Total Synthesis of the Sesquiterpenoid Polyols (±)-Euonyminol and (±)-3,4-Dideoxymaytol, Core Constituents of Esters of the *Celastraceae*

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Abstract: A general synthetic route to the set of polyhydroxylated agarofurans that comprise the core structures of esters present in plants of the *Celastraceae* family has been devised. The pathway is exemplified with total syntheses of (±)-3,4-dideoxymaytol (**3**), the nucleus of ever-1 (**6**), and (±)-euonyminol (**4**), the sesquiterpenoid core of several cathedulins including K-19 (**5**). A focal intermediate **19**, prepared by Diels−Alder addition of **11** to **12**, was identified that permitted stereoselective introduction of an isopropenyl substituent via chelation-controlled, conjugate Grignard addition to give **34**. Triflic acid-catalyzed cyclization of **39** afforded the agarofuran skeleton of **3**, and subsequent epimerization of the hydroxyl substituent at C1 via a reversible aldol sequence gave **41**. Sequential reductions using hydride and catalytic hydrogenation yielded **3** and 4-*epi*-3,4-dideoxymaytol (**51**). The route from **19** was extended toward **4** via **56**, prepared by directed epoxidation of **34**. A trifuoroacetic acid-catalyzed "epoxide-cascade" cyclization of **56** furnished **61**, which was advanced to γ-lactone **63** prior to epimerization at C1. Introduction of the 8β hydroxyl function of **69** was followed by an α-ketol transposition to give **71** which was reduced and protected as polysilyl ether **80**. Osmylation and replacement of protecting groups produced euonyminol octaacetate **78** which underwent methanolysis to (±)-**4**.

Plants of the *Celastraceae* family are a rich source of hydroxylated sesquiterpene esters based on the dihydroagarofuran skeleton (**1**). These compounds have attracted a great deal of interest on account of their cytotoxic,[1] antitumor,[2] immunosuppressive,[3] and insect antifeedant activities.[4] The most commonly encountered derivatives of **1** among Celastraceous sesquiterpenes are esters of maytol (**2**),[5] 3,4-dideoxymaytol (**3**),[6] and euonyminol (**4**).[7] The latter is the core structure of several of the cathedulins[8] including K-19 (**5**).[9] These substances, isolated from leaves and twigs of the shrub *Catha edulis* (Forsk), are present in the drug "khat" used extensively in east Africa for its appetite-suppressant and euphoriant properties.[10] 3,4-Dideoxymaytol (**3**) is the sesquiterpene nucleus of ever-1 (**6**) and several congeners present in the fruits of *Euonymus verrucosus*[11] as well as maymyrsine (**7**).[6]

Extensive structural studies of the cathedulins by Crombie's group[12] and others[13] that included chemical degradation as well as X-ray crystallographic analysis have contributed to the elucidation of over 35 structures based on **2**, **3**, and **4.** In spite of these comprehensive efforts, however, no synthetic routes to these complex sesquiterpenoids have been reported. Herein, we describe total syntheses of (±)-3,4-dideoxymaytol (**3**) and (±)-euonyminol (**4**) using a strategy based on a "cascade cyclization" to establish the dihydroagarofuran framework of these structures.[14]

Our goal from the outset was to develop a general plan for synthesis of *all* hydroxylated agarofurans of the *Celastraceae*. 3,4-Dideoxymaytol (**3**) containing five hydroxyl groups and euonyminol (**4**) with nine represent the two extreme degrees of hydroxylation within this class. Structures at intermediate hydroxylation levels such as **2** would, in principle, be accessible through minor modification of the pathways leading to **3** or **4.** An efficient strategy for achieving this goal should identify a key substance that represents the latest possible point from which routes to **3**, **4**, and their congeners could diverge. Analysis of the functional group arrays present in these sesquiterpene polyols led to the selection of the decalone **8** as the pivotal intermediate

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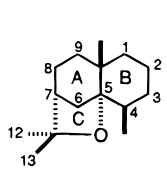

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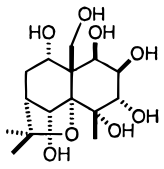
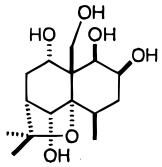
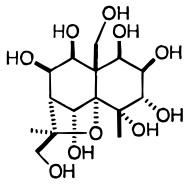


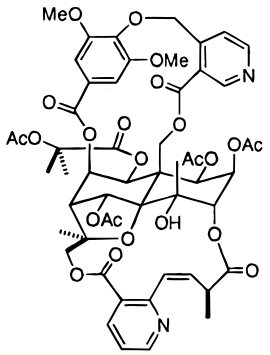
Maytol (**2**)



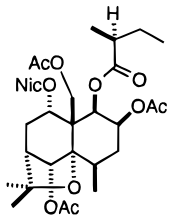
3,4-Dideoxymaytol (**3**)



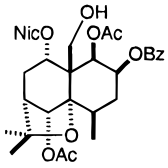
Euonyminol (**4**)



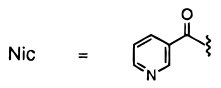
Cathedulin K-19 (**5**)

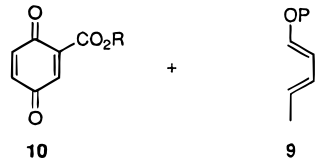


Ever-1 (**6**)

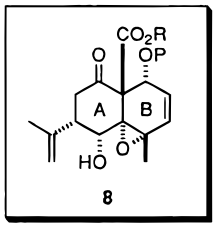


Maymyrsine (**7**)





10 **9**



8

3 **4**

for this purpose. An avenue to the bicyclic framework of **8** was envisioned through *endo* Diels−Alder cycloaddition of diene **9** to benzoquinone **10**. Subsequent elevation of the oxidation levels of rings A and B, followed by attachment of an isopropenyl substituent at C7, would lead to **8**.

The synthesis of **8** began from 2-pentenal, which upon exposure to *tert*-butyldimethylsilyl triflate, gave all four geometrical isomers of 1-*tert*-butyldimethylsilyloxypenta-1,3-diene (**11**).[15] Although the (*E*,*E*) isomer constituted only 25−30% of the total, addition of the diene mixture to 2-carbomethoxy-1,4-benzoquinone (**12**), prepared *in situ* by oxidation of methyl gentisate (**13**), afforded a single Diels−Alder adduct **14**. Assignment of *endo* configuration to this substance was made from the H_4-H_5 coupling constant ($J = 4.6$ Hz) which supported a *cis* (axial−equatorial) relationship of these two protons. In contrast, *trans* isomer **15**, which was obtained in quantitative yield upon passage of **14** through neutral alumina, exhibits a coupling constant ($J = 9.9$ Hz) consistent with an axial−axial orientation of H_4-H_5. The clean *endo* stereochemistry seen in the reaction of **11** with **12** is in accord with results reported by Kraus on a related Diels−Alder cycloaddition[16] and presumably reflects the rapid interconversion of diene isomers **11** under the reaction conditions. The process is all the more remarkable for its taking place at room temperature.

With a route to **14** secured, efforts were next directed toward introduction of the epoxide into ring B. For this transformation, it was necessary to first install a $\Delta^{4,5}$ double bond. Bromination of **14** with *N*-bromosuccinimide unexpectedly gave the rearranged allylic bromide **16** which, due to its instability, was immediately treated with triethylamine to yield the desired homoannular diene **17**. In order to circumvent the likelihood of a mixture of regio- and stereoisomeric epoxides arising from the reaction of **17** with peracid, it was decided to use an allylic hydroxyl function to direct epoxidation toward the α face of the $\Delta^{4,5}$ olefin. An energy minimization study of **17** revealed that ring A in this structure prefers a boat conformation, and that in this conformation the β face of the C6 ketone is the more exposed to hydride attack. Furthermore, selectivity should be enhanced by reduction in the presence of a Lewis acid which would presumably complex to the more open and basic C6 ketone. In the event, Luche reduction[17] of **17** was found to give a near quantitative yield of an alcohol identified as **18**. Epoxidation of this allylic alcohol with *m*-chloroperbenzoic acid furnished, as expected, a single epoxide **19**.[18]

Attention was now turned to construction of the tetrahydrofuran portion of **3** and **4**. Before attempting this, however, it seemed prudent to test the reactivity of **19** for its sensitivity toward reagents that could impact the sensitive allylic epoxide moiety. Ultimately, these efforts not only provided reassurance that our hopes with **19** would be fulfilled but also suggested an innovative means for inserting oxygen functionality into ring B. Thus, exposure of **19** to acetic acid at 60 °C gave **20**, whereas trifluoroacetic acid gave a 1:2 mixture of **21** and the triol **22** from which the silyl ether had been removed. In another experiment with **19**, *p*-toluenesulfonic acid in acetone gave a 1:2 mixture of **23** and γ-lactone **24**. The latter was the sole product when **19** was treated with pyridinium *p*-toluenesulfonate. The recurring observation from these experiments, that opening of the allylic epoxide of **19** occurs predominantly in S_N2' fashion

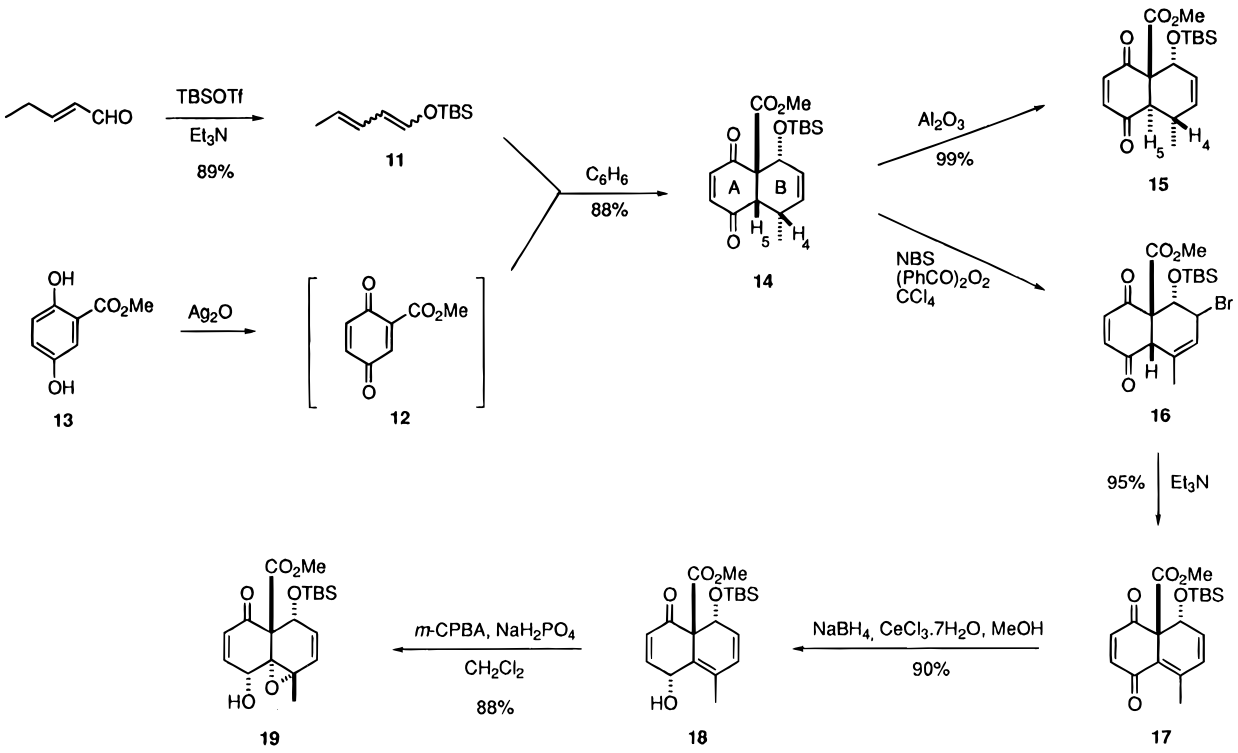
(15) Mander, L. N.; Sethi, S. P. *Tetrahedron Lett.* **1984**, *25*, 5953.

(16) Kraus, G. A.; Taschner, M. J. *J. Org. Chem.* **1980**, *45*, 1175.

(17) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.

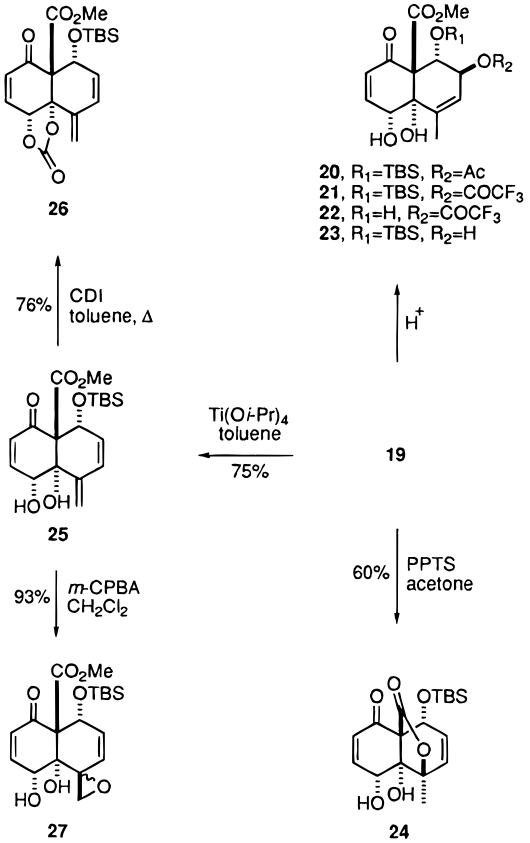
(18) (a) Henbest, H. B.; Wilson, R. A. *J. Chem. Soc.* **1957**, 1958. (b) Berti, G. *Top. Stereochem.* **1973**, 9, 93. (c) Hirayama, M.; Gamoh, K.; Ikeyama, N. *Tetrahedron Lett.* **1982**, *23*, 4725.

Scheme 1



with entry of the nucleophile from the β face (i.e., opposite epoxide bond cleavage), augured well for the future elaboration of ring B of **3** and **4**.

Surprisingly, the behavior of **19** with Lewis acids followed a different course. With titanium tetraisopropoxide, **19** gave exclusively the product **25** of epoxide elimination,[19] in which the *cis*-1,2-diol relationship was confirmed by formation of cyclic carbonate **26** with carbonyldiimidazole. The dienol **25** underwent quantitative epoxidation to **27** with *m*-chloroperbenzoic acid.



The foregoing results indicated that both Brönsted and Lewis acids were to be avoided if the allylic epoxide of **19** was to survive during functionalization of ring A. Our hope was that a cuprate species would selectively target the rear face of enone **19**, leading to a 7α isopropenyl substituent. In fact, the reaction of **19** with the higher order isopropenylcuprate **28** in the presence of trimethylsilyl chloride[20] afforded a bis TMS ether, later found to be **29**, as a single epimer. The H_6-H_7 proton coupling constant ($J = 6.2$ Hz) in this substance as well as the hydroxy ketone **30** derived by treatment of **29** with the triethylamine−hydrofluoric acid complex[21] resulted in an inconclusive determination of configuration of the isopropenyl substituent, and the synthetic sequence was therefore continued from **30**. In analogy with **19**, treatment of **30** with titanium tetraisopropoxide in toluene led via epoxide elimination to **31**, in which the $H_7-H_{8\beta}$ coupling ($J = 11.4$ Hz) strongly suggested a *trans* diaxial relationship of these protons. That the isopropenyl substituent had indeed entered **19** from the wrong face was confirmed by epoxidation of **29** which, after removal of the two trimethylsilyl groups, produced **32**. The configuration of **32** was revealed when it was found to undergo conversion to the crystalline ortho ester **33** in the presence of an acid catalyst. X-ray crystallographic analysis of **33** established the stereostructure shown in Figure 1.

Although the β orientation of the isopropenyl substituent in **29** would appear to confound established principles of stereoelectronic control in 1,4-addition to enones,[22] a simple explanation for this result can be offered in the form of prior complexation of cuprate with the 6α hydroxyl group. This

(19) (a) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557. (b) Masaki, Y.; Hashimoto, K.; Serizawa, Y.; Koji, K. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 3476.

(20) For mechanistic speculation regarding variations in stereoselectivity in organocopper additions to carbocyclic enones in the presence of trimethylsilyl chloride, see: (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015. (b) Horiguchi, Y.; Komatu, M.; Kuwajima, I. *Tetrahedron Lett.* **1989**, *30*, 7087. (c) Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1990**, *31*, 1393. (d) Corey, E. J.; Boaz, N. W. *Tetrahedron* **1989**, *45*, 545.

(21) Hunig, S.; Wehner, G. *Synthesis* **1975**, 181.

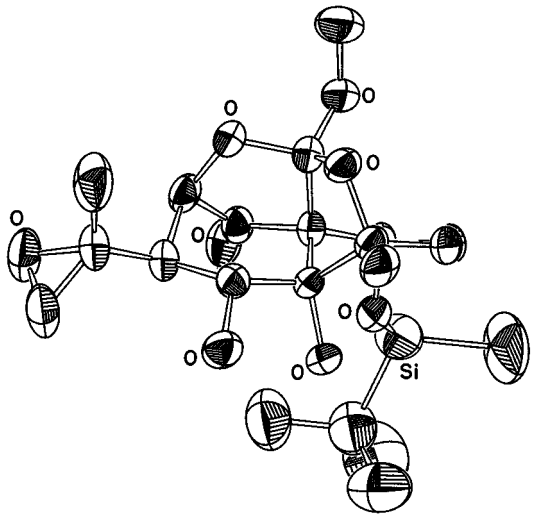
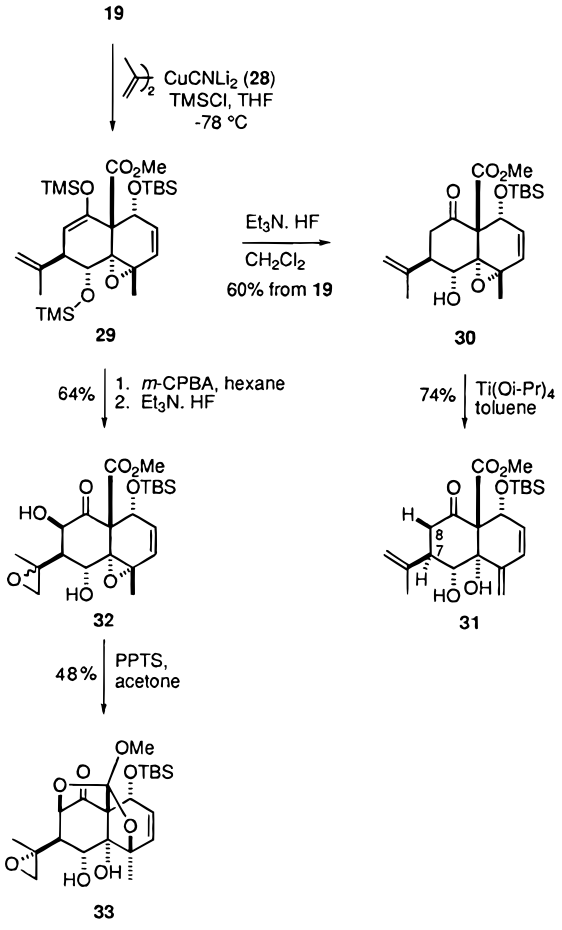


Figure 1. X-ray crystal structure of **33**.



