Enantiospecific Total Synthesis of Natural (+)-Taxusin. 1. Retrosynthesis, Advancement to Diastereomeric *trans*-$\Delta^{9,10}$-Tricyclic Olefinic Intermediates, and the Stereocontrol Attainable Because of Intrinsic Rotational Barriers Therein

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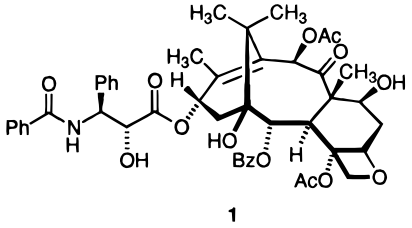
Abstract: In a study directed toward the expeditious construction of heavily functionalized taxane intermediates, 1-vinyl-2-cyclohexenyl-7,7-dimethyl-*exo*-norbornan-2-ols such as **9**, which are derived from *D*-camphor are shown to undergo stereocontrolled oxyanionic Cope rearrangement to give tricyclic unsaturated ketones. In the specific example of **13**, only three subsequent steps are required to effect 1,2-bridge migration with formation of triketone **6**. Once the relative reactivities of the carbonyl groups in **6** were elucidated, its direct conversion to the diastereomeric trans olefins **25** and **26** was accomplished. As expected, both intermediates exhibit restricted rotation due to transannular steric constraints, with **25** being the more thermodynamically stable. These compounds can be regioselectively dihydroxylated, but the more advanced substrates **30** and **32** were shown not to perform well under Wittig olefination conditions. This warranted prior exocyclic olefination in ring C, a strategy which allowed for the highly efficient conversion of **33** to **39** having the complete array of functionality demanded of the B and C rings in taxusin.

For more than three decades, taxane diterpenes have been isolated and structurally characterized with considerable frequency.[1,2] The interest in this compound class, which now numbers in excess of 100, stems from a combination of molecular complexity, structural diversity, and in some cases significant biological activity. The proven efficacy of taxol (**1**)[3] against a number of important human cancers[4] has caused it to be a major focus of preparative work,[5] which has culminated in five successful total syntheses.[6−10] In a more recent development, taxinine (**2**) was shown to inhibit the drug transport activity of P-glycoprotein, a property of potential utility in overcoming the drug resistance problem.[11]



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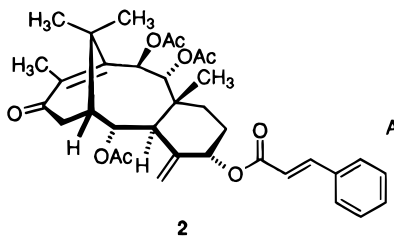

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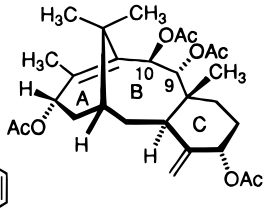

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These and many related findings have given impetus to a wider range of synthetic investigations for the express purpose of developing satisfactory protocols for accessing the taxanes with their characteristic bridgehead unsaturation feature.[12] Though it has no known curative properties,[13] taxusin (**3**) has

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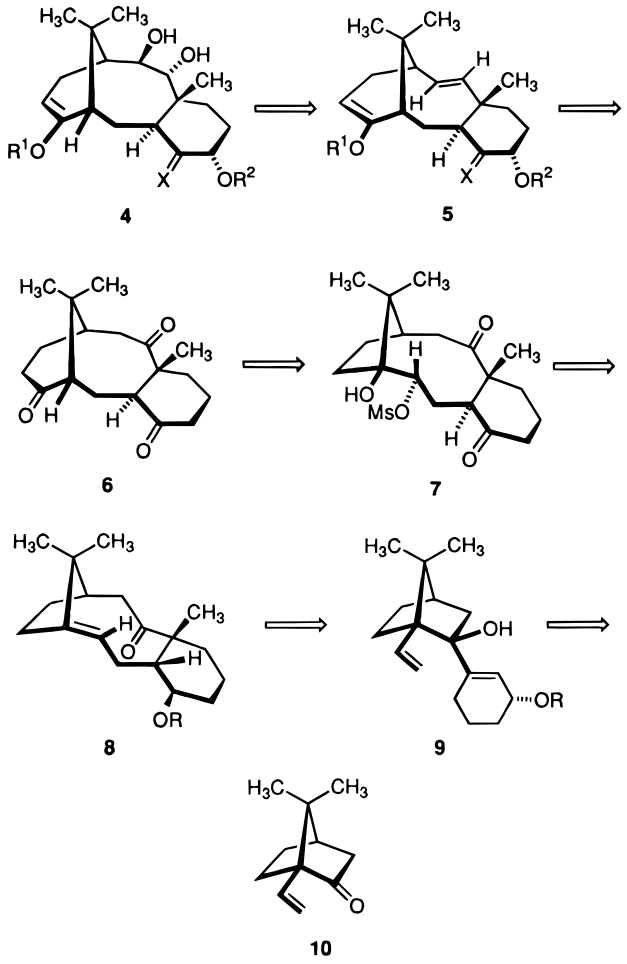
emerged as an exemplary resource. The high interest engendered by Holton's pioneering report in 1988 of a successful route to **3**[14] has been followed more recently by a more concise second-generation total synthesis at the hands of Kuwajima and his colleagues.[15]

The studies to be detailed herein and in the following article[16] were formulated for the explicit purpose of reaching natural taxusin, and to do so in a fashion as correlatable as possible with a companion route to taxol.[17] An added challenge was to achieve these goals in as expedient a manner as possible. In pursuit of this program, we envisioned an unrivaled opportunity to deploy oxyanionic sigmatropy,[18] and in so doing, to utilize *D*-camphor as the enantiopure precursor to both **1** and **3**.[19]

Retrosynthetic Analysis and Strategy

The main theme that was presently followed was influenced particularly by the expectation that the C(9)−C(10) B-ring oxygenation pattern resident in taxusin could be most expediently introduced by *cis*-dihydroxylation of *trans*-olefinic precursor **5** (Scheme 1). Although the intended **5** → **4** transformation was viewed to be on secure grounds, our ability to preserve the structural integrity of **5** once generated was much less so. Although the structural implications of the molecular dynamics capable of operation within *trans*-cycloalkenes have been appreciated for several decades, none had previously been applied in a synthetic context. Nevertheless, it seemed appropriate to explore the elaboration of **5** from triketone **6** in a manner that would suitably distinguish between its three carbonyl groups. In this way, the absolute configuration of all of the several stereogenic centers in rings B and C would be established quickly and properly.

Scheme 1



In continuation of this line of reasoning, the availability of **6** was projected to arise from a stereocontrolled Wagner−Meerwein bridge migration within hydroxy mesylate **7**. Following the examination of molecular models, we came to expect that 1,2-migration of the *gem*-dimethyl-substituted carbon would be kinetically preferred to an overwhelming extent provided that the leaving group was α-oriented. The stage for this key step could be set by proper oxygenation of **8**, a compound that we envisioned being assembled in one step by anionic oxy-Cope rearrangement of **9** followed by in situ methylation of the regiospecifically formed enolate. In this way, the crucial convergency would rest simply on the coupling of readily available ketone **10**[20] with the proper cycloalkenyl anion from the more sterically accessible endo direction. Refinement of the problem down to the level of **10** constitutes the linkup with *D*-camphor alluded to above.

Preparation of Triketone 6 and the Need to Circumvent Intramolecular Aldolization across Rings A and B

Several options for approaching **6** have previously been evaluated.[19c,19d,21] Of these, the possibility of producing quantities of enantiomerically pure cyclohexenyl bromides **11** and **12** was reduced to practice via lipase P-30 hydrolysis of chloroacetate precursors. As satisfying as it was to combine their lithio derivatives with **10** to arrive at pure diastereomeric adducts,

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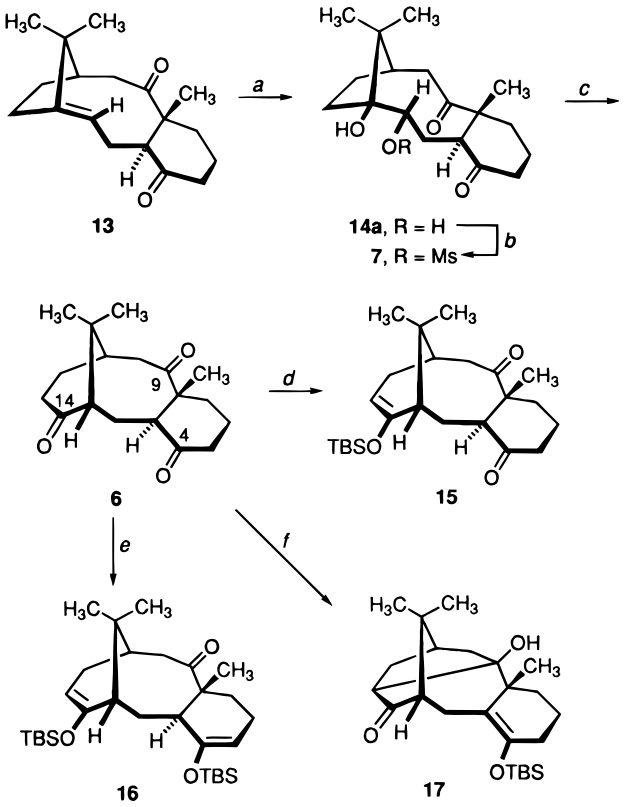
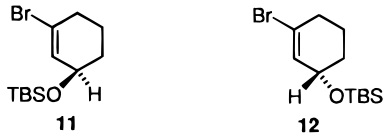
Scheme 2



[a] OsO_4, CH_2Cl_2; py, $NaHSO_3$, H_2O (100%). [b] CH_3SO_2Cl, py, 0° → 25 °C. [c] Et_2AlCl, CH_2Cl_2, hexanes, -78° → -15 °C (96% for 2 steps). [d] $KN(SiMe_3)_2$, TBSCl, THF, -78° → 25 °C (71%). [e] TBSOTf, Et_3N, CH_2Cl_2, -78° → 0 °C (95%). [f] $LiN(i\text{-}Pr)_2$ or $LiN(SiMe_3)_2$, TBSCl, THF, -78° → 25 °C (35%).

the prior resolution was rendered unnecessary by the fact that each adduct could be quite satisfactorily transformed into the



identical diketone **13** of 100% ee.[21] In effect, *only five laboratory steps are required to advance from **10** to **13***.

