Taxane Synthesis through Intramolecular Pinacol Coupling at C-1−C-2. Highly Oxygenated C-Aromatic Taxanes

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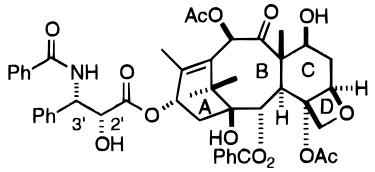
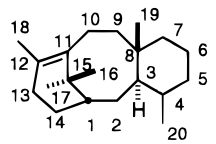
Chiral, nonracemic intramolecular pinacol coupling substrates **3**/**20** and **30** have been prepared from ethyl isopropyl ketone and acryloyl chloride, which provide the A-ring and either *o*-iodobenzyl alcohol or 2,4-dimethoxybenzyl alcohol, which provide the respective aromatic C-rings, in 14−16 linear steps in overall yields of approximately 20%. Potential pinacol coupling substrate **23** could not be made available for investigation due to intervening pinacol rearrangement in the acetonide formation step. **3**/**20** undergo stereoselective cyclizations mediated by $TiCl_4$−Zn in which the C-9 oxygen substituent plays the dominant role in determining the stereochemical outcome at C-1 and C-2 in the respective tricyclic products **4** and **21**. The formation of **21** is the more stereoselective process. The reagent of choice for the transformation of **30** into **31** is SmI_2, which, although less stereoselective than $TiCl_4$−Zn, leads to higher yielding carbon−carbon bond formation relative to carbonyl reduction. These pinacol cyclizations are interpreted to occur through endo boat-chair transition structures that prefer to orient the developing C-2 substituent and the preexisting C-9 substituent equatorially. Pinacol product **31** was converted through three additional steps into **40** having a B-ring closely related to that of taxol. We believe that these studies indicate pinacol cyclizations at C-1−C-2 to have considerable potential for producing advanced intermediates for syntheses of taxol and related complex taxanes.

Introduction

In the preceding article,[1] we showed that a taxane (cf. taxol[2]) synthesis strategy having an intramolecular pinacol coupling at C-1−C-2 as the key step could efficiently deliver potential advanced tricyclic intermediates. The appropriate relative stereochemistry at the conjoined carbons in the example demonstrated (**1** → **2**; Scheme 1) is a presumed reflection of an endo transition structure closely related in conformation to the product. Herein we examine more complex intramolecular pinacol couplings (e.g., **3** → **4**)[3] in which the issue is whether preexisting stereogenic centers at C-9 and C-10 can exert productive stereochemical control over the closure of the C-1−C-2 bond.[4]



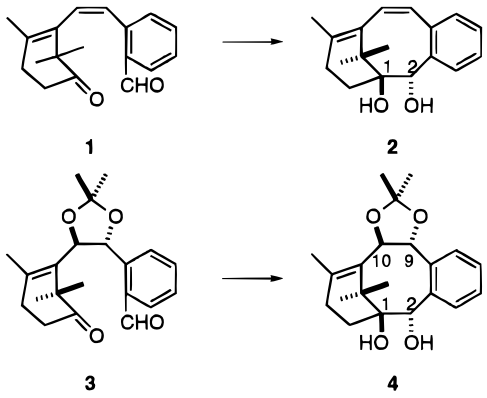
TAXOL



Results and Discussion

The concept behind the construction of the necessary pinacol coupling substrates (e.g., **3**) required the three aromatic C-ring progenitors **12**−**14** (Scheme 2). They were prepared, in the first case, from commercially available *o*-iodobenzyl alcohol (**5**), with **13** and **14** arising from commercially available 2,4-dimethoxybenzyl alcohol (**6**). The latter starting material was converted to iodide **7**, and **5** and **7** were then processed further in similar fashion. Palladium-induced coupling with the acetylene

Scheme 1



equivalent 1,1-dimethylpropargyl alcohol followed by silylation, base-catalyzed ejection of acetone, and partial hydrogenation of the terminal acetylene group thus revealed led to styrenes **8** and **9**, respectively. These materials were subjected to Sharpless hydroxylation,[5] and the vicinal diols so produced were converted to the

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(1) Swindell, C. S.; Chander, M. C.; Heerding, J. M.; Klimko, P. G.; Rahman, L. T.; Raman, J. V.; Venkataraman, H. *J. Org. Chem.* **1996**, *61*, 1101−1108.

(2) Isolation: (a) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325−2327. Synthesis: (b) Holton, R. A.; *et al. J. Am. Chem. Soc.* **1994**, *116*, 1597−1598, 1599−1600. (c) Nicolaou, K. C.; *et al. J. Am. Chem. Soc.* **1995**, *117*, 624−633, 634−644, 645−652, 653−659. Recent reviews: (d) Kingston, D. G. I.; Molinero, A. A.; Rimoldi, J. M. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Kirby, G. W., Moore, R. E., Steglich, W., Tamm, Ch., Eds.; Springer-Verlag: Vienna, 1993; Vol. 61, pp 1−206. (e) Nicolaou, K. C.; Dai, W.-M.; Guy, R. K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 15−44. (f) Boa, A. N.; Jenkins, P. R.; Lawrence, N. J. *Contemp. Org. Synth.* **1994**, *1*, 47−75.

(3) For a preliminary report of part of this work, see: Swindell, C. S.; Fan, W.; Klimko, P. G. *Tetrahedron Lett.* **1994**, *35*, 4959−4962.

(4) For an analysis of stereoselective medium and large ring formation through the pinacol coupling, see: McMurry, J. E.; Siemers, N. O. *Tetrahedron Lett.* **1993**, *34*, 7891−7894.

(5) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768−2771.

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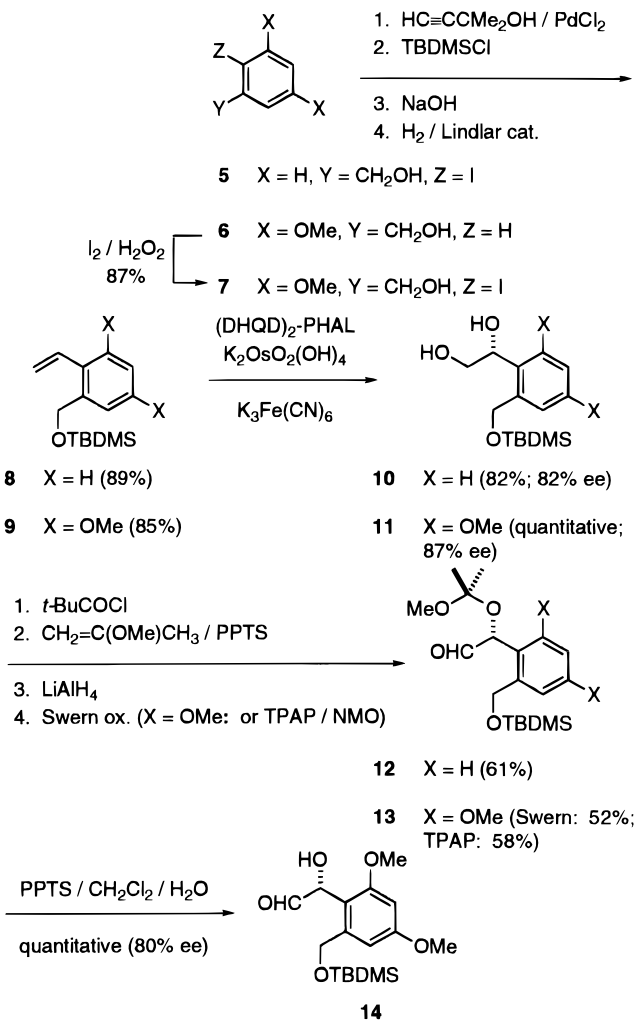
Scheme 2



respective protected hydroxy aldehydes **12** and **13** through a series of unremarkable functional group manipulations. Hydroxy aldehyde **14** was derived from **13** through acid-catalyzed hydrolysis. The enantiomeric purity of **12** was assumed to reflect closely that of its vicinal diol precursor **10**, which was established by Mosher ester analysis.[6] The ee of **14**, however, was determined by reduction to **11** and remeasurement, which revealed a modest level of epimerization either at the stage of **13** or **14**. Through these routes, C-ring intermediates **12**−**14** were available in 9−11 steps in overall yields of approximately 45%.

The desmethoxy series was pursued as outlined in Scheme 3. Thioacetal iodide **16** was derived from known[7] dioxolane iodide **15**, and the former was lithiated and subsequently involved in an addition to protected hydroxy aldehyde **12**. The formation of **17** and **18** was planned to occur without emphasis on achieving stereochemical control since the investigation of the pinacol closures of both **3** and **20** were, in fact, of interest, and since it seemed likely that the formation of either stereochemical type could be optimized as desired. By pairing the lithium reagent derived from **16** with **12**, Cram−Felkin−Ahn adduct **18** predominated over chelation-controlled adduct **17**. The further processing of **17** and **18** into pinacol coupling substrates **3** and **20** was uneventful.

Following the protocol that had succeeded in the transformation of **1** into **2**,[1] keto aldehyde **3** was exposed to the $TiCl_4$−Zn reagent[8] whereupon expected tricycle **4** was formed as the major component of a three-isomer product mixture. The structure of pinacol **4** was confirmed upon its conversion to benzoate **19**, a substance previously prepared and characterized through X-ray crystallography by Nicolaou[9] whose published spectral parameters matched those we observed. However, it was keto aldehyde **20** that proved to be the more effective pinacol coupling substrate, delivering **21** in high yield and without contamination by alternative diastereomers. Benzoate **22**, epimerically related to **19**, could be prepared from **21**. The cleavage of the *cis*-fused acetonide in the sequence that produced **22** was considerably more difficult under hydrolytic conditions, which made necessary the use of BCl_3. That **21** and **22** differ from **4** and **19** only in configuration at C-10 was indicated by a number of NOE experiments carried out on these substances.[10] The endo conformation of **21** (and thus **22**) follows from the NOE's observed for protons at C-13/C-14 and protons on the aromatic C-ring; equivalent data were obtained for **4**. Furthermore, **22** reveals its Me-18 signal to possess the shielded chemical shift ($\delta = 0.81$) characteristic of the endo conformation of C-aromatic taxanes.[11] This conformational assignment is also implied by the stereochemical relationships in **22** defined by NOE's involving Me-16 and H-2, H-9, and H-10, as well as ones involving H-2 and H-9. Pinacol **21** yields analogous data, as does pinacol **4**, except the latter substance replaces the NOE involving Me-16 and H-10 with one involving Me-18 and H-10. The signals for Me-16, Me-17, and Me-18 could be assigned from the mutual NOE relationship of the first two.

We interpret the successful formation of **4** and **21** to be the result of pinacol coupling transition structures that have conformational properties similar to those of the products.[1] It is noteworthy that the configuration of C-9 plays the dominant role in determining the stereochemical outcome at the linked C-1 and C-2 sites. Still[12] has estimated the energetic penalty for moving substituents from equatorial to axial positions at the five unique sites on the boat-chair conformation of the eight-membered ring. This penalty is greatest at the position characteristic of C-9 and essentially nil at that characteristic of C-10 (cf. conformational structures **19** and **22**, Scheme 3) in **4** and **21**. Thus, the stereochemical induction exemplified in these intramolecular pinacol couplings largely reflects the preference for the developing oxygen group at C-2 and the pre-existing one at C-9 to be equatorial in the endo boat-chair transition structures we believe to be involved;[13] the configuration of C-10 appears to be of secondary importance. Nevertheless, the highly efficient formation of **21** indicates it to represent the stereochemical manifold of choice given a protocol for

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

(7) DiGrandi, M. J.; Jung, D. K.; Krol, W. J.; Danishefsky, S. J. *J. Org. Chem.* **1993**, *58*, 4989−4992.

