Convergent Synthesis of Polyether Ionophore Antibiotics: Synthesis of the Spiroketal and Tricyclic Glycal Segments of Monensin[1]

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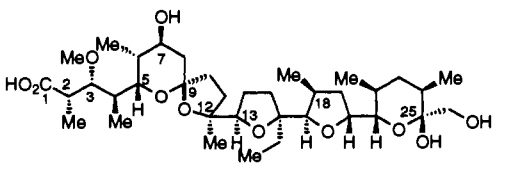
Abstract: The syntheses of the spiroketal II and tricyclic glycal III portions of the polyether antibiotic monensin (I) are described. The butyric acid side chain of spiroketal II is constructed through either Sharpless epoxidation of a *cis*-2-butenol residue or by Brown crotylation of an α-methylacetaldehyde unit. The spiroketal is then generated through a hetero-Diels–Alder addition between a tetrahydropyranoid methylene ketone and acrolein. Finally, [6.5]-spiroketal structure II is prepared by mild acid catalyzed rearrangement of [6.6]-spiroketal epoxide **23**. Glycal III was made from the C/D subunit **44**. This subunit was prepared by the ester enolate Claisen rearrangement that unites the tetrahydrofuranoid C and D rings **40** and **41** by Brown crotylation, Wittig condensation, and then cyclization to form the E ring. The synthesis of the two fragments set the stage for a final ester enolate Claisen rearrangement that will form the skeleton of the polyether monensin (I).

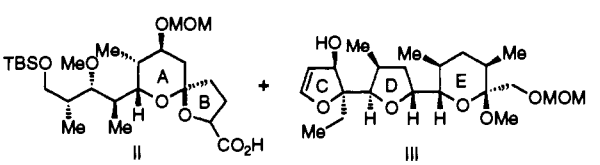
The antibiotic monensin (I)[2] is an important representative of a large class[3] of polyether antibiotics that has been the subject of many chemical, biochemical, and medicinal investigations.[3] Monensin (I) has been synthesized on two occasions[4] and has served as the platform for the development of new synthetic methodology[5] that relates to the construction of tetrahydropyran and tetrahydrofuran systems. The total syntheses of several other very complex members of this class of polyether antibiotics have also been accomplished.[6]

Some time ago, a program was initiated in these laboratories for the synthesis of such polyether systems. The basic strategy undertaken for the construction of these polycyclic molecules was the union of preformed carbohydrate-based acids and glycals by the ester enolate Claisen rearrangement.[7] The goal of this work, in addition to the total synthesis of important members of this large class of antibiotics, was the exploration of the scope of the ester enolate Claisen rearrangement for the synthesis of large complex molecules. Success with this strategy and methodology was initially realized in the synthesis of the nonactic acids[8] and then progressed through the synthesis of lasalocid and *enantio*-lasalocid[6b] in an attempt to prepare monensin.[9] The monensin target represented the initial phase of a program aimed at the application of these techniques to the synthesis of more common poly(tetrahydrofuran)–poly(tetrahydropyran) based ionophores. The techniques necessary for the synthesis of this prototypical polyether antibiotic can then be utilized for the construction of other even more complex members of this class.[3]

An important facet of this program is that the convergency[10] inherent in the union of large prefabricated subunits by the ester enolate Claisen rearrangement will allow for the preparation of substantial quantities of the target molecules. Such a result will mean that the protocols developed here can be used to make sufficient amounts of some of the less common members of this class as well as pertinent analogs of important members for biological evaluation.



MONENSIN I



II III

(1) No reprints of this paper are available.

(2) Agtarap, A.; Chamberlin, J. W.; Pinkerton, M.; Steinrauf, L. *J. Am. Chem. Soc.* **1967**, *84*, 5737–5739. Pinkerton, M.; Steinrauf, L. K. *J. Mol. Biol.* **1970**, *49*, 533. Haney, M. E., Jr.; Hoehn, M. M. *Antimicrob. Agents Chemother.* **1967**, 349. Stark, W. M.; Knox, M. G.; Westhead, J. E. *Ibid.* **1967**, 353. Agtarap, A.; Chamberlin, J. W. *Ibid.* **1967**, 359. Gorman, M.; Chamberlin, J. W.; Hamill, R. L. *Ibid.* **1967**, 363.

(3) *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Westley, J. W., Ed.; Marcel Dekker Inc.: New York, 1982; Vol. 1–2. *Dictionary of Antibiotics and Related Substances*, Chapman and Hall: New York, 1988.

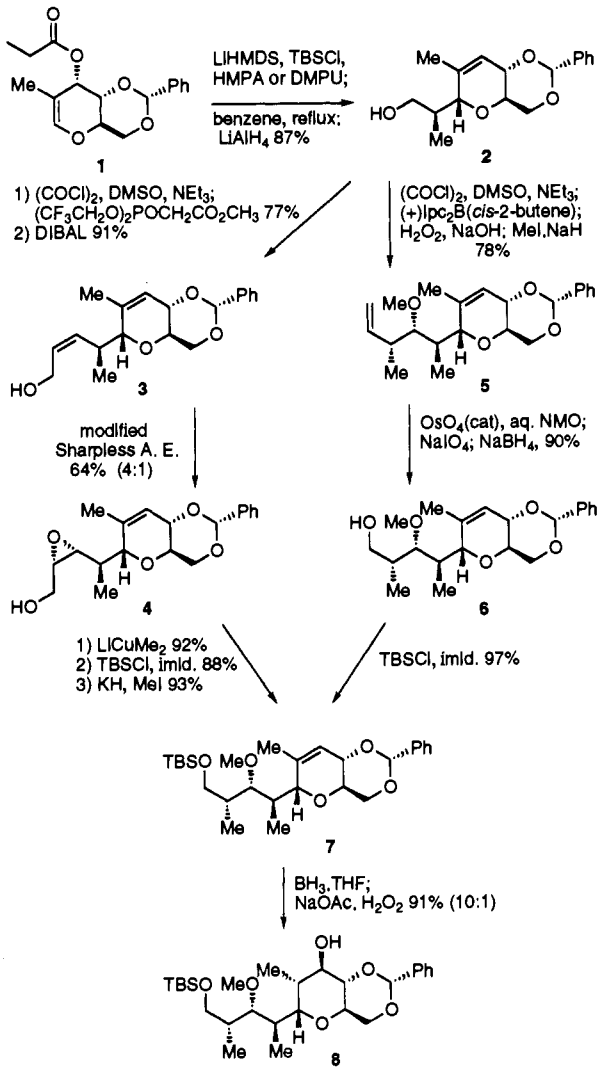
(4) Schmid, G.; Fukuyama, T.; Akasaka, K.; Kishi, Y. *J. Am. Chem. Soc.*, **1979**, *101*, 259–260. Fukuyama, T.; Wang, C.-L. J.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 260–262. Fukuyama, T.; Akasaka, K.; Karanewsky, D. S.; Wang, C.-L. J.; Schmid, G.; Kishi, Y. *J. Am. Chem. Soc.*, **1979**, *101*, 262–263. Collum, D. B.; McDonald, J. H., III; Still, W. C. *J. Am. Chem. Soc.* **1980**, *102*, 2117–2118; 2118–2120; 2120–2121.

(5) Wierenga, W. *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. IV, pp 263–351. Walba, D. M.; Thurmes, W. N.; Haltiwanger, R. C. *J. Org. Chem.* **1988**, *53*, 1046–1056.

(6) (a) *Calcimycin*: Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Tabor, T. R. *J. Am. Chem. Soc.* **1979**, *101*, 6789. Grieco, P. A.; Williams, E.; Tanaka, H.; Gilman, S. G. *J. Org. Chem.* **1980**, *45*, 3537. (b) *Lasalocid A*: Nakata, T.; Schmid, G.; Vranesic, B.; Okogawa, M.; Smith-Palmer, T.; Kishi, Y. *J. Am. Chem. Soc.* **1978**, *100*, 2933. Ireland, R. E.; Anderson, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988. (c) *Antibiotic X-14574A*: Nicolaou, K. C.; Papahatjis, D. P.; Claremon, D. A.; Dolle, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 6967. Roush, W. R.; Meyers, A. G. *J. Org. Chem.* **1981**, *46*, 1509. Edwards, M. P.; Ley, S. V.; Lister, S. G. *Tetrahedron Lett.* **1981**, 361. (d) *Narasin*: Kishi, Y. *Aldrichim. Acta* **1980**, *13*, 23. (e) *Salinomycin*: Kishi, Y.; Hatakeyama, S.; Lewis, M. D. *Front. Chem. Plenary Keynote Lect. IUPAC Congr. 28th* **1981**, 287. Horita, K.; Nagoto, S.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron Lett.* **1987**, *28*, 3253. (f) *Antibiotic X-206*: Evans, D. A.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506. (g) *Ferensimycin B*: Evans, D. A.; Polniaszek, R. P.; DeVries, K. M.; Guinn, D. E.; Mathre, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 7613–7630. (h) *Ionomycin*: Evans, D. A.; Dow, R. L.; Shih, T. I.; Takacs, J. M.; Zahler, R. *J. Am. Chem. Soc.* **1990**, *112*, 5290.

0002-7863/93/1515-7152$04.00/0

Scheme I



The previous monensin project faltered[9c] when it was found that tricyclic glycal **III** could not be made in the stereochemically requisite D/E syn configuration by a radical decarboxylation of the acid derived from the ester enolate Claisen rearrangement union of the C/D acid with the E ring glycal. In addition, the synthesis of monensin spiroketal **II** seemed cumbersome, and the construction of the carboxylic acid side chain was completed at the end of the total synthesis. There were clearly some significant obstacles that had to be overcome before the implementation of this strategy could be applied to the synthesis of this important group of aliphatic polyether antibiotics. In this and the following paper, these drawbacks are addressed and a synthesis of monensin is realized.

Synthesis of the Spiroketal Fragment of Monensin. In order to have the final ester enolate Claisen rearrangement[7] that joins the left-side spiroketal subunit II with the right-side tricyclic subunit III as close to the end of the monensin synthesis as possible, the spiroketal target becomes acid II. Selection of acid II as the target for that portion of the synthesis requires the early addition of the monensin butyric acid side chain.[9a] For this process, two procedures were developed (Scheme I).

The first approach used for the side-chain construction relies on Sharpless stereoselective epoxidation[11] of *Z*-allylic alcohol **3**, which itself can be readily prepared as shown (Scheme I). Not surprisingly, with *Z*-allylic alcohol **3**, the standard Sharpless oxidation conditions[11] were stereochemically inefficient and the reaction was very slow. However, modification[12] of these conditions such that allylic alcohol **3** was precomplexed with the titanium catalyst before hydroperoxide addition resulted in an expeditious reaction rate and the satisfactory isomeric ratio quoted. Lithium dimethylcuprate cleavage of the epoxide mixture **4** proceeded normally, and recrystallization of the resulting diol mixture served to remove the minor isomer. After silylation of the primary alcohol, the secondary alcohol was easily methylated. Completion of the blocked side chain was thus accomplished in 30% overall yield from ester **1**. The stereochemical outcome of the reactions in this sequence was based on ^{1}H NMR precedence,[9] and confirmed later through a single-crystal X-ray structure analysis[13] of alcohol **8**.

As useful as this sequence was, an alternate, more direct route for the side-chain construction was also explored (Scheme I). For this approach, the aldehyde derived by oxidation of alcohol **2** was crotylated by the method of Brown.[14] The use of the borane derived from *cis*-2-butene and (−)-*B*-methoxydiisopinocampheylborane set the desired *S,R* stereochemistry of the C-2 methyl group and the C-3 hydroxyl function. After methylation of the C-3 hydroxyl, olefin **5** was available on large scale in 78% overall yield. Conversion of this olefin **5** to the previously prepared silylated alcohol **7** with the blocked monensin side chain was easily accomplished in 87% overall yield as shown (Scheme I). This alternate scheme for the construction of the side chain gave a 64% overall yield of silylated derivative **7** and is clearly more efficient than the former approach through epoxide **3**. This procedure has been used to make multigram quantities of this key intermediate **7**.

The bicyclic portion of silylated derivative **7** is a rigid trans-fused system in which approach from the α-face is hindered by the newly constructed axial side chain. It is not surprising, then, that hydroboration of the double bond is stereoselective (10:1 isomer ratio) and efficient (91% yield). Purification of major isomer **8** is facile, and it is this crystalline intermediate with six new contiguous stereocenters that was used for single-crystal X-ray analysis. Subsequent blocking of the β-oriented hydroxyl group with either a MEM or MOM grouping is readily accomplished. This completes the stereoselective construction of the tetrahydropyran portion of monensin spiroketal II and sets the stage for the formation of spiroketal II itself.

For the spiroketal construction, it was planned to use a hetero-Diels–Alder condensation with an exomethylene derivative of tetrahydropyran systems **9** and **10** (Scheme II). Such a scheme had been demonstrated earlier[15] in model systems and attempted initially in the first approach to this spiroketal.[9a] This earlier attempt failed when the exocyclic double bond migrated to the endocyclic position in preference to condensation with acrolein. Subsequently, it was found[16] that if exocyclic–endocyclic rearrangement was blocked by substitution adjacent to the exocyclic methylene grouping, the hetero-Diels–Alder condensation proceeded in a satisfactory manner. In particular, a ketone at this

(7) Ireland, R. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 5897–5898. Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868–2877.

(8) Ireland, R. E.; Vevert, J.-P. *J. Org. Chem.* **1980**, *45*, 4259–4260.

(9) (a) Ireland, R. E.; Häbich, D.; Norbeck, D. W. *J. Am. Chem. Soc.* **1985**, *107*, 3271–3278. (b) Ireland, R. E.; Norbeck, D. W. *J. Am. Chem. Soc.* **1985**, *107*, 3279–3285. (c) Ireland, R. E.; Norbeck, D. W.; Mandel, G. S.; Mandel, N. S. *J. Am. Chem. Soc.* **1985**, *107*, 3285–3294.

(10) For a comment on the relevance of efficient methodology in the synthesis of complex molecules, see: Heathcock, C. A. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 665–681.

(11) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974–5976.

(12) M. G. Finn, University of Virginia, personal communication.

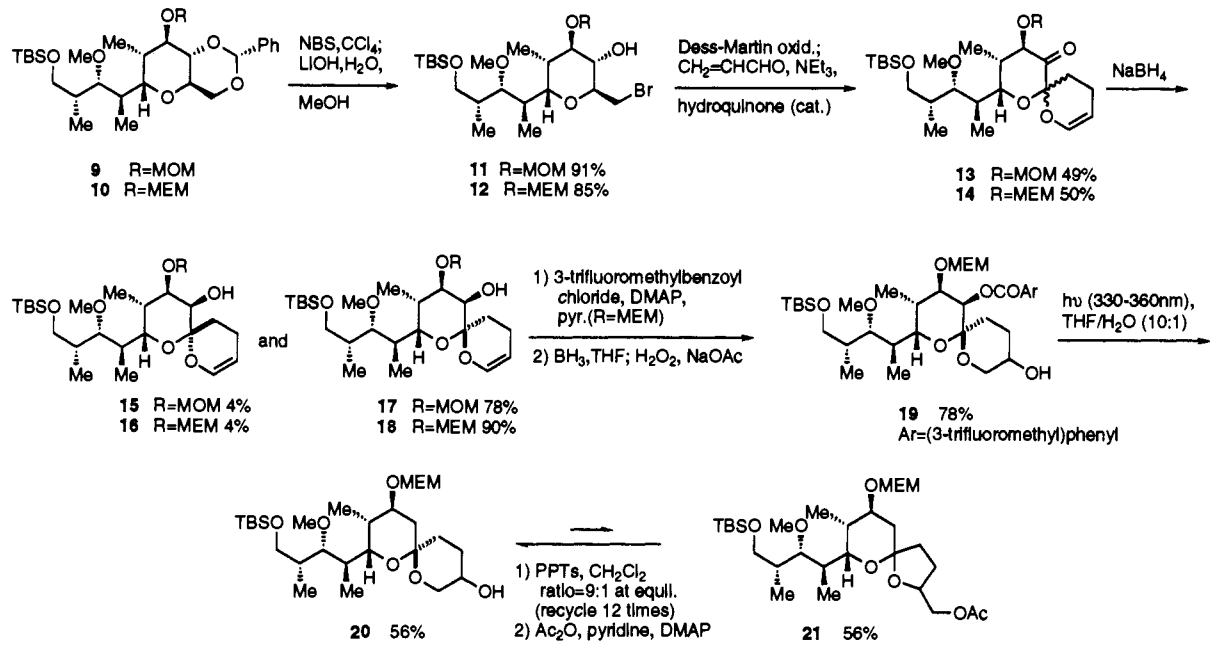
(13) The single-crystal X-ray structure analysis of alcohol **8** was done by Professor R. Bryan, University of Virginia. The data pertaining to this analysis are contained in the supplementary material.

(14) Brown, H. G.; Bhat, K. S.; Ramnarayan, S. R. *J. Org. Chem.* **1989**, *54*, 1570–1576.

(15) Ireland, R. E.; Häbich, D. *Chem. Ber.* **1981**, *114*, 1418–1427.

(16) (a) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1983**, *48*, 1303–1312. (b) Ireland, R. E.; Thaisrivongs, S.; Dussault, P. H. *J. Am. Chem. Soc.* **1988**, *110*, 5768–5779.

Scheme II



adjacent position served to block the exocyclic–endocyclic migration and assist in the formation of the methylene group. The current synthesis was planned to utilize a C-8–C-9[17] methylene ketone as the hetero-Diels–Alder dienophile. Experience[16a] has shown that such methylene ketones were very labile and self-condensed easily at room temperature. To avoid this dimerization, the dienophile is generated *in situ*[16a] in the presence of a large excess of diene (acrolein). Mild base treatment of the ketone derived from bromo alcohol **11** or **12** served this purpose. This sequence of reactions went well and produced spiroketals **13** or **14** which now possess the required carbons of monensin spiroketal II. The stereochemistry at the spirocenter obtained as a result of this hetero-Diels–Alder spiro ketal formation could not be proven conclusively at this juncture.

It was then necessary to convert the [6.6]-spiroketal system in **13** or **14** to the monensin-like [6.5]-spiroketal found in spiroketal subunit II. In a similar, less substituted system, mild acid equilibration of a 3-hydroxy [6.6]-spiroketal gave a 1:1 mixture of a 2-hydroxymethyl [6.5]-spiroketal and a 3-hydroxy [6.6]-spiroketal.[16a] As a result, hydroxy spiroketal **20** was the next logical target. Several schemes were explored for the removal of the ketone group in hetero-Diels–Alder adduct **14**. Since direct ketone reduction under Wolff–Kishner conditions[18] failed to generate recognizable products, deoxygenation of the derived alcohol was pursued. An added bonus from this decision was that alcohols **16** and **18** obtained as a result of sodium borohydride reduction of ketone **14** separated readily on flash chromatography. That these isomers were spiro-center isomers and not alcohol epimers was shown from ^{1}H NMR and ^{13}C NMR spectroscopy and later confirmed by single-crystal X-ray analysis of a derivative of **17**[19] (*vide infra*). The isolation of alcohol **18** as by far the major component of this mixture establishes that the hetero-Diels–Alder condensation had resulted from top (β) face addition to the intermediate methylenetetrahydropyran and that **18** was the anomerically favorable spiroketal.