As a direct consequence of the adoption of an "endo-chair" transition state during the **9** → **8** isomerization,[19a] the olefinic center in **13** is properly disposed for *cis*-dihydroxylation. Since access by osmium tetraoxide to this double bond can be gained only from the exo surface for obvious reasons, the conversion to **14a** occurs cleanly and quantitatively (Scheme 2). The mesylation of **14a** in pyridine at 0 to 25 °C proceeds with the usual total kinetic bias for esterification of the secondary hydroxyl to give **7**. Of the several promoters screened for effecting the important rearrangement to **6**, diethylaluminum chloride emerged as the most suitable since it gave rise to the triketone in 96% overall yield for the two steps.[22] For the dual purpose of corroborating the structural assignment to **6** and to ascertain its conformational features, a single-crystal X-ray crystallographic analysis was undertaken. As revealed in Figure 1, its B-ring adopts a "carbonyl-up" topology, a structural

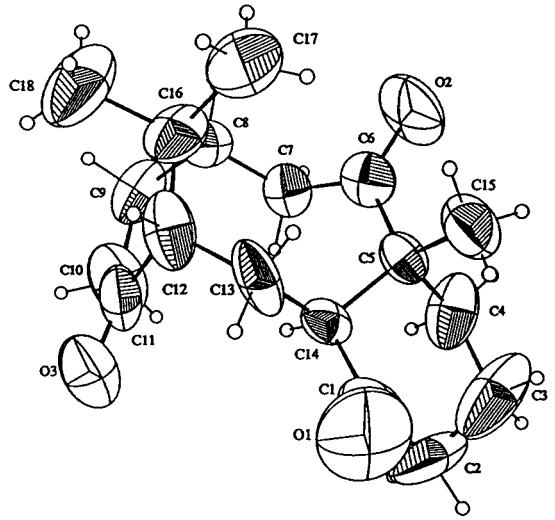
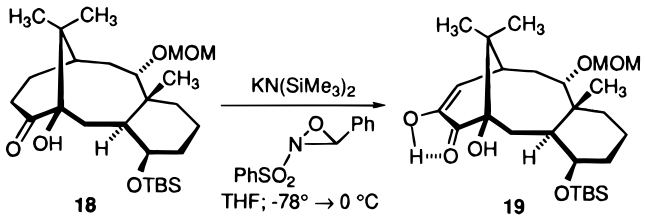


Figure 1. Computer-generated perspective drawing of the final X-ray model of **6**.

parameter that will emerge as significant when the time arrives to undertake stereocontrolled reduction of this functionality.

Our analysis of the relative ease of enolization of the three available sites in **6** began with controlled O-silylation studies. The A-ring in taxanes is well recognized to be subject to significant steric blockade.[1,2] Prior experience in this laboratory with related molecules hinted that the C(9) carbonyl might well be reasonably unreactive.[21] Consequently, the relative rate of deprotonation α to C(4) was originally expected to be most rapid, unless steric acceleration[23] was to operate at one of the other sites. The latter presumption proved to be correct, in that treatment of **6** with 1 equiv each of potassium hexamethyldisilazide and *tert*-butyldimethylsilyl chloride (TBSCl) in THF at −78 °C gave **15** in 71% yield. The preceding observation prompted parallel studies in which the susceptibility of A-ring ketones to oxygenation under anionic conditions was probed. When **18** was found to be transformed into the α-diketone **19** following exposure of its potassium enolate to the Davis



oxaziridine at 0 °C,[24] we concluded that simultaneous attainment of sp^2 character by C(13) and C(14) is energetically advantaged because of substantive nonbonded decompression.

At this stage, it was timely to observe that a change to 2 equiv of TBSOTf and triethylamine at low temperature led predominantly to the desired **16** (92%). Lithium amide bases had to be avoided since under these conditions intramolecular aldolization is kinetically dominant and **17** is produced. This outcome is believed to be due to a decreased reactivity on the part of the enolate anion toward the silyl halide, thereby providing an opportunity for 1,2-addition to C(9) whose proximity to C(14) arises from the highly folded conformation associated with **6**. Once the new C−C bond has been installed,

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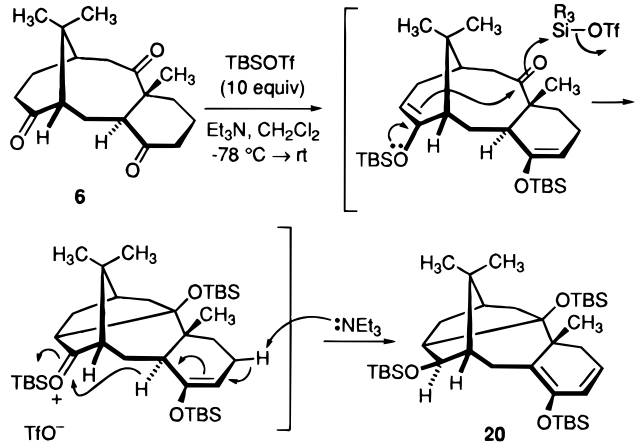
(24) Elmore, S. W.; Paquette, L. A. *J. Org. Chem.* **1993**, *58*, 4963.

Scheme 3



C-ring enolization occurs toward the ring junction rather than in the lesser substituted direction.

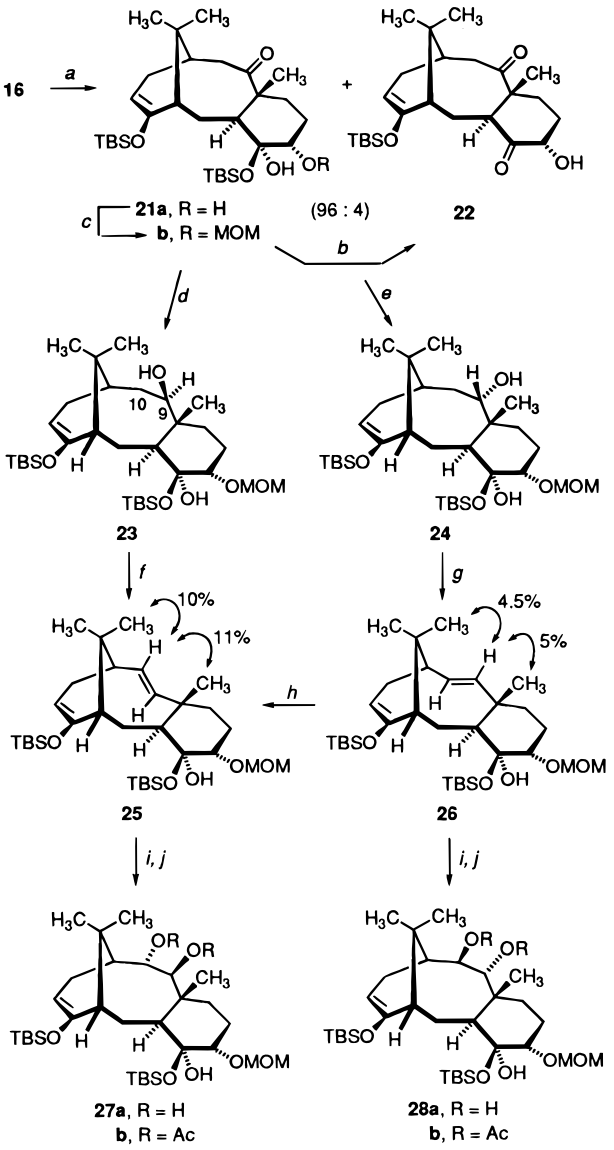
With these observations as a platform, the challenge of engaging C-9 in reaction was irresistible. To this end, **6** was treated overnight with 10 equiv of TBSOTf and triethylamine in CH_2Cl_2 at −78 °C to room temperature. The "swamping" conditions afforded a colorless oil recognized by ^{1}H NMR and ^{13}C NMR to have incorporated three TBS groups, but only two double bonds. One of these was tetrasubstituted, and the other necessarily disubstituted, *Z*-configured, devoid of bonding to oxygen, and connected to an adjacent methylene group. The remaining two oxygen-bearing centers appear as low-field quaternary and methine carbons. Crucial connectivity information, unambiguously provided by 1-D long-range ^{1}H/^{13}C correlation[25] of those protons accessible for selective excitation, was consistent only with structure **20**. A mechanism for the redox process involved in the formation of **20**, λ_{max}^{hexane} 281 nm (ϵ 4060), is summarized in Scheme 3.

Arrival at the Enantiopure *trans*-Tricyclopentadecenes and Kinetic Analysis of Their Diastereomeric Interconversion

Differentiation between the triad of carbonyl groups in **6** having been accomplished, the distinctive steric factors prevailing in bis(silyl enol ether) **16** were next relied upon to direct subsequent reaction to ring C without anticipated interference from the functionality in ring A (Scheme 4). While there was little apprehension for this regioselectivity pattern, we were not prepared to find that oxidation with dimethyl dioxirane[26] at −78 °C would lead predominantly to the unusual hemiacetal **21a** (96%). The minor product **22** (3%) can be generated in 92% yield by treatment of **21a** with potassium carbonate in methanol at room temperature. To confirm both the structural assignment to, and absolute stereochemistry of, **21a**, recourse was made to X-ray crystallographic analysis (Figure 2).

The formation of **21a** and its stability under acidic conditions are worthy of comment. It is presumed that attack by the dioxirane proceeds via the more sterically accessible endo trajectory to deliver the α-epoxide **A** (Scheme 5). The customary pathway for strain release, which likely involves the transient

Scheme 4



[a] Me(Me)C(O)O, acetone, CH_2Cl_2, -78 → -10 °C (93%). [b] K_2CO_3, CH_3OH (92%). [c] MOMCl, $(i\text{-Pr})_2NEt$, CH_2Cl_2 (97%). [d] $(i\text{-Bu})_2AlH$, hexanes, -78 → -10 °C (97%). [e] $(i\text{-Bu})_2AlH$, C_6H_6, 6 °C (99%). [f] $CH_3O_2\bar{C}N\overset{+}{S}O_2N(C_2H_5)_3$, C_6H_6, 25-45 °C (73%). [g] $[C_6H_5C(CF_3)_2O]_2SPh_2$, C_6H_6, 25 °C (91%). [h] C_6H_6, Δ. [i] OsO_4, CH_2Cl_2; $NaHSO_3$, py (71% of **27a**, 84% of **28a**). [j] Ac_2O, py, DMAP (56% for **27b**, 92% for **28b**).

generation of oxonium ion **B**, is followed in this instance by the nucleophilic attack of water from the α-surface as before to provide **C**. This accomplished, proton loss leads to **21a**. When this diol is treated with aqueous acid, protonation of the hemiacetal hydroxyl presumably occurs rapidly due to the greater accessibility of its nonbonded electron pairs. This return to **C** does not result in facile evolution of a ketone carbonyl. The hydrolytic outcome requires alternative oxygen-centered protonation at the more crowded OTBS site. Contrariwise, deprotonation of the acetal hydroxyl is followed by rapid loss of *tert*-butyldimethylsilanoxide ion and generation of **22**.