(8) (a) Mukaiyama, T.; Sato, T.; Hanna, J. *Chem. Lett.* **1973**, 1041−1044. (b) Kato, N.; Takeshita, H.; Kataoka, H.; Ohbuchi, S.; Tanaka, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 165−174.

(9) Nicolaou, K. C.; Claiborne, C. F.; Nantermet, P. G.; Couladouros, E. A.; Sorensen, E. J. *J. Am. Chem. Soc.* **1994**, *116*, 1591−1592.

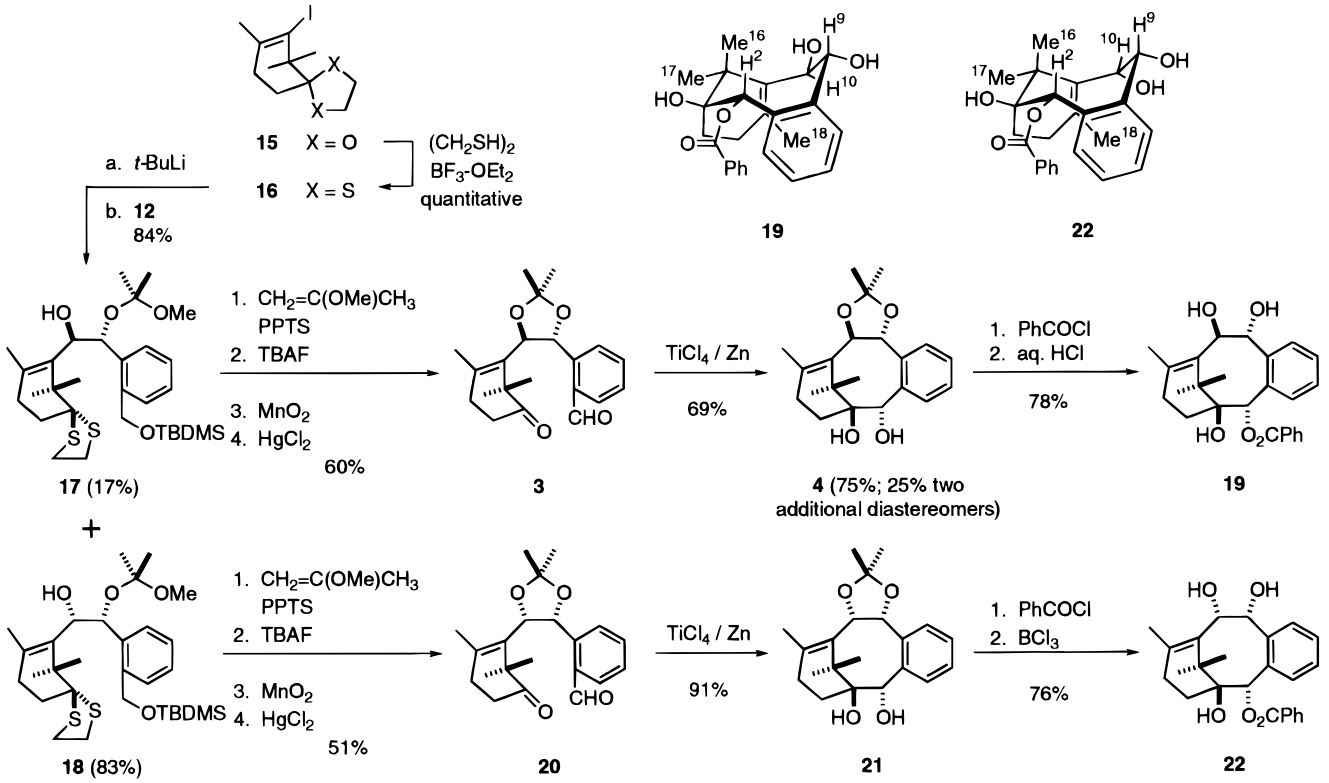
(10) Woods, M. C.; Chiang, H.-C.; Nakadaira, Y.; Nakanishi, K. *J. Am. Chem. Soc.* **1968**, *90*, 522−523.

(11) Shea, K. J.; Gilman, J. W.; Haffner, C. D.; Dougherty, T. K. *J. Am. Chem. Soc.* **1986**, *108*, 4953−4956.

(12) For an excellent discussion of some aspects of medium ring conformational analysis, see: Still, W. C.; Galynker, I. *Tetrahedron* **1981**, *37*, 3981−3996.

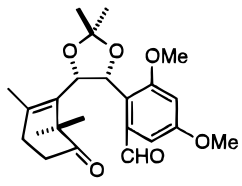
(13) For a counterexample, see ref 2c.

Scheme 3

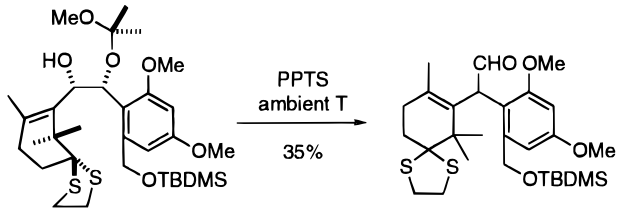


addressing the C-9−C-10 substructure in the final stages of sequences to the natural product targets of interest.

In the face of the above experience with the conversion of **20** to **21**, and with the expectation that Birch reduction would offer the best opportunity for downstream processing of the aromatic C-ring, the preparation of dimethoxy pinacol coupling substrate **23** was of interest. Addition of the lithium reagent derived from **16** to **13** (Scheme 4) led to Cram−Felkin−Ahn adduct **24** in high yield as the sole detectable isomer. However, closure of the acetonide ring proved unavoidably problematic. Mild treatment of **24** with acid, even in the presence of excess 2-methoxypropene, gave only **25**. When harsher conditions were employed, as when **24** was exposed to acid at higher temperatures (again, even in the presence of excess 2-methoxypropene), pinacol rearrangement intervened to give **28**.[14] Given the high migratory aptitude of the electron-rich aromatic ring, this complication is perhaps not surprising. Neither were we successful in carrying out modifications of the vicinal diol substructure under basic conditions. For example, conversion to a cyclic carbonate could not be brought about. The only scheme we could reduce to practice was the conversion of **25** to diacetate **26**. However, **26** was not a competent intramolecular pinacol coupling substrate, either because it lacks the rotational restriction afforded by the acetonide, which favors eight-membered ring formation, or because the acetyl groups are incompatible with the reductive conditions required. We were unable to characterize tricyclic products from the exposure of **26** to the $TiCl_4$−Zn reagent or to SmI_2[15] (*vide infra*).



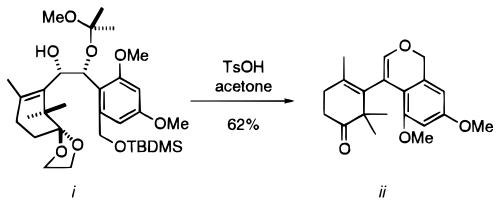
23



24 **28**

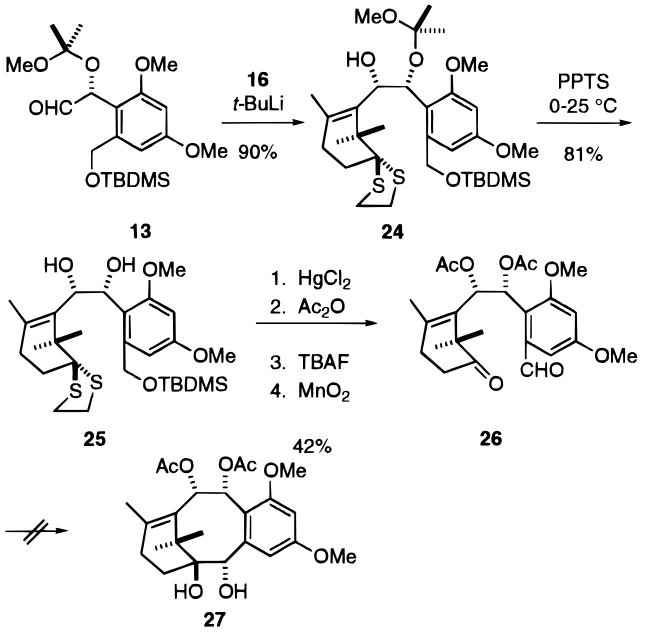
Fortunately, the alternative diastereomeric series proved amenable to providing a viable intramolecular pinacol coupling substrate in **30** (Scheme 5). The addition of the A-ring lithium reagent to **14** now provided chelation-controlled product **29**, again without detectable contamination by its diastereomer. Unlike previously encountered **24**, **29** was readily convertible to acetonide **30**. Keto aldehyde **30** could then by cyclized through the use of the $TiCl_4$−Zn reagent or by treatment with SmI_2.

(14) Likewise with the corresponding oxygen acetal, we observed the following:

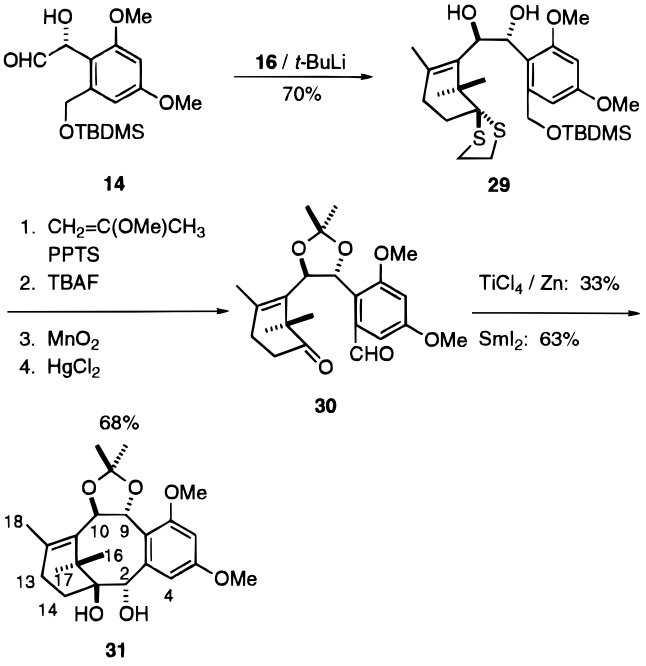


(15) (a) Namy, J. L.; Souppe, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765−766. (b) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1988**, *53*, 2132−2134. (c) Chiara, J. L.; Cabri, W.; Hanessian, S. *Tetrahedron Lett.* **1991**, *32*, 1125−1128.