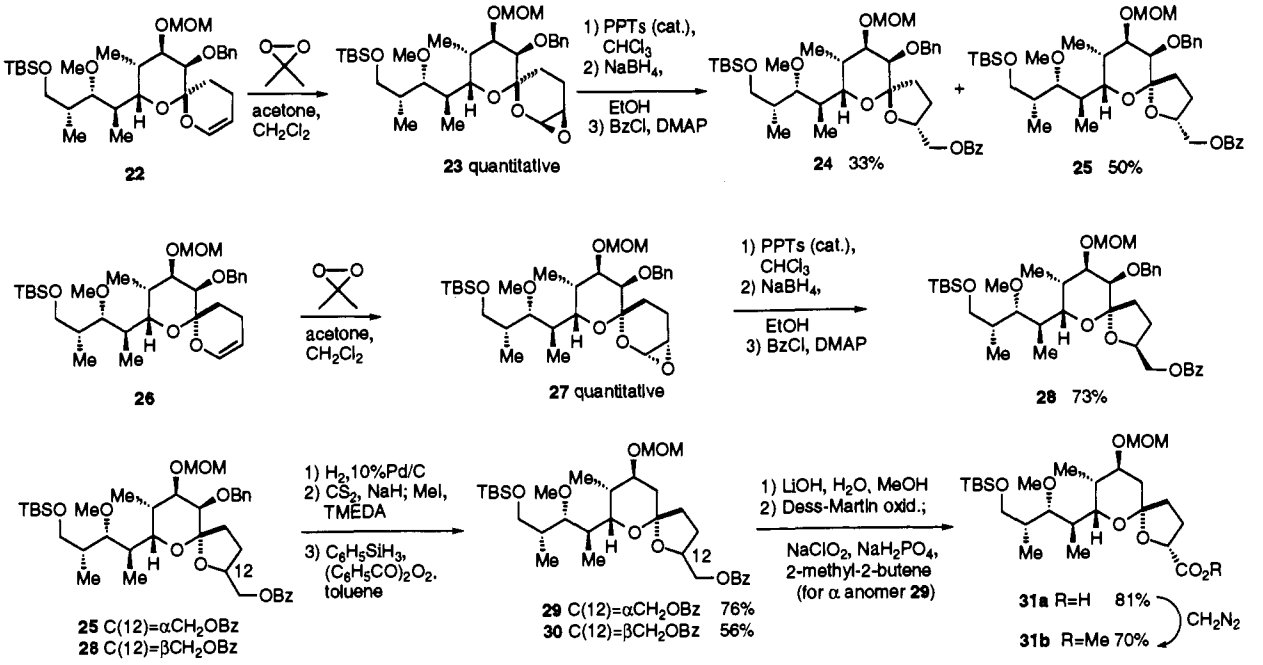
Removal of the hydroxyl group in alcohol **18** through reduction of the derived xanthate[20a] failed when the intermediate radical participated with the dihydropyran double bond to form new cyclic products. Finally, after protection of the hydroxyl group of alcohol **18** as the *m*-(trifluoromethyl)benzoate, the double bond was removed by hydroboration and then benzoates **19** were reduced photochemically.[21] Alcohol **20**, as a mixture of isomers about the hydroxyl function, was then obtained in modest yield and only in relatively small scale batches. Since the stereochemistry at this hydroxyl center was of no ultimate concern (enolization of the derived ester with the right-side tricyclic subunit would destroy the stereocenter), the rearrangement of alcohols **20** was explored.

The mild acid-catalyzed rearrangement of [6.6]-spiroketal alcohols **20** did not follow the precedence[15] from the earlier unsubstituted model systems. The equilibrium between this [6.6]- and [6.5]-spiroketal system appears to strongly favor the starting [6.6]-isomer. While an acceptable yield of the desired [6.5]-spiroketal (characterized as its derived acetate **21**) can be achieved after 12 cycles of equilibration/separation, this process is clearly not amenable for large-scale preparations. It is interesting to note the dramatic effect that the multiple substitution on [6.6]-spiroketal **20** has on the equilibration. This step alone is not the only flaw in the latter stages of this synthesis, for the deoxygenation process of benzoate **19** also leaves much to be desired.

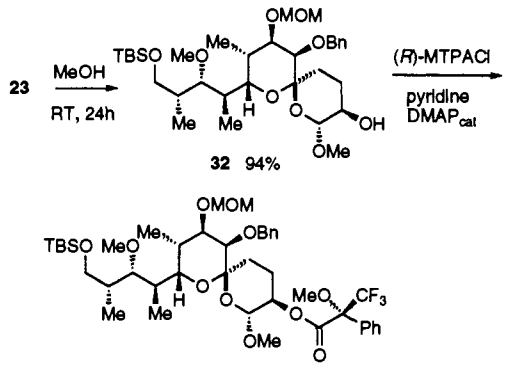
With the problems in the latter stages of the above spiroketal II synthesis in mind, we sought a new route for the conversion of the [6.6]-spiroketal hetero-Diels–Alder product. From the above results, it was clear that the desired equilibration to the [6.5]-system could not be achieved through a vicinal diol precursor of the tetrahydrofuran ring. Some means had to be devised such that only the secondary hydroxyl function was available during the rearrangement. Such an opportunity presented itself when it was found that the double bond of the dihydropyran ring of benzyl ether **22**[22] could be smoothly oxidized to a single epoxide, **23**, with dimethyldioxirane[23] (Danishefsky conditions[24]) (Scheme III). That this epoxide **23** had the stereochemistry shown was demonstrated by the following experiments.

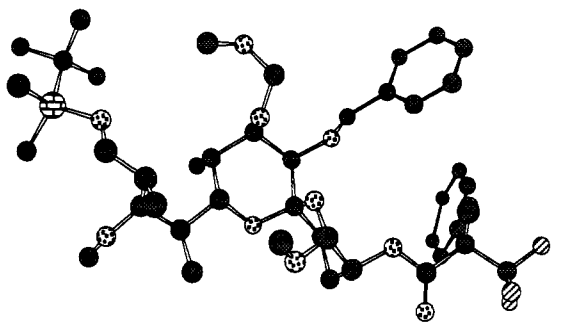
(17) The monensin (I) numbering system is used.
(18) Huang-Minlon, *J. Am. Chem. Soc.* **1946**, *68*, 2487–2487.
(19) The single-crystal X-ray structure analysis of (*R*)-MPTA ester **33** was done by Dr. Michal Sabat. The data pertaining to this analysis are contained in the supplementary material.
(20) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. I* **1975**, 1574–1585. (b) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. C. *Synlett* **1991**, 435–438.
(21) Saito, I.; Ikehira, H.; Kasatani, R.; Watanabe, M.; Matsuura, T. *J. Am. Chem. Soc.* **1986**, *108*, 3115–3117.
(22) Readily prepared in 94% yield from alcohol **17**; see Experimental Part.
(23) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847–2853. For a more convenient and higher yielding preparation of dimethyldioxirane, see: Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.
(24) Danishefsky, S. J.; Halcomb, R. L., *J. Org. Chem.* **1989**, *111*, 6662–6666. See, also: Baertschi, S. W.; Raney, K. D.; Stone, M. P.; Harris, T. M. *J. Am. Chem. Soc.* **1988**, *110*, 7929–7931.

Scheme III



Scheme IV





X-ray structure of ester **33** (hydrogen atoms are omitted)

Treatment[24] of epoxide **23** with methanol led, in high yield, to methyl hydroxyglycoside **32** which in turn was esterified with (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (Scheme IV). The resulting Mosher ester[25] **33** crystallized, and the structure was then determined by single-crystal X-ray structure analysis.[19] This structure confirms the earlier spectral analysis that led to the conclusion that the spiro center of the major isomer from the hetero-Diels–Alder reaction had the anomerically more favorable, axially oriented carbon–oxygen bond. As spectrally deduced earlier, the hydroxyl group (now a benzyl ether) formed on sodium borohydride reduction of the ketonic product of the hetero-Diels–Alder condensation is β (equatorially) oriented. Most importantly, the hydroxyl group (now an (*R*)-MTPA ester) formed by methanolysis of epoxide **23** is shown to be β (axially) oriented. Since this hydroxyl group arose by antiperiplanar cleavage of original epoxide **23**, this epoxide **23** must itself be β-oriented, as shown.

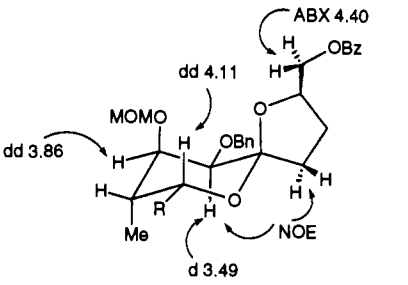
With the stereochemistry of epoxide **23** clearly defined, rearrangement of this epoxide to the [6.5]-spiroketal system was explored (Scheme III). While strong acid completely destroyed epoxide **23**, treatment with mild acid and then sodium borohydride reduction of the presumed intermediate aldehyde and subsequent benzoylation led to the formation of two readily separable new products **24** and **25** in a combined overall yield of 83%. Similar treatment of benzyl ether **26**[26] from minor hetero-Diels–Alder adduct **15** led, in 73% overall yield, to a single product, **28.** In both cases, epoxidation by dimethyldioxirane had occurred *exclusively* from the face of the enol ether (β-face of **22** and a face of **26**) opposite to the C-9 axial oxygen substituent. That the products **24, 25,** and **28** had the desired [6.5]-spiroketal structure shown was determined by the following analysis.

In addition to the expected spectral characteristics of the tetrahydropyran ring and its substituents, the ^{1}H NMR spectra of both products **24** and **25** showed ABX resonances centered at ~4.40 ppm which result from the (benzoyloxy)methylene group on the tetrahydrofuran ring (Figure 1). Particularly noteworthy is the deshielding[16a] of the C-5 hydrogen (dd, δ 4.11) by the axial oxygen atom in minor isomer **24**; in major isomer **25**, this C-5 hydrogen resonance occurs at higher field (dd, δ 3.66). A significant NOE in major isomer **25** between the C-5 hydrogen and the axial methylene hydrogen of the tetrahydrofuran ring was also observed. The structure of spiroketal **28** also arose from a similar spectral analysis.

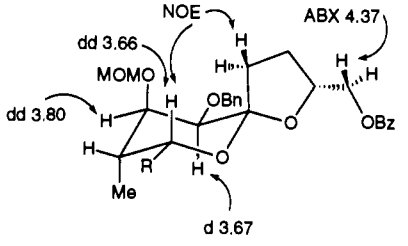
A possible rationalization for the formation of two spiro-center isomers as a result of this rearrangement is shown in Figure 2. Initial mild acid cleavage of epoxide **23** will generate an α-hydroxy aldehyde and a tetrahydropyranoid oxonium ion. As desired, this α-hydroxy aldehyde can readily collapse to form a new [6.5]-spiroketal but may do so by attack on the top (β) or bottom (α) face of the tetrahydropyranoid oxonium ion. In this case, attack on either face is acceptable but top-side (β) attack is somewhat hindered by the interaction (**A**) of the hydroxyl group and the axial C-7–OMOM substituent. Thus, attack through trajectory

(25) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

(26) Readily prepared in 86% yield from alcohol **15**; see Experimental Part.



24 (Minor)



25 (Major)

Figure 1. ^{1}H NMR data for [5.6]-spiroketals.

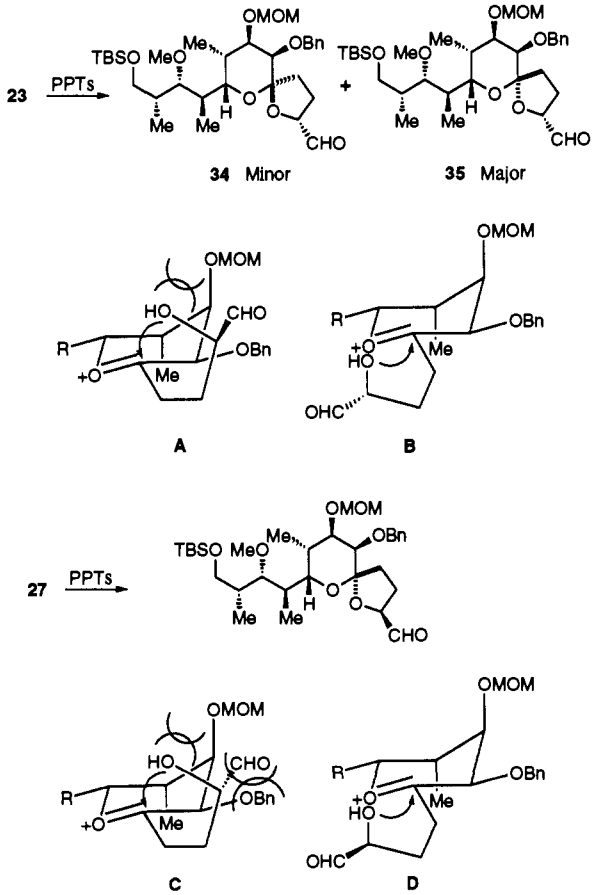
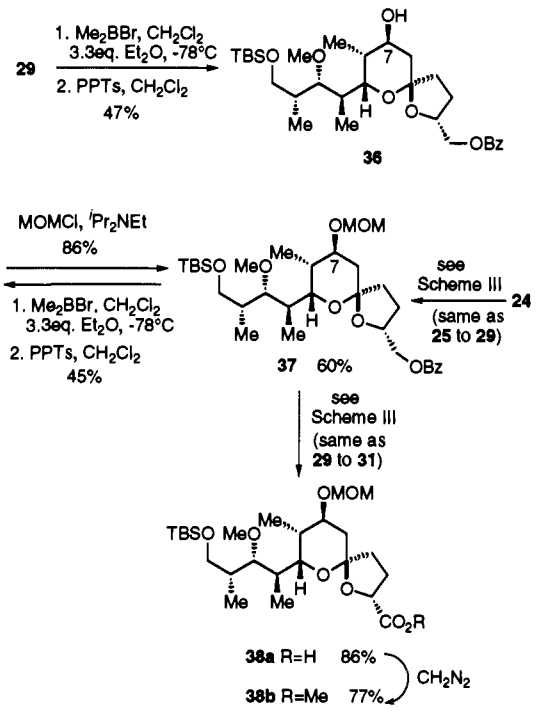


Figure 2.

B will be more favorable, and correspondingly, the major isomer is aldehyde **35** and the minor isomer aldehyde **34**.

Support for this analysis is found in the fact that epoxide **27** from dimethyldioxirane oxidation of minor isomer **26** from the hetero-Diels–Alder condensation gives only one spiroketal isomer, **28**, on treatment with mild acid. As can be seen, spiroketal formation from the top (β) face of the tetrahydropyranoid oxonium ion is now severely hindered in the β-trajectory **C** and unhindered in that from the bottom (α) face **D**.

Scheme V



It is interesting to note that in both cases, the sterically more favored trajectory for kinetic spiroketal formation (**B** and **D**) generates an equatorial C–O bond at the anomeric center rather than the stereoelectronically more favorable axial C–O bond.

Confident that the rearrangement products of epoxides **23** and **27** were the desired [6.5]-spiroketals **24**, **25**, and **28**, we explored the removal of the C-8 oxygen function (Schemes III and V). After debenzylation and reductive deoxygenation of the derived xanthate with a modified Barton procedure,[20b] spiroketals **29, 30** (Scheme III), and **37** (Scheme V) were obtained. The conversions on deoxgenation were moderate, but in each case, the byproducts were the starting xanthate or alcohol which was recycled. Extended reaction times in the radical deoxygenation resulted in production of undesired byproducts.

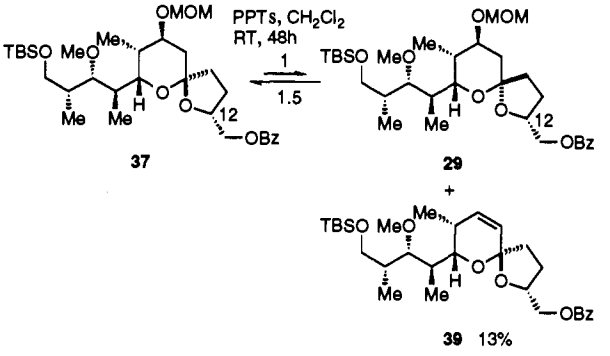
As further confirmation of the stereochemistry of spiroketals **29** and **37**, removal[27] of the blocking group on the C-7 hydroxyl function of [6.5]- spiroketal **29** and then mild acid-catalyzed treatment of the product provided hydroxy [6.5]-spiroketal **36** (Scheme V). The infrared spectrum of spiroketal **36** clearly showed an absorption at 3530 cm^{-1} (sharp, unaffected by dilution) which was assigned to the C-7 hydroxyl O–H which is hydrogen-bonded to the tetrahydrofuranoid ether oxygen. Such hydrogen bonding is also evident in monensin itself.[28] Further corroboration of this structural assignment comes from the similar treatment of spiroketal **37** from minor isomer **24** of the mild acid rearrangement of epoxide **23** wherein the same hydroxy [6.5]-spiroketal **36** is formed. Finally, reintroduction of the blocking group on the C-7 hydroxyl group of spiroketal **36** regenerated spiroketal **37** and not spiroketal **29**. Not only does this analysis confirm the structures depicted, it also demonstrates that the stereochemistry at the spiroketal center can be changed to the correct monensin (I) configuration.

Treatment of either spiroketal isomer **29** or **37** with mild acid gave an equilibrium mixture (ratio 1.5:1) favoring isomer **37**. A small amount of a byproduct, alkene **39**, was also isolated, and its structure followed from its spectral properties. Therefore, compounds **29** and **37** are isomeric only about the spiro center, and it appears that no equilibration at C-12 of intermediate

(27) Guindon, Y.; Yoakim, C.; Morton, H. E. *J. Org. Chem.* **1984**, *49*, 3912–3920.

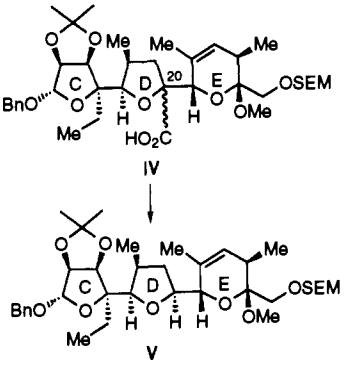
(28) Lutz, W. K.; Winkler, F. K.; Dunitz, J. D. *Helv. Chim. Acta* **1971**, *54*, 1103–1108.

aldehydes **34** and **35** (Figure 2) had occurred under the acid conditions of the rearrangement. It follows that the stereochemistry at C-12 is set at the epoxidation step.



Completion of the preparation of the monensin spiroketal subunits, characterized as methyl esters **31b** and **38b**, was then readily achieved as shown (Schemes III and V). Each of the crude acids **31a** and **38a** is pure enough to be utilized in the esterification step to give the required precursor for the Claisen rearrangement. Since the stereochemistry at the spiro center can be changed at a later stage and the stereochemistry adjacent to the carboxyl group will be destroyed by enolization, each of the individual spiroketal isomers will serve the purposes sought.

Synthesis of the Tricyclic Glycal Fragment of Monensin. An effort to prepare subunit III by the union of a preformed C/D bis(tetrahydrofuran) acid and a tetrahydropyran glycal with the ester enolate Claisen rearrangement and then decarboxylation of resulting tricyclic acid IV failed when the decarboxylation led only to the undesired tricyclic system V with the anticonnection between the D and E rings.[9c]

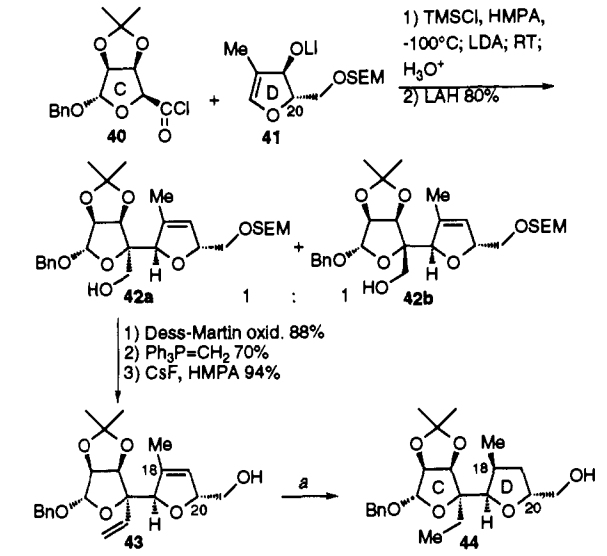


Since it was shown in this earlier study and concurrent work by Giese[29] in the pyranose series that an α-alkoxy carbon centered radical is stabilized by the anomeric effect, the bonding lobe of the intermediate radical in this decarboxylation process must be α (axially) oriented in these cyclic structures. It was clear, then, that the desired trans disposition of the 2,5 substituents on the tetrahydrofuranoid D ring would not result from a radical decarboxylation process. Other procedures involving decarboxylative substitution followed by reduction were explored without success. The C-20 position of tricyclic molecule IV is highly hindered,[9c] and intermolecular reactions appear to be virtually excluded.

