^{13}C NMR spectra were obtained with the use of a Varian Associates Model FT-80 spectrometer equipped with a multinuclei broad-band variable-temperature probe. The chemical shifts were referenced from an external capillary of tetramethylsilane.

Acknowledgment. Support of our work by the National Science Foundation and National Institutes of Health is gratefully acknowledged.

Registry No. 2a, 82732-48-7; **2a**-OH, 82732-52-3; **2b**, 82732-49-8; **2b**-OH, 79575-90-9; **2c**, 82732-50-1; **2c**-OH, 82732-53-4; **2d**, 82732-51-2; **2d**-OH, 82732-54-5; **3a**, 71939-89-4; **3b**, 71939-86-1; **3c**, 82732-55-6; **3c**-OH, 82732-57-8; **3d**, 82732-56-7; **3d**-OH, 54549-72-3; **4a**, 82732-58-9; **4a**-OH, 17138-80-6; **4b**, 82732-59-0; **4b**-OH, 36169-67-2; **4c**, 82732-60-3; **4c**-OH, 82732-61-4; **4d**-OH, 82732-62-5; **5a**, 82732-63-6; **5a**-OH, 82732-66-9; **5b**, 82732-64-7; **5b**-OH, 82732-67-0; **5c**, 82732-65-8; **5c**-OH, 82732-68-1; **6a**, 82732-69-2; **6a**-OH, 82732-71-6; **6b**, 82732-70-5; **6b**-OH, 82732-72-7; **7a**, 82732-73-8; **7a**-OH, 82740-51-0; **7b**, 82732-74-9; **7b**-OH, 4229-86-1; **8a**, 82732-75-0; **8a**-OH, 82740-53-2; **8b**, 82740-52-1; **8b**-OH, 82740-54-3; **9a**, 82732-76-1; **9a**-OH, 82732-80-7; **9b**, 82732-77-2; **9b**-OH, 82732-81-8; **9c**, 82732-78-3; **9c**-OH, 82732-82-9; **9d**, 82732-79-4; **9d**-OH, 82732-83-0; **10a**, 82732-84-1; **10a**-OH, 82732-87-4; **10b**, 82732-85-2; **10b**-OH, 82732-88-5; **10d**, 82732-86-3; **10d**-OH, 82732-89-6; **11d**, 82732-90-9; **11d**-OH, 82732-91-0; **12d**-OH, 82732-92-1; **13d**-OH, 82732-93-2; **15**, 82732-94-3; **16**, 82732-95-4.

Syntheses of Arborescin, 1,10-Epiarborescin, and (11*S*)-Guaia-3,10(14)-dieno-13,6α-lactone, the Key Intermediate in Greene and Crabbé's Estafiatin Synthesis, and the Stereochemical Assignment of Arborescin[1]

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Received February 25, 1982

Arborescin (**2**), 1,10-epiarborescin (**3**), and (11*S*)-guaia-3,10(14)-dieno-13,6α-lactone (**33**), the key intermediate in Greene and Crabbé's synthesis of estafiatin (**4**), have been synthesized from (11*S*)-1,1-(ethylenedioxy)eudesm-3-eno-13,6α-lactone (**6**) in 12 steps and 11 steps, respectively. The key step involves the solvolytic rearrangement of (11*S*)-3α-(benzoyloxy)-1β-(mesyloxy)eudesmano-13,6α-lactone (**18**). The stereochemistry of the epoxide ring of arborescin has been determined to be β orientation from this synthesis.

Guaianolides are a rapidly expanding group of natural products, comprising to date ca. 200 varieties.[2] Some of them have been shown to possess high antitumor,[3,4] allergenic,[3,5] antischistosomal,[3,6] antihelmintic,[7] contraceptive,[8] root growth stimulatory,[3,9] root growth and germination inhibitory activities.[3,10] Because of their high biological activities and because they are available from natural sources often only in small quantities, their efficient syntheses are a synthetic challenge that has received much attention during the past few years.[11]

Chart I

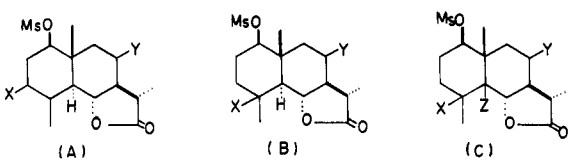
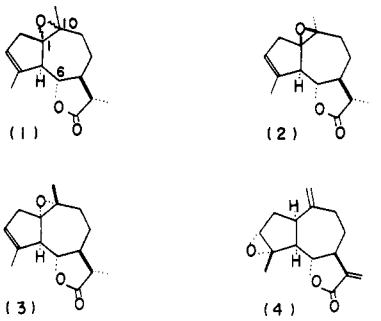


Chart II



With only a few exceptions guaianolides possess a cis-fused (α-H) hydroazulene skeleton and a functionality at C_{10} (double bond, hydroxyl or epoxide group). Furthermore, most have the γ-lactone moiety closed in a trans