Scheme 4

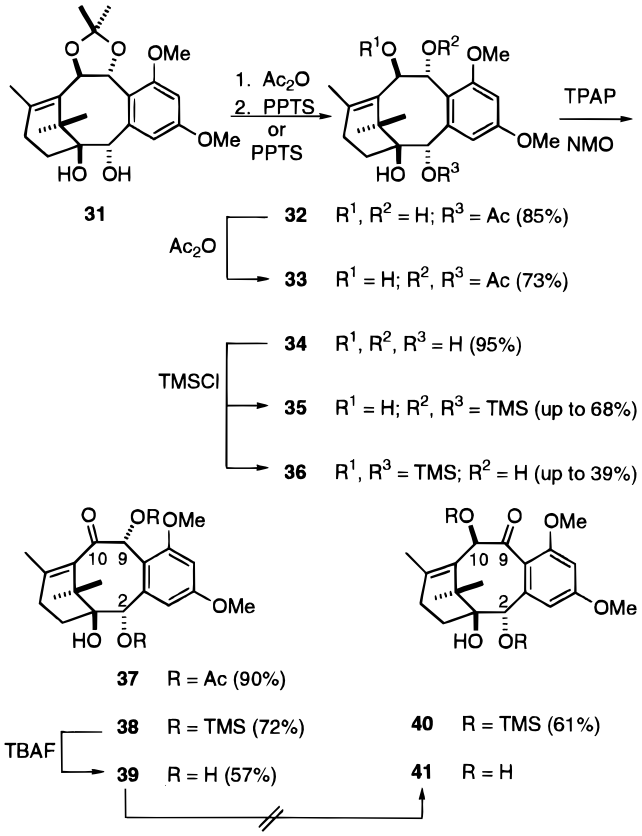


Scheme 5



Several features of the pinacol cyclizations of **30** are particularly noteworthy. Both reagent systems proved to be sensitive to temperature, with lower temperatures favoring simple carbonyl reduction and higher temperatures favoring carbon−carbon bond formation. With the $TiCl_4$−Zn reagent, only reduction occurred at −78 °C, whereas the optimal yield indicated in Scheme 5 was obtained in an experiment conducted at 65 °C that also produced an equivalent amount of keto alcohol reduction byproduct. SmI_2 behaved similarly. At −78 °C, only reduction took place, but when **30** was exposed to a 10-fold excess of SmI_2 at room temperature, a 63% yield of **31** was obtained along with an approximately 10% yield of reduction byproduct. Its relative inefficiency notwithstanding, the $TiCl_4$−Zn reagent mediated inherently more stereoselective pinacol cyclizations. In none of the experiments with $TiCl_4$−Zn was another diastereomer of **31** detected (in contrast to previous experience with **3** → **4**), whereas the cyclizations carried out with SmI_2 consistently produced an approximately 10% yield of an additional uncharacterized stereoisomer. NOE experiments again proved decisive in defining the endo conformation and stereochemistry of **31** (cf. conformational structure **19**, Scheme 3) by classifying important proton signals into three interacting sets: one involving Me-16, H-2, and H-9; another involving Me-18 and H-10; and a third including protons at C-13/C-14 and H-4.

Scheme 6



It proved possible to manipulate the B-ring of **31** to provide materials clearly relevant to the construction of taxol and to demonstrate the structures of the latter by taking advantage of the NOE relationships exploited above. Monoacetate **32** was readily available and exhibited selective reactivity toward acetylation at C-9 to give **33** (Scheme 6). Oxidation of **33** then furnished keto diacetate **37** having its B-ring C-9−C-10 substructure in the correct oxidation state relative to taxol but with an incorrect arrangement of functional groups. Cleavage of the acetonide group from **31** led to tetrol **34**. The silylation of **34** was somewhat capricious but generally supported the notion that of the secondary hydroxyls those at C-2 and C-9 were the more reactive. Thus **35** was easily accessible and amenable to oxidation to give bis(silyloxy) ketone **38**. Precedent established by Nicolaou[2c] and Holton[2b] suggested that the α-hydroxy ketone subunit at C-9−C-10 might be made subject to a keto−enol equilibrium that would lead predominantly to the natural arrangement having the carbonyl at C-9 and a *β*-oriented oxygen at C-10.[16] However, attempted saponification (KOH, MeOH−water) of **37** simply led to its destruction, fluoride-induced desilylation of **38** pro-

(16) For another solution, see: Young, W. B.; Link, J. T.; Masters, J. J.; Snyder, L. B.; Danishefsky, S. J.; De Gala, S. *Tetrahedron Lett.* **1995**, *36*, 4963−4966.

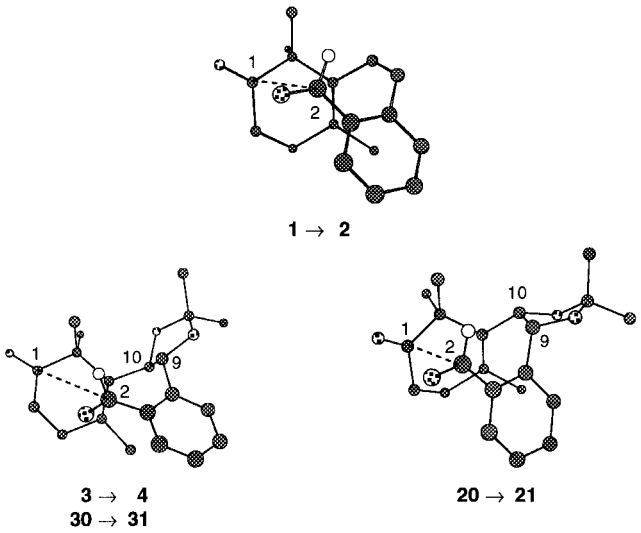


Figure 1. Proposed endo transition structures for the pinacol cyclizations reported in this and the preceding[1] paper.

duced **39**, and base treatment of **39** either left it unchanged (Et_3N, CH_2Cl_2) or decomposed it to uncharacterizeable material (MeONa, MeOH). 2,9-Disilyl derivative **36**, which was available in modest yield from **34**, furnished **40** on oxidation. Tricycle **40** possesses the B-ring functionality and stereochemistry characteristic of taxol except for the placement of the acyl groups on the C-2 and C-10 oxygens.

Conclusion

In this and the preceding article,[1] we have demonstrated four intramolecular pinacol cyclizations (**1** → **2**; **3** → **4**; **20** → **21**; and **30** → **31**) that serve to join C-1 and C-2 of the taxane skeleton with the appropriate stereochemical disposition of the substituents at these sites. All of these processes can be interpreted to proceed through endo transition structures that prefer to orient the developing oxygen group at C-2 equatorially on the boat-chair-like eight-membered being formed. In similar fashion, the cyclizations that allow for stereoinduction by pre-existing substituents at C-9 and C-10 show a preference for equatorial orientation of the C-9 acetonide oxygen, as well. The configuration of C-10 plays a subordinate role in determining the stereochemical outcome at conjoined C-1 and C-2. Nevertheless, the stereochemical manifold represented by the transformation **20** → **21** is characterized by greater selectivity. Given the variable endo−exo selectivity of intramolecular (A-ring) Diels−Alder[17] and (C-9−C-10-linking) vinylogous aldol[18] routes to tricyclic taxane synthesis intermediates with heavily functionalized B-rings, the consistently favorable transition structure features that typify the pinacol cyclizations leading to **2**, **4**, **21**, and **31** are noteworthy. The three endo transition structures that we believe apply to these processes are illustrated in Figure 1. On the basis of these studies, pinacol cyclizations that connect C-1 and C-2 appear capable of playing the key role in the delivery of advanced intermediates for syntheses of taxol and related complex taxanes. Indeed, potential intermediate **40** has been produced from pinacol **31** in three additional steps. Recent reports from the Wender[19] group have highlighted the use of Birch reduction chemistry to process the aromatic C-rings of intermediates related to **40**.

Experimental Section[20]

2-Methyl-4-[2-(hydroxymethyl)phenyl]-3-butyn-2-ol. A solution of 2-iodobenzyl alcohol (**5**; 46.8 g, 0.2 mol), 2-methyl-3-butyn-2-ol (29 mL, 0.3 mol), and Ph_3P (3.67 g, 0.014 mol) in diethylamine (200 mL) at 25 °C was sparged with N_2 for 30 min, $PdCl_2$ (1.42 g, 0.008 mol) and CuI (1.52 g, 0.008 mol) were added, and cooling with an ice−water bath was applied. After being stirred for 2 h, the reaction mixture was concentrated to afford a residue which was taken up in ether (250 mL) and water (50 mL), the organic layer was washed with saturated brine (2 × 50 mL), the aqueous layer was extracted with ether (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$). Concentration gave a brown solid (37.6 g, quantitative) which could be purified by dissolution in ethyl acetate followed by precipitation with hexane to give a yellow solid: mp 69−71 °C; ^{1}H NMR δ 7.36−7.13 (m, 4H), 4.70 (s, 2H), 4.48 (s, 1H), 4.00 (s, 1H), 1.57 (s, 6H); ^{13}C NMR δ 142.2, 131.9, 128.3, 127.7, 127.3, 121.4, 98.7, 79.4, 65.2, 63.2, 31.2; IR (CH_2Cl_2) 3600, 2200 (w) cm^{-1}. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.77; H, 7.41. Found: C, 75.67; H, 7.23.

Aryl Iodide 7. A mixture of 3,5-dimethoxybenzyl alcohol (33.6 g, 0.20 mol) and I_2 (50.8 g, 0.20 mol) in acetic acid (300 mL) was cooled to 0 °C, and 30% aqueous H_2O_2 (24.9 g, 0.22 mol) added slowly. After the reaction mixture was stirred at 0 °C for 0.5 h, intermittent cooling was employed to keep the reaction mixture at 25 °C for 2 h. At this time, the reaction mixture was poured into cold 1:1 ethyl acetate−saturated aqueous sodium metabisulfite. The aqueous layer was extracted with ethyl acetate (2 × 200 mL), and the combined organic layers were washed with saturated aqueous NaCl (3 × 200 mL) and saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated. The white solid product (50.7 g, 87%) could be further purified through dissolution in ethyl acetate and precipitation with hexane: mp 90−92 °C; ^{1}H NMR δ 6.68 (d, J = 2.5, 1H), 6.33 (d, J = 2.5, 1H), 4.63 (s, 2H), 3.82 (s, 3H), 3.78 (s, 3H).

2-Methyl-4-[2,4-dimethoxy-6-(hydroxymethyl)phenyl]-3-butyn-2-ol was prepared as for 2-methyl-4-[2-(hydroxymethyl)phenyl]-3-butyn-2-ol (97%) from **7** with a reaction time of 50 h: mp 115−117 °C; ^{1}H NMR δ 6.61 (d, J = 2.3, 1H), 6.34 (d, J = 2.3, 1H), 4.74 (d, J = 5.6, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 2.76 (s, 1H), 2.53 (t, J = 5.6, OH), 1.63 (s, 6H); ^{13}C NMR δ 161.9, 161.0, 145.7, 103.4, 102.2, 101.9, 97.4, 75.8, 65.9, 63.8, 56.2, 55.5, 31.4; IR (CH_2Cl_2) 3580, 2200 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.19; H, 7.25. Found: C, 67.34; H, 7.42.

2-Methyl-4-[2-[((*tert*-butyldimethylsilyl)oxy]methyl]-phenyl]-3-butyn-2-ol. A solution of 4-[2-(hydroxymethyl)-phenyl]-2-methyl-3-butyn-2-ol (37.6 g, 0.20 mol), imidazole (20.00 g, 0.30 mol), and *tert*-butyldimethylsilyl chloride (30.15 g, 0.20 mol) in CH_2Cl_2 (500 mL) at room temperature was stirred for 2 h, washed with saturated brine (3 × 150 mL), dried ($MgSO_4$), and concentrated to give a yellow solid (56.8 g, 93%) sufficiently pure for the next step. Further purification could be carried out by chromatography: mp 26−28 °C; ^{1}H NMR δ 7.54 (d, J = 7.7, 1H), 7.38−7.18 (m, 3H), 4.87 (s, 2H), 1.63 (s, 6H), 0.96 (s, 9H), 0.12 (s, 6H); ^{13}C NMR δ 143.2, 131.5, 128.5, 126.4, 125.7, 119.3, 98.8, 79.5, 65.7, 63.1, 31.5, 25.9, 18.4,

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−5.3. Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.26. Found: C, 71.00; H, 9.29.

2-Methyl-4-[2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]phenyl]-3-butyn-2-ol was prepared similarly (98%) from 2-methyl-4-[2,4-dimethoxy-6-(hydroxymethyl)phenyl]-3-butyn-2-ol: mp 78−80 °C; ^{1}H NMR δ 6.76 (d, J = 2.3, 1H), 6.31 (d, J = 2.3, 1H), 4.81 (s, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 2.29 (s, 1H), 1.63 (s, 6H), 0.96 (s, 9H), 0.11 (s, 6H); ^{13}C NMR δ 160.9, 160.9, 146.7, 102.2, 102.1, 100.7, 96.6, 75.6, 65.8, 63.2, 55.9, 55.3, 31.7, 25.9, 18.4, −5.4. Anal. Calcd for $C_{20}H_{32}O_4Si$: C, 65.90; H, 8.84. Found: C, 66.08; H, 9.00.