In order to overcome the unfavorable stereochemical result of the decarboxylation, it was decided that the E ring would be appended on to a C/D bis(tetrahydrofuran) ring system that already contained the correct stereochemistry at C-20. This modification entailed using glycal **41**, prepared from L-arabinose, and the original acid chloride **40** in the ester enolate Claisen rearrangement[7,9b] (Scheme VI).

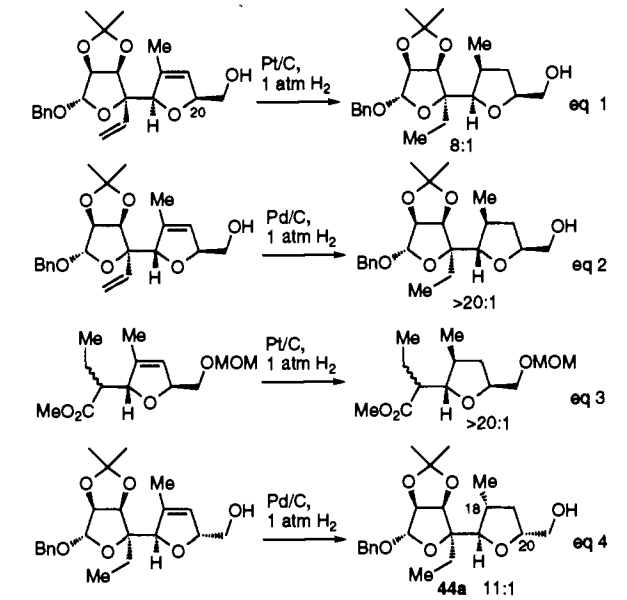
(29) Giese, B.; Dupuis, J. *Tetrahedron Lett.* **1984**, *25*, 1349–1352.

Scheme VI[a]



[a] (a) [Rh(COD)DIPHOS-4]BF_4, 640 psi H_2 96%.

Scheme VII

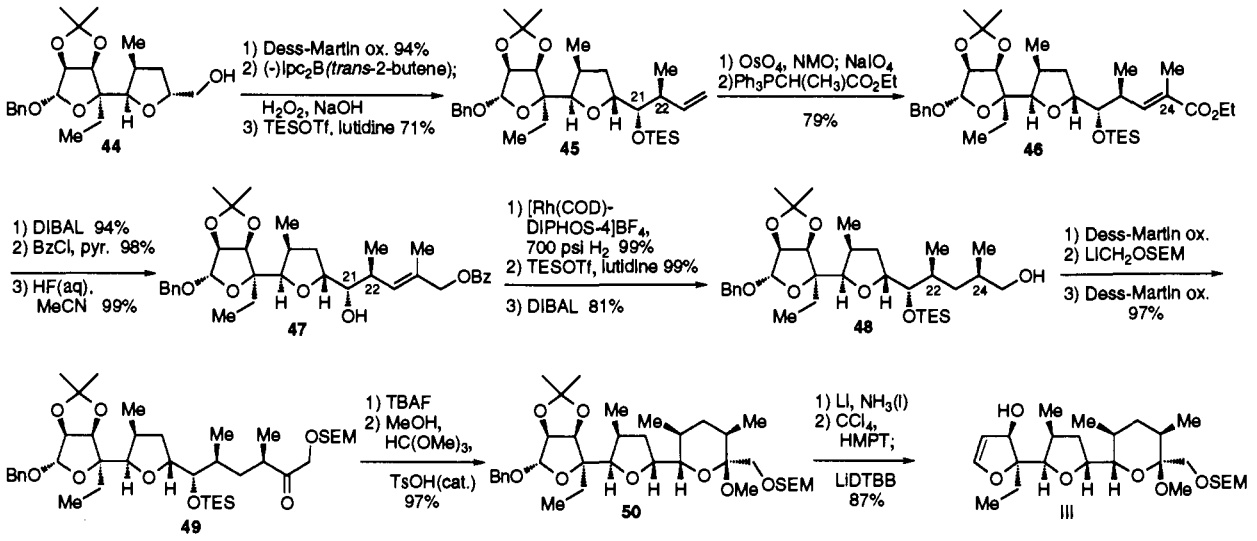


The mixture of acids obtained from this reaction gave a separable mixture of alcohols **42a** and **42b** after reduction with LAH. Alcohol **42a**, later shown to have the desired syn relationship between the two rings, was then refunctionalized in several steps so as to form ethylenic alcohol **43**. Conversion to the required C/D subunit **44** then required hydrogenation of bis(olefin) **43** with α-facial selectivity at the endocyclic double bond. In related systems, it has been found that the orientation of the C-20 methanol side chain is the overriding steric factor in hydrogenation catalyzed by Pd(0) or Pt(0) (Scheme VII).[30]

In each of these cases, hydrogen addition came from, predominantly, the face opposite this appendage (eqs 1, 2, and 3, Scheme VII). This precedent proved applicable to the current substrate, in which hydrogenation gave the incorrect methyl orientation (eq 4). This result, as well as the stereochemical assignment of the Claisen products, was proven by the single-crystal X-ray structure determination of the 2,4-dinitrobenzoate of alcohol **44a**.[31] Since it was apparent that hydrogenation from the same face of the olefin as that of the alcohol would solve this

(30) The reactions of eqs 1 and 2 are from refs 9b and 6a (Ireland, Anderson *et al.*), respectively. For the reaction of eq 3, see the supplementary material in: Ireland, R. E.; Meissner, R. S.; Rizzacasa, M. A. *J. Am. Chem. Soc.* Following paper in this issue.

Scheme VIII



problem, the hydroxyl-tethered catalyst utilized by Evans[32] was the logical choice. Hydrogenation of substrate **43** under the prescribed conditions gave a complete reversal of selectivity (>95:5) and excellent yield of the fully fuctionalized C/D subunit **44** (Scheme VI).

With the requisite functionality of the C/D portion completed, the addition of the E ring followed (Scheme VIII). Oxidation of alcohol **44** to the corresponding aldehyde, crotylation with a Brown crotyl boronate,[14] and silylation of the resulting alcohol gave alkene **45**, containing the required protected C-21 alcohol and C-22 methyl group. Dihydroxylation and oxidative cleavage of the terminal olefin provided the corresponding aldehyde, which was immediately subjected to Wittig olefination. This reaction installed two skeletal carbons, C-24 and C-25, as well as the methyl appendage at C-24 with the expected *E*-olefin geometry in enoate **46**. After reduction of ester **46** and then benzoylation of the resulting alcohol, cleavage of the C-21 silyl ether gave alcohol **47**. The stereochemical dyad formed by the C-21 hydroxyl and C-22 methyl was then exploited in another hydroxyl-tethered hydrogenation.[33] The procedure provided a single diastereoisomer in excellent yield and established the syn-C-22/C-24 dimethyl relationship. In preparation for the addition of the remaining skeletal carbon, the secondary C-21 alcohol was reprotected and the primary C-25 alcohol unmasked to give alcohol **48**. After oxidation of the alcohol, the resulting aldehyde was alkylated with a SEM-protected methanol carbanion.[34] Reoxidation of the resulting alcohol to the ketone gave the complete right-side skeleton **49** in excellent yield over the three-step sequence. Cleavage of the TES ether allowed cyclization to the lactol, which was then converted[35] to methyl ketal **50**. This completed the synthesis of the E ring, and the refunctionalization of the C ring then remained. Reductive cleavage of the benzyl acetal followed by chlorination and reductive elimination[9b,c] gave tricyclic glycal III.

With tricyclic glycal III and spiroketal acids II now in hand, we approached the union of these fragments by an ester enolate Claisen rearrangement to form the monensin skeleton. These efforts are discussed in the following paper.

(31) The single-crystal X-ray structure analysis of the dinitrobenzoate of alcohol **44a** was done by Dr. Michal Sabat, University of Virginia. The data pertaining to this analysis are contained in the supplementary material.

(32) Evans, D. A.; Morrissey, M. M. *J. Am. Chem Soc.* **1984**, *106*, 3866–3868.

(33) Evans, D. A.; Morrissey, M. M.; Dow, R. L. *Tetrahedron Lett.* **1985**, *26*, 6005–6008. The present hydrogenation is functionally and stereochemically very similar to a reference example, and the assumption of the outcome is based on this precedence.

(34) The anion was derived from tri-*n*-butyl stannane by the method of Still. See: Still, W. C. *J. Am. Chem Soc.* **1978**, *100*, 1481–1487.

(35) Cai, D.; Still, W. C. *J. Org. Chem.* **1988**, *53*, 4643–4644.

Experimental Part

General. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively, for solutions in $CDCl_3$. NOESY and COSY spectra were obtained at 500 MHz. Optical rotations were measured in 1-dm or 1-cm cells. Analytical TLC was conducted on 2.5- × 5-cm precoated aluminum TLC plates (silica gel 60 F_{254}, layer thickness 0.2 mm) manufactured by E. Merck and Co., Darmstadt, Germany. Preparative TLC was conducted on 20- × 20-cm glass plates coated with silica gel 150A fluorescent at 254 nm to a layer thickness of 0.25 mm (manufactured by Whatman International LTD., Maidstone, England). Flash chromatography was performed using Merck silica gel 60 (230–400 mesh). All anhydrous solvents were purified according to standard methods. All ^{1}H NMR *J* values are given in hertz.

(*R*)-1,5-Anhydro-2-deoxy-2-methyl-4,6-*O*-(phenylmethylene)-D-*ribo*-hex-1-enitol Propionate (1). To a solution of glycal[36] (21.3 g, 85.8 mmol) and pyridine (12.8 mL, 158.1 mmol) in CH_2Cl_2 (250 mL) at 0 °C was added dropwise propionyl chloride (9.2 mL, 105.6 mmol). After 1 h at 0 °C, saturated aqueous NH_4Cl was added and the reaction mixture was diluted with Et_2O (20 mL), washed with saturated aqueous NaCl, and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel with 15% EtOAc–hexanes as eluent afforded ester **1** (25.1 g, 96%) as a white solid. An analytical sample was obtained by recrystallization of the solid ester from hexane, mp 51 °C: $[\alpha]^{23}_D$ +175° (*c* 2.22, $CHCl_3$); IR (neat) 3010, 2900, 1730, 1670, 1460, 1380, 1220, 1185, 1080, 1020, 920, 740, 680 cm^{-1}; ^{1}H NMR δ 1.15 (t, *J* = 7.6, 3H), 1.64 (s, 3H), 2.38 (q, *J* = 7.6, 2H), 3.68–4.01 (br m, 3H), 4.43 (dd, *J* = 4.6, 10.2, 1H), 5.54 (d, *J* = 3.7, 1H), 5.58 (s, 1H), 6.32 (s, 1H), 7.36 (m, 3H), 7.50 (m, 2H); ^{13}C NMR δ 174.8, 142.5, 137.7, 129.4, 128.6, 126.4, 106.9, 101.5, 76.6, 69.1, 65.6, 64.8, 28.2, 16.0, 9.8. Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.31; H, 6.31. Found: C, 67.21; H, 6.31.

[2*R*(2′*R*, 4a′*R*, 6′*R*, 8a′*S*)]-2-(4,4a,6,8a-Tetrahydro-7-methyl-2-phenylpyrano[3,2-*d*]-1, 3-dioxin-6-yl)propanol (2): HMPA–THF Reaction Solvents. To a stirred solution of LHMDS [from hexamethyldisilazane (51.5 mL, 0.244 mol) and *n*-BuLi (0.2 mol) in hexanes] in dry THF (407 mL) cooled to −100 °C was added dropwise a solution of propanoate **1** (30.3 g, 0.10 mol) in dry THF (119 mL) over 20 min. After 30 min, a solution of TBSCl (36.8 g, 0.244 mol) in dry HMPA (174 mL) was added rapidly with vigorous stirring. After being stirred for 30 min at −100 °C, the resulting mixture was allowed to warm to 0 °C for 30 min and then to room temperature for 30 min. The reaction mixture was diluted with hexanes (3000 mL) and washed with water. The aqueous washings were extracted with hexanes. After being dried ($MgSO_4$), the combined organic layers were concentrated under reduced pressure followed by further concentration under vacuum (0.5 mmHg). An aliquot was removed, and inspection of the characteristic resonances in the ^{13}C NMR spectrum mainly showed one silyl ketene acetal. The crude silyl ketene acetals were dissolved in dry benzene (300 mL), dried briefly over $MgSO_4$, and diluted with dry benzene (1780 mL). This solution was heated at reflux for 19 h under a nitrogen atmosphere and then concentrated under reduced

(36) Sharma, M.; Brown, R. K. *Can. J. Chem.* **1968**, *46*, 757–766.

pressure. The crude epimeric silyl esters (yellow oil) were hydrolyzed by stirring with water (285 mL), THF (690 mL), and 2 N aqueous NaOH (570 mL) for 3 h. This mixture was diluted with water (2600 mL), washed with Et_2O, carefully acidified at 0 °C to pH 3.0–3.5 with 10% aqueous HCl (~500 mL), and extracted with Et_2O. The ethereal layer was dried ($MgSO_4$) and concentrated under reduced pressure, affording the epimeric acids (29.6 g, 97.5%) as a white solid [1:7 mixture of α: β, as determined by the integration of the characteristic resonances of the β- and α-methyl in the ^1H NMR, δ (β, CH_3) 1.27 (d, J = 7.5, 3H), (α, CH_3) 1.38 (d, J = 7.2, 3H)]. This material was directly used in the next reaction without further purification.

To a suspension of $LiAlH_4$ (11.1 g, 0.29 mol) in Et_2O (393 mL) at 0 °C was added dropwise a solution of the epimeric acids (29.6 g, 0.10 mol) in Et_2O (393 mL). After 3 h at 0 °C, the reaction mixture was allowed to stir at room temperature for 8 h. The solution was then cooled to 0 °C, and water (13 mL) was cautiously added followed by 15% aqueous NaOH (13 mL) and then water (39 mL). The suspension was filtered through 2 in. of Celite in a 350-mL coarse fritted funnel, and the filtered solids were washed with Et_2O. Removal of the solvent under reduced pressure and chromatography of the residue on silica gel with 30–40% EtOAc–hexanes as eluent afforded the alcohol (3.48 g, 12%, C-2$_\alpha$ epimer) as a colorless oil: $[\alpha]^{23}_D$ +28.84° (c 0.52, $CHCl_3$); IR (neat) 3460, 2900, 1460, 1380, 1280, 1185, 1060, 1020, 890, 690 cm^{-1}; ^1H NMR δ 1.16 (d, J = 7.2, 3H), 1.79 (s, 3H), 2.17 (m, 1H), 3.43 (m, 1H), 3.58 (m, 1H), 3.73 (m, 2H), 4.06 (br s, 2H), 4.30 (dd, J = 4.5, 10.2, 1H), 5.57 (s, 1H), 5.79 (br s, 1H), 7.36 (m, 3H), 7.50 (m, 2H); ^{13}C NMR δ 138.0, 137.0, 129.5, 128.7, 126.7, 123.7, 102.1, 80.3, 76.3, 70.0, 68.5, 64.4, 39.4, 20.6, 15.9. Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.70; H, 7.46.

There was then eluted alcohol **2** (24.5 g, 87%, C-2$_\beta$ epimer) as a colorless oil: $[\alpha]^{23}_D$ +52.4° (c 2.9, $CHCl_3$); IR (neat) 3460, 2900, 1460, 1380, 1280, 1185, 1090, 1020, 980, 760, 690 cm^{-1}; ^1H NMR δ 1.01 (d, J = 7.2, 3H), 1.72 (s, 3H), 2.03 (m, 1H), 3.62 (m, 1H), 3.68–3.78 (br m, 4H), 4.04 (m, 1H), 4.30 (dd, J = 4.2, 9.9, 1H), 4.41 (br s, 1H), 5.57 (s, 1H), 5.87 (br s, 1H), 7.36 (m, 3H), 7.50 (m, 2H); ^{13}C NMR δ 138.0, 136.2, 129.5, 128.7, 126.7, 124.7, 102.0, 77.2, 76.1, 70.0, 69.1, 65.8, 38.8, 20.0, 11.9. Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.29; H, 7.68.

DMPU–THF Reaction Solvents. To a stirred solution of LHMDS [from hexamethyldisilazane (4.2 mL, 20.1 mmol) and n-BuLi (16.5 mmol) in hexanes] in dry THF (33 mL) cooled to –78 °C was added dropwise a solution of ester **1** (2.4 g, 7.9 mmol) in THF (10 mL). A solution of TBSCl (3.0 g, 20.1 mmol) in DMPU (40 mL) was then added rapidly, and the mixture was stirred at –78 °C for 30 min, 0 °C for 30 min and room temperature for 30 min. Extraction with hexanes gave the crude mixture of Z:E silyl ketene acetals which were dissolved in anhydrous benzene (160 mL), and the resulting solution was heated at reflux for 19 h. Workup, as described above, gave the crude acids (2.1 g, 88%) which were reduced with $LiAlH_4$ as before and chromatographed to give the alcohol (192 mg, 10%, C-2$_\alpha$ epimer) and alcohol **2** (1.50 g, 75%, C-2$_\beta$ epimer).

[2*R*,4a*R*,6*R*(1′*S*,2′*S*,3′*R*),8a*S*]-4,4a,6,8a-Tetrahydro-6-(2-methoxy-1,3-dimethylpent-4-enyl)-7-methyl-2-phenylpyrano[3,2-*d*]-1,3-dioxin (5). To a solution of oxalyl chloride (6.7 mL, 77.2 mmol) in CH_2Cl_2 (213 mL) at –78 °C was added slowly a solution of DMSO (15.1 mL, 212 mmol) in CH_2Cl_2 (10 mL). After 5 min, a solution of alcohol **2** (11.2 g, 38.6 mmol) in CH_2Cl_2 (50 mL) was added dropwise over 1 h. The reaction mixture was stirred for 30 min at –78 °C, and then triethylamine (19.1 mL, 115.8 mmol) was added. The resulting mixture was stirred for 40 min at –78 °C and allowed to warm to 0 °C over 2 h. The reaction mixture was poured into water, and the suspension was extracted with Et_2O. The combined organic extracts were washed with water and saturated aqueous NaCl and then dried ($MgSO_4$). Removal of the solvent under reduced pressure gave the crude product (19.2 g), which was used in the following reaction without further purification.

