H, m) 1.08 (3 H, d, J = 7.5 Hz), 0.13 (9 H, s); ^{13}C NMR δ 136.5, 100.0, 85.0, 84.9, 42.7, 32.1, 31.8, 19.7, 11.7, −0.1; IR (neat, film) 2183, 1454, 1408, 844 cm^{-1}.

(*Z*)-1-(5-Methylcyclopentenyl)-1-penten-4-yne (18). A mixture of 0.12 g (0.56 mmol) of **21**, 0.02 g of Lindlar catalyst, 0.01 g of quinoline, and 2 mL of heptane was placed in a flask and attached to a hydrogenation apparatus. The system was flushed three times with hydrogen, filled again with hydrogen, and sealed. Measurable uptake of hydrogen ceased after 3 h at 759 mmHg and 22 °C. The catalyst was filtered off and washed with hexane, and the solvents were evaporated, giving 0.15 g of crude material. Chromatography on silica, eluting with hexane, gave 0.088 g (73%) of impure silylated dienyne, which was used directly in the next step: ^{1}H NMR δ 5.87 (1 H, d, J = 11.4 Hz), 5.60 (1 H, s), 5.52 (1 H, d of t, J = 11.4, 6.9 Hz), 3.13 (2 H, d, J = 6.9 Hz), 2.70 (1 H, m), 2.22 (3 H, series of m), 1.41 (1 H, m), 0.99 (3 H, d, J = 6.6 Hz), 0.13 (9 H, s). This material contained a small amount of the triene overreduction product: ^{1}H NMR δ 6.28 (1 H, d of t, J = 13.9, 7.1 Hz), 5.84 (1 H, d, J = 11.7 Hz), 5.58 (1 H, s), 5.52 (1 H, d of t, J = 13.9, 1.2 Hz), 5.43 (1 H, d of t, J = 11.7, 7.0 Hz), 3.06 (2 H, d of t, J = 1.2, 7.0 Hz), 2.71 (1 H, m), 2.35 (2 H, m), 2.09 (1 H, m), 1.45 (1 H, m), 1.01 (3 H, d, J = 7.2 Hz), 0.11 (9 H, s).

To a solution of 1.3 g (13.8 mmol) of potassium fluoride dihydrate in 8 mL of DMF was added 0.20 g (0.92 mmol) of impure dienyne dissolved in 2 mL of DMF. After being stirred for 3.5 h, the reaction mixture was poured into 30 mL of 1 M HCl and extracted with 5 × 15 mL ether. The extracts were washed with 3 × 50 mL of water and 2 × 50 mL of saturated aqueous NaCl. Drying ($MgSO_4$), filtration, and solvent evaporation gave 0.16 g of crude product that was further purified by MPLC with hexane to yield 0.053 g (41%) of **18**: ^{1}H NMR δ 5.89 (1 H, d, J = 11.2 Hz), 5.63 (1 H, s), 5.53 (1 H, d of t, J = 11.2, 7.0 Hz), 3.06 (2 H, d of t, J = 2.0, 7.0 Hz), 2.71 (1 H, m), 2.5–2.0 (3 H, series of m), 1.98 (1 H, t, J = 2.5 Hz), 1.43 (1 H, m), 0.99 (3 H, d, J = 6.9 Hz); ^{13}C NMR δ 129.7, 126.2, 125.5, 92.8, 68.0, 42.0, 32.3, 31.3, 19.9, 18.8; IR 3310, 2120, 631 cm^{-1}.

α-Bromostyrene by Bromoboration of Phenylacetylene Using Dibromoborane.[48] To a solution of 0.07 g (0.7 mmol) of phenylacetylene in 2 mL of 1,2-dichloroethane at 0 °C was added 0.7 mL (1 M in CH_2Cl_2, 0.7 mmol) of dibromoborane–methyl sulfide complex. The reaction was stirred for 20 min at 0 °C and 30 min at rt. Glacial acetic acid (0.2 mL) was added and the mixture refluxed for 2.5 h. The reaction was cooled in an ice bath, and 2 mL of 2.5 M sodium hydroxide solution was added. The mixture was dissolved in 3 mL of water and extracted with 3 × 5 mL of hexane. The combined hexane layers were washed with 2 × 10 mL of saturated aqueous $NHCl_4$ and 10 mL of saturated aqueous NaCl and then dried ($MgSO_4$). Filtration and solvent evaporation gave 0.10 g of yellow liquid. The NMR spectrum of this crude product showed no phenylacetylene and no styrene: ^{1}H NMR δ 7.57 (2 H, m), 7.32 (3 H, m), 6.10 (1 H, d, J = 2.0 Hz), 5.77 (1 H, d, J = 2.0 Hz). Low-resolution GC/MS showed only one major product of this reaction: base peak m/e 103 (loss of Br); other peaks at m/z 182 and 184 (M^+), 77, 63, and 51.

Representative Attempted Synthesis of 2-Methyltricyclo[6.3.0.0^{1,5}]undeca-7,10-dien-6-one (17). A mixture of 0.11 g (0.75 mmol) of dienyne **18** and 0.25 g (0.75 mmol) of $Co_2(CO)_8$ in 5 mL of heptane was stirred under CO for 1 h. The mixture was transferred to a sealed tube and heated at 115 °C for 18 h. After the reaction had cooled, 10 mL of Florisil was added and the solvents were evaporated. The purple solids were loaded onto a Florisil column and eluted with 300 mL of hexane, 450 mL of ether, and 200 mL of ethyl acetate, collecting 50-mL fractions. None of these fractions had NMR spectra displaying any vinyl protons although some did have peaks in the aromatic region. No carbonyl signals were observed in any of the IR spectra of these fractions.

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Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra of compounds lacking elemental analysis data (17 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Spongian Pentacyclic Diterpenes. Stereoselective Synthesis of (−)-Dendrillol-1

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A formal total synthesis of the spongian diterpene (−)-dendrillol-1 (**3**), through a consice approach that could be used for the synthesis of other pentacyclic spongian diterpenes, is reported. The synthesis is based on the intramolecular acetalization of an acid–dialdehyde **4**, which is prepared from (+)-podocarp-8(14)-en-13-one (**5**) via a sequence of transformations involving (a) introduction of a latent dialdehyde unit on **5** by photochemical reaction with acetylene, (b) reductive carboxylation at C-13 of photoadduct **6** to obtain acid **18**, and (c) elaboration of the dialdehyde moiety at C-8 and C-14 of **18** by ozonolysis. Several procedures that have been examined for the reductive carboxylation at C-13 of **6** are described. A simple three-step procedure to effect the conversion of a podocarp-8-en-13-one system into a C-17-functionalized beyerane compound is also reported.

Introduction

A family of diterpenes sharing the hypothetical spongian carbon skeleton (**1**) have been reported from various marine organisms.[1] In recent years, a small group of novel spongian pentacyclic terpenoids have been isolated from various marine sponges[2] and nudibranches.[3] These compounds have a common skeleton represented by **2** with

(1) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 251; **1984**, *1*, 551; **1986**, *3*, 1; **1987**, *4*, 539; **1988**, *5*, 613; **1990**, *7*, 269; **1991**, *8*, 97.

(2) (a) Molinski, T. F.; Faulkner, D. J. *J. Org. Chem.* **1986**, *51*, 1144. (b) Schmitz, F. J.; Chang, J. S.; Hossain, M. B.; van der Helm, D. *J. Org. Chem.* **1985**, *50*, 2862. (c) Karuso, P.; Taylor, W. C. *Aust. J. Chem.* **1986**, *39*, 1629. (d) Karuso, P.; Bergquist, P. R.; Cambie, R. C.; Buckleton, J. S.; Clark, G. R.; Rickard, C. E. F. *Aust. J. Chem.* **1986**, *39*, 1643. (e) Gunasekera, S. P.; Schmitz, F. J. *J. Org. Chem.* **1991**, *56*, 1250.

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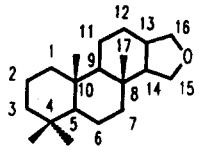
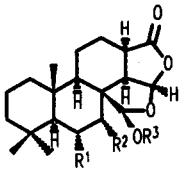
different oxidation patterns at the B ring and have the oxygens in the lactone–tetrahydrofuran moieties (DE rings) conveniently arrayed to serve as a complexing moiety for cations.[2b]



1



2

$R^1=R^2=R^3=H$

$R^1=H$; $R^2=OH,OAc,OCOPr$; $R^3=H$

$R^1=OH,OCOPr$; $R^2=OCOPr,OH$; $R^3=H$

$R^1=OCOPr,OAc$; $R^2=R^3=H$

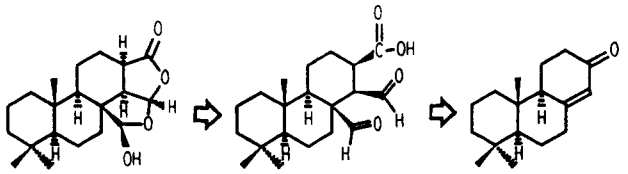
$R^1=OAc,OCOPr$; $R^2=H$; $R^3=Ac$

Despite the biological properties shown by some members of this group and their unusual pentacyclic structure, there have not been synthetic efforts to date with these compounds as the target.[4] Here we report a formal enantioselective total synthesis of the simplest member of the group, dendrillol-1 (3), which has been isolated from the sponge *Dendrilla rosea* as well as from the nudibranch *Ceratosoma brevicaudatum*,[2d,3] through a concise approach that could be viewed as a general one to other spongian pentacyclic diterpenoids.[5]

Results and Discussion

Retrosynthesis of 3 is described in Scheme I. Our approach to compound 3 envisaged construction of rings D–E by an intramolecular acetalization of a suitable acid–dialdehyde (4) (ABC + DE approach). The α,β-unsaturated ketone 5 was considered to be an attractive chiron since it can be easily obtained from natural sources[6] and it possesses a convenient tricyclic skeleton (ABC rings) with the necessary functional groups for building up the acid and 1,4-dialdehyde moieties of 4. This strategy also permits access to other members of this group if additional oxygen functions are incorporated at the 6- and/or 7-position of the starting podocarpenone in the aforementioned retrosynthetic analysis. A critical step in this approach could be the intramolecular cyclization of acid–dialdehyde 4 which ought to take place to give the natural 17β-OH hemiacetal. Molecular mechanics calculations[7] of the two epimeric hemiacetals, namely 3 and its 17α-epimer,[8] indicated that 3 is significantly more stable

Scheme I



3 4 5

(3.4–4.6 kcal/mol) than its epimer, and consequently, it seemed reasonable to consider that the intramolecular acetalization should occur with the desired stereoselectivity.[10]

We envisioned the 1,4-dialdehyde function of key intermediate 4 as arising from ozonolysis of a cyclobutene moiety. Toward this end, enone 5 was transformed into cyclobutenone 6 by stereoselective photoaddition of acetylene (Scheme II). As shown previously,[11] the addition occurred stereoselectively from the more hindered β side of the enone,[12] giving only 6 in about 60% yield.