The time had arrived to examine how **21a** might be integrated into the main synthetic pathway. The first option to be pursued consisted of its initial transformation into the MOM-protected derivative **21b**.[27] To pursue dehydrative studies, **21b** was subjected in turn to the action *of diisobutylaluminum hydride*

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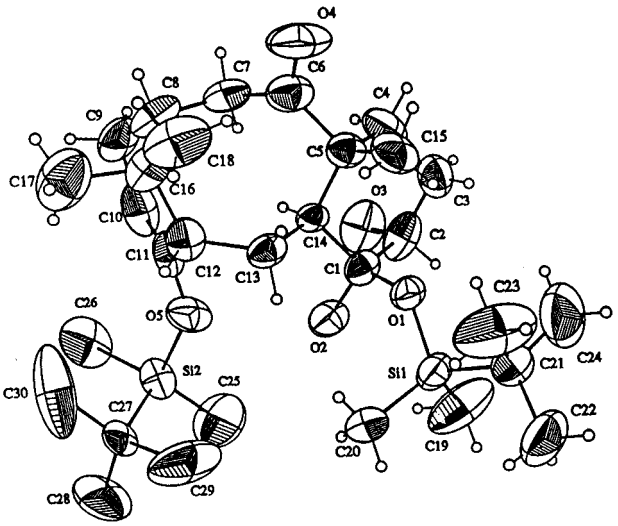
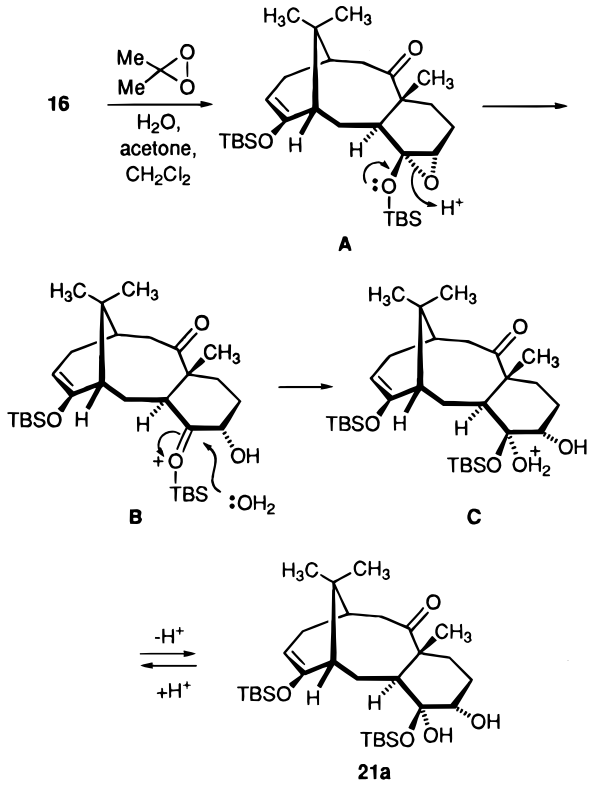


Figure 2. Computer-generated perspective drawing of the final X-ray model of **21a**.

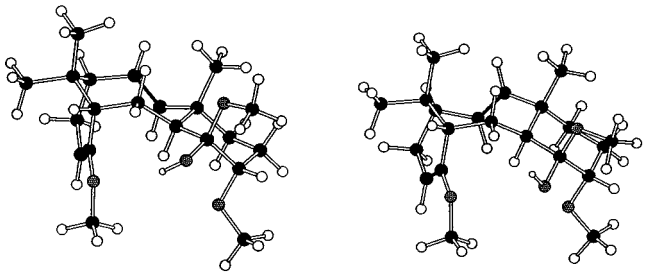
Scheme 5



in hexane at −78 to −10 °C. These conditions led to the exclusive formation of β-alcohol **23**, isolatable in 97% yield as a consequence of direct attack on the preferred "carbonyl-up" conformer (see above). At about the same time, the remarkable discovery was made that this diastereoselectivity was amenable to complete reversal simply by performing the reduction *in benzene solution at 8 °C.* This remarkable crossover is attributed to the ability of the **21b**-Dibal-H complex to adopt the less sterically congested "carbonyl-down" geometry at the more elevated reaction temperature, with hydride delivery occurring from the exo direction as always. The configurations assigned to **23** and **24** are based on the stereospecificity of their respective dehydrations.

(27) Paquette, L. A.; Zhao, M. *J. Am. Chem. Soc.* **1993**, *115*, 354.

Table 1. Global Minimum Energy Conformations of Simplified Analogues of **23** (as **D**) and **24** (as **E**) as Determined by Molecular Mechanics Calculations (Chem 3-D output)



D	**E**
ΔE_{strain} = 46.19 kcal/mol	ΔE_{strain} = 49.25 kcal/mol
ΔE_{total} = 73.20 kcal/mol	ΔE_{total} = 76.26 kcal/mol
ΔH_f = -144.57 kcal/mol	ΔH_f = -141.51 kcal/mol

With both diastereomeric carbinols in hand, advantage could next be taken of their latent potential for independent conversion to the diastereomeric *trans*-cyclooctenes **25** and **26**. Evidence was garnered from the inspection of molecular models concerning the rather inflexible conformational nature of **23**, which serves to project its C(9)-hydroxyl into an arrangement essentially coplanar with H(10α) and orthogonal to H(10β). Since the Burgess reagent[28] has been demonstrated to prefer a cis-eliminative pathway, our expectation was that warming **23** with this inner salt in benzene up to 45 °C would result in smooth conversion to **25**. Indeed, this enantiopure olefin, $[\alpha]^{20}_D$ −125 (*c* 1.03, hexanes), was isolated in 70% yield. When the α-alcohol **24** was found to be unreactive toward the Burgess reagent at a reasonable temperature, recourse was made instead to the Martin sulfurane.[29] This more powerful reagent induced dehydration in benzene at room temperature and gave rise only to **26**, $[\alpha]^{20}_D$ +42.3 (*c* 1.96, hexanes), in 91% yield. Evidence that both olefinic products were (*E*)-cycloalkenes was garnered from their large characteristic vinyl/vinyl coupling constants (J = 17.4 Hz for **25**; J = 18.7 Hz, for **26**).[30] The more crucial question of their specific identity was resolved by undertaking one-bond $^1H/^{13}C$ COSY correlation and NOE experiments.[31] Several of the key measurements are overlayed on the structural formulas.

Now that the general concept of stereoselective dehydration proved to be fruitful, we turned to molecular mechanics calculations (MODEL version KS 2.96)[32] in order to gain insight into which diastereomer is the more stable. For simplification purposes, the OTBS and OMOM substituents were replaced by OCH_3 as shown in **D** and **E** (Table 1). Under these circumstances, indication was provided that **D** might be as much as 3 kcal/mol more thermodynamically favored than **E**. At the experimental level, heating **26** in C_6D_6 at 67 °C resulted in its *unidirectional conversion* to **25** with a first-order rate constant of 2.58×10^{-4} s^{-1} and $t_{1/2}$ of 45 min. The relative ease of this

(28) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.

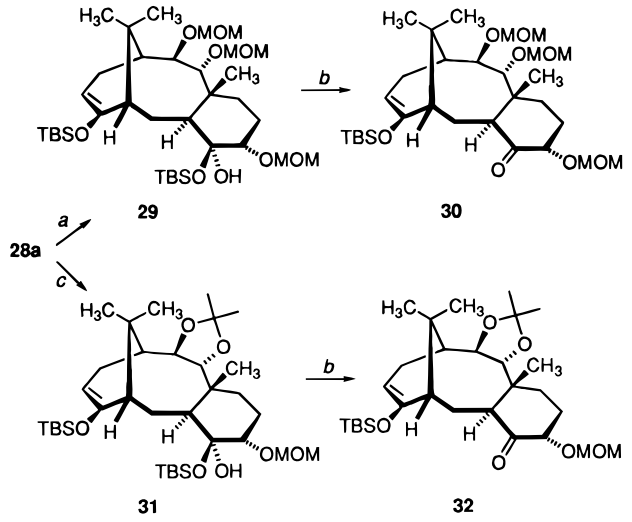
(29) Martin, J. C.; Arhart, R. J. *J. Am. Chem. Soc.* **1971**, *93*, 4327; **1972**, *94*, 5003.

(30) (a) Chapman, O. L. *J. Am. Chem. Soc.* **1963**, *85*, 2014. (b) Pegg, N. A.; Paquette, L. A. *J. Org. Chem.* **1991**, *56*, 2461.

(31) (a) Keeler, J.; Neuhaus, D.; Williamson, M. P. *J. Magn. Reson.* **1987**, *73*, 45. (b) Neuhaus, D.; Williamson, M. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*; VCH Publishers: Deerfield Beach, FL, 1989; pp 194 ff.

(32) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC, 1982. We thank Professors W. C. Still and K. Steliou for making this program available to us.

Scheme 6



[a] MOMCl, (*i*-Pr)$_2$NEt, CH_2Cl_2 (90%). [b] CH_3Li, THF, -78° → 25 °C (88% for **30**, 90% for **32**). [c] $(CH_3)_2C(OCH_3)_2$, (TsOH), DMF (94%).

interconversion places **26** closer to *trans*-cyclononene ($t_{1/2} \approx 4$ min at 0 °C)[33] than to *trans*-cyclooctene ($t_{1/2} = 122$ h at 132.7 °C)[34] in the intrinsic ability of these molecules to overcome their internal rotational barriers. Accordingly, fusion of A- and C-rings to a central *trans*-cyclooctene core in a manner characteristic of taxane frameworks facilitates internal rotation relative to the parent unsaturated hydrocarbon. Nonetheless, the thermal stability of **26** proved to be more than adequate to allow for its individual utilization in the synthetic sequence.