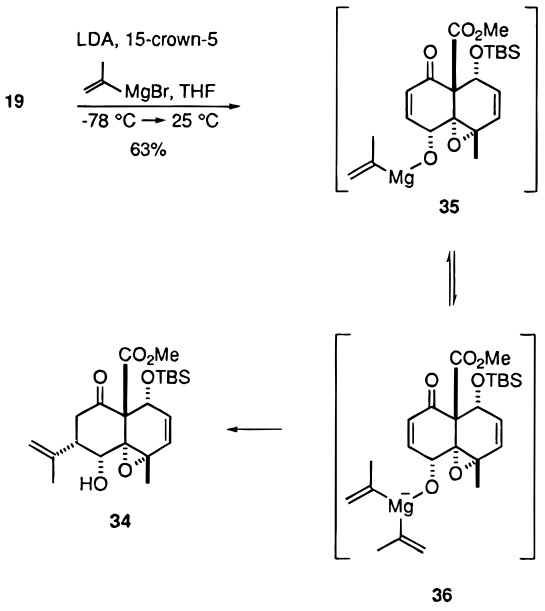
would effectively block the α face of the enone with a bulky organometallic species that is rendered incapable of alkyl group transfer through its coordination to oxygen. The appropriate counter would, of course, be a conjugate addition in which *the isopropenyl group is guided into place by the* 6α hydroxyl substituent. For this tactic to be successful, a complexed species more reactive than a cuprate was required. Liotta and Maryanoff have shown that addition of Grignard reagents to α,β-unsaturated ketones can be strongly directed by a γ alkoxy substituent,[23] and after considerable experimentation it was found that **34** was obtained in good yield when **19** was first treated with lithium diisopropylamide, then with 15-crown-5, and finally with

(22) (a) Toromanoff, E. *Bull. Soc. Chim. Fr.* **1962**, 708. (b) Deslongchamps, P. In *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983; pp 221−231.

Table 1. Conjugate Addition of Isopropenylmagnesium Bromide to **19**

Base	Additive (eq)	Eq of 	Yield of **34** (%)
LDA	HMPA (6)	1.1	9
LDA	DMPU (6)	2.2	21
KHMDS	none	1.1	17
n-BuLi	DMPU (10)	1.0	0
LDA	15-crown-5 (1.2)	1.1	63

isopropenylmagnesium bromide. This sequence ensures that a Schlenk equilibrium is established in which the binary complex **35** is forced toward the more reactive ternary ate complex **36**. The latter is believed to be the species responsible for stereoselective intramolecular transfer of the isopropenyl group to the β carbon. Additives such as HMPA were less effective in promoting the desired conjugate addition (see Table 1). The epimeric relationship of **34** with **30** was clearly apparent from comparison of their ^{1}H NMR spectra, confirming that we had indeed reached the point at which paths toward **3** and **4** could now diverge.

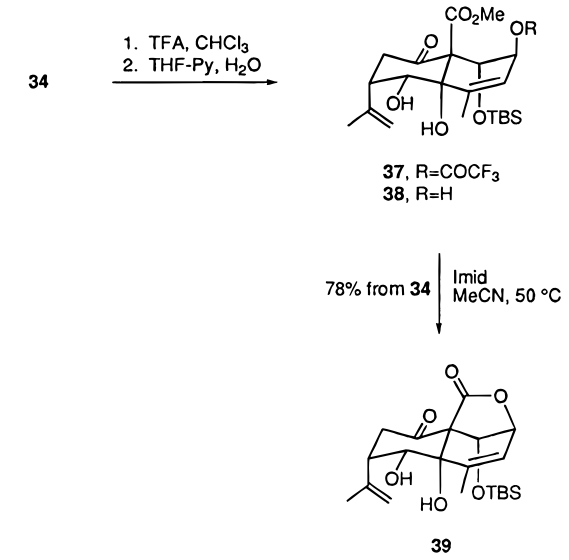


Synthesis of (±)-3,4-Dideoxymaytol (3). With **34** in hand, we were now able to exploit the chemistry developed with **19**, specifically the conversion that had led to **21**. Treatment of **34** with trifluoroacetic acid produced the hydroxy trifluoracetate **37** resulting from the expected *anti* S_N2' opening of the allylic epoxide. Mild hydrolysis of the trifluoroacetate gave hydroxy ester **38** which underwent facile lactonization to **39** when catalyzed by imidazole.

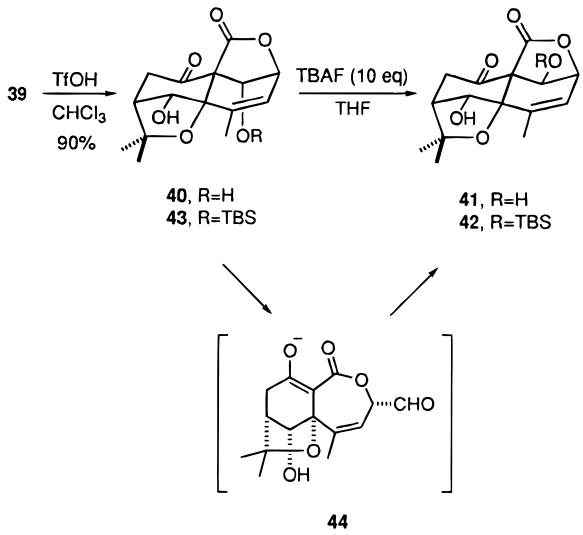
Ample literature exists to suggest that **39** should undergo cyclization to the tricyclic skeleton of **3** with ease.[24] In practice, no less than 2 equiv of trifluoromethanesulfonic acid in chloroform would suffice for the conversion of **39** to **40**; neither trifluoroacetic acid nor other sulfonic acids were effective for this purpose. The yield of this cyclization, however, was a welcome surprise, and as a bonus it was discovered that the silyl ether had been removed from **40** in a process that

(23) (a) Solomon, M.; Jamison, C. L.; McCormick, M.; Liotta, D. C.; Cherry, D. A.; Mills, J. E.; Shah, R. D.; Rodgers, J. D.; Maryanoff, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 3702. (b) Swiss, K. A.; Liotta, D. C.; Maryanoff, C. A. *J. Am. Chem Soc.* **1990**, *112*, 9393. (c) Swiss, K. A.; Hinkley, W.; Maryanoff, C. A.; Liotta, D. C. *Synthesis* **1992**, 127.

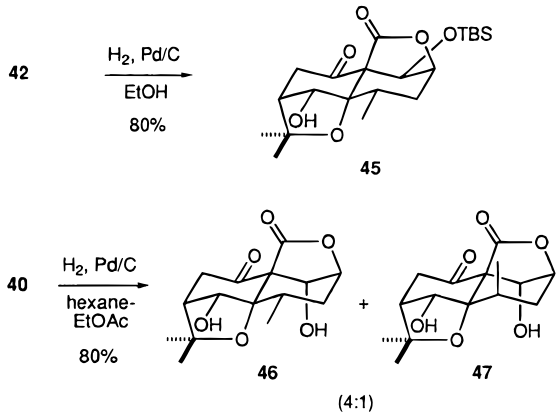
(24) Barrett, H. C.; Büchi, G. *J. Am. Chem. Soc.* **1967**, *89*, 5665.



presumably consumes one of the 2 equiv of triflic acid. The newly liberated α hydroxyl group at C1 now gave us an opportunity to test the stratagem we had reserved for its inversion—retroaldol fission followed by recondensation that would allow the C1 alcohol to equilibrate to its more stable β configuration. Several organic and inorganic bases left **40** unchanged, but tetra-*n*-butylammonium fluoride was found to effect clean conversion of **40** to its C1 epimer **41**. Optimization of this reaction, which typically gave a **41**:**40** ratio of 13−18:1, required that it be carried out in dilute solution with a large excess of the fluoride reagent. That inversion of hydroxyl configuration at C1 was the sole event in this reaction was demonstrated by conversion of **41** to its silyl ether **42**, shown to be epimeric with the minor product **43** formed in the cyclization of **39**. Steric strain due to the axial orientation of the C1 alcohol in the boat-shaped B ring of **40** is undoubtedly the principal driving force for inversion. The lactone carbonyl contributes little toward stabilization of the developing enolate **44** since its π orbital is badly aligned with respect to the fragmenting ring bond, but the bridging lactone of **40** plays a crucial role by forcing the forward aldol toward **41**. Thus, inversion does not take place if the constraining lactone of **40** is opened, as in **38**, and only a complex mixture of products is obtained.



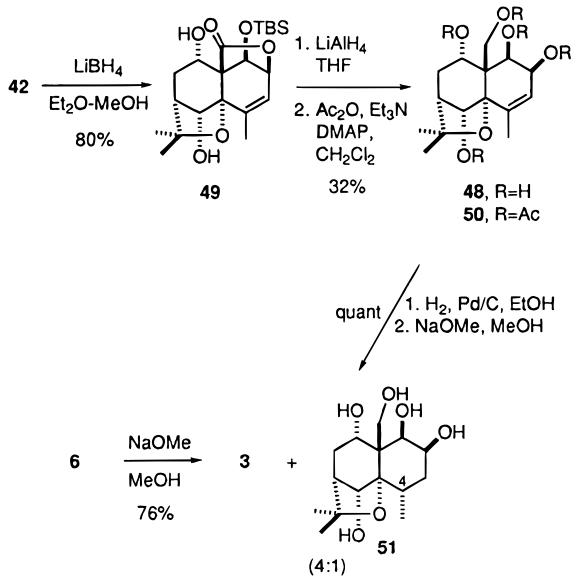
In principle, **41** is only two steps—hydrogenation of the double bond and hydride reduction of ketone and lactone carbonyls—from 3,4-dideoxymaytol (**3**). In fact, neither of these operations was straightforward. Hydrogenation of **42** in ethanol did lead to a single dihydro compound, but a nuclear Overhauser experiment in which irradiation of H_6 caused enhancement of the signal due to H_4 revealed that this product was the undesired stereoisomer **45** bearing a 4α methyl substituent. On the supposition that the C1 hydroxyl of **40** could be used to direct *syn* hydrogenation to the α face of the $\Delta^{3,4}$ bond in an aprotic solvent,[25] this olefin was reacted with hydrogen in a mixture of hexane and ethyl acetate as solvent. Again, the major product **46** resulted from attack at the β face, although a minor quantity of the desired stereoisomer **47** was also formed.



A possible solution to the unfavorable outcome from hydrogenation of **42** appeared to lie in reversing the sequence of the final steps to **3** in order to position more steric bulk above the double bond. It was expected that reaction of **42** with lithium aluminum hydride would reduce both the lactone and the C9 ketone, the latter from the β face since α approach is obstructed by the *endo* methyl substituent of the geminal pair. However, even this seemingly trivial task proved to be troublesome. Reduction of **41** with lithium aluminum hydride was found to yield none of the expected pentaol **48**. Instead, only uncharacterized products devoid of the angular carbon substituent were obtained. These are believed to arise by preferential reduction of the lactone rather than the ketone of **41**, which is followed by retroaldol fission of either the derived hemiacetal or primary alcohol. Resistance of the C9 ketone toward reduction by hydride is attributed to its facile formation of an enolate, a property that is consistent with other observations on **41** and which was to have important consequences for our later approach to euonyminol. Fortunately, an easy exit from this impasse was available by stepwise reduction of **42**, first with lithium borohydride in ether containing an equiv of methanol to yield hydroxy lactone **49** and then with lithium aluminum hydride to give the pentaol **48**. The latter was isolated and characterized as its crystalline pentaacetate **50**. With the upper face of ring B now effectively blockaded by acetoxy substituents, hydrogenation of **50** took place predominantly from below the double bond to give a 4:1 mixture of saturated C4 epimers. Since these were inseparable, the mixture was subjected to methanolysis, resulting after chromatographic purification in 3,4-dideoxymaytol (**3**) and a small amount of its unnatural 4-*epi* stereoisomer **51**. The identity of synthesized (±)-**3** was confirmed by comparison with material obtained by methanolysis of a sample of natural ever-1 (**6**).

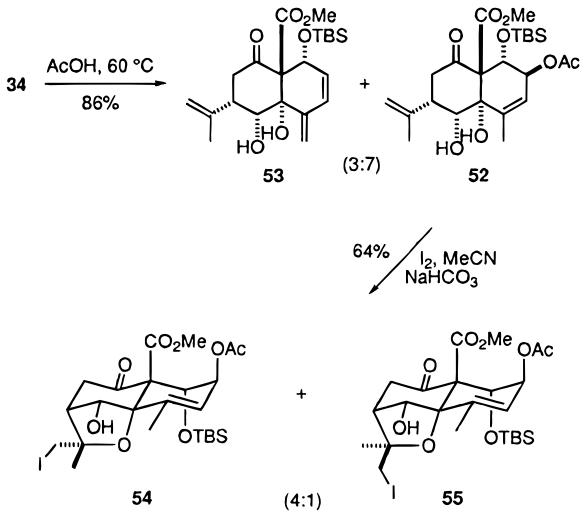
Synthesis of (±)-Euonyminol (4). With nine hydroxyl groups and all 11 ring carbons of its structure stereogenic, euonyminol (**4**) presents a particularly demanding target for synthesis. As with **3**, our intention was to use the bicyclic structure **8** as a

(25) (a) Thompson, H. W. *J. Org. Chem.* **1971**, *36*, 2577. (b) Thompson, H. W.; McPherson, E.; Lences, B. L. *J. Org. Chem.* **1976**, *41*, 2903.



template upon which serial oxidation of rings A and B would be imposed. The greater complexity of **4** as compared to **3**, particularly the additional hydroxyl functions at C3, 4, and 13 and the reversed hydroxyl configuration at C9, clearly required a judicious selection of the sequence of operations by which **8** would be carried forward. After the successful result with **39**, it was decided to proceed directly toward the tricyclic nucleus of **4** by employing a variation of the cyclization used to construct **40**.

Our initial efforts focused on intramolecular iodoetherification[26] of **52**, obtained from **34** with hot acetic acid along lines used for the preparation of **37**. In contrast to the reaction of **34** with trifluoroacetic acid, however, **52** was accompanied by a substantial quantity of **53**, the C7 epimer of **31**. Treatment of **52** with iodine in acetonitrile afforded an inseparable mixture of primary iodides **54** and **55** in which the major isomer (**54**) was subsequently found to have the undesired configuration at the new quaternary center.[27]



An alternative tactic for constructing the tetrahydrofuran ring of **4** which appeared to offer a better prospect for stereocontrol

(26) Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol 3, Chapter 6.

(27) Attempts to effect substitution of the iodo group of **54** using potassium superoxide or cesium acetate afforded a crystalline cyclobutane resulting from initial formation of the ketone enolate followed by intramolecular displacement of iodide. The structure of the cyclobutane was confirmed by X-ray crystallographic analysis, proving that the major product from **52** possessed an *endo* iodomethyl substituent.

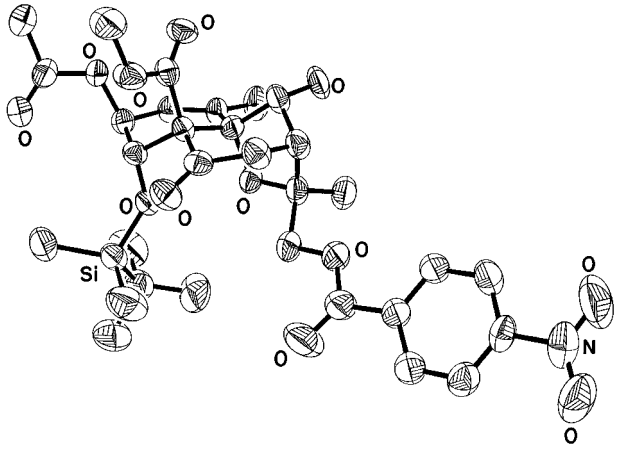
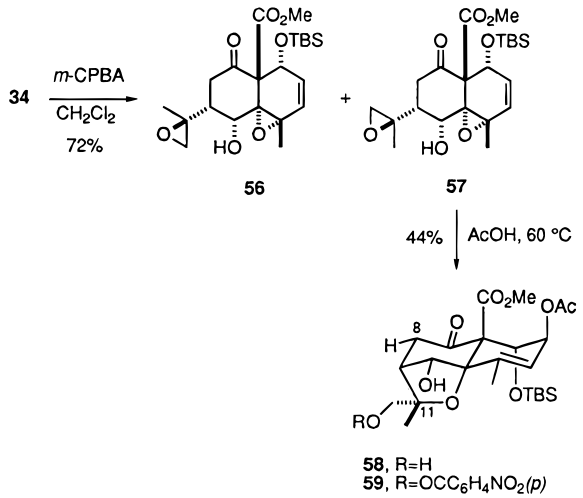


Figure 2. X-ray crystal structure of **59**.

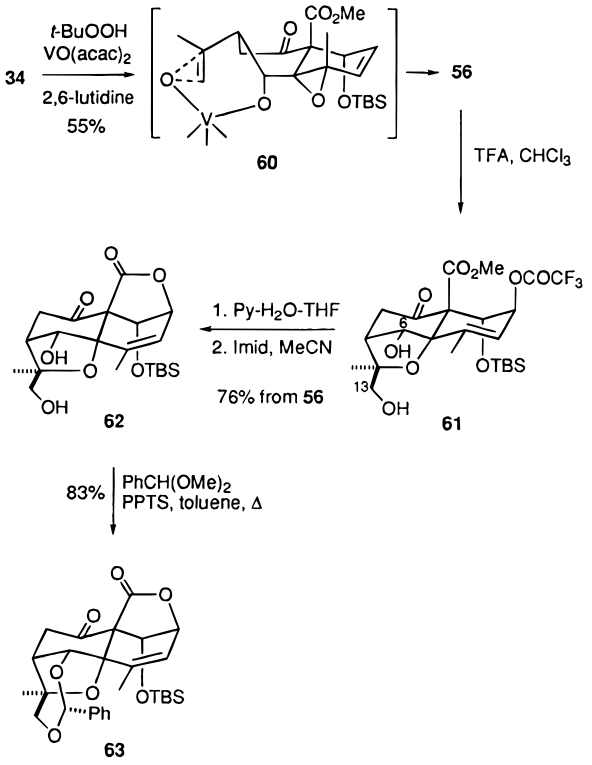
was cyclization of **56**, since opening of this terminal epoxide leaves no doubt as to the configurational outcome at the quaternary carbon of the heterocyclic ring. It was already known from experiments with **34** that epoxidation with *m*-chloroperbenzoic acid would occur selectively at the isopropenyl substituent rather than the cyclohexene double bond, but it was disappointing to find that no stereoselectivity was observed in this epoxidation. To complicate matters further, no reliable means could be found for assigning configuration to the terminal epoxide of either **56** or **57**. This uncertainty forced us to make an arbitrary selection of one epimer of the pair for cyclization studies, and when the crystalline stereoisomer **57** was subjected to the action of hot acetic acid in the hope that the two epoxide functions would open in tandem and lead to the tricyclic nucleus of **4**, our best expectations seemed to have been fulfilled. The "epoxide cascade cyclization" had indeed produced the tricyclic framework of an agarofuran. However, nuclear Overhauser enhancement of the resonance due to the equatorial proton at C8 caused by irradiation of the methylene protons of the primary alcohol of the cyclization product clearly pointed to **58**, containing the undesired C11 configuration, as the product from **57**. This was subsequently confirmed by X-ray analysis of the crystalline *p*-nitrobenzoate **59** derived from **58** (Figure 2).



