Stereochemical Models for the Enantiocontrolled Construction of Fully Functionalized C Rings via Intramolecular Aldolization in Advanced Precursors to Paclitaxel

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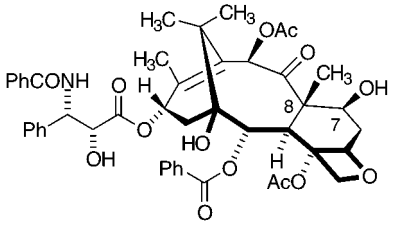
Six transition-state models for intramolecular aldol C-ring annulation in suitably substituted bicyclo-[6.2.1]undecanones have been defined. The first consideration is the inherent conformational flexibility of the nine-membered ketonic ring which does not limit effective deprotonation to a single C-8 epimer. When the oxygen substituents at C-4 and C-5 are not covalently linked, the configuration at C-5 defines the stereochemical course of the ring closure, with only the β series being amenable to the proper elaboration of paclitaxel. When C-4 and C-5 are incorporated into a 1,3-dioxane ring instead, the principal stereocontrol element is translocated into the aryl-substituted carbon of the cyclic acetal. To the extent that the Ar group remains equatorially disposed, then proper aldolization will materialize in only one of the four possible diastereomers. Experimental tests that are provided for three of the models are shown to conform to expectations. This analysis of the origin of stereoselectivity has, for the first time, defined the scope and limitations associated with C-ring closure by means of the aldol protocol.

Of the five successfully completed total syntheses of paclitaxel (**1**),[1−5] two rely on an intramolecular aldol reaction to construct ring C and establish proper configuration at C-7 and C-8 (Scheme 1).[4,5a] The two research groups involved have recently addressed in explicit terms the fact that the transformation of **2** into **3** as well as of **4** into **5** requires that the methyl substituent positioned at the enolizable center be β-oriented.[4−6] Only when this condition is met is proper orbital overlap for proton abstraction realized. In contrast, **6** is inert to aldol closure and even to base-catalyzed H/D exchange because the relevant proton is rigidly positioned orthogonal to the carbonyl π-bond.



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Our group has also approached the paclitaxel problem by taking advantage of a comparable aldol ring closure. The major distinction is that this process is initiated by us within appropriately functionalized bicyclo[6.2.1]-undecanones prior to bridge migration via α-ketol rearrangement. The conversion of **7** to **8**, and subsequently via **9** to **10**, is illustrative of the tactic (Scheme 2).[7] We were guided in this venture by early knowledge of the fact that bicyclic ketones such as **7** and higher tricyclic congeners thereof are more conformationally flexible than **2** and **4**.[8] Although atropisomerization has been observed

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(4) (a) Wender, P. A.; Badham, N. F.; Conway, S. P.; Floreancig, P. E.; Glass, T. E.; Gränicher, C.; Houze, J. B.; Jänichen, J.; Lee, D.; Marquess, D. G.; McGrane, P. L.; Meng, W.; Mucciaro, T. P.; Mühlebach, M.; Natchus, M. G.; Paulsen, H.; Rawlins, D. B.; Satkofsky, J.; Shuker, A. J.; Sutton, J. C.; Taylor, R. E.; Tomooka, K. *J. Am. Chem. Soc.* **1997**, *119*, 2755. (b) Wender, P. A.; Badham, N. F.; Conway, S. P.; Floreancig, P. E.; Glass, T. E.; Houze, J. B.; Krauss, N. E.; Lee, D.; Marquess, D. G.; McGrane, P. L.; Meng, W.; Natchus, M. G.; Shuker, A. J.; Sutton, J. C.; Taylor, R. E. *J. Am. Chem. Soc.* **1997**, *119*, 2757.

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(6) For an earlier discussion of the preferred ground-state conformation of trans-fused B/C taxoids, see: (a) Swindell, C. S.; de Solms, S. J. *Tetrahedron Lett.* **1987**, *28*, 3801. (b) Wender, P. A.; Ihle, N. C. *Tetrahedron Lett.* **1987**, *28*, 2451.

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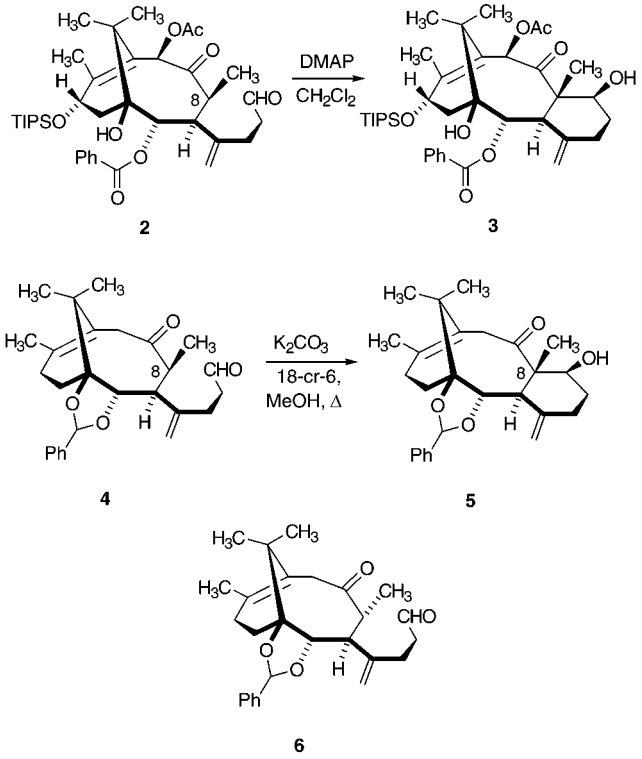
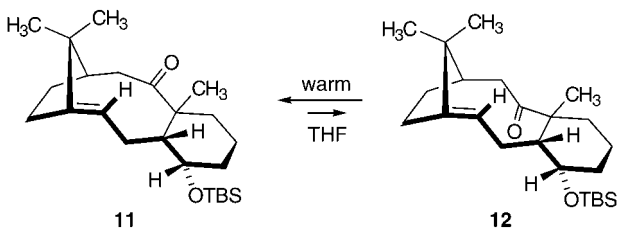
Scheme 1



in systems exemplified by **11** and **12**, warming in THF is adequate to achieve conformational interconversion in most cases. The significance of this heightened flexibility gains importance when deprotonation of ketones such as **7** is being considered. As a direct consequence of the molecular motion attainable within **7** and analogues thereof, no difficulty arises in the transient population of conformers conducive to proper overlap of the C-8 proton for enolate generation. These considerations hold importance because they allow attention to be redirected to other central stereochemical factors associated with the intramolecular aldol process. These issues gain particular significance when the confluence of functionality present in the side chain reaches the heightened level found in **7**. Thus, successful aldol ring closure will materialize only if the enolate anion adds to the aldehyde carbonyl at a rate faster than unwanted β-elimination of *p*-methoxybenzyl alcohol. Additionally, the nucleophilic C-8 center must be conjoined to the C-7 electrophilic site from the appropriate π-surface at each terminus. Such an event must not be forced to operate against prevailing low-energy conformational preferences that would dictate otherwise. The minimization of these risk factors is directly relevant to the success of this protocol. In this paper, we document the issues considered to be critical to the successful deployment of the aldol process in paclitaxel C-ring construction when beginning with **7** and related structural congeners.



Conformational Analysis

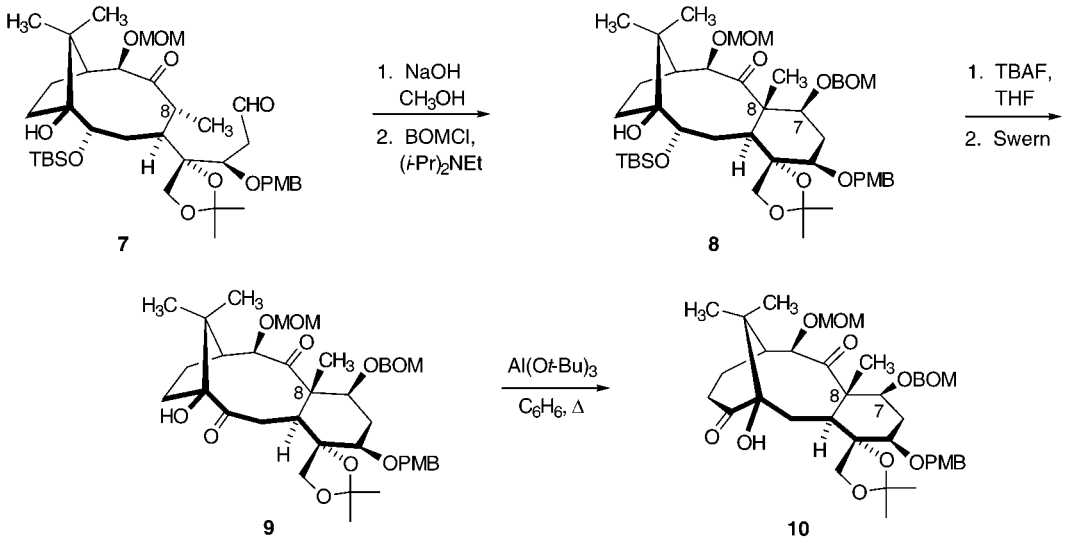
Construction of the oxetane ring in paclitaxel can ultimately be approached from two directions. If OR^3 is designed to serve as the nucleofugal substituent, this functionality must originally reside on the α-surface in order to allow for anticipated configurational inversion during the S_N2 displacement step. The stereochemical arrangement defined by this precondition is found in structural formula $\mathbf{A_1}$ in Figure 1. If, on the other hand, OR^2 is predetermined to be the leaving group, OR^3 must already be predisposed β as in $\mathbf{B_1}$. For simplification purposes, OR^2 and OR^3 are initially considered to be structurally independent of each other. The low-energy conformations anticipated to be operational during intramolecular aldol cyclization within each of these diastereomers are depicted as $\mathbf{A_2}$ and $\mathbf{B_2}$, respectively. In these illustrations, the major controller of conformational bias is the equatorial orientation of two of the three groups at C-4 and C-5. Although enolate geometry is comparable in both series, the nine-membered nature of the B ring is, as previously indicated, sufficiently flexible to accommodate the adoption of conformers $\mathbf{A_2}$ and $\mathbf{B_2}$.[9] As a consequence, the precise relationship imposed between the enolate double bond and the aldehyde functionality becomes paramount. Thus, the ring closure of $\mathbf{A_2}$ to $\mathbf{A_3}$ necessarily orients the C-7 hydroxyl and C-8 methyl groups α while projecting the C-9 carbonyl in a downward direction. On the other hand, the electrophilic aldehyde center in $\mathbf{B_2}$ is constrained to approaching the opposite face of the enolate. Under these circumstances, C−C bond formation proceeds with proper installation of the stereocenters at C-7 and C-8, along with upward orientation of the C-9 keto group (see $\mathbf{B_3}$ and $\mathbf{B_4}$). A 1,3-diaxial interaction is noted to develop along the **A** reaction trajectory. *On the basis of this analysis, we conclude that the stereochemical disposition of the oxygenated substituents at C-4 and C-5 as in* $\mathbf{B_1}$ *is a very important consideration for aldolization favorable to the acquisition of paclitaxel*. The successful conversion of **7** to **8** exemplifies the anticipated diastereoselectivity. Other examples in support of this analysis are provided below.

We next consider the option of achieving hydroxyl protection by conversion to a benzylidene acetal (see section B of Figure 1). With the introduction of a new stereocenter (labeled with an asterisk (*)), it becomes additionally necessary to specify the configuration of the Ar substituent. Our evaluation of the stereochemically induced interrelationship of C-5 and C* on conformation has once again led us to the conclusion that aldol-related matters should be manageable. Two conditions are considered to be fundamental and intrinsic to the 1,3-dioxane subunit. The first is the expectation that steric interactions will be minimized upon adoption of a chair geometry. Additionally, equatorial projection of the Ar substituent should be favored. Therefore, structures $\mathbf{C_2}$−$\mathbf{F_2}$ presumably experience the lowest level of conformational destabilization in the four possible diastereomers.

These restrictions support the proposition that conformers $\mathbf{C_2}$ and $\mathbf{D_2}$ should experience complementary interactions that are expected to favor bonding of the

(9) For the dynamic behavior of diastereomeric *trans*-$\Delta^{9,10}$-tricyclo-[9.3.1.$0^{3,8}$]pentadecenes, consult ref 8c and the following: Paquette, L. A.; Zhao, M. *J. Am. Chem. Soc.* **1998**, *120*, 5953.

Scheme 2



aldehyde to the *si* face of the enolate anion, resulting in incorrect installation of C-7 and C-8 stereochemistry. Thus, matching of the configuration at C-5 and C* in either the α sense (see $\mathbf{C_1}$) or in a dual β direction (as in $\mathbf{D_1}$) has the untoward consequence of constraining the aldol process to unwanted stereoinduction pathways. Likewise, the arrangement of the key substituents as in $\mathbf{F_1}$ is clearly not in a reinforcing relationship and is unquestionably unattractive on that basis. In contrast, the anti relationship present in $\mathbf{E_1}$ contributes simultaneously to a selectivity for bonding to the *re* face of the enolate (see $\mathbf{E_2}$), this diastereomeric relationship contributing to the preferential formation of $\mathbf{E_4}$. By inspection, therefore, it is evident that any deployment of an acetal protecting group for the hydroxyls resident at C-4 and C-5 must accord due consideration to a number of configurational and conformational factors.

Support for the Conformational Models

On the basis of the preceding analysis, the stereochemical features associated with $\mathbf{B_1}$ are seen to be particularly conducive to intramolecular aldolization with the proper facial selectivity when R_2 and R_3 are not part of a dioxane ring. This working hypothesis has been substantiated on the basis of three case studies. Previous disclosure has been made of the stereoselective cyclization of **7** to **8** in 85% yield,[7] and of the unidirectional conversion of **13** into **14** (Scheme 3).[10] The third example is represented by the transformation of **27** into **29**. Arrival at **27** requires that access first be gained to the *Z* vinyl iodide **21**. To this end, the known diol **15**[7] was chemoselectively protected in turn at its primary (as in **16**) and secondary hydroxyl groups to give **17** (Scheme 4). Heating **17** in ethanol containing pyridinium *p*-toluenesulfonate resulted in near-quantitative conversion to **18**, thereby making possible the formation of primary iodide **19** in conventional fashion.[11] The production of **19** as an anomeric mixture is of no long-range consequence since its ensuing reductive cleavage with zinc in refluxing methanol[12] gives rise to aldehyde **20** with destruction of this stereogenic center. The stringent requirement that the homologation of **20** to **21** proceed with *Z* stereoselectivity in order to guarantee the orientation of this side chain later in **24** was ideally met by Wittig condensation with (iodomethylene)triphenylphosphorane.[13] In agreement with this assignment, the coupling constant observed for the vinylic protons located in the iodoethylene moiety of **21** is 8.9 Hz.

The vinyl anion corresponding to **21** could be generated by treatment with *n*-butyllithium in ether at −78 °C and added to norbornanone **22**.[8d] As is customary for these systems, the presence of an apical syn methyl group directs nucleophilic attack to the endo surface. This more sterically congested reaction trajectory is reflected in the observation that the desired 1,2-addition proceeded at a reasonable rate only when room temperature conditions were approached. Notwithstanding, the yield of **23** was excellent (Scheme 5). Exposure of **23** to potassium hexamethyldisilazide and 18-crown-6 in THF *at low temperatures* (−78 °C → −60 °C) promoted anionic oxy-Cope rearrangement[14] via an endo-chair transition state.[8a] This process occurs readily to generate an enolate anion regiospecifically. The presence of the crown ether sequesters the potassium ion, thereby significantly enhancing the reactivity of the enolate intermediate to the point where C-alkylation with methyl iodide takes place rapidly at −78 °C. Under these conditions, ketone **24** is formed uniquely in 80% overall isolated yield. Detailed NOE studies performed on this product revealed the absence of interactions involving the newly introduced CH_3 group and the vinylic proton of the bridgehead,[15] thereby requiring an α-orientation for this substituent.

The low-temperature conditions utilized for the production of **24** were expected to favor delivery of the carbonyl-up atropisomer as shown. Proper documenta-

(10) Paquette, L. A.; Bailey, S. *J. Org. Chem.* **1995**, *60*, 7849.
(11) (a) Garegg, P. J.; Samulesson, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866. (b) Corbett, D. F.; Dean, D. K.; Robinson, S. R. *Tetrahedron Lett.* **1993**, *34*, 1525.
(12) (a) Gallos, J. K.; Goga, E. G.; Koumbis, A. E. *J. Chem. Soc., Perkin Trans. 1* **1994**, 613. (b) Gallos, J. K.; Koftis, T. V.; Koumbis, A. E. *J. Chem. Soc., Perkin Trans. 1* **1994**, 611.
(13) Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 2173.
(14) (a) Paquette, L. A. *Tetrahedron* **1997**, *53*, 13971. (b) Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 609.
(15) The proximity of the bridgehead vinylic proton to the syn apical methyl group was clearly evidenced by a strong mutual signal enhancement at the 5.9% level.

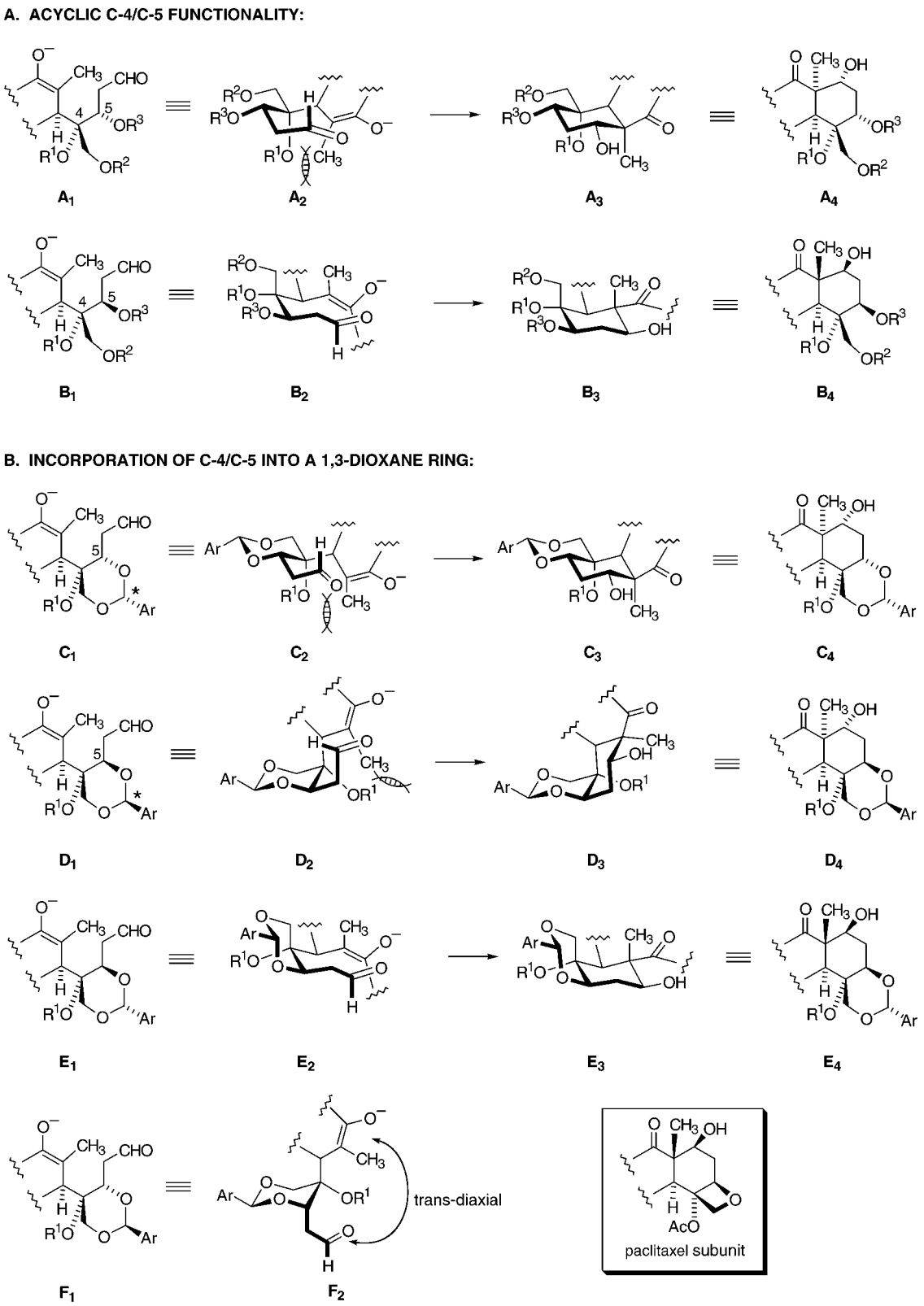
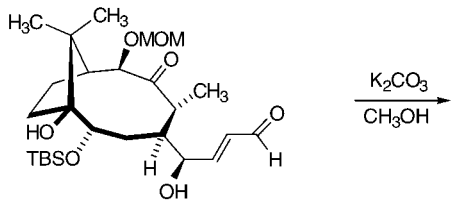
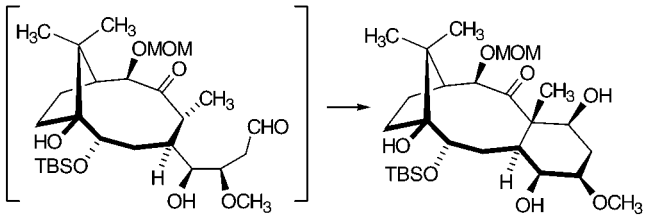