1-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2-ethynylbenzene. A mixture of 2-methyl-4-[2-[[(*tert*-butyldimethylsilyl)-oxy]methyl]phenyl]-3-butyn-2-ol (56.8 g, 0.187 mol) and crushed NaOH (7.48 g, 0.187 mol) in benzene (300 mL) was heated to reflux for 3.5 h. After being cooled to ambient temperature, the reaction mixture was washed with saturated brine (3 × 100 mL), the combined aqueous layers were extracted with ether (3 × 150 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a brown oil (44.3 g, 96%). Further purification could be carried out by kugelrohr distillation (115−120 °C; 0.55 mmHg) to give a colorless oil: ^{1}H NMR δ 7.61−7.20 (m, 4H), 4.93 (s, 2H), 3.32 (s, 1H), 0.99 (s, 9H), 0.15 (s, 6H); ^{13}C NMR δ 143.8, 132.3, 129.0, 126.4, 125.8, 118.8, 82.0, 81.1, 63.1, 26.0, 18.4, −5.3; IR (CCl_4) 3300, 2100 (w) cm^{-1}. Anal. Calcd for $C_{15}H_{22}OSi$: C, 73.12; H, 8.99. Found: C, 73.30; H, 9.09.

2,4-Dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]ethynylbenzene was prepared similarly (91%) from 2-methyl-4-[2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-phenyl]-3-butyn-2-ol with a reaction time of 30 h: ^{1}H NMR (C_6D_6) δ 6.97 (s, 1H), 6.19 (s, 1H), 5.04 (s, 2H), 3.42 (s, 3H), 3.30 (s, 3H), 3.27 (s, 1H), 0.97 (s, 9H), 0.05 (s, 6H); ^{13}C NMR δ 161.8, 161.2, 147.4, 102.2, 100.0, 96.5, 85.0, 77.3, 63.1, 55.9, 55.3, 25.9, 18.3, −5.4; IR (CH_2Cl_2) 3300 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_3Si$: C, 66.63; H, 8.55. Found: C, 66.81; H, 8.71.

Styrene 8. A mixture of 1-[[(*tert*-butyldimethylsilyl)oxy]-methyl]-2-ethynylbenzene (44.3 g, 0.182 mol), commercial Lindlar's catalyst (Aldrich; 3.1 g), and quinoline (0.93 mL) in hexane (300 mL) was stirred at room temperature under an atmoshphere of H_2 for 3.5 h, then diluted with ether (200 mL), filtered through Celite, and concentrated to give a yellow oil contaminated by quinoline (quantitative). Further purification could be carried out by Kugelrohr distillation (125−130 °C; 0.55 mmHg) to give a colorless oil: ^{1}H NMR δ 7.50−7.22 (m, 4H), 7.00 (dd, J = 11, 17.4, 1H), 5.66 (dd, J = 1.4, 17.4, 1H), 5.32 (dd, J = 1.4, 11, 1H), 4.80 (s, 2H), 0.95 (s, 9H), 0.11 (s, 6H); ^{13}C NMR δ 138.1, 135.7, 133.9, 127.6, 127.2, 126.9, 125.4, 115.8, 63.1, 25.9, 18.4, −5.3. Anal. Calcd for $C_{15}H_{24}OSi$: C, 72.52; H, 9.73. Found: C, 72.40; H, 9.86.

Styrene 9 was prepared similarly (94%) from 2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]ethynylbenzene with a reaction time of 20 h: ^{1}H NMR δ 6.79 (d, J = 2.3, 1H), 6.68 (dd, J = 11.8, 17.9, 1H), 6.38 (d, J = 2.3, 1H), 5.50 (dd, J = 2.2, 17.9, 1H), 5.41 (dd, J = 2.2, 11.8, 1H), 4.77 (s, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 0.95 (s, 9H), 0.10 (s, 6H); ^{13}C NMR δ 159.5, 158.4, 141.4, 129.8, 118.1, 117.4, 103.0, 97.1, 63.1, 55.5, 55.1, 25.9, 18.3, −5.3. Anal. Calcd for $C_{17}H_{28}O_3Si$: C, 66.19; H, 9.14. Found: C, 65.97; H, 9.12.

***R* Diol 10.** A mixture of *tert*-butyl alcohol (20 mL), water (20 mL), and AD-mix-β (5.60 g) was stirred at ambient temperature until two clear phases were produced and then cooled to 0 °C, and a solution of **8** (0.99 g, 4.0 mmol) in *tert*-butyl alcohol (5 mL) and water (5 mL) was added. After being stirred at 0 °C for 20 h, the mixture was treated with Na_2SO_3 (6 g) with stirring at ambient temperature for 30 min. The aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave a colorless oil (0.92 g, 82%): 82% ee; $[\alpha]^{20}_D$ −18.7° (*c* 0.0113, CH_2Cl_2); ^{1}H NMR δ 7.48−7.24 (m, 4H), 5.01 (dd, J = 5.3, 6.6, 1H), 4.79 (d, J = 12.4, 1H), 4.72 (d, J = 12.4, 1H), 3.76 (app d, J = 6.6, 1 H), 3.75 (app d, J = 5.3, 1H), 0.92 (s, 9H), 0.11 (s, 6H); ^{13}C NMR δ 139.0, 137.7, 128.4, 128.0, 127.8, 126.3, 70.9, 66.8, 63.8, 25.8, 18.3, −5.3. Anal. Calcd for $C_{15}H_{26}O_3Si$: C, 63.79; H, 9.27. Found: C, 64.00; H, 9.18.

***R* Diol 11** was prepared similarly (quantitative) from **9** with a reaction time of 9 h: 87% ee; $[\alpha]^{20}_D$ −4.6° (*c* 0.020, CH_2Cl_2); ^{1}H NMR (C_6D_6) δ 6.81 (d, J = 2.2, 1H), 6.26 (d, J = 2.2, 1H), 5.28−5.26 (m, 1H), 4.86 (d, J = 13.1, 1H), 4.72 (d, J = 13.1, 1H), 4.03 (t, J = 9.9, 1H), 3.92−3.82 (m, 2H), 3.41 (s, 3H), 3.06 (s, 3H), 2.98 (d, J = 5.4, 1H), 0.97 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR δ 160.3, 159.1, 141.7, 119.0, 105.1, 98.5, 71.4, 66.4, 64.0, 54.9, 54.8, 26.1, 18.5, −5.3. Anal. Calcd for $C_{17}H_{30}O_5Si$: C, 59.62; H, 8.82. Found: C, 59.57; H, 8.98.

***(R)*-1-[1-Hydroxy-2-(pivaloyloxy)ethyl]-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene.** To a solution of **10** (15.1 g, 53.5 mmol) and DMAP (0.065 g, 0.54 mmol) in pyridine (100 mL) at 0 °C was added slowly pivaloyl chloride (5.58 mL, 45.6 mmol). After 1 h, the mixture was diluted with CH_2Cl_2 (150 mL) and washed with saturated brine (100 mL), the aqueous layer was extracted with ether (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave a colorless oil (15.8 g, 81%): $[\alpha]^{20}_D$ −20.9° (*c* 0.0109, CH_2Cl_2); ^{1}H NMR δ 7.52−7.25 (m, 4H), 5.22 (dd, J = 3.6, 7.2, 1H), 4.81 (d, J = 12.3, 1H), 4.77 (d, J = 12.3, 1H), 4.36−4.25 (m, 2H), 3.10 (d, J = 3 Hz, OH), 1.21 (s, 9H), 0.92 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR δ 178.7, 138.5, 137.7, 128.5, 128.0, 128.0, 126.7, 69.1, 68.4, 64.0, 38.8, 27.1, 25.9, 18.3, −5.3; IR (CCl_4) 3600, 1760 cm^{-1}. Anal. Calcd for $C_{20}H_{34}O_4Si$: C, 65.53; H, 9.34. Found: C, 65.64; H, 9.36.

***(R)*-1-[1-Hydroxy-2-(pivaloyloxy)ethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene** was prepared similarly (80%) from **11**: $[\alpha]^{20}_D$ −16° (*c* 0.028, CH_2Cl_2); ^{1}H NMR (C_6D_6) δ 6.74 (d, J = 2.3, 1H), 6.22 (d, J = 2.3, 1H), 5.36−5.29 (m, 1H), 4.86 (d, J = 13, 1H), 4.79 (dd, J = 9.1, 11.2, 1H), 4.72 (d, J = 13, 1H), 4.36 (dd, J = 4.6, 11.2, 1H), 3.73 (d, J = 10.3, 1H), 3.41 (s, 3H), 3.08 (s, 3H), 1.19 (s, 9H), 0.95 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (C_6D_6) δ 178.1, 160.4, 159.4, 141.5, 118.6, 105.0, 98.3, 68.5, 67.6, 64.0, 54.9, 54.8, 38.9, 27.4, 26.1, 18.4, −5.3, −5.3; IR (CH_2Cl_2) 3540, 1715 cm^{-1}. Anal. Calcd for $C_{22}H_{38}O_6Si$: C, 61.94. H, 8.97. Found: C, 61.99; H, 8.81.

***(R)*-1-[1-[(2-Methoxyprop-2-yl)oxy]-2-(pivaloyloxy)ethyl]-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene.** A mixture of (*R*)-1-[1-hydroxy-2-(pivaloyloxy)ethyl]-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene (14.6 g, 39.8 mmol), 2-methoxypropene (7.65 mL, 80 mmol), and PPTS (1.0 g, 4.0 mmol) in CH_2Cl_2 (150 mL) was stirred at 0 °C for 3.5 h and then washed with saturated aqueous $NaHCO_3$ (100 mL), the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a colorless oil (17.1 g, 98%). Further purification could be carried out by chromatography: $[\alpha]^{20}_D$ −41.4° (*c* 0.0105, CH_2Cl_2); ^{1}H NMR δ 7.53−7.21 (m, 4H), 5.23 (dd, J = 5, 6.7, 1H), 4.88 (d, J = 12.5, 1H), 4.76 (d, J = 12.5, 1H), 4.13 (app d, J = 6.7, 1H), 4.12 (app d, J = 5, 1H), 3.07 (s, 3H), 1.42 (s, 3H), 1.17 (s, 9H), 1.11 (s, 3H), 0.93 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR δ 178.3, 139.2, 137.2, 127.5, 127.4, 127.4 (double signal), 101.1, 68.2, 67.2, 63.4, 49.1, 38.7, 27.2, 26.0, 25.9, 25.1, 18.4, −5.3, −5.4; IR (CCl_4) 1735 cm^{-1}. Anal. Calcd for $C_{24}H_{42}O_5Si$: C, 65.72; H, 9.65. Found: C, 65.56; H, 9.71.

***(R)*-1-[1-[(2-Methoxyprop-2-yloxy)-2-(pivaloyloxy)ethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-benzene** was prepared similarly (quantitative) from (*R*)-1-[1-hydroxy-2-(pivaloyloxy)ethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene: $[\alpha]^{20}_D$ −29° (*c* 0.026, CH_2Cl_2); ^{1}H NMR (CD_3CN) δ 6.80 (br s, 1H), 6.46 (d, J = 2.2, 1H), 5.05 (v br s, 1H), 5.00 (s, 2H), 4.40 (br s, 1H), 4.09 (dd, J = 5.8, 11.1, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.05 (s, 3H), 1.39 (s, 3H), 1.13 (s, 9H), 1.12 (s, 3H), 0.99 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (C_6D_6) δ 178.3, 159.7, 157.5 (w, br), 142.6 (w, br), 117.7, 102.9, 100.9, 96.3 (w, br), 66.4, 64.7 (w, br), 62.6 (w, br), 55.6, 55.0, 48.9, 38.6, 27.1, 25.9, 25.1, 24.8, 18.3, −5.3, −5.3; IR (CCl_4) 1735 cm^{-1}. Anal. Calcd for $C_{26}H_{46}O_7Si$: C, 62.62; H, 9.29. Found: C, 62.39; H, 9.15.