With the secure knowledge that the terminal epoxide stereochemistry of **56** rather than **57** was required in order to produce the C11 configuration corresponding to euonyminol, efforts were charted toward obtaining a more favorable ratio of these epoxides from **34**. Careful scrutiny of the ^{1}H NMR spectrum of **34** revealed the fact that protons H6 and H8 were W coupled (J = 2 Hz), stipulating that the cyclohexanone ring of this decalin system must exist in a boat conformation.[28] Epoxidation

in this conformation directed by the 6α hydroxyl substituent should occur at the *si* face of the isopropenyl group, leading to **56**. In fact, the reaction of **34** with *tert*-butyl hydroperoxide in the presence of vanadium oxyacetylacetonate[29] afforded a 3:1 mixture of **56** and **57**, respectively, via a transition state that is presumed to resemble **60**. Inclusion of 2,6-lutidine was essential for a satisfactory yield in this epoxidation.

After examining several acidic reagents for the "cascade cyclization" of **56**, we selected trifluoroacetic acid in chloroform as the best medium. The transformation to **61** under these conditions was exceptionally clean, and the structure of the product was apparent not only from its epimeric relationship to **58** but also from subsequent chemistry that connected the C6 and C13 hydroxyl groups via an acetal *(vide infra)*. Following the analogous sequence **37** → **39** employed en route to 3,4-dideoxymaytol, **61** was taken to lactone **62** which was reacted with benzaldehyde dimethyl acetal in the presence of pyridinium *p*-toluenesulfonate. A single acetal **63** was obtained which was later shown to have α configuration at the benzylidene carbon.



Our initial plan with **63** was to use this material as a substrate for introducing the *syn* diol functionality of ring B, reasoning that the bridging γ lactone would block access to the top face of the double bond and therefore promote osmylation from the underside of the $\Delta^{3,4}$ olefin. However, **63** was completely unreactive toward osmium tetroxide, suggesting that the *tert*-butyldimethylsilyl ether at C1 was as much a steric impediment to osmylation from the lower face as the lactone was from above the double bond. Fortunately, a resolution of this difficulty was already at hand in the reversible aldol sequence that had inverted **40** to **41** via **44**, and when this protocol was applied to **63**, a nearly quantitative conversion to the crystalline alcohol **64** took place. An X-ray analysis of this substance (Figure 3) fully confirmed its structure, and resilylation gave the expected ether **65** epimeric with **63**.

In contrast to the osmylation of **63**, the corresponding reaction of **65** proceeded with ease, yielding a diol that was confidently

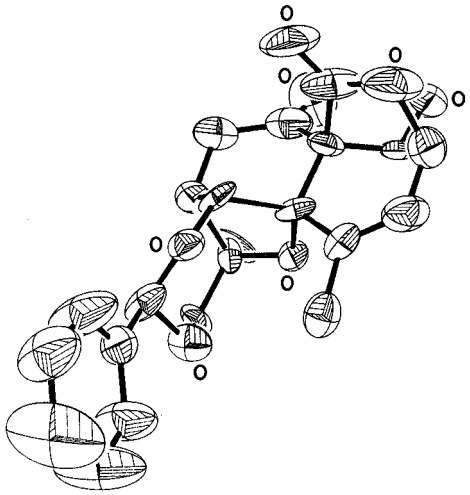
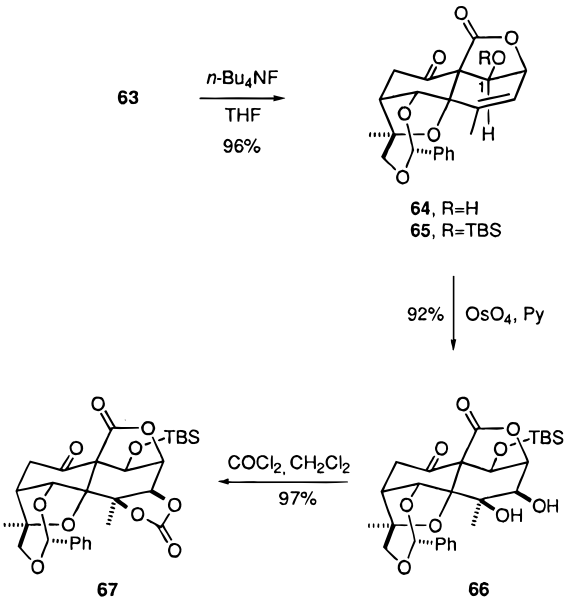


Figure 3. X-ray crystal structure of **64**.

predicted to have the desired α configuration at C3 and C4. The diol reacted quantitatively with phosgene to give a crystalline cyclic carbonate **67** for which X-ray analysis (Figure 4) disclosed the disquieting result that hydroxylation of **70** had occurred exclusively from the top face of the double bond to give **66**. A convincing rationale for this outcome must await more detailed study of the reaction of osmium tetraoxide with other sterically crowded olefins, but it should be noted that allylic substituents can have a powerful directing effect on facial selectivity in osmylation.[30] In particular, dihydroxylation tends to occur *syn* to an allylic ester and *anti* to an allylic ether, a generalization with which our results including those described below are consistent.



Our failure to negotiate the dihydroxylation of ring B in a satisfactory manner led to a revision of the planned sequence from **65** in which the manipulation of oxygen functionality in ring A now became the main endeavor. Anticipating that the lactone bridge and protecting groups of **65** would be retained until the last stages of the synthesis, we chose hydroxylation at C8 as the next move. This was accomplished in straightforward fashion by reaction of the enolate of **65** with the Davis oxaziridine **68**.[31] A single hydroxy ketone was obtained, and, since it is clear from a molecular model that the lower face of

(28) Günther, H. In *NMR Spectroscopy*; Wiley: Chichester, U.K., 1995; pp 124−125.

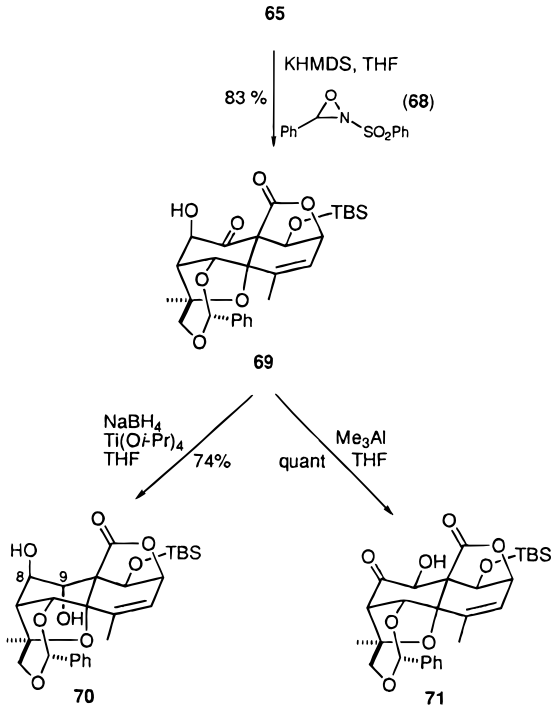
(29) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136.

(30) Arjona, O.; de Dios, A.; Plumet, J.; Saez, B. *J. Org. Chem.* **1995**, *60*, 4932.

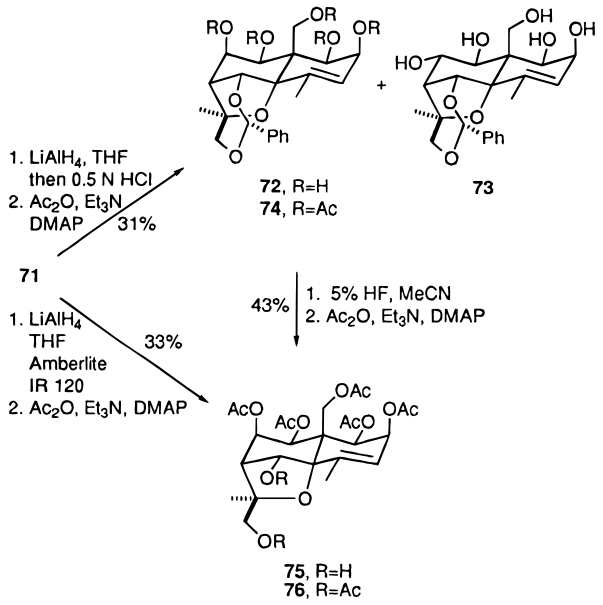
(31) Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.

the enolate from **65** is severely obstructed by the *endo* C12 methyl substituent, the reasonable assumption was made that hydroxylation had taken place to give the desired 8β configuration shown in **69**. This was subsequently confirmed, but the *raison d'être* for this assignment augured badly for the stereochemical outcome of reduction at the C9 ketone. Indeed, when **69** was treated with a variety of hydride and other reducing agents, only the undesired *trans* diol **70** was obtained. This result was clear from the absence of coupling (J = 0 Hz) between the C8 and C9 protons, indicating a diequatorial relationship.

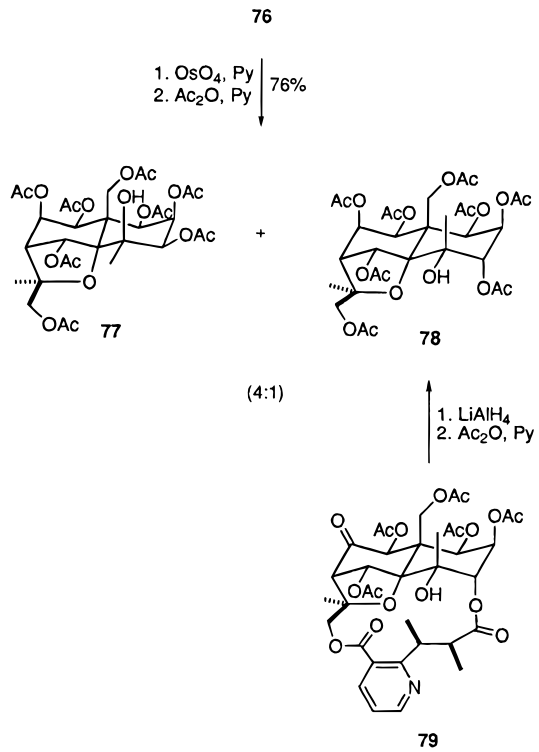
Fortunately, an incidental observation made in the course of studies with **65** that this ketone undergoes exceptionally facile enolization suggested an escape from this stereochemical dilemma. Reasoning that hydroxy ketone **69** would be similarly disposed toward enolization, we envisioned a 1,2-transposition that would take place via an enediol and would place a C9 hydroxyl in the correct β orientation. The interchange of a vicinal hydroxyl group and ketone is a version of the Lobry de Bruyn−Alberda van Eckenstein transformation conventionally used for converting aldoses to ketoses[32] and proved to be extremely efficient in the case of **69**. Lewis acids, particularly trimethylaluminum in excess, accomplished the transformation of **69** to **71** in quantitative yield. The rearrangement, which is believed to occur via an aluminum-complexed enediol species, is driven by relief of an unfavorable diaxial interaction between the C8 hydroxyl and lactone, where no hydrogen bond is possible, toward an equatorial C9 alcohol which can form a hydrogen bond with the equatorial silyl ether at C1.



With the C9 hydroxyl substituent now correctly set in place, **71** was exhaustively reduced with lithium aluminum hydride. An acidic workup that cleaved the silyl ether, but not the benzylidene acetal, produced a 4:1 mixture of pentaols **72** and **73**, respectively. The mixture was acetylated, and the major pentaacetate **74**, after chromatographic purification, was again acidified in order to hydrolyze the benzylidene acetal. The resultant diol **75** was acetylated to give heptaacetate **76.** The same heptaacetate was also obtained directly from **71** by reduction, followed by treatment with Amberlite resin to remove the silyl and benzylidene protecting groups simultaneously and final acetylation of the resulting heptaol.



The result of osmylating **76** had already been foreshadowed by the outcome with **65** which furnished the undesired diol **66**, and, true to form, the reaction of **76** with osmium tetraoxide in pyridine followed by acetylation gave as the major product an octaacetate **77** stereoisomeric with the corresponding octaacetate derivative of euonyminol. As with **65**, it appears that the allylic substituents again act in concert to direct osmylation *syn* to the acetoxy group and *anti* to the ether oxygen. Happily, there was produced in this reaction a small amount of a substance **78** that was identical with a sample of authentic euonyminol octaacetate, obtained from reduction of evonine[13a] (**79**) followed by acetylation.[13c]



With the aim of improving the stereoselectivity of osmylation, pentaol **72** from reduction of **71** was exhaustively silylated with *tert*-butyldimethylsilyl triflate to afford an inseparable mixture

(32) Speck, J. C. *Adv. Carbohydr. Chem.* **1958**, *13*, 63.

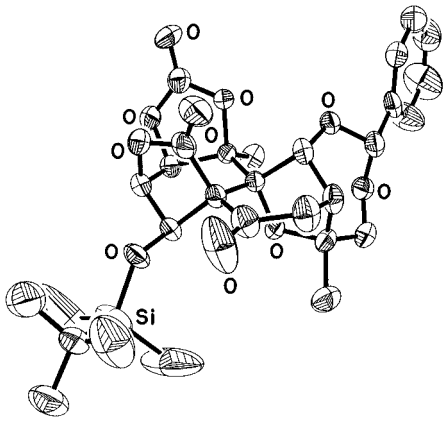
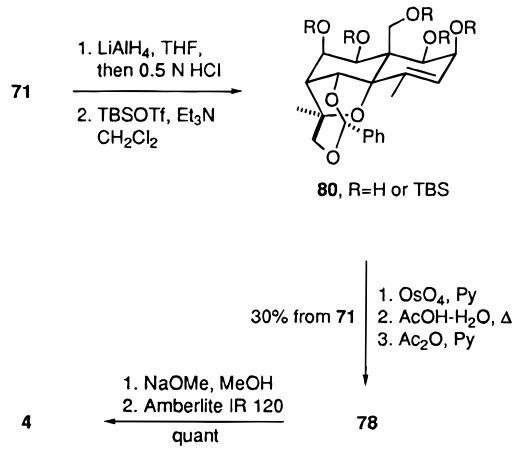


Figure 4. X-ray crystal structure of **67**.

of tetra- and pentasilyl ethers **80**. The mixture was reacted with osmium tetraoxide in pyridine, and the product was exposed to warm aqueous acetic acid in order to hydrolyze both the benzylidene group and all silyl ethers. The resultant, very polar nonaol was acetylated to give euonyminol octaacetate **78**, this time as the sole product. Final methanolysis of **78** followed by purification on Amberlite resin[13c] delivered (±)-euonyminol (**4**), identical by comparison of chromatographic and spectroscopic properties with naturally derived material. The structure of the latter has previously been established by X-ray crystallographic analysis.[13d]



Experimental Section

General Methods. Starting materials and reagents were obtained from commercial sources and, unless stated otherwise, were used without further purification. Solvents were dried by distillation from the appropriate drying agent immediately prior to use. Toluene, tetrahydrofuran, and ether were distilled from potassium and benzophenone under an argon atmosphere. Diisopropylamine, triethylamine, diisopropylethylamine, dimethylformamide, acetonitrile, pyridine, and dichloromethane were distilled from calcium hydride under argon. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Moisture and air sensitive reactions were carried out under an atmosphere of argon. Alkyllithium reagents, sodium hexamethyldisilazide, and potasium hexamethyldisilazide were titrated following Kofron's procedure.[33]

Residual solvent was removed by vacuum pump at pressures less than 2 Torr. Reaction flasks were flame-dried under a stream of argon. Syringes were oven dried at 200 °C and cooled to room temperature in a desiccator over anhydrous calcium sulfate.

Analytical thin-layer chromatography (TLC) was carried out using E. Merck precoated glass TLC plates (0.25 mm layer thickness of silica gel 60 F-254). Spots were visualized by ultraviolet light or by heating the plate after dipping in a 3−5% solution of phosphomolybdic acid in ethanol, 10% ammonium molybdate, or a 1% solution of vanillin in 0.1 M H_2SO_4 in methanol. Column chromatography refers to the flash chromatographic purification method of Still[34] and was carried out using E. Merck silica gel 60 (230−400 mesh ASTM). Radial chromatography was carried out on individually prepared rotors with layer thickness of 1, 2, or 4 mm using a Chromatotron manufactured by Harrison Research, Palo Alto, CA.

Melting points were measured using a Büchi melting point apparatus. Infared (IR) spectra were recorded on a Nicolet 5DXB FT-IR spectrometer. Proton and carbon nuclear magnetic resonance (NMR) spectra were obtained using either a Bruker AC-300 or Bruker AM-400 spectrometer. All chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane using the δ scale. ^{1}H NMR spectral data are reported in the following order: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad), coupling constant (J) in Hertz, and number of protons. Chemical ionization mass spectra MS(CI) were obtained using a Finnigan 4023 quadrupole GC-MS 4500 spectrometer with a source temperature of 140 °C and a pressure of 0.7 Torr. Electron impact mass spectra MS(EI) were obtained using a Varian MAT 311 spectrometer with an ionization potential of 70 eV. High resolution mass spectra were obtained using a Kratos MS-50 RF spectrometer. X-ray crystallographic data were collected using a Rigaku AFC6R or Siemens P4 diffractometer. Structures were solved using the direct method contained in TEXAN (VAX/VMS) and SHELXTL (Silicon Graphics/UNIX) software package. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

1-(*tert*-Butyldimethylsilyl)oxypenta-1,3-diene (11). To a stirred solution of *trans*-2-pentenal (10 g, 118.8 mmol) and triethylamine (24.8 mL, 177.9 mmol) in 200 mL of methylene chloride was added dropwise *tert*-butyldimethylsilyl triflate (26.4 mL, 115.2 mmol) at 0 °C. After the addition was complete, the mixture was refluxed for 4 h. To the resulting mixture was added aqueous sodium bicarbonate solution, and the organic layer was separated. The separated organic layer was washed with saturated brine, dried, and concentrated in vacuo. Vacuum distillation (1 mm Hg, 100−110 °C) of the residue afforded 20.9 g (89%) of an oily mixture of stereoisomeric 1-*tert*-butyldimethylsilyl)-oxypenta-1,3-dienes (**11**) which contained 25−30% of the (*E*,*E*) isomer.

