Found: C, 56.75; H, 5.30. The structure of **36** was determined by means of X-ray analysis.[17]

syn isomer: $[\alpha]^{25}{}_{D}$ −120.3° (c 1.1, CH_2Cl_2); mp 58.5–61 °C (EtOAc/hexane); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.36 (3 H, s), 1.47 (3 H, s) 3.49 (1 H, dd, J = 13.7, 1.7 Hz), 3.70 (3 H, s), 3.84 (1 H, d, J = 13.7 Hz), 4.31–4.39 (1 H, m), 4.81–5.00 (2 H, m), 6.05 (1 H, d, J = 5.6 Hz), 7.08–7.35 (5 H, m); IR ($CHCl_3$) 1690, 1585 cm^{-1}; MS, m/z 380 (M^+). Anal. Calcd for $C_{18}H_{20}O_7S$ (380.42): C, 56.83; H, 5.30. Found: C, 56.56; H, 5.27.

Acknowledgment. We thank Dr. K. Kawai, M. Moroki, and Dr. H. Kasai of Hoshi University for the X-ray structure determination and the preparation of the manuscript. Financial support from the Ministry of Education, Science, and Culture is also acknowledged.

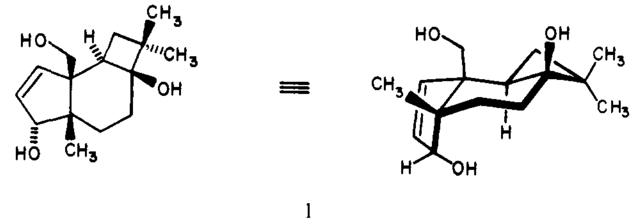
Enantiospecific Total Synthesis of the Sesquiterpene Antibiotics (−)-Punctatin A and (+)-Punctatin D

Takashi Sugimura and Leo A. Paquette*

Contribution from the Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received November 10, 1986*

Abstract: Total syntheses of the levorotatory enantiomer of punctatin A (antibiotic M95464) and the dextrorotatory enantiomer of punctatin D (antibiotic M167906) have been achieved. The identities of the synthetic materials with the corresponding natural products, which were confirmed spectroscopically and by $[\alpha]_D$, permitted the assignment of absolute configuration. These structurally novel trans fused tertiary cyclobutyl alcohol antibiotics were constructed in 16–19 steps from optically pure (99.6% ee) dextrorotatory diketone **5**. Central to the synthetic strategy was (i) utilization of the Still rearrangement as a viable means for elaborating an angular hydroxymethylated *cis*-perhydroindan system and (ii) construction of the completely functionalized four-membered ring in proper stereochemical disposition by application of Norrish type II photochemistry. The conformational bias shown by selected intermediates and certain of their stereoisomers is also briefly touched upon.

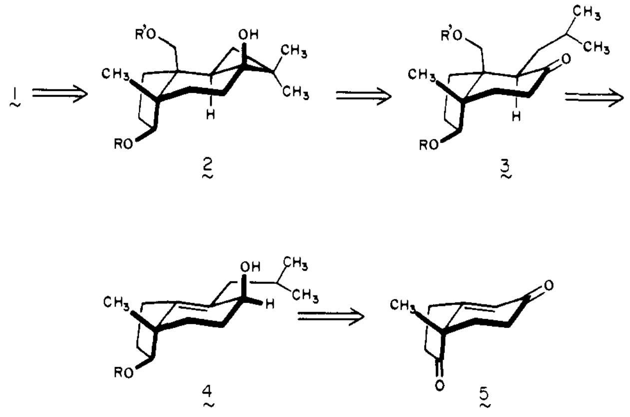
Growing of the dung fungus *Poronia punctata* (Linnaeus *ex* Fries) on malt solution in still culture has recently been shown to provide a rich source of new sesquiterpenes.[1,2] The major C_{15} constituent has been characterized as the trishydroxylated tricyclic substance **1** possessing a previously unknown caryophyllene-related framework. The structural assignment to **1**, originally known as antibiotic M95464 but now recognized trivially as punctatin A,[3] rests upon chemical transformations and spectra as well as an X-ray crystallographic analysis.[1] A second more polar metabolite (punctatin D, antibiotic M167906) is epimeric with **1** at the allylic hydroxyl group.[2b]



1

The remarkable biological activity of these colorless, crystalline solids and the presence within their structure of a trans fused tertiary cyclobutyl alcohol hold particular fascination. Our interest in punctatins A and D stemmed also from the realization that their absolute configurations were unknown.

Scheme I



Accordingly, we embarked on stereospecific total syntheses of **1** and **33b** and set as our overall goal the assembling of their five contiguous chiral centers in proper relative configuration starting with a simple enantiomerically pure substrate.[4] From the retrosynthetic perspective, we envisioned introduction of the ring A double bond and setting of the associated allylic alcohol stereochemistry to be capable of implementation in the very late stages of the synthesis (Scheme I). This simplification would permit proper laboratory assessment of the elaboration of **2** from **3** by photochemical means. Thus, the plan was to construct the completely functionalized four-membered ring of punctatin A in its proper stereochemical disposition by utilization of Norrish type II photochemistry.[5] The success of this scenario rested on gaining access to **4** which we hoped to do from **5**, with appropriate at-

---

(1) Anderson, J. R.; Briant, C. E.; Edwards, R. L.; Mabelis, R. P.; Poyser, J. P.; Spencer, H.; Whalley, A. J. S. *J. Chem. Soc., Chem. Commun.* **1984**, 405.

(2) Five additional metabolites that co-occur with **1** have been assigned the names punctatin B–F and structurally characterized: (a) Anderson, J. R.; Edwards, R. L.; Fraer, A. A.; Mabelix, R. P.; Poyser, J. P.; Spencer, H.; Whalley, A. J. S. *J. Chem. Soc., Chem. Commun.* **1984**, 917. (b) Poyser, J. P.; Edwards, R. L.; Anderson, J. R.; Hursthouse, M. B.; Walker, N. P. C.; Sheldrick, G. M.; Whalley, A. J. S. *J. Antibiot.* **1986**, *39*, 167.

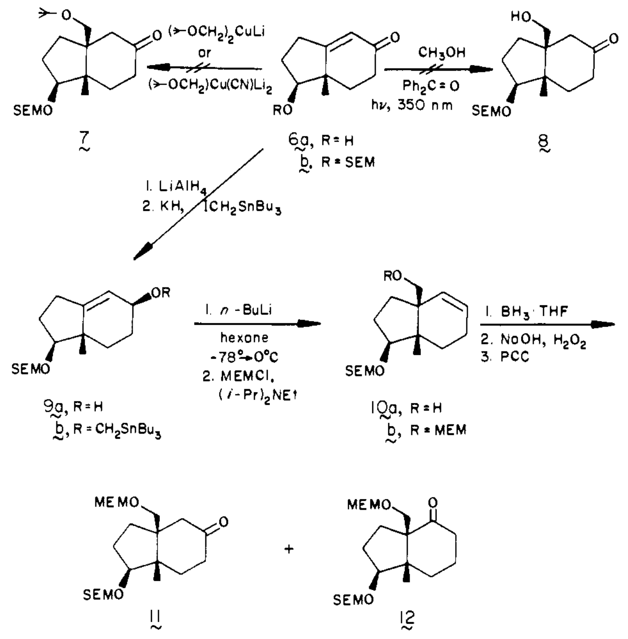
(3) Care should be exercised not to confuse punctatin A with punctatin, a germacranolide obtained from *Liatris punctata* Hook (Herz, W.; Wahlberg, I *Phytochemistry* **1973**, *12*, 1421). This substance was later renamed punctaliatrin (Herz, W.; Wahlberg, I. *Phytochemistry* **1974**, *13*, 315). An even earlier use of the name for a group of homoisoflavones has turned up (Heller, W.; Tamm, C. *Prog. Chem. Org. Nat. Prods.* **1981**, *40*, 105). We have been more recently informed by Dr. Edwards and Dr. Poyser that they are implementing a proposal to alter the names of punctatins A–F to punctaporonins A–F in order to eliminate further overlap of common nomenclature.

(4) Preliminary communication: Paquette, L. A.; Sugimura, T. *J. Am. Chem. Soc.* **1986**, *108*, 3841.

(5) (a) Fleming, I.; Kemp-Jones, A. V.; Long, W. E.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 2* **1976**, 7. (b) Fleming, I.; Long, W. E. *Ibid.* **1976**, 14. (c) Singh, S.; Usha, G.; Tung, C.-H.; Turro, N. J.; Ramamurthy, V. *J. Org. Chem.* **1986**, *51*, 941 and relevant references cited in these papers.

0002-7863/87/1509-3017$01.50/0

Scheme II



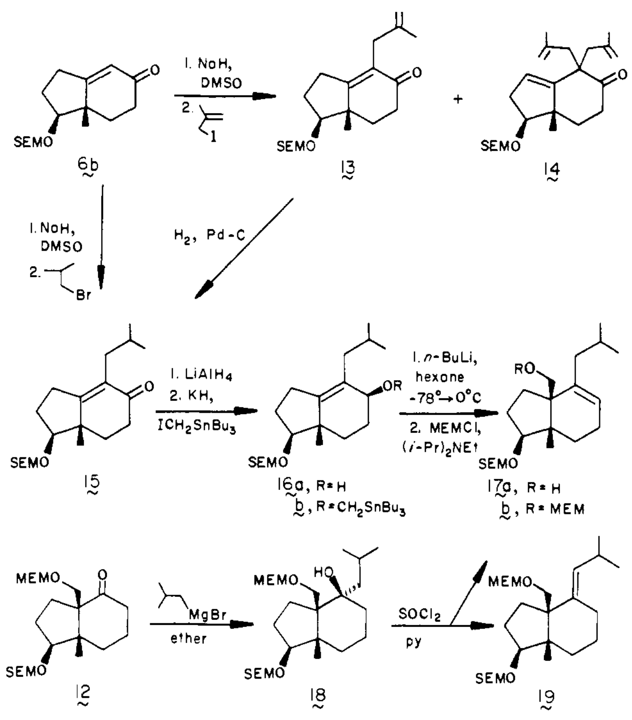
tention being given to regio- and stereochemical control. With **4** in hand, the plan was to utilize the Still rearrangement[6] as the tool for proper elaboration of the angularly hydroxymethylated *cis*-perhydroindane framework.

In line with the above, our synthesis was initiated by controlled hydride reduction[7] of the dextrorotatory diketone **5**. This substance, whose absolute stereochemistry is recognized to be 7a*S*,[8] is readily available in 99.6% enantiomeric purity.[9] Keto alcohol **6a** was next transformed into its SEM ether **6b** in preparation for several preliminary experimental studies. Quickly established was the fact that exposure of **6b** to the Gilman reagent derived from *tert*-butoxymethyllithium[10] or to higher order cuprates of the same reagent[11] did not afford **7** or any product of conjugate addition (Scheme II). Equally unsuccessful were all attempts to add methanol photochemically to **6b** under triplet-sensitized conditions.[12] On this basis, it was already apparent that the β carbon of the enone experiences appreciable steric congestion.

For this reason, our attention turned to the implementation of an intramolecular rearrangement protocol, specifically the [2,3]-sigmatropic Wittig process introduced by Still.[6] The preparation of **9a**, achieved in line with precedent,[15] was followed by conversion to stannylmethyl ether **9b**. Subsequent transmetalation with *n*-butyllithium furnished **10a** in 45% yield, accompanied by 10% of the [1,2] rearranged product. The latter side reaction was expected in the light of comparable complications witnessed by Still and Mitra with structurally related octalols.[6b]

A mixture of **11** and **12** was obtained in isolated yields of 49% and 30%, respectively, when MEM ether **10b** was treated with the borane–tetrahydrofuran complex and directly oxidized with pyridinium chlorochromate. When recourse was made to thexylborane, a product distribution of 66% and 16% was realized. This absence of regiocontrol provided the impetus for the strategic introduction of the desired sidechain at C-7 prior to hydroboration.