With 6 in hand, we then examined its 1-carbon homologation to acid 18 and explored methods for making it. Our first choice was to effect a reductive nucleophilic acylation at the C-13 carbonyl group of 6 by means of Wittig, Wittig–Horner, or Peterson reagents.[13] In all cases a low percent conversion of ketone 6 to the homologated product was obtained, probably due to competitive enolization. For instance, treatment of 6 with the lithium derivative of α-methoxymethyldiphenylphosphine oxide at −78 °C and then at rt for 5 h afforded a 6:4 mixture of *E* and *Z* enol ethers 7, separated by chromatography from the recovered 6 (35–40% recovery), which were hydrolyzed with aqueous perchloric acid in ether to provide a mixture of epimeric aldehydes 8 in ca. 40–45% yield from 6. On account of their instability the mixture of aldehydes 8 was not separated but directly oxidized with oxygen and platinum[14] to give a ca. 1:2 mixture of the epimeric C-13 acids 17 and 18 in 75% yield. These two acids were separated by careful flash chromatography, and their stereochemistries were assigned on the basis of the magnitude of the *J* values of the signal due to H-13. In the case of 18 a 1 H signal was observed at δ 2.75 ppm (ddd, *J* 13, 6, and 4 Hz), while in the case of 17, a 1 H signal was observable at δ 2.7 ppm (ddd, *J* 9.8, 2.6, and 2.6 Hz). Since it is assumed that ring C is in a boat conformation,[15] the greater magnitude of the coupling constants observed for 18 are in agreement with the axial (α) orientation of H-13 ($J_{a,a}$, $J_{a,e}$, $J_{a,e}$), while the small values observed for 17 are consistent only with an equatorial (β) orientation of H-13 ($J_{e,a}$, $J_{e,e}$, $J_{e,e}$). Further support for these stereochemical assignments was derived from nuclear Overhauser effect

(3) Ksebati, M. B.; Schmitz, F. J. *J. Org. Chem.* **1987**, *52*, 3766.

(4) For previous syntheses of tetracyclic spongian compounds, see: (a) Inmamura, P. M., González Sierra, M.; Rûveda, E. A. *J. Chem. Soc., Chem. Commun.* **1981**, 734. (b) Nakano, T.; Hernández, M. I. *Tetrahedron Lett.* **1982**, *23*, 1423. (c) Nakano, T.; Hernández, M. I. *J. Chem. Soc., Perkin Trans. 1* **1983**, 135. (d) Nishizawa, M.; Takenaka, H.; Hayashi, Y. *Chem. Lett.* **1983**, 1459. (e) Mischne, M. P.; González Sierra, M.; Rûveda, E. A. *J. Org. Chem.* **1984**, *49*, 2035. (f) Nakano, T.; Hernández, M. I.; Gomez, M.; Medina, J. D. *J. Chem. Res. Synop.* **1989**, 54. (g) Goldsmith, D. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; John Wiley and Sons: New York, 1992; Vol. 8, p 228.

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(6) (a) Do Khac Manh, D.; Fetizon, M.; Kone, M. *Tetrahedron* **1975**, *31*, 1903. (b) Abad, A.; Arnó, M.; Domingo, L. R.; Zaragozá, R. J. *Tetrahedron* **1985**, *41*, 4937.

(7) Calculated by PCMODEL version 4.0 and MACROMODEL version 3.1 (MM2), W. C. Still, Columbia University.

(8) The numbering system used throughout this paper is one proposed by Kazlauskas[9] for the hypothetical compound spongian (1). Systematic *Chemical Abstracts* names are used for title compounds in the Experimental Section.

(9) Kazlauskas, R.; Murphy, P. T.; Wells, R. J.; Noack, K.; Oberhansli, W. E.; Sconholzer, P. *Aust. J. Chem.* **1979**, *32*, 867.

(10) In addition, the intramolecular cyclization of 4 to 3 is predicted[7] to have a free energy difference of ca. −10 kcal/mol, which shows that the ring closure is strongly favored.

(11) Bastard, J.; Do Khac, D.; Fetizon, M.; Prevost, C.; Beloeil, J. C. *Tetrahedron* **1991**, *47*, 229.

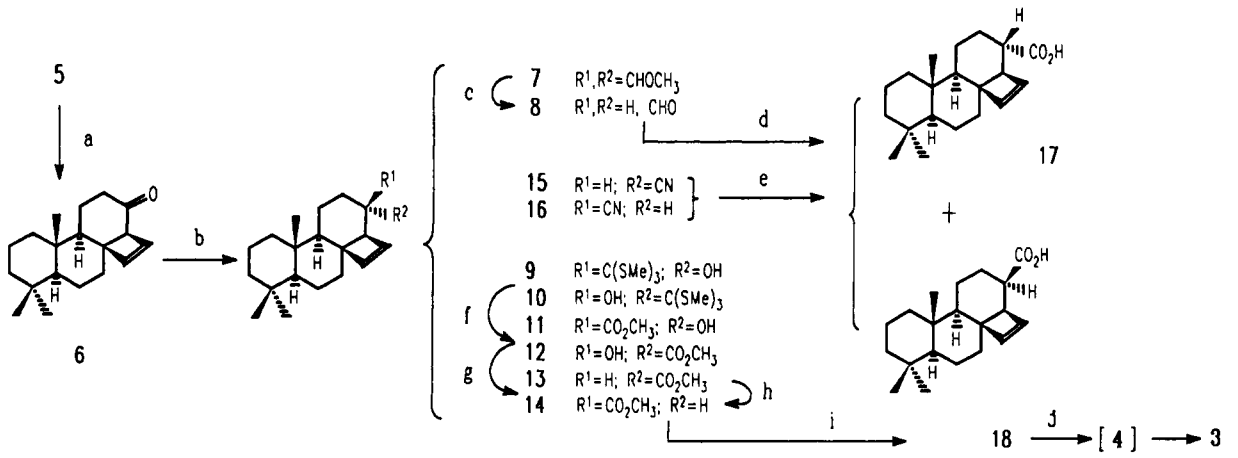
(12) For a theoretical treatment of this stereochemical result, see: Wiesner, K. *Tetrahedron* **1975**, *31*, 1655.

(13) (a) Martin, S. F. *Synthesis* **1979**, 633. (b) Magnus, P.; Burford, C.; Cooke, F.; Roy, G. *Tetrahedron* **1983**, *39*, 867. (c) Cooke, F.; Roy, G.; Magnus, P. *Organometallics* **1982**, *1*, 893.

(14) Fried, J.; Sih, J. C. *Tetrahedron Lett.* **1973**, 3899.

(15) The bicyclo[4.2.0]octane ring system present in compounds 17 and 18, and also in most compounds described in this paper, is relatively rigid, and there is a strong preference for the six-membered ring of this moiety (ring C) to exist in the boat conformation (vide infra). Consequently, in these cases the 12β- and 13α-substituents, which are equatorially oriented in the chair conformation of C ring, became axial.

Scheme II[a]



[a] Reagents: (a) C_2H_2, acetone, $h\nu$, 60%; (b) from **6** to **7**: $Ph_2P(O)CHLiOCH_3$, THF, 78%; from **6** to **9** + **10**: $Cl_2CeC(SCH_3)_3$, THF, 99%; from **6** to **15** + **16**: TosMIC, *t*-BuOK, DME–*t*-BuOH, 67%; (c) $HClO_4$, ether, 90%; (d) Pt, O_2, acetone, 75%; (e) KOH, $HOCH_2CH_2OCH_2CH_3$, 90%; (f) HgCl, HgO, CH_3OH–H_2O and then $NaOCH_3$–CH_3OH, 85%; (g) SmI_2, THF–HMPT, pivalic acid, 90%; (h) $NaOCH_3$–CH_3OH, 100%; (i) KOH, CH_3OH–H_2O, 100%; (j) O_3, CH_2Cl_2 and then $S(CH_3)_2$, 80% from **18**.

(NOEDIF) experiments performed on the corresponding methyl esters (vide infra).

An alternative, and more efficient, method to produce the acid **18** involved initial treatment of ketone **6** with [tris(methylthio)methyl]lithium[16] followed by hydrolysis of the ortho thioester moiety, reductive dehydroxylation, and saponification of the ester group. Treatment of **6** with [tris(methylthio)methyl]lithium gave, after chromatographic purification, alcohols **9** and **10**, in 45% combined yield, along with the unreacted starting material (55%). The also low percent conversion of this reaction could be significantly improved by conversion of the lithium reagent to the corresponding dichlorocerate.[17] Thus, treatment of ketone **6** with $Cl_2CeC(SMe)_3$ at −78 °C afforded adducts **9** and **10** in 64% combined yield, together with 34% of unreacted ketone **6**, which could be recycled. Although both epimeric adducts were easily separated by chromatography, the assignment of the correct stereochemistry at C-13 could only be realized after their conversion to the corresponding α-hydroxy esters. Thus, each of the alcohols was separately treated with mercuric chloride and mercuric oxide in aqueous methanol[18] to afford methyl esters **11** and **12**, respectively, in 62–64% yield. In both cases, a second product, assigned as the corresponding methyl thiol ester of **11** (R^1 = COSMe, R^2 = OH) and **12** (R^1 = OH, R^2 = COSMe), respectively, was isolated in ca. 15% yield. An increase in reaction time resulted in no appreciable change in the proportion of both products. However, when the crude mixture obtained from **9** (or **10**) was treated with sodium methoxide in methanol, prior to chromatographic purification, methyl ester **11** (or **12**) was obtained as sole product (85% yield; see Experimental Section). The isomeric hydroxy esters **11** and **12** were assigned as such on the basis of their spectral data. Of special significance was the NOE effect observed between the methyl of the carbomethoxy moiety (irradiated) and the olefinic proton at C-15, which conclusively proved the stereochemistry of the less polar isomer **11**. In the same way, irradiation of H-15 of the more polar isomer **12** gave a NOE enhancement to 13-OH. This fact, together with the absence of NOE enhancement to H-15 from the methyl of the carbomethoxy group, indicated the α-disposition of the methyl ester function in this isomer. Reductive elimination of α-hydroxy esters **12** and **11** to the corresponding saturated esters **13** and **14**, respectively, was accomplished in high yield by using the electron-transfer system SmI_2–THF–HMPA and pivalic acid as the proton source.[19] Either hydroxy ester **11** or its epimer **12** gave a 2:3 mixture of methyl esters **13** and **14** in ca. 90% yield when subjected to the above conditions. Because of this result, which is a consequence of the initial formation of an ester enolate that is kinetically protonated to give the final products, it was more convenient, for synthetic purposes, to effect the transformation of cyclobutenone **6** into **13** and **14** without separation of epimeric intermediates at C-13. It was subsequently shown that equilibration of the 2:3 mixture of esters **13** and **14** with 2% sodium methoxide in methanol at 80 °C for 1 h changed the original ratio to 1:4. That this mixture represented the position of the thermodynamic equilibrium in this system was shown by treating each ester with sodium methoxide in methanol to give the same ratio.[20] The two isomers could be separated by either careful flash chromatography or preparative HPLC, and thus the minor isomer **13** could be conveniently recycled without loss of material. For instance, ca. 70% overall yield could be achieved for the whole reductive nucleophilic carboxylation process (conversion of **6** into **14**, taking into account unreacted starting material) after repeated treatment of the 13α-ester **13** with sodium methoxide under the above-stated conditions. The spectroscopic data found for **13** and **14** were in total agreement with the assigned stereochemistries at C-13 in both compounds; in addition to the same arguments given above supporting the proposed stereochemistry for structurally related acids **17** and **18**, the NOE enhancement observed in **14** between the methyl of the carbomethoxy moiety (irradiated) and the olefinic proton at C-15 confirmed beyond doubt the stereochemistry assigned to both **14** and **13**.