Figure 1. Putative low-energy conformations associated with intramolecular aldol cyclization of stereochemically varied C-ring precursors to paclitaxel.

tion of this conclusion comes from two directions. First, regioselective dihydroxylation of **24** followed by silylation of the resulting secondary OH functionality gave rise to **25** without any evidence for transannular hemiketalization. This reluctance to undergo intramolecular bonding across the nine-membered ring is generally encountered when the carbonyl is oriented up because of the reduced flexibility of this conformer.[7,8] More revealing yet was the discovery that the charge-accelerated [3,3] sigmatropic rearrangement of **23** *at 0 °C* followed by low-temperature methylation furnished only the carbonyl-down ketone **31** (Scheme 6). To define the direction of

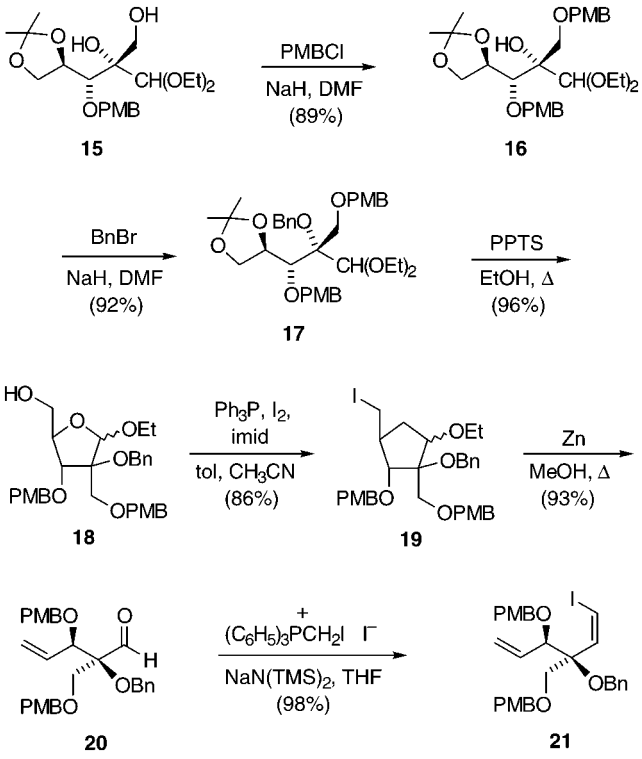
Scheme 3





13 **14**

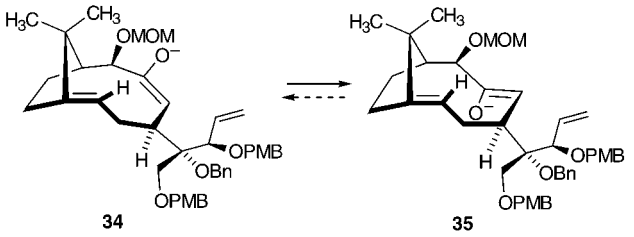
Scheme 4



15 **16** **17** **18** **19** **20** **21**

entry of the methyl group, **31** was reduced with lithium aluminum hydride and the α-alcohol was protected as the SEM ether. These chemical transformations positioned H-8 in a unique region of the high-field NMR spectrum. It was then possible to establish stereochemistry convincingly by NOE methods. Two key observations are indicated directly on the structural formula. When **31** was subjected to osmylation, hemiacetal **33** was formed, in line with expectations.

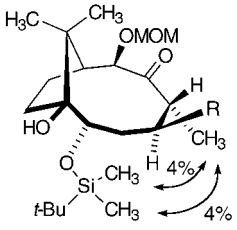
The remarkable atropisomeric control associated with the oxy-Cope rearrangement of **23** suggests that while enolate anion **34** is generated under kinetic control and is capable of retaining its geometry at or below −60 °C, strain factors facilitate its conformational inversion to produce **35** at more elevated temperatures. Both of these reactive intermediates exhibit a proclivity for the capture of methyl iodide from that surface anti to the side chain at C-7.



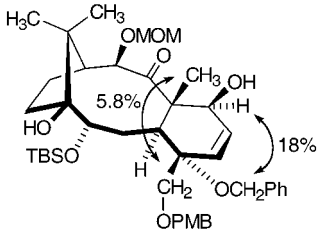
34 **35**

With the stereochemical features of **25** secure,[16] the planned elaboration of ring C could now be given consideration. Hydroboration−oxidation of the terminal vinyl group in **25** was accomplished with thexylborane in order to maximize the level of primary carbinol **26** produced. Recourse to Swern oxidation subsequently afforded **27** without complication, thereby setting the stage for intramolecular aldol ring closure. Initial experiments involving the use of sodium hydroxide in a mixed methanol/THF solvent system at −5 °C or of titanium tetraisopropoxide in THF at room temperature were met with rapid *β*-elimination of *p*-methoxybenzyl alcohol and slower ring closure to give **28** in 65−79% yield. The *β*-orientation of the hydroxyl and angular methyl substituents in this tricyclic product was corroborated by definitive NOE measurements.[17] Although the stereochemical outcome of the intramolecular aldolization conformed to expectation, permutations in the reaction conditions were necessary in order to demonstrate feasibility without loss of important oxygenated functionality. Our efforts were soon rewarded with the discovery that recourse to lithium hydroxide in THF at −12 °C was capable of delivering **29**. As a consequence of overlapping proton signals in the high-field ^{1}H NMR spectrum of **29**, the configurations at C-7 and C-8 could not be rigorously defined. Therefore, the benzoate **30** was prepared. At this point, it was an easy matter to confirm by NOE methods that the features present in paclitaxel were resident in this product, as depicted in the inset. With the completion of this phase of our investigation, little doubt remained that the

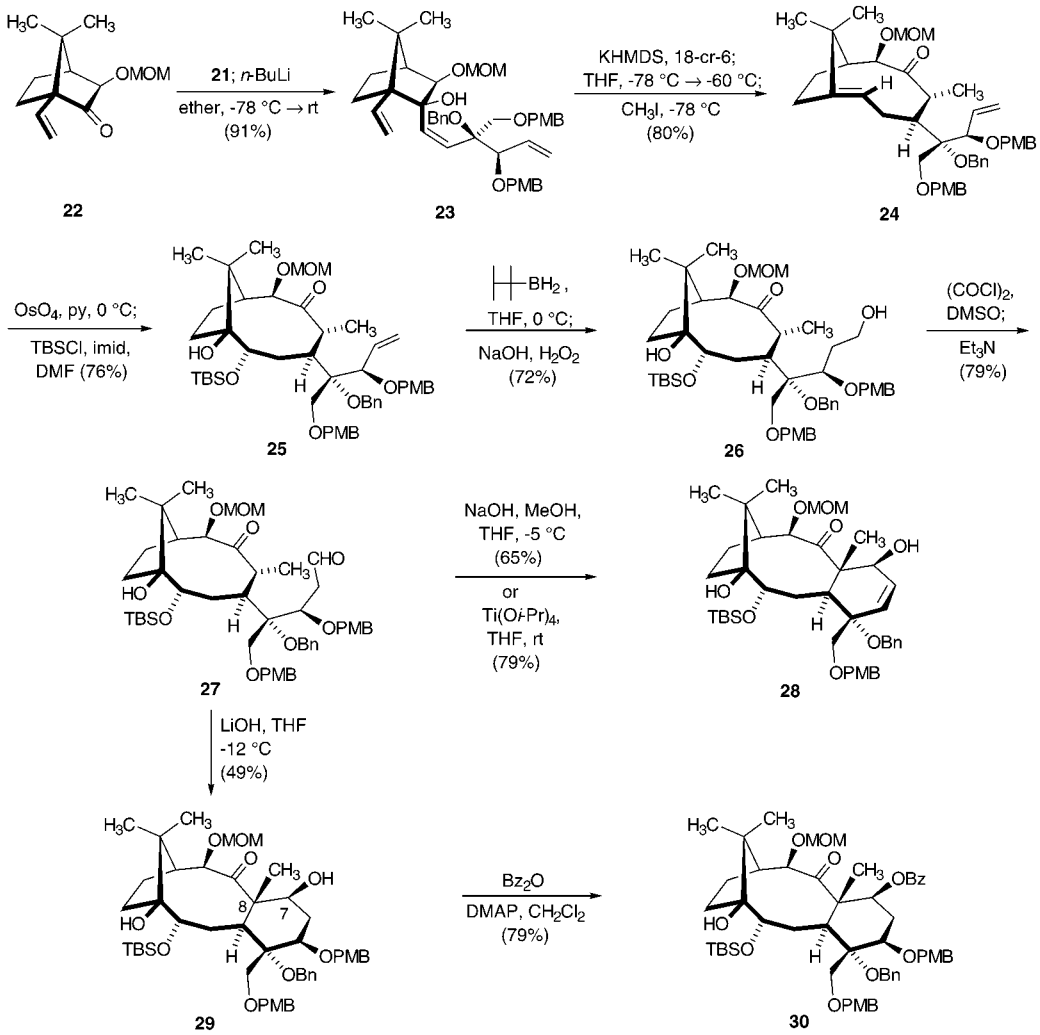
(16) The distinctive chemical shift of the C-8 methyl in this advanced intermediate provided an opportunity for added verification of the α-orientation of this substituent as shown below:



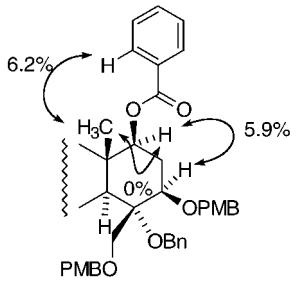
(17) Among the more definitive signal enhancements are those shown below:



Scheme 5



$\mathbf{B_1}-\mathbf{B_4}$ transition model in Figure 1 is particularly conducive to paclitaxel synthesis.



The occasion to evaluate the $\mathbf{C_1}-\mathbf{C_4}$ option arose during our probing of an alternate route to **1** in which the $C(CH_3)_2$ bridge was projected to undergo the α-ketol rearrangement along the "back" of the molecule as it is typically drawn. This variant invited pursuit because of the real possibility that some minimization of the total number of steps could result. The issue of accessing carbinol **52** involved the improvisations depicted in Schemes 7 and 8. With D-glucose as starting material, aldehyde **37** was obtained by preparation of the 4,6-*O*-benzylidene derivative **36** in advance of periodate cleavage according to precedent.[18] Following one-carbon chain extension via Wittig olefination, the directed hydroboration of **38** with 9-BBN produced **39**, which was subjected to positionally specific silylation and oxidation with formation of **41**.

With the availability of this ketone, we turned to the preparation of its coupling partner. The first step in this direction involved the subjection of enantiopure keto aldehyde **42**[19] to the Corey−Fuchs protocol.[20] The treatment of this bifunctional intermediate with methylene dibromide and triphenylphosphine proceeded with anticipated high chemoselectivity to give **43** (Scheme 8). The ketone carbonyl was next reduced with sodium borohydride in order to achieve its temporary masking. Exo alcohol **45** predominated over the endo isomer **44** by a factor of 5:1. Since these epimers were readily separated, it was an easy matter to effect the oxidation of **44** for recycling purposes. The next step involved the conversion of **45** into the lithium acetylide by exposure to 3 equiv of *n*-butyllithium. With this accomplished, dry cerium(III) chloride was added in advance of **41** in order to curtail enolization and maximize the level of 1,2-addition.[21] The coupling proved to be highly stereoselective in favor of the *S*-carbinol **46** (14:1). The

(18) Baker, S. R.; Clissold, D. W.; McKillop, A. *Tetrahedron Lett.* **1988**, *29*, 991.
(19) Paquette, L. A.; Huber, S. K.; Thompson, R. C. *J. Org. Chem.* **1993**, *58*, 6874.
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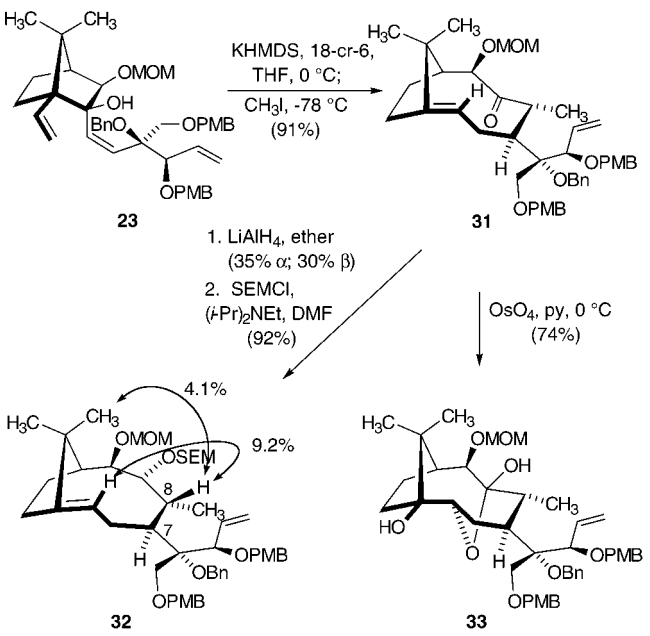
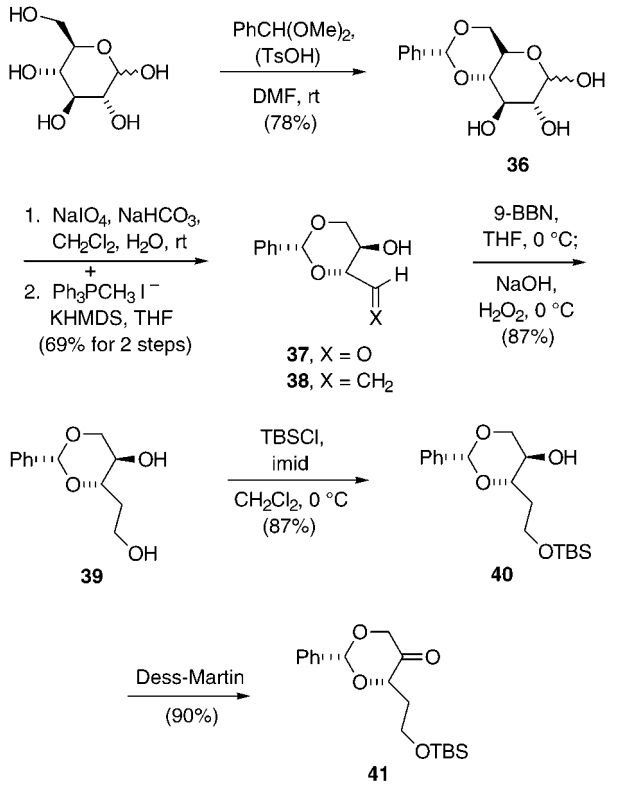
(21) (a) Paquette, L. A., Ed. *Encyclopedia of Reagents for Organic Synthesis*; Wiley: New York, 1995; Vol. 1, pp 1031−1034. (b) Dimitrov, V.; Kostova, K.; Genov, M. *Tetrahedron Lett.* **1996**, *37*, 1787.

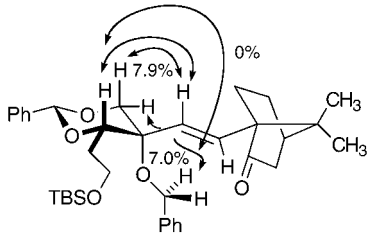
Scheme 6



Scheme 7



expectation that equatorial attack would materialize on the more stable chair conformer of **41**[22] was confirmed by NOE analysis following conversion to the benzyl ether **49**. Thus, Red-Al reduction[23] of propargyl alcohol **46** gave the trans olefin **47**, the two hydroxyl groups in which were differentiated by sequential Dess−Martin oxidation[24] and O-alkylation. Several of the more diagnostic signal enhancements observed for **49** are shown in the inset.



α-Oxygenation of this ketone was accomplished by the action of oxone on the silyl enol ether.[25] No complication was experienced either during predominant formation of the exo carbinol[26] or during its protection as the MOM ether.[27] Addition of *trans*-1-propenyllithium[28] to **51** provided the fully functionalized oxy-Cope rearrangement precursor **52** in 86% yield.

The sequence of steps that would allow for examination of the intramolecular aldol cyclization began with isomerization of **52** in the presence of potassium hexamethyldisilazide and 18-crown-6 in THF at −78 °C. The desired [3,3] sigmatropic rearrangement proceeded very efficiently with formation of an enolate anion that was directly oxygenated (O_2, then Ph_3P)[29] in order to generate **53** (Scheme 9). In this instance, the configuration at C-8 is properly set as the direct consequence of the transition state that is invariably adopted in the course of such transpositions.[8a] When our initial pursuit of a sequence involving desilylation[30] of **53** and dual oxidation of the two hydroxyl-bearing carbons was found to be unsuccessful, the possibility of a stepwise approach to **56** was eventually shown to be feasible. Thus, compound **53** was first oxidized under Swern conditions[31] to the α-diketone level, as in **54** in advance of generation of aldehyde **56**. It was well-appreciated that successful C-ring closure in this substrate depended on the absence of any disruption from competing nucleophilic attack at either of the neighboring carbonyl groups. This was accomplished by treatment of **56** with tetrabutylammonium fluoride in acetonitrile at 20 °C. This reagent is sufficiently basic to deprotonate **56** and bring about the aldol process. The stereochemistry of **57** was assessed following conversion to acetate **58**. The proximity of the α-acetoxy proton but not the neighboring angular methyl group to the bridgehead vinyl proton in **58** corroborated our expectation in the form of $\mathbf{C_1}-\mathbf{C_4}$ (Figure 1) that the stereochemistry resident in **56** is unsuited to achieving the proper paclitaxel configuration at both C-7 and C-8.

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(25) (a) Adam, W.; Chan, Y. Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800. (b) Adam, W.; Prechtl, F. *Chem. Ber.* **1991**, *124*, 2369.

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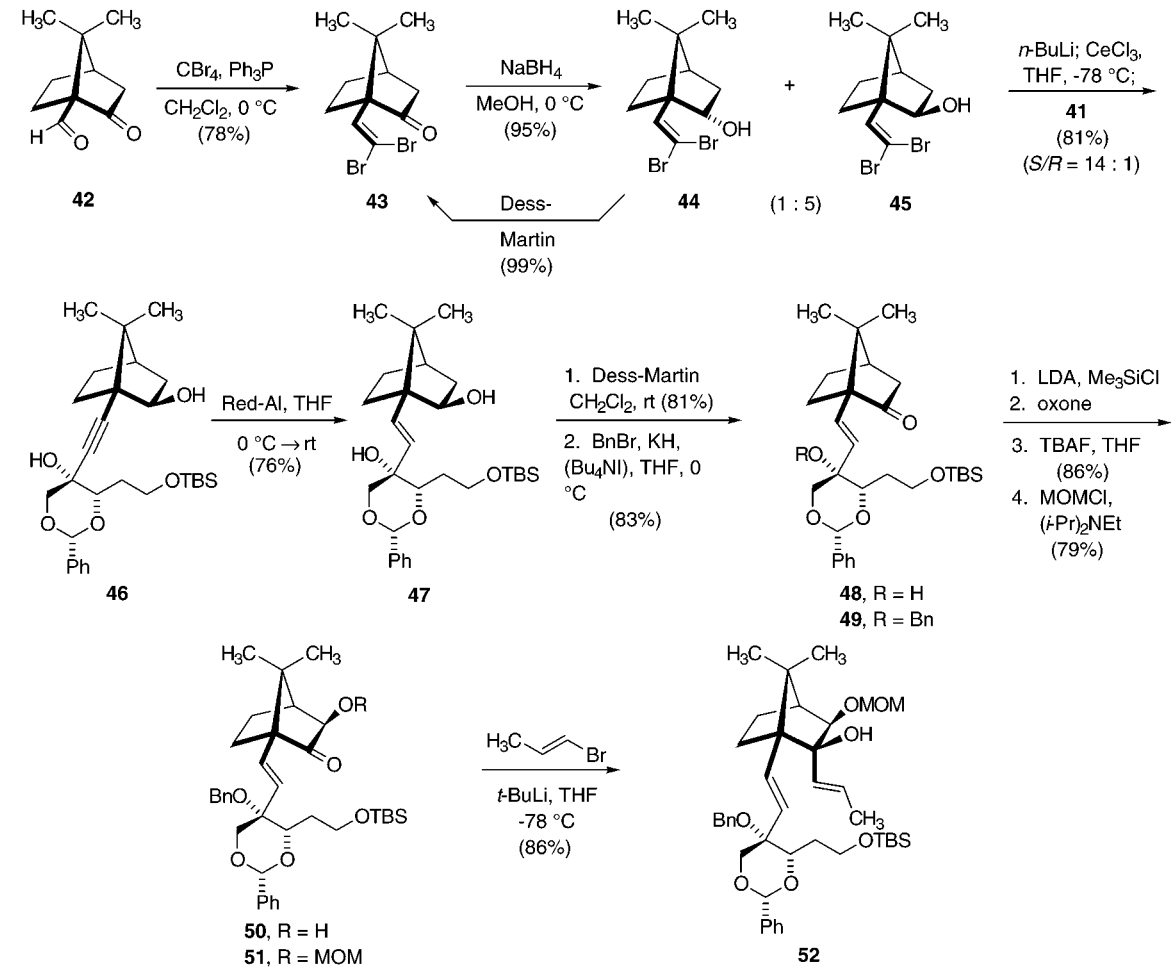
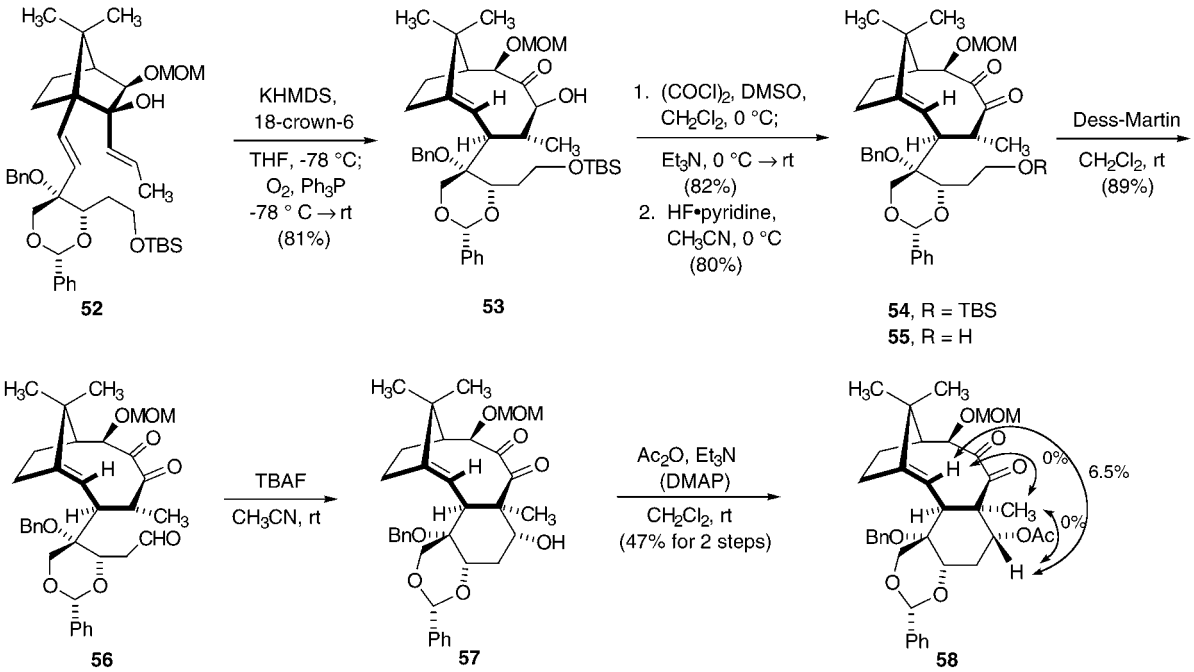
(31) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