Scheme III



Toward this end, the thermodynamic enolate of **6b**[14] was exposed to the highly reactive 3-iodo-2-methyl-1-propene reagent. Workup gave rise to a mixture of the desired **13** (40%) as well as **14**, the product of twofold alkylation (20%, Scheme III). One obvious means for overcoming the latter complication was to proceed instead with 1-bromo-2-methylpropane. Indeed, reduction of electrophilic reactivity in this manner resulted in the exclusive formation of **15**. It should be recalled here that the saturated alkyl side chain is destined to become ultimately the carbocyclic backbone of the four-membered ring.

We were well aware of the possibility that the added appendage in **15** might serve to kinetically retard operation of the Still rearrangement. Hydride reduction of **15** did lead to a single allylic alcohol, the carbinol stereochemistry of which was temporarily assigned as β (see **16a**). Following the formation of stannane **16b**, we proceeded to generate the α-lithio ether and to induce [2,3]-sigmatropy. Smooth rearrangement was observed to deliver homoallylic alcohol **17a** in 34% overall yield. In order to unravel the stereochemistry of **16** and to establish that complete transfer of chirality[15] had occurred while progressing to **17**, MEM ether **17b** was prepared. To complete the relay, ketone **12** of established absolute stereochemistry was treated with 2-methyl-1-propylmagnesium bromide giving **18**. Dehydration of this tertiary alcohol with thionyl chloride in pyridine resulted in the coproduction of **17b** and **19**. The sample of chromatographically purified **17b** thus obtained was identical in all respects with that produced earlier. The stereochemical efficacy of this phase of the synthesis was thereby demonstrated.

With the structure of **17b** assurred, we set out to assess its response to various hydroborating agents. Detailed conformational analysis suggested that electrophilic attack should be less encumbered from the β face. Use of the borane–tetrahydrofuran complex gave alcohols **20** and **21** (ratio 1:2), which were therefore tentatively formulated as having the large alkyl side chain in an α disposition. Substitution of borane–dimethylsulfide did not alleviate the complication of concomitant deblocking of the MEM group. The heightened sensitivity of this blocking group to the mild conditions employed probably arises because of its proximity to the reaction center. The Lewis acidity of boranes is well-recognized.

The readily separated alcohols were individually oxidized to **22** and **23**. To gain support for the stereochemistry of the isobutyl substituent, **23** was directly irradiated in dioxane solution through

---

(6) (a) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1480. (b) Still, W. C.; Mitra, A. *Ibid.* **1978**, *100*, 1927.

(7) Hajos, Z. G.; Parrish, D. R.; Oliveto, E. P. *Tetrahedron* **1968**, *24*, 2039.

(8) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615.

(9) Hajos, Z. G.; Parrish, D. R. *Org. Synth.* **1984**, *63*, 26.

(10) Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, 3165.

(11) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005.

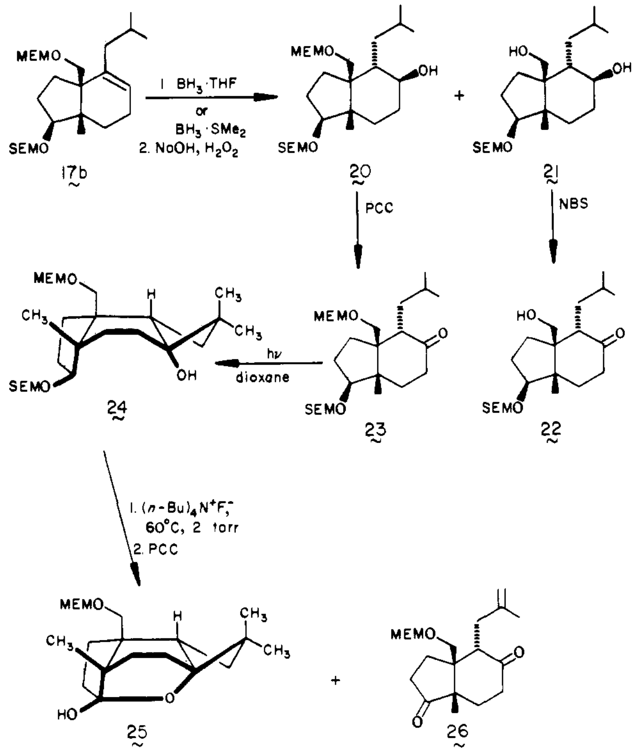
(12) (a) Fitzsimmons, B. J.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1979**, *101*, 6123. (b) Fraser-Reid, B.; Holder, N. L.; Hicks, D. R.; Walker, D. L. *Can. J. Chem.* **1977**, *55*, 3978 and relevant references cited in these papers.

(13) Marshall, J. A.; Ellison, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 4312.

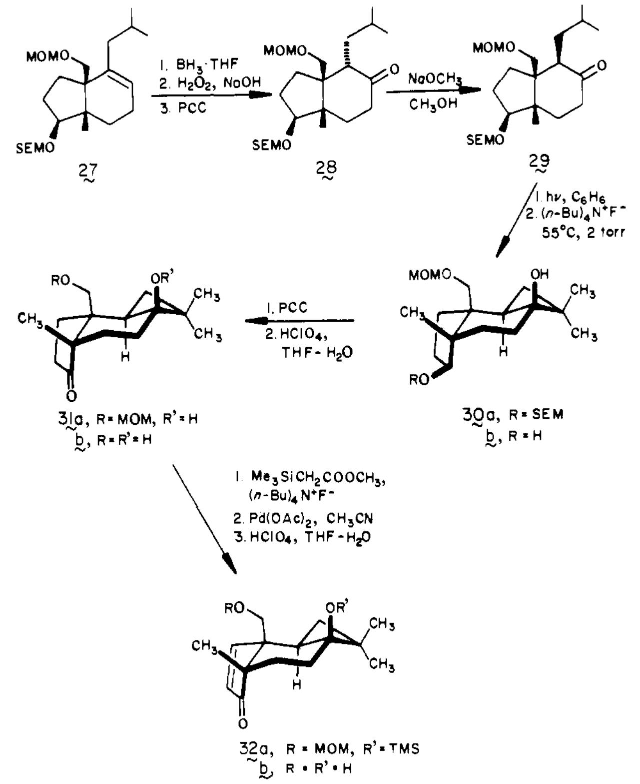
(14) Hajos, Z. G.; Micheli, R. A.; Parrish, D. R.; Oliveto, E. P. *J. Org. Chem.* **1967**, *32*, 3008.

(15) Midland, M. M.; Kwon, Y. C. *Tetrahedron Lett.* **1985**, 5013.

Scheme IV



Scheme V



pyrex with a 450-W Hanovia lamp for 10 h. Workup gave a single cyclobutyl alcohol in 62% yield with no trace of an isomeric cyclized product. One consequence of the α orientation of the isobutyl side chain on the course of this Norrish type II cyclization is particularly noteworthy. Specifically, formation of a trans fused cyclobutyl alcohol in this instance requires that biradical capture proceed from the equatorial direction onto a six-membered ring forced to adopt a boat conformation. The efficient production of hemiketal **25** reflects not only the close proximity of the two oxygen functionalities but also the existing conformational bias.

We were well aware of the fact that the above findings do not prove unequivocally the configuration of the isobutyl group. Nonetheless, the low level of β-cleavage[5,16] associated with the photocyclization of **23** was viewed as a harbinder of success in the stereoisomeric series required to arrive at punctatins A and D as long as the isobutyl group remained in an orientation unfavorable for fragmentation. Ultimately, the correctness of all the structural assignments in Scheme IV was confirmed by the experiments that follow.

To guard against excessive deblocking under the conditions of hydroboration, the MEM group was replaced by MOM as indicated in **27**, and the solvent was changed from tetrahydrofuran to diglyme. When this substance was treated in the predescribed manner, the overall extent of conversion to **28** was gratifyingly observed to be 62%. That MOM is indeed more resistant toward the borane–tetrahydrofuran complex was further revealed in the coproduction of only 9% of diol.

The ready availability of **28** set the stage for base-promoted equilibration to **29**, a process that occurs upon warming with sodium methoxide. When benzene solutions of **29** were irradiated with 253.7-nm light, **30a** was isolated in 49% yield (Scheme V).[17] Approximately 20% of Norrish β-fragmentation was noted under these conditions. Since the ensuing chromatographic purification of **30a** posed no problem, a key step toward the completion of our synthetic goal had been successfully accomplished.

Consider for the moment the events required for the appropriate excited-state closure of **29**. Following γ-hydrogen transfer, the diradical intermediate likely exists with the six-membered ring in a chair conformation; the isobutyl radical substituent is projected equatorially. Under these circumstances, the two singly occupied orbitals can find it possible to enter into bonding from the equatorial direction with formation of a trans fused cyclobutanol. If production of the four-membered ring were to involve elaboration of an axial bond, severe impedance would develop because one of the methyl groups from the geminal pair would be brought into close spatial proximity to the angular $MOMOCH_2$– side chain. It is widely recognized[5,16,18] that while cyclobutyl alcohol production is not strictly governed by the orientation of the C_2–C_3 bond in the 1,4-biradical, fragmentation is. In view of the fact that the triplet state reaction involving **29** results in greater levels of fragmentation than in the case of **23**, there is evidently greater opportunity for the C_2–C_3 σ bond to become oriented parallel to the singly occupied p orbitals at the radical centers within **29**.[18g]

At this juncture, our synthetic strategy called for removal of the SEM blocking group. In order to accomplish this maneuver efficiently, **30a** was heated at 55 °C in a solvent-free melt with tetra-*n*-butylammonium fluoride under a vacuum of 2 mmHg. Failure to do this led to appreciable protolytic removal of the trimethylsilyl group *without* fragmentation and release of the hydroxyl functionality. The aforementioned technique, entirely comparable to that utilized earlier for the conversion of **24** to **25**, has proven to be highly reproducible and efficacious.

The pyridinium chlorochromate oxidation of **30b** to **31a** set the stage for introduction of a conjugated double bond into the A ring. This conversion was most conveniently accomplished by treatment with methyl trimethylsilylacetate and tetra-*n*-butylammonium fluoride[19] followed by oxidation with 1.5 equiv of palladium acetate

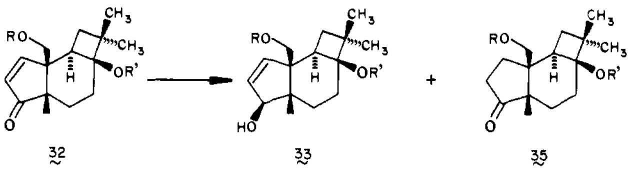
---

(16) See, for example: (a) Yang, N. C.; Thap, D.-M. *Tetrahedron Lett.* **1966**, 3671. (b) Lewis, F. D.; Hilliard, T. A. *J. Am. Chem. Soc.* **1972**, *94*, 3852. (c) Wagner, P. J. *Acc. Chem. Res.* **1971**, *4*, 168. (d) Turro, N. J.; Wan P. *Tetrahedron Lett.* **1984**, 3655.

(17) Use of dioxane as solvent and a 450-W Hanovia lamp (Pyrex vessel) as previously described for **23** gave **30a** in only 18–22% yield. The extent of fragmentation was 10%. We have no explanation for this difference in photochemical response between **23** and **29**.

(18) (a) Wagner, P. J.; Kemppainen, A. E. *J. Am. Chem. Soc.* **1968**, *90*, 5896. (b) Wagner, P. J.; Kelso, P. A.; Kemppainen, A. E.; McGrath, J. M.; Zepp, R. G. *Ibid.* **1972**, *94*, 7506. (c) Wagner, P. J.; McGrath, J. M. *Ibid.* **1972**, *94*, 3849. (d) Padwa, A.; Alexander, E.; Niemczyk, M. *Ibid.* **1969**, *91*, 456. (e) Sauers, R. R.; Gorodetsky, M.; Whittle, J. A.; Hu, C. K. *Ibid.* **1971**, *93*, 5520. (f) Lewis, F. D.; Johnson, R. W.; Ruden, R. A. *Ibid.* **1972**, *94*, 4292. (g) Gagosian, R. B.; Dalton, J. C.; Turro, N. J. *Ibid.* **1970**, *92*, 4752.