(1) A portion of this work has appeared in preliminary form: M. Ando, A. Akahane, and K. Takase, *Chem. Lett.*, 727 (1978).
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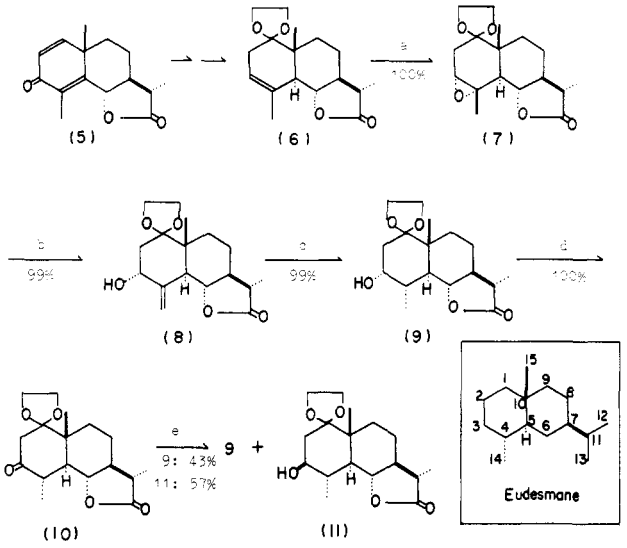
Scheme I[a]



[a] a, m-CPBA; b, $Al(iPrO)_3$, toluene; c, H_2, Pt/C; d, $CrO_3 \cdot 2Py$, CH_2Cl_2; e, $Zn(BH_3)_2$, DME.

manner toward C_6 (6α-lactone). The wide variety of natural guaianolides arises from additional functionalities in the five-membered ring and at C_8. Keeping these structural requirements in mind, we envisioned a general synthetic approach to the guaianolides that consisted of the solvolytic rearrangements of the appropriately functionalized eudesmanolides such as compounds **A**, **B**, and **C** (Chart I).

Solvolytic rearrangements of *cis*- and *trans*-decalin derivatives with an equatorial tosyloxy group at C_1 have been applied to the syntheses of guaiane-type sesquiterpenes with rather simple structures, such as bulnesol, bulnesene, and kessane,[12] but have not yet been applied to the syntheses of guaianolides probably because of difficulties in syntheses of appropriately functionalized intermediates such as **A**, **B**, and **C**.[13] In the present paper we report efficient syntheses of arborescin (**2**), 1,10-epiarborescin (**3**), and diene **33**, the key intermediate in Greene and Crabbé's synthesis of estafiatin (**4**), to demonstrate the utility of the solvolytic rearrangement of an appropriately functionalized eudesmanolide (**18**), which was conveniently prepared from α-santonin (Chart II).

Results and Discussion

Syntheses of Arborescin (2) and 1,10-Epiarborescin (3). Arborescin was isolated by Meisels and Weizman[14] from *Artemisia arborescens* (Compositae), a plant used for contraceptive purpose by the ancient Greeks and Arabs.[8] The structure of this compound was proposed as shown in structure **1** by Herout et al. on the basis of its synthesis from *O*-acetylisophotosantonic lactone,[15] but the stereochemistry of the epoxide ring at $C_{1,10}$ was not clear from this chemical transformation. This paper gives details of the total syntheses of **2** and **3** in a regio- and stereoselective manner with the object of establishing the

Chart III

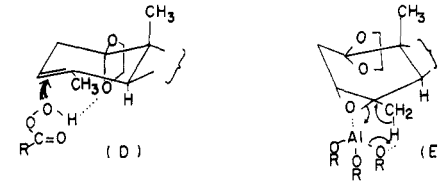


Chart IV

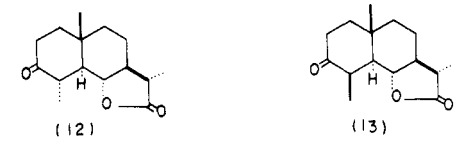


Table I. ($\delta_{CDCl_3} - \delta_{C_6D_6}$) Values in ^1H NMR Spectral Data of Compounds 10, 12, and 13

H	10	12	13
C_4-Me	−0.24	−0.12	0.15
C_{11}-Me	0.26	0.26	0.22
C_{10}-Me	0.43	0.59	0.54

structure of "arborescin". It was also interesting to determine whether the compound **2** or **3** is identical with sieversinin since the structure proposed for sieversinin is a stereoisomer of arborescin.[16]

The starting material is the acetal **6**, which can be prepared from α-santonin (**5**) in 23% yield in eight steps.[17] The epoxidation of **6** with *m*-chloroperoxybenzoic acid in dichloromethane proceeded stereoselectively from the α face to give 3α,4α-epoxide **7** in a quantitative yield. The stereochemistry of **7** was fully supported by the ^1H NMR spectrum[18] as well as the subsequent transformations shown in Scheme I. The high stereoselectivity of this reaction can be explained by steric hindrance due to the angular methyl group and the directing effect of the α-(a)-oxygen of the acetal group at C_1 by hydrogen bonding as shown in the possible intermediate complex **D** (Chart III).

Treatment of **7** with aluminum isopropoxide[19] in boiling toluene gave allyl alcohol **8** in 99% yield. The high regioselectivity of this reaction is presumed due to the preferred geometry of the possible intermediate complex **E**. This procedure is remarkable in the following points: (1) aluminum isopropoxide is cheap and easy to handle; (2) this reaction proceed in high yield and high regioselectivity; (3) this procedure can be applied to compounds sensitive to strong base. The generality and the utility of this procedure will be reported separately elsewhere.

