**Methyl 6-Acetamido-2,3,4,7-tetra-*O*-acetyl-6,8-dideoxy-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside (23).** Peracetylation of **22** as for preparation of **17**, and chromatography using 4:1 ether–petroleum ether as eluant afforded 11.5 mg of **23** (quantitative yield for two steps), mp 213–214 °C; mixed melting point (with natural **23**, mp 215–216 °C) 213–214 °C; [α] +224° (*c* = 0.364, $CHCl_3$), lit.[4] +223° (*c* = 0.906, $CHCl_3$); NMR 1.26 (d, 3 H, *J* = 7), 1.90 (s, 3 H), 1.96 (s, 3 H), 2.03 (s, 3 H), 2.06 (s, 3 H), 2.11 (s, 3 H), 2.12 (s, 3 H), 4.24 (d, 1 H, *J* = 10), 4.57 (td, 1 H, *J* = 11, 2), 5.03 (qd, 1 H, *J* = 7, 2), 5.08 (dd, 1 H, *J* = 11, 3), 5.24 (dd, 1 H, *J* = 11, 6), 5.37 (d, 1 H, *J* = 3), 5.55 (d, 1 H, *J* = 11), 5.61 (d, 1 H, *J* = 6); IR 1750, 1649; CI-MS 464 ($M^+$ + 1).

**Methyl 6-Amino-6,8-dideoxy-1-thio-D-*erythro*-α-D-*galacto*-octopyranoside (2).** A solution of 50 mg (0.179 mmol) of **22** in 1.5 mL of hydrazine hydrate was heated at reflux for 3 h. The reaction mixture was cooled and concentrated, and the resulting white solid was recrystallized from 70% aqueous methanol–ether to afford 39 mg (91%) of **2**, mp 216–217 °C (with decomposition), mixed mp 216–217 °C (with **2** obtained from **1** by degradation, mp 216–217 °C, lit.[4] mp 225–228 °C): NMR ($D_2O$, 3-(trimethylsilyl)-1-propanesulfonic acid, sodium salt as internal reference) δ 1.15 (d, 3 H, *J* = 7), 2.13 (s, 3 H), 3.19 (dd, 1 H, *J* = 10, 4), 3.66 (dd, 1 H, *J* = 10, 3), 4.00 (d, 1 H, *J* = 9), 4.09–4.13 (m, 3 H), 5.33 (d, 1 H, *J* = 6).

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**Registry No.** **1**·HCl, 859-18-7; **2**, 14810-93-6; **3** hydrazide, 13380-37-5; **6**, 3396-99-4; **6** (1-*o*-silyl deriv), 114217-35-5; **6** (3,4-*o*-isopropylidene-6-*o*-silyl deriv), 114217-36-6; **7**, 27851-16-7; **7** (6-*o*-silyl deriv), 124780-61-6; **7** (6-aldehyde), 124780-62-7; **8**, 124780-53-6; **8** (8-uronic acid ethyl ester), 124780-63-8; **8** (8-alcohol), 124780-64-9; **8** (desisopropylidene deriv), 124780-65-0; **9**, 124780-54-7; **9** (4-*o*-debenzoyl deriv), 124780-66-1; **10**, 124780-55-8; **10** (4-*o*-benzoyl deriv), 124820-53-7; **14**, 124780-56-9; **15**, 124780-57-0; **16**, 124780-58-1; **17**, 124915-82-8; **17** (2,3,4-de-*o*-acetyl deriv), 124780-67-2; α-**18**, 6991-35-1; β-**18**, 6982-19-0; **19**, 124780-59-2; **20**, 124780-60-5; **21**, 124915-83-9; **22**, 6982-20-3; **22** (2,3,4,-tri-*o*-benzyl deriv), 124820-33-3; **23**, 13038-00-1.

**Supplementary Material Available:** Full experimental details for the preparation of epoxy alcohol **10** (Scheme I) and for the degradation of **1** leading to **2**, **18**, **22**, and **23** (5 pages). Ordering information is given on any current masthead page.

# Development of a Fully Synthetic Stereoselective Route to 6-Deoxyerythronolide B by Reiterative Applications of the Lewis Acid Catalyzed Diene Aldehyde Cyclocondensation Reaction: A Remarkable Instance of Diastereofacial Selectivity†

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The synthesis of racemic **2**, which contains the relative stereochemistry appropriate to a synthesis of (9*S*)-dihydro-6-deoxyerythronolide B (see compound **38**), is described. The synthesis features three Lewis acid catalyzed diene aldehyde cyclocondensation reactions, using, in each instance, (*E*,*E*)-1-methoxy-2-methyl-3-(trimethylsilyloxy)penta-1,3-diene (**3**). In the first cycle, carried out with formaldehyde as the heterodienophile, a single stereogenic center is constructed (see compound **4**). By a series of steps featuring stereoselective reactions in pyranoid matrices, as well as two additional cyclocondensation reactions, the stereogenicity of $C_2$ (erythronolide numbering) is used to induce the required configurations at carbons 3, 4, 5, 6, 8, 9, 10, and 11 of the target system (see formation of glycal **20**). To achieve stereoselectivity from this point onward, it was necessary to open the pyranoid substructure with attendant loss of configuration at $C_{11}$ (see *E* enal **31**). Subsequently, the configurations required at carbons 11, 12, and 13 to reach compound **2** were introduced in highly selective reactions, carried out on acyclic intermediates. The enantiomerically homogeneous (9*S*) version of compound **2** was obtained from 6-deoxyerythronolide (**1**) by way of tetraol **38**. Compound **2** (9*S*) was converted to **1**, again by way of **38**. Macrolactonization (17% yield) was carried at the stage of seco acid **44** to produce **45**, which was, in turn, converted to **1**. A totally synthetic route to **1** is thus accomplished in a formal sense.

## Introduction

In 1981 we began to investigate the potentialities of the Lewis acid catalyzed diene aldehyde cyclocondensation (LACDAC) process as a device for the assembly of a variety of goal structures.[1,2] The new chemistry has been of value in addressing the total synthesis of targets bearing multiple stereogenic centers such as pyranoid antibiotics[3,4] and complex monosaccharides.[5,6] An important element in the applicability of the method has been the finding that the stereochemical outcome of the cyclocondensation is re-

† Dedicated to the contributions of Professor Satoru Masamune in the macrolide field.

(1) Danishefsky, S. J. *Aldrichimica Acta* **1986**, *19*, 59.
(2) Danishefsky, S. J.; DeNinno, M. P. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 15.
(3) Danishefsky, S. J.; Selnick, H. G.; DeNinno, M. P.; Zelle, R. E. *J. Am. Chem. Soc.* **1987**, *109*, 1572.
(4) Danishefsky, S. J.; Armistead, D. M.; Wincott, F. E.; Selnick, H. G.; Hungate, R. W. *J. Am. Chem. Soc.* **1988**, *110*, 8117.
(5) Danishefsky, S. J.; Maring, C. J. *J. Am. Chem. Soc.* **1985**, *107*, 1269.
(6) Danishefsky, S. J.; DeNinno, S. L.; Chen, S.-H.; Boisvert, L.; Barbachyn, M. *J. Am. Chem. Soc.*, in press.

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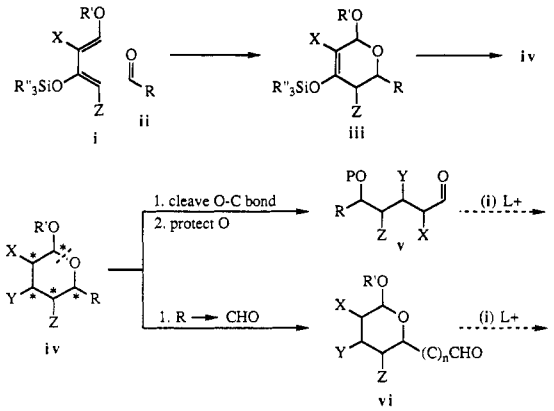


**Figure 1.**

sponsive to variations of the substitution pattern of the diene, the particular Lewis acid employed, the solvent, and the nature of the aldehyde. Moreover, the pyranoid rings (iii) that are elaborated from the reaction have proven to be useful matrices for stereoselective transformations, cf. iii → iv. Finally the overall logic is reiteratable. Aldehydes of the type v or vi can be unveiled from the pyranoid constructure in the first cycle and used in another cyclocondensation.

Exploiting the basic protocols and the potentialities for reiteration implied in Figure 1, the LACDAC methodology was successfully applied to the fashioning of systems with a multiplicity of stereogenic centers. In this paper, we describe the application of this strategy to the total synthesis of 6-deoxyerythronolide B (1).[7] The first total synthesis of 1 was accomplished in a landmark effort by the Masamune laboratory.[8] The achievements of the Masamune group in the total synthesis of 1 have expanded the range of stereoselective transformations and feasible functional group accommodation in syntheses directed at 1.[9]

Our interest in compound 1 centered around studying its synthesis as a heuristic framework to probe the outer limits of the LACDAC process and to explore new possibilities for arranging the stereochemistry of the resultant

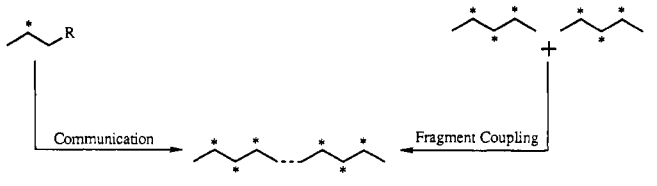


**Figure 2.**

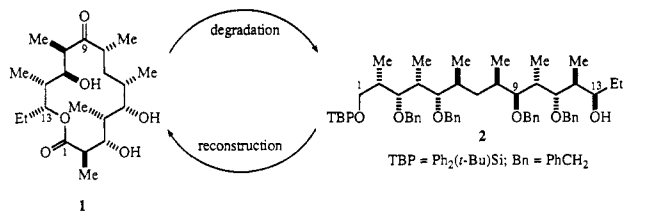


**Figure 3.** The position numbers in this figure and subsequent figures are unrelated to the numbers in the *CA* names.

pyranoid rings to advantage. *We hoped to demonstrate that the bias inherent in a single stereogenic center could be conveyed in a serial sense to elaborate all of the configurational requirements of our goal structure.*[10] Elsewhere[2] we have characterized this approach as one of stereochemical communication. This strategy is quite distinct from one in which the arrangement of relative stereochemistry is ordered by coupling of appropriately matched chiral fragments.

We emphasize that our commitment, in this study, to establishing stereochemistry by induction (cf. stereocommunication) rather than by merging of appropriately matched chiral subunits (cf. fragment coupling) does not necessarily derive from generic considerations of efficiency and practicality (Figure 2). Such comparisons cannot be offered in the abstract. To be meaningful, they require a detailed analysis of specific propositions for the synthesis of specific molecules. Rather, we approached this problem as a test case where previously developed findings could be critically evaluated and, hopefully, expanded.

While compound 1 was the focusing device, its critical "stereochemical code" can be expressed in various seco systems. The specific seco system **2** was selected as our subtarget (Figure 3). It will be recognized that in compound **2** the stereogenicity at $C_9$ is not per se critical to reaching the natural product, 1. The reasons for adding still another dissymmetry element are several. First, as a general proposition, it is easier to convey stereochemistry to emerging carbon centers by *drawing upon biases of nearest neighbors, as opposed to remote areas of dissymmetry.* Indeed, the stereogenicity at $C_9$ was used to advantage to induce the required stereochemistry at carbons 10, 11, 12, and 13. Furthermore, as will be described, the synthetic route that was developed involved reaching an intermediate that was available from the natural product itself. It was demonstrated (vide infra) that reduction of 1 with sodium borohydride afforded compound **38**, which has the *S* configuration at $C_9$. It was useful for the target seco system to be accessible from the macrolide itself.

For purposes of convenience, we operated in the racemic series. At no point would we be coupling chiral fragments. In our design, resident chirality would determine the sense of emerging chirality. The lessons to be garnered in such

(7) Myles, D. C. Ph.D. Dissertation, Yale University, May 1989. A preliminary report on part of this work was given at the 14th International Carbohydrate Symposium, Stockholm, Sweden, August 15, 1988.

(8) Masamune, S.; Hirama, M.; Mori, S.; Ali, S. A.; Garvey, D. S. *J. Am. Chem. Soc.* **1981**, *103*, 1568.

(9) For other key papers in the macrolide area, cf. inter alia: (a) Masamune, S.; Yamamoto, H.; Kamata, S.; Fukuzawa, A. *J. Am. Chem. Soc.* **1975**, *97*, 3513. (b) Corey, E. J.; Trybulski, E. J.; Melvin, L. S., Jr.; Nicolaou, K. C.; Secrist, J. A.; Lett, R.; Sheldrake, P. W.; Falck, J. R.; Brunell, D. J.; Haslanger, M. F.; Kim, S.; Yoo, S.-E. *J. Am. Chem. Soc.* **1978**, *100*, 4618. (c) Corey, E. J.; Kim, S.; Yoo, S.-E.; Nicolaou, K. C.; Melvin, L. S., Jr.; Brunell, D. J.; Falck, J. R.; Trybulski, E. J.; Lett, R.; Sheldrake, P. W. *Ibid.* **1978**, *100*, 4620. (d) Woodward, R. B.; et al. *Ibid.* **1981**, *103*, 3210, 3213, 3215. (e) Corey, E. J.; Hopkins, P. B.; Kim, S.; Yoo, S.-E.; Nambiar, F. P.; Falck, J. R. *Ibid.* **1979**, *101*, 7131. (f) Masamune, S.; Hirama, M.; Mori, S.; Ali, S. A.; Garvey, D. S. *Ibid.* **1981**, *103*, 1568. (g) Hannessian, S.; Rancourt, G.; Guindon, Y. *Can J. Chem.* **1978**, *56*, 1843. (h) Sauvé, G.; Schwartz, D. A.; Ruest, L.; Deslonchamps, P. *Can J. Chem.* **1984**, *62*, 2929. (i) Bernet, B.; Bishop, P. M.; Caron, M.; Kawamata, T.; Roy, B. L.; Ruest, L.; Sauvé, G.; Soucy, P.; Deslongchamps, P. *Ibid.* **1985**, *63*, 2810, 2814, 2818. (j) Stork, G.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1987**, *109*, 1564, 1565; *Pure Appl. Chem.* **1986**, *58*, 767. For a review covering recent efforts directed at macrolide synthesis through mid-1984, see: (k) Paterson, I.; Mansuri, M. M. *Tetrahedron* **1985**, *41*, 3569. For recent efforts in the synthesis of erythronolide fragments, see: (l) Oikawa, Y.; Nishi, T.; Yonemitsu, O. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1, 7, 19, 27. (m) Heathcock, C. H.; Young S. D.; Hagen, J. P.; Pilli, R.; Badertscher, U. *J. Org. Chem.* **1985**, *50*, 2095. (n) Kobayashi, Y.; Uchiyama, H.; Kanbara, H.; Sato, F. *J. Am. Chem. Soc.* **1985**, *107*, 5541. (o) Kinoshita, M.; Arai, M.; Tomooka, K.; Nakata, M. *Tetrahedron Lett.* **1986**, *27*, 1811. (p) Ziegler, F. E.; Kneisley, A. *Heterocycles* **1987**, *25*, 105. (q) Chamberlin, A. R.; Sall, D. *J. Am. Chem. Soc.* in press.

(10) To our knowledge, no previous syntheses of erythronolide structures have been accomplished without at some point relying on the coupling of subunits containing previously formed chirality. For a synthesis that is particularly notable for its demonstration of reiterative methodology, see ref. 9j. See also: Stork et al. (Stork, G., Paterson, I., Lee, F. K. C. *J. Am. Chem. Soc.* **1982**, *104*, 4686 for a total synthesis which exploited an interesting symmetry element.

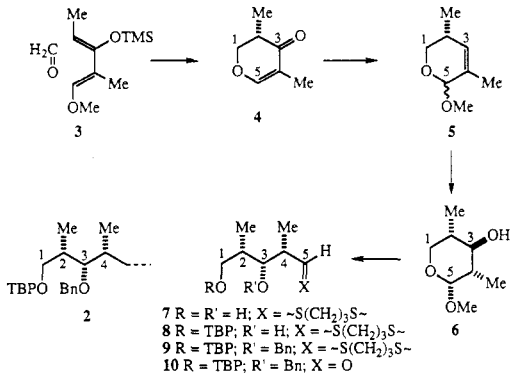


**Figure 4.**

an effort would not be blurred by working with racemates.