(16) Damon, R. E.; Schlessinger, R. H. *Tetrahedron Lett.* **1976**, 1561.
(17) To our knowledge the use of this organocerium(III) reagent had not been previously described. For 1,2-addition of other organocerium reagents to easily enolizable ketones, see: Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamija, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392 and references cited therein.
(18) Woessner, W. D. *Chem. Lett.* **1976**, 43.
(19) Kusuda, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1989**, *30*, 2945.
(20) Molecular mechanics calculations[7] of the equilibrium [**13** ⇌ **14**] showed a free energy difference of −0.95 kcal/mol (**14** being the more stable epimer); this means a 79:21 ratio of **14**:**13** at the equilibrium (at 80 °C), which is in good agreement with the experimental result.

Saponification of the ester moiety of 14 was accomplished, in nearly quantitative yield, by treatment of 14 with potassium hydroxide in aqueous methanol at room temperature for 72 h. The acid 18 obtained in this way was identical in all respects to that previously obtained through the reductive nucleophilic acylation route (vide supra).

Although the above results allowed us to effect the required reductive carboxylation of photoadduct 6 in good overall yield, we also examined the possibility of employing the reductive cyanation[21a] of 6 as an indirect way for introducing the required carboxylic group at C-13. Treatment of ketone 6 with tosylmethyl isocyanide (TosMIC) and *t*-BuOK in HMPT (containing some MeOH) under standard conditions[21b,c] afforded a 3:7 mixture of nitriles 15 and 16, respectively, in 57% yield after column chromatography. Better results were obtained by reverse addition of TosMIC to a mixture of ketone and base. Thus, when a solution of TosMIC in DME was added dropwise to a solution of 6 and *t*-BuOK in *t*-BuOH–DME at rt,[21d] a 67% yield of the 3:7 mixture of α- and β-nitriles was obtained after chromatographic purification. In contrast with the above nucleophilic additions to the C-13 carbonyl group (conversion of 6 into 7 or 9 and 10), no starting material was recovered and the α/β ratio of both nitriles reflected the thermodynamic control followed by this process.[21b] The two C-13 epimers could be separated chromatographically at this stage (preparative HPLC) and elaborated further independently. Fortunately, for synthetic purposes, this separation was unnecessary (vide infra). As in the case of the above-mentioned compounds 13/14 and 17/18, the splitting pattern showed by the H-13 signals supported the assigned stereochemistries at C-13 in both epimers.

Alkaline hydrolysis of the 13β-nitrile 16 by treatment with potassium hydroxide in ethylene glycol ethyl ether at 135 °C overnight afforded a 93:7 mixture of acids 18 and its epimer 17, respectively, in high yield. Hydrolysis of the minor 13α-isomer 15 also took place under the same circumstances to give the same mixture with comparable yield. It is obvious that the equilibrium between both nitriles, 15 and 16, is established rapidly under the alkaline conditions used, and faster hydrolysis of the 13β-nitrile 16 then occurs. It is likely that steric hindrance around the axially (α) oriented nitrile group of 15 is the cause of its slow hydrolysis relative to 16.[22] As expected, hydrolysis of the 7:3 mixture directly obtained in the reductive cyanation also afforded the same result. By this means the required acid 18 could be obtained in two steps from photo-adduct 6 in acceptable yield (ca. 54%, 93% purity) without the need of separation by chromatography of epimers at C-13, which was generally difficult. In our experience, this two-step conversion is the most direct and practicable pathway to acid 18 from 6.

With all the stereocenters in ring C established, the construction of D and E rings of the target molecule (3) required oxidative cleavage of the double bond of 18. Toward this end, compound 18, either pure or as directly obtained from the above hydrolysis step, was exposed to ozone in dichloromethane at −78 °C and then treated with dimethyl sulfide for decomposition of the resultant ozonide. However, the initially formed acid–dialdehyde 4 could not be isolated since spontaneous internal lactone–hemiacetal formation took place, furnishing the pentacyclic compound 3 in 80% yield for the whole process, after purification by chromatography. The stereochemistry shown at C-17 in 3 was consistent with the enhancements observed at the 10β-Me and H-6β signals upon irradiation of H-17 at δ 5.50 ppm, in a NOE experiment. As predicted, the intramolecular cyclization of 4 occurred with complete stereoselectivity; none of the 17α-OH epimeric hemiacetal or of the ring-opened dialdehyde form was obtained from this reaction.

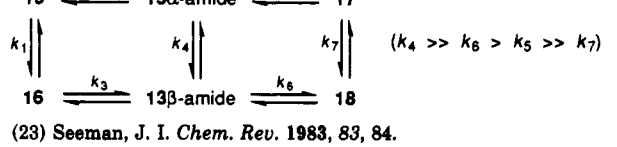
The physical and spectroscopic data of synthetic 3 were in complete agreement with those of the natural product. Since the optical rotation of 3 agreed well with that reported ($[\alpha]_D$ −29.2° (lit.[2d] $[\alpha]_D$ −31.8°)), the synthesis described here establishes the absolute configuration of natural dendrillol-1 as shown in formula 3 (5*S*,8*S*,9*R*,10*S*,13*R*,14*R*,15*R*,17*R*).

During the course of this work, we examined an alternative approach to effect the one-carbon homologation of ketone 6 based on the known two-step sequence involving addition of methylene to the carbonyl group followed by acid-catalyzed rearrangement of the so-formed oxirane moiety to a formyl group.[24] Although the approach was not successful, some results of interest emerged from this attempt.

Treatment of a solution of dimethylsulfonium methylide[25] in THF and HMPT with 6 and then stirring the mixture at room temperature for 40 h afforded a 3:5 mixture of unstable epoxides 19 and 20 in nearly quantitative yield (Scheme III). These could be separated, not without difficulty and with some loss of material, by preparative HPLC using a 98:1:1 mixture of hexane, ethyl acetate, and triethylamine, respectively, as the eluent. The first eluted, less polar epoxide 19, was obtained in 32% yield, and the more polar epoxide 20 was obtained in 49% yield. The assignment of structure to these epoxides followed from analysis of ^1H and ^{13}C NMR shift data. Although the ^{13}C NMR spectra of both isomers are essentially identical, they differ significantly in the shielding of C-16; in the α-epoxide 20 this carbon resonates at 6.15 ppm upfield compared with the β-isomer 19 (50.17 and 56.32 ppm, respectively), probably due to the γ-effect exerted by C-15. The assigned stereochemistry at C-13 in both epoxides also accounts for the difference in the NMR shift of 15 H protons induced by tris(2,2-dimethyl-6,6,7,7,8,8,8-heptafluoro-3,5-octadionato)europium(III) [Eu(fod)$_3$]. When 1 equiv of the shift reagent was added to a mixture of both epoxides, the signals of the olefinic protons moved to lower field, but while the shift reagent causes the same deshielding in the 17 H protons of both

(21) (a) van Lausen, A. M. *Lect. Heterocycl. Chem.* **1980**, *5*, S111. (b) Oldenziel, O. H.; van Lausen, D.; van Lausen, A. M. *J. Org. Chem.* **1977**, *42*, 3114. (c) Oldenziel, O. H.; van Lausen, A. M. *Tetrahedron Lett.* **1973**, 1357. (d) Bull, J. R.; Tuinman, A. *Tetrahedron* **1975**, *31*, 2151.