An attempt to effect catalytic hydrogenation of **8** in the presence of palladium on carbon was unsuccessful, but catalytic hydrogenation of **8** in the presence of 13% platinum on carbon, which was prepared in situ from platinum oxide and activated charcoal powder, proceeded well to give alcohol **9** as a single product in nearly quantitative yield. Benzoylation of **9** with benzoyl chloride in pyridine gave benzoate **14**. Although the stereochemistry

(12) C. H. Heathcock and R. Ratcliffe, *J. Am. Chem. Soc.*, **93**, 1746 (1971); M. Kato, H. Kosugi, and A. Yoshikoshi, *J. Chem. Soc., Chem. Commun.*, **1970**, 185, 934.

(13) After we had completed our work, the transformation of vulgarin to (11*S*)-4α-hydroxyguai-10(1)-eno-13,6α-lactone and (11*S*)-4α-hydroxyguai-10(14)-eno-13,6α-lactone (compressanolide) via the solvolytic rearrangement of 4α-hydroxy-1β-(tosyloxy)eudesmano-13,6α-lactone was reported; A. G. González, A. Galindo, and H. Mansilla, *Tetrahedron*, **36**, 2015 (1980).

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(19) The reaction of epoxides with aluminum isopropoxide in no solvent or in isopropyl alcohol has already been reported; E. H. Eschinasi, *Israel J. Chem.*, **6**, 713 (1968); E. H. Eschinasi, *J. Org. Chem.*, **35**, 1598 (1970); K. H. Schulte-Elte, F. Gautschi, W. Renold, A. Hauser, P. Frankhauser, J. Limacher, and G. Ohloff, *Helv. Chim. Acta*, **61**, 1125 (1978).

Chart V

of the methyl groups at C_4 in **9** and **14** could not be determined from an analysis of their NMR spectra, their α(e) configuration was established as following.

Oxidation of **9** by the Collins procedure gave keto acetal **10** in nearly quantitative yield. In the NMR spectrum of **10** the C_4-methyl proton resonance showed a 0.24 ppm downfield shift on passing from deuteriochloroform to benzene.[20] In a model study, we examined the same solvent effect of **12** and **13** bearing the α-equatorial and β-axial methyl groups at C_4, respectively (Chart IV). The results summarized in Table I strongly suggest the α-equatorial configuration of the C_4-methyl group of **10**. This is further supported by the following observation. Reduction of **10** with zinc borohydride gave a 3:4 mixture of **9** and the corresponding β-alcohol **11**. Formation of **9** showed that no epimerization of the C_4-methyl group occurred in the oxidation of **9** and the following reduction of **10**. The β(e)-alcohol (**11**) showed C_3-H at 3.30 ppm as ddd with J = 6.0, 9.5, and 11.0 Hz. These coupling constants and the chemical transformation of **9** to **11** showed without doubt that the the C_4-methyl group of **9** was equatorial.

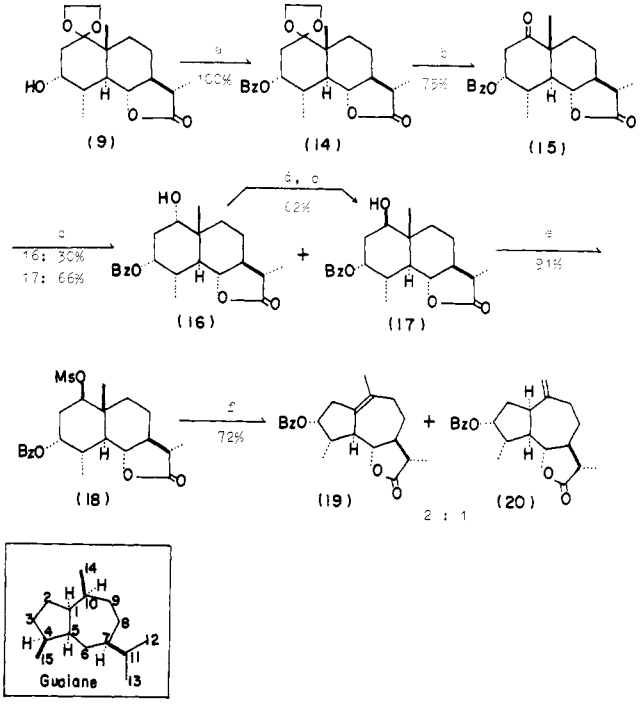
Treatment of benzoate **14** with boiling 50% aqueous acetic acid for 30 min gave the desired keto benzoate **15** in 75% yield. Treatment of **14** under more acidic conditions or for a longer reaction period gave the corresponding α,β-unsaturated ketone **34** formed by elimination of benzoic acid.

For introduction of β(e)-hydroxyl group at the C_1 position, we examined several conditions. Reduction of **15** with sodium borohydride or lithium tri-*tert*-butoxyaluminum hydride gave a complex mixture of epimeric C_1 alcohols **16** and **17**, α,β-unsaturated ketone **34**, and allyl alcohol **35** even at low temperature. The undesired compounds, **34** and **35** (Chart V), were probably produced by the elimination of benzoic acid from **15** under the basic reaction conditions. To avoid the formation of **34** and **35**, we employed a neutral reducing agent, zinc borohydride.[21] Reduction of **15** with zinc borohydride in DME at room temperature gave the desired β-alcohol **17** in 66% yield and the corresponding α-alcohol **16** in 30% yield. The latter was further converted to **17** by Collins oxidation and successive reduction of the resulting **15** with zinc borohydride in 62% yield. The stereochemistries of **16** and **17** were assigned from the ^{1}H NMR spectra shown in the Experimental Section.