Below we describe the realization of these goals. The work presented herein underscores the possibilities that are provided by the assembly, manipulation, and disconnection of pyranoid matrices. A particularly striking example of a highly stereoselective LACDAC reaction is provided in the transformation of **17** + **5** to yield **18** (vide infra, Figure 6). The excellent margin of diastereoface selectivity in this reaction could not have been anticipated by precedent. That this stereoselectivity is realized even in the absence of unsaturated or hetero substituents at the $\alpha$, $\beta$, or $\gamma$ carbons is particularly remarkable.

## Discussion of Results

The first retrosynthetic dissection upon which we focused was that between $C_1$ and the four-carbon ensemble destined to emerge as $C_2$–$C_5$ (inclusive). Formaldehyde served as the ultimately achiral aldehyde. Diene **3** would serve as the $C_2$–$C_5$ progenitor. That this diene comes endowed with branching methyl groups at the carbons destined to become $C_2$ and $C_4$, and is equipped with exploitable functionality at the future carbons 3 and 5, did not go unnoticed.

The reaction of paraformaldehyde with diene **3** was conducted in THF under reflux in the presence of anhydrous zinc chloride. A 69% yield of the racemic dihydropyrone **4** was obtained (Figure 4). Reduction of the keto group was carried out with sodium borohydride in the presence of cerium(III) chloride.[11a] Solvolytic, Ferrier-type rearrangement[11b] with methanol afforded the methyl glycoside mixture **5**. While in our earlier works[2-4] the Ferrier rearrangement provided substantially a single isomer, arising from axial solvolysis, in the case at hand a nearly 1:1 mixture was obtained (78%).[12]

Previous experience[4,13] had shown that the hydroboration of dihydropyrans such as **5** occurred anti to the $C_5$-alkyl group with remarkable fidelity. With this maxim well in mind, anomer mixture **5** was treated with borane–dimethyl sulfide.[14] After oxidation with alkaline hydrogen peroxide, there was obtained an 80% yield of a single methyl glycoside whose NMR spectrum showed it to be properly represented as structure **6**. The precise stage where configurational convergence at the anomeric center had occurred is not clear. The stereochemistry at the anomeric center was, at this stage, of little consequence, in light of the very next transformation (see **6** → **7**).

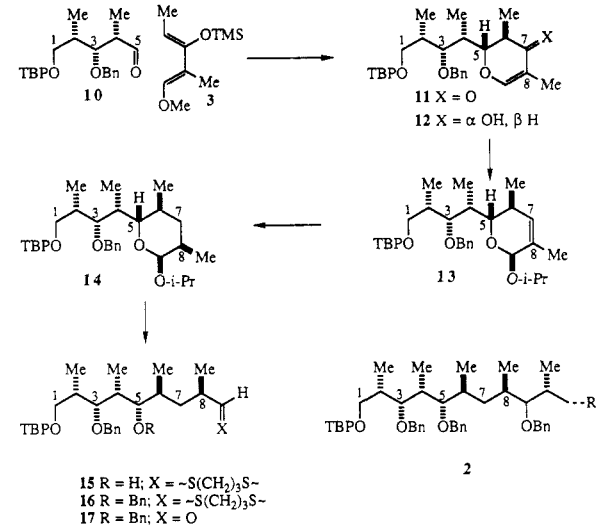


**Figure 5.**

However, the formation of a single stereoisomer was certainly helpful for spectral characterization and for purposes of structural assignment.

Having fulfilled its stereochemical template role, the pyran ring could now be disassembled. The groundwork for the next installment of the LACDAC method was prepared through the reaction of **6** with propanedithiol in the presence of titanium tetrachloride. A 64% yield of the dithiane diol **7** was obtained. The primary alcohol, destined to become the $C_1$ carbon of goal system **2** and, eventually, the carboxyl group of the seco acid **44** (see Figure 9), was now differentiated through protection of its alcohol as a *tert*-butyldiphenylsilyl (TBP) ether.[15] Reaction of compound **8** with sodium hydride/benzyl bromide provided **9** (88%) from **7**. The dithiane was cleaved through the action of *N*-bromosuccinimide and aqueous acetone.[16] Aldehyde **10**, thus generated, was unstable and was used without complete characterization (vide infra).

Analysis of the relevant section of the seco system **2**, in the context of our capabilities, reveals that dihydropyrone **11** (Figure 5) could well be a useful intermediate for the synthesis. The required stereochemistry would have been introduced at carbons 5 and 6. The branching methyl group at carbon 7 would already be available. It is recognized that the diastereofacial sense of the LACDAC reaction required to go from aldehyde **10** to system **11** would be that in accord with the models offered by Cram[17] and by Felkin[18,19] (CF).[20a] Although based on quite different premises, both viewpoints converge in predicting the preferential formation of the "syn" $C_4$–$C_5$ isomer.[20b] Our previous work[21,22] suggested that such an outcome would be particularly favored by dint of the presence of the electron-withdrawing group (benzyloxy) at the $\beta$-car-

(11) (a) Luche, J. L.; Gemal, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 5848. (b) Ferrier, R. *J. Chem. Soc.* **1964**, 5443.

(12) Pyran **5** is purified by distillation (see Experimental Section). It is likely that the epimerization occurs at this stage.

(13) Danishefsky, S. J.; Myles, D. C.; Harvey, D. F. *J. Am. Chem. Soc.* **1987**, *109*, 862.

(14) See: *Borane Reagents*; Pelter, A., Smith, K., Brown, H. G., Eds.; Academic Press: New York, 1988.

(15) Hanessian, S.; Lavalle, P. *Can. J. Chem.* **1977**, *55*, 562.

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(19) Ahn, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.

(20) (a) The descriptor CF is used to designate those products formed under diastereofacial guidance that would have been predicted from either the acyclic Cram rule[17] or the Felkin analyses.[18] Although the premises are totally different, the actual predictions in almost all cases converge. The descriptor CC is used to designate a product formed under chelation control. (b) Masamune, S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557.

(21) Danishefsky, S. J.; Kato, N.; Askin, D.; Kerwin, J. F., Jr. *J. Am. Chem. Soc.* **1982**, *104*, 360.

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bon. Furthermore, precedent suggested[23] that the use of $BF_3{\cdot}OEt_2$ as the Lewis acid catalyst would particularly promote the CF[20a] outcome and would favor the formation of trans-disubstituted dihydropyrone. As previously discussed, the latter stereorelationship arises, formally, from an exo transition state in cycloaddition terms or from a threo aldol in the two-stage mechanistic variation.[24]

In practice, the crude aldehyde **10** obtained from **9** was subjected to the action of diene **3** in the presence of $BF_3{\cdot}OEt_2$. There was obtained only one recognizable dihydropyran. Its NMR spectrum at 250 mHz indicated it to be a trans-disubstituted system ($J_{C5H-C6H}$ = 13.8 Hz (pyrone numbering)). It was the weight of precedent rather than any firm chemical data that led us to formulate the $C_4$–$C_5$ stereochemical relationship as syn[20b] (vide supra). As will be shown through unfolding events, this assignment turned out to be correct, and the dihydropyrone obtained is properly represented as **11**.

Examination of the substitution pattern and stereochemistry of carbons 2, 3, and 4 in relation to those of carbons 6, 7, and 8 in seco structure **2** reveals the nature of the next obstacle to be overcome. The syn 1,3-dimethyl relationship of carbons 2 and 4 is of course duplicated at carbons 6 and 8. *However, there is a significant difference in the intervening carbon 3 is oxygenated while $C_7$ is not substituted.* Application of the hydroboration strategy used in the first cycle to produce a pyranoside of the type **14** would presumably provide the desired stereochemistry at $C_8$ but would oblige us to deal with a potentially problematic deoxygenation at carbon 7.

Fortunately, our earlier work in the Prelog–Djerassi lactone synthesis[25] called to mind a more straightforward solution to the problem. Reduction of compound **11** with sodium borohydride–cerium(III) chloride[11a] provided an 86% yield of **12**. Ferrier rearrangement[11b] with isopropyl alcohol as the nucleophile[25] gave a 91% yield of **13**. With the methyl and isopropoxy groups hindering the $\beta$ face, catalytic reduction ($H_2$, Pd–$Al_2O_3$) occurred from the $\alpha$ face to afford pyran **14**.

The relative stereochemistry required for the $C_2$–$C_8$ segment of the subgoal system **2** had been implemented. The next phase of the effort would focus on installation of the required configurations at carbons 9–13. For this purpose, the pyran ring was disassembled through the action of propanedithiol–titanium tetrachloride. Dithiane **15** was thus obtained in 69% yield and converted to its benzyl ether derivative **16** in the usual way. Treatment of this compound with *N*-bromosuccinimide in aqueous acetone resulted in cleavage of the dithiane and provided the aldehyde **17**. The third LACDAC reaction was now at hand.

*In the third cyclocondensation reaction a major new issue of facial selectivity would be confronted.* The subgoal structure would be dihydropyran **18** in which the $C_8$, $C_9$, and $C_{10}$ stereochemistry is appropriate for reaching the seco structure **2** (Figure 6). Indeed, the diastereofacial sense of the LACDAC reaction required to convert aldehyde **17** to dihydropyrone **18** corresponds, at least in formal terms, to that anticipated by the Cram–Felkin models.[18,19] While we often encountered high margins of CF[20a] selectivity (in the absence of circumstances that favored chelation), in the cyclocondensation of diene **3** with aldehyde **17** we would be facing a situation that has not

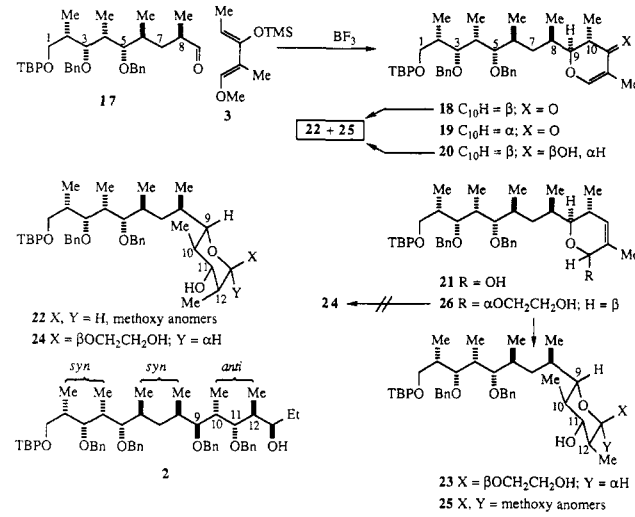



**Figure 6.**

yet been encountered. Hitherto, we had taken advantage of rather special groups ($\alpha$-phenyl,[21] $\alpha$-vinyl,[3] $\alpha$- or $\beta$-alkoxyl[22]) that were perceived to be crucial to success, at least in terms of the Felkin–Anh[19] models. However in the most concise route that we would now be investigating, where $C_7$ would be unsubstituted, there would be no such precedented "selectivity enhancing" group at either the $\alpha$ or the $\beta$ carbon. The nearest electron-withdrawing group if the benzyloxy function at the $\delta$ carbon. The branching characteristics of the aldehyde **17** are roughly those of a "2-methyl-2-isobutylacetaldehyde" system. There was no known data that would lead one to suppose that such aldehydes would exhibit useful margins of stereoselectivity.

That we were emboldened to plan our synthesis allowing for the possibility of selectivity in a LACDAC reaction of an aldehyde such as **17** arose from several considerations. *Foremost among these was our earlier finding that Lewis acid catalysis was providing notably higher margins of diastereofacial preference in addition reactions to aldehydes than were available from more conventional nucleophilic processes.* Indeed this phenomenon was first revealed in our early experiments in the LACDAC area.[19] Another recent example of such an application, which occurred in the compactin problem, indicated that the origins of the facial selectivity are still not well understood.[26]

Moreover, if no useful selectivity could be achieved, we had access to an alternative route wherein a $C_7$ oxygen function would have been introduced via hydroboration–oxidation of **13**. Such a program (which would necessitate special protecting group arrangements to permit eventual deoxygenation at $C_7$) constituted a fall back position, albeit a difficult one.

In the event, the LACDAC reaction of **3** with aldehyde **17** was carried out with $BF_3{\cdot}OEt_2$. The crude product, containing varying amounts of aldol-type components, was subjected to reaction with pyridinium *p*-toluenesulfonate in benzene under reflux. After preliminary silica gel chromatography, there was obtained a dihydropyrone fraction in 76% yield. Through NMR analysis, there could

(23) Heathcock, C. H.; Flippin, L. A. *J. Am. Chem. Soc.* **1983**, *105*, 1667.
(24) Larson, E. R.; Danishefsky, S. J. *Tetrahedron Lett.* **1982**, *23*, 1975.
(25) Danishefsky, S. J.; Larson, E. R.; Askin, D.; Kato, N. *J. Am. Chem. Soc.* **1985**, *107*, 1246.

(26) (a) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc.* **1989**, *111*, 2599. (b) We have observed significant selectivity margins (~3–5:1) with LACDAC reactions of even unbranched versions of diene **3** and simple $\alpha$-branched aldehydes. At this writing the sense of the selectivity in these simple model cases is not proven.[7] The realization of selectivity with simple $\alpha$-branched aldehyde substrates holds out considerable prospects for stereoselective synthesis once the scope and sense of the effect is rigorously established in a broad range of cases.

clearly be discerned the presence of major and minor products (6:1).

The pyrones were separated and each compound was characterized. The major compound was a trans-disubstituted dihydropyrone, and the minor was cis-disubstituted dihydropyrone. The diastereofacial selectivity in each series seemed to be complete. It is well recognized that the configuration at $C_9$ is not in of itself decisive, since this center would become a ketone in compound **1**. However, if $C_9$ were of the *S* configuration as shown in **18**, we would be able to link with the degradative series for relay purposes (vide infra). In addition, *cis*-dihydropyrone **19** does not contain the required $C_{10}$ stereochemistry. With no significant precedent for assignment of $C_9$, but with data establishing the relative relationship at $C_9$ and $C_{10}$ to guide our selection, we adopted as a working model the notion that the major isomer was indeed **18** (and the minor one, **19**). The matter would be clarified only by experiment.

While completion of the total syntheses (vide infra) did indeed confirm that the major compound corresponds to **18**, the diastereoface sense of formation of the minor product was not established. In the unlikely event that the cis compound belongs to the anti-Cram–Felkin series (contrary to that shown in **19**) the overall face selectivity with aldehyde **17** would still be 6:1. Even this minimum estimate serves to underscore the extraordinary improvement in stereoselectivity margins associated with Lewis acid mediated nucleophilic additions to aldehydes. What makes this case particularly striking is that the selectivity is realized in the absence of the traditional directing functions at proximal carbons.[26b]

Assuming the assignments to this stage were correct, the nature of the next synthetic problem to be addressed is foretold by analysis of the pairwise relationships of branching methyl groups at $C_2$–$C_4$ (syn), $C_6$–$C_8$ (syn), and $C_{10}$–$C_{12}$ (anti) in structure **2**. In the context of the pyranoid matrix paradigm for transcribing stereochemistry, this subgoal required the conversion of the presumed **18** to system **22**. Of course, there was no concern over the introduction of the equatorial alcohol at $C_{11}$. The problem that proved to be insurmountable was the one of installing an axial methyl group at the future $C_{12}$ with high stereoselectivity. The Ferrier-hydroboration based strategy that had served us well in our first cycle (see **4** → **5** → **6**) could not of itself solve the problem in this case, since the configuration at either $C_{11}$ or $C_{12}$ must emerge opposite to that needed. Hoping that the stereochemistry at $C_{11}$ could be adjusted via the corresponding ketone, we focused on directing the hydroboration from the $\beta$ face. In this way, the problem of the $C_{12}$ stereochemistry could be solved.