Table I. Product Ratios from Reductions of **32**



substituents	reducing conditions	product distribution, % 33	 35
R = R′ = H	$LiAlH_4$, ether, −78 °C, 3 h	<5	>95
	Red-Al, THF, rt,[b] 2 h	0	100
	Dibal, THF, 0 °C, 3	>95	<5
	$NaBH_4$, $CeCl_3$, CH_3OH, 0 °C, 2 h[a]	0	100
R = TBDMS, R′ = H	$LiAlH_4$, ether, −78 °C, 3 h	10	90
	Dibal, THF, 0 °C, 3 h	100	0
R = TBDMS, R′ = TMS	$LiAlH_4$, ether −78 °C, 3 h	10	90
	Dibal, THF, 0 °C, 3 h	100	0
	$NaBH_4$, $CeCl_3$, CH_3OH, 0 °C, 20 min	100	0
R = R′ = TMS	Dibal, THF, 0 °C, 3 h	50	50
R = MOM, R′ = TMS	$NaBH_4$, $CeCl_3$, CH_3OH, 0 °C, 20 min	100	0

[a] When this reduction was carried out at 20 °C for 3 h, a mixture of the fully saturated α- and β-alcohols was also isolated. [b] rt is abbreviation for room temperature.

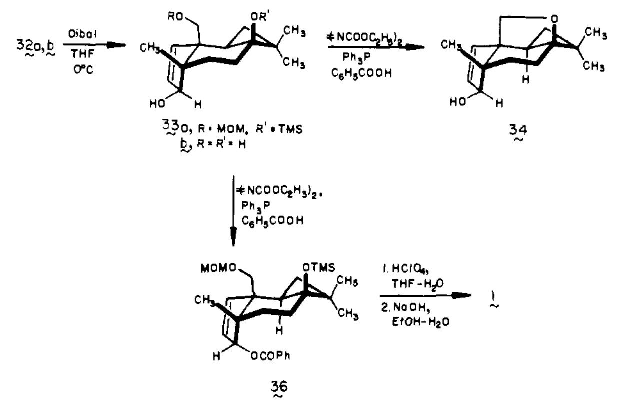
in acetonitrile. Several comments concerning these transformations are in order. First, the Kuwajima method for generation of the silyl enol ether also served to silylate the tertiary hydroxyl functionality. Secondly, under the conditions utilized for the Pd(II) oxidation, no benzoquinone or other comparable oxidant proved necessary to achieve the conversion to enone. Finally, the free hydroxyl groups in **32b** can be unmasked without any evidence of complications resulting from carbocation-induced structural rearrangement.

If the stereochemical outcome of the photocyclization of **29** is as indicated, the tertiary hydroxyl group in **30–32** is necessarily cis oriented to the MOM ether functionality. Specific confirmation of this relative stereochemical relationship was sought by conversion of **32a** to **34**. Given the concave–convex nature of enone **32a** and its analogues, it was not surprising to observe that reduction with lithium aluminum hydride proceeds predominantly in a 1,4 manner (Table I). While both diisobutylaluminum hydride and cerium trichloride-doped sodium borohydride gave rise only to 1,2-reduction, the chemical shift of the newly introduced carbinol proton clearly indicated that the hydroxyl group stereochemistry in **33a** was β. Alterations in the nature of the blocking groups had little impact on the course of these reactions. However, when **32b** was comparably examined, it was determined that reductions with Red-Al and $NaBH_4$-$CeCl_3$ also now proceed in a 1,4 manner (Table I). Evidently, prior covalent bonding of the reducing agent to the primary carbinol center kinetically directs hydride attack to the β carbon of the conjugated enone moiety.

Elaboration of the tetrahydrofuran ring in **34** was next accomplished under conditions of the Mitsunobu reaction.[20] Cyclization occurred at a sufficiently rapid rate that chemical modification of the secondary allylic alcohol was easily obviated. Ultimately, arrival at punctatin D (**33b**) was accomplished by Dibal reduction of **32b**. Not only were the spectra of this triol identical with the natural product,[2b] but the dextrorotatory $[\alpha]_D$ revealed that the natural enantiomer was in hand.

Armed with the preceding knowledge, there was no question that the stereochemistry of the secondary hydroxyl in **33a** had to be inverted in order to conform to that present in punctatin A. Suffice it to say that the conversion to **36** by the Mitsunobu procedure was uneventful (Scheme VI).

Scheme VI



For the purpose of ascertaining the order in which the protective groups should be removed from this penultimate intermediate, a small sample of natural punctatin A was shaken with aqueous perchloric acid for 30 min. Total decomposition occurred. In view of this acid sensitivity, we proceeded to remove the MOM and TMS substituents first on the assumption that the destruction of **1** was triggered by allylic cation formation in the A ring. This deblocking maneuver proceeded satisfactorily, and the resulting dihydroxy benzoate was then cleanly saponified to punctatin A (**1**). Examination of the IR and high field ^1H NMR spectra of the synthetic material showed it to be identical with the natural product. That the correct levorotatory enantiomer of **1** had been prepared became evident upon determination of the optical rotation, $[\alpha]^{22}_D$ −27° (*c* 0.4, methanol) of the totally synthetic antibiotic. Anderson et al. have reported $[\alpha]^{20}_D$ −26° (*c* 1.0, methanol) for the natural antibiotic.[1]

In summary, the enantiospecific total syntheses of natural (−)-punctatin A and (+)-punctatin D have been achieved for the first time. The route consists of 16–19 steps and permits unequivocal assignment of absolute configuration. In fact, all of the formulas depicted herein are drawn with proper absolute stereochemical perspective and depict pure enantiomers. The synthetic achievement was made possible in large part by preparative application of the Norrish type II cyclization. To our knowledge, this is the first occasion that such an excited-state reaction has been applied to natural products synthesis.

Experimental Section

(1*S*,7a*S*)-7,7a-Dihydro-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5(6*H*)-indanone (6b). Ketone **5**, $[\alpha]^{22}_D$ 360.5° (*c* 8.8, benzene) of 99.6% ee, was reduced with lithium tri-*tert*-butoxyaluminum hydride as earlier described[7] to give **6a**, $[\alpha]^{22}_D$ 26.6° (*c* 2.4, benzene). To a solution of **6a** (5.57 g, 30.0 mmol) and diisopropylethylamine (6.4 mL, 1.2 equiv) in dry dichloromethane (15 mL) was added dropwise 6.5 mL (1.2 equiv) of 2-(trimethylsilyl)ethoxymethyl chloride at room temperature. After 4 h of stirring, petroleum ether was added, and the precipitate was separated by filtration. The filtrate was concentrated, and the residue was chromatographed on silica gel (elution with 5% ethyl acetate in petroleum ether) to give **6b** as a colorless oil (8.24 g, 95.5%): $[\alpha]^{22}_D$ 26.6° (*c* 2.4, benzene); IR (neat, cm^{-1}) 2945, 1670, 1240, 1052; ^1H NMR (300 MHz, $CDCl_3$) δ 5.70 (s, 1 H), 4.65 (d, *J* = 6.9 Hz, 1 H), 4.64 (d, *J* = 6.9 Hz, 1 H), 3.64 (dd, *J* = 10.2, 7.6 Hz, 1 H), 3.56 (t, *J* = 8.5 Hz, 2 H), 2.65 (ddm, *J* = 19.7, 11.6 Hz, 1 H), 2.47–2.02 (m, 3 H), 1.83–1.69 (m, 2 H), 1.09 (s, 3 H), 0.91–0.84 (m, 2 H), −0.03 (s, 9 H).

The semicarbazone of **6b** was prepared conventionally and isolated as colorless needles, mp 176.2–176.8 °C.

Anal. Calcd for $C_{17}H_{31}N_3O_5Si$: C, 57.75; H, 8.84. Found: C, 57.69; H, 8.84.

(1*S*,5*S*,7a*S*)-5,6,7,7a-Tetrahydro-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5-indanol (9a). A solution of **6b** (3.0 g, 10.1 mmol) in anhydrous ether (10 mL) was added dropwise to a cold (−78 °C), magnetically stirred slurry of lithium aluminum hydride (384 mg, 4 equiv) in the same solvent (30 mL). The reaction mixture was stirred at this temperature for 2 h and treated in turn with ethyl acetate, methanol, and

---

(19) Nakamura, E.; Murofushi, T.; Shimizu, M.; Kuwajima, I *J. Am. Chem. Soc.* **1976**, *98*, 2346.

(20) Mitsunobu, O *Synthesis* **1981**, 1.

water. The product was extracted into ether, dried, and concentrated. Filtration through a short column of silica gel (5 g) afforded 2.47 g (81.8%) of **9a** as a colorless oil: $[\alpha]^{22}_{\mathrm{D}}$ −2.0° (*c* 1.4, benzene); IR (neat, cm^{-1}) 3350, 2952, 1060; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.34 (m, 1 H), 4.67 (d, *J* = 6.9 Hz, 1 H), 4.66 (d, *J* = 6.9 Hz, 1 H), 4.24 (m, 1 H), 3.64–3.48 (m, 3 H), 2.45 (m, 1 H), 2.15–1.96 (m, 3 H), 1.80 (ddd, *J* = 13.0, 3.8, 3.0 Hz, 1 H), 1.74–1.49 (m, 2 H), 1.41–1.31 (m, 2 H), 1.02 (s, 3 H), 0.94–0.88 (m, 2 H), 0.00 (s, 9 H); MS, m/z ($\mathrm{M}^+ - \mathrm{C_3H_8O}$) calcd 238.1389, obsd 238.1385.

(1*S*,3a*S*,7a*S*)-7,7a-Dihydro-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-3a(6*H*)-indanmethanol (10a). To a solution of **9a** (50 mg, 0.168 mol) in dry tetrahydrofuran (1 mL) was added 0.3 mL of potassium hydride (24% in oil) followed by 120 mg (1.5 equiv) of iodomethyltri-*n*-butylstannane. The reaction mixture was stirred for 1.5 h, cooled to −78 °C, and treated during 2 min with 0.33 mL of *n*-butyllithium in hexane (1.54 N, 3 equiv). After 2 h, saturated ammonium chloride solution (2 mL) was added, and the product was extracted into ether. Solvent evaporation gave 290 mg of colorless oil which was purified by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether). There was obtained 23 mg (45%) of **10a**, $[\alpha]^{22}_{\mathrm{D}}$ 91.7° (*c* 0.5, methanol): IR (neat, cm^{-1}) 3502, 2978, 1066; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.53 (dt, *J* = 10.0, 3.6 Hz, 1 H), 5.00 (dm, *J* = 10.0 Hz, 1 H), 4.68 (d, *J* = 6.9 Hz, 1 H), 4.64 (d, *J* = 6.9 Hz, 1 H), 3.90 (t, *J* = 7.0 Hz, 1 H), 3.68–3.53 (m, 2 H), 3.49 (d, *J* = 11.0 Hz, 1 H), 3.36 (d, *J* = 11.0 Hz, 1 H), 2.09–1.97 (m, 3 H), 1.78–1.37 (series of m, 6 H), 0.95 (s, 3 H), 0.92 (m, 1 H), 0.01 (s, 9 H); MS, m/z ($\mathrm{M}^+ - \mathrm{C_3H_8O}$) calcd 254.1702, obsd 254.1687.