(22) In reality, since nitriles (15 and 16) are initially hydrolyzed to the corresponding amides (see scheme below), and provided the interconversion of these is significantly faster than their hydrolysis, the product distribution [17]/[18] is solely controlled by the relative hydrolysis rates of the intermediate amides (k_5 and k_6). The possibility that the product distribution represents the position of the thermodynamic equilibrium 17 ⇌ 18 can be rejected since control experiments demonstrated that 17 and 18 were not significantly interconverted under the reaction conditions used in the hydrolysis. We note here that this system is a good illustration of the Curtin–Hammett principle.[23]

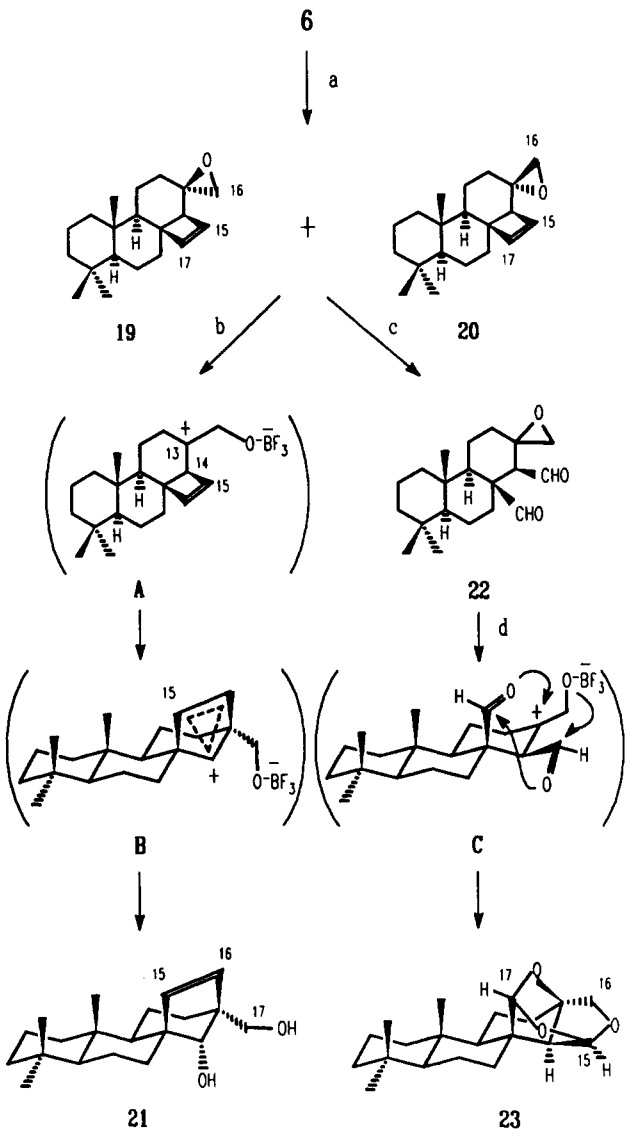


(23) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 84.

(24) (a) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353. (b) Corey, E. J.; Nozoe, S. *J. Am. Chem. Soc.* **1965**, *87*, 5728.

(25) (a) March, J. In *Advanced Organic Chemistry*, 3rd ed.; John Wiley and Sons: New York, 1985; p 274. (b) White, J. D.; Sheean, R. W.; Trammell, G. L. *J. Org. Chem.* **1985**, *50*, 1939.

Scheme III[a]



[a] Reagents: (a) $(CH_3)_2S{=}CH_2$, THF–HMPA; (b) $BF_3{\cdot}Et_2O$, 67% from **19** + **20**; (c) O_3, CH_2Cl_2 then $S(CH_3)_2$, 80% from **19** + **20**; (d) $BF_3{\cdot}Et_2O$, 48% from **19** + **20**.

epoxides, the deshielding in the 15 H protons is much greater for the β-epoxide **19**, indicating a shorter C-13 oxygen to 15 H proton distance for **19** than for **20**.

Several attempts were made to effect acid-catalyzed rearrangement of both epoxides to aldehyde **8**. All attempts led to mixtures in which there was no indication of the desired aldehyde **8** by ^1H NMR analysis of the crude reaction mixture. The sole identifiable product was the beyerane compound **21**, the structure of which was determined from its spectroscopic data. Particularly significant in its ^1H NMR spectrum were a one-proton singlet at δ 3.36 ppm and a two-proton singlet at δ 3.55 ppm which indicated the presence of oxygenated functions on methine and methylene carbon atoms. Also, the ^{13}C NMR spectrum provided support for the assigned structure; in particular, the shielding of C-9 (δ 44.90 ppm) produced by the γ-effect of the 14α-hydroxyl group confirmed the stereochemistry at C-14.

It is notable that when the rearrangement was performed in the presence of water ($BF_3{\cdot}Et_2O$ in wet dichloromethane, rt, 30–60 min) the diol **21** was obtained in good yield (up to 70%). Comparable results were eventually obtained when either epoxide **19** or **20** was subjected to similar reactions conditions. Taking into account these results, it seems reasonable to postulate (Scheme III) that the rearrangement of **19** and **20** occurs by acid-catalyzed opening of the oxirane ring to give a carbocation (**A**) which may evolve toward **21** by migration of bond 15–14 to 15–13 together with attack on C-14 by a hydroxylic species, either by a concerted or a nonconcerted mechanism. Although a concerted mechanism has been established for the last-mentioned step in the rearrangement of a related bicyclo[4.2.0]octane system,[11] the possibility that rearrangement of carbocation **A** may occur in a nonconcerted manner, by a two-step process, via a nonclassical or bridged carbocation (**B**) cannot be discarded. The presumed stability of a carbocation such as this may be inferred from the chemical ionization spectra of **21**.[26] The great intensity of the $[MH - H_2O]^+$ peak at 287 (base peak, relative intensity 100%) may be related with the formation of such an ion, which could be specially stabilized by the neighbor C(15)–C(16)[27] double bond.

The aforementioned rearrangement is of interest since it permits the conversion of a podocarpane system into a C-17-funtionalized[27] beyerane compound by a simple three-step procedure, in synthetically useful yield. To our knowledge this conversion has not been described previously.[28]

In an attempt to avoid the above skeletal rearrangement, we exchanged the order of projected steps to transform the epoxides into the target spongian compound. Accordingly, the crude mixture of epoxides **19** and **20** was exposed to ozone in dichloromethane at −78 °C and then treated with dimethyl sulfide. Although the product we were seeking (**22**) was formed in the reaction, the sole identifiable product was compound **23**, isolated in 10–15% yield following column chromatography. It seems that silica gel-catalyzed opening of the oxirane moiety gives a carbocation (**C**), in a manner similar to that described for **19**–**20**, which evolves toward compound **23** via a concerted process (Scheme III). All spectral data were consistent with the structure assigned to **23**. In particular, the ^1H and ^{13}C NMR spectra showed signals corresponding to the two acetal moieties [H-15/C-15 at δ 5.59 (d, J = 2.9 Hz)/102.88 ppm; H-17/C-17 at δ 5.26 (s)/100.96 ppm] and the methylene group of the tetrahydrofuran ring [two H-16 at δ 3.95 and 3.69 (an AB system, J = 9.2 Hz); C-16 at δ 73.76 ppm]; also the quaternary carbon atom (C-13) adjacent to an oxygen atom was evidenced by the ^{13}C NMR absorption at δ 84.78 ppm. As expected, irradiation of the H-17 signal enhanced the signal at 0.93 assigned to the methyl group at C-10.

Although compound **23** has the spongian skeleton, and the yield of this reaction could be considerably improved (ca. 50% overall yield of **23** from **6**) by treatment of the crude ozonation mixture with $BF_3{\cdot}Et_2O$ in dry dichloromethane prior to the chromatographic purification (see Experimental Section), its conversion to target **3** was not investigated further.

During the course of this work, the ^{13}C NMR spectra of all synthesized compounds were recorded. Unambiguous assignment of the ^{13}C resonance signals for each compound

(26) Bastard, J.; Do Khac Manh, D.; Fetizon, M.; Tabet, J. C.; Fraisse, D. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1591.

(27) Usual beyerane numbering is used for carbocation **B** and compound **21**; see: Nakanishi, K.; Goto, T. Itô, S.; Natori, S.; Nozoe, S. *Natural Products Chemistry*; Kodansha Scientific Books; Tokio, 1974; Vol. 1, p 187.

(28) For rearrangements of other related bicyclo[4.2.0]octane systems, see: (a) Do Khac Manh, D.; Fetizon, M.; Flament, J. P. *Tetrahedron* **1975**, *31*, 1897. (b) Do Khac Manh, D.; Fetizon, M.; Lazare, S. *J. Chem. Res., Synop.* **1978**, 22; *J. Chem. Res., Miniprint* 167. (c) Do Khac Manh, D.; Fetizon, M.; Lazare, S. *Tetrahedron* **1978**, *34*, 1207.

was made on the basis of a combination of homonuclear COSY, DEPT, and inverse-detected heteronuclear multiple quantum coherence (HMQC) experiments. The results are presented in Table I. In addition to the useful information obtained by analysis of these data concerning structural and stereochemical assignments, some of which have already been described, the ^{13}C NMR data for the compounds included here are sufficiently characteristic to make them useful for conformational analysis. In particular, the signals due to C-9 and C-12 are shifted upfield appreciably in those compounds which possess a boat ring-C conformation, due to the shielding effect (γ-effect) exerted by C-13 and C-15 on C-9 and C-12, respectively. On this basis, a boat ring-C conformation is predicted for all compounds possessing the bicyclo[4.2.0]octane ring system except compounds **6** and **10**, for which a chair ring C is predicted. In the case of epoxides **19** and **20** the shielding effect on C-9 is slightly lower, reflecting some deformation of the boat ring-C conformation. These ^{13}C NMR based conformational predictions coincide with that obtained from molecular mechanics energy minimizations.[7]

Experimental Section

^1H NMR spectra were recorded in $CDCl_3$ at 400 MHz unless specified otherwise. HPLC was performed on a Waters Associates Prep LC System equipped with a RCM 25 × 10 compression module and two PrePak 25 × 10 cartridges (Nova Silica HR 60 Å, 6 μm). Other general experimental information and spectroscopic instrumentation used have been described in ref 29.

Podocarp-8,14-en-13-one (**5**) was obtained from commercial colophony following the procedure previously described by us.[6b]

[3a*S*-(3aα,5a*S*,7aα,11aβ,11bα)]-(+)-1,6,7,7a,8,9,10,11,11a,-11b-Decahydro-8,8,11a-trimethyl-2*H*-cyclobuta[*j*]-phenanthren-3(3a*H*)-one (6). A solution of podocarpenone **5** (250 mg, 1.02 mmol) in dry acetone (200 mL) was placed in a photoreactor and exhaustively purged with nitrogen. The mixture was cooled to −20 °C, and prepurified acetylene[30] was bubbled through the solution until its saturation (1 h). The mixture was irradiated at −15 °C through a Pyrex filter with a 125-W OSRAM high-pressure mercury lamp, while acetylene was slowly bubbled through the reaction mixture. Analysis (TLC) of the reaction mixture showed only a small amount of starting material after 2 h. Irradiation of the reaction (whose temperature rose to 0 °C during this time) was continued for an additional $^1/_4$ h. The slightly yellow mixture was concentrated to dryness to give an oil which was taken up in hexane. Usual workup and chromatography on silica gel, using hexane–ether (8:2) as eluent, afforded photoadduct **6** (165 mg, 60%), as a white solid: mp 75–77 °C (from ether) (lit.[11] mp 76–77 °C); $[\alpha]^{26}_D$ +226° (*c* 1.6, $CHCl_3$); IR (KBr) 3060, 3040, 1700, 790 cm^{-1}; ^1H NMR δ 6.53 (d, *J* = 2.7 Hz, 1 H, H-17), 5.99 (dd, *J* = 2.7, 1.2 Hz, 1 H, H-15), 2.88 (br s, 1 H, H-14), 2.61 (dddd, *J* = 19.0, 5.9, 1.7, 0.7 Hz, 1 H, H-12β), 2.15 (dddd, *J* = 19.0, 11.0, 8.1, 2.0 Hz, 1 H, H-12α), 0.95 (dd, *J* = 11.7, 2.0 Hz, 1 H, H-5), 0.86 (s, 3 H, 4α-Me), 0.84 (s, 3 H, 10β-Me), 0.82 (s, 3 H, 4β-Me); ^{13}C NMR: see Table I; MS *m/e* (relative intensity) 272 (M^+, 5.4), 257 (4.7), 254 (4.5), 244 (14.5), 239 (7.0), 229 (6.5), 136 (53), 91 (100), 69 (36), 55 (53), 41 (63).