Reduction of **18** under Luche-type conditions[11a] afforded **20**. This system was subjected to Ferrier rearrangement,[11b] this time with ethylene glycol, to produce **26** (R = $OCH_2CH_2OH$). The reason for recourse to such an unusual nucleophile in the Ferrier step was the hope that the axial hydroxyethyl glycoside would direct hydroboration from the $\alpha$ face. Such directivity would be required to counteract the natural tendency of the $\alpha$-disposed methyl group at $C_{10}$ to deflect the borane electrophile to the $\beta$ face. In the event, hydroboration even of compound **26** occurred from the $\beta$ face to give, upon oxidation, the all-equatorial product **23**.

Attempts to install the required configuration at $C_{12}$ included the study of various solvomercuration–reductive demercuration sequences with dihydropyrone **18**. Thus, methoxymercuration of dihydropyrone **18** followed by sequential reduction with sodium trithiocarbonate followed by further reduction with sodium borohydride provided

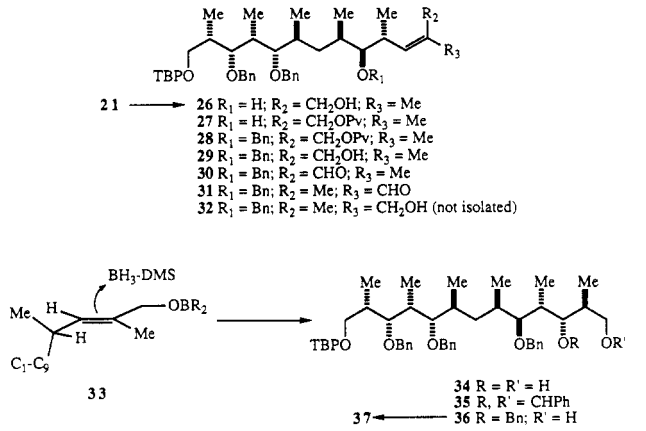



**Figure 7.**

the difficultly separable pyran mixture **22** + **25** in a ratio of 1.3:1. An even less favorable ratio (<1:1) of **22** and **25** was generated from either methoxymercuration or methoxybormination of the glycal **20** followed by reduction with sodium borohydride or tri-*n*-butyltin hydride, respectively. *The absence of a selective route that is responsive to the stereochemical pattern in pyran type 22 is a limitation on the pyranoid approach to polypropionates.*

At this point we abandoned the pyranoid matrix in favor of an acyclic determinant, falling back upon important principles developed by Kishi[27] and by Matsumoto[28] in the field of hydroboration of allylic alcohols. For an allylic alcohol to serve our needs, the double bond had to be of the *E* configuration. We proceeded as follows.

Glycal **20** was treated with aqueous TsOH in tetrahydrofuran to afford **21**. The latter compound was reduced in situ with lithium borohydride to provide diol **26** (Figure 7). Our plan to reach the *E* allylic alcohol contemplated isomerization of a *Z* enal to an *E* system. To allow for oxidation of the $C_{13}$ allylic alcohol to the aldehyde, it was necessary to protect the $C_9$ alcohol, since, in all probability, a $C_9$ hydroxy–$C_{13}$ aldehyde would revert to **21** faster than it would undergo double-bond isomerization. Accordingly, compound **26** was selectively pivaloylated to afford **27** (82%). The secondary alcohol was "tagged" as its benzyl ether (benzytrichloracetimidate, catalytic trifluoromethanesulfonic acid)[29] to afford **28**. Reductive cleavage of the pivalate (lithium aluminum hydride) afforded **29** in 89% yield from **27**). Oxidation of the allylic alcohol with the Dess–Martin periodinane[30] gave *Z* enal **30** (87%). Upon exposure of **30** to the action of lithium thiophenolate, also in tetrahydrofuran, the desired *E* enal **31** (92% yield, **31**:**30** > 30:1) was in hand.

Compound **31** was treated with borane–dimethyl sulfide complex[14] in THF. The hope was to achieve, thereby, the *in situ* reduction of the aldehyde and to follow this reduction with hydroboration of the borate derivative (**33**) of the hypothetical alcohol **32**. It was further presumed that the operative transition state for hydroboration of the double bond would be that implied in **33**. Attack of borane reagent anti to the functionalized long-chain polypropionate would produce the desired diastereomer **34**. This plan worked quite smoothly. Following hydroboration and oxidation with alkaline hydrogen peroxide, there was obtained, after silica gel chromatography, a single

(27) Schmid, G.; Fukuyama, T.; Akasaka, K.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 259.
(28) Matsumoto, T.; Hosoda, Y.; Mori, K.; Fukui, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3516.
(29) Widmer, U. *Synthesis* **1987**, 568 and references therein.
(30) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156.

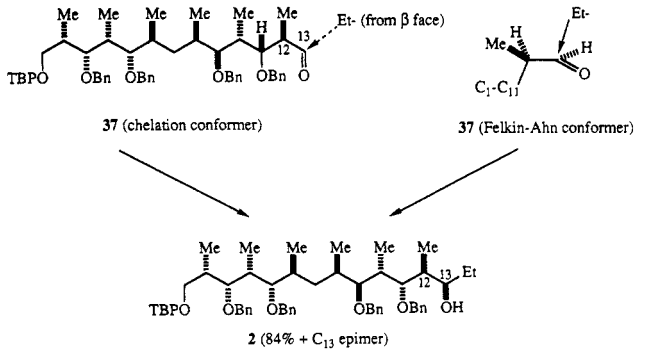


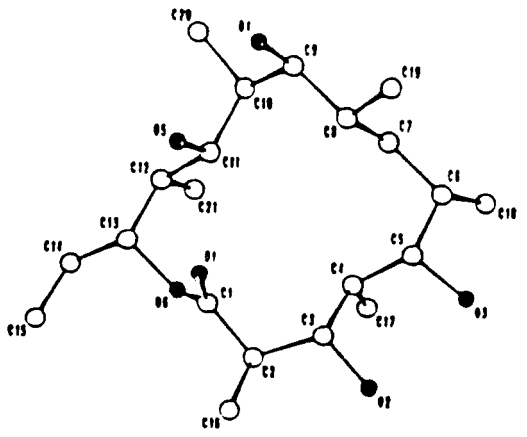

**Figure 8.**

diol. Given our formulation of the enal as **31** (based on our tentative assignment going back to compound 18), the diol obtained is represented as structure **34**.

The next stage of the plan involved distinguishing the $C_{11}$ and $C_{13}$ hydroxyl groups. To this end, compound **34** was treated with benzaldehyde dimethyl acetal in the presence of pyridinium *p*-toluenesulfonate. The resulting benzylidene acetal **35** (not characterized) suffered reduction with diisobutylaluminum hydride. There was thus obtained the monoalcohol **36**. Oxidation of **36** again as above (see **29** → **30**) with the Des–Martin periodinane[30] afforded aldehyde **37**.

The last stereogenic center to be addressed was that at $C_{13}$. Assuming all assignments to this point were correct, the diastereofacial sense of the addition of a "metalloethyl" equivalent, to aldehyde **36** was that envisioned by the convergent Cram[17] and Felkin[18,19] models. In a chelation control model (see reacting conformer **37c**), the required $C_{13}$ *R* configuration would arise only if the large α-disposed polypropionate side chain attached to the remote $C_{11}$ directed the nucleophile to the β face notwithstanding the β-methyl group at the neighboring $C_{12}$. In the event, aldehyde **37** (not characterized) reacted with ethylmagnesium bromide in THF. From this reaction there was isolated an 84% yield of alcohol **2** (Figure 8). Spectroscopic examination of the crude reaction mixture indicated that the presence of small amounts of another product, presumably the $C_{13}$ epimer of **2**.

A four-step sequence provided the enantiomerically homogeneous 9*S* version of **2** from 6-deoxyerythronolide B (**1**). Treatment of **1** with sodium borohydride in the presence of alumina gave rise to a pentol (Figure 9). *That this compound was the 9S system 38 was unambiguously shown by X-ray diffraction analysis of a single crystal (mp 188–190 °C).* Perbenzylation was accomplished, albeit only in 31% yield, by reaction of **38** with benzyl tri-



**38**

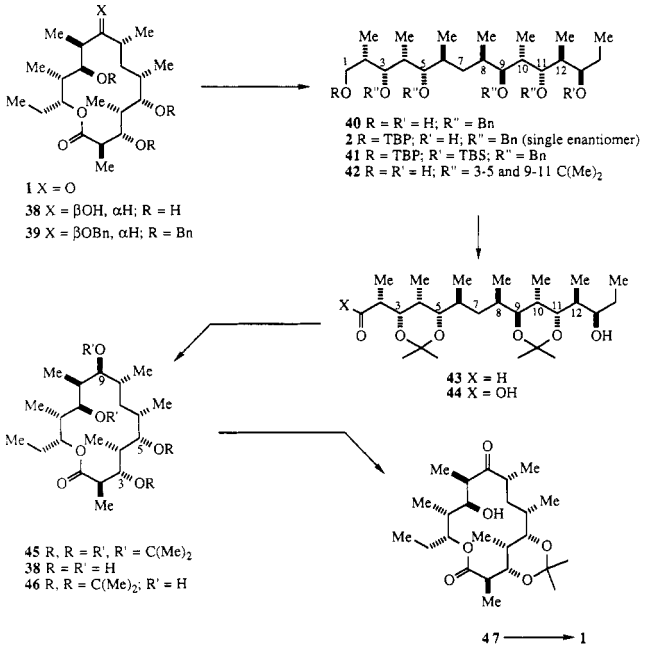



**Figure 9.**

chloroacetimidate[29] in the presence of catalytic trifluoromethanesulfonic acid. The tetrabenzyl compound **39** was treated with lithium aluminum hydride to produce diol **40**. Treatment of **40** with *tert*-butyldiphenylchlorosilane in the presence of triethylamine and 4-(dimethylamino)pyridine led to the formation of **2** in enantiomerically homogeneous (9*S*) form. The high-field NMR and infrared spectra as well as chromatographic mobility served to establish the identity (except for optical rotation) of fully synthetic **2** with the material derived from **1**. This identity serves to validate all of the assignments of the synthetic series. *Thus a fully synthetic route involving selective continuous asymmetric induction for introducing all of the relative stereochemistry of a macrolide antibiotic had been achieved.*

There remained only the goal of converting system **2** back to **1** to complete a totally synthetic pathway. We resorted to naturally derived **2** (vide supra) to complete the cycle. Given the fact that our fully synthetic material had not been resolved, our report describes the development of a formal totally synthetic route, rather than the execution of an actual total synthesis.

Treatment of **2** with *tert*-butyldimethylsilyl triflate in the presence of triethylamine produced the differentially functionalized disilyl derivative **41**. Perdebenzylation was accomplished with sodium in ammonia. This reaction was followed by ketalization (2,2-dimethoxypropane, CSA) and *bis*-desilylation. This sequence afforded compound **42** in 90% yield. Selective oxidation of the primary alcohol according to Nozaki[31] produced aldehyde **43**. Lingren oxidation[32] of **43** provided the seco acid bis-acetonide **44** (57% for the two steps). Macrolactionization using 2,4,6-trichlorobenzoyl chloride was accomplished to give **45**. Unfortunately, the yield in the macrolactonization step was only 17%. Hydrolysis of both acetonides (methanol, CSA) afforded the previously encountered 9*S* dihydro compound **38** (77% yield).

(31) Tomioka, H.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1605.
(32) Bal, B. S.; Childers, W. F.; Pinnick, H. W. *Tetrahedron* **1981**, *22*, 1605.
(33) Sutter, M. A.; Seebach, D. *Liebigs Ann. Chem.* **1983**, 939.

At this point there remained to be accomplished only the conversion of tetraol **38** to the tin hydroxy keto goal structure **1**. For this purpose the hydroxyl groups at carbons 3 and 5 had to be protected. Fortunately it was possible to carry out selective formation of the 3,5-acetonide (74% yield) through the action of 2,2-dimethoxypropane (CSA). Some recyclable bis-acetonide **45** was also obtained. Following the previously described protocol of Masamune,[8] selective oxidation of **46** could be achieved with pyridinium chlorochromate. *The relay cycle was now completed through cleavage of the acetonide of 47 with aqueous acid in acetonitrile. There was thus obtained 6-deoxyerythronolide B (1) indistinguishable by proton NMR and infrared spectroscopy as well as chromatographic mobility from an authentic sample of the natural product.*

## Summary

A total synthesis of the racemic differentiated seco erythronolide derivative **2** has been accomplished. Since the 9*S* enantiomer of **2** has now been reconverted to 6-deoxyerythronolide B (**1**), a formal synthetic route to the latter has been charted.

The synthesis started with the merger of two achiral components (formaldehyde and diene **3**) to provide a product with a single stereogenic center. *All subsequently installed stereocenters involved building, in a serial fashion, from this original chirality element.* To this end, it was possible to use to advantage various diastereofacial or topographic biases in the reactions of chiral molecules with achiral building blocks and reagents. The key resources we exploited were (i) the selectivities associated with the LACDAC reaction and (ii) the ability of variously substituted pyranoid rings to function as matrices for stereoselective addition reactions. The most notable instance of selectivity (>6:1 in the desired sense) came in the LACDAC reaction of aldehyde **7**, which has the $\alpha$-methyl-$\alpha$-isobutylacetaldehyde substitution pattern.

Eventually a limitation in our capacity to manipulate pyranoid matrices to advantage was revealed by our inability to obtain pyran **22** with useful stereoselectivity margins. Fortunately, previously developed methods[25,26] for achieving relative asymmetric induction using acyclic structures were used to advantage to solve the remaining problems.

**Prospects.** The chemistry described herein provides a powerful base for assembling polypropionate arrays with excellent margins of stereocontrol. The next frontier would appear to lie in understanding the basis for the selectivity in cases where the induction determinant is, at least superficially, somewhat removed from the area of bond formation. Quite likely through such improved comprehension will come new applications to even more challenging goals.

## Experimental Section[34]

**2,3-Dihydro-3,5-dimethyl-4*H*-pyran-4-one (Pyrone 4).** Zinc chloride (57.0 g, 420 mmol) was fused three times in a 1-L round-bottom flask, under high vacuum. The resulting zinc chloride glass was then dissolved in tetrahydrofuran (500 mL). To the resulting solution were then added paraformaldehyde (60 g) and diene **3** (80.0 g, 400 mmol). The stirred mixture was then heated at reflux for 3 h. After that time, the reaction mixture was allowed to cool to room temperature. Hexane (400 mL) was added to precipitate the zinc salts. The slurry was then filtered through a pad of Celite and concentrated to afford the crude pyrone as a yellow oil. This was then fractionally distilled under vacuum (85 °C, 15 mmHg) to furnish pyrone **4** (35.0 g, 69%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.14 (d, $J$ = 1.1 Hz, 1 H), 4.30 (dd, $J$ = 11.1, 6.0 Hz, 1 H), 3.97 (dd, $J$ = 11.1, 11.1 Hz, 1 H), 2.61–2.46 (m, 1 H), 1.59 (d, 3 *H*, $J$ = 1.2 Hz), 1.05 (d, $J$ = 7.1 Hz, 3 H); IR ($CHCl_3$) 2975, 2931, 2875, 1670, 1621, 1462, 1398, 1380, 1298, 1247, 1165, 1125, 1024, 920 cm$^{-1}$; MS (20 eV) 126 ($M^+$, 44), 84 (52), 83 (44), 59 (52), 57 (61), 56 (100).