To a mixture of ^{t}BuOK (15.8 g, 140 mmol) and *cis*-2-butene (8.8 g, 156 mmol) in THF (170 mL) was added dropwise at –78 °C n-BuLi (2.5 M in hexanes, 56.1 mL, 140 mmol). The yellow mixture was stirred at –78 °C for 15 min and –20 °C for 20 min and then recooled to –78 °C. A solution of (–)-*B*-methoxydiisopinocampheylborane (46.5 g, 147 mmol) in THF (170 mL) was added by cannula. The resultant, clear solution was stirred at –78 °C for 1 h and treated with BF_3·OEt_2 (22.8 mL, 185 mmol). A solution of the above aldehyde (19.2 g, 66 mmol) in THF (90 mL) was then added dropwise, and the mixture became viscous. Stirring was continued for 2.5 h, and then 3 N aqueous NaOH (102 mL) and 30% aqueous H_2O_2 (42 mL) were added, and the mixture was boiled for 16 h. The crude product was isolated by extraction with Et_2O, and the residue remaining upon removal of the solvent was dissolved in THF (125 mL) and added dropwise at room temperature to a suspension of NaH (80% in oil, hexane washed × 3, 13.4 g, 447 mmol) in THF (125 mL). After 1 h, iodomethane (29.2 mL, 469 mmol) was added, and the mixture was stirred at room temperature for 24 h. Water was cautiously added, the mixture was extracted with Et_2O (×3), and the organic layer was washed with brine and dried ($MgSO_4$). Removal of the solvent gave an oil which was subjected to vacuum distillation to remove the majority of the methylated isopinocampheol (bp 55–58 °C at 0.2 mmHg). The pot residue was purified by flash chromatography with 0–5% EtOAc–hexanes as eluent to give alkene **5** (18.6 g, 78%) which crystallized from hexane as colorless prisms: mp 95–96 °C; $[\alpha]^{25}_D$ +86.6° (c 3.94, $CHCl_3$); IR (CCl_4) 2960, 2920, 1440, 1370, 1290, 1180, 1090, 1075, 905, 690 cm^{-1}; ^1H NMR δ 0.92 (d, J = 7.2, 3H), 1.01 (d, J = 6.9, 3H), 1.71 (s, 3H), 1.86–1.92 (m, 1H), 2.40–2.45 (m, 1H), 3.36 (dd, J = 1.6, 10.2, 1H), 3.47 (s, 3H), 3.57–3.76 (m, 2H), 4.05–4.08 (m, 1H), 4.35 (dd, J = 9.9, 4.2, 1H), 4.51 (br s, 1H), 5.06 (d, J = 10.2, 1H), 5.12 (d, J = 17.1, 1H), 5.58 (s, 1H), 5.88 (br s, 1H), 6.04 (ddd, J = 17.1, 10.2, 7.2, 1H), 7.35–7.37 (m, 3H), 7.49–7.52 (m, 2H); ^{13}C NMR δ 143.7, 138.2, 137.1, 129.4, 128.7, 126.7, 124.6, 113.9, 102.0, 85.7, 74.4, 76.3, 70.3, 68.7, 61.6, 39.8, 39.7, 20.1, 12.2, 12.17. Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.77; H, 8.49.

[2*R*,3*S*,4*S*(2′*R*,4a′*R*,6′*R*,8a′*S*)]-4-(4,4a,6,8a-Tetrahydro-7-methyl-2-phenylpyrano[3,2-*d*]-1,3-dioxin-6-yl)-3-methoxy-2,4-dimethylbutanol (6). A solution of alkene **5** (17.2 g, 48.0 mmol) in THF (130 mL) and water (20 mL) was vigorously stirred with an aqueous solution of N-methylmorpholine N-oxide (11.2 g, 60%, 58 mmol) and OsO_4 (0.96 mmol, 4.9 mL of a 0.2 M solution in benzene) for 5 h at room temperature. Solid $NaIO_4$ (12.3 g, 57.0 mmol) and water (30 mL) were added, and the mixture was stirred for 2 h, after which time a thick, white precipitate had formed. The mixture was poured into water and extracted with Et_2O to provide the crude aldehyde which was dissolved in ethanol (150 mL) and treated with $NaBH_4$ (3.6 g, 95.2 mmol). After 15 min, the solvents were removed *in vacuo*, the residue was stirred with water, and Et_2O and 10% aqueous HCl were added until effervescence ceased. The organic layer was washed with saturated aqueous $NaHCO_3$, water, and brine. Removal of the solvent and chromatography of the crude product on silica gel with 40% EtOAc–hexanes as eluent gave alcohol **6** (15.6 g, 90%) which crystallized from Et_2O–hexanes as prisms: mp 156–157 °C; $[\alpha]^{25}_D$ +56.9° (c 1.74, $CHCl_3$); IR (CCl_4) 3600, 2960, 2900, 1370, 1290, 1180, 1085, 1070, 1020, 690; ^1H NMR δ 0.86 (d, J = 6.9, 3H), 0.87 (d, J = 7.2, 3H), 1.71 (s, 3H), 1.84–1.95 (m, 2H), 3.50 (s, 3H), 3.50–3.74 (m, 5H), 4.05 (m, 1H), 4.33 (dd, J = 10.2, 4.5, 1H), 4.47 (br s, 1H), 5.57 (s, 1H), 5.87 (br s, 1H), 7.34–7.36 (m, 3H, ArH), 7.50–7.52 (m, 2H, ArH); ^{13}C NMR δ 138.0, 136.9, 129.4, 128.7, 126.7, 124.6, 102.0, 82.3, 76.4, 76.1, 70.3, 68.7, 66.7, 61.4, 39.3, 37.7, 20.1, 12.0, 9.7. Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.63; H, 8.45.

[2*R*,4a*R*,6*R*(1′*S*,2′*S*,3′*R*),8a*S*]-4,4a,6,8a-Tetrahydro-6-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-7-methyl-2-phenylpyrano[3,2-*d*]-1,3-dioxin (7). A solution of alcohol **6** (8.0 g, 22.1 mmol), TBSCl (3.9 g, 25.8 mmol), and imidazole (4.0 g, 58.7 mmol) in dry DMF (140 mL) was stirred at room temperature for 12 h. The reaction mixture was poured into water and extracted with Et_2O. Chromatography of the crude product on silica gel with 10% EtOAc–hexanes as eluent gave ether **7** (10.2 g, 97%) as an oil: $[\alpha]^{23}_D$ +35.51° (c 3.88, $CHCl_3$); IR (neat) 2900, 1460, 1380, 1250, 1110, 1020, 970, 830, 760, 700 cm^{-1}; ^1H NMR δ 0.07 (s, 6H), 0.76 (d, J = 6.9, 3H), 0.92 (s, 9H), 0.85 (d, J = 7.2, 3H), 1.56–1.69 (m, 1H), 1.71 (s, 3H), 1.77–1.90 (m, 2H), 3.49 (s, 3H), 3.48–3.62 (m, 3H), 3.66, 3.73 (2d, J = 10.5, 2H), 4.06 (m, 1H), 4.28 (dd, J = 4.2, 9.9, 1H), 5.58 (s, 1H), 5.86 (s, 1H), 7.38 (m, 3H), 7.51 (m, 2H); ^{13}C NMR δ 138.1, 137.3, 129.4, 128.7, 126.6, 124.4, 102.0, 80.4, 76.4, 76.3, 70.2, 68.6, 65.8, 61.4, 39.3, 38.0, 26.3, 20.0, 18.6, 12.3, 9.2, –4.9, –4.8. Anal. Calcd for $C_{27}H_{44}O_5Si$: C, 68.03; H, 9.30. Found: C, 67.89; H, 9.42.

[2*R*,4a*R*,6*R*(1′*S*,2′*S*,3′*R*),7*R*,8*R*,8a*S*]-4,4a,6,7,8,8a-Hexahydro-6-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-7-methyl-2-phenylpyrano[3,2-*d*]-1,3-dioxin-8-ol (8). To a solution of alkene **7** (2.42 g, 5.09 mmol) in THF (27.5 mL) at –5 °C was slowly added a 1 M solution of borane (25.4 mL, 25.4 mmol) in THF. After 32 h at –5 °C, the reaction mixture was cautiously treated with water (4 mL). After the evolution of hydrogen ceased (ca. 15 min), aqueous 3 M NaOAc (8.5 mL) and 10% H_2O_2 (4.2 mL) were added to the reaction mixture. After 12 h at room temperature, the solution was poured into water and extracted with Et_2O. The combined organic extracts were washed with water, saturated aqueous $NaHCO_3$ solution, and brine and dried (Na_2SO_4).

Removal of the solvent under reduced pressure and chromatography on silica gel with 30% EtOAc–hexanes as eluent gave the alcohol (0.21 g, 8.3%) as a glass: $[\alpha]^{23}_D$ +42.74° (*c* 6.19, $CHCl_3$); IR ($CHCl_3$) 3500, 2900, 1460, 1380, 1250, 1110, 1030, 980, 840, 770, 700, 670 cm^{-1}; ^1H NMR δ 0.07 (s, 6H), 0.76 (d, *J* = 6.9, 3H), 0.93 (s, 9H), 0.99 (d, *J* = 7.2, 3H), 1.10 (d, *J* = 6.9, 3H), 1.83–1.98 (m, 2H), 2.28 (m, 1H), 2.60 (m, 1H), 3.45 (s, 3H), 3.48–3.78 (m, 7H), 3.90 (m, 1H), 4.24 (m, 2H), 5.53 (s, 1H), 7.38 (m, 3H), 7.51 (m, 2H); ^{13}C NMR δ 137.9, 129.6, 128.8, 126.7, 102.3, 84.9, 80.5, 76.3, 72.4, 70.3, 67.5, 65.9, 61.1, 40.7, 38.0, 37.6, 26.7, 26.4, 18.6, 15.7, 13.0, 9.5, –4.8, –4.9. Anal. Calcd for $C_{27}H_{46}O_6Si$: C, 65.55; H, 9.37. Found: C, 65.35; H, 9.21.

There was then eluted isomeric alcohol **8** (2.28 g, 91%) as a white solid. An analytical sample, which was used for single-crystal X-ray analysis, was obtained by recrystallization from hexane: mp 131.5–132.5 °C; $[\alpha]^{23}_D$ +53.05° (*c* 2.19, $CHCl_3$); IR ($CHCl_3$) 3500, 2900, 1460, 1380, 1250, 1110, 1030, 980, 840, 770, 700 cm^{-1}; ^1H NMR δ 0.06 (s, 6H), 0.75 (d, *J* = 6.9, 3H), 0.92 (s, 9H), 1.01 (d, *J* = 7.5, 3H), 1.12 (d, *J* = 6.9, 3H), 1.83–1.93 (m, 2H), 2.30 (m, 1H), 3.45 (s, 3H), 3.44–3.50 (m, 5H), 3.55, 3.62 (2d, *J* = 9.6, 2H), 3.73 (dd, *J* = 4.5, 9.6, 1H), 3.94 (dd, *J* = 9.3, 9.3, 1H), 4.23 (dd, *J* = 4.8, 10.2, 1H), 4.28 (dd, *J* = 3.6, 7.5, 1H), 5.54 (s, 1H), 7.36 (m, 3H), 7.51 (m, 2H); ^{13}C NMR δ 137.8, 129.6, 128.8, 126.7, 102.3, 84.8, 80.5, 76.3, 72.4, 70.3, 67.5, 65.9, 61.1, 40.7, 38.0, 37.6, 26.3, 18.6, 15.7, 13.0, 9.5, –4.9, –4.8. Anal. Calcd for $C_{27}H_{46}O_6Si$: C, 65.55; H, 9.37. Found: C, 65.44; H, 9.42.

[2*R*,4a*R*,6*R*(1′*S*,2′*S*,3′*R*),7*R*,8*R*,8a*S*]-4,4a,6,7,8,8a-Hexahydro-6-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-8-[(methoxymethyl)oxy]-7-methyl-2-phenylpyrano[3,2-*d*]-1,3-dioxin (9). A solution of alcohol **8** (1.0 g, 2.0 mmol) in THF (5 mL) and TMEDA (0.9 mL) was added dropwise to a suspension of KH (344 mg, 4.0 mmol, 35% wt in oil, hexane washed × 3) in THF (5 mL) at 0 °C. After 1 h, MOMCl (228 μL, 3.0 mmol) was added and the mixture was stirred for 30 min at 0 °C. Water was added, and extraction with Et_2O gave the crude product which was chromatographed on silica gel with 5% EtOAc–hexanes as eluent to provide MOM ether **9** (1.08 g, 99%) as a clear oil: $[\alpha]^{23}_D$ +63.0° (*c* 0.92, $CHCl_3$); IR (neat) 2920, 1455, 1370, 1245, 1080, 1020, 910, 830, 720, 690 cm^{-1}; ^1H NMR δ 0.06 (s, 6H), 0.76 (d, *J* = 6.9, 3H), 0.91 (s, 9H), 1.03 (d, *J* = 7.2, 3H), 1.15 (d, *J* = 7.2, 3H), 1.80–1.98 (m, 2H), 2.30 (m, 1H), 3.40 (s, 3H), 3.44 (s, 3H), 3.47–3.69 (m, 5H), 3.77 (m, 1H), 3.94 (dd, *J* = 8.7, 1H), 4.21–4.26 (m, 2H), 4.71 (d, *J* = 6.6, 1H), 4.97 (d, *J* = 6.6, 1H), 7.33–7.35 (m, 3H), 7.47–7.52 (m, 2H); ^{13}C NMR δ 138.0, 129.3, 128.6, 126.4, 101.7, 97.5, 84.6, 80.4, 77.4, 76.1, 70.4, 67.4, 65.9, 60.8, 56.4, 39.8, 37.9, 37.6, 26.3, 18.6, 15.5, 13.9, 9.7, –4.9, –4.8. Anal. Calcd for $C_{29}H_{50}O_7Si$: C, 64.65; H, 9.35. Found: C, 64.94; H, 9.34.

[2*S*,3*S*,4*R*,5*R*,6*R*(1′*S*,2′*S*,3′*R*)]-2-(Bromomethyl)-6-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-3,4,5,6-tetrahydro-4-[(methoxymethyl)oxy]-5-methyl-2*H*-pyran-3-yl Benzoate. To a solution of MOM ether **9** (11.63 g, 21.6 mmol) in anhydrous CCl_4 (230 mL) was added *N*-bromosuccinimide (4.23 g, 23.8 mmol), and the solution was boiled for 30 min. Immediate removal of the solvent under reduced pressure and chromatography of the residue on silica gel with 10% EtOAc–hexanes as eluent gave the bromo benzoate (12.2 g, 91%) as a colorless oil: $[\alpha]^{23}_D$ –18.4° (*c* 1.28, $CHCl_3$); IR (neat) 2920, 1720, 1460, 1260, 1140, 1080, 830, 770, 710 cm^{-1}; ^1H NMR δ 0.037 (3, 3H), 0.04 (s, 3H), 0.85 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 1.09 (d, *J* = 6.9, 3H), 1.23 (d, *J* = 7.2, 3H), 1.73 (m, 1H), 2.06–2.17 (m, 2H), 3.38 (s, 3H), 3.40 (s, 3H), 3.34–3.52 (m, 3H), 3.74–3.94 (m, 4H), 4.26 (m, 1H), 4.73 (ABq, *J* = 6.8, 2H), 5.10 (d, *J* = 2.4, 1H), 7.42–7.47 (m, 2H), 7.58 (m, 1H), 8.05 (m, 1H); ^{13}C NMR δ 165.9, 133.7, 130.2, 130.1, 128.9, 95.9, 78.9, 77.0, 76.2, 69.8, 69.4, 66.7, 58.6, 56.4, 37.5, 36.1, 33.6, 31.0, 26.3, 18.7, 13.3, 11.8, 11.5, –5.0. Anal. Calcd for $C_{29}H_{49}O_7SiBr$: C, 56.39; H, 8.00; Br, 12.94. Found: C, 56.49; H, 7.88; Br, 12.91.

[2*S*,3*S*,4*R*,5*R*,6*R*(1′*S*,2′*S*,3′*R*)]-2-(Bromomethyl)-6-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-3,4,5,6-tetrahydro-4-[(methoxymethyl)oxy]-5-methyl-2*H*-pyran-3-ol (11). To a solution of the bromo benzoate (12.2 g, 19.8 mmol) in MeOH (190 mL) was added $LiOH·H_2O$ (1 g, 23.7 mmol). After 2 h at ambient temperature, the reaction mixture was poured into 300 mL of water and extracted with Et_2O. The combined organic extracts were washed with saturated aqueous NaCl and dried (Na_2SO_4). Removal of the solvent under reduced pressure and flash filtration of the residue on silica gel with 20% EtOAc–hexanes gave alcohol **11** (9.12 g, 90%) which crystallized from hexane as needles: mp 87–88 °C; $[\alpha]^{23}_D$ +13.1° (*c* 1.68, $CHCl_3$); IR ($CHCl_3$) 3500, 2900, 1460, 1260, 1100, 1040, 840, 770, 670 cm^{-1}; ^1H NMR δ 0.06 (s, 6H), 0.77 (d, *J* = 6.9, 3H), 0.90 (s, 9H), 0.99 (d, *J* = 7.5, 3H), 1.06 (d, *J* = 7.2, 3H), 1.77–1.96 (m, 2H), 2.20 (ddq, *J* = 7.2, 1H), 3.46 (s, 3H), 3.38–3.65 (m, 5H), 3.49 (s, 3H), 3.76–3.81 (m, 2H), 4.17–4.21 (m, 2H), 4.74 (ABq, *J* = 6.9, 2H); ^{13}C NMR δ 98.5, 87.6, 80.3, 76.3, 74.6, 72.8, 66.4, 60.6, 56.3, 38.4, 37.7, 37.6, 35.1, 26.4, 18.7, 15.3, 13.2, 10.0, –4.93, –4.89. Anal. Calcd for $C_{22}H_{45}O_6SiBr$: C, 51.45; H, 8.83; Br, 15.56. Found: C, 51.58; H, 8.77; Br, 15.49.

[6*R*,8*R*(1′*S*,2′*S*,3′*R*),9*R*,10*R*]-8-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-[(methoxymethyl)oxy]-9-methyl-1,7-dioxaspiro[5.5]undec-2-en-11-one (13). To a solution of bromo alcohol **11** (1.29 g, 2.5 mmol) in CH_2Cl_2 (46 mL) was added Dess–Martin periodinane (1.53 g, 3.6 mmol). After 2 h at room temperature, the reaction mixture was cooled to 0 °C and hydroquinone (20 mg) was added. Acrolein (17.2 mL, 257.4 mmol) was then added dropwise followed by the dropwise addition of Et_3N (4.27 mL, 25.1 mmol). The cooling bath was removed, and the reaction mixture was allowed to stir at ambient temperature. After 24 h, the dark brown solution was filtered through a 2-in. pad of Florisil in a 350-mL coarse glass fritted funnel. The filtrate was washed with 10% EtOAc–hexanes. Removal of the solvent under reduced pressure and chromatography of the residue on silica gel with 5% EtOAc–hexanes gave enol ether **13** (0.599 g, 49%) as a colorless oil: $[\alpha]^{23}_D$ +50.5° (*c* 3.78, $CHCl_3$); IR (neat) 2600, 1730, 1645, 1450, 1380, 1250, 1210, 1080, 1040, 980, 830, 770 cm^{-1}; ^1H NMR δ 0.04 (s, 6H), 0.80 (d, *J* = 6.9, 3H), 0.89 (s, 9H), 0.93 (d, *J* = 6.9, 3H), 1.12 (d, *J* = 6.9, 3H), 1.76–2.20 (m, 6H), 2.48 (m, 1H), 3.37 (s, 3H), 3.39 (s, 3H), 3.35–3.51 (m, 3H), 4.03 (d, *J* = 5.4, 1H), 4.34 (dd, *J* = 6.9, 4.2, 1H), 4.67 (s, 2H), 4.85 (m, 1H), 6.27 (m, 1H); ^{13}C NMR δ 203.9, 140.4, 102.5, 98.1, 96.2, 80.7, 79.9, 72.1, 66.3, 59.7, 56.3, 40.2, 37.4, 36.3, 26.9, 26.3, 18.6, 16.2, 12.7, 12.3, 10.7, –5.1, –5.0. Anal. Calcd for $C_{25}H_{46}O_7Si$: C, 61.69; H, 9.53. Found: C, 61.78; H, 9.58.

[6*R*,8*R*(1′*S*,2′*S*,3′*R*),9*R*,10*R*,11*R*]- and [6*S*,8*R*(1′*S*,2′*S*,3′*R*),9*R*,10*R*,11*R*]-8-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-[(methoxymethyl)oxy]-9-methyl-1,7-dioxaspiro[5.5]undec-2-en-11-ol (17 and 15). To a solution of ketone **13** (1.0 g, 2.0 mmol) in EtOH (15 mL) was added $NaBH_4$ (158 mg, 4.0 mmol) at 0 °C. After 30 min h at 0 °C, the reaction mixture was concentrated under reduced pressure and diluted with 200 mL of Et_2O and 40 mL of water; 2% aqueous HCl (10 mL) was added until the aqueous phase was slightly acidic. The organic phase was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl and dried (Na_2SO_4). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel with 10% EtOAc–hexanes as eluent gave alcohol **15** (0.040 g, 4%) as a colorless oil: $[\alpha]^{23}_D$ +88.4°(*c* 1.16, $CHCl_3$); ^1H NMR δ 0.04 (s, 6H), 0.80 (d, *J* = 6.9, 3H), 0.89 (s, 9H), 0.93 (d, *J* = 6.9, 3H), 1.12 (d, *J* = 7.2, 3H), 1.58–2.26 (m, 7H), 3.35 (s, 3H), 3.40 (s, 3H), 3.36–3.51 (m, 3H), 3.69–3.72 (m, 2H), 4.03 (dd, *J* = 5.1, 3.6, 1H), 4.70 and 4.72 (ABq, *J* = 6.6, 2H), 4.82 (m, 1H), 6.15 (d, *J* = 6, 1H); ^{13}C NMR δ 139.4, 103.1, 98.4, 95.2, 79.4, 74.6, 72.8, 71.5, 66.6, 58.9, 56.1, 37.4, 36.3, 34.3, 27.8, 26.4, 18.6, 16.5, 12.4, 11.3, 9.0, –5.05, –5.01. Anal. Calcd for $C_{25}hdH_{48}O_7Si$: C, 61.44; H, 9.90. Found: C, 61.37; H, 9.94.