Trimethyl[2-[[[(1*S*,3a*S*,7a*S*)-3a,6,7,7a-tetrahydro-3a-[(2-methoxyethoxy)methoxy]-7a-methyl-1-indanyl]oxy]methoxy]ethyl]silane (10b). A solution of **10a** (300 mg, 0.56 mmol) and diisopropylethylamine (0.374 mL, 2 equiv) in dry dichloromethane (10 mL) was treated with 0.164 mL (1.5 equiv) of chloromethyl methyl ether at room temperature. After 33 h, ether and water were added, and the organic phase was dried and evaporated. The residue was eluted through a short silica gel column (10% ethyl acetate in petroleum ether) to give 370 mg (96.2%) of **10b** as a colorless oil: $[\alpha]^{22}_{\mathrm{D}}$ 74.8° (*c* 1.0, benzene); IR (neat, cm^{-1}) 2924, 1252, 1116, 1050; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.63 (ddd, *J* = 10.1, 3.8, 3.3 Hz, 1 H), 5.43 (ddd, *J* = 10.1, 2.0, 1.9 Hz, 1 H), 4.83–4.63 (m, 4 H), 3.98 (t, *J* = 8.1 Hz, 1 H), 3.73–3.54 (m, 6 H), 3.50 (d, *J* = 9.3 Hz, 1 H), 3.40 (d, *J* = 9.3 Hz, 1 H), 3.39 (s, 3 H), 2.07–1.97 (m, 3 H), 1.73 (ddd, *J* = 12.7, 11.4, 4.3 Hz, 1 H), 1.59–1.36 (m, 4 H), 0.98–0.87 (m, 2 H), 0.89 (s, 3 H), 0.01 (s, 9 H); MS, m/z ($\mathrm{M}^+ - \mathrm{C_4H_9O_2}$) calcd 283.1729, obsd 283.1755.

Hydroboration–Oxidation of 10b. To a cold (0 °C), magnetically stirred solution of **10b** (370 mg, 0.92 mmol) in dry tetrahydrofuran (10 mL) was added 1.5 mL of 1 M borane–tetrahydrofuran complex in tetrahydrofuran under an argon atmosphere. After 3 h at 0 °C, there was introduced in sequence of ca. 1 mL of water, 2 mL of 2 M sodium hydroxide solution, and 2 mL of 30% hydrogen peroxide. The reaction mixture was stirred at 50 °C for 2 h, cooled, and extracted with ether. The combined organic layers were dried and evaporated to provide 540 mg of alcohol mixture.

The alcohols were dissolved in dry dichloromethane (13 mL), cooled in ice water, and treated in 1 portion with pyridinium chlorochromate (397 mg, 1.84 mmol). The reaction mixture was stirred at room temperature for 3 h, treated with 5 mL of 3 M sodium hydroxide solution, and extracted with ether. The combined organic layers were dried and concentrated to leave 390 mg of ketone mixture. By means of MPLC on silica gel (elution with 50% ethyl acetate in petroleum ether), it proved possible to separate **11** (180 mg, 49%) from **12** (110 mg, 30%).

For **11**: colorless oil, $[\alpha]^{22}_{\mathrm{D}}$ 14.2° (*c* 0.9, benzene); IR (neat, cm^{-1}) 2964, 1719, 1248, 1026; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.66 (d, *J* = 3.0 Hz, 1 H), 4.61 (d, *J* = 3.0 Hz, 1 H), 4.57 (d, *J* = 6.9 Hz, 1 H), 4.55 (d, *J* = 6.9 Hz, 1 H), 4.20 (dd, *J* = 7.0, 6.7 Hz, 1 H), 3.65–3.48 (m, 7 H), 3.33 (s, 3 H), 3.29 (d, *J* = 9.4 Hz, 1 H), 2.33–2.08 (m, 5 H), 1.84–1.77 (m, 2 H), 1.69–1.57 (m, 2 H), 1.25 (m, 1 H), 0.96 (s, 3 H), 0.85 (m, 2 H), 0.02 (s, 9 H); MS, m/z (M^+) calcd 342.2226, obsd 342.2214.

For **12**: colorless oil, $[\alpha]^{22}_{\mathrm{D}}$ −3.4° (*c* 1.0, benzene); IR (neat, cm^{-1}) 2966, 1713, 1246, 1034; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.60–4.50 (m, 4 H), 3.89 (d, *J* = 9.4 Hz, 1 H), 3.69 (t, *J* = 8.4 Hz, 1 H), 3.58–3.34 (m, 7 H), 3.33 (s, 3 H), 2.55–2.47 (m, 2 H), 2.30 (br d, *J* = 13.8 Hz, 1 H), 1.95–1.67 (m, 5 H), 1.44–1.30 (m, 2 H), 0.90 (s, 3 H), 0.84 (m, 2 H), −0.05 (s, 9 H); MS, m/z ($\mathrm{M}^+ - \mathrm{C_5H_{11}O_3}$) calcd 297.1886, obsd 297.1901.

Use of thexylborane in an entirely analogous manner transformed 560 mg of **10b** into 380 mg (66%) of **11** and 90 mg (16%) of **12**.

(1*S*,7a*S*)-7,7a-Dihydro-4-(2-methyl-2-propenyl)-7a-methyl-1[[2-(trimethylsilyl)ethoxy]methoxy]-5(6*H*)-indanone (13). A 1.34-g sample of sodium hydride (50% in oil) was placed in a reaction flask and washed with pentane. Following evaporation of the traces of pentane under reduced pressure, 40 mL of freshly distilled (from CaH$_2$) dimethyl sulfoxide was introduced. The suspension was warmed to 65 °C for 1 h with stirring. After having been cooled to room temperature, a solution of **6b** (7.5 g, 25.3 mmol) in dry dimethyl sulfoxide was added during 5 min. Following 1.5 h of stirring, 3-iodo-2-methylpropene (5.07 g, 1.1 equiv) was next introduced, and stirring was continued for an additional hour. Ether and water were carefully added, and the combined organic phases were washed with water, dried, and evaporated. Purification of the residue by HPLC on silica gel (elution with 10% ethyl acetate in petroleum ether) afforded 3.54 g (40%) of **13** and 2.09 g (20%) of **14**.

For **13**: colorless oil, $[\alpha]^{22}_{\mathrm{D}}$ 11.4° (*c* 9.8, benzene); IR (neat, cm^{-1}) 2968, 1665, 1246, 1056; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.73 (d, *J* = 6.9 Hz, 1 H), 4.71 (d, *J* = 6.9 Hz, 1 H), 4.66 (m, 1 H), 4.47 (m, 1 H), 3.71 (dd, *J* = 10.5, 7.2 Hz, 1 H), 3.65–3.59 (m, 2 H), 2.95–2.81 (m, 2 H), 2.63–2.53 (m, 2 H), 2.46–2.32 (m, 2 H), 2.17–2.08 (m, 2 H), 1.89–1.77 (m, 2 H), 1.68 (s, 3 H), 1.15 (s, 3 H), 0.96–0.91 (m, 2 H), 0.02 (s, 9 H); MS, m/z (M^+) calcd 350.2313, obsd 350.2295.

For **14**: colorless oil; IR (neat, cm^{-1}) 2960, 1705, 1244, 1056; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.47 (dd, *J* = 3.5, 1.7 Hz, 1 H), 4.90 (m, 1 H), 4.79–4.73 (m, 3 H), 4.68 (m, 1 H), 4.51 (m, 1 H), 3.94 (dd, *J* = 9.2, 3.4 Hz, 1 H), 3.70–3.63 (m, 2 H), 2.73–2.56 (m, 3 H), 2.48–2.42 (m, 4 H), 1.97 (ddd, *J* = 13.2, 6.1, 2.6 Hz, 1 H), 1.80 (dd, *J* = 13.4, 5.2 Hz, 1 H), 1.71 (s, 3 H), 1.67 (m, 1 H), 1.63 (s, 3 H), 1.19 (s, 3 H), 0.98–0.94 (m, 2 H), 0.06 (s, 9 H); MS, m/z (M^+) calcd 404.2747, obsd 404.2747.

(1*S*,7a*S*)-7,7a-Dihydro-4-isobutyl-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5(6*H*)-indanone (15). A. Alkylation of 6b. Sodium hydride (6.02 g of 50% in oil, 0.125 mol) was washed with pentane and dried in the predescribed fashion. Freshly distilled (from CaH$_2$) dimethyl sulfoxide (480 mL) was added, and the stirred suspension was heated at 65 °C for 1 h. After cooling, a solution of **6b** (39.15 g, 0.132 mol) in the same solvent (100 mL) was added dropwise during 3 h. The reaction mixture was stirred for an additional hour to complete enolate formation, at which point 14.43 mL (0.95 equiv) of 1-iodo-2-methylpropane was slowly introduced while the flask was cooled in a water bath. After 40 min, a small amount of saturated ammonium chloride solution was added followed by 50 mL of saturated sodium bicarbonate solution and 500 mL of water. The product was extracted into ether (2 × 500 mL and 2 × 300 mL), and the combined organic layers were washed with water (2×) and brine prior to drying. Solvent evaporation left a residual oil that was purified by HPLC on a Waters Prep 500 system (silica gel). Elution with 6% ethyl acetate in petroleum ether gave 19.81 g of **15**, while elution with 20% ethyl acetate returned 8.41 g of **6b**. The yield of **15** was therefore 54%: colorless oil: $[\alpha]^{22}_{\mathrm{D}}$ 14.2° (*c* 2.7, benzene); IR (neat, cm^{-1}) 2954, 1665, 1056, 832; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.75 (d, *J* = 6.9 Hz, 1 H), 4.71 (d, *J* = 6.9 Hz, 1 H), 3.69 (dd, *J* = 10.5, 7.3 Hz, 1 H), 3.66–3.59 (ABm, 2 H), 2.62–2.37 (m, 4 H), 2.20–1.93 (m, 4 H), 1.88–1.69 (m, 3 H), 1.13 (s, 3 H), 0.96–0.91 (ABm, 2 H), 0.82 (d, *J* = 6.6 Hz, 6 H), 0.02 (s, 9 H); MS, m/z (M^+) calcd 352.2434, obsd 352.2431.

B. Catalytic Hydrogenation of 13. A solution of **13** (3.20 g, 9.14 mmol) in 200 mL of absolute ethanol was stirred with 10% palladium on carbon (300 mg) under hydrogen (1 atm) for 26 h. The reaction mixture was filtered through Celite and concentrated to leave 3.06 g of colorless oil that was purified by preparative HPLC on silica gel (elution with 10% ethyl acetate in petroleum ether). There was isolated 2.22 g of reduction products and 620 mg of unreacted **13**. The reduced products proved to be a difficult, separable three-component mixture (5:5:1). The two major compounds had an infrared carbonyl maximum at 1710 cm^{-1} while the minor component exhibited its carbonyl stretching at 1663 cm^{-1} and was identical with the material produced in part A.

(1*S*,5*S*,7a*S*)-5,6,7,7a-Tetrahydro-4-isobutyl-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5-indanol (16a). A stirred solution of **15** (10.0 g, 28.36 mmol) in anhydrous ether (100 mL) was treated portionwise with a suspension of lithium aluminum hydride (1.07 g, 4 equiv) in ether (50 mL) at −78 °C. Upon completion of the addition, the reaction mixture was sitrred at −30 °C for 30 min and subsequently treated in turn with ethyl acetate, methanol, and water. The resulting suspension was diluted with water and extracted 3 times with ether. The combined organic layers were dried and evaporated to give 9.75 g (97%) of **16a** as a colorless solid: mp 31.8–32.0 °C; $[\alpha]^{22}_{\mathrm{D}}$ 2.06° (*c* 4.7, benzene); IR (neat, cm^{-1}) 3550, 2958, 1246, 1152; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.70 (d, *J* = 6.8 Hz, 1 H), 4.68 (d, *J* = 6.8 Hz, 1 H), 4.17 (m, 1 H), 3.65–3.57 (m, 2 H), 3.49 (dd, *J* = 10.2, 7.7 Hz, 1 H), 2.32–1.60 (series of m, 11 H), 1.35 (m, 1 H), 1.01 (s, 3 H), 0.98–0.85 (m, 2 H), 0.93 (d, *J* = 6.3 Hz, 3 H), 0.79 (d, *J* = 6.3 Hz, 3 H), 0.01 (s, 9 H).