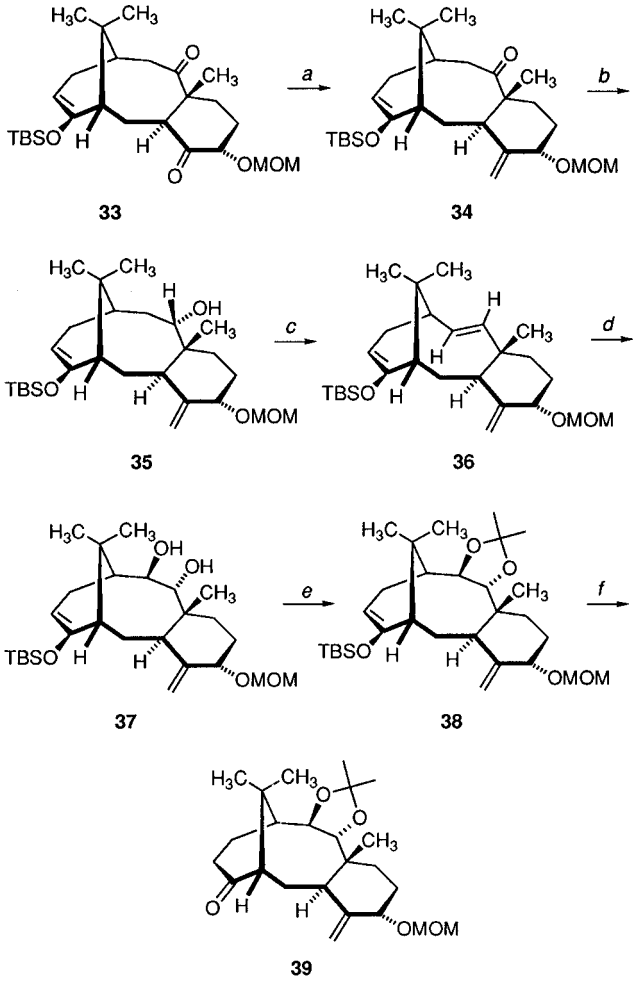
Dihydroxylation Studies and the Timing of Ring C Olefination

The pursuit of dihydroxylation studies on **25** and **26** was also motivated by the desire to demonstrate that the *E* double bond would prove more reactive than the silyl enol ether functionality in ring A. In fact, osmylation of these substrates proceeded to give diols **27a** (71%) and **28a** (84%), respectively, by electrophilic attack from the only available direction external to the ring. Conventional acetylation provided **27b** and **28b** efficiently, with the latter exhibiting the distinguishing C(9)/C(10) stereochemical pattern demanded by the target.

With this chemistry at hand, we proceeded to investigate the installation of hydroxyl protecting groups more suited to our goals than acetate. As outlined in Scheme 6, it proved to be equally facile to mask these substituents as methoxymethyl ethers as in **29** and **30**, or as an acetonide as in **31** and **32**. Clearly, this region of the taxane nucleus offers no complications with regard to structural modification.

Surprisingly, however, when either **30** or **32** was submitted to a range of conditions designed to bring about Wittig olefination at C(4), very little or no reaction occurred. When heat was applied to accelerate the process, decomposition occurred. This setback was construed to be the result of conformational factors brought on by the heavy substitution at C(9) and C(10), the consequence of which was to screen the C-ring carbonyl group from nucleophilic attack by the bulky phosphorane reagent. On this basis, it seemed possible that certain substrates, most notably C(9) ketones residing in a "carbonyl-up" B-ring geometry, might be more amenable to

Scheme 7



[a] $(C_6H_5)_3PCH_3^+ I^-$, *n*-BuLi, THF, 0° → 25 °C (97%). [b] (*i*-Bu)$_2$AlH, C_6H_6, 6 °C (100%). [c] $[C_6H_5C(CF_3)_2O]_2SPh_2$, C_6H_6, 25 °C (98%). [d] OsO_4, py; $NaHSO_3$, H_2O (91%). [e] $(CH_3)_2C(OCH_3)_2$, (TsOH), DMF (97%). [f] (*n*-Bu)$_4N^+ F^-$, THF, H_2O, -78° → 0 °C (96%).

olefination at C(4). It had earlier been established that the C(9) position was so sterically encumbered so not to offer competitive reactivity. To probe this matter further, **22** was converted into its MOM-protected derivative **33** in 93% yield for evaluation as a candidate substrate. Remarkably, the homologation to give **34** proceeded very efficiently at 0 → 25 °C to give **34** in 97% yield (Scheme 7). This experiment was to have significant implications for our taxusin strategy in that the Wittig process was now to be deployed much earlier than originally anticipated.

With arrival at **34**, we next had to garner evidence that stereocontrolled generation of the proper *trans*-cyclooctene could be accomplished. This phase of the synthesis took advantage of lessons previously learned. Thus, diisobutylaluminum hydride reduction of **34** in benzene at 6 °C resulted in quantitative conversion to α-alcohol **35**, subsequent dehydration of which with the Martin sulfurane delivered **36** with exceptional ease (98%). We were now in a position to evaluate the regioselectivity of the dihydroxylation of this trienyl product. Within the limits of our detection, osmylation was directed uniquely to the central B-ring, such that **37** could be isolated with an efficiency of 91%. Presumably, this outcome reflects once again the significant ring strain introduced in molecules of type **36**.

At this point, we confined ourselves to diol protection as acetonide **38**. Fluoride ion-induced desilylation of **38** gave rise

(33) Cope, A. C.; Banholzer, K.; Keller, H.; Pawson, B. A.; Whang, J. J.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1965**, *87*, 3644.

(34) Cope, A. C.; Pawson, B. A. *J. Am. Chem. Soc.* **1965**, *87*, 3649.

to ketone **39**, thereby setting the stage for those A-ring functionalization studies described in the following paper.[16]

Conclusion

Described herein is the evolution of a synthetic route that opens access to a number of functionalized taxane intermediates. Specifically, it has been established that the central framework can be assembled efficiently in only eight steps from **10** (as **10** → **13** → **14** → **6**) and that the level of substitution in rings B and C is amenable to introduction with proper control of absolute configuration in concise fashion (as **6** → **16** → **22** → **23** → **39**). Ultimately, all stereochemistry in this domain is induced from the bridged bicyclic features resident in *D*-camphor.

Stereoselective conversion of carbinol epimers into diastereomeric *trans*-olefins has been demonstrated, as has the interconversion of these strained systems. Also illustrated in these studies are the interplay of configurational arrangements on chemical reactivity and the power of the anionic oxy-Cope rearrangement in assembling taxane frameworks rapidly.

At this point, enough knowledge has been gained to recognize that the final push toward taxusin requires that attention now be focused principally on elaboration of the A-ring sector.

Experimental Section

General. THF and ether were distilled from sodium benzophenone ketyl under nitrogen just prior to use. For CH_2Cl_2 and benzene, the drying agent was calcium hydride. All reactions were performed under a N_2 atmosphere. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} aluminum-backed plates. All chromatographic purifications were performed on E. Merck silica gel 60 (230−400 mesh) using the indicated solvent systems. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker instruments at 300 and 75 MHz, respectively. Elemental analyses were performed at the Scandinavian Microanalytical Laboratory, Herlev, Denmark. The organic extracts were dried over anhydrous $MgSO_4$. IR spectra were recorded with a Perkin-Elmer 1320 spectrometer and optical rotations were measured with a Perkin-Elmer Model 241 polarimeter. The high-resolution mass spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center.

(4a*R*,7*R*,10*S*,11*S*,12a*S*)-Dodecahydro-10,11-dihydroxy-4a,13,13-trimethyl-7,10-methanobenzocyclodecene-1,5-dione (14a). To a solution of **13** (1.00 g, 3.64 mmol) in CH_2Cl_2 (15 mL) was added osmium tetraoxide (1.00 g, 3.9 mmol) at 25 °C. After 1 h of stirring, the solvent was evaporated in vacuo and the black solid was taken up in pyridine (15 mL), treated with $NaHSO_3$ (5 g in 15 mL of H_2O), and stirred overnight. The product was extracted into CH_2Cl_2 and the combined organic layers were dried and concentrated in vacuo. Chromatography of the residue on silica gel (elution with 1:1 ethyl acetate in hexanes) afforded 1.16 g (100%) of **14a** as a colorless crystalline solid, mp 123−124.5 °C (from ethyl acetate−hexanes): IR ($CHCl_3$, cm^{-1}) 3640−3300, 1715, 1683, 1010; ^{1}H NMR (300 MHz, C_6D_6) δ 3.80 (d, J = 6.9 Hz, 1 H), 3.06 (br s, 1 H), 2.96 (br s, 1 H), 2.86−2.76 (m, 2 H), 2.66−2.63 (m, 1 H), 2.20−1.15 (series of m, 12 H), 1.12 (s, 3 H), 0.93 (s, 3 H), 0.65 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 212.5, 210.5, 85.6, 73.4, 55.2, 48.0, 47.6, 45.9, 41.1, 39.1, 34.0, 33.2, 30.4, 25.5, 24.4, 21.3, 18.2, 17.1; MS m/z (M^+) calcd 308.1987, obsd 308.2012; $[\alpha]^{20}_D$ +144.6 (c 1.08, $CHCl_3$).

(4a*S*,6*S*,10*R*,12a*R*)-Decahydro-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,7,12(1*H*)-trione (6). To a solution of **14a** (0.90 g, 2.92 mmol) in pyridine (5 mL) at 0 °C was added methanesulfonyl chloride (1.00 g, 8.75 mmol). The mixture was stirred overnight and the pyridine was removed in vacuo. The residue was taken up in CH_2Cl_2 (50 mL) and washed sequentially with 0.1 N HCl (2 × 20 mL), water (2 × 15 mL), and saturated $NaHCO_3$ solution prior to drying and solvent removal. The resulting monomesylate **7** was directly reacted by dissolution in CH_2Cl_2 (40 mL), cooling to −78 °C, and treatment with diethylaluminum chloride (16 mL of 1.0 M in hexanes, 16 mmol, 8 equiv) during 5 min. The mixture was stirred at −78 °C for 12 h and at −15 °C for 9 h prior to being quenched with methanol (2 mL) and then water (15 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic solutions were evaporated. Purification of the residue by chromatography on silica gel furnished 550 mg (96%) of **6** as a white solid, mp 154−156 °C (from 1:1 ethyl acetate−hexanes): IR ($CHCl_3$, cm^{-1}) 1700 (br), 1445, 1394, 1382, 1338, 1220, 1096; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.80 (d, J = 10.9 Hz, 1 H), 2.72−2.61 (m, 2 H), 2.50−2.40 (m, 2 H), 2.36−2.22 (m, 4 H), 2.19−2.12 (m, 1 H), 2.04−1.86 (m, 4 H), 1.69−1.62 (m, 1 H), 1.57−1.47 (m, 1 H), 1.41 (d, J = 8.8 Hz, 1 H), 1.08 (s, 3 H), 1.06 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 215.1, 214.3, 209.8, 56.3, 55.7, 52.7, 41.1, 40.1, 38.5, 37.4, 36.1, 35.5, 33.7, 28.1, 25.1, 22.6, 22.1, 14.9; MS m/z (M^+) calcd 290.1882, obsd 290.1886; $[\alpha]^{20}_D$ −122.1 (c 0.98, $CHCl_3$).

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.36; H, 9.02.

This triketone was subjected to X-ray crystallographic analysis (Figure 1).

(4a*S*,6*S*,10*R*,12a*R*)-7-(*tert*-Butyldimethylsiloxy)-1,2,3,4a,5,6,9,10,11,12a-decahydro-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,12-dione (15). A solution of **6** (158 mg, 0.544 mmol) in dry THF (15 mL) was cooled to −78 °C, treated with potassium hexamethyldisilazide (1.20 mL of 0.5 M in toluene, 0.60 mmol), and stirred at this temperature for 1 h prior to the addition of a solution of *tert*-butyldimethylsilyl chloride (164 mg, 1.08 mmol) in hexanes (2 mL). The reaction mixture was allowed to warm to room temperature for 4 h, quenched with saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. The combined extracts were dried and concentrated to leave a residue that was chromatographed on silica gel. There was isolated 156 mg (71%) of **15** and 30 mg (6%) of **16**.