Scheme 8

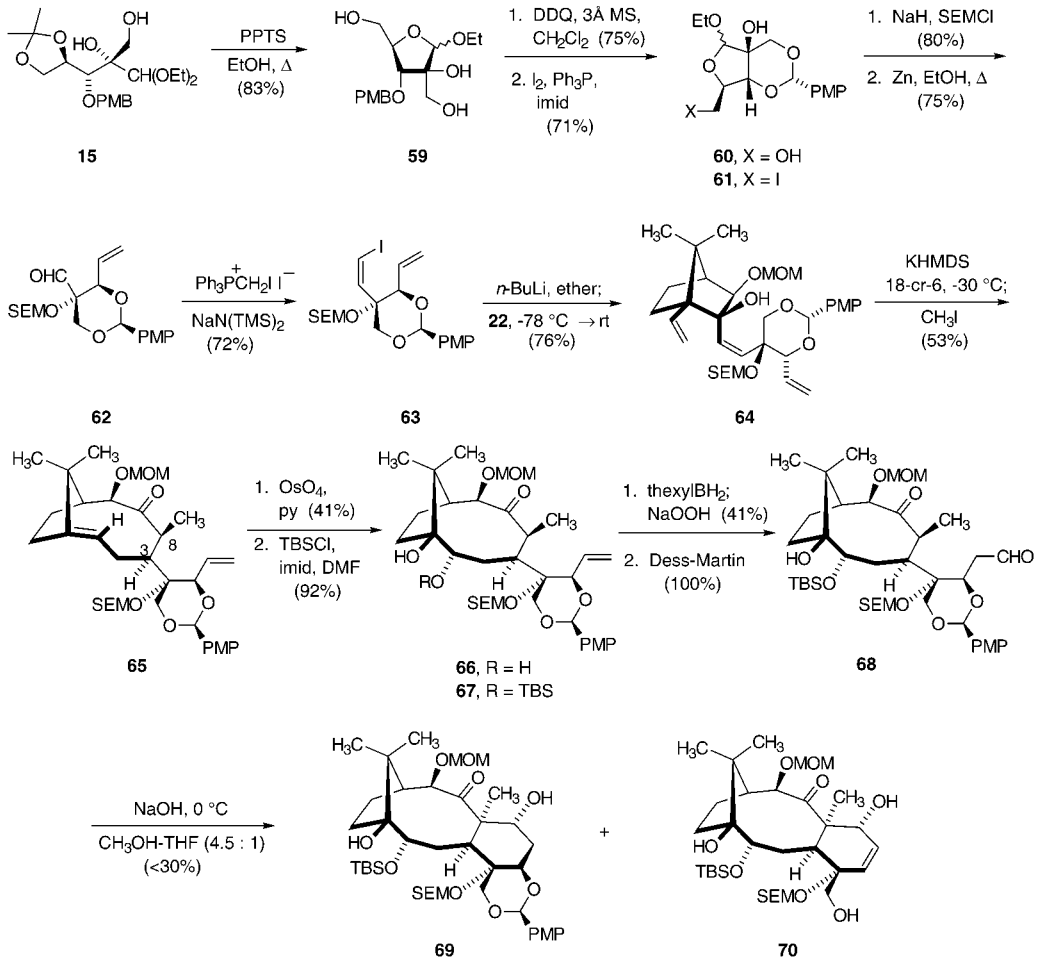


Scheme 9



In our original transition-state analysis, we had envisioned that **D**$_1$, the C* epimer of **C**$_1$, would be conformationally constrained to produce **D**$_4$. Reassurance that this correlation holds came from those experiments summarized in Scheme 10. The enantiopure diol **15** was first heated with pyridinium *p*-toluenesulfonate in ethanol in order to effect hydrolysis and equilibration. Subsequent treatment of the resulting **59** with DDQ in anhydrous dichoromethane proceeded with exceptionally high regio- and stereoselectivity. Thus, cyclization in-

Scheme 10



volved exclusive nucleophilic attack by the primary hydroxyl to form a 1,3-dioxane.[32] Furthermore, only that *p*-methoxybenzylidene acetal wherein the aromatic ring is projected equatorially on a chairlike six-membered ring was seen. The success of this tactic carried further with conversion of primary carbinol **60** into iodide **61**,[11] protection of the tertiary carbinol as its trimethylsilylethoxymethyl ether,[33] and fragmentation of the fully protected furanose by way of the Bernet−Vasella protocol.[34] Aldehyde **62** was alkenylated as before[13] to deliver vinyl iodide **63**, thereby making possible halogen−metal exchange and 1,2-addition to **22**. Carbinol **64** so formed underwent charge-accelerated sigmatropic rearrangement and direct methylation efficiently to produce **65**. As defined earlier in a related example,[35] ketone **65** is produced at −30 °C in the carbonyl-up geometry and with the C-8 methyl substituent oriented β. Chemoselective dihydroxylation of the bridgehead double bond in **65** was accomplished without any attempt at optimization. Once monoprotection of the diol had been accomplished as in **67**, the side chain was elaborated to the aldehyde level found in **68**.

The amalgamation of the 1,3-dioxane ring in this manner into the pendant C-3 unit destined to become ring C appreciably restricts the conformational flexibility attainable during the annulation process. The limiting features of the aldol transition state are given by $\mathbf{D_2}$ in Figure 1. This combination of factors is likely responsible for the inability of **68** to undergo cyclization with an acceptable degree of efficiency. The two tricyclic products **69** and **70** were produced in a 2:1 ratio (<30%) in addition to *p*-methoxybenzaldehyde. The identities of the aldols were suggested by comparative analyses of their ^{1}H NMR spectra with those of **28**, **29**, and **57**. The most diagnostic chemical shifts are those associated with the C-8 methyl signals which in both **57** and **69** appear downfield at δ 1.46 and 1.43, respectively, because of their α-orientation. In contrast, β-orientation of this substituent as in **29** (δ 1.32) is accompanied by characteristic shielding in excess of 0.1 ppm. When the C ring carries a double bond as in **28** (δ 1.46) and **70** (δ 1.15), this trend is reversed.

Conclusions

Transition-state models that incorporate the stereochemical consequences of C-4/C-5 substituents on the intramolecular C-ring-forming aldol reactions in highly functionalized bicyclo[6.2.1]undecanones related to paclitaxel are provided. When the C-4 and C-5 groups are not covalently linked, the configurational pattern given in transition-state model $\mathbf{B_2}$ is shown to be particularly amenable to adoption of that chairlike arrangement

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conducive to proper stereoinduction at C-7 and C-8 of the paclitaxel C ring. The dominant stereochemical determinants are believed to be the equatorial orientation of at least two pendant groups and avoidance of 1,3-diaxial interaction. An additional important stereochemical influence appears upon incorporation of the oxygenated centers at C-4 and C-5 into a 1,3-dioxane ring. When this structural feature is present, the stereogenic carbon labeled as C* exerts a dominant effect by preferentially projecting the aryl group equatorially. From among the four transition-state models $\mathbf{D_2}-\mathbf{F_2}$, the first is subject to destabilization as a consequence of a prominent 1,3-diaxial interaction. The $\mathbf{F_2}$ option is impossible because of large interatomic distances. Of the remaining two, $\mathbf{D_2}$ is subject to a facial bias unsuited to paclitaxel construction. The stereoselective nature of three cyclizative options is herein exemplified at the experimental level. These results provide the first unambiguous picture of the full intricacies of the intramolecular aldol cyclization. Work directed to the preparation of a diastereoisomer of the $\mathbf{E_1}$ class for the purpose of evaluating the level and direction of operational stereoinduction will soon be initiated and is expected to be the subject of a future report.

Experimental Section

General Methods. Melting points are uncorrected. The column chromatographic separations were performed with Woelm silica gel (230−400 mesh). Solvents were reagent grade and in most cases dried prior to use. The purity of all compounds was shown to be >95% by TLC and high-field ^{1}H and ^{13}C NMR. The high-resolution and fast-atom-bombardment spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark, or at Atlantic Microlab, Inc., Norcross, GA.

(α*S*,*βR*,4*R*)-α-Hydroxy-*β*-[(*p*-methoxybenzyl)oxy]-α-[[(*p*-methoxybenzyl)oxy]methyl]-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde Diethyl Acetal (16). Sodium hydride (380 mg, 15.8 mmol) was added to a solution of **15**[7] (5.50 g, 13.3 mmol) in DMF (40 mL) at 0 °C. After 30 min of stirring at this temperature, *p*-methoxybenzyl chloride was introduced, and the mixture was stirred at room temperature for 1 h, quenched with ice, diluted with saturated NH_4Cl solution, and extracted with ethyl acetate. The combined extracts were washed with water, dried, and concentrated. The residue was chromatographed on silica gel (elution with 30% ethyl acetate in hexanes) to give **16** (6.29 g, 89%) as a colorless oil: IR (film, cm^{-1}) 3532, 1613; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27−7.22 (m, 4 H), 6.87−6.83 (m, 4 H), 4.82 (d, J = 10.7 Hz, 1 H), 4.62−4.58 (m, 2 H), 4.51−4.40 (m, 3 H), 4.05−3.96 (m, 3 H), 3.79 (s, 6 H), 3.78−3.74 (m, 2 H), 3.61−3.55 (m, 2 H), 3.49−3.41 (m, 2 H), 2.89 (s, 1 H), 1.42 (s, 3 H), 1.33 (s, 3 H), 1.23−1.14 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 158.8, 158.7, 130.7, 129.6, 129.0 (2 C), 128.9 (2 C), 113.3 (2 C), 113.2 (2 C), 107.1, 103.6, 78.8, 76.8, 76.2, 74.6, 72.8, 69.3, 65.4, 65.0, 64.7, 54.7 (2 C), 26.0, 24.7, 15.0 (2 C); HRMS m/z (M^+) calcd for $C_{29}H_{42}O_9$ 534.2828, obsd 534.2867; $[\alpha]^{20}_D$ +2.1 (*c* 3.3, $CHCl_3$).

α*S*,*βR*,4*R*)-α-(Benzyloxy)-*β*-[(*p*-methoxybenzyl)oxy]-α-[[(*p*-methoxybenzyl)oxy]methyl]-2,2-dimethyl-1,3-dioxolane-4-propionaldehyde Diethyl Acetal (17). Sodium hydride (0.95 g, 39.6 mmol) was added to a solution of **16** (10.60 g, 19.8 mmol) in DMF (250 mL) at 0 °C. After 30 min of stirring at this temperature, benzyl bromide (6.78 g, 43.2 mmol) was introduced. The reaction mixture was processed in the predescribed manner to give 11.45 g (92%) of **17** as a colorless oil: IR (film, cm^{-1}) 1612; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.19 (m, 9 H), 6.90−6.84 (m, 4 H), 4.94−4.81 (m, 2 H), 4.79 (d, J = 5.7 Hz, 2 H), 4.69 (s, 1 H), 4.55 (d, J = 10.7 Hz, 1 H), 4.44 (s, 2 H), 4.33 (s, 1 H), 4.11 (t, J = 7.7 Hz, 1 H), 3.91−3.84 (m, 2 H), 3.80−3.67 (m, 9 H), 3.58−3.43 (m, 2 H), 1.44 (s, 3 H), 1.32 (s, 3 H), 1.30−1.16 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 158.8, 139.9, 131.6, 130.3, 129.1 (2 C), 128.9 (2 C), 128.0 (2 C), 127.1 (2 C), 126.8, 113.6 (2 C), 113.5 (2 C), 106.9, 104.4, 82.1, 80.4, 77.2, 74.9, 73.1, 68.0, 66.4, 65.8, 65.3, 64.8, 55.2 (2 C), 26.4, 24.5, 15.51, 15.45; HRMS m/z ($M^+ - CH_3$) calcd for $C_{35}H_{45}O_9$ 609.3063, obsd 609.3095; $[\alpha]^{20}_D$ +5.0 (*c* 1.6, $CHCl_3$).

Ethyl 2-*O*-Benzyl-3-*O*-(*p*-methoxybenzyl)-2-*C*-[[(*p*-methoxybenzyl)oxy]methyl]-D-arabinofuranoside (18). A solution of **17** (11.20 g, 17.95 mmol) in ethanol (420 mL) containing pyridinium *p*-toluenesulfonate (770 mg, 3.07 mmol) was refluxed for 1 h, concentrated, taken up in ether, washed with water, dried, and reconcentrated. Purification of the residue by chromatography on silica gel (elution with 40% ethyl acetate in hexanes) furnished **18** as a colorless oil (9.30 g, 96%). This inseparable mixture of α- and *β*-anomers was used without further characterization.

Ethyl 2-*O*-Benzyl-5-deoxy-5-iodo-3-*O*-(*p*-methoxybenzyl)-2-*C*-[[(*p*-methoxybenzyl)oxy]methyl]-D-arabinofuranoside (19). A solution of **18** (9.29 g, 17.3 mmol) in 4:1 toluene/acetonitrile (185 mL) was treated with triphenylphosphine (13.56 g, 51.76 mmol) and imidazole (4.65 g, 68.4 mmol) under nitrogen. The mixture was stirred at room temperature for 10 min and at 50 °C for an identical period of time before being returned to 20 °C, at which point iodine (8.73 g, 34.4 mmol) was introduced. The resulting suspension was stirred at 70 °C for 1 h, cooled, diluted with ether, washed with water, dried, and concentrated. Chromatography of the residue on silica gel (elution with 15% ethyl acetate in hexanes) afforded **19** (9.66 g, 86%). A further column separation led to the isolation of individual pure isomers.

Isomer A: IR (film, cm^{-1}) 1612; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.20 (m, 9 H), 6.87−6.82 (m, 4 H), 5.32 (s, 1 H), 4.90 (d, J = 11.6 Hz, 1 H), 4.71−4.60 (m, 2 H), 4.53−4.45 (m, 4 H), 4.17 (d, J = 6.2 Hz, 1 H), 4.05 (d, J = 6.9, 6.4 Hz, 1 H), 3.86 (d, J = 6.8 Hz, 2 H), 3.79 (s, 3 H), 3.78 (s, 3 H), 3.59−3.49 (m, 1 H), 3.28 (d, J = 6.9 Hz, 2 H), 1.26 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.3, 159.1, 139.5, 130.0, 129.9, 129.7 (2 C), 129.2 (2 C), 128.0 (2 C), 127.3 (2 C), 127.1, 113.7 (2 C), 113.6 (2 C), 102.0, 87.9, 86.6, 81.0, 73.4, 72.6, 71.2, 68.7, 63.8, 55.2, 15.3, 8.6 (one signal overlaps); HRMS m/z (M^+ − OBn) calcd for $C_{24}H_{30}IO_6$ 541.1087, obsd 541.1113; $[\alpha]^{20}_D$ −25.2 (*c* 0.62, $CHCl_3$).

Isomer B: IR (film, cm^{-1}) 1612; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.25 (m, 9 H), 6.91−6.85 (m, 4 H), 5.19 (s, 1 H), 4.63 (d, J = 1.8 Hz, 2 H), 4.59−4.48 (m, 4 H), 4.26−4.21 (m, 1 H), 3.88 (d, J = 1.5 Hz, 2 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.78−3.76 (m, 2 H), 3.57−3.52 (m, 1 H), 3.22−3.11 (m, 2 H), 1.25 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.2, 159.1, 138.4, 130.3, 130.0, 129.5 (2 C), 129.3 (2 C), 128.2 (2 C), 127.4 (2 C), 127.3, 113.7 (2 C), 113.6 (2 C), 105.8, 88.7, 85.1, 84.3, 73.2, 72.5, 65.8, 65.7, 63.6, 55.2, 15.1, 7.1 (one signal overlaps); HRMS molecular ion too fleeting for accurate measurement; $[\alpha]^{20}_D$ +8.0 (*c* 0.9, $CHCl_3$).

(2*S*,3*R*)-2-(Benzyloxy)-3-[(*p*-methoxybenzyl)oxy]-2-[[(*p*-methoxybenzyl)oxy]methyl]-4-pentenal (20). A solution of **19** (9.66 g, 14.9 mmol) in methanol (105 mL) was treated with zinc dust (9.60 g, 148 mmol), refluxed for 1.5 h, cooled to room temperature, and filtered. The filtrate was diluted with ether, washed with saturated NH_4Cl solution and water, dried, and concentrated. Chromatography of the residue on silica gel (elution with 15% ethyl acetate in hexanes) gave **20** as a colorless oil (6.62 g, 93%): IR (film, cm^{-1}) 1737, 1612; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1 H), 7.39−7.28 (m, 5 H), 7.27−7.15 (m, 4 H), 6.89−6.83 (m, 4 H), 5.98−5.89 (m, 1 H), 5.43−5.29 (m, 2 H), 4.79 (s, 2 H), 4.60 (d, J = 11.5 Hz, 1 H), 4.43−4.33 (m, 3 H), 4.30 (d, J = 11.5 Hz, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.73 (d, J = 10.2 Hz, 1 H), 3.66 (d, J = 10.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.6, 159.3, 159.2, 138.9, 132.9, 129.8, 129.5, 129.4 (2 C), 129.3 (2 C), 128.1 (2 C), 127.3 (2 C), 120.4, 113.71 (2 C), 113.68 (2 C), 85.3, 80.8, 73.2, 70.5, 69.7, 68.2, 55.2 (two signals overlap); HRMS m/z (M^+) calcd for $C_{29}H_{32}O_6$ 476.2194, obsd 476.2212; $[\alpha]^{20}_D$ −18.9 (*c* 0.32, $CHCl_3$).

(1*Z*,3*S*,4*R*)-2-(Benzyloxy)-1-iodo-4-[(*p*-methoxybenzyl)-oxy]-3-[[(*p*-methoxybenzyl)oxy]methyl]-1,5-hexadiene (21). A solution of sodium hexamethyldisilazide (50 mL of 1 M in THF, 50 mmol) was added to a suspension of (iodomethyl)-triphenylphosphonium iodide (27.0 g, 50.9 mmol) in THF (170 mL) under nitrogen. This mixture was stirred at room temperature for 5 min and at −78 °C for 10 min prior to the introduction of **20** (14.0 g, 29.4 mmol) dissolved in THF (10 mL). After 1.5 h at −78 °C, water was added and the product was extracted into ether. The combined organic extracts were washed with water, dried, and concentrated in advance of chromatographic purification (silica gel, elution with 15% ethyl acetate in hexanes). There was isolated 17.25 g (98%) of **21** as a colorless oil: IR (film, cm^{-1}) 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.41 (m, 2 H), 7.35−7.20 (m, 7 H), 6.91−6.86 (m, 4 H), 6.77 (d, J = 8.9 Hz, 1 H), 6.68 (d, J = 8.9 Hz, 1 H), 6.04−5.90 (m, 1 H), 5.40−5.31 (m, 2 H), 4.82 (d, J = 11.6 Hz, 1 H), 4.67 (t, J = 11.1 Hz, 2 H), 4.42 (s, 2 H), 4.38−4.33 (m, 2 H), 3.97 (d, J = 9.8 Hz, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.71 (d, J = 9.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 139.4, 138.2, 134.1, 130.5, 130.1, 129.3 (2 C), 128.0 (2 C), 127.6, 126.9, 119.7, 113.7 (2 C), 113.6, 82.6, 81.5, 80.4, 72.9, 70.9, 70.4, 66.5, 55.3 (six signals overlap); HRMS m/z (M^+ − PMB) calcd for $C_{22}H_{24}IO_4$ 479.0681, obsd 479.0700; $[\alpha]^{20}_D$ −9.3 (*c* 0.28, $CHCl_3$).