***(R)*-1-[1-[(2-Methoxyprop-2-yl)oxy]-2-hydroxyethyl]-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene.** To a mixture of $LiAlH_4$ (1.67 g, 44 mmol) in ether (200 mL) at 0 °C

was added dropwise a solution of (*R*)-1-[1-[(2-methoxyprop-2-yl)oxy]-2-(pivaloyloxy)ethyl]-2-[[(*tert*-butyldimethylsilyl)oxy]-methyl]benzene (17.0 g, 39 mmol) in ether (50 mL). The reaction mixture was stirred at 0 °C for an additional 1 h, then water (100 mL) was added dropwise, and the mixture was extracted with ether (2 × 100 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a colorless oil (12.8 g, 92%) sufficiently pure for the next step. Further purification could be carried out by chromatography: $[\alpha]^{20}_D$ −38° (*c* 0.0091, CH_2Cl_2); ^{1}H NMR δ 7.52−7.49 (m, 1H), 7.34−7.21 (m, 3H), 5.09 (dd, J = 5.2, 7.3, 1H), 4.82 (d, J = 12.4, 1H), 4.73 (d, J = 12.4, 1H), 3.74−3.56 (m, 2H), 3.13 (s, 3H), 2.60−2.52 (m, OH), 1.42 (s, 3H), 1.13 (s, 3H), 0.95 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H); ^{13}C NMR δ 139.7, 137.0, 127.7, 127.7, 127.3, 127.1, 101.2, 69.8, 67.2, 63.5, 49.2, 25.9, 25.8, 25.1, 18.4, −5.3, −5.4; IR (CCl_4) 3600 cm^{-1}. Anal. Calcd for $C_{19}H_{39}O_4Si$: C, 64.37; H, 9.66. Found: C, 64.30; H, 9.80.

(*R*)-1-[1-[(2-Methoxyprop-2-yl)oxy]-2-hydroxyethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-benzene was prepared similarly (96%) from (*R*)-1-[1-[(2-methoxyprop-2-yl)oxy]-2-(pivaloyloxy)ethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene: $[\alpha]^{20}_D$ −39° (*c* 0.0091, CH_2Cl_2); ^{1}H NMR δ 6.81 (d, J = 2.2, 1H), 6.35 (d, J = 2.2, 1H), 5.42 (dd, J = 5.4, 7.8, 1H), 4.96 (d, J = 14.4, 1H), 4.90 (d, J = 14.4, 1H), 3.79 (s, 3H), 3.79 (s, 3H), 3.75−3.52 (m, 2H), 3.17 (s, 3H), 2.43 (dd, J = 3.7, 8.3, 1H), 1.38 (s, 3H), 1.16 (s, 3H), 0.96 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3 H); ^{13}C NMR δ 159.7, 157.5, 142.7, 117.6, 103.3, 101.1, 97.0, 68.8, 64.9, 62.9, 55.7, 55.1, 49.2, 25.9, 24.9, 24.8, 18.4, −5.3, −5.3; IR (CH_2Cl_2) 3590 cm^{-1}. Anal. Calcd for $C_{21}H_{38}O_6Si$: C, 60.84; H, 9.23. Found: C, 60.79; H, 9.34.

***R* Aldehyde 12.** To a solution of oxalyl chloride (6.77 g, 56 mmol) in CH_2Cl_2 (150 mL) at −78 °C was added dropwise a solution of DMSO (10.50 g, 134 mmol) in CH_2Cl_2 (35 mL). The mixture was stirred at −78 °C for an addtional 20 min; then a solution of (*R*)-1-[1-[(2-methoxyprop-2-yl)oxy]-2-hydroxyethyl]-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene (9.94 g, 28 mmol) in CH_2Cl_2 (35 mL) was added dropwise. After an additional 20 min, triethylamine (37 mL) was added slowly dropwise. After this addition was complete, the mixture was warmed slowly to 0 °C; then water (50 mL) added. The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave a yellow oil (8.16 g, 83%): $[\alpha]^{20}_D$ −20.2° (*c* 0.0062, CH_2Cl_2); ^{1}H NMR δ 9.57 (d, J = 1.7, 1H), 7.52−7.28 (m, 4H), 5.43 (d, J = 1.7, 1H), 4.82 (s, 2H), 3.12 (s, 3H), 1.45 (s, 3H), 1.27 (s, 3H), 0.94 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR δ 198.6, 138.7, 133.7, 128.3, 127.8, 127.7, 127.7, 101.8, 75.0, 63.3, 49.1, 25.9, 25.4, 25.0, 18.4, −5.3, −5.4; IR (CCl_4) 1740 cm^{-1}. Anal. Calcd for $C_{19}H_{32}O_4Si$: C, 64.73; H, 9.14. Found: C, 64.66; H, 8.96.

***R* Aldehyde 13** was prepared similarly (65%) from (*R*)-1-[1-[(2-methoxyprop-2-yl)oxy]-2-hydroxyethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene: $[\alpha]^{20}_D$ −62° (*c* 0.011, CH_2Cl_2); ^{1}H NMR δ 9.64 (s, 1H), 6.81 (d, J = 2.2, 1H), 6.38 (d, J = 2.2, 1H), 5.72 (s, 1H), 4.90 (d, J = 14.5, 1H), 4.57 (d, J = 14.5, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.08 (s, 3H), 1.39 (s, 3H), 1.23 (s, 3H), 0.93 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 199.8, 160.7, 157.9, 143.9, 113.8, 103.4, 101.4, 97.1, 71.7, 62.6, 55.9, 55.1, 49.0, 25.9, 24.9, 24.7, 18.3, −5.3, −5.4; IR (CCl_4) 1750 cm^{-1}. Anal. Calcd for $C_{21}H_{36}O_6Si$: C, 61.14; H, 8.79. Found: C, 61.24; H, 9.00.

Alternatively, a mixture of (*R*)-1-[1-[(2-methoxyprop-2-yl)-oxy]-2-hydroxyethyl]-2,4-dimethoxy-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]benzene (20.5 g, 50 mmol), *N*-methylmorpholine *N*-oxide (8.74 g, 75 mmol), powdered activated 4 Å molecular sieves (24.9 g), and tetrapropylammonium perruthenate (0.44 g, 1.3 mmol) in CH_2Cl_2 (100 mL) was stirred at ambient temperature for 1.5 h at which time additional tetrapropylammonium perruthenate (0.43 g, 0.12 mmol) was added. After 7 h, the mixture was filtered through silica gel, eluting with CH_2Cl_2, and concentrated. Chromatography of the residue gave **13** (15.8 g, 76%).

***R* Aldehyde 14.** A mixture of **13** (12.7 g, 31 mmol), PPTS (231 mg, 0.92 mmol), and four drops of water in CH_2Cl_2 (500 mL) was stirred initially at 0 °C and subsequently at ambient temperature for 3.5 h. After being washed with saturated aqueous $NaHCO_3$ (150 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a yellow oil (10.6 g; quantitative): 80% ee; $[\alpha]^{20}_D$ −21° (*c* 0.013, CH_2Cl_2); ^{1}H NMR δ 9.67 (s, 1H), 6.62 (d, J = 2.3, 1H), 6.41 (d, J = 2.3, 1H), 5.33 (s, 1H), 4.84 (d, J = 12.8, 1H), 4.68 (d, J = 12.8, 1 H), 3.83 (s, 3H), 3.77 (s, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR δ 199.7, 160.9, 158.6, 142.7, 114.8, 105.2, 97.6, 73.4, 63.5, 55.5, 55.1, 25.6, 18.0, −5.5, −5.6; IR (CH_2Cl_2) 3525, 1760 cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_5Si$: C, 59.98; H, 8.28. Found: C, 59.78; H, 8.12.

Vinyl Iodide 16. To a solution of **15** (15.5 g, 50 mmol) and ethanedithiol (8.4 mL) in CH_2Cl_2 (100 mL) at ambient temperature was added $BF_3{\cdot}OEt_2$ (5.2 mL). After being stirred 3 h, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with 10% aqueous NaOH (100 mL), the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a yellow solid (17.7 g; quantitative) sufficiently pure for the next step. Further purification could be carried out by chromatography: mp 46−48 °C; ^{1}H NMR δ 3.22 (s, 4H), 2.38−2.25 (m, 4H), 1.85 (s, 3H), 1.37 (s, 6H); ^{13}C NMR δ 137.4, 114.5, 76.0, 47.6, 39.1 (double signal), 36.6, 32.9, 31.0, 29.1, 28.6. Anal. Calcd for $C_{11}H_{17}IS_2$: C, 38.83; H, 5.03. Found: C, 38.92; H, 5.18.

Adducts 17 and 18. To a solution of **16** (15.30 g, 43 mmol) in THF (150 mL) at −78 °C was added dropwise *tert*-butyllithium (52.94 mL, 1.7 M in pentane, 90 mmol), and the mixture was stirred for 30 min. At this time, a solution of **12** (7.92 g, 22.5 mmol) in THF (25 mL) was added rapidly, the mixture was stirred for 30 min, diluted with ether (100 mL), and warmed to 0 °C, and water (50 mL) was added. The aqueous layer was extracted with ether (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave **17** (1.78 g, 14%) and **18** (8.85 g, 70%), both as colorles oils. **17**: $[\alpha]^{20}_D$ −6.4° (*c* 0.017, CH_2Cl_2); ^{1}H NMR δ 7.53−7.20 (m, 4H), 5.27 (d, J = 9.7, 1H), 4.88 (d, J = 13.4, 1H), 4.52 (d, J = 13.4, 1H), 4.29 (d, J = 9.7, 1H), 3.25−3.04 (m, 7H), 2.33−2.15 (m, 4H), 2.08 (s, 3H), 1.41 (s, 3H), 1.23 (s, 3H), 1.09 (s, 3H), 0.95 (s, 9H), 0.13 (s, 6H), 0.10 (s, 3H); ^{13}C NMR δ 138.9, 138.7, 136.4, 134.6, 127.8, 127.4, 126.5, 125.9, 101.8, 79.0, 74.5, 69.3, 62.1, 49.5, 43.7, 38.9, 38.8, 36.7, 33.0, 26.3, 26.0, 25.4, 25.2, 23.5 (w), 21.5, 18.4, −5.2, −5.2. Anal. Calcd for $C_{30}H_{50}O_4S_2Si$: C, 63.56; H, 8.88. Found: C, 63.38; H, 8.65. **18**: $[\alpha]^{20}_D$ −1.7° (*c* 0.0092, CH_2Cl_2); ^{1}H NMR δ 7.63−7.24 (m, 4H), 5.23 (d, J = 9.5, 1H), 5.03 (d, J = 13.1, 1H), 4.92 (d, J = 13.1, 1H), 4.37 (dd, J = 3.4, 9.5, 1H), 3.26 (s, 4H), 2.80 (s, 3H), 2.50−2.05 (m, 4H), 1.96 (s, 3H), 1.53 (s, 3H), 1.36 (s, 3H), 1.35 (s, 3H), 1.03 (s, 3H), 0.95 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR δ 141.7, 138.7, 138.6, 131.3, 127.4, 127.1, 126.5, 126.1, 101.3, 79.0, 74.9, 69.0, 63.1, 48.8, 44.0, 38.8, 38.6, 36.8, 32.6, 25.9, 25.9, 25.8, 24.8, 23.5 (w), 20.9, 18.4, −5.3, −5.4. Anal. Calcd for $C_{30}H_{50}O_4S_2Si$: C, 63.56; H, 8.88. Found: C, 63.73; H, 8.93.