There was then eluted alcohol **17** (0.783 g, 78%) as a colorless oil: $[\alpha]^{23}_D$ +56.3° (*c* 1.26, $CHCl_3$); IR (neat) 3500, 1460, 1380, 1250, 1220, 1075, 1040, 985, 830, 770 cm^{-1}; ^1H NMR δ 0.03 (s, 6H), 0.81 (d, *J* = 6.9, 3H), 0.89 (s, 9H), 0.92 (d, *J* = 6.9, 3H), 1.02 (d, *J* = 7.2, 3H), 1.61–2.23 (m, 7H), 3.08 (d, *J* = 12, 1H), 3.31–3.50 (m, 2H), 3.34 (s, 3H), 3.43 (s, 3H), 3.70 (dd, *J* = 6.6, 3.3, 1H), 3.97 (d, *J* = 8.7, 1H), 4.69–4.80 (m, 3H), 6.28 (m, 1H); ^{13}C NMR δ 140.5, 102.1, 97.9, 97.0, 81.2, 79.3, 69.0, 68.9, 66.6, 58.7, 56.3, 37.2, 35.9, 35.8, 29.1, 26.3, 18.6, 16.4, 12.8, 11.4, –5.0. Anal. Calcd for $C_{25}H_{48}O_7Si$: C, 61.44; H, 9.90. Found: C, 61.41; H, 9.88.

[6*R*,8*R*(1′*S*,2′*S*,3′*R*),9*R*,10*R*,11*R*]-11-(Benzyloxy)-8-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-[(methoxymethyl)oxy]-9-methyl-1,7-dioxaspiro[5.5]undec-2-ene (22). A solution of alcohol **17** (580 mg, 1.2 mmol) in THF (10 mL) was added dropwise to a suspension of KH (272 mg, 2.4 mmol, 35% wt in oil, hexane washed × 3) in THF (10 mL) at 0 °C. After 30 min, benzyl bromide (183 μL, 1.5 mmol) was added dropwise and the mixture was stirred for 30 min at 0 °C. Water was cautiously added, and the aqueous layer was extracted with Et_2O. Chromatography of the crude product on silica gel with 10% EtOAc–hexanes as eluent provided ether **22** (644 mg, 94%) as a colorless oil: $[\alpha]^{23}_D$ +7.0° (*c* 3.43, $CHCl_3$); ^1H NMR δ 0.04 (s, 6H), 0.80 (d, *J* = 6.6, 3H), 0.89 (s, 9H), 0.89 (d, *J* = 6.3, 3H), 0.96 (d, *J* = 7.2, 3H), 1.34–1.40 (m, 1H), 1.75–2.23 (m, 6H), 3.34 (s, 3H), 3.30–3.50 (m, 3H), 3.41 (s, 3H), 3.88 (dd, *J* = 3.3, 1H), 4.07 (dd, *J* = 8.4, 1.5, 1H), 4.50 (d, *J* = 12.0, 1H), 4.72–4.80 (m, 4H), 6.31 (br d, *J* = 6.0, 1H), 7.30–7.35 (m, 5H); ^{13}C NMR δ 141.1, 138.0, 129.8, 128.8, 128.3, 101.6, 97.4, 96.4, 79.5, 75.8, 75.6, 71.7, 69.1, 66.6, 58.7, 56.1, 37.3, 36.0, 29.4, 26.3, 18.7,

16.7, 12.7, 11.8, 11.3, −5.0. Anal. Calcd for $C_{32}H_{54}O_7Si$: C, 66.40; H, 9.40. Found: C, 66.52; H, 9.33.

[6*S*,8*R*(1′*S*,2′*S*,3′*R*),9*R*,10*R*,11*R*]-11-(Benzyloxy)-8-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-[(methoxymethyl)oxy]-9-methyl-1,7-dioxaspiro[5.5]undec-2-ene (26). A solution of alcohol **15** (116 mg, 0.24 mmol) in THF (2 mL) was added dropwise to a suspension of KH (54.4 mg, 0.47 mmol, 35% wt in oil, hexane washed × 3) in THF (1 mL) at 0 °C. After 1 h, benzyl bromide (37 μL, 0.31 mmol) was added dropwise and the mixture was stirred for 1 h at 0 °C and 2 h at room temperature. Water was cautiously added, and the aqueous layer was extracted with Et_2O. Chromatography of the crude product on silica gel with 5% EtOAc–hexanes as eluent provided ether **26** (118 mg, 86%) as a colorless oil: $[\alpha]^{23}_D$ +65.8° (*c* 1.14, $CHCl_3$); IR (neat) 2920, 1650, 1460, 1380, 1250, 1210, 1090, 1030, 990, 825, 770, 700 cm^{-1}; ^1H NMR δ 0.040 (s, 3H), 0.043 (s, 3H), 0.81 (d, *J* = 6.6, 3H), 0.89 (s, 9H), 0.92 (d, *J* = 6.9, 3H), 1.19 (d, *J* = 7.2, 3H), 1.46 (m, 1H), 1.71–1.89 (m, 2H), 2.09–2.18 (m, 3H), 2.30 (m, 1H), 3.35 (s, 3H), 3.36–3.47 (m, 3H), 3.41 (s, 3H), 3.52 (d, *J* = 3.3, 1H), 3.69 (dd, *J* = 7.8, 2.1, 1H), 4.16 (dd, *J* = 4.8, 3.3, 1H), 4.58 (d, *J* = 11.4, 1H), 4.70 (ABq, *J* = 6.6, 2H), 4.80 (br t, *J* = 5.4, 1H), 4.94 (d, *J* = 11.4, 1H), 6.15 (m, 1H), 7.31–7.36 (m, 5H); ^{13}C NMR δ 139.5, 128.5, 128.0, 127.7, 103.1, 99.0, 95.0, 79.3, 75.4, 73.6, 66.6, 58.8, 56.0, 37.5, 36.3, 34.9, 28.2, 26.4, 18.7, 16.8, 12.4, 11.3, 9.0, −5.01, −4.99. Anal. Calcd for $C_{32}H_{54}O_7Si$: C, 66.40; H, 9.40. Found C, 66.43; H, 9.23.

[2*R*,5*R*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*R*,10*R*]- and [2*R*,5*S*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*R*,10*S*]-10-(Benzyloxy)-7-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate (24 and 25). A solution of dimethyldioxirane in acetone (16 mL, 0.11 M, 1.7 mmol) was added dropwise to a solution of ether **22** (822 mg, 1.4 mmol) in CH_2Cl_2 (16 mL) at 0 °C. After the addition was complete, the solvents were removed *in vacuo* (0.2 mmHg) at 0 °C. The residue was dissolved in dry $CHCl_3$ (16 mL), and freshly recrystallized PPTs (50 mg, 0.2 mmol) was added. The solution was stirred at room temperature for 1 h, and an aliquot was removed and showed a 1.5:1 ratio of aldehydes by ^1H NMR spectroscopy. EtOH (35 mL) and $NaBH_4$ (104 mg, 2.8 mmol) were added at room temperature, and after 15 min, the solvents were removed *in vacuo*. Et_2O (50 mL) and water (10 mL) were added to the residue, and the aqueous layer was acidified to pH 4 at 0 °C with 5% aqueous HCl. The organic layer was washed with saturated aqueous $NaHCO_3$, water, and brine. Removal of the solvent gave the crude alcohols which were dissolved in CH_2Cl_2 (10 mL) and treated with pyridine (345 μL, 4.2 mmol), DMAP (10 mg), and benzoyl chloride (330 μL, 2.8 mmol) at 0 °C. The solution was stirred at room temperature for 16 h, diluted with Et_2O, and washed, in turn, with saturated $NaHCO_3$, 5% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. Removal of the solvent and chromatography of the residue on silica gel with 5% EtOAc–hexanes as eluent gave [5.6]-spiroketal **25** (497 mg, 50%) as an oil: $[\alpha]^{23}_D$ −5.5° (*c* 2.16, $CHCl_3$); R_f 0.38 (20% EtOAc–hexanes); IR (neat) 2920, 2880, 1720, 1445, 1375, 1310, 1265, 1145, 1080, 1035, 830, 770, 705 cm^{-1}; ^1H NMR δ 0.03 (s, 6H), 0.84 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.97 (d, *J* = 7.2, 3H), 1.00 (d, *J* = 6.9, 3H), 1.74 (m, 1H), 1.86 (m, 1H), 2.01–2.34 (m, 5H), 3.32 (s, 3H), 3.35 (s, 3H), 3.34–3.50 (m, 2H), 3.65–3.68 (m, 2H), 3.80 (t, *J* = 3.0, 1H), 4.33 (dd, *J* = 11.1, 5.6, 1H), 4.40 (dd, *J* = 11.1, 4.2, 1H), 4.60–4.78 (m, 5H), 7.10–7.58 (m, 8H), 8.04–8.06 (m, 2H); ^{13}C NMR δ 167.0, 139.0, 133.3, 130.5, 130.2, 128.7, 128.6, 128.1, 127.8, 111.2, 96.6, 78.9, 78.5, 76.2, 75.1, 73.6, 67.0, 66.7, 58.3, 55.9, 37.3, 36.1, 35.4, 28.2, 26.8, 26.3, 18.7, 13.2, 11.65, 11.60, −5.0. Anal. Calcd for $C_{39}H_{60}O_9Si$: C, 66.82; H, 8.63. Found: C, 66.73; H, 8.73.

Further elution with 20% EtOAc–hexanes gave isomeric spiroketal **24** (328 mg, 33%) as an oil: $[\alpha]^{23}_D$ −3.2° (*c* 1.48, $CHCl_3$); R_f 0.18 (20% EtOAc–hexanes); IR (neat) 2920, 2880, 1720, 1445, 1375, 1310, 1265, 1080, 1035, 1000, 830, 770, 710 cm^{-1}; ^1H NMR δ 0.03 (s, 6H), 0.78 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.93 (d, *J* = 7.2, 3H), 0.99 (d, *J* = 6.9, 3H), 1.74–1.88 (m, 2H), 1.96–1.22 (m, 5H), 3.31 (s, 3H), 3.36 (s, 3H), 3.28–3.45 (m, 3H), 3.49 (d, *J* = 3.6, 1H), 3.86 (dd, *J* = 3.6, 3.0, 1H), 4.11 (dd, *J* = 9.6, 1.8, 1H), 4.33 (dd, *J* = 10.8, 6.0, 1H), 4.43–4.49 (m, 2H), 4.64 (m, 1H), 4.71 (d, *J* = 7.0, 1H), 4.74 (d, *J* = 12.6, 1H), 4.78 (d, *J* = 7.0, 1H), 7.27–7.58 (m, 8H), 8.04–8.06 (m, 2H); ^{13}C NMR δ 166.7, 138.2, 133.2, 130.8, 130.1, 128.8, 128.6, 128.3, 108.1, 96.4, 79.6, 79.2, 75.5, 73.6, 71.6, 69.7, 68.5, 66.8, 58.3, 56.1, 37.2, 36.1, 35.7, 35.2, 27.4, 26.3, 18.6, 13.4, 11.6, 11.5, −5.1. Anal. Calcd for $C_{39}H_{60}O_9Si$: C, 66.82; H, 8.63. Found: C, 66.66; H, 8.72.

[2*R*,3*R*,6*R*,8*R*(1′*S*,2′*S*,3′*R*),9*R*,10*R*,11*R*]-11-(Benzyloxy)-8-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-2-methoxy-10-[(methoxymethyl)oxy]-9-methyl-1,7-dioxaspiro[5.5]undecan-3-ol (32). A solution of dimethyldioxirane in acetone (3.2 mL, 0.075 M, 0.24 mmol) was added dropwise to a solution of ether **22** (115 mg, 0.2 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After the addition was complete, the solvents were removed *in vacuo* (0.2 mmHg) at 0 °C. The residue was dissolved in dry MeOH (2 mL) and stirred at room temperature for 20 h. Removal of the solvent and chromatography on silica gel with 40% EtOAc–hexanes as eluent gave alcohol **32** (117 mg, 94%) as an oil: $[\alpha]^{23}_D$ −32.1° (*c* 0.38, $CHCl_3$); IR (neat) 3450, 2920, 1460, 1375, 1250, 1110, 1085, 980, 830, 770, 695 cm^{-1}; ^1H NMR δ 0.04 (s, 6H), 0.84 (d, *J* = 6.9, 3H), 0.89 (s, 9H), 0.91 (d, *J* = 6.9, 3H), 0.99 (d, *J* = 6.9, 3H), 1.45–1.81 (m, 3H), 1.96–2.17 (m, 4H), 2.20 (d, *J* = 5.4, 1H), 3.24 (d, *J* = 3.3, 1H), 3.32 (s, 3H), 3.34–3.49 (m, 3H), 3.39 (s, 3H), 3.53 (s, 3H), 3.83–3.87 (m, 2H), 4.16 (dd, *J* = 9.9, 1.5, 1H), 4.47 (d, *J* = 11.7, 1H), 4.69–4.78 (m, 4H), 7.34–7.36 (m, 5H); ^{13}C NMR δ 137.7, 129.1, 128.9, 128.5, 103.9, 99.1, 96.3, 79.2, 76.4, 75.0, 71.7, 69.1, 67.7, 66.6, 58.2, 56.7, 56.1, 37.4, 35.3, 35.1, 29.8, 26.3, 23.7, 18.7, 12.7, 11.7, 11.5, −5.0. Anal. Calcd for $C_{33}H_{58}O_9Si$: C, 63.23; H, 9.33. Found: C, 63.27; H, 9.25.

(*R*)-Mosher Ester 33. To a solution of alcohol **32** (30 mg, 47.9 μmol) in anhydrous pyridine (0.5 mL) was added a solution of (*R*)-methoxy-(trifluoromethyl)phenylacetic acid chloride (24.2 mg, 98.5 μmol) in pyridine (0.5 mL) at 0 °C. The solution was stirred at room temperature for 2 h and diluted with Et_2O. The organic layer was washed, in turn, with 1.5% aqueous HCl, saturated aqueous $NaHCO_3$, water, and brine. Chromatography of the crude product on silica gel with 10% EtOAc–hexanes as eluent gave (*R*)-MTPA ester **33** (28.0 mg, 69%) which crystallized on standing. Recrystallization from MeOH gave colorless lathes suitable for a single-crystal X-ray structural determination: mp 122–123 °C; $[\alpha]^{23}_D$ −5.6° (*c* 0.46, $CHCl_3$); ^1H NMR δ 0.04 (s, 6H), 0.84 (d, *J* = 6.9, 3H), 0.89 (s, 9H), 0.91 (d, *J* = 6.9, 3H), 1.01 (d, *J* = 6.9, 3H), 1.38 (m, 1H), 1.63 (m, 1H), 1.77 (m, 1H), 2.02–2.24 (m, 4H), 3.21 (d, *J* = 3.3, 1H), 3.33 (s, 3H), 3.37 (s, 3H), 3.35 (m, 1H), 3.46–3.53 (m, 2H), 3.52 (s, 3H), 3.53 (s, 3H), 3.86 (t, *J* = 3.0, 1H), 4.16 (dd, *J*=9.9, 1.8, 1H), 4.39 (d, *J* = 11.7, 1H), 4.66 (d, *J* = 11.7, 1H), 4.73 (AB q, *J* = 6.6, 2H), 4.85 (d, *J* = 4.5, 1H), 5.21 (m, 1H), 7.26 (br s, 5H), 7.37–7.39 (m, 3H), 7.52–7.58 (m, 2H). Anal. Calcd for $C_{43}H_{65}O_{11}F_3Si$: C, 61.26; H, 7.77. Found: C, 61.05; H, 7.67.

[2*S*,5*S*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*R*,10*R*]-10-(Benzyloxy)-7-[4-((*tert*-butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)-oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate (28). Oxidation of ether **26** (100 mg, 0.17 mmol) with dimethyldioxirane followed by rearrangement, reduction, and benzoylation in a manner similar to that described above furnished, after chromatography on silica gel with 5% EtOAc–hexanes as eluent, [5.6]-spiroketal **28** (89 mg, 73%) as an oil: $[\alpha]^{23}_D$ +47.7° (*c* 0.86, $CHCl_3$); IR (neat) 2920, 2880, 1720, 1445, 1375, 1310, 1265, 1145, 1080, 1035, 830, 770, 705 cm^{-1}; ^1H NMR δ 0.02 (s, 6H), 0.80 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 1.01 (d, *J* = 6.9, 3H), 1.18 (d, *J* = 7.2, 3H), 1.68–1.89 (m, 3H), 2.02–2.12 (m, 2H), 2.23–2.30 (m, 2H), 3.32 (s, 3H), 3.42 (s, 3H), 3.26–3.50 (m, 2H), 3.52 (d, *J* = 2.7, 1H), 3.75 (dd, *J* = 9.6, 1.8, 1H), 4.04 (dd, *J* = 4.8, 2.7, 1H), 4.29–4.59 (m, 3H), 4.60 (d, *J* = 11.4, 1H), 4.71 (AB q, *J* = 6.6, 2H), 4.99 (d, *J* = 11.4, 1H), 7.26–7.58 (m, 8H), 8.05–8.07 (m, 2H); ^{13}C NMR δ 166.8, 139.6, 133.4, 130.6, 130.2, 128.8, 128.5, 128.1, 127.7, 109.3, 95.2, 80.4, 79.5, 78.6, 76.6, 75.0, 73.8, 68.7, 66.8, 58.1, 56.1, 37.5, 37.1, 35.7, 34.0, 27.6, 26.4, 18.7, 13.1, 11.7, 8.6, −5.0. Anal. Calcd for $C_{39}H_{60}O_9Si$: C, 66.82; H, 8.63. Found: C, 66.90; H, 8.64.

[2*R*,5*S*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*R*,10*R*]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-hydroxy-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate. A solution of ether **25** (764 mg, 1.1 mmol) in EtOAc/EtOH (1:1, 22 mL) containing palladized charcoal (10%, 80 mg) and a crystal of oxalic acid was stirred under an atmosphere of hydrogen for 4 h. The catalyst was removed by filtration through a bed of Celite, and concentration of the filtrate gave the crude product which was purified by chromatography on silica gel. Elution with 20% EtOAc–hexanes yielded the alcohol (639 mg, 96%) as a clear oil: $[\alpha]^{23}_D$ −19.8° (*c* 1.77, $CHCl_3$); IR (neat) 3470, 2920, 1720, 1445, 1380, 1310, 1270, 1090, 1030, 830, 770, 710 cm^{-1}; ^1H NMR δ 0.031 (s, 3H), 0.034 (s, 3H), 0.83 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.99 (d, *J* = 6.9, 3H), 1.03 (d, *J* = 6.9, 3H), 1.68–1.82 (m, 2H), 2.08–2.24 (m, 5H), 3.32 (s, 3H), 3.34–3.49 (m, 3H), 3.40 (s, 3H), 3.64 (dd, *J* = 8.7, 1.8, 1H), 3.80–3.86 (m, 2H), 4.15 (m, 1H), 4.58 (m, 2H), 4.67 (d, *J* = 6.6, 1H), 4.76 (d, *J* = 6.6, 1H), 7.39–7.55 (m, 3H), 8.04–8.06 (m, 2H); ^{13}C NMR δ 167.5, 133.5, 130.5, 130.2, 128.7, 111.5, 97.3, 81.4, 78.9, 76.6, 73.9, 68.0, 67.0, 66.7, 58.3, 56.2, 37.3, 36.0, 35.5, 27.3, 26.7, 26.2, 18.6, 13.2, 11.7, 11.6, −5.1. Anal. Calcd for $C_{32}H_{54}O_9Si$: C, 62.92; H, 8.91. Found: C, 62.67; H, 8.76.