The *p*-nitrobenzoate of **16a** was prepared conventionally and obtained as colorless prisms, mp 83.5–83.9 °C.

Anal. Calcd for $\mathrm{C_{27}H_{41}NO_6Si}$: C, 64.38; H, 8.20. Found: C, 64.51; H, 8.24.

(1*S*,3a*S*,7a*S*)-7,7a-Dihydro-4-isobutyl-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-3a(6*H*)-indanmethanol (17a). A solution of **16a** (9.75 g, 27.5 mmol) in dry tetrahydrofuran (50 mL) was added to a suspension of potassium hydride (2.0 g, 1.8 equiv) in the same solvent (50 mL), and the mixture was stirred at room temperature for 2 h. At this point, iodomethyltri-*n*-butylstannane (12.5 g, 1.06 equiv) was added, and stirring was continued for 1.5 h longer. A small amount of water was carefully introduced followed by 50 mL of saturated ammonium chloride solution. The product was extracted into petroleum ether (3×), and the combined organic layers were dried and concentrated. The residue was chromatographed on 40 g of silica gel (elution with 3% ethyl acetate in petroleum ether) to furnish 17.22 g (95.1%) of **16b** as a yellowish oil.

A cold (−78 °C), magnetically stirred solution of the above material (17.22 g, 26.2 mmol) in dry hexane (250 mL, distilled from CaH_2) was blanketed with argon and treated dropwise with *n*-butyllithium (17.8 mL of 1.55 N in hexane) during 5 min. After 2 h, another 9 mL of the *n*-butyllithium solution was introduced, and the reaction mixture was allowed to warm to room temperature during 6 h and stand overnight. Following careful addition of water, the product was extracted into dichloromethane (3×), and the combined extracts were dried and evaporated. The crude product (18.43 g) was purified by HPLC on silica gel (elution with 10% ethyl acetate in petroleum ether) to give 3.45 g (34%) of **17a** and 2.82 g (27.8%) of the [1.2] rearrangement product.

For **17a**: colorless oil, $[\alpha]^{22}_D$ 59.3° (*c* 4.0, benzene); IR (neat, cm^{-1}) 3500, 2942, 1244, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 5.69 (t, J = 3.8 Hz, 1 H), 4.68 (d, J = 6.9 Hz, 1 H), 4.65 (d, J = 6.9 Hz, 1 H), 3.90 (t, J = 7.0 Hz, 1 H), 3.68–3.52 (m, 3 H), 3.44 (d, J = 11.3 Hz, 1 H), 2.10–2.07 (m, 2 H), 1.96 (m, 1 H), 1.82–1.79 (m, 3 H), 1.68–1.43 (m, 6 H), 0.99 (s, 3 H), 0.95–0.87 (m, 8 H), 0.01 (s, 9 H); MS, m/z ($M^+-C_4H_8$) calcd 310.1964, obsd 310.2000.

Its *p*-nitrobenzoate proved to be a pale yellow oil.

Anal. Calcd for $C_{28}H_{43}NO_6S$: C, 64.96; H, 8.37. Found: C, 64.97; H, 8.36.

Trimethyl[2-[[[(1*S*,3a*S*,7a*S*)-3a,6,7,7a-tetrahydro-4-isobutyl-3a-[(2-methoxyethoxy)methoxy]-7a-methyl-1-indanyl]oxy]methoxy]ethyl]silane (17b). A solution of **17a** (187 mg, 0.507 mmol) and diisopropylethylamine (0.17 mL, 2 equiv) in dry dichloromethane (5 mL) was treated with (methoxyethoxy)ethyl chloride (0.1 mL, 1.5 equiv) and allowed to stand for 23 h. Water and additional dichloromethane were added, and the organic layer was dried and concentrated. The residue was purified by MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether) to give 208 mg (90.2%) of **17b** as a colorless oil: $[\alpha]^{22}_D$ 72.8° (*c* 6.5, benzene); IR (neat, cm^{-1}) 2950, 1964, 1248, 1054; ^1H NMR (300 MHz, $CDCl_3$) δ 5.50 (t, J = 3.6 Hz, 1 H), 4.68–4.58 (m, 4 H), 3.95 (t, J = 8 Hz, 1 H), 3.76–3.52 (m, 7 H), 3.42 (d, J = 10.2 Hz, 1 H), 3.38 (s, 3 H), 2.15–1.39 (series of m, 11 H), 0.98–0.92 (m, 2 H), 0.94 (s, 3 H), 0.89 (d, J = 6.0 Hz, 3 H), 0.86 (d, J = 6.2 Hz, 3 H), 0.01 (s, 9 H); MS, m/z ($M^+-C_6H_{13}O_2$) calcd 339.2356, obsd 339.2400.

Isobutylmagnesium Bromide Addition to 12. A solution of **12** (140 mg, 0.336 mmol) in dry ether (3 mL) was treated with 1 mL of 1 M isobutylmagnesium bromide at 0 C and stirred at this temperature for 1 h. Water was added, the product was extracted into ether (2×), and the combined organic layers were dried and concentrated. The residue was purified by MPLC on silica gel (elution with 50% ethyl acetate in petroleum ether) to give 60 mg (38%) of **18**, 40 mg (29%) of unreacted **12**, and 20 mg (15%) of the alcohol derived from **12**.

For **18**: colorless oil; ^1H NMR (300 MHz, $CDCl_3$) δ 4.71 (d, J = 6.8 Hz, 1 H), 4.69 (d, J = 6.8 Hz, 1 H), 4.60 (d, J = 6.9 Hz, 1 H), 4.53 (d, J = 6.9 Hz, 1 H), 4.23 (d, J = 10.5 Hz, 1 H), 4.13 (br s, 1 H), 3.80 (d, J = 10.5 Hz, 1 H), 3.84–3.71 (m, 2 H), 3.63–3.53 (m, 3 H), 3.49 (br d, J = 7.5 Hz, 1 H), 3.38 (s, 3 H), 2.13 (m, 1 H), 1.96–168 (m, 4 H), 1.58–1.44 (m, 2 H), 1.40–1.12 (m, 6 H), 1.29 (s, 3 H), 0.95 (d, J = 6.6 Hz, 3 H), 0.92–0.83 (m, 2 H), 0.87 (d, J = 6.6 Hz, 3 H), −0.01 (s, 9 H).

Dehydration of 18. To a magnetically stirred solution of **18** (55 mg, 0.116 mmol) in dry pyridine (2 mL) was added 0.1 mL of freshly distilled thionyl chloride at room temperature. After an elapsed time of 50 min, the mixture was taken up in ether and washed sequentially with water, cuprous sulfate solution, water, and brine prior to drying. Following solvent evaporation, the residue was subjected to MPLC purification on silica gel (elution with 15% ethyl acetate in petroleum ether) to give 24 mg (45%) of **17b** and 20 mg (38%) of **19**.

For **19**: colorless oil, $[\alpha]^{22}_D$ −11.7° (*c* 0.7, benzene); IR (neat, cm^{-1}) 2928, 1116, 1046; ^1H NMR (300 MHz, $CDCl_3$) δ 5.10 (d, J = 8.5 Hz, 1 H), 4.65–4.56 (m, 4 H), 4.01 (dd, J = 8.7, 6.9 Hz, 1 H), 3.83 (d, J = 9.5 Hz, 1 H), 3.65–3.48 (m, 6 H), 3.44 (d, J = 9.5 Hz, 1 H), 3.39 (s, 3 H), 2.58 (m, 1 H), 2.49 (dm, J = 14.3 Hz, 1 H), 2.15–1.87 (m, 3 H), 1.75–1.35 (m, 6 H), 0.97 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.6 Hz, 3 H), 0.96–0.87 (m, 2 H), 0.86 (s, 3 H), 0.01 (s, 9 H); MS, m/z ($M^+-C_4H_9O$) calcd 383.2527, obsd 383.2572.

Hydroboration of 17b. To a solution of **17b** (1.0 g, 2.19 mmol) in anhydrous tetrahydrofuran (5 mL) was added 18 mL of 1 M borane–tetrahydrofuran complex in tetrahydrofuran during 15 min. After 2 h, an additional 5 mL of the borane complex was introduced, and the reaction mixture was allowed to stand at room temperature for 5 h more, treated in turn with 10 mL of 3 M sodium hydroxide solution followed by 10 mL of 30% hydrogen peroxide, and warmed to 50 °C for 1 h. The cooled reaction mixture was extracted with dichloromethane, and the combined organic layers were dried and evaporated. Purification of the residue by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) afforded 283 mg (27.2%) of **20**, 463 mg (54.7%) of **21**, and 100 mg (10%) of unreacted **17b**.

For **20**: colorless oil, $[\alpha]^{22}_D$ 26.1° (*c* 3.9, benzene); IR (neat, cm^{-1}) 3450, 2952, 1248, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 4.70 (d, J = 7.5 Hz, 1 H), 4.63–4.61 (m, 2 H), 4.56 (d, J = 7.0 Hz, 1 H), 3.83–3.40 (m, 10 H), 3.39 (s, 3 H), 2.11 (m, 1 H), 1.76–1.18 (series of m, 11 H), 1.07 (s, 3 H), 1.04–0.84 (m, 9 H), 0.02 (s, 9 H); MS, m/z ($M^+-C_7H_{15}O_3$) calcd 327.2355, obsd 327.2354.

For **21**: colorless needles, mp 64.0–65.2 °C; $[\alpha]^{22}_D$ 23.1° (*c* 1.4, methanol); IR (KBr, cm^{-1}) 3480, 2960, 1386, 1028; ^1H NMR (300 MHz, $CDCl_3$) δ 4.70 (d, J = 7.0 Hz, 1 H), 4.64 (d, J = 7.0 Hz, 1 H), 3.70 (d, J = 7.6 Hz, 1 H), 3.66–3.55 (m, 2 H), 3.52–3.42 (m, 3 H), 2.16 (m, 1 H), 1.87 (d, J = 12.0 Hz, 1 H), 1.78–1.67 (m, 4 H), 1.45 (m, 1 H), 1.40–1.19 (m, 5 H), 1.08 (s, 3 H), 1.01–0.89 (m, 4 H), 0.91 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.6 Hz, 3 H), 0.02 (s, 9 H); MS, m/z ($M^+-C_3H_8O_2$) calcd 310.2328, obsd 310.2370.

(1*S*,3a*S*,4*S*,7a*S*)-Tetrahydro-3a-(hydroxymethyl)-4-isobutyl-7a-methyl-1[[2-(trimethylsilyl)ethoxy]methoxy]-5(4*H*)-indanone (22). Diol **21** (77 mg, 0.20 mmol) was dissolved in 10% aqueous dimethoxyethane (1.5 mL) at room temperature and treated with recrystallized *N*-bromosuccinimide (70.9 mg, 2 equiv). The reaction mixture was stirred for 45 min, and the product was extracted into ether. The combined organic layers were dried and evaporated to leave a residue that was purified by MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether). There was isolated 23 mg (36%) of **22** as a colorless oil: IR (neat, cm^{-1}) 3530, 2952, 1707, 1248, 1056; ^1H NMR (300 MHz, $CDCl_3$) δ 4.68 (d, J = 6.9 Hz, 1 H), 4.64 (d, J = 6.9 Hz, 1 H), 3.75–3.55 (m, 5 H), 2.51 (td, J = 12.2, 6.0 Hz, 1 H), 2.42 (d, J = 8.9 Hz, 1 H), 2.26 (dt, J = 13.9, 4.8 Hz, 1 H), 2.05 (m, 1 H), 1.91–1.33 (m, 9 H), 1.31 (s, 3 H), 0.97–0.87 (m, 2 H), 0.86 (d, J = 6.7 Hz, 3 H), 0.80 (d, J = 6.5 Hz, 3 H), 0.02 (s, 9 H); MS, m/z ($M^+-C_5H_{11}O_3$) calcd 309.2250, obsd 309.2199.