Attempts at tosylation of **17** under various conditions was unsuccessful probably because of steric hindrance by the angular methyl group and the α-axial benzoyloxy group at C_3. Thus we tried the introduction of a smaller mesyloxy group at C_1. Treatment of **17** with methanesulfonyl chloride in pyridine at room temperature for 2 h gave mesylate **18** in 91% yield.

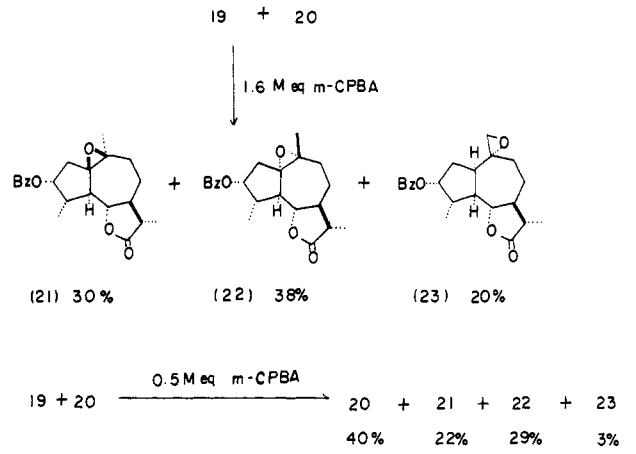
Solvolytic rearrangement of **18** in refluxing 0.5 M acetic acid solution of potassium acetate gave a 72% yield of an

Scheme II[a]



[a] a, BzCl, Py; b, 50% AcOH, reflux; c, $Zn(BH_3)_2$, DME; d, $CrO_3 \cdot 2Py$, CH_2Cl_2; e, MsCl, Py; f, 0.5 M AcOK-AcOH, reflux.

Scheme III



ca. 2:1 mixture of endo- and exocyclic olefins (**19** and **20**),[22] which showed a single spot on silica gel TLC in various solvent systems. Although we could separate some **19** and **20** from the mixture by column chromatography on silver nitrate impregnated silica gel, repeated chromatography was necessary for complete separation (Scheme II). For the practical purpose, we employed the mixture in the next step without separation.

Epoxidation of this mixture with an excess of *m*-chloroperoxybenzoic acid gave epoxides **21**, **22**, and **23** in 30%, 38%, and 20% yields, respectively. When 0.5 molar equiv of *m*-chloroperoxybenzoic acid was employed, the endocyclic olefin **19** was selectively epoxidized to give the recovered exocyclic olefin **20** and stereoisomeric epoxides **21** and **22** in 40%, 22%, and 29% yields, respectively (Scheme III). The ^{1}H NMR spectrum (90 MHz, in $CDCl_3$) of **20** showed C_1-H at 3.18 ppm as ddd with J = ca. 9, 9, and 9 Hz. The cis ring fusion for **20** was fully supported by the relatively small mutual coupling constant ($J_{1,5}$ =

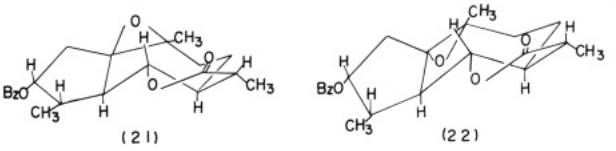
(20) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Fransisco, 1964, p 165.
(21) W. J. Gensler, F. Johnson, and A. D. B. Sloan, *J. Am. Chem. Soc.*, **82**, 6074 (1960); M. Fieser and L. F. Fieser, "Reagent for Organic Synthesis", Wiley, New York, 1971, Vol. 3, p 337, 1975, Vol. 5, p 761, 1976, Vol. 6, p 222.

(22) The ratio of **19** and **20** was estimated from NMR spectral analysis.

Table II. Comparison of the Chemical Shift Values of C_6-H in Pairs of Compounds 21 and 22, 2 and 3, 24 and 26, and 29 and 30

21 and its derivatives (A)	21	2	24	29
δ values of C_6-H	3.97	4.02	3.93	3.90
22 and its derivatives (B)	22	3	26	30
δ values of C_6-H	3.78	3.77	3.73	3.69
$\delta_A - \delta_B$	0.19	0.25	0.20	0.21