For **15**: white solid, mp 85−88 °C; IR (CH_2Cl_2, cm^{-1}) 1710 (br), 1656, 1210, 1160, 1090, 844; ^{1}H NMR (300 MHz, C_6D_6) δ 4.79 (d, J = 5.7 Hz, 1 H), 2.99−2.89 (m, 2 H), 2.85−2.65 (m, 1 H), 2.23−2.16 (m, 3 H), 1.94 (br d, J = 6.8 Hz, 1 H), 1.88−1.73 (m, 2 H), 1.60−1.31 (m, 6 H), 1.05 (s, 3 H), 0.97 (s, 9 H), 0.82 (s, 3 H), 0.81 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 214.3, 208.6, 151.5, 102.6, 56.1, 52.3, 48.4, 41.1, 39.5, 36.6, 36.1, 32.6, 29.3, 28.0, 25.8, 22.7, 20.8, 18.1, 15.5, −4.1, −4.7; MS m/z (M^+) calcd 404.2747, obsd 404.2732; $[\alpha]^{20}_D$ −156.8 (c 0.98, $CHCl_3$).

Compound **16** is characterized below.

(4a*S*,6*S*,10*R*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,4a,5,6,9,10,11,12a-octahydro-12a,13,13-trimethyl-6,10-methanobenzocyclodecen-12(2*H*)-one (16). To a solution of **6** (185 mg, 0.637 mmol) in CH_2Cl_2 (10 mL) at 0 °C were added triethylamine (193 mg, 1.91 mmol) and *tert*-butyldimethylsilyl triflate (420 mg in 3 mL of CH_2Cl_2, 1.59 mmol). The reaction mixture was stirred for 5 h at 0 °C, quenched with saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2. After the combined extracts had been dried and concentrated, the residue was purified by chromatography on silica gel (elution with 1:20 ether/hexanes) to give 304 mg (95%) of **16** as a colorless solid, mp 80−82 °C: IR ($CHCl_3$, cm^{-1}) 1682, 1655, 1471, 1461, 1361, 1252, 1192, 1148, 1075, 1010, 870, 837; ^{1}H NMR (300 MHz, C_6D_6) δ 4.76 (br s, 1 H), 4.75 (m, 1 H), 2.98 (dd, J = 7.3, 15.6 Hz, 1 H), 3.00−1.10 (series of m, 12 H), 1.02 (s, 9 H), 1.01 (s, 3 H), 0.99 (br s, 12 H), 0.91 (s, 3 H), 0.19 (s, 3 H), 0.17 (s, 3 H), 0.16 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 215.5, 151.2, 103.6, 103.4, 101.7, 36.7, 32.5, 26.7, 26.5, 26.3, 26.0, 21.04, 21.01, 20.9, 20.8, 18.5, 18.2, 14.9, −3.97, −4.02; MS m/z (M^+) calcd 518.3612, obsd 518.3611; $[\alpha]^{20}_D$ −75.0 (c 1.01, hexanes).

Anal. Calcd for $C_{30}H_{54}O_3Si_2$: C, 69.45; H, 10.50. Found: C, 69.31; H, 10.44.

Oxidation of 16 with Dimethyldioxirane. A cold (−78 °C), magnetically stirred solution of **16** (2.30 g, 4.43 mmol) in CH_2Cl_2 (90 mL) was treated with dimethyldioxirane (53.2 mL of 0.1 M in acetone, 5.32 mmol), stirred for 3 h, quenched with saturated $NaHCO_3$ solution, and freed of organic solvent in vacuo. The residual aqueous mixture was extracted with CH_2Cl_2, the combined organic extracts were evaporated, and the residue was chromatographed on silica gel (elution with 9:1 hexanes/ethyl acetate); 2.36 g (96%) of **21a** and 0.06 g (3%) of **22**, were obtained.

For **21a**: white solid, mp 147−149 °C (from hexanes); IR (hexanes, cm^{-1}) 1702, 1255, 1191, 1138, 1060, 1012, 839, 778; ^{1}H NMR (300

MHz, C_6D_6) δ 5.08 (s, 1 H), 4.84 (d, J = 5.6 Hz, 1 H), 3.69 (t, J = 2.6 Hz, 1 H), 2.90 (d, J = 7.3 Hz, 1 H), 2.85 (dd, J = 9.0, 12.1 Hz, 1 H), 2.61 (br s, 1 H), 2.21 (dd, J = 9.8, 12.1 Hz, 1 H), 2.20−1.67 (series of m, 8 H), 1.61 (s, 3 H), 1.34 (dd, J = 5.9, 17.0 Hz, 1 H), 1.05 (td, J = 3.2, 12.6 Hz, 1 H), 1.00 (s, 9 H), 0.94 (s, 9 H), 0.85 (s, 3 H), 0.78 (s, 3 H), 0.31 (s, 3 H), 0.23 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.2, 150.9, 106.9, 99.4, 72.1, 53.4, 50.0, 40.6, 40.4, 38.7, 37.0, 33.0, 30.3, 29.8, 27.9, 26.2, 26.0, 24.3, 21.7, 18.2, 15.8, −1.7, −2.3, −4.0, −4.3; MS *m*/*z* (M^+) calcd 552.3666, obsd 552.3684; $[\alpha]^{20}_D$ −71.6 (*c* 0.99, hexanes).

Anal. Calcd for $C_{30}H_{56}O_5Si_2$: C, 65.17; H, 10.21. Found: C, 65.21; H, 10.30.

This diol was subjected to X-ray crystallographic analysis (Figure 2).

For **22**: white solid, mp 184−185 °C (from hexanes−benzene); IR (C_6H_6, cm^{-1}) 3586, 1723, 1702, 1215, 1201, 1152; ^{1}H NMR (30 MHz, C_6D_6) δ 4.74 (d, J = 5.6 Hz, 1 H), 3.90 (d, J = 9.7 Hz, 1 H), 3.75 (td, J = 3.0, 3.6 Hz, 1 H), 3.00−2.90 (br s, 1 H), 2.75 (dd, J = 6.9, 16.3 Hz, 1 H), 2.25−2.13 (m, 3 H), 1.95 (br d, J = 6.9 Hz, 1 H), 1.75 (d, J = 3.6 Hz, 1 H), 1.76−1.42 (m, 5 H), 1.07 (s, 3 H), 1.02−0.91 (m, 1 H), 0.98 (s, 9 H), 0.83 (s, 3 H), 0.81 (s, 3 H), 0.16 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 213.6, 209.9, 151.4, 102.3, 74.3, 56.0, 48.8, 46.9, 39.7, 39.6, 36.9, 32.7, 30.7, 30.4, 29.2, 28.0, 25.9, 20.8, 18.2, 15.5, −4.1, −4.6; MS *m*/*z* (M^+) calcd 420.2696, obsd 420.2682; $[\alpha]^{20}_D$ −125.5 (*c* 1.02, C_6H_6).

Anal. Calcd for $C_{24}H_{40}O_4Si$: C, 68.53; H, 9.59. Found: C, 68.46; H, 9.62.

(3*S*,4a*S*,6*S*,10*R*,12a*R*)-7-(*tert*-Butyldimethylsiloxy)-1,2,3,4a,5,6,9,10,11,12a-decahydro-3-hydroxy-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,12-dione (22). A mixture of **21a** and **22** (60 mg, 0.11 mmol), K_2CO_3 (40 mg, 0.29 mmol), and methanol (4 mL) was stirred for 30 min, then quenched with saturated NH_4Cl solution. Removal of the methanol in vacuo followed by extraction with CH_2Cl_2 and the usual workup afforded 43 mg of white solid. Column chromatography on silica gel afforded 42 mg (92%) of pure **22**.

(3*S*,4*S*,4a*S*,6*S*,10*R*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,3,4,4a,5,6,9,10,11,12a-decahydro-4-hydroxy-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecen-12(2*H*)-one (21b). To a solution of **21a** (241 mg, 0.436 mmol) in CH_2Cl_2 (10 mL) were added diisopropylethylamine (1.41 g, 10.9 mmol) and MOM chloride (702 mg, 8.72 mmol). The reaction mixture was stirred for 48 h, quenched with saturated NH_4Cl and $NaHCO_3$ solutions, and allowed to hydrolyze for 10 min. The separated aqueous phase was extracted with hexanes (2 × 15 mL) and the combined organic layers were dried and evaporated. Chromatography of the residue on silica gel afforded 252 mg (97%) of **21b** as a colorless oil; IR (neat, cm^{-1}) 3465, 1693, 1659, 1253, 1146, 1050, 1030, 839; ^{1}H NMR (300 MHz, C_6D_6) δ 4.86 (d, J = 6.4 Hz, 1 H), 4.86 (m, 1 H), 4.63 (d, J = 6.4 Hz, 1 H), 4.43 (s, 1 H), 3.67 (d, J = 3.5 Hz, 1 H), 3.24 (s, 3 H), 2.90 (dd, J = 10.3, 10.3 Hz, 1 H), 2.80 (d, J = 8.0 Hz, 1 H), 2.34 (dd, J = 16.3, 7.2 Hz, 1 H), 2.27 (dd, J = 11.8, 9.5 Hz, 1 H), 2.11−2.03 (m, 3 H), 1.89 (br d, J = 6.6 Hz, 1 H), 1.75−1.61 (m, 3 H), 1.66 (s, 3 H), 1.45−1.35 (br m, 1 H), 1.12−1.07 (m, 1 H), 1.02 (s, 9 H), 0.98 (s, 9 H), 0.88 (s, 3 H), 0.80 (s, 3 H), 0.36 (s, 3 H), 0.30 (s, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.2, 151.3, 106.4, 99.2, 96.6, 77.8, 55.2, 53.5, 49.9, 41.6, 40.3, 39.0, 37.1, 32.9, 31.0, 29.5, 28.0, 26.3, 25.9, 24.6, 21.0, 18.3, 16.1, −1.7, −2.3, −4.1, −4.3; MS *m*/*z* (M^+) calcd 596.3883, obsd 596.3906; $[\alpha]^{20}_D$ −87.3 (*c* 1.71, hexanes).

Anal. Calcd for $C_{32}H_{60}O_6Si_2$: C, 64.38; H, 10.13. Found: C, 64.37; H, 10.17.