Methyl (4a*β*,5α,8α,8a*β*)-1,5,8,8a-Tetrahydro-5-(*tert*-butyldimethylsilyl)oxy-1,4-dioxo-8-methyl-4a(4*H*)-naphthalenecarboxylate (14). To a stirred solution of methyl gentisate (**13**, 4.28 g, 25.5 mmol) and 1-*tert*-butyldimethylsilyloxypenta-1,3-diene (16 g, 80.6 mmol, mixture of stereoisomers) in 24 mL of toluene at 10 °C was added silver(I) oxide (11.8 g, 50.9 mmol) in one portion. The mixture was warmed to room temperature and stirred for 19 h, then was diluted with diethyl ether (100 mL), and filtered through Celite. The Celite was washed thoroughly with diethyl ether, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (hexane−ethyl acetate, 6:1) to give 8.2 g (88%) of **14** as a pale yellow solid: mp 57−59 °C; IR (KBr) 1749, 1710, 1686, 1253, 1227, 1089, 1058, 1037, 842 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (d, J = 10 Hz, 1H), 6.57 (d, J = 10 Hz, 1H), 5.68 (m, 2H), 4.77 (m, 1H), 3.76 (s, 3H), 3.64 (d, J = 5 Hz, 1H), 2.17 (m, 1H), 1.42 (d, J = 7 Hz, 3H), 0.73 (s, 9H), 0.01 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 169.1, 144.3, 138.4, 132.7, 125.8, 67.1, 66.2, 53.0, 50.4, 30.0, 25.5, 17.7, 17.1, −4.6, −5.2; MS (CI) *m/z* (rel intensity) 365 (M + 1, 100), 349 (43), 307 (65). Anal. Calcd for $C_{19}H_{28}O_5Si$: C, 62.59; H, 7.76. Found: C, 62.79; H, 7.67.

Methyl (4a*β*,5α,8α,8aα)-1,5,8,8a-Tetrahydro-5-(*tert*-butyldimethylsilyl)oxy-1,4-dioxo- 8-methyl-4a(4*H*)-naphthalenecarboxylate (15). A mixture of **14** (117 mg, 0.321 mmol) and neutral alumina (3 g, Brockman Activity 1, 80−100 mesh) in 8 mL of benzene was stirred for 4 h at room temperature. The resulting mixture was filtered through Celite, and the Celite was washed with ethyl acetate (20 mL). Concentration of the filtrate afforded 113 mg (97%) of **15** as a viscous oil (*trans:cis* > 30:1 based on ^{1}H NMR analysis): IR (film) 1748, 1733, 1697, 1273, 1252, 1212, 1180, 1073, 1047, 1009, 991, 864, 850, 839, 779 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.81 (d, J = 10 Hz, 1H), 6.57 (d, J = 10 Hz, 1H), 5.79 (m, 1H), 5.62 (dd, J = 10, 3 Hz, 1H), 4.99 (d, J = 7 Hz, 1H), 3.58 (s, 3H), 3.32 (d, J = 10 Hz, 1H), 2.82 (m, 1H), 1.19 (d, J = 7 Hz, 3H), 0.79 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 191.6, 167.1, 142.6, 137.5, 136.2, 125.7, 68.0, 65.1, 53.0, 50.3, 29.9, 25.6, 20.7, 17.8, −4.0, −5.0;

(33) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1876.

(34) Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

MS (CI) *m/z* (rel intensity) 365 (M + 1, 26), 363 (5), 351 (3), 350 (8), 349 (34), 308 (8), 307 (44), 234 (14), 233 (100); HRMS (CI) *m/z* 365.1785 (M^+ + 1) (calcd for $C_{19}H_{28}O_5Si$: 365.1784).

Methyl (4a*β*,5α)-1,5-Dihydro-5-(*tert*-butyldimethylsilyl)oxy-8-methyl-1,4-dioxo-4a(4*H*)-naphthalenecarboxylate (17). A solution of **14** (7.51 g, 20.6 mmol), N-bromosuccinimide (3.86 g, 21.7 mmol), and a catalytic amount of benzoyl peroxide in 140 mL of carbon tetrachloride was refluxed for 3 h. To the mixture was added 8 mL of triethylamine, and reflux was continued for an additional 2 h. The mixture was cooled to room temperature and poured into aqueous, saturated sodium bicarbonate solution (100 mL). The resulting mixture was extracted with methylene chloride (150 mL), and the separated organic layer was dried and concentrated in vacuo. Column chromatography (hexane−ethyl acetate, 5:1) of the residue afforded 7.29 g (98%) of **17** which slowly solidified in the refrigerator to give an amorphous yellow solid: IR (KBr) 1745, 1685, 1661, 1559, 1074, 839 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.89 (d, J = 10 Hz, 1H), 6.68 (d, J = 10 Hz, 1H), 6.32 (dd, J = 6, 10 Hz, 1H), 6.05 (d, J = 10 Hz, 1H), 5.06 (d, J = 6 Hz, 1H), 3.59 (s, 3H), 2.32 (s, 3H), 0.74 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.8, 186.6, 166.8, 145.0, 144.3, 137.1, 133.4, 131.4, 122.9, 65.8, 63.8, 53.3, 25.5, 20.7, 17.8, −4.0, −5.1; MS (CI) *m/z* (rel intensity) 363 (M + 1, 53), 347 (28), 305 (24), 231 (100), 198 (15), 170 (96); HRMS (CI) *m/z* 363.1627 (M^+ + 1) (calcd for $C_{19}H_{27}O_5Si$: 363.1627).

Methyl (1α,4a*β*,5α)-1,5-Dihydro-5-(*tert*-butyldimethylsilyl)oxy-1-hydroxy-8-methyl-4-oxo-4a(4*H*)-naphthalenecarboxylate (18). To a stirred solution of **17** (7.29 g, 20.1 mmol) and cerium chloride heptahydrate (7.84 g, 22.1 mmol) in 1.4 L of methanol was added solid sodium borohydride (0.76 g, 20.1 mmol) portionwise during 30 min at 0 °C. After the addition was complete, the mixture was warmed to room temperature, and stirring was continued for 30 min. Acetone (5 mL) was added to destroy residual sodium borohydride, and the volatile material was evaporated in vacuo. The residue was diluted with methylene chloride (150 mL) and washed with water (200 mL). The separated aqueous layer was extracted with methylene chloride (50 mL × 2), and the combined organic layer was washed with saturated brine, dried, and concentrated in vacuo to give crude **18** (6.6 g, 90%) which was used in the next step without further purification. A pure sample of **18** was obtained by column chromatography (hexane−ethyl acetate, 5:1): IR (KBr) 3463, 1727, 1663, 1466, 1440, 1253, 1224, 1099, 839 $cm^{-1;}$ ^1H NMR (300 MHz, $CDCl_3$) δ 6.95 (dd, J = 4, 10 Hz, 1H), 6.14 (dd, J = 2, 10 Hz, 1H), 6.00 (dd, J = 5, 9 Hz, 1H), 5.85 (d, J = 9 Hz, 1H), 5.20 (br. d, J = 12 Hz, 1H), 3.60 (s, 3H), 2.07 (d, J = 1 Hz, 3H), 0.76 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0, 168.0, 149.3, 133.8, 131.1, 127.9, 127.5, 126.5, 65.8, 64.1, 53.1, 25.7, 19.8, 17.9, −4.1, −5.1; MS (CI) *m/z* (rel intensity) 365 (M + 1, 12), 349 (39), 347 (86), 331 (24), 317 (20), 289 (22), 275 (15), 235 (20), 233 (100), 201 (75), 175 (30), 173 (70); HRMS (CI) *m/z* 365.1783 (M^+ + 1) (calcd for $C_{19}H_{29}O_5Si$: 365.1776).

Methyl (1α,4a*β*,5α,8a,8aα)-1,5-Dihydro-5-(*tert*-butyldimethylsilyl)oxy-1-hydroxy-8(*β*)-methyl-4-oxo-4a(4*H*)-8,8a-epoxynaphthalenecarboxylate (19). To a stirred solution of crude **18** (2.34 g, 6.43 mmol) in 200 mL of methylene chloride and 800 mL of aqueous phosphate buffer (pH 8) was added *m*-chloroperbenzoic acid (1.35 g, 13.5 mmol) portionwise at 0 °C. After the addition was complete, the mixture was warmed to room temperature and stirred for 50 min. Excess dimethyl sulfide was added to remove residual *m*-chloroperbenzoic acid, and stirring was continued for 15 min. The organic layer was separated and concentrated in vacuo. Column chromatography (hexane−ethyl acetate, 4:1) of the residue gave 2.12 g (88%) of **19** as colorless plates: mp 89.5−90.5 °C; IR (KBr) 3487, 1731, 1691, 1253, 1213, 1109, 1091, 1046, 840, 813 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.93 (dd, J = 11, 2 Hz, 1H), 6.10 (dd, J = 11, 2 Hz, 1H), 5.96 (m, 2H), 5.11 (m, 2H), 3.66 (s, 3H), 2.71 (d, J = 11 Hz, 1H, OH), 1.76 (s, 3H), 0.79 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.9, 167.2, 152.2, 134.4, 132.1, 127.2, 67.7, 67.5, 63.0 (two peaks), 58.3, 53.3, 25.6, 17.8, 17, −4.0, −5.0; MS (CI) *m/z* (rel intensity) 381 (M + 1, 100), 365 (98), 323 (79), 331 (33), 277 (10), 249 (80), 217 (22); Anal. Calcd for $C_{19}H_{28}O_6Si$: C, 59.96; H, 7.43. Found: C, 59.63; H, 7.54.

Methyl (1α,4a*β*,5α,6*β*,8aα)-1,5,6,8a-Tetrahydro-6-acetoxy-5-(*tert*-butyldimethylsilyl)-oxy-1,8a-dihydroxy-8-methyl-4a(4*H*)-naphthalenecarboxylate (20). A solution of **19** (145 mg, 0.3810 mmol) in 2 mL of acetic acid was refluxed for 5 h. The mixture was cooled to room temperature, and volatile material was removed in vacuo. Column chromatography (hexane−ethyl aceate, 3:1) of the residue afforded 119 mg (71%) of **20** as a colorless oil: IR (film) 3421, 3399, 1737, 1701, 1371, 1251, 1226, 1031, 838, 784 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.66 (dd, J = 11, 3 Hz, 1H), 6.00 (dd, J = 11, 2 Hz, 1H), 5.46 (m, 1H), 5.39 (s, 1H, OH), 5.16∼5.07 (m, 2H), 4.87 (t, J = 2 Hz, 1H), 3.62 (s, 3H), 3.18 (d, J = 12 Hz, 1H, OH), 2.14 (br. s, 3H), 2.00 (s, 3H), 0.85 (s, 9H), 0.31 (s, 3H), 0.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.1, 169.6, 166.8, 149.2, 144.8, 126.5, 117.9, 75.3, 71.0, 69.2, 68.7, 63.7, 52.7, 25.7, 21.4, 20.9, 17.9, −4.9, −5.3; MS (CI) *m/z* (rel intensity) 441 (M+ 1, 24), 425 (31), 424 (25), 422 (100), 407 (14), 383 (35), 382 (24), 381 (99), 367 (12), 365 (32), 364 (18), 363 (70), 323 (27), 249 (11), 231 (15); HRMS (CI) *m/z* 441.1944 (M^+ + 1) (calcd for $C_{21}H_{32}O_8Si$: 441.1944).

Methyl (1α,4a*β*,5α,6*β*,8aα)-1,5,6,8a-Tetrahydro-5-(*tert*-butyldimethylsilyl)oxy-1,8a-dihydroxy-8-methyl-4-oxo-6-trifluoroacetoxy-4a(4*H*)-naphthalenecarboxylate (21). A solution of **19** (24.4 mg, 0.0641 mmol) in 0.2 mL of trifluoroacetic acid was stirred for 2 h at room temperature. The resulting mixture was diluted with diethyl ether (10 mL) and washed with aqueous sodium bicarbonate solution. The separated organic layer was washed with brine, dried, and concentrated in vacuo. Column chromatography (hexane−ethyl acetate, 3:1 to 2:1) of the residue afforded 6.5 mg (33%) of **21** and 10 mg (67%) of **22**, each as an oil. Spectroscopic data for **22**: IR (film) 3425, 1785, 1745, 1697, 1378, 1252, 1221, 1172, 1149, 1095, 1031, 925 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.73 (dd, J = 11, 3 Hz, 1H), 6.09 (dd, J = 11, 2 Hz, 1H), 5.61 (m, 1H), 5.44 (m, 1H), 5.12 (dt, J = 15, 1 Hz, 1H), 4.95 (m, 1H), 4.46 (d, J = 1 Hz, 1H, OH), 3.78 (d, J = 5 Hz, 1H, OH), 3.62 (s, 3H), 3.15 (d, J = 12 Hz, 1H, OH), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 165.9, 150.1, 146.5, 126.3, 116.4, 116.1, 75.7, 72.4, 68.5, 63.9, 53.7, 52.9, 52.8, 21.3; MS (CI) *m/z* (rel intensity) 381 (M + 1, 6), 379 (2), 363 (14), 345 (3), 313 (1), 301 (2), 295 (2), 268 (15), 267 (100), 250 (11), 249 (71), 231 (14), 221 (18), 217 (29), 189 (14), 115 (63); HRMS (CI) *m/z* 381.0797 (M^+ + 1) (calcd for $C_{15}H_{16}F_3O_8$: 381.0797).

Spectroscopic data for **21**: IR (film) 3416, 1784, 1745, 1703, 1375, 1253, 1223, 1176, 1145, 1101, 1026, 1032, 935, 837, 785 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.68 (dd, J = 10, 3 Hz, 1H), 6.03 (dd, J = 10, 2 Hz, 1H), 5.49 (m, 1H), 5.29 (m, 2H), 5.11 (br d, J = 12 Hz, 1H), 4.94 (t, J = 2 Hz, 1H), 3.59 (s, 3H), 3.16 (d, J = 12 Hz, 1H, OH), 2.18 (t, J = 2 Hz, 3H), 0.86 (s, 9H), 0.32 (s, 3H), 0.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.6, 166.1, 149.3, 147.7, 126.4, 115.5, 75.0, 73.2, 70.5, 68.6, 63.6, 53.0, 25.7, 21.5, 17.9, −5.0, −5.2; MS (CI) *m/z* (rel intensity) 495 (M + 1, 20), 479 (17), 478 (11), 477 (40), 437 (16), 383 (14), 382 (30), 381 (M − CF_3CO_2, 100), 365 (13), 363 (35), 249 (20), 115 (38); HRMS (CI) *m/z* 495.1662 (M^+ + 1) (calcd for $C_{21}H_{30}F_3O_8Si$: 495.1662).

Methyl (1α,4a*β*,5α,6*β*,8aα)-1,5,6,8a-Tetrahydro-5-(*tert*-butyldimethylsilyl)oxy-8-methyl-4-oxo-1,6,8a-trihydroxy-4a(4*H*)-naphthalenecarboxylate (23). A mixture of **19** (62 mg, 0.163 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg, 0.0526 mmol) in 2 mL of acetone was stirred for 30 min at room temperature. The mixture was neutralized with a few drops of triethylamine and was passed through a short pad of silica gel using diethyl ether as eluent. Column chromatography (hexane−ethyl acetate, 3:1 to 2:1) of the concentrated eluent afforded 27 mg of **24** and 16 mg of **23**. Spectroscopic data for **23**: IR (KBr) 3453, 3427, 3381, 1743, 1685, 1466, 1431, 1391, 1258, 1220, 1174, 1084, 1034, 841, 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.60 (dd, J = 10, 2 Hz, 1H), 5.99 (d, J = 10 Hz, 1H), 5.53 (m, 1H), 5.28 (s, 1H, OH), 5.00 (d, J = 12 Hz, 1H), 4.82 (m, 1H), 4.05 (br s, 1H), 3.56 (s, 3H), 3.12 (d, J = 12 Hz, 1H), 2.09 (s, 3H), 1.48 (d, J = 5 Hz, 1H, OH), 0.81 (s, 9H), 0.25 (s, 3H), 0.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.6, 148.7, 142.7, 126.9, 121.4, 75.5, 73.2, 68.8, 68.4, 63.3, 52.8, 25.7, 21.3, 17.9, −5.0, −5.1; MS (CI) *m/z* (rel intensity) 399 (M + 1, 23), 383 (29), 382 (22), 381 (100), 363 (65), 341 (28), 305 (20), 249 (23), 231 (22); HRMS (CI) *m/z* 399.1840 (M^+ + 1) (calcd for $C_{19}H_{31}O_7Si$: 399.1839).

Lactone 24. A mixture of **19** (7 mg, 0.0184 mmol) and pyridinium *p*-toluenesulfonate (4 mg, 0.016 mmol) in reagent grade acetone (1 mL) was stirred for 24 h at room temperature. The mixture was concentrated in vacuo and was purified by column chromatography (hexane−ethyl acetate, 2:1) to give 4 mg (59%) of **24** as a colorless

amorphous solid: IR (KBr) 3390, 1777, 1692, 1385, 1257, 1228, 1202, 1081, 1054, 1001, 905, 843, 787 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.98 (dd, $J = 11$, 2 Hz, 1H), 6.15 (dd, $J = 11$, 2 Hz, 1H), 6.03 (m, 2 H), 5.76 (s, 1H, OH), 5.04 (m, 1H), 4.69 (dt, $J = 11$, 2 Hz, 1H), 3.22 (d, $J = 11$ Hz, 1H), 1.69 (s, 3H), 0.82 (s, 9H), 0.20 (s, 3H), 0.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.8, 167.1, 152.8, 134.6, 130.8, 128.0, 83.6, 81.8, 67.6, 65.3, 60.5, 26.9, 25.4, 18.2, 17.7, −4.6, −5.5; MS (CI) *m/z* (rel intensity) 367 (M + 1, 100), 351 (11), 235 (22), 191 (27); HRMS (CI) *m/z* 367.1575 ($M^+ + 1$) (calcd for $C_{18}H_{27}O_6Si$: 367.1569).

Carbonate 26. A mixture of **25** (18.5 mg, 0.486 mmol) and carbonyldiimidazole (15.8 mg, 0.972 mmol) in 1.5 mL of toluene was refluxed for 6 h. The mixture was cooled to room temperature and purified by column chromatography (hexane−ethyl acetate, 6:1 to 2:1) to give 15 mg (76%) of **26** as a colorless amorphous solid: ^1H NMR (300 MHz, $CDCl_3$) δ 6. 81 (dd, $J = 10$, 3 Hz, 1H), 6.27 (d, $J = 10$ Hz, 1H), 6.18 (d, $J = 10$ Hz, 1H), 6.01 (dd, $J = 10$, 5 Hz, 1H), 5.86 (d, $J = 3$ Hz, 1H), 5.61 (s, 1H), 5.38 (s, 1H), 5.25 (d, $J = 5$ Hz, 1H), 3.63 (s, 3H), 0.83 (s, 9H), 0.17 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$,) δ 186.1, 166.0, 152.3, 139.5, 139.1, 129.26, 129.22, 128.5, 117.1, 83.6, 74.2, 65.2, 64.8, 53.8, 25.6, 17.9, −3.9, −5.1; MS (CI) *m/z* 407 (M + 1, 100), 391 (31), 349 (54), 275 (44), 231 (46), 203 (39); Anal. Calcd for $C_{20}H_{27}O_7Si$: C, 59.09; H, 6.45. Found: C, 59.07; H, 6.38.

