentally new intermediate for aldol annulation of the C-ring. In all cases to this point, free rotation about the four side chain carbon-carbon bonds was possible, thereby granting the aldehyde a certain degree of mobility for accessing the desired chair conformation necessary to annulate ring-C while forging the correct configurations at C(7) and C(8). By fusing a 1,3-dioxane ring to the side chain, we had restricted the conformational freedom available to the aldehyde during the annulation process. This combination of factors are likely responsible for the failure of 116b to undergo the desired aldol process with an acceptable degree of efficiency. Instead, the formation of p-anisaldehyde was clearly observed, and only two products could be isolated in significant amounts. These oils were produced in a 2:1 ratio, and their ¹H NMR spectra suggested their identities as 117 and 118, respectively. Although the planar structure of 118 is consistent with our targeted intermediate, it is likely that the chair conformation of the acetal was preserved in the aldol transition state, thereby demanding the C-ring carbons to assume a boat-like arrangement.
Scheme 29. The aldol annulation reaction in a similar system. Reagents and Conditions: (a) TBAF, CH$_3$CN.

As a result, the most likely configurational assignment for 117 and 118 is as shown, but the vanishing amount (<30% yield) that was generated failed to warrant further inspection. This result parallels a second example recently discovered by Mr. Hon-Chung Tsui (Scheme 29).

Although the topology of the B-ring in this approach is significantly different, the expected transition state should come under similar energy-driven requirements for bond formation. The B-ring demands the necessary flexibility to accommodate an intermediate enolate double bond, but poses little conformation constraint on the side chain. The second heuristic concern is that the 1,3-dioxolane remain in the chair conformation that it has presumably maintained throughout its existence. As a result, the lowest energy conformation involving the atoms of the nascent C-ring will be a chair conformation if possible, and the ultimate ramification is the setting of stereochemistry at C(7) and C(8).

Considering these two examples (120b$\rightarrow$122 and 123$\rightarrow$124), a hypothesis may be developed for predicting the factors necessary to effect a successful C-ring aldol ring closure to give the desired C(7) and C(8) configurations when protecting the side chain oxygens in tandem using a 1-substituted acetal. The analysis in Figure 15 rests on the assumption that cases A-C,
where the two reactive arms of the acetal are unable to approach one another; of course, our assumption that the benzylidene acetal retains a chair conformation may be overridden here. As

Figure 15. Putative intramolecular aldol low energy conformations for the four possible permutations at C* (see 120b and 123).
the analysis reveals, only one permutation (C) enables bond formation with the desired stereochemistry via a chair conformation.

2.4.5 Implementation of the Second Generation C-Ring Synthon: Coupling With a 1-[(Z)-2-p-methoxyphenyloxy]vinyl]-2-norbornanone and Subsequent Elaboration: A Direct Solution to the C(2) Oxygenation Problem

Despite the fact that incorporation of oxygen into the camphor skeleton prior to coupling and anionic oxy-Cope rearrangement failed when using the first-generation side chain due to competing basic elimination (vide supra), we decided that a second look at this tactic was necessary. We were motivated by our hypothesis that the steric compression generated by the original side chain was the responsible factor for competing elimination. Also, since we had attempted to eliminate this congestion when remodeling the side chain, perhaps the sigmatropic process would once again predominate. Secondly, we had preemptively removed the possibility

![Scheme 30](image)

**Scheme 30.** Deployment of C-ring synthon 110 when C(6) is substituted with a p-methoxyphenoxymo moiety. *Reagents and Conditions:* (a) 110, n-BuLi, Et₂O (65%); (b) KHMDS, 18-cr-6, THF, 0 °C→rt (73%); (c) KHMDS, 18-cr-6, THF, 0 °C (92%).
for anti-elimination due to the locking of the leaving group (now an OSEM) and the adjacent tertiary hydrogen in a syn-arrangement. We were aware, however, that a potentially anti-oriented hydrogen occupied the adjacent methylene. In the event, we were delighted when a product could be retrieved that clearly showed the entire side chain to be unchanged after treatment of carbinol 125, itself the result of the coupling of 48a and 110 using the usual protocol, with potassium hexamethyldisilazide and 18-crown-6 in tetrahydrofuran at 0 °C to room temperature (Scheme 30). Interestingly, it was clear that the elements of ρ-methoxyphenol were absent from

![Diagram A](image1)

![Diagram B](image2)

![Diagram C](image3)

**Figure 16.** Mechanism for the tandem anionic oxy-Cope rearrangement/transannular SN' displacement.

the 1H NMR spectrum, while a 1,2-disubstituted alkene (J = 6.0 Hz) had been generated instead of the expected trisubstituted bridgehead olefin. Based on others’ reports of facile tandem anionic oxy-Cope rearrangement/SN' transannular displacement, it was not difficult to propose and verify its identity as 120. This mechanism, which is shown in detail in Figure 16, is fully consistent with the observed stereochemistry.

It was very pleasing to learn after significant experimentation that the deleterious SN' process could be obviated. It appears that the enolate which is the immediate product of
rearrangement may actually be protonated by either hexamethyldisilazane or unrearranged carbinol, although the evidence is circumstantial at best. Such an explanation would account for our general inability to methylate the putative enolate, and also the need to warm the reaction mixture to room temperature to effect the tandem process; it has been observed on occasion that the bicyclo[6.2.1]undecane intermediates (viz. 80a) require warmer temperatures for deprotonation. This working hypothesis may also be extended to the varying success with which methylation products 42 and 118 could be accessed.

Without further success in methylating ketone 127 before initiating the competing SN' displacement of p-methoxyphenoxide, we turned our attention to the subject of elaboration and advancement to more taxol-like intermediates (Scheme 31). We soon discovered that the presence of substitution at C(6) required slight modifications of our previous strategy. Immediate osmylation of 127 returned a mixture of products among which the dihydroxylation of the terminal olefin predominated. The oxygen-containing group at C(6) had now become the dominating steric force, and hydroboration/oxidation was effected in advance of dihydroxylation to deliver 128. As if to exert its true steric bias, the C(6) substituent drove the initial diol 129 to hemiketalization in a highly efficient manner overall. This event was followed by disappearance of the carbonyl 13C absorption concommittant with the formation of a quaternary carbon peak at 100.1 ppm. The conclusion that the impetus for this process was purely steric appears reasonable on the grounds that 119a, a close relative of 129, could be isolated in good yield even after silica gel chromatography.

This behavior required the obvious decision to reduce the C(3) carbonyl prior to formation of a discrete bridgehead diol. The use of a distinct reduction step immediately following the sigmatropic rearrangement was considered first, and side chain and B-ring functionalization would immediately follow. The details of this approach are also outlined in Scheme 28. Reduction of the C(3) carbonyl was cleanly achieved by lithium aluminum hydride at reduced temperature to give
Scheme 31. Functionalization of 127. Reagents and Conditions: (a) thexyloborane, THF, then KOOH (128, 59%; 132, 48%); (b) OsO₄, py, -30 °C (130, 87%; 133, 78%); (c) LiAlH₄, Et₂O, 0 °C (79%).
Chemoselective functionalization of this diene then delivered diol 132 in a modest yield. Osmylation and hydrolysis of the osmate ester using the usual protocol produced 133 in an overall yield of 30% for the three steps. Simultaneous reduction of the C(3) carbonyl and osmate ester, while shortening the sequence by one step, was slightly less efficient producing 133 from 127 in an overall yield of 24%. What remains to be demonstrated is the ability to protect tetraol 127 orthogonally so that the C(4) methyl can be installed. The protection of the primary hydroxyl as a TBS ether proceeds in near quantitative yield.

2.5.1 Conclusion

Some of the considerations necessary for effecting an early incorporation of the C(6) oxygen have been delineated. Among these, methylation of the nascent enolate immediately following the sigmatropic event appears to be the most problematic, as it requires an otherwise unnecessary protection/deprotection scheme for the numerous sites of oxygenation. Another point of note is the steric "swelling" of the p-methoxyphenoxy substituent at C(6) that causes facile hemiketalization of diol 129, but ultimately imparts little resistance to entry of a molecule of osmium tetroxide. This behavior mandates an otherwise unnecessary reduction of the C(3) carbonyl.

The incorporation of oxygen at C(6) does indeed give rise to its own unique set of consequences, but still carries the advantage that 1) an oxygen has been incorporated at C(6) in the correct configuration and 2) the oxygen is suitably protected for late removal. At present, it is not clear which of the several tactics outlined above will achieve the same goal(s) in a more expedient and efficient manner.

2.5.2 Future Work

We have already begun work on a third generation side chain of the general formula 134 that should remedy the problems associated with protecting the oxygens on the side chain in
Scheme 32. A possible third-generation C-ring synthon and its implementation.

tandem as a PMB-acetal (Scheme 32). To maintain the ease of deprotection prior to oxetane formation, it should be possible to cloak the involved oxygens as $p$-methoxybenzyl ethers. Once again, only a single additional step is necessary relative to the original vinyl iodide synthesis. The implementation of this third-generation vinyl iodide is expected to proceed smoothly when utilizing the unsubstituted camphor-derived ketone (Method A), and direct oxygenation via the enolate derived from 135 should be possible now that there is no acetonide methyl rigidly held near the front edge of the B-ring. Use of pre-oxygenated 48a (Method B) could also be possible, but the degree to which the conformationally flexible nature of this side chain will allow the destructive elimination process encountered with 49a is largely unpredictable. Nonetheless, either approach should once again offer annulation of the C-ring via an aldol strategy since the protecting groups associated with the side chain no longer impose a strict conformational bias upon the side chain.
CHAPTER 3

Experimental

All manipulations were performed under a nitrogen atmosphere. Solvents were dried over 4 Å molecular sieves prior to distillation. Fat extraction diethyl ether was used for extractions, and organic extracts were dried over magnesium sulfate unless noted otherwise. Diethyl ether and tetrahydrofuran were distilled from sodium/benzophenone ketyl. Benzene and toluene were distilled from sodium. Acetonitrile, diisopropylamine, chlorotrimethylsilane, triethylamine, dichloromethane, dimethylsulfoxide, and N,N-dimethylformamide were each distilled from calcium hydride. All reagents were reagent grade and typically used without further purification. Separations were performed with Woelm silica gel (230-400 mesh). The purity of all compounds was shown to be >95% by TLC and high field 1H and 13C NMR.

Melting points were measured on a Thomas Hoover (Uni-Melt) capillary melting point apparatus and are uncorrected. Optical rotations were obtained using a Perkin-Elmer Model 241 Polarimeter. Rotations were measured at 589 nm with a sodium lamp and concentrations are expressed in g/100 mL. Infrared spectra were recorded with a Perkin-Elmer 1320 spectrometer and are reported in reciprocal centimeters (cm⁻¹). The high-resolution and fast-atom-bombardment spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center. Proton and carbon magnetic resonance spectra were recorded at 300 MHz and 75 MHz, respectively, on a Bruker AC 300 FT NMR spectrometer. Chemical shifts are reported in parts per million relative to residual non-deuterated solvent, and splitting patterns are designated as: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad and all coupling
patterns are measured in hertz (Hz). Elemental analyses were performed at either the Scandinavia Microanalysis Laboratory, Herlev, Denmark, or Atlantic Microlab Inc., Norcross, Georgia, USA.

** Allyl L-Fucopyranoside (8).**

L-Fucose (1.00 g, 6.09 mmol), calcium sulfate (0.830 g, 6.09 mmol), and concentrated sulfuric acid (98 μL, 1.83 mmol) in allyl alcohol (12.4 mL) were heated to 80 °C for 16 h. Following the addition of K₂CO₃, the mixture was filtered through Celite, concentrated *in vacuo*, and purified by silica gel chromatography (10% methanol in chloroform) to provide 8 (1.09 g, 88%) as a white solid, mp 145-148 °C; IR (CHCl₃, cm⁻¹) 3568, 3422, 2936, 2877, 1407, 1383, 1069; ¹H NMR (300 MHz, d₆-DMSO) δ 5.94-5.82 (m, 2H), 5.30 (dd, J = 17, 2 Hz, 2H), 5.12 (dd, J = 10, 2 Hz, 2H), 4.84 (br s, 1H), 4.62 (br s, 2H), 4.49-4.42 (br m, 1H), 4.36 (t, J = 2 Hz, 2H), 4.20 (tdd, J = 13, 5, 2 Hz, 1H), 4.11-3.86 (m, 4H), 3.76 (q, J = 7 Hz, 1H), 3.58 (br s, 1H), 3.48 (q, J = 7 Hz, 2H), 3.39 (br s, 1H), 3.25 (br s, 4H), 1.67 (d, J = 6 Hz, 3H), 1.07 (d, J = 6 Hz, 3H); ¹³C NMR (75 MHz, d₆-DMSO) ppm 135.1, 135.0, 116.2, 116.1, 102.6, 98.5, 73.5, 71.6, 71.0, 70.2, 69.9, 69.6, 68.7, 68.0, 67.4, 66.0, 16.6, 16.4; HRMS (El) m/z (M+) calcd for C₉H₁₆O₅ 204.0998, obsd 204.0996.

** Allyl 3,4-O-isopropylidene-L-fucopyranoside (9).**

A mixture of 8 (5.26 g, 25.8 mmol), 2,2-dimethoxypropane (15.8 mL, 129 mmol), and p-toluenesulfonic acid monohydrate (99 mg, 0.52 mmol) in dry benzene (50 mL) was stirred for 45 min. Dilution with ether was followed by a wash with saturated aq NaHCO₃ solution. Drying of the organic layer and concentration provided the dimethyl acetal as an oil that was used immediately in the next step.
Careful purification of an aliquot via silica gel chromatography (40% ethyl acetate in hexanes) provided both anomers as colorless oils.

For the \( \alpha \)-anomer: \( R_f = 0.27; [\alpha]_D^{25} = -140 \) (c 0.60, CHCl₃); IR (CHCl₃, cm⁻¹) 3574, 2989, 1382, 1246, 1219, 1179, 1129, 1082; \( ^1H \) NMR (300 MHz, CDCl₃) \( \delta \) 5.98-5.85 (m, 1H), 5.30 (dt, \( J = 17, 1 \text{ Hz}, 1 \text{H} \)), 5.21 (dt, \( J = 10, 1 \text{ Hz}, 1 \text{H} \)), 4.87 (d, \( J = 4 \text{ Hz}, 1 \text{H} \)), 4.28-4.19 (m, 2H), 4.14 (qd, \( J = 7, 2 \text{ Hz}, 1 \text{H} \)), 4.08-4.01 (m, 2H), 3.83-3.77 (m, 1H), 2.28 (d, \( J = 7 \text{ Hz}, 1 \text{H} \)), 1.51 (s, 3H), 1.35 (s, 3H), 1.31 (d, \( J = 7 \text{ Hz}, 3 \text{H} \)); \( ^13C \) NMR (75 MHz, CDCl₃) ppm 133.7, 117.6, 109.2, 96.7, 76.2, 75.6, 69.4, 68.5, 64.0, 27.8, 25.9, 16.2.

For the \( \beta \)-anomer, \( R_f = 0.18; [\alpha]_D^{25} = -16.8 \) (c 0.57, CHCl₃); \( ^1H \) NMR (300 MHz, CDCl₃) \( \delta \) 6.00-5.84 (m, 1H), 5.31 (dd, \( J = 17, 2 \text{ Hz}, 1 \text{H} \)), 5.22 (dd, \( J = 10, 1 \text{ Hz}, 1 \text{H} \)), 4.39 (ddt, \( J = 13, 5, 1 \text{ Hz}, 1 \text{H} \)), 4.20 (d, \( J = 8 \text{ Hz}, 1 \text{H} \)), 4.13-3.99 (m, 3H), 3.85 (qd, \( J = 7, 2 \text{ Hz}, 1 \text{H} \)), 3.57 (ddd, \( J = 9, 9, 2 \text{ Hz}, 1 \text{H} \)), 2.35 (d, \( J = 2 \text{ Hz}, 1 \text{H} \)), 1.53 (s, 3H), 1.42 (d, \( J = 7 \text{ Hz}, 3 \text{H} \)), 1.36 (s, 3H); \( ^13C \) NMR (75 MHz, CDCl₃) ppm 133.8, 118.0, 109.9, 101.1, 78.8, 76.3, 73.7, 70.0, 69.2, 28.2, 26.3, 16.5; HRMS (El) m/z (M⁺) calcd for C₁₂H₂₀O₅ 244.1311, obsd 244.1314.

**Allyl 3,4-O-Isopropylidene-2-O-methyl-L-fucopyranoside (10).**

The unpurified carbinol 9 was stirred with sodium hydride (1.24 g, 51.5 mmol) in N,N-dimethylformamide (30 mL) at 0 °C for 20 min prior to the addition of methyl iodide (3.21 mL, 51.5 mmol). The low temperature was maintained for 30 min before removal of the cooling bath. Mechanical stirring of the paste was continued until methanol (1 mL) was added after 1 h. The mixture was poured into water (30 mL) and extracted with ether. The combined organic layers were dried, filtered, and concentrated to provide an oil that was used in the next step without further purification. The two anomers could be purified as a mixture using silica gel chromatography (25% ethyl acetate in hexanes) to provide...
10 as a colorless oil; IR (CHCl₃, cm⁻¹) 2988, 1456, 1382, 1104, 1050, 991; ¹H NMR (300 MHz, CDCl₃) δ 5.99-5.85 (m, 2H), 5.34-5.26 (dt, J = 17, 2 Hz, 2H), 5.18 (td, J = 10, 1 Hz, 2H), 4.93 (d, J = 4 Hz, 1H), 4.36 (dd, J = 13, 5 Hz, 1H), 4.26-3.95 (m, 15H), 3.81-3.73 (m, 1H), 3.57 (s, 3H), 3.49 (s, 3H), 3.35 (dd, J = 8, 4 Hz, 1H), 3.17 (dd, J = 7, 7 Hz, 1H), 1.53 (s, 3H), 1.38 (d, J = 7 Hz, 3H), 1.34 (s, 3H), 1.33 (d, J = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 134.0, 133.7, 117.9, 117.2, 109.6, 108.7, 101.4, 95.3, 82.2, 79.1, 76.4, 76.0, 75.7, 69.6, 68.7, 68.2, 63.2, 60.1, 58.5, 28.3, 28.0, 26.3, 26.2, 16.5, 16.2; HRMS (El) m/z (M⁺) calcd for C₁₃H₂₂O₅ 258.1467, obsd 258.1459.

Anal. Calcd for C₁₃H₂₂O₅: C, 60.45; H, 8.58. Found: C, 60.65; H, 8.70.

Allyl 2-0-Methyl L-fucopyranoside (11).

Allyl glycoside 10 from the previous step was stirred in methanol (30 mL) with water (1 mL) and p-toluenesulfonic acid (99 mg, 0.52 mmol) for 24 h. The desired diol could be retrieved by dilution with saturated NaHCO₃ solution, extraction with EtOAc, and drying and concentration of the organic layers. Silica gel chromatography (ethyl acetate) of the residue furnished both anomers (5.20 g, 93%, 3 steps).

For the α-anomer: colorless oil, Rf = 0.21; [α]D₂⁰ = -159 (c 0.67, CHCl₃); IR (CHCl₃, cm⁻¹) 3693, 3583, 2936, 1602, 1458, 1234, 1094; ¹H NMR (300 MHz, CDCl₃) δ 5.99-5.85 (m, 1H); 5.32 (dd, J = 17, 2 Hz, 1H), 5.21 (dd, J = 10, 1 Hz, 1H), 5.04 (d, J = 4 Hz, 1H), 4.19 (ddt, J = 13, 5, 1 Hz, 1H), 4.05 (dd, J = 13, 7, 1H), 3.97 (d, J = 7 Hz, 1H), 3.96 (d, J = 10 Hz, 1H), 3.81 (br s, 1H), 3.51 (dd, J = 10, 4 Hz, 1H), 3.46 (s, 3H), 2.73 (s, 1H), 2.49 (s, 1H), 1.28 (d, J = 7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 133.8, 117.9, 94.6, 77.9, 71.5, 69.5, 68.3, 65.6, 57.7, 16.1.

For the β-anomer: white solid, mp 58-60 °C; Rf = 0.28; [α]D₂⁰ = +19.8 (c 0.54, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 6.00-5.85 (m, 1H), 5.31 (ddd, J = 17, 2, 2 Hz, 1H), 5.18 (dd, J = 11, 2
Hz, 1H), 4.39 (ddt, J = 13, 5, 2 Hz, 1H), 4.29 (d, J = 8 Hz, 1H), 4.10 (ddt, J = 13, 6, 1 Hz, 1H), 3.72 (br s, 1H), 3.62 (s, 3H), 3.58 (q, J = 7 Hz, 1H), 3.54 (d, J = 9 Hz, 1H), 3.20 (dd, J = 9, 8 Hz, 1H), 2.74 (br d, J = 3 Hz, 1H), 2.30 (br d, J = 5 Hz, 1H), 1.33 (d, J = 7 Hz, 3H); 13C NMR (75 MHz, CDCl3) ppm 134.0, 117.0, 102.5, 81.1, 73.7, 71.4, 70.3, 69.9, 60.9, 16.2; HRMS (El) m/z (M+) calcd for C10H18O5 218.1154, obsd 218.1190.

Anal. Calcd for C10H18O5: C, 55.03; H, 8.31. Found: C, 55.34; H, 8.32.

**Allyl 2,3-Di-O-methyl-L-fucopyranoside (12).**

The tin acetal was formed by refluxing 11 (0.500 g, 2.29 mmol) and di-n-butyltin oxide (0.599 g, 2.41 mmol) in methanol (40 mL) for 18 h. The colorless solution was concentrated to a white solid, which was dried under high vacuum (2 h), followed by the addition of anhydrous cesium fluoride (0.644 g, 4.37 mmol). Dissolution into DMF (12 mL), addition of methyl iodide (0.72 mL, 12 mmol), and stirring for 24 h gave a paste that was diluted with water, extracted with ether, dried, and concentrated prior to silica gel chromatography (ethyl acetate) to provide both anomers as colorless oils (0.404 g, 76%).

For the α-anomer: Rf = 0.33; [α]D22 = -139 (c 1.03, CHCl3); IR (CHCl3, cm⁻¹) 3568, 2936, 2877, 1212, 1095; 1H NMR (300 MHz, CDCl3) δ 6.00-5.87 (m, 1H), 5.32 (ddd, J = 17, 3, 1 Hz, 1H), 5.20 (br dd, J = 10, 1 Hz, 1H), 4.99 (d, J = 3 Hz, 1H), 4.18 (dddd, J = 13, 5, 1, 1 Hz, 1H), 4.06 (br dd, J = 13, 7 Hz, 1H), 3.93 (br q, J = 6 Hz, 1H), 3.88 (br d, J = 1 Hz, 1H), 3.57 (dd, J = 10, 3 Hz, 1H), 3.53 (dd, J = 10, 3 Hz, 1H), 3.49 (s, 3H), 3.47 (s, 3H), 2.34 (s, 3H), 1.29 (d, J = 6 Hz, 3H); 13C NMR (75 MHz, CDCl3) ppm 133.9, 117.9, 95.4, 79.3, 77.1, 69.0, 68.2, 65.3, 58.5, 57.6, 16.1.

For the β-anomer: Rf = 0.38; [α]D22 = +15.3 (c 0.72, CHCl3); 1H NMR (300 MHz, CDCl3) δ 6.00-5.87 (m, 1H), 5.31 (ddd, J = 17, 2, 2 Hz, 1H), 5.18 (ddd, J = 11, 2, 1 Hz, 1H), 4.39 (ddt, J = 13, 5, 2 Hz, 1H), 4.28 (d, J = 8 Hz, 1H), 4.10 (ddt, J = 13, 6, 1 Hz, 1H), 3.80 (dd, J = 4, 3 Hz, 1H), 3.72 (br s, 1H), 3.62 (s, 3H), 3.58 (q, J = 7 Hz, 1H), 3.54 (d, J = 9 Hz, 1H), 3.20 (dd, J = 9, 8 Hz, 1H), 2.74 (br d, J = 3 Hz, 1H), 2.30 (br d, J = 5 Hz, 1H), 1.33 (d, J = 7 Hz, 3H); 13C NMR (75 MHz, CDCl3) ppm 134.0, 117.0, 102.5, 81.1, 73.7, 71.4, 70.3, 69.9, 60.9, 16.2; HRMS (El) m/z (M+) calcd for C10H18O5 218.1154, obsd 218.1190.
3.59 (s, 3H), 3.52 (q, J = 7 Hz, 1H), 3.50 (s, 3H), 3.24 (dd, J = 9, 8 Hz, 1H), 3.15 (dd, J = 9, 3 Hz, 1H), 2.21 (d, J = 4 Hz, 1H), 1.35 (d, J = 7 Hz, 3H); 13C NMR (75 MHz, CDCl3) ppm 134.2, 116.9, 102.4, 83.1, 80.2, 70.0, 69.8, 68.5, 60.8, 57.8, 16.4; HRMS (El) m/z (M+) calcd for C11H20O5 232.1311, obsd 232.1284.

**Allyl 4-O-Benzyl-2,3-di-O-methyl-L-fucopyranoside (13).**

Sodium hydride (54 mg, 2.26 mmol) was carefully added to a cold (0 °C) solution of 12 (0.372 g, 1.60 mmol) and n-Bu4NI (0.064 g, 0.17 mmol) in DMF (5 mL). Stirring for 15 min at this temperature was followed by the addition of benzyl bromide (0.22 mL, 1.8 mmol) and removal of the ice bath. The reaction mixture was quenched with water and extracted with ether. The combined organic layers were dried, concentrated in vacuo, and purified (SiO2, 40% ether in hexanes) to yield anomers 13 (0.518 g, 99%), each as a colorless oil.

For the α-anomer: Rf = 0.22; [α]D23 ^ = -105 (c 0.83, CHCl3); IR (CHCl3, cm^-1) 2936, 2884, 1455, 1355, 1094, 1069; 1H NMR (300 MHz, CDCl3) δ 7.42-7.24 (m, 5H), 5.98-5.87 (m, 1H), 5.30 (ddd, J = 17, 3, 2 Hz, 1H), 5.19 (br ddd, J = 10, 3, 2 Hz, 1H), 5.01 (d, J = 4 Hz, 1H), 4.95 (d, J = 12 Hz, 1H), 4.63 (d, J = 12 Hz, 1H), 4.16 (ddddd, J = 13, 5, 1, 1 Hz, 1H), 4.06 (ddddd, J = 13, 6, 1, 1 Hz, 1H), 3.89 (br q, J = 7 Hz, 1H), 3.76 (dd, J = 10, 4 Hz, 1H), 3.69 (dd, J = 3, 1 Hz, 1H), 3.61 (dd, J = 10, 3 Hz, 1H), 3.51 (s, 3H), 3.50 (s, 3H), 1.16 (d, J = 7 Hz, 3H); 13C NMR (75 MHz, CDCl3) ppm 138.7, 134.1, 128.3, 128.2, 127.6, 117.8, 95.6, 80.9, 77.6, 76.5, 74.8, 68.2, 66.3, 58.4, 58.2, 16.7.

For the β-anomer: Rf = 0.27; [α]D23 ^ = +38.6 (c 1.17, CHCl3); 1H NMR (300 MHz, CDCl3) δ 7.41-7.24 (m, 5H), 5.98-5.88 (m, 1H), 5.30 (ddd, J = 17, 3, 2 Hz, 1H), 5.16 (ddd, J = 10, 3, 1 Hz, 1H), 4.93 (d, J = 12 Hz, 1H), 4.66 (d, J = 12 Hz, 1H), 4.38 (ddddd, J = 13, 5, 2, 2 Hz, 1H), 4.25 (d, J = 8 Hz, 1H), 4.08 (ddddd, J = 13, 6, 1, 1 Hz), 3.62 (s, 3H), 3.59 (br d, J = 3 Hz, 1H), 3.50 (s, 3H),
3.47-3.39 (m, 2H), 3.15 (dd, J = 10, 3 Hz, 1H), 1.19 (d, J = 6 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 138.6, 134.4, 128.3, 128.1, 127.5, 116.6, 102.7, 84.8, 80.5, 75.1, 74.5, 70.2, 69.7, 60.7, 58.5, 16.9; HRMS (El) m/z (M$^+$-C$_3$H$_6$O) calcd for C$_{15}$H$_{29}$O$_4$ 264.1362, obsd 264.1387.

4-O-Benzyl-2,3-di-O-methyl-L-fucopyranose (14a).

A mixture of 13 (50 mg, 0.16 mmol), palladium (II) chloride (19 mg, 0.11 mmol), and sodium acetate (19 mg, 0.23 mmol) in 95% (v/v) aqueous acetic acid (0.65 mL) was heated at 60 °C for 6 h. Cooling to rt preceded dilution with water and extraction with chloroform. Drying of the organic layers, filtration, and concentration allowed purification by silica gel chromatography (80% ethyl acetate in hexanes) to furnish 14a (42 mg, 96%) as a colorless oil ($\alpha: \beta$ = 2.9:1); $\alpha$: $\alpha$$_{D}^{20}$ = -62.9 (c 0.56, CHCl$_3$, 37 h); $\alpha$: R$_f$ = 0.29; IR (CHCl$_3$, cm$^{-1}$) 3691, 2936, 1602, 1095, 1068; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.61-7.25 (m, 5H), 5.38 (d, J = 4 Hz, 1H), 4.94 (d, J = 12 Hz, 1H), 4.64 (d, J = 12 Hz, 1H), 4.10 (q, J = 7 Hz, 1H), 3.62 (dd, J = 3, 1 Hz, 1H), 3.54 (s, 3H), 3.51 (s, 3H), 3.57-3.49 (m, 2H), 2.89 (br s, 1H), 1.18 (d, J = 7 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 138.5, 128.3, 128.2, 127.6, 91.1, 80.8, 78.1, 76.1, 74.8, 66.6, 58.7, 58.2, 16.8; $\beta$: R$_f$ = 0.35; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.61-7.25 (m, 5H), 4.94 (d, J = 12 Hz, 1H), 4.66 (d, J = 12 Hz, 1H), 4.98 (d, J = 7 Hz, 1H), 3.73 (d, J = 3 Hz, 1H), 3.64 (s, 3H), 3.53 (s, 3H), 3.57-3.49 (m, 1H), 3.35 (dd, J = 10, 7 Hz, 1H), 3.19 (dd, J = 10, 3 Hz, 1H), 2.89 (br s, 1H), 1.22 (d, J = 6 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 138.5, 128.3, 128.2, 127.6, 97.6, 84.8, 82.2, 75.2, 74.7, 70.7, 60.7, 58.4, 17.0; HRMS (El) m/z (M$^+$) calcd for C$_{15}$H$_{22}$O$_5$ 282.1467, obsd 282.1487.
4-O-Benzyl-2,3-di-O-methyl-L-fucopyranosyl Chloride (14b).

Treatment of 14a (20 mg, 71 μmol) in dichloromethane (1 mL) with the Vilsmeier reagent, formed in situ from oxalyl chloride (8.1 mL, 92 μmol) and DMF (7.7 mL, 99 μmol), at rt for 2 h provided a yellow solution that was concentrated in vacuo to provide 14b as a yellow oil. The crude oil was too unstable to purify/characterize and was therefore used without further processing.

4-O-Benzyl-2,3-di-O-methyl-β-L-fucopyranosyl 2,2,2-Trichloroacetimidate (14c).

Reducing sugar 14a (50 mg, 180 μmol), trichloroacetonitrile (0.18 mL, 1.8 mmol), and potassium carbonate (25 mg, 180 μmol) were stirred at rt in dichloromethane (0.5 mL) for 3 h. Evaporation of solvent was followed by chromatography on silica gel (30:70:5 ethyl acetate:hexanes:triethylamine) to provide 73 mg (96%) of 14c (single anomer): β: colorless oil; [α]D = -3.13 (c 0.48, CHCl3); IR (CHCl3, cm⁻¹) 2936, 1732, 1674, 1304, 1096, 1062; ¹H NMR (300 MHz, CDCl3) δ 8.57 (s, 1H), 7.43-7.27 (m, 5H), 5.60 (d, J = 8 Hz, 1H), 4.96 (d, J = 12 Hz, 1H), 4.69 (d, J = 12 Hz, 1H), 3.71-3.64 (m, 3H), 3.62 (s, 3H), 3.54 (s, 3H), 3.28 (dd, J = 10, 3 Hz, 1H), 1.23 (d, J = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl3) ppm 161.8, 138.4, 128.4, 128.2, 127.7, 98.8, 84.8, 79.7, 77.2, 75.1, 74.7, 71.6, 61.0, 58.8, 16.8; HRMS (EI) m/z (M+Cl₂H₂Cl₃NO) calcd for C₁₅H₂₀O₄ 264.1362, obsd 264.1399.

4-O-Benzyl-2,3-di-O-methyl-L-fucopyranosyl Diphenyl Phosphate (14d).

To a solution of 4-O-benzyl-2,3-di-O-methyl-L-fucose (20 mg, 71 μmol) in THF (0.5 mL) was added 1.6 M n-butyllithium (53 μL, 85
μmol), then diphenylphosphoryl chloride (18 μL, 85 μmol). The mixture was quenched after 10 min with saturated sodium bicarbonate solution (2 mL) and rapidly extracted with ether. The organic fractions were dried, concentrated, and used without further purification in the glycosylation attempts.

Phenyl 4-O-Benzyl-2,3-di-O-methyl-1-thio-L-fucopyranoside (14e).

For the α-anomer: colorless crystals, mp 80-81 °C; Rf = 0.31; [α]D22 = -244 (c 0.58, CHCl3); IR (CHCl3, cm⁻¹) 2936, 2894, 1480, 1454, 1357, 1106, 1072; ¹H NMR (300 MHz, CDCl3) δ 7.51-7.20 (m, 10H), 5.81 (d, J = 5 Hz, 1H), 4.97 (d, J = 12 Hz, 1H), 4.65 (d, J = 12 Hz, 1H), 4.34 (q, J = 7 Hz, 1H), 4.08 (dd, J = 10, 5 Hz, 1H), 3.75 (d, J = 2 Hz, 1H), 3.55 (s, 3H), 3.53 (s, 3H), 3.50 (dd, J = 10, 2 Hz, 1H), 1.19 (d, J = 7 Hz, 3H); ¹³C NMR (75 MHz, CDCl3) ppm 138.5, 135.0, 131.1, 128.8, 86.8, 81.7, 78.6, 76.3, 75.0, 67.5, 58.5, 57.8, 57.8, 16.6.

For the β-anomer: colorless oil; Rf = 0.21; [α]D22 = -8.4 (c 0.67, CHCl3); ¹H NMR (300 MHz, CDCl3) δ 7.59-7.19 (m, 10H), 4.96 (d, J = 12 Hz, 1H), 4.64 (d, J = 12 Hz, 1H), 4.47 (d, J = 10 Hz, 1H), 3.65 (dd, J = 3, 1 Hz, 1H), 3.57 (s, 3H), 3.52 (s, 3H), 3.55-3.47 (m, 2H), 3.24 (dd, J = 9, 3 Hz, 1H), 1.27 (d, J = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl3) ppm 138.8, 134.3, 131.6, 128.6, 128.1.

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127.9, 127.4, 126.9, 87.3, 86.9, 78.7, 75.7, 74.54, 74.50, 61.0, 58.4, 17.3; HRMS (El) m/z (M⁺) calcd for C₂₁H₂₆O₄S 374.1552, obsd 374.1554.

4-O-Benzyl-2,3-di-O-methyl-L-fucopyranosyl Fluoride (14f).

To a solution of thioglycoside 14e (29 mg, 0.077 mmol) and diethylamino-sulfur trifluoride (12 μL, 93 μmol) in dichloromethane (1.3 mL) at 0 °C was added N-bromosuccinimide (15 mg, 85 μmol). The solution was stirred for 15 min before being poured into saturated sodium bicarbonate solution and extracted with ether. Drying of the combined organic layers, concentration in vacuo, and chromatography of the crude oil (SiO₂, 20% ethyl acetate in hexanes) provided 22 mg (100%) of the glycosyl fluoride 14f.

For the α-anomer: colorless crystals, mp 79-80 °C; Rf = 0.27; [α]₂₂° = -113 (c 0.88, CHCl₃); IR (CHCl₃, cm⁻¹) 2936, 1099, 1020, 985; ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.27 (m, 5H), 5.71 (dd, J = 54, 3 Hz, 1H), 4.96 (d, J = 12 Hz, 1H), 4.64 (d, J = 12 Hz, 1H), 4.06 (q, J = 6 Hz, 1H), 3.75 (d, J = 3 Hz, 1H), 3.74 (ddd, J = 25, 10, 3 Hz, 1H), 3.59 (dd, J = 10, 3 Hz, 1H), 3.56 (s, 3H), 3.54 (s, 3H), 1.22 (d, J = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 138.3, 128.2, 128.2, 127.7, 105.7 (d, J = 225 Hz), 80.5, 77.4 (d, J = 24 Hz), 75.8, 74.8, 69.1 (d, J = 3 Hz), 59.0, 58.3, 16.6.