Further elution with the same eluent gave unreacted starting enone **5** (10 mg, 5%).

[3*S*-(3α,3aα,5a*R*,7aα,11aβ,11bα)]- and [3*R*-(3β,3aα,5a*R*,7aα,11aβ,11bα)]-(+)-1,3,3a,6,7,7a,8,9,10,11,11a,-11b-Dodecahydro-8,8,11a-trimethyl-2*H*-cyclobuta[*j*]-phenanthrene-3-carboxylic Acids (17) and (18). To a stirred slurry of methoxymethyldiphenylphosphine oxide (294 mg, 1.19 mmol) in THF (3 mL) at −30 °C was added, dropwise via syringe, 1.68 mL of a 0.6 M solution of lithium diisopropylamide (LDA, 1.01 mmol) in THF. The mixture was stirred at the same temperature for 30 min and then cooled to −78 °C, and the ketone

Table I. ^{13}C Chemical Shifts (δ) in ppm from TMS of Compounds 3, 6, 9–21, and 23[a]

	3[b]	6	9	10	11	12	13	14	15	16	17	18	19	20	21	23
C-1	39.08	38.89	38.57	38.87	38.47	38.67	38.49	38.66	38.24	38.52	38.85*	38.64	38.94	38.64	39.05	38.87
C-2	18.76	18.46	18.53	18.62	18.58	18.52	18.57	18.56	18.48	18.46	18.58	18.56	18.58	18.63	18.60	18.62
C-3	41.94	41.97	42.11	42.27	42.08	42.04	42.03	42.07	41.87	41.93	42.08	42.06	42.11	42.07	42.00	41.90
C-4	33.30	33.30	33.21	33.41	33.27	33.27	33.29	33.28	33.26	33.25	33.30	33.27	33.32	33.31	33.17	33.29
C-5	56.75	56.00	56.25	56.45	56.12	56.36	56.19	56.34	55.85	56.20	56.17	56.32	56.25	55.87	55.33	56.51
C-6	20.03	20.53	20.82	20.59	20.74	20.52	20.64	20.71	20.57	20.52	20.64**	20.70	20.69	20.69	20.90	20.12
C-7	41.46	38.49	39.52	40.22	39.27	38.67	38.93	38.66	38.53	38.38	38.49*	38.64	38.62	38.44	33.13	30.92
C-8	46.90	53.74	53.49	53.52	51.72	52.23	50.97	51.00	50.67	50.56	51.03	51.00	53.11	52.05	49.82*	55.49
C-9	55.51	54.72	49.54	57.44	49.70	50.53	51.13	51.17	50.01	50.61	51.20	51.17	52.77	52.13	44.90	51.34
C-10	38.10	38.25	38.24	38.56	38.31	38.37	38.41	38.30	38.53	38.28	38.40	38.31	38.37	38.23	36.94	38.20
C-11	16.52	18.24	16.66	16.37	15.33	16.96	15.89	16.14	15.20	15.83	15.87	16.08	17.48	16.32	19.66**	19.70
C-12	23.85	39.98	28.72	40.22	28.18	30.33	20.20	20.31	20.64	21.59	20.09**	20.13	26.85	27.83	18.20**	26.65
C-13	37.79	213.08	85.34	82.35	77.46	75.65	39.86	39.57	25.18	25.29	39.66	39.45	58.70	58.58	49.71*	84.78
C-14	49.60	63.14	58.59	55.91	57.43	55.54	50.64	51.56	50.72	50.80	50.37	51.34	56.46	57.12	81.50	58.05
C-15	104.40	132.40	136.13	135.75	134.74	134.70	136.40	136.02	134.17	134.10	136.26	135.83	135.44	133.54	136.85	102.88
C-16	177.40		81.22	81.48	177.39	176.60	177.08	176.28	123.93	122.30	182.50	181.73	56.32	50.17	129.76	73.76
C-17	103.91	147.14	144.19	142.57	145.47	145.79	144.75	145.06	146.73	146.51	144.91	145.22	145.34	145.84	67.40	100.96
4α-Me	33.33	33.42	33.40	33.28	33.45	33.40	33.41	33.57	33.36	33.51	33.46	33.57	33.58	33.56	33.56	33.29
4β-Me	21.34	21.56	21.54	21.30	21.68	21.64	21.72	21.75	21.69	21.71	21.73	21.75	21.74	21.77	21.92	21.55
10β-Me	15.96	15.12	14.87	16.22	14.75	14.77	14.80	14.77	14.78	14.72	14.84	14.77	14.70	14.77	15.71	14.76
SMe			16.30	16.09												
CO_2Me					52.66	52.46	51.61	51.41								

[a] At 75.4 MHz in $CDCl_3$. The signals with the same superscript may be interchanged within the same column. [b] This spectral assignment differs from the published one[3] in that the signals from the pairs C-3/C-7 and C-5/C-9 have been reversed.

(29) Abad, A.; Agulló, C.; Arnó, M.; Cuñat, A. C.; Zaragozá, R. J. *J. Org. Chem.* **1992**, *57*, 50.

(30) Purified by successive passage through two dry ice traps and a drying tube containing 3-Å molecular sieves.

6 (250 mg, 0.92 mmol) in THF (1.5 mL) was added dropwise. After 18 h at −78 °C the mixture was allowed to warm slowly to rt and then stirred for 3 h. The reaction mixture was quenched by the addition of saturated NH_4Cl solution, and the product was isolated by extraction with hexane. The residue obtained after usual workup was purified by chromatography on silica gel using hexane–ether (85:15) as eluent to give a mixture of enol ethers 7 (134 mg, 48%, 78% based on consumed 6) and unreacted 6 (94 mg). ^1H NMR (300 MHz) analysis indicated a 6:4 mixture of *E*- and *Z*-isomer of 7; main signals of each isomer, deduced from the spectrum (300 MHz) of the mixture of both, are as follows: ***E*-isomer**, δ 6.25 (d, J = 3 Hz, 1 H, H-17), 6.06 (d, J = 3 Hz, 1 H, H-15), 5.73 (dd, J = 1.8, 2.2 Hz, 1 H, H-16) 3.53 (s, 3 H, OMe), 2.55 (br s, 1 H, H-14); ***Z*-isomer**, 6.3 (d, J = 3 Hz, 1 H, H-17), 6.09 (d, J = 3 Hz, 1 H, H-15), 5.78 (d, J = 1.6, 1 H, H-16), 3.49 (s, 3 H, OMe), 3.26 (br s, 1 H, H-14).

A solution of the above mixture (134 mg, 0.45 mmol) in diethyl ether (4 mL), previously saturated with 60% $HClO_4$, was stirred at 0 °C for 15 min. After another 20 min the mixture was diluted with ether, washed with 5% $NaHCO_3$ solution, and worked up as usual to give a light yellow oil which was filtered through a short pad of silica gel with hexane–ether (9:1) to provide a 6:4 mixture of 13α- and 13β-aldehydes 8 (115 mg, 90%). This was used directly without further purification: ^1H NMR (200 MHz) δ 9.81 (s, 0.6 H, 13β-CHO), 9.66 (d, J = 1.6 Hz, 0.4 H, 13α-CHO).

To a suspension of platinum, generated by hydrogenation of PtO_2 (37 mg) in water (4 mL) at 2 atm for 2 h, was added a solution of the mixture of aldehydes 8 (36 mg, 0.13 mmol) in acetone (4 mL) at 40 °C, and oxygen was bubbled through the suspension for 6 h. The solution was filtered and concentrated in vacuo. The residue was chromatographed on silica gel, eluting with hexane–ethyl acetate (85:15), to afford the epimeric acids 17 and 18 (28 mg, 75%).

17 (13α-epimer; less polar isomer): 10 mg; amorphous solid; $[\alpha]^{20}_D$ +16° (*c* 1.8, $CHCl_3$); IR (KBr) 3300–2600, 3010, 1680, 1240, 785, 715 cm^{-1}; ^1H NMR (300 MHz) δ 6.35 (d, J = 2.9 Hz, 1 H, H-17), 6.05 (dd, J = 2.9, 0.9 Hz, 1 H, H-15), 2.85 (br s, 1 H, H-14), 2.7 (ddd, J = 9.8, 2.6, 2.6 Hz, 1 H, H-13), 1.14 (ddd, J = 13.0, 13.0, 4.2 Hz, 1 H, H-1α), 0.90 (dd, J = 12.1, 2.2 Hz, 1 H, H-5), 0.85 (s, 3 H, 10β-Me), 0.81 (s, 6 H, 4α-Me and 4β-Me); ^{13}C NMR: see Table I; MS (CI) m/e (relative intensity) 304 (M^+ + 2, 22), 303 (M^+ + 1, 100), 302 (M^+, 31), 301 (74), 287 (38), 286 (14), 285 (55), 257 (32), 179 (38), 137 (23).

18 (13β-epimer; more polar isomer): 18 mg; mp 197–200 °C (from hexane at −20 °C); $[\alpha]^{19}_D$ +63° (*c* 2.09, $CHCl_3$); IR (KBr) 3500–2300, 1695, 800, 730 cm^{-1}; ^1H NMR (200 MHz) δ 6.33 (d, J = 3 Hz, 1 H, H-17), 6.10 (d, J = 3 Hz, 1 H, H-15), 2.75 (ddd, J = 13, 6, 4 Hz, 1 H, H-13), 2.58 (d, J = 4 Hz, 1 H, H-14), 0.84 (s, 3 H, 4α-Me), 0.80 (s, 6 H, 4β-Me and 10β-Me); ^{13}C NMR: see Table I; MS (CI) m/e (relative intensity) 304 (M^+ + 2, 22), 303 (M^+ + 1, 100), 302 (M^+, 18), 301 (46), 288 (5), 287 (23), 286 (6), 285 (22), 257 (12), 179 (6). Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 9.99. Found: C, 78.98; H, 10.03.