Keto Aldehyde 3. A mixture of **17** (2.04 g, 3.60 mmol), 2-methoxypropene (3.16 mL, 33.0 mmol), and PPTS (50 mg, 0.20 mmol) in CH_2Cl_2 (300 mL) at 0 °C was stirred at ambient temperature for 3.5 h and then washed with saturated aqueous $NaHCO_3$ (50 mL), the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give the acetonide as a yellow oil (1.89 g, 98%) sufficiently pure for the next step. Further purification could be carried out by chromatography: $[\alpha]^{20}_D$ +14.3° (*c* 0.017, CH_2Cl_2); ^{1}H NMR δ 7.59−7.24 (m, 4H), 5.50 (d, J = 9.1, 1H), 4.92 (d, J = 13.4, 1H), 4.66 (d, J = 13.4, 1H), 4.42 (d, J = 9.1, 1H), 3.51−3.08 (m, 4H), 2.34−2.16 (m, 4H), 1.97 (br s, 3H), 1.63 (s, 3H), 1.62 (s, 3H), 1.28 (br s, 3H), 0.93 (s, 9H), 0.50 (br s, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 139.5, 135.4, 134.6, 131.2, 127.8, 127.1, 126.3, 126.1, 107.6, 82.2, 78.5, 76.0, 62.4, 43.5, 38.9, 38.9, 36.6, 33.2, 27.5, 26.9, 26.0, 25.9, 23.5 (br and w), 20.4, 18.3, −5.1, −5.3. Anal. Calcd for $C_{29}H_{46}O_3S_2Si$: C, 65.12; H, 8.66. Found: C, 64.80; H, 8.60.

A mixture of the above acetonide (1.89 g, 3.54 mmol) and tetrabutylammonium fluoride (7.08 mL, 1 M in THF, 7.08 mmol) in THF (150 mL) at ambient temperature was stirred

for 30 min and then washed with saturated aqueous NaCl (50 mL), the aqueous layer was extracted with ether (3 × 50 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a yellow oil. To this oil in benzene (100 mL) was added MnO_2 (6.16 g, 71 mmol), and the mixture was stirred at ambient temperature for 19 h, filtered through Celite, and concentrated. Chromatography of the residue gave a yellow viscous oil (1.21 g, 82%): $[\alpha]^{20}_D$ −5.2° (*c* 0.011, CH_2Cl_2); ^{1}H NMR δ 10.23 (s, 1H), 7.83−7.38 (m, 4H), 6.14 (d, J = 8.9, 1H), 4.45 (d, J = 8.9, 1H), 3.16−3.05 (m, 4H), 2.28−2.14 (m, 4H), 1.88 (br s, 3H), 1.63 (s, 6H), 1.29 (br s, 3H), 0.51 (br s, 3H); ^{13}C NMR δ 190.9, 140.5, 136.7, 134.5, 134.0, 129.7, 129.6, 128.2, 127.2, 108.2, 82.8, 78.5, 75.0, 43.5, 38.9, 38.9, 36.5, 33.0, 27.5, 26.7, 25.6 (w, br), 23.5 (w, br), 20.5; IR (CH_2Cl_2) 1700 cm^{-1}. Anal. Calcd for $C_{23}H_{30}O_3S_2$: C, 65.99; H, 7.22. Found: C, 65.79; H, 7.49.

A mixture of the above thioketal aldehyde (0.84 g, 2.0 mmol), $CaCO_3$ (4.80 g, 48 mmol), $HgCl_2$ (6.02 g, 24 mmol), and water (33 mL) in acetonitrile (130 mL) at ambient temperature was stirred for 13 h and then filtered through Celite. After being washed with saturated brine (50 mL), the aqueous layer was extracted with ether (3 × 30 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave **3** as a yellow oil (0.49 g, 71%): $[\alpha]^{20}_D$ −49.2° (*c* 0.012, CH_2Cl_2); ^{1}H NMR δ 10.14 (s, 1H), 7.87−7.42 (m, 4H), 6.15 (d, J = 9, 1H), 4.27 (d, J = 9, 1H), 2.53−2.33 (m, 4H), 1.97 (s, 3H), 1.66 (s, 3H), 1.64 (s, 3H), 1.17 (s, 3H), 0.34 (s, 3H); ^{13}C NMR δ 213.9, 190.9, 140.3, 137.6, 134.5, 134.4, 130.5, 128.6, 128.4, 127.0, 108.7, 82.6, 74.9, 47.5, 35.6, 32.6, 27.5, 26.6, 24.9, 23.1, 20.4; IR (CH_2Cl_2) 1710, 1690 cm^{-1}. Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.49; H, 7.80.

Keto Aldehyde 20. A similar sequence was applied to the stereoisomeric series to deliver first an analogous acetonide (94%): $[\alpha]^{20}_D$ −13.3° (*c* 0.0092, CH_2Cl_2); ^{1}H NMR δ 7.56−7.22 (m, 4H), 5.65 (d, J = 7.9, 1H), 5.14 (br s, 1H), 4.92 (d, J = 13.1, 1H), 4.75 (d, J = 13.1, 1H), 3.24−2.99 (m, 4 H), 2.29−1.92 (m, 4H), 1.77 (s, 3 H), 1.72 (s, 3H), 1.51 (s, 3H), 1.28 (br s, 3H), 1.16 (br s, 3H), 0.94 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 138.8, 135.4, 134.0, 132.1, 128.8, 127.4, 126.9, 126.2, 106.5, 78.4 (br, double signal), 76.2, 63.3, 43.6, 38.9, 38.7, 36.5, 32.9, 26.0, 25.9, 25.8, 23.1, 22.6, 22.5, 18.2, −5.2, −5.3. Anal. Calcd for $C_{29}H_{46}O_3S_2Si$: C, 65.12; H, 8.66. Found: C, 64.94; H, 8.66.

This acetonide was converted to the analogous thioketal aldehyde (73%): $[\alpha]^{20}_D$ −31.2° (*c* 0.0095, CH_2Cl_2); ^{1}H NMR δ 10.22 (s, 1H), 7.80−7.39 (m, 4H), 6.40 (d, J = 6.1, 1H), 5.22 (br s, 1H), 3.11−3.01 (m, 4H), 2.33−1.93 (m, 4H), 1.72 (s, 3H), 1.57 (s, 3H), 1.53 (s, 3H), 1.30 (s, 3H), 1.19 (s, 3H); ^{13}C NMR δ 192.8, 140.3, 135.3, 134.2, 132.6, 132.3, 131.6, 129.2, 127.6, 107.1, 78.4, 78.2, 75.5, 43.8, 38.9 (double signal), 36.4, 32.6, 28.4, 25.9, 25.6, 23.1, 22.6; IR (CCl_4) 1700 cm^{-1}. Anal. Calcd for $C_{23}H_{30}O_3S_2$: C, 65.99; H, 7.22. Found: C, 65.80; H, 7.24.

The thioketal aldehyde was converted to **20** (74%): $[\alpha]^{20}_D$ −44.6° (*c* 0.0033, CH_2Cl_2); ^{1}H NMR δ 10.05 (s, 1H), 7.90−7.42 (m, 4H), 6.28 (d, J = 7.9, 1H), 5.20 (br s, 1H), 2.20−2.11 (m, 4H), 1.77 (s, 3H), 1.56 (s, 3H), 1.60−1.11 (br s, 6H), 1.11 (s, 3H); ^{13}C NMR δ 214.5, 191.2, 140.9, 138.5 (br), 133.7, 133.2, 131.8 (br), 130.4 (br), 128.6, 127.9, 107.7, 78.3 (br), 76.2, 48.2, 35.7, 31.6, 26.4, 24.9 (br, double signal), 23.7, 22.2; IR (CCl_4) 1715, 1695 cm^{-1}. Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.64; H, 7.41.

Tricycle 4. To THF (200 mL) at 0 °C was added dropwise $TiCl_4$ (1.17 mL, 10.7 mmol), the mixture was warmed to ambient temperature, and Zn dust (1.40 g, 21.4 mmol) was added, followed after 10 min by pyridine (0.91 mL, 10.7 mmol). A solution of **3** (187 mg, 0.54 mmol) in THF (20 mL) was added dropwise via syringe pump over 2 h, and the mixture was stirred for an additional 30 min and then treated with 10% aqueous K_2CO_3 (100 mL). The aqueous layer was extracted with ethyl acetate (3 × 100 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave a white solid (129 mg, 69%) comprised of **4** (75%) and two minor diastereomers (25%). **4**: mp 179−181 °C; $[\alpha]^{20}_D$ +42.2° (*c* 0.013, CH_2Cl_2); ^{1}H NMR δ 7.65 (d, J = 7.8, 1H, H-4), 7.48 (d, J =2.8, 1H, H-7), 7.46−7.14 (m, 2H), 5.00 (d, J = 8.8, 1H, H-9), 4.77 (s, 1 H, H-2), 4.16 (d, J = 8.8, 1H, H-10), 3.17 (br s, OH), 3.04 (br s, OH), 2.39−2.25 (m, 2H, H-13), 1.60 (s, 3H), 1.59 (s, 3H), 1.56 (s, 3H, H-16), 1.50−1.20 (m, 2H, H-14), 1.15 (s, 3H, H-17), 0.66 (s, 3H, H-18); ^{13}C NMR δ 141.4, 140.5, 134.3, 127.3, 127.1, 126.6, 125.4, 122.1, 110.3, 86.3, 80.6, 77.9, 71.4, 41.1, 30.5, 27.4, 27.3, 26.8, 24.9, 20.6, 19.2. Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found: C, 73.47; H, 8.20.

Benzoate 19. To a mixture of **4** (86 mg, 0.25 mmol) and pyridine (0.85 mL, 10 mmol) in CH_2Cl_2 (35 mL) was added dropwise benzoyl chloride (0.58 mL, 5.0 mmol). The mixture was stirred at ambient temperature for 36 h and washed with saturated aqueous $NaHCO_3$ (15 mL), the aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave the acetonide benzoate as a colorless oil (105 mg, 94%): $[\alpha]^{20}_D$ −20.2° (*c* 0.0047, CH_2Cl_2); ^{1}H NMR δ 8.11−8.07 (m, 2H), 7.61−7.45 (m, 5H), 7.24−7.15 (m, 2H), 6.36 (s, 1H), 5.35 (d, J = 8.9, 1H), 4.22 (d, J = 8.9, 1H), 2.52−2.35 (m, 3H), 1.91−1.80 (m, 1H), 1.73 (s, 3H), 1.69 (s, 3H), 1.64 (s, 3H), 1.20 (s, 3H), 0.70 (s, 3H); ^{13}C NMR δ 165.9, 141.4, 137.7, 134.9, 133.3, 130.0, 129.7, 128.5, 127.4, 127.1 (double signal), 124.7, 122.7, 110.6, 86.5, 80.2, 78.3, 74.4, 41.5, 30.4, 27.5, 27.4, 26.9, 25.8, 20.6, 19.2; IR (CH_2Cl_2) 3600, 1730 cm^{-1}. Anal. Calcd for $C_{28}H_{32}O_5$: C, 74.98; H, 7.19. Found: C, 75.16, H, 7.38.

A mixture of the above acetonide benzoate (33 mg, 0.074 mmol) and 1 N aqueous HCl (0.30 mL) in methanol (15 mL) at ambient temperature was stirred for 20 min, diluted with $CHCl_3$ (30 mL), and washed with saturated aqueous $NaHCO_3$ (30 mL). The aqueous layer was extracted with $CHCl_3$ (3 × 25 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave a white solid (25.4 mg, 83%): mp 85−88 °C; $[\alpha]^{20}_D$ −6.3° (*c* 0.0071, CH_2Cl_2); ^{1}H NMR δ 8.09−8.06 (m, 2H), 7.75−7.72 (m, 1H), 7.61−7.44 (m, 4H), 7.17 (m, 2H), 6.32 (s, 1H), 5.40 (d, J = 8.9, 1H), 4.51 (d, J = 8.9, 1H), 2.97 (br s, OH), 2.65 (br s, OH), 2.45−2.22 (m, 3H), 1.84 (m, 1H), 1.74 (s, 3H), 1.16 (s, 3H), 0.64 (s, 3H); IR (CH_2Cl_2) 3560−3430, 1700 cm^{-1}.