(1*S*,3a*S*,4*S*,7a*S*)-Tetrahydro-4-isobutyl-3a-[(2-methoxyethoxy)methoxy]-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5(4*H*)-indanone (23). To a solution of **20** (283 mg, 0.596 mmol) in dry dichloromethane (18 mL) was added pyridinium chlorochromate (257 mg, 2 equiv) in 1 portion at room temperature. After being stirred for 3 h, the reaction mixture was treated with aqueous 2 M sodium hydroxide solution to dissolve the inorganic salts and extracted with ether. The combined organic layers were dried and concentrated. Purification of the residue by MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether) afforded 208 mg (74%) of **23** as a colorless oil: $[\alpha]^{22}_D$ 82.7° (*c* 5.0, benzene); IR (neat, cm^{-1}) 2958, 1708, 1250; ^1H NMR (300 MHz, $CDCl_3$) δ 4.75 (d, J = 6.6 Hz, 1 H), 4.66–4.63 (m, 2 H), 4.59 (d, J = 6.8 Hz, 1 H), 3.84 (d, J = 10.3 Hz, 1 H), 3.77–3.66 (m, 2 H), 3.63–3.53 (m, 5 H), 3.40 (s, 3 H), 3.34 (d, J = 10.3 Hz, 1 H), 2.96 (d, J = 9.1 Hz, 1 H), 2.45 (m, 1 H), 2.33 (m, 1 H), 1.90 (m, 1 H), 1.70 (m, 1 H), 1.60–1.15 (series of m, 6 H), 1.21 (s, 3 H), 0.98–0.85 (m, 2 H), 0.87 (d, J = 6.6 Hz, 3 H), 0.80 (d, J = 6.6 Hz, 3 H), 0.02 (s, 9 H); MS, m/z ($M^+-C_4H_{10}Si$) calcd 386.2668, obsd 386.2616.

(2a*R*,4a*S*,5*S*,7a*S*,7b*S*)-Decahydro-7a-[(2-methoxyethoxy)methoxy]-2,2,4a-trimethyl-5-[[2-(trimethylsilyl)ethoxy]methoxy]-2a*H*-cyclobut[*e*]inden-2a-ol (24). A solution of **23** (108 mg) in dry dioxane (10 mL, freshly distilled from CaH_2) was placed in a Pyrex tube and deoxygenated (N_2) for 30 min. The solution was irradiated with a 450-W medium pressure Hanovia lamp for 10 h. The solvent was evaporated, and the residue was purified by MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether). There was isolated 67 mg (62%) of **24** as a colorless oil; IR (neat, cm^{-1}) 3480, 2942, 1050; ^1H NMR (300 MHz, $CDCl_3$) δ 4.66 (d, J = 6.9 Hz, 1 H), 4.63 (d, J = 6.7 Hz, 1 H), 4.62 (d, J = 6.7 Hz, 1 H), 4.56 (d, J = 6.9 Hz, 1 H), 3.68–3.60 (m, 4 H), 3.58–3.52 (m, 3 H), 3.48 (d, J = 8.8 Hz, 1 H), 3.38 (s, 3 H), 3.31 (d, J = 8.8 Hz, 1 H), 2.40 (m, 1 H), 2.21–2.02 (m, 3 H), 1.81 (m, 1 H), 1.71–1.53 (m, 5 H), 1.27–1.18 (m, 2 H), 1.15 (s, 3 H), 1.02 (s, 3 H), 0.99 (s, 3 H), 0.96–0.83 (m, 2 H), 0.01 (s, 9 H); MS, m/z ($M^+-C_6H_{14}O_2$) calcd 354.2226, obsd 354.2279.

(2a*R*,4a*S*,5*R*,7a*S*,7b*S*)-Octahydro-7a-[(2-methoxyethoxy)methoxy]-2,2,4a-trimethyl-2a,5-epoxy-2a*H*-cyclobut[*e*]inden-5(2*H*)-ol (25). Tetra-*n*-butylammonium fluoride trihydrate (1.0 g) was heated at 90 °C and 2 torr for 3 h. To the solid was added a solution of **24** (196 mg, 0.415

mmol) in dry tetrahydrofuran (4 mL), and the solvent was removed in vacuo (2 torr). While still under vacuum, the reaction mixture was heated at 60 °C for 18 h, cooled, and extracted with dichloromethane (3×). The combined organic layers were dried, concentrated, and chromatographed (MPLC) on silica gel (elution first with 50% ethyl acetate in petroleum ether and then pure ethyl acetate). There was isolated 25 mg (12.8%) of unreacted **24** and 103 mg (72.5%) of diol: $[\alpha]^{22}{}_{D}$ −3.2° (*c* 1.1, methanol); IR (neat, cm^{-1}) 3400, 2928, 1448, 1030; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.76 (d, *J* = 6.9 Hz, 1 H), 4.73 (d, *J* = 6.9 Hz, 1 H), 3.76–3.66 (m, 2 H), 3.62–3.49 (m, 2 H), 3.45 (m, 1 H), 3.39 (s, 3 H), 3.29 (d, *J* = 9.5 Hz, 1 H), 3.12 (d, *J* = 9.5 Hz, 1 H), 2.51 (t, *J* = 10.5 Hz, 1 H), 2.33 (m, 1 H), 1.99 (dd, *J* = 12.3, 8.8 Hz, 1 H), 1.90–1.80 (m, 2 H), 1.71–1.53 (m, 6 H), 1.35–1.21 (m, 2 H), 1.14 (s, 3 H), 1.05 (s, 6 H).

The mono *p*-nitrobenzoate, prepared in customary fashion, was obtained as pale yellow needles, mp 108.0–109.5 °C.

Anal. Calcd for $C_{26}H_{37}NO_8$: C, 63.53; H, 7.59. Found: C, 64.03; H, 7.78.

The above diol (103 mg, 0.301 mmol) dissolved in dry dichloromethane (5 mL) was stirred magnetically while pyridinium chlorochromate (134.5 mg, 0.60 mmol) was added in 1 portion at room temperature. After an elapsed time of 3.5 h, saturated sodium bicarbonate solution was added to dissolve the solids, and this solution was extracted with dichloromethane. The combined organic layers were dried and evaporated, and the residue was purified by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) to afford 56 mg (54.6%) of **25** and 10 mg (9.8%) of **26**.

For **25**: colorless solid, mp 35.5–36.1 °C; $[\alpha]^{22}{}_{D}$ +3.7° (*c* 0.6, methanol); IR (KBr, cm^{-1}) 3450, 2930, 1464, 1380; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.70 (d, *J* = 6.8 Hz, 1 H), 4.68 (d, *J* = 6.8 Hz, 1 H), 3.72–3.68 (m, 2 H), 3.59–3.55 (m, 2 H), 3.51 (d, *J* = 9.2 Hz, 1 H), 3.40 (s, 3 H), 3.37 (d, *J* = 9.2 Hz, 1 H), 2.37 (dd, *J* = 10.0, 8.1 Hz, 1 H), 1.98–1.40 (series of m, 11 H), 1.09 (s, 3 H), 1.01 (s, 3 H), 0.82 (s, 3 H); ^{13}C NMR (75 MHz, CDCl$_3$) ppm 108.48, 96.02, 79.51, 73.60, 71.91, 66.93, 59.06, 47.58, 44.08, 41.13, 38.39, 35.22, 34.79, 27.08, 25.16, 24.73, 23.63, 22.16, 16.80; MS, *m/z* (M$^+$) calcd 340.2249, obsd 340.2230.

For **26**: colorless oil; IR (CCl$_4$, cm^{-1}) 2975, 2938, 2880, 1742, 1718, 1450, 1110, 1050, 910; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.72 (m, 1 H), 4.65 (d, *J* = 6.8 Hz, 1 H), 4.61 (m, 1 H), 4.60 (d, *J* = 6.8 Hz, 1 H), 3.66–3.62 (m, 3 H), 3.60–3.51 (m, 3 H), 3.38 (s, 3 H), 2.77 (dd, *J* = 9.1, 2.3 Hz, 1 H), 2.62 (dd, *J* = 15.4, 8.8 Hz, 1 H), 2.53 (dd, *J* = 13.0, 6.0 Hz, 1 H), 2.36–2.29 (m, 3 H), 1.93–1.65 (m, 5 H), 1.71 (s, 3 H), 1.33 (s, 3 H); MS, *m/z* (M$^+$) calcd 338.2093, obsd 338.2130.

Trimethyl[2-[[[(1*S*,3a*S*,7a*S*)-3a,6,7,7a-tetrahydro-4-isobutyl-3a-(methoxymethoxy)-7a-methyl-1-indanyl]oxy]methoxy]ethyl]silane (27). To a solution of **17a** (74 mg, 0.201 mmol) and diisopropylethylamine (0.1 mL) in dry dichloromethane (1 mL) was added chloromethyl methyl ether (0.02 mL) at room temperature. After 20 min, the reaction mixture was treated with water, the product was extracted into ether (3×), and the combined organic layers were dried and evaporated. Purification by column chromatography (silica gel, elution with 10% ethyl acetate in petroleum ether) afforded 83 mg (100%) of **27** as a colorless oil: $[\alpha]^{22}{}_{D}$ 76.7° (*c* 1.0, methanol); IR (neat, cm^{-1}) 2975, 2926, 1465, 1250, 1150, 1120, 1055, 1045; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.52 (m, 1 H), 4.69 (d, *J* = 6.8 Hz, 1 H), 4.67 (d, *J* = 6.8 Hz, 1 H), 4.57 (d, *J* = 6.5 Hz, 1 H), 4.52 (d, *J* = 6.5 Hz, 1 H), 3.96 (t, *J* = 8.0 Hz, 1 H), 3.68–3.65 (m, 2 H), 3.52 (d, *J* = 10.2 Hz, 1 H), 3.40 (d, *J* = 10.2 Hz, 1 H), 3.35 (s, 3 H), 2.07–1.28 (series of m, 11 H), 0.96 (s, 3 H), 0.93–0.87 (m, 8 H), 0.02 (s, 9 H); MS, *m/z* (M$^+$–C$_4$H$_9$O) calcd 339.2355, obsd 339.2385.

(1*S*,3a*S*,4*S*,7a*S*)-Tetrahydro-4-isobutyl-3a-(methoxymethoxy)-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5(4*H*)-indanone (28). A solution of **27** (845 mg, 2.05 mmol) in 20 mL of dry 2-methoxyethyl ether (distilled from CaH$_2$) was treated with 20 mL of the borane–tetrahydrofuran complex (1 M in tetrahydrofuran) under an argon atmosphere at room temperature. The reaction mixture was stirred for 24 h, treated sequentially with 25 mL of 3 M sodium hydroxide solution and 20 mL of 40% hydrogen peroxide, and heated at 50 °C for 1 h. The product was extracted into dichloromethane (3×), passed through a column of magnesium sulfate, and concentrated. Purification of the residue by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) afforded 546 mg (62%) of the desired β alcohol and 74 mg (9.3%) of the derived diol lacking the MOM group.

For the major product: colorless oil, $[\alpha]^{22}{}_{D}$ 22.8° (*c* 1.1, methanol); IR (neat, cm^{-1}) 3440, 2954, 1252, 1048; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.65–4.52 (m, 4 H), 3.75 (d, *J* = 10.2 Hz, 1 H), 3.62–3.38 (m, 5 H), 3.37 (s, 3 H), 2.13–2.00 (m, 2 H), 1.81–1.13 (series of m, 11 H), 1.08 (s, 3 H), 0.94–0.86 (m, 8 H), 0.01 (s, 9 H).

The *p*-nitrobenzoate was obtained as a colorless oil.

Anal. Calcd for $C_{30}H_{49}NO_2Si$: C, 62.15; H, 8.52. Found: C, 62.36; H, 8.59.