***cis*-(±)-5,6-Dihydro-2-methoxy-3,5-dimethyl-2*H*-pyran and *trans*-(±)-5,6-Dihydro-2-methoxy-3,5-dimethyl-2*H*-pyran (Pyran 5).** A 1-L round-bottom flask containing a solution of pyrone **4** (35.0 g, 278 mmol) and cerium trichloride heptahydrate (30.0 g, 80.5 mmol) in anhydrous ethanol (300 mL) was cooled to ca. −15 °C in an ice/acetone bath. To the solution was added, via addition funnel, approximately 35 mL of a saturated solution of sodium borohydride in anhydrous ethanol. The reaction was judged to be complete when no starting material was visible by TLC (4:1 hexane/ethyl acetate, $R_f$ = 0.4). The solution was allowed to stir for an additional 15 min while being warmed to room temperature. The reaction was then quenched by addition of pH 7 buffer (500 mL). The resulting white emulsion was extracted (3 × 500 mL) with ether. The combined ethereal extracts were washed with brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo to afford a colorless or slightly yellow oil. This was dissolved in anhydrous methanol (300 mL) and treated with *p*-toluenesulfonic acid (500 mg, 2.6 mmol). The mixture was stirred for 1 h at room temperature. Saturated sodium bicarbonate solution (100 mL) was then added and this mixture stirred for 10 min. Distilled water (200 mL) was then added and the resulting two-phase mixture extracted (3 × 200 mL) with pentane. The organic extracts were combined, dried over anhydrous magnesium sulfate, and concentrated in vacuo to a volume of approximately 150 mL. The concentrate was then transferred to a distillation apparatus and the remaining pentane removed by distillation. This furnished crude pyrans **5** as a slightly yellow oil. This was then fractionally distilled (55–58 °C, 20 mmHg) to afford pyrans **5** (30.8 g, 78%) in a 6:4 ratio as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 5.59 (dd, $J$ = 5.1, 0.6 Hz, 0.4 H), 5.47 (br s, 0.6 H), 4.56 (d, $J$ = 2.0 Hz, 0.6 H), 4.56 (d, $J$ = 0.8 Hz, 0.4 H), 3.94 (dd, $J$ = 11.0, 3.9 Hz, 0.4 H), 3.63 (ddd, $J$ = 10.8, 5.7, 1.3 Hz, 0.6 H), 3.41 (s, 3 H), 3.41–3.32 (m, 1 H), 2.48–2.3 (m, 0.6 H), 2.12–1.96 (m, 0.4 H), 1.59 (m, 3 H), 1.04 (d, $J$ = 7.1 Hz, 1.2 H), 0.86 (d, $J$ = 7.5 Hz, 1.8 H); IR (neat) 2962, 2876, 1451, 1190, 1064, 964 cm$^{-1}$.

**Methyl 2,4-Dideoxy-2,4-dimethyl-$\alpha$-L-xylopyranoside (Pyran 6).** A solution of pyran **5** (30.8 g, 217 mmol) in tetrahydrofuran (300 mL) was cooled to 0 °C. Borane–dimethyl sulfide complex (30 mL, 10.0 M in DMS, 300 mmol) was then added via syringe. The homogeneous solution was then placed in a freezer at −5 °C for 12 h. The reaction flask was then removed from the freezer and placed in an ice bath. To the magnetically stirred solution were then slowly added sodium hydroxide (40.0 g, 1 mol) and 30% hydrogen peroxide (113 mL). The resulting two-phase mixture was stirred for 4 h and extracted (3 × 200 mL) with dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulfate and concentrated in vacuo to afford crude product as a colorless oil. This was purified by flash chromatography (4:1 hexane/ethyl acetate) to afford **6** (27.9 g, 80%) as a colorless oil that solidified on standing. Analytically pure samples were prepared by recrystallization (ether/hexane) to afford colorless needles (mp 74–76 °C): $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 3.92 (d, $J$ = 8.5 Hz, 1 H), 3.88 (dd, $J$ = 11.9, 4.8 Hz, 1 H), 3.49 (s, 3 H), 3.06 (dd, $J$ = 11.4, 11.4 Hz, 1 H), 2.90 (ddd, $J$ = 11.2, 11.2, 6.3 Hz, 1 H), 1.73–1.60 (m, 1 H), 1.60 (d, 6.6 Hz, 1 H), 1.59–1.39 (m, 1 H), 1.07 (d, $J$ = 6.5 Hz, 3 H), 0.95 (d, $J$ = 6.6 Hz, 3 H); IR ($CDCl_3$) 3605, 3579, 3450, 2960, 2913, 2828, 1430, 1393, 1102, 1062, 1053, 1006 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_8H_{17}O_3$ ($M^+$ + H) 161.1197, found 161.1185.

**2,4-Dideoxy-2,4-dimethyl-L-xylose, Cyclic 1,3-Propanediyl Mercaptal (Diol 7).** A solution of pyran **6** (12.19 g, 76.6 mmol) and 1,3-propanedithiol (12.85 g, 119 mmol) in dichloromethane (200 mL) was cooled to 0 °C in an ice bath. Titanium tetrachloride (15.2 g, 78.0 mmol) was then added dropwise via syringe. With the addition of the first drop of titanium tetrachloride, the solution immediately turned dark red. After the addition was completed,

(34) NMR spectra of all fully characterized compounds are included as supplementary material. The purity of all intermediates is >90%.

the solution was allowed to warm to room temperature and was stirred for 1.5 h. The reaction was then quenched by slow addition of distilled water (200 mL), during which time the mixture gradually changed from dark red to milky white. This mixture was then extracted (3 × 200 mL) with dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude product as a yellow oil. Gradient elution (4:1 to 2:1 hexane/ethyl acetate) flash chromatography afforded diol **7** (11.6 g, 64%) as a slightly yellow oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 4.17 (d, $J$ = 4.3 Hz), 1 H, 3.95 (ddd, $J$ = 6.1, 4.6, 4.6 Hz, 1 H), 3.78–3.74 (m, 2 H), 3.05–2.84 (m, 4 H), 2.30 (d, $J$ = 4.5 Hz, 1 H), 2.19–1.80 (m, 4 H), 1.69 (s, 1 H), 1.20 (d, $J$ = 6.9 Hz, 3 H), 1.03 (d, $J$ = 7.0 Hz, 3 H); IR ($CDCl_3$) 3600, 3480, 2955, 2920, 2885, 1420, 1272, 1070, 1020, 960 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{10}H_{21}O_2S_2$ ($M^+$ + H) 237.09829, found 237.0964.

**2,4-Dideoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-2,4-dimethyl-L-xylose, Cyclic 1,3-Propanediyl Mercaptal (Alcohol 8).** A solution of diol **7** (32.3 g, 136 mmol) in dichloromethane (300 mL) was treated with triethylamine (75 g, 0.75 mol), *tert*-butyldimethylchlorosilane (22.5 g, 149.6 mmol), and 4-(dimethylamino)pyridine (830 mg, 6.8 mmol). The resulting mixture was stirred for 12 h at room temperature. The reaction was then quenched by addition of saturated sodium bicarbonate (100 mL) and extracted (3 × 200 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a crude product as a viscous yellow oil. This was purified by flash chromatography (4:1 hexane/ethyl acetate) to furnish alcohol **8** (57.1 g, 88%) as a colorless viscous oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.67–7.42 (m, 4 H), 7.49–7.36 (m, 6 H), 4.15 (d, $J$ = 4.4 Hz, 1 H), 4.05–3.90 (m, 1 H), 3.69 (d $AB_q$, $J_{AB}$ = 10.1 Hz, Dn = 19.0 Hz, $J_{AX}$ = 4.1 Hz, $J_{BX}$ = 2.4 Hz, 2 H), 3.05–2.81 (m, 4 H), 1.18 (d, $J$ = 6.8 Hz, 3 H), 1.08 (s, 9 H), 1.04 (d, $J$ = 6.9 Hz, 3 H); IR ($CDCl_3$) 3475, 3060, 2955, 2921, 2890, 2851, 1426, 1112, 1080, 823 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{26}H_{39}O_2S_2Si$ ($M^+$ + H) 475.2161, found 275.2156.

**2,4-Dideoxy-5-*O*-[(1,1-dimethylethyl)diphenylsilyl]-2,4-dimethyl-3-*O*-(phenylmethyl)-L-xylose, Cyclic 1,3-Propanediyl Mercaptal (Dithiane 9).** A solution of alcohol **8** (57.1 g, 120 mmol) in tetrahydrofuran (350 mL) was treated with 95% sodium hydride (4.34 g, 181 mmol) in small portions, maintaining a moderate rate of gas evolution. Benzyl bromide (27.1 g, 158 mmol) and tetrabutylammonium iodide (558 mg, 1.51 mmol) were then added, and the mixture was brought to reflux. After being stirred at reflux for 8 h, the mixture was cooled to room teperature and excess sodium hydride was quenched by slow addition of methyl alcohol (40 mL). Saturated sodium bicarbonate solution (400 mL) was then added. The resulting mixture was then extracted (3 × 300 mL) with ether. The combined organic extracts were washed with brine and dried over anhydrous magnesium sulfate. Filtration and concentration in vacuo followed by flash chromatography (9:1 hexane/ethyl acetate) afforded dithiane **9** (68 g, quantitative yield) as a slightly yellow oil: $^1$H NMR ($CDCl_3$, 490 MHz) $\delta$ 7.74–7.68 (m, 4 H), 7.46–7.28 (m, 11 H), 4.68 ($AB_q$, $J_{AB}$ = 9.1 Hz, $\Delta\nu$ = 16.5 Hz, 2 H), 4.11 (d, $J$ = 5.1 Hz, 1 H), 3.96 (dd, $J$ = 6.5, 4.1 Hz, 1 H), 3.70 (dd, $J$ = 10.1, 7.5 Hz, 1 H), 3.57 (dd, $J$ = 10.1, 5.8 Hz, 1 H), 2.95–2.80 (m, 4 H), 2.18–2.05 (m, 3 H), 1.90–1.86 (m, 1 H), 1.23 (d, $J$ = 6.9 Hz, 3 H), 1.11 (s, 9 H), 0.95 (d, $J$ = 6.8 Hz, 3 H); IR ($CDCl_3$) 3050, 2945, 2919, 2881, 2743, 1465, 1447, 1420, 1105, 820 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{33}H_{45}O_2S_2Si$ ($M^+$ + H) 565.2632, found 565.2614.

**1,5-Anhydro-2,4,6,8-tetradeoxy-9-*O*-[(1,1-dimethylethyl)diphenylsilyl]-2,4,6,8-tetramethyl-7-*O*-(phenylmethyl)-L-*glycero*-D-*gulo*-non-1-en-3-ulose (Pyrone 11).** A solution of dithiane **9** (1.35 g, 2.38 mmol) in acetone containing 5% water (total volume 15 mL) was cooled to ca. −15 °C in an ice/methanol bath. To this solution was added solid sodium bicarbonate (1.5 g, 17.9 mmol). *N*-Bromosuccinimide (NBS) (2.51 g, 14.5 mmol) was then washed into the reaction mixture with acetone (approximately 20 mL). During the addition the solution took on a dark orange color, which slowly (5 min) faded to a light yellow. After the completion of the addition, excess NBS was then quenched by addition of a 1 to 1 mixture of saturated sodium sulfite and saturated sodium bicarbonate (40 mL), at which time the solution became colorless. The mixture was then extracted (3 × 100 mL) with ether. The combined organic extracts were then washed with brine and dried over anhydrous magnesium sulfate. Filtration and concentration in vacuo furnished the crude aldehyde as a slightly yellow oil contaminated with crystalline succinimide, which was removed by filtration of a pentane solution of aldehyde **10**. After removal of the pentane in vacuo, the crude aldehyde was dissolved in dichloromethane (15 mL) and cooled to −78 °C in a dry ice/acetone bath, and diene **3** (480 mg, 2.4 mmol) was added via syringe. The mixture was then treated with boron trifluoride etherate (340 mg, 2.4 mmol), which was also added by syringe. After being stirred for 40 min, the mixture was poured into a rapidly stirred saturated sodium bicarbonate solution (50 mL). The resulting two-phase mixture was then extracted (3 × 50 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a mixture of products as a dark yellow oil. This oil was dissolved in benzene (25 mL) and treated with pyridinium *p*-toluenesulfonate (PPTS) (40 mg, 0.16 mmol). The solution was heated at reflux for 1 h, cooled to room temperature, washed through a plug of silica gel (ca. 15 g) with ether, and concentrated in vacuo to afford crude pyrone as a yellow oil. This was purified by flash chromatography (4:1 hexane/ether) to afford pyrone **11** (549 mg, 40%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.67–7.64 (m, 4 H), 7.418–7.21 (m, 11 H), 4.68 ($AB_q$, $J_{AB}$ = 10.8 Hz, $\Delta\nu$ = 10.9 Hz, 2 H), 4.01 (dd, $J$ = 11.1, 2.0 Hz, 1 H), 3.95 (dd, $J$ = 4.8, 2.0 Hz, 1 H), 3.76 (dd, $J$ = 9.9, 9.9 Hz, 1 H), 3.59 (dd, $J$ = 9.9, 5.8 Hz, 1 H), 2.6 (dq, $J$ = 13.8, 6.9 Hz, 1 H), 2.11–1.95 (m, 1 H), 1.72 (d, $J$ = 1.1 Hz, 3 H), 1.17 (d, $J$ = 7.1 Hz, 3 H), 1.10 (s, 9 H), 1.08 (d, $J$ = 6.9 Hz, 3 H), 0.78 (d, $J$ = 6.9 Hz, 3 H); IR ($CDCl_3$) 3000, 2919, 2842, 1657, 1619, 1451, 1422, 1347, 1300, 1163, 1106, 905 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{36}H_{47}O_4Si$ ($M^+$ + H) 571.3245, found 571.3263.

**1,5-Anhydro-2,4,6,8-tetradeoxy-9-*O*-[(1,1-dimethylethyl)diphenylsilyl]-2,4,6,8-tetramethyl-7-*O*-(phenylmethyl)-L-*threo*-L-*galacto*-non-1-enitol (Pyran 12).** A solution of pyrone **11** (7.27 g, 14.04 mmol) and cerium trichloride heptahydrate (8.0 g, 21.5 mmol) in ethyl alcohol (150 mL) was cooled to ca. −15 °C in an ice/methanol bath. To this cooled, stirred solution was added dropwise a saturated solution of sodium borohydride in ethyl alcohol (15 mL). TLC analysis of the reaction mixture showed complete consumption of starting material (4:1 hexane/ethyl acetate, $R_f$ = 0.4) at the conclusion of the addition. The reaction was then quenched by the addition of pH 7 buffer (300 mL). The resulting mixture was extracted (3 × 200 mL) with ether. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a colorless oil. This was purified by flash chromatography (4:1 hexane/ethyl acetate) to furnish pyran **12** (6.92 g, 86%): $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.67–7.61 (m, 4 H), 7.48—7.26 (m, 11 H), 6.23 (bs, 1 H), 4.65 ($AB_q$, $J_{AB}$ = 11.2 Hz, $\Delta\nu$ = 10.8 Hz, 2 H), 3.89 (dd, $J$ = 9.4, 2.0 Hz, 1 H), 3.83–3.71 (m, 2 H), 32.60–3.52 (m, 2 H), 2.11–1.99 (m, 2 H), 1.90–1.79 (m, 1 H), 1.66 (bs, 3 H), 1.15 (d, $J$ = 6.9 Hz, 3 H), 1.10 (s, 9 H), 1.03 (d, $J$ = 6.3 Hz, 3 H), 0.79 (d, $J$ = 6.7 Hz, 3 H); IR ($CDCl_3$) 3610, 3576, 3062, 2960, 2925, 2855, 1668, 1472, 1428, 1376, 1162, 1114, 1030 cm$^{-1}$; MS (FAB-TEGDME) 572 ($M^+$, 1.2) 555 (2.7), 449 (4.7), 447 (3.9), 407 (3.2), 346 (2.2), 329 (2.3), 297 (3.1), 269 (5.4), 267 (7.7), 249 (5.5), 239 (5.4), 224 (10.6), 223 (100), 221 (39.5), 199 (12.2), 197 (10.4).