[2R,5R,7R(1'S,2'S,3'R),8R,9R,10R]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-hydroxy-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate. A solution of ether **24** (291 mg, 0.42 mmol) in EtOAc/EtOH (1:1, 5 mL) containing palladized charcoal (10%, 20 mg) and a crystal of oxalic acid was stirred under an atmosphere of hydrogen for 24 h. The catalyst was removed by filtration through a bed of Celite, and concentration of the filtrate gave the crude product which was purified by chromatrography on silica gel. Elution with 20% EtOAc–hexanes yielded the alcohol (246 mg, 97%) as a clear oil: $[\alpha]^{23}_D$ +2.2° (*c* 1.36, $CHCl_3$); IR (neat) 3400, 2920, 1720, 1450, 1310, 1265, 1085, 1030, 1000, 830, 770, 710 cm^{-1}; ^1H NMR δ 0.01 (s, 3H), 0.02 (s, 3H), 0.79 (d, *J* = 6.6, 3H), 0.87 (s, 9H), 0.98 (d, *J* = 7.5, 3H), 1.00 (d, *J* = 6.9, 3H), 1.71 (m, 1H), 1.82–2.11 (m, 4H), 2.20 (m, 1H), 2.31 (m, 1H), 3.31 (s, 3H), 3.38 (s, 3H), 3.27–3.47 (m, 3H), 3.57–3.65 (m, 2H), 4.01, 3.64 (dd, *J* = 9.6, 1.5, 1H), 4.32–4.45 (m, 3H), 4.66 (AB q, *J* = 6.9, 2H), 7.39–7.56 (m, 3H), 8.04–8.06 (m, 2H); ^{13}C NMR δ 166.6, 133.3, 130.7, 130.0, 128.7, 108.9, 97.1, 82.0, 80.0, 78.9, 69.6, 68.8, 66.8, 66.4, 58.2, 56.4, 37.1, 35.9, 35.6, 35.5, 27.4, 26.3, 18.6, 13.3, 11.7, 11.1, –5.1. Anal. Calcd for $C_{32}H_{54}O_9Si$: C, 62.92; H, 8.91. Found: C, 62.90; H, 9.01.

[2S,5S,7R(1'S,2'S,3'R),8R,9R,10R]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-10-hydroxy-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate. A solution of ether **28** (86 mg, 0.12 mmol) in EtOH (2 mL) was stirred with 10% $Pd(OH)_2$ on carbon (5 mg) under an atmosphere of hydrogen for 3 h at room temperature. The suspension was filtered through Celite, and the solvent was removed. ^1H NMR and TLC analysis of the crude product showed a mixture of product and diol. A solution of this crude mixture in DMF (2 mL) was treated with TBSCl (18 mg, 0.12 mmol) and imidazole (20 mg, 0.30 mmol) at room temperature for 2 h. Water was added, and the crude product was isolated by extraction with Et_2O. Chromatography on silica gel with 20% EtOAc–hexanes as eluent gave the alcohol (70.4 mg, 94%) as a colorless oil: $[\alpha]^{23}_D$ +44.7°(*c* 0.94, $CHCl_3$); ^1H NMR δ 0.02 (s, 6H), 0.80 (d, *J* = 6.9, 3H), 0.87 (s, 9H), 1.02 (d, *J* = 6.9, 1H), 1.10 (d, *J* = 7.2, 3H), 1.70 (m, 1H), 1.89 (m, 1H), 2.01, 2.28 (m, 5H), 3.29–3.48 (m, 3H), 3.30 (s, 3H), 3.40 (s, 3H), 3.72 (m, 1H), 3.76 (dd, *J* = 9.3, 1.8 , 1H), 3.93 (dd, *J* = 5.1, 3.3, 1H), 4.31–4.48 (m, 3H), 4.69 (d, *J* = 6.6, 1H), 4.75 (d, *J* = 6.6, 1H), 7.44–7.56 (m, 3H), 8.04–8.07 (m, 2H); ^{13}C NMR δ 167.2, 133.4, 130.5, 130.1, 128.8, 108.7, 95.4, 79.6, 78.9, 75.4, 73.12, 73.07, 68.7, 66.8, 58.4, 56.2, 37.5, 36.4, 35.8, 33.4, 27.6, 26.4, 18.6, 13.1, 11.7, 8.7, –5.06, –5.02. Anal. Calcd for $C_{32}H_{54}O_9Si$: C, 62.92; H, 8.91. Found: C, 63.07; H, 8.76.

[2R,5R,7R(1'S,2'S,3'R),8R,9S]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate (29). A solution of the alcohol (375 mg, 0.61 mmol) in anhydrous CS_2 (6 mL) was added dropwise to a suspension of hexane washed with NaH (80%, 36 mg, 1.2 mmol) in CS_2 (12 mL) at 0 °C under argon. The mixture was stirred at room temperature for 3 h, and MeI (380 μL, 6.1 mmol) and TMEDA (0.5 mL) were added. After the solution was stirred for 12 h, water was added and the crude product was isolated by extraction with Et_2O. Chromatography on silica gel with 10% EtOAc–hexanes as eluent gave the xanthate (395 mg, 92%) as a light yellow oil.

To a boiling solution of the above xanthate (750 mg, 1.07 mmol) and $PhSiH_3$ (264 μL, 2.1 mmol) in desulfurized anhydrous toluene (10 mL) under argon was added benzoyl peroxide [400 μL of a 1.04 g (4.28 mmol) solution in toluene (8 mL)] every 30 min. After five additions, extra $PhSiH_3$ (264 μL, 2.1 mmol) was added followed by five more additions of the benzoyl peroxide solution at 30-min intervals. The solvents were removed *in vacuo*, and the residue remaining was purified by chromatography on silica gel. Elution with 10% EtOAc–hexanes gave unreacted xanthate (192 mg) followed by the deoxygenated spiroketal **29** (409 mg, 64%, 86% based on recovered xanthate) as a colorless oil: $[\alpha]^{23}_D$ –5.4°(*c* 1.12, $CHCl_3$); IR (neat) 2920, 1720, 1445, 1380, 1310, 1270, 1150, 1090, 1035, 830, 770, 710 cm^{-1}; ^1H NMR δ 0.03 (s, 3H), 0.04 (s, 3H), 0.84 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 1.00 (d, *J* = 6.9, 6H), 1.67–1.92 (m, 5H), 2.10–2.26 (m, 3H), 2.56 (m, 1H), 3.33 (s, 3H), 3.34 (s, 3H), 3.36–3.50 (m, 3H), 3.66 (dd, *J* = 9.0, 1.5, 1H), 3.77 (m, 1H), 4.31 (dd, *J* = 11.4, 5.1, 1H), 4.36 (dd, *J* = 11.4, 4.2, 1H), 4.58 (m, 1H), 4.63 (s, 2H), 7.40–7.55 (m, 3H), 8.03–8.06 (m, 2H); ^{13}C NMR δ 167.0, 133.4, 130.6, 130.1, 128.7, 108.1, 95.0, 78.6, 76.6, 75.8, 74.0, 67.2, 66.7, 58.2, 55.8, 37.2, 35.7, 34.5, 34.1, 33.3, 27.2, 26.3, 18.6, 13.1, 11.7, 11.5, –5.1. Anal. Calcd for $C_{32}H_{54}O_8Si$: C, 64.61; H, 9.15. Found: C, 64.80; H, 9.03.

[2R,5S,7R(1'S,2'S,3'R),8R,9S]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate (37). The alcohol (537 mg, 0.88 mmol) was converted into the xanthate (468 mg, 76%) and then deoxygenated with $PhSiH_3$ and benzoyl peroxide in a manner similar to that described above. Chromatography on silica gel and elution with 10% EtOAc–hexanes gave the deoxygenated spiroketal **37** (206 mg, 52%) as a colorless oil: $[\alpha]^{23}_D$ +23.6° (*c* 1.25, $CHCl_3$); IR (neat) 2920, 1725, 1450, 1310, 1270, 1090, 1045, 980, 830, 775, 710 cm^{-1}; ^1H NMR δ 0.02 (s, 3H), 0.03 (s, 3H), 0.80 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.94 (d, *J* = 6.9, 3H), 1.02 (d, *J* = 6.9, 3H), 1.71–2.94 (m, 9H), 3.31–3.49 (m, 3H), 3.33 (s, 3H), 3.34 (s, 3H), 3.66 (m, 1H), 4.08 (dd, *J* = 9.6, 1.5, 1H), 4.33 (m, 1H), 4.44–4.53 (m, 2H), 4.69 (s, 2H), 7.40–7.58 (m, 3H), 8.03–8.06 (m, 2H); ^{13}C NMR δ 166.7, 133.2, 130.8, 130.1, 128.6, 106.3, 94.9, 78.8, 75.5, 69.9, 69.0, 66.8, 58.2, 55.8, 40.1, 37.1, 35.9, 33.4, 32.6, 27.6, 26.3, 18.6, 13.4, 11.7, 11.2, –5.1. Anal. Calcd for $C_{32}H_{54}O_8Si$: C, 64.61; H, 9.15. Found: C, 64.54; H, 9.02.

Further elution gave the starting alcohol (119 mg, 30%).

[2S,5R,7R(1'S,2'S,3'R),8R, 9S]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate (30). The alcohol (70 mg, 0.11 mmol) was converted into the xanthate (69.1 mg, 86%) and then deoxygenated with $PhSiH_3$ and benzoyl peroxide. Chromatography on silica gel and elution with 5–10% EtOAc–hexanes gave unreacted xanthate (6.0 mg) followed by the deoxygenated spiroketal **30** (27.7 mg, 64%, 72% based on recovered xanthate) as a colorless oil: $[\alpha]^{23}_D$ +52.9° (*c* 1.02, $CHCl_3$); IR (neat) 2950, 1735, 1460, 1395, 1280, 1100, 1055, 850, 790, 720 cm^{-1}; ^1H NMR δ 0.02 (s, 6H), 0.87 (d, *J* = 6.9, 3H), 0.87 (s, 9H), 0.91 (d, *J* = 6.9, 3H), 0.99 (d, *J* = 6.9, 3H), 1.70–1.93 (m, 5H), 2.04–2.15 (m, 4H), 3.30–3.49 (m, 3H), 3.33 (s, 3H), 3.35 (s, 3H), 3.71 (dd, *J* = 9.3, 1.5, 1H), 4.04 (m, 1H), 4.28–4.48 (m, 3H), 4.61 (d, *J* = 6.6, 1H), 4.69 (d, *J* = 6.6, 1H), 7.40–7.58 (m, 3H), 8.05–8.08 (m, 2H); ^{13}C NMR δ 166.8, 133.3, 130.6, 130.2, 128.7, 107.5, 95.1, 79.0, 78.7, 74.2, 73.7, 66.8, 66.0, 58.4, 55.8, 39.0, 37.4, 36.05, 35.96, 34.2, 27.7, 26.4, 18.7, 13.1, 11.7, 5.4, –5.06, –5.02. Anal. Calcd for $C_{32}H_{54}O_8Si$: C, 64.61; H, 9.15. Found: C, 64.69; H, 9.21.

[2R,5S,7R(1'S,2'S,3'R),8R,9S]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-hydroxy-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol Benzoate (36). To a solution of MOM ether **29** (36.9 mg, 62.1 μmol) and anhydrous Et_2O (21.2 μL, 0.205 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added dropwise Me_2BBr (118 μL of a 1.58 M solution in CH_2Cl_2, 0.186 mmol). After 20 min at –78 °C, a mixture of THF and saturated aqueous $NaHCO_3$ was added and the mixture was allowed to warm to room temperature and stirred for 3 h. Et_2O was added, and the organic layer was washed with water and brine. Removal of the solvent gave an oil which was dissolved in CH_2Cl_2 (1.0 mL) and stirred with PPTs (5 mg, 20 μmol) for 24 h at room temperature. Saturated aqueous $NaHCO_3$ and Et_2O were added, and the aqueous layer was further extracted with Et_2O. Chromatography of the crude product on silica gel with 10% EtOAc–hexanes as eluent gave alcohol **36** (16.1 mg, 47%) as an oil: $[\alpha]^{23}_D$ +1.2° (*c* 0.40, $CHCl_3$); IR (neat) 3530, 2920, 2840, 1720, 1440, 1265, 1090, 1020, 830, 720, 705 cm^{-1}; ^1H NMR δ 0.02 (s, 6H), 0.78 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.91 (d, *J* = 7.2, 3H), 1.02 (d, *J* = 6.9, 3H), 1.66–2.17 (m, 9H), 3.30 (m, 1H), 3.33 (s, 3H), 3.39–3.46 (m, 2H), 3.75 (m, 1H), 3.80 (d, *J* = 9.6, 1H), 4.06 (dd, *J* = 9.6, 2.1, 1H), 4.35 (dd, *J* = 11.4, 8.1, 1H), 4.41 (dd, *J* = 11.4, 4.1, 1H), 4.51 (m, 1H), 7.41–7.46 (m, 2H), 7.56 (m, 1H), 8.03–8.06 (m, 2H); ^{13}C NMR δ 166.7, 133.4, 130.4, 130.1, 128.8, 108.0, 79.4, 78.8, 71.5, 69.6, 68.7, 66.7, 58.3, 39.3, 37.2, 36.0, 35.6, 34.9, 26.9, 26.3, 18.6, 13.1, 11.8, 11.4, –5.1, -.5.0. Anal. Calcd for $C_{30}H_{50}O_7Si$: C, 65.42; H, 9.15. Found: C, 65.33; H, 9.15.

Treatment of ether **37** (21.3 mg, 35.9 μmol) in a similar manner to that described above gave alcohol **36** (8.9 mg, 45%). To a solution of alcohol **36** (6.0 mg, 10.9 μmol) in CH_2Cl_2 (0.4 mL) under argon were added $^iPr_2NEt$ (19.0 μL, 0.109 mmol) and MOMCl (8.3 μL, 0.109 mmol). The solution was stirred at room temperature for 48 h and concentrated *in vacuo*. The residue was filtered through a small plug of silica gel with 20% EtOAc–hexanes as eluent to give the MOM ether **37** (5.6 mg, 86%).

Equilibration of Spiroketal 37. A solution of spiroketal **37** (50 mg, 84.2 μmol) and recrystallized PPTs (20 mg) in CH_2Cl_2 (2 mL) was stirred at room temperature for 48 h. The reaction was quenched with saturated aqueous $NaHCO_3$, and the crude product was isolated with Et_2O. Chromatography on silica gel with 10% EtOAc–hexanes as eluent gave alkene **39** (5.8 mg, 13%) as an oil: $[\alpha]^{23}_D$ –66.3° (*c* 1.01, $CHCl_3$); IR (neat) 2920, 1720, 2840, 1440, 1265, 1085, 990, 830, 770, 705 cm^{-1}; ^1H NMR δ 0.017 (s, 3H), 0.022 (s, 3H), 0.80 (d, *J* = 6.9, 3H), 0.87 (s, 9H), 0.96 (d, *J* = 6.9, 3H), 1.03 (d, *J* = 6.9, 3H), 1.75 (m, 1H), 1.87–2.33 (m, 6H), 3.30–3.48 (m, 3H), 3.35 (s, 3H), 3.82 (dd, *J* = 9.3, 2.7 Hz, 1H), 4.39–4.50 (m, 3H), 5.54 (d, *J* = 10.0, 1H), 6.00 (dd, *J* = 10.0, 6, 1H),

7.44–7.59 (m, 3H), 8.04–8.07 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 166.1, 136.7, 133.3, 130.6, 130.2, 128.7, 127.0, 105.0, 79.1, 78.3, 73.2, 69.3, 66.9, 58.6, 38.8, 37.2, 36.2, 30.5, 28.7, 26.3, 18.7, 13.1, 12.9, 11.6, –5.1, –5.0. Anal. Calcd for $C_{30}H_{49}O_6Si$: C, 67.63; H, 9.08. Found: C, 67.72; H, 9.07.

Further elution provided spiroketal **29** (16.5 mg, 32%). This was followed by spiroketal **37** (23.5 mg, 47%).

[2*R*,5*R*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*S*]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol. To a solution of benzoate **29** (223 mg, 0.37 mmol) in MeOH (10 mL) was added $LiOH·H_2O$ (18.9 mg, 0.45 mmol), and the resultant, yellow solution was stirred at room temperature for 2 h. Water and CH_2Cl_2 were added, and the organic layer was washed with water. The aqueous layer was extracted further with CH_2Cl_2, and the combined organic layers were washed with brine and dried (Na_2SO_4). Removal of the solvent and chromatography of the residue on silica gel with 40% EtOAc–hexanes as eluent gave the alcohol (155 mg, 84%) as an oil: $[\alpha]^{23}_D$ –7.8° (*c* 1.48, $CHCl_3$); IR (neat) 3460, 2920, 1460, 1380, 1250, 1145, 1085, 1035, 1000, 830, 770, cm^{-1}; ^{1}H NMR δ 0.02 (s, 3H), 0.03 (s, 3H), 0.83 (d, *J* = 6.6, 3H), 0.88 (s, 9H), 0.98 (d, *J* = 6.6, 3H), 0.99 (d, *J* = 7.2, 3H), 1.57–1.91 (m, 5H), 2.03–2.15 (m, 3H), 2.40 (m, 1H), 3.32 (s, 3H), 3.34 (s, 3H), 3.30–3.51 (m, 4H), 3.63–3.72 (m, 2H), 3.76 (m, 1H), 4.33 (m, 1H), 4.62 (s, 2H); ^{13}C NMR δ 108.0, 95.0, 78.6, 78.4, 76.5, 73.9, 66.7, 65.5, 58.2, 55.9, 37.2, 35.8, 34.6, 34.4, 33.3, 26.4, 26.3, 18.6, 13.1, 11.7, 11.5, –5.1. Anal. Calcd for $C_{25}H_{50}O_7Si$: C, 61.19; H, 10.27. Found: C, 61.25; H, 10.38.

[2*R*,5*R*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*S*]-Methyl 7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-carboxylate (31b). To a solution of the alcohol (135 mg, 0.28 mmol) in CH_2Cl_2 (5 mL) were added pyridine (332 μL, 4.2 mmol) and Dess–Martin reagent (152 mg, 0.35 mmol), and the solution was stirred at room temperature for 1.5 h. Peroxide-free Et_2O, saturated aqueous $NaHCO_3$, and 1.5 M aqueous $Na_2S_2O_3$ were added, and the mixture was stirred until both layers were clear. The organic layer was washed, in turn, with saturated $NaHCO_3$, saturated aqueous $CuSO_4$, water, and brine. Removal of the solvent gave the crude aldehyde (135 mg) which was dissolved in ^{t}BuOH (3.5 mL) and 2-methyl-2-butene (1 mL). A freshly prepared solution of $NaClO_2$ (100 mg, 1.10 mmol) and NaH_2PO_4 (66 mg, 0.55 mmol) in water (1.9 mL) was added, and the mixture was stirred vigorously at room temperature for 2 h. Water was then added, and the product was isolated by extraction with Et_2O. Acid **31a** (135 mg, 97%) was pure by ^{1}H NMR spectroscopy. A portion was methylated with ethereal diazomethane, and chromatography on silica gel with 20% EtOAc–hexanes as eluent furnished ester **31b** (70%) as an oil: $[\alpha]^{23}_D$ +2.6° (*c* 1.17, $CHCl_3$); R_f 0.31 (20% EtOAc–hexanes); IR (neat) 2940, 2920, 1750, 1460, 1250, 1195, 1145, 1085, 1025, 990, 820, 770 cm^{-1}; ^{1}H NMR δ 0.03 (s, 3H), 0.04 (s, 3H), 0.83 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.98 (d, *J* = 6.6, 3H), 1.00 (d, *J* = 6.9, 3H), 1.64–1.72 (m, 2H), 1.84–2.24 (m, 5H), 2.34–2.48 (m, 2H), 3.32 (s, 3H), 3.35 (s, 3H), 3.30–3.49 (m, 3H), 3.65 (dd, *J* = 9.0, 1.8, 1H), 3.74 (s, 3H), 3.80 (m, 1H), 4.63 (s, 2H), 4.82 (dd, *J* = 9.1, 3.2, 1H); ^{13}C NMR δ 173.6, 109.0, 94.9, 78.5, 76.2, 76.1, 74.5, 66.7, 58.2, 55.9, 52.4, 37.2, 35.6, 34.2, 33.3, 33.2, 29.3, 26.3, 18.6, 13.1, 11.7, 11.4, –5.1. Anal. Calcd for $C_{26}H_{50}O_8Si$: C, 60.20; H, 9.72. Found: C, 60.39; H, 9.80.