[3*S*-(3α,3aα,5a*S*,7aα,11aβ,11bα)]- and [3*R*-(3β,3aα,5a*S*,7aα,11aβ,11bα)]-(+)-1,3,3a,6,7,7a,8,9,10,11,11a,-11b-Dodecahydro-8,8,11a-trimethyl-3-[tris(methylthio)-methyl]-2*H*-cyclobuta[*j*]phenanthren-3-ols (9) and (10). *n*-BuLi (518 μL of a 1.6 M solution in hexane, 0.82 mmol) was added to a solution of tris(methylthio)methane (145 mg, 124 μL, 0.94 mmol) in anhyd THF (3 mL) at −78 °C. The solution was stirred at the same temperature during 30 min, at which time it was cooled to −90 °C and quickly transferred, via cannula, into a suspension of powdered, anhyd[31] $CeCl_3$ (272 mg, 1.1 mmol) in dry THF (3 mL) at −78 °C. After vigorous stirring for 45 min at −78 °C, a solution of ketone 6 (100 mg, 0.36 mmol) in dry THF (1 mL) was added and the stirring was continued for 12 h at −78 °C. The reaction was treated with saturated aqueous NH_4Cl (4 mL), poured into water, extracted with hexane, and worked up as usual. ^1H NMR analysis of the residue obtained showed it to be a mixture of 65% of adducts 9–10 and 35% of starting ketone 6. Careful chromatography of this mixture, using hexane–ether (9:1) as eluent, separated the three compounds. The first eluted compound (27 mg, 17%) was identified as alcohol 9, an oil: $[\alpha]^{20}_D$ +38° (*c* 1.17, $CHCl_3$); IR (film) 3700–3300, 3070, 3050, 965, 810 cm^{-1}; ^1H NMR δ 6.31 (d, J = 3.0 Hz, 1 H, H-17), 6.29 (dd, J = 3.0, 0.7 Hz, 1 H, H-15), 2.66 (d, J = 0.7 Hz, 1 H, H-14), 2.26 (s, 9 H, 3×SMe), 1.90 (dd, J = 11.9, 5.2 Hz, 1 H, H-9), 1.13 (ddd, J = 13.5, 13.5, 4.8 Hz, 1 H, H-3α), 0.98 (dd, J = 12.5, 2.7 Hz, 1 H, H-5), 0.83 (s, 3 H, 4α-Me), 0.79 (s, 3 H, 4β-Me), 0.77 (s, 3 H, 10β-Me); ^{13}C NMR see Table I; MS m/e (relative intensity) 411 (M^+ − Me, 0.1), 379 (1), 331 (0.5), 255 (4), 153 (100), 91 (58), 55 (43), 41 (58). Anal. Calcd for $C_{23}H_{38}OS_3$: C, 64.73; H, 8.97. Found: C, 65.01; H, 9.08.

The second compound eluted (74 mg, 48%) was identified as the C-13 epimeric alcohol 10, a white solid: mp 117–120 °C (from hexane–ether); $[\alpha]^{20}_D$ +60° (*c* 2.0, $CHCl_3$); IR (film) 3700–3300, 3070, 3050, 1100, 800 cm^{-1}; ^1H NMR δ 6.25 (d, J = 2.9 Hz, 1 H, H-17), 6.17 (dd, J = 2.9, 1.0 Hz, 1 H, H-15), 2.99 (d, J = 1.0 Hz, 1 H, H-14), 2.28 (s, 9 H, 3×SMe), 1.15 (ddd, J = 13.2, 13.2, 4.4 Hz, 1 H, H-3α), 1.05 (dd, J = 10.0, 3.5 Hz, 1 H, H-9), 0.95 (dd, J = 12.4, 2.3 Hz, 1 H, H-5), 0.84 (s, 3 H, 4α-Me), 0.79 (s, 3 H, 4β-Me), 0.76 (s, 3 H, 10β-Me); ^{13}C NMR see Table I; MS m/e (relative intensity) 379 (M^+ − SMe, 3), 331 (1.6), 303 (1.7), 283 (1.8), 255 (6), 153 (72), 91 (100), 69 (39), 41 (27). Anal. Calcd for $C_{23}H_{38}OS_3$: C, 64.73; H, 8.97. Found: C, 64.95; H, 9.12.

The latter fractions afforded unreacted ketone 6 (36 mg, giving a 99% yield of 9 and 10 based on recovered starting material).

[3*S*-(3β,3aα,5a*S*,7aα,11aβ,11bα)]- and [3*R*-(3α,3aα,5a*S*,7aα,11aβ,11bα)]-(+)-1,3,3a,6,7,7a,8,9,10,11,11a,-11b-Dodecahydro-3-hydroxy-8,8,11a-trimethyl-2*H*-cyclobuta[*j*]phenanthrene-3-carboxylic Acid Methyl Esters (11) and (12). A mixture of 10 (127 mg, 0.30 mmol), $HgCl_2$ (329 mg, 1.21 mmol), and HgO (108 mg, 0.5 mmol) in 12:1 MeOH–water (7.3 mL) and ether (1 mL) was stirred at rt for 2 h. The mixture was filtered and the residue washed with ether. The combined filtrates were washed with saturated aqueous NH_4OAc and saturated aqueous NH_4Cl, dried, and evaporated. The residue was dissolved in MeOH (2.5 mL) and treated with a solution of NaOMe in MeOH (1 mL of a solution prepared from 100 mg of Na in 2.5 mL of MeOH) at 0 °C. After being stirred at rt for 30 min, the mixture was poured into water and extracted with ether. The combined extracts were washed with dilute HCl and 5% aqueous $NaHCO_3$ solution. Usual workup followed by column chromatography of the residue on silica gel, using hexane–ether (8:2) as eluent, afforded hydroxy ester 12 (83 mg, 84%) as a solid: mp 118–119 °C (from hexane at 0 °C); $[\alpha]^{20}_D$ +45° (*c* 2.0, $CHCl_3$); IR (KBr) 3500, 3600–3100, 3050, 1715, 1250 cm^{-1}; ^1H NMR δ 6.44 (d, J = 2.9 Hz, 1 H, H-17), 6.18 (dd, J = 2.9, 0.9 Hz, 1 H, H-15), 3.80 (s, 3 H, CO_2Me), 2.71 (dd, J = 1.7, 0.9 Hz, 1 H, H-14), 2.03 (dddd, J = 14.1, 10.3, 6.0, 1.7 Hz, 1 H, H-12α), 1.87 (ddd, J = 14.1, 9.8, 5.6 Hz, 1 H, H-12β), 1.71 (m, 2 H, H-7), 1.29 (dd, J = 12.2, 5.6 Hz, 1 H, H-9), 1.14 (ddd, J = 13.7, 13.7, 4.7 Hz, 1 H, H-3α), 0.85 (s, 3 H, 4α-Me), 0.81 (s, 6 H, 4β-Me and 10β-Me); ^{13}C NMR see Table I; MS m/e (relative intensity) 317 (M^+ − Me, 2), 314 (1), 299 (3), 271 (4), 255 (4), 239 (5), 91 (82), 69 (100), 59 (51), 55 (92), 43 (82), 41 (76). Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.64; H, 9.76.

When the chromatographic purification was effected prior to the NaOMe/MeOH treatment, hydroxy ester 12 was obtained in 63% yield, and a slightly more polar product, identified as the corresponding hydroxy thiolester (12: R^1 = OH; R^2 = COSMe), in 15% yield was also obtained. The latter product was an oil: IR (film) 3600–3200, 3060, 1730, 1690 cm^{-1}; ^1H NMR (200 MHz) δ 6.42 (d, J = 3 Hz, 1 H, H-17), 6.15 (d, J = 3 Hz, 1 H, H-15), 2.65 (br s, 1 H, H-14), 2.27 (s, 3 H, SMe), 0.84 (s, 3 H, 4α-Me) 0.79 (s 6 H, 4β-Me and 10β-Me).

In similar fashion, epimer 9 was transformed into 11 (85% overall yield): an oil; $[\alpha]^{20}_D$ +48° (*c* 2.0, $CHCl_3$); IR (film) 3700–3200, 3050, 1730, 1250 cm^{-1}; ^1H NMR δ 6.42 (d, J = 2.8 Hz, 1 H, H-17), 6.01 (dd, J = 2.8, 0.9 Hz, 1 H, H-15), 3.78 (s, 3 H, CO_2Me), 2.31 (dd, J = 2.2, 0.9 Hz, 1 H, H-14), 2.21 (m, 1 H, H-12), 1.76 (ddd, J = 12.5, 12.5, 4.0 Hz, 1 H, H-7α), 1.71 (ddd, J = 12.5, 4.9, 3.3 Hz, 1 H, H-7β), 1.16 (ddd, J = 14.0, 14.0, 4.7 Hz, 1 H, H-3α), 1.03 (dd, J = 12.6, 2.4 Hz, 1 H, H-5), 0.97 (ddd, J = 13.7, 13.7, 4.4 Hz, 1 H, H-1α), 0.85 (s, 3 H, 4α-Me), 0.83 (s, 3 H, 10β-Me) and 0.82 (s, 3 H, 4β-Me); ^{13}C NMR see Table I; MS m/e (relative intensity) 332 (M^+, 0.5), 317 (3), 314 (8), 299 (14), 271 (9), 255 (17), 83 (84), 69 (66), 41 (100). Anal. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.56; H, 9.63.

(31) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Mita, T.; Hatanaka, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904.

The corresponding thiolester (12: R^1 = COSMe; R^2 = OH), also obtained in 14% yield if NaOMe/MeOH treatment was omitted, was an oil: IR (film) 3600–3200, 3060, 1680 cm^{-1}; ^1H NMR (200 MHz) δ 6.38 (d, J = 3 Hz, 1 H, H-17), 6.05 (d, J = 3 Hz, 1 H, H-15), 2.26 (br s, 1 H, H-14), 2.23 (s, 3 H, SMe), 0.84, 0.81, and 0.80 (each s, 3 H each, 3×Me).