For the β-anomer: colorless oil; Rf = 0.20; ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.27 (m, 5H), 5.04 (dd, J = 53, 7 Hz, 1H), 4.95 (d, J = 12 Hz, 1H), 4.66 (d, J = 12 Hz, 1H), 3.60 (s, 3H), 3.51 (s, 3H), 3.63-3.46 (m, 3H), 3.20 (dd, J = 10, 3 Hz, 1H), 1.27 (d, J = 6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 138.3, 128.2, 128.2, 127.7, 110.4 (J = 225 Hz), 83.7, 83.6, 80.2 (J = 24 Hz), 74.6, 70.8 (J=3 Hz), 60.5, 58.7, 16.7.
1,2-O-isopropylidene-5-O-trityl-α-D-xylofuranose (15a).

\[
\begin{align*}
\text{TrO} & \quad \text{O} \quad \text{O} \quad \text{CH}_3 \\
\text{HO} & \quad \text{O} \quad \text{O} \quad \text{CH}_3
\end{align*}
\]

1,2-O-isopropylidene-α-D-xylofuranose (6) (15.0 g, 78.9 mmol), triphenylmethyl chloride (23.1 g, 82.8 mmol), triethylamine (16.5 mL), and N,N-dimethylaminopyridine (0.483 g, 3.95 mmol) were stirred for 20 h in DMF (50 mL). The resulting mixture was poured into ice water and extracted with dichloromethane. The organic layers were washed collectively with saturated NH₄Cl solution and water, then dried and concentrated to leave a red oil. An aliquot was purified via silica gel chromatography (50% ether in hexanes) to give analytically pure 15a as white crystals, mp 60-62 °C; [α]₀° = +13 (c 1.0, CHCl₃); IR (CHCl₃, cm⁻¹) 3458, 2937, 1491, 1449, 1384; ¹H NMR (300 MHz, CDCI₃) δ 7.47-7.43 (m, 6H), 7.35-7.22 (m, 9H), 6.01 (d, J = 3.7 Hz, 1H), 4.53 (d, J = 3.7 Hz, 1H), 4.30-4.26 (m, 2H), 3.58 (dd, J = 10.2, 5.0 Hz, 1H), 3.49 (dd, J = 10.0, 3.2 Hz, 1H), 3.16 (d, J = 2.7 Hz, 1H), 1.50 (s, 3H), 1.33 (s, 3H); ¹³C NMR (75 MHz, CDCI₃) ppm 143.2, 128.5, 128.3, 127.3, 111.5, 105.0, 87.5, 85.1, 78.4, 76.3, 61.8, 26.8, 26.1; HRMS (El) m/z (M⁺) calcd for C₂₇H₂₈O₅ 432.1937, obsd 432.1937.

3-O-Benzyl-1,2-O-isopropylidene-α-D-xylofuranose (15b).

\[
\begin{align*}
\text{TrO} & \quad \text{O} \quad \text{O} \quad \text{CH}_3 \\
\text{BnO} & \quad \text{O} \quad \text{O} \quad \text{CH}_3
\end{align*}
\]

The oil from above and n-Bu₄NI (2.91 g, 7.89 mmol) were cooled to 0 °C in DMF (50 mL), at which point sodium hydride (3.79 g, 78.9 mmol) was added in several portions. Following a period of 15 min, benzyl bromide (10.3 mL, 86.8 mmol) was added slowly, and the resulting mixture was stirred for 2.5 h in the absence of a cooling bath. Saturated NH₄Cl solution was added, and the mixture was extracted with ether. The organic layers were combined, washed with brine, dried, and concentrated to leave a red oil that could be purified (SiO₂, 25% ether in hexanes) to a white foam, mp 55-56.5 °C; [α]₀° = -42 (c 0.9, CHCl₃); IR (CHCl₃, cm⁻¹) 2937, 1491, 1449; ¹H NMR (300 MHz, CDCI₃) δ 7.46 (d, J = 6.6 Hz, 6H), 7.31-
7.21 (m, 12H), 7.14-7.11 (m, 2H), 5.92 (d, J = 3.8 Hz, 1H), 4.62-4.58 (m, 2H), 4.45 (d, J = 12.8 Hz, 1H), 4.44-4.38 (m, 1H), 4.02 (d, J = 3.1 Hz, 1H), 3.57 (dd, J = 9.3, 5.8 Hz, 1H), 3.33 (dd, J = 9.3, 6.8 Hz, 1H), 1.55 (s, 3H), 1.34 (s, 3H); \( ^{13}\text{C NMR (75 MHz, CDCl}_3 \text{ ppm 143.9, 137.5, 128.7, 128.3, 128.0, 127.8, 127.7, 127.5, 127.0, 111.6, 105.0, 86.9, 82.4, 81.6, 79.5, 72.0, 61.3, 26.8, 26.2}; \) HRMS (EI) m/z (M+) calcd for C\(_{34}\)H\(_{34}\)O\(_{5}\) 522.2406, obsd 522.2405.

**3-O-Benzyl-1,2-O-isopropylidene-\( \alpha \)-D-xylofuranose (15c).**

The crude oil and \( \rho \)-toluenesulfonic acid (6.00 g, 31.5 mmol) were stirred in methanol (200 mL), ether (20 mL), and water (2 mL) for 5.5 h before being treated with saturated NaHCO\(_3\) solution (200 mL) and extracted with EtOAc. A brine wash was followed by drying, concentration, and purification over silica gel (20% - 50% ethyl acetate in hexanes) to provide 15c (17.9 g, 81%) as a colorless oil; \([\alpha]^{25}_D = -139 \) (c 0.5, CHCl\(_3\)); IR (CHCl\(_3\), cm\(^{-1}\)) 3692, 3570, 3012, 2935, 1602, 1461, 1222; \( ^1\text{H NMR (300 MHz, CDCl}_3 \text{ ppm 7.45-7.26 (m, 5H), 5.99 (d, J = 3.8 Hz, 1H), 4.72 (d, J = 12.0 Hz, 1H), 4.64 (d, J = 3.8 Hz, 1H), 4.50 (d, J = 12.0 Hz, 1H), 4.31-4.26 (m, 1H), 4.02 (d, J = 3.5 Hz, 1H), 3.97-3.81 (m, 2H), 2.16 (br s, 1H), 1.49 (s, 3H), 1.33 (s, 3H); \( ^{13}\text{C NMR (75 MHz, CDCl}_3 \text{ ppm 137.1, 128.6, 128.2, 127.7, 111.8, 105.1, 82.8, 82.5, 80.1, 71.9, 61.0, 26.8, 26.3}; \) HRMS (EI) m/z (M+) calcd for C\(_{15}\)H\(_{20}\)O\(_{5}\) 280.1311, obsd 280.1429.

**Allyl 3-O-Benzyl-D-xylopyranoside (16).**

Carbinol 15c (1.00 g, 3.56 mmol) was warmed to 80 °C in 60% aqueous acetic acid (10 mL) for 8 h, and refluxed for an additional 11 h. The mixture was concentrated in vacuo to afford a white solid, which was dissolved in allyl alcohol (5.8
mL) and stirred with calcium sulfate (0.486 g, 3.57 mmol) and concentrated sulfuric acid (0.06 mL, 0.1 mmol) at 80 °C for 10 h. The reaction mixture was diluted with water and extracted with chloroform. The combined organic layers were washed successively with saturated NH₄Cl and NaHCO₃ solutions prior to drying and concentration to furnish a crude yellow oil. Careful purification of an aliquot on silica gel chromatography (50% ethyl acetate in hexanes) gave analytically pure 16 (anomeric mixture: α:β = 1.7:1) as a white solid, mp 83-84 °C; IR (CHCl₃, cm⁻¹) 3576, 2910, 1454, 1350, 1103, 993, 939; ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.28 (m, 10H), 6.00-5.87 (m, 2H), 5.32 (d, J = 12.7, 1.5 Hz, 2H), 5.23 (d, J = 10.4, 1.2 Hz, 2H), 4.99 (d, J = 11.7 Hz, 1H), 4.94 (d, J = 11.5 Hz, 1H), 4.82 (d, J = 3.2 Hz, 1H), 4.74 (d, J = 11.7 Hz, 1H), 4.71 (d, J = 11.5 Hz, 1H), 4.35 (d, J = 12.7, 5.3, 1.5, 1.5 Hz, 1H), 4.31 (d, J = 7.2 Hz, 1H), 4.28 (d, J = 12.7, 5.3, 1.5, 1.5 Hz, 1H), 4.11 (d, J = 12.7, 6.3, 1.2, 1.2 Hz, 1H), 4.05 (d, J = 12.7, 6.3, 1.2, 1.2 Hz, 1H), 4.00 (d, J = 11.5, 5.2 Hz, 1H), 3.76-3.52 (m, 7H), 3.37 (t, J = 8.5 Hz, 1H), 3.24 (d, J = 11.5, 9.8 Hz, 1H), 2.57 (d, J = 3.4 Hz, 1H), 2.50 (d, J = 2.8 Hz, 1H), 2.30 (d, J = 7.7 Hz, 1H), 2.28 (d, J = 3.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 138.5, 138.4, 133.7, 133.6, 128.6, 128.0, 127.92, 127.85, 118.0, 102.4, 97.7, 83.3, 81.7, 74.4, 73.8, 72.1, 70.1, 69.2, 68.8, 68.7, 65.1, 62.9; HRMS (El) m/z (M⁺) calcd for C₁₅H₂₀O₅ 280.1311, obsd 280.1617.

Allyl 3-O-Benzyl-2,4-di-O-methyl-D-xylopyranoside (17).

Crude 16 was dissolved in DMF (10 mL), cooled to 0 °C, and treated with sodium hydride (0.256g, 10.7 mmol) and methyl iodide (0.66 mL, 11 mmol). The mixture was stirred for an additional hour while the cooling bath slowly warmed to rt. The resulting brown paste was carefully diluted with saturated NH₄Cl solution and water, extracted with ether, dried, concentrated in vacuo, and purified (SiO₂, 40 % ether in hexanes) to yield anomers 17 (0.540 g, 49% from 15c), each as a colorless oil.
For the α-anomer: \( R_f = 0.38; [\alpha]^2_{D}^2 = +93.3 \) (c 2.36, CHCl\(_3\)); IR (CHCl\(_3\), cm\(^{-1}\)) 2934, 2871, 1455, 1359, 1095; \(^1\)H NMR (300 MHz, CDCI\(_3\)) \( \delta \) 7.41-7.24 (m, 5H), 6.02-5.84 (m, 1H), 5.34 (dm, \( J = 17.2, 1.5 \) Hz, 1H), 5.23 (dm, \( J = 10.5, 1.2 \) Hz, 1H), 4.94 (d, \( J = 3.6 \) Hz, 1H), 4.86 (d, \( J = 11.0 \) Hz, 1H), 4.80 (d, \( J = 11.0 \) Hz, 1H), 4.21 (dddd, \( J = 12.9, 5.1, 1.4, 1.4 \) Hz, 1H), 4.05 (dddd, \( J = 12.9, 5.1, 1.4 \) Hz, 1H), 3.75 (dd, \( J = 10.8, 9.1 \) Hz, 1H), 3.71 (dd, \( J = 10.8, 5.7 \) Hz, 1H), 3.52 (s, 3H), 3.50 (dd, \( J = 10.6, 10.6 \) Hz, 1H), 3.49 (s, 3H), 3.33 (dddd, \( J = 10.6, 8.7, 5.7 \) Hz, 1H), 3.26 (dd, \( J = 9.5, 3.6 \) Hz, 1H); \(^1\)C NMR (75 MHz, CDCI\(_3\)) ppm 139.1, 133.7, 128.2, 127.8, 127.4, 118.0, 95.1, 81.8, 81.4, 79.9, 75.4, 68.0, 59.7, 59.13, 59.06.

For the β-anomer: \( R_f = 0.43; [\alpha]^2_{D}^2 = -29.2 \) (c 1.10, CHCl\(_3\)); \(^1\)H NMR (300 MHz, CDCI\(_3\)) \( \delta \) 7.41-7.28 (m, 5H), 6.00-5.88 (m, 1H), 5.33 (dddd, \( J = 17.3, 3.3, 1.6 \) Hz, 1H), 5.20 (dddd, \( J = 10.4, 2.8, 1.3 \) Hz, 1H), 4.82 (d, \( J = 1.7 \) Hz, 2H), 4.34 (dddd, \( J = 13.1, 5.2, 1.5, 1.5 \) Hz, 1H), 4.29 (d, \( J = 7.5 \) Hz, 1H), 4.11 (dddd, \( J = 13.1, 5.9, 1.4, 1.4 \) Hz, 1H), 4.00 (dd, \( J = 11.6, 4.8 \) Hz, 1H), 3.59 (s, 3H), 3.47 (s, 3H), 3.42-3.31 (m, 2H), 3.17-3.07 (m, 2H); \(^1\)C NMR (75 MHz, CDCI\(_3\)) ppm 138.9, 134.1, 128.3, 127.8, 127.5, 117.1, 103.1, 83.7, 83.5, 79.7, 75.1, 70.0, 63.3, 60.6, 58.9; HRMS (EI) m/z (M\(^+\)) calcd for C\(_{17}\)H\(_{24}\)O\(_5\) 308.1624, obsd 308.1635.

2,4-Di-O-methyl-D-xylopyranose (18).

\[
\text{Allyl glycoside 17 (74 mg, 240 \mu\text{mol}) in THF (2 mL) was cannulated into a -78 °C solution of sodium (28 mg, 1.2 mmol) in ammonia (ca. 15 mL).}
\]

Persistence of a blue color for 5 min was followed by the addition of water (2 drops) and warming to rt overnight. Purification of the residue by flash chromatography (SiO\(_2\), 10% methanol-chloroform) afforded 18 (0.043 g, 100%) as a colorless oil.
Allyl 2,4-Di-O-methyl-D-xylopyranoside (4).

From 18. Xylopyranose 18 (34 mg, 190 µmol), calcium sulfate (52 mg), and concentrated sulfuric acid (1 drop) were heated to 80 °C in allyl alcohol (3 mL) for 24 h. The mixture was cooled, neutralized with K₂CO₃, filtered through Celite, concentrated, and purified (SiO₂, 70 % ether in hexanes) to afford 4 (17 mg, 41%).

From 19. Methyl glycoside 19 (68 mg, 350 µmol), calcium sulfate (46 mg), and concentrated sulfuric acid (1 drop) were heated to 80 °C in allyl alcohol (1 mL) for 24 h. The mixture was cooled, neutralized with K₂CO₃, filtered through Celite, concentrated, and similarly purified to afford 4 (62 mg, 81%) as a colorless oil.

For the α-anomer: colorless oil; Rf = 0.35; [α]D²⁶ = -55.0 (c 0.28, CHCl₃); IR (CHCl₃, cm⁻¹) 3588, 2935, 1226, 1208, 1090; ¹H NMR (300 MHz, CDCl₃) δ 5.99-5.83 (m, 1H), 5.32 (ddt, J = 17.2, 3.1, 1.6 Hz, 1H), 5.21 (dd, J = 10.3, 2.7 Hz, 1H), 4.97 (d, J = 3.5 Hz, 1H), 4.20 (ddt, J = 13.0, 5.1, 1.4 Hz, 1H), 4.02 (ddt, J = 13.0, 6.5, 1.2 Hz, 1H), 3.88 (dd, J = 9.4, 9.4, 1.6 Hz, 1H), 3.74 (dd, J = 10.9, 5.5 Hz, 1H), 3.49 (s, 3H), 3.48 (s, 3H), 3.47 (dd, J = 10.9, 10.7 Hz, 1H), 3.27 (ddd, J = 10.7, 8.8, 5.5 Hz, 1H), 3.16 (dd, J = 9.5, 3.5 Hz, 1H), 2.63 (d, J = 1.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 133.9, 117.3, 102.6, 82.6, 78.9, 74.9, 70.0, 62.9, 60.5, 58.5.

For the β-anomer: colorless oil, Rf = 0.25; [α]D²⁶ = +132 (c 0.26, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 5.99-5.86 (m, 1H), 5.31 (ddt, J = 17.2, 3.2, 1.6 Hz, 1H), 5.20 (dd, J = 10.4, 2.7 Hz, 1H), 4.34 (ddt, J = 12.9, 5.2, 1.4 Hz, 1H), 4.32 (d, J = 6.7 Hz, 1H), 4.09 (ddt, J = 12.9, 5.9, 1.4 Hz, 1H), 4.04 (dd, J = 11.3, 4.7 Hz, 1H), 3.60 (s, 3H), 3.53 (dd, J = 8.7, 2.0 Hz, 1H), 3.48 (s, 3H), 3.29 (ddd, J = 9.4, 9.4, 4.8 Hz, 1H), 3.17 (dd, J = 11.3, 9.5 Hz, 1H), 3.01 (dd, J = 8.9, 7.2 Hz, 1H), 2.75 (d, J = 2.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 133.6, 118.0, 94.4, 81.2, 79.3, 72.3, 68.1, 59.3, 58.6, 58.2; HRMS (El) m/z (M⁺) calcd for C₁₀H₁₈O₅ 218.1154, obsd 218.1160.

Methyl 2,4-Di-O-methyl-D-xylopyranoside (19).

Carbinol 15c (1.00 g, 3.57 mmol) was dissolved in an 80% methanol-water soln (24 mL) containing concentrated sulfuric acid (0.560 g) and refluxed for 2 h, cooled to rt, neutralized with NaOCH₃, and concentrated to leave a white solid. This solid was refluxed for 7 h in methanolic HCl solution (19:1 v/v) which was cooled to rt, neutralized with NaOCH₃, diluted with water, and extracted with chloroform. The organic layers were washed with saturated NaHCO₃ solution, dried, and concentrated to provide the methyl glycoside as a colorless oil.

Sodium hydride (0.257 g, 10.7 mmol) was added to a cold (0 °C) solution of the crude diol in DMF (5 mL). Stirring for 15 min was followed by the careful addition of methyl iodide (0.67 mL, 11 mmol). Stirring at 0 °C and rt ensued for periods of 30 min and 1 h, respectively. Dilution with water and extraction with ether preceded drying and concentration in vacuo of the organic layers to provide the fully protected methyl glycoside as a colorless oil.

Without purification, this oil was immediately shaken with 10% Pd/C (48 mg) in EtOAc (50 mL) under a hydrogen atmosphere (50 psi) for 23 h using a Parr apparatus. Filtration through Celite and concentration in vacuo furnished an oil that was purified via silica gel chromatography (80% ethyl acetate in hexanes) to afford 19 (0.519 g, 76%).

For the α-anomer: colorless oil; Rf = 0.28; [α]²⁴
₇ = +131 (c 0.62, CHCl₃); IR (CHCl₃, cm⁻¹) 3588, 2936, 2835, 1214, 1088, 1048; ¹H NMR (300 MHz, CDCl₃) δ 4.82 (d, J = 4 Hz, 1H), 3.85 (dd, J = 9, 9 Hz, 1H), 3.75 (dd, J = 11, 5 Hz, 1H), 3.51 (s, 3H), 3.49 (s, 3H), 3.43 (dd, J = 11, 11 Hz, 1H), 3.41 (s, 3H), 3.27 (ddd, J = 11, 9, 5 Hz, 1H), 3.16 (dd, J = 9, 4 Hz, 1H), 2.59 (d, J = 2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) 96.9, 81.3, 79.3, 72.4, 59.0, 58.6, 58.5, 55.2.

For the β-anomer: colorless needles, mp 75-76.5 °C; Rf = 0.35; [α]²⁴
₇ = -48.1 (c 0.53, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 4.19 (d, J = 7.1 Hz, 1H), 4.05 (dd, J = 11.2 Hz, 4.5 Hz, 1H).
3.58 (s, 3H), 3.54 (dd, J = 8.7, 8.7 Hz, 1H), 3.51 (s, 3H), 3.48 (s, 3H), 3.28 (ddd, J = 8.4, 8.4, 4.6 Hz, 1H), 3.18 (dd, J = 11.2, 9.4 Hz, 1H), 2.97 (dd, J = 8.8, 7.2 Hz, 1H), 2.70 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 104.5, 82.6, 79.0, 74.8, 62.9, 60.4, 58.5, 56.7; HRMS (El) m/z (M⁺⁻H) calcd for C₈H₁₅O₅ 191.0919, obsd 191.0892.

Acetyl 2,4-Di-O-acetyl-D-xylopyranoside (20).

AcO
\[ \text{HO} \longrightarrow \text{OAc} \]
AcO
A methanolic solution (10 mL) of 22 (171 mg, 467 µmol) and 10% Pd/C (40 mg) was flushed and pressurized (1200 psi) with hydrogen in a Parr reactor. The mixture was stirred for three days, filtered through Celite, and concentrated to leave an oil that was subjected to silica gel chromatography (elution with 60% ethyl acetate in hexanes) to furnish 124 mg (96%) of 20 as a crystalline solid.

For the α-anomer: colorless oil; [α]D²⁰ = +79 (c 1.35, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 6.20 (d, J = 3.6 Hz, 1H), 4.94-4.85 (m, 2H), 4.02 (d, J = 9.5 Hz, 1H), 3.88 (dd, J = 11.1, 5.7 Hz, 1H), 3.61 (t, J = 11.1 Hz, 1H), 2.90 (br s, 1H), 2.12 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 170.5, 170.4, 169.0, 89.4, 71.7, 71.0, 69.3, 60.7, 20.7, 20.6; HRMS (El) m/z (M⁺-C₄H₇O₄) calcd for C₇H₉O₄ 157.0501, obsd 157.0510.

Phenyl 2,4-Di-O-acetyl-1-thio-D-xylopyranoside (21).

Triacetate 20 (650 mg, 2.98 mmol) and phenylthiotrimethylsilane (0.85 mL, 4.47 mmol) were stirred in the presence of tin(IV) chloride (0.17 mL, 1.45 mmol) for 15 min prior to the addition of BF₃·OEt₂ (0.73 mL, 5.96 mmol) and an additional 20 min of stirring. Saturated NH₄Cl was added to give a biphasic mixture that was extracted with ethyl
acetate. The combined organic layers were dried, concentrated, and purified (SiO₂, 50% ethyl acetate in hexanes) to provide 647 mg (66%) of 21.

For the α-anomer: colorless oil; Rf = 0.28; [α]D²³ = +1586 (c 0.21, CHCl₃); IR (CHCl₃, cm⁻¹) 2946, 1746, 1210, 1037; ¹H NMR (300 MHz, CDCl₃) δ 7.51-7.22 (m, 5H), 5.79 (d, J = 5 Hz, 1H), 4.95-4.84 (m, 2H), 4.13-4.00 (m, 2H), 3.91-3.85 (m, 1H), 2.17 (s, 3H), 2.13 (s, 3H), 1.95 (br s, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 170.7, 170.3, 133.3, 131.7, 129.1, 127.6, 85.5, 73.4, 71.5, 69.8, 59.8, 20.90, 20.88.

For the β-anomer: colorless oil; Rf = 0.21; [α]D²⁴ = (c 0.00, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.51-7.45 (m, 2H), 7.33-7.27 (m, 3H), 4.87-4.80 (m, 2H), 4.73 (d, J = 8.7 Hz, 1H), 4.23 (dd, J = 11.6, 5.0 Hz, 1H), 3.78 (dd, J = 8.3, 8.3 Hz, 1H), 3.35 (dd, J = 11.6, 9.0 Hz, 1H), 2.46 (br s, 1H), 2.16 (s, 3H), 2.09 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 170.6, 170.3, 132.6, 132.4, 129.0, 128.1, 86.2, 73.4, 72.4, 71.3, 65.5, 20.9, 20.8; HRMS (El) m/z (M⁺) calcd for C₁₅H₁₈O₈S 326.0824, obsd 326.0825.

3-O-Benzyl-1,2,4-tri-O-acetyl-D-xylopyranose (22).

A hot (100 °C) solution of 15c (1.04 g, 3.71 mmol) in 50% aqueous acetic acid (25 mL) was stirred for 3 h, cooled to rt, and freed of solvent in vacuo. The resulting white solid and N,N-dimethylamino pyridine (45 mg, 371 μmol) and treated in a dropwise fashion with acetic anhydride (1.40 mL, 14.8 mmol). The mixture was stirred for 1 h, diluted with ethyl acetate, and washed with 10% aq HCl and brine. The organic layer was dried and concentrated to leave a residue that was purified by silica gel chromatography (elution with 40% ethyl acetate in hexanes) to give 22 (1.22 g, 85%) as an inseparable mixture of anomers (β:α = 7:1).
For the α-anomer: colorless oil; $^1$H NMR (300 MHz, C$_6$D$_6$) $\delta$ 7.26-7.19 (m, 2H), 7.16-7.02 (m, 3H), 6.52 (d, $J = 3.5$ Hz, 1H), 5.18 (dd, $J = 9.5$, 3.6 Hz, 1H), 5.09 (ddd, $J = 10.7$, 9.2, 5.7 Hz, 1H), 4.58 (s, 2H), 3.96 (dd, $J = 9.2$, 9.2 Hz, 1H), 3.85 (dd, $J = 11.1$, 5.7 Hz, 1H), 3.54 (dd, $J = 10.7$, 10.7 Hz, 1H), 1.65 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 169.3 (3C), 138.9, 128.6, 128.1, 127.5, 90.2, 77.0, 74.4, 71.5, 70.5, 61.3, 20.2 (2C), 20.1.

For the β-anomer: colorless oil; $^1$H NMR (300 MHz, C$_6$D$_6$) $\delta$ 7.26-7.19 (m, 2H), 7.16-7.02 (m, 3H), 5.96 (d, $J = 5.5$ Hz, 1H), 5.26 (dd, $J = 6.9$, 5.6 Hz, 1H), 4.95 (ddd, $J = 6.8$, 6.6, 4.2 Hz, 1H), 4.53 (s, 2H), 4.04 (dd, $J = 12.1$, 4.2 Hz, 1H), 3.65 (dd, $J = 6.8$, 6.8 Hz, 1H), 3.26 (dd, $J = 12.1$, 6.6 Hz, 1H), 1.63 (s, 3H), 1.62 (s, 3H), 1.59 (s, 3H); $^{13}$C NMR (75 MHz, C$_6$D$_6$) ppm 168.9 (3C), 138.5, 128.5, 127.9, 92.5, 76.7, 73.2, 69.84, 69.80, 62.1, 20.3 (3C); HRMS (El) m/z (M$^+$) calcd for C$_{18}$H$_{22}$O$_8$ 366.1315, obsd 366.1332.

1,2,4-Tri-O-acetyl-3-O-(4-O-benzyl-2,3-di-O-methyl-α-L-fucopyranosyl)-α-D-xylopyranose (23).

To a mixture of 14e (15 mg, 40 µmol), 20 (9 mg, 40 µmol), N-trifluoromethanesulfonic acid, iodosuccinimide (11 mg, 48 µmol), 4 Å molecular sieves (25 mg), and dichloromethane (0.75 mL) was added a catalytic amount of trifluoromethanesulfonic acid. The deep red solution was stirred at rt for 5 min, saturated sodium bicarbonate solution was added, and the aqueous layer was extracted with ether. Drying and concentration in vacuo provided a crude oil that was purified by column chromatography (SiO$_2$, 50% ethyl acetate in hexanes) to furnish 23 as a colorless oil (7 mg, 36%).
Phenyl 2,4-Di-O-acetyl-3-O-(4-O-benzyl-2,3-di-O-methyl-α-L-fucopyranosyl)-1-thio-β-D-xylopyranoside (24).

Glycosyl fluoride 14f (10 mg, 35 μmol) in ether (0.5 mL) was added via cannula at rt to a mixture of glycosyl acceptor 2c (12 mg, 37 μmol), silver perchlorate (8 mg, 39 μmol), tin(II) chloride (7 mg, 39 μmol), and 4 Å molecular sieves (50 mg) in ether (0.75 mL). Following 1.5 h of stirring at rt, the mixture was filtered, and the filter cake was washed with ether. Concentration in vacuo and silica gel chromatography (40% ethyl acetate in hexanes) of the crude oil provided disaccharide 24 as a colorless oil, 18 mg (87%): [α]D23 = -62.9 (c 0.79, CHCl3); IR (CHCl3, cm⁻¹) 2938, 1745, 1369, 1100, 1059, 1035; ¹H NMR (300 MHz, CDCl3) δ 7.54-7.45 (m, 2H), 7.39-7.27 (m, 8H), 5.04 (d, J = 4 Hz, 1H), 5.00-4.88 (m, 2H), 4.92 (d, J = 12 Hz, 1H), 4.77 (d, J = 8 Hz, 1H), 4.60 (d, J = 12 Hz, 1H), 4.21 (dd, J = 12, 5 Hz, 1H), 3.94 (br q, J = 7 Hz, 1H), 3.78 (dd, J = 8, 8 Hz, 1H), 3.66 (dd, J = 10, 4 Hz, 1H), 3.64-3.63 (m, 1H), 3.52 (dd, J = 10, 3 Hz, 1H), 3.49 (s, 3H), 3.48 (s, 3H), 3.33 (dd, J = 12, 8 Hz, 1H), 1.22 (s, 3H), 2.04 (s, 3H), 1.09 (d, J = 7 Hz, 3H); ¹³C NMR (75 MHz, CDCl3) ppm 170.0, 169.3, 138.5, 132.8, 132.5, 128.9, 128.4, 128.2, 127.9, 127.6, 98.9, 86.2, 80.5, 79.3, 78.1, 76.7, 74.9, 70.2, 70.0, 67.6, 65.0, 58.7, 58.4, 21.0, 21.0, 16.5; HRMS (EI) m/z (M⁺-C₆H₅S) calcd for C₂₄H₃₃O₁₀ 481.2074, obsd 481.2054.

1,2,3-Tri-O-acetyl-4-O-(tert-butyldimethylsilyl)-L-fucopyranose (25a).

To a solution of L-fucose (8.89 g, 54.2 mmol) and N,N-dimethylaminopyridine (0.662 g, 5.43 mmol) in pyridine (50 mL) at rt was added acetic anhydride (15.3 mL, 0.162 mmol) in two portions, a third equivalent being added after 2 h. The solution was stirred for an additional 1.5 h prior to its dilution with water and...
extraction with ether and ethyl acetate. Drying of the organic layers and concentration in vacuo provided a crude oil that was chromatographed (SiO₂, 50% ethyl acetate in hexanes) to remove all undesired partially acetylated starting material. A pure sample of 27 was also obtained in this manner and shown to be an anomic mixture (α:β = 4.6:1) of triacetates, the α-anomer of which was characterized: colorless prisms, mp 134.5-135.5 °C (ether); IR (CHCl₃, cm⁻¹) 3610, 3028, 2988, 2940, 1750, 1372, 1244, 1140, 1071, 1012; ¹H NMR (300 MHz, CDCl₃) δ 6.29 (d, J = 3.7 Hz, 1H), 5.39 (dd, J = 10.8, 3.8 Hz, 1H), 5.26 (dd, J = 10.8, 3.0 Hz, 1H), 4.17 (q, J = 6.7 Hz, 1H), 3.98 (d, J = 1.0 Hz, 1H), 2.13 (s, 3H), 2.11 (s, 3H), 1.99 (s, 3H), 1.28 (d, J = 6.7 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 170.2, 169.9, 169.2, 90.0, 70.5, 70.2, 68.4, 66.4, 20.8, 20.8, 20.5, 16.0; HRMS (El) m/z (M+ - C₂H₃O₂) calcd for C₁₀H₁₅O₇ 231.0869, obsd 231.0872.

Anal. Calcd for C₁₂H₁₈O₈: C, 49.65; H, 6.25. Found: C, 49.68; H, 6.05.

The mixture of desired triacetates and peracetylated L-fucose was warmed (60 °C) with imidazole (3.11 g, 45.7 mmol), N,N-dimethylaminopyridine (0.559 g, 4.58 mmol), and t-butyldimethylsilyl triflate (10.49 mL, 45.7 mmol) in dimethylformamide (14 mL) for 6 h. Dilution of the cooled solution with saturated sodium bicarbonate solution and extraction of the mixture with ether was followed by drying of the organic layers, evaporation of the solvent under reduced pressure, and chromatography of the residue (SiO₂, 20% ethyl acetate in hexanes) to provide peracetylated L-fucose (5.86 g, 33%) as an oil and the desired triacetate 25a (9.51 g, 43%): colorless oil; [α]D₂² = -94.5 (c 0.83, CHCl₃); IR (CHCl₃, cm⁻¹) 2931, 2858, 1752, 1372, 1253, 1240, 1143, 1070, 1040, 1011; ¹H NMR (300 MHz, CDCl₃) δ 6.29 (d, J = 4 Hz, 1H), 5.44 (dd, J = 11, 4 Hz, 1H), 5.25 (dd, J = 11, 2 Hz, 1H), 4.10 (q, J = 7 Hz, 1H), 3.96 (d, J = 2 Hz, 1H), 2.12 (s, 3H), 2.08 (s, 3H), 1.99 (s, 3H), 1.19 (d, J = 7 Hz, 3H), 0.95 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 170.4, 169.9, 169.4, 90.4, 71.8, 70.7, 69.4, 66.5, 25.9 (3C), 21.2,
Phenyl 2,3-Di-0-acetyl-4-0-(tert-butyldimethylsilyl)-1-thio-β-L-fucopyranoside (25b).

To a stirred solution of 25a (2.00 g, 4.94 mmol) and (phenylthio)trimethylsilane (3.36 mL, 19.8 mmol) in dichloromethane (10 mL) at rt was added boron trifluoride etherate (0.61 mL, 4.94 mmol). The solution was stirred for 6 h prior to its concentration in vacuo and purification (SiO2, 25% ether-hexanes) to provide 1.94 g (86%) of 25b as colorless crystals, mp 76-78 °C; [a]D = +11.9 (c 0.93, CHCl3); IR (CHCl3, cm⁻¹) 2957, 2951, 2858, 1750, 1373, 1252, 1207, 1176, 1086, 1057, 1025; ¹H NMR (300 MHz, CDCl3) δ 7.51-7.47 (m, 2H), 7.31-7.24 (m, 3H), 5.23 (dd, J = 9.9 Hz, 9.9 Hz, 1H), 4.95 (dd, J = 9.9, 2.6 Hz, 1H), 4.63 (d, J = 9.8 Hz, 1H), 3.85 (d, J = 2.6 Hz, 1H), 3.70 (q, J = 6.3 Hz, 1H), 2.03 (s, 3H), 2.02 (s, 3H), 1.27 (d, J = 6.3 Hz, 3H), 0.88 (s, 9H), 0.02 (s, 6H); ¹³C NMR (75 MHz, CDCl3) ppm 170.3, 169.2, 132.9, 132.0, 128.7, 127.8, 85.2, 75.4, 75.3, 71.6, 67.4, 25.8, 21.0, 20.8, 18.3, 17.5, -4.44, -4.47; HRMS (El) m/z (M⁺-C₆H₅S) calcd for C₁₆H₂₉O₆Si 345.1733, obsd 345.1738.

2,3-Di-0-acetyl-4-0-(tert-butyldimethylsilyl)-L-fucopyranosyl Fluoride (25c).

Glycosyl sulfide 25b (829 mg, 2.49 mmol) and diethylaminosulfur trifluoride (0.48 mL, 3.7 mmol) were stirred with 4Å mol sieves in dichloromethane (18 mL) at rt prior to the addition of boron trifluoride etherate (0.34 mL, 2.7 mmol). The hazy solution was stirred for 10 min, then partitioned between saturated sodium bicarbonate solution and ether. Further extraction with ether, drying of the organic layers, and
silica gel chromatography (gradient, 15-30% ethyl acetate-hexanes) provided colorless crystals (665 mg, 91%).

Further purification furnished homogeneous α-anomer: colorless oil; Rf = 0.20; [α]23 = -115 (c 0.93, CHCl₃); IR (CHCl₃, cm⁻¹) 2958, 2931, 1746, 1483, 1372, 1253, 1230, 1206, 1068, 1040, 839; ¹H NMR (300 MHz, CDCl₃) δ 5.40-5.30 (m, 1H), 5.20 (dd, J = 53.1, 7.0 Hz, 1H), 4.93-4.89 (m, 1H), 3.87 (br s, 1H), 3.77 (q, J = 6.3 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H), 1.31 (d, J = 6.3 Hz, 3H), 0.96 (s, 9H), 0.080 (s, 3H), 0.056 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 170.2, 169.3, 107.3 (d, J = 214 Hz), 72.9 (d, J = 10.4 Hz), 71.6 (d, J = 3.9 Hz), 70.7, 69.2 (d, J = 24.6 Hz), 25.8 (3C), 21.0, 20.6, 18.3, 16.9, -4.39, -4.47; HRMS (EI) m/z (M+H) calcd for C₁₈H₂₃O₅Si 345.1733, obsd 345.1734.

Phenyl 2,3,4-Tri-O-acetyl-1-thio-L-fucopyranoside (28).

A solution of L-fucose (5.04 g, 30.7 mmol), acetic anhydride (14.5 mL, 153 mmol), and DMAP (50 mg, 0.41 mmol) in pyridine (12 mL) was stirred at rt for 12 h. The solution was diluted with ethyl acetate, and the resulting mixture washed successively with saturated NaHCO₃, 10% v/v aq HCl, and brine. The organic layer was dried and concentrated in vacuo to provide a crude oil.

This oil was taken up in benzene (30 mL) before being treated with thiophenol (3.79 mL, 36.8 mmol) and tin(IV) chloride (21.5 mL, 1M in CH₂Cl₂, 21.5 mmol). Stirring for 1.5 h was followed by dilution with ethyl acetate and washing of the organic layer with 10% v/v aq HCl and brine before drying and evaporation of solvent to leave a yellow oil. An aliquot could be purified using silica gel chromatography (35% ethyl acetate in hexanes) to provide both anomers of 28 as colorless oils.
For the α-anomer: \( R_f = 0.38; [\alpha]_D^{22} = -225 \text{ (c 0.47, CHCl}_3) \); IR (CHCl\(_3\), cm\(^{-1}\)) 3003, 2838, 2872, 1750, 1369, 1030; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.44-7.39 (m, 2H), 7.33-7.22 (m, 3H), 5.93 (d, \( J = 5 \text{ Hz, 1H} \)), 5.38-5.25 (m, 3H), 4.61 (q, \( J = 7 \text{ Hz, 1H} \)), 2.16 (s, 3H), 2.09 (s, 3H), 2.01 (s, 3H), 1.13 (d, \( J = 7 \text{ Hz, 3H} \)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) ppm 170.5, 170.2, 169.9, 133.3, 131.8, 129.1, 127.5, 85.6, 70.9, 68.6, 68.2, 65.5, 20.8, 20.7, 20.6, 15.9.