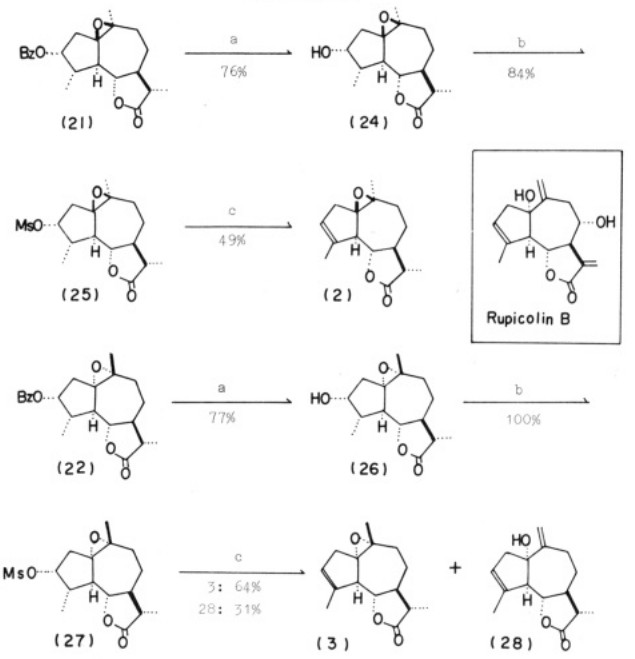
Chart VI



ca. 9 Hz)[23] as well as the subsequent transformations shown in Scheme VI. The stereochemical assignment of the epoxide ring in **23** is based on the consideration that the reagent attacks the exocyclic double bond of **20** from the less hindered α or outer side. The stereochemistries of the endocyclic epoxides **21** and **22** were deduced from the following observation in their NMR spectra. The C_6-H resonance of **21** appeared at 0.19 ppm lower field than that of **22**. Since it has been reported that the epoxide function deshields protons that are situated on the same side of the oxygen atom,[24] the above-mentioned result strongly suggests a cis relationship between the $C_{1,10}$-epoxide ring and the C_6 proton in **21**. As shown in Table II, the C_6-proton resonances of the derivatives of **21** always appeared at lower field than those of the corresponding derivatives of **22**. It is remarkable that the deshielding of the C_6 proton by an epoxide ring at $C_{1,10}$ and a hydroxyl group at C_{10} were of the same degree. An NOE experiment also supports the β and α orientations of the epoxide rings in **21** and **22**, respectively. Thus, in **22** irradiation of the C_{10}-methyl protons produced a 6% increase in the integrated intensity of the C_6 proton, while no NOE effect was observed between the C_{10}-methyl protons and the C_6-proton in **21** under the same experimental conditions. In the ^{13}C NMR spectra, the C_6 resonance of **21** appeared at 0.8 ppm higher field than the corresponding signal of **22**. Although the difference is small, this observation is probably explained by steric compression (γ effect)[25] due to the β-oriented epoxide ring in **21** (Chart VI).

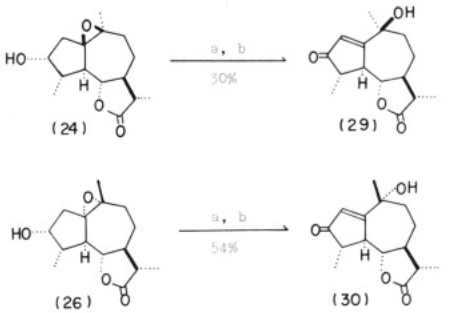
Hydrolysis of **21** and **22** with 1 M K_2CO_3 in refluxing methanol gave the corresponding alcohols **24** and **26** in 76% and 77% yields, respectively (Schemes IV and V). For the syntheses of arborescin and its 1,10-epimer, the regioselective introduction of a trisubstituted double bond at the C_3 position is a crucial step. As had been expected from observations made in similar systems,[15,26] conversion of the alcohols **24** and **26** to the trisubstituted olefins **2** and **3** proved to be difficult. Attempted dehydration of **24** and **26** with thionyl chloride–pyridine and methanesulfonyl chloride–pyridine at 0 °C or at room temperature gave chlorides and mesylates, respectively. When these reactions were carried out at elevated temperature, both **24** and **26** gave complex mixtures. Finally, dehydration of **24** and **26** in the desired direction was accomplished by the following two-step conversion.

Scheme IV[a]



[a] a, 1 M K_2CO_3 aqueous solution, MeOH; b, MsCl, Py; c, Li_2CO_3, LiBr, DMF, Δ.

Scheme V[a]



[a] a, $CrO_3 \cdot 2Py$, CH_2Cl_2; b, silica gel.

Treatment of **24** with methanesulfonyl chloride in pyridine at room temperature gave mesylate **25** in 84% yield. Successive treatment of **25** with lithium carbonate and lithium bromide in DMF at 118–129 °C for 2 h gave compound **2** in 49% yield as a sole product. Another possible regioisomer, a disubstituted olefin, could not be detected by TLC, HPLC, and NMR analysis of the crude product. **2** was identical with arborescin by comparison of their NMR spectra under the same conditions.[8]

On the other hand, treatment of **26** with methanesulfonyl chloride in pyridine at room temperature gave a mesylate **27** in quantitative yield. Successive treatment of **27** with lithium carbonate and lithium bromide in DMF at 118–135 °C for 3 h gave compounds **3** and **28** in 64% and 31% yields, respectively. When the reaction temperature was elevated to refluxing, the same treatment of **27** gave **3** and **28** in 19% and 45% yields, respectively. Another possible regioisomer of **3**, a disubstituted olefin,

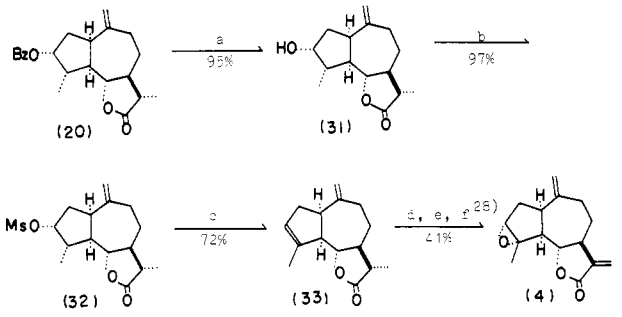
(23) The coupling constant of cis compounds is less than 10 Hz, while that of trans compound is around 13 Hz; T. Tahara, Y. Sakuda, M. Kodama, Y. Fukazawa, and S. Ito, *Tetrahedron Lett.*, **21**, 1861 (1980), and references cited therein.