[3*S*-(3α,3aα,5a*R*,7aα,11aβ,11bα)]- and [3*R*-(3β,3aα,5a*R*,7aα,11aβ,11bα)]-(+)-1,3,3a,6,7,7a,8,9,10,11,11a,-11b-Dodecahydro-8,8,11a-trimethyl-2*H*-cyclobuta[*j*]-phenanthrene-3-carboxylic Acid Methyl Esters (13) and (14). A solution of hydroxy ester 12 (60 mg, 0.18 mmol) in anhyd THF (0.5 mL) was treated with a solution of SmI_2 in THF (7.3 mL of a 0.1 M solution of SmI_2 in THF, 0.73 mmol)[32] at rt. Anhydrous HMPT (275 μL, 0.24 mmol) was then added, and the resulting purple solution was stirred at rt while a solution of pivalic acid (46.9 mg, 0.40 mmol) in THF (1 mL) was added dropwise over 2 h. After the solution was stirred for 15 min at rt, water was added, and the mixture was extracted with CH_2Cl_2. The combined organic extracts were washed with 5% $NaHCO_3$ solution followed by workup as usual. Short column chromatography of the residue left after evaporation of the solvent furnished an oil, whose ^1H NMR showed it to be a 2:3 mixture of C-13 epimeric methyl esters 13 and 14 (52 mg, 90%). Although both compounds could be separated at this step, it was more convenient for synthetic purposes to effect the separation of 13α- and 13β-epimers after their base-mediated equilibration (see below).

In the same manner as that described for 12, 11 afforded also a 2:3 mixture of 13 and 14. This could be carried out also on a mixture of 11 and 12.

Sodium Methoxide Equilibration of 13 and 14. The 2:3 mixture of esters 13 and 14 obtained above (60 mg, 0.19 mmol) was treated with 2% NaOMe in MeOH (2 mL) at 80 °C in a sealed tube for 30–40 min. The mixture was poured into cold 5% HCl and extracted with CH_2Cl_2. Usual workup gave a crude mixture of epimeric methyl esters 13 and 14 (59.5 mg, ca. 100%) in a ratio of 1:4 (^1H NMR analysis). The two isomers were separated by careful chromatography with hexane–ether (98:2) as eluent.

13 (11.4 mg, 19%): a white solid, mp 75–76 °C (from MeOH–H_2O at −20 °C); $[\alpha]^{19}_D$ +18° (*c* 2.0, $CHCl_3$); IR (film) 3040, 1735, 1200 cm^{-1}; ^1H NMR (200 MHz) δ 6.31 (d, J = 3.0 Hz, 1 H, H-17), 6.0 (d, J = 3.0 Hz, 1 H, H-15), 3.69 (s, 3 H, CO_2Me), 2.79 (br s, 1 H, H-14), 2.62 (ddd, J = 6.9, 3.0, 2.5 Hz, 1 H, H-13), 0.83 and 0.79 (two s, 3 H and 6 H, 4α-Me, 4β-Me and 10β-Me); ^{13}C NMR see Table I; MS *m/e* (relative intensity) 316 (M^+, 4), 302 (3), 301 (15), 269 (6), 241 (9), 117 (60), 91 (100), 55 (54), 41 (51). Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.41; H, 10.28.

14 (47.1 mg, 79%): a solid, mp 88–89 °C (from hexane at −20 °C); $[\alpha]^{20}_D$ +69° (*c* 5.94, $CHCl_3$); IR (KBr) 3040, 1730, 1160 cm^{-1}; ^1H NMR δ 6.36 (d, J = 2.9 Hz, 1 H, H-17), 6.11 (dd, J = 2.9, 0.9 Hz, 1 H, H-15), 3.66 (s, 3 H, CO_2Me), 2.74 (ddd, J = 12.9, 5.7, 3.7 Hz, 1 H, H-13), 2.56 (ddd, J = 3.7, 0.9, 0.9 Hz, 1 H, H-14), 1.86 (dddd, J = 13.4, 13.4, 10.9, 5.1 Hz, 1 H, H-12α), 1.28 (dd, J = 12.4, 5.5 Hz, 1 H, H-9), 1.13 (ddd, J = 13.8, 13.8, 4.2 Hz, 1 H, H-3α), 0.88 (dd, J = 12.5, 2.2 Hz, 1 H, H-5), 0.84 (s, 3 H, 4α-Me), 0.79 (s, 6 H, 4β-Me and 10β-Me); ^{13}C NMR see Table I; MS *m/e* (relative intensity) 316 (M^+, 2) 301 (3), 257 (2), 241 (4), 117 (37), 91 (92), 59 (100). Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.81; H, 10.42.

Hydrolysis of Methyl Ester 14 to Acid 18. To a solution of methyl ester 14 (29 mg, 0.09 mmol) in MeOH (2.5 mL) was added a solution of KOH in MeOH–water (2.5 mL of a 4% solution of KOH in 6:1 MeOH–water, ca. 20 equiv), and the mixture was stirred for 72 h at rt. Water was added, the mixture was acidified with 2 N HCl and extracted with ether. The combined organic layers were worked up as usual to give nearly pure acid 18 as a white solid (27.7 mg, ca. 100%). This material, which was identical with acid 18 obtained by oxidation of aldehyde 8 (see above), could be used without further purification for the next step.

[3*S*-(3α,3aα,5a*R*,7aα,11aβ,11bα)]- and [3*R*-(3β,3aα,5a*R*,7aα,11aβ,11bα)]-1,3,3a,6,7,7a,8,9,10,11,11a,11b-Dodecahydro-8,8,11a-trimethyl-2*H*-cyclobuta[*j*]-phenanthrene-3-carbonitriles (15) and (16). Method a. *t*-BuOK (215 mg, 2.64 mmol) was added to a solution of TosMIC (296 mg, 2.64 mmol) in anhyd HMPT (1.3 mL) at −30 °C. The brown mixture was stirred at 0 °C for 20 min, and then a mixture of ketone 6 (100 mg, 0.37 mmol) and dry MeOH (24 μL) in HMPT (0.6 mL) was added. After stirring for 20 h at 40 °C, the dark mixture was diluted with water, acidified with 2 N HCl, and extracted with hexane. The combined organic solutions were worked up as usual to give a dark residue which was chromatographed on silica gel. Elution with hexane–ether (98:2) afforded a 3:7 mixture of 13α- and 13β-nitriles (59.3 mg, 57%). Both isomers were separated by preparative HPLC, with hexane–ethyl acetate (95:5) as eluent (flow rate 16 mL/min), to give pure 13α-isomer (15) (17.6 mg) and 13β-isomer (16) (40.2 mg).

Method b. A solution of ketone 6 (30 mg, 0.11 mmol) in anhyd DME (2.5 mL) was treated with 1 M *t*-BuOK–*t*-BuOH (1.1 mL, 1.1 mmol). The resulting orange mixture was then slowly treated (1 h) with a solution of TosMIC (22.6 mg, 0.12 mmol) in DME (0.5 mL) at rt. After completion of the addition, stirring was continued for 6 h and the mixture poured into cold 2 N HCl, extracted with ethyl acetate, and worked up. Purification as above gave a 3:7 mixture of 15 and 16 (21 mg, 67%).

15 (second isomer eluted): mp 89–90 °C (from hexane at −20 °C); $[\alpha]^{20}_D$ nearly zero (*c* 1.5, $CHCl_3$); IR (KBr) 3060, 3040, 2230, 810, 740, 730 cm^{-1}; ^1H NMR δ 6.42 (d, J = 2.9 Hz, 1 H, H-17), 5.93 (dd, J = 2.9, 0.9 Hz, 1 H, H-15), 2.82 (ddd, J = 6.4, 2.2, 2.2 Hz, 1 H, H-13), 2.65 (ddd, J = 2.2, 1.4, 0.9 Hz, 1 H, H-14), 1.82 (dd, J = 13.1, 4.6 Hz, 1 H, H-9), 1.17 (dd, J = 12.4, 2.3 Hz, 1 H, H-5), 0.87 (s, 3 H, 4α-Me), 0.82 (s, 3 H, 10β-Me) and 0.81 (s, 3 H, 4β-Me); ^{13}C NMR, see Table I; MS (CI) *m/e* (relative intensity) 285 (M^+ + 2, 21), 284 (M^+ + 1, 100), 283 (M^+, 8), 282 (14), 268 (13), 267 (12), 257 (5), 256 (17), 215 (4), 146 (12). Anal. Calcd for $C_{20}H_{29}N$: C, 84.75; H, 10.31; N, 4.94. Found: C, 84.71; H, 10.40; N, 5.02.

16 (first isomer eluted): mp 65–68 °C (from MeOH–H_2O at −20 °C); $[\alpha]^{21}_D$ +84° (*c* 3.6, $CHCl_3$); IR (KBr) 3050, 3040, 2240, 800, 730 cm^{-1}; ^1H NMR δ 6.44 (d, J = 2.9 Hz, 1 H, H-17), 6.19 (dd, J = 2.9, 0.7 Hz, 1 H, H-15), 2.85 (ddd, J = 11.5, 7.2, 3.8 Hz, 1 H, H-13), 2.59 (ddd, J = 3.8, 0.9, 0.7 Hz, 1 H, H-14), 1.90 (m, 2 H, H-12), 1.23 (dd, J = 12.6, 6.0 Hz, 1 H, H-9), 1.12 (ddd, J = 13.4, 13.4, 4.7 Hz, 1 H, H-3α), 0.86 (s, 3 H, 4α-Me), 0.81 (s, 6 H, 4β-Me and 10β-Me); ^{13}C NMR see Table I; MS (CI) *m/e* (relative intensity) 285 (M^+ + 2, 23), 284 (M^+ + 1, 100), 282 (5), 268 (4), 257 (8), 214 (3), 160 (14), 137 (13), 95 (6). Anal. Calcd for $C_{20}H_{29}N$: C, 84.75; H, 10.31; N, 4.94. Found: C, 84.53; H, 10.24; N, 5.06.

Hydrolysis of Nitriles 15 and 16. To a solution of nitrile 16 (13.7 mg, 0.05 mmol) in ethylene glycol ethyl ether (2 mL) was added aqueous KOH (0.15 mL of a solution of 1.3 g of KOH in 1 mL of water, 3.4 mmol), and the mixture was stirred and heated under reflux overnight. The reaction mixture was cooled to rt, water was added, and the mixture was acidified with 2 N HCl and extracted with ethyl acetate. The extract was worked up as usual to give a solid residue. ^1H NMR analysis indicated a 93:7 mixture of acids 18 and 17. Although this material was used directly without further purification in the next step (see below) the product mixture was separated by preparative HPLC, using hexane–ethyl acetate (1:1) as eluent (flow rate 16 mL/min), to give acid 18 (12.3 mg, 84%) and its epimer 17 (0.8 mg, 6%). These products were identical with those obtained by the oxidation of aldehydes 8 as shown by the identity of ^1H NMR spectra.