(1*S*,2*S*,3*R*,4*S*)-2-[(1*Z*,3*S*,4*R*)-2-(Benzyloxy)-4-[(*p*-methoxybenzyl)oxy]-3-[[(*p*-methoxybenzyl)oxy]methyl]-1,5-hexadienyl]-3-(methoxymethoxy)-7,7-dimethyl-1-vinylbicyclo[2.2.1]heptan-2-ol (23). A cold (−78 °C), magnetically stirred solution of **21** (2.35 g, 3.92 mmol) in anhydrous ether (30 mL) under N_2 was treated with *n*-butyllithium (3 mL of 1.3 M, 3.9 mmol) and stirred for 2 min prior to the introduction of **22**[8d] (0.87 g, 3.88 mmol) dissolved in dry ether. After 40 min of continued agitation at −78 °C, the reaction mixture was warmed to room temperature, quenched with water, and extracted with ether. The combined organic extracts were washed with water, dried, and concentrated to leave a residue that was purified chromatographically (silica gel, elution with 15% ethyl acetate in hexanes). There was isolated 2.46 g (91%) of **23** as a colorless oil: IR (film, cm^{-1}) 3340, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.28 (m, 5 H), 7.25−7.15 (m, 4 H), 6.85 (d, J = 8.3 Hz, 4 H), 5.92−5.80 (m, 1 H), 5.67 (s, 1 H), 5.52 (s, 2 H), 5.42−5.29 (m, 3 H), 4.81−4.68 (m, 4 H), 4.63−4.51 (m, 4 H), 4.48−4.36 (m, 3 H), 3.96 (d, J = 10.9 Hz, 1 H), 3.89 (d, J = 10.9 Hz, 1 H), 3.795 (s, 3 H), 3.791 (s, 3 H), 3.56 (s, 1 H), 3.31 (s, 3 H), 1.84 (d, J = 7.1 Hz, 1 H), 1.76−1.65 (m, 1 H), 1.58−1.48 (m, 1 H), 1.36−1.27 (m, 1 H), 1.21 (s, 3 H), 1.19−1.00 (m, 1 H), 0.64 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.13, 159.05, 140.2, 137.5, 136.0, 134.7, 130.4, 130.3, 129.3 (2 C), 128.9 (2 C), 128.0 (2 C), 127.7, 126.5, 118.5, 116.0, 113.7 (2 C), 113.6 (2 C), 96.1, 89.6, 84.0, 82.4, 78.0, 72.9, 71.7, 70.0, 67.0, 60.8, 55.21, 55.16, 50.8, 25.6, 24.4, 21.9, 21.7 (four signals overlap); HRMS molecular ion too fleeting for accurate mass measurement; $[\alpha]^{20}_D$ −34.1 (*c* 0.16, $CHCl_3$).

(1*S*,2*R*,4*R*,5*S*,7*E*)-5-[(1*S*,2*R*)-2-(Benzyloxy)-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]methyl]-3-butenyl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]-undec-7-en-3-one (24). A solution of potassium hexamethyldisilazide (11 mL of 0.5 M in toluene, 5.5 mmol) was added to a solution of **23** (1.30 g, 1.86 mmol) and 18-crown-6 (1.45 g, 5.49 mmol) in dry THF (60 mL) cooled to −78 °C under N_2. The reaction mixture was stirred at −78 °C for 1 h and at −60 °C for 30 min before being returned to −78 °C in advance of treatment with methyl iodide (1.18 g, 8.30 mmol) and another 40 min of stirring. After addition of water and warming to room temperature, the product was extracted into ether, washed with water, dried, concentrated, and chromatographed on silica gel (elution with 15% ethyl acetate in hexanes). There was isolated 1.06 g (80%) of **24** as a white foam: IR (film, cm^{-1}) 1709, 1613; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, J = 7.0 Hz, 2 H), 7.30−7.16 (m, 7 H), 6.90−6.80 (m, 4 H), 6.16−6.05 (m, 1 H), 5.31−5.10 (m, 3 H), 5.01−4.92 (m, 2 H), 4.67−4.63 (m, 2 H), 4.57−4.53 (m, 2 H), 4.50 (d, J = 1.9 Hz, 1 H), 4.44−4.31 (m, 3 H), 4.06−4.00 (m, 2 H), 3.80 (s, 3 H), 3.77 (s, 3 H), 3.34 (s, 3 H), 2.58−2.27 (m, 5 H), 2.14−2.01 (m, 3 H), 1.54−1.46 (m, 1 H), 1.19 (d, J = 7.6 Hz, 3 H), 1.07 (s, 3 H), 0.98 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.3, 159.0, 158.8, 146.5, 140.6, 136.8, 131.2, 130.8, 129.2 (2 C), 128.9 (2 C), 127.9 (2 C), 127.6 (2 C), 126.5, 124.6, 116.0, 113.62 (2 C), 113.57 (2 C), 95.0, 86.2, 84.4, 81.8, 72.7, 70.9, 70.4, 66.8, 55.5, 55.21, 55.16, 54.6, 47.9, 47.7, 45.4, 28.9, 26.9, 26.1, 23.2, 19.78, 19.76; HRMS molecular ion too fleeting for accurate mass measurement; $[\alpha]^{20}_D$ −31.4 (*c* 0.18, $CHCl_3$).

(1*S*,2*R*,4*R*,5*S*,7*S*,8*S*)-5-[(1*S*,2*R*)-1-(Benzyloxy)-4-hydroxy-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]-methyl]butyl]-7-(*tert*-butyldimethylsiloxy)-8-hydroxy-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]-undecan-3-one (26). A solution of **24** (370 mg, 0.52 mmol) in cold (0 °C) pyridine (7 mL) was admixed with osmium tetraoxide (80 mg, 0.32 mmol), stirred at this temperature for 1.5 h, treated with a solution of sodium dithionite (2.0 g of 85% purity, 9.8 mmol) in water (7 mL), stirred at 20 °C for 12 h, and extracted with ether. The combined organic extracts were washed with water, dried, and concentrated. The residue was dissolved in DMF (0.7 mL), treated with imidazole (0.20 g, 2.9 mmol) and *tert*-butyldimethylsilyl chloride (0.27 g, 1.8 mmol), stirred for 2 h prior to quenching with saturated Na_2CO_3 solution, and extracted with ether. The combined organic layers were washed with water, dried, and concentrated. Chromatography of the residue on silica gel (elution with 15% ethyl acetate in hexanes) gave **25** as a colorless oil (208 mg, 76%). This material was used without further purification.

A solution of borane in THF (2.7 mL of 1.0 M, 2.7 mmol) was added at 0 °C under N_2 to a solution of 2,3-dimethyl-2-butene in the same solvent (2.7 mL of 1.0 M, 2.7 mmol). The resulting solution was stirred at 0 °C for 50 min before a solution of **25** (700 mg, 0.81 mmol) in THF (5 mL) was introduced. The mixture was stirred at 0 °C for 100 min and treated successively with aqueous NaOH solution (2.7 mL of 3 M, 8.1 mmol) and 30% hydrogen peroxide (2.1 mL, 32 mmol). After further stirring for 30 min at room temperature, a solution of sodium sulfite (3.0 g, 23.8 mmol) in water (10 mL) was added, to be followed 30 min later by extraction with ether. The combined extracts were washed with water, dried, and concentrated to leave a residue that was chromatographed on silica gel (elution with 50% ethyl acetate in hexanes) to give **26** as a white foam (512 mg, 72%): IR (film, cm^{-1}) 3453, 1701, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.17 (m, 7 H), 7.11 (d, J = 8.7 Hz, 2 H), 6.89 (d, J = 8.7 Hz, 2 H), 6.84 (d, J = 8.7 Hz, 2 H), 4.83 (d, J = 11.8 Hz, 1 H), 4.75 (d, J = 11.7 Hz, 1 H), 4.61 (d, J = 10.7 Hz, 1 H), 4.57 (d, J = 10.7 Hz, 1 H), 4.52−4.47 (m, 3 H), 4.44 (dd, J = 9.4, 2.4 Hz, 1 H), 4.33 (d, J = 7.0 Hz, 1 H), 4.17 (s, 2 H), 3.95 (d, J = 10.3 Hz, 1 H), 3.85−3.76 (m, 9 H), 3.75−3.65 (m, 1 H), 3.61 (dd, J = 11.9, 2.2 Hz, 1 H), 3.25 (s, 3 H), 3.06−3.02 (m, 1 H), 2.64 (d, J = 13.1 Hz, 1 H), 2.47−2.36 (m, 2 H), 2.23−2.10 (m, 2 H), 1.96−1.86 (m, 1 H), 1.79−1.64 (m, 4 H), 1.17 (d, J = 6.4 Hz, 3 H), 1.06 (s, 3 H), 0.96 (s, 3 H), 0.89 (s, 9 H), 0.15 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.3, 159.4, 159.1, 139.3, 129.7 (2 C), 129.3, 129.1 (2 C), 128.2 (2 C), 127.1, 126.7 (2 C), 113.8 (2 C), 113.6 (2 C), 94.9, 87.1, 82.8, 82.1, 74.3, 73.2, 70.1, 66.2, 60.6, 55.9, 55.7, 55.2, 50.4, 48.2, 35.6, 34.4, 32.1, 30.0, 25.8 (3 C), 18.1, 16.9, 10.6, −3.2, −4.8 (six signals overlap); FAB MS m/z (M^+) calcd for $C_{50}H_{74}O_{11}Si$ 878.50, obsd 878.60; $[\alpha]^{20}_D$ +7.1 (*c* 0.4, $CHCl_3$).

(*βR*,*γS*,1*S*,4*S*,5*R*,7*R*,8*S*)-*γ*-(Benzyloxy)-2-(*tert*-butyldimethylsiloxy)-1-hydroxy-*β*-[(*p*-methoxybenzyl)oxy]-*γ*-[[(*p*-methoxybenzyl)oxy]methyl]-7-(methoxymethoxy)-5,11,11-trimethyl-6-oxobicyclo[6.2.1]undecane-4-butyraldehyde (27). A solution of oxalyl chloride (0.017 mL, 0.195 mmol) in CH_2Cl_2 (1 mL) was added to a solution of DMSO (0.014 mL, 0.195 mmol) in CH_2Cl_2 (1 mL) at −78 °C under N_2. After 10 min, a solution of 26 (38 mg, 0.043 mmol) in the same solvent (0.7 mL) was introduced, and stirring was maintained at −78 °C for 40 min prior to the addition of triethylamine (0.38 mL, 2.7 mmol), warming to 0 °C for 10 min, quenching with water, and extraction with ether. The combined organic layers were washed with water, dried, and

concentrated. Chromatography of the residue on silica gel (elution with 30% ethyl acetate in hexanes) gave **27** as a colorless oil (30 mg, 79%): IR (film, cm^{-1}) 3454, 1723, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 9.73 (s, 1 H), 7.32−7.21 (m, 7 H), 7.08 (d, J = 8.7 Hz, 2 H), 6.89 (d, J = 8.7 Hz, 2 H), 6.82 (d, J = 8.7 Hz, 2 H), 4.95 (dd, J = 7.5, 3.3 Hz, 1 H), 4.68 (s, 2 H), 4.51−4.45 (m, 5 H), 4.35 (d, J = 7.0 Hz, 1 H), 4.16 (d, J = 9.5 Hz, 2 H), 3.89 (d, J = 9.7 Hz, 1 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 3.61 (dd, J = 11.4, 1.9 Hz, 1 H), 3.27 (s, 3 H), 3.10−3.04 (m, 1 H), 2.89−2.86 (m, 2 H), 2.61 (dd, J = 13.6, 0.5 Hz, 1 H), 2.40−2.30 (m, 3 H), 2.10−2.00 (m, 1 H), 1.76−1.60 (m, 4 H), 1.18 (d, J = 6.5 Hz, 3 H), 1.04 (s, 3 H), 0.95 (s, 3 H), 0.88 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.0, 200.3, 159.4, 159.2, 138.7, 130.1, 129.7 (2 C), 129.3 (2 C), 129.2, 128.2 (2 C), 127.3, 126.8 (2 C), 113.9 (2 C), 113.6 (2 C), 100.0, 95.0, 87.3, 82.4, 82.1, 73.9, 73.3, 70.7, 70.1, 66.2, 55.8, 55.2, 50.4, 48.1, 45.9, 35.4, 32.1, 31.9, 30.0, 28.6, 25.8 (3 C), 18.1, 16.9, 10.6, −3.3, −4.8 (two signals overlap); FAB MS m/z (M^+) calcd for $C_{50}H_{72}O_{11}Si$ 876.48, obsd 876.53; $[\alpha]^{20}_D$ +7.9 (c 0.15, $CHCl_3$).

(1*S*,4*S*,4a*S*,6*S*,7*S*,10*S*,11*S*,12a*S*)-1-(Benzyloxy)-11-(*tert*-butyldimethylsiloxy)-4,4a,6,7,8,9,10,11,12,12a-decahydro-4,10-dihydroxy-1-[[(*p*-methoxybenzyl)oxy]methyl]-6-(methoxymethoxy)-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (28). A. Use of Sodium Hydroxide. A mixture of **27** (34 mg, 0.039 mmol) and aqueous NaOH solution (0.28 mL of 0.5 M, 0.14 mmol) in methanol (1 mL) and THF (0.2 mL) was stirred at −5 °C for 30 h, quenched with saturated NH_4Cl solution (1 mL), warmed to room temperature, and extracted with ether (3 × 15 mL). The combined extracts were washed with water, dried, and concentrated. Product **28**, purified by chromatography on silica gel (elution with 30% ethyl acetate in hexanes), was isolated as a colorless oil (17 mg, 65% based on recovered **27** (3 mg)): IR (film, cm^{-1}) 3457, 1697; ^1H NMR (300 MHz, C_6D_6) δ 7.44 (d, J = 7.2 Hz, 2 H), 7.23−7.15 (m, 5 H), 6.80 (d, J = 8.6 Hz, 2 H), 6.08 (dd, J = 10.6, 2.6 Hz, 1 H), 5.97 (d, J = 10.7 Hz, 1 H), 4.75 (br s, 1 H), 4.56 (d, J = 11.5 Hz, 1 H), 4.44−4.18 (m, 7 H), 3.73 (d, J = 10.2 Hz, 1 H), 3.64 (d, J = 10.2 Hz, 1 H), 3.54 (d, J = 4.7 Hz, 1 H), 3.27 (s, 3 H), 3.26−3.23 (m, 1 H), 2.98 (s, 3 H), 2.83 (dd, J = 11.3, 0.4 Hz, 1 H), 2.55−2.08 (m, 5 H), 1.82−1.72 (m, 1 H), 1.46 (s, 3 H), 1.41 (s, 3 H), 1.29 (s, 3 H), 1.10 (t, J = 7.0 Hz, 1 H), 0.82 (s, 9 H), 0.16 (s, 3 H), 0.14 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 213.4, 159.8, 139.7, 136.0, 130.7, 129.5 (2 C), 128.6 (2 C), 127.6, 114.1 (2 C), 100.2, 96.3, 84.4, 82.0, 80.1, 74.2, 73.7, 73.6, 69.8, 65.8, 61.0, 56.9, 55.8, 54.8, 50.4, 37.9, 33.2, 32.4, 29.9, 26.9, 25.9 (3 C), 18.2, 18.1, 12.0, −3.2, −4.4 (two signals overlap); FAB MS m/z (M^+) calcd for $C_{42}H_{62}O_9Si$ 738.42, obsd 738.47; $[\alpha]^{20}_D$ +65.1 (c 0.08, C_6H_6).

B. Use of Titanium Tetraisopropoxide. A solution of titanium isopropoxide in CH_2Cl_2 (0.1 mL of 0.5 M, 0.05 mmol) was added to a solution of **27** (15 mg, 0.017 mmol) in THF (1 mL). This mixture was stirred at 20 °C for 8 h, quenched with saturated NH_4Cl solution, and extracted with ether. Adaptation of the preceding workup led to the isolation of 10 mg (79%) of **28**.

(1*S*,2*R*,4*S*,4a*S*,6*R*,7*S*,10*S*,11*S*,12a*S*)-1-(Benzyloxy)-11-(*tert*-butyldimethylsiloxy)dodecahydro-4,10-dihydroxy-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]-methyl]-6-(methoxymethoxy)-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one (29). A solution of lithium hydroxide in water (0.6 mL of 0.5 M, 0.3 mmol) was added to a solution of **27** (95 mg, 0.108 mmol) in THF (5 mL) at −12 °C. The reaction mixture was stirred at this temperature for 17 h and worked up in the predescribed manner. Chromatography on silica gel (elution with 15% ethyl acetate in hexanes) gave **29** (18.2 mg) and returned unreacted **27** (58.2 mg) for an adjusted yield of 49%: colorless oil; IR (film, cm^{-1}) 3444, 1699, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.20 (m, 7 H), 7.16 (d, J = 8.6 Hz, 2 H), 6.87−6.79 (m, 4 H), 4.87 (d, J = 11.3 Hz, 1 H), 4.74 (d, J = 11.5 Hz, 1 H), 4.62−4.50 (m, 4 H), 4.43 (s, 2 H), 4.35 (d, J = 11.0 Hz, 1 H), 4.23 (s, 1 H), 4.16−4.12 (m, 1 H), 3.96 (s, 2 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.78−3.69 (m, 2 H), 3.34 (s, 3 H), 3.25 (d, J = 5.0 Hz, 1 H), 2.58−2.46 (m, 2 H), 2.44−2.36 (m, 2 H), 2.27−2.14 (m, 1 H), 2.06−2.01 (m, 1 H), 1.83−1.65 (m, 3 H), 1.32 (s, 3 H), 1.28 (d, J = 7.9 Hz, 1 H), 1.05 (s, 3 H), 0.99 (s, 3 H), 0.86 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 213.0, 159.1, 139.8, 130.3, 129.9, 129.4 (2 C), 128.9 (2 C), 128.1 (2 C), 127.0, 126.9 (2 C), 113.8 (2 C), 113.7 (2 C), 96.2, 84.4, 83.5, 82.0, 81.1, 73.3, 72.6, 70.7, 69.7, 67.3, 66.9, 59.7, 56.8, 56.0, 55.2, 49.9, 40.9, 33.8, 32.7, 31.6, 29.6, 28.1, 25.8 (3 C), 18.0, 17.2, 10.6, −3.2, −4.6 (two signals overlap); FAB MS m/z (M^+) calcd for $C_{50}H_{72}O_{11}Si$ 876.48, obsd 876.53; $[\alpha]^{20}_D$ −42.0 (c 0.04, $CHCl_3$).

(1*S*,2*R*,4*S*,4a*S*,6*R*,7*S*,10*S*,11*S*,12a*S*)-1-(Benzyloxy)-11-(*tert*-butyldimethylsiloxy)dodecahydro-4,10-dihydroxy-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]-methyl]-6-(methoxymethoxy)-4a,13,13-trimethyl-7,10-methanobenzocyclodecen-5(1*H*)-one 4-Benzoate (30). A solution of **29** (8 mg, 0.009 mmol), benzoic anhydride (100 mg, 0.44 mmol), and DMAP (50 mg, 0.41 mmol) in CH_2Cl_2 (1.5 mL) was stirred at 20 °C for 6 h, quenched with saturated $NaHCO_3$ solution (1 mL), and extracted with ether (3 × 10 mL). The combined extracts were washed with water, dried, and concentrated. The residue was purified by chromatography (silica gel, elution with 20% ethyl acetate in hexanes) to provide **30** as a colorless oil (7 mg, 79%): IR (film, cm^{-1}) 3458, 1723, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 7.4 Hz, 2 H), 7.55 (t, J = 7.4 Hz, 1 H), 7.41−7.21 (m, 9 H), 7.17 (d, J = 8.5 Hz, 2H), 6.84−6.81 (m, 4H), 5.31 (dd, J = 11.5, 3.3 Hz, 1 H), 4.89 (d, J = 11.3 Hz, 1 H), 4.73 (d, J = 11.3 Hz, 1 H), 4.64 (d, J = 11.4 Hz, 1 H), 4.60 (s, 1 H), 4.59 (d, J = 11.7 Hz, 1 H), 4.44 (d, J = 11.9 Hz, 1 H), 4.38 (d, J = 10.9 Hz, 1 H), 4.19 (d, J = 2.5 Hz, 1 H), 4.17 (s, 1 H), 4.06 (d, J = 10.1 Hz, 1 H), 4.04 (d, J = 6.7 Hz, 1 H), 3.93−3.82 (m, 2 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.73−3.70 (m, 1 H), 3.07 (s, 3 H), 2.71−2.40 (m, 5 H), 2.07−1.67 (m, 4 H), 1.61 (s, 3 H), 1.32−1.20 (br m, 1 H), 1.03 (s, 3 H), 0.97 (s, 3 H), 0.87 (s, 9 H), 0.15 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.4, 165.4, 159.2, 159.1, 139.5, 133.1, 130.1, 130.0, 129.8, 129.5 (2 C), 129.4 (2 C), 129.0 (2 C), 128.4 (2 C), 128.2 (2 C), 127.1, 127.0 (2 C), 113.8 (2 C), 113.7 (2 C), 94.4, 82.3, 82.0, 81.0, 77.2, 75.3, 73.4, 70.6, 69.7, 67.2, 67.0, 57.3, 56.3, 55.5, 55.2, 50.0, 41.0, 33.4, 31.6, 29.4, 29.0, 27.3, 25.8 (3 C), 18.1, 17.3, 12.5, −3.2, −4.6 (one signal overlaps); FAB MS m/z (M^+) calcd for $C_{57}H_{76}O_{12}Si$ 980.51, obsd 980.58; $[\alpha]^{20}_D$ +17.7 (c 0.03, $CHCl_3$).