(24) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Franscisco, 1964, pp 99–102; L. A. Paquette, W. E. Fristad, C. A. Schuman, M. A. Beno, and G. G. Christoph, *J. Am. Chem. Soc.*, **101**, 4645 (1979); L. A. Maçaira, F. W. L. Machado, M. Garcia, and J. A. Rabi, *Tetrahedron Lett.*, **21**, 773 (1980); L. A. Maçaira, M. Garcia, and J. A. Rabi, *J. Org. Chem.*, **42**, 4207 (1977).

(25) G. C. Levy, R. L. Lichter, and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance Spectroscopy", 2nd ed., Wiley, New York, 1980, p 55.

(26) E. H. White, S. Eguchi, and J. N. Marx, *Tetrahedron*, **25**, 2099 (1969); E. Piers and K. F. Cheng, *Can. J. Chem.*, **48**, 2234 (1970).

Scheme VI



[a] a, 1 M K_2CO_3 aqueous solution, MeOH; b, MsCl, Py; c, LiBr, Li_2CO_3, DMF; d, LDA, PhSeSePh; e, H_2O_2; f, m-CPBA.

could not be detected in both cases in the reaction mixture. **3** was completely different from arborescin by comparison of their NMR spectra.[8] Although sieversinin was described as a stereoisomer of arborescin by Nazarenko and Leont'eva, the NMR data reported in the literature were different from those of **3**.[16] It is interesting that **28** possesses a structure similar to that of rupicolin B.[27]

Synthesis of Estafiatin (4). Estafiatin (**4**) is a constituent of *Artemisia mexicana* whose extracts have been used as an antihelmintic in Mexico. Isolation and structure elucidation of this compound were carried out by Sánchez-Viesca and Ramo except for the stereochemistry of the epoxide ring.[7] Recently Greene et al. established the stereochemistry of the epoxide ring of **4** by synthesis of **4** from *O*-acetylisophotosantonic lactone via diene **33** although the introduction of the double bond at C_3 of **33** was nonregioselective.[28]

The starting material of our synthesis of **4** was benzoate **20**. The hydrolysis of **20** with 1 M K_2CO_3 in refluxing methanol gave the corresponding alcohol **31** in 95% yield. The regioselective introduction of the double bond at C_3 was accomplished as follows. Treatment of **31** with methanesulfonyl chloride in pyridine at room temperature gave a mesylate **32** in 97% yield. Successive treatment of **32** with lithium carbonate and lithium bromide in DMF at 115–120 °C for 1.5 h gave diene **33** in 72% yield. The ^1H NMR spectrum (in CCl_4) of **33** was identical with that reported in the literature.[28] The structure of **33** was fully supported by the ^1H NMR (90 MHz, in $CDCl_3$) of **33** shown in the Experimental Section. The cis ring fusion for **33** was indicated by the relatively small mutual coupling constant ($J_{1,5}$ = ca. 7 Hz).[23] Another possible regioisomer, a disubstituted olefin, could not be detected by TLC, HPLC, and NMR analysis of the crude product.

Diene **33** has already been converted to estafiatin **4** by Greene et al. in a three-step conversion with 41% overall yield (Scheme VI).[28]

Experimental Section

All melting points were uncorrected. IR spectra were recorded on a Shimadzu IRG-1 spectrometer. NMR spectra were recorded on Varian XL-200, Varian EM-390, Varian HA-100, and Hitachi R-24B spectrometers in $CDCl_3$ containing 1% Me_4Si as the internal standard. Mass spectra were recorded on Hitachi RMU-6D spectrometer with a direct inlet system operating at 25 eV. Optical rotations were determined on a Perkin-Elmer 241 polarimeter.

(11*S*)-3α,4α-Epoxy-1,1-(ethylenedioxy)eudesmano-13,6α-lactone (7). A mixture of (11*S*)-1,1-(ethylenedioxy)eudesm-3-eno-13,6α-lactone (**6**; 103 mg, 0.35 mmol) and *m*-chloroperoxybenzoic acid (64 mg, 0.37 mmol) in CH_2Cl_2 (5 mL) was allowed to stand at room temperature for 100 h. The mixture was poured into an aqueous solution of KI and extracted with $CHCl_3$ (10 mL × 3). The combined extracts were washed successively with a 0.2 M $Na_2S_2O_3$ aqueous solution, a saturated $NaHCO_3$ aqueous solution, and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give 109 mg (100%) of spectroscopically pure **7** as a crystalline material, which was recrystallized from a mixture of chloroform and ether (1:1) to give colorless needles: mp 257 °C dec; NMR ($CDCl_3$) δ 1.12 (3 H, s, C_{10}-CH_3), 1.23 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.49 (3 H, s, C_4-CH_3), 2.16 (1 H, d, J = 3.0 Hz, C_2-H), 2.20 (1 H, d, J = 1.5 Hz, C_2-H), 2.43 (1 H, d, J = 12.0 Hz, C_5-H), 3.01 (1 H, dd, J = 1.5, 3.0 Hz, C_3-H), 3.6–4.1 (5 H, m, OCH_2CH_2O, C_6-H); $[\alpha]^{20}_D$ +81.6° (*c* 0.85, $CHCl_3$).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.26; H, 7.89.