Epoxide 27. To a stirred solution of **25** (13 mg, 0.0341 mmol) in 0.5 mL of methylene chloride was added *m*-chloroperbenzoic acid (1.5 equiv, 10.7 mg, 0.051 mmol) at 0 °C. After 0.5 h the mixture was warmed to room temperature, and stirring was continued for 7 h. A few drops of dimethyl sulfide was then added to destroy residual *m*-chloroperbenzoic acid, and aqueous sodium bicarbonate solution was then added. After 2 h of vigorous stirring, the mixture was extracted with diethyl ether (10 mL), and the separated organic layer was washed with saturated brine, dried, and concentrated in vacuo. Thin-layer chromatography (0.25 mm, hexane−ethyl acetate, 3:1) of the residue afforded 6.5 mg (47%) of a high R_f isomer **27** and 6.0 mg (44%) of a lower R_f isomer, each as oils. Spectroscopic data for high R_f **27**: IR (film) 3528, 3382, 1738, 1689, 1254, 1229, 1188, 1100, 1058, 1045, 1017, 933, 844, 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (dd, $J = 10$, 2 Hz, 1H), 6.52 (s, 1H), 6.30 (dd, $J = 10$, 5 Hz, 1H), 6.05 (dd, $J = 10$, 2 Hz, 1H), 5.37 (d, $J = 10$ Hz, 1H), 5.26 (d, $J = 5$ Hz, 1H), 4.95 (dt, $J = 12$, 2 Hz, 1H), 3.93 (d, $J = 5$ Hz, 1H), 3.65 (s, 3H), 2.98 (d, $J = 12$ Hz, 1H), 2.77 (d, $J = 5$ Hz, 1H), 0.83 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.6, 166.2, 152.0, 131.9, 131.2, 126.2, 75.6, 68.6, 67.9, 64.7, 61.4, 54.6, 53.3, 25.6, 17.8, 14.2, −4.4, −5.3; MS (CI) *m/z* (rel intensity) 397 ($M^+ + 1$, 17), 381 (25), 379 (17), 363 (13), 347 (21), 339 (31), 305 (11), 293 (22), 266 (11), 265 (80), 249 (17), 247 (88), 231 (13), 229 (24), 219 (37), 215 (44), 187 (100), 171 (11), 159 (12), 133 (20), 117 (11) ; HRMS (CI) *m/z* 397.1681 ($M^+ +$ 1) (calcd for $C_{19}H_{29}O_7Si$: 397.1682).

Spectroscopic data for low R_f **27**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.77 (dd, $J = 11$, 2 Hz, 1H), 6.22 (s, 1H), 6.18 (dd, $J = 10$, 2 Hz, 1H), 6.04 (dd, $J = 11$, 2 Hz, 1H), 5.30 (d, $J = 10$ Hz, 1H), 5.23 (d, $J = 5$ Hz, 1H), 5.13 (br d, $J = 7$ Hz, 1H), 3.63 (s, 3H), 3.57 (d, $J = 4$ Hz, 1H), 3.19 (d, $J = 7$ Hz, 1H), 2.91 (d, $J = 4$ Hz, 1H), 0.82 (s, 9H), 0.19 (s, 6H).

Methyl (1α,2*β*,4a*β*,5α,8α,8aα)-1,2,3,5,8,8a-Hexahydro-5-(*tert*-butyldimethylsilyl)oxy-1-hydroxy-8(*β*)-methyl-2-(1-methyl)ethenyl-4-oxo-4a(4*H*)-8,8a-epoxynaphthalenecarboxylate (30). To a stirred solution of 2-bromopropene (121 μL, 1.366 mmol) in 4 mL of tetrahydrofuran at −78 °C was added dropwise *tert*-butyllithium (1.7 M in pentane, 1.61 mL, 2.73 mmol). After 45 min, the resulting pale yellow solution of 2-lithiopropene was transferred rapidly via cannula to a suspension of cuprous cyanide in 2 mL of tetrahydrofuran at −78 °C. After the transfer was complete, the mixture was allowed to warm slowly by removing the cooling bath until the solution became homogeneous (3−5 min). The mixture was then recooled to −78 °C. To the resulting light yellow solution was added slowly via the wall of the flask a solution of trimethylsilyl chloride (1 M in THF, 3.4 mL, 3.42 mmol). Immediately after the addition of trimethylsilyl chloride was complete, a solution of **19** in 1 mL of tetrahydrofuran was added to the yellow-orange solution via cannula, and the mixture was stirred for 50 min. Saturated ammonium chloride (4 mL), saturated ammonium hydroxide (4 mL), and diethyl ether (10 mL) were added, the mixture was allowed to warm to ice-bath temperature, and stirring was continued until the solution became clear. The organic layer was separated and washed with saturated sodium bicarbonate solution and saturated brine, dried, and concentrated to give 50 mg of crude **29**.

To a stirred solution of crude **29** (50 mg) in 2 mL of methylene chloride was added excess triethylamine−hydrofluoric acid complex at room temperature. The mixture was allowed to stand for 17 h and passed through a short pad of silica gel using diethyl ether (25 mL) as eluent. Column chromatography (hexane−ethyl acetate, 4:1) of the concentrated eluent afforded 30 mg (60%) of **30** as a colorless amorphous solid: IR (film) 3509, 1748, 1723, 1250, 1224, 1195, 1098, 1060, 840, 776 cm^{-1};^1H NMR (300 MHz, $CDCl_3$) δ 6.81 (d, $J = 9$ Hz, 1H), 5.88 (dd, $J = 9$, 6 Hz, 1H), 4.98 (d, $J = 6$ Hz, 1H), 4.83 (s, 1H), 4.56 (dd, $J = 8$, 6 Hz, 1H), 3.61 (s, 3H), 2.73 (m, 3H), 2.55 (d, $J = 8$ Hz, 1H, OH), 1.81 (s, 3H), 1.74 (s, 3H), 0.82 (s, 9H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$,) δ 200.6, 167.1, 144.4, 135.4, 131.4, 113.1, 68.7, 68.0, 66.2, 64.7, 59.4, 53.2, 48.3, 42.1, 25.7, 19.9, 17.8, 17.3, −4.0, −5.0; MS (CI) *m/z* (rel intensity) 407 ($M^+ -$ 15, 100), 409 (6), 408 (16), 407 (59), 406 (23), 405 (79), 392 (10), 391 (38), 389 (36), 387 (22), 381 (14), 375 (15), 374 (9), 373 (26), 366 (17), 365 (69), 363 (13), 357 (14), 348 (11), 347 (41), 333 (15), 331 (19), 323 (12), 319 (17), 315 (11), 309 (15), 292 (13), 291 (75), 279 (10), 277(40), 273 (84), 259 (37), 249 (15), 245 (14), 241 (21), 237 (21), 229 (14), 227 (15), 213 (39), 199 (10), 197 (14), 177(31), 167 (19). Anal. Calcd for $C_{22}H_{34}O_6Si$: C, 62.53; H, 8.11. Found: C, 62.30; H, 7.98.

Methyl (1α,2*β*,4a*β*,5α,8aα)-1,2,3,5,8,8a-Hexahydro-5-(*tert*-butyldimethylsilyl)oxy-1,8a-dihydroxy-8-methylene-2-(1-methyl)ethenyl-4-oxo-4a(4*H*)-naphthalenecarboxylate (31). To a stirred solution of **30** (5.7 mg, 0.0135 mmol) in 1 mL of toluene at room temperature was added neat titanium tetraisopropoxide (16 μL, 0.0540 mmol). After 7 h, the mixture was passed through a short pad of silca gel, using diethyl ether as eluent, and the concentrated eluent was purified by column chromatography (hexane−ethyl acetate, 6:1 to 3:1) to give 4.2 mg (74%) of **31** as an oil: IR (film) 3356, 3508, 1723, 1467, 1235, 1190, 1044, 1014, 1005, 843, 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (s, 1H, OH), 6.17 (d, $J = 10$ Hz, 1H), 6.11 (s, 1H), 5.82 (dd, $J = 10$, 6 Hz, 1H), 5.26 (s, 1H), 5.12 (d, $J = 6$ Hz, 1H), 4.86 (m, 3H), 3.61 (s, 3H), 2.94 (m, 1H), 2.64 (dd, $J = 15$, 14 Hz, 1H), 2.35 (m, 2H, 1 proton exchanged with D_2O), 1.83 (s, 3H), 0.85 (s, 9H), 0.25 (s, 3H), 0.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.8, 166.9, 144.5, 144.0, 132.7, 125.4, 119.4, 113.8, 71.1, 68.0, 67.4, 53.2, 48.1, 42.2, 25.7, 18.9, 17.9, −4.5, −5.1; MS (CI) *m/z* (rel intensity) 423 (M + 1, 17), 407 (31), 405 (11), 389 (5), 366 (7), 365 (30), 331 (7), 319 (20), 293 (9), 292 (18), 291 (100), 274 (11), 273 (61), 259 (10), 213 (10), 177 (44), 133 (24); HRMS (CI) *m/z* 423.2202 ($M^+ + 1$) (calcd for $C_{22}H_{35}O_6Si$: 423.2203).

Epoxide 32. To a stirred solution of *m*-chloroperbenzoic acid (172 mg, 0.800 mmol) in 5 mL of hexane at 0 °C was added dropwise a solution of **29** (205 mg, 0.3616 mmol) in 5 mL of hexane. After the addition was complete, the mixture was warmed to room temperature, and stirring was continued for 19 h. The mixture was cooled to 0 °C, and the deposited solid was filtered and washed with pentane (3 mL × 2). The filtrate was concentrated in vacuo, and the residue was diluted with methylene chloride (8 mL) and then treated with triethylamine−hydrofluoric acid complex (350 mg, 2.9 mmol). After 22 h, the mixture was passed through a short pad of silica gel, using diethyl ether as eluent, and the concentrated eluent was purified by column chromatography (silica gel 10 g, hexane−ethyl acetate, 2:1 to 3:2) to give 104 mg (64%) of **32** as an epimeric mixture at the terminal epoxide in a 3:1 ratio based on ^1H NMR analysis.

Orthoester 33. A mixture of **32** (4.8 mg, 0.0106 mmol) and pyridinium *p*-toluenesulfonate (10 mg, 0.040 mmol) in 1 mL of acetone was stirred for 1.5 h at room temperature. The mixture was passed through a short pad of silica gel, using diethyl ether as eluent, and the concentrated eluent was purified by column chromatography (hexane−ethyl acetate, 6:1) to give 2.1 mg (48%) of **33** as a colorless solid: mp 141−141.5 °C; IR (KBr) 3500, 1778, 1256, 1197, 1177, 1088, 1045, 1020, 951, 901, 839, 814 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.19 (s, 1H, OH), 5.92 (dd, $J = 10$, 4 Hz, 1H), 5.80 (d, $J = 10$ Hz, 1H), 4.57 (d, $J = 4$ Hz, 1H), 4.44 (s, 1H), 4.38 (t, $J = 10$ Hz, 1H), 3.34 (s, 3H), 2.94 (d, $J = 10$ Hz, 1H, OH), 2.82 (d, $J = 5$ Hz, 1H), 2.72 (d, J

= 5 Hz, 1H), 1.51 (s, 3H), 1.47 (s, 3H), 0.88 (s, 9H), 0.27 (s, 3H), 0.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 133.8, 129.1, 119.8, 86.1, 84.9, 79.8, 68.3, 65.7, 59.3, 57.7, 56.9, 55.3, 49.8, 25.7, 18.1, 17.8, 17.7, 15.2, −4.5, −5.1; MS (CI) *m/z* (rel intensity) 455 (M + 1, 80), 439 (12), 437 (25), 423 (34), 421 (12), 405 (11), 379 (12), 365 (15), 363 (15), 351 (27), 324 (15), 323 (86), 322 (18), 302 (63), 287 (15), 277 (19), 273 (19), 247 (30), 229 (42), 201 (34), 167 (46), 60 (100); HRMS (CI) *m/z* 455.2103 (M^+ + 1) (calcd for $C_{22}H_{35}O_8Si$: 455.2101).

Compound **33** crystallized from octane in the space group P2(1)/c with a = 11.696 (3) Å, b = 14.867 (2) Å, c = 14.541 (2) Å, β = 93.77 (2)°, z = 4, and d_{calcd} = 1.197 g/cm^3. The intensity data were measured on a Rikagu AFC6R diffractometer (Mo Kα radiation). There were 2168 observed reflections [$I > 3.00(I)$], and the structure was solved by direct methods. The final discrepancy indices were R = 0.066 and R_w = 0.095.

Methyl (1α,2α,4a*β*,5α,8α,8aα)-1,2,3,5,8,8a-Hexahydro-5-(*tert*-butyl-dimethylsilyl)oxy-1-hydroxy-8(*β*)-methyl-2-(1-methyl)ethenyl-4-oxo-4a(4*H*)-8,8a-epoxynaphthalenecarboxylate (34). To a stirred solution of diisopropylamine (0.088 mL, 0.67 mmol) in tetrahydrofuran (2 mL) was added *n*-butyllithium (1.6 M in hexane, 0.42 mL, 0.67 mmol) dropwise at 0 °C. After 30 min, the resulting lithium diisopropylamide solution was added to a stirred solution of **19** (244 mg, 0.64 mmol) in tetrahydrofuran (1.8 mL) at −78 °C, and the mixture was stirred for 15 min. A solution of 15-crown-5 (0.15 mL, 0.77 mmol) in tetrahydrofuran (0.8 mL) was added, and stirring was continued for 15 min. To the mixture was added isopropenylmagnesium bromide (0.50 M in THF, 1.34 mL, 0.67 mmol), and stirring was continued for 30 min at −78 °C. The mixture was allowed to warm to room temperature and stirred for 1 h. The mixture was quenched with aqueous ammonium chloride solution and extracted with ether. The organic extract was washed with brine, dried over magnesium sulfate, and concentrated in vacuo, and the residue was chromatographed on silica (hexanes−ethyl acetate, 4:1) to give **34** (169 mg, 63%) as an oil: IR (film) 3479, 1752, 1723, 1251, 1203, 1096, 841, 775 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.02 (1H, d, J = 10 Hz), 5.91 (1H, dd, J = 10, 6 Hz), 5.02 (1H, d, J = 6 Hz), 5.00 (1H, d, J = 1 Hz), 4.72 (1H, s), 4.51 (1H, ddd, J = 4, 4, 2 Hz), 3.69 (3H, s), 2.93 (1H, d, J = 4 Hz), 2.69 (1H, d, J = 15 Hz), 2.53 (2H, m), 1.90 (3H, s), 1.63 (3H, s), 0.81 (9H, s), 0.07 (3H, s), 0.03 (3H, s); ^{13}C NMR ($CDCl_3$) δ 200.8, 167.3, 143.2, 133.9, 131.4, 112.1, 69.1, 67.1, 63.9, 63.8, 58.3, 53.3, 42.9, 39.9, 25.5, 21.9, 17.7, 16.6, −4.0, −5.1; MS (CI) *m/z* 423 (M^+ + 1), 407, 406, 405, 391, 389, 373, 291, 277, 273, 259, 249, 241, 231, 213, 177, 165, 59; HRMS (CI) *m/z* 423.2202 (M^+ + 1) (calcd for $C_{22}H_{35}O_6Si$: 423.2203).

Lactone 39. To a solution of **34** (175 mg, 0.415 mmol) in chloroform (5 mL) at room temperature was added trifluoroacetic acid (48 mL, 0.622 mmol) in one portion. After 1 h, triethylamine (58 mL, 0.415 mmol) was added, and the reaction mixture was concentrated under reduced pressure to give crude **37**. This was taken up into THF−pyridine−water (4:1:1, 6 mL), and after 3 h ethyl acetate (6 mL) was added to the mixture. The solution was dried over magnesium sulfate and concentrated under reduced pressure to give crude **38**. This was taken up into acetonitrile (15 mL), and imidazole (283 mg, 4.15 mmol) was added. The solution was stirred at 50 °C for 12 h and concentrated. The residue was chromatographed on silica (hexanes−ethyl acetate, 8:1) to give **39** (132 mg, 78%) as a colorless crystalline solid: mp 87.5−88.5 °C; IR (KBr) 3418, 2927, 1776, 1718, 1397, 1246, 1159, 1149, 954 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.83 (1H, m), 5.21 (1H, d, J = 5 Hz), 4.97 (1H, d, J = 1 Hz), 4.85 (1H, OH, s), 4.68 (1H, s), 4.59 (1H, dd, J = 6, 5 Hz), 4.07 (1H, dd, J = 10, 7 Hz), 3.75 (1H, m), 2.97 (1H, OH, d, J = 10 Hz), 2.94 (1H, dd, J = 18, 15 Hz), 2.55 (1H, dd, J = 18, 4 Hz), 2.01 (3H, d, J = 2 Hz), 1.87 (3H, s), 0.85 (9H, s), 0.19 (3H, s), 0.17 (3H, s); ^{13}C NMR ($CDCl_3$) δ 203.0, 169.5, 146.2, 143.8, 120.5, 111.4, 73.9, 73.2, 71.9, 68.2, 62.7, 39.1, 37.9, 25.3, 22.5, 18.3, 17.6, −5.21, −5.26; MS (CI) *m/z* 409 (M^+ + 1), 391, 363, 347, 333, 305, 271, 259, 231, 1512, 135, 75; HRMS (CI) *m/z* 409.2048 (M^+ + 1) (calcd for $C_{21}H_{33}O_6Si$: 409.2046).

Diol 40. To a solution of **39** (8.0 mg, 19.6 μmol) in THF (1.5 mL) was added trifluoromethanesulfonic acid (4 μL, 39.2 μmol). The resulting solution was warmed to 50 °C, stirred for 5 h, and poured into aqueous $NaHCO_3$ solution. The mixture was extracted with ether, dried over magnesium sulfate, concentrated, and purified by column chromatography on silica (hexanes−ethyl acetate, 2:1) to give **40** (5.1 mg, 90%) as a colorless crystalline solid: mp 176−177 °C dec: IR (KBr) 3477, 2913, 1770, 1720, 1401, 1161, 1112, 962 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.06 (1H, m), 5.09 (1H, s), 5.02 (1H, dd, J = 9, 5 Hz), 4.76 (1H, dd, J = 6, 5 Hz), 4.09 (1H, OH, d, J = 9 Hz), 2.93 (2H, d, J = 4 Hz), 2.48 (1H, t, J = 4 Hz), 2.09 (3H, d, J = 1 Hz), 1.67 (3H, s), 1.28 (3H, s); ^{13}C NMR ($CDCl_3$) δ 201.4, 171.9, 141.9, 125.7, 86.9, 85.2, 81.9, 74.2, 70.2, 65.3, 49.4, 44.2, 28.5, 26.1, 19.7; MS (CI) *m/z* 295 (M^+ + 1), 277, 266, 259, 253, 233, 215, 205, 163, 135, 125, 97, 85; HRMS (CI) *m/z* 295.1181 (M^+ + 1) (calcd for $C_{15}H_{19}O_6$: 295.1182).