**[2*S*-[2$\alpha$(2*R**,3*S**,4*R**),3$\beta$,6$\beta$]]-[[4-[3,6-Dihydro-3,5-dimethyl-6-(1-methylethoxy)-2*H*-pyran-2-yl]-2-methyl-3-(phenylmethoxy)pentyl]oxy](1,1-dimethylethyl)diphenylsilane (Pyran 13).** A solution of pyran **12** (6.92 g, 12.1 mmol) in isopropyl alcohol (150 mL) was treated with *p*-toluenesulfonic acid monohydrate (100 mg, 0.526 mmol). This mixture was stirred at room temperature for 2 h. At that time saturated sodium bicarbonate solution (100 mL) was then added and the resulting mixture was extracted (3 × 200 mL) with ether. The combined ethereal extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to give the crude product as a colorless oil. Flash chromatography afforded pyran **13** (6.76 g, 91%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.69–7.64 (m, 4 H), 7.47–7.10 (m, 11 H), 5.48 (bs, 1 H), 4.88 (bs, 1 H), 4.44 ($AB_q$, $J_{AB}$ = 10.8 Hz, $\Delta\nu$ = 28.9 Hz, 2 H), 4.05 (dq, $J$ = 6.3, 6.3 Hz, 1 H), 3.83–3.52 (m, 4 H), 2.36–2.30 (m,

2 H), 2.10–2.01 (m, 1 H), 1.71 (t, $J$ = 1.7 Hz, 1 H), 1.24 (d, $J$ = 6.3 Hz, 3 H), 1.18 (d, $J$ = 6.3 Hz, 3 H), 1.09 (d, $J$ = 6.9 Hz, 3 H), 1.08 (s, 9 H), 0.94 (d, $J$ = 6.9 Hz, 3 H), 0.92 (d, $J$ = 7.1 Hz, 3 H); IR ($CHCl_3$) 2955, 2915, 2858, 1448, 1375, 1105, 1015, 905 $cm^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{39}H_{55}O_4Si$ ($M^+$ + H) 615.3871, found 615.3832.

**[2*S*-[2α(2*R**,3*S**,4*R**),3β,5β,6β]]-(1,1-Dimethylethyl)[[2-methyl-3-(phenylmethoxy)-4-[tetrahydro-3,5-dimethyl-6-(1-methylethoxy)-2*H*-pyran-2-yl]pentyl]oxy]diphenylsilane (Pyran 14).** A solution of pyran **13** (6.76 g, 11.01 mmol) in ethyl acetate (75 mL) was treated with 5% palladium on alumina (6.0 g). The suspension was placed in a Parr shaker and exposed to hydrogen gas at 50 psi for 36 h. After depressurization the catalyst was removed by filtration and the solution concentrated in vacuo. Flash chromatography (19:1 hexane/ethyl acetate) afforded pyran **14** (5.40 g, 80%) as a colorless oil: $^1H$ NMR ($CDCl_3$, 250 MHz) δ 7.69–7.63 (m, 4 H, 7.51–7.28 (m, 9 H), 7.19–7.13 (m, 2 H), 4.74 (d, $J$ = 3.3 Hz, 1 H), 4.53 ($AB_q$, $J_{AB}$ = 10.8 Hz, Δν = 19.7 Hz, 2 H), 4.02 (dq, $J$ = 6.1, 6.1 Hz, 1 H), 3.83–3.66 (m, 3 H), 3.52 (dd, $J$ = 10.1, 2.0 Hz, 1 H), 2.36–2.24 (m, 1 H), 2.11–1.99 (m, 1 H), 1.91–1.68 (m, 2 H), 1.42–1.20 (m, 2 H), 1.22 (d, $J$ = 6.3 Hz, 3 H), 1.13 (s, 9 H), 1.11 (d, $J$ = 6 Hz, 3 H), 1.00 (d, $J$ = 6 Hz, 3 H), 0.95 (d, $J$ = 7.5 Hz, 3 H), 0.60 (d, $J$ = 7.1 Hz, 3 H), 0.82 (d, $J$ = 7.1 Hz, 3 H); IR ($CDCl_3$) 2940, 2903, 1500, 1415, 1367, 1100, 1054, 1010, 992, 816 $cm^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{39}H_{57}O_4Si$ ($M^+$ + H) 617.4026, found 617.3937.

**[α*S*-[α*R**(1*S**,2*S**,3*R**),β*R**,δ*S**]]-α-[4-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1,3-dimethyl-2-(phenylmethoxy)butyl]-β,δ-dimethyl-1,3-dithiane-2-butanol (Dithiane–Alcohol 15).** A solution of pyran **14** (992 mg, 1.61 mmol) and 1,3-propanedithiol (174 mg, 1.61 mmol) in dichloromethane (16 mL) was cooled to −78 °C in a dry ice/acetone bath. To this cooled solution was added a solution of titanium tetrachloride (1.61 mL, 1.0 M in dichloromethane). The resulting dark orange mixture was then allowed to warm to room temperature over 15 min. The reaction was then quenched by addition of saturated sodium bicarbonate solution (25 mL), at which time it became milky white in appearance. The mixture was then extracted (3 × 25 mL) with ether. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to furnish a crude product as a yellow oil. Flash chromatography (4:1 hexane/ethyl acetate) afforded dithiane alcohol **15** (746.1 mg, 69%) as a colorless oil: $^1H$ NMR ($CDCl_3$, 490 MHz) δ 7.70–7.69 (m, 4 H), 7.48–7.28 (m, 11 H), 4.59 ($AB_q$, $J_{AB}$ = 11.1 Hz, Δν = 36.9 Hz, 2 H), 4.22 (d, $J$ = 3.0 Hz, 1 H), 3.75–3.71 (m, 3 H), 3.62 (dd, $J$ = 10.0, 6.2 Hz, 1 H), 3.31 (ddd, $J$ = 8.6, 3.8, 2.0 Hz, 1 H), 2.99–2.84 (m, 4 H), 1.94–1.83 (m, 2 H), 1.71–1.67 (m, 1 H), 1.16 (d, $J$ = 6.6 Hz, 3 H), 1.00 (s, 9 H), 0.99 (d, $J$ = 6.6 Hz, 3 H), 0.97 (d, $J$ = 7.5 Hz, 3 H), 0.84 (d, $J$ = 7.2 Hz, 3 H); IR ($CDCl_3$) 3460, 3050, 2948, 2918, 1450, 1420, 1375, 1107, 820 $cm^{-1}$; MS (20 eV) 664 ($M^+$, 7), 607 (15), 499 (78), 351 (15), 331 (19), 289 (16), 269 (60), 249 (20), 219 (50), 197 (30), 159 (40), 119 (55), 91 (100); HRMS (CI, $NH_4^+$) mass calcd for $C_{39}H_{56}O_3S_2Si$ ($M^+$ + H) 644.3440, found 664.3479.

**[2*S*-(2*R**,3*S**,4*S**,5*R**,6*R**,8*S**)]-(1,1-Dimethylethyl)-[[8-(1,3-dithian-2-yl)-2,4,6-trimethyl-3,5-bis(phenylmethoxy)nonyl]oxy]diphenylsilane (Dithiane 16).** A solution of dithiane alcohol **15** (195.1 mg, 0.289 mmol) in tetrahydrofuran (10 mL) was treated with 95% sodium hydride (75 mg, 3.13 mmol), benzyl bromide (216 mg, 1.26 mmol), and tetrabutylammonium iodide (25 mg, 0.096 mmol). The mixture was then heated at reflux for 12 h. After allowing the reaction mixture to cool to room temperature, excess sodium hydride was quenched by slow addition of methanol (5 mL). Saturated sodium bicarbonate solution (25 mL) was then added and the mixture was extracted (3 × 50 mL) with ether. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude product. Flash chromatography (9:1 hexane/ethyl acetate) furnished dithiane **16** (205.1 mg, 94%) as a colorless oil: $^1H$ NMR ($CDCl_3$, 490 MHz) δ 7.67–7.61 (m, 4 H), 7.48–7.26 (m, 16 H), 4.57 ($AB_q$, $J_{AB}$ = 11.3 Hz, Δν = 17.5 Hz, 2 H), 4.11 (d, $J$ = 3.2 Hz, 1 H), 3.72 (dd, $J$ = 9.9, 6.8 Hz, 1 H), 3.66 (dd, $J$ = 7.2, 3.4 Hz, 1 H), 3.57 (dd, $J$ = 9.9, 6.8 Hz, 1 H), 3.21 (dd, $J$ = 5.3, 3.9 Hz, 1 H), 2.88–2.72 (m, 4 H), 2.20–2.16 (m, 1 H), 2.09–1.99 (m, 2 H), 1.91–1.80 (m, 2 H), 1.12 (d, $J$ = 6.7 Hz, 3 H), 1.10 (d, $J$ = 6.7 Hz, 3 H), 1.05 (s, 9 H), 0.96 (d, $J$ = 7.5 Hz, 3 H), 0.94 (d, $J$ = 6.7 Hz, 3 H); IR ($CDCl_3$) 2942, 2118, 2880, 2840, 1448, 1420, 1375, 1100, 1060 $cm^{-1}$; MS (20 eV) 697 ($M^+$ -$t$-Bu, 20), 589 (20), 483 (25), 309 (85), 249 (30), 197 (75), 165 (50), 91 (100); HRMS (CI, $NH_4^+$) mass calcd for $C_{42}H_{53}O_3S_2Si$ ($M^+$ − $t$-Bu) 697.3205, found 697.3206.

**[2*S*-[2α(1*S**,3*R**,4*R**,5*S**,6*S**,7*R**),3β]]-2-[8-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1,3,5,7-tetramethyl-4,6-bis(phenylmethoxy)octyl]-2,3-dihydro-3,5-dimethyl-4*H*-pyran-4-one (Pyrone 18).** Dithiane **16** (417.7 mg, 0.554 mmol) was dissolved in acetone containing 5% water (15 mL total volume) and the resulting solution cooled to ca. −15 °C in an ice/methanol bath. The solution became dark orange in color as *N*-bromosuccinimide (601.5 mg, 3.38 mmol) in acetone (25 mL) was added dropwise. After the addition was completed, the solution was stirred an additional 10 min. Saturated sodium bicarbonate solution (25 mL) and saturated sodium sulfite solution (25 mL) were then added. The resulting colorless slurry was extracted (3 × 100 mL) with ether. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The resulting paste was suspended in pentane and filtered to remove the solid succinimide byproduct. The solution was then concentrated to afford crude aldehyde **17** as a colorless oil. This was dissolved in dichloromethane (5 mL) to which was added diene **3** (130 mg, 0.65 mmole). The solution was then cooled to −78 °C in a dry ice/acetone bath and boron trifluoride ethereate (92.3 mg, 0.65 mmole) was added via syringe. The mixture was stirred at −78 °C for 45 min, after which time it was poured into a rapidly stirred sodium bicarbonate solution (25 mL, 1.0 M). The resulting mixture was then extracted (3 × 50 mL) with ether. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a mixture of products as a yellow oil. This oil was dissolved in benzene (25 mL) and treated with pyridinium *p*-toluenesulfonate (10 mg, 0.040 mmol). The solution was then heated at reflux for 2 h, cooled to room temperature, washed through a plug of silica gel (ca. 15 g) with ether (ca. 100 mL), and concentrated in vacuo to afford crude pyrone **18** as a yellow oil. This was purified by flash chromatography (50:48:2 hexane/dichloromethane/ethyl acetate) to afford pyrone **18** and another pyrone in a 6:1 ratio (319.4 mg, 76%). Pyrone **18**: $^1H$ NMR ($CDCl_3$, 250 MHz) δ 7.67–7.61 (m, 4 H), 7.49–7.24 (m, 16 H), 7.04 (bs, 1 H), 4.59 ($AB_q$, $J_{AB}$ = 11.3 Hz, Δν = 32.1 Hz, 2 H), 4.57 (bs, 2 H), 3.88 (bd, $J$ = 13.6 Hz, 1 H), 3.76–3.55 (m, 3 H), 3.19 (dd, $J$ = 6.4, 3.3 Hz, 1 H), 2.51 (dq, $J$ = 13.7, 6.9 Hz, 1 H), 2.26–2.17 (m, 1 H), 2.11–2.07 (m, 1 H), 1.89–1.71 (m, 2 H), 1.65 (d, $J$ = 1.0 Hz, 3 H), 1.14 (d, $J$ = 6.7 Hz, 3 H), 1.06 (s, 9 H), 1.03 (d, $J$ = 6.9 Hz, 3 H), 0.97 (d, $J$ = 6.6 Hz, 3 H), 0.94 (d, $J$ = 7.1 Hz, 3 H), 0.92 (d, $J$ = 6.7 Hz, 3 H), 0.90 (d, $J$ = 6.9 Hz, 3 H); IR ($CDCl_3$) 3000, 2975, 2908, 1700, 1618, 1450, 1420, 1375, 1175, 1105, 1059 $cm^{-1}$; MS (20 eV) 703 ($M^+$, 52), 315 (75), 289 (40), 269 (10), 249 (20), 225 (10), 193 (12), 167 (13), 125 (35), 91 (100); HRMS (20 eV) mass calcd for $C_{45}H_{55}O_3Si$ ($M^+$ − $t$-Bu) 703.3821, found 703.3824.

**[2*S*-[2α(1*S**,3*R**,4*R**,5*S**,6*S**,7*R**),3]]-2-[8-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1,3,5,7-tetramethyl-4,6-bis(phenylmethoxy)octyl]-2,3-dihydro-3,5-dimethyl-4*H*-pyran-4-one (Minor Pyrone 19).** $^1H$ NMR ($CDCl_3$, 490 MHz) δ 7.65–7.62 (m, 4 H), 7.44–7.30 (M, 16 H), 7.17 (bs, 1 H), 4.57 ($AB_q$, $J_{AB}$ = 11.3 Hz, Δν v 84.3 Hz, 2 H), 4.56 ($AB_q$, $J_{AB}$ = 11.3 Hz, Δν = 14.7 Hz, 2 H), 3.86 (dd, $J$ = 8.5, 3.0 Hz, 1 H), 3.71–3.66 (m, 2 H), 3.57 (dd, $J$ = 9.9, 6.3 Hz, 1 H), 3.15 (dd, $J$ = 6.8, 2.7 Hz, 1 H), 2.46 (dq, $J$ = 7.3, 3.0 Hz, 1 H), 2.23–2.18 (m, 1 H), 2.06–2.00 (m, 1 H), 1.97–1.90 (m, 1 H), 1.89–1.82 (m, 1 H), 1.74–1.68 (m, 2 H), 1.65 (d, $J$ = 1.1 Hz, 3 H), 1.12 (d, $J$ = 6.9 Hz 3 H), 1.05 (d, $J$ = 6.6 Hz, 3 H), 1.03 (s, 9 H), 0.95 (d, $J$ = 6.8 Hz, 3 H), 0.94 (d, $J$ = 7.4 Hz, 3 H), 0.89 (d, $J$ = 6.9 Hz, 3 H); IR ($CDCl_3$) 2960, 2920, 2850, 1655, 1618, 1451, 1426, 1386, 1302, 1179, 1110, 1060 $cm^{-1}$.

**[2*S*-[2α(1*S**,3*R**,4*R**,5*S**,6*S**,7*R**),3β,4α]]-2-[8-[[(1,1-dimethylethyl)diphenylsilyl]oxy]-1,3,5,7-tetramethyl-4,6-bis(phenylmethoxy)octyl]-3,4-dihydro-3,5-dimethyl-2*H*-pyran-4-ol (Pyran 20).** Pyrone **18** (336 mg, 0.441 mmol) and cerium trichloride heptahydrate (400 mg, 1.07 mmol) were dissolved in ethyl alcohol (15 mL). This solution was cooled to −15 °C in an ice/methanol bath. A saturated solution of sodium borohydride in ethanol (ca. 10 mL) was added over 30 min via an additional funnel. The reaction was judged to be complete when no more

starting material could be seen by TLC ($R_f$ = 0.35, 4:1 hexane/ethyl acetate) and the mixture stirred an additional 10 min. The reaction was then quenched by addition of pH 7 buffer (50 mL) and extracted (3 × 100 mL) with ether. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude product as a colorless oil. Flash chromatography (4:1 hexane/ethyl acetate) afforded pyran **20** (310 mg, 92%) as a colorless oil: $^1$H NMR ($CDCl_3$, 490 MHz) $\delta$ 7.67–7.61 (m, 4 H), 7.48–7.28 (m, 16 H), 6.14 (bs, 1 H), 4.58 ($AB_q$, $J_{AB}$ = 10.8 Hz, $\Delta\nu$ = 16.2 Hz, 2 H), 4.55 (bs, 2 H), 3.75–3.59 (m, 4 H), 3.43 (dd, $J$ = 10.8, 0.8 Hz, 1 H), 3.18 (dd, $J$ = 5.7, 3.5 Hz, 1 H), 2.25–2.14 (m, 1 H), 2.12–2.02 (m, 1 H), 1.90–1.79 (m, 2 H), 1.75–1.69 (m, 1 H), 1.59 (bs, 3 H), 1.12 (d, $J$ = 6.7 Hz, 3 H), 1.05 (s, 9 H), 0.93 (d, $J$ = 7.1 Hz, 3 H), 0.88 (d, $J$ = 7.0 Hz, 3 H), 0.86 (d, $J$ = 6.9 Hz, 3 H); IR ($CDCl_3$) 3610, 3579, 3060, 3020, 2960, 2622, 2858, 1665, 1455, 1425, 1380, 1160, 1112, 1005, 1030 cm$^{-1}$; MS (FAB-THIO) 762 ($M^+$, 33), 745 (52), 653 (28), 529 (38), 485 (27), 401 (24), 371 (32), 325 (49), 301 (100); HRMS (FAB-THIO) mass calcd for $C_{49}H_{66}O_5Si$ ($M^+$ + H) 763.4760, found 763.4733.