In a reaction using the 13α-nitrile or even the 3:7 mixture of 13α/13β-nitriles obtained in the TosMIC reaction, run under essentially the same conditions, an identical result was obtained.

[5α,8(*S*),13α,15β]-(−)-8,15-Hydroxy-4,4-dimethyl-17-oxo-18-nor-16-oxaandrostane-8-carboxaldehyde Cyclic-8,15-hemiacetal (17β-Hydroxy-15,17-oxidospongian-16-one) (Dendrillol-1, 3). A stream of ozone (O_2 flow = 12 L/h; 7 mmol O_3/h) was passed through a solution of acid 18 (27.7 mg, 0.09 mmol) in dry CH_2Cl_2 (5 mL) for approximately 2 min at −78 °C. Nitrogen was bubbled through the mixture which was then treated with Me_2S (1 mL). The reaction was stirred at rt for 24 h. The solvent and the excess of Me_2S were removed under reduced pressure, and the residue was chromatographed on silica gel, using hexane–ether (6:4) as eluent, giving dendrillol-1 (3) (25 mg, 80%) as a solid: mp 224–226 °C (from hexane–CH_2Cl_2) (lit.[2d] mp 229–231 °C); $[\alpha]^{21}_D$ −29° (*c* 1.44, $CHCl_3$) (lit.[2d] $[\alpha]_D$ −31.8°); IR (KBr) 3380, 3040, 1760, 1110, 1065, 970, 940 cm^{-1}; ^1H NMR δ 6.09

(32) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693.

(d, J = 5.9 Hz, 1 H, H-15), 5.50 (d, J = 2.2 Hz, 1 H, H-17), 2.92 (d, J = 2.2 Hz, 1 H, OH), 2.71 (ddd, J = 11.2, 7.6, 1.0 Hz, 1 H, H-13), 2.57 (dd, J = 11.2, 5.9 Hz, 1 H, H-14), 2.38 (dddd, J = 13.9, 3.7, 2.2, 1.7 Hz, 1 H, H-12β), 1.96 (dddd, J = 12.9, 12.9, 12.9, 3.7 Hz, 1 H, H-11β), 1.85 (ddd, J = 12.9, 3.2, 3.2 Hz, 1 H, H-7β), 1.70 (m, 1 H, H-1β), 1.35 (dddd, J = 13.7, 13.7, 13.7, 3.2 Hz, 1 H, H-6β), 1.23 (dd, J = 12.9, 2.7 Hz, 1 H, H-9), 1.14 (ddd, J = 13.2, 13.2, 4.03 Hz, 1 H, H-3α), 1.08 (ddd, J = 13.7, 12.9, 3.8 Hz, 1 H, H-7α), 0.94 (dd, J = 13.7, 2.6 Hz, 1 H, H-5), 0.91 (s, 3 H, 10β-Me), 0.84 (s, 3 H, 4α-Me), 0.82 (s, 3 H, 4β-Me); ^{13}C NMR see Table I; MS m/e (relative intensity) 301 ($M^+ - H_2O$ - Me, 1.5), 290 (3), 289 (8), 288 (42), 273 (8), 91 (55), 41 (100).

When the crude 7:93 mixture of acids **17** and **18**, obtained from the hydrolysis of nitriles **15** and/or **16**, was directly subjected to the above reaction conditions a 75–80% overall yield of **3** was obtained.

[3*R*-(3β,3aα,5a*S*,7aα,11aβ,11bα)]- and [3*S*-(3α,3aα,5a*S*,7aα,11aβ,11bα)]-1,3,3a,6,7,7a,8,9,10,11,11a,11b-Dodecahydro-3,3-(epoxymethano)-8,8,11a-trimethylcyclobuta[*j*]phenanthrenes (19) and (20). A solution of trimethylsulfonium iodide (115 mg, 0.56 mmol) in anhyd THF (1.2 mL) and HMPT (1.4 mL) was treated with n-BuLi (473 μL of a 1.2 M solution in hexane, 0.56 mmol) at −20 °C. After being stirred at −40 °C for 15 min, the mixture was cooled to −78 °C and a solution of ketone **6** (52 mg, 0.19 mmol) in THF (1 mL) was added. The reaction mixture was allowed to warm to rt and then stirred for 15 h (no starting material remaining). Water was added, and the mixture was extracted with hexane. Workup as usual furnished an oily product (53 mg, ca. 100%) whose ^{1}H NMR indicated that it was exclusively a 4:6 mixture of epoxides **19** and **20**. Since their separation by column chromatography produced some material loss, the mixture was used directly in the next reaction. A small amount of this mixture (18 mg) was separated by preparative HPLC using a 98:1:1 mixture of hexane–ethyl acetate–triethylamine as eluent (flow rate 16 mL/min). The first material eluted (6 mg, 32%) was identified as the β-epoxide **19**, an oil: ^{1}H NMR (300 MHz) δ 6.43 (d, J = 2.8 Hz, 1 H, H-17), 6.24 (dd, J = 2.8, 0.9 Hz, 1 H, H-15), 2.61 (d, J = 5.2 Hz, 1 H, H-16), 2.56 (dd, J = 5.2, 1.5 Hz, 1 H, H-16′), 2.21 (dddd, J = 14, 7.5, 5.5, 1.5 Hz, 1 H, H-12), 1.91 (dd, J = 1.9, 0.9 Hz, 1 H, H-14), 0.87 (s, 3 H, 4α-Me), 0.83 (2s, 6 H, 4β-Me and 10β-Me); ^{13}C NMR see Table I.

The second material eluted (9 mg, 49%) was identified as the α-epoxide **20**, a solid: $[\alpha]^{20}_D$ +55° (c 1.2, $CHCl_3$); ^{1}H NMR δ 6.41 (d, J = 2.9 Hz, 1 H, H-17), 6.04 (dd, J = 2.9, 0.9 Hz, 1 H, H-15), 2.52 (d, J = 4.8 Hz, 1 H, H-16), 2.49 (d, J = 4.8 Hz, 1 H, H-16′), 2.28 (ddd, J = 15.2, 10.1, 2.5 Hz, 1 H, H-12), 1.86 (dd, J = 2.5, 0.9 Hz, 1 H, H-14), 1.75 (m, 2 H, H-7), 1.16 (ddd, J = 12.7, 12.7, 4.3 Hz, 1 H, H-3α), 1.03 (dd, J = 12.5, 2.3 Hz, 1 H, H-5), 0.98 (ddd, J = 12.9, 12.9, 3.7 Hz, 1 H, H-1α), 0.86 (s, 3 H, 4α-Me), 0.82 (s, 6 H, 4β-Me and 10β-Me); ^{13}C NMR see Table I.

(5α,9α,10β,14α)-(−)-13-(Hydroxymethyl)-17-norkaur-15-en-14-ol (21). To a solution of the 4:6 mixture of α- and β-epoxides **19** and **20** (20 mg, 0.07 mmol) in CH_2Cl_2 (4 mL) were added a drop of water and a catalytic amount of BF_3·Et_2O. The mixture was stirred at rt for 1 h and diluted with ether. Workup as usual gave a solid, which after chromatography on silica gel, eluting with 6:4 hexane:ethyl acetate, afforded **21** (14.3 mg, 67%) as a white solid: mp 131–133 °C (from hexane at −20 °C); $[\alpha]^{21}_D$ −41° (c 3.8, $CHCl_3$); IR (KBr) 3600, 3490, 3460–3000, 3040, 1020, 980, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$–D_2O, 300 MHz) δ 5.84 (d, J = 6.3 Hz, 1 H, H-15), 5.52 (d, J = 6.3 Hz, 1 H, H-16), 3.55 (s, 2 H, H-17), 3.36 (s, 1 H, H-14), 0.86 (s, 3 H, 4α-Me), 0.82 (s, 3 H, 4β-Me), 0.78 (s, 3 H, 10 β-Me); ^{13}C NMR see Table I; MS (CI) m/e (relative intensity) 305 (M^+ + 1, 11), 304 (M^+, 8), 303 (18), 289 (12), 288 (23), 287 (100), 285 (22), 269 (13). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.70; H, 10.73.

Preparation of Compound 23. A stream of ozone was passed through a solution of the mixture of epoxides obtained above (**19** and **20**) (26.8 mg, 0.09 mmol) in dry CH_2Cl_2 (2 mL) cooled at −78 °C until no starting material remained (TLC). Me_2S was added, and the reaction mixture was stirred at rt for 24 h. The solvent and the excess of Me_2S were removed under reduced pressure and the residue dissolved in CH_2Cl_2 (2 mL) and treated with a catalytic amount of BF_3·Et_2O. After being stirred at rt for 1 h, the brownish mixture was diluted with hexane and worked up as usual to give an oily residue which was chromatographed on silica gel, using hexane–ethyl acetate (5:5) as eluent, to afford compound **23** (14.4 mg, 48%) as an amorphous solid: $[\alpha]^{20}_D$ +13° (c 2.7, $CHCl_3$); IR (KBr) 3040, 1460, 1035, 915, 860, 845 cm^{-1}; ^{1}H NMR δ 5.59 (d, J = 2.9 Hz, 1 H, H-15), 5.26 (s, 1 H, H-17), 3.95 (d, J = 9.2 Hz, 1 H, H-16), 3.69 (d, J = 9.2 Hz, 1 H, H-16′), 2.09 (dd, J = 12.6, 6.7 Hz, 1 H, H-12β), 1.96 (m, 1 H, H-7β), 1.85 (d, J = 2.9 Hz, 1 H, H-14), 1.48 (dd, J = 10.3, 5.1 Hz, 1 H, H-9), 1.15 (ddd, J = 12.6, 12.6, 4.1 Hz, 1 H, H-3α), 0.93 (s, 3 H, 10β-Me), 0.85 (s, 3 H, 4α-Me), 0.82 (s, 3 H, 4β-Me); ^{13}C NMR see Table I; MS (CI) m/e (relative intensity) 320 (M^+ + 2, 23), 319 (M^+ + 1, 100), 317 (18), 303 (10), 302 (19), 301 (78), 283 (11), 273 (18), 257 (8).

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