(3*S*,4*S*,4a*S*,6*S*,10*R*,12*R*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,12-diol (23). A solution of **21b** (66 mg, 0.11 mmol) in hexanes (7 mL) was cooled to −78 °C, treated with diisobutylaluminum hydride (0.33 mL of 1.0 M in hexanes, 0.33 mmol), stirred for 2 h at −78 °C and for 2 h more during warming to −10 °C, and quenched with saturated NH_4Cl solution. After 15 min, the aqueous phase was separated and extracted with hexanes. The combined organic solutions were dried and concentrated to leave a colorless oil which became a white foam (64 mg, 97%) when placed under high vacuum: ^{1}H NMR (300 MHz, C_6D_6) δ 4.88 (d, J = 6.4 Hz, 1 H), 4.77 (dd, J = 4.9, 2.4 Hz, 1 H), 4.70 (d, J = 6.4 Hz, 1 H), 3.78 (s, 1 H), 3.71 (dd, J = 2.7, 2.7 Hz, 1H), 3.34 (d, J = 8.5 Hz, 1 H), 3.28 (s, 3H), 2.35−2.17 (m, 3 H), 2.09−1.97 (m, 1 H), 1.94−1.58 (series of m, 7 H), 1.46−1.22 (m, 1 H), 1.16 (s, 3 H), 1.03 (s, 9 H), 0.96 (s, 12 H), 0.93 (s, 3 H), 0.38 (s, 3 H), 0.30 (s, 3 H), 0.14 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 152.7, 105.1, 99.9, 96.2, 77.8, 55.1, 47.2, 45.3, 42.3, 37.5, 36.7, 34.6, 31.6, 31.5, 26.3, 26.1, 25.92, 25.89, 24.0, 18.4, 18.3, 18.2, 12.6, −1.8, −2.3, −3.8, −4.0; MS *m*/*z* (M^+) calcd 598.4085, obsd 598.4067; $[\alpha]^{20}_D$ −54.1 (*c* 0.92, hexanes).

Anal. Calcd for $C_{32}H_{62}O_6Si_2$: C, 64.16; H, 10.43. Found: C, 64.24; H, 10.50.

(3*S*,4*S*,4a*S*,6*S*,10*R*,11*E*,12a*S*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,12a-decahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecen-4-ol with H-11 Up (25). A mixture of **23** (20 mg, 0.033 mmol) and the Burgess reagent (12 mg) was dissolved in benzene (5 mL) and stirred for 3 h at 25 °C and for 2 h at 40−45 °C. Additional Burgess reagent (10 mg) was introduced and dehydration was allowed to proceed overnight at room temperature. After the addition of saturated $NaHCO_3$ solution, the aqueous layer was extracted with hexanes, and the combined organic solutions were dried and evaporated. Purification of the residue by chromatograpy on silica gel (elution with 1:30 ether/hexanes) led to the isolation of **25** (14 mg, 73%) as a colorless oil: IR (neat, cm^{-1}) 3580, 2668, 1256, 1142, 1061, 1030, 922, 834, 780; ^{1}H NMR (300 MHz, C_6D_6) δ 5.72 (dd, J = 17.4, 2.7 Hz, 1 H), 5.60 (d, J = 17.4 Hz, 1 H), 4.87 (dd, J = 3.6, 3.6 Hz, 1 H), 4.62 (d, J = 6.5 Hz, 1 H), 4.58 (d, J = 6.5 Hz, 1 H), 3.60 (br s, 1 H), 3.32 (s, 1 H), 3.22 (s, 3 H), 2.28 (dd, J = 15.9, 10.6 Hz, 1 H), 2.23−2.19 (m, 2 H), 2.08−1.87 (m, 4 H), 1.81−1.69 (m, 2 H), 1.61−1.35 (m, 2 H), 1.33 (s, 3 H), 1.08 (s, 3 H), 1.05 (s, 9 H), 0.99 (s, 3 H), 0.98 (s, 9 H), 0.37 (s, 3 H), 0.29 (s, 3 H), 0.16 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 151.5, 140.8, 126.9, 104.9, 99.2, 95.6, 78.8, 55.3, 52.3, 48.9, 44.2, 44.0, 42.8, 32.4, 29.1, 26.3, 25.9, 25.7, 24.7, 23.4, 19.8, 18.3, 18.2, 15.9, −1.8, −2.3, −3.97, −4.00; MS *m*/*z* (M^+) calcd 680.3979, obsd 680.3962; $[\alpha]^{20}_D$ −125.0 (*c* 1.03, hexanes).

(3*S*,4*S*,4a*S*,6*S*,10*R*,11*E*,12a*S*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,12a-decahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecen-4-ol with H-11 Down (26). To a solution of **21b** (40 mg, 0.067 mmol) in benzene (8 mL) at 6 °C was added diisobutylaluminum hydride (0.25 mL of 1.0 M in hexanes, 0.25 mmol). The mixture was stirred for 30 min, quenched with saturated NH_4Cl and $NaHCO_3$ solutions, and agitated 15 min longer. The separated aqueous phase was extracted with hexanes and the combined organic layers were dried and concentrated to give 40 mg (99%) of

24 as a colorless oil which was dehydrated directly.

A solution of Martin's sulfurane (183 mg, 0.27 mmol) in benzene (7 mL) was treated with a solution of **24** (130 mg, 0.217 mmol) in benzene (4 mL), stirred at 25 °C for 3 h, and quenched with saturated $NaHCO_3$ solution. The mixture was extracted with hexanes, and the combined organic layers were dried and concentrated. Purification of the residue by chromatography on silica gel afforded 115 mg (91%) of **26** as a colorles oil: IR (neat, cm^{-1}) 3490, 1648, 1465, 1255, 1130, 1102, 1055, 1032, 860, 840, 780; ^{1}H NMR (300 MHz, C_6D_6) δ 5.94 (d, J = 18.7 Hz, 1 H), 5.86 (dd, J = 6.4, 18.7 Hz, 1 H), 4.93 (d, J = 6.5 Hz, 1 H), 4.87 br d, J = 5.2 Hz, 1 H), 4.70 (d, J = 6.5 Hz, 1 H), 4.01 (s, 1 H), 3.69 (t, J = 2.7 Hz, 1 H), 3.28 (s, 3 H), 2.39−2.03 (m, 5 H), 1.91−1.77 (m, 4 H), 1.60−1.52 (m, 2 H), 1.36 (s, 3 H), 1.044 (s, 9 H), 1.036 (s, 3 H), 0.99 (s, 9 H), 0.89 (s, 3 H), 0.37 (s, 3 H), 0.33 (s, 3 H), 0.15 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 153.5, 142.2, 139.1, 107.4, 100.2, 96.6, 78.7, 55.2, 54.8, 51.7, 42.6, 41.4, 39.9, 31.4, 30.3, 29.9, 27.0, 26.3, 26.0, 25.3, 23.0, 21.4, 18.3, −1.7, −2.2, −4.1, −4.2; MS *m*/*z* (M^+) calcd 580.3979, obsd 580.3985; $[\alpha]^{20}_D$ +41.3 (*c* 1.96, hexanes).

(3*S*,4*S*,4a*S*,6*S*,10*S*,11*S*,12*S*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,11,12-triol (27a). A solution of **25** (36 mg, 0.062 mmol) in CH_2Cl_2 (5 mL) at 25 °C was treated with osmium tetraoxide (20 mg), stirred for 10 min, and freed of solvent in vacuo to leave a dark green solid. This material was

taken up in pyridine (2 mL), $NaHSO_3$ was introduced (1 g in 2 mL of H_2O), and the mixture was stirred overnight prior to extraction with ether (4 × 15 mL). The combined organic extracts were dried under high vacuum, and the residue was subsequently chromatographed on silica gel. Elution with 1:3 ethyl acetate/hexanes furnished 217 mg (71%) of **27a** as a white solid, mp 182−183 °C (from hexanes/ethyl acetate): IR (CCl_4, cm^{-1}) 3650, 3490, 3360, 1253, 1147, 1102, 1040, 839, 826; ^1H NMR (300 MHz, C_6D_6) δ 4.84 (d, J = 6.4 Hz, 1 H), 4.78 (dd, J = 3.6, 3.6 Hz, 1 H), 4.69 (d, J = 6.4 Hz, 1 H), 4.02 (d, J = 7.5 Hz, 1 H), 3.72 (s, 1 H), 3.69 (br s, 1 H), 3.29 (d, J = 7.5 Hz, 1 H), 3.28 (s, 3 H), 2.90−2.70 (br s, 1 H), 2.34 (dd, J = 16.4, 11.5 Hz, 1 H), 2.18−2.13 (m, 2 H), 2.09−1.98 (m, 1 H), 1.91−1.68 (m, 6 H), 1.59 (dd, J = 16.8, 7.5 Hz, 1 H), 1.37−1.20 (m, 1 H), 1.19 (s, 3 H), 1.07 (s, 3 H), 1.03 (s, 9 H), 0.98 (s, 3 H), 0.96 (s, 9 H), 0.37 (s, 3 H), 0.29 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 153.0, 104.5, 99.8, 96.1, 78.0, 77.8, 68.0, 55.2, 48.0, 47.6, 45.2, 43.0, 36.3, 32.3, 31.6, 26.3, 25.9, 25.7, 23.7, 22.6, 18.7, 18.24, 18.15, 12.9, −1.8, −2.4, −3.8, −4.1; FAB MS (M^+) calcd 614.40, obsd 614.40; $[\alpha]^{20}_D$ −49.8 (*c* 1.00, CCl_4).

Anal. Calcd for $C_{32}H_{62}O_7Si_2$: C, 62.50; H, 10.16. Found: C, 62.53; H, 10.18.

(3*S*,4*S*,4a*S*,6*S*,10*S*,11*S*12*S*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,11,12-triol 11,12-Diacetate (27b). A solution of **27a** (23 mg, 0.038 mmol), pyridine (0.20 mL, 2.5 mmol), acetic anhydride (0.10 mL, 1.06 mmol), and 4-(dimethylamino)pyridine (2 mg) in CH_2Cl_2 (3 mL) was stirred overnight at room temperature, quenched with saturated NH_4Cl solution, and extracted with CH_2Cl_2. The combined extracts were dried and evaporated, and the residue was chromatographed on silica gel to provide 15 mg (56%) of **27b** and 7 mg (28%) of the monoacetate.