(1*S*,2*R*,4*R*,5*S*,7*E*)-5-[(1*S*,2*R*)-2-(Benzyloxy)-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]methyl]-3-butenyl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]-undec-7-en-3-one (31). A solution of potassium hexamethyldisilazide (0.44 mL of 0.5 M, 0.22 mmol) in toluene was added to a solution of **23** (53 mg, 0.076 mmol) and 18-crown-6 (59 mg, 0.23 mmol) in THF (3 mL) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 5 min, cooled to −78 °C, treated with methyl iodide (45 mg, 0.32 mmol) dissolved in THF (1 mL), stirred at −78 °C for 2 h, quenched with water, warmed to 20 °C, and extracted with ether. The combined extracts were processed in the usual way, and the residue was chromatographed on silica gel (elution with 10% ethyl acetate in hexanes) to give 49 mg (91%) of **31** as a white foam: IR (film, cm^{-1}) 1687, 1613; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.21 (m, 9 H), 6.89−6.85 (m, 4 H), 6.09−5.97 (m, 1 H), 5.47−5.27 (m, 3 H), 5.01 (d, J = 11.7 Hz, 1 H), 4.69 (d, J = 6.7 Hz, 1 H), 4.59−4.51 (m, 3H), 4.49 (d, J = 11.2 Hz, 1 H), 4.35 (d, J = 9.9 Hz, 2 H), 4.12 (d, J = 11.1 Hz, 1 H), 3.87 (d, J = 5.1 Hz, 2 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.70 (d, J = 9.7 Hz, 1 H), 3.51−3.38 (m, 2 H), 3.37 (s, 3 H), 2.43−2.01 (m, 4 H), 1.93−1.88 (m, 3 H), 1.37 (s, 3 H), 1.03 (d, J = 3.6 Hz, 3 H), 1.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.4, 159.0, 158.8, 146.5, 139.6, 135.8, 130.9, 130.4, 129.1 (2 C), 128.6 (2 C), 128.1 (2 C), 127.4 (2 C), 127.0, 124.1, 120.1, 113.6 (2 C), 113.5 (2 C), 96.1, 87.4, 85.0, 81.9, 73.0, 72.5, 69.4, 65.6, 56.1, 55.2, 53.4, 45.7, 41.8, 40.6, 26.1, 23.6, 23.0, 22.0, 18.0 (two signals overlap); FAB MS m/z (M^+) calcd for $C_{44}H_{56}O_8$ 712.40, obsd 712.47; $[\alpha]^{20}_D$ −33.1 (c 0.38, $CHCl_3$).

[2-[[[(1*S*,2*R*,3*R*,4*R*,5*S*,7*E*)-5-[(1*S*,2*R*)-1-(Benzyloxy)-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]-methyl]-3-butenyl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]undec-7-en-3-yl]oxy]methoxy]ethyl]tri-

methylsilane (32). Lithium aluminum hydride (200 mg, 5.26 mmol) was added to a solution of **31** (860 mg, 1.21 mmol) in dry ether (30 mL), and the resulting suspension was stirred at 20 °C for 3 h, quenched with water, and extracted with ether. Following the predescribed workup and chromatography on silica gel (elution with 15% ethyl acetate in hexanes), there was isolated 303 mg (35%) of the α-carbinol and 260 mg (30%) of the *β*-carbinol.

α-Isomer: colorless oil; IR (film, cm^{-1}) 3446, 1612; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.20 (m, 9 H), 6.89 (d, J = 8.6 Hz, 4 H), 6.04−5.92 (m, 1 H), 5.39 (dd, J = 10.2, 2.0 Hz, 1 H), 5.30−5.24 (m, 2 H), 4.96 (d, J = 11.8 Hz, 1 H), 4.68 (d, J = 6.2 Hz, 1 H), 4.61−4.59 (m, 2 H), 4.54−4.46 (m, 3 H), 4.41 (d, J = 8.6 Hz, 1 H), 4.37 (d, J = 11.3 Hz, 1 H), 4.16 (d, J = 11.2 Hz, 1 H), 3.81 (s, 3 H), 3.81−3.80 (m, 1 H), 3.79 (s, 3 H), 3.67 (d, J = 9.9 Hz, 1 H), 3.58 (d, J = 4.2 Hz, 1 H), 3.47 (d, J = 10.9 Hz, 1 H), 3.38 (s, 3 H), 3.07−2.84 (m, 1 H), 2.83−2.78 (m, 1 H), 2.68−2.45 (m, 3 H), 2.17−1.99 (m, 3 H), 1.73 (br s, 1 H), 1.32 (s, 3 H), 1.23 (d, J = 6.3 Hz, 3 H), 1.07 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.0, 158.7, 145.0, 139.6, 136.0, 131.1, 130.4, 129.2 (2 C), 128.6, 128.5, 128.1 (2 C), 127.2 (2 C), 126.9, 120.7, 120.2, 113.9, 113.7, 113.5, 96.3, 91.7, 85.4, 82.6, 73.2, 73.1, 72.4, 69.3, 65.3, 55.8, 55.2, 50.4, 45.9, 37.4, 34.5, 26.9, 24.3, 23.8, 22.5, 13.2 (three signals overlap); FAB MS m/z (M^+) calcd for $C_{44}H_{58}O_8$ 714.41, obsd 714.48; $[\alpha]^{20}_D$ −48.7 (c 0.40, $CHCl_3$).

***β*-Isomer:** colorless oil; IR (film, cm^{-1}) 3541, 1613; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.17 (m, 9 H), 6.88−6.81 (m, 4 H), 6.14−5.92 (m, 1 H), 5.44−5.39 (m, 1 H), 5.32−5.24 (m, 2 H), 4.80−4.50 (m, 7 H), 4.45−4.38 (m, 2 H), 4.29 (s, 1 H), 4.27 (d, J = 3.4 Hz, 1 H), 4.09 (d, J = 8.8 Hz, 1 H), 3.79 (s, 6 H), 3.39 (s, 3 H), 3.30 (dd, J = 9.4, 1.1 Hz, 1 H), 3.13 (s, 1 H), 2.63−2.41 (m, 4 H), 2.20−1.96 (m, 4 H), 1.51−1.47 (m, 1 H), 1.02 (d, J = 8.3 Hz, 3 H), 0.97 (s, 3 H), 0.80 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 158.8, 145.5, 139.8, 135.9, 131.0, 130.9, 129.1 (2 C), 128.9 (2 C), 128.1 (2 C), 128.06 (2 C), 127.0, 119.3 (2 C), 118.7 (2 C), 113.6, 113.5, 98.0, 90.6, 86.8, 84.3, 73.0, 72.9, 69.8, 69.4, 66.7, 56.0, 55.2, 51.6, 45.6, 44.9, 38.5, 26.7, 24.4, 24.2, 23.1, 20.8, 15.8 (two signals overlap); FAB MS m/z (M^+) calcd for $C_{44}H_{58}O_8$ 714.41, obsd 714.43; $[\alpha]^{20}_D$ −8.3 (c 0.21, $CHCl_3$).

SEM chloride (470 mg, 2.82 mmol) was added to a solution of the α-alcohol (270 mg, 0.378 mmol) and diisopropylethylamine (0.5 mL, 2.9 mmol) in DMF (1 mL). The reaction mixture was stirred at room temperature for 2.5 h, treated with saturated $NaHCO_3$ solution (5 mL), and extracted with ether. The combined organic extracts were washed with water, dried, concentrated, and chromatographed on silica gel. Elution with 15% ethyl acetate in hexanes provided 295 mg (92%) of **32** as a colorless oil: IR (film, cm^{-1}) 1613; ^1H NMR (300 MHz, C_6D_6) δ 7.44 (d, J = 7.2 Hz, 2 H), 7.35 (d, J = 8.6 Hz, 2 H), 7.28 (d, J = 8.6 Hz, 2 H), 7.19 (d, J = 7.1 Hz, 2 H), 7.09 (d, J = 7.3 Hz, 1 H), 6.84 (d, J = 8.0 Hz, 2 H), 6.82 (d, J = 8.4 Hz, 2 H), 6.18−6.06 (m, 1 H), 5.57−5.52 (m, 1 H), 5.26−5.14 (m, 3 H), 4.74−4.61 (m, 6 H), 4.55 (d, J = 10.7 Hz, 1 H), 4.44 (d, J = 11.3 Hz, 1 H), 4.25 (d, J = 11.3 Hz, 1 H), 4.16 (d, J = 10.7 Hz, 1 H), 3.88 (d, J = 4.9 Hz, 1 H), 3.82 (d, J = 9.8 Hz, 1 H), 3.79−3.70 (m, 2 H), 3.68−3.52 (m, 2 H), 3.32 (s, 3 H), 3.30 (s, 3 H), 3.29 (s, 3 H), 3.28−3.24 (m, 1 H), 3.13−2.99 (m, 2 H), 2.81−2.68 (m, 2 H), 2.21−2.06 (m, 2 H), 1.93−1.89 (m, 1 H), 1.67 (d, J = 6.5 Hz, 3 H), 1.54 (s, 3 H), 1.52−1.44 (m, 1 H), 1.08 (s, 3 H), 0.96−0.86 (m, 2 H), −0.04 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 159.6, 159.5, 144.8, 140.2, 136.9, 131.5, 130.7, 129.7 (2 C), 129.6 (2 C), 128.5 (2 C), 127.2, 121.6, 120.3, 113.9 (2 C), 96.8, 93.5, 87.7, 86.3, 83.1, 76.8, 73.5, 70.1, 65.9, 65.6, 55.6, 54.7, 51.8, 46.6, 38.4, 35.3, 27.2, 24.8, 24.6, 23.1, 22.7, 18.5, 15.0, −1.3 (four signals overlap); FAB MS m/z (M^+) calcd for $C_{50}H_{72}O_9Si$ 844.49, obsd 844.62; $[\alpha]^{20}_D$ −32.8 (c 0.12, benzene).

Analogous treatment of the *β*-alcohol gave the corresponding derivative in 91% yield.

(1*S*,2*S*,5*S*,6*R*,7*R*,8*R*,9*S*)-9-[(1*S*,2*R*)-1-(Benzyloxy)-2-[(*p*-methoxybenzyl)oxy]-1-[[(*p*-methoxybenzyl)oxy]methyl]-3-butenyl]-6-(methoxymethoxy)-8,12,12-trimethyl-11-oxatricyclo[5.3.1.1^{2,5}]dodecane-2,7-diol (33). A solution of osmium tetraoxide (85 mg, 0.33 mmol) in pyridine (0.5 mL) was added to a solution of **31** (246 mg, 0.35 mmol) in pyridine (7 mL) at 0 °C. The reaction mixture was stirred at this temperature for 2 h, treated with a solution of sodium dithionite (1.4 g of 85% purity, 6.8 mmol) in water (10 mL), stirred at 20 °C overnight, and extracted with ether. The combined extracts were washed with water, dried, and concentrated. Chromatography of the residue on silica gel (elution with 30% ethyl acetate in hexanes) afforded **33** as a colorless oil (190 mg, 74%): IR (film, cm^{-1}) 3440, 1613; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.21 (m, 9 H), 6.88−6.84 (m, 4 H), 6.03−5.91 (m, 1 H), 5.40−5.25 (m, 2 H), 4.92 (d, J = 12.2 Hz, 1 H), 4.67−4.56 (m, 3H), 4.54 (d, J = 10.1 Hz, 1 H), 4.39−4.26 (m, 3 H), 4.13−4.06 (m, 2 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 3.61 (d, J = 10.1 Hz, 1 H), 3.56−3.42 (m, 1 H), 3.39 (s, 3 H), 3.21 (dd, J = 12.1, 6.6 Hz, 1 H), 2.84 (m, 1 H), 2.50 (s, 1 H), 2.08−1.66 (m, 9 H), 1.41 (s, 3 H), 1.17 (d, J = 6.6 Hz, 3 H), 1.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.1, 158.9, 139.6, 135.3, 130.8, 130.2, 129.2 (2 C), 128.9 (2 C), 128.1 (2 C), 126.9 (2 C), 126.8, 120.3, 113.7 (2 C), 113.6 (2 C), 103.4, 97.7, 92.8, 84.9, 83.2, 81.7, 79.4, 73.1, 71.7, 69.7, 65.2, 55.6, 55.2, 50.4, 46.8, 38.2, 37.9, 32.7, 30.0, 25.0, 24.7, 22.8, 15.1 (one signal overlaps); FAB MS m/z (M^+) calcd for $C_{44}H_{56}O_{10}$ 746.40, obsd 746.49; $[\alpha]^{20}_D$ +7.8 (c 0.50, $CHCl_3$).

(2*R*,4*S*,5*R*)-2-Phenyl-4-vinyl-*m*-dioxan-5-ol (38). To a mixture of 4,6-*O*-benzylidene-D-glucose[18] (**36**, 14.0 g, 0.052 mmol) and $NaHCO_3$ (4.37 g, 0.052 mmol) in CH_2Cl_2 (200 mL) and water (100 mL) was added sodium periodate (25.0 g, 0.12 mol) in small portions. After 30 min of agitation, the solvents were removed in vacuo, and the white residue was extracted five times with ethyl acetate. The combined extracts were dried, filtered, and evaporated to give aldehyde **37**, which was used directly without purification.

A solution of methyltriphenylphosphonium iodide (21.4 g, 0.053 mol) in dry THF (100 mL) at 0 °C was treated with potassium hexamethyldisilazide (106 mL of 0.5 M in toluene, 0.053 mmol), stirred at 0 °C for 1 h, and treated with the above aldehyde dissolved in THF (100 mL). The resultant brown suspension was allowed to warm to 20 °C, stirred for an additional 3 h, and quenched with saturated NH_4Cl solution. Ether was added, and the white solids were removed by filtration through a Celite pad. The filtrate was extracted with ether, the combined organics were dried and concentrated, and the residue was chromatographed on silica gel. Elution with 25% ethyl acetate in hexanes yielded 7.44 g (69% overall) of **38** as a white solid: mp 87−89 °C; IR (film, cm^{-1}) 3443; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55−7.35 (m, 5 H), 5.98 (ddd, J = 17.3, 10.5, 6.6 Hz, 1 H), 5.54 (s, 1 H), 5.50 (dt, J = 17.3, 1.3 Hz, 1 H), 5.37 (dd, J = 10.6, 1.0 Hz, 1 H), 4.33−4.25 (m, 1 H), 4.03−3.98 (t, J = 7.3 Hz, 1H), 3.65−3.54 (m, 2 H), 2.19 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.4, 134.5, 129.0, 128.2 (2 C), 126.1 (2 C), 119.0, 100.8, 83.1, 70.7, 65.1; HRMS m/z (M^+) calcd 206.0943, obsd 206.0936; $[\alpha]^{20}_D$ −59.1 (c 1.96, $CHCl_3$).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.99; H, 6.85.

(2*R*,4*S*,5*R*)-5-Hydroxy-2-phenyl-*m*-dioxane-4-ethanol (39). A solution of **38** (7.44 g, 0.036 mol) in THF (50 mL) at 0 °C was treated with a solution of 9-BBN (217 mL of 0.5 M in THF, 0.108 mol), allowed to warm to 20 °C, and stirred overnight. The mixture was cooled in an ice−water bath, treated carefully with aqueous sodium hydroxide (60 mL, 2 N) followed by hydrogen peroxide (60 mL, 30% in water), allowed to warm to 20 °C, and stirred for another 2 h. Solvents were removed in vacuo to leave a white residue, which was partitioned between ether and water. The separated aqueous phase was extracted with ether (2×), and the combined organic phases were dried, filtered, and concentrated. Chromatographic purification of the residue on silica gel (elution with 25% ethyl acetate in hexanes) provided 7.0 g (87%) of **39** as a colorless oil: IR (film, cm^{-1}) 3395; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49−7.32 (m, 5 H), 5.46 (s, 1 H), 4.30−4.20 (m, 1 H), 3.94 (br s, 2 H), 3.85−3.70 (m, 2 H), 3.69−3.62 (m, 1 H), 3.60−3.52 (m, 2 H), 2.12−2.01 (m, 1 H), 1.96−1.87 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.5, 129.0, 128.2 (2 C), 126.0 (2 C),

100.9, 81.0, 71.0, 65.6, 59.3, 35.6; HRMS *m/z* (M^+) calcd for $C_{12}H_{16}O_4$ 224.1048, obsd 224.1049; $[\alpha]^{20}_D$ −23.0 (*c* 3.79, $CHCl_3$).

(2*R*,4*S*,5*R*)-4-[2-(*tert*-Butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-ol (40). A solution of **39** (9.56 g, 0.043 mol) in CH_2Cl_2 (100 mL) at 0 °C was treated with imidazole (4.36 g, 0.064 mol) and *tert*-butyldimethylsilyl chloride (7.07 g, 0.049 mol), warmed to 20 °C, and stirred overnight. The mixture was quenched with saturated $NaHCO_3$ solution, and the separated phase was extracted with CH_2Cl_2 (2×). The combined organic solutions were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 25% ether in hexanes) afforded **40** as a colorless oil (12.5 g, 87%): IR (film, cm^{-1}) 3405; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.33 (m, 5 H), 5.47 (s, 1 H), 4.56 (s, 1 H), 4.38−4.34 (m, 1 H), 3.94−3.77 (m, 2 H), 3.65−3.56 (m, 3 H), 2.04−1.99 (m, 2 H), 0.94 (s, 9 H), 0.134 (s, 3 H), 0.127 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.9, 128.8, 128.2 (2 C), 126.1 (2 C), 100.9, 81.8, 71.0, 66.1, 60.3, 37.7, 25.8 (3 C), 18.2, −5.5, −5.6; HRMS *m/z* (M^+) calcd for $C_{18}H_{30}O_4Si$ 338.1913, obsd 338.1908; $[\alpha]^{20}_D$ −26.6 (*c* 3.57, $CHCl_3$).

(2*R*,4*S*)-4-[2-(*tert*-Butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-one (41). To a solution of **40** (3.85 g, 0.011 mol) in CH_2Cl_2 (50 mL) was added the Dess−Martin periodinane (7.25 g, 0.017 mol). The mixture was stirred for 30 min, diluted with ether, filtered, and washed with aqueous NaOH (1.0 N) and brine prior to drying and filtration. The removal of solvents in vacuo followed by chromatography on silica gel (elution with 25% ether in hexanes) gave **41** (3.44 g, 90%) as a colorless oil: IR (film, cm^{-1}) 1737; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57−7.36 (m, 5 H), 5.95 (s, 1 H), 4.66 (dd, *J* = 7.8, 4.0 Hz, 1 H), 4.51 and 4.43 (ABq, *J* = 17.3 Hz, 2 H), 3.91−3.78 (m, 2 H), 2.33−2.22 (m, 1 H), 2.07−1.96 (m, 1 H), 0.93 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 205.7, 137.2, 129.1, 128.3 (2 C), 126.0 (2 C), 99.1, 79.4, 72.0, 58.0, 32.9, 25.8 (3 C), 18.3, −5.4, −5.5; HRMS *m/z* (M^+) calcd for $C_{18}H_{28}O_4Si$ 336.1757, obsd 336.1738; $[\alpha]^{20}_D$ −33.7 (*c* 4.60, $CHCl_3$).

(1*S*,4*R*)-1-(2,2-Dibromovinyl)-7,7-dimethylbicyclo[2.2.1]-heptan-2-one (43). To a solution of triphenylphosphine (12.6 g, 0.084 mol) in CH_2Cl_2 (50 mL) at 0 °C was added solid carbon tetrabromide (8.0 g, 0.024 mol) in small portions. The resultant brown suspension was stirred at 0 °C for 5 min, at which point a solution of **42**[19] (2.0 g, 0.012 mol) in CH_2Cl_2 (5 mL) was treated dropwise. After 10 min at this temperature, ether was added and the solid was removed by filtration through a pad of Celite. Removal of solvents from the filtrate followed by chromatography on silica gel (elution with 10% ether in hexanes) gave **43** as a white solid (3.0 g, 78%): mp 72−73 °C; IR (film, cm^{-1}) 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 6.39 (s, 1 H), 2.39 (dt, *J* = 18.3, 3.3 Hz, 1 H), 2.24−2.14 (m, 2 H), 2.07−1.95 (m, 2 H), 1.90 (d, *J* = 18.3 Hz, 1 H), 1.47−1.39 (m, 1 H), 0.99 (s, 3 H), 0.92 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.3, 132.9, 91.4, 65.2, 49.1, 43.1, 42.2, 27.2, 25.9, 20.2, 19.9; HRMS *m/z* (M^+) calcd for $C_{11}H_{14}Br_2O$ 319.9412, obsd 319.9405; $[\alpha]^{20}_D$ −93.4 (*c* 4.68, $CHCl_3$).

Anal. Calcd for $C_{11}H_{14}Br_2O$: C, 41.03; H, 4.38. Found: C, 40.92; H, 4.32.