A solution of this alcohol (527 mg, 1.22 mmol) in dry dichloromethane (40 mL) was stirred with pyridinium chlorochromate (527 mg, 2 equiv) for 2.5 h. The dark red mixture was stirred with 10% sodium bicarbonate solution for 10 min and extracted with dichloromethane (3×). The combined organic layers were dried and concentrated, and the residue was purified by silica gel chromatography to give 530 mg (100%) of **28**: colorless oil, $[\alpha]^{22}{}_{D}$ 57.7° (*c* 2.0, methanol); IR (neat, cm^{-1}) 2950, 2922, 2880, 1712, 1464, 1247, 1160, 1108, 1080; ^{1}H NMR (300 MHz, CDCl^3) δ 4.66–4.62 (m, 2 H), 4.60 (d, *J* = 6.9 Hz, 1 H), 4.56 (d, *J* = 6.5 Hz, 1 H), 3.80 (d, *J* = 10.3 Hz, 1 H), 3.66–3.53 (m, 2 H), 3.40 (s, 3 H), 3.32 (d, *J* = 10.3 Hz, 1 H), 2.98 (d, *J* = 8.7 Hz, 1 H), 2.45 (m, 1 H), 2.33 (m, 1 H), 1.97–1.83 (m, 2 H), 1.79–1.63 (m, 3 H), 1.53–1.45 (m, 2 H), 1.43–1.17 (m, 2 H), 1.23 (s, 3 H), 0.94–0.84 (m, 2 H), 0.87 (d, *J* = 6.6 Hz, 3 H), 0.80 (d, *J* = 6.6 Hz, 3 H), 0.01 (s, 9 H); MS, *m/z* (M$^+$–C$_4$H$_8$) calcd 372.2332, obsd 372.2333.

(1*S*,3a*S*,4*R*,7a*S*)-Tetrahydro-4-isobutyl-3a-(methoxymethoxy)-7a-methyl-1-[[2-(trimethylsilyl)ethoxy]methoxy]-5(4*H*)-indanone (29). A solution of **28** (530 mg) in 40 mL of 1 M sodium methoxide in methanol was heated at the reflux temperature for 9.5 h, cooled, and diluted with water (50 mL). The product was extracted into dichloromethane (4 × 150 mL), and the combined organic layers were dried and concentrated. MPLC of the residue on silica gel (elution with 10% ethyl acetate in petroleum ether) afforded 348 mg of **29**; the balance of the material was unisomerized **28**.

For **29**: colorless oil, $[\alpha]^{22}{}_{D}$ 13.9° (*c* 1.0, methanol); IR (neat, cm^{-1}) 2950, 2922, 2880, 1715, 1460, 1248, 1150, 1110, 1035; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.75 (d, *J* = 7.0 Hz, 1 H), 4.68 (d, *J* = 7.0 Hz, 1 H), 4.46 (t, *J* = 8.1 Hz, 1 H), 4.42 (d, *J* = 6.6 Hz, 1 H), 4.39 (d, *J* = 6.6 Hz, 1 H), 3.72–3.54 (m, 2 H), 3.43 (d, *J* = 10.1 Hz, 1 H), 3.32 (s, 3 H), 3.26 (d, *J* = 10.1 Hz, 1 H), 2.40 (ddd, *J* = 14.7, 11.2, 7.2 Hz, 1 H), 2.31 (dt, *J* = 14.7, 4.6 Hz, 1 H), 2.25–2.10 (m, 2 H), 2.04–1.88 (m, 3 H), 1.70 (m, 1 H), 1.53–1.35 (m, 3 H), 1.00 (s, 3 H), 0.97–0.85 (m, 2 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 0.79 (d, *J* = 6.5 Hz, 3 H), 0.77 (m, 1 H), 0.01 (s, 9 H); MS, *m/z* (M$^+$–C$_4$H$_8$) calcd 372.2332, obsd 372.2318.

(2a*S*,4a*S*,7a*S*,7b*R*)-Decahydro-7a-(methoxymethoxy)-2,2,4a-trimethyl-5-[[2-(trimethylsilyl)ethoxy]methoxy]-2a*H*-cyclobut[*e*]inden-2a-ol (30a). A solution of **29** (110 mg, 0.257 mmol) in 100 mL of benzene (freshly distilled from KMnO$_4$) was placed in a quartz tube and deoxygenated with an argon stream. The flow of argon was utilized for agitation as the solution was irradiated in a Rayonet reactor with 253.7-nm lamps. After 9.5 h, the yellow solution was concentrated, and the residue was submitted to MPLC on silica gel (elution with 9% ethyl acetate in petroleum ether). There was isolated 27.6 mg (25.1%) of unreacted **29** and 40.5 mg (36.8%) of **30a**. Increase in the solvent polarity to 30% ethyl acetate afforded 16.7 mg (17.5%) of cleavage product.

For **30a**: colorless oil, $[\alpha]^{22}{}_{D}$ 23.4° (*c* 0.5, methanol); IR (neat, cm^{-1}) 3425, 2954, 2928, 1468, 1375, 1250, 1108, 1050, 1025; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.71 (d, *J* = 6.9 Hz, 1 H), 4.70–4.65 (m, 3 H), 4.36 (t, *J* = 8.7 Hz, 1 H), 3.70–3.38 (m, 4 H), 3.46 (s, 3 H), 2.21–2.09 (m, 2 H), 1.98 (dd, *J* = 12.4, 8.6 Hz, 1 H), 1.76–1.53 (m, 5 H), 1.41–1.21 (m, 4 H), 1.14 (s, 3 H), 1.09 (s, 3 H), 0.97–0.88 (m, 2 H), 0.92 (s, 3 H), 0.02 (s, 9 H); MS, *m/z* (M$^+$–C$_3$H$_{13}$Si) calcd 339.2171, obsd 339.2206.

For cleavage product: IR (neat, cm^{-1}) 2954, 1709, 1252, 1154, 1110, 1078; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.72 (d, *J* = 6.9 Hz, 1 H), 4.66 (d, *J* = 6.9 Hz, 1 H), 4.53 (d, *J* = 6.5 Hz, 1 H), 4.51 (d, *J* = 6.5 Hz, 1 H), 4.24 (dd, *J* = 8.3, 6.6 Hz, 1 H), 3.68–3.53 (m, 2 H), 3.57 (d, *J* = 9.6 Hz, 1 H), 3.33 (s, 3 H), 3.29 (d, *J* = 9.6 Hz, 1 H), 2.39–2.14 (m, 5 H), 1.89–1.81 (m, 2 H), 1.75–1.59 (m, 2 H), 1.31 (m, 1 H), 1.02 (s, 3 H), 0.96–0.87 (m, 2 H), 0.02 (s, 9 H); MS, *m/z* (M$^+$–C$_4$H$_9$O) calcd 283.1729, obsd 283.1741.

(2a*S*,4a*S*,5*S*,7b*R*)-Decahydro-7a-(methoxymethoxy)-2,2,4a-trimethyl-2a*H*-cyclobut[*e*]indene-2a,5-diol (30b). A mixture of **30a** (99 mg), tetra-*n*-butylammonium fluoride trihydrate (300 mg), and 2 mL of 2-methoxyethyl ether was heated at 55 °C and 2 torr for 36 h. The brown mixture was dissolved in dichloromethane, washed with water, dried, and concentrated. The residue was subjected to MPLC on silica gel (elution with 60% ethyl acetate in petroleum ether) to give 56 mg (81.2%) of **30b** as colorless needles: mp 102.5–103.4 °C; $[\alpha]^{22}{}_{D}$ 8.5° (*c* 0.4, methanol); IR (neat, cm^{-1}) 3410, 2950, 2932, 1472, 1441, 1150, 1108, 1043, 1022; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.68 (br s, 2 H), 4.42 (t, *J* = 8.3 Hz, 1 H), 3.56 (br s, 2 H), 3.45 (s, 3 H), 2.18–2.11 (m, 2 H), 2.00 (dd, *J* = 12.5, 8.6 Hz, 1 H), 1.76–1.23 (series of m, 10 H), 1.13 (s, 3 H), 1.08 (s, 3 H), 0.93 (s, 3 H); MS, *m/z* (M$^+$–H$_2$O) calcd 280.2038, obsd 280-2041.

Anal. Calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.69; H, 9.90.

(2a*S*,4a*S*,7a*S*,7b*R*)-Decahydro-2a-hydroxy-7a-(methoxymethoxy)-2,2,4a-trimethyl-5*H*-cyclobut[*e*]inden-5-one (31a). A solution of **30b** (8 mg) in 1 mL of dry dichloromethane was stirred with 10 mg of pyridinium chlorochromate at room temperature for 1 h. The reaction mixture was partitioned between dichloromethane and sodium bicarbonate solution. The organic phase was dried and evaporated, and the residue was purified by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether). There was isolated 6.4 mg (80.5%) of **31a** as a colorless oil: $[\alpha]^{22}_{D}$ 60.3° (*c* 1.1, methanol); IR (neat, cm^{-1}) 3430, 2929, 1737, 1463, 1150, 1108, 1048; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.70 (ABd, *J* = 7.1 Hz, 2 H), 3.73 (d, *J* = 10.1 Hz, 1 H), 3.72 (d, *J* = 10.1 Hz, 1 H), 3.46 (s, 3 H), 2.45 (dt, *J* = 19.9, 6.8 Hz, 1 H), 2.38 (dt, *J* = 19.9, 9.2 Hz, 1 H), 2.09 (dd, *J* = 12.0, 8.9 Hz, 1 H), 1.97 (dt, *J* = 14.0, 3.4 Hz, 1 H), 1.78–1.56 (m, 6 H), 1.33–1.21 (m, 4 H), 1.07 (s, 3 H), 1.05 (s, 3 H), 0.96 (s, 3 H); MS, *m/z* (M^+) calcd 296.1987, obsd 296.1963.

(2a*S*,4a*S*,7a*S*,7b*R*)-Decahydro-2a,7a-dihydroxy-2,2,4a-trimethyl-5*H*-cyclobut[*e*]inden-5-one (31b). A solution of **31a** (4.2 mg, 0.014 mol) in 2 mL of tetrahydrofuran and 0.4 mL of 35% perchloric acid was stirred for 12 h at room temperature. The pale yellow reaction mixture was neutralized with saturated sodium bicarbonate solution and extracted with dichloromethane. The combined organic layers were dried and concentrated, and the residue was purified by MPLC on silica gel (elution with ethyl acetate). There was isolated 1.7 mg (47%) of **31b** as a colorless solid: mp 153.5–155.0 °C; IR (KBr, cm^{-1}) 3425, 3250, 3165, 2966, 2938, 1735, 1384; ^{1}H NMR (300 (MHz, $CDCl_3$) δ 4.02 (d, *J* = 11.2 Hz, 1 H), 3.89 (d, *J* = 11.2 Hz, 1 H), 2.53–2.48 (m, 2 H), 2.32 (dd, *J* = 12.1, 8.9 Hz, 1 H), 2.25 (m, 1 H), 1.97 (dd, *J* = 12.6, 7.4 Hz, 1 H), 1.65–1.56 (m, 3 H), 1.22 (s, 3 H), 1.21 (s, 3 H), 1.06 (s, 3 H); MS, *m/z* (M^+) calcd 252.1726, obsd 252.1723.

(2a*S*,4a*S*,7a*S*,7b*R*)-1,2,2a,3,4,4a,7a,7b-Octahydro-7a-(methoxymethoxy)-2,2,4a-trimethyl-2a-(trimethylsiloxy)-5*H*-cyclobut[*e*]inden-5-one (32a). A solution of **31a** (39 mg, 0.13 mmol) and methyl trimethylsilylacetate (0.2 mL) in dry tetrahydrofuran (0.5 mL) was added to tetra-*n*-butylammonium fluoride (10 mg, predried to 70 °C and 1 mm for 30 min) and allowed to stand for 30 min. The reaction mixture was taken up in hexane, washed with saturated sodium bicarbonate solution, dried, and concentrated.