There was also obtained **43** (0.9 mg, 10%) as a colorless oil: IR (film) 3493, 2925, 1770, 1720, 1252, 1202, 1132, 833 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.88 (1H, m), 5.04 (1H, s), 4.91 (1H, d, J = 5 Hz), 4.51 (1H, dd, J = 2, 2Hz), 2.96 (1H, dd, J = 16, 4 Hz), 2.81 (1H, dd, J = 16, 3 Hz), 2.38 (1H, dd, J = 4, 3 Hz), 2.05 (3H, d, J = 2 Hz), 1.54 (3H, s), 1.18 (3H, s), 0.83 (9H, s), 0.08 (6H, s); ^{13}C NMR ($CDCl_3$) δ 202.5, 173.1, 144.0, 123.4, 84.9, 84.6, 82.9, 74.1, 69.2, 67.1, 49.3, 44.1, 28.6, 26.6, 25.3, 19.3, 17.7, −5.0, −5.2; MS (CI) *m/z* 409 (M^+ + 1), 391, 365, 351, 333, 289, 231, 75; HRMS (CI) *m/z* 409.2043 (M^+ + 1) (calcd for $C_{21}H_{33}O_6Si$: 409.2046).

Silyl Ether 42. To a solution of **40** (12.0 mg, 40.8 μmol) in THF (12 mL) was added tetra-*n*-butylammonium fluoride (0.48 mL, 0.476 mmol, 1.0 M in THF) at room temperature under argon. After 0.5 h, the mixture was poured into water, extracted with ether, dried over magnesium sulfate, concentrated, and purified by chromatography on silica (hexanes−ethyl acetate, 3:1) to give a mixture of **41** and **40** (10.0 mg, 83%) in a ratio of 13:1, respectively. The mixture was used in the next step without separation.

To a solution of the mixture of **41** and **40** (11.8 mg, 40.1 μmol) in CH_2Cl_2 (3 mL) at 0 °C was added triethylamine (34 μL, 392 μmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (36 mL, 160.5 μmol). The solution was warmed to room temperature and stirred for 2 h. The mixture was poured into saturated aqueous $NaHCO_3$ solution, extracted with CH_2Cl_2, dried over magnesium sulfate, concentrated, and purified by chromatography on silica (hexanes−ethyl acetate, 3:1) to give **42** (14.4 mg, 88%) as a colorless oil: IR (film) 3490, 2928, 1760, 1724, 1260, 1121, 833 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.06 (1H, m), 5.11 (1H, s), 4.61 (1H, s), 4.39 (1H, d, J = 6 Hz), 3.01 (1H, dd, J = 16, 4 Hz), 2.74 (1H, dd, J = 16, 3 Hz), 2.38 (1H, dd, J = 4, 3 Hz), 2.00 (3H, d, J = 2 Hz), 1.58 (3H, s), 1.30 (3H, s), 0.88 (9H, s), 0.16 (3H, s), 0.09 (3H, s); ^{13}C NMR ($CDCl_3$) δ 200.1, 174.3, 141.2, 126.6, 88.6, 86.5, 82.3, 80.1, 67.8, 61.2, 49.7, 45.5, 28.9, 28.4, 25.6, 19.4, 18.2, −5.0, −5.5; MS (CI) *m/z* 409 (M^+ + 1), 391, 365, 351, 333, 307, 289, 233, 75; HRMS (CI) *m/z* 409.2048 (M^+ + 1) (calcd for $C_{21}H_{33}O_6Si$: 409.2046). There was also obtained **43** (0.8 mg, 5%).

Hydroxy Ketone 45. To a solution of **42** (4.0 mg, 9.8 μmol) in ethanol (2 mL) was added 10% palladium-on-charcoal (2.0 mg), and the suspension was stirred under hydrogen at 20 psi. After 1.5 h, the mixture was filtered over Celite, concentrated under reduced pressure, and purified by chromatography on silica (hexanes−ethyl acetate, 6:1) to give **45** (3.3 mg, 80%) as a colorless oil: IR (film) 3494, 2953, 2933, 1783, 1716, 1228, 1136, 846 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.75 (1H, s), 4.63 (1H, s), 4.46 (1H, d, J = 5 Hz), 2.80 (1H, dd, J = 10, 2 Hz), 2.68 (1H, dd, J = 10, 5 Hz), 2.0−2.4 (4H, m), 1.52 (3H, s), 1.28 (3H, s), 1.23 (3H, d, J = 6 Hz), 0.90 (9H, s), 0.06 (3H, s), 0.03 (3H, s); ^{13}C NMR ($CDCl_3$) δ 200.9, 173.5, 86.8, 84.6, 84.4, 81.4, 78.6, 70.6, 47.1, 44.9, 35.8, 29.3, 28.8, 26.9, 25.6, 18.0, 16.1, −4.8, −5.1; MS (CI) *m/z* 411 (M^+ + 1), 395, 353, 279, 251, 233, 95; HRMS (CI) *m/z* 411.2197 (M^+ + 1) (calcd for $C_{21}H_{35}O_6Si$: 411.2203).

Diol 46. To a solution of **40** (5.0 mg, 17.1 μmol) in hexanes-ethyl acetate (10:1, 2 mL) was added 10% palladium-on-charcoal (2.5 mg), and the suspension was stirred under hydrogen at 18 psi. After 2 h, the mixture was filtered over Celite, concentrated under reduced pressure, and purified by chromatography on silica (hexanes−ethyl acetate, 2:1 to 1:1) to give **46** (3.1 mg, 62%) as a colorless oil: IR (film) 3408, 2968, 2927, 1761, 1715, 1443, 1244, 1136, 978 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.92 (1H, dd, J = 8, 6 Hz), 4.86 (1H, s), 4.73 (1H, t, J = 5 Hz), 2.88 (1H, dd, J = 19, 3 Hz), 2.75 (1H, dd, J = 19, 4 Hz), 2.37 (1H, dd, J = 4, 3 Hz), 2.26 (1H, m), 2.05 (1H, m), 1.88 (1H, d, J = 15, 11 Hz), 1.55 (3H, s), 1.28 (3H, s), 1.27 (3H, d, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 202.7, 171.1, 87.3, 86.6, 81.2, 78.7, 71.8, 64.4, 47.7,

44.4, 29.7, 28.9, 28.8, 26.2, 16.2; MS (CI) *m/z* 296 (M^+), 279, 261, 251, 233, 217, 147, 85; HRMS (CI) *m/z* 296.1261 (M^+) (calcd for $C_{15}H_{20}O_6$: 296.1260).

There was also obtained **47** (0.9 mg, 18%) as an oil: ^{1}H NMR ($CDCl_3$) δ 4.93 (1H, dd, J = 6, 9 Hz), 4.83 (1H, t, J = 5 Hz), 4.66 (1H, d, J = 4 Hz), 2.75 (1H, dd, J = 19, 3 Hz), 2.73 (1H, dd, J = 19, 4 Hz), 2.4−2.6 (3H, m), 1.89 (1H, m), 1.85 (1H, d, J = 15, 4 Hz), 1.57 (3H, s), 1.35 (3H, d, J = 7 Hz), 1.27 (3H, s).

Diol 49. To a suspension of lithium borohydride (80 mg, 3.7 mmol) in ether (4 mL) was added a solution of **42** (25 mg, 0.061 mmol) in ether (4 mL) and methanol (160 μL, 3.7 mmol). After 20 min, the mixture was poured into aqueous $NaHCO_3$ solution, extracted with ether, washed with brine, dried over magnesium sulfate, concentrated, and purified by chromatography on silica (hexanes−ethyl acetate, 4:1) to give **49** (20 mg, 80%) as a colorless oil: IR (film) 3397, 2933, 1759, 1466, 1365, 1123 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.05 (1H, m), 4.65 (1H, d, J = 4 Hz), 4.55 (1H, s), 4.48 (1H, d, J = 7 Hz), 4.15 (1H, m), 2.36 (1H, dd, J = 4, 3 Hz), 2.21 (1H, dd, J = 3, 3 Hz), 2.01 (3H, d, J = 2 Hz), 1.66 (3H, s), 1.62 (3H, s), 0.88 (9H, s), 0.13 (6H, s); ^{13}C NMR ($CDCl_3$) δ 178.4, 141.9, 126.4, 87.6, 86.1, 82.9, 78.0, 65.9, 64.1, 50.9, 33.8, 29.7, 29.4, 25.9, 25.5, 19.8, 17.8, −4.4, −5.0; MS (CI) *m/z* 409 ($M^+ - 1$), 393, 377, 335, 307, 233, 217, 209, 137, 75; HRMS (CI) *m/z* 409.2043 ($M^+ - 1$) (calcd for $C_{21}H_{33}O_6Si$: 409.2046).

Pentaacetate 50. To a solution of **49** (20 mg, 49 μmol) in THF (10 mL) at 0 °C under argon was added excess lithium aluminum hydride (0.6 mL, 1.0 M in THF). The mixture was stirred for 2.5 h at 0 °C and quenched with 0.1 N HCl solution. The mixture was extracted with ethyl acetate, dried over sodium sulfate, concentrated, and purified by chromatography on silica ($CHCl_3$−methanol, 8:1) to give the crude pentaol **48** (10 mg), which was subjected to the next reaction without purification.

To a solution of crude **48** at room temperature was added a crystal of 4-(dimethylamino)pyridine in CH_2Cl_2 (6 mL), triethylamine (0.35 mL, 2.53 mmol), and acetic anhydride (0.16 mL, 1.65 mmol). The mixture was stirred for 4 days, poured into water, extracted with CH_2Cl_2, dried over magnesium sulfate, concentrated under reduced pressure, and purified by chromatography on silica (hexanes−ethyl acetate, 6:1 to 3:1) to give **50** as a colorless crystalline solid (8.0 mg, 32%): mp 195−197 °C: IR (KBr) 2984, 2937, 1746 (br), 1366, 1230, 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.96 (1H, s), 5.65 (1H, m), 5.62 (1H, d, J = 5 Hz), 5.53 (1H, dd, J = 5, 5 Hz), 5.12 (1H, d, J = 7 Hz), 4.40 (1H, d, J = 13 Hz), 4.32 (1H, d, J = 13 Hz), 2.45 (1H, m), 2.0∼2.3 (2H, m), 2.15 (3H, s), 2.09 (3H, s), 2.05 (3H, s), 1.99 (3H, s), 1.98 (3H, s), 1.90 (3H, s) 1.54 (3H, s) 1.48 (3H, s); ^{13}C NMR ($CDCl_3$) δ 170.3, 170.1, 169.8, 169.5, 169.3, 138.2, 124.9, 87.2, 83.4, 79.6, 67.4, 66.9, 64.7, 64.3, 52.7, 49.4, 34.0, 29.7, 25.1, 21.9, 21.6, 21.2, 21.1, 20.9, 20.5; MS (CI) *m/z* 510 (M^+), 468, 451, 408, 350, 289, 217, 159; HRMS (CI) *m/z* 510.2100 ($M^+ - 1$) (calcd for $C_{25}H_{34}O_{11}$: 510.2101).

3,4-Dideoxymaytol (3). A. From 50. To a solution of **50** (4.5 mg, 8.8 μmol) in EtOH (2 mL) was added 10% palladium-on-charcoal (2.5 mg), and the suspension was stirred under a hydrogen atmosphere at 100 psi. After 4 h, the mixture was filtered over Celite and concentrated under reduced pressure. The crude product was added to a solution of sodium methoxide (3 mL, 0.1 N in methanol), and the mixture was stirred for 18 h. Solid ammonium chloride (42 mg) was added, and the resulting suspension was concentrated. The residue was purified by chromatography on silica ($CHCl_3$−methanol, 14:1) to give 3,4-dideoxymaytol (**3**, 2.1 mg, 80%) as an amorphous solid: IR (KBr) 3337, 2924, 1556, 1260, 1105 cm^{-1}; ^{1}H NMR (CD_3OD) δ 4.59 (1H, d, J = 11 Hz) 4.37 (1H, d, J = 3 Hz), 4.34 (1H, s), 4.17 (2H, m), 3.69 (1H, d, J = 11 Hz), 2.0∼2.3 (5H, m), 1.76 (1H, m), 1.54 (3H, s), 1.46 (3H, s), 1.37 (3H, d, J = 9 Hz); ^{13}C NMR (CD_3OD) δ 93.6, 83.5, 77.9, 74.6, 73.4, 69.9, 66.9, 55.4, 52.6, 35.4, 35.2, 35.1, 31.4, 27.3, 20.3; MS (CI) *m/z* 287 ($M^+ - 15$), 249, 231, 219, 204, 147, 125, 86; HRMS (CI) *m/z* 287.1495 ($M^+ - 15$) (calcd for $C_{14}H_{23}O_6$: 287.1495). There was also obtained 4-*epi*-3,4-dideoxymaytol (**51**, 0.5 mg, 20%).

B. From Ever-1 (6). Ever-1 (**6**, 15.0 mg, 24.3 mmol) was added to a solution of sodium methoxide (1.2 mL, 0.1 N in methanol), and the mixture was stirred for 40 h. The mixture was concentrated under reduced pressure and purified by chromatography on silica (ethyl acetate−methanol, 20:1 to methanol) to give **3** (5.6 mg, 76%): $[\alpha]^{23}_D$ −2.5 (*c* 0.12, MeOH). This substance was identical with **3** prepared from **50** (method A) by comparison of IR, ^{1}H and ^{13}C NMR, and mass spectra.

Methyl (1α,2α,4a*β*,5α,6*β*,8aα)-1,5,6,8a-Tetrahydro-6-acetoxy-5-(*tert*-butyldimethylsilyl)-oxy-1,8a-dihydroxy-8-methyl-2-(1-methylethenyl)-4-oxo-4a(4*H*)-naphthalenecarboxy-late (52). A solution of **34** (5.2 mg, 0.012 mmol) in 0.5 mL of acetic acid was heated at 60−65 °C for 4 h. The volatile material was evaporated in vacuo, and the residue was purified by column chromatography (hexane−ethyl acetate, 4:1 to 3:1) to give 4.0 mg (67%) of **52** and 1.5 mg (19%) of **53**, each as an oil. Spectroscopic data for **52**: IR (film) 3535, 3384, 1735, 1438, 1370, 1231, 1153, 1104, 1071, 1020, 838, 785 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.43 (m, 1H), 5.31 (s, 1H), 5.12 (d, J = 5 Hz, 1H), 4.93 (s, 1H), 4.85 (d, J = 1 Hz, 1H), 4.61 (s, 1H), 4.56 (m, 1H), 3.68 (s, 3H), 3.33 (br d, J = 10 Hz, 1H), 2.87 (dd, J = 18, 15 Hz, 1H), 2.50 (m, 2H), 2.08 (s, 3H), 1.98 (s, 3H), 1.86 (s , 3H), 0.82 (s, 9H), 0.28 (s, 3H), 0.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 169.6, 166.6, 144.9, 143.7, 117.1, 111.4, 72.3, 72.0, 69.2, 68.0, 64.5, 52.7, 41.7, 38.3, 25.7, 22.3, 20.9, 19.4, 17.8, −4.9, −5.5; LRMS (CI) *m/z* (rel intensity) 483 (M + 1, 12), 467 (10), 466 (22), 465 (65), 449 (24), 433 (10), 425 (11), 424 (22), 423 (72), 409 (17), 408 (10), 407 (41), 406 (17), 405 (58), 391 (17), 389 (22), 381 (16), 373 (10), 366 (12), 365 (49), 351 (33), 349 (12), 347 (23), 335 (11), 333 (39), 323 (29), 301 (13), 291 (22), 273 (100), 267 (12), 259 (12), 249 (77), 219 (44), 177 (33); HRMS (CI) *m/z* 423.2202 (M^+ − OAc) (calcd for $C_{22}H_{35}O_6Si$: 423.2203).

Methyl (1α,2*β*,6α,11*R and *S**)-2-Acetoxy-1-(*tert*-butyldimethylsilyl)oxy-6-hydroxy-13-iodo-9-oxo-(7*β*H)-5,11-oxy-8-eudesmen-14-oates (54 and 55).** To a stirred solution of **52** (37 mg, 0.0766 mmol) and solid sodium bicarbonate (64 mg, 0.766 mmol) in 1 mL of acetonitrile in an amber-colored bottle was added iodine (49 mg, 0.192 mmol). After 10 h, the mixture was treated with aqueous sodium bisulfite solution and was extracted with ether (10 mL). The separated organic layer was washed with saturated brine, dried, and concentrated in vacuo. Column chromatography (hexane−ethyl acetate, 3:1) of the residue afforded 30 mg (64%) of a 4:1 diastereomeric mixture of **54** and **55**, respectively (based on ^{1}H NMR analysis): MS (CI) *m/z* (rel intensity) 609 (M + 1, 16), 550 (14), 549 (49), 533 (25), 531 (16), 491 (34), 482 (22), 481 (68), 465 (13), 424 (23), 422 (47), 421 (100), 407 (34), 405 (64), 403 (28), 389 (42), 365 (40), 363 (22), 349 (22), 333 (22), 309 (27), 307 (22), 291 (61), 289 (38), 277 (38), 177 (52); HRMS (CI) *m/z* 609.1383 ($M^+ + 1$) (calcd for $C_{24}H_{38}IO_8Si$: 609.1381).

Methyl (1α,2α,4a*β*,5α,8α,8aα)-1,2,3,5,8,8a-Hexahydro-5-(*tert*-butyldimethylsilyl)oxy-1-hydroxy-8(*β*)-methyl-2-[1(R* and S*)-methyl]-epoxyethenyl-4-oxo-4a(4*H*)-8,8a-epoxynaphthalenecarboxylates (56 and 57). To a stirred solution of **34** (36 mg, 0.085 mmol), 2,6-lutidine (10 μL, 0.085 mmol), and *tert*-butyl hydroperoxide (5.0−6.0 M in isooctane, 51 μL, 0.256 mmol) in 1 mL of toluene was added solid vanadium oxyacetylacetonate (0.7 mg, 0.00256 mmol) at room temperature. After 2 days, the mixture was passed through a short pad of silica gel, using ether as eluent, and the eluent was concentrated in vacuo. Column chromatography (hexane−ethyl acetate, 6:1 to 3:1) of the residue afforded 19.2 mg (53%) of **56** and 6.8 mg (19%) of **57**, each as an oil. Spectroscopic data for **56**: IR (film) 3469, 1752, 1723, 1437, 1391, 1252, 1202, 1144, 1097, 910, 842, 776 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.98 (d, J = 10 Hz, 1H), 5.89 (dd, J = 10, 6 Hz, 1H), 5.01 (d, J = 6 Hz, 1H), 4.67 (ddd, J = 5, 5, 2 Hz, 1H), 3.65 (s, 3H), 3.07 (d, J = 5 Hz, 1H), 2.81 (d, J = 4 Hz, 1H), 2.66 (m, 2H), 2.51 (ddd, J = 15, 2, 2 Hz, 1H), 1.82 (ddd, J = 14, 4, 3 Hz, 1H), 1.61 (s, 3H), 1.46 (s, 3H), 0.80 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 167.3, 133.9, 131.5, 69.0, 66.8, 64.6, 64.0, 58.5, 57.1, 53.4, 52.2, 43.2, 38.1, 25.6, 20.0, 17.8, 16.6, 04.0, −5.1; MS (CI) *m/z* (rel intensity) 439 (M + 1, 43), 423 (42), 421 (100), 407 (49), 403 (40), 389 (87), 381 (50), 373 (44), 363 (57), 345 (37), 331 (36), 307 (85), 277 (58), 275 (82), 247 (42), 243 (50), 229 (71), 213 (42), 167 (33). Anal. Calcd for $C_{22}H_{34}O_7Si$: C, 60.25; H, 7.81. Found: C, 60.10; H, 7.80.