Borohydride Reduction of 43. A solution of **43** (556 mg, 1.74 mmol) in methanol (10 mL) at 0 °C was treated with sodium borohydride (66 mg, 1.74 mmol) in small portions. The cooling bath was removed, and the mixture was allowed to warm to room temperature, stirred for a further 2 h, and freed of solvent. Chromatographic separation of the epimeric alcohols (silica gel, elution with 10% ethyl acetate in hexanes) provided in turn the less polar exo alcohol **45** (443 mg, 79%), followed by the more polar endo alcohol **44** (88 mg, 16%).

44: white solid, mp 128−129 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 6.53 (s, 1 H), 4.50 (br d, *J* = 9.5 Hz, 1 H), 2.62−2.55 (m, 1 H), 2.35−2.25 (m, 1 H), 1.87−1.62 (m 4 H), 1.42−1.35 (m, 1 H), 1.06 (dd, *J* = 13.3, 3.4 Hz, 1 H), 0.96 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 139.1, 86.9, 75.2, 58.7, 51.6, 44.3, 38.4, 28.5, 23.4, 20.8, 19.1; HRMS *m/z* (M^+) calcd for $C_{11}H_{16}Br_2O$ 321.9568, obsd 321.9565; $[\alpha]^{20}_D$ +5.9 (*c* 2.49, $CHCl_3$).

Anal. Calcd for $C_{11}H_{16}Br_2O$: C, 40.77; H, 4.98. Found: C, 40.67; H, 4.96.

45: colorless oil, IR (film, cm^{-1}) 3453; ^1H NMR (300 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 4.38 (ddd, *J* = 7.5, 3.6, 3.6 Hz, 1 H), 2.12 (d, *J* = 3.2 Hz, 1 H), 1.89−1.60 (m, 7 H), 1.09 (s, 3 H), 0.86 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 138.4, 88.3, 76.1, 57.8, 48.3, 43.9, 39.7, 29.1, 27.3, 20.5, 20.1; HRMS *m/z* (M^+) calcd for $C_{11}H_{16}Br_2O$ 321.9568, obsd 321.9567; $[\alpha]^{20}_D$ −64.7 (*c* 7.02, $CHCl_3$).

Anal. Calcd for $C_{11}H_{16}Br_2O$: C, 40.77; H, 4.98. Found: C, 40.81; H, 4.94.

(2*R*,4*S*,5*S*)-4-[2-(*tert*-Butyldimethylsiloxy)ethyl]-5-[[(1*R*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]hept-1-yl]ethynyl]-2-phenyl-*m*-dioxan-5-ol (46). Into a solution of **45** (4.31 g, 13.4 mmol) in THF (30 mL) at −78 °C was introduced a solution of *n*-butyllithium (25.1 mL of 1.6 M in hexanes, 40.2 mmol). The mixture was stirred at −78 °C for 1 h and cannulated into a stirred suspension of **41** (3.0 g, 8.93 mmol) and anhydrous cerium trichloride [prepared from cerium trichloride heptahydrate (16.6 g, 44.6 mol)] in THF (100 mL) at −78 °C. The mixture was allowed to warm to 20 °C overnight. After being returned to −78 °C, the mixture was quenched with saturated NH_4Cl solution, and the white suspension was warmed to room temperature and diluted with ether and water. The solid was removed by filtration through a pad of Celite. The aqueous phase was extracted with ether (2×) and the combined organic solutions were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 25% ethyl acetate in hexanes) gave diol **46** (2.90 g, 65%) as the major product: white solid, mp 92−94 °C; IR (film, cm^{-1}) 3401, 1737; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50−7.31 (m, 5 H), 5.57 (s, 1 H), 4.19 (d, *J* = 11.5 Hz, 1 H), 4.11 (dd, *J* = 9.5, 2.2 Hz, 1 H), 4.02 (d, *J* = 11.5 Hz, 1 H), 3.81−3.74 (m, 3 H), 3.72 (s, 1 H), 3.03 (br s, 1 H), 2.25−2.14 (m, 1 H), 2.01−1.70 (m, 7 H), 1.33−1.25 (m, 1 H), 1.18 (s, 3 H), 0.96 (s, 3 H), 0.91 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.6, 129.0, 128.2 (2 C), 125.9 (2 C), 101.5, 87.6, 81.9, 79.9, 78.0, 76.1, 66.0, 58.3, 50.5, 49.7, 44.0, 39.5, 32.7, 32.6, 27.2, 25.9 (3 C), 21.1, 20.4, 18.3, −5.3, −5.5; HRMS *m/z* (M^+ − ^{t}Bu − H_2O) calcd for $C_{25}H_{33}O_4Si$ 425.2148, obsd 425.2150; $[\alpha]^{20}_D$ −22.8 (*c* 1.76, $CHCl_3$).

Anal. Calcd for $C_{29}H_{44}O_5Si$: C, 69.56; H, 8.86. Found: C, 69.65; H, 8.92.

(2*R*,4*S*,5*S*)-4-[2-(*tert*-Butyldimethylsiloxy)ethyl]-5-[(*E*)-2-[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]hept-1-yl]vinyl]-2-phenyl-*m*-dioxan-5-ol (47). A solution of **46** (838 mg, 1.68 mmol)) in THF (15 mL) at 0 °C was treated with a solution of Red-Al (2.46 mL of 3.4 M in toluene, 8.38 mmol). The cooling bath was removed, and the mixture was stirred at 20 °C for another 2 h. After being returned to an ice−water bath, the mixture was quenched carefully with saturated NH_4Cl solution. The mixture was diluted with ether and water, solids were removed by filtration, and layers were separated. The aqueous phase was extracted with ether (5×), the combined organic solutions were dried and filtered, and the concentrate was chromatographed on silica gel (elution with 25% ethyl acetate in hexanes). There was obtained 639 mg (76%) of **47** as a colorless oil: IR (film, cm^{-1}) 3417, 1664; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53−7.30 (m, 5 H), 6.20 (d, *J* = 16.3 Hz, 1 H), 5.58 (s, 1 H), 5.30 (d, *J* = 16.3 Hz, 1 H), 4.03 (dd, *J* = 9.3, 2.3 Hz, 1 H), 3.93 (s, 2 H), 3.80−3.64 (m, 4 H), 2.93 (br s, 1 H), 1.90−1.71 (m, 7 H), 1.19 (s, 3 H), 1.14−1.01 (m, 2 H), 0.91 (s, 9 H), 0.80 (s, 3 H), 0.054 (s, 3 H), 0.046 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.9, 131.8, 128.8, 128.2, 128.1 (2 C), 125.9 (2 C), 101.3, 80.3, 79.1, 76.6, 70.7, 58.7, 54.9, 47.9, 45.5, 40.2, 31.6, 29.5, 27.0, 25.9 (3 C), 20.8, 20.3, 18.3, −5.3, −5.4; HRMS *m/z* (M^+ − $C_7H_7O_2$) calcd for $C_{22}H_{39}O_3Si$ 379.2668, obsd 379.2668; $[\alpha]^{20}_D$ −51.5 (*c* 4.34, $CHCl_3$).

(1*S*,4*R*)-1-[(*E*)-2-[(2*R*,4*S*,5*S*)-4-[2-(*tert*-Butyldimethylsiloxy)ethyl]-5-hydroxy-2-phenyl-*m*-dioxan-5-yl]vinyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-one (48). A solution of **47** (607 mg, 1.21 mmol) in CH_2Cl_2 (15 mL) was treated with the Dess−Martin periodinane (771 mg, 1.81 mmol), stirred for 1 h, diluted with ether, and filtered. The filtrate was washed with 1 N NaOH and brine, dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 20% ethyl acetate in hexanes) delivered **48** (491 mg, 81%) as a

colorless oil: IR (film, cm^{-1}) 3460, 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54−7.35 (m, 5 H), 5.94 (d, J = 16.2 Hz, 1 H), 5.57 (s, 1 H), 5.52 (dd, J = 16.2, 1.0 Hz, 1 H), 4.04 (t, J = 5.5 Hz, 1 H), 3.93 and 3.90 (ABq, J = 11.6 Hz, 2 H), 3.82−3.71 (m, 2 H), 3.12 (d, J = 0.9 Hz, 1 H), 2.44 (ddd, J = 18.3, 4.8, 2.2 Hz, 1 H), 2.14 (t, J = 3.9 Hz, 1 H), 2.05−1.79 (m, 5 H), 1.58−1.39 (m, 2 H), 0.96 (s, 3 H), 0.94 (s, 3 H), 0.90 (s, 9 H), 0.049 (s, 3 H), 0.046 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.2, 137.9, 131.0, 128.9, 128.2 (2 C), 126.8, 125.9 (2 C), 101.3, 79.4, 76.2, 70.4, 62.9, 58.7, 48.8, 43.6, 43.2, 31.9, 27.1 (2 C), 25.9 (3 C), 20.2, 19.5, 18.2, −5.3, −5.4; HRMS m/z ($M^+ - {}^t$Bu) calcd for $C_{25}H_{35}O_5Si$ 443.2254, obsd 443.2279; $[\alpha]^{20}_D$ +16.0 (c 3.94, $CHCl_3$).

Anal. Calcd for $C_{29}H_{44}O_5Si$: C, 69.56; H, 8.86. Found: C, 69.37; H, 8.79.

(1*S*,4*R*)-1-[(*E*)-2-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]vinyl]-7,7-dimethylbicyclo[2.2.1]heptan-2-one (49). To a suspension of potassium hydride (606 mg, 15.1 mmol) in dry THF (10 mL) at 0 °C was added a solution of **48** (3.78 g, 7.56 mol) in THF (10 mL). The mixture was stirred at 0 °C for 15 min, benzyl bromide (1.80 mL, 15.1 mol) and a catalytic amount of tetra-*n*-butylammonium iodide were added, and warming to 20 °C was effected. After 30 min, the mixture was recooled in an ice−water bath, quenched carefully with ethyl acetate followed by saturated NH_4Cl solution, and diluted with water and ether. The separated aqueous layer was extracted with ether, and the combined organic solutions were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 18% ethyl acetate in hexanes) furnished **49** (3.9 g, 83%) as a colorless oil: IR (film, cm^{-1}) 1742; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62−7.25 (m, 10 H), 5.84 (d, J = 16.4 Hz, 1 H), 5.64 (s, 1 H), 5.49 (d, J = 16.4 Hz, 1 H), 4.91 (d, J = 11.4 Hz, 1 H), 4.75 (d, J = 11.4 Hz, 1 H), 4.55 (d, J = 12.9 Hz, 1 H), 4.04 (dd, J = 11.4, 2.1 Hz, 1 H), 4.00 (d, J = 12.9 Hz, 1 H), 3.85−3.70 (m, 2H), 2.46 (ddd, J = 18.3, 4.7, 2.2 Hz, 1 H), 2.16 (t, J = 4.1 Hz, 1 H), 2.10−1.86 (m, 6 H), 1.61−1.42 (m, 1 H), 0.95 (s, 3 H), 0.92 (s, 12 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.2, 139.5, 138.4, 130.8, 128.7, 128.1 (2 C), 128.0 (3 C), 127.2 (2 C), 126.9, 126.3 (2 C), 101.5, 79.6, 74.5, 70.7, 65.6, 63.1, 58.9, 48.8, 43.6, 43.2, 31.2, 27.0, 26.9, 25.9 (3 C), 20.2, 19.5, 18.2, −5.3, −5.5; HRMS m/z (M^+) calcd for $C_{36}H_{50}O_5Si$ 590.3428, obsd 590.3466; $[\alpha]^{20}_D$ −13.8 (c 4.38, $CHCl_3$).

(1*S*,3*R*,4*S*)-1-[(*E*)-2-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]vinyl]-3-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-2-one (50). A solution of diisopropylamine (0.16 mL, 1.14 mmol) in THF (5 mL) at −78 °C was treated with a solution of *n*-butyllithium (0.71 mL of 1.6 M hexanes, 1.14 mmol) and later with a solution of **49** (380 mg, 0.64 mmol) in THF (4 mL). The mixture was stirred at −78 °C for another 1 h, and trimethylsilyl chloride (0.15 mL, 1.14 mmol) was introduced, followed by warming to 20 °C and further treatment with triethylamine (1 mL). The white suspension was diluted with ether and washed with saturated $NaHCO_3$ solution. The separated organic layer was dried, filtered, and concentrated. The silyl enol ether was dissolved in a mixture of water (10 mL), acetone (10 mL), and CH_2Cl_2 (10 mL). A catalytic amount of 18-crown-6 and solid $NaHCO_3$ (5.0 g, 59.5 mmol) were added, and the mixture was cooled to 0 °C. Oxone (4.67 g, 7.60 mmol) was introduced, the cooling bath was removed, and the mixture was stirred for another 1 h prior to dilution with water and CH_2Cl_2. The organic layer was extracted twice with ether, and the combined organic solutions were dried, filtered, and concentrated. The residue was dissolved in THF (10 mL), cooled to 0 °C, treated with TBAF (0.76 mL of 1.0 M in THF, 0.76 mmol), stirred at 0 °C for 1 h, and finally diluted with ether and water. The aqueous layer was extracted with ether, and the combined organic solutions were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 25% ethyl acetate in hexanes) gave **50** as a colorless oil: IR (film, cm^{-1}) 3442, 1750; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62−7.26 (m, 10 H), 5.93 (d, J = 16.5 Hz, 1 H), 5.69 (s, 1 H), 5.53 (d, J = 16.5 Hz, 1 H), 4.94 (d, J = 11.3 Hz, 1 H), 4.78 (d, J = 11.3 Hz, 1 H), 4.57 (d, J = 12.8 Hz, 1 H), 4.10−4.01 (m, 2 H), 3.88−3.74 (m, 3 H), 3.42 (br s, 1 H), 2.16−1.89 (m, 5 H), 1.59−1.39 (m, 2 H), 1.11 (s, 3 H), 0.95 (s, 9 H), 0.94 (s, 3 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.5, 139.5, 138.5, 131.2, 128.9, 128.3 (2 C), 128.2 (2 C), 127.6, 127.4 (2 C), 127.1, 126.4 (2 C), 101.7, 79.7, 77.6, 74.6, 70.8, 65.8, 62.4, 59.0, 49.6, 49.0, 31.3, 26.1 (3 C), 25.8, 25.1, 21.56, 20.6, 18.4, −5.2, −5.3; FAB MS m/z (M^+ + H) calcd 607.35, obsd 607.43; $[\alpha]^{20}_D$ +0.22 (c 2.67, $CHCl_3$).

(1*S*,3*R*,4*S*)-1-[(*E*)-2-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]vinyl]-3-(methoxymethoxy)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (51). A solution of **50** (190 mg, 0.31 mmol) in CH_2Cl_2 (5 mL) at 0 °C was treated with diisopropylethylamine (0.32 mL, 1.84 mmol) and MOM chloride (0.084 mL, 1.11 mmol). The cooling bath was removed, and the mixture was stirred overnight, quenched with saturated $NaHCO_3$ solution, and diluted with ether. The separated aqueous phase was extracted with ether. The combined organic solutions were dried, filtered, and freed of solvent to leave a residue that was chromatographed on silica gel. Elution with 18% ethyl acetate in hexanes delivered **51** as a colorless oil (160 mg, 79%): IR (film, cm^{-1}) 1755; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.26 (m, 10 H), 5.90 (d, J = 16.5 Hz, 1 H), 5.66 (s, 1 H), 5.51 (d, J = 16.5 Hz, 1 H), 4.92 (d, J = 11.3 Hz, 1 H), 4.87 (d, J = 6.6 Hz, 1 H), 4.76 (d, J = 11.3 Hz, 1 H), 4.75 (d, J = 6.6 Hz, 1 H), 4.55 (d, J = 12.9 Hz, 1 H), 4.06−4.02 (m, 1 H), 4.00 (d, J = 13.0 Hz, 1 H), 3.74 (s, 1 H), 3.82−3.45 (m, 2 H), 3.44 (s, 3 H), 2.20 (d, J = 4.4 Hz, 1 H), 2.10−1.92 (m, 4 H), 1.56−1.46 (m, 2 H), 1.10 (s, 3 H), 0.94 (s, 3 H), 0.93 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 214.6, 139.4, 138.4, 131.1, 128.7, 128.1 (2 C), 128.0 (2 C), 127.5, 127.2 (2 C), 126.9, 126.2 (2 C), 101.5, 96.6, 81.2, 79.5, 74.5, 70.7, 65.6, 62.2, 58.9, 55.5, 48.7, 48.4, 31.2, 25.9 (4 C), 24.9, 21.3, 20.3, 18.2, −5.3, −5.5; FAB MS m/z (M^+ + H) calcd for $C_{38}H_{55}O_7Si$ 651.19, obsd 651.33; $[\alpha]^{20}_D$ +16.2 (c 5.98, $CHCl_3$).

(1*S*,2*S*,3*R*,4*S*)-1-[(*E*)-2-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]-vinyl]-3-(methoxymethoxy)-7,7-dimethyl-2-[(*E*)-1-propenyl]bicyclo[2.2.1]heptan-2-ol (52). To a solution of *trans*-1-bromo-1-propene (0.20 mL, 2.36 mmol) in THF (5 mL) at −78 °C under N_2 was added *tert*-butyllithium (2.70 mL, 4.72 mmol), and the mixture was stirred at −78 °C for 15 min. A solution of **51** (428 mg, 0.66 mmol) in THF (5 mL) was introduced, and the reaction mixture was stirred at −78 °C for another 30 min, quenched with saturated $NaHCO_3$ solution, and diluted with ether. The separated aqueous layer was extracted with ether, and the combined organic solutions were dried, filtered, and concentrated. Purification of the residue on silica gel (elution with 18% ethyl acetate in hexanes) afforded **52** (393 mg, 86%) as a colorless oil: IR (film, cm^{-1}) 3533; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57−7.22 (m, 10 H), 6.12 (d, J = 16.8 Hz, 1 H), 5.71 (dq, J = 15.3, 6.4 Hz, 1 H), 5.63 (s, 1 H), 5.54 (dd, J = 15.4, 1.2 Hz, 1 H), 5.20 (d, J = 16.7 Hz, 1 H), 4.79 (d, J = 11.3 Hz, 1 H), 4.71 (s, 2 H), 4.65 (d, J = 11.2 Hz, 1 H), 4.48 (d, J = 12.8 Hz, 1 H), 4.00 (d, J = 12.8 Hz, 1 H), 3.98 (dd, J = 9.9, 2.2 Hz, 1 H), 3.82−3.71 (m, 2 H), 3.69 (s, 1 H), 3.39 (s, 3 H), 2.94 (s, 1 H), 2.09−1.91 (m, 2 H), 1.95 (d, J = 5.1 Hz, 1 H), 1.89−1.74 (m, 1 H), 1.71 (dd, J = 6.3, 1.0 Hz, 3 H), 1.60−1.49 (m, 1 H), 1.49−1.35 (m, 1 H), 1.32 (s, 3 H), 1.12−1.03 (m, 1 H), 0.89 (s, 9 H), 0.79 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 139.7, 138.6, 135.6, 131.4, 129.4, 128.7, 128.1 (2 C), 128.0 (2 C), 127.5 (2 C), 127.0, 126.3 (2 C), 124.4, 101.5, 97.1, 88.2, 82.3, 80.3, 74.6, 70.6, 65.4, 59.1, 58.8, 55.6, 50.6, 50.5, 31.1, 26.3, 26.0 (3 C), 24.2, 22.6, 22.2, 18.3, 18.0, −5.3, −5.4; FAB MS m/z (M^+ + H) calcd for $C_{41}H_{61}O_7Si$ 693.42, obsd 693.44; $[\alpha]^{20}_D$ −11.7 (c 1.54, $CHCl_3$).

(1*S*,2*R*,5*R*,6*S*,7*E*)-6-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]-4-hydroxy-2-(methoxymethoxy)-5,11,11-trimethylbicyclo-[6.2.1]undec-7-en-3-one (53). To a solution of **52** (48 mg, 0.069 mmol) and 18-crown-6 (38 mg, 0.14 mmol) in THF (5 mL) at −78 °C under oxygen was added a solution of triphenylphosphine (18 mg, 0.069 mmol) in THF (0.2 mL). The

solution was transferred to a beaker of cold silica gel, suction filtered, and washed with ether. The filtrate was concentrated and chromatographed (silica gel, elution with 33% ethyl acetate in hexanes). After the recovery of unreacted **52** (8 mg, 17%), there was obtained 35 mg (72%; 81% based on recovered **52**) of **53** as a colorless oil: IR (film, cm^{-1}) 3406, 1706; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53−7.20 (m, 10 H), 5.59 (s, 1 H), 5.14 (d, J = 11.7 Hz, 1 H), 5.07 (d, J = 7.1 Hz, 1 H), 5.06 (d, J = 11.7 Hz, 1 H), 4.64 (d, J = 6.7 Hz, 1 H), 4.48 (d, J = 13.1 Hz, 1 H), 4.43 (d, J = 6.7 Hz, 1 H), 4.36 (dd, J = 10.2, 1.6 Hz, 1 H), 4.26 (d, J = 13.1 Hz, 1 H), 4.18 (d, J = 2.0 Hz, 1 H), 3.88 (dt, J = 10.0, 4.1 Hz, 1 H), 3.79−3.73 (m, 1 H), 3.43 (t, J = 10.3 Hz, 1 H), 3.37 (s, 3 H), 2.62 (q, J = 10.2 Hz, 1 H), 2.57−2.26 (m, 4 H), 2.22 (dd, J = 8.2, 1.8 Hz, 1 H), 2.15−2.11 (m, 1 H), 2.06−1.96 (m, 1 H), 1.77−1.68 (m, 1 H), 1.52 (d, J = 11.3 Hz, 1 H), 1.38 (d, J = 6.3 Hz, 3 H), 1.21 (s, 3 H), 1.09 (s, 3 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 208.5, 145.3, 140.0, 138.4, 128.8, 128.2 (2 C), 128.0, 127.1 (2 C), 126.9, 126.2, 125.7 (2 C), 101.0, 95.3, 86.2, 79.2, 76.8, 74.3, 70.9, 67.9, 58.8, 55.7, 53.2, 47.5, 45.6, 39.1, 32.1, 26.0 (3 C), 25.9, 25.6, 23.7, 20.3, 19.4, 18.4, −5.3, −5.4; FAB MS m/z (M^+ + H) calcd for $C_{41}H_{61}O_8Si$ 709.41, obsd 709.60; $[\alpha]^{20}_D$ −89.7 (c 1.38, $CHCl_3$).