**[2*R*-[2$\alpha$,5$\alpha$,6$\beta$(1*R**,3*S**,4*S**,5*R**,6*R**,7*S**)]]-2-[[6-[8-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-1,3,5,7-tetramethyl-4,6-bis(phenylmethoxy)octyl]-5,6-dihydro-3,5-dimethyl-2*H*-pyran-2-yl]oxy]ethanol (Allylic Alcohol 26).** A solution of pyran **20** (310 mg, 0.406 mmol) and water (150 mg, 8.3 mmol) in tetrahydrofuran (5 mL) was treated with *p*-toluenesulfonic acid monohydrate (15 mg, 0.079 mmol). This mixture was heated at reflux for 45 min. It was then cooled to room temperature and lithium borohydride (ca. 100 mg, 4.6 mmol) was added. The resulting slurry was stirred at room temperature for 2 h. Phosphate buffer (25 mL, pH 7) was then added dropwise with the evolution of gas. The mixture was then extracted (3 × 30 mL) with ether. The combined organic extracts were then dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude product as a colorless oil. Flash chromatography (3:2 hexanes/ethyl acetate) afforded allylic alcohol **26** 4.1 mg, 56%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.71–7.59 (m, 4 H), 7.48–7.23 (m, 16 H), 5.04 (dd, $J$ = 1.12, 9.9 Hz, 1 H), 4.60 ($AB_q$, $J_{AB}$ = 10.97, $\Delta\nu$ = 44.29 Hz, 2 H), 4.60 ($AB_q$, $J_{AB}$ = 13.33, $\Delta\nu$ = 14.63 Hz, 2 H), 4.25 (d, $J$ = 11.42 Hz, 1 H), 3.81–3.58 (m, 4 H), 3.17–3.11 (m, 2 H), 2.65–2.51 (m, 1 H), 2.32–2.26 (m, 1 H), 2.25–2.06 (m, 1 H), 1.85 (d, $J$ = 3.0 Hz, 3 H), 1.79 (bs, 2 H), 1.13 (d, $J$ = 8.1 Hz, 3 H), 1.03 (s, 9 H), 0.92 (d, $J$ = 7.5 Hz, 3 H), 0.90 (d, $J$ = 6.9 Hz, 3 H), 0.89 (d, $J$ = 7.9 Hz, 3 H), 0.84 (d, $J$ = 7.5 Hz, 3 H); IR ($CHCl_3$) 3400, 300, 2950, 2909, 2860, 1445, 1420, 1105 cm$^{-1}$; MS (CI, $NH_4^+$) 765 (M + 1), 764, 736, 709, 683, 657, 639, 622, 611, 605, 531, 491, 471, 457, 449, 249, 211, 193, 175, 135, 123, 105, 91 (base peak), 83; HRMS (FAB-TEGDME) mass calcd for $C_{49}H_{69}O_5Si$ ($M^+$ + H) 765.4917, found 765.4989.

**[4*R*-(2*Z*,4*R**,5*S**,6*R**,8*S**,9*S**,10*R**,11*R**,12*S**)]-13-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,4,6,8,10,12-hexamethyl-5,9,11-tris(phenylmethoxy)-2-tridecenyl 2,2-Dimethylpropanoate (Allylic Ester 27).** A solution of allylic alcohol **26** (174.1 mg, 0.228 mmol), triethylamine (296 mg, 2.93 mmol), and 4-(dimethylamino)pyridine, (10 mg, 0.082 mmol) in dichloromethane (4 mL) was treated with trimethylacetyl chloride (200 mg, 1.66 mmol). The resulting mixture was stirred at room temperature for 12 h. It was then washed through a plug of silica gel and concentrated in vacuo to afford a crude yellow oil. This was purified by flash chromatography (4:1 hexanes/ether) to furnish the allylic pivaloyl ester **27** (156.4 mg, 82.3%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 7.69–7.61 (m, 4 H), 7.46–7.21 (m, 16 H), 5.21 (dd, $J$ = 9.93, 0.35 Hz, 1 H), 4.58 ($AB_q$, $J_{AB}$ = 11.0, $\Delta\nu$ = 52.7 Hz, 2 H), 4.65–4.53 (m, 4 H), 3.73–3.66 (m, 2 H), 3.57 (dd, $J$ = 9.8, 9.8 Hz, 1 H), 3.21–3.17 (m, 2 H), 2.65–2.52 (m, 1 H), 2.26–2.13 (m, 1 H), 2.11–1.99 (m, 1 H), 1.78 (bs, 3 H), 1.63 (bs, 1 H), 1.13 (d, $J$ = 7.1 Hz, 3 H), 1.04 (s, 9 H), 0.93–0.82 (m, 12 H); IR ($CDCl_3$) 3500, 2960, 2930, 2873, 2858, 1720, 1454, 1283, 1161, 1113, 1067 cm$^{-1}$; MS (CI, $NH_4^+$) 850 ($M^+$ + 1, 1.14), 849 (1.1), 832 (1.0), 531 (1.0), 346 (1.1), 339 (1.1), 327 (1.2), 323 (1.0), 309 (1.4), 301 (1.1), 296 (1.6), 295 (7.0), 249 (4.6), 224 (11.6), 223 (100), 222 (3.1), 221 (32.1), 220 (4.7); HRMS (FAB-TEGDME) mass calcd for $C_{54}H_{77}O_6Si$ ($M^+$ + H) 849. 5492, found 849.5552.

**[4*R*-(2*Z*,4*R**,5*S**,6*R**,8*S**,9*S**,10*R**,11*R**,12*S**)]-13-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,4,6,8,10,12-hexamethyl-5,9,11-tris(phenylmethoxy)-2-tridecen-1-ol (Allylic Alcohol 29).** A solution of alcohol **27** (128 mg, 0.153 mmol) and benzyl trichloroacetimidate (ca. 200 mg, 0.839 mmol) in cyclohexane (1.5 mL) was treated with trifluoromethanesulfonic acid (2 $\mu$L, 3.4 mg, 0.023 mmol). This mixture was stirred for 12 h, over which time a colorless precipitate slowly formed. At the conclusion of the 12-h reaction period the suspension was filtered through a pad of Celite with cyclohexane, washed through silica gel with ether, and concentrated in vacuo to afford a yellow oil. This was dissolved in ether, cooled to 0 °C in an ice bath, and treated with excess lithium aluminum hydride (LAH) (250 mg, 6.59 mmol). The suspension was then allowed to warm to room temperature and stir for 2 h. At that time, excess LAH was quenched by dropwise addition of saturated sodium/potassium tartrate solution (25 mL). The resulting two-phase mixture was then stirred rapidly for 45 min. It was then extracted (3 × 50 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a slightly yellow oil. This was purified by gradient elution flash chromatography (9:1 to 3:1 hexane/ethyl acetate) to furnish allylic alcohol **29** (101.6 mg, 88.5%) as a colorless oil: $^1$H NMR ($CDCl_3$, 490 MHz) $\delta$ 7.72–7.67 (m, 4 H), 7.51–7.24 (m, 21 H), 5.20 (ddd, $J$ = 10.1, 1.2, 1.2 Hz, 1 H) 4.63 ($AB_q$, $J_{AB}$ = 11.37, $\Delta\nu$ = 48.80 Hz, 2 H), 4.63 ($AB_q$, $J_{AB}$ = 11.20, $\Delta\nu$ = 19.60 Hz, 2 H), 4.49 ($AB_q$, $J_{AB}$ = 10.60, $\Delta\nu$ = 11.30 Hz, 2 H), 4.23 (ddd, $J$ = 12.0, 2.6, 0.8 Hz, 1 H), 3.79–3.76 (m, 2 H), 3.74–3.69 (m, 2 H), 3.64 (dd, $J$ = 9.9, 6.3 Hz, 1 H), 3.22, (dd, $J$ = 7.5, 1.4 Hz, 1 H), 3.06 (dd, $J$ = 9.3, 1.6 Hz, 1 H), 2..1–2.86 (m, 1 H), 2.48 (dd, $J$ = 8.5, 3.5 Hz, 1 H), 2.30–2.23 (m, 1 H), 2.18–2.12 (m, 1 H), 2.15–1.90 (m, 3 H), 1.85 (d, $J$ = 1.4 Hz, 3 H), 1.21 (d, $J$ = 6.9 Hz, 3 H), 1.07 (s, 9 H), 1.05 (d, $J$ = 6.6 Hz, 3 H), 0.99 (d, $J$ = 6.7 Hz, 3 H), 0.94 (d, $J$ = 6.6 Hz, 3 H), 0.94 (d, $J$ = 6.8 Hz, 3 H); IR ($CDCl_3$) 3420, 3030, 3013, 2960, 2924, 2877, 1710, 1497, 1455, 1438, 1112, 1066 cm$^{-1}$; MS (FAB-TEGDME), 855 ($M^+$, 78), 760 (30), 705 (34), 639 (28), 557 (32), 491 (31), 443 (100), 355 (59), 301 (79); HRMS (FAB-TEGDME) mass calcd for $C_{56}H_{75}O_5Si$ ($M^+$ + H) 855.5387, found 855.5385.

**[4*R*-(2*Z*,4*R**,5*S**,6*R**,8*S**,9*S**,10*R*,11*R**,12*S**)]-13-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,4,6,8,10,12-hexamethyl-5,9,11-tris(phenylmethoxy)-2-tridecenal (*Z* Enal 30).** A solution of allylic alcohol **29** (68.9 mg, 0.092 mmol) in dichloromethane (5 mL) was treated with the Dess–Martin periodinane (50 mg, 0.118 mmol). The mixture was stirred at room temperature for 1 h. A saturated solution of sodium sulfite (5 mL) was then added and the resulting biphasic mixture stirred for an additional 0.5 h. The mixture was then extracted (3 × 15 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a slightly yellow oil. This was purified by preparative thin layer chromatography (0.50-mm silica gel plates, 4:1 hexane/ethyl acetate) to furnish the unstable enal **30** (59.6 mg, 87%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) $\delta$ 10.06 (s, 1 H), 7.66–7.61 (m, 4 H), 7.43–7.12 (m, 21 H), 6.39 (bd, $J$ = 9.4 Hz, 1 H), 4.70–4.32 (m, 6 H), 3.75–3.60 (m, 4 H), 3.48–3.37 (m, 1 H), 3.13 (bt, $J$ = 7.7 Hz, 2 H), 2.36–2.20 (m, 1 H), 2.19–2.08 (m, 1 H), 2.07–1.83 (m, 3 H), 1.73 (d, $J$ = 1.1 Hz, 3 H), 1.16 (d, $J$ = 6.8 Hz, 3 H), 1.00 (s, 9 H), 0.99 (d, $J$ = ca. 7 Hz, 3 H), 0..98 (d, $J$ = ca. 7 Hz, 3 H), 0.92 (d, $J$ = 6.7 Hz, 3 H), 0.87 (d, $J$ = 6.8 Hz, 3 H); IR ($CDCl_3$) 2945, 2916, 2843, 1657, 1496, 1105 cm$^{-1}$.

**[4*R*-(2*E*,4*R**,5*S**,6*R**,8*S**,9*S**,10*R**,11*R**,12*S**)]-13-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,4,6,8,10,12-hexamethyl-5,9,11-tris(phenylmethoxy)-2-tridecenal (*E* Enal 31).** A solution of thiophenol (40 mg, 0.36 mmol) in tetrahydrofuran (0.5 mL) was cooled to −78 °C in a dry ice/acetone bath. The solution was then treated with *n*-butyllithium (0.1 mL, 2.2 M solution in hexanes, 0.22 mmol). A portion (ca. 0.1 mL) of this solution was transferred to a previously prepared solution of *Z* enal **30** (59.6 mg, 0.080 mmol) in tetrahydrofuran (3 mL). The enal-containing solution was stirred at room temperature for 1.5 h, after which time it was washed through a plug of silica gel (ca. 5 g) with ether (ca. 50 mL). Concentration in vacuo then afforded crude product as a slightly yellow oil. This was purified by preparative TLC (0.5-mm silica gel plate, 4:1 hexanes/ethyl acetate) to afford *E* enal **31** (54.8 mg, 92%): $^1$H NMR ($CDCl_3$, 490 MHz) $\delta$ 9.32 (s, 1 H), 7.67–7.60 (m, 4 H), 7.53–7.15 (m, 21 H), 6.44 (dd, $J$ = 9.8, 1.3 Hz), 4.67 (d, $J$ = 11.3 Hz, 1 H), 4.61 (d, $J$ = 11.2 Hz, 1 H), 4.59–4.51 (m, 3 H), 4.40 (d, $J$ = 11.1 Hz, 1 H),

3.76–3.68 (m, 2 H), 3.60 (dd, $J$ = 9.9, 6.2 Hz, 1 H), 3.25 (dd, $J$ = 6.7, 3.0 Hz, 1 H), 3.15 (dd, $J$ = 7.6, 1.2 Hz, 1 H), 2.97–2.92 (m, 1 H), 2.24–2.11 (m, 1 H), 2.10–2.08 (m, 1 H), 1.98–1.92 (m, 2 H), 1.87–1.85 (m, 1 H), 1.72 (d, $J$ = 1.3 Hz, 3 H), 1.15 (d, $J$ = 6.9 Hz, 3 H), 1.02 (s, 9 H), 1.01 (d, $J$ = ca. 7 Hz, 3 H), 0.98 (d, $J$ = 6.9 Hz, 3 H), 0.93 (d, $J$ = 6.7 Hz, 3 H), 0.88 (d, $J$ = 6.9 Hz, 3 H); IR ($CDCl_3$) 2959, 2922, 2864, 2856, 1679, 1631, 1452, 1112 $cm^{-1}$.

**[2*S*-(2*R**,3*R**,4*S**,5*R**,6*S**,8*R**,9*R**,10*S**,11*S**,12*R**)]-13-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,4,6,8,10,12-hexamethyl-5,9,11-tris(phenylmethoxy)-1,3-tridecanediol (Diol 34).** A solution of *E* enal **31** (54.8 mg, 0.0733 mol) in THF (3 mL) was cooled in an ice bath. Borane–dimethyl sulfide complex (0.040 mL of a 10.0 M solution in dimethyl sulfide, 0.40 mmol) was then added via syringe. The resulting solution was stirred for 3 h while being warmed slowly to room temperature. The mixture was then recooled in an ice bath and 15% sodium hydroxide solution (2 mL) and 30% hydrogen peroxide (1 mL) solution were added dropwise. The resulting two-phase mixture was warmed to room temperature and stirred vigorously for 2 h. The reaction was quenched with saturated sodium bicarbonate solution and extracted (3 × 15 mL) with dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude product as a slightly yellow oil. Preparative TLC (0.5-mm silica gel, 254-nm indicator, 3:2 hexanes/ethyl acetate) furnished diol **34** (46.0 mg, 81%) as a colorless oil: $^1H$ NMR ($CDCl_3$, 250 MHz) $\delta$ 7.66–7.62 (m, 4 H), 7.48–7.23 (m, 21 H), 4.72–4.45 (m, 6 H), 3.84 (bd, $J$ = 8.7 Hz, 1 H), 3.76 (bd, $J$ = 9.8 Hz, 1 H), 3.68 (bd, $J$ = 8.5 Hz, 1 H), 3.62–3.53 (m, 3 H), 3.40–3.35 (m, 1 H), 3.30–3.28 (m, 1 H), 3.13 (bd, $J$ = 7.0 Hz, 1 H), 2.33–2.26 (m, 1 H), 2.14–2.03 (m, 1 H), 1.97–1.69 (m, 3 H), 1.14 (d, $J$ = 6.7 Hz, 3 H), 1.05 (d, $J$ = 6.3 Hz, 3 H), 1.00 (s, 9 H), 0.92 (d, $J$ = 7.5 Hz, 3 H), 0.87 (d, $J$ = 7.5 Hz, 3 H), 0.69 (d, $J$ = 7.1 Hz, 3 H); IR ($CDCl_3$) 3448, 2958, 2921, 2870, 1451, 1425, 1108, 1033 $cm^{-1}$; MS (FAB-DBPTH) 874 ($M^+$, 15), 833 (14), 619 (13), 554 (14), 483 (27), 434 (45), 419 (48), 383 (24), 335 (100); HRMS (FAB-TEGDME) mass calcd for $C_{56}H_{77}O_6Si$ ($M^+$ + H) 873.5492, found 873.5472.