For the β-anomer: \( R_f = 0.30; [\alpha]_D^{22} = -6.72 \text{ (c 0.66, CHCl}_3) \); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.53-7.48 (m, 2H), 7.35-7.28 (m, 3H), 5.26 (d, \( J = 3 \text{ Hz, 1H} \)), 5.20 (d, \( J = 10 \text{ Hz, 1H} \)), 5.05 (dd, \( J = 10, 3 \text{ Hz, 1H} \)), 4.70 (d, \( J = 10 \text{ Hz, 1H} \)), 3.83 (q, \( J = 7 \text{ Hz, 1H} \)), 2.14 (s, 3H), 2.08 (s, 3H), 1.97 (s, 3H), 1.24 (d, \( J = 7 \text{ Hz, 3H} \)); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) ppm 170.6, 170.1, 169.4, 132.9, 132.4, 128.8, 127.9, 86.5, 73.2, 72.4, 70.4, 67.4, 20.8, 20.8, 20.6, 16.5; HRMS (El) \( m/z \) (\( \text{M}^+ - \text{C}_6\text{H}_5\text{S} \)) calcd for C\(_{12}\)H\(_{17}\)O\(_7\) 273.0974, obsd 273.0968.


Phenyl 2-O-Methyl-1-thio-β-L-fucopyranoside (29).

The crude oil 28 was dissolved in methanol (100 mL) and stirred with potassium hydroxide (1.03 g, 18.4 mmol) which had been introduced in aliquots of 0.1 eq. The resulting turbid mixture was agitated for an additional 5 h before concentration under reduced pressure and purification of the crude oil by silica gel chromatography (10% methanol-chloroform) to afford the triol as a white foam (7.18 g, 91% for 3 steps).

Zinc(II) chloride (5.85 g, 42.9 mmol) and phosphoric acid (0.05 mL) in acetone (80 mL) was slowly added to a suspension of the triol (7.18 g, 28.0 mmol) in acetone (80 mL). The resulting solution was stirred for 10 h before KOH (1 g) was added and the mixture was concentrated \textit{in vacuo}. The residue was treated with water and extracted with ethyl acetate. The
combined organic layers were washed with saturated NaHCO$_3$ solution and brine before drying. The solvent was removed under vacuum, and the residue was chromatographed (SiO$_2$, 40 % ethyl acetate in hexanes) to furnish the acetonide as a colorless oil (6.9 g, 83%).

A portion of the acetonide (5.80 g, 19.6 mmol) in DMF (55 mL) was treated with methyl iodide (2.44 mL, 39.1 mmol) and sodium hydride (704 mg, 29.4 mmol). The low temperature was maintained for 30 min prior to removal of the ice bath. Stirring for an additional 1 h was immediately followed by quenching with saturated NaHCO$_3$ solution and water before extraction of the mixture with ether. The combined organic layers were washed with brine, dried, and concentrated in vacuo to provide a yellow oil.

The crude oil was warmed to 100 °C in a 50% aqueous AcOH solution (150 mL) for 2 h. Removal of the solvent under reduced pressure, and filtering of the residue through silica gel (100% ethyl acetate) provided 29 as a colorless oil (5.28 g, 99%): [α]$^2_{D}$ = +22.9 (c 1.06, CHCl$_3$; IR (CHCl$_3$, cm$^{-1}$) 3600-3200, 2930, 2856, 1463, 1175, 1137, 1102; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.55-7.51 (m, 2H), 7.32-7.22 (m, 3H), 4.51 (d, J = 9.7 Hz, 1H), 3.75 (brd, J=3.2 Hz, 1H), 3.64 (s, 3H), 3.62-3.58 (m, 2H), 3.27 (dd, J = 9.4 Hz, 1H), 2.65 (s, 2H), 1.33 (d, J = 6.5 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 133.8, 131.7, 128.8, 127.4, 87.2, 79.9, 75.4, 74.4, 71.8, 61.2, 16.6; HRMS (EI) m/z (M$^+$) calcd for C$_{13}$H$_{18}$O$_4$S 270.0926, obsd 270.0928.

Anal. Calcd for C$_{13}$H$_{18}$O$_4$S: C, 57.76; H, 6.71. Found: C, 57.80; H, 6.85.

**Phenyl 2,3-Di-O-methyl-1-thio-β-L-fucopyranoside (30).**

A solution of 29 (406 mg, 1.50 mmol) in methanol (6 mL) was refluxed in the presence of di-n-butyltin oxide (392 mg, 1.58 mmol) for 2 h. Concentration of the mixture to leave a white solid was followed by addition of DMF (3 mL), methyl iodide (0.47 mL, 7.51 mmol), and cesium fluoride (342 mg, 2.25 mmol). The mixture was stirred...
for 12 h, at which point the foamy solution was diluted with 10% v/v aq HCl (5 mL) and extracted with ethyl acetate. The organic layers were combined and dried, concentrated in vacuo, and chromatographed (SiO₂, 60% ethyl acetate in hexanes) to provide 30 as a colorless oil (424 mg, 99%): [α]₂⁰° ≈ +9.56 (c 1.13, CHCl₃); IR (CHCl₃, cm⁻¹) 3569, 2936, 2836, 1479, 1440, 1381, 1128, 1104, 1077, 1045, 998; ¹H NMR (300 MHz, CDCl₃) δ 7.59-7.53 (m, 2H), 7.32-7.21 (m, 3H), 4.48 (d, J = 9.3 Hz, 1H), 3.85 (dd, J = 3.1, 1.0 Hz, 1H), 3.57 (s, 3H), 3.59-3.52 (m, 1H), 3.50 (s, 3H), 3.29 (dd, J = 9.0, 9.0 Hz, 1H), 3.22 (dd, J = 8.8, 3.1 Hz, 1H), 2.04 (br s, 1H), 1.36 (d, J = 6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 133.8, 132.0, 128.8, 127.3, 87.2, 85.0, 78.4, 74.2, 68.6, 61.1, 57.6, 16.7; HRMS (EI) m/z (M⁺) calcd for C₁₄H₂₀O₄S 284.1082, obsd 284.1081.

Phenyl 4-O-(tert-Butyldimethylsilyle)-2,3-di-O-methyl-1-thio-β-L-fucopyranoside (31).

A warm (80 °C) solution of 30 (3.34 g, 11.7 mmol), imidazole (1.60 g, 23.5 mmol) and DMAP (287 mg, 2.35 mmol) in N,N-dimethylformamide (8 mL) was treated with t-butyldimethylsilyle triflate (3 mL, 13.1 mmol) in three aliquots, each separated by 1 h. Continued heating for a 14 h period was followed by cooling and quenching of the solution with saturated NaHCO₃ solution. The mixture was extracted with ether and the combined organic layers were washed with water and saturated NH₄Cl solution, then dried and concentrated in vacuo. The resulting oil was chromatographed (SiO₂, 15% ethyl acetate in hexanes) to provide 31 as a colorless oil (3.61 g, 77%): [α]₁⁰° = +123 (c 0.50, CHCl₃); IR (CHCl₃, cm⁻¹) 3004, 2934, 2857, 1584, 1472, 1440, 1368, 1250, 1178, 1136, 1111, 1078, 1025, 984, 954, 837; ¹H NMR (300 MHz, CDCl₃) δ 7.60-7.55 (m, 2H), 7.29-7.18 (m, 3H), 4.41 (d, J = 9.5 Hz, 1H), 3.80 (d, J = 2.6 Hz, 1H), 3.52 (q, J = 6.4 Hz, 1H), 3.46 (s, 3H), 3.44 (s, 3H), 3.36 (dd, J = 9.4, 9.4 Hz, 1H), 3.06 (dd, J = 9.2, 2.7 Hz, 1H), 1.28 (d, J = 6.4 Hz, 3H), 0.92 (s, 9H), 0.058 (s, 3H), 0.054 (s, 3H); ¹³C
NMR (75 MHz, CDCl₃) ppm 133.7, 131.7, 128.6, 126.9, 86.6, 86.3, 77.5, 75.3, 71.2, 60.6, 58.5, 26.0, 18.6, 17.7, -4.13, -4.96; HRMS (El) m/z (M⁺) calcd for C₂₀H₃₄O₄Si 398.1947, obsd 398.1939.

Anal. Calcd for C₂₀H₃₄O₄Si: C, 60.26; H, 8.60. Found: C, 60.61; H, 8.69.

4-O-(tert-Butyldimethylsilyl)-2,3-di-O-methyl-L-fucopyranosyl Fluoride (26).

To a solution of 31 (250 mg, 0.627 mmol) and diethylaminosulfur trifluoride (91 μL, 0.690 mmol) in cold (0 °C) dichloromethane (5 mL) was added NBS (117 mg, 0.658 mmol). The orange solution was stirred for 15 min, diluted with triethylamine (1 mL) and ethyl acetate, washed with water, dried, concentrated in vacuo, and chromatographed (SiO₂, 15% ethyl acetate in hexanes with TEA) to provide 26 as a colorless oil (170 mg, 88%). The instability of 26 in most solvents limited its characterization to: α-anomer: colorless oil; Rf = 0.28; ¹H NMR (300 MHz, CDCl₃) δ 5.68 (dd, J = 54.5 Hz, 2.7 Hz, 1H), 4.03 (q, J = 6.5 Hz, 1H), 3.90 (d, J = 2.2 Hz, 1H), 3.59 (ddd, J = 25.2, 10.1, 2.7 Hz, 1H), 3.54 (s, 3H), 3.47 (s, 3H), 3.44 (dd, J = 7.5, 2.6 Hz, 1H), 1.23 (d, J = 6.5 Hz, 3H), 0.93 (s, 9H), 0.13 (s, 3H), 0.074 (s, 3H).

Phenyl 2,4-Di-O-acetyl-3-O-[2,3-di-O-acetyl-4-O-(tert-butyldimethylsilyl)-α-L-fucopyranosyl]-1-thio-β-D-xylopyranoside (32).

From 25a. Glycosyl fluoride 25a (68 mg, 0.187 mmol), glycosyl donor β-21 (76 mg, 0.233 mmol), and 4 Å molecular sieves (100 mg) were stirred vigorously in dichloromethane at 0 °C while a catalytic amount of boron trifluoride etherate was added. Following 10 min of stirring, the mixture
was filtered through Celite, concentrated under reduced pressure, and chromatographed (SiO₂, 30% ethyl acetate-hexanes) to furnish 83 mg (66%) of 32 as a colorless oil.

From 25c. Glycosyl fluoride 25c (65 mg, 0.178 mmol), glycosyl acceptor β-21 (58 mg, 0.178 mmol), tin(II) chloride (44 mg, 0.214 mmol), and 4 Å molecular sieves (75 mg) were stirred vigorously in dichloromethane at 0 °C while silver perchlorate (41 mg, 0.214 mmol) was introduced. Following 15 min of stirring, the mixture was concentrated under reduced pressure, filtered through Celite with ether, and chromatographed (SiO₂, 50% ether in hexanes) to furnish 24 mg (20%) 32 as a colorless oil: [α]D²³ = -119 (c 0.94, CHCl₃); IR (CHCl₃, cm⁻¹) 2958, 1746, 1371, 1244, 1066, 1039, 839; ¹H NMR (300 MHz, CD₅D₅) δ 7.55-7.51 (m, 2H), 7.04-6.92 (m, 3H), 5.59 (dd, J = 10.9, 3.6 Hz, 1H), 5.51 (dd, J = 10.9, 2.5 Hz, 1H), 5.42 (dd, J = 3.6 Hz, 1H), 5.25 (dd, J = 7.7 Hz, 1H), 4.77 (dd, J = 7.7, 7.7, 4.8 Hz, 1H), 4.58 (dd, J = 7.7 Hz, 1H), 4.13 (dd, J = 11.8, 4.8 Hz, 1H), 4.05 (q, J = 6.4 Hz, 1H), 3.83 (dd, J = 7.7, 7.7, 1H), 3.74 (br d, J = 2.0 Hz, 1H), 2.88 (dd, J = 11.8, 7.7 Hz, 1H), 1.94 (s, 3H), 1.84 (s, 3H), 1.79 (s, 3H), 1.63 (s, 3H), 1.15 (d, J = 6.4 Hz, 3H), 1.00 (s, 9H), 0.062 (s, 3H), -0.014 (s, 3H); ¹³C NMR (75 MHz, CD₅D₅) ppm 170.5, 169.4, 169.1, 169.0, 134.2, 132.6, 129.1, 127.9, 97.0, 86.8, 75.8, 72.7, 71.3, 70.7, 70.3, 68.6, 67.5, 64.6, 26.1, 23.0, 20.82, 20.76, 20.4, 18.6, 17.2, -4.2, -4.3; HRMS (El) m/z (M+-C₆H₅S) calcd for C₂₅H₄₁O₁₂Si 561.2367, obsd 561.2420.

**Anal.** Calcd for C₃₁H₄₆O₁₂Si: C, 55.50; H, 6.91. Found: C, 55.80; H, 7.48.

**Phenyl 2,4-Di-O-acetyl-3-O-[4-O-(tert-butyl(dimethyl)silyl)-2,3-di-O-methyl-α-L-fucopyranosyl]-1-thio-β-D-xylopyranoside (34).**

A solution of 26 (170 mg, 0.551 mmol) in ether (5 mL) was added to a vigorously stirred suspension of β-21 (170 mg, 0.521 mmol), silver perchlorate (114 mg, 0.521 mmol), and tin(II)
chloride (104 mg, 0.521 mmol) in ether (5 mL). The mixture was stirred for 15 min prior to dilution with brine and extraction of the mixture with ether. The ether layers were dried and concentrated, and the residue was chromatographed (SiO₂, 20% ethyl acetate in hexanes) to afford 34 as a white foam (182 mg, 57%): [α]²⁴ D = −99.0 (c 0.92, CHCl₃); IR (CHCl₃, cm⁻¹) 3004, 2954, 2931, 1240, 1236, 1196, 1134, 1102, 1065, 1027, 971, 838; ¹H NMR (300 MHz, CDCl₃) δ 7.63-7.59 (m, 2H), 7.05-6.91 (m, 3H), 5.27 (dd, J = 8.4, 8.4 Hz, 1H), 5.02 (ddd, J = 8.8, 7.9, 5.1 Hz, 1H), 4.88 (d, J = 3.4 Hz, 1H), 4.64 (d, J = 8.6 Hz, 1H), 4.02 (dd, J = 11.7, 5.0 Hz, 1H), 3.76 (q, J = 6.4 Hz, 1H), 3.58 (dd, J = 10.1, 3.3 Hz, 1H), 3.56 (dd, J = 7.9, 7.9 Hz, 1H), 3.44 (d, J = 0.9 Hz, 1H), 3.41 (dd, J = 10.3, 0.9 Hz, 1H), 3.32 (s, 3H), 3.24 (s, 3H), 2.93 (dd, J = 11.7, 8.8 Hz, 1H), 1.89 (s, 3H), 1.75 (s, 3H), 1.15 (d, J = 6.5 Hz, 3H), 1.05 (s, 9H), 0.21 (s, 3H), 0.067 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 169.3, 168.7, 133.4, 133.4, 133.1, 129.1, 129.1, 128.1, 128.1, 100.0, 86.3, 81.0, 80.1, 78.8, 72.9, 70.5, 70.4, 68.5, 65.4, 58.9, 58.7, 26.4, 26.4, 26.4, 20.8, 20.7, 18.9, 17.1, 3.71, -4.68; HRMS (EI) m/z (M⁺-C₆H₅S) calcd for C₂₃H₄₁O₁₀Si 505.2469, obsd 505.2467.

Phenyl 3-O-[4-O(tert-butyldimethylsilyl)-2,3-di-O-methyl-α-L-fucopyranosyl]-2,4-di-O-methyl-1-thio-β-D-xylopyranoside (35).

Disaccharide 34 (101 mg, 0.164 mmol) was stirred for 15 min in methanol (5 mL) in the presence of potassium hydroxide (7 mg, 0.125 mmol). The solvent was evaporated, and the residue was redissolved in DMF (1 mL), cooled to 0 °C and treated successively with methyl iodide (102 µL, 1.64 mmol) and sodium hydride (10 mg, 0.411 mmol). The ice bath was removed, and after 1 h of stirring, water was added carefully. The mixture was extracted with ether, and the organic layers were dried and concentrated in vacuo to provide a residue that could be purified by silica gel chromatography (25% ethyl acetate in hexanes) to furnish 35 as a colorless oil (77 mg, 84%).
$[\alpha]_D^{24} = -17.1 \ (c \ 1.01, \ CHCl_3); \ \text{IR (CHCl}_3, \ \text{cm}^{-1}) \ 3000, \ 2933, \ 2857, \ 1463, \ 1365, \ 1253, \ 1101, \ 1028, \ 970; \ ^1H \ \text{NMR} \ (300 \ MHz, \ C_6D_6) \ \delta \ 7.58-7.55 \ (m, \ 2H), \ 7.05-6.92 \ (m, \ 3H), \ 5.46 \ (d, \ J = 3.6 \ Hz, \ 1H), \ 4.53 \ (d, \ J = 9.3 \ Hz, \ 1H), \ 4.23 \ (q, \ J = 6.5 \ Hz, \ 1H), \ 3.83 \ (dd, \ J = 11.4, \ 5.1 \ Hz, \ 1H), \ 3.78 \ (dd, \ J = 8.9, \ 8.9 \ Hz, \ 1H), \ 3.75-3.70 \ (m, \ 2H), \ 3.61 \ (s, \ 3H), \ 3.54 \ (dd, \ J = 10.1, \ 2.6 \ Hz, \ 1H), \ 3.31 \ (s, \ 3H), \ 3.29 \ (s, \ 3H), \ 3.27 \ (dd, \ J = 9.1, \ 9.1 \ Hz, \ 1H), \ 3.09 \ (ddd, \ J = 9.4, \ 9.4, \ 5.1 \ Hz, \ 1H), \ 3.00 \ (s, \ 3H), \ 2.85 \ (dd, \ J = 11.4, \ 9.6 \ Hz, \ 1H), \ 1.29 \ (d, \ J = 6.5 \ Hz, \ 3H), \ 1.09 \ (s, \ 9H), \ 0.25 \ (s, \ 3H), \ 0.12 \ (s, \ 3H); \ ^{13}C \ \text{NMR} \ (75 \ MHz, \ C_6D_6) \ \text{ppm} \ 135.0, \ 132.1, \ 129.0, \ 127.4, \ 98.5, \ 88.6, \ 83.8, \ 81.0, \ 79.9, \ 78.64, \ 78.60, \ 73.0, \ 67.1, \ 66.4, \ 60.4, \ 59.4, \ 58.5, \ 57.4, \ 26.4, \ 19.0, \ 17.4, \ -3.63, \ -4.60; \ \text{HRMS (EI)} \ m/z \ (M^+) \ \text{calcd for C}_{27}H_{46}O_8Si: \ 558.2683, \ \text{obsd} \ 558.2702.$

*Anal. Calcd for C$_{27}$H$_{46}$O$_8$Si: C, 58.03; H, 8.30. Found: C, 57.89; H, 8.50.*
(1S,2S,3R,4S)-2-[(Z)-2-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]2,2-dimethyl-1,3-dioxolan-4-yl]vinyl]-3-(methoxymethoxy)-1-[(Z)-2-(p-methoxyphenoxy)vinyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-ol (49a).

Ketone 48a and (4S)-4-[(Z)-2-iodovinyl]-4-[(1R)-1-[(p-methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolane were reacted in an identical manner to provide 49a as a colorless oil (64 mg, 34%); 

\[ \alpha \text{D}^1 = -104 \ (c 0.62, \text{CHCl}_3) \]; IR (film, cm\(^{-1}\)) 3455, 2937, 1664, 1612, 1506, 1466, 1370, 1222, 1178, 1148, 1112, 1044; \( ^1H \) NMR (300 MHz, \( \text{C}_6\text{D}_6 \)) \( \delta \) 7.25 (d, \( J = 8.6 \) Hz, 2H), 6.85 (d, \( J = 9.1 \) Hz, 2H), 6.76 (d, \( J = 8.7 \) Hz, 2H), 6.68 (d, \( J = 9.1 \) Hz, 2H), 6.33 (d, \( J = 7.0 \) Hz, 1H), 5.97 (ddd, \( J = 17.0, 10.5, 6.1 \) Hz, 1H), 5.73 (d, \( J = 13.4 \) Hz, 1H), 5.57 (d, \( J = 13.4 \) Hz, 1H), 5.36 (d, \( J = 16.9 \) Hz, 1H), 5.23 (d, \( J = 10.5 \) Hz, 1H), 5.14 (d, \( J = 7.0 \) Hz, 1H), 4.90 (s, 1H), 4.63 (s, 2H), 4.52 (d, \( J = 11.3 \) Hz, 1H), 4.49 (d, \( J = 6.4 \) Hz, 1H), 4.35 (d, \( J = 11.4 \) Hz, 1H), 4.30 (d, \( J = 6.5 \) Hz, 1H), 4.26 (d, \( J = 6.1 \) Hz, 1H), 3.48 (s, 1H), 3.26 (s, 3H), 3.25 (s, 3H), 3.20 (s, 3H), 2.26 (ddd, \( J = 5.4, 5.4, 2.0 \) Hz, 1H), 2.09 (ddd, \( J = 14.3, 9.3, 3.3 \) Hz, 1H), 1.90 (d, \( J = 5.1 \) Hz, 1H), 1.74 (s, 3H), 1.72-1.64 (m, 1H), 1.45 (s, 3H), 1.42 (s, 3H), 1.00 (s, 3H), 0.97-0.92 (m, 1H); \( ^{13}C \) NMR (75 MHz, \( \text{C}_6\text{D}_6 \)) ppm 160.0, 155.7, 152.1, 143.4, 138.7, 135.5, 130.9, 130.5, 129.8, 117.9, 117.7, 114.9, 114.1, 109.0, 108.9, 96.8, 90.6, 85.1, 84.2, 83.3, 73.4, 71.8, 58.7, 55.1, 55.0, 54.7, 52.3, 49.8, 27.7, 27.4, 26.2, 25.3, 22.9, 22.8; HRMS (EI) m/z (M\(^+\)) calcd for C\(_{38}\)H\(_{50}\)O\(_9\) 650.3455, obsd 650.3428.

_Anal._ Calcd for C\(_{38}\)H\(_{50}\)O\(_9\): C, 70.13; H, 7.74. Found: C, 69.73; H, 7.77.
(1S,2S,3R,4S)-2-[(Z)-2-[[4S]-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]2,2-dimethyl-1,3-dioxolan-4-ylvinyl]-3-(methoxymethoxy)-1-[(E)-2-[(p-methoxyphenoxy)vinyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-ol (49b).

Ketone 48b (101 mg, 0.292 mmol) and (4S)-4-[(Z)-2-iodovinyl]-4-[(1R)-1-[(p-methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolane (132 mg, 0.306 mmol) in dry ether (3 mL) were cooled to -78 °C and treated with two equal portions of n-butyllithium (0.19 mL, 1.6 M in hexanes) the addition of which was separated by 30 min. The solution was stirred for 20 min, quenched with saturated NH₄Cl solution, and warmed to rt. The reaction mixture was diluted with ether, the layers were separated, and the combined organic layers were dried, concentrated, and chromatographed (20% ethyl acetate in hexanes) to provide 49b as a colorless oil (53 mg, 29%); [α]D²¹ = -46.6 (c 0.35, CHCl₃); IR (film, cm⁻¹) 3442, 2941, 1664, 1613, 1505, 1250, 1179, 1148, 1116, 1044; ¹H NMR (300 MHz, CDCl₃) δ 7.27 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 9.1 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.82 (d, J = 9.1 Hz, 2H), 6.23 (d, J = 12.6 Hz, 1H), 5.77 (ddd, J = 17.3, 10.6, 6.9 Hz, 1H), 5.62 (d, J = 12.6 Hz, 1H), 5.57 (d, J = 13.4 Hz, 1H), 5.43 (d, J = 13.4 Hz, 1H), 5.30 (d, J = 10.3 Hz, 1H), 5.26 (d, J = 17.1 Hz, 1H), 4.49 (d, J = 11.1 Hz, 1H), 4.41 (d, J = 11.2 Hz, 1H), 4.33 (d, J = 6.6 Hz, 1H), 4.28 (d, J = 9.9 Hz, 1H), 4.21 (d, J = 9.9 Hz, 1H), 4.16 (d, J = 6.6 Hz, 1H), 3.96 (d, J = 6.8 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.40 (s, 1H), 3.22 (s, 3H), 2.17 (s, 1H), 1.86 (d, J = 5.1 Hz, 1H), 1.81-1.74 (m, 1H), 1.60 (ddd, J = 13.0, 13.0, 5.1 Hz, 1H), 1.52-1.43 (m, 1H), 1.39 (s, 3H), 1.32 (s, 3H), 1.26 (s, 3H), 1.15-1.06 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 159.3, 155.1, 151.2, 144.3, 137.2, 134.4, 130.8, 130.1, 129.4, 119.0, 118.0, 114.5, 113.7, 109.7, 108.4, 96.2, 89.6, 84.5, 83.6, 83.4, 72.3, 71.4, 57.1, 55.6, 55.2, 55.0, 51.1, 49.8, 27.0, 26.0, 25.5, 24.6, 22.2, 22.0; HRMS (EI) m/z (M⁺) calcd for C₃₈H₅₀O₉ 650.3455, obsd 650.3450.
(1S,2R,5S,6S,7E)-5-[(E)-1-(Hydroxymethyl)-2-[(p-methoxybenzyl)oxy]-1,3-butadienyl]-2-(methoxymethoxy)-6-(p-methoxyphenoxy)-11,11-dimethylbicyclo[6.2.1]undec-7-en-3-one (51a) and (1S,2R,5S,6S,7E)-5-[(E)-2-[(p-methoxybenzyl)oxy]-1-[(trimethylsiloxy)methyl]-1,3-butadienyl]-2-(methoxymethoxy)-6-(p-methoxyphenoxy)-11,11-dimethylbicyclo[6.2.1]undec-7-en-3-one (51b).

A solution of 49b (9.9 mg, 16 µmol) and 18-crown-6 (21 mg, 78 µmol) in THF (0.75 mL) was purged with dry argon for 10 min, cooled to 0°C, and treated with potassium hexamethyldisilazide (0.16 mL, 0.5 M in toluene). The solution was stirred for 5 min, quenched with water, and extracted with ether. The combined ether layers were dried and concentrated to furnish a crude oil that was subjected to flash chromatography (45% ethyl acetate in hexanes) to provide 51a (5.1 mg, 55%) and 51b (1.4 mg, 14%) as colorless oils.

For 51a: [α]D23 = -18.1 (c 0.36, CHCl3); IR (film, cm⁻¹) 3519, 2943, 1693, 1613, 1505, 1248, 1036; ¹H NMR (300 MHz, C₆D₆) δ 7.40 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 9.1 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 6.62 (d, J = 9.1 Hz, 2H), 5.84 (br d, J = 9.0 Hz, 1H), 5.72 (dd, J = 17.2, 2.1 Hz, 1H), 5.22-5.11 (m, 3H), 4.80 (d, J = 11.2 Hz, 1H), 4.72 (d, J = 11.1 Hz, 1H), 4.54 (d, J = 12.3, 7.2 Hz, 1H), 4.39 (dd, J = 12.3, 2.5 Hz, 1H), 4.21 (d, J = 6.6 Hz, 1H), 4.14 (d, J = 6.6 Hz, 1H), 3.87 (d, J = 5.4 Hz, 1H), 3.68 (dd, J = 15.4, 11.7 Hz, 1H), 3.25 (s, 3H), 3.21 (s, 3H), 3.05 (br s, 1H), 2.97 (s, 3H), 2.32 (ddd, J = 14.3, 10.4, 5.5 Hz, 1H), 1.96-1.83 (m, 4H), 1.71-1.61 (m, 2H), 1.42 (s, 3H), 0.85 (s, 3H); ¹³C NMR (75 MHz, C₆D₆) ppm 210.3, 159.9, 154.9, 153.6, 152.3, 149.0, 130.3, 130.1, 129.0, 128.6, 124.4, 117.7, 117.2, 114.9, 114.2, 96.2, 88.2, 77.6, 73.3, 59.2, 55.4, 55.0, 54.8, 54.7, 46.4, 41.2, 40.3, 26.3, 24.7, 23.5, 22.4; HRMS (El) m/z (M⁺) calcd for C₃₅H₄₄O₈ 592.3036, obsd 592.3036.
For 51b: IR (film, cm\(^{-1}\)) 2955, 1693, 1562, 1465, 1249, 1172, 1130, 1037; \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \(\delta\) 7.43 (d, \(J = 8.6\) Hz, 2H), 6.95 (d, \(J = 9.1\) Hz, 2H), 6.79 (d, \(J = 8.6\) Hz, 2H), 6.71 (d, \(J = 9.1\) Hz, 2H), 5.91 (br d, \(J = 2.2\) Hz, 1H), 5.67 (d, \(J = 16.5\) Hz, 1H), 5.29-5.17 (m, 3H), 4.81-4.68 (m, 3H), 4.30 (d, \(J = 6.5\) Hz, 1H), 4.20 (d, \(J = 6.6\) Hz, 1H), 4.01-3.96 (m, 1H), 3.89 (d, \(J = 5.5\) Hz, 1H), 3.26 (s, 3H), 3.25 (s, 3H), 3.04 (s, 3H), 2.45-2.35 (m, 1H), 2.01-1.86 (m, 4H), 1.73-1.62 (m, 1H), 1.60-1.49 (br s, 2H), 0.92 (s, 3H), 0.40 (s, 3H), 0.19 (s, 9H).

\((1S,3R,4S)-3-(M ethoxym ethoxy)-1-[2-m ethoxy-2-(m ethylthio)vinyl]-7,7-
\textit{dimethylbicyclo[2.2.1]heptan-2-one (53b).}\)

\begin{center}
\includegraphics[width=0.2\textwidth]{diagram}
\end{center}

A solution of O,S-dimethylthioacetal diethyl formylyphosphonate (116 mg, 509 \(\mu\)mol) in tetrahydrofuran (1 mL) was cooled to -78 \(^\circ\)C, treated with tert-butyllithium, and stirred for 1 h. Ketone 52 (114 mg, 504 \(\mu\)mol) in tetrahydrofuran (0.5 mL) was added, and the reaction flask was immediately warmed to rt and stirred for 45 min prior to the addition of water and extraction with ether. The ethereal extracts were dried and freed of solvent to leave a residue that was subjected to silica gel chromatography (elution with 15% ethyl acetate in hexanes containing 2% triethylamine) to furnish 53b (50 mg, 33%) as a very unstable colorless oil. The 1.4:1 mixture of stereoisomers thus isolated was found to be too labile to characterize beyond acquisition of their magnetic resonance spectra.

For the major stereoisomer: \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \(\delta\) 5.17 (s, 1H), 4.80 (d, \(J = 6.4\) Hz, 1H), 4.52 (d, \(J = 6.8\) Hz, 1H), 3.63 (s, 1H), 3.23 (s, 3H), 3.22 (s, 3H), 2.13-1.91 (m, 1H), 1.86 (s, 3H), 1.84-1.55 (series of m, 3H), 1.10 (s, 3H), 1.07-0.92 (m, 1H), 0.76 (s, 3H); \(^13\)C NMR (75 MHz, C\(_6\)D\(_6\)) ppm 212.5, 156.7, 108.4, 96.5, 80.9, 61.9, 57.2, 55.2, 48.4, 48.2, 27.1, 25.4, 21.6, 20.7, 15.5.
For the minor stereoisomer: $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 4.85 (s, 1H), 4.82 (d, $J = 5.9$ Hz, 1H), 4.54 (d, $J = 4.5$ Hz, 1H), 3.68 (s, 1H), 3.47 (s, 3H), 3.26 (s, 3H), 2.09 (s, 3H), 2.13-1.91 (m, 1H), 1.84-1.55 (series of m, 3H), 1.13 (s, 3H), 1.07-0.92 (m, 1H), 0.81 (s, 3H); $^{13}$C NMR (75 MHz, $C_6D_6$) ppm 212.3, 157.1, 99.1, 96.6, 80.8, 60.3, 56.4, 55.2, 48.7, 48.2, 27.0, 25.6, 21.6, 20.9, 14.8.

\((1\text{S},3\text{R},4\text{S})\)-3-(Methoxymethoxy)-7,7-dimethyl-1-[(Z)-2-(phenylthio)vinyl]bicyclo[2.2.1]heptan-2-one (53c).

A solution of potassium hexamethyldisilazide (95.0 mL of 0.5M in toluene, 47.5 mmol) was added dropwise to a chilled (0 °C), magnetically stirred suspension of commercial phenylthiomethyl triphenylphosphonium chloride (19.7 g, 47 mmol) in dry THF (100 mL). After 30 min at this temperature, a solution of 52 (8.7 g, 39 mmol) in THF (20 mL) was introduced slowly into the yellow reaction mixture. The cooling bath was removed and stirring was maintained for an additional 2 h, at which point saturated $\text{NH}_4\text{Cl}$ solution and hexanes were added. The separated organic layer was dried and concentrated to leave an oil, which was purified by chromatography on silica gel (7% ethyl acetate in hexanes) to furnish 53c (8.1 g, 63%) and its slightly impure trans isomer (2.7 g, 21%) which was not further purified.

For 53c: white solid, mp 70-70.5 °C; $[\alpha]_{D}^{20} = -68.3$ (c 1.26, CHCl$_3$); IR (film, cm$^{-1}$) 1755, 1586; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.38-7.18 (m, 5H), 6.57 (d, $J = 10.7$ Hz, 1H), 5.68 (d, $J = 10.6$ Hz, 1H), 4.85 (d, $J = 6.6$ Hz, 1H), 4.72 (d, $J = 6.6$ Hz, 1H), 3.75 (s, 1H), 3.41 (s, 3H), 2.37-2.27 (m, 1H), 2.17-2.03 (m, 3H), 1.54-1.45 (m, 1H), 1.12 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 213.3, 136.5, 129.7, 129.2, 128.9, 126.5, 124.0, 96.6, 81.1, 62.7, 55.5, 49.0, 47.8, 25.4.
25.3, 21.3, 20.7; HRMS (El) m/z (M+) calcd for C_{19}H_{24}O_{3}S 332.1446, obsd 332.1448.

Anal. Calcd for C_{19}H_{24}O_{3}S: C, 68.64; H, 7.28. Found: C, 68.91; H, 7.33.

(1S,2S,3R,4S)-2-[(Z)-2-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-ylvinyl]-3-(methoxymethoxy)-7,7-dimethyl-1-[(Z)-2-(phenylthio)viny1]bicyclo[2.2.1]heptan-2-ol (54b).

\[
\begin{align*}
&n-\text{Butyllithium (3.07 mL of 1.5 M in hexanes, 4.60 mmol) was added to a solution of (4S)-4-[(Z)-2-iodovinyl]-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolane (1.98 g, 4.60 mmol), in anhydrous ether (12 mL) at -78 °C. After 1 min of stirring, a solution of 53c in dry ether (5 mL) was cannulated into the reaction mixture, which was agitated for another 20 min at -78 °C before being diluted with water, allowed to warm to rt, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel (10% ethyl acetate in hexanes) to furnish 54b (2.25 g, 85%) as a colorless oil; [\alpha]_{D}^{20} = -205 (c 0.81, CHCl_{3}); \text{IR (film, cm}^{-1}\text{)} 3423, 1612, 1586; ^1\text{H NMR (300 MHz, CDCl}_{3}\text{)} \delta 7.29-7.13 (m, 7H), 6.87-6.83 (m, 2H), 6.32 (d, J = 10.9 Hz, 1H), 5.90 (d, J = 10.9 Hz, 1H), 5.79 (ddd, J = 17.9, 10.0, 6.6 Hz, 1H), 5.63 (d, J = 13.4 Hz, 1H), 5.59 (d, J = 13.4 Hz, 1H), 5.29 (d, J = 4.9 Hz, 1H), 5.24 (s, 1H), 4.58 (s, 1H), 4.52 (d, J = 11.3 Hz, 1H), 4.45 (d, J = 11.3 Hz, 1H), 4.35 (d, J = 6.6 Hz, 1H), 4.30-4.20 (m, 3H), 4.01 (d, J = 6.3 Hz, 1H), 3.78 (s, 3H), 3.37 (s, 1H), 3.73 (s, 3H), 2.12-2.07 (m, 2H), 1.87-1.78 (m, 2H), 1.40 (s, 3H), 1.38 (s, 3H), 1.32 (s, 3H), 1.29-1.10 (m, 1H), 0.86 (s, 3H); ^13\text{C NMR (75 MHz, CDCl}_{3}\text{)} ppm 159.3, 137.9, 137.4, 134.6, 130.8, 130.0, 129.4, 128.8, 128.7, 126.1, 125.8, 118.6, 113.6, 108.6, 96.5, 90.4, 84.6, 84.0, 83.2, 72.6,
\end{align*}
\]
71.4, 60.4, 55.2, 55.0, 52.4, 49.3, 27.0, 26.7, 25.7, 24.9, 22.33, 22.26; HRMS (El) m/z (M+)
calcd for C_{37}H_{48}O_7S 636.3120, obsd 636.3141.

Anal. Calcd for C_{37}H_{48}O_7S: C, 69.78; H, 7.60. Found: C, 69.81; H, 7.63.

(1S,2R,4S,5S,6R,7E)-5-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethyl-6-(phenythio)bicyclo[6.2.1]undec-7-en-3-one (55b).

A solution of 54b (816 mg, 1.28 mmol) and 18-crown-6 (1.00 g, 3.78 mmol) in dry THF (20 mL) was deoxygenated (Ar), cooled to -78 °C, treated dropwise with potassium hexamethyldisilazide (7.7 mL of 0.5 M in toluene, 3.85 mmol), and allowed to stir at -78 °C for 15 min prior to the introduction of methyl iodide (0.80 mL, 12.8 mmol) in one portion. After a final hour of agitation at -78 °C, the white suspension was quenched with saturated NH_4Cl solution (10 mL), allowed to warm to rt, and diluted with ethyl acetate (20 mL). The separated organic layer was dried and concentrated, leaving a residue that was purified by chromatography on silica gel (15% ethyl acetate in hexanes) to give 55b as a white foam (667 mg, 80%): [α]_D^{20} = -105 (c 0.77, CHCl_3); IR (film, cm⁻¹) 1613, 1584, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.31-7.13 (m, 7H), 6.86-6.81 (m, 2H), 6.05 (br s, 1H), 5.40 (br m, 1H), 5.29 (d, J = 11.6 Hz, 1H), 5.24 (d, J = 6.8 Hz, 1H), 4.61 (d, J = 6.9 Hz, 1H), 4.54 (d, J = 11.3 Hz, 1H), 4.36-4.25 (m, 3H), 4.23 (d, J = 9.1 Hz, 1H), 4.09 (s, 1H), 3.79 (s, 3H), 3.30 (s, 3H), 3.01-2.97 (m, 1H), 2.85 (br s, 1H), 2.33-2.15 (m, 2H), 2.13 (d, J = 8.2 Hz, 1H), 1.49 (s, 3H), 1.41 (s, 3H), 1.21 (d, J = 7.5 Hz, 3H), 1.13 (s, 3H), 0.99 (s, 3H); ^13C NMR (75 MHz, CDCl_3) ppm 217.8, 159.3, 137.3, 134.6, 130.8, 130.1, 129.5, 128.9, 128.84, 128.77, 126.2, 125.9, 118.7, 113.7, 108.7, 99.8, 98.2, 96.5,
HRMS (FAB) m/z (M+H) calcd for C_{38}H_{50}O_{7}S 651.33, obsd 651.22.