Spectroscopic data for **57**: IR (film) 3474, 1753, 1723, 1253, 1200, 1096, 1064, 842, 814, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (d, J = 10 Hz, 1H), 5.90 (dd, J = 10, 6 Hz, 1H), 5.00 (d, J = 6 Hz, 1H), 4.51 (m, 1H), 3.68 (s, 3H), 2.95 (d, J = 4 Hz, 1H), 2.67 (d, J = 4 Hz, 1H), 2.63 (d, J = 4 Hz, 1H), 2.32 (m, 3H), 1.63 (s, 3H), 1.52 (s, 3H), 0.79 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$)

δ 199.8, 167.3, 133.7, 131.6, 69.1, 67.2, 64.0, 63.8, 58.5, 56.6, 53.4, 51.1, 41.3, 36.0, 25.6, 21.1, 17.8, 16.7, −4.0, −5.1.

Methyl (1α,2*β*,6α,11R*)-2-Acetoxy-1-(*tert*-butyldimethylsilyl)oxy-6,13-dihydroxy-9-oxo-(7*β*H)-5,11-epoxy-8-eudesmen-14-oate (58). A solution of **57** (16.6 mg, 0.0379 mmol) in 1 mL of acetic acid was heated at 60−65 °C for 4 h. The mixture was cooled to room temperature, and the volatile material was removed in vacuo. Column chromatography (hexane−ethyl acetate, 2:3 to 1:2) of the residue afforded 8.2 mg (44%) of **58** as an oil: IR (film) 3510, 3477, 1718, 1236, 1143, 1112, 1085, 1026, 992, 963, 840 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.59 (d, J = 4 Hz, 1H), 5.24 (d, J = 2 Hz, 1H), 5.12 (s, 1H), 4.82 (s, 1H), 3.68 (s, 3H), 3.57 (d, J = 12 Hz, 1H), 3.45 (d, J = 12 Hz, 1H), 2.97 (dd, J = 18, 3 Hz, 1H), 2.49 (dd, J = 18, 4 Hz, 1H), 2.42 (m, 1H), 2.13 (s, 3H), 2.01 (s, 3H), 1.52 (s, 3H), 0.87 (s, 9H), 0.21 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.5, 169.4, 168.2, 139.5, 123.4, 84.9, 84.6, 84.7, 72.7, 72.0, 69.8, 67.4, 52.8, 47.8, 44.0, 25.8, 24.3, 21.7, 21.0, 18.2, −4.3, −6.1; MS (CI) *m/z* (rel intensity) 499 (M + 1, 16), 498 (M, 2), 481 (10), 441 (16), 440 (31), 439 (100), 425 (8), 424 (15), 423 (53), 422 (15), 421 (46), 407 (32), 405 (15), 403 (25), 391 (25), 382 (17), 381 (68), 367 (27), 349 (33), 307 (44), 289 (58), 275 (55), 257 (51), 243 (22), 233 (22), 231 (25), 229 (21), 177 (56), 141 (30), 133 (31); HRMS (CI) *m/z* 499.2361 (M^+ + 1) (calcd for $C_{24}H_{39}O_9Si$: 499.2363).

Methyl (1α,2*β*,6α,11R*)-2-Acetoxy-1-(*tert*-butyldimethylsilyl)oxy-6-hydroxy-13-*p*-nitrobenzoyloxy-9-oxo-(7*β*H)-5,11-epoxy-8-eudesmen-14-oate (59). To a stirred solution of **58** (8 mg, 0.016 mmol), triethylamine (7 μL, 0.0481 mmol), and *p*-nitrobenzoyl chloride (6 mg, 0.0321 mmol) in 0.2 mL of methylene chloride at room temperature was added a catalytic amount of *N*,*N*-dimethylaminopyridine (DMAP). After 6 h, aqueous sodium bicarbonate was added, and the mixture was extracted with ether (8 mL). The separated organic layer was dried and concentrated in vacuo. Column chromatography (hexane−ethyl acetate, 3:1 to 1:1) of the residue afforded 5 mg (48%) of **59** as a colorless solid: mp 213−214 °C; IR (KBr) 35011, 1728, 1529, 1349, 1273, 1264, 1259, 1235, 1142, 1110, 1017, 993, 840, 724 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 9 Hz, 2H), 8.17 (d, J = 9 Hz, 2H), 5.63 (d, J = 6 Hz, 1H), 5.24 (br s, 2H), 4.79 (s, 1H), 4.30 (d, J = 11 Hz, 1H), 4.25 (d, J = 11 Hz, 1H), 3.69 (s, 3H), 2.81 (dd, J = 16, 2 Hz, 1H), 2.60 (m, 2H), 2.15 (s, 3H), 2.02 (s, 3H), 1.66 (s, 3H), 0.85 (s, 9H), 0.20 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.0, 169.6, 168.1, 163.9, 150.6, 138.9, 135.1, 130.6, 124.6, 124.6, 123.5, 85.6, 83.2, 82.8, 72.2, 70.2, 69.8, 52.9, 47.7, 43.6, 25.8, 24.9, 21.7, 21.0, 18.2, −4.4, −6.1; MS (CI) *m/z* (rel intensity) 648 (M^+ + 1, 13), 589 (17), 588 (47), 572 (17), 570 (34), 556 (14), 531 (11), 530 (23), 456 (35), 422 (11), 421 (32), 403 (14), 333 (16), 307 (14), 289 (35), 257 (14), 224 (19), 177 (100), 168 (35), 159 (15); HRMS (CI) *m/z* 648.2476 (M^+ + 1) (calcd for $C_{31}H_{42}O_{13}NSi$: 648.2476).

Compound **59** crystallized from octane−ethyl acetate in the space group P2(1)/c with a = 13.361 (3) Å, b = 13.611 (2) Å, c = 18.573 (2) Å, β = 91.57 (2)°, z = 4, and d_{calcd} = 1.306 g/cm^3. The intensity data were measured on a Siemens P4 diffractometer (Cu Kα radiation). There were 3118 unique reflections, and the structure was solved by direct methods. The final discrepancy indices were R = 0.0535 and R_w = 0.0546.

Lactone 62. To a solution of **56** (486 mg, 1.11 mmol) in chloroform (17 mL) was added trifluoroacetic acid (0.13 mL, 1.67 mmol) in one portion at room temperature. After 1 h, triethylamine (0.15 mL, 1.11 mmol) was added, and the reaction mixture was concentrated under reduced pressure to give **61**. An analytical sample of **61** was obtained by chromatography on silica (hexane:ethyl acetate, 2:1 to 1:1) to give the pure substance as a colorless oil: IR (film) 3292, 1782, 1721, 1379, 1221, 1151, 1115, 1039, 966, 934, 840, 779 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.51 (1H, s), 5.46 (1H, br s), 5.04 (1H, s), 4.95 (1H, d, J = 2 Hz), 3.73 (1H, d, J = 12 Hz), 3.69 (1H, d, J = 12 Hz), 3.67 (3H, s), 2.81 (1H, dd, J = 19, 3 Hz), 2.72 (1H, dd, J = 19, 4 Hz), 2.49 (1H, t, J = 3 Hz), 2.12 (3H, s), 1.20 (3H, s), 0.83 (9H, s), 0.18 (3H, s), 0.09 (3H, s); MS (CI) *m/z* 553 (M^+ + 1) , 440, 439, 423, 381, 307, 289, 177, 133, 129, 115; HRMS (CI) *m/z* 553.2078 (M^+ + 1) (calcd for $C_{24}H_{36}F_3O_9Si$: 553.2080).

To **61** was added THF−pyridine-water (4:1:1, 18 mL) at room temperature, and, after 3 h, ethyl acetate (20 mL) was added to the reaction mixture. The solution was dried over magnesium sulfate, concentrated under reduced pressure, and diluted with acetonitrile (17 mL). Imidazole (755 mg, 11.1 mmol) was added to the solution, which was stirred for 20 h. The mixture was concentrated under reduced pressure and chromatographed on silica (hexanes−ethyl acetate, 1:1) to give **62** (357 mg, 76% from **56**) as a colorless oil: IR (film) 3412, 2952, 2929, 2895, 1771, 1720, 1249, 1178 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.88 (1H, d, J = 5 Hz), 4.94 (1H, d, J = 5 Hz), 4.89 (1H, s), 4.51 (1H, dd, J = 5, 5 Hz), 3.73 (2H, s), 3.03 (1H, dd, J = 17, 4 Hz), 2.80 (1H, dd, J = 5, 3 Hz), 2.54 (1H, t, J = 3 Hz), 2.02 (3H, s), 1.13 (3H, s), 0.81 (9H, s), 0.07 (3H, s), 0.06 (3H, s); ^{13}C NMR ($CDCl_3$) δ 203.0, 173.1, 143.7, 123.6, 86.3, 84.8, 81.7, 74.0, 69.2, 69.0, 67.1, 46.3, 44.3, 25.3, 21.7, 19.4, 17.6, −5.0, −5.2; MS *m/z* 425 (M^+ + 1), 407, 381, 275, 231, 133; HRMS (CI) *m/z* 425.1994 (M^+ + 1) (calcd for $C_{21}H_{32}O_7$-Si: 425.1995).

Benzylidene Acetal 63. To a stirred solution of **62** (356 mg, 0.839 mmol) in toluene (20 mL) was added benzaldehyde dimethyl acetal (1.2 mL, 8.40 mmol) and a catalytic amount of pyridinium *p*-toluenesulfonate. The mixture was refluxed for 2 h, concentrated under reduced pressure, and chromatographed on silica (hexanes−ethyl acetate, 20:1 to 4:1) to give **63** (359 mg, 83%) as a colorless amorphous solid: mp 252−254 °C; IR (KBr) 2956, 1770, 1723, 666 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.52 (2H, m), 7.36 (3H, m), 5.87 (1H, dd, J = 6, 2 Hz), 5.85 (1H, s), 5.32 (1H, s), 4.96 (1H, d, J = 5 Hz), 4.51 (1H, dd, J = 6, 5 Hz), 3.84 (1H, d, J = 12 Hz), 3.56 (1H, d, J = 12 Hz), 3.20 (2H, m), 2.92 (1H, dd, J = 17, 4 Hz), 2.10 (3H, d, J = 2 Hz), 1.20 (3H, s), 0.84 (9H, s), 0.10 (3H, s), 0.09 (3H, s); ^{13}C NMR ($CDCl_3$) δ 201.8, 172.5, 144.5, 138.5, 128.4, 128.1, 125.9, 123.8, 98.0, 86.2, 85.8, 85.6, 76.3, 73.9, 69.0, 67.2, 42.8, 41.8, 25.3, 20.9, 19.9, 17.7, −5.0, −5.2; MS *m/z* 513 (M^+ + 1), 469, 455, 407, 349, 305, 231, 159; HRMS (CI) *m/z* 513.2306 (M^+ + 1) (calcd for $C_{28}H_{37}O_7Si$: 513.2308).

Lactone 64. To a solution of **63** (359 mg, 0.699 mmol) in THF (26 mL) was added tetra-*n*-butylammonium fluoride (7.0 mL, 7.0 mmol, 1 M in THF). After 2 h, water was added to the mixture, which was extracted with ether. The ethereal extract was dried over magnesium sulfate, concentrated under reduced pressure, and chromatographed on silica (hexanes−ethyl acetate, 1:1) to give **64** (268 mg, 96%) as colorless plates: mp 236 °C dec; IR (KBr) 3485, 2927, 1765, 1702, 1134, 998 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47 (2H, m), 7.37 (3H, m), 6.06 (1H, dd, J = 7, 2 Hz), 5.83 (1H, s), 5.41 (1H, s), 5.15 (1H, s), 4.82 (1H, s), 4.57 (1H, d, J = 7 Hz), 3.90 (1H, d, J = 13 Hz), 3.58 (1H, d, J = 13 Hz), 3.28 (2H, m), 2.92 (1H, dd, J = 17, 5 Hz), 2.02 (3H, s), 1.30 (3H, s); ^{13}C NMR ($CDCl_3$) δ 208.9, 172.2, 141.4, 138.0, 128.5, 128.2, 127.2, 125.9, 98.2, 88.9, 87.4, 84.7, 77.6, 77.4, 76.6, 67.7, 43.9, 42.2, 21.2, 19.2; MS *m/z* 399 (M^+ + 1), 381, 355, 321, 231, 107; HRMS (CI) *m/z* 399.1444 (M^+ + 1) (calcd for $C_{22}H_{22}O_7$: 399.1444).

Compound **64** crystallized in the monoclinic space group $p2_1$ with a = 8.744 (2) Å, b = 9.658 (2) Å, c = 22.430 (4) Å, β = 93.76 (3), V = 1890.1 (7) Å^3, Z = 4, D_{calc} = 1.4 Mg/m^3. All 2320 nonequivalent reflections were measured on a Siemens P4 diffractometer with graphite monochromated Cu Kα radiation (λ = 1.54178 Å). The structure was solved by direct methods (SHELXS) using 1981 unique reflections with $F > 3\sigma(F)$. Full matrix least squares refinement with anistropic temperature factors for all non-hydrogen atom positions led to the final discrepancy indices of R = 8.34 and R_w = 8.13.

Silyl Ether 65. To a solution of **64** (59 mg, 0.148 mmol) in dichloromethane (5 mL) at 0 °C was added triethylamine (67 mg, 0.666 mmol) and *tert*-butyldimethylsilyl triflate (0.1 mL, 0.444 mmol). After 1.2 h, the mixture was diluted with saturated, aqueous sodium bicarbonate solution, extracted with ether, dried over magnesium sulfate, concentrated, and chromatographed on silica (hexanes−ethyl acetate, 1:1) to give **65** (76 mg, 100%) as a colorless amorphous solid: mp 180−181°C; IR (KBr) 2926, 1768, 1729, 1129, 966 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.46 (2H, m), 7.35 (3H, m), 6.03 (1H, dd, J = 7, 2 Hz), 5.82 (1H, s), 5.38 (1H, s), 4.64 (1H, s), 4.38 (1H, d, J = 7 Hz), 3.88 (1H, d, J = 13 Hz), 3.57 (1H, d, J = 13 Hz), 1.31 (3H, s), 0.87 (9H, s), 0.17 (3H, s), 0.13 (3H, s); ^{13}C NMR ($CDCl_3$) δ 200.3, 184.2, 173.2, 141.5, 138.1, 128.5, 128.1, 127.4, 125.9, 97.9, 90.2, 87.8, 85.1, 79.5, 76.6, 76.2, 68.3, 44.0, 42.2, 25.6, 21.4, 18.9, −4.9, −5.4; MS *m/z* 513 (M^+ + 1) , 411, 349, 305, 231, 159; HRMS (CI) *m/z* 513.2292 (M^+ + 1) (calcd for $C_{28}H_{37}O_7Si$: 513.2308).

Diol 66. To a solution of **65** (6.1 mg, 0.012 mmol) in pyridine (0.2 mL) was added osmium tetraoxide (0.057 mL, 0.014 mmol, 0.25 M in pyridine). The mixture was stirred for 48 h at room temperature, diluted with water (3 drops) and sodium bisulfite (10 mg), and stirred for 5 h.

The suspension was diluted with ethyl acetate, and the resultant solution was dried over sodium sulfate, concentrated, and chromatographed on silica (hexanes−ethyl acetate, 2:1) to give **66** (6.0 mg, 92%) as a colorless amorphous solid: mp 238−240 °C; IR (KBr) 3528, 2952, 2929, 2856, 1778, 1712, 1128, 1078, 860, 734 $cm^{-1;}$ ^1H NMR ($CDCl_3$) δ 7.39 (2H, m), 7.36 (3H, m), 5.96 (1H, s), 5.37 (1H, s), 4.58 (1H, s), 4.49 (1H, d, J = 2 Hz), 3.94 (1H, d, J = 13 Hz), 3.61 (1H, d, J = 13 Hz), 3.45 (1H, d, J = 11 Hz), 3.36 (1H, d, J = 11 Hz), 3.19 (1H, m), 2.91 (3H, m), 1.67 (3H, s), 1.29 (3H, s), 0.92 (9H, s), 0.11 (3H, s), 0.05 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.5, 171.9, 137.7, 128.9, 128.4, 125.9, 98.1, 90.6, 88.6, 87.9, 84.0, 77.2, 76.2, 76.1 (two lines), 72.6, 68.3, 43.7, 39.3, 25.7, 25.0, 20.3, 18.2, −4.7, −5.1; MS (CI) *m/z* 547 (M^+ + 1), 531, 489, 441, 263, 187; HRMS (CI) *m/z* 547.2365 (M^+ + 1) (calcd for $C_{28}H_{39}O_9Si$: 547.2363)

Carbonate 67. To a solution of **66** (15.9 mg, 0.0291 mmol) in methylene chloride (3 mL) at 0 °C was added pyridine (0.12 mL, 1.46 mmol) and phosgene (0.15 mL, 0.29 mmol, 1.93 M solution in toluene). The mixture was stirred for 1.3 h at room temperature, and the excess phosgene was removed under reduced pressure until the volume of the mixture had decreased to approximately half of the original volume. The residue was diluted with saturated, aqueous sodium bicarbonate, extracted with ethyl acetate (3×), dried over sodium sulfate, concentrated, and chromatographed on silica (hexanes−ethyl acetate, 3:1) to give **67** (16.0 mg, 97%) as a colorless crystalline solid: mp 210 °C dec; IR (KBr) 2925, 2852, 1803, 1785, 1718, 1122, 1035, 777 $cm^{-1;}$ ^1H NMR ($CDCl_3$) δ 7.49 (2H, m), 7.36 (3H, m), 5.92 (1H, s), 5.37 (1H, s), 4.61 (1H, s), 4.59 (1H, d, J = 3 Hz), 4.32 (1H, d, J = 3Hz), 3.88 (1H, d, J = 13 Hz), 3.65 (1H, d, J = 13 Hz), 3.26 (1H, m), 3.03 (1H, dd, J = 18, 4 Hz), 2.90 (1H, dd, J = 18, 4 Hz), 1.85 (3H, s), 1.28 (3H, s), 0.91 (9H, s), 0.15 (3H, s), 0.07 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2, 169.7, 152.3, 137.8, 128.8, 128.4, 126.2, 98.0, 89.4, 87.7, 86.0, 82.9, 82.9, 77.4, 75.7, 74.1, 65.9, 44.1, 39.9, 25.5, 23.9, 20.0, 18.3, −4.8, −5.3; MS (CI) *m/z* 573 (M^+ + 1), 557, 537, 529, 515, 485, 467, 459, 409; HRMS (CI) *m/z* 573.2156 (M^+ + 1) (calcd for $C_{29}H_{37}O_{10}Si$: 573.2156).