Tricycle 21 was prepared (91%) from **20** as in the case of **4**: mp 130−132 °C; $[\alpha]^{20}_D$ +211° (*c* 0.016, CH_2Cl_2); ^{1}H NMR δ 7.67 (d, J = 7.8, 2H, H-4 and H-7), 7.29−7.12 (m, 2H), 5.25 (d, J = 6.1, 1H, H-10), 5.10 (d, J = 6.1, 1H, H-9), 4.56 (s, 1H, H-2), 3.18 (br s, 1H, OH), 2.89 (br s, OH), 2.37−2.25 (m, 2H, H-13), 1.76 (s, 3H, H-20), 1.65−1.57 (m, 2H), 1.53 (s, 3H, H-19), 1.33 (s, 3H, H-16), 1.14 (s, 3H, H-17), 0.76 (s, 3H, H-18); ^{13}C NMR δ 141.6, 139.0, 137.5, 126.7, 125.8, 125.8, 125.3, 124.4, 109.7, 80.9, 80.1, 79.6, 69.8, 41.2, 31.1, 27.2, 26.1, 25.3, 25.1, 20.3, 19.6. Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found: C, 73.00; H, 7.91.

Benzoate 22. The acetonide benzoate derived from **21** was prepared (96%) as in the case of the corresponding acetonide benzoate derived from **4** except for the inclusion of an equivalent amount of DMAP: mp 61−63 °C; $[\alpha]^{20}_D$ +48.8° (*c* 0.010, CH_2Cl_2); ^{1}H NMR δ 8.07−7.13 (m, 9H), 6.07 (s, 1H), 5.51 (d, J = 6.2, 1H), 5.40 (d, J = 6.2, 1H), 2.54−2.34 (m, 3H), 1.88−1.84 (m, 1H), 1.79 (s, 3H), 1.59 (s, 3H), 1.49 (s, 3H), 1.20 (s, 3H), 0.81 (s, 3H); ^{13}C NMR δ 165.7, 139.4, 138.8, 137.9, 133.3, 129.9, 129.6, 128.5, 126.7, 126.3, 126.2, 125.4, 124.0, 109.8, 81.0, 80.2, 79.0, 73.0, 41.7, 31.0, 27.2, 26.8, 25.3, 25.2, 20.3, 19.7; IR (CH_2Cl_2) 3600, 1730 cm^{-1}.

To a solution of the above acetonide benzoate (88 mg, 0.196 mmol) in CH_2Cl_2 (30 mL) at −78 °C was added BCl_3 (0.80 mL, 1 M in CH_2Cl_2, 0.80 mmol). The mixture was stiirred for 1 h and then diluted with CH_2Cl_2 (30 mL), and saturated aqueous $NaHCO_3$ (30 mL) was added. The aqueous layer was extrated with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave a colorless viscous oil (63 mg, 79%): $[\alpha]^{20}_D$ +20.8° (*c* 0.0037, CH_2Cl_2); ^{1}H NMR δ 8.10−8.07 (m, 2H), 7.62−7.45 (m, 5H), 7.23−7.11 (m, 2H), 6.09 (s, 1H, H-2), 5.36 (d, J = 4.7, 1H, H-9), 4.99 (m, 1H, H-10), 3.43 (br s, OH), 2.83 (br s, OH), 2.50−2.27 (m, 3H), 1.80 (m, 1H), 1.39 (s, 3H, H-16), 1.14 (s, 3H, H-17), 0.81 (s, 3H, H-18); ^{13}C NMR δ 166.1, 138.8, 137.9, 137.1, 133.3, 129.8, 129.7, 129.6, 128.5, 126.8, 126.3, 125.3, 123.0, 79.4, 75.5, 74.3, 71.6, 41.1, 31.7, 26.4, 26.1, 19.9, 19.3; IR (CH_2Cl_2) 3600, 1720 cm^{-1}. Anal. Calcd for $C_{25}H_{28}O_5$: C, 73.51; H, 6.91. Found: C, 73.75; H, 7.19.

Diol 29 was prepared (70%) from **14** and **16** similarly to the preparation of **17/18** except that excess **16**−*tert*-butyllithium was employed: mp 40−42 °C; $[\alpha]^{20}_D$ +35° (*c* 0.029, CH_2Cl_2); ^{1}H NMR δ 6.76 (d, J = 2.4, 1H), 6.36 (d, J = 2.4, 1H), 5.03 (app t, J = 10.2, 1H), 4.78 (d, J = 14.2, 1H), 4.61 (d, J = 10.2, 1H), 4.57 (d, J = 14.2, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.44 (s, 1H), 3.16−3.01 (m, 4H), 2.36−2.04 (m, 4H), 2.00 (s, 3H), 1.26 (s, 3H), 0.95 (s, 9H), 0.43 (br s, 3H), 0.12 (s, 6H); ^{13}C NMR δ 160.1, 158.7, 142.5, 137.1, 133.6, 116.9, 103.4, 97.2, 78.7, 71.5, 70.6, 62.5, 55.4, 55.2, 43.7, 38.8 (double signal), 36.7, 32.9, 27.3 (br), 25.8, 23.1 (br), 21.4, 18.2, −5.1, −5.3.

Keto Aldehyde 30. A sequence similar to that applied in the preparation of **3** delivered first an intermediate acetonide (96%): mp 47−49 °C; $[\alpha]^{20}_D$ +36° (*c* 0.023, CH_2Cl_2); ^{1}H NMR δ 6.77 (d, J = 2.2, 1H), 6.32 (d, J = 2.2, 1H), 5.46 (br s, 1H), 5.06 (br s, 1H), 4.93 (d, J = 13.9, 1H), 4.80 (br s, 1H), 3.79 (s, 6H), 3.17−3.03 (m, 4H), 2.34−2.12 (m, 4H), 1.97 (s, 3H), 1.58 (s, 6H), 1.32 (s, 3H), 0.95 (s, 9H), 0.66 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR δ 160.4, 159.6, 143.5, 134.4, 131.7, 112.1, 107.5, 102.7, 97.4, 78.9, 76.1, 75.0, 62.7, 55.2, 55.1, 43.5, 38.9, 38.9, 36.7, 33.4, 27.8, 27.2, 26.5 (br), 25.9, 23.7 (br), 20.3, 18.3, −5.1, −5.2. Anal. Calcd for $C_{31}H_{50}O_5S_2Si$: C, 62.59; H, 8.47. Found: C, 62.70; H, 8.39.

This acetonide was then converted (quantitative) to an intermediate thioketal aldehyde: mp 56−59 °C; $[\alpha]^{20}_D$ +34° (*c* 0.024, CH_2Cl_2); ^{1}H NMR δ 10.76 (s, 1H), 6.93 (d, J = 2.5, 1H), 6.56 (d, J = 2.5, 1H), 5.96 (d, J = 9.4, 1H), 4.78 (d, J = 9.4, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.12−3.01 (m, 4H), 2.28−2.02 (m, 4H), 1.92 (s, 3H), 1.57 (s, 3H), 1.55 (s, 3H), 1.27 (s, 3H), 0.60 (s, 3H); ^{13}C NMR δ 192.2, 160.2, 159.5, 138.2, 135.3, 130.0, 118.8, 107.7, 103.8, 102.4, 79.8, 78.7, 73.7, 55.6, 55.3, 43.3, 38.8, 38.7, 36.5, 33.3, 27.5, 27.2, 26.2, 24.3, 20.3; IR (CH_2Cl_2) 1695 cm^{-1}. Anal. Calcd for $C_{25}H_{34}O_5S_2$: C, 62.73; H, 7.16. Found: C, 62.65; H, 7.01.

The thioketal aldehyde was then converted (71%) to **30**: mp 109−111 °C; $[\alpha]^{20}_D$ +64° (*c* 0.0063, CH_2Cl_2); ^{1}H NMR δ 10.80 (s, 1H), 6.94 (d, J = 2.5, 1H), 6.60 (d, J = 2.5, 1H), 5.94 (d, J = 9.3, 1H), 4.72 (d, J = 9.3, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 2.43−2.31 (m, 4H), 1.90 (s, 3H), 1.62 (s, 3H), 1.60 (s, 3H), 1.25 (s, 3H), 0.58 (s, 3H); ^{13}C NMR δ 214.1, 192.5, 160.5, 159.4, 138.6, 135.7, 129.3, 118.3, 108.4, 103.9, 103.3, 80.0, 74.2, 55.7, 55.5, 47.6, 35.7, 32.9, 27.5, 27.2, 25.2, 23.4, 20.3; IR (CH_2Cl_2) 1710, 1685 cm^{-1}. Anal. Calcd for $C_{23}H_{30}O_6$: C, 68.64; H, 7.51. Found: C, 68.47; H, 7.65.

Tricycle 31. To Sm (2.61 g, 17.4 mmol) in THF (90 mL) at ambient temperature was added slowly diiodomethane (0.70 mL, 8.7 mmol). The mixture was stirred for an additional 1.5 h; then a solution of **30** (0.35 g, 0.87 mmol) in THF (3 mL) was added. The reaction mixture was stirred for 0.5 h, diluted with ether (90 mL), and washed with saturated aqueous $NaHCO_3$ (50 mL), the aqueous layer was extracted with ether (2 × 40 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a 5.5:1:1 mixture of **31**, an uncharacterized reduction product, and an uncharacterized diasteromer, respectively (0.30 g, 86% total yield, 63% yield of **31**). Chromatography and trituration with ether gave **31** as a white solid: mp 175−177 °C; $[\alpha]^{20}_D$ +132° (*c* 0.0033, CH_2Cl_2); ^{1}H NMR δ 6.90 (d, J = 2.4, 1H, H-4), 6.22 (d, J = 2.4, 1H, H-6), 4.88 (d, J = 9.5, 1H, H-9), 4.73 (s, 1H, H-2), 4.61 (d, J = 9.5, 1H, H-10), 3.78 (s, 3H), 3.77 (s, 3H), 2.32−2.10 (m, 2H, H-13), 1.65−1.35 (m, 2H, H-14), 1.56 (s, 3H), 1.55 (s, 3H), 1.51 (s, 3H, H-16), 1.12 (s, 3H, H-17), 0.82 (s, 3H, H-18); ^{13}C NMR δ 159.4, 159.0, 144.5, 140.3, 128.5, 113.8, 110.2, 103.4, 97.6, 82.2, 80.3, 77.8, 71.5, 55.8, 55.2, 41.2, 30.7, 27.6, 27.5, 26.7, 25.2, 20.7, 19.4. Anal. Calcd for $C_{23}H_{32}O_6$: C, 68.30; H, 7.97. Found: C, 68.23; H, 8.19.

Acetate 32. A solution of **31** (0.40 g, 1.0 mmol), pyridine (3.40 mL, 40 mmol), DMAP (0.12 g, 1 mmol), and acetic anhydride (0.66 mL, 10.0 mmol) in CH_2Cl_2 (50 mL) was stirred at ambient temperature for 2 h, diluted with CH_2Cl_2 (100 mL), and washed with saturated aqueous $NaHCO_3$ (70 mL), the aqueous layer extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave the corresponding acetate as a white solid (0.41 g, 92%): mp 122−124 °C; $[\alpha]^{20}_D$ +137° (*c* 0.0095, CH_2Cl_2); ^{1}H NMR δ 6.68 (d, J = 2.4, 1H), 6.31 (d, J = 2.4, 1H), 6.06 (s, 1H), 5.16 (d, J = 9.6, 1H), 4.67 (d, J = 9.6, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 2.24−2.16 (m, 2H), 2.13 (s, 3H), 1.76−1.70 (m, 1H), 1.62 (s, 3H), 1.61 (s, 3H), 1.60 (s, 3H), 1.47−1.32 (m, 1H), 1.13 (s, 3H), 0.86 (s, 3H); ^{13}C NMR δ 170.4, 159.6, 159.5, 141.4, 140.2, 128.5, 114.7, 110.5, 103.6, 97.9, 82.2, 80.0, 78.2, 73.9, 56.3, 55.3, 41.5, 30.5, 27.6, 27.5, 26.8, 25.6, 21.3, 20.7, 19.2; IR (CH_2Cl_2) 3590, 1735 cm^{-1}.