For **27b**: white solid, mp 60 °C; IR (neat, cm^{-1}) 3480, 1740, 1465, 1370, 1250, 1148, 1102, 1030, 830, 780; ^1H NMR (300 MHz, C_6D_6) δ 5.85 (d, J = 8.2 Hz, 1 H), 5.11 (d, J = 8.2 Hz, 1 H), 5.00 (dd, J = 4.9, 2.4 Hz, 1 H), 4.78 (d, J = 6.5 Hz, 1 H), 4.63 (d, J = 6.5 Hz, 1 H), 3.78 (s, 1 H), 3.69 (m, 1 H), 3.23 (s, 3 H), 3.02 (dd, J = 18.6, 4.9 Hz, 1 H), 2.44 (dd, J = 16.6, 11.5 Hz, 1 H), 2.28 (br dd, J = 18.6, 7.5 Hz, 1 H), 2.10 (d, J = 6.8 Hz, 1 H), 2.09−1.97 (m, 1 H), 1.90 (d, J = 11.5 Hz, 1 H), 1.83−1.53 (m, 4 H), 1.72 (s, 3 H), 1.67 (s, 3 H), 1.50 (s, 3 H), 1.21 (s, 3 H), 1.01 (s, 9 H), 0.94 (s, 9 H), 0.93 (s, 3 H), 0.37 (s, 3 H), 0.29 (s, 3 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 169.3, 168.2, 152.6, 105.2, 99.5, 96.0, 78.5, 77.5, 69.6, 55.2, 47.4, 46.9, 45.0, 42.8, 36.6, 32.1, 31.1, 26.2, 25.9, 23.5, 22.7, 20.7, 20.3, 18.6, 18.2, 18.1, −1.8, −2.4, −3.8, −4.2; FAB MS *m*/*z* (M^+) calcd 698.42, obsd 698.50; $[\alpha]^{20}_D$ −54.8 (*c* 2.08, hexanes).

Anal. Calcd for $C_{36}H_{66}O_9Si_2$: C, 61.85; H, 9.52. Found: C, 61.87; H, 9.46.

(3*S*,4*S*,4a*S*,6*S*,10*S*,11*R*,12*R*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,11,12-triol (28a). *trans*-Olefin **26** (115 mg, 0.198 mmol) dissolved in CH_2Cl_2 (7 mL) was osmylated in the manner described above to give 102 mg (84%) of **28a** as a white foam, mp 65−67 °C; IR (neat, cm^{-1}) 3440, 1060, 1030, 837, 775; ^1H NMR (300 MHz, C_6D_6) δ 5.01 (d, J = 6.3 Hz, 1 H), 4.98−4.95 (m, 1 H), 4.82 (s, 1 H), 4.74 (d, J = 6.3 Hz, 1 H), 3.99 (br d, J = 6.6 Hz, 1 H), 3.73 (br t, J = 2.6 Hz, 1 H), 3.65 (dd, J = 7.1, 6.6 Hz, 1 H), 3.30 (s, 3 H), 2.34−2.23 (m, 2 H), 2.18−2.02 (m, 4 H), 1.88−1.79 (m, 2 H), 1.72−1.55 (m, 3 H), 1.45 (s, 3 H), 1.34−1.30 (m, 2 H), 1.15 (s, 3 H), 1.05 (s, 9 H), 0.97 (s, 9 H), 0.92 (s, 3 H), 0.37 (s, 3 H), 0.34 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 151.6, 108.0, 100.2, 96.8, 78.5, 73.2, 72.9, 55.2, 50.0, 49.5, 43.0, 39.6, 36.1, 35.0, 30.3, 28.6, 26.4, 25.9, 24.7, 23.5, 19.6, 19.0, 18.3, 18.2, −1.6, −2.2, −4.0, −4.3; MS *m*/*z* (M^+) calcd 614.4034, obsd 614.4028; $[\alpha]^{23}_D$ −30.6 (*c* 1.13, hexanes).

(3*S*,4*S*,4a*S*,6*S*,10*S*,11*R*,12*R*,12a*R*)-4,7-Bis(*tert*-butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,11,12-triol 11,12-Diacetate (28b). Acetylation of diol **28a** (40 mg, 0.065 mmol) as before afforded 42 mg (92%) of **28b** as a white foam, mp 63−66 °C: IR (neat, cm^{-1}) 3460, 1745, 1370, 1250, 1230, 1020, 857, 840, 780; ^1H NMR (300 MHz, C_6D_6) δ 5.59 (d, J = 7.4 Hz, 1 H), 5.29 (dd, J = 7.2, 7.4 Hz, 1 H), 5.00 (br d, J = 3.6 Hz, 1 H), 4.93 (d, J = 6.5 Hz, 1 H), 4.75 (s, 1 H), 4.75 (d, J = 6.5 Hz, 1 H), 3.70 (t, J = 2.6 Hz, 1 H), 3.40 (s, 3 H), 2.49−2.40 (m, 2 H), 2.31−2.14 (m, 2 H), 2.03−1.84 (m, 4 H), 1.79−1.66 (m, 2 H), 1.74 (s, 3 H), 1.69 (s, 3 H), 1.56 (s, 3 H), 1.45−1.35 (m, 1 H), 1.26 (s, 3 H), 1.04 (s, 9 H), 0.98 (s, 9 H), 0.93 (s, 3 H), 0.38 (s, 3 H), 0.33 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 170.0, 168.9, 151.7, 107.5, 99.9, 96.5, 78.5, 75.3, 73.7, 55.2, 49.6, 46.2, 41.9, 39.6, 36.3, 35.0, 29.3, 28.5, 26.4, 25.9, 24.5, 24.3, 20.6, 20.1, 19.5, 19.1, 18.3, 18.2, −1.6, −2.2, −4.0, −4.3; MS *m*/*z* (M^+) calcd 698.4245, obsd 698.4259; $[\alpha]^{23}_D$ −7.4 (*c* 1.05, hexanes).

Anal. Calcd for $C_{36}H_{66}O_9Si_2$: C, 61.85; H, 9.52. Found: C, 61.80, H, 9.39.

(3*S*,4a*S*,6*S*,10*R*,12a*R*)-7-(*tert*-Butyldimethylsiloxy)-1,2,3,4a,5,6,9,10,11,12a-decahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-6,10-methanobenzocyclodecene-4,12-dione (33). A solution of **22** (1.64 g, 3.90 mmol) in CH_2Cl_2 (8.0 mL) was reacted with diisopropylethylamine (1.70 mL, 97.5 mmol) and MOM chloride (5.9 mL, 78.0 mmol) at room temperature for 72 h and worked up in the predescribed manner to provide **33** (1.69 g, 93%) as a white solid, mp 102−103 °C (from hexanes−ethyl acetate): IR (neat, cm^{-1}) 1723, 1704, 1657; ^1H NMR (300 MHz, C_6D_6) δ 4.74 (d, J = 5.6 Hz, 1 H), 4.59 (d, J = 6.4 Hz, 1 H), 4.55 (d, J = 6.4 Hz, 1 H), 3.95 (t, J = 2.8 Hz, 1 H), 3.88 (d, J = 9.5 Hz, 1 H), 3.16 (s, 3 H), 2.97 (br t, J = 10.5 Hz, 1 H), 2.73 (dd, J = 6.8, 16.3 Hz, 1 H), 2.31−2.08 (m, 3 H), 1.89 (br d, J = 6.5 Hz, 1 H), 1.81−1.56 (m, 3 H), 1.49−1.40 (m, 2 H), 1.08 (s, 3 H), 1.00 (m, 1 H), 0.92 (s, 9 H), 0.81 (s, 3 H), 0.80 (s, 3 H), 0.09 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 214.0, 209.7, 151.3, 103.3, 94.9, 77.8, 56.7, 55.5, 48.8, 47.2, 39.9, 36.7, 32.7, 31.2, 29.4, 28.8, 28.0, 25.8, 20.7, 18.1, 15.2, −3.9, −5.0; MS *m*/*z* (M^+) calcd 464.2958, obsd 464.2964; $[\alpha]^{20}_D$ −146.1 (*c* 1.15, hexanes).

Anal. Calcd for $C_{26}H_{44}O_5Si$: C, 67.20; H, 9.55. Found: C, 67.24; H, 9.51.

(3*S*,4a*R*,6*S*,10*R*,12a*R*)-7-(*tert*-Butyldimethylsiloxy)-1,4,4,4a,5,6,9,10,11,12a-decahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-4-methylene-6,10-methanobenzocyclodecen-12(2*H*)-one (34). A slurry of methyltriphenylphosphonium iodide (800 mg, 1.98 mmol) in THF (10 mL) was treated with *n*-butyllithium (1.08 mL of 1.65 M in hexanes, 1.78 mmol) at 0 °C. The mixture was stirred at 0 °C for 2 h and at 25 °C for 2 h prior to the addition of **33** (225 mg, 0.484 mmol) in dry THF (4 mL). After 14 h, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with hexanes. The combined organic extracts were dried and concentrated to leave a residue which was purified chromatographically (silica gel, elution with 1:7 ethyl acetate/hexanes) to give 217 mg (97%) of **34** as a white solid, mp 81−85 °C: IR (CH_2Cl_2, cm^1) 1692, 1658, 1217, 1210, 1150, 1035, 848; ^1H NMR (300 MHz, C_6D_6) δ 4.99 (s, 1 H), 4.82 (s, 1 H), 4.81 (d, J = 6.4 Hz, 1 H), 4.76 (br d, J = 5.6 Hz, 1 H), 4.58 (d, J = 6.4 Hz, 1 H), 4.16 (dd, J = 2.8, 2.8 Hz, 1 H), 3.35 (br d, J = 10 Hz, 1 H), 3.23 (s, 3 H), 3.1−3.0 (m, 1 H), 2.23−2.11 (m, 4 H), 1.84−1.73 (m, 3 H), 1.64−1.44 (m, 3 H), 1.19 (s, 3 H), 1.16−1.06 (m, 1 H), 0.95 (s, 9 H), 0.91 (s, 3 H), 0.86 (s, 3 H), 0.13 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 216.1, 151.4, 150.9, 112.2, 103.1, 93.1, 76.2, 55.1, 54.5, 50.1, 39.6, 39.2, 37.9, 36.7, 32.8, 32.4, 29.5, 28.8, 28.4, 25.9, 25.2, 18.1, 13.9, −3.8, −5.1; FAB MS *m*/*z* (M^+) calcd 462.32, obsd 462.47; $[\alpha]^{23}_D$ −207.7 (*c* 1.45, hexanes).

Anal. Calcd for $C_{27}H_{46}O_4Si$: C, 70.08; H, 10.02. Found: C, 70.29; H, 10.11.

(3*S*,4a*R*,6*S*,10*R*,12*S*,12a*R*)-7-(*tert*-Butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-4-methylene-6,10-methanobenzocyclodecen-12-ol (35). A cold (6 °C) solution of **34** (765 mg, 1.65 mmol) in benzene (30 mL) was treated with diisobutylaluminum hydride (3.64 mL of 1.0 M in hexanes, 3.64 mmol) during 5 min, stirred for 1 h at this temperature, and quenched with saturated NH_4Cl solution (10 mL). The reaction mixture was stirred for 1 h and diluted with hexanes. The separated aqueous phase was extracted with hexanes (2 × 20 mL), and the combined organic solutions were dried and concentrated to give **35** (768 mg, 100%) as a white foam: IR (neat, cm^{-1}) 3500, 1654, 1254, 1200, 1150, 1094, 1035; ^1H NMR (300 MHz, C_6D_6) showed two conformational isomers to be present in an approximate ratio of

3:2; ^{13}C NMR (75 MHz, C_6D_6) ppm 155.1, 154.0, 152.2, 112.0, 111.2, 104.1, 102.9, 93.6, 93.1, 81.5, 77.8, 76.8, 64.2, 55.0, 50.2, 47.2, 44.1, 44.0, 40.0, 39.2, 38.2, 37.4, 37.1, 35.5, 34.8, 34.7, 34.5, 33.0, 31.7, 31.2, 29.5, 29.2, 28.4, 27.1, 27.0, 26.8, 25.93, 25.88, 24.0, 22.3, 18.14, 18.07, 17.7, 16.4, −3.4, −4.2, −5.0; FAB MS (M^++1) calcd 465.45, obsd 465.51; $[\alpha]^{23}_D$ −146.8 (*c* 0.13, hexanes).