(11*S*)-1,1-(Ethylenedioxy)-3α-hydroxyeudesm-4(14)-eno-13,6α-lactone (8). A solution of **7** (416 mg, 1.35 mmol) in anhydrous toluene (50 mL) was refluxed with aluminum isopropoxide (1.39 g, 6.76 mmol) under N_2 for 13 h. After further addition of aluminum isopropoxide (1.41 g, 6.89 mmol) the reflux was continued for 5 h. The solvent was removed from the reaction mixture under reduced pressure. The residue was stirred with a mixture of ethyl acetate (20 mL) and 2 M HCl (20 mL) until the residue was dissolved. The organic layer was separated and the aqueous layer was further extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed successively with a saturated $NaHCO_3$ aqueous solution and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give spectroscopically pure **8** (426 mg, 99%) as a crystalline material, which was recrystallized from a mixture of chloroform and ether (1:1) to give colorless needles: mp 234–235 °C; IR (KBr) 3500, 1772, 1657, 910 cm^{-1}; NMR ($CDCl_3$ + D_2O) δ 0.98 (3 H, s, C_{10}-CH_3), 1.23 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.89 (2 H, d, J = 3.2 Hz, C_2-H), 2.94 (1 H, dt, J = 1.8, 11.0 Hz, C_5-H), 3.85–4.32 (5 H, m, OCH_2CH_2O, C_6-H), 4.23 (1 H, t, J = 3.2 Hz, C_3-H), 5.05 (1 H, dd, J = 1.0, 1.8 Hz, C_{14}-H), 5.21 (1 H, m, C_{14}-H).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.16; H, 7.88.

(11*S*)-1,1-(Ethylenedioxy)-3α-hydroxyeudesmano-13,6α-lactone (9). A mixture of **8** (331 mg, 1.07 mmol), ethyl acetate (40 mL), PtO_2 (27 mg), and activated charcoal powder (151 mg) was shaken under 1 atm of hydrogen for 1 h. The filtrate was concentrated to give spectroscopically pure **9** (330 mg, 99%) as colorless needles, which was subsequently recrystallized from a mixture of chloroform and ether (1:1) to give colorless needles: mp 188–190 °C; IR (KBr) 3550, 1775 cm^{-1}; NMR ($CDCl_3$) δ 1.09 (3 H, s, C_{10}-CH_3), 1.21 (6 H, d, J = 6.3 Hz, C_4-CH_3, C_{11}-CH_3), 3.60–4.13 (6 H, m, C_3-H, C_6-H, OCH_2CH_2O); $[\alpha]^{20}_D$ +20.8° (*c* 0.85, $CHCl_3$).

Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.59; H, 8.50.

(11*S*)-1,1-(Ethylenedioxy)-3-oxoeudesmano-13,6α-lactone (10). Chromic anhydride (94 mg, 0.93 mmol) was added into a mixture of anhydrous methylene chloride (0.5 ml) and anhydrous pyridine (191 μL, 1.64 mmol) at 0 °C and the mixture was stirred for 10 min. Then **9** (11.7 mg, 0.038 mmol) dissolved in anhydrous methylene chloride (1.5 mL) was added over 5 min, and the mixture was stirred at 0 °C for 6 h and filtered through Celite under reduced pressure. The filtrate was washed successively with a saturated $NaHCO_3$ aqueous solution, 2 M HCl, and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give 11.6 mg (100%) of **10** as colorless needles: mp 202 °C; IR (KBr) 1770, 1708 cm^{-1}; NMR ($CDCl_3$) δ 1.22 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.27 (3 H, s, C_{10}-CH_3), 1.28 (3 H, d, J = 6.0 Hz, C_4-CH_3), 3.80–4.20 (5 H, m, OCH_2CH_2O, C_6-H); NMR (C_6D_6) δ 0.84 (3 H, s, C_{10}-CH_3), 0.96 (3 H, d, J = 6.0 Hz, C_{11}-CH_3), 1.52 (3 H, d, J = 5.5 Hz, C_4-CH_3).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 65.91; H, 7.84.

Formation of 9 and (11*S*)-1,1-(Ethylenedioxy)-3β-hydroxyeudesmano-13,6α-lactone (11) from 10. To a stirred solution of **10** (47 mg, 0.15 mmol) in dimethoxyethane (2 mL) was added a 0.5 M solution of $Zn(BH_4)_2$ (4 mL). The solution was stirred for 2 h at room temperature and poured into a mixture of a saturated NaCl aqueous solution (10 mL), 2 M HCl (0.3 mL), and ice. The mixture was extracted with ethyl acetate (10 mL).

(27) M. A. Irwin and T. A. Geissman, *Phytochemistry*, **12**, 863 (1973).
(28) M. T. Edgar, A. E. Greene, and P. Crabbé, *J. Org. Chem.*, **44**, 159 (1979).