**Anal.** Calcd for C_{38}H_{50}O_{7}S: C, 70.12; H, 7.75. Found: C, 69.90; H, 7.92.

\[ \text{(1S,2R,4S,5S,6R,7E)-5-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethyl-6-(phenylsulfinyl)bicyclo[6.2.1]undec-7-en-3-one (57).} \]

\[ \text{m-Chloroperbenzoic acid (16 mg, 90 \mu mol) was added to a solution of 55b (55 mg, 86 \mu mol) in CH}_2\text{Cl}_2 (3 mL) containing sodium bicarbonate (2 mg, 24 \mu mol) at -78 °C. After 5 min of stirring at this temperature, the reaction mixture was warmed to 0 °C for 15 min before being diluted with saturated NaHCO}_3 solution and CH}_2\text{Cl}_2. The separated organic phase was dried and concentrated to leave an oil that was purified by chromatography on silica gel (30% ethyl acetate in hexanes). The less polar sulfoxide (34 mg, 60%) was isolated as a colorless oil; the more polar diastereomer (20 mg, 36%) exhibited the same physical characteristics. These sulfoxides are unstable at rt, readily undergoing elimination to 58. Consequently, no characterization was undertaken.} \]
Reaction of m-chloroperbenzoic acid (232 mg, 1.35 mmol) with 55b (727 mg, 1.12 mmol) in the predescribed manner gave an oily mixture of sulfoxides, which was taken up in THF (20 mL), heated to reflux for 3 h, cooled to rt, and concentrated.

Purification of the residue by chromatography on silica gel (20% ethyl acetate in hexanes) afforded triene 58 as a colorless oil (374 mg, 62%): \([\alpha]_D^{20} = -219 \) (c 1.70, CHCl₃); IR (film, cm⁻¹) 1705, 1613, 1586; \(^1\)H NMR (300 MHz, C₆D₆, 60 °C) δ 7.29-7.25 (m, 2H), 6.85-6.82 (m, 2H), 6.59 (br s, 1H), 6.09 (ddd, \(J = 17.4, 10.7, 6.9 \) Hz, 1H), 5.65 (s, 1H), 5.37 (d, \(J = 17.4 \) Hz, 1H), 5.31 (d, \(J = 10.4 \) Hz, 1H), 4.60-4.55 (m, 3H), 4.35-4.30 (m, 2H), 4.19-4.08 (m, 3H), 3.39 (s, 3H), 3.31-3.27 (m, 1H), 3.22 (s, 3H), 2.60-2.52 (m, 1H), 2.16-2.15 (m, 1H), 2.14-1.98 (m, 2H), 1.60-1.58 (m, 1H), 1.54 (s, 6H), 1.39 (s, 3H), 1.34 (d, \(J = 6.9 \) Hz, 3H), 1.06 (s, 3H); \(^{13}\)C NMR (75 MHz, C₆D₆, 30 °C) ppm 209.2, 159.8, 146.7, 135.5, 130.7, 129.8, 126.5, 118.5, 114.0, 109.0, 95.2, 85.3, 71.5, 55.4, 54.7, 54.0, 47.0, 46.5, 26.9, 25.5, 25.0, 24.9, 21.7, 17.5; HRMS Molecular ion too fleeting for accurate mass measurement.
(1S,2R,4S,5S,6R,7E)-5-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethyl-6-(phenylsulfonyl)bicyclo[6.2.1]undec-7-en-3-one (59).

m-Chloroperbenzoic acid (9.8 mg, 57 µmol) was added directly to a mixture of sodium bicarbonate (7.0 mg, 83 µmol) and 55b (18 mg, 28 µmol) in cold (0 °C) CH_2Cl_2 (1 mL). Stirring was continued at that temperature for 30 min and at rt for a total of 23 h. The reaction mixture was diluted with water and extracted with ether, and the organic layer was dried and concentrated to leave a residue that was purified by silica gel chromatography (35% ethyl acetate in hexanes) to provide 59 (12.6 mg, 67%) as a colorless oil: [α]^23_D = -71.9 (c 1.82, CHCl_3); IR (film, cm^-1) 2940, 1717, 1614, 1515, 1447, 1380, 1300, 1249, 1145, 1107, 1086, 1042, 1003; ^1H NMR (300 MHz, C_6D_6) δ 7.96 (d, J = 7.8 Hz, 2H), 7.27 (d, J = 8.4 Hz, 1H), 7.00-6.93 (m, 3H), 6.82 (d, J = 8.5 Hz, 2H), 5.94 (d, J = 11.3 Hz, 1H), 5.24 (br d, 3H), 4.84 (d, J = 10.6 Hz, 1H), 4.68 (d, J = 8.1 Hz, 1H), 4.49 (d, J = 6.8 Hz, 1H), 4.47 (d, J = 11.1 Hz, 1H), 4.37 (d, J = 6.8 Hz, 1H), 4.19 (d, J = 11.3 Hz, 1H), 4.13 (s, 1H), 3.87 (d, J = 7.0 Hz, 1H), 3.85 (d, J = 10.8 Hz, 1H), 3.66 (br s, 1H), 3.31 (s, 3H), 3.29-3.20 (m, 2H), 3.10 (s, 3H), 2.86-2.61 (br m, 1H), 2.16 (br d, J = 8.2 Hz, 1H), 2.11-2.02 (m, 1H), 1.45 (d, J = 7.7 Hz, 3H), 1.44-1.37 (m, 1H), 1.31 (s, 3H), 1.31-1.23 (m, 1H), 1.04 (br s, 3H), 1.01 (s, 3H), 0.73 (br s, 3H); ^13C NMR (75 MHz, C_6D_6) ppm 210.5, 159.7, 155.5, 142.2, 135.7, 132.7, 131.0, 129.7, 129.1, 128.5, 119.4, 115.6, 114.0, 108.1, 95.4, 88.4, 85.4, 83.6, 71.2, 70.2, 65.5, 55.4, 54.9, 54.8, 48.3, 47.6, 45.4, 28.3, 27.4, 26.7, 26.4, 25.9, 20.7, 18.9; HRMS (El) m/z (M+CH_3) calcd for C_{37}H_{47}O_{9}S 667.2941, obsd 667.2972.
(1S,2R,3S,4S,5S,6R,7E)-5-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethyl-6-(phenylthio)bicyclo[6.2.1]undec-7-en-3-ol (62a) and (1S,2R,3R,4S,5S,6R,7E)-5-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethyl-6-(phenylthio)bicyclo[6.2.1]undec-7-en-3-ol (62b).

Lithium aluminum hydride (141 mg, 3.72 mmol) was added to a cold (0 °C) solution of 55b (2.02 g, 3.10 mmol) in anhydrous ether (30 mL). The suspension was stirred for 2 h, treated with saturated Rochelle’s salt solution, and stirred for an additional 12 h. Following extraction with ethyl acetate, the combined organic layers were dried and concentrated. The residue was chromatographed on silica gel (20% ethyl acetate in hexanes) to furnish 1.57 g (77%, 80% purity) of 62a and 134 mg (7%) of 62b, both as colorless oils.

For 62a: $[\alpha]_D^{21} = -284$ (c 1.10, CHCl$_3$); IR (film, cm$^{-1}$) 3485, 2946, 1613, 1514, 1478, 1439, 1380, 1378, 1248, 1211, 1172, 1148, 1036; $^1$H NMR (300 MHz, C$_6$D$_6$) $\delta$ 7.33 (d, $J = 7.3$ Hz, 2H), 7.22 (d, $J = 8.6$ Hz, 2H), 7.04 (dd, $J = 7.2$ Hz, 2H), 6.93 (dd, $J = 7.3$ Hz, 1H), 6.73 (dd, $J = 8.6$ Hz, 2H), 6.28 (ddd, $J = 17.3$, 10.4, 6.8 Hz, 1H), 5.78 (d, $J = 7.5$ Hz, 1H), 5.39 (d, $J = 10.3$ Hz, 1H), 5.34 (br d, $J = 17.3$ Hz, 1H), 4.53 (d, $J = 11.1$ Hz, 1H), 4.45 (d, $J = 6.4$ Hz, 1H), 4.37 (d, $J = 11.1$ Hz, 1H), 4.33 (d, $J = 6.5$ Hz, 1H), 4.31 (d, $J = 11.1$ Hz, 1H), 4.19 (d, $J = 6.9$ Hz, 1H), 4.16 (d, $J = 11.2$ Hz, 1H), 3.92-3.85 (m, 2H), 3.77 (d, $J = 5.7$ Hz, 1H), 3.36 (d, $J = 11.5$ Hz, 1H), 3.25 (s, 3H), 3.10 (s, 3H), 3.08-2.97 (m, 1H), 2.79 (br s, 1H), 2.31 (br dd, $J = 12.3$ Hz, 1H), 1.87 (dd, $J = 6.9$ Hz, 1H), 1.64 (ddd, $J = 12.4$, 12.4, 5.4 Hz, 1H), 1.45 (s, 3H), 1.44 (s, 3H), 1.41 (d, $J = 6.8$ Hz, 3H), 1.33 (s, 3H), 1.16-1.07 (m, 2H), 0.82 (s, 3H); $^{13}$C NMR (75 MHz, C$_6$D$_6$) ppm 159.8, 148.5, 148.4,
For 62b: [α]_D^21 = -103 (c 0.64, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 7.36 (d, J = 6.9 Hz, 2H), 7.26-7.15 (m, 5H), 6.85 (d, J = 8.7 Hz, 2H), 5.97 (ddd, J = 17.6, 10.2, 7.1 Hz, 1H), 5.42 (d, J = 6.6 Hz, 1H), 5.32 (d, J = 17.6 Hz, 1H), 5.26 (d, J = 10.2 Hz, 1H), 4.72 (d, J = 6.7 Hz, 1H), 4.66 (d, J = 6.7 Hz, 1H), 4.55 (d, J = 11.6 Hz, 1H), 4.54 (d, J = 6.6 Hz, 1H), 4.41 (d, J = 9.2 Hz, 1H), 4.32 (d, J = 11.6 Hz, 1H), 4.14 (d, J = 9.5 Hz, 1H), 4.07 (d, J = 9.2 Hz, 1H), 4.07 (d, J = 7.1 Hz, 1H), 3.78 (s, 3H), 3.77-3.71 (m, 2H), 3.41 (s, 1H), 3.39 (s, 3H), 3.31 (d, J = 9.5 Hz, 1H), 2.59 (br s, 1H), 2.25 (q, J = 7.6 Hz, 1H), 2.21-2.16 (m, 3H), 1.41 (s, 3H), 1.40 (s, 3H), 1.31 (d, J = 1.3 Hz, 1H), 1.09 (d, J = 7.6 Hz, 3H), 1.03 (s, 3H); ^13C NMR (75 MHz, CDCl_3) ppm 159.0, 152.0, 136.8, 134.6, 130.7, 130.1, 129.3, 128.4, 126.2, 119.5, 116.8, 113.6, 108.4, 97.6, 88.3, 88.1, 82.5, 70.7, 69.8, 68.0, 55.8, 55.2, 51.8, 50.2, 47.1, 46.3, 33.0, 27.7, 27.5, 26.7, 26.1, 25.2, 21.7, 16.2; HRMS (El) m/z (M^+ calcd for C_{38}H_{52}O_{7}S_{6} 652.3434, obsd 652.3451.

(3S,4S,4aS,5R,6S,6aR,11bR,11cR)-2,3,4,4a,5,6,6a,11c-Octahydro-6-[(4S)-4-[(1R)-1-[(p-methoxybenzyl oxy)allyl]-2,2-dimethyl-1,3-dioxolan-4-y1]-4-(methoxym ethoxy)-5,12,12-trimethyl-1H-3,11-methanoazuleno[1,8-bc][1]benzothiopyran (63).

Carbinol 61a (16.7 mg, 25.6 μmol), tert-butyldimethylsilyl chloride (5.8 mg, 38.4 μmol), imidazole (5.2 mg, 76.7 μmol), and a catalytic amount of DMAP were taken up in DMF and stirred at rt for 1 h. tert-Butyldimethylsilyl triflate (18 μL, 77 μmol) was added and stirring was continued for 14 h before dilution with water, extraction with ether, drying and
concentration of the organic extracts, and purification of the resulting crude oil by silica gel chromatography (15% ethyl acetate in hexanes) to furnish 9.0 mg (56%) of 63 as a colorless oil; \([\alpha]^2_{D} = -66.3 \ (c \ 0.65, \text{CHCl}_3)\); \(\text{IR (film, cm}^{-1}\) 2951, 1612, 1514, 1459, 1371, 1248; \(^1\text{H NMR (300 MHz, CDCls)} \delta 7.59 (d, J = 7.8, 1.3 \text{ Hz, 1H}), 7.50 (dd, J = 7.4, 1.6 \text{ Hz, 1H}), 7.14 (d, J = 8.7 \text{ Hz, 2H}), 7.03 (ddd, J = 7.4, 1.6 \text{ Hz, 1H}), 6.95 (ddd, J = 7.4, 1.4 \text{ Hz, 1H}), 6.75 (d, J = 8.7 \text{ Hz, 2H}), 6.15 (ddd, J = 17.4, 10.6, 5.2 \text{ Hz, 1H}), 4.54 (d, J = 8.5 \text{ Hz, 1H}), 4.50 (d, J = 11.1 \text{ Hz, 1H}), 4.35 (d, J = 6.5 \text{ Hz, 1H}), 4.21 (d, J = 9.2 \text{ Hz, 1H}), 4.16 (d, J = 11.1 \text{ Hz, 1H}), 4.11 (br d, J = 5.2 \text{ Hz, 1H}), 3.76 (ddd, J = 3.8 \text{ Hz, 1H}), 3.65 (d, J = 9.1 \text{ Hz, 1H}), 3.53 (ddd, J = 13.6, 9.3, 3.9 \text{ Hz, 1H}), 3.28 (s, 3H), 3.18 (s, 3H), 3.24-3.17 (m, 1H), 2.96 (dd, J = 14.1, 10.3 \text{ Hz, 1H}), 2.85 (dd, J = 9.2, 5.4 \text{ Hz, 1H}), 2.63 (qd, J = 6.7, 5.1 \text{ Hz, 1H}), 2.29 (ddd, J = 14.1, 4.3, 4.3 \text{ Hz, 1H}), 1.75 (dd, J = 7.1, 3.6 \text{ Hz, 1H}), 1.64 (s, 3H), 1.59-1.52 (m, 1H), 1.49 (s, 3H), 1.48 (s, 3H), 1.46-1.37 (m, 1H), 1.29 (s, 3H), 1.04 (d, J = 6.9 \text{ Hz, 3H}), 0.88-0.79 (m, 1H); \(^{13}\text{C NMR (75 MHz, CDCls)} \text{ ppm} 159.7, 146.8, 140.1, 134.9, 132.2, 130.8, 129.6, 126.1, 125.8, 125.7, 117.6, 114.0, 108.6, 95.2, 86.3, 83.5, 80.3, 72.3, 67.3, 55.5, 55.3, 54.7, 54.1, 53.5, 46.4, 46.0, 43.8, 43.3, 38.1, 30.1, 28.9, 28.7, 26.7, 26.0, 25.8, 21.1; \text{HRMS (EI) m/z (M}^+) \text{ calcd for C}_{38}\text{H}_{50}\text{O}_{6}\text{S 634.3328, obsd 634.3348.}
\[ (1S,2R,3S,4S,5S,6R,7R,8S)-7,8-Epoxy-5-[(4S)-4-[(1R)-1-[(\rho-
\text{methoxybenzyl})oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-
4,11,11-trimethyl-6-(phenylsulfinyl)bicyclo[6.2.1]undec-3-ol \] (64).

A cold (0 °C) solution of 62a (25 mg, 38 μmol) and sodium bicarbonate (10 mg, 114 μmol) in CH\(_2\)Cl\(_2\) (1 mL) was treated with \textit{m}-chloroperbenzoic acid (20 mg, 114 μmol). The low temperature was maintained for 1 h, then raised to rt while stirring was continued for 24 h. The addition of water and ether was followed by separation, drying, and concentration of the organic layer. The resulting crude oil was purified by means of silica gel chromatography (45% ethyl acetate in hexanes) to afford 64 (21 mg, 80%) as a colorless oil; \( \alpha^2_{D} = -3.28 \) (c 0.98, CHCl\(_3\)); IR (film, cm\(^{-1}\)) 3542, 2940, 1613, 1515, 1448, 1380, 1306, 1250, 1144, 1038; \(^1\)H NMR (300 MHz, CD\(_2\)D\(_2\)) \( \delta \) 7.98 (m, 2H), 7.12 (d, \( J = 8.7 \) Hz, 2H), 7.08-6.96 (m, 3H), 6.73 (d, \( J = 6.8 \) Hz, 2H), 5.97 (ddd, \( J = 17.5 \), 10.5, 7.2 Hz, 1H), 5.39 (br d, \( J = 17.3 \) Hz, 1H), 5.30 (d, \( J = 10.7 \) Hz, 1H), 4.67 (d, \( J = 6.0 \) Hz, 1H), 4.47 (d, \( J = 10.5 \) Hz, 1H), 4.40 (d, \( J = 10.4 \) Hz, 1H), 4.36 (d, \( J = 7.1 \) Hz, 1H), 4.29 (d, \( J = 6.7 \) Hz, 1H), 4.17 (d, \( J = 10.5 \) Hz, 1H), 4.15 (d, \( J = 6.6 \) Hz, 1H), 3.95 (d, \( J = 6.1 \) Hz, 1H), 3.83 (d, \( J = 10.5 \) Hz, 1H), 3.56-3.51 (m, 1H), 3.46 (d, \( J = 3.0 \), 3.0 Hz, 1H), 3.44-3.33 (m, 2H), 3.30 (s, 3H), 3.04 (s, 3H), 2.85-2.76 (br m, 2H), 2.42 (ddd, \( J = 12.3 \), 12.3, 6.1 Hz, 1H), 2.11 (dd, \( J = 10.2 \), 2.0 Hz, 1H), 2.03-1.94 (br m, 1H), 1.32 (d, \( J = 7.2 \) Hz, 3H), 1.25 (s, 3H), 1.17 (s, 3H), 1.10 (s, 3H), 0.96 (s, 3H), 0.77-0.66 (br m, 1H); \(^{13}\)C NMR (75 MHz, CD\(_2\)D\(_2\)) ppm 159.7, 142.7, 134.8, 132.6, 130.6, 130.2, 129.8, 128.3, 120.6, 114.0, 108.3, 95.6, 88.1, 83.5, 83.0, 75.1, 72.5, 70.4, 70.1, 63.7, 61.7, 55.3, 54.7, 50.7, 44.7, 42.8, 33.4, 27.7, 27.4, 25.9, 24.8, 23.8, 22.7, 19.5; HRMS (El) \( m/z \) (M\(^+\)) calcd for C\(_{38}\)H\(_{52}\)O\(_{10}\)S 685.3046, obsd 685.3100.

\textit{Anal.} Calcd for C\(_{38}\)H\(_{52}\)O\(_{10}\)S: C, 65.12; H, 7.48. Found: C, 64.97; H, 7.55.
(1S,2S,5S,6R,7S,8S,9S,10S)-9-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-6-(methoxymethoxy)-8,12,12-trimethyl-10-(phenylsulfonyl)-11-oxatricyclo[5.3.1.1^-'][dodecan-2-ol (66).

A solution of epoxy sulfone 64 (7.7 mg, 11 μmol) and disodium phosphate (16 mg, 110 μmol) in refluxing methanol was treated with 6% Na(Hg) (17 mg, 44 μmol Na°). Further heating for 5 h was followed by dilution with water and extraction of the resulting mixture with ether. The combined organic layers were dried and concentrated in vacuo prior to purification of the residue by flash chromatography (SiO₂, 35% ethyl acetate in hexanes) to furnish 66 as a colorless oil (7 mg, 91%); [α]D²¹ = +34.4 (c 0.43, CHCl₃); IR (film, cm⁻¹) 3466, 2938, 1514, 1290, 1250, 1140, 1029; ¹H NMR (300 MHz, CD₂Cl₂) δ 7.82 (d, J = 7.2 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 6.97 (dd, J = 7.3 Hz, 1H), 6.89-6.84 (m, 4H), 6.24 (s, 1H), 5.69 (ddd, J = 17.5, 10.3, 7.5 Hz, 1H), 5.24 (d, J = 9.4 Hz, 1H), 5.18 (dd, J = 10.3, 1.8 Hz, 1H), 5.03 (dd, J = 17.4, 1.5 Hz, 1H), 4.84 (dd, J = 9.4, 2.6 Hz, 1H), 4.50 (d, J = 6.9 Hz, 1H), 4.48 (d, J = 11.0 Hz, 1H), 4.42 (d, J = 6.9 Hz, 1H), 4.16 (d, J = 11.0 Hz, 2H), 3.81 (dd, J = 6.9 Hz, 1H), 3.81 (d, J = 11.0 Hz, 1H), 3.66 (d, J = 12.6 Hz, 1H), 3.59 (d, J = 7.6 Hz, 1H), 3.50 (d, J = 3.2 Hz, 1H), 3.28 (s, 3H), 3.26-3.12 (m, 1H), 3.11 (s, 3H), 2.61 (qd, J = 6.4, 5.2 Hz, 1H), 2.44 (ddd, J = 12.0, 8.9, 0.8 Hz, 1H), 2.17 (dd, J = 9.7 Hz, 1H), 2.13-2.01 (m, 1H), 1.98 (s, 3H), 1.42 (s, 3H), 1.04-0.91 (m, 1H), 0.89 (s, 3H), 0.85 (s, 3H), 0.75 (d, J = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CD₂Cl₂) ppm 160.2, 141.6, 135.4, 132.7, 130.9, 130.2, 129.7, 128.2, 118.9, 114.2, 108.6, 95.5, 86.7, 83.9, 83.8, 82.3, 80.7, 79.6, 70.5, 67.2, 65.9, 55.0, 54.8, 50.3, 50.2, 37.6, 35.9, 29.7, 28.9, 25.92, 25.87, 25.3, 20.7, 18.2; HRMS (FAB) m/z (M⁺+H) calcd for C₃₈H₅₃O₁₀S 701.34, obsd 701.45.

(1R,2Z,4S,5S,6S,7R,8S)-4-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-7-(methoxymethoxy)-5,11,11-trimethylbicyclo[6.2.1]undec-2-ene-1,6-diol 1-(trifluoroacetate) (69a).

A mixture of 62a (231 mg of 80% purity, 0.354 mmol) and sodium bicarbonate (29 mg, 0.354 mmol) in dry CH$_2$Cl$_2$ (5 mL) at -78 °C was treated with m-chloroperbenzoic acid (79 mg, 0.460 mmol), stirred for 1.5 h, diluted with water, and extracted with ether. The combined organic layers were dried and concentrated to give a foam that was immediately dissolved in cold (-78 °C) CH$_2$Cl$_2$ (5 mL) and treated with trifluoroacetic anhydride (100 μL, 0.708 mmol). After an additional 30 min of stirring, the reaction mixture was diluted with water and extracted with ether. The combined organic layers were dried and concentrated to leave a residue that was subjected to chromatography on silica gel. Elution with 20% ethyl acetate in hexanes furnished 69a (97 mg, 53%) as a colorless oil: [α]$_D^{23}$ = -6.90 (c 0.71, CHCl$_3$); IR (film, cm$^{-1}$) 3498, 2939, 1783, 1613, 1515, 1467, 1371, 1257, 1215, 1164, 1090, 1031, 923; $^1$H NMR (300 MHz, CD$_2$D$_2$) δ 7.14 (d, $J = 8.6$ Hz, 2H), 6.79 (d, $J = 8.6$ Hz, 2H), 6.53 (d, $J = 6.9$ Hz, 1H), 6.42 (d, $J = 7.0$ Hz, 1H), 4.09 (d, $J = 10.5$ Hz, 1H), 4.04 (d, $J = 11.0$ Hz, 1H), 4.47 (d, $J = 11.0$ Hz, 1H), 4.31 (d, $J = 9.2$ Hz, 1H), 3.95 (d, $J = 5.6$ Hz, 1H), 3.75 (dd, $J = 3.4$, 3.4 Hz, 1H), 3.47-3.37 (m, 2H), 3.29 (s, 3H), 3.32-3.24 (m, 1H), 3.06 (s, 3H), 2.42 (br d, $J = 11.8$ Hz, 1H), 2.17-2.09 (m, 1H), 2.08-1.71 (series of m, 4H), 1.50 (s, 6H), 1.46 (s, 3H), 1.10 (s, 3H), 1.08 (d, $J = 7.0$ Hz, 3H); $^{13}$C NMR (75 MHz, CD$_2$D$_2$) ppm 159.9, 135.5, 132.6, 130.35, 130.26, 129.5, 117.9, 114.1, 109.3, 97.8, 95.8, 87.5, 87.0, 84.2, 79.9, 72.3, 66.4, 55.5, 54.7, 53.4, 51.6, 39.6, 35.0, 32.7, 30.1, 27.9, 26.9.
25.6, 20.4, 15.7 (CF₃CO carbons not observed); HRMS (FAB) m/z (M^+H) calcd for C₉₄H₄₈F₃O₉
657.33, obsd 657.32.

(1R,2Z,4S,5S,6S,7R,8S)-4-[(4S)-4-[(1-fl)-1-(p-Methoxybenzyl)oxy]allyl]-2,2-
dimethyl-1,3-dioxolan-4-yl]-7-(methoxymethoxy)-5,11,11-
trimethylbicyclo[6.2.1]undec-2-ene-1,6-diol bis(trifluoroacetate) (70a).

\[ \text{m-Chloroperbenzoic acid (231 mg, 1.34 mmol) was added to a} \]
cold (0 °C) mixture of 62a (796 mg of 80% purity, 1.22 mmol) and NaHCO₃ (51 mg, 0.61 mmol) in CH₂Cl₂(15 mL), stirred for
1.5 h, and treated with trifluoroacetic anhydride (0.86 mL, 6.1
mmol) followed by pyridine (0.69 mL, 8.5 mmol). After 1 h, water
was introduced and the separated aqueous layer was further extracted with CH₂Cl₂. The
combined organic layers were dried and concentrated. Purification of the residue by
chromatography on silica gel (elution with 8-20% ethyl acetate in hexanes) provided 70a as a
colorless oil (403 mg, 55%): [\alpha]D^21 = +28.4 (c 1.33, CHCl₃); IR (film, cm⁻¹) 2939, 1783, 1613,
1515, 1468, 1372, 1249, 1217, 1168, 1091, 1026; ¹H NMR (300 MHz, CDCl₃) δ 7.24 (d, J = 8.7
Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 6.08 (dd, J = 17.2, 10.6, 5.6 Hz, 1H), 5.62 (dd, J = 12.1, 12.1
Hz, 1H), 5.49 (m, 2H), 5.45 (d, J = 10.2 Hz, 1H), 5.29 (dd, J = 3.4, 3.4 Hz, 1H), 4.61 (d, J = 11.2
Hz, 1H), 4.58 (d, J = 7.4 Hz, 1H), 4.51 (d, J = 7.4 Hz, 1H), 4.33 (d, J = 11.2 Hz, 1H), 3.97 (d, J = 9.2
Hz, 1H), 3.93 (d, J = 9.2 Hz, 1H), 3.92 (d, J = 5.7 Hz, 1H), 3.82 (s, 3H), 3.57 (dd, J = 3.6, 3.6 Hz,
1H), 3.41 (s, 3H), 3.55-3.37 (m, 1H), 3.20 (ddd, J = 13.7, 11.4, 4.5 Hz, 1H), 2.47 (br d, J = 12.9
Hz, 1H), 2.43-2.29 (m, 1H), 2.29-2.20 (m, 1H), 2.07-1.82 (series of m, 2H), 1.45 (s, 3H), 1.31 (s,
3H), 1.20 (s, 3H), 1.16 (s, 3H), 0.77 (d, J = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 159.5,
134.4, 133.8, 130.1, 129.5, 127.2, 118.6, 113.9, 109.3, 96.6, 95.2, 86.7, 83.0, 82.9, 82.4,
(1R,2Z,4S,5S,6S,7R,8S)-4-[(4S)-4-[(1R)-1-Hydroxyallyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-7-(methoxymethoxy)-5,11,11•trimethylbicyclo[6.2.1]undec-2-ene-1,6-diol 1,6-bis(trifluoroacetate) (70b).

A solution of 70a (12.5 mg, 17 µmol) and DDQ (10 mg, 46 µmol) in CH₂Cl₂ (1 mL) containing water (2 drops) was stirred vigorously at rt for 3 h, treated with saturated NaHCO₃ solution, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel. Elution with 30% ethyl acetate in hexanes yielded 8.3 mg (79%) of 70b as colorless crystals, mp 155-156 °C; [α]D²⁵ = +44.2 (c 0.79, CHCl₃); IR (film, cm⁻¹) 3414, 2988, 1784, 1374, 1217, 1167, 1028; ¹H NMR (300 MHz, C₆D₆) δ 6.09 (ddd, J = 17.3, 10.7, 4.0 Hz, 1H), 5.84-5.40 (m, 2H), 5.37 (dd, J = 3.7, 3.7 Hz, 1H), 5.22 (ddd, J = 17.3, 1.8, 1.8 Hz, 1H), 5.11 (ddd, J = 10.7, 1.8 Hz, 1H), 4.36 (d, J = 7.3 Hz, 1H), 4.28 (d, J = 7.3 Hz, 1H), 3.78 (br s, 1H), 3.64 (s, 2H), 3.52 (dd, J = 3.8 Hz, 1H), 3.42 (m, 1H), 3.30-3.19 (m, 2H), 3.15 (s, 3H), 2.37 (br d, J = 12.8 Hz, 1H), 2.08-1.98 (m, 2H), 1.85-1.74 (m, 2H), 1.41 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.04 (s, 3H), 0.52 (d, J = 7.0 Hz, 3H); ¹³C NMR (75 MHz, C₆D₆) ppm 137.8, 134.3, 127.3, 115.7, 109.5, 97.0, 95.4, 87.0, 83.2, 82.8, 74.8, 65.6, 56.1, 53.2, 51.6, 38.9, 35.4, 32.6, 29.9, 27.4, 26.8, 25.5, 19.2, 13.4 (CF₃CO carbons not observed); HRMS (FAB) m/z (M⁺+H) calcld for C₃₂H₃₆F₆O₉ 633.25, obsd 633.33.

**Anal.** Calcd for C₃₂H₃₆F₆O₉: C, 53.16; H, 6.05. Found: C, 53.22; H, 6.06.

The structural assignment for 70b was corroborated by X-ray crystallographic analysis.
A solution of 69a (3.0 mg, 5.4 μmol) in CH₂Cl₂ (1 mL) was stirred with the Dess-Martin periodinane (7.6 mg, 18 μmol) for 1 h, filtered through Celite, and concentrated. The resulting oil was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to provide 3.0 mg (100%) of 71 as a colorless oil: [α]D

$\text{C} \equiv \text{HClO}_3$

$\text{CHCl}_3$

$\text{C}_3\text{H}_2\text{D}_5$

$\text{C}_3\text{D}_5\text{O}_9$

$\text{C}_5\text{D}_6$

$\text{C}_6\text{H}_5\text{F}_3$
(1R,2Z,4S,5S,6S,7R,8S)-4-(((4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-7-(methoxymethoxy)-5,11,11-trimethylbicyclo[6.2.1]undec-2-ene-1,6-diol (72a).

A solution of 69a (37 mg, 49 µmol) in methanol (0.5 mL) was added to a suspension of K₂CO₃ (75 mg, 540 µmol) in methanol (2.5 mL). The reaction mixture was stirred at rt for 30 min, diluted with water, and extracted with ether. The combined ethereal layers were dried and concentrated, and the residue was purified by flash chromatography (SiO₂, elution with 30% ethyl acetate in hexanes) to furnish 72a (23.6 mg, 86%) as a colorless oil; [α]D²¹ = -35.0 (c 0.50, CHCl₃); IR (film, cm⁻¹) 3488, 2932, 1614, 1515, 1456, 1380, 1251, 1214, 1143, 1054; ¹H NMR (300 MHz, CDCl₃) δ 7.14 (d, J = 8.6 Hz, 2H), 6.12 (ddd, J = 17.2, 10.5, 6.3 Hz, 1H), 5.64-5.62 (m, 2H), 5.30 (br d, J = 11.3 Hz, 1H), 5.26 (dd, J = 3.2, 1.2 Hz, 1H), 4.47 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 7.0 Hz, 1H), 4.38 (d, J = 7.0 Hz, 1H), 4.08 (d, J = 9.2 Hz, 1H), 4.05 (d, J = 11.2 Hz, 1H), 3.94 (d, J = 9.2 Hz, 1H), 3.86 (br d, J = 5.9 Hz, 2H), 3.51 (dd, J = 5.9, 5.9 Hz, 1H), 3.42 (dd, J = 3.4, 3.4 Hz, 1H), 3.30 (s, 4H), 3.14 (s, 3H), 2.92 (ddd, J = 14.1, 10.3, 3.7 Hz, 1H), 2.57 (ddd, J = 12.2, 2.7, 2.7 Hz, 1H), 2.34 (d, J = 5.1 Hz, 1H), 2.17-2.11 (m, 2H), 1.97-1.85 (m, 1H), 1.80-1.70 (m, 1H), 1.49 (s, 3H), 1.37 (s, 6H), 1.16 (s, 3H), 1.14 (d, J = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 160.0, 139.2, 135.7, 130.5, 130.3, 126.8, 118.5, 114.1, 108.7, 95.8, 87.8, 87.6, 84.2, 84.0, 80.5, 71.9, 66.9, 55.4, 55.1, 54.7, 50.3, 39.5, 35.7, 35.6, 29.7, 27.6, 27.3, 25.3, 20.6, 15.9; HRMS (FAB) m/z (M⁺+H) calcd for C₃₂H₄₉O₈ 561.34, obsd 561.45.
A solution of 62b (47 mg, 72 μmol) in CH₂Cl₂ containing NaHCO₃ (3.0 mg, 36 μmol) was cooled to 0 °C (3 mL) and treated with m-chloroperbenzoic acid (14 mg, 79 μmol). The mixture was stirred for 1 h, treated with trifluoroacetic anhydride (106 μL, 0.50 mmol), and stirred an additional 2 h while the temperature was maintained below 15 °C. Saturated aqueous NaHCO₃ solution and ether were added, and the organic layer was dried and concentrated to leave a crude oil that was diluted with methanol (2 mL) and added to a suspension of potassium carbonate (99 mg, 0.72 mmol) in methanol (2 mL) at rt for 30 min. Water was added and the mixture was extracted with ether. The organic layers were dried and concentrated, and the resulting residue was chromatographed (SiO₂, 30% ethyl acetate in hexanes) to yield 72b (11.3 mg, 23%) as a colorless oil; [α]²⁰ D = -36.5 (c 1.10, CHCl₃); IR (film, cm⁻¹) 3488, 2932, 1614, 1515, 1456, 1380, 1251, 1214, 1143, 1054; ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 6.04 (ddd, J = 17.5, 10.4, 7.2 Hz, 1H), 5.62 (dd, J = 11.7, 0.8 Hz, 1H), 5.54 (ddd, J = 11.7, 11.7 Hz, 1H), 5.47 (dd, J = 10.4, 0.8 Hz, 1H), 5.39 (dd, J = 17.5 Hz, 1H), 4.73 (d, J = 6.6 Hz, 1H), 4.63 (d, J = 6.6 Hz, 1H), 4.58 (d, J = 10.9 Hz, 1H), 4.17 (d, J = 10.9 Hz, 1H), 4.17 (d, J = 9.3 Hz, 1H), 3.84 (d, J = 9.3 Hz, 1H), 3.81 (d, J = 7.2 Hz, 1H), 3.79 (s, 3H), 3.57 (dd, J = 9.3, 9.3 Hz, 1H), 3.44 (s, 3H), 3.33 (br s, 1H), 3.22 (dd, J = 11.7, 4.1 Hz, 1H), 3.07 (dd, J = 9.3, 2.6 Hz, 1H), 2.76-2.67 (m, 1H), 2.56 (br d, J = 12.0 Hz, 1H), 2.14-2.01 (m, 1H), 1.86-1.39 (series of m, 4H), 1.37 (s, 3H), 1.34 (s, 3H), 1.08 (s, 3H), 1.05 (s, 3H), 0.99 (d, J = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 159.3, 139.8, 135.1, 130.4, 129.8, 125.3, 119.7, 113.7, 108.6, 97.6, 90.8, 87.4, 84.2, 84.1, 75.2, 71.4, 66.8, 56.3, 55.2, 52.7, 51.3, 38.5, 38.1, 36.1,
29.4, 27.1, 27.0, 24.8, 19.6, 13.4; HRMS (FAB) m/z (M++H) calcd for C_{32}H_{49}O_8 561.34, obsd 561.45.