Compound **67** crystallized in the monoclinic space group $p2_1/c$ with a = 12.947 (3) Å, b = 10.980 (2) Å, c = 20.621 (4) Å, β = 96.09 (3), V = 2914.9 (10) Å^3, Z = 4, D_{calc} = 1.305 Mg/m^3. All 3895 nonequivalent reflections in the range of 22.2° < 2Θ < 53.4° were measured on a Siemens P4 diffractometer with graphite monochromated Cu Kα radiation (λ = 1.54178 Å). The structure was solved by direct methods (SHELXS) using 3124 unique reflections with $F > 4\sigma(F)$. Full matrix least squares refinement with anistropic temperature factors for all non-hydrogen atom positions led to the final discrepancy indices of R = 5.94 and R_w = 6.38.

α-Hydroxy Ketone 69. To a stirred solution of **65** (30 mg, 58.5 μmol) in THF (3 mL) at −78 °C under argon was added potassium hexamethyldisilazide (116 μL, 87.9 μmol, 0.5 M in toluene). After 15 min, the oxaziridine **68** (23 mg, 0.0879 mmol, prepared from *N*-benzylidenebenzenesulfonamide) in THF (1 mL) was added to the mixture. The solution was stirred for 45 min at −78°C, and aqueous ammonium chloride solution was added slowly. The mixture was extracted with ether, dried over magnesium sulfate, and chromatographed on silica (hexane: ethyl acetate, 7:1) to give **69** (26 mg, 83%) as a colorless amorphous solid: mp 230 °C dec; IR (KBr) 3409, 2953, 1729, 1131, 984 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47 (2H, m), 7.35 (3H, m), 6.06 (1H, d, J = 7 Hz), 5.83 (1H, s), 5.53 (1H, d, J = 9 Hz), 5.49 (1H, s), 4.68 (1H, s), 4.49 (1H, d, J = 7 Hz), 4.37 (1H, dd, J = 4 Hz), 3.86 (1H, d, J = 13 Hz), 3.59 (1H, d, J = 13 Hz), 3.31 (1H, d, J = 4 Hz), 2.04 (3H, s), 1.27 (3H, s), 0.89 (9H, s), 0.19 (3H, s), 0.12 (3H, s); ^{13}C NMR ($CDCl_3$) δ 197.5, 176.3, 141.8, 138.1, 128.6, 128.2, 126.9, 125.9, 98.4, 90.5, 85.9, 81.7, 81.1, 77.1, 77.0, 71.2, 49.7, 29.7, 25.7, 21.5, 18.5, 18.2, −4.9, −5.3; MS *m/z* 529 (M^+ + 1), 467, 427, 303, 247, 174; HRMS (CI) *m/z* 529.2252 (M^+ + 1) (calcd for $C_{28}H_{37}O_8Si$: 529.2258).

Diol 70. To a stirred solution of **69** (3.8 mg, 0.0072 mmol) in tetrahydrofuran (1.2 mL) at room temperature was added titanium tetraisopropoxide (6.4 μL, 0.022 mmol). After 15 min, the mixture was cooled to −78 °C, and solid sodium borohydride (1.0 mg, 0.022 mmol) was added. The mixture was stirred for 1.5 h at −78 °C, warmed to room temperature, and stirred for 30 min. The residual sodium borohydride was destroyed with a few drops of acetone, and the mixture was diluted with ethyl acetate, washed with saturated aqueous ammonium chloride solution, dried over sodium sulfate, and concentrated under reduced pressure. The residual oil was purified by chromatography on silica (hexanes−ethyl acetate, 9:1) to give **70** (2.8 mg, 74%) as a colorless oil: IR (film) 2918, 2851, 1746, 1464, 909, 733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45 (2H, m), 7.33 (3H, m), 6.05 (1H, dd, J = 7, 1 Hz), 5.79 (1H, s), 5.11 (1H, s), 4.59 (1H, s), 4.54 (1H, dd, J = 10, 4 Hz), 4.25 (1H, d, J = 5 Hz), 4.17 (1H, d, J = 10 Hz), 3.88 (1H, d, J = 13 Hz), 3.57 (1H, d, J = 13 Hz), 3.21 (1H, d, J = 4 Hz), 2.99 (1H, d, J = 5 Hz), 2.08 (3H, d, J = 1 Hz), 1.56 (3H, s), 0.90 (9H, s), 0.21 (6H, s); MS (CI) *m/z* 531 (M^+ + 1), 473, 409, 367, 341, 231, 209; HRMS (CI) *m/z* 531.2414 (M^+ + 1) (calcd for $C_{28}H_{39}O_8Si$ 531.2414).

α-Hydroxy Ketone 71. To a solution of trimethylaluminum (0.080 mL, 0.16 mmol, 2.0 M in toluene) in tetrahydrofuran (1.7 mL) at 0°C was added **69** (0.0142 g, 0.027 mmol) in tetrahydrofuran (0.8 mL). After stirring for 2 h at 0 °C, the mixture was stirred at room temperature for a further 3 h. The mixture was cooled to 0 °C and diluted with saturated aqueous ammonium chloride (0.1 mL), and the aqueous layer was extracted with ethyl acetate (3×) and tetrahydrofuran (3×). The combined organic extracts were dried over sodium sulfate, and the solvent was removed under reduced pressure to give pure **71** (0.0142 g, 100%) as a colorless oil. An analytical sample of **71** was obtained by chromatography on silica (hexanes−ethyl acetate, 6:1): IR (film) 3480, 2959, 2933, 2858, 1772, 1729, 1456, 1384, 1132, 781 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42 (2H, m), 7.34 (3H, m), 6.13 (1H, d, J = 6 Hz), 5.71 (1H, s), 5.21 (1H, s), 4.76 (1H, s), 4.65 (1H, d, J = 5 Hz), 4.50 (1H, d, J = 6 Hz), 3.95 (1H, d, J = 13 Hz), 3.85 (1H, s), 3.56 (1H, d, J = 13 Hz), 3.21 (1H, d, J = 5 Hz), 2.02 (3H, s), 1.38 (3H, s), 0.93 (9H, s), 0.18 (3H, s), 0.17 (3H, s); ^{13}C NMR ($CDCl_3$) δ 201.9, 173.5, 140.9, 137.6, 129.0, 128.7, 128.2, 125.9, 99.0, 90.4, 85.9, 82.2, 79.2, 77.8, 76.6, 73.4, 61.9, 59.4, 25.5, 21.1, 18.7, 18.0, −4.8, −4.9; MS *m/z* 529 (M^+ + 1), 513, 471, 467, 451, 427, 423, 397, 365, 247, 174; HRMS (CI) *m/z* 529.2260 (M^+ + 1) (calcd for $C_{28}H_{37}O_8Si$: 529.2258).

Pentaacetate 74. To a solution of **71** (22.2 mg, 0.042 mmol) in tetrahydrofuran (1.5 mL) at 0 °C was added lithium aluminum hydride (20 mg, 0.53 mmol) in small portions. The mixture was stirred for 18 h at room temperature and then cooled to 0 °C. An ice-cold, aqueous solution of 0.5 N HCl was added until the stirred mixture became homogeneous. The aqueous layer was extracted with ethyl acetate (5 × 10 mL), and the combined organic extract was washed with saturated, aqueous sodium bicarbonate and dried over sodium sulfate. The solution was concentrated, and the resultant mixture of **72** and **73** was used without further purification.

To a solution of crude **72** (14.6 mg, 0.035 mmol) in methylene chloride (1.8 mL) at 0 °C was added triethylamine (0.22 mL), acetic anhydride (0.11 mL), and a catalytic amount of 4-(dimethylamino)-pyridine. The mixture was stirred at room temperature for 72 h, concentrated under reduced pressure, diluted with saturated, aqueous sodium bicarbonate (0.5 mL), and extracted with ethyl acetate (4 × 5 mL). The organic layer was dried over sodium sulfate, concentrated, and chromatographed on silica (hexanes−ethyl acetate, 2:1) to give **74** (7.8 mg, 31%) as an oil: IR (film) 2935, 2915, 2858, 1747, 1371, 1231, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48 (2H, m), 7.37 (3H, m), 5.77 (1H, s), 5.67 (1H, d, J = 4 Hz), 5.53 (3H, m), 5.34 (1H, d, J = 6 Hz), 5.30 (1H, s), 4.84 (1H, d, J = 13 Hz), 4.32 (1H, d, J = 13 Hz), 3.90 (1H, d, J = 13 Hz), 3.56 (1H, d, J = 13 Hz), 3.10 (1H, d, J = 4 Hz), 2.25 (3H, s), 2.19 (3H, s), 2.05 (3H, s), 2.04 (3H, s), 1.98 (3H, s), 1.90 (3H, s), 1.48 (3H, s); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.3, 169.8, 169.4, 169.0, 141.6, 138.2, 128.6, 128.2, 126.1, 123.4, 98.9, 88.3, 83.4, 79.8, 77.2, 72.2, 71.6, 69.7, 64.6, 60.8, 49.3, 47.4, 24.1, 21.1 (two lines), 20.7, 20.6, 20.5, 17.8; MS *m/z* 631 (M^+ + 1), 571, 527, 513, 481, 465, 405, 345, 298; HRMS (CI) *m/z* 631.2387 (M^+ + 1) (calcd for $C_{32}H_{39}O_{13}$ 631.2391).

Heptaacetate 76. A. From 74. To a solution of **74** (6.1 mg, 9.7 μmol) in acetonitrile (1 mL) at 0 °C was added HF (two drops of a 48% aqueous solution). The mixture was warmed to room temperature, stirred for 75 min, cooled to 0° C, diluted with saturated, aqueous sodium bicarbonate (0.5 mL), and extracted with ethyl acetate (3 × 10 mL). The organic extract was dried over sodium sulfate and concentrated under reduced pressure to give the crude diol **75**. To a solution of crude **75** in methylene chloride (0.5 mL) was added triethylamine (0.060 mL), acetic anhydride (0.030 mL), and a catalytic amount of

4-(dimethylamino)pyridine. The mixture was stirred for 48 h and then concentrated under reduced pressure. The residue was diluted with saturated, aqueous sodium bicarbonate (0.5 mL), and the solution was extracted with ethyl acetate (4 × 5 mL) and dried over sodium sulfate. The extract was concentrated, and the residual oil was chromatographed on silica (hexanes−ethyl acetate, 1:1) to yield **76** (2.7 mg, 43%) as a colorless oil: IR (film) 3467, 2964, 2933, 2856, 1747, 1440, 1371, 1236, 1128, 1043, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.17 (1H, s), 5.58 (2H, m), 5.20 (2H, m), 5.34 (1H, d, J = 6 Hz), 4.80 (1H, d, J = 13 Hz), 4.65 (1H, d, J = 11 Hz), 4.39 (1H, d, J = 13 Hz), 3.96 (1H, d, J = 11 Hz), 2.55 (1H, d, J = 4 Hz), 2.17 (3H, s), 2.13 (3H, s), 2.08 (3H, s), 2.02 (3H, s), 1.99 (6H, s), 1.97 (3H, s), 1.90 (3H, s), 1.55 (3H,s); ^{13}C NMR ($CDCl_3$) δ 170.4, 170.3, 169.8, 169.3 (two lines), 169.0 (two lines), 138.7, 124.5, 87.1, 81.8, 71.6, 71.4, 69.9, 69.0, 64.2, 60.8, 50.2, 49.6, 21.8, 21.5, 20.9 (three lines), 20.7, 20.6, 20.5, 19.6; MS (CI) *m/z* 627 ($M^+ + 1$) 626, 567, 553, 525, 507, 465, 447, 405, 391, 357; HRMS (CI) *m/z* 567.2075 ($M^+ - OAc$) (calcd for $C_{27}H_{35}O_{13}$ 567.2077).

B. From 71. To a solution of **71** (7.7 mg, 14.6 μmol) in tetrahydrofuran (0.7 mL) at 0 °C was added lithium aluminum hydride (0.11 mL, 0.11 mmol, 1.0 M in tetrahydrofuran). The mixture was stirred for 30 min at 0 °C and then for 15 h at room temperature. The mixture was cooled to 0 °C, and water (5 drops) was added. The mixture was concentrated under reduced pressure, diluted with water (2 mL), and filtered through Amberlite 120 (plus) resin (water−acetic acid, 1:1). The filtrate was concentrated under reduced pressure, and the residue was taken up into methylene chloride (1 mL) containing triethylamine (0.2 mL), acetic anhydride (0.1 mL), and a catalytic amount of 4-(dimethylamino)pyridine. The mixture was stirred for 4 days at room temperature, concentrated under reduced pressure, diluted with saturated, aqueous sodium bicarbonate (0.1 mL), and extracted with ethyl acetate (4 × 10 mL). The extract was dried over sodium sulfate and was concentrated to leave a residual oil which was chromatographed on silica (hexanes−ethyl acetate, 1:1) to give **76** (3.2 mg, 33%) as a colorless oil.

Euonyminol Octaacetate (78). **A. From 76.** To a solution of **76** (1.8 mg, 0.0027 mmol) in pyridine (0.050 mL) was added osmium tetraoxide (0.043 mL, 0.011 mmol, 0.26 M in pyridine). The mixture was stirred for 48 h, diluted with aqueous sodium bisulfite solution, stirred for 5 h, and extracted with ethyl acetate (4 × 10 mL). The organic layer was washed with brine, dried over sodium sulfate, and concentrated under reduced pressure to give a mixture of diols that was used without further purification. To a solution of this mixture in pyridine (0.15 mL) at room temperature was added acetic anhydride (0.050 mL, 0.54 mmol). The mixture was stirred for 4 days at room temperature and concentrated under reduced pressure. The residue was diluted with saturated, aqueous sodium bicarbonate (0.1 mL), extracted with ethyl acetate (4 × 5 mL), dried over sodium sulfate, concentrated under reduced pressure, and chromatographed on silica (hexanes−ethyl acetate, 3:1 to 4:1) to give euonyminol octaacetate (**78**) (0.3 mg, 16%) as an oil: IR (film) 3430, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.76 (1H, s), 5.57 (1H, d, J = 6 Hz), 5.47 (1H, dd, J = 6, 4 Hz), 5.33 (1H, J = 6 Hz), 5.26 (1H, m), 5.20 (1H, d, J = 13 Hz), 4.88 (1H, d, J = 12 Hz), 4.81 (1H, d, J = 2 Hz), 4.40 (1H, d, J = 13 Hz), 3.94 (1H, d, J = 12 Hz), 2.31 (1H, d, J = 4 Hz), 2.24 (3H, s), 2.15 (3H, s), 2.14 (3H, s), 2.12 (3H, s), 2.11 (3H, s), 2.10 (3H, s), 1.97 (3H, s), 1.87 (3H, s), 1.56 (3H, s), 1.46 (3H, s); MS (CI) *m/z* 703 ($M^+ + 1$) 685, 643, 629, 601, 583, 541, 523, 407, 123; HRMS (CI) *m/z* ($M^+ - OH$) 685.2341 (calcd for $C_{31}H_{41}O_{17}$ 703.2345).

There was also obtained **77** (1.1 mg, 60%) as an amorphous solid: mp 242−244 °C; IR (KBr) 3444, 2956, 2918, 2848, 1747, 1369, 1238, 1109, 1043 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.77 (1H, s), 5.54 (1H, d, J = 13 Hz), 5.44 (3H, m), 5.29 (1H, d, J = 6 Hz), 5.09 (1H, d, J = 4 Hz), 4.68 (1H, d, J = 13 Hz), 4.57 (1H, d, J = 11 Hz), 3.98 (1H, d, J = 11 Hz), 2.53 (1H, s), 2.45 (1H, d, J = 4 Hz), 2.19 (3H, s), 2.18 (3H, s), 2.13 (3H, s), 2.11 (3H, s), 2.09 (3H, s), 2.08 (3H, s), 1.97 (3H, s), 1.91 (3H, s), 1.57 (3H, s), 1.42 (3H, s); MS (CI) *m/z* 703 ($M^+ + 1$) 685, 661, 643, 629, 601, 583, 541, 523, 497, 481, 463, 407, 379, 361; HRMS (CI) *m/z* ($M^+ + 1$) 703.2446 (calcd for $C_{31}H_{43}O_{18}$ 703.2449).

B. From 71. To a mixture of the pentaols **72** and **73** (2:1, 3.0 mg, 0.0071 mmol), obtained from **71** as described above, in methylene chloride (0.5 mL) at 0 °C was added triethylamine (0.040 mL, 0.284 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.050 mL, 0.214 mmol). The mixture was stirred for 1 h at 0 °C and for 4 h at room temperature. The mixture was diluted with saturated, aqueous sodium bicarbonate (five drops) and ethyl acetate (5 mL), and the separated ethyl acetate layer was dried over sodium sulfate and filtered through a short pad of silica using hexanes−ethyl acetate, 4:1 as eluent. The filtrate was concentrated to leave an oil which was taken up into pyridine (0.075 mL). Osmium tetraoxide (0.057 mL, 0.036 mmol, 0.62 M in pyridine) was added, and the mixture was stirred for 72 h. The mixture was diluted with water (0.1 mL), sodium bisulfite (20 mg) was added, and the solution was stirred for 5 h and extracted with ethyl acetate (4 × 10 mL). The extract was filtered through a short pad of Celite (ethyl acetate), dried over sodium sulfate, and concentrated under reduced pressure to leave an oily residue that was used without further purification. The oil was taken up into acetic acid, water, and tetrahydrofuran (3:1:1, 2 mL) and was heated at 85 °C for 36 h. The solution was concentrated under reduced pressure and filtered through a short pad of Amberlite 120 (plus) resin (50% aqueous acetic acid, 5 mL), and the filtrate was concentrated under reduced pressure to give a crude nonaol.

A solution of the crude nonaol in pyridine (1.5 mL) and acetic anhydride (1.0 mL) was heated at 65 °C for 16 h. The solution was concentrated, diluted with ethyl acetate (10 mL) and saturated aqueous sodium bicarbonate (0.2 mL), and extracted with ethyl acetate (3×). The extract was dried over sodium sulfate and concentrated under reduced pressure, and the residue was chromatographed on silica (hexanes−ethyl acetate, 1:1 to 1:4) to give **78** (1.4 mg, 30% from **71**).

Euonyminol (4). To a solution of **78** (1.1 mg, 1.6 μmol) in methanol (0.4 mL) was added freshly prepared sodium methoxide (3.5 μL of a 0.22 M solution in MeOH, 0.77 μmol). The mixture was stirred for 25 h, filtered through a small pad of Amberlite-120 (plus) resin, and concentrated under reduced pressure to give pure **4** (0.6 mg, 100%) as an amorphous solid: IR (KBr) 3367, 2907, 1659, 1049 cm^{-1}; ^1H NMR (D_2O) δ 5.10 (1H, s), 4.30 (4H, m), 4.09 (1H, d, J = 11 Hz), 4.00 (1H, m), 3.95 (1H, m), 3.68 (1H, d, J = 11 Hz), 3.65 (1H, d, J = 4 Hz), 2.30 (1H, s), 1.58 (3H, s), 1.36 (3H, s), identical by comparison of these data with those of the naturally derived material.

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Supporting Information Available: Full crystal structure data for X-ray analyses of **33**, **59**, **64**, and **67**, including atomic coordinates and equivalent isotropic displacement coefficients, interatomic distances and bond angles, and anisotropic displacement coefficients (37 pages). See any current masthead page for ordering and Internet access instructions.

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