(1*S*,2*R*,5*R*,6*S*,7*E*)-6-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[2-(*tert*-butyldimethylsiloxy)ethyl]-2-phenyl-*m*-dioxan-5-yl]-2-(methoxymethoxy)-5,11,11-trimethylbicyclo[6.2.1]undec-7-ene-3,4-dione (54). Oxalyl chloride (0.81 mL of 0.68 M in CH_2Cl_2, 0.56 mmol) was added to a solution of dimethyl sulfoxide (0.81 mL of 1.38 M in CH_2Cl_2, 1.12 mmol) at −78 °C, followed 10 min later by a solution of **53** (132 mg, 0.19 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred at −78 °C for 1 h, at which point a solution of triethylamine (0.30 mL, 2.27 mmol) in CH_2Cl_2 (1 mL) was introduced. The mixture was allowed to warm to 20 °C and diluted with ether and brine. The separated organic layer was extracted with ether, and the combined organic phases were dried, filtered, and concentrated. Chromatography of the residue on silica gel (elution with18% ether in hexanes) gave **54** as a yellowish oil (108 mg, 82%): IR (film, cm^{-1}) 1699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54−7.22 (m, 10 H), 5.59 (s, 1 H), 5.43 (d, J = 10.4 Hz, 1 H), 5.15 (d, J = 11.6 Hz, 1 H), 5.08 (d, J = 11.6 Hz, 1 H), 4.69 (s, 1 H), 4.67 (d, J = 6.9 Hz, 1 H), 4.52 (d, J = 13.0 Hz, 1 H), 4.47 (d, J = 6.8 Hz, 1 H), 4.38 (dd, J = 9.9, 1.5 Hz, 1 H), 4.22 (d, J = 13.0 Hz, 1 H), 3.93−3.74 (m, 2 H), 3.38 (s, 3 H), 2.80 (t, J = 10.5 Hz, 1 H), 2.26−1.98 (m, 7 H), 1.75−1.65 (m, 1 H), 1.32 (d, J = 3.3 Hz, 3 H), 1.20 (s, 3 H), 1.08 (s, 3 H), 0.92 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.5, 201.2, 146.4, 139.6, 138.3, 128.9, 128.2 (2 C), 128.1 (2 C), 127.1 (2 C), 127.0, 126.2 (2 C), 123.6, 101.0, 95.8, 82.9, 78.9, 74.1, 71.0, 67.9, 58.7, 55.8, 53.9, 46.7, 45.9, 39.7, 32.5, 26.2, 26.0 (3 C), 24.6, 23.5, 20.7, 18.3, 15.7, −5.3, −5.5; FAB MS m/z (M^+ + H) calcd for $C_{41}H_{59}O_8Si$ 707.40, obsd 707.47; $[\alpha]^{20}_D$ −38.3 (c 2.65, $CHCl_3$).

(1*S*,2*R*,5*R*,6*S*,7*E*)-6-[(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-(2-hydroxyethyl)-2-phenyl-*m*-dioxan-5-yl]-2-(methoxymethoxy)-5,11,11-trimethylbicyclo-[6.2.1]undec-7-ene-3,4-dione (55). To a solution of **54** (273 mg, 0.39 mmol) in acetonitrile (10 mL) at 0 °C was added 1.0 mL of hydrogen fluoride−pyridine. The mixture was stirred at 0 °C for 15 min, quenched with solid $NaHCO_3$, and diluted with water and ether. The separated aqueous phase was extracted with ether, and the combined organic solutions were dried, filtered, and chromatographed on silica gel (elution with 50% ethyl acetate in hexanes) to provide **55** as a yellow oil (185 mg, 85%): IR (film, cm^{-1}) 3440, 1698; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52−7.23 (m, 10 H), 5.62 (s, 1 H), 5.42 (d, J = 10.3 Hz, 1 H), 5.17 (d, J = 11.3 Hz, 1 H), 5.02 (d, J = 11.3 Hz, 1 H), 4.68 (d, J = 6.6 Hz, 1 H), 4.66 (d, J = 11.8 Hz, 1 H), 4.63−4.39 (m, 3 H), 4.12 (d, J = 13.1 Hz, 1 H), 3.94−3.81 (m, 3 H), 3.36 (s, 3 H), 2.73 (t, J = 10.6 Hz, 1 H), 2.30−1.93 (m, 7 H), 1.74−1.67 (m, 1 H), 1.28 (d, J = 6.6 Hz, 3 H), 1.20 (s, 3 H), 1.08 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.6, 201.5, 147.2, 139.2, 137.9, 129.1, 128.4 (2 C), 128.2 (2 C), 127.22 (2 C), 127.17, 126.1 (2 C), 123.2, 101.0, 95.8, 82.8, 81.4, 73.9, 71.4, 67.7, 60.1, 55.8, 53.8, 46.7, 46.0, 39.8, 32.6, 26.3, 24.6, 23.5, 20.7, 15.8; FAB MS m/z (M^+ + H) calcd for $C_{35}H_{45}O_8$ 593.31, obsd 593.41; $[\alpha]^{20}_D$ −50.7 (c 0.91, $CHCl_3$).

(2*R*,4*S*,5*S*)-5-(Benzyloxy)-4-[(1*E*,3*S*,4*R*,7*R*,8*S*)-7-(methoxymethoxy)-4,11,11-trimethyl-5,6-dioxobicyclo-[6.2.1]-undec-1-en-3-yl]-2-phenyl-*m*-dioxane-4-acetaldehyde (56). A solution of **55** (92 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) was treated with the Dess−Martin periodinane (99 mg, 0.23 mmol), stirred for 30 min, and diluted with ether. The solid was filtered, and the filtrate was concentrated. Chromatography on silica gel (elution with 18% ethyl acetate in hexanes) furnished **56** as a yellow oil (81 mg, 89%): IR (film, cm^{-1}) 1727, 1698; ^1H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1 H), 7.49−7.27 (10 H), 5.64 (s, 1 H), 5.45 (d, J = 10.3 Hz, 1 H), 5.14 (d, J = 11.3 Hz, 1 H), 5.04 (d, J = 11.3 Hz, 1 H), 4.71−4.61 (m, 4 H), 4.58 (d, J = 13.1 Hz, 1 H), 4.46 (d, J = 6.8 Hz, 1 H), 4.15 (d, J = 13.0 Hz, 1 H), 3.91−3.81 (m, 1 H), 3.36 (s, 3 H), 2.99−2.95 (m, 2 H), 2.66 (t, J = 10.4 Hz, 1 H), 2.27−2.08 (m, 2 H), 2.02−1.90 (m, 1 H), 1.74−1.60 (m, 1 H), 1.27 (d, J = 6.5 Hz, 3 H), 1.19 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.3, 201.1, 199.6, 147.5, 138.9, 137.6, 129.2, 128.4 (2 C), 128.3 (2 C), 127.3, 127.2 (2 C), 126.2 (2 C), 122.9, 101.1, 95.8, 82.8, 78.0, 73.9, 71.5, 67.8, 55.8, 53.8, 47.0, 46.1, 44.9, 39.2, 26.2, 24.6, 23.6, 20.6, 15.9; FAB MS m/z (M^+ + H) calcd for $C_{35}H_{43}O_8$ 591.30, obsd 591.18; $[\alpha]^{20}_D$ −49.6 (c 0.66, $CHCl_3$).

(3*R*,4a*R*,6*R*,6a*R*,9*R*,10*S*,13*E*,14a*S*,14b*S*)-14b-(Benzyloxy)-4a,5,6,6a,9,10,11,12,14a,14b-decahydro-6-hydroxy-9-(methoxymethoxy)-6a,15,15-trimethyl-3-phenyl-10,13-methano-1*H*-cyclodeca[*f*][1,3]-benzodioxin-7,8-dione Acetate (58). To a solution of tetra-*n*-butylammonium fluoride (0.5 mL, 0.5 mmol) in acetonitrile (1.0 mL) was added a solution of **56** (10 mg, 0.017 mg, 0.017 mol) in acetonitrile. The resulting solution was immediately diluted with ether, and the mixture was washed with saturated NH_4Cl solution. The aqueous phase was extracted with ether, dried, and filtered. Solvent evaporation furnished the aldol product as a yellow oil: IR (film, cm^{-1}) 3424, 1687; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53−7.27 (m, 10 H), 5.66 (s, 1 H), 5.42 (d, J = 11.5 Hz, 1 H), 5.02 (ddd, J = 12.1, 5.6, 4.1 Hz, 1 H), 4.81 (d, J = 10.5 Hz, 1 H), 4.67 (d, J = 6.8 Hz, 1 H), 4.66 (s, 1 H), 4.58 (d, J = 10.5 Hz, 1 H), 4.44 (d, J = 6.8 Hz, 1 H), 4.26 (dd, J = 12.1, 3.9 Hz, 1 H), 4.22 (d, J = 12.6 Hz, 1 H), 3.76 (d, J = 12.7 Hz, 1 H), 3.38 (s, 3 H), 3.21 (d, J = 11.6 Hz, 1 H), 2.69 (d, J = 5.9 Hz, 1 H), 2.43 (q, J = 12.1 Hz, 1 H), 2.31−2.18 (m, 4 H), 2.06 (dt, J = 11.8, 3.9 Hz, 1 H), 1.78−1.71 (m, 1 H), 1.46 (s, 3 H), 1.18 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 204.1, 202.3, 152.0, 138.3, 137.8, 192.2, 128.4 (2 C), 128.2 (2 C), 127.7 (2 C), 127.3, 126.5 (2 C), 117.0, 102.3, 96.1, 84.2, 78.2, 71.9, 68.5, 67.1, 64.1, 58.0, 55.9, 55.2, 46.0, 44.2, 30.7, 26.2, 24.7, 24.0, 21.1, 16.0; FAB MS m/z (M^+ + H) calcd for $C_{35}H_{43}O_8$ 591.30, obsd 591.37; $[\alpha]^{20}_D$ +8.1 (c 0.37, $CHCl_3$).

The unpurified aldol from above was dissolved in CH_2Cl_2 and treated with triethylamine (0.40 mL, 0.28 mmol), acetic anhydride (0.021 mL, 0.14 mmol), and a catalytic amount of DMAP. The mixture was stirred for 3 h and diluted with CH_2Cl_2 and saturated NH_4Cl solution. The separated aqueous phase was extracted with CH_2Cl_2, and the combined organic solutions were dried, filtered, and evaporated. The residue was chromatographed on silica gel (elution with 25% ethyl acetate in hexanes) to give **58** as a yellow oil (5 mg, 47% for 2 steps): IR (film, cm^{-1}) 1742, 1693; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.27 (m, 10 H), 6.08 (dd, J = 11.7, 4.2 Hz, 1 H), 5.65 (s, 1 H), 5.41 (d, J = 11.7 Hz, 1 H), 4.83 (d, J = 10.4 Hz, 1 H), 4.65−4.56 (m, 3 H), 4.37 (d, J = 6.9 Hz, 1 H), 4.33 (dd, J = 11.8, 4.0 Hz, 1 H), 4.22 (d, J = 12.7 Hz, 1 H), 3.79 (d, J = 12.8 Hz, 1 H), 3.35 (s, 3 H), 3.23 (d, J = 11.6 Hz, 1 H), 2.43−2.13 (m, 6 H), 1.91 (s, 3 H), 1.76−1.65 (m, 1 H), 1.53 (s, 3 H), 1.18 (s, 3 H), 1.08 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 203.0, 199.7, 169.9, 152.2, 138.3, 137.8, 129.2, 128.4 (2 C), 128.3 (2 C), 127.8 (2 C), 127.4, 126.4 (2 C), 117.3, 102.3, 95.9, 83.7, 77.1, 71.8, 70.9, 68.5, 64.3, 55.8, 55.2, 54.9, 46.2, 44.7, 27.5, 26.4, 24.7, 24.0, 21.1, 20.7, 17.6; FAB MS m/z (M^+ + H) calcd for $C_{37}H_{45}O_9$ 633.31, obsd 633.23; $[\alpha]^{20}_D$ +21.6 (c 0.19, $CHCl_3$).

Ethyl 2-*C*-(Hydroxymethyl)-3-*O*-(*p*-methoxybenzyl)-D-arabinofuranoside (59). Diol **15** (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 evaporated, and the residue was purified by chromatography on silica gel (elution with 60% ethyl acetate in hexanes) to furnish **59** (7.43 g, 83%) as an oily mixture of anomers.

α-Anomer: IR (film, cm^{-1}) 3444, 1614; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 4.93 (s, 1 H), 4.70 (d, J = 11.3 Hz, 1 H), 4.51 (d, J = 11.3 Hz, 1 H), 4.10 (d, J = 6.6 Hz, 1 H), 3.99−3.95 (m, 1 H), 3.96 (d, J = 12.1 Hz, 1 H), 3.87 (dq, J = 9.8, 7.1 Hz, 1 H), 3.79 (s, 3H), 3.72−3.68 (m, 1 H), 3.69 (d, J = 12.1 Hz, 1 H), 3.62 (dq, J = 9.8, 7.1 Hz, 1 H), 3.52 (dd, J = 11.9, 4.3 Hz, 1 H), 2.51 (br s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.4, 129.6, 129.4 (2 C), 113.9 (2 C), 102.9, 83.3, 82.2, 81.4, 72.7, 65.1, 63.2, 62.4, 55.3, 15.2; $[\alpha]^{20}_D$ −8.52 (*c* 1.59, $CHCl_3$).

***β*-Anomer:** ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 4.87 (s, 1 H), 4.62 (d, J = 11.8 Hz, 1 H), 4.52 (d, J = 11.8 Hz, 1 H), 4.13 (ddd, J = 4.7, 2.7, 2.7 Hz, 1 H), 3.93 (d, J = 12.0 Hz, 1 H), 3.88 (d, J = 12.0 Hz, 1 H), 3.79 (s, 3 H), 3.83−3.72 (series of m, 3 H), 3.50 (dq, J = 9.8, 7.0 Hz, 1 H), 3.45 (dd, J = 11.9, 2.8 Hz, 1 H), 2.81 (br s, 3 H), 1.20 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 159.4, 129.9, 129.5 (2 C), 113.9 (2 C), 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 $C_{16}H_{24}O_7$ 328.1522, obsd 328.1511; $[\alpha]^{20}_D$ +90.0 (*c* 0.66, $CHCl_3$).

Anal. Calcd for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.27; H, 7.31.

(2*S*,4a*S*,7*S*,7a*R*)-5-Ethoxydihydro-7-(iodomethyl)-2-(*p*-methoxyphenyl)-4*H*-furo[3,4-*d*]-*m*-dioxin-4a(5*H*)-ol (61). A mixture of **59** (7.10 g, 21.6 mmol) and 3 Å molecular sieves in CH_2Cl_2 (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 and filtered through Celite into saturated $NaHCO_3$ and $Na_2S_2O_7$ solutions. The organic layer was separated, dried, and concentrated to leave a crude solid, which was purified (chromatography on silica gel, elution with 50% ethyl acetate in hexanes) to yield unreacted **59** (0.96 g, 14%) together with **60** (4.31 g, 61%) as a white amorphous solid, which was used immediately in the next step.

Diol **60** (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 yellow oil, which was purified by silica gel chromatography (elution with 10−25% ethyl acetate in hexanes) to provide α-**61** (2.95 g, 27%) and *β*-**61** (7.83 g, 71%) as colorless oils.

α-Anomer: IR (film, cm^{-1}) 3460, 1684, 1614; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, J = 8.7 Hz, 2 H), 6.89 (d, J = 8.7 Hz, 2 H), 5.51 (s, 1 H), 5.03 (s, 1 H), 4.38 (d, J = 12.0 Hz, 1 H), 4.28 (ddd, J = 5.3, 5.3, 3.0 Hz, 1 H), 3.94 (d, J = 2.8 Hz, 1 H), 3.85 (d, J = 12.0 Hz, 1 H), 3.86−3.81 (m, 1 H), 3.80 (s, 3H), 3.56 (dq, J = 7.0, 7.0 Hz, 1 H), 3.51 (dd, J = 10.6, 5.8 Hz, 1 H), 3.43 (dd, J = 10.6, 4.9 Hz, 1 H), 2.49 (br s, 1 H), 1.27 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 160.0, 130.1, 127.6 (2 C), 113.6 (2 C), 109.0, 98.3, 84.9, 83.0, 82.9, 67.3, 63.5, 55.2, 15.0, 7.38; $[\alpha]^{20}_D$ +89.1 (*c* 1.42, $CHCl_3$).

***β*-Anomer:** ^1H NMR (300 MHz, C_6D_6) δ 7.47 (d, J = 8.7 Hz, 2 H), 6.80 (d, J = 8.8 Hz, 2 H), 5.45 (s, 1 H), 5.19 (s, 1 H), 4.46 (dd, J = 9.6, 6.3 Hz, 1 H), 4.30 (s, 1 H), 3.84 (d, J = 11.6 Hz, 1 H), 3.64 (d, J = 11.6 Hz, 1 H), 3.71−3.61 (m, 1 H), 3.36 (dd, J = 9.7 Hz, 1 H), 3.26 (s, 3 H), 3.30−3.24 (m, 1 H), 3.20 (dd, J = 9.7, 6.3 Hz, 1 H), 3.01 (s, 1 H), 0.90 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) 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 *m*/*z* (M^+) calcd for $C_{16}H_{21}IO_6$ 436.0383, obsd 436.0389; $[\alpha]^{20}_D$ +11.6 (*c* 1.71, $CHCl_3$).

Anal. Calcd for $C_{16}H_{21}IO_6$: C, 44.05; H, 4.85. Found: C, 43.93; H, 4.80.

[2-[[[(2*S*,4a*S*,7*S*,7a*R*)-5-Ethoxydihydro-7-(iodomethyl)-2-(*p*-methoxyphenyl)-4*H*-furo[3,4-*d*]-*m*-dioxin-4a(5*H*)-yl]-oxy]methoxy]ethyl]trimethylsilane (62). Sodium hydride (107 mg, 4.45 mmol) was added in several portions to a solution of **61** (971 mg, 2.23 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride (985 μL, 5.56 mmol) in THF (20 mL). The mixture was stirred for 40 min in advance of the careful addition of water. The reaction mixture was extracted with ether, and the combined organic layers were dried in the presence of triethylamine. The ethereal solution was concentrated to a total volume of 10 mL, treated with triethylamine, filtered through silica gel, treated again with triethylamine, and finally fully concentrated and chromatographed (silica gel, elution with 5% ethyl acetate in hexanes) to furnish the SEM derivatives as a colorless oil (1.00 g, 80%).

α-Anomer: IR (film, cm^{-1}) 1615; ^1H NMR (300 MHz, C_6D_6) δ 7.56 (d, J = 8.7 Hz, 2 H), 6.81 (d, J = 8.7 Hz, 2 H), 5.60 (s, 1 H), 5.41 (s, 1 H), 4.64 (d, J = 7.7 Hz, 1 H), 4.61 (d, J = 7.7 Hz, 1 H), 4.54 (d, J = 12.1 Hz, 1 H), 4.45 (ddd, J = 6.7, 6.7, 3.2 Hz, 1 H), 4.18 (d, J = 3.2 Hz, 1 H), 4.06 (d, J = 12.1 Hz, 1 H), 3.77 (dq, J = 9.6, 7.0 Hz, 1 H), 3.63 (ddd, J = 8.5, 8.5, 1.4 Hz, 2 H), 3.31 (dq, J = 9.6, 7.0 Hz, 1 H), 3.25 (s, 3 H), 3.21 (dd, J = 7.0, 2.0 Hz, 2 H), 1.09 (t, J = 7.0 Hz, 3 H), 0.93 (dd, J = 8.8, 7.8 Hz, 2 H), −0.0090 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 160.6, 131.6, 127.8 (2 C), 113.8 (2 C), 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; $[\alpha]^{20}_D$ +58.2 (*c* 1.31, $CHCl_3$).