(1S,2R,3S,4S,5S,6Z,8R)-8-Chloro-5-[(4S)-4-[(1R)-1-[(p-methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-4,11,11-trimethylbicyclo[6.2.1]undec-6-ene-2,3-diol (73).

m-Chloroperbenzoic acid (28 mg, 170 µmol) was added to a cold (0 °C) mixture of 62a (98 mg of 80% purity, 120 µmol) and NaHCO_3 (6.3 mg, 75 µmol) in CH_2Cl_2 (3 mL). After 15 min of stirring water and ether were added. The separated ether layer was dried and concentrated to leave a residue that was subjected to silica gel chromatography (30% ethyl acetate in hexanes) to furnish 73 (7.5 mg, 11%) as a colorless oil: [α]_D^{22} = -16.3 (c 0.49, CHCl_3); IR (film, cm⁻¹) 3406, 2922, 1614, 1514, 1463, 1381, 1249, 1058; 

$^1$H NMR (300 MHz, CDCl_3) δ 7.22 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 6.03 (ddd, J = 17.5, 10.4, 7.2 Hz, 1H), 5.96 (d, J = 12.4 Hz, 1H), 5.69 (dd, J = 12.4, 12.4 Hz, 1H), 5.52 (dd, J = 10.4, 0.5 Hz, 1H), 5.40 (d, J = 17.5 Hz, 1H), 4.60 (d, J = 11.2 Hz, 1H), 4.24 (d, J = 11.2 Hz, 1H), 4.11 (d, J = 9.3 Hz, 1H), 3.83-3.80 (m, 1H), 3.80 (s, 3H), 3.70 (ddd, J = 11.3, 3.6, 3.6 Hz, 1H), 3.53-3.43 (m, 2H), 3.10-2.95 (m, 1H), 2.87 (brd, J = 8.5 Hz, 1H), 2.72 (ddd, J = 12.4, 2.9, 2.9 Hz, 1H), 2.46 (d, J = 11.1 Hz, 1H), 2.41 (ddd, J = 13.4, 5.8, 5.8 Hz, 1H), 2.27-2.16 (m, 1H), 1.97-1.91 (m, 1H), 1.72-1.43 (m, 2H), 1.38 (s, 3H), 1.36 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H), 0.99 (d, J = 7.1 Hz, 3H);

$^{13}$C NMR (75 MHz, CDCl_3) ppm 159.5, 139.9, 134.9, 130.5, 129.3, 127.2, 120.2, 113.7, 109.1, 86.9, 83.9, 82.7, 82.1, 80.3, 71.0, 66.6, 55.3, 55.1, 51.4, 38.9, 37.3, 35.3, 32.1, 26.9, 26.7, 25.2, 19.9, 15.3; HRMS (FAB) m/z (M++H) calcd for C_{30}H_{44}ClO_6 535.28, obsd 535.27.
Borane-tetrahydrofuran complex (52 μmol, 0.5 M in THF) was added to a rt solution of 70a (11.7 mg, 17.8 μmol) in tetrahydrofuran (0.8 mL). The solution was stirred for 3 h and treated with 0.5 M NaOH and 30% aqueous hydrogen peroxide for 2 h. Extraction with ethyl acetate was followed by drying of the organic layers to give a residual oil that was chromatographed (SiO2, 85% ethyl acetate in hexanes) to deliver 74 as a colorless oil (5.6 mg, 54%); [α]D²¹ = -13.6 (c 1.99, CHCl₃); IR (film, cm⁻¹): 3443, 2932, 1613, 1515, 1466, 1382, 1250, 1145, 1091, 1031; ¹H NMR (300 MHz, CDCl₃) δ 7.25 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.71 (dd, J = 11.9, 11.9 Hz, 1H), 5.62 (d, J = 12.2 Hz, 1H), 4.68 (d, J = 7.1 Hz, 1H), 4.62-4.53 (series of m, 4H), 4.13 (d, J = 9.4 Hz, 1H), 4.03 (d, J = 9.5 Hz, 1H), 3.80 (s, 3H), 3.83-3.67 (series of m, 4H), 3.48-3.40 (m, 1H), 3.39 (s, 3H), 3.28 (dd, J = 11.2, 4.9 Hz, 1H), 2.67-2.57 (m, 1H), 2.56 (br d, J = 10.8 Hz, 1H), 2.39-2.02 (series of m, 5H), 2.00-1.78 (series of m, 2H), 1.62-1.48 (m, 1H), 1.38 (s, 3H), 1.29 (s, 3H), 1.23 (s, 3H), 1.10 (s, 3H), 1.05 (d, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 159.3, 138.6, 130.1, 129.6, 126.7, 113.8, 108.4, 95.6, 87.1, 86.9, 83.9, 81.8, 80.6, 74.3, 67.0, 60.7, 55.8, 55.2, 54.0, 49.8, 39.1, 35.8, 35.2, 33.2, 29.3, 27.4, 26.8, 25.7, 20.0, 15.2; HRMS (El) m/z (M⁺-CH₃) calcd for C₃₁H₄₇O₉ 563.3220, obsd 563.3232.
(1R,2S,3S,6S,7R,8S,9S,10R)-10-[(4S)-4-[(1R)-3-Hydroxy-1-[(p-methoxybenzyl)oxy]propyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-7-(methoxymethoxy)-9,12,12-trimethyl-11-oxatricyclo[6.2.1.1*']dodecane-2,3-diol (75).

A rt solution of 74 (13 mg, 23 μmol) in dichloromethane (0.5 mL) was treated with m-chloroperbenzoic acid (16 mg, 90 μmol) and stirred for 30 min. Water was added, the mixture was extracted with ethyl acetate, and the combined organic layers were dried, concentrated, and chromatographed (SiO₂, 70% ethyl acetate in hexanes) to provide the triol 75 as an oil (5.3 mg, 40%); ¹H NMR (300 MHz, CD₆D₆) δ 7.15 (d, J = 8.6 Hz, 2H), 6.77 (d, J = 8.6 Hz, 2H), 4.93 (d, J = 7.6 Hz, 1H), 4.39 (series of m, 6H), 4.23 (s, 1H), 4.11 (d, J = 9.6 Hz, 1H), 4.04 (d, J = 9.9 Hz, 1H), 3.71 (d, J = 9.6 Hz, 1H), 3.57-3.52 (m, 2H), 3.26 (s, 3H), 3.15 (dd, J = 9.4, 9.4 Hz, 1H), 3.15 (s, 3H), 2.50-2.45 (m, 1H), 2.33-1.99 (series of m, 5H), 1.88 (s, 3H), 1.59-1.50 (m, 1H), 1.47 (s, 3H), 1.43 (s, 3H), 1.28 (s, 3H), 1.15-1.06 (m, 1H), 1.03 (d, J = 7.0 Hz, 3H), 0.94-0.84 (m, 3H); ¹³C NMR (75 MHz, CD₆D₆) ppm 160.0, 130.4, 130.0, 114.1, 109.0, 95.6, 93.4, 86.6, 85.6, 84.1, 82.1, 78.6, 75.8, 74.2, 67.2, 59.4, 55.1, 54.7, 50.3, 46.3, 42.0, 41.7, 33.4, 33.0, 32.2, 28.1, 26.5, 22.4, 21.4, 21.3.
(2S,3R)-3-[(p-Methoxybenzyl)oxy]-2-[(3S,4R,4aS,5S,6S,6aS,11bR,11aS)-
2,3,4,4a,5,6,6a,11c-octahydro-4a-hydroxy-4-(methoxymethoxy)-5,12,12-
trimethyl-1H-3,11b-methanoazuleno[1,8-bc][1]benzothiopyran-6-yl]-4-pentene-
1,2-diol (76).

Acetonide 55b (47.5 mg, 73 μmol) was stirred in 80% acetic acid-
water (1 mL) at rt for 2 d. The solvent was removed under vacuum
(0.2 Torr) and the residue was chromatographed (silica gel, 30%
ehxane) to provide 76 (26.7 mg, 60%) as a
colorless oil; [α]D21 = -11.1 (c 1.60, CHCl3); IR (film, cm⁻¹) 3391,
2954, 1613, 1514, 1464, 1034; ¹H NMR (300 MHz, CDCl3) δ 7.54 (dd, J = 5.0, 4.4 Hz, 1H), 7.35-
7.24 (m, 3H), 7.11-7.06 (m, 2H), 6.86 (d, J = 8.6 Hz, 2H), 6.04 (ddd, J = 17.5, 10.3, 7.4 Hz, 1H),
5.46 (br d, J = 16.2 Hz, 1H), 4.77 (dd, J = 8.7, 1.6 Hz, 1H), 4.82 (d, J = 6.8 Hz, 1H), 4.65 (d, J = 6.8
Hz, 1H), 4.64 (d, J = 11.7 Hz, 1H), 4.35 (d, J = 11.5 Hz, 1H), 4.21 (dd, J = 10.5, 5.0 Hz, 1H), 4.14
(d, J = 7.4 Hz, 1H), 3.79 (s, 3H), 3.66 (s, 3H), 3.55-3.43 (m, 1H), 3.42 (s, 3H), 3.32 (ddd, J = 14.5,
12.4, 4.6 Hz, 1H), 2.81 (dd, J = 10.9, 4.9 Hz, 1H), 2.60 (d, J = 10.4 Hz, 1H), 2.27 (dq, J = 10.9, 7.2
Hz, 1H), 2.06-1.95 (m, 2H), 1.44 (s, 6H), 1.29-1.18 (m, 3H), 1.05 (d, J = 7.3 Hz, 3H), 0.94-0.85 (m,
1H); ¹³C NMR (75 MHz, CDCl3) ppm 159.2, 144.7, 136.8, 134.7, 130.4, 130.3, 129.7, 125.9,
125.7, 125.1, 119.8, 113.7, 96.0, 81.9, 80.7, 79.3, 77.9, 70.1, 64.8, 59.0, 56.0, 55.2, 53.4,
53.1, 52.0, 46.5, 44.0, 43.7, 28.7, 25.5, 25.1, 21.4, 10.1; HRMS (EI) m/z (M⁺) calcd for
C₃₅H₄₆O₇S 610.2964, obsd 610.2970.
(1R,2S,3S,6S,7R,8S,9S,10R)-10-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-7-(methoxymethoxy)-9,12,12-trimethyl-11-oxatricyclo[6.2.1.13^6]dodecane-2,3-diol (77a).

A mixture of 72a (100 mg, 0.18 mmol), m-chloroperbenzoic acid (123 mg, 0.71 mmol), and NaHCO₃ (30 mg, 0.36 mmol) in CH₂Cl₂ (8 mL) was stirred at rt for 9 h, treated with triphenylphosphine (140 mg, 0.53 mmol) for 30 min, and then diluted with saturated NaHCO₃ solution, and extracted with ether. The combined organic layers were dried and concentrated, leaving a residue that was subjected to chromatography (SiO₂, elution with 20% ethyl acetate in hexanes). There was isolated 77 mg (75%) of 77a as a colorless oil; [α]D²⁰ = +38.6 (c 0.92, CHCl₃); IR (film, cm⁻¹) 3528, 3389, 2921, 1614, 1515, 1464, 1375, 1249, 1147; ¹H NMR (300 MHz, CDCl₃) δ 7.23 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 5.97 (ddd, J = 17.4, 10.7, 4.5 Hz, 1H), 5.48 (ddd, J = 17.4, 1.7, 1.7 Hz, 1H), 5.40 (ddd, J = 10.7, 1.5, 1.5 Hz, 1H), 4.68 (d, J = 7.8 Hz, 1H), 4.64 (d, J = 7.0 Hz, 1H), 4.58 (d, J = 11.0 Hz, 1H), 4.55 (d, J = 7.0 Hz, 1H), 4.45 (dd, J = 8.0, 4.8 Hz, 1H), 4.31 (d, J = 11.0 Hz, 1H), 4.19 (d, J = 9.5 Hz, 1H), 4.12 (ddd, J = 4.5, 1.3, 1.3 Hz, 1H), 4.02 (s, 1H), 3.99 (dd, J = 7.8, 4.8 Hz, 1H), 3.85 (d, J = 9.4 Hz, 1H), 3.82 (s, 3H), 3.57 (s, 1H), 3.36 (d, J = 5.3 Hz, 1H), 3.35 (s, 3H), 3.09 (dd, J = 8.2, 8.2 Hz, 1H), 2.43-2.34 (m, 2H), 2.12-1.96 (m, 2H), 1.82-1.78 (m, 1H), 1.49 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H), 1.11 (s, 3H), 1.07 (d, J = 7.0 Hz, 3H), 1.09-1.04 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) ppm 159.3, 133.3, 129.7, 129.5, 118.2, 113.8, 108.9, 95.0, 93.0, 86.6, 85.2, 83.3, 81.8, 81.5, 73.5, 72.4, 67.2, 55.4, 55.2, 49.4, 45.8, 41.6, 41.5, 32.0, 31.60, 31.57, 28.2, 26.3, 21.2, 20.7; HRMS (FAB) m/z (M⁺+H) calcd for C₃₂H₄₉O₉ 577.34, obsd 577.39.

A solution of 77a (73 mg, 130 μmol) and triethylamine (0.17 mL, 1.3 mmol) in dimethylsulfoxide (1 mL) was treated with SO₃•py complex (60 mg, 380 μmol). A second aliquot of triethylamine and SO₃•py complex was added after 24 h of stirring, and a third aliquot of the latter reagent was added after an additional 12 h of stirring. A final 12 h period of stirring was ended by the addition of water and ethyl acetate, separation and drying of the organic layer, and concentration to leave a residue. Purification of the crude oil using silica gel chromatography (15-30% ethyl acetate in hexanes) provided unchanged 77a (14 mg, 19%) and 77b (51 mg, 70%), both as colorless oils. For 77b: $\alpha^2_{D} = +39.0$ (c 0.80, CHCl₃); IR (film, cm⁻¹) 3440, 2933, 1683, 1613, 1515, 1465, 1303, 1250, 1034, 931; ¹H NMR (300 MHz, CDCl₃) δ 7.23 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 5.98 (ddd, J = 17.5, 10.7, 4.3 Hz, 1H), 5.47 (ddd, J = 17.5, 1.7, 1.7 Hz, 1H), 5.34 (ddd, J = 10.7, 1.6 Hz, 1H), 4.68 (d, J = 9.0 Hz, 1H), 4.64 (d, J = 7.1 Hz, 1H), 4.61 (s, 1H), 4.57 (d, J = 10.9 Hz, 1H), 4.56 (d, J = 7.1 Hz, 1H), 4.30 (d, J = 10.9 Hz, 1H), 4.19 (s, 1H), 4.06 (d, J = 9.2 Hz, 1H), 4.05 (d, J = 4.3 Hz, 1H), 3.89 (d, J = 9.2 Hz, 1H), 3.81 (s, 3H), 3.45 (d, J = 4.6 Hz, 1H), 3.41 (dd, J = 8.6, 8.6 Hz, 1H), 3.35 (s, 3H), 3.62 (ddd, J = 12.0, 3.5, 3.5 Hz, 1H), 2.41 (dq, J = 7.2, 7.2 Hz, 1H), 2.37-2.19 (m, 2H), 2.05 (ddd, J = 15.4, 12.7, 7.2 Hz, 1H), 1.48-1.37 (m, 1H), 1.37 (s, 3H), 1.33 (s, 3H), 1.22 (s, 3H), 1.14 (s, 3H), 1.01 (d, J = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 209.8, 159.3, 133.8, 129.8, 129.4, 117.5, 113.8, 108.8, 95.1, 94.7, 89.8, 86.4, 85.8, 82.9, 81.7, 72.3,
66.9, 55.5, 55.2, 50.6, 50.0, 44.8, 40.4, 34.8, 32.0, 28.2, 26.5, 22.7, 21.0, 19.3; HRMS (El) m/z (M+) calcd for C$_{32}$H$_{46}$O$_9$ 574.3142, obsd 574.3146.

Anal. Calcd for C$_{32}$H$_{46}$O$_9$: C, 66.88; H, 8.07. Found: C, 66.60; H, 8.16.

(1$R$,2$R$,3$R$,4$S$,5$S$,6$R$,7$S$)-1-Hydroxy-3-[(4$S$)-4-[(1$R$)-1-[(p-methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-6-(methoxymethoxy)-4,8,8-trimethyl-12-oxatricyclo[5.2.2.1$^b$]dodecan-9-one (78a).

A mixture of 77b (28 mg, 49 μmol) and aluminum tri-tert-butoxide (48 mg, 190 μmol) was refluxed in benzene (4 mL) for 1.25 h, cooled to rt, diluted with water, and extracted with ether. The combined ethereal layers were dried and concentrated, thereby affording a crude oil that was purified using silica gel chromatography (elution with 20% ethyl acetate in hexanes) to give 78a (28 mg, 100%) as a colorless oil; $[\alpha]_D^{25} = -15.7$ (c 1.46, CHCl$_3$); IR (film, cm$^{-1}$) 3461, 2935, 1704, 1613, 1515, 1467, 1372, 1250, 1213, 1172, 1147, 1093, 1033, 971, 916, 733; $^1$H NMR (300 MHz, CD$_3$OD) $\delta$ 7.22 (d, $J = 8.6$ Hz, 2H), 6.75 (d, $J = 8.6$ Hz, 2H), 6.07 (ddd, $J = 17.4$, 10.5, 6.9 Hz, 1H), 5.23 (dd, $J = 10.5$, 1.1 Hz, 1H), 5.16 (br d, $J = 17.4$ Hz, 1H), 4.45 (d, $J = 10.8$ Hz, 1H), 4.38 (d, $J = 6.9$ Hz, 1H), 4.22 (d, $J = 6.9$ Hz, 1H), 4.21 (s, 1H), 4.11 (d, $J = 10.8$ Hz, 1H), 4.08 (d, $J = 6.3$ Hz, 1H), 3.99 (br s, 1H), 3.91 (d, $J = 8.8$ Hz, 1H), 3.86 (d, $J = 8.8$ Hz, 1H), 3.74 (br d, $J = 6.9$ Hz, 1H), 3.45 (d, $J = 2.4$ Hz, 1H), 3.27 (s, 3H), 3.02 (s, 3H), 2.97 (br d, $J = 6.3$ Hz, 1H), 2.44 (dq, $J = 6.3$, 6.3 Hz, 1H), 2.18 (br dd, $J = 12.6$ Hz, 12.6 Hz, 1H), 2.04-1.77 (series of m, 4H), 1.74 (s, 3H), 1.43 (s, 3H), 1.36 (s, 3H), 1.29 (d, $J = 6.3$ Hz, 3H), 1.12 (s, 3H); $^{13}$C NMR (75 MHz, CD$_3$OD) ppm 218.5, 160.0, 135.5, 130.9, 129.7, 128.6, 118.9, 113.9, 110.3, 95.0, 91.3, 88.9, 86.7, 85.4, 82.5, 78.0, 71.2, 70.91, 70.89, 55.0,
54.7, 48.4, 46.6, 46.0, 41.8, 31.0, 27.8, 27.3, 27.2, 25.3, 21.4, 16.0; HRMS (El) m/z (M+) calcd for C\textsubscript{32}H\textsubscript{46}O\textsubscript{9} 574.3142, obsd 574.3164.

\((1S,2R,3R,4S,5S,6R,7S,9R)-3-[(4S)-4-[(1R)-1-[(p-Methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-6-(methoxymethoxy)-4,8,8-trimethyl-12-oxatricyclo[5.2.2.1"dodecan-9-one (78b).

Lithium aluminum hydride (1.4 mg, 36 µmol) was added to a cold (0 °C) solution of 78a (19 mg, 33 µmol) in ether (1 mL) and stirred for 1 h before the addition of saturated Rochelle’s salt solution. Extraction with ether, drying of the ethereal layers, and concentration to a residue was followed by flash chromatography (SiO\textsubscript{2}, 40% ethyl acetate in hexanes) to furnish 78b (13.3 mg, 70%) as a colorless oil; \([\alpha]_D^{21} = +9.40 \text{ (c 1.34, CHCl}_3\text{)}\); IR (film, cm\textsuperscript{-1}) 3416, 2932, 1614, 1515, 1464, 1379, 1249, 1149, 1095, 1033, 1008, 976; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \delta 7.25 (d, \(J = 8.6\text{ Hz}, 2\text{H})\), 6.85 (d, \(J = 8.6\text{ Hz}, 2\text{H})\), 5.98 (ddd, \(J = 17.2, 10.5, 6.5\text{ Hz}, 1\text{H})\), 5.44 (dd, \(J = 10.5, 1.0\text{ Hz}, 1\text{H})\), 5.37 (d, \(J = 17.2\text{ Hz}, 1\text{H})\), 4.59 (d, \(J = 11.2\text{ Hz}, 1\text{H})\), 4.55 (d, \(J = 6.9\text{ Hz}, 1\text{H})\), 4.39 (d, \(J = 6.9\text{ Hz}, 1\text{H})\), 4.25 (d, \(J = 11.2\text{ Hz}, 1\text{H})\), 4.17 (d, \(J = 3.4\text{ Hz}, 1\text{H})\), 3.95 (d, \(J = 8.9\text{ Hz}, 1\text{H})\), 3.89 (d, \(J = 6.5\text{ Hz}, 1\text{H})\), 3.88 (d, \(J = 4.1\text{ Hz}, 1\text{H})\), 3.79 (s, 3\text{H})\), 3.78 (d, \(J = 8.9\text{ Hz}, 1\text{H})\), 3.35 (d, \(J = 11.9\text{ Hz}, 1\text{H})\), 3.33 (d, \(J = 2.9\text{ Hz}, 1\text{H})\), 3.26 (s, 3\text{H})\), 2.84 (dd, \(J = 4.0\text{ Hz}, 3.8\text{ Hz}, 1\text{H})\), 2.52 (s, 1\text{H})\), 2.48 (d, \(J = 11.9\text{ Hz}, 1\text{H})\), 2.31-2.16 (m, 2\text{H})\), 1.84 (dd, \(J = 9.5, 2.6\text{ Hz}, 1\text{H})\), 1.78-1.57 (series of m, 3\text{H})\), 1.43 (s, 3\text{H})\), 1.41 (s, 3\text{H})\), 1.25 (s, 3\text{H})\), 1.21 (s, 3\text{H})\), 0.99 (d, \(J = 7.0\text{ Hz}, 3\text{H})\); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) ppm 159.1, 134.4, 130.2, 129.8, 118.9, 113.6, 109.5, 94.8, 91.3, 86.6, 86.4, 85.5, 84.3, 81.5, 78.0, 70.9, 69.4, 55.2 (2\text{C})\), 45.8, 41.7, 39.4, 37.4, 28.9, 27.4, 27.2 (2\text{C})\), 23.6, 22.5, 16.6; HRMS (El) m/z (M+) calcd for C\textsubscript{32}H\textsubscript{48}O\textsubscript{9} 576.3298, obsd 576.3291.
(1S,2R,4S,5S,6Z,8R)-8-Hydroxy-5-[(4S)-4-[[1R]-1-[(p-methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]undec-6-en-3-one (80a).

A solution of 72a (73 mg, 130 μmol) in CH₂Cl₂ (5 mL) was stirred with the Dess-Martin periodinane (113 mg, 260 μmol) for 30 min, filtered through Celite, and concentrated. The resulting oil was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to provide 66.4 mg (91%) of 80a and 3.5 mg (5%) of unreacted 72a.

For 80a: colorless oil; [α]₁⁰⁹ = +0.38 (c 0.80, CHCl₃); IR (film, cm⁻¹) 3495, 2938, 1714, 1614, 1515, 1464, 1381, 1250, 1212, 1038; ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.11 (ddd, J = 17.4, 10.5, 6.8 Hz, 1H), 5.56 (d, J = 10.4 Hz, 1H), 5.48 (d, J = 12.1 Hz, 1H), 5.45 (d, J = 17.4 Hz, 1H), 5.40 (dd, J = 12.1, 12.1 Hz, 1H), 4.65 (d, J = 11.2 Hz, 1H), 4.50 (d, J = 7.0 Hz, 1H), 4.31 (d, J = 7.0 Hz, 1H), 4.28 (d, J = 11.2 Hz, 1H), 4.07 (d, J = 9.3 Hz, 1H), 3.95 (d, J = 2.2 Hz, 1H), 3.85-3.80 (m, 3H), 3.79 (s, 3H), 3.31 (s, 3H), 2.79-2.73 (m, 1H), 2.71 (ddd, J = 13.9, 9.9, 3.3 Hz, 1H), 2.49 (d, J = 11.9 Hz, 1H), 2.43-2.37 (m, 1H), 2.07-1.94 (m, 1H), 1.94-1.88 (m, 1H), 1.65 (br s, 1H), 1.36 (s, 3H), 1.33 (s, 3H), 1.03 (s, 3H), 1.00 (s, 3H), 0.86 (d, J = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 210.2, 159.5, 140.1, 134.9, 130.4, 129.3, 125.0, 119.9, 113.8, 109.0, 95.3, 88.1, 86.5, 83.9, 82.8, 71.2, 66.6, 56.1, 55.7, 55.2, 51.8, 46.6, 36.0, 35.8, 29.2, 26.92, 26.89, 26.3, 18.1, 10.8; HRMS (FAB) m/z (M⁺+H) calcd for C₃₂H₄₇O₈ 559.33, obsd 559.24.
(1S,2R,4S,5S,6Z,8R)-2,8-Dihydroxy-5-[(4S)-4-[(1R)-1-[(p-
methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-4,11,11-
trimethylbicyclo[6.2.1]undec-6-en-3-one (80b).

A solution of 80a (57 mg, 100 μmol) and pyridinium p-
toluenesulfonate (128 mg, 510 μmol) in tert-butyl alcohol (3 mL)  
was warmed to 80 °C, stirred for 48 h, cooled, diluted with water,  
and extracted with ether. The combined organic layers were  
dried and evaporated to leave a residue, chromatography of  
which on silica gel (elution with 30% ethyl acetate in hexanes) furnished 80b (36.5 mg, 70%) as a  
colorless oil; [α]_D superscript 21 = -15.4 (c 0.65, CHCl₃); IR (film, cm⁻¹) 3478, 2968, 1694, 1615, 1515, 1462,  
1371, 1251, 1173, 1075; ¹H NMR (300 MHz, CDCl₃) δ 7.22 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H),  
6.13 (ddd, J = 17.2, 10.6, 6.0 Hz, 1H), 5.54 (ddd, J = 10.6, 1.1, 1.1 Hz, 1H), 5.47 (ddd, J = 17.2, 1.5, 1.5 Hz, 1H),  
5.47 (d, J = 12.2 Hz, 1H), 5.41 (dd, J = 12.2 Hz, 1H), 4.63 (d, J = 11.1 Hz, 1H), 4.29 (d, J = 11.1 Hz, 1H),  
4.08 (d, J = 9.3 Hz, 1H), 3.91 (d, J = 6.0 Hz, 1H), 3.89 (d, J = 9.3 Hz, 1H), 3.87-3.82 (m, 3H), 3.79 (s, 3H),  
2.87 (qd, J = 6.6, 6.5 Hz, 1H), 2.72 (ddd, J = 14.3, 10.0, 4.0 Hz, 1H), 2.62 (ddd, J = 11.7, 2.1, 2.1 Hz, 1H),  
2.39-2.30 (m, 1H), 2.09-1.99 (m, 1H), 1.88 (ddd, J = 13.3, 13.3, 5.9 Hz, 1H), 1.37 (s, 3H), 1.32 (s, 3H), 1.25 (br s, 1H),  
1.04 (s, 3H), 0.95 (d, J = 6.6 Hz, 3H), 0.90 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 214.9, 159.5, 140.1, 134.6,  
130.0, 129.4, 124.6, 119.2, 113.8, 109.0, 86.3, 83.8(2C), 83.1, 71.7, 66.7, 57.0, 55.3, 51.6, 46.2, 36.0, 35.6,  
28.7, 27.1, 26.8, 24.6, 18.0, 10.9; HRMS (El) m/z (M⁺) calcd for C₃₀H₄₂O₇ 514.2931, obsd  
514.2903.
A solution of 80b (12 mg, 23 nmol), m-chloroperbenzoic acid (16 mg, 93 nmol), and NaHCO₃ (3.9 mg, 47 nmol) in CH₂Cl₂ (0.75 mL) was stirred for 22 h at rt, diluted with saturated NaHCO₃ solution, and extracted with ether. Following the prescibed workup and chromatography (SiO₂, elution with 30% ethyl acetate in hexanes), there was isolated 9.5 mg (77%) of 81 as a colorless oil; [α]ₒ²⁰¹ = +8.90 (c 0.98, CHCl₃); IR (film, cm⁻¹) 3460, 2986, 1695, 1614, 1515, 1455, 1372, 1303, 1249, 1215, 1173, 1057; ¹H NMR (300 MHz, CDCl₃) δ 7.23 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.05 (ddd, J = 17.2, 10.6, 5.5 Hz, 1H), 5.45 (ddd, J = 17.2, 1.5, 1.5 Hz, 1H), 5.43 (ddd, J = 10.6, 1.3, 1.3 Hz, 1H), 4.59 (d, J = 11.1 Hz, 1H), 4.36 (d, J = 11.1 Hz, 1H), 4.16 (s, 2H), 4.12 (br d, J = 5.5 Hz, 1H), 3.99 (dd, J = 6.2, 4.3 Hz, 1H), 3.80 (s, 3H), 3.56 (d, J = 6.3 Hz, 1H), 3.21 (dq, J = 6.4, 6.4 Hz, 1H), 3.08 (dd, J = 11.7, 4.2 Hz, 1H), 2.73 (dd, J = 4.1, 1.1 Hz, 1H), 2.66 (dd, J = 11.7, 5.9 Hz, 1H), 2.59-2.53 (m, 1H), 2.32-2.22 (m, 1H), 2.14-2.03 (m, 1H), 1.95 (s, 1H), 1.77-1.57 (series of m, 2H), 1.48 (s, 3H), 1.44 (s, 3H), 1.10 (s, 3H), 1.10 (d, J = 6.4 Hz, 3H), 1.09 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 216.2, 159.3, 134.4, 129.7, 129.6, 118.4, 113.8, 109.4, 86.7, 83.7, 83.0, 81.8, 72.0, 67.2, 59.5, 57.5, 55.3, 54.4, 46.9, 45.7, 34.9, 30.7, 29.3, 27.3, 26.6, 22.5, 17.3, 13.2; HRMS (FAB) m/z (M^++H) calcd for C₃₀H₄₃O₇ 531.30, obsd 531.37.
(1S,2S,5S,6R,7R,8S,9S,10S)-9-[(4S)-4-[[p-Methoxybenzyl]oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-8,12,12-trimethyl-11-oxatetracyclo[5.3.1.12\(^{2}\),5.0\(^{6},10\)]dodecane-2,6,7-triol (82).

Aqueous KOH (5.5 µL of 3 M) was added to a solution of 81 (8.7 mg, 16 µmol) in DMSO (0.5 mL) and the reaction mixture was stirred for 30 min, diluted with water, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue that was purified by chromatography on silica gel (elution with 40% ethyl acetate in hexanes) to give 82 as a colorless oil (8.1 mg, 93%); \([\alpha]_D^{21} = -7.1 \, (c 0.72, \text{CHCl}_3)\); IR \( (\text{film, cm}^{-1}) 3474, 2920, 1614, 1515, 1456, 1372, 1303, 1250, 1175, 1036, 937, 824, 738\); \(^1\)H NMR \( (300 \text{ MHz, CDCl}_3) \delta \) 7.24 (d, \( J = 8.7 \text{ Hz}, 2\)H), 6.86 (d, \( J = 8.7 \text{ Hz}, 2\)H), 6.06 (ddd, \( J = 17.4, 10.5, 6.8 \text{ Hz}, 1\)H), 5.47 (d, \( J = 10.5 \text{ Hz}, 1\)H), 5.35 (d, \( J = 17.4 \text{ Hz}, 1\)H), 4.61 (d, \( J = 11.1 \text{ Hz}, 1\)H), 4.28 (d, \( J = 11.1 \text{ Hz}, 1\)H), 4.03 (br s, 1H), 3.86 (d, \( J = 6.8 \text{ Hz}, 1\)H), 3.85 (s, 1H), 3.80 (s, 3H), 3.74 (d, \( J = 8.8 \text{ Hz}, 1\)H), 3.61 (d, \( J = 8.8 \text{ Hz}, 1\)H), 3.29 (s, 1H), 2.12-2.04 (m, 1H), 1.97 (ddd, \( J = 9.6, 1.5 \text{ Hz}, 1\)H), 1.85 (d, \( J = 4.0 \text{ Hz}, 1\)H), 1.83 (d, \( J = 3.9 \text{ Hz}, 1\)H), 1.87-1.78 (m, 1H), 1.62 (s, 1H), 1.68-1.56 (m, 2H), 1.51 (d, \( J = 3.9 \text{ Hz}, 1\)H), 1.47 (s, 3H), 1.38 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H), 1.05 (s, 3H); \(^{13}\)C NMR \( (75 \text{ MHz, CDCl}_3) \) ppm 159.4, 135.1, 130.0, 129.4, 119.4, 113.9, 109.0, 105.8, 87.2, 85.7, 83.7, 83.2, 82.0, 70.9, 68.6, 55.2, 52.0, 46.1, 35.7, 34.8, 29.4, 27.6, 27.02, 26.98, 26.4, 19.6, 12.0; HRMS (EI) \( m/z \, (M^+OH) \) calcd for C\(_{30}\)H\(_{41}\)O\(_{7}\) 513.2852, obsd 513.2884.
(1S,2R,4R,5S,6Z,8R)-4,8-Dihydroxy-5-[(4S)-4-[(1R)-1-[(p-methoxybenzyl)oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]undec-6-en-3-one (83a).

A solution of 80a (30.8 mg, 55 μmol) and 18-crown-6 (15 mg, 55 μmol) in cold (0 °C) THF (3 mL) was oxygenated while being treated with potassium hexamethyldisilazide in toluene (0.23 mL of 0.5 M, 115 μmol). Oxygen was bubbled through the solution for an additional 20 min before triphenylphosphine (16 mg, 61 μmol) was introduced. The reaction mixture was stirred for 20 min at rt, diluted with water, and extracted with ether. The combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to give 83a (20.8 mg, 66%) and bridgehead silylated 83b (2.0 mg, 6%), both as colorless oils.

Deprotection of the silylated product (17.9 mg, 28.4 μmol) was effected by stirring with tetra-n-butylammonium fluoride (142 μL of 1 M in THF) in THF (4 mL) for 24 h at rt. The reaction mixture was concentrated and the residue was chromatographed on silica gel as above to give 83a (15.4 mg, 94%).

For 83a: [α]D22 = -15.4 (c 0.39, CHCl3); IR (film, cm⁻¹) 3390, 2926, 1717, 1614, 1464, 1372, 1252, 1144, 1100, 1026; ¹H NMR (300 MHz, CDCl3) δ 7.24 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 1H), 6.43 (ddd, J = 17.1, 10.8, 6.2 Hz, 1H), 5.49 (d, J = 12.4 Hz, 1H), 5.44 (d, J = 17.7 Hz, 1H), 5.41 (d, J = 10.9 Hz, 1H), 5.26 (s, 1H), 5.15 (dd, J = 12.4, 12.4 Hz, 1H), 5.01 (d, J = 3.8 Hz, 1H), 4.69 (d, J = 11.0 Hz, 1H), 4.51 (d, J = 6.9 Hz, 1H), 4.40 (d, J = 11.0 Hz, 1H), 4.30 (d, J = 6.9 Hz, 1H), 4.12 (d, J = 6.2 Hz, 1H), 4.04 (d, J = 9.4 Hz, 1H), 3.98 (d, J = 9.4 Hz, 1H), 3.81 (s, 3H), 3.72 (d, J = 12.4 Hz, 1H), 3.31 (s, 3H), 2.57-2.52 (m, 1H), 2.50-2.20 (series of m, 3H), 1.91 (ddd, J = 12.8 Hz, 12.8 Hz, 6.4 Hz, 1H), 1.38 (s, 3H), 1.25 (s, 1H), 1.23 (s, 3H), 1.16 (s, 3H), 1.07
(s, 3H), 1.04 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 211.2, 159.8, 138.6, 132.8, 130.2, 128.1, 125.5, 120.5, 114.1, 108.6, 95.5, 86.2, 83.5, 83.2, 80.8, 80.0, 72.5, 66.5, 55.7, 55.2, 54.5, 50.6, 43.8, 34.6, 28.6, 28.0, 26.4, 23.5, 22.0, 18.1; HRMS (FAB) m/z (M$^+$+H) calcd for C$_{32}$H$_{47}$O$_9$ 575.32, obsd 575.43.

For 83b: $[\alpha]_{D}^{20} = +10.4$ (c 1.10, CHCl$_3$); IR (film, cm$^{-1}$) 3416, 2962, 1722, 1614, 1515, 1468, 1372, 1303, 1251, 1148, 1043, 921, 885, 844, 757; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.24 (d, $J = 8.7$ Hz, 2H), 6.89 (d, $J = 8.7$ Hz, 2H), 6.11 (ddd, $J = 12.5$, 12.5 Hz, 1H), 5.05-5.41 (series of m, 3H), 5.28 (s, 1H), 5.08 (dd, $J = 12.5$, 12.5 Hz, 1H), 4.99 (d, $J = 4.0$ Hz, 1H), 4.70 (d, $J = 10.9$ Hz, 1H), 4.51 (d, $J = 6.9$ Hz, 1H), 4.42 (d, $J = 10.9$ Hz, 1H), 4.29 (d, $J = 6.9$ Hz, 1H), 4.17 (d, $J = 5.6$ Hz, 1H), 3.93 (d, $J = 9.2$ Hz, 1H), 3.91 (s, 3H), 3.74 (d, $J = 12.5$ Hz, 1H), 3.30 (s, 3H), 2.51-2.26 (series of m, 4H), 1.93-1.86 (m, 1H), 1.39 (s, 3H), 1.24 (s, 3H), 1.13 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H), 0.033 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 211.7, 159.8, 139.7, 132.7, 130.1, 128.1, 124.5, 119.9, 114.1, 108.4, 95.5, 86.5, 85.8, 82.5, 81.0, 80.1, 72.8, 66.3, 55.6, 55.2, 52.9, 51.9, 43.7, 34.7, 29.1, 28.2, 26.4, 23.5, 22.5, 18.2, 2.03; HRMS (FAB) m/z (M$^+$+H) calcd for C$_{35}$H$_{55}$O$_8$Si 631.37, obsd 631.41.