[2*R*,5*S*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*S*]-7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-methanol. Hydrolysis of benzoate **37** (120 mg, 0.2 mmol) in a manner similar to that described for compound **29** gave the alcohol (86 mg, 88%) as an oil: $[\alpha]^{23}_D$ –32.7° (*c* 1.5, $CHCl_3$); IR (neat) 3440, 2930, 2860, 1470, 1255, 1130, 1090, 10405, 980, 840, 780 cm^{-1}; ^{1}H NMR δ 0.03 (s, 3H), 0.04 (s, 3H), 0.85 (d, *J* = 6.9, 3H), 0.88 (s, 9H), 0.93 (d, *J* = 6.9, 3H), 0.99 (d, *J* = 7.2, 3H), 1.787–2.11 (m, 9H), 2.16 (br s, 1H), 3.34 (s, 3H), 3.37 (s, 3H), 3.31–3.5 (m, 3H), 3.56 (dd, *J* = 11.4, 6.0, 1H), 3.66–3.71 (m, 2H), 4.04 (dd, *J* = 9.0, 1.8, 1H), 4.29 (m, 1H), 4.70 (AB q, *J* = 6.9, 2H); ^{13}C NMR δ 106.1, 94.9, 82.6, 79.3, 75.3, 69.8, 66.7, 66.6, 58.5, 55.8, 40.7, 37.2, 36.0, 33.6, 33.3, 26.1, 25.8, 18.6, 13.2, 11.9, 11.2, –5.1. Anal. Calcd for $C_{25}H_{50}O_7Si$: C, 61.19; H, 10.27. Found: C, 61.32; H, 10.39.

[2*R*,5*S*,7*R*(1′*S*,2′*S*,3′*R*),8*R*,9*S*]-Methyl 7-[4-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-1,3-dimethylbutyl]-9-[(methoxymethyl)oxy]-8-methyl-1,6-dioxaspiro[4.5]decane-2-carboxylate (38b). Oxidation and methylation of the alcohol (66.2 mg, 0.13 mmol) in a similar method to that described above gave acid **38a** (67 mg, 98%). A portion was treated with ethereal diazomethane to give ester **38b** (77%) as an oil: $[\alpha]^{23}_D$ +47.6° (*c* 1.25, $CHCl_3$); R_f 0.26 (20% EtOAc–hexanes); IR (neat) 2920, 2850, 1760, 1460, 1250, 1205, 1085, 1040, 980, 840, 680 cm^{-1}; ^{1}H NMR δ 0.03 (s, 3H), 0.04 (s, 3H), 0.85–0.90 (m, 6H), 0.89 (s, 9H), 0.93 (d, *J* = 7.2, 3H), 1.65–1.83 (m, 3H), 1.98–2.08 (m, 4H), 2.20–2.25 (m, 2H), 3.33 (s, 3H), 3.37 (s, 3H), 3.31–3.52 (m, 3H), 3.71 (s, 3H), 4.19 (dd, *J* = 10.2, 1.5, 1H), 4.64 (dd, *J* = 8.7, 8.4, 1H), 4.72 (AB q, *J* = 6.0, 2H); ^{13}C NMR δ 173.6, 106.8, 94.4, 78.9, 78.6, 74.5, 69.8, 66.7, 58.1, 55.7, 52.2, 39.9, 37.2, 35.5, 33.1, 32.0, 28.0, 26.3, 18.7, 12.2, 11.7, 11.2, –5.1. Anal. Calcd for $C_{26}H_{50}O_8Si$: C, 60.20; H, 9.72. Found: C, 60.38; H, 9.51.

2(*R*)-Vinyl-2-[2,5-dihydro-5(*R*)-(hydroxymethyl)-3-methyl-2(*R*)-furyl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (43). To a solution of 0.514 g (0.991 mmol) of the ether in 6 mL of HMPA was added 1.13 g (7.43 mmol) of undried CsF. The slurry was heated to 125 °C and stirred for 15 h. After cooling, the mixture was poured into water and extracted with ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure. Chromatography on silica gel (2.5- × 12-cm, 40% ethyl acetate/hexane) gave 0.362 g (94%) of alcohol **43** as a colorless oil: $[\alpha]^{22}_D$ +138° (*c* 1.20, $CHCl_3$); IR (neat) 3010, 2970, 1450, 1370, 1260, 1150, 930, 855 cm^{-1}; ^{1}H NMR δ 1.36 (s, 3H), 1.50 (s, 3H), 1.87 (s, 3H), 3.20 (br s, 1H), 3.54 (m, 2H), 4.47 (d, *J* = 12.0, 1H), 4.65 (m, 3H), 4.89 (d, *J* = 5.7, 1H), 4.98 (d, *J* = 5.4, 1H), 5.16 (m, 2H), 5.84 (dd, *J* = 11.4, 17.7, 1H), 7.3 (m, 5H); ^{13}C NMR δ 139.3, 138.5, 137.7, 128.8, 128.2, 128.1, 124.1, 116.7, 113.0, 109.1, 91.1, 89.4, 88.0, 86.0, 85.3, 69.9, 65.7, 27.0, 25.7, 14.2. Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27. Found: C, 67.96; H, 7.34.

2(*R*)-Ethyl-2-[5(*R*)-(hydroxymethyl)-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (44). To a dry glass bomb (1.5 × 4-cm, narrow neck) were added 6.3 mg (8.89 μmol) of [Rh(NBD)DIPHOS-4]BF_4 and 0.034 g (0.0889 mmol) of dihydrofuran **43** in 2 mL of dry CH_2Cl_2, and the bomb was flushed with argon. After several flushes with hydrogen (200 psi), the bomb was pressurized to 640 psi and allowed to stand, with occasional shaking, for 2 h. The reaction solution was filtered through a 1-g plug of silica gel, washing with 1:1 ethyl acetate–hexane. Rotary evaporation afforded 0.0335 g (96%) of tetrahydrofuran **44** as a colorless oil: $[\alpha]^{22}_D$ +65.0° (*c* 1.0, $CHCl_3$); IR (neat) 3440, 3030, 2930, 1450, 1375, 1265, 1205, 1160, 1075, 1015, 870 cm^{-1}; ^{1}H NMR δ 0.995 (t, *J* = 7.5, 3H), 1.16 (d, *J* = 7.2, 3H), 1.31 (s, 3H), 1.50 (s, 3H), 1.62–2.04 (m, 5H), 2.67 (m, 1H), 3.48 (m, 1H), 3.63 (m, 1H), 4.00 (d, *J* = 4.5, 1H), 4.26 (m, 1H), 4.44 (d, *J* = 12, 1H), 4.58 (d, *J* = 6, 1H), 4.74 (d, *J* = 12, 1H), 4.77 (d, *J* = 6, 1H), 5.16 (s, 1H), 7.32 (m, 5H); ^{13}C NMR δ 138.2, 130.3, 128.2, 128.0, 112.9, 107.7, 91.7, 87.1, 84.1, 80.3, 76.2, 69.8, 65.8, 37.3, 36.0, 31.0, 26.0, 24.5, 17.2, 9.8. Anal. Calcd for $C_{22}H_{32}O_6$: C, 67.32; H, 8.22. Found: C, 67.16; H, 8.13.

2(*R*)-Ethyl-2-[5(*R*)-(formyl)-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (Precursor to 45). To a solution of 0.283 g (0.721 mmol) of alcohol **44** in 4 mL of dry CH_2Cl_2 was added 0.46 g (1.08 mmol) of the Dess–Martin periodinane. After the solution was stirred for 4 h, the solvent was evaporated under reduced pressure and to the residue were added 2 mL of 1.3 N NaOH and 3 mL of ether. After separation, the aqueous layer was extracted with three 2-mL portions of ether. The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure to give 0.271 g (94%) of the crude aldehyde, which was used immediately in the next reaction.

2(*R*)-Ethyl-2-[5(*R*)-[2(*S*)-methyl-1(*S*)-[(triethylsilyl)oxy]-3-butenyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (45). To a solution of 0.165 g (1.47 mmol) of KO^{t}Bu and 0.203 mL (2.18 mmol) of *trans*-2-butene in 3 mL of THF at –78 °C was added 0.613 mL (2.4 M in hexane, 1.47 mmol) of *n*-BuLi dropwise. After being warmed to –48 °C for 15 min, the solution was recooled to –78 °C. To the solution was then added 0.559 g (1.77 mmol) of (–)-β-methoxydiisopinocampheylborane in 3 mL of THF, and after 30 min, 0.235 mL (1.91 mmol) of $BF_3·OEt_2$ was added dropwise. A solution of 0.230 g (0.589 mmol) of the above aldehyde in 3 mL of THF was then added and the resulting mixture stirred vigorously for 3 h. A 3 M solution of aqueous NaOH and 30% H_2O_2 (0.3 mL of each) was then added and the solution allowed to warm and stir for 2 h. To the solution were then added 2 mL of water and 2 mL of ether. After separation, the aqueous layer was extracted with three 2-mL portions of ether. The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure to give a mixture of the product alcohol and isopinocampheol.

To a solution of this mixture in 1 mL of CH_2Cl_2 were added 0.137 mL (1.17 mmol) of 2,6-lutidine and 0.200 mL (0.883 mmol) of TESOTf. After 1 h, the solution was diluted with 3 mL of ether and 5 mL of water. After separation, the aqueous layer was extracted with three 2-mL portions

of ether. The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure. Chromatography on silica gel (2.5 × 12 cm, 5% ethyl acetate/hexane) gave 0.235 g (71%) of silyl ether **45** as a colorless oil: $[\alpha]^{22}_D$ +31.0° (*c* 1.0, $CHCl_3$); IR (neat) 3040, 2950, 2870, 1455, 1370, 1205, 1070, 1010, 870, 735 cm^{-1}; ^1H NMR δ 0.654 (d, *J* = 7.8, 6H), 0.994 (t, *J* = 7.8, 12H), 1.081 (d, *J* = 6.9, 3H), 1.15 (d, *J* = 7.2, 3H), 1.322 (s, 3H), 1.522 (s, 3H), 1.70 (m, 2H), 2.01 (m, 2H), 2.51 (m, 1H), 2.66 (m, 1H), 3.60 (q, *J* = 3, 1H), 3.96 (d, 1H), 4.05 (m, 1H), 4.45 (d, *J* = 12, 1H), 4.59 (d, *J* = 6.3, 1H), 4.76 (d, *J* = 6.3, 1H), 4.79 (d, *J* = 12, 1H), 4.98–5.07 (m, 2H), 5.15 (s, 1H), 5.95 (m, 1H), 7.27–7.35 (m, 5H); ^{13}C NMR δ 141.5, 138.3, 128.8, 128.3, 128.0, 114.6, 112.8, 107.7, 92.2, 87.0, 83.9, 80.1, 79.5, 76.7, 69.8, 43.1, 39.1, 37.3, 31.2, 26.0, 24.4, 17.3, 16.1, 10.0, 7.5, 5.9. Anal. Calcd for $C_{32}H_{52}O_6Si$: C, 68.53; H, 9.35. Found: C, 68.52; H, 9.24.

2(*R*)-Ethyl-2-[5(*R*)-[4-carbethoxy-2(*S*)-methyl-1(*S*)-[(triethylsilyl)oxy]-3-pentenyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (46). To a solution of 0.135 g (0.240 mmol) of alkene **45** in 1 mL of 2:1 THF–water were added 0.048 mL of a 0.2 M solution of OsO_4 in benzene (9.6 μmol) and 0.70 mL of a 5.12 M solution of NMO in water (0.361 mmol). After the solution was stirred vigorously for 12 h, a solution of 0.077 g (0.361 mmol) of $NaIO_4$ in 0.5 mL of water was added. After 2 h, 3 mL of ether and 1 mL of water were added. After separation, the aqueous layer was extracted with three 2-mL portions of ether. The combined organic extracts were dried over Na_2SO_4 and evaporated under reduced pressure to give 0.131 g (98%) of the crude aldehyde.

To a solution of the crude aldehyde in 2 mL of toluene was added 0.174 g (0.481 mmol) of (carbethoxyethylidene)triphenylphosphorane and the solution stirred at 70 °C for 10 h and then at reflux for 12 h. After the solution was cooled, the solvent was evaporated under reduced pressure and the residue subjected to chromatography on silica gel (2.5 × 12 cm, 5% ethyl acetate/hexane) to give 0.123 g (79%) of the desired ester **46** as a colorless oil: $[\alpha]^{22}_D$ +35.2° (*c* 0.85, $CHCl_3$); IR (neat) 2925, 2830, 1700, 1450, 1365, 1230, 1080, 1010, 865, 730 cm^{-1}; ^1H NMR δ 0.642 (q, *J* = 7.8, 6H), 0.979 (m, 12H), 1.06 (d, *J* = 3.9, 3H), 1.15 (d, *J* = 7.2, 3H), 1.28 (m, 6H), 1.49 (s, 3H), 1.68 (m, 2H), 1.89 (d, *J* = 1.2, 3H), 1.96 (m, 2H), 2.63 (m, 1H), 2.88 (m, 1H), 3.56 (q, *J* = 3, 1H), 3.93 (m, 2H), 4.16 (dq, *J* = 1.8, 5.1, 2H), 4.42 (d, *J* = 11.7, 1H), 4.55 (d, *J* = 6, 1H), 4.74 (d, *J* = 6, 1H), 4.75 (d, *J* = 11.7, 1H), 5.11 (s, 1H), 6.85 (dd, *J* = 1.2, 10, 1H), 7.25–7.32 (m, 5H); ^{13}C NMR δ 168.8, 144.7, 138.3, 128.8, 128.8, 127.6, 112.7, 107.6, 92.1, 87.0, 83.8, 80.2, 79.3, 77.0, 69.7, 60.7, 39.4, 38.1, 37.3, 31.3, 25.9, 24.3, 17.2, 17.1, 14.7, 13.0, 10.0, 7.5, 5.9. Anal. Calcd for $C_{36}H_{58}O_8Si$: C, 66.84; H, 9.04. Found: C, 66.73; H, 8.92.

2(*R*)-Ethyl-2-[5(*R*)-[4-(hydroxymethyl)-2(*S*)-methyl-1(*S*)-[(triethylsilyl)oxy]-3-pentenyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran. To a solution of 0.595 g (0.920 mmol) of ester **46** in 25 mL of dichloromethane at –78 °C was added 2.02 mL of a 1.0 M solution of DIBAL in hexane (2.02 mmol). After 30 min, the solution was warmed to 0 °C and stirred for 15 min. Excess aqueous potassium sodium tartrate (10 mL, 0.5 M) was then added and the heterogeneous mixture stirred vigorously for 3 h. Following the addition of 2 mL of water and 20 mL of ether, the phases were separated and the aqueous layer was extracted with three 5-mL portions of ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give an oily residue. Chromatography on silica gel (2.5 × 12 cm, 15% ethyl acetate/hexane) gave 0.522 g (94%) of the alcohol as a colorless oil: $[\alpha]^{22}_D$ +43.3° (*c* 1.2, $CHCl_3$); IR (neat) 3400, 2950, 2870, 1450, 1370, 1200, 1160, 1070, 1010, 870, 730 cm^{-1}; ^1H NMR δ 0.63 (q, *J* = 7.8, 6H), 0.98 (m, 15H), 1.12 (d, *J* = 7.2, 3H), 1.31 (s, 3H), 1.50 (s, 3H), 1.66 (m, 3H), 1.71 (s, 3H), 1.96 (m, 2H), 2.60 (m, 1H), 2.74 (m, 1H), 3.52 (dd, *J* = 3.0, 6.9, 1H), 3.94 (AB q, *J* = 4.8, 2H), 4.00 (s, 2H), 4.43 (d, *J* = 11.4, 1H), 4.56 (d, *J* = 6.0, 1H), 4.73 (d, *J* = 6.0, 1H), 4.75 (d, *J* = 11.4, 1H), 5.11 (s, 1H), 5.48 (d, *J* = 9.3, 1H), 7.31 (m, 5H); ^{13}C NMR δ 138.2, 129.0, 128.8, 128.3, 128.0, 112.8, 107.5, 96.6, 92.1, 87.0, 84.0, 80.2, 79.5, 77.6, 69.7, 39.4, 37.2, 37.0, 31.1, 26.0, 24.5, 17.6, 17.2, 14.3, 10.0, 7.6, 5.9. Anal. Calcd for $C_{34}H_{56}O_7Si$: C, 67.51; H, 9.33. Found: C, 67.51; H, 9.17.

2(*R*)-Ethyl-2-[5(*R*)-[4-((benzyloxy)methyl)-2(*S*)-methyl-1(*S*)-[(triethylsilyl)oxy]-3-pentenyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (Precursor to 47). To a solution of 0.044 g (0.0727 mmol) of the above alcohol in 1 mL of dichloromethane was added 0.014 mL (0.170 mmol) of pyridine followed by 0.018 mL (0.154 mmol) of benzoyl chloride. After 2 h, the solution was poured into 3 mL of saturated aqueous $NaHCO_3$ and 3 mL of ether. After separation, the aqueous layer was extracted with three 2-mL portions of ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give an oily residue. Chromatography on silica gel (1.0 × 10 cm, 5% ethyl acetate/hexane) gave 0.051 g (98%) of the benzoate as a colorless oil: $[\alpha]^{22}_D$ +39.3° (*c* 1.2, $CHCl_3$); IR (neat) 3060, 3020, 2935, 1715, 15.95, 1450, 1370, 1310, 1265, 1205, 1160, 1080, 1010, 870, 710 cm^{-1}; ^1H NMR δ 0.65 (q, *J* = 7.8, 6H), 0.97 (m, 12H), 1.04 (d, *J* = 6.9, 3H), 1.14 (d, *J* = 6.9, 3H), 1.30 (s, 3H), 1.50 (s, 3H), 1.69 (m, 2H), 1.78 (s, 3H), 1.98 (m, 2H), 2.62 (m, 1H), 2.80 (m, 1H), 3.56 (dd, *J* = 2.7, 6.6, 1H), 3.96 (AB q, *J* = 4.8, 2H), 4.44 (d, *J* = 11.7, 1H), 4.56 (d, *J* = 6.3, 1H), 4.73 (m, 4H), 5.11 (s, 1H), 5.64 (d, *J* = 9.9, 1H), 7.2–7.31 (m, 5H), 7.40–7.55 (m, 3H), 8.07 (d, *J* = 7.2, 2H); ^{13}C NMR δ 166.7, 138.3, 133.2, 132.1, 131.0, 130.1, 129.9, 128.8, 128.7, 128.3, 128.0, 112.7, 107.6, 92.2, 87.0, 84.0, 80.2, 79.6, 77.4, 71.2, 69.7, 39.2, 37.3, 37.0, 31.2, 26.0, 24.4, 18.0, 17.3, 14.7, 10.1, 7.6, 6.0. Anal. Calcd for $C_{41}H_{60}O_8Si$: C, 69.46; H, 8.53. Found: C, 69.31; H, 8.63.