**[2*S*-(2*R**,3*R**,4*R**,5*R**,6*S**,8*R**,9*R**,10*S**,11*S**,12*R**)]-13-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,4,6,8,10,12-hexamethyl-3,5,9,11-tetrakis(phenylmethoxy)-1-tridecanol (Alcohol 36).** A solution of diol **34** (45.6 mg, 0.059 mmol) and benzaldehyde dimethyl acetal (100 mg, 0.66 mmol) in benzene (2 mL) was treated with pyridinium *p*-toluenesulfonate (2.0 mg, 0.008 mmol). This mixture was the stirred at reflux for 2 h, then cooled to room temperature, and washed through a plug of basic alumina (ca. 2 g, activity grade I) with ether (ca. 20 mL). Concentration in vacuo and then exposure to high vacuum for 2 h to remove excess benzaldehyde dimethyl acetal reagent furnished the crude acetal. This was dissolved in dichloromethane (1.0 mL), treated with diisobutylaluminum hydride (0.050 mL of 1.0 M solution in hexanes, 0.050 mmol), and stirred at room temperature for 1.5 h. A saturated solution of sodium/potassium tartrate (4.0 mL) was then added dropwise and the resulting two-phase mixture was stirred for an additional 1 h. It was then extracted (3 × 15 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude product. Flash chromatography (4:1 hexanes/ethyl acetate) provided alcohol **36** (30 mg, 58%) as a colorless oil: $^1H$ NMR ($CDCl_3$, 490 MHz) $\delta$ 7.67–7.61 (m, 4 H), 7.45–7.13 (m, 26 H), 4.68–4.49 (m, 7 H), 4.23 (d, $J$ = 11.4 Hz, 1 H), 3.76–3.68 (m, 3 H), 3.61–3.52 (m, 3 H), 3.34 (d, $J$ = 9.7 Hz, 1 H), 3.15 (d, $J$ = 7.9 Hz, 1 H), 2.63 (dd, $J$ = 7.8, 4.3 Hz, 1 H), 2.24–2.21 (m, 1 H), 2.13–2.10 (m, 1 H), 2.06–1.92 (m, 3 H), 1.89–1.84 (m, 1 H), 1.29 (s, 1 H), 1.16 (d, $J$ = 6.8 Hz, 3 H), 1.01 (s, 9 H), 0.98 (d, $J$ = 6.7 Hz), 3 H, 0.93 (d, $J$ = 6.8 Hz), 6 H, 0.88 (d, $J$ = 6.9 Hz, 6 H); IR ($CDCl_3$) 3490, 2959, 2925, 2875, 2552, 1453, 1428, 1115, 1066 $cm^{-1}$; HRMS (FAB-TEGDME) mass calcd for $C_{63}H_{83}O_6Si$ ($M^+$ + H) 963.5962, found 963.5968.

**[3*R*-(3*R**,4*S**,5*S**,6*S**,7*S**,8*R**,10*S**,11*S**,12*R**,13*R**,14*S**)]-15-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-5,7,11,13-tetrakis(phenylmethoxy)-3-pentadecanol (Alcohol 2 (Synthetic)).** A solution of alcohol **36** (22.6 mg, 0.0263 mmol) in dichloromethane (5 mL) was treated with the Dess–Martin periodinane (25 mg, 0.059 mmol). The mixture was stirred at room temperature for 1 h. A saturated solution of sodium sulfite (5 mL) was then added and the resulting biphasic mixture was stirred for an additional 0.5 h. The mixture was then extracted (3 × 5 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford crude aldehyde **37** as a colorless oil. This was dissolved in THF (3 mL) and cooled to −78 °C in a dry ice/acetone bath. Ethylmagnesium bromide (0.10 mL of 1.0 M solution in ether, 0.10 mmol) was then added via syringe. The mixture was stirred at −78 °C for 10 min and then quenched by addition of saturated sodium bicarbonate solution (5 mL). After being warmed to room temperature, the mixture was extracted (3 × 10 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to furnish crude product as a slightly yellow oil. This was purified by flash chromatography (5:1 hexanes/ethyl acetate) to afford alcohol **2** (19.7 mg, 84.1%) as a colorless oil: $^1H$ NMR ($CDCl_3$, 490 MHz) $\delta$ 7.64–7.60 (m, 4 H), 7.45–7.06 (m, 26 H), 4.62–4.48 (m, 7 H), 4.29 (d, $J$ = 11.4 Hz, 1 H), 3.74–3.66 (m, 4 H), 3.58 (dd, $J$ = 9.9, 6.3 Hz, 1 H) 3.29 (d, $J$ = 8.1 Hz, 1 H), 3.13 (d, $J$ = 8.1 Hz, 1 H), 2.72 (d, $J$ = 2.7 Hz, 1 H), 2.23–2.21 (m, 1 H), 2.11–2.08 (m, 1 H), 2.06–1.87 (m, 4 H), 1.72–1.69 (m, 1 H), 1.10 (d, $J$ = 6.7 Hz, 3 H), 1.01 (s, 9 H), 0.97 (d, $J$ = 7.0 Hz, 3 H), 0.96 (d, $J$ = 6.4 Hz, 3 H), 0.91–0.81 (M, 14 H); IR ($CHCl_3$) 3400, 3010, 2980, 2922, 2875, 1427, 1109, 1056, 937 $cm^{-1}$; HRMS (FAB-THIO) mass calcd for $C_{65}H_{87}O_6Si$ ($M^+$ + H) 991.6272, found 991.6263.

**Alcohol 2 (Natural).** A solution of diol **40** (65.9 mg, 0.088 mmol) (vide infra), triethylamine (0.10 mL, 0.76 mmol), and 4-(dimethylamino)pyridine (1 mg, 0.008 mmol) was treated with *tert*-butyldiphenylchlorosilane (75 mg, 0.27 mmol). This mixture was stirred for 24 h, after which time it was washed through a plug of silica gel and concentrated in vacuo to furnish a yellow oil. Preparative TLC (1.0 mm, 5:1 hexanes/ethyl acetate) afforded alcohol **2** (69 mg, 89%): $^1H$ NMR ($CDCl_3$, 490 MHz) 7.64–7.60 (m, 4 H), 7.45–7.06 (m, 26 H), 4.62–4.48 (m, 7 H), 4.29 (d, 1 H, $J$ = 11.4 Hz), 3.74–3.66 (m, 4 H), 3.58 (dd, 1 H, $J$ = 9.9, 6.3 Hz) 3.29 d, 1 H, $J$ = 8.1 Hz), 3.13 (d, 1 H, $J$ = 8.1 Hz), 2.72 (d, 1 H, $J$ = 2.7 Hz), 2.23–2.21 (m, 1 H), 2.11–2.08 (m, 1 H), 2.06–1.87 (m, 4 H), 1.72–1.69 (m, 1 H), 1.10 (d, 3 H, $J$ = 6.7 Hz), 1.01 (s, 9 H), 0.97 (d, 3 H, $J$ = 7.0 Hz), 0.96 (d, 3 H, $J$ = 6.4 Hz, 0.91–0.81 (M, 14 H); IR ($CHCl_3$) 3400, 3010, 2980, 2922, 2875, 1427, 1109, 1056, 937 $cm^{-1}$; $[\alpha]_D$ = +17.6° (*c*, 1.17, $CHCl_3$).

**(9*S*)-9-Deoxo-12-deoxy-9-hydroxyerythronolide [(9*S*)-Dihydro-6-deoxyerythronolide B (38)]. Method A.** Solid sodium borohydride (200 mg, 5.3 mmol) was added to a solution of 6-deoxyerythronolide B (1) (311 mg, 0.774 mmol) in tetrahydrofuran (5 mL) in which alumina (200 mg) has been suspended. The slurry was stirred at room temperature for 2 h, after which time it was washed through a plug of silica gel (ca. 5 g) with ether and concentrated in vacuo to afford a colorless gum. This was purified by gradient elution flash chromatography (7:3 to 1:1 hexanes/ethyl acetate) to furnish (9*S*)-dihydro-6-deoxyerythronolide B (**38**) (296 mg, 95%) as a colorless gum. Crystalization from ether/hexanes affords colorless needles (mp 188–190 °C).

**Method B.** A solution of bis-acetonide **45** (8.6 mg, 0.018 mmol) (vide infra) in methanol (1 mL) was treated with camphorsulfonic acid (1 mg, 0.004 mmol). The mixture was stirred at room temperature for 1.5 h, after which time it was diluted with ether (ca. 10 mL) and washed through a plug of silica gel. The washings were then concentrated in vacuo and the residue was chromatographed as in method A to afford (9*S*)-dihydro-6-deoxyerythronolide B (**38**) (5.5 mg, 77%): $^1H$ NMR ($CDCl_3$, 250 MHz) (ddd, $J$ = 9.4, 4.2, 1.4 Hz, 1 H), 4.32 (bs, 1 H), 3.98 (dd, $J$ = 5.3, 1.2 Hz, 1 H), 3.86 (d, $J$ = 10.4 Hz, 1 H), 3.78 (bs, 1 H), 3.38 (bd, $J$ = 11.1 Hz, 1 H), 3.00 (bd, $J$ = 9.2 Hz, 1 H), 2.76 (dq, $J$ = 10.4, 6.7 Hz, 1 H), 2.16–2.03 (m, 1 H), 2.00–1.89 (m, 1 H), 1.87–1.77 (m, 2 H), 1.56–1.32 (m, 2 H), 1.28 (d, $J$ = 6.7 Hz, 3 H), 1.10 (d, $J$ = 7.2 Hz, 3 H), 1.06 (d, $J$ = 7.3 Hz, 3 H), 1.02 (d, $J$ = 6.9 Hz, 3 H), 1.01 (d, $J$ = 7.2 Hz, 3 H), 0.93 (t, $J$ = 7.3 Hz, 3 H), 0.80 (d, $J$ = 7.0 Hz, 3 H); IR ($CDCl_3$) 3090, 3458, 2962, 2923, 1693, 1454, 1370, 1332, 1187, 1070, 1040, 973 $cm^{-1}$; $[\alpha]_D$ = +22.7° (*c* 1.63, $CHCl_3$).

**[2*S*-(2*R**,3*S**,4*S**,5*R**,6*R**,8*S**,9*R**,10*R**,11*R**,12*R**,13*S**)]-2,4,6,8,10,12-Hexamethyl-3,5,9,11-tetrakis(phenylmethoxy)-1,13-pentadecanediol (Diol 40).** A solution of benzyl trichloroacetimidate (500 mg, 2.1 mmol) and (9*S*)-dihydro-6-

deoxyerythronolide B (38) (122 mg, 0.302 mmol) in cyclohexane (3 mL) was treated with trifluoromethanesulfonic acid (0.005 mL, 8.5 mg, 0.055 mmol). As the mixture was stirred for 48 h, a colorless precipitate slowly formed. At the conclusion of the 2-day reaction period, the slurry was filtered through Celite with cyclohexane followed by basic alumina with ether. The filtrate was then concentrated in vacuo to afford a colorless oil. This was chromatographed (9:1 hexanes/ether). The fastest running fraction ($R_f$ = 0.8 in 4:1 hexanes/ethyl acetate) was collected. This contains tetrabenzyl lactone **39** heavily contaminated with benzyl trichloroacetimidate. The mixture was dissolved in ether (10 mL) and the solution was treated with excess lithium aluminum hydride (LAH) (100 mg, 2.6 mmol). The resulting slurry was stirred at room temperature for 1 h. Excess LAH was then quenched by dropwise addition of saturated sodium/potassium tartrate solution (10 mL). The resulting two-phase mixture was stirred until colorless and then extracted (3 × 25 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. Flash chromatography (4:1 hexanes/ethyl acetate) afforded diol **40** (66 mg, 31%) as a colorless oil: $^1$H NMR ($CDCl_3$, 490 MHz) 7.41–7.10 (m, 20 H), 4.65–4.47 (m, 7 H), 4.38 (d, $J$ = 11.4 Hz, 1 H), 3.74–3.70 (m, 2 H), 3.55 (dd, $J$ = 8.2, 2.5 Hz, 1 H), 3.49–3.45 (m, 2 H), 3.33 (dd, $J$ = 8.2, 2.5 Hz, 1 H), 3.49–3.45 (m, 2 H), 3.33 (d, $J$ = 9.0 Hz, 1 H), 3.1 (dd, $J$ = 7.2, 2.0 Hz, 1 H), 2.69 (bd, $J$ = 3.4 Hz, 1 H), 2.09–1.89 (m, 4 H), 1.73–1.71 (m, 1 H), 1.52–1.24 (m, 3 H), 1.13 (d, $J$ = 6.9 Hz, 3 H), 0.99 (d, $J$ = 6.6 Hz, 3 H), 0.98 (d, $J$ = 7.1 Hz, 3 H), 0.94–0.87 (m, 14 H); IR ($CDCl_3$) 3480, 2971, 2925, 2870, 1491, 1450, 1345, 1095, 1064, 1027, 952 cm$^{-1}$; $[\alpha]_D$ = +23.6° (c 0.56 $CHCl_3$); HRMS (CI, $NH_4^+$) mass calcd for $C_{49}H_{69}O_6$ ($M^+$ + H) 753.5094, found 753.5069.

**[5*R*-(5*R**,6*R**,7*R**,8*S**,9*S**,10*R**,12*S**,13*S**,14*R**,15-*R**,16*S**)]-5-Ethyl-2,2,3,3,6,8,10,12,14,16,20,20-dodecamethyl-19,19-diphenyl-7,9,13,15-tetrakis(phenylmethoxy)-4,18-dioxa-3,19-disilaheneicosane (Protected Hexaol 41).** A solution of alcohol **2** (33.7 mg, 0.034 mmol) and triethylamine (34 mg, 0.034 mmol) in dichloromethane (2 mL) was treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate (10.8 mg, 0.041 mmol) and stirred at room temperature for 15 min. It was then washed through a plug of silica gel with ether and concentrated. The residue was chromatographed (9:1 hexane/ethyl acetate) to afford protected hexol **41** (36 mg, 96%): $^1$H NMR ($CDCl_3$, 250 MHz) δ 7.67–7.63 (m, 4 H), 7.42–7.13 (m, 26 H), 4.77 (d, $J$ = 11.3 Hz, 1 H), 4.65–4.45 (m, 6 H), 5.37 (d, $J$ = 10.8 Hz, 1 H), 3.96–3.51 (m, 5 H), 3.45 (d, $J$ = 9.1 Hz, 1 H), 3.13 (d, $J$ = 7.9 Hz, 1 H), 2.30–1.81 (m, 6 H), 1.63–1.42 (m, 2 H), 1.12 (d, $J$ = 7.1 Hz, 3 H), 0.98 (s, 9 H), 0.90–0.80 (m, 18 H), 0.86 (s, 9 H), 0.04 (s, 3 H), 0.00 (s, 3 H); IR ($CDCl_3$) 3080, 3028, 2980, 2918, 1496, 1455, 1429, 1382, 1255, 1115, 1075, 1031, 840 cm$^{-1}$.