(1S,2R,4R,5S,6S,7S,8S)-6,7-Epoxy-4,8-dihydroxy-5-[(4S)-4-[[[p-methoxybenzyl]oxy]allyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]undecan-3-one (84).

A magnetically stirred mixture of 83a (13 mg, 23 µmol) and NaHCO$_3$ (3.8 mg, 45 µmol) in CH$_2$Cl$_2$(0.5 mL) was treated with m-CPBA (16 mg, 91 µmol), stirred for 16 h prior to the introduction of triphenylphosphine (18 mg, 69 µmol), and concentrated. Chromatography of the residue (SiO$_2$, elution with 30% ethyl...
acetate in hexanes) furnished 84 (12.8 mg, 96%) as a colorless oil; \([\alpha]_D^{19} = +0.29 \text{ (c 0.35, CHCl}_3\text{)};\)

IR (film, cm\(^{-1}\)) 3397, 2935, 1716, 1613, 1515, 1469, 1249, 1214, 1143, 1102, 1024; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.25 (d, J = 8.6 \text{ Hz, 2H}), 6.89 (d, J = 8.6 \text{ Hz, 2H}), 5.99-5.89 \text{ (m, 1H), 5.44 \text{ (br d, J = 10.9 Hz, 1H), 5.39 \text{ (d, J = 18.0 Hz, 1H), 5.04 \text{ (d, J = 4.7 Hz, 1H), 4.67 \text{ (d, J = 11.2 Hz, 1H), 4.53 \text{ (d, J = 6.8 Hz, 1H), 4.41 \text{ (d, J = 11.2 Hz, 1H), 4.37 \text{ (d, J = 6.8 Hz, 1H), 4.27-4.24 \text{ (br m, 1H), 4.21 \text{ (br s, 2H), 3.82 \text{ (s, 3H), 3.29 \text{ (s, 3H), 2.96 \text{ (dd, J = 11.7, 4.2 Hz, 1H), 2.80 \text{ (d, J = 4.2 Hz, 1H), 2.57 \text{ (d, J = 11.7 Hz, 1H), 2.46 \text{ (dd, J = 10.0, 4.3, 4.3 Hz, 1H), 2.24-2.11 \text{ (m, 2H), 1.99-1.62 \text{ (series of m, 2H), 1.47 \text{ (s, 3H), 1.44 \text{ (s, 2H), 1.31 \text{ (s, 3H), 1.27 \text{ (s, 6H), 1.09 \text{ (s, 3H)}; \(^1\)\)C NMR (75 MHz, CDCl\(_3\)) ppm 213.5, 159.6, 133.0, 132.5, 130.1, 120.3, 114.0, 109.1, 96.1, 87.8, 83.1, 81.3, 79.5, 71.9, 67.4, 60.0, 55.7, 55.2, 52.2, 47.2, 43.5, 31.6, 30.7, 29.3, 26.2, 25.4, 22.6, 20.1, 17.8, 14.1; HRMS (FAB) \text{ m/z (M}^+\text{+H)} \text{ calcd for C}_{32}\text{H}_{47}\text{O}_{15} 591.32, \text{ obsd 591.22.}\)

\((1S,2R,3S,6S,7S,11R)-6,7-\text{Dihydroxy-11-}((4S)-4-(((1R)\text{-1-([p-methoxybenzyl]oxy})allyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-(methoxymethoxy)-10,10-dimethyl-4-oxatricyclo[5.2.1.1^\text{2,6}]undec-3-yl methyl ketone (85).\)

A solution of 84 (18 mg, 31 \text{ pmol}) and aqueous potassium hydroxide (0.40 mL of a 3 M solution) in DMSO (4 mL) was warmed to 55 °C for 2 h, cooled, and diluted with water. Following exhaustive extraction with ethyl acetate, the organic layers were dried and concentrated to leave a crude oil that was purified by means of silica gel chromatography (30% ethyl acetate in hexanes) to give 85 as a colorless oil (10.0 mg, 56%); \([\alpha]_D^{21} = +10.0 \text{ (c 0.89, CHCl}_3\text{)};\)

IR (film, cm\(^{-1}\)) 3467, 2950, 1712, 1615, 1516, 1466, 1387, 1252, 1150, 1024, 928, 825; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.25 (d, J = 8.6 \text{ Hz, 2H}), 6.86 (d, J = 8.6 \text{ Hz, 2H}, 6.08 \text{ (dd, J = 17.7, 10.5, 7.7 Hz, 1H), 5.47 \text{ (d, J = 10.5 Hz, 1H), 5.37 \text{ (d, J = 7.3 Hz, 1H), 4.88 \text{ (dd, J = 5.0, 3.6 Hz, 1H),}\)
1H), 4.57 (d, J = 10.8 Hz, 1H), 4.52 (d, J = 6.9 Hz, 1H), 4.33 (d, J = 6.9 Hz, 1H), 4.31 (d, J = 10.8 Hz, 1H), 4.09 (d, J = 7.7 Hz, 1H), 3.96 (dd, J = 8.4, 3.6 Hz, 1H), 3.94 (d, J = 8.7 Hz, 1H), 3.80 (s, 3H), 3.65 (d, J = 5.0 Hz, 1H), 3.64 (d, J = 3.7 Hz, 1H), 3.60 (d, J = 8.7 Hz, 1H), 3.31 (s, 3H), 2.73 (s, 1H), 2.60 (d, J = 8.4 Hz, 1H), 2.45 (dd, J = 10.5, 3.7 Hz, 1H), 2.32 (s, 3H), 2.19-2.04 (m, 3H), 1.60-1.46 (m, 1H), 1.44 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.12 (s, 3H); ^13C NMR (75 MHz, CDCl3) ppm 214.3, 159.6, 134.7, 130.5, 129.3, 120.6, 113.8, 97.0, 90.4, 86.5, 86.0, 84.2, 82.6, 76.7, 75.9, 71.5, 68.3, 56.2, 55.2, 50.8, 46.5, 40.0, 31.2, 30.7, 29.5, 28.0, 26.4, 24.6, 20.1; HRMS (FAB) m/z (M+H) calcd for C32H47O10 591.32, obsd 591.16.

\[(1S,2R,3S,5R,6S,7S,11R)-6,7-Dihydroxy-11-\{[(4S)-4-[(1R)-3-hydroxy-1-[(p-methoxybenzyl)oxy]propyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-10,10-dimethyl-4-oxatricyclo[5.2.1.1^{13}]undec-3-yl methyl ketone (86) and (1S,3R,3aS,4R,5S,8S,9S,10R,10aR)-Hexahydro-1-\{[(1R)-2-hydroxy-1-[(p-methoxybenzyl)oxy]propyl]-1-(isopropoxymethyl)-4-(methoxymethoxy)-3,12,12-trimethyl-3H-3a,10-epoxy-5,8-methano-1H-cyclonona[c]furan-3,8,9(9H)-triol (87).\]

Borane-tetrahydrofuran (0.41 mL, 1M in THF) was added to a cold (0 °C) solution of 85 (24 mg, 41 μmol) in tetrahydrofuran (1 mL). The mixture was stirred for 20 min, warmed to rt for 30 min, and treated with 2M aqueous sodium hydroxide (0.82 mL) and 30% hydrogen peroxide (0.82 mL). The reaction mixture was extracted with ether, the organic layers were dried and concentrated,
and the residue was chromatographed (silica gel, elution with 60% ethyl acetate in hexanes) to furnish 86 (9.0 mg, 36%) and 87 (7.0 mg, 28%) as colorless oils.

For 86: $\left[\alpha\right]_{D}^{22} = +11.9$ (c 0.85, CHCl$_3$); IR (film, cm$^{-1}$) 3428, 2935, 1712, 1614, 1515, 1249, 1074, 1019; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.22 (d, $J = 8.5$ Hz, 2H), 6.86 (d, $J = 8.5$ Hz, 2H), 5.01 (dd, $J = 5.3$, 3.8 Hz, 1H), 4.71 (d, $J = 10.6$ Hz, 1H), 4.51 (d, $J = 6.8$ Hz, 1H), 4.49 (d, $J = 10.6$ Hz, 1H), 4.36 (d, $J = 6.8$ Hz, 1H), 3.98 (dd, $J = 10.0$, 1.9 Hz, 1H), 3.95 (d, $J = 10.0$, 3.8 Hz, 1H), 3.91 (d, $J = 8.3$ Hz, 2H), 3.80 (s, 3H), 3.79 (d, $J = 5.7$ Hz, 2H), 3.88-3.71 (m, 2H), 3.51 (d, $J = 8.3$ Hz, 1H), 3.40 (d, $J = 5.3$ Hz, 1H), 3.31 (s, 3H), 3.16 (d, $J = 10.0$ Hz, 1H), 2.86 (s, 1H), 2.51 (dd, $J = 3.8$, 0.3 Hz, 1H), 2.33 (s, 3H), 2.36-2.21 (m, 1H), 2.18-2.07 (m, 1H), 2.03-1.94 (m, 1H), 1.45 (s, 3H), 1.41 (s, 3H), 1.40 (s, 3H), 1.45-1.20 (series of m, 4H), 1.13 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 213.8, 159.8, 130.2, 129.2, 114.0, 111.7, 97.4, 90.3, 86.9, 85.9, 83.8, 80.8, 76.8, 76.6, 75.1, 70.2, 60.4, 56.2, 55.3, 50.9, 46.5, 39.1, 33.3, 30.8, 30.7, 29.9, 29.0, 25.4, 25.2, 20.1; HRMS (FAB) $m/z$ (M$^+$H) calcd for C$_{32}$H$_{49}$O$_{11}$ 609.33, obsd 609.65.

For 87: $\left[\alpha\right]_{D}^{22} = +71.3$ (c 0.70 CHCl$_3$); IR (film, cm$^{-1}$) 3360, 2928, 1613, 1514, 1464, 1372, 1249, 1148, 1077, 1010; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.32 (d, $J = 8.6$ Hz, 2H), 6.88 (d, $J = 8.6$ Hz, 2H), 5.61 (s, 1H), 5.00 (d, $J = 10.6$ Hz, 1H), 4.87 (d, $J = 6.9$ Hz, 1H), 4.73 (dd, $J = 3.5$, 3.5 Hz, 1H), 4.65 (d, $J = 6.9$ Hz, 1H), 4.61 (d, $J = 10.6$ Hz, 1H), 4.07 (br d, $J = 4.0$ Hz, 1H), 3.92 (d, $J = 4.4$ Hz, 1H), 3.86-3.81 (m, 2H), 3.81 (s, 3H), 3.77-3.63 (m, 2H), 3.56-3.43 (series of m, 4H), 3.45 (s, 3H), 2.67 (dd, $J = 10.0$, 4.4 Hz, 1H), 2.42-2.27 (m, 2H), 2.04 (s, 1H), 1.75-1.59 (m, 2H), 1.55 (s, 3H), 1.48 (s, 3H), 1.22 (d, $J = 6.4$ Hz, 9H), 1.18 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 159.3, 130.7, 130.2, 113.7, 106.5, 98.5, 95.5, 87.5, 86.9, 86.1, 81.9, 75.8, 75.2, 74.9, 73.1, 70.8, 69.2, 55.9, 55.3, 52.6, 46.8, 43.7, 31.5, 30.7, 23.9, 22.0, 21.88, 21.86, 21.6, 20.2; HRMS (FAB) $m/z$ (M$^+$H) calcd for C$_{32}$H$_{51}$O$_{11}$ 611.34, obsd 611.50.
(1S,2R,4S,5S,6R,7E)-5-[(4S)-4-[(1R)-3-Hydroxy-1-[(p-methoxybenzyl)oxy]propyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethyl-6-(phenylthio)bicyclo[6.2.1]undec-7-en-3-one (88a) and (1S,2R,4S,5S,6Z,8S)-5-[(4S)-4-[(1R)-3-Hydroxy-1-[(p-methoxybenzyl)oxy]propyl]-2,2-dimethyl-1,3-dioxolan-4-yl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]undec-6-en-3-one (89a).

CH₂OH

P  OPMB

CH₃

OMOM

CH₂OH

P  OPMB

H₃C

^CH₃

\[
\text{Borane-dimethyl sulfide complex (2.01 mL, 20.1 mmol) was added to 2-methyl-2-butene (25.2 mL, 2 M in THF) at 0 °C, and the resulting solution was stirred for 2.25 h. A solution of 55b (1.31 g, 2.01 mmol) in THF (65 mL) was added and the temperature was immediately raised to 25 °C while stirring was maintained for 2 d. The reaction mixture was recooled to 0 °C and treated with 0.5 M NaOH (4.82 g in 100 mL) and 30% H₂O₂ (30 mL). Stirring was continued at 0 °C for 15 min and at rt for 30 min before extraction with ether. The combined organic layers were dried and concentrated prior to flash chromatography (SiO₂, 30% ethyl acetate in hexanes) to furnish 88a (858 mg, 64%) and 89a (62 mg, 5%), both as colorless oils.}
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For 88a: [\(\alpha\)]\⁰ = -126 (c 0.18, CHCl₃); IR (film, cm⁻¹) 3488, 2958, 1713, 1612, 1514, 1479, 1248, 1043; \(^1\)H NMR (300 MHz, C₆D₆) and \(^{13}\)C NMR (75 MHz, C₆D₆): too broadened to record, see spectra; HRMS (EI) \(m/z\) (M⁺-CH₃) calcd for C₃₇H₄₉O₈S 653.3148, obsd 653.3117.

Anal. Calcd for C₃₇H₄₉O₈S: C, 68.24; H, 7.84. Found: C, 68.00; H, 7.97.

For 89a: [\(\alpha\)]\⁰ = -17.9 (c 0.28, CHCl₃); IR (film, cm⁻¹) 3507, 2955, 1714, 1613, 1515, 1465, 1381, 1251; \(^1\)H NMR (300 MHz, C₆D₆) δ 7.13 (d, J = 8.6 Hz, 2H), 6.77 (d, J = 8.6 Hz, 2H), 6.71 (d, J = 8.6 Hz, 2H), 5.68 (t, J = 7.8 Hz, 1H).
5.61 (dd, J = 11.8, 8.1 Hz, 1H), 5.44 (dd, J = 11.8, 11.8 Hz, 1H), 4.48 (d, J = 11.2 Hz, 1H), 4.42 (d, J = 7.0 Hz, 1H), 4.39 (d, J = 7.0 Hz, 1H), 4.31 (d, J = 11.0 Hz, 1H), 4.29 (s, 1H), 4.03 (d, J = 9.4 Hz, 1H), 3.97 (d, J = 9.4 Hz, 1H), 3.93-3.83 (m, 2H), 3.63-3.56 (m, 2H), 3.26 (s, 3H), 3.25-3.20 (m, 1H), 3.10 (s, 3H), 2.64-2.46 (m, 3H), 2.30-2.20 (m, 2H), 2.18 (dd, J = 9.2, 9.2 Hz, 1H), 2.09-1.98 (m, 1H), 1.94-1.85 (m, 1H), 1.47 (s, 3H), 1.40 (s, 3H), 1.28 (s, 3H), 1.26-1.17 (m, 1H), 1.14 (d, J = 6.5 Hz, 3H), 0.96 (s, 3H). $^{13}$C NMR (75 MHz, C$_{6}$D$_{6}$) ppm 209.6, 136.0, 130.6, 129.7, 126.3, 114.1, 108.7, 95.7, 89.2, 87.2, 81.4, 74.1, 67.4, 60.4, 57.6, 55.5, 54.7, 51.1, 50.5, 47.9, 36.8, 35.2, 33.7, 31.8, 28.1, 27.6, 26.9, 21.2, 21.2, 11.5; HRMS (El) m/z (M$^+$) calcd for C$_{32}$H$_{48}$O$_{8}$ 560.3349, obsd 560.3327.

Anal. Calcd for C$_{32}$H$_{48}$O$_{8}$: C, 68.55; H, 8.63. Found: C, 68.29; H, 8.52.

(βR,4S)-β-[(p-Methoxybenzyl)oxy]-4-[(1E,3R,4S,5S,7R,8S)-7-(methoxymethoxy)-5,11,11-trimethyl-6-oxo-3-(phenylthio)bicyclo[6.2.1]undec-1-en-4-yl]-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde (88b).

Dimethyl sulfoxide (0.76 mL, 0.5 M in CH$_{2}$Cl$_{2}$) and oxalyl chloride (0.51 mL, 0.5 M in CH$_{2}$Cl$_{2}$) were stirred at -78 °C for 15 min, then treated with 88a (33.9 mg, 50.7 µmol) in CH$_{2}$Cl$_{2}$ (0.5 mL). The solution was stirred for 30 min, treated with triethylamine (2.02 mL, 0.5 M in CH$_{2}$Cl$_{2}$), and stirred for an additional 10 min at -78 °C and 15 min at 0 °C. The reaction mixture was then poured into brine and extracted with CH$_{2}$Cl$_{2}$. The organic layers were dried and concentrated to a crude oil that was chromatographed (SiO$_{2}$, 35% ethyl acetate in hexanes) to deliver 88b (30.8 mg, 91%) as a colorless oil; [α]$_{D}^{19}$ = -113 (c 1.60, CHCl$_{3}$); IR (film, cm$^{-1}$) 2938, 1721, 1613, 1515, 1479, 1371, 1302, 1248, 1108, 1042; $^1$H NMR (300 MHz, C$_{6}$D$_{6}$) δ 9.55 (br s, 1H), 7.41 (d, J = 7.8 Hz, 2H), 7.16 (d, J = 8.6 Hz, 2H), 7.01 (dd, J = 139
7.3 Hz, 2H), 6.89 (dd, J = 7.3 Hz, 1H), 6.76 (d, J = 8.6 Hz, 2H), 5.46 (br s, 1H), 4.76 (br d, J = 7.6 Hz, 1H), 4.54 (br d, J = 10.3 Hz, 1H), 4.43 (d, J = 6.9 Hz, 1H), 4.34 (br d, J = 6.8 Hz, 1H), 4.28 (d, J = 8.5 Hz, 1H), 4.02 (br s, 1H), 3.29 (s, 3H), 3.10 (s, 3H), 3.06-2.86 (br m, 3H), 2.21-1.95 (m, 4H), 1.67 (br s, 3H), 1.42 (s, 3H), 1.36-1.25 (br m, 8H), 1.20-0.96 (br s, 3H), 0.84 (s, 3H); 13C NMR (75 MHz, CDCl3) ppm 200.3, 150.6, 137.7, 130.8, 129.9, 129.0, 126.5, 123.6, 114.0, 109.0, 95.3, 85.8, 76.8, 73.8, 60.0, 55.4, 54.7, 47.0, 46.0, 26.9, 26.0, 12.6, 20.5, 20.3, 14.2 (not all peaks clearly observed due to fluxional behavior); HRMS (El) m/z (M+−C6H5O) calcd for C30H41O7S 545.2573, obsd 545.2663.

(βR,4S)-β-[(p-Methoxybenzyl)oxy]-4-[(1S,2Z,4S,5S,7R,8S)-7-(methoxymethoxy)-5,11,11-trimethyl-6-oxobicyclo[6.2.1]undec-2-en-4-yl]-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde (89b).

Oxalyl chloride (0.66 mL, 0.5 M in CH2Cl2) was stirred with dimethyl sulfoxide (0.99 mL, 0.5 M in CH2Cl2) at -78 °C for 15 min, then treated with 89a (37 mg, 66 μmol) in CH2Cl2 (0.5 mL). The mixture was stirred for 30 min, triethylamine (0.18 mL, 1.32 mmol) was added, and stirring was continued for 10 min at -78 °C and 1 h at 0 °C prior to the addition of water and ether. Separation, drying, and concentration of the organic layer gave a residue that was purified using silica gel chromatography (30% ethyl acetate in hexanes) to afford 89b (26 mg, 71%) as a colorless oil; [α]D20 = -40.9 (c 1.04, CHCl3); IR (film, cm−1) 2945, 1721, 1613, 1515, 1464, 1382, 1251, 1212, 1144, 1040; 1H NMR (300 MHz, CDCl3) δ 9.50 (dd, J = 1.4, 1.4 Hz, 1H), 7.12 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 5.56 (dd, J = 11.8, 8.2 Hz, 1H), 5.33 (dd, J = 11.9, 11.9 Hz, 1H), 4.45 (d, J = 7.0 Hz, 1H), 4.41 (d, J = 7.0 Hz, 1H), 4.31 (d, J = 10.9 Hz, 1H), 4.23 (qd, J = 6.6, 4.0 Hz, 1H), 4.20 (d, J = 1.9 Hz, 1H),

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4.07 (d, J = 10.9 Hz, 1H), 3.91 (d, J = 9.4 Hz, 1H), 3.89 (dd, J = 11.8, 4.6 Hz, 1H), 3.77 (d, J = 9.5 Hz, 1H), 3.27 (s, 3H), 3.14 (s, 3H), 3.05 (dd, J = 6.5, 4.4 Hz, 1H), 2.94 (ddd, J = 17.0, 4.0, 1.2 Hz, 1H), 2.57 (ddd, J = 17.0, 6.6, 1.6 Hz, 1H), 2.52-2.44 (m, 2H), 2.41-2.31 (m, 1H), 2.16-2.10 (m, 2H), 2.07-1.92 (m, 1H) 1.43 (s, 3H), 1.34 (s, 3H), 1.20 (s, 3H), 1.02 (d, J = 6.6 Hz, 3H), 0.94 (s, 3H); $^{13}$C NMR (75 MHz, CD$_3$D$_6$) ppm 209.4, 199.2, 160.0, 136.4, 130.2, 129.9, 125.8, 114.1, 108.9, 95.6, 89.0, 87.0, 77.6, 72.7, 66.9, 57.4, 55.6, 54.7, 51.1, 47.6, 45.2, 36.8, 35.1, 21.2, 27.9, 27.4, 27.0, 21.1, 11.5; HRMS (El) m/z (M$^+$-CH$_3$) calcd for C$_{31}$H$_{43}$O$_8$ 543.2958, obsd 543.2952.

$(\beta R,4S)-4-[(1 R,2 Z,4 S,5 S,7 R,8 S)-1$-hydroxy-7-(methoxymethoxy)-5,11,11-trimethyl-6-oxobicyclo[6.2.1]undec-2-ene-4-yl]-3-[($\rho$-methoxybenzyl)oxy]-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde (90).

Triol 74 (29 mg, 50 μmol) was stirred at rt in dichloromethane (1 mL) with the Dess-Martin periodinane (53 mg, 125 μmol) for 1 h before silica gel was introduced and the mixture was concentrated. The powder was loaded onto a flash column and chromatographed (SiO$_2$, 60% ethyl acetate in hexanes) to give 90 as a colorless oil (22.2 mg, 77%); [α]$^D$ = +8.86 (c 0.44, CHCl$_3$); IR (film, cm$^{-1}$) 3468, 2930, 1715, 1613, 1515, 1463, 1383, 1250, 1213, 1144, 1094; $^1$H NMR (300 MHz, CDCl$_3$) δ 9.92 (s, 1H), 7.23 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.50-5.39 (m, 2H), 4.54 (d, J = 10.9 Hz, 1H), 4.52 (d, J = 7.0 Hz, 1H), 4.34 (d, J = 10.4 Hz, 1H), 4.33 (d, J = 7.3 Hz, 1H), 4.24 (ddd, J = 6.6, 4.3 Hz, 1H), 4.08 (d, J = 9.6 Hz, 1H), 4.00 (br s, 1H), 3.86 (d, J = 9.6 Hz, 1H), 3.80 (s, 3H), 3.83-3.73 (m, 1H), 3.31 (s, 3H), 3.10 (dd, J = 16.9, 4.0 Hz, 1H), 2.94-2.85 (m, 2H), 2.66-2.45 (series of m, 4H), 2.09-1.85 (m, 2H), 1.40 (s, 3H), 1.27 (s, 3H), 1.05 (s, 3H), 1.03 (s, 3H), 0.92 (d, J = 6.6 Hz,
$^3$H; $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 209.8, 200.0, 159.6, 140.3, 130.1, 129.1, 124.5, 113.9, 109.1, 95.3, 88.2, 86.4, 83.8, 77.2, 72.8, 66.7, 55.9, 55.8, 55.3, 51.8, 47.4, 45.0, 35.6, 35.5, 29.1, 27.2, 26.9, 26.7, 18.0, 10.9; HRMS (ESI) m/z (M$^+$) calcd for C$_{32}$H$_{46}$O$_9$ 574.3142, obsd 574.3095.

$(\alpha$E, 4S)-4-[(1E, 3R, 4S, 5S, 7R, 8S)-7-(Methoxymethoxy)-5, 11, 11-trimethyl-6-oxo-3-(phenylthio)bicyclo[6.2.1]undec-1-en-4-yi]-2, 2-dimethyl-1, 3-dioxolane-4-acrolein (93).

Aldehyde 88b (30 mg, 45 μmol) in cold (0 °C) methanol-THF (10:1, 1 mL) was treated with 0.5 M NaOH (0.36 mL, 0.18 mmol). Stirring was continued for a total of 17 h as the ice bath slowly warmed to rt. The solvent was removed in vacuo, and the residue was adsorbed onto silica gel with dichloromethane prior to chromatography (SiO$_2$, 40% ethyl acetate in hexanes) to provide 93 as a colorless oil (18.2 mg, 77%); $[\alpha]_D^{19} = -68.1$ (c 1.81, CHCl$_3$); IR (film, cm$^{-1}$) 2986, 1690, 1479, 1372, 1267, 1213, 1145, 1127, 1109, 1044, 1014; $^1$H NMR (300 MHz, CD$_2$D$_6$) δ 9.38 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 7.1 Hz, 2H), 7.26 (d, J = 15.7 Hz, 1H), 7.47-6.91 (m, 3H), 6.48 (dd, J = 15.7, 7.8 Hz, 1H), 5.39 (d, J = 7.0 Hz, 1H), 4.56 (d, J = 6.9 Hz, 1H), 4.47 (d, J = 6.9 Hz, 1H), 4.42 (d, J = 6.9 Hz, 1H), 4.29 (d, J = 10.3 Hz, 1H), 4.20 (d, J = 10.3 Hz, 1H), 3.98 (d, J = 1.8 Hz, 1H), 3.56 (m, 1H), 3.12 (s, 3H), 2.92 (qd, J = 7.5, 2.8 Hz, 1H), 2.54 (d, J = 2.8 Hz, 1H), 2.24-1.93 (m, 3H), 1.28-1.24 (m, 1H), 1.20 (s, 3H), 1.17 (s, 3H), 1.04 (s, 3H), 0.87 (d, J = 7.6 Hz, 3H), 0.83 (s, 3H); $^{13}$C NMR (75 MHz, CD$_2$D$_6$) ppm 211.8, 192.6, 161.0, 152.1, 136.8, 132.2, 130.3, 129.0, 127.3, 121.7, 109.2, 95.5, 86.7, 85.9, 71.2, 62.4, 55.5, 54.7, 47.0, 46.8, 43.8, 26.5, 26.54, 26.47, 26.2, 25.7, 20.9, 20.5; HRMS (ESI) m/z (M$^+$-OCH$_3$) calcd for C$_{29}$H$_{37}$O$_5$S 497.2362, obsd 497.2370.
A cold (0 °C) solution of aldehyde 89b (11.6 mg, 208 μmol) in 4:1 methanol-tetrahydrofuran (1 mL) was treated with an aqueous sodium hydroxide solution (0.5 M, 0.17 mL). The homogeneous solution was stirred at 0 °C for 6 h and allowed to warm slowly to rt overnight. The solvent was removed under vacuum, and the residue was adsorbed onto silica gel for flash chromatography (SiO₂, 40% ethyl acetate in hexanes) to provide alcohols 94 (34%) and 95 (26%) as a 1:1 inseparable mixture (6 mg).

Repetition of this experiment with the addition of aqueous sodium hydroxide solution at room temperature and stirring for 21 h furnished alcohols 94 (48%) and 95 (18%) as a 2:1 mixture (6 mg).

For 94 and 95: IR (film, cm⁻¹) 3443, 2956, 1709, 1613, 1514, 1462, 1250, 1215, 1152, 1098, 1032; see ¹H NMR (300 MHz, C₆D₆) spectrum of mixture.
(2R,4R,4'R,5S)-5-(Hydroxymethyl)-2-((p-methoxyphenyl)-2',2'-dimethyl[4,4'-bi-
1,3-dioxolane]-5-carboxaldehyde, diethyl acetal, acetate (102).

A rapidly stirred solution of 100 (39.3 mg, 94.8 µmol) and 3 Å molecular sieves in CH$_2$Cl$_2$ (5 mL) was treated with DDQ (32.0 mg, 142 µmol). The mixture was stirred for 5 h, filtered through Celite, concentrated, and the residue was redissolved in pyridine (1 mL) with acetic anhydride (36 µL, 379 µmol) and a catalytic amount of 4-(N,N-dimethylamino)pyridine. The mixture was stirred for 10 h, diluted with water, extracted with ether, and the combined organic layers were dried and concentrated. The resulting residue was chromatographed (silica gel, elution with 30% ethyl acetate in hexanes) to furnish 23.4 mg (54%) of 102 as a colorless oil.

For the major anomer: R$_f$ = 0.31; [α]$^2$$_D$ = -3.70 (c 1.65, CHCl$_3$); IR (film, cm$^{-1}$) 2978, 2899, 1745, 1615, 1518, 1382, 1249, 1171, 1072; $^1$H NMR (300 MHz, CD$_2$D$_6$) δ 7.52 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 6.18 (s, 1H), 4.86 (d, J = 11.7 Hz, 1H), 4.76 (d, J = 7.8 Hz, 1H), 4.74 (s, 1H), 4.72 (d, J = 11.7 Hz, 1H), 4.48-4.42 (m, 1H), 4.21 (dd, J = 8.5, 5.1 Hz, 1H), 4.02 (dd, J = 8.5, 6.3 Hz, 1H), 3.68-3.52 (m, 3H), 3.34 (dq, J = 9.3, 6.9 Hz, 1H), 3.24 (s, 3H), 1.71 (s, 3H), 1.47 (s, 3H), 1.27 (s, 3H), 1.10 (t, J = 7.0 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H); $^{13}$C NMR (75 MHz, CD$_2$D$_6$) ppm 169.5, 160.8, 130.0, 128.5, 113.7, 109.4, 104.2, 103.7, 84.0, 79.8, 74.3, 67.7, 65.0, 64.4, 63.9, 54.5, 26.7, 25.4, 20.3, 15.4, 15.0; HRMS (El) m/z (M$^+$) calcd for C$_{23}$H$_{34}$O$_9$ 454.2203, obsd 454.2180.

Anal. Calcd for C$_{23}$H$_{34}$O$_9$: C, 60.78; H, 7.54. Found: C, 60.92; H, 7.47.
(αS,βR,4R)-α,β-Dihydroxy-α-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde, diethyl acetal, α-(p-methoxybenzoate) (103) and (αS,βR,4R)-α,β-Dihydroxy-α-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde, diethyl acetal, β-(p-methoxybenzoate) (104).

A suspension of 2-C-(hydroxymethyl)-4,5-O-isopropylidene-3-O-(p-methoxybenzyl)-D-arabinose diethyl acetal (100 mg, 241 μmol), DDQ (82.0 mg, 362 μmol), and 3 Å molecular sieves in CH₂Cl₂ (5 mL) was stirred for 2 h. Water (0.5 mL) and additional oxidant (82.0 mg) were added and the mixture was stirred for 3 h, diluted with water, and extracted with ether. The combined organic layers were dried and concentrated, and the residue was chromatographed (silica gel, 30% ethyl acetate in hexanes) to give regioisomeric 103 and 104 (1.2:1) as colorless oils (78.7 mg, 76%).

For 103: Rf = 0.15; [α]D²1 = +19.5 (c 1.79, CHCl₃); IR (film, cm⁻¹) 3485, 2980, 2932, 1715, 1607, 1513, 1460, 1372, 1317, 1259, 1169, 1103, 1061; ¹H NMR (300 MHz, CDCl₃) δ 8.24 (d, J = 8.9 Hz, 2H), 6.64 (d, J = 8.8 Hz, 2H), 4.96-4.83 (m, 2H), 4.73 (s, 1H), 4.57 (dd, J = 14.4, 6.2 Hz, 1H), 4.23-4.13 (m, 3H), 3.79 (br s, 1H), 3.55-3.44 (m, 3H), 3.40-3.25 (m, 2H), 3.14 (s, 3H), 1.36 (s, 3H), 1.26 (s, 3H), 1.00-0.90 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) ppm 166.2, 163.7, 132.1, 123.5, 113.9, 109.6, 106.9, 76.4, 76.1, 73.5, 68.3, 66.8, 66.1, 65.7, 54.8, 26.7, 25.7, 15.4, 15.2; HRMS (FAB) m/z (M⁺+H) calcd for C₂₁H₃₃O₈ 429.21, obsd 429.25.


Ethyl 2-C-(hydroxymethyl)-3-O-(p-methoxybenzyl)-D-arabinofuranoside (105).

The requisite diol 100 (10.0 g, 27.1 mmol) and pyridinium p-toluenesulfonate (354 mg, 1.41 mmol) in ethanol (150 mL) were refluxed
for 4 h and cooled to rt. The solvent was removed in vacuo, and the residue was purified by means of silica gel chromatography (60% ethyl acetate in hexanes) to furnish 105 (7.43 g, 83%) as an oily mixture of anomers.

For the α-anomer: \([\alpha]_{D}^{25} = \text{value} \text{ (c 1.59, CHCl}_3\text{); IR (film, cm}^{-1}\text{) 3444, 2928, 1614, 1515, 1250, 1098; }^{1}\text{H NMR (300 MHz, CDCl}_3\text{) \delta 7.24 (d, } J = 8.7 \text{ Hz, 2H), 6.87 (d, } J = 8.7 \text{ Hz, 2H), 4.93 (s, 1H), 4.70 (d, } J = 11.3 \text{ Hz, 1H), 4.51 (d, } J = 11.3 \text{ Hz, 1H), 4.10 (d, } J = 6.6 \text{ Hz, 1H), 3.99-3.95 (m, 1H), 3.96 (d, } J = 12.1 \text{ Hz, 1H), 3.87 (dq, } J = 9.8 \text{ Hz, 7.1 Hz, 1H), 3.79 (s, 3H), 3.72-3.68 (m, 1H), 3.69 (d, } J = 12.1 \text{ Hz, 1H), 3.62 (dq, } J = 9.8 \text{, 7.1 Hz, 1H), 3.52 (dd, } J = 11.9, 4.3 \text{ Hz, 1H), 2.51 (br s, 3H), 1.25 (t, } J = 7.1 \text{ Hz, 3H); }^{13}\text{C NMR (75 MHz, CDCl}_3\text{) ppm 159.4, 129.6, 129.4, 113.9, 102.9, 83.3, 82.2, 81.4, 72.7, 65.1, 63.2, 62.4, 55.3, 15.2.}

For the β-anomer: \([\alpha]_{D}^{22} = +90.0 \text{ (c 0.66, CHCl}_3\text{); }^{1}\text{H NMR (300 MHz, CDCl}_3\text{) \delta 7.25 (d, } J = 8.5 \text{ Hz, 2H), 6.87 (d, } J = 8.5 \text{ Hz, 2H), 4.87 (s, 1H), 4.62 (d, } J = 11.8 \text{ Hz, 1H), 4.52 (d, } J = 11.8 \text{ Hz, 1H), 4.13 (ddd, } J = 4.7, 2.7, 2.7 \text{ Hz, 1H), 3.93 (d, } J = 12.0 \text{ Hz, 1H), 3.88 (dd, } J = 12.0 \text{ Hz, 1H), 3.79 (s, 3H), 3.83-3.72 \text{ (series of m, 3H), 3.50 (dq, } J = 9.8 \text{, 7.0 Hz, 1H), 3.45 (dd, } J = 11.9, 2.8 \text{ Hz, 1H), 2.81 (br s, 3H), 1.20 (t, } J = 7.1 \text{ Hz, 3H); }^{13}\text{C NMR (75 MHz, CDCl}_3\text{) ppm 159.4, 129.9, 129.5, 113.9, 108.3, 83.8, 82.9, 82.6, 72.7, 63.7, 62.2, 61.4, 55.3, 15.1; HRMS (EI) m/z (M+) calcd for C}_{16}\text{H}_{24}\text{O}_7: 328.1522, obsd 328.1511.}

\text{Anal. Calcd for C}_{16}\text{H}_{24}\text{O}_7: \text{C, 58.53; H, 7.37. Found: C, 58.27; H, 7.31.}

(2S,4aS,7S,7aR)-5-Ethoxydihydro-7-(iodomethyl)-2-(p-methoxyphenyl)-4H-furo[3,4-d]-2,3-dioxin-4a(5H)-ol (107).

\[\text{EtO} \quad \text{CH} \quad \text{O} \quad \text{O} \quad \text{PMP}\]

A mixture of 105 (7.10 g, 21.6 mmol) and 3 Å molecular sieves in dichloromethane (250 mL) at rt was treated with DDQ (9.82 g, 43.2 mmol) in three portions separated by 15 min intervals. The murky mixture was stirred...
for 5 h, filtered through Celite into saturated sodium bicarbonate and sodium thiosulfite solutions. The organic layer was separated, dried, and concentrated to a crude solid that was purified (SiO₂ chromatography, 50% ethyl acetate in hexanes) to yield 105 (0.96 g, 14%) and 106 (4.31 g, 61%) as white amorphous solids which were used immediately in the next step.

The diol 106 (8.26 g, 25.3 mmol) was warmed (90 °C) with imidazole (6.03 g, 88.6 mmol) and triphenylphosphine (16.6 g, 63.3 mmol) in a 4:1 toluene-acetonitrile (300 mL) solution. Iodine (15.4 g, 60.6 mmol) was added in two portions, and the mixture was stirred for 1 h prior to cooling and removal of the solvent in vacuo. The residue was partitioned between water and ether, and the latter was recovered, dried, and concentrated to provide a crude yellow oil that was purified by silica gel chromatography (10-25% ethyl acetate in hexanes) to provide α-107 (2.95 g, 27%) and β-107 (7.83 g, 71%) as colorless oils.