A mixture of the above acetonide monoacetate (19 mg, 0.043 mmol), PPTS (10 mg, 0.043 mmol), and water (2 drops) in CH_2Cl_2 (10 mL) at ambient temperature was stirred for 18 h, diluted with CH_2Cl_2 (30 mL), washed with saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$), and concentrated. Chromatography of the residue gave **32** as a white solid (16 mg, 92%): mp 79−81 °C; $[\alpha]^{20}_D$ +109° (*c* 0.0014, CH_2Cl_2); ^{1}H NMR δ 6.68 (d, J = 2.3, 1H), 6.29 (d, J = 2.3, 1H), 6.00 (s, 1H, H-2), 5.04 (app t, J = 10, 1H, H-9), 4.91 (d, J = 10, OH), 4.66 (d, J = 10, 1H, H-10), 3.84 (s, 3H), 3.77 (s, 3H), 3.06 (br s, 1H, OH), 2.35 (s, OH), 2.24−2.16 (m, 2H), 2.12 (s, 3H), 1.73−1.65 (m, 1H), 1.63 (s, 3H, H-16); 1.29−1.17 (m, 1H), 1.09 (s, 3H, H-17), 0.84 (s, 3H, H-18); ^{13}C NMR δ 170.2, 159.0, 158.7, 141.8, 137.6, 132.5, 118.4, 103.8, 96.9, 79.2, 77.4, 75.3, 73.8, 55.9, 55.3, 41.7, 30.0, 27.6, 25.9, 21.2, 20.5, 19.5; IR (CH_2Cl_2) 3590−3500, 1735 (br) cm^{-1}.

Diacetate 33. A solution of **32** (73 mg, 0.18 mmol), pyridine (0.25 mL, 2.90 mmol), DMAP (22 mg, 0.18 mmol), and acetic anhydride (36 μL, 0.38 mmol) in CH_2Cl_2 (6 mL) was stirred at ambient temperature for 1.5 h, diluted with CH_2Cl_2 (40 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave **33** (59 mg, 73%) and the 2,9,10-triacetate (6 mg, 7%), both as a colorless oils. **33**: $[\alpha]^{20}_D$ +112° (*c* 0.0037, CH_2Cl_2); ^{1}H NMR δ 6.68 (d, J = 2.4, 1H), 6.27 (d, J = 2.4, 1H), 6.20 (s, 1H), 6.14 (d, J = 10.5, 1H), 5.08 (d, J = 10.5, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 2.40−2.20 (m, 2H), 2.17 (s, 3H), 2.15 (s, 3H), 1.76−1.66 (m, 1H), 1.69 (s, 3H), 1.32−1.20 (m, 1H), 1.13 (s, 3H), 0.90 (s, 3H); ^{13}C NMR δ 170.7, 170.2, 159.3, 158.9, 142.1, 138.8, 131.9, 116.8, 103.5, 97.5, 79.1, 74.8, 73.8, 73.8, 55.9, 55.3, 41.8, 30.1, 27.7, 26.0, 21.2, 20.9, 20.7, 19.5; IR (CH_2Cl_2) 3590, 1740 cm^{-1}.

Tetrol 34. A mixture of **31** (0.51 g, 1.26 mmol), PPTS (0.17 g, 0.63 mmol), and H_2O (0.20 mL) in CH_2Cl_2 (40 mL) at ambient temperature was stirred for 20 h and washed with saturated aqueous $NaHCO_3$ (20 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to give a white solid (0.44 g, 95%) sufficiently pure for the next step. Further purification could be carried out by chromatography: mp 87−89 °C; $[\alpha]^{25}_D$ +70° (*c* 0.0052, CH_2Cl_2); ^{1}H NMR ($CDCl_3$−D_2O) δ 6.97 (d, J = 2.4, 1H), 6.27 (d, J = 2.4, 1H), 4.88 (d, J = 9.8, 1H), 4.73 (s, 1H), 4.66 (d, J = 9.8, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 2.45−2.05 (m, 2H), 1.65−1.45 (m, 1H), 1.55 (s, 3H), 1.22−1.04 (m, 1H), 1.07 (s, 3H), 0.83 (s, 3H); ^{13}C NMR δ 158.8, 158.2, 144.6, 137.4, 132.5, 118.0, 103.3, 97.3, 79.9, 77.2, 75.1, 71.1, 55.7, 55.3, 41.3, 30.1, 27.5, 25.3, 20.5, 19.7. Anal. Calcd for $C_{20}H_{28}O_6$: C, 65.92; H, 7.74. Found: C, 65.74; H, 7.62.

Disilyl Ethers 35 and 36. A solution of **34** (73 mg, 0.20 mmol), triethylamine (0.56 mL, 4.0 mmol), and trimethylsilyl chloride (152 μl, 1.20 mmol) in CH_2Cl_2 (10 mL) at ambient temperature was stirred for 4 h, diluted with CH_2Cl_2 (30 mL), and washed with saturated aqueous $NaHCO_3$ (20 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave **35** (69 mg, 68%) as a white solid and **36** (12 mg, 12%) as a colorless oil. **35**: mp 125−127 °C; $[\alpha]^{20}_D$ +43° (*c* 0.0022, CH_2Cl_2); ^{1}H NMR δ 6.81 (d, J = 2.5, 1H), 6.25 (d, J = 2.5, 1H), 5.09 (d, J = 9.6, 1H), 4.85 (d, J = 9.6, 1H), 4.81 (s, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.25 (s, OH), 2.70 (s, OH), 2.22−1.96 (m, 2H), 1.66−1.61 (m, 1H), 1.58 (s, 3H), 1.17−1.04 (m, 1H), 1.13 (s, 3H), 0.88 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H); ^{13}C NMR δ 159.7, 158.7, 144.7, 138.3, 132.2, 118.9, 103.2, 97.5, 78.7, 76.1, 74.1, 73.4, 55.3, 55.2, 41.0, 30.4, 28.1, 26.2, 20.9, 20.0, 0.1, 0.0. Anal. Calcd for $C_{26}H_{44}O_6Si_2$: C, 61.38; H, 8.71. Found: C, 61.52; H, 8.58. **36**: $[\alpha]^{20}_D$ +103° (*c* 0.0053, CH_2Cl_2); ^{1}H NMR δ 6.83 (d, J = 2.5, 1H), 6.27 (d, J = 2.5, 1H), 4.99 (app t, J = 10.6, 1H), 4.80 (s, 1H),

4.69 (d, $J = 9.5$, 1H), 4.54 (d, $J = 10.6$, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.29 (s, 1H, OH), 2.14−1.96 (m, 2H), 1.66−1.63 (m, 1H), 1.59 (s, 3H), 1.17−1.04 (m, 1H), 1.08 (s, 3H), 0.87 (s, 3H), 0.18 (s, 3H), 0.03 (s, 3H); ^{13}C NMR δ 158.4, 158.4, 145.1, 135.1, 134.8, 119.7, 103.9, 97.3, 78.4, 77.2, 75.0, 73.3, 55.7, 55.3, 41.1, 30.2, 28.0, 26.3, 20.5, 20.0, 0.2, 0.0. Anal. Calcd for $C_{26}H_{44}O_6Si_2$: C, 61.38; H, 8.71. Found: C, 61.58; H, 8.64.

Keto Diacetate 37. A mixture of **33** (41 mg, 0.092 mmol), *N*-methylmorpholine *N*-oxide (100 mg, 0.85 mmol), powdered activated 4 Å molecular sieves (125 mg), and tetrapropylammonium perruthenate (16 mg, 0.046 mmol) in CH_2Cl_2 (4 mL) was stirred at ambient temperature for 1.5 h and then subjected to chromatography to afford a yellow oil (37 mg, 90%): $[\alpha]^{20}_D$ −66° (*c* 0.0075, CH_2Cl_2); ^{1}H NMR δ 6.74 (d, $J =$ 2.4, 1H), 6.69 (s, 1H, H-2), 6.29 (d, $J = 2.4$, 1H), 6.26 (s, 1H, H-9), 3.79 (s, 3H), 3.77 (s, 3H), 2.50−2.05 (m, 2H), 2.26 (s, 3H), 2.18 (s, 3H), 1.90−1.60 (m, 2H), 1.52 (s, 3H, H-16), 1.12 (s, 3H, H-17), 0.81 (s, 3H, H-18); ^{13}C NMR δ 198.3, 170.3, 169.9, 160.1, 160.0, 141.9, 140.1, 134.4, 114.8, 104.2, 97.8, 78.1, 76.9, 74.2, 56.3, 55.3, 39.6, 29.5, 26.8, 26.2, 21.1, 20.8, 20.4, 20.2; IR (CH_2Cl_2) 3580, 1740, 1720 cm^{-1}. Anal. Calcd for $C_{24}H_{30}O_8$: C, 64.56; H, 6.77. Found: C, 64.36; H, 6.76.

Keto Disilyl Ether 38 was prepared (72%) similarly from **35** with a reaction time of 16 h and purification by chromatography: mp 84−86 °C; $[\alpha]^{20}_D$ −65° (*c* 0.0022, CH_2Cl_2); ^{1}H NMR δ 6.78 (d, $J = 2.5$, 1H), 6.15 (d, $J = 2.5$, 1H), 5.52 (s, 1H, H-2), 4.86 (s, 1H, H-9), 3.70 (s, 3H), 3.62 (s, 3H), 3.25 (s, 1H, OH), 2.17−1.96 (m, 2H), 1.65−1.49 (m, 1H), 1.25 (s, 3H, H-16), 1.18−1.05 (m, 1H), 1.02 (s, 3H, H-17), 0.68 (s, 3H, H-18), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR δ 202.8, 160.2, 159.2, 144.0, 139.1, 134.9, 118.3, 104.0, 97.8, 77.8, 77.1, 73.9, 55.6, 55.2, 38.7, 29.6, 27.1, 26.0, 20.7, 20.2, 0.1, −0.1; IR (CH_2Cl_2) 3535, 1715 cm^{-1}. Anal. Calcd for $C_{26}H_{42}O_6Si_2$: C, 61.62; H, 8.35. Found: C, 61.83; H, 8.16.

Keto Disilyl Ether 40 was prepared (61%) as a colorless oil as in the case of **37** with a reaction time of 24 h and purification by chromatography: $[\alpha]^{20}_D$ −1.4 (*c* 0.0076, CH_2Cl_2); ^{1}H NMR δ 6.73 (d, $J = 2.1$, 1H), 6.24 (d, $J = 2.1$, 1H), 5.24 (s, 1H, H-10), 4.67 (s, 1H, H-2), 3.80 (s, 3H), 3.74 (s, 3H), 3.24 (s, OH), 2.35−1.55 (m, 3H), 1.34 (s, 3H, H-16), 1.33−1.25 (m, 1H), 1.09 (s, 3H, H-17), 1.05 (d, $J = 0.5$, 3H, H-18), 0.20 (s, 3H), 0.00 (s, 3H); ^{13}C NMR δ 206.8, 160.2, 155.6, 144.0, 137.5, 132.5, 120.8, 103.1, 96.3, 81.8, 78.1, 73.2, 55.8, 55.4, 41.6, 29.9, 26.8, 25.8, 20.9, 18.5, 0.1, −0.2; IR (CH_2Cl_2) 3530, 1715 cm^{-1}. Anal. Calcd for $C_{26}H_{42}O_6Si_2$: C, 61.62; H, 8.35. Found: C, 61.46; H, 8.39.

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Supporting Information Available: Experimental details for the preparation of **24**−**26** and **28** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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