***β*-Anomer:** ^1H NMR (300 MHz, C_6D_6) δ 7.49 (d, J = 8.7 Hz, 2 H), 6.81 (d, J = 8.7 Hz, 2 H), 5.60 (s, 1 H), 5.35 (s, 1 H), 5.16 (d, J = 7.5 Hz, 1 H), 4.73 (d, J = 7.5 Hz, 1 H), 4.46 (dd, J = 9.9, 6.0 Hz, 1 H), 4.41 (d, J = 11.7 Hz, 1 H), 4.38 (s, 1 H), 4.26 (d, J = 11.7 Hz, 1 H), 3.87−3.72 (series of m, 2 H), 3.57 (dd, J = 9.7, 9.7 Hz, 1 H), 3.52−3.44 (m, 1 H), 3.32 (dd, J = 9.5, 5.9 Hz, 1 H), 3.26 (s, 3 H), 3.31−3.23 (m, 1 H), 0.98 (t, J = 7.1 Hz, 3 H), 0.95−0.92 (m, 2 H), 0.011 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 160.9, 130.9, 128.0 (2 C), 114.1 (2 C), 106.8, 100.2, 92.2, 84.8, 84.1, 76.1, 67.2, 66.6, 66.1, 55.0, 18.6, 15.7, 6.78, −0.99 (3 C); HRMS *m*/*z* (M^+) calcd for $C_{22}H_{35}IO_7Si$ 566.1197, obsd 566.1205; $[\alpha]^{20}_D$ −83.9 (*c* 0.93, $CHCl_3$).

Anal. Calcd for $C_{22}H_{35}IO_7Si$: C, 46.64; H, 6.23. Found: C, 46.71; H, 6.18.

A solution of iodide anomers (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 wash), concentrated, and chromatographed (silica gel, elution with 5% ethyl acetate in hexanes) to provide **62** as a colorless oil (291 mg, 75%): IR (film, cm^{-1}) 1732, 1616; ^1H NMR (300 MHz, C_6D_6) δ 10.1 (s, 1 H), 7.49 (d, J = 8.7 Hz, 2 H), 6.80 (d, J = 8.7 Hz, 2 H), 6.24 (ddd, J = 17.3, 11.0, 4.0 Hz, 1 H), 5.55 (ddd, J = 17.4, 1.8, 1.8 Hz, 1 H), 5.41 (s, 1 H), 5.16 (ddd, J = 10.9, 1.8, 1.8 Hz, 1 H), 4.74 (d, J = 7.6 Hz, 1 H), 4.65 (d, J = 11.3 Hz, 1 H), 4.57 (d, J = 7.6 Hz, 1 H), 4.30 (ddd, J = 3.8, 1.8, 1.8 Hz, 1 H), 3.78 (d, J = 11.3 Hz, 1 H), 3.64 (ddd, J = 9.4, 9.4, 7.1 Hz, 1 H), 3.44 (ddd, J = 9.4, 9.4, 7.1 Hz, 1 H), 3.26 (s, 3 H), 0.87−0.82 (m, 2 H), −0.033 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 200.5, 160.7, 131.9, 130.5, 128.2 (2 C), 117.5, 113.9 (2 C), 102.0, 91.5, 81.6, 75.7, 71.0, 65.9, 54.8, 18.2, −1.41 (3 C); HRMS *m*/*z* (M^+) calcd for $C_{20}H_{30}O_6Si$ 394.1812, obsd 394.1792; $[\alpha]^{20}_D$ −24.2 (*c* 0.38, $CHCl_3$).

[2-[[[(2*S*,4*R*,5*S*)-5-[(*Z*)-2-Iodovinyl]-2-(*p*-methoxyphenyl)-4-vinyl-*m*-dioxan-5-yl]oxy]methoxy]ethyl]trimethylsilane (63). 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 of 1 M 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 **62** (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 on silica gel (elution with 3% ethyl acetate in hexanes) to yield **63** as a colorless oil (1.18 g, 72%): IR (film, cm^{-1}) 1616; ^1H NMR (300 MHz, C_6D_6) δ 7.53 (d, J = 8.7 Hz, 2 H), 6.84 (d, J = 9.0 Hz, 1 H), 6.81 (d, J = 8.7 Hz, 2 H), 6.48 (ddd, J = 17.3, 10.9, 4.0 Hz, 1 H), 6.29 (d, J = 9.0 Hz, 1 H), 5.61 (ddd, J = 17.3, 2.0, 2.0 Hz, 1 H), 5.43 (s, 1

H), 5.30 (ddd, J = 10.9, 1.9, 1.9 Hz, 1 H), 4.82 (d, J = 7.9 Hz, 1 H), 4.78 (d, J = 7.9 Hz, 1 H), 4.58 (d, J = 11.0 Hz, 1 H), 4.38−4.36 (m, 1 H), 3.94 (d, J = 11.0 Hz, 1 H), 3.81 (ddd, J = 9.6, 9.6, 6.4 Hz, 1 H), 3.50 (ddd, J = 9.4, 9.4, 7.1 Hz, 1 H), 3.27 (s, 3 H), 0.96−0.89 (m, 2 H), −0.0069 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 160.6, 136.9, 133.4, 130.9, 128.0 (2 C), 117.3, 113.8 (2 C), 101.7, 91.8, 83.6, 80.2, 75.8, 73.9, 66.0, 54.7, 18.3, −1.33 (3 C); HRMS m/z (M^+) calcd for $C_{21}H_{31}IO_5Si$ 518.0986, obsd 518.0951; $[\alpha]^{20}_D$ +31.6 (c 0.89, $CHCl_3$).

Anal. Calcd for $C_{21}H_{31}IO_5Si$: C, 48.65; H, 6.03. Found: C, 48.93; H, 6.04.

(1*S*,2*S*,3*R*,4*S*)-3-(Methoxymethoxy)-2-[(*Z*)-2-[(2*S*,4*R*,5*S*)-2-(*p*-methoxyphenyl)-5-[[2-(trimethylsilyl)ethoxy]-methoxy]-4-vinyl-*m*-dioxan-5-yl]vinyl]-7,7-dimethyl-1-vinylbicyclo[2.2.1]heptan-2-ol (64). A cold (−78 °C) solution of **63** (685 mg, 1.32 mmol) in dry ether (15 mL) was treated with *n*-butyllithium (0.90 of 1.6 M in pentane, 1.44 mmol) and stirred for 5 min prior to the addition of **22** (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 (silica gel, elution with 15% ethyl acetate in hexanes) to provide **64** as a colorless oil (564 mg, 76%): IR (film, cm^{-1}) 3400; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, J = 8.7 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 6.06 (dd, J = 17.7, 11.0 Hz, 1 H), 5.95 (ddd, J = 17.4, 10.9, 4.4 Hz, 1 H), 5.81 (d, J = 14.0 Hz, 1 H), 5.65 (d, J = 14.0 Hz, 1 H), 5.55 (s, 1 H), 5.46 (ddd, J = 17.4, 1.7, 1.7 Hz, 1 H), 5.28 (s, 1 H), 5.28 (ddd, J = 10.9, 1.7, 1.7 Hz, 1 H), 5.18 (dd, J = 11.0, 2.0 Hz, 1 H), 4.98 (dd, J = 17.7, 2.0 Hz, 1 H), 4.95 (d, J = 8.0 Hz, 1 H), 4.87 (d, J = 8.0 Hz, 1 H), 4.71 (d, J = 6.5 Hz, 1 H), 4.68 (d, J = 6.5 Hz, 1 H), 4.62 (ddd, J = 4.4, 1.8, 1.8 Hz, 1 H), 4.36 (d, J = 10.3 Hz, 1 H), 4.11 (d, J = 10.3 Hz, 1 H), 3.80 (s, 3 H), 3.78−3.63 (series of m, 3 H), 3.37 (s, 3 H), 1.94 (d, J = 5.0 Hz, 1 H), 1.80 (dddd, J = 12.4, 12.4, 3.4, 3.4 Hz, 1 H), 1.65 (ddd, J = 13.1, 13.1, 4.7 Hz, 1 H), 1.51−1.42 (m, 1 H), 1.38 (s, 3 H), 1.17−1.09 (m, 1 H), 0.96 (dd, J = 8.5, 8.5 Hz, 2 H), 0.78 (s, 3 H), 0.046 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 160.1, 138.5, 136.0, 133.2, 130.1, 127.6 (2 C), 126.8, 118.2, 116.3, 113.6 (2 C), 101.4, 96.6, 90.0 (2 C), 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 (3 C); HRMS m/z (M^+) calcd for $C_{34}H_{52}O_8Si$ 616.3431, obsd 616.3444; $[\alpha]^{20}_D$ −17.0 (c 0.92, $CHCl_3$).

Anal. Calcd for $C_{34}H_{52}O_8Si$: C, 66.20; H, 8.50. Found: C, 66.12; H, 8.54.

(1*S*,2*R*,4*S*,5*S*,7*E*)-2-(Methoxymethoxy)-5-[(2*S*,4*R*,5*S*)-2-(*p*-Methoxyphenyl)-5-[[2-(trimethylsilyl)ethoxy]methoxy]-4-vinyl-*m*-dioxan-5-yl]-4,11,11-trimethylbicyclo[6.2.1]-undec-7-en-3-one (65). A solution of **64** (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 0.5 M 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, which was purified via silica gel chromatography (elution with 15% ethyl acetate in hexanes) to furnish **65** as a colorless oil (115 mg, 53%): IR (film, cm^{-1}) 1709, 1615; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 6.23 (ddd, J = 17.3, 10.8, 4.6 Hz, 1 H), 5.58 (s, 1 H), 5.40 (d, J = 8.2 Hz, 1 H), 5.37 (ddd, J = 17.3, 1.7, 1.7 Hz, 1 H), 5.23 (dd, J = 11.3, 3.8 Hz, 1 H), 5.17 (ddd, J = 10.8, 1.7, 1.7 Hz, 1 H), 5.09 (d, J = 11.2 Hz, 1 H), 4.64 (d, J = 8.6 Hz, 1 H), 4.63 (d, J = 6.8 Hz, 1 H), 4.44−4.40 (m, 2 H), 4.38 (d, J = 6.8 Hz, 1 H), 4.07 (d, J = 1.6 Hz, 1 H), 3.91 (ddd, J = 11.1, 9.6, 5.7 Hz, 1 H), 3.79 (s, 3 H), 3.57 (ddd, J = 11.1, 9.7, 6.3 Hz, 1 H), 3.30 (s, 3H), 2.73 (dd, J = 7.6, 2.1 Hz, 1 H), 2.61−2.32 (series of m, 4 H), 2.20−2.09 (series of m, 3 H), 1.56 (ddd, J = 14.1, 9.6, 4.8 Hz, 1 H), 1.36 (d, J = 7.8 Hz, 3 H), 1.17 (s, 3 H), 1.05 (s, 3 H), 1.03−0.88 (m, 2 H), 0.050 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.8, 159.8, 146.6, 134.5, 130.7, 127.5 (2 C), 124.3, 114.6, 113.5 (2 C), 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 (2 C), 18.3, −1.40 (3 C); FAB MS m/z (M^+ + H) calcd for $C_{35}H_{55}O_8Si$ 631.37, obsd 631.34; $[\alpha]^{20}_D$ −70.0 (c 0.61, $CHCl_3$).

(1*S*,2*R*,4*S*,5*S*,7*S*,8*S*)-7,8-Dihydroxy-2-(methoxymethoxy)-5-[(2*S*,4*R*,5*S*)-2-(*p*-methoxyphenyl)-5-[[2-(trimethylsilyl)-ethoxy]methoxy]-4-vinyl-*m*-dioxan-5-yl]-4,11,11-trimethylbicyclo[6.2.1]undecan-3-one (66). Osmium tetraoxide (4.9 mg, 19 μmol) was added to a chilled (0 °C) solution of **65** (13 mg, 21 μmol) in pyridine (1 mL) and stirred for 2 h before being quenched with saturated $Na_2S_2O_4$ 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, which was subjected to flash chromatography (silica gel, elution with 30% ethyl acetate in hexanes). There was isolated **66** (5.2 mg, 41%) and some unreacted **65**.

66: colorless oil; IR (film, cm^{-1}) 3384, 1698, 1615; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.7 Hz, 2 H), 6.89 (d, J = 8.7 Hz, 2 H), 6.32 (ddd, J = 17.6, 11.0, 2.6 Hz, 1 H), 5.65 (s, 1 H), 5.56 (ddd, J = 17.6, 1.7, 1.7 Hz, 1 H), 5.38 (ddd, J = 11.0, 2.1, 2.1 Hz, 1 H), 4.91 (d, J = 8.1 Hz, 1 H), 4.85 (d, J = 8.1 Hz, 1 H), 4.72 (ddd, J = 2.6, 1.9, 1.9 Hz, 1 H), 4.48 (d, J = 6.9 Hz, 1 H), 4.32 (d, J = 11.9 Hz, 1 H), 4.31 (d, J = 6.9 Hz, 1 H), 4.22 (s, 1 H), 4.19 (d, J = 11.9 Hz, 1 H), 3.82 (s, 3 H), 3.71 (dd, J = 8.4 Hz, 2 H), 3.42 (br d, J = 11.4 Hz, 1 H), 3.23 (s, 3H), 3.18 (s, 1 H), 2.95 (q, J = 6.4 Hz, 1 H), 2.77 (d, J = 13.1 Hz, 1 H), 2.45−2.26 (series of m, 4 H), 2.04 (ddd, J = 12.6, 12.6, 2.4 Hz, 1 H), 1.85 (dd, J = 13.1, 13.1, 1.2 Hz, 1 H), 1.80−1.66 (series of m, 2 H), 1.29 (d, J = 6.4 Hz, 3 H), 1.05 (s, 3 H), 0.98 (s, 3 H), 0.96 (dd, J = 8.4 Hz, 2 H), 0.043 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.2, 160.0, 132.5, 129.8, 127.3 (2 C), 116.3, 113.5 (2 C), 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 (3 C); FAB MS m/z (M^+ + H) calcd for $C_{35}H_{57}O_{10}Si$ 665.37, obsd 665.38; $[\alpha]^{20}_D$ +17.8 (c 0.41, $CHCl_3$).

(1*S*,2*R*,4*S*,5*S*,7*S*,8*S*)-7-(*tert*-Butyldimethylsiloxy)-8-hydroxy-2-(methoxymethoxy)-5-[(2*S*,4*R*,5*S*)-2-(*p*-methoxyphenyl)-5-[[2-(trimethylsilyl)ethoxy]methoxy]-4-vinyl-*m*-dioxan-5-yl]-4,11,11-trimethylbicyclo[6.2.1]undecan-3-one (67). A solution of **66** (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 equiv of TBDMSCl and imidazole were next added, and 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 **67** as a colorless oil (23 mg, 73%) and 5.0 mg (19%) of unreacted **66**: IR (film, cm^{-1}) 3460, 1698, 1615; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.7 Hz, 2 H), 6.90 (d, J = 8.7 Hz, 2 H), 6.34 (ddd, J = 17.4, 11.0, 2.6 Hz, 1 H), 5.64 (s, 1 H), 5.57 (ddd, J = 17.4, 1.7, 1.7 Hz, 1 H), 5.42 (ddd, J = 11.0, 1.8, 1.8 Hz, 1 H), 4.93 (d, J = 8.1 Hz, 1 H), 4.86 (d, J = 8.1 Hz, 1 H), 4.70 (ddd, J = 2.3, 2.3, 2.3 Hz, 1 H), 4.49 (d, J = 6.9 Hz, 1 H), 4.31 (d, J = 6.9 Hz, 1 H), 4.28 (d, J = 12.0 Hz, 1 H), 4.24 (s, 1 H), 4.19 (s, 1 H), 4.15 (d, J = 12.0 Hz, 1 H), 3.82 (s, 3 H), 3.72 (dd, J = 8.4, 8.4 Hz, 2 H), 3.57 (dd, J = 11.7, 2.4 Hz, 1 H), 3.25 (s, 3 H), 3.01 (qd, J = 6.8, 0.6 Hz, 1 H), 2.77 (br d, J = 12.9 Hz, 1 H), 2.47−2.40 (m, 1 H), 2.38 (br s, 1 H), 2.33−2.29 (m, 1 H), 1.98 (dd, J = 13.8, 13.8 Hz, 1 H), 1.82−1.70 (m, 3 H), 1.32 (d, J = 6.5 Hz, 3 H), 1.05 (s, 3 H), 0.96 (dd, J = 9.7 Hz, 2 H), 0.94 (s, 3 H), 0.88 (s, 9 H), 0.16 (s, 3 H), 0.12 (s, 3 H), 0.043 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.5, 160.0, 132.4, 129.7, 127.4 (2 C), 116.5, 113.5 (2 C), 101.4, 94.8, 89.3, 86.6, 82.5, 81.2, 75.5, 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 (2 C), 18.2, 18.1, 16.9, 10.7, −1.42 (3 C), −3.08, −4.76; HRMS m/z (M^+) calcd for $C_{41}H_{70}O_{10}Si_2$ 778.4508, obsd 778.4506; $[\alpha]^{20}_D$ +33.3 (c 0.27, $CHCl_3$).

(1*S*,2*R*,4*S*,5*S*,7*S*,8*S*)-7-(*tert*-Butyldimethylsiloxy)-8-hydroxy-5-[(2*S*,4*R*,5*S*)-4-(2-hydroxyethyl)-2-(*p*-methoxyphenyl)-5-[[2-(trimethylsilyl)ethoxy]methoxy]-*m*-dioxan-5-yl]-2-(methoxymethoxy)-4,11,11-trimethylbicyclo[6.2.1]-

undecan-3-one (68). Thexylborane was prepared by combining 2,3-dimethylbutene (0.15 mL, 1 M in THF) and borane−tetrahydrofuran (0.15 mL, 1 M in THF) at 0 °C for 1.5 h. To this solution was added **67** (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 3 M soln) and 30% H_2O_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 (silica gel, elution with 30% ethyl acetate in hexanes) to furnish the primary (12.7 mg, 41%) and secondary carbinols (6.3 mg, 21%), both as colorless oils.

Primary Carbinol: IR (film, cm^{-1}) 3464, 1699, 1616; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 8.7 Hz, 2 H), 6.87 (d, J = 8.7 Hz, 2 H), 5.61 (s, 1 H), 4.90 (d, J = 8.2 Hz, 1 H), 4.83 (d, J = 8.2 Hz, 1 H), 4.51 (d, J = 7.0 Hz, 1 H), 4.39 (d, J = 7.9 Hz, 1 H), 4.36 (d, J = 7.0 Hz, 1 H), 4.25 (d, J = 12.0 Hz, 1 H), 4.23 (s, 2 H), 4.03 (d, J = 12.0 Hz, 1 H), 3.90−3.86 (m, 1 H), 3.80 (s, 3 H), 3.80−3.62 (series of m, 4 H), 3.26 (s, 3 H), 3.00 (q, J = 6.7 Hz, 1 H), 2.89 (br d, J = 12.6 Hz, 1 H), 2.44−2.28 (series of m, 3 H), 2.20−1.66 (series of m, 7 H), 1.36 (d, J = 6.7 Hz, 3 H), 1.07 (s, 3 H), 0.97 (s, 3 H), 0.89 (s, 9 H), 0.94−0.85 (m, 2 H), 0.17 (s, 3 H), 0.14 (s, 3 H), 0.035 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 212.1, 160.0, 129.5, 127.3 (2 C), 113.6 (2 C), 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 (3 C), 18.12, 18.09, 16.8, 10.8, −1.47 (3 C), −3.07, −4.78; FAB MS m/z (M^+ + H) calcd for $C_{41}H_{73}O_{11}Si_2$ 797.47, obsd 797.48; $[\alpha]^{20}_D$ +18.1 (c 1.27, $CHCl_3$).

The Dess−Martin periodinane (9.6 mg, 23 μmol) was stirred in CH_2Cl_2 (1 mL) with the primary carbinol (12 mg, 15 μmol) for 1 h, concentrated to about 0.2 mL, transferred to a flash column, and purified (silica gel, elution with 20% ethyl acetate in hexanes) to give 9.8 mg (82%) **68** and unchanged alcohol (2.2 mg, 18%), both as colorless oils.

68: IR (film, cm^{-1}) 3464, 1731, 1701; ^1H NMR (300 MHz, $CDCl_3$) δ 9.86 (s, 1 H), 7.36 (d, J = 8.7 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 5.68 (s, 1 H), 4.81 (s, 2 H), 4.81 (d, J = 11.7 Hz, 1 H), 4.51 (d, J = 7.0 Hz, 1 H), 4.37 (d, J = 7.0 Hz, 1 H), 4.33 (d, J = 11.8 Hz, 1 H), 4.22 (s, 1H), 4.21 (d, J = 8.9 Hz, 1 H), 4.18 (d, J = 11.8 Hz, 1 H), 3.80 (s, 3 H), 3.68−3.57 (m, 3 H), 3.27 (s, 3 H), 3.08 (d, J = 5.8 Hz, 2 H), 2.94 (q, J = 6.4 Hz, 1 H), 2.98−2.88 (m, 1 H), 2.40 (d, J = 10.9 Hz, 1 H), 2.36−2.22 (m, 2 H), 1.95−1.82 (m, 3 H), 1.70−1.62 (m, 1 H), 1.33 (d, J = 6.4 Hz, 3 H), 1.06 (s, 3 H), 0.97 (s, 3 H), 0.89 (s, 9 H), 0.95−0.86 (m, 2 H), 0.17 (s, 3 H), 0.14 (s, 3 H), 0.026 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 211.9, 119.2, 160.0, 129.2, 127.2 (2 C), 113.5 (2 C), 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 (3 C), 18.1 (2 C), 16.8, 10.5, −1.46 (3 C), −3.10, −4.78; FAB MS m/z (M^+ + H) calcd for $C_{41}H_{71}O_{11}Si_2$ 795.45, obsd 795.63; $[\alpha]^{20}_D$ +17.7 (c 0.87, $CHCl_3$).

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Supporting Information Available: Copies of the high-field ^1H NMR spectra for all compounds reported herein (52 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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