**[4*S*-[4α(α*S**,β*R**),5α,6β[1*S**,3*R**[4*R**,5*S**,6*S**(*R**)]]]]-α-Ethyl-6-[3-[6-(2-hydroxy-1-methylethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl]-1-methylbutyl]-β,2,2,5-tetramethyl-1,3-dioxane-4-ethanol (Diol 42). Method A.** Liquid ammonia (ca. 8 mL) was collected via a dry ice condenser in a 50-mL, three-neck flask cooled to −78 °C in a dry ice/acetone bath. To the ammonia was added sodium metal (ca. 8 mg, 0.35 mmol). To the resulting dark blue solution was added a solution of protected hexol **41** (23 mg, 0.020 mmol) in THF (3 mL). After stirring for 5 min, solid ammonium chloride was added, at which time the solution became colorless. The dry ice condenser and dry ice/acetone bath were removed and the liquid ammonia was allowed to evaporate as the mixture slowly warmed to room temperature. The resulting slurry was filtered through anhydrous magnesium sulfate and the filter cake washed with ether. The filtrate was concentrated in vacuo, and the residue was dissolved in 2,2-dimethoxypropane (3 mL). To this was added camphorsulfonic acid (2 mg, 0.008 mmol). This mixture was stirred at room temperature for 45 min, after which time it was then washed through a plug of basic alumina with ether and concentrated in vacuo. The residue was dissolved in a tetrahydrofuran solution of tetra-*n*-butylammonium fluoride (TBAF) (1.5 mL, 1.0 M in TBAF, 1.5 mmol). The solution was refluxed for 8 h and then saturated sodium bicarbonate solution (5 mL) was added. The resulting two-phase mixture was extracted (3 × 5 mL) with ether. The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo afford a yellow oil. This was chromatographed (6:4 hexanes/ether) to yield diol **42** (9.0 mg, 90%) as a colorless oil.

**Method B.** A solution of bis-acetonide **45** (265 mg, 0.548 mmol, method B) in ether (15 mL) was treated with lithium aluminum hydride (LAH) (ca. 20 mg, 0.53 mmol). The resulting slurry was stirred at room temperature for 2 h. Excess LAH was then quenched by dropwise addition of saturated sodium/potassium tartrate solution (10 mL) and the mixture was stirred until colorless (ca. 30 min). It was then extracted (3 × 15 mL) with ether, and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered, concentrated in vacuo, and chromatographed as in method A to afford diol **42** (244 mg, 91%) as a colorless oil: $^1$H NMR ($CDCl_3$, 250 MHz) δ 3.67 (dd, $J$ = 10.7, 4.0 Hz, 1 H), 3.67–3.50 (m 4 H), 3.33 (dd, $J$ = 9.6, 1.9 Hz, 1 H), 3.18 (dd, $J$ = 7.6, 2.3 Hz, 1 H), 1.94–1.73 (m, 4 H), 1.70–1.40 (m, 5 H), 1.36 (s, 3 H), 1.35 (s, 3 H), 1.34 (s, 3 H), 1.31 (s, 3 H), 1.04–0.98 (m, 6 H), 0.91 (d, $J$ = 6.8 Hz, 3 H), 0.84 (d, $J$ = 6.8 Hz, 3 H), 0.79 (d, $J$ = 6.6 Hz, 3 H), 0.78 (d, $J$ = 7.0 Hz, 3 H); IR ($CDCl_3$) 3602, 3460, 2958, 2622, 2865, 1457, 1377, 1223, 1196, 1150, 1100, 1010, 980 cm$^{-1}$; MS (CI, $NH_4^+$) 473 ($M^+$ + 1, 2.1), 457 (4.5), 415 (6.5), 357 (372), 339 (30.9), 321 (14.3), 287 (8.8), 239 (14.4), 211 (9.3), 181 (5.7), 157 (7.0), 99 (11.8); HRMS (CI, $NH_4^+$) mass calcd for $C_{27}H_{53}O_6$ ($M^+$ + H) 473.3842, found 473.3854.

**[4*S*-[4α[1*R**[4*R**(*S**),5*S**,6*R**],3*S**],5β,6β(1*R**,2*S**)]]-6-[3-[6-(2-Hydroxy-1-methylbutyl)-2,2,5-trimethyl-1,3-dioxan-4-yl]-1-methylbutyl]-α,2,2,5-tetramethyl-1,3-dioxane-4-acetaldehyde (Aldehyde 43).** A solution of diol **42** (86.4 mg, 0.177 mmol, method B) in benzene (2 mL) was treated with tris(triphenylphosphine)ruthenium(II) chloride (186.7 mg, 0.195 mmol). The dark brown mixture was stirred at room temperature for 18 h. It was then diluted with ether (5 mL) and washed through a short, packed alumina (ca. 5 g) column. The resulting pale green solution was then concentrated in vacuo and chromatographed (4:1 hexanes/ether) to furnish aldehyde **43** (49 mg, 57%) as a colorless oil: $^1$H NMR ($CDCl_3$, 490 MHz) δ 9.73 (d, 1 H, $J$ = 2.4 Hz), 3.94 (dd, $J$ = 9.1, 2.1 Hz, 1 H), 3.76 (dd, $J$ = 10.8, 4.3 Hz, 1 H), 3.57 (m, 1 H), 3.35 (dd, $J$ = 9.6, 1.0 Hz, 1 H), 3.17 (dd, $J$ = 7.5, 2.5 Hz, 1 H), 2.69–2.63 (m, 1 H), 2.58 (bs, 1 H), 1.90–1.78 (m, 2 H), 1.67–1.54 (m, 2 H), 1.48–1.43 (m, 1 H), 1.39 (s, 3 H), 1.34 (s, 3 H), 1.34 (s, 3 H), 1.30 (s, 3 H), 1.13 (d, $J$ = 6.9 Hz, 3 H), 1.00 (t, $J$ = 7.3 Hz, 3 H), 0.91 (d, $J$ = 6.8 Hz, 3 H), 0.85 (d, $J$ = 6.7 Hz, 3 H), 0.84 (d, $J$ = 6.8 Hz, 3 H), 0.78 (d, $J$ = 7.1 Hz, 3 H), 0.76 (d, $J$ = 7.1 Hz, 3 H); IR ($CDCl_3$) 3600, 3460, 2958, 2920, 2865, 1717, 1456, 1376, 1222, 1197, 1146, 1105, 1010, 970 cm$^{-1}$.

**[4*S*-[4α[1*R**[4*R**(*S**),5*S**,6*R**],3*S**],5β,6β(1*R**,2*S**)]]-6-[3-[6-(2-Hydroxy-1-methylbutyl)-2,2,5-trimethyl-1,3-dioxan-4-yl]-1-methylbutyl]-α,2,2,5-tetramethyl-1,3-dioxane-4-acetic Acid (Seco Acid 44).** Aldehyde **43** (48 mg, 0.099 mmol) was dissolved in *tert*-butyl alcohol (1 mL) and water (1 mL). To this solution was added 2-methyl-2-butene (330 mg, 4.7 mmol), sodium dihydrogen phosphate (100 mg, 0.833 mmol), and sodium chlorite (100 mg of 80%, 0.885 mmol). The biphasic mixture was stirred at room temperature for 1 h. It was then extracted (4 × 15 mL) with ether. The combine organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to provide the crude seco acid **44** (51 mg, quantitative). This was characterized as its methyl ester prepared by treatment of an ethereal solution of the seco acid with excess diazomethane solution in ether followed by concentration in vacuo. $^1$H NMR ($CDCl_3$, 250 MHz) δ 3.82 (dd, $J$ = 9.2, 2.1 Hz, 1 H), 3.77 (dd, $J$ = 11.7, 5.4 Hz, 1 H), 3.69 (s, 3 H), 3.63–3.52 (m, 1 H), 3.35 (dd, $J$ = 9.6, 1.6 Hz, 1 H), 3.18 (dd, $J$ = 7.7, 2.9 Hz, 1 H), 2.71–2.58 (m 2 H), 1.99–1.76 (m, 3 H), 1.71–1.41 (m, 4 H), 1.39 (s, 3 H), 1.36 (s, 3 H), 1.34 (s, 3 H), 1.30 (s, 3 H), 1.21 (d, 3 H, $J$ = 7.1 Hz), 1.01 (d, 3 H, $J$ = 8.3 Hz), 0.91 (d, 3 H, $J$ = 6.7 Hz), 0.84 (d, $J$ = 6.8 Hz, 3 H), 0.83 (d, $J$ = 6.9 Hz, 3 H), 0.79 (d, $J$ = 7.5 Hz, 3 H), 0.75 (d, $J$ = 6.7 Hz, 3 H); IR ($CDCl_3$) 3450, 2960, 2920, 2863, 1725, 1451, 1376, 1223, 1195, 1165, 1100, 1050, 1008, 980 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{28}H_{53}O_6$ ($M^+$ + H) 501.3791, found 501.3809.

**(9*S*)-9-Deoxo-6,11,12-trideoxy-3,5-*O*-(1-methylethylidene)-9,11-[oxy(1-methylethylidene)oxy]erythronolide A [(9*S*)-Dihydro-6-deoxyerythronolide B, Bis(acetonide) (45)]. Method A.** A solution of seco acid bis-acetonide **44** (8.4 mg, 0.017 mmol) and triethylamine (38 mg, 0.37 mmol) in THF (0.5 mL) was treated with 2,4,6-trichlorobenzoyl chloride (4.7 mg,

0.019 mmol). The mixture was stirred at room temperature for 4 h. It was then filtered and loaded into a 1-mL gas-tight syringe. The mixture was then added by syringe pump over 1.5 h to a refluxing solution of 4-(dimethylamino)pyridine (40 mg, 0.33 mmol) in freshly distilled xylenes (1.5 mL). After the addition was complete, the mixture was refluxed an additional 12 h. It was then concentrated in vacuo and chromatographed (9:1 hexanes/ether) to afford bis-acetonide **45** (1.4 mg, 17%) as a colorless oil.

**Method B.** A solution of (9*S*)-dihydro-6-deoxyerythronolide B **38** (296 mg, 0.733 mmol) in 2,2-dimethoxypropane (5 mL) was treated with *p*-toluenesulfonic acid monohydrate (5 mg, 0.026 mmole). The mixture was stirred at room temperature for 24 h. It was then diluted with ether (ca. 10 mL) and washed through a plug of basic alumina. The filtrate was concentrated in vacuo and chromatographed (9:1 hexanes/ether) to furnish bis-acetonide **45** (287 mg, 81%) as a colorless oil: $^1$H NMR ($CDCl_3$, 490 MHz) $\delta$ 5.35–5.32 (m, 1 H), 3.91 (dd, $J$ = 6.5, 1.2 Hz, 1 H), 3.75 (dd, $J$ = 10.6, 0.9 Hz, 1 H), 3.58 (d, $J$ = 9.2 Hz, 1 H), 3.20 (d, $J$ = 10.8 Hz, 1 H), 2.76–2.71 (dq, $J$ = 10.7, 6.6 Hz, 1 H), 2.20–2.15 (m, 1 H), 2.09–2.05 (m, 1 H), 1.84 (bq, $J$ = 6.7 Hz, 1 H), 1.74–1.58 (m, 2 H), 1.52–1.47 (m, 1 H), 1.46 (s, 3 H), 1.45 (s, 3 H), 1.42 (s, 3 H), 1.41 (s, 3 H), 1.16 (d, $J$ = 6.6 Hz, 3 H), 1.10 (d, $J$ = 6.6 Hz, 3 H), 1.04 (d, $J$ = 6.6 Hz, 3 H), 0.99 (d, $J$ = 6.8 Hz, 3 H), 0.89 (d, $J$ = 7.3 Hz, 3 H), 0.88 (t, $J$ = 7.3 Hz, 3 H); IR ($CDCl_3$) 2958, 2920, 2863, 1710, 1450, 1378, 1239, 1194, 1094, 1008 cm$^{-1}$; HRMS (CI, $NH_4^+$) mass calcd for $C_{27}H_{49}O_6$ ($M^+$ + H), 469.3531, found 469.3536; $[\alpha]_D$ = +25.6° (*c* 1.61, $CHCl_3$).

**(9*S*)-6,12-Dideoxy-9-deoxo-9-hydroxy-3,5-*O*-(1-methylethylidene)erythronolide A [(9*S*)-Dihydro-6-deoxyerythronolide B 3,5-Acetonide (46)].** A solution of (24 mg, 0.060 mmol, method A) and 2,2-dimethoxypropane (7.2 mg, 0.069 mmol) in dichloromethane (0.15 mL) was treated with camphorsulfonic acid (1 mg, 0.004 mmole). The mixture was stirred at room temperature for 4 h. Saturated sodium bicarbonate solution (2 mL) was then added and the mixture extracted (3 × 5 mL) with ether. The combine organic extracts were dried over anhydrous magnesium sulfate, filtered, concentrated in vacuo, and chromatographed (4:1 hexanes/ether) to afford **46** (19.8 mg, 74%) as a colorless oil: $^1$H NMR ($CDCl_3$, 490 MHz) $\delta$ 5.26–5.23 (m, 1 H), 3.88 (d, $J$ = 6.2 Hz, 1 H), 3.73 (d, $J$ = 10.6 Hz, 1 H), 3.69–3.66 (m, 1 H), 3.59 (d, $J$ = 3.8 Hz, 1 H), 3.33 (d, $J$ = 8.6 Hz, 1 H), 3.10–3.06 (m, 1 H), 2.80–2.74 (m, 1 H), 2.19–2.15 (m, 1 H), 2.00–1.98 (m, 1 H), 1.82–1.59 (m, 2 H), 1.55–1.38 (m, 2 H), 1.47 (s, 6 H), 1.18 (d, $J$ = 6.5 Hz, 3 H), 1.10 (d, $J$ = 7.3 Hz, 3 H), 1.08 (d, $J$ = 7.2 Hz, 3 H), 1.01 (d, $J$ = 6.6 Hz, 3 H), 0.97 (d, $J$ = 7.2 Hz, 3 H), 0.92 (t, $J$ = 7.3 Hz, 3 H), 0.84 (d, $J$ = 7.1 Hz, 3 H); IR ($CDCl_3$) 3480, 2975, 2936, 2880, 1700, 1458, 1383, 1198, 1100, 923, 914 cm$^{-1}$; $[\alpha]_D$ = +26.4° (*c* 0.81, $CHCl_3$); HRMS (CI $NH_4^+$) mass calcd for $C_{24}H_{45}O_6$ ($M^+$ + H) 429.3216, found 429.3323.

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**Registry No.** 1, 15797-36-1; 2, 123992-29-0; 3, 72486-93-2; (±)-4, 123992-03-0; 4 (alcohol derivative), 123992-04-1; (±)-*cis*-5, 123992-05-2; (±)-*trans*-5, 123992-06-3; 6, 124095-53-0; 7, 123992-07-4; 8, 123992-08-5; 9, 123992-09-6; 10, 123992-10-9; 11, 123992-11-0; 12, 123992-12-1; 13, 123992-13-2; 14, 123992-14-3; 15, 123992-15-4; 16, 123992-16-5; 17, 123992-17-6; 18, 123992-18-7; 19, 124095-54-1; 20, 123992-19-8; 22 (anomer 1), 123992-41-6; 22 (anomer 2), 124095-58-5; 23, 123992-40-5; 25 (anomer 1), 124095-56-3; 25 (anomer 2), 124095-57-4; 26, 123992-20-1; 27, 123992-21-2; 28, 123992-22-3; 29, 123992-23-4; 30, 123992-24-5; 31, 124095-55-2; 34, 123992-25-6; 35, 123992-26-7; 36, 123992-27-8; 37, 123992-28-9; 38, 28316-66-7; 39, 123992-32-5; 40, 123992-30-3; 41, 123992-33-6; 41 (perdebenzylated derivative), 123992-34-7; 41 (perdebenzylated ketalized derivative), 123992-35-8; 42, 123992-36-9; 43, 123992-37-0; 44, 123992-38-1; 44 (methyl ester), 123992-39-2; 45, 123992-31-4; 46, 77480-16-1; formaldehyde, 50-00-0; 1,3-propanedithiol, 109-80-8; benzyl trichloroacetimidate, 81927-55-1; thiophenol, 108-98-5.

**Supplementary Material Available:** Results of the single-crystal X-ray analysis of compound **38** including positional parameters, intramolecular distances, bond angles, torsional angles, and $U$ values and NMR spectra (250 or 490 MHz; $CDCl_3$) of all intermediates (38 pages). Ordering information is given on any current masthead page.