For the α-anomer: \([\alpha]_D^{20} = +89.1 \text{ (c 1.42, CHCl}_3\); IR (film, cm⁻¹) 3460, 2918, 1684, 1614, 1518, 1384, 1243, 1167, 1088; \(^1\)H NMR (300 MHz, CDCl₃) δ 7.41 (d, \(J = 8.7\) Hz, 2H), 6.89 (d, \(J = 8.7\) Hz, 2H), 5.51 (s, 1H), 5.03 (s, 1H), 4.38 (d, \(J = 12.0\) Hz, 1H), 4.28 (ddd, \(J = 5.3, 5.3, 3.0\) Hz, 1H), 3.94 (d, \(J = 2.8\) Hz, 1H), 3.85 (d, \(J = 12.0\) Hz, 1H), 3.86-3.81 (m, 1H), 3.80 (s, 3H), 3.56 (dq, \(J = 7.0, 7.0\) Hz, 1H), 3.51 (dd, \(J = 10.6, 5.8\) Hz, 1H), 3.43 (dd, \(J = 10.6, 4.9\) Hz, 1H), 2.49 (br s, 1H), 1.27 (t, \(J = 7.0\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl₃) ppm 160.0, 130.1, 127.6, 113.6, 109.0, 98.3, 84.9, 83.0, 82.9, 67.3, 63.5, 55.2, 15.0, 7.38.

For the β-anomer: \([\alpha]_D^{20} = +11.6 \text{ (c 1.71, CHCl}_3\); \(^1\)H NMR (300 MHz, C₆D₆) δ 7.47 (d, \(J = 8.7\) Hz, 2H), 6.80 (d, \(J = 8.8\) Hz, 2H), 5.45 (s, 1H), 5.19 (s, 1H), 4.46 (dd, \(J = 9.6, 6.3\) Hz, 1H), 4.30 (s, 1H), 3.84 (d, \(J = 11.6\) Hz, 1H), 3.64 (d, \(J = 11.6\) Hz, 1H), 3.71-3.61 (m, 1H), 3.36 (dd, \(J = 9.7\) Hz, 1H), 3.26 (s, 3H), 3.30-3.24 (m, 1H), 3.20 (dd, \(J = 9.7, 6.3\) Hz, 1H), 3.01 (s, 1H), 0.90 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (75 MHz, C₆D₆) ppm 160.6, 130.5, 113.7 (2C), 104.8, 99.9, 86.0, 83.1, 71.4, 69.0, 65.9, 54.8, 15.2, 6.25; HRMS (El) m/z (M⁺) calcd for C₁₈H₂₁IO₆ 436.0383, obsd 436.0389.

Anal. Calcd for C₁₈H₂₁IO₆: C, 44.05; H, 4.85. Found: C, 43.93; H, 4.80.
Sodium hydride (107 mg, 4.45 mmol) was added in several portions to a solution of 107 (971 mg, 2.23 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (985 µL, 5.56 mmol) in THF (20 mL) at rt. The mixture was stirred for 40 min in advance of the careful addition of water. The reaction mixture was extracted with ether and the organic layers were dried in the presence of triethylamine. The ethereal solution was concentrated to a total volume of ca 10 mL, treated with triethylamine, filtered through silica gel, treated again with triethylamine, and finally fully concentrated and chromatographed (5% ethyl acetate in hexanes) to furnish 108 (1.00 g, 80%) as a colorless oil.

For the α-anomer: [α]D 19° = +58.2 (c 1.31, CHCl3); IR (film, cm−1) 2952, 1615, 1518, 1393, 1309, 1103, 922, 833; 1H NMR (300 MHz, C6D6) δ 7.56 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 7.7 Hz, 1H), 5.61 (s, 1H), 5.41 (s, 1H), 4.64 (d, J = 7.7 Hz, 1H), 4.61 (d, J = 7.7 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.45 (ddd, J = 6.7, 6.7, 3.2 Hz, 1H), 4.18 (d, J = 3.2 Hz, 1H), 4.06 (d, J = 12.1 Hz, 1H), 3.77 (dq, J = 9.6, 7.0 Hz, 1H), 3.63 (ddd, J = 8.5, 8.5, 1.4 Hz, 2H), 3.31 (dq, J = 9.6, 7.0 Hz, 1H), 3.25 (s, 3H), 3.21 (dd, J = 7.0, 2.0 Hz, 2H), 1.09 (t, J = 7.0 Hz, 3H), 0.93 (dd, J = 8.8, 7.8 Hz, 2H), -0.0090 (s, 9H); 13C NMR (75 MHz, C6D6) ppm 160.6, 131.6, 127.8, 113.8, 107.1, 98.4, 90.8, 84.6, 83.7, 82.0, 66.0, 64.9, 63.8, 54.7, 18.2, 15.2, 6.12, -1.34.

For the β-anomer: [α]D 19° = -83.9 (c 0.93, CHCl3); 1H NMR (300 MHz, C6D6) δ 7.49 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 5.60 (s, 1H), 5.35 (s, 1H), 5.16 (d, J = 7.5 Hz, 1H), 4.73 (d, J = 7.5 Hz, 1H), 4.46 (dd, J = 9.9, 6.0 Hz, 1H), 4.41 (d, J = 11.7 Hz, 1H), 4.38 (s, 1H), 4.26 (d, J = 11.7 Hz, 1H), 3.87-3.72 (series of m, 2H), 3.57 (dd, J = 9.7, 9.7 Hz, 1H), 3.52-3.44 (m, 1H), 3.32 (dd, J = 9.5, 5.9 Hz, 1H), 3.26 (s, 3H), 3.31-3.23 (m, 1H), 0.98 (t, J = 7.1 Hz, 3H), 0.95-0.92 (m, 2H), 0.011 (s, 9H); 13C NMR (75 MHz, C6D6) ppm 160.9, 130.9, 128.0, 114.1, 106.8, 100.2.

A solution of iodide 108 (557 mg, 0.98 mmol) in 95% ethanol (15 mL) containing pyridine (0.5 mL) was treated with zinc dust (3.05 g, 46.6 mmol) and heated at 80-90 °C for 5 h. The mixture was cooled, concentrated in vacuo, filtered through Celite (ether), concentrated, and chromatographed (5% ethyl acetate in hexanes) to provide 109 (291 mg, 75%) as a colorless oil; [α]D<sup>21</sup> = -24.2 (c 0.38, CHCl<sub>3</sub>); IR (film, cm<sup>-1</sup>) 2955, 1732, 1616, 1519, 1456, 1392, 1304, 1252, 1088; <sup>1</sup>H NMR (300 MHz, CD<sub>3</sub>OD) δ 10.13 (s, 1H), 7.49 (d, J = 8.7 Hz, 2H), 6.80 (d, J = 8.7 Hz, 2H), 6.24 (ddd, J = 17.3, 11.0, 4.0 Hz, 1H), 5.55 (ddd, J = 17.4, 1.8, 1.8 Hz, 1H), 5.41 (s, 1H), 5.16 (ddd, J = 10.9, 1.8, 1.8 Hz, 1H), 4.74 (d, J = 7.6 Hz, 1H), 4.65 (d, J = 11.3 Hz, 1H), 4.57 (d, J = 7.6 Hz, 1H), 4.30 (ddd, J = 3.8, 1.8, 1.8 Hz, 1H), 3.78 (d, J = 11.3 Hz, 1H), 3.64 (ddd, J = 9.4, 9.4, 7.1 Hz, 1H), 3.44 (ddd, J = 9.4, 9.4, 7.1 Hz, 1H), 3.26 (s, 3H), 0.87-0.82 (m, 2H), -0.033 (s, 9H); <sup>13</sup>C NMR (75 MHz, CD<sub>3</sub>OD) ppm 200.5, 160.7, 131.9, 130.5, 128.2, 117.5, 113.9, 102.0, 91.5, 81.6, 75.7, 71.0, 65.9, 54.8, 18.2, -1.41; HRMS (EI) m/z (M<sup>+</sup>) calcd for C<sub>20</sub>H<sub>30</sub>O<sub>6</sub>Si 394.1812, obsd 394.1792.
a suspension of (iodomethyl)triphenylphosphonium iodide (2.53 g, 4.78 mmol) in THF (45 mL) was stirred at rt while sodium hexamethyldisilazide (4.78 mL, 1M in THF) was added dropwise. The clear red solution was stirred at rt for 10 min and cooled to 0 °C prior to addition via cannula of a solution of 109 (1.25 g, 3.18 mmol) in THF (15 mL). The cloudy red mixture was immediately warmed to rt, stirred for an additional 15 min, diluted with water, and extracted with ether. The ethereal layers were combined, dried, and concentrated before chromatography over silica gel (3% ethyl acetate in hexanes) to yield 110 (1.18 g, 72%) as a colorless oil; [α]D = +31.6 (c 0.89, CHCl3); IR (film, cm⁻¹) 2953, 1616, 1518, 1389, 1296, 1250, 1172, 1089, 833; ¹H NMR (300 MHz, CDCl3) δ 7.53 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 9.0 Hz, 1H), 6.81 (d, J = 8.7 Hz, 2H), 6.48 (ddd, J = 17.3, 10.9, 4.0 Hz, 1H), 6.29 (d, J = 9.0 Hz, 1H), 5.61 (ddd, J = 17.3, 2.0, 2.0 Hz, 1H), 5.43 (s, 1H), 5.30 (ddd, J = 10.9, 1.9, 1.9 Hz, 1H), 4.82 (d, J = 7.9 Hz, 1H), 4.78 (d, J = 7.9 Hz, 1H), 4.58 (d, J = 11.0 Hz, 1H), 4.38-4.36 (m, 1H), 3.94 (d, J = 11.0 Hz, 1H), 3.81 (ddd, J = 9.6, 9.6, 6.4 Hz, 1H), 3.50 (ddd, J = 9.4, 9.4, 7.1 Hz, 1H), 3.27 (s, 3H), 0.96-0.89 (m, 2H), -0.0069 (s, 9H); ¹³C NMR (75 MHz, CDCl3) ppm 160.6, 136.9, 133.4, 130.9, 128.0, 117.3, 113.8, 101.7, 91.8, 83.6, 80.2, 75.8, 73.9, 66.0, 54.7, 18.3, -1.33; HRMS (EL) m/z (M⁺) calcd for C₂₁H₂₃IO₅Si 518.0986, obsd 518.0951.


n-Butyllithium (0.54 mL, 1.6M in hexanes) was added to a cold (-78 °C) solution of vinyl iodide 110 (380 mg, 733 μmol) in ether (7 mL). The resulting solution was stirred for 1 min, treated with a rt solution of vinyl sulfide 53c (222 mg, 666 μmol) in THF (3 mL), stirred for 10 min, treated with water, and extracted with ether. The organic layers were combined, dried, and concentrated prior to silica gel chromatography (15% ethyl acetate in hexanes) to furnish the adduct (346 mg, 72%) as a colorless oil; \([\alpha]_D^{21} = -157 (c 1.28, \text{CHCl}_3)\); IR (film, cm\(^{-1}\)) 3394, 2954, 1616, 1591, 1391, 1250, 1150, 1109, 1047; \(^1\)H NMR (300 MHz, CD\(_2\)D\(_2\)) \& 7.57 (d, \(J = 8.7 \text{ Hz}, 2\)H), 7.35 (d, \(J = 7.2 \text{ Hz}, 2\)H), 7.03 (dd, \(J = 7.3, 7.3 \text{ Hz}, 2\)H), 6.92 (ddd, \(J = 7.4, 7.4, 1\)H), 6.80 (d, \(J = 8.8 \text{ Hz}, 2\)H), 6.46 (d, \(J = 10.8 \text{ Hz}, 1\)H), 6.36 (ddd, \(J = 17.2, 10.9, 4.0 \text{ Hz}, 1\)H), 6.11 (d, \(J = 10.8 \text{ Hz}, 1\)H), 6.04 (d, \(J = 13.9 \text{ Hz}, 1\)H), 5.81 (d, \(J = 13.9 \text{ Hz}, 1\)H), 5.65 (ddd, \(J = 17.3, 1.8, 1.8 \text{ Hz}, 1\)H), 5.45 (s, 1H), 5.35 (ddd, \(J = 10.9, 1.8, 1.8 \text{ Hz}, 1\)H), 5.23 (s, 1H), 4.79-4.72 (m, 4H), 4.67 (d, \(J = 6.3 \text{ Hz}, 1\)H), 4.56 (ddd, \(J = 4.0, 2.0, 2.0 \text{ Hz}, 1\)H), 4.09 (d, \(J = 10.3 \text{ Hz}, 1\)H), 3.72 (s, 1H), 3.69 (ddd, \(J = 8.5, 8.5, 8.5 \text{ Hz}, 1\)H), 3.64 (ddd, \(J = 8.5, 8.5, 8.5 \text{ Hz}, 1\)H), 3.26 (s, 3H), 3.25 (s, 3H), 2.25-2.18 (m, 2H), 1.92 (d, \(J = 5.1 \text{ Hz}, 1\)H), 1.77 (s, 3H), 1.73-1.64 (m, 1H), 0.96 (s, 3H), 1.02-0.89 (series of m, 3H), -0.021 (s, 9H); \(^{13}\)C NMR (75 MHz, CD\(_2\)D\(_2\)) ppm 160.5, 139.7, 138.3, 134.0, 131.0, 129.7, 129.2, 129.1, 128.6, 127.9, 126.35, 126.27, 117.6, 113.8, 101.7, 97.0 (2C), 90.2, 85.0, 80.9, 74.5, 73.9, 66.7, 62.0, 55.3, 54.7, 52.6, 50.3, 27.5, 25.1, 22.9, 22.8, 18.2, -1.38; HRMS (EI) \(m/z\) calcd for C\(_{40}\)H\(_{56}\)O\(_8\)SSi 724.3465, obsd 724.3459.

Anal. Calcd for C\(_{40}\)H\(_{56}\)O\(_8\)SSi: C, 66.27; H, 7.79. Found: C, 66.23; H, 7.75.

Potassium hexamethyldisilazide (108 μL, 0.5 M in toluene) was added to a cold (-78 °C), deoxygenated (Ar, 15 min) solution of tertiary carbinol 111 (13 mg, 18 μmol) and 18-crown-6 (14 mg, 54 μmol) in THF (2 mL). The mixture was stirred for 15 min, treated with methyl iodide (25 μL, 179 μmol), stirred for 1.5 h, and quenched with water prior to its extraction with ether. The combined organic layers were dried and concentrated to leave a crude oil that was purified using silica gel chromatography (15% ethyl acetate in hexanes) to afford 112 (12.4 mg, 94%) as a colorless oil; [α]D 20 = -90.7 (c 1.08, CHCl3); IR (film, cm⁻¹) 2951, 1711, 1616, 1518, 1392, 1302, 1250, 1146, 1107; ¹H NMR (300 MHz, C6D6) δ 7.54 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 7.2 Hz, 2H), 6.99 (dd, J = 7.4 Hz, 2H), 6.86 (dd, J = 7.4, 7.4 Hz, 1H), 6.80 (d, J = 8.7 Hz, 2H), 6.85-6.73 (m, 1H), 5.71-5.61 (series of m, 3H), 5.64 (s, 1H), 5.33 (d, J = 11.3 Hz, 1H), 5.13 (d, J = 10.7 Hz, 1H), 5.00 (d, J = 5.8 Hz, 1H), 4.80 (d, J = 8.2 Hz, 1H), 4.66 (d, J = 6.3 Hz, 1H), 4.64 (d, J = 11.3 Hz, 1H), 4.53 (d, J = 6.9 Hz, 1H), 4.44 (d, J = 6.9 Hz, 1H), 4.35-4.28 (m, 1H), 4.14 (d, J = 1.3 Hz, 1H), 3.96 (ddd, J = 10.0, 10.0, 5.9 Hz, 1H), 3.61 (ddd, J = 9.8, 9.8, 6.6 Hz, 1H), 3.28 (s, 3H), 3.13 (s, 3H), 3.07 (dd, J = 7.9, 2.3 Hz, 1H), 2.15 (br d, J = 7.5 Hz, 1H), 2.11-1.94 (m, 1H), 1.47 (d, J = 7.8 Hz, 3H), 1.41 (s, 3H), 1.36-1.23 (m, 2H), 1.20-0.85 (series of m, 3H), 0.83 (s, 3H), 0.019 (s, 9H); ¹³C NMR (75 MHz, C6D6) ppm 210.7, 160.5, 150.4, 138.2, 133.3, 131.3, 131.3, 128.8, 128.6, 127.9, 125.3, 121.8, 117.5, 113.8, 102.2, 95.4, 91.2, 86.9, 86.2, 77.3, 72.6, 65.9, 55.4, 55.2, 54.7, 54.4, 47.13, 47.08, 46.5, 26.9, 26.6, 24.4, 20.6, 20.0, 18.6, -1.27; HRMS (El) m/z (M⁺) calcd for C₅₁H₅₈O₃Si 738.3622, obsd 738.3582.

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A solution of 112 (25 mg, 34 μmol) in cold (-78 °C) CH₂Cl₂ was treated with m-chloroperbenzoic acid (7.0 mg, 40.8 μmol), stirred at that temperature for 30 min, warmed to 0 °C for 30 min, and treated with additional peracid (0.6 mg, 3.4 μmol). The reaction mixture was washed with saturated NaHCO₃ solution, the organic layers were dried and concentrated, and the residue was chromatographed (silica gel, 30% ethyl acetate in hexanes) to provide both sulfoxide diastereomers as colorless oils (24.6 mg, 96%).

For 113: [α]ºD = -172 (c 0.32, CHCl₃); IR (film, cm⁻¹) 2953, 1714, 1613, 1519, 1449, 1390, 1249, 1147, 1107, 1044; ¹H NMR (300 MHz, CDCl₃) δ 7.48 (d, J = 8.7 Hz, 2H), 7.45-7.35 (m, 5H), 6.92 (d, J = 8.7 Hz, 2H), 6.37 (ddd, J = 17.3, 10.9, 4.9 Hz, 1H), 5.65 (s, 1H), 5.58 (br d, J = 17.3 Hz, 1H), 5.50 (d, J = 8.2 Hz, 1H), 5.31 (br d, J = 10.9 Hz, 1H), 5.12-5.07 (m, 2H), 4.62 (d, J = 8.2 Hz, 1H), 4.62 (d, J = 6.9 Hz, 1H), 4.57 (br d, J = 4.9 Hz, 1H), 4.50-4.44 (m, 2H), 4.36 (d, J = 6.9 Hz, 1H), 4.06 (s, 1H), 3.94 (ddd, J = 9.6, 9.6, 5.7 Hz, 1H), 3.83 (s, 3H), 3.65 (d, J = 6.5 Hz, 1H), 3.58 (ddd, J = 10.3, 10.3, 6.5 Hz, 1H), 3.52-3.41 (m, 1H), 3.28 (s, 3H), 2.73 (qd, J = 7.8, 2.2 Hz, 1H), 2.29-2.20 (m, 1H), 2.07 (d, J = 8.6 Hz, 1H), 1.78-1.67 (m, 1H), 1.61-1.52 (m, 1H), 1.44 (d, J = 7.8 Hz, 3H), 1.01 (s, 3H), 0.82 (s, 3H), 0.074 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) ppm 211.1, 160.1, 151.9, 142.8, 133.3, 130.4, 129.5, 128.4, 127.8, 124.5, 120.0, 117.5, 113.7, 102.4, 94.9, 91.3, 86.0, 85.9, 77.2, 72.4, 65.7, 61.4, 55.6, 55.3, 54.0, 48.8, 47.0, 46.7, 28.3, 26.9, 25.7, 20.0, 19.6, 18.4, -1.30.

For the sulfoxide epimer 113: [α]ºD = -90.1 (c 1.42, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.71-7.67 (m, 2H), 7.49-7.44 (m, 5H), 6.88 (d, J = 8.7 Hz, 2H), 6.64 (ddd, J = 18.3, 10.4, 8.2 Hz,
1H), 5.59 (s, 1H), 5.41 (d, J = 8.2 Hz, 1H), 5.20 (dd, J = 18.3, 1.0 Hz, 1H), 5.20 (d, J = 6.8 Hz, 1H), 5.09 (d, J = 11.4 Hz, 1H), 4.91 (dd, J = 10.4, 1.5 Hz, 1H), 4.69 (d, J = 6.8 Hz, 1H), 4.64 (d, J = 6.9 Hz, 1H), 4.53 (d, J = 8.2 Hz, 1H), 4.39 (d, J = 11.4 Hz, 1H), 4.39 (d, J = 6.9 Hz, 1H), 4.39 (d, J = 8.2 Hz, 1H), 4.17 (d, J = 1.0 Hz, 1H), 3.92 (d, J = 2.1 Hz, 1H), 3.81 (ddd, J = 9.1, 9.1, 5.7 Hz, 1H), 3.80 (s, 3H), 3.49 (ddd, J = 9.7, 9.7, 6.5 Hz, 1H), 3.31 (s, 3H), 2.99 (qd, J = 7.8, 2.2 Hz, 1H), 2.50-2.43 (m, 2H), 2.22 (br d, J = 7.3 Hz, 1H), 1.76-1.65 (m, 2H), 1.49 (d, J = 7.7 Hz, 3H), 1.10 (s, 3H), 1.08 (s, 3H), 1.05-0.87 (m, 2H), 0.014 (s, 9H); 1H NMR (75 MHz, CDCl₃) ppm 210.6, 160.0, 150.9, 144.7, 135.9, 130.62, 130.59, 128.8, 127.9, 124.7, 120.3, 118.0, 113.6, 102.1, 95.0, 91.0, 88.0, 86.0, 75.7, 72.6, 66.5, 65.6, 55.6, 55.3, 54.3, 47.3, 46.8, 46.5, 29.2, 27.2, 26.5, 20.1, 19.6, 18.3, -1.35; HRMS (FAB) m/z (M+H) calcd for C₄₁H₅₉O₉Si 755.36, obsd 755.44.


Sodium acetate (8.3 mg, 101 μmol) was warmed to 120 °C with 113 (7.6 mg, 10 μmol) in acetic anhydride (2 mL) for 6.5 h. The reaction mixture was cooled, freed of solvent, and chromatographed (SiO₂, 15% ethyl acetate in hexanes) to furnish 4.8 mg (76%) 111 as a colorless oil; [α]D²⁰ = -185 (c 0.43, CHCl₃); IR (film, cm⁻¹) 2919, 1704, 1616, 1519, 1457, 1390, 1250, 1146, 1108, 1042; ¹H NMR (300 MHz, CDCl₃) δ 7.41 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.69 (br s, 1H), 6.59 (ddd, J = 17.2, 11.0, 3.6 Hz, 1H), 5.75 (s, 1H), 5.48 (ddd, J = 17.2, 2.0, 2.0 Hz, 1H), 5.44 (br s, 1H), 5.28 (ddd, J = 11.0, 2.0, 2.0 Hz, 1H), 4.96 (d, J = 7.1 Hz, 1H), 4.78 (d, J = 7.1 Hz, 1H), 4.59 (s, 1H), 4.58 (d, J = 6.8 Hz, 1H), 4.39 (d, J = 6.9 Hz, 1H), 4.35 (d, J = 11.1 Hz, 1H), 4.04 (d, J = 2.0 Hz, 1H), 3.92 (d, J = 11.1 Hz, 1H), 3.80 (s, 3H).
3H), 3.74 (ddd, J = 9.7, 9.7, 7.1 Hz, 1H), 3.64 (ddd, J = 9.2, 9.2, 7.8 Hz, 1H), 3.34 (s, 3H), 3.28-3.26 (m, 1H), 2.52-2.37 (m, 1H), 2.30-2.05 (series of m, 3H), 1.30 (d, J = 7.2 Hz, 3H), 1.27 (s, 3H), 1.12 (s, 3H), 0.95 (m, 2H), 0.027 (s, 9H); 13C NMR (75 MHz, CDCl3) ppm 209.3, 160.1, 146.9, 136.6, 135.0, 132.4, 130.9, 127.9, 127.9, 116.2, 113.6, 100.6, 94.9, 91.1, 84.9, 83.8, 78.4, 70.9, 66.2, 55.6, 55.3, 53.6, 46.4, 46.2, 25.2, 24.9, 24.8, 21.2, 18.2, 17.3, -1.40; HRMS (FAB) m/z (M+ + H) calcd for C35H53O8Si 629.35, obsd 629.44.


A solution of 112 (10 mg, 14 μmol) in cold (0 °C) ether (1 mL) was stirred rapidly as lithium aluminum hydride (0.6 mg, 16 μmol) was added. After a 2 h period of stirring, a saturated solution of Rochelle's salt was added, and the mixture was stirred for 12 h. The organic layer was dried and concentrated to give a crude oil that yielded to chromatographic purification (SiO2, 25% ethyl acetate in hexanes) to provide 115 (7 mg, 70%) as a colorless oil; [α]D20 = -122 (c 0.99, CHCl3); IR (film, cm⁻¹) 3446, 2949, 1616, 1519, 1479, 1392, 1303, 1250, 1147, 1096, 1039; 1H NMR (300 MHz, CDCl3) δ 7.57 (d, J = 8.7 Hz, 2H), 7.45 (d, J = 7.3 Hz, 2H), 7.02 (dd, J = 7.4, 7.4 Hz, 2H), 6.87 (dd, J = 7.4, 7.4 Hz, 1H), 6.89-6.84 (m, 1H), 6.79 (d, J = 8.8 Hz, 2H), 5.88 (d, J = 5.5 Hz, 1H), 5.58 (br d, J = 17.2 Hz, 1H), 5.51 (s, 1H), 5.14 (d, J = 10.7 Hz, 1H), 4.88 (d, J = 7.6 Hz, 1H), 4.85 (d, J = 5.5 Hz, 1H), 4.73 (d, J = 7.8 Hz, 1H), 4.66 (d, J = 11.4 Hz, 1H), 4.55 (s, 1H), 4.53 (s, 2H), 4.32 (d, J = 11.4 Hz, 1H), 4.30-4.22 (m, 1H), 4.09 (ddd, J = 6.9, 3.6, 3.6 Hz, 1H), 3.85 (ddd, J = 9.6, 9.6, 6.3 Hz, 1H), 3.67 (ddd, J = 9.6, 9.6, 6.9 Hz, 1H), 3.55 (dd, J = 3.8, 2.0 Hz, 1H), 3.51 (d, J = 2.5 Hz, 1H), 3.31 (s, 1H), 3.27 (s, 3H), 3.19
(s, 3H), 2.71 (dq, J = 7.8, 7.8 Hz, 1H), 2.20-2.14 (m, 1H), 2.14 (br d, J = 9.1 Hz, 1H), 2.05-1.97 (m, 1H), 1.79 (s, 3H), 1.53 (d, J = 7.4 Hz, 3H), 1.50-1.18 (m, 1H), 1.16-1.11 (m, 1H), 1.00 (s, 3H), 0.94-0.85 (m, 1H), 0.034 (s, 9H); \(^{13}\)C NMR (75 MHz, C\(_{6}\)D\(_{6}\)) ppm 160.5, 150.4, 138.8, 133.1, 131.0, 128.7, 128.3, 128.2, 125.3, 118.4, 117.4, 113.9, 102.3, 95.8, 90.4, 85.1 (2C), 78.1, 77.9, 71.6, 66.6, 55.3, 54.7, 54.4, 53.9, 47.1, 46.3, 35.5, 28.3, 26.7, 26.0, 24.8, 22.1, 18.4, -1.30; HRMS (EI) m/z (M\(^+\)) calcd for C\(_{41}\)H\(_{60}\)O\(_{9}\)Si 740.3778, obsd 740.3764.

\((1S,2S,3R,4S)-3-(\text{Methoxymethoxy})-2-[(\text{Z})-2-[(2S,4R,5S)-2-(\text{p-methoxyphenyl})-\text{5}-\text{[2-(trimethylsilyl)ethoxy}]-\text{methoxy}]-4-\text{vinyl-m-dioxan-5-yl}]-\text{vinyl}]-7,7-\text{dimethyl}-1-\text{vinylbicyclo[2.2.1]heptan-2-ol}\) (116).

A cold (-78 °C) solution of vinyl iodide 110 (685 mg, 1.32 mmol) in dry ether (15 mL) was treated with \(\nu\)-butyllithium (0.90 of a 1.6 M soln in pentane, 1.44 mmol) and stirred for 5 min prior to the addition of ketone 39 (269 mg, 1.20 mmol) in ether (5 mL). The reaction mixture was stirred for 20 min, quenched with water, warmed to rt, and diluted with ether. Following separation of the biphasic mixture, the organic layer was dried and concentrated to give an oil that was chromatographed (SiO\(_2\), 15% ethyl acetate in hexanes) to provide 116 (564 mg, 76%) as a colorless oil; \([\alpha]_D^{31} = -17.0\) (c 0.92, CHCl\(_3\)); IR (film, cm\(^{-1}\)) 3400, 2951, 1519, 1461, 1414, 1389, 1249, 1149, 1108, 1091, 1044; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.41 (d, \(J = 8.7\) Hz, 2H), 6.88 (d, \(J = 8.7\) Hz, 2H), 6.06 (dd, \(J = 17.7, 11.0\) Hz, 1H), 5.95 (ddd, \(J = 17.4, 10.9, 4.4\) Hz, 1H), 5.81 (d, \(J = 14.0\) Hz, 1H), 5.65 (d, \(J = 14.0\) Hz, 1H), 5.55 (s, 1H), 5.46 (ddd, \(J = 17.4, 1.7, 1.7\) Hz, 1H), 5.28 (s, 1H), 5.28 (ddd, \(J = 10.9, 1.7, 1.7\) Hz, 1H), 5.18 (dd, \(J = 11.0, 2.0\) Hz, 1H), 4.98 (dd, \(J = 17.7, 2.0\) Hz, 1H), 4.95 (d, \(J = 8.0\) Hz, 1H), 4.87 (d, \(J = 8.0\) Hz, 1H), 4.71 (d, \(J = 6.5\) Hz, 1H), 4.68 (d, \(J = 6.5\) Hz, 1H), 4.62 (ddd, \(J = 4.4, 1.8, 1.8\) Hz, 1H), 4.36 (d, \(J = 10.3\) Hz, 1H), 4.11
(d, J = 10.3 Hz, 1H), 3.80 (s, 3H), 3.78-3.63 (series of m, 3H), 3.37 (s, 3H), 1.94 (d, J = 5.0 Hz, 1H), 1.80 (ddddd, J = 12.4, 12.4, 3.4, 3.4 Hz, 1H), 1.65 (ddd, J = 13.1, 13.1, 4.7 Hz, 1H), 1.51-1.42 (m, 1H), 1.38 (s, 3H), 1.17-1.09 (m, 1H), 0.96 (dd, J = 8.5, 8.5 Hz, 2H), 0.78 (s, 3H), 0.046 (s, 9H). 13C NMR (75 MHz, CDCl3) ppm 160.1, 138.5, 136.0, 133.2, 130.1, 127.6, 126.8, 118.2, 116.3, 113.6, 101.4, 96.6, 90.0 (2C), 84.0, 80.0, 74.1, 73.7, 66.7, 60.9, 55.4, 55.3, 50.83, 50.78, 25.9, 24.3, 22.1, 21.9, 18.1, -1.40; HRMS (EI) m/z (M+) calcd for C34H52O8Si 616.3431, obsd 616.3444.

Anal. Calcd for C34H52O8Si: C, 66.20; H, 8.50. Found: C, 66.12; H, 8.54.


A deoxygenated (Ar) solution of 116 (462 mg, 750 μmol) and 18-crown-6 (396 mg, 1.50 mmol) in cold (-30 °C) tetrahydrofuran was treated with potassium hexamethyldisilazide (3.00 mL of a 0.5 M in toluene, 1.50 mmol) and stirred for 30 min. Water was added, the mixture was extracted with ether, the organic layers were dried and concentrated, and the resulting residue was chromatographed on silica gel (elution with 15% ethyl acetate in hexanes) to provide 391 mg (85%) of 117 as a colorless oil; [α]D22 = +8.54 (c 1.27, CHCl3); IR (film, cm⁻¹) 2898, 1693, 1615, 1519, 1464, 1428, 1411, 1391, 1303, 1250, 1173, 1147, 1103, 1037, 991, 834; 1H NMR (300 MHz, CDCl3) δ 7.45 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.16 (ddd, J = 17.2, 10.8, 4.6 Hz, 1H), 5.55 (s, 1H), 5.37 (ddd, J = 17.2, 1.6, 1.6 Hz, 1H), 5.37 (dd, J = 12.0, 3.6 Hz, 1H), 5.27 (ddd, J = 10.8, 1.3 Hz, 1H), 4.93 (d, J = 7.7 Hz, 1H), 4.79 (d, J = 7.7 Hz, 1H), 4.56 (d, J = 6.6 Hz, 1H), 4.52 (ddd, J = 4.6, 2.3, 2.3 Hz, 1H), 4.45 (d, J =
6.6 Hz, 1H), 4.41 (d, J = 12.0 Hz, 1H), 4.02 (d, J = 12.0 Hz, 1H), 3.81 (d, J = 5.5 Hz, 1H), 3.80 (s, 3H), 3.78-3.61 (m, 2H), 3.56 (dd, J = 16.0, 13.1 Hz, 1H), 3.24 (s, 3H), 3.13-3.08 (br m, 1H), 2.30-2.14 (series of m, 3H), 2.11-2.01 (m, 2H), 1.97-1.77 (series of m, 3H), 1.43 (s, 3H), 1.09 (s, 3H), 0.95 (dd, J = 8.4, 8.4 Hz, 2H), 0.035 (s, 9H); 13C NMR (75 MHz, CDCl3) ppm 211.0, 160.0, 146.8, 132.7, 130.3, 127.8, 123.6, 117.3, 113.5, 101.8, 95.8, 89.3, 87.8, 82.3, 74.2, 71.1, 65.8, 55.6, 55.3, 54.6, 45.9, 39.2, 38.5, 26.4, 23.5, 23.31, 23.25, 22.3, 18.2, -1.42; HRMS (FAB) m/z (M+H) calcd for C34H53O8Si 617.35, obsd 617.28.


A solution of 116 (214 mg, 347 µmol) and 18-crown-6 (275 mg, 1.04 mmol) in dry tetrahydrofuran (8 mL) was deoxygenated (Ar), cooled to -78 °C, and treated with potassium hexamethyldisilazide (2.78 mL of a 0.5 M soln in toluene, 1.39 mmol). The solution was stirred at -78 °C for 1 h, warmed to -30 °C for 1 h, and treated with methyl iodide (216 µL, 3.37 mmol). The cloudy mixture was stirred for an additional 2 h before the addition of water, warming to rt, and extraction with ether. The ethereal layers were dried and concentrated to leave a crude oil that was purified via silica gel chromatography (elution with 15% ethyl acetate in hexanes) to furnish 118 (115 mg, 53%) as a colorless oil; [α]D 20 = -70.0 (c 0.61, CHCl3); IR (film, cm⁻¹) 2954, 1709, 1615, 1518, 1462, 1391, 1302, 1250, 1146, 1108, 1092, 1044, 859, 834; 1H NMR (300 MHz, CDCl3) δ 7.42 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.23 (ddd, J = 17.3, 10.8, 4.6 Hz, 1H), 5.58 (s, 1H), 5.40 (d, J = 8.2 Hz, 1H), 5.37 (ddd, J = 17.3, 1.7, 1.7 Hz, 1H), 5.23
(dd, J = 11.3, 3.8 Hz, 1H), 5.17 (ddd, J = 10.8, 1.7, 1.7 Hz, 1H), 5.09 (d, J = 11.2 Hz, 1H), 4.64 (d, J = 8.6 Hz, 1H), 4.63 (d, J = 6.8 Hz, 1H), 4.44-4.40 (m, 2H), 4.38 (d, J = 6.8 Hz, 1H), 4.07 (d, J = 1.6 Hz, 1H), 3.91 (ddd, J = 11.1, 9.6, 5.7 Hz, 1H), 3.79 (s, 3H), 3.57 (ddd, J = 11.1, 9.7, 6.3 Hz, 1H), 3.30 (s, 3H), 2.73 (dd, J = 7.6, 2.1 Hz, 1H), 2.61-2.32 (series of m, 4H), 2.20-2.09 (series of m, 3H), 1.56 (ddd, J = 14.1, 9.6, 4.8 Hz, 1H), 1.36 (d, J = 7.8 Hz, 3H), 1.17 (s, 3H), 1.05 (s, 3H), 1.03-0.88 (m, 2H), 0.050 (s, 9H); δ 211.8, 159.8, 146.6, 134.5, 130.7, 127.5, 124.3, 114.6, 113.5, 101.5, 94.8, 90.4, 85.6, 85.1, 76.2, 72.1, 65.2, 55.5, 55.2, 54.4, 47.8, 46.9, 45.2, 30.2, 26.7, 26.1, 23.1, 19.7 (2C), 18.3, -1.40; HRMS (FAB) m/z (M+H) calcd for C35H55O8Si 631.37, obsd 631.34.


Osmium tetraoxide (4.9 mg, 19 μmol) was added to a chilled (0 °C) solution of 118 (13 mg, 21 μmol) in pyridine (1 mL) and stirred for 2 h before being quenched with saturated aq Na2S2O4 solution. Following an additional 2 h period of stirring at rt, the mixture was extracted with ether, and the ethereal layers were dried and concentrated to provide a residue that was subjected to flash chromatography (SiO2, 30% ethyl acetate in hexanes). There was isolated 119a (5.2 mg, 41%) and an undetermined amount of 118, both as colorless oils.