The colorless silyl enol ether was dissolved in dry acetonitrile (3 mL), treated with palladium acetate (47 mg, 0.2 mmol), and stirred for 33.5 h. Direct preparative TLC purification (silica gel, elution with 10% ethyl acetate in petroleum ether) furnished 40 mg (80.2%) of **32a** as a colorless oil: $[\alpha]^{22}_{D}$ 32.3° (*c* 0.9, methanol); IR (neat, cm^{-1}) 2950, 2934, 1709, 1454, 1250, 1114, 1052; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 6.0 Hz, 1 H), 6.03 (d, *J* = 6.0 Hz, 1 H), 4.63 (d, *J* = 6.6 Hz, 1 H), 4.61 (d, *J* = 6.6 Hz, 1 H), 3.99 (d, *J* = 10.4 Hz, 1 H), 3.94 (d, *J* = 10.4 Hz, 1 H), 3.38 (s, 3 H), 2.27 (ddm, *J* = 14.6, 5.1 Hz, 1 H), 2.10 (dd, *J* = 12.3, 9.4 Hz, 1 H), 1.75 (ddd, *J* = 14.2, 12.9, 5.9 Hz, 1 Hz, 1 H), 1.59–1.20 (m, 4 H), 1.05 (s, 3 H), 1.03 (s, 3 H), 0.99 (s, 3 H), 0.21 (s, 9 H); MS, *m/z* ($M^+-C_3H_7O_2$) calcd 291.1781, obsd 291.1769.

(2a*S*,4a*S*,7a*S*,7b*R*)-1,2,2a,3,4,4a,7a,7b-Octahydro-2a,7a-dihydroxy-2,2,4a-trimethyl-5*H*-cyclobut[*e*]inden-5-one (32b). A solution of **32a** (34 mg) in 15 mL of tetrahydrofuran was treated with 2.8 mL of 35% perchloric acid, stirred at room temperature for 70 h, and poured into saturated sodium bicarbonate solution. The product was extracted into dichloromethane (5×), and the combined organic layers were dried and evaporated. Following purification of the residue by spinning plate chromatography on silica gel (elution with 50% ethyl acetate in petroleum ether), 17 mg (73%) of **32b** was isolated as a colorless solid: mp 152.0–152.9 °C (lit.[1] mp 154–155 °C); $[\alpha]^{22}_{D}$ 98.9° (*c* 1.0, methanol); IR (KBr, cm^{-1}) 3438, 3150, 2930, 1695, 1364; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (d, *J* = 5.9 Hz, 1 H), 6.06 (d, *J* = 5.9 Hz, 1 H), 3.85 (d, *J* = 11.6 Hz, 1 H), 3.71 (d, *J* = 11.6 Hz, 1 H), 2.87 (m, 2 H), 2.29 (m, 1 H), 2.18 (dd, *J* = 15.2, 11.9 Hz, 1 H), 1.87 (ddd, *J* = 13.8, 11.3, 4.5 Hz, 1 H), 1.70–1.56 (m, 2 H), 1.43–1.35 (m, 2 H), 1.23 (s, 3 H), 1.11 (s, 3 H), 1.07 (s, 3 H); MS, *m/z* (M^+) calcd 250.1569, obsd 250.1594.

Prototypical Reductions of 32b. A. Use of Cerium Trichloride-Doped Sodium Borohydride. A cold (0 °C), magnetically stirred solution of **32b** (2.0 mg, 0.008 mmol) and cerium(III) chloride heptahydrate (3.0 mg) in methanol (2 mL) was treated with sodium borohydride (3 mg) in 1 portion. Stirring was maintained for 15 min before water was added, and the product was extracted into dichloromethane (3×). The combined and dried organic layers were concentrated, and the residue was purified by short column chromatography on silica gel (elution with 30% ethyl acetate in petroleum ether). There was isolated 2.0 mg (100%) of **31c** as a colorless solid, mp 140.5–141.9 °C. The spectra of this substance proved identical with those reported earlier.

B. Use of Diisobutylaluminum Hydride. (+)-Punctatin D. Dibal (1 mL of 1 M in tetrahydrofuran) was added dropwise to a cold (0 °C), magnetically stirred solution of **32b** (1.1 mg, 0.004 mmol) in dry tetrahydrofuran (1 mL). After 3 h at 0 °C, water was introduced, and threefold extraction with dichloromethane followed. Drying and evaporation left 1.5 mg of colorless solid identified as **33b**: $[\alpha]^{22}_{D}$ +26° (*c* 0.2, methanol); IR (KBr, cm^{-1}) 3400–3200, 2924, 1088, 1012; ^{1}H NMR (300 MHz, C_5D_5N) δ 6.01 (d, *J* = 5.7 Hz, 1 H), 5.75 (d, *J* = 5.7 Hz, 1 H), 5.37 (m, 1 H), 4.08 (d, *J* = 12.9 Hz, 1 H), 3.96 (dm, *J* = 13 Hz, 1 H), 2.39–1.94 (series of m, 5 H), 1.65–1.60 (m, 2 H), 1.61 (s, 3 H), 1.27 (s, 3 H), 1.14 (s, 3 H); MS, *m/z* (M^+-H_2O) calcd 234.1620, obsd 234.1659.

(2a*S*,4a*S*,5*S*,7a*S*,7b*R*)-2,2a,3,4,4a,5,7a,7b-Octahydro-7a-(methoxymethoxy)-2,2,4a-trimethyl-2a-(trimethylsiloxy)-1*H*-cyclobut[*e*]inden-5-ol (33a). To a cold (0 °C) solution of **32a** (12.3 mg, 0.034 mmol) and cerium(III) chloride heptahydrate (15 mg) in methanol (8 mL) was added sodium borohydride (10 mg). After being stirred for 20 min, the mixture was extracted with dichloromethane, and the product was purified by MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether). There was isolated 12.2 mg (97%) of **33a** as a colorless oil: $[\alpha]^{22}_{D}$ 37.3° (*c* 1.1, methanol); IR (neat, cm^{-1}) 3380, 2948, 1254, 1040, 838; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (dd, *J* = 6.0, 1.8 Hz, 1 H), 5.61 (dd, *J* = 6.0, 1.4 Hz, 1 H), 4.67 (dm, *J* = 8.2 Hz, 1 H), 4.59 (s, 2 H), 3.76 (d, *J* = 10.2 Hz, 1 H), 3.74 (d, *J* = 10.2 Hz, 1 H), 3.34 (s, 3 H), 2.01 (dd, *J* = 12.3, 9.0 Hz, 1 H), 1.77–1.63 (m, 3 H), 1.57 (br s, 1 H), 1.51–1.41 (m, 3 H), 1.05 (s, 3 H), 0.99 (s, 3 H), 0.86 (s, 3 H), 0.17 (s, 9 H); MS, *m/z* ($M^+-C_3H_7O_2$) calcd 293.1936, obsd 293.1927.

(2a*S*,4a*S*,5*S*,7a*S*,7b*R*)-1,3,4,4a,5,7b-Hexahydro-2,2,4a-trimethyl-2*H*-2a,7a-(epoxymethanol)-2a*H*-cyclobut[*e*]inden-5-ol (34). To a solution of **33b** (0.7 mg), benzoic acid (1.0 mg), and triphenylphosphine (2.0 mg) in 0.5 mL of dry benzene was added a benzene solution (2 mL) of diethyl azodicarboxylate (2.0 mg/mL) at room temperature. The progress of reaction was monitored by TLC. When the reactant had been consumed (ca. 1 h), the solvent was evaporated, and the residue was purified by MPLC on silica gel (elution with benzene–ethyl acetate–acetic acid, 50:49:1) to give 0.5 mg (80%) of **34** as a colorless solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92 (m, 1 H), 5.70 (m, 1 H), 4.65 (m, 1 H), o982 (d, *J* = 13 Hz, 1 H), 3.79 (dm, *J* = 13 Hz, 1 H), 2.39–1.40 (series of m, 8 H), 1.15 (s, 3 H), 1.06 (s, 3 H), 0.94 (s, 3 H); MS the molecular ion peak was too transient for accurate high resolution measurement.

(2a*S*,4a*S*,5*R*,7a*S*,7b*R*)-2,2a,3,4,4a,5,7a,7b-Octahydro-7a-(methoxymethoxy)-2,2,4a-trimethyl-2a-(trimethylsiloxy)-1*H*-cyclobut[*e*]inden-5-ol (36). To a solution of **33a** (10.5 mg, 0.0285 mmol) in dry benzene (4 mL) was added triphenylphosphine (30 mg, 4 equiv) and benzoic acid (14 mg, 4 equiv) followed by dropwise addition of diethyl azodicarboxylate (10 mg, 2 equiv) at room temperature. after 3 h, the reaction mixture was concentrated and directly subjected to preparative TLC (silica gel, elution with 10% ethyl acetate in petroleum ether) followed by spinning plate chromatography (same parameters). There was obtained 8.4 mg (62.4%) of **36** as a colorless oil: IR (neat, cm^{-1}) 2944, 1714, 1270, 1042; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (br d, *J* = 7.2 Hz, 2 H), 7.55 (br t, *J* = 7.3 Hz, 1 H), 7.42 (br t, *J* = 7.3 Hz, 1 H), 6.30 (d, *J* = 5.9 Hz, 1 H), 5.81 (dd, *J* = 5.9, 2.6 Hz, 1 H), 5.60 (d, *J* = 2.6 Hz, 1 H), 4.63 (d, *J* = 6.3 Hz, 1 H), 4.60 (d, *J* = 6.3 Hz, 1 H)8 4.01 (d, *J* = 10.0 Hz, 1 H), 3.81 (d, *J* = 10.0 Hz, 1 H), 3.38 (s, 3 H)8 2.25–2.11 (m, 2 H), 1.89–1.75 (m, 2 H), 1.64–1.56 (m, 2 H), 1.44 (m, 1 H), 1.14 (s, 3 H), 1.07 (s, 3 H), 1.04 (s, 3 H), 0.19 (s, 9 H); MS, *m/z* ($M^+-C_3H_7O_2$) calcd 397.2199, obsd 397.2182.

(−)-Punctatin A (1). A solution of **36** (7.6 mg, 0.016 mmol) in tetrahydrofuran (1 mL) was slowly treated with 35% perchloric acid (0.4 mL). The reaction mixture was stirred for 25 h, neutralized with saturated sodium bicarbonate solution, and extracted with dichloromethane. Spinning plate chromatographic purification (silica gel, elution with 30% ethyl acetate in petroleum ether) afforded 3.5 mg (61%) of diol as a colorless solid, mp 165–170 °C, and returned 1.2 mg (16%) of unreacted **36**.

The diol (3.5 mg, 0.01 mmol) was dissolved in 2 mL of 5% potassium hydroxide in 95% ethanol and heated to 50 °C for 3 h under a nitrogen atmosphere. Following the addition of saturated ammonium chloride solution, the product was extracted into dichloromethane, dried, and concentrated. Purification by MPLC on silica gel (elution with 50:49:1 benzene/ethyl acetate/acetic acid) gave 1.9 mg (77%) of **1** as a colorless solid, mp 184–185 °C (lit.[1] mp 187–192 °C), $[\alpha]^{22}_{D}$ −27° (*c* 0.4, methanol) (lit.[1] $[\alpha]^{20}$ −26° (*c* 1.0, methanol)]. The spectra of the synthetic sample were superimposable on those of the natural product.

Acknowledgment. This investigation was made possible by grants from the National Institutes of Health (GM 30827) and Eli Lilly Company. We also thank Drs. R. L. Edwards (University of Bradford) and Kurt Loening (Chemical Abstracts Service). Dr. Edwards generously made available to us a sample of authentic (−)-**1** and copies of its spectra. Dr. Loening provided needed assistance with nomenclature.