2(*R*)-Ethyl-2-[5(*R*)-[4-((benzyloxy)methyl)-1(*S*)-hydroxy-2(*S*)-methyl-3-pentenyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (47). A solution of 0.433 g (0.611 mmol) of the above silyl ether in 25 mL of dilute HF in CH_3CN (0.5 mL, 48% aqueous HF in 99.5 mL of CH_3CN) was stirred for 40 min, and 1.5 mL of saturated $NaHCO_3$ was added. The CH_3CN was then evaporated under reduced pressure and the residue diluted with 5 mL of ether and 3 mL of water. After separation, the aqueous layer was extracted with three 2-mL portions of ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give an oily residue. Chromatography on silica gel (2.5 × 12 cm, 15% ethyl acetate/hexane) gave 0.361 g (99%) of alcohol **47** as a colorless oil: $[\alpha]^{22}_D$ +45.0° (*c* 1.2, $CHCl_3$); IR (neat) 3500, 3060, 3025, 2940, 1720, 1450, 1370, 1270, 1205, 1160, 1075, 1000, 870, 710 cm^{-1}; ^1H NMR δ 1.02 (m, 6H), 1.15 (d, *J* = 67.2, 3H), 1.30 (s, 3H), 1.50 (s, 3H), 1.5–1.7 (m, 2H), 1.79 (s, 3H), 2.00 (m, 1H), 2.18 (m, 1H), 2.63 (m, 2H), 3.63 (dd, *J* = 4.8, 6.9, 1H), 4.04 (d, *J* = 4.2, 1H), 4.18 (m, 1H), 4.42 (d, *J* = 11.7, 1H), 4.57 (d, *J* = 6.0, 1H), 4.75 (m, 4H), 5.13 (s, 1H), 5.53 (d, *J* = 9.3, 1H), 7.25–7.33 (m, 5H), 7.40–7.55 (m, 3H), 8.05 (d, *J* = 7.2, 2H); ^{13}C NMR δ 166.8, 138.2, 133.3, 132.3, 131.4, 130.1, 128.8, 128.2, 128.0, 112.8, 107.5, 91.9, 87.0, 83.9, 80.7, 77.4, 77.0, 71.1, 69.7, 37.1, 35.9, 35.8, 31.2, 26.0, 24.4, 17.7, 17.2, 14.9, 10.1. Anal. Calcd for $C_{35}H_{46}O_8$: C, 70.68; H, 7.80. Found: C, 70.70; H, 7.75.

2(*R*)-Ethyl-2-[5(*R*)-[4(*R*)-((benzyloxy)methyl)-1(*S*)-hydroxy-2(*S*)-methyl-3-pentyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran. To a dry glass bomb (2 × 4 cm, narrow neck) were added 37.0 mg (51.2 μmol) of [Rh(COD)DIPHOS]BF_4 and 0.3046 g (0.170 mmol) of the above alkene in 15 mL of dry CH_2Cl_2, and the bomb was flushed with argon. After several flushes with hydrogen (200 psi), the bomb was pressurized to 1000 psi and allowed to stand, with occasional shaking, for 3.5 h. The reaction solution was filtered through an 8-g plug of silica gel, washing with 1:1 ethyl acetate–hexane. Rotary evaporation afforded 0.302 g (99%) of the alcohol as a colorless oil: $[\alpha]^{22}_D$ +55° (*c* 1.6, $CHCl_3$); IR (neat) 3490, 3060, 3020, 2940, 1730, 1450, 1375, 1265, 1200, 1155, 1070, 1010, 870, 710 cm^{-1}; ^1H NMR δ 0.93 (d, *J* = 6.6, 3H), 0.99 (t, *J* = 7.5, 3H), 1.07 (d, *J* = 6.6, 3H), 1.15 (d, *J* = 6.9, 3H), 1.30 (s, 3H), 1.49 (s, 3H), 1.50 (m, 1H), 1.70 (m, 2H), 1.8–2.2 (m, 6H), 2.64 (m, 1H), 3.58 (m, 1H), 4.07 (m, 2H), 4.27 (m, 2H), 4.13 (d, *J* = 11.7, 1H), 4.58 (d, *J* = 6.3, 1H), 4.75 (d, *J* = 6.3, 1H), 4.76 (d, *J* = 11.7, 1H), 5.14 (s, 1H), 7.25–7.35 (m, 5H), 7.43 (t, *J* = 7.2, 2H), 7.54 (t, *J* = 7.5, 1H), 8.05 (d, *J* = 7.2, 2H); ^{13}C NMR δ 167.1, 138.2, 133.2, 131.0, 130.0, 128.7, 128.2, 128.0, 112.8, 107.6, 91.8, 87.1, 84.0, 81.3, 77.1, 69.9, 69.8, 38.3, 36.9, 34.5, 33.5, 30.8, 30.7, 26.0, 24.5, 19.3, 17.2, 16.5, 10.1. Anal. Calcd for $C_{35}H_{48}O_8$: C, 70.44; H, 8.11. Found: C, 70.59; H, 7.96.

2(*R*)-Ethyl-2-[5(*R*)-[4(*R*)-((benzyloxy)methyl)-2(*S*)-methyl-1(*S*)-[(triethylsilyl)oxy]-3-pentyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (Precursor to 48). To a solution of 0.044 g (0.0737 mmol) of the above alcohol in 1 mL of dichloromethane was added 0.015 mL (0.133 mmol) of 2,6-lutidine followed by 0.023 mL (0.103 mmol) of TESOTf. After 10 min, the solution was flash-filtered through 2 g of silica gel, eluting with 10% ethyl acetate–hexane, affording 0.0518 g (99%) of the silyl ether as a colorless oil: $[\alpha]^{22}_D$ +42° (*c* 1.6, $CHCl_3$); IR (neat) 3055, 3020, 2920, 1715, 1450, 1370, 1260, 1070, 870, 700 cm^{-1}; ^1H NMR δ 0.63 (m, 6H), 0.97 (m, 15H), 1.08 (d, *J* = 6.9, 3H), 1.13 (d, *J* = 7.2, 3H), 1.27 (m, 1H), 1.31 (s, 3H), 1.51 (s, 3H), 1.70 (m, 3H), 2.00 (m, 5H), 2.66 (m, 1H), 3.55 (dd, *J* = 3.3, 6.6, 1H), 3.97 (d, *J* = 4.5, 1H), 4.08 (m, 2H), 4.32 (dd, *J* = 4.5, 11.0, 1H), 4.40 (d, *J* = 11.7, 1H), 4.57 (d, *J* = 6.3, 1H), 4.73 (d, *J* = 11.7, 1H), 4.74 (d, *J* = 6.3, 1H), 5.12 (s, 1H), 7.2–7.35

(m, 5H), 7.4–7.6 (m, 3H), 8.06 (d, J = 7.5, 2H); ^{13}C NMR δ 167.0, 138.3, 133.1, 131.0, 130.0, 128.7, 128.3, 127.9, 112.7, 107.6, 92.1, 87.0, 83.8, 80.2, 79.8, 76.0, 69.8, 69.7, 39.8, 37.2, 36.6, 35.7, 31.2, 30.8, 26.0, 24.4, 19.3, 17.3, 16.6, 10.1, 7.5, 5.9. Anal. Calcd for $C_{41}H_{62}O_8Si$: C, 69.26; H, 8.79. Found: C, 69.31; H, 8.81.

2(*R*)-Ethyl-2-[5(*R*)-[4(*R*)-(hydroxymethyl)-2(*S*)-methyl-1(*S*)-[(triethylsilyl)oxy]-3-pentyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)tetrahydrofuran (48). To a solution of 0.340 g (0.478 mmol) of the above benzoate in 10 mL of dichloromethane at –78 °C was added 1.19 mL (1.0 M in hexanes,1.19 mmol) of DIBAL. After 30 min, the solution was allowed to warm to 0 °C, and 2 mL of 0.5 M aqueous potassium sodium tartrate was added. After being stirred vigorously for 2 h, the solution was poured into 20 mL of ether. After separation, the aqueous layer was extracted with three portions of ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give an oily residue. Chromatography on silica gel (2.5 × 12 cm, 15% ethyl acetate/hexane) gave 0.234 g (81%) of alcohol **48** as a colorless oil: $[\alpha]^{22}_D$ +45° (c 1.8, $CHCl_3$); IR (neat) 3490, 2950, 1455, 1370, 1205, 1070, 1020, 870, 760 cm^{-1}; ^{1}H NMR δ 0.62 (q, J = 8.1, 6H), 0.98 (m, 18H), 1.16 (d, J = 7.2, 3H), 1.31 (s, 3H), 1.51 (s, 3H), 1.71 (m, 4H), 1.95 (m, 4H), 2.41 (br s, 1H), 2.64 (m, 1H), 3.50 (m, 3H), 4.01 (d, J = 4.8, 1H), 4.09 (m, 1H), 4.43 (d, J = 11.7, 1H), 4.57 (d, J = 6.0, 1H), 4.74 (d, J = 6.0, 1H), 4.77 (d, J = 11.7, 1H), 5.12 (s, 1H), 7.2–7.35 (m, 5H); ^{13}C NMR δ 138.2, 128.7, 128.3, 127.9, 112.7, 107.5, 91.7, 87.0, 84.0, 80.4, 79.8, 76.4, 69.7, 67.2, 40.1, 36.9, 35.1, 34.8, 33.4, 30.8, 26.0, 24.4, 19.0, 17.3, 17.0, 9.9, 7.5, 5.9. Anal. Calcd for $C_{34}H_{58}O_7Si$: C, 67.29; H, 9.63. Found: C, 67.22; H, 9.72.

([(2-(Trimethylsilyl)ethoxy)methoxy]methyl)tributylstannane was prepared by a variation of the Still method (ref 33). To a solution of 2.5 mL (17.8 mmol) of diisopropylamine in 10 mL of THF and 2 mL of HMPA at 0 °C was added 6.5 mL (2.5 M in hexanes, 16.3 mmol) of n-BuLi dropwise. After 5 min, 4.0 mL (14.9 mmol) of n-Bu_3SnH was added. After 20 min, 1.11 g (37.1 mmol) of paraformaldehyde was added in 3 mL HMPA. After being stirred for 1 h at room temperature, the solution was poured into 50 mL of water and 50 mL of hexanes. Following separation, the organic layer was washed with three 20-mL portions of water. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give the crude alcohol as an oily residue. The alcohol was dissolved in 20 mL of dichloromethane and 4.71 mL of N,N-dimethylaniline and cooled to 0°C. Then, 3.94 g of SEMCl was added and the solution allowed to warm and stir for 15 h. The solution was then poured into 100 mL hexanes and washed with three 20-mL portions of 1.5% HCl (aqueous) and then 30 mL of water. The organics were dried over $MgSO_4$ and evaporated under reduced pressure to give the crude SEM stannane as an oily residue. Chromatography on silica gel (5 × 20 cm, 2% ethyl acetate/hexanes) gave 5.76 g (77%) of the stannane as a colorless oil: ^{1}H NMR δ 0.01 (s, 9H), 0.88 (m, 17H), 1.30 (m, 6H), 1.48 (m, 6H), 3.56 (t, J = 8.4, 2H), 3.73 (s, 2H), 4.54 (s, 2H); ^{13}C NMR δ 98.3, 65.2, 58.0, 29.5, 27.7, 18.6, 14.1, 9.3, –1.0. Anal. Calcd for $C_{19}H_{44}O_2SiSn$: C, 50.56; H, 9.83. Found: C, 50.84; H, 9.77.

2(*R*)-Ethyl-2-[5(*R*)-[2(*S*),4(R)-dimethyl-1(*S*)-[(triethylsilyl)oxy]-6-[(2-(trimethylsilyl)ethoxy)methoxy]-5-oxohexyl]-3(*S*)-methyl-2(*R*)-tetrahydrofuryl]-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)-tetrahydrofuran (49). To a solution of 0.108 g (0.178 mmol) of alcohol **48** in 2 mL of dichloromethane and 0.144 mL (1.77 mmol) of pyridine was added 0.121 g (0.284 mmol) of the Dess–Martin periodinane. After 1.5 h, 1 mL of saturated $NaHCO_3/Na_2S_2O_3$ was added followed by vigorous stirring for 10 min. The solution was then diluted and extracted with ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give the crude aldehyde as an oily residue.

To a solution of 0.161 mL of the above stannane in 2 mL of THF at –78 °C was added 0.142 mL of n-butyllithium (2.5 M in hexanes, 0.355 mmol). After 5 min, the crude aldehyde was added dropwise in 1 mL of THF. After an additional 10 min, 0.5 mL of saturated NH_4Cl was added and the solution allowed to warm. The solution was then diluted and extracted with ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give a mixture of the product alcohols and stannane byproducts. This mixture was submitted to oxidation and workup under the same conditions as above. Chromatography of the residue on silica gel (2.5 × 12 cm, 10% ethyl acetate/hexane) gave 0.131 g (97%) of ketone **49** as a colorless oil $[\alpha]^{22}_D$ +38.9° (c 1.31, $CHCl_3$); IR (neat) 2950, 2870, 1710, 1455, 1370, 1205, 1155, 1015, 830, 735 cm^{-1}; ^{1}H NMR δ 0.01 (s, 9H), 0.58 (q, J = 8.1, 6H), 0.95 (m, 17H), 1.11 (m, 6H), 1.30 (s, 3H), 1.31(m, 1H), 1.50 (s, 3H), 1.70 (m, 3H), 2.00 (m, 3H), 2.63 (m, 1H), 2.79 (m, 1H), 3.49 (m, 1H), 3.63 (t, J = 8.7, 2H), 3.93 (d, J = 4.5, 1H), 4.05 (m, 1H), 4.25 (AB q, J = 13.5, 2H), 4.43 (d, J = 11.7, 1H), 4.56 (d, J = 6.0, 1H), 4.74 (m, 4H), 5.12 (s, 1H), 7.31 (m, 5H); ^{13}C NMR δ 211.7, 138.3, 128.7, 128.2, 127.9, 112.7, 107.6, 95.2, 92.1, 86.9, 83.8, 80.2, 79.4, 76.0, 71.66, 66.74, 66.0, 41.1, 39.8, 37.0, 36.7, 36.2, 31.1, 25.9, 24.3, 18.51, 18.2, 17.2, 15.9, 10.1, 7.4, 5.7, –1.0. Anal. Calcd for $C_{41}H_{72}O_9Si_2$: C, 64.36; H, 9.48. Found: C, 64.41; H, 9.55.

2(*S*)-[2(*R*)-[2(*R*)-Ethyl-3(*R*),4(*S*)-[(dimethylmethylene)dioxy]-5(*S*)-(benzyloxy)-2-tetrahydrofuryl]-3(*S*)-methyl-5-tetrahydrofuryl]-3(*S*),5(*R*)-dimethyl-6(*R*)-methoxy-6-[[(2-(trimethylsilyl)ethoxy)methoxy]methyl]-tetrahydropyran (50). To a solution of 0.037 g (0.0484 mmol) of ketone **49** in 1 mL of THF was added 0.025 g (0.0967 mmol) of TBAF monohydrate. After 2 h, the solvent was evaporated and the residue chromatographed on silica gel (1.0 × 10 cm, 25% ethyl acetate/hexane) to give the crude lactols. The lactols were dissolved in 0.7 mL of dichloromethane and 0.3 mL of 9:1 MeOH/$(MeO)_3CH$, and a trace of TsOH was added. After 2 h, the solution was diluted with hexane and filtered through silica gel (3 × 4 cm, 20% ethyl acetate/hexane) to give 0.031 g (97%) of methyl ketal **50** as a colorless oil: $[\alpha]^{22}_D$ +91.9° (c 1.36, $CHCl_3$); IR (neat) 2925, 1455, 1370, 1245, 1205, 1060, 970, 835 cm^{-1}; ^{1}H NMR δ 0.02 (s, 9H), 0.87–1.01 (m, 11H), 1.13 (s, 3H), 1.30 (s, 3H), 1.35 (m, 2H), 1.51 (s, 3H), 1.58 (m, 1H), 1.68 (m, 2H), 1.90 (m, 1H), 2.04 (m, 1H), 2.20 (m, 1H), 2.70 (m, 1H), 3.28 (s, 3H), 3.60 (m, 5H), 3.97 (d, J = 3.9, 1H), 4.32 (m, 1H), 4.42 (d, J = 11.7, 1H), 4.58 (d, J = 6.3, 1H), 4.68 (AB q, 2H), 4.78 (m, 2H), 5.14 (s, 1H), 7.31 (m, 5H); ^{13}C NMR δ 138.3, 128.7, 128.2, 127.9, 112.7, 107.4, 99.7, 95.5, 92.0, 87.0, 83.3, 80.2, 77.0, 75.5, 69.8, 69.7, 65.4, 48.5, 37.5, 37.0, 36.2, 35.2, 33.3, 31.6, 25.7, 24.1, 18.4, 17.9, 16.8, 16.4, 10.2, –1.0. Anal. Calcd for $C_{36}H_{60}O_9Si$: C, 65.03; H, 9.10. Found: C, 65.04; H, 9.13.

2(*S*)-[2(*R*)-[2,3-Dihydro-2(*R*)ethyl-3(*R*)-hydroxy-2-furyl]-3(*S*)-methyl-5-tetrahydrofuryl]-3(*S*),5(*R*)-dimethyl-6(*R*)-methoxy-6-[[(2-(trimethylsilyl)ethoxy)methoxy]methyl]tetrahydropyran (III). To a vigorously stirred solution of 0.012 g of lithium (1.77 mmol) in 10 mL of liquid ammonia at –78 °C was added 0.118 g (0.177 mmol) of benzyl ether **50** in 3 mL of THF. After 10 min, NH_4Cl was added until the color dissipated. After the addition of ether and evaporation of the ammonia at room temperature, $MgSO_4$ was added and the solution filtered. Evaporation gave the crude lactols. To a solution of the crude lactols in 1 mL of THF and 0.022 mL (0.221 mmol) of carbon tetrachloride at –78 °C was added 0.037 mL (0.204 mmol) of HMPT dropwise. After 30 min, the solution was allowed to warm to room temperature and stir for 45 min. This solution was then added dropwise to 8.2 mL of a 0.250 M solution (2.05 mmol) of LiDTBB in THF at –78 °C. After 10 min, water was added until the color dissipated and the solution warmed to room temperature. The solution was diluted and extracted with ether. The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give the crude glycal. Chromatography of the residue on silica gel (1.5 × 12 cm, 2.5–30% ethyl acetate/hexane) gave 0.078 g (87%) of glycal **III** as a colorless oil: $[\alpha]^{22}_D$ +37.2° (c 1.2, $CHCl_3$); IR (neat) 3425, 2930, 2840, 1610, 1455, 1030, 835 cm^{-1}; ^{1}H NMR δ 0.0 (s, 9H), 0.879 (m, 11H), 1.12 (d, J = 7.2, 3H), 1.25–1.90 (m, 7H), 2.29 (m, 1H), 2.56 (m, 1H), 3.24 (s, 3H), 3.41–3.70 (m, 5H), 4.28 (m, 1H), 4.35 (d, J = 4.8, 1H) 5.56 (d, J = 4.8, 1H), 4.67 (AB q, J = 4.8, 6.6, 2H), 5.06 (t, J = 2.7, 1H), 6.43 (d, J = 2.4, 1H); ^{13}C NMR δ 148.6, 104.5, 99.8, 95.5, 90.4, 84.0, 79.5, 77.1, 69.6, 65.5, 48.4, 37.5, 36.0, 35.9, 34.5, 33.1, 29.2, 18.5, 17.8, 16.6, 16.3, 8.1, –1.0. Anal. Calcd for $C_{26}H_{48}O_7Si$: C, 62.36; H, 9.66. Found: C, 62.45; H, 9.57.

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Supplementary Material Available: Experimental procedures and characterization data for compounds **3, 4, 10, 12, 14, 16, 18, 19, 20, 21, 42a, 42b,** and **44a** as well as ^{1}H NMR, ^{13}C NMR, NOESY and COSY spectra for compounds **24** and **25** and data pertaining to the X-ray crystal-structure determinations of compounds **8, 33,** and the dinitrobenzoate of **44a** (58 pages). Ordering information is given on any current masthead page.