For 119a: [α]D20 = +17.8 (c 0.41, CHCl3); IR (film, cm⁻¹) 3384, 2951, 1698, 1615, 1519, 1461, 1392, 1304, 1251, 1150, 1095, 1036, 834; 1H NMR (300 MHz, CDCl3) δ 7.43 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 6.32 (ddd, J = 17.6, 11.0, 2.6 Hz, 1H), 5.65 (s, 1H), 5.56 (ddd, J
= 17.6, 1.7, 1.7 Hz, 1H), 5.38 (dd, J = 11.0, 2.1, 2.1 Hz, 1H), 4.91 (d, J = 8.1 Hz, 1H), 4.85 (d, J = 8.1 Hz, 1H), 4.72 (ddd, J = 2.6, 1.9, 1.9 Hz, 1H), 4.48 (d, J = 6.9 Hz, 1H), 4.32 (d, J = 11.9 Hz, 1H), 4.31 (d, J = 6.9 Hz, 1H), 4.22 (s, 1H), 4.19 (d, J = 11.9 Hz, 1H), 3.82 (s, 3H), 3.71 (dd, J = 8.4 Hz, 2H), 3.42 (br d, J = 11.4 Hz, 1H), 3.23 (s, 3H), 3.18 (s, 1H), 2.95 (q, J = 6.4 Hz, 1H), 2.77 (d, J = 13.1 Hz, 1H), 2.45-2.26 (series of m, 4H), 2.04 (dd, J = 12.6, 12.6, 2.4 Hz, 1H), 1.85 (dd, J = 13.1, 13.1, 1.2 Hz, 1H), 1.80-1.66 (series of m, 2H), 1.29 (d, J = 6.4 Hz, 3H), 1.05 (s, 3H), 0.98 (s, 3H), 0.96 (dd, J = 8.4 Hz, 2H), 0.043 (s, 9H); 13C NMR (75 MHz, CDCl₃) ppm 212.2, 160.0, 132.5, 129.8, 127.3, 116.3, 113.5, 101.5, 94.9, 89.4, 86.5, 82.5, 81.2, 75.5, 70.0, 69.0, 66.3, 55.9, 55.6, 55.3, 50.4, 47.6, 34.4, 32.7, 32.1, 29.8, 27.8, 18.2, 16.3, 10.4, -1.42; HRMS (FAB) m/z (M+H) calcd for C₃₅H₅₇O₁₀Si 665.37, obsd 665.38.


A solution of diol 119a (27 mg, 41 µmol), tert-butyldimethylsilyl chloride (12 mg, 82 µmol), imidazole (14 mg, 200 µmol), and a catalytic amount of 4-(N,N-dimethylamino)pyridine in DMF (0.2 mL) was stirred at rt for 12 h. An additional 2.6 eq of TBDMSI and imidazole were next added, and the stirring was continued for 2 days. Water was introduced, the mixture was extracted with ether, the organic layers were dried and concentrated, and the residue was chromatographed on silica gel (elution with 15% ethyl acetate in hexanes) to furnish 119a (5.0 mg, 19%) and 119b (23.2 mg, 73%), both as colorless oils.
For 119b: $[\alpha]^\circ_{D}^{20} = +33.3$ (c 0.27, CHCl$_3$); IR (film, cm$^{-1}$) 3460, 2943, 1698, 1615, 1519, 1470, 1384, 1251, 1150, 1039, 931, 836; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.43 (d, $J = 8.7$ Hz, 2H), 6.90 (d, $J = 8.7$ Hz, 2H), 6.34 (ddd, $J = 17.4$, 11.0, 2.6 Hz, 1H), 5.64 (s, 1H), 5.57 (ddd, $J = 17.4$, 1.7, 1.7 Hz, 1H), 5.42 (ddd, $J = 11.0$, 1.8, 1.8 Hz, 1H), 4.93 (d, $J = 8.1$ Hz, 1H), 4.86 (d, $J = 8.1$ Hz, 1H), 4.70 (ddd, $J = 2.3$, 2.3, 2.3 Hz, 1H), 4.49 (d, $J = 6.9$ Hz, 1H), 4.31 (d, $J = 6.9$ Hz, 1H), 4.28 (d, $J = 12.0$ Hz, 1H), 4.24 (s, 1H), 4.19 (s, 1H), 4.15 (d, $J = 12.0$ Hz, 1H), 3.82 (s, 3H), 3.72 (dd, $J = 8.4$, 8.4 Hz, 2H), 3.57 (dd, $J = 11.7$, 2.4 Hz, 1H), 3.25 (s, 3H), 3.01 (qd, $J = 6.8$, 0.6 Hz, 1H), 2.77 (br d, $J = 12.9$ Hz, 1H), 2.47-2.40 (m, 1H), 2.38 (br s, 1H), 2.33-2.29 (m, 1H), 1.98 (dd, $J = 13.8$, 13.8 Hz, 1H), 1.82-1.70 (m, 3H), 1.32 (d, $J = 6.5$ Hz, 3H), 1.05 (s, 3H), 0.96 (dd, $J = 9.7$ Hz, 2H), 0.94 (s, 3H), 0.88 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H), 0.043 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 212.5, 160.0, 132.4, 129.7, 127.4, 116.5, 113.5, 101.4, 94.8, 89.3, 86.6, 82.5, 81.2, 70.8, 69.5, 66.2, 55.9, 55.6, 55.3, 50.4, 47.4, 34.4, 32.6, 32.3, 30.3, 27.8, 25.8, 18.2, 18.1, 16.9, 10.7, -1.42, -3.08, -4.76; HRMS (EI) m/z (M$^+$) calcd for C$_{41}$H$_{70}$O$_{10}$Si$_2$ 778.4508, obsd 778.4506.


The thexylborane was prepared by combining 2,3-dimethylbutene (0.15 mL, 1 M in THF) and borane-tetrahydrofuran (0.15 mL, 1M in THF) at 0°C for 1.5 h. To this solution was added 119b (30 mg, 39 µmol) in THF (0.6 mL), and the resulting mixture was stirred for 30 min at 0°C, treated with aqueous KOH (1.5 mL of a 3M soln) and 30% H$_2$O$_2$ (1.5 mL), warmed to rt for 12 h, and extracted with ether. The combined
organic layers were dried and concentrated, and the residue was purified via flash chromatography (SiO$_2$; 30% ethyl acetate in hexanes) to furnish 120a (12.7 mg, 41%) and the secondary carbinol isomer (6.3 mg, 21%), both as colorless oils.

For 120a: $[\alpha]_D^{21} = +18.1$ (c 1.27, CHCl$_3$); IR (film, cm$^{-1}$) 3464, 2954, 1699, 1616, 1518, 1471, 1383, 1304, 1037, 932, 835, 780, 757; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.37 (d, $J = 8.7$ Hz, 2H), 6.87 (d, $J = 8.7$ Hz, 2H), 5.61 (s, 1H), 4.90 (d, $J = 8.2$ Hz, 1H), 4.83 (d, $J = 8.2$ Hz, 1H), 4.51 (d, $J = 7.0$ Hz, 1H), 4.39 (d, $J = 7.9$ Hz, 1H), 4.36 (d, $J = 7.0$ Hz, 1H), 4.25 (d, $J = 12.0$ Hz, 1H), 4.23 (s, 2H), 4.03 (d, $J = 12.0$ Hz, 1H), 3.90-3.86 (m, 1H), 3.80 (s, 3H), 3.80-3.62 (series of m, 4H), 3.26 (s, 3H), 3.00 (q, $J = 6.7$ Hz, 1H), 2.89 (br d, $J = 12.6$ Hz, 1H), 2.44-2.28 (series of m, 3H), 2.20-1.66 (series of m, 7H), 1.36 (d, $J = 6.7$ Hz, 3H), 1.07 (s, 3H), 0.97 (s, 3H), 0.89 (s, 9H), 0.94-0.85 (m, 2H), 0.17 (s, 3H), 0.14 (s, 3H), 0.035 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 212.1, 160.0, 129.5, 127.3, 113.6, 102.0, 94.7, 88.9, 86.6, 82.3, 80.8, 74.7, 70.9, 70.4, 66.3, 60.3, 55.7, 55.6, 55.3, 50.4, 48.2, 33.7, 32.7, 32.2, 30.3, 28.1, 25.8, 18.12, 18.09, 16.8, 10.8, -1.47, -3.07, -4.78; HRMS (FAB) m/z (M$^+$+H) calcd for C$_{41}$H$_{72}$O$_{11}$Si$_2$ 797.47, obsd 797.48.

(2S,4R,5S)-5-[(1S,2S,4S,5S,7R,8S)-2-(tert-Butyldimethylsiloxy)-1-hydroxy-7-(methoxy methoxy)-5,11,11-trimethyl-6-oxobicyclo[6.2.1]undec-4-yl]-2-(p-methoxyphenyl)-5-[[2-(trimethylsilyl)ethoxy]methoxy]-m-dioxane-4-acetaldehyde (120b).

The Dess-Martin periodinane (9.6 mg, 23 µmol) and 120a (12 mg, 15 µmol) were stirred in CH$_2$Cl$_2$ (1 mL) for 1 h, concentrated to about 0.2 mL, transferred to a flash column, and purified (SiO$_2$, elution with 20% ethyl acetate in hexanes) to give 9.8 mg (82%) 120b and unchanged 120a (2.2 mg, 18%), both as colorless oils.
For 120b: \([\alpha]_D^{21} = +17.7\) (c 0.87, CHCl₃); IR (film, cm⁻¹) 3464, 2930, 1731, 1701, 1616, 1518, 1468, 1390, 1252, 1145, 1098, 836; \(^1\)H NMR (300 MHz, CDCl₃) \(\delta 9.86\) (s, 1H), 7.36 (d, \(J = 8.7\) Hz, 2H), 6.86 (d, \(J = 8.7\) Hz, 2H), 5.68 (s, 1H), 4.81 (s, 2H), 4.81 (d, \(J = 11.7\) Hz, 1H), 4.51 (d, \(J = 7.0\) Hz, 1H), 4.37 (d, \(J = 7.0\) Hz, 1H), 4.33 (d, \(J = 11.8\) Hz, 1H), 4.22 (s, 1H), 4.21 (d, \(J = 8.9\) Hz, 1H), 4.18 (d, \(J = 11.8\) Hz, 1H), 3.80 (s, 3H), 3.68-3.57 (m, 3H), 3.27 (s, 3H), 3.08 (d, \(J = 5.8\) Hz, 2H), 2.94 (q, \(J = 6.4\) Hz, 1H), 2.98-2.88 (m, 1H), 2.40 (d, \(J = 10.9\) Hz, 1H), 2.36-2.22 (m, 2H), 1.95-1.82 (m, 3H), 1.70-1.62 (m, 1H), 1.33 (d, \(J = 6.4\) Hz, 3H), 1.06 (s, 3H), 0.97 (s, 3H), 0.89 (s, 9H), 0.95-0.86 (m, 2H), 0.17 (s, 3H), 0.14 (s, 3H), 0.026 (s, 9H); \(^{13}\)C NMR (75 MHz, CDCl₃) ppm 211.9, 119.2, 160.0, 129.2, 127.2, 113.5, 102.0, 94.8, 89.3, 86.6, 82.3, 77.4, 74.2, 71.1, 70.9, 66.4, 55.7, 55.5, 55.3, 50.4, 48.3, 44.2, 33.4, 33.0, 32.4, 30.2, 28.0, 25.8, 18.1, 16.8, 10.5, -1.46, -3.10, -4.78; HRMS (FAB) m/z (M+H) calcd for C₄₁H₇₁O₁₁Si₂ 795.45, obsd 795.63.

\((1S,2S,3R,4S)-3-(\text{Methoxymethoxy})-1-\text{[}(Z)-2-\text{(p-methoxyphenoxy)vinyl}]-2-\text{[(Z)-2-\text{(2S,4R,5S)-2-(p-methoxyphenyl)-5-\text{[(2-trimethylsilyl)ethoxy)methoxy]-4-vinyl-}m-dioxan-5-yl}vinyl]-7,7\text{-dimethylbicyclo[2.2.1]heptan-2-ol} (125).}

To a cold (-78 °C) solution of iodide 110 (292 mg, 680 \(\mu\)mol) in ether (8 mL) was added \(n\)-butyllithium (0.46 mL of a 1.6 M soln in hexanes, 740 \(\mu\)mol), and the resulting solution was stirred for 2 min prior to the addition of ketone 48a (214 mg, 620 \(\mu\)mol) in ether (2 mL). Following a 30 min period of stirring at low temperature, water was added and the reaction mixture was warmed to rt before being extracted with ether. The combined organic layers were dried and concentrated, and the residue was purified via silica gel chromatography (elution with 15% ethyl acetate in hexanes) to give 125 (294 mg, 65%) as a colorless oil; \([\alpha]_D^{22} = -105\) (c 0.48, CHCl₃); IR (film, cm⁻¹) 3398, 2952, 1661, 1505, 1461, 1390, 1250, 1220, 1149, 1110, 110.
$^{1}$H NMR (300 MHz, C$_6$D$_6$) δ 7.57 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H), 6.80 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 9.0 Hz, 2H), 6.44 (d, J = 6.9 Hz, 1H), 6.31 (ddd, J = 17.3, 10.9, 4.2 Hz, 1H), 6.01 (d, J = 14.0 Hz, 1H), 5.90 (d, J = 14.0 Hz, 1H), 5.63 (ddd, J = 17.3, 1.8, 1.8 Hz, 1H), 5.47 (s, 1H), 5.31 (ddd, J = 10.8, 1.8, 1.8 Hz, 1H), 5.16 (s, 1H), 5.09 (d, J = 6.9 Hz, 1H), 4.83 (d, J = 6.1 Hz, 1H), 4.84-4.80 (m, 1H), 4.80-4.77 (m, 1H), 4.76 (d, J = 10.2 Hz, 1H), 4.69 (d, J = 6.3 Hz, 1H), 4.45 (ddd, J = 4.1, 2.0, 2.0 Hz, 1H), 4.11 (d, J = 10.4 Hz, 1H), 3.74 (s, 1H), 3.74-3.63 (m, 2H), 3.28 (s, 3H), 3.27 (s, 3H), 3.26 (s, 3H), 2.30 (ddd, J = 12.0, 8.8, 6.6 Hz, 1H), 1.96 (s, J = 5.2 Hz, 1H), 1.80 (s, 3H), 1.77-1.64 (m, 1H), 1.05 (s, 3H), 1.03-0.96 (m, 1H), 0.95 (ddd, J = 8.2 Hz, 8.2 Hz, 2H), 0.0073 (s, 9H); $^{13}$C NMR (75 MHz, C$_6$D$_6$) ppm 160.6, 155.7, 152.1, 143.5, 140.1, 134.1, 131.0, 126.9, 117.8, 117.7, 115.0, 113.8, 108.5, 101.7, 100.2, 97.1, 90.3 (2C), 84.5, 81.2, 74.6, 74.0, 66.7, 59.6, 55.3, 55.1, 54.7, 52.0, 50.2, 28.0, 25.3, 23.1, 23.0, 18.2, -1.38; HRMS (FAB) m/z (M$^+$+H) calcd for C$_{41}$H$_{59}$O$_{10}$Si 739.39, obsd 739.49.

Anal. Calcd for C$_{41}$H$_{59}$O$_{10}$Si: C, 66.64; H, 7.91. Found: C, 66.54; H, 7.92.

(1$^S$,3a$^R$,6$^S$,7$^R$,8a$^S$)-1,4,5,6,7,8a-Hexahydro-7-(methoxymethoxy)-1-[(2$^S$,4$^R$,5$^S$)-2-[p-methoxyphenyl]-5-[[2-(trimethylsilyl)ethoxy]methoxy]-4-vinyl-m-dioxan-5-yl]-9,9-dimethyl-8$^H$-3a,6-methanoazulen-8-one (126).
\[ \beta \delta = +60.0 \ (c \ 0.41, \text{CHCl}_3); \ \text{IR} \ (\text{film}, \ \text{cm}^{-1}) \ 2952, 1724, 1615, 1518, 1464, 1391, 1250, 1151, 1101, 835; \ \text{H NMR} \ (300 \ \text{MHz}, \ \text{CDCl}_3) \ 5 \ 7.50 \ (d, \ J = 8.7 \ \text{Hz}, \ 2\text{H}), 6.89 \ (d, \ J = 8.7 \ \text{Hz}, \ 2\text{H}), 6.39 \ (ddd, \ J = 17.1, 10.6, 6.1 \ \text{Hz}, \ 1\text{H}), 6.01 \ (dd, \ J = 6.0, 1.5 \ \text{Hz}, \ 1\text{H}), 5.59 \ (dd, \ J = 6.0, 2.4 \ \text{Hz}, \ 1\text{H}), 5.56 \ (s, \ 1\text{H}), 5.37 \ (ddd, \ J = 17.1, 1.5, 1.5 \ \text{Hz}, \ 1\text{H}), 5.29 \ (ddd, \ J = 10.7, 1.4, 1.4 \ \text{Hz}, \ 1\text{H}), 4.88 \ (d, \ J = 7.9 \ \text{Hz}, \ 1\text{H}), 4.77 \ (d, \ J = 7.9 \ \text{Hz}, \ 1\text{H}), 4.43 \ (d, \ J = 7.0 \ \text{Hz}, \ 1\text{H}), 4.41 \ (d, \ J = 6.6 \ \text{Hz}, \ 1\text{H}), 4.26 \ (d, \ J = 9.1 \ \text{Hz}, \ 1\text{H}), 4.23 \ (d, \ J = 11.4 \ \text{Hz}, \ 1\text{H}), 4.11 \ (d, \ J = 6.6 \ \text{Hz}, \ 1\text{H}), 4.07 \ (d, \ J = 11.4 \ \text{Hz}, \ 1\text{H}), 3.80 \ (s, \ 3\text{H}), 3.71-3.60 \ (\text{series of m}, \ 4\text{H}), 3.25 \ (s, \ 3\text{H}), 2.09 \ (dd, \ J = 6.6, 3.7 \ \text{Hz}, \ 1\text{H}), 1.87-1.74 \ (m, \ 1\text{H}), 1.46-1.43 \ (m, \ 1\text{H}), 1.43 \ (s, \ 3\text{H}), 1.08 \ (dd, \ J = 13.6, 6.9 \ \text{Hz}, \ 1\text{H}), 1.05 \ (s, \ 3\text{H}), 0.94 \ (dd, \ J = 8.4 \ \text{Hz}, \ 2\text{H}), 0.94-0.86 \ (m, \ 1\text{H}), 0.029 \ (s, \ 9\text{H}); \ 1^3\text{C NMR} \ (75 \ \text{MHz}, \ \text{C}_6\text{D}_6) \ 207.6, 159.8, 134.1, 132.0, 130.5, 127.7, 117.7, 113.5, 101.6, 95.6, 89.7, 87.4, 84.1, 73.34, 73.27, 65.5, 64.6, 55.5, 55.3, 55.1, 52.4, 46.2, 44.2, 28.8, 24.9, 23.0, 21.2, 18.2, -1.38; \ \text{HRMS} \ (\text{El}) \ m/z (M^+) \ \text{calcd for } C_{34}H_{50}O_8Si \ 614.3275, \ \text{obsd} \ 614.3256.

\text{Anal. Calcd for } C_{34}H_{50}O_8Si: \ C, 66.42; \ H, 8.20. \ \text{Found: } C, 66.50; \ H, 8.23.

(1S,2R,5R,6R,7E)-2-(\text{Methoxymethoxy})-6-(\text{p-methoxyphenoxy})-5-[[2S,4R,5S]-2-(\text{p-methoxyphenyl})-5-[[2-(\text{trimethylsilyl})ethoxy]methoxy]-4-vinyl-\text{m-dioxan-5-yl}]-11,11-\text{dimethylbicyclo[6.2.1]undec-7-en-3-one} \ (127).

A solution of 125 (137 mg, 185 \mu\text{mol}) and 18-crown-6 (147 mg, 560 \mu\text{mol}) in dry tetrahydrofuran (8 mL) was deoxygenated (Ar), chilled (0 \degree\text{C}) prior to the addition of potassium hexamethyldisilazide (1.11 mL of a 0.5 M in toluene), stirred for 20 min, quenched with water, and extracted with ether. After the ethereal layers were dried and concentrated, a residue was obtained and subjected to silica gel chromatography (elution with 10% ethyl acetate in hexanes) to furnish 127 (126 mg, 92%) as a colorless oil; \[ \beta \delta = -20.6 \ (c}
0.50, CHCl₃); IR (film, cm⁻¹) 2954, 1694, 1615, 1506, 1464, 1389, 1228, 1148, 1105, 1040; 

^{1}H NMR (300 MHz, C₆D₆) δ 7.50 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 9.1 Hz, 2H), 6.78 (d, J = 8.7 Hz, 2H), 6.72 (d, J = 9.1 Hz, 2H), 6.52 (ddd, J = 17.2, 10.9, 4.6 Hz, 1H), 5.64 (ddd, J = 17.2, 1.8, 1.8 Hz, 1H), 5.50 (br s, 1H), 5.45 (s, 1H), 5.38 (br s, 1H), 5.28 (ddd, J = 10.9, 1.8, 1.8 Hz, 1H), 5.01 (d, J = 8.0 Hz, 1H), 4.63 (d, J = 8.0 Hz, 1H), 4.61 (br s, 1H), 4.50 (d, J = 11.9 Hz, 1H), 4.35 (d, J = 6.4 Hz, 1H), 4.29 (d, J = 6.4 Hz, 1H), 4.21 (br d, J = 11.9 Hz, 1H), 4.03 (d, J = 11.9 Hz, 1H), 3.97 (d, J = 5.5 Hz, 1H), 3.70 (dd, J = 15.8, 12.7 Hz, 1H), 3.68 (ddd, J = 9.5, 8.1, 8.1 Hz, 1H), 3.42 (ddd, J = 9.5, 8.1, 8.1 Hz, 1H), 3.30 (s, 3H), 3.28 (s, 3H), 3.01 (s, 3H), 2.87 (dd, J = 15.8, 1.7 Hz, 1H), 1.94 (ddd, J = 11.8, 8.6, 1.9 Hz, 1H), 1.88 (dd, J = 6.0, 6.0 Hz, 1H), 1.78 (br d, J = 12.9 Hz, 1H), 1.66-1.57 (m, 1H), 1.55 (s, 3H), 1.35-1.30 (m, 1H), 0.87 (dd, J = 9.1, 9.1 Hz, 2H), 0.87 (s, 3H), -0.038 (s, 9H); 

^{13}C NMR (75 MHz, C₆D₆) ppm 209.1, 160.5, 154.1, 152.8, 147.8, 133.5, 131.0, 128.1, 123.5, 117.5, 116.2, 114.8, 113.8, 101.6, 96.5, 89.6, 89.0, 83.0, 75.5, 73.7, 73.0, 65.8, 55.6, 55.1, 54.8, 54.2, 49.6, 46.7, 40.0, 26.8, 25.3, 24.2, 22.8, 18.3, -1.34; HRMS (EI) m/z (M⁺) calcd for 

C₄₁H₅₈O₁₀Si 738.3799, obsd 738.3806.


Thexylborane was prepared by combining 2,3-dimethylbutene (87 µL, 1 M in THF) and borane-tetrahydrofuran (87 µL, 1M in THF) at 0 °C for 1.5 h. To this solution was added 127 (16 mg, 22 µmol) in THF (0.8 mL), and the resulting mixture was stirred for 45 min at 0°C, treated with aqueous KOH (0.29 mL of a 3M soln) and 30%
$\text{H}_2\text{O}_2$ (0.29 mL), warmed to rt for 3 h, and extracted with ether. The combined organic layers were
dried and concentrated, and the residue was purified via flash chromatography ($\text{SiO}_2$, 30% ethyl
acetate in hexanes) to furnish 128 (9.6 mg, 59%) and its secondary isomer (4.2 mg, 26%), both
as colorless oils.

For 128: $[\alpha]_D^{21} = -26.9$ (c 0.96, CHCl$_3$); IR (film, cm$^{-1}$) 3421, 2952, 1695, 1616, 1506,
1461, 1390, 1250, 1230, 1144, 1104, 1040, 1033, 828, 759; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.33
(d, $J = 8.7$ Hz, 2H), 6.84 (d, $J = 8.7$ Hz, 2H), 6.82 (d, $J = 9.3$ Hz, 2H), 6.75 (d, $J = 9.3$ Hz, 2H), 5.52
(s, 1H), 5.32 (d, $J = 4.1$ Hz, 1H), 5.06 (d, $J = 8.5$ Hz, 1H), 4.91 (dd, $J = 4.1, 4.1$ Hz, 1H), 4.57 (d, $J =
6.4$ Hz, 1H), 4.52 (d, $J = 8.5$ Hz, 1H), 4.47 (d, $J = 6.4$ Hz, 1H), 4.33 (d, $J = 9.7$ Hz, 1H), 4.27 (d, $J =
12.1$ Hz, 1H), 3.95 (d, $J = 5.7$ Hz, 1H), 3.88 (dd, $J = 12.1, 1.6$ Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H),
3.80-3.64 (m, 4H), 3.49-3.39 (m, 2H), 3.22 (s, 3H), 2.67 (d, $J = 15.2$ Hz, 1H), 2.57-2.48 (m, 1H),
2.26 (ddd, $J = 13.9, 9.0, 5.1$ Hz, 1H), 2.24-2.18 (m, 1H), 2.10 (dd, $J = 5.9, 5.9$ Hz, 1H), 2.07-1.96
(m, 1H), 1.84-1.67 (series of m, 3H), 1.46 (s, 3H), 0.98 (s, 3H), 0.89 (dd, $J = 9.8, 8.6$ Hz, 2H),
-0.019 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 210.6, 160.1, 153.4, 152.2, 148.2, 130.1, 127.5,
122.7, 115.8, 114.2, 113.6, 101.5, 95.9, 89.3, 88.0, 81.2, 75.0, 72.3, 72.2, 66.0, 60.3, 55.7,
55.6, 55.3, 53.6, 47.8, 46.4, 39.9, 32.1, 26.7, 24.9, 23.8, 22.2, 18.1, -1.48; HRMS (FAB) $m/z$
(M$^+$+H) calcd for C$_{41}$H$_{61}$O$_{11}$Si 757.40, obsd 757.56.
Osmium tetroxide (2.4 mg, µmol) was added to a solution of 128 (6.4 mg, 8.5 µmol) in cold (-30 °C) pyridine and stirred at that temperature for 1 h, warmed to rt for 3 h, treated with 20% Na₂S₂O₄ solution, and agitated for 12 h. The resulting light green solution was diluted with water and extracted with ether. The combined organic phases were dried and concentrated to retrieve an oily residue that was chromatographed on silica gel (elution with 60% ethyl acetate in hexanes) to furnish 5.8 mg (87%) of 130 as a colorless oil; [α]_D^20 = -18.8 (c 0.43, CHCl₃); IR (film, cm⁻¹) 3451, 2952, 1616, 1506, 1463, 1400, 1250, 1227, 1100, 1034; ¹H NMR (300 MHz, CDCl₃) δ 7.42 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 9.1 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 9.1 Hz, 2H), 5.53 (s, 1H), 5.05 (dd, J = 9.9, 3.0 Hz, 1H), 4.69 (d, J = 8.7 Hz, 1H), 4.65 (d, J = 6.7 Hz, 1H), 4.60 (d, J = 6.7 Hz, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.45 (d, J = 8.7 Hz, 1H), 4.23 (d, J = 9.5 Hz, 1H), 4.13 (d, J = 3.0 Hz, 1H), 3.97 (d, J = 12.0 Hz, 1H), 3.80 (s, 3H), 3.79-3.77 (m, 3H), 3.75 (s, 3H), 3.60-3.44 (m, 2H), 3.29 (s, 3H), 3.13 (dd, J = 15.7, 15.7 Hz, 1H), 2.97-2.87 (m, 2H), 2.49 (dd, J = 15.7, 4.0 Hz, 1H), 2.36 (br s, 1H), 2.24-2.19 (m, 1H), 2.13-1.99 (series of m, 3H), 1.86-1.77 (m, 2H), 1.70-1.61 (m, 1H), 1.40 (s, 3H), 1.04 (s, 3H), 1.02 (s, 1H), 0.87 (dd, J = 8.7, 8.7 Hz, 2H), -0.0041 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) ppm 160.1, 154.0, 150.8, 130.2, 127.8, 117.8, 114.7, 113.6, 102.0, 100.1, 96.3, 91.3, 89.8, 89.0, 83.0, 82.3, 74.2, 72.2, 71.2, 65.8, 60.8, 55.61, 55.55, 55.3, 50.0, 46.4, 38.6, 36.7, 32.7, 31.4, 29.8, 26.0, 21.6, 18.1, -1.46; HRMS (FAB) m/z (M+H) calcd for C₄₁H₆₃O₁₃Si 790.40, obsd 790.52.
Lithium aluminum hydride (7.3 mg, 192 µmol) was added in two portions to a chilled (0 °C) solution of 127 (88 mg, 120 µmol) in dry ether (2 mL), and the resulting suspension was agitated for 1 h at 0 °C and 15 min at rt prior to the addition of saturated Rochelle’s salt solution. The biphasic mixture was extracted with ether, the combined organic layers were dried and concentrated, and the residue was chromatographed (SiO2, elution with 20% ethyl acetate in hexanes) to furnish 131 (69.2 mg, 79%) as a colorless oil; 

$\alpha$\textsubscript{D} = -23.2 (c 1.25, CHCl₃); IR (film, cm\textsuperscript{-1}) 3554, 2953, 1615, 1506, 1389, 1250, 1232, 1149, 1091, 1032; \textsuperscript{1}H NMR (300 MHz, CDCl₃) δ 7.44 (d, \textit{J} = 6.7 Hz, 2H), 6.88 (d, \textit{J} = 8.7 Hz, 2H), 6.75 (s, 4H), 5.98 (ddd, \textit{J} = 17.0, 10.6, 6.1 Hz, 1H), 5.72 (d, \textit{J} = 11.4 Hz, 1H), 5.56 (s, 1H), 5.31-5.22 (m, 3H), 4.95 (d, \textit{J} = 7.7 Hz, 1H), 4.90 (d, \textit{J} = 7.7 Hz, 1H), 4.88 (d, \textit{J} = 10.7 Hz, 1H), 4.73 (d, \textit{J} = 6.6 Hz, 1H), 4.65 (d, \textit{J} = 6.6 Hz, 1H), 4.54 (d, \textit{J} = 6.1 Hz, 1H), 4.33 (br d, \textit{J} = 9.3 Hz, 1H), 4.05 (d, \textit{J} = 11.4 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.78-3.65 (m, 3H), 3.40 (s, 3H), 3.26 (dd, \textit{J} = 9.4, 1.4 Hz, 1H), 3.21 (d, \textit{J} = 3.6 Hz, 1H), 3.14-3.05 (m, 2H), 2.15-1.86 (series of m, 3H), 1.61 (s, 1H), 1.47-1.40 (m, 1H), 1.27 (s, 3H), 1.06-0.97 (m, 2H), 0.95 (s, 3H), 0.061 (s, 9H); \textsuperscript{13}C NMR (75 MHz, CDCl₃) ppm 160.0, 153.0, 151.4, 149.0, 133.3, 130.7, 127.7, 118.5, 116.7, 115.7, 114.0, 113.4, 101.5, 97.3, 91.2, 89.4, 83.6, 76.9, 76.0, 71.4, 70.3, 65.8, 56.0, 55.6, 55.3, 49.5, 46.7, 45.1, 29.8, 27.2, 25.3, 24.9, 21.6, 18.3, -1.40; HRMS (FAB) m/z (M+H) calcd for C₄₁H₆₁O₁₀Si 741.40, obsd 741.61.

Thehexylborane was prepared by combining 2,3-dimethylbutene (220 µL, 1 M in THF) and borane-tetrahydrofuran (220 µL, 1 M in THF) at 0 °C for 2 h. To this solution was added 131 (32 mg, 43 µmol) in THF (1 mL), and the resulting mixture was stirred for 45 min at 0 °C, treated with aqueous KOH (0.73 mL of a 3 M soln) and 30% H₂O₂ (0.73 mL), and warmed to rt for 1 h. The mixture was extracted with ether, the combined organic layers were dried and concentrated, and the residue was purified via flash chromatography (SiO₂, 30% ethyl acetate in hexanes) to furnish 132 (15.7 mg, 48%) as a colorless oil; [α]D²² = -40.6 (c 1.56, CHCl₃); IR (film, cm⁻¹) 3505, 2936, 1616, 1558, 1506, 1456, 1398, 1303, 1250, 1213, 1070, 830; ¹H NMR (300 MHz, CDCl₃) δ 7.40 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.79 (d, J = 9.4 Hz, 2H), 6.75 (d, J = 9.4 Hz, 2H), 5.75 (d, J = 11.3 Hz, 1H), 5.56 (s, 1H), 5.24 (d, J = 4.7 Hz, 1H), 5.21 (d, J = 4.7 Hz, 1H), 4.93 (d, J = 7.7 Hz, 1H), 4.80 (d, J = 7.7 Hz, 1H), 4.73 (d, J = 6.5 Hz, 1H), 4.65 (d, J = 6.5 Hz, 1H), 4.30 (br d, J = 10.2 Hz, 1H), 4.27 (br d, J = 10.5 Hz, 1H), 3.97 (d, J = 11.4 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H), 3.77-3.61 (series of m, 1H), 3.40 (s, 3H), 3.26 (dd, J = 13.9, 1.2 Hz, 1H), 3.24 (s, 3H), 3.62 (s, 1H), 3.09-3.07 (m, 1H), 2.16-1.91 (series of m, 5H), 1.78-1.70 (m, 1H), 1.45-1.35 (m, 1H), 1.28 (s, 3H), 1.03-0.98 (m, 2H), 0.96 (s, 3H), 0.061 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) ppm 160.0, 153.2, 151.4, 149.3, 130.5, 127.5, 118.3, 115.8, 114.2, 113.5, 101.8, 97.3, 91.3, 89.3, 82.8, 75.7, 71.7, 70.5, 65.8, 61.3, 56.0, 55.6, 55.3, 49.5, 47.0, 45.1, 31.6, 30.1, 27.2, 25.3, 25.0, 21.6, 18.2, -1.42; HRMS (FAB) m/z (M⁺+H) calcd for C₄₁H₆₃O₁₁Si 759.41, obsd 759.53.
From 132. A cold (-30 °C) solution of 132 (15 mg, 20 μmol) in pyridine (0.5 mL) was stirred with osmium tetraoxide (6.0 mg, 24 μmol) for 30 min and warmed to rt for 30 min prior to treatment with 20% Na₂S₂O₄ solution. The murky mixture was extracted with ethyl acetate, the combined organic layers were dried and freed of solvent, and the residue was subjected to flash chromatography (silica gel, elution with 60% ethyl acetate in hexanes) to provide 133 (12.2 mg, 78%) as a colorless oil.

From 128. Ketone 128 (8.4 mg, 11 μmol) and osmium tetraoxide (3.4 mg, 13 μmol) were stirred in cold (-30 °C) pyridine (0.3 mL) for 30 min and at rt for an additional 30 min. The solvent was removed under vacuum (0.2 torr), the residue was taken up in dry tetrahydrofuran (1 mL), and lithium aluminum hydride (4.2 mg, 110 μmol) was added. The resulting mixture was stirred at rt for 24 h, quenched with saturated Rochelle’s salt solution, and extracted with ethyl acetate. Drying and concentration of the organic extracts provided a residue that was subjected to silica gel chromatography (60% ethyl acetate in hexanes) to furnish 3.6 mg (41 %) of 133 as a colorless oil; [α]D²¹ = -54.7 (c 1.18, CHCl₃); IR (film, cm⁻¹) 3402, 2958, 1615, 1506, 1484, 1250, 1215, 1114, 1035, 835; ¹H NMR (300 MHz, CDCl₃) δ 7.42 (d, J = 8.7 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 6.89 (d, J = 6.7 Hz, 2H), 6.81 (d, J = 9.0 Hz, 2H), 5.60 (s, 1H), 5.20 (d, J = 8.1 Hz, 1H), 5.08-5.01 (m, 1H), 4.90 (d, J = 8.1 Hz, 1H), 4.78 (d, J = 6.6 Hz, 1H), 4.73 (d, J = 6.6 Hz, 1H), 4.34-4.26 (m, 4H), 3.94-3.82 (m, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.72-3.61 (m, 1H), 3.45 (s, 3H), 3.28 (br s, 2H), 3.24-3.13 (m, 1H), 3.10 (br s, 1H), 2.46-2.09 (series of m, 7H), 1.94-1.82 (m, 2H), 1.36-1.30
(m, 1H), 1.13 (s, 3H), 1.05 (s, 3H), 1.03-0.44 (m, 2H), 0.039 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) ppm 160.1, 151.0, 129.9, 127.9, 127.8, 120.2, 114.9, 113.8, 101.7, 97.5, 91.5, 89.8, 86.5, 81.5, 80.1, 75.7, 75.2, 71.6, 69.2, 66.7, 60.9, 56.2, 55.6, 55.3, 52.0, 45.8, 36.9, 33.9, 33.1, 30.5, 23.3, 19.1, 18.1 (2C), -1.40; HRMS (FAB) $m/z$ (M$^+$+H) calcd for C$_{41}$H$_{85}$O$_3$Si 793.42, obsd 793.70.
LIST OF REFERENCES

1 Thirteen people became ill, three of whom died.


7 Several members of the penicillin class have yielded to total synthesis; for lead references: Corey, E. J., Cheng, X.-M. *The Logic of Chemical Synthesis* Wiley: New York; 1989, p. 387. The chemistry developed in these undertakings is undoubtedly responsible for their thorough biological evaluation.

8 A total synthesis of amphotericin B was recently reported by Nicolaou and coworkers: *J. Am. Chem. Soc.* 1988, 110, 4660, 4672, 4685, 4696.


31 Pissamitski, D., unpublished results.


34 Bristol-Meyers Squibb has since retained the designation "Taxol" as a trade name, thereby relegating the designation "paclitaxel" as the generic name for the natural product.


44 Dr. T.-Z. Wang, unpublished results.


47 The following IUPAC numbering system is used in the ensuing discussion:

![IUPAC numbering system diagram]

We thank Dr. Kurt Loening for this information.


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52 Two molecular ions corresponding to $^{35}\text{Cl}$- and $^{37}\text{Cl}$-containing M$^+$$\text{H}$ were observed as expected.


58 We are deeply indebted to Dr. Dirk Friedrich (Hoechst-Marion-Roussel) for this structural elucidation.

59 Q. Zeng, unpublished results.


Appendix A

$^1$H NMR Spectra
T = 303K
\[ \text{Structure Image} \]