Anal. Calcd for $C_{27}H_{48}O_4Si$: C, 69.78; H, 10.41. Found: C, 69.47; H, 10.47.

***tert*-Butyl[[(3*S*,4a*S*,6*S*,10*R*,11*E*,12a*S*)-1,2,3,4,4a,5,6,9,10,12a-decahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-4-methylene-6,10-methanobenzocyclodecen-7-yl]oxy]dimethylsilane (36).** To a solution of the Martin sulfurane (2.14 g, 3.18 mmol) in benzene (20 mL) was added a solution of **35** (738 mg, 1.59 mmol) in benzene (10 mL). The reaction mixture was stirred overnight, quenched with saturated $NaHCO_3$ soution (10 mL), and extracted with hexanes. The combined organic phases were concentrated and the residue was chromatographed on silica gel to furnish **36** (755 mg, 98%) as a colorless oil: IR (neat, cm^{-1}) 1647, 1470, 1461, 1254, 1200, 1152, 1133, 1033, 870, 832, 777; ^{1}H NMR (300 MHz, C_6D_6) δ 6.05 (dd, J = 18.6, 7.5 Hz, 1 H), 5.91 (d, J = 18.6 Hz, 1 H), 4.96 (t, J = 1.4 Hz, 1 H), 4.85 (d, J = 6.5 Hz, 1 H), 4.80 (d, J = 6.1 Hz, 1 H), 4.76 (t, J = 1.4 Hz, 1 H), 4.60 (d, J = 6.5 Hz, 1 H), 4.20 (t, J = 2.9 Hz, 1 H), 3.26 (s, 3 H), 3.00 (d, J = 9.8 Hz, 1 H), 2.45 (dt, J = 4.5, 13.3 Hz, 1 H), 2.19 (qd, J = 2.3, 16.7 Hz, 1 H), 2.05 (dd, J = 7.2, 15.2 Hz, 1 H), 1.97−1.88 (m, 3 H), 1.79−1.68 (m, 2 H), 1.53 (ddd, J = 1.9, 4.6, 12.3 Hz, 1 H), 1.42 (ddd, J = 1.6, 10.0, 15.2 Hz, 1 H), 1.04 (s, 3 H), 0.95 (s, 12 H), 0.90 (s, 3 H), 0.14 (s, 3H), 0.09 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 153.5, 151.8, 140.3, 138.9, 110.5, 104.4, 93.1, 76.7, 55.0, 51.9, 50.4, 43.1, 41.4, 39.9, 33.2, 29.9, 29.7, 26.9, 26.0, 25.8, 20.2, 18.2, −3.7, −4.9; MS *m*/*z* (M^+) calcd 446.3216, obsd 446.3208; $[\alpha]^{23}_D$ −76.3 (*c* 1.08, hexanes).

(3*S*,4a*R*,6*S*,10*S*,11*R*.12*R*,12a*R*)-7-(*tert*-Butyldimethylsiloxy)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-4-methylene-6,10-methanobenzocyclodecene-11,12-diol (37). A solution of **36** (790 mg of 90% purity, 1.49 mmol) in pyridine (10 mL) at 0 °C was treated with osmium tetraoxide (1.49 mmol) and stirred for 1 h prior to the addition of $NaHSO_3$ (16 g in 17 mL of H_2O). After overnight stirring and the usual workup, there was obtained 650 mg (91%) of **37** as a white solid, mp 150−151 °C: IR (CH_2Cl_2, cm^{-1}) 3600−3200, 1655, 1463, 1388, 1360, 1195, 1150, 1137, 1090, 980; ^{1}H NMR (300 MHz, C_6D_6) δ 5.05 (s, 1 H), 4.89 (d, J = 6.6 Hz, 1 H), 4.85−4.82 (m, 2 H), 4.59 (d, J = 6.6 Hz, 1 H), 4.26 (t, J = 2.7 Hz, 1 H), 4.07 (br s, 1 H), 3.76 (br s, 1 H), 3.28 (s, 3 H), 2.83 (d, J = 7.5 Hz, 1 H), 2.58 (br s, 1 H), 2.38−2.29 (m, 2 H), 2.19 (dd, J = 5.2, 17.0 Hz, 1 H), 1.99 (dd, J = 7.3, 15.4 Hz, 1 H), 1.98−1.36 (series of m, 7 H), 1.20 (s, 3 H), 1.01 (s, 3 H), 0.99 (s, 3 H), 0.95 (s, 9 H), 0.12 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 152.5, 151.5, 111.6, 104.6, 93.0, 76.8, 73.1, 72.2, 55.1, 50.4, 49.1, 44.0, 36.5, 35.7, 35.2, 30.1, 29.0, 28.7, 25.9, 24.3, 22.4, 18.1, 17.6, −3.4, −5.1; FAB MS (M^++1) calcd 481.34, obsd 481.48; $[\alpha]^{23}_D$ −140.0 (*c* 1.02, CH_2Cl_2).

Anal. Calcd for $C_{27}H_{48}O_5Si$: C, 67.46; H, 10.06. Found: C, 67.38; H, 10.12.

***tert*-Butyl[[(3*S*,4a*R*,6*S*,10*S*,11*R*,12*R*,12a*S*)-1,2,3,4,4a,5,6,9,10,11,12,12a-dodecahydro-3-(methoxymethoxy)-12a,13,13-trimethyl-4-methylene-6,10-methanobenzocyclodecen-7-yl]oxy]dimethylsilane (38).** A mixture of **37** (640 mg, 1.33 mmol), *p*-toluenesulfonic acid (5 mg), and 2,2-dimethoxypropane (0.82 mL, 6.6 mmol) in DMF (4 mL) was stirred at 25 °C for 2 h and processed in the usual way to deliver 672 mg (97%) of **38** as a colorless oil: IR (neat, cm^{-1}) 1652, 1460, 1448, 1378, 1366, 1257, 1202, 1145, 1092, 1030, 920; ^{1}H NMR (300 MHz, C_6D_6) δ 5.06 (s, 1 H), 4.90 (d, J = 6.6 Hz, 1 H), 4.84 (s, 1 H), 4.70 (dd, J = 2.2, 5.2 Hz, 1 H), 4.60 (d, J = 8.0 Hz, 1 H), 4.58 (d, J = 6.6 Hz, 1 H), 4.27 (t, J = 2.7 Hz, 1 H), 4.16 (dd, J = 5.3, 8.0 Hz, 1 H), 3.29 (s, 3 H), 2.88 (d, J = 6.5 Hz, 1 H), 2.37 (tdd, J = 2.2, 6.1, 17.4 Hz, 1 H), 2.21 (dd, J = 5.0, 17.4 Hz, 1 H), 2.06 (dd, J = 4.8, 13.9 Hz, 1 H), 2.01−1.61 (series of m, 6 H), 1.51−1.44 (m, 1 H), 1.45 (s, 3 H), 1.41 (s, 3 H), 1.26 (s, 3 H), 1.06 (s, 3 H), 0.98 (s, 3 H), 0.95 (s, 9 H), 0.10 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 152.2, 151.1, 111.3, 107.4, 104.2, 93.1, 83.1, 83.0, 76.5, 55.0, 50.0, 46.2, 41.2, 37.8, 36.2, 35.0, 31.0, 29.1, 27.7, 27.2, 27.1, 25.9, 25.7, 22.1, 18.6, 18.1, −3.4, −5.1; MS *m*/*z* (M^+) calcd 520.3584, obsd 520.3572; $[\alpha]^{23}_D$ −108.2 (*c* 1.00, hexanes).

Anal. Calcd for $C_{30}H_{52}O_5Si$: C, 69.18; H, 10.06. Found: C, 69.41; H, 10.16.

(3*S*,4a*R*,6*S*,10*S*,11*R*,12*R*,12a*R*)-Dodecahydro-11,12-(isopropylidenedioxy)-3-(methoxymethoxy)-12a,13,13-trimethyl-4-methylene-6,10-methanobenzocyclodecen-7(1*H*)-one (39). To a solution of **38** (672 mg, 1.29 mmol) in THF (5 mL) and H_2O (0.10 mL) at −78 °C was added tetra-*n*-butylammonium fluoride (1.42 mL of 1.0 M in THF, 1.42 mmol). The mixture was allowed to warm to 0 °C, stirred at this temperature for 1 h, quenched with saturated NH_4Cl solution, and extracted with 1:1 ethyl acetate/hexanes. The combined organic layers were dried and concentrated to leave a residue, purification of which by chromatography on silica gel afford 504 mg (96%) of **39** as a white solid, mp 159−161 °C (from hexanes/ethyl acetate): IR (CH_2Cl_2, cm^{-1}) 1697, 1210, 1152, 1092, 1030, 910; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 (br s, 1 H), 4.85 (br s, 1 H), 4.49 (d, J = 8.9 Hz, 1 H), 4.48 (d, J = 6.5 Hz, 1 H), 4.41 (d, J = 6.5 Hz, 1 H), 4.15 (dd, J = 3.8, 8.9 Hz, 1 H), 4.14 (br s, 1 H), 3.33 (s, 3 H), 2.52−2.33 (m, 4 H), 2.22−1.59 (series of m, 9 H), 1.41 (s, 3 H), 1.39 (s, 3 H), 1.37 (s, 3 H), 1.02 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 214.7, 148.0, 112.5, 106.7, 92.8, 82.9, 81.7, 76.4, 57.9, 55.3, 44.5, 40.3, 38.5, 36.6, 36.5, 35.8, 28.3, 27.14, 27.11, 27.0, 26.8, 25.2, 23.7, 17.3; MS *m*/*z* (M^+) calcd 406.2719, obsd 406.2720; $[\alpha]^{23}_D$ −50.5° (*c* 0.92, CH_2Cl_2).

Anal. Calcd for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 70.89; H, 9.49.

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Supporting Information Available: Experimental details for the preparation of **17**, **20**, and **29**−**32**, as well as final calculated atomic coordinates for **D** and **E** in Table 1, along with crystallographic experimental details and tables of X-ray crystal data, bond distances and angles, final fractional coordinates, and thermal parameters for **6** and **21a** (22 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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