The extract was washed with a saturated NaCl solution, dried (Na_2SO_4), and concentrated to give an oily product (50 mg), which was then purified by preparative TLC [Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$ (1:9)]. The first band (R_f 0.24) gave 14 mg (30%) of recovered starting material. The second band (R_f 0.13) gave 14 mg (30%) of **9**. The third band (R_f 0.05) gave 19 mg (40%) of **11**, which was recrystallized from a mixture of ether and hexane (1:1) to give colorless needles: mp 203–204 °C; IR ($CHCl_3$) 3600, 1765 cm^{-1}; NMR ($CDCl_3$) δ 1.11 (3 H, s, C_{10}-CH_3), 1.20 (3 H, d, J = 6.8 Hz, C_{11}-CH_3), 1.24 (3 H, d, J = 6.0 Hz, C_4-CH_3), 3.30 (1 H, ddd, J = 6.0, 9.5, 11.0 Hz, C_3-H), 3.62–4.18 (5 H, m, OCH_2CH_2O, C_6-H); MS, m/e 310 (M^+).

(11*S*)-3α-(Benzoyloxy)-1,1-(ethylenedioxy)eudesmano-13,6α-lactone (14). To a stirred solution of **9** (513 mg, 1.65 mmol) in anhydrous pyridine (2 mL) was added benzoyl chloride (290 μL, 2.48 mmol) at room temperature. The mixture was stirred for 18 h at room temperature and poured into a saturated NaCl aqueous solution (50 mL). The mixture was extracted with ethyl acetate (20 mL, 10 mL). The combined extracts were washed successively with 2 M HCl (20 mL), a saturated $NaHCO_3$ aqueous solution (20 mL), and a saturated NaCl aqueous solution (30 mL), dried (Na_2SO_4), and concentrated to give an oil (733 mg). This was subsequently chromatographed over silica gel (35 g, Merck, finner than 230 mesh) and eluted with chloroform to give **14** (685 mg, 100%) as an oil: IR ($CHCl_3$) 1768, 1710, 1212, 1605 cm^{-1}; NMR ($CDCl_3$) δ 1.14 (3 H, s, C_{10}-CH_3), 1.17 (3 H, d, J = 6.0 Hz, C_4-CH_3), 1.22 (3 H, d, J = 7.5 Hz, C_{11}-CH_3), 3.68–3.98 (5 H, m, OCH_2CH_2O, C_6-H), 5.14 (1 H, ddd, J = 3.0, 3.0, 3.0 Hz, C_3-H), 7.37–7.67 (3 H, m, aromatic H), 7.96–8.22 (2 H, m, aromatic H); MS, m/e 414 (M^+).

(11*S*)-3α-(Benzoyloxy)-1-oxoeudesmano-13,6α-lactone (15). A solution of **14** (376 mg, 0.91 mmol) in 50% aqueous acetic acid was refluxed under N_2 for 30 min. The mixture was cooled, poured into a saturated NaCl aqueous solution (40 mL), and extracted with ethyl acetate (20 mL, 10 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (30 mL × 3) and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give a crystalline material (312 mg), which was recrystallized from a mixture of ether and chloroform to give 253 mg (75%) of spectroscopically pure **15**.

An analytical sample was prepared by recrystallization from a mixture of ether and chloroform, affording colorless prisms: mp 165–167 °C; IR (KBr) 1782, 1717 cm^{-1}; NMR ($CDCl_3$) δ 1.26 (3 H, d, J = 6.5 Hz), 1.27 (3 H, d, J = 6.5 Hz), 1.30 (3 H, s, C_{10}-CH_3), 4.11 (1 H, t, J = 10.0 Hz, C_6-H), 5.59 (1 H, ddd, J = 3.0, 3.0, 3.0 Hz, C_3-H), 7.52–7.78 (3 H, m, aromatic H), 8.01–8.25 (2 H, m, aromatic H).

Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08. Found: C, 71.17; H, 7.20.

(11*S*)-3α-(Benzoyloxy)-1α-hydroxyeudesmano-13,6α-lactone (16) and (11*S*)-3α-(Benzoyloxy)-1β-hydroxyeudesmano-13,6α-lactone (17). To a stirred solution of **15** (57 mg, 0.15 mmol) in dimethoxyethane (3 mL) under N_2 was added 0.5 M solution of $Zn(BH_3)_2$ in dimethoxyethane (6 mL, 3 mmol). The mixture was stirred for 1 h at room temperature under N_2 and poured into a mixture of ice, saturated NaCl aqueous solution (30 mL), and 0.5 M HCl (10 mL) and filtered. The filtrate was extracted with ethyl acetate (20 mL, 5 mL × 2). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (20 mL) and a saturated NaCl aqueous solution (20 mL), dried (Na_2SO_4), and concentrated to give an oily material (65 mg), which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9).

The first band (R_f 0.29) gave spectroscopically pure **16** (17 mg, 30%) as a crystalline material, which was recrystallized from a mixture of ether and chloroform to give colorless prisms: mp 274–276 °C; IR (KBr) 3475, 1778, 1692, 1602, 1583, 737, 717 cm^{-1}; NMR ($CDCl_3$) δ 1.00 (3 H, s, C_{10}-CH_3), 1.18 (3 H, d, J = 6.0 Hz, C_4-CH_3), 1.23 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 3.40 (1 H, t, J = 3.0 Hz, C_1-H), 3.93 (1 H, t, J = 10.0 Hz, C_6-H), 5.40 (1 H, ddd, J = 3.0, 3.0, 3.0 Hz, C_3-H), 7.43–7.67 (3 H, m, aromatic H), 7.93–8.13 (2 H, m, aromatic H); MS, m/e 372 (M^+); $[\alpha]^{20}_D$ + 5.3° (c 0.85, $CHCl_3$).

The second band (R_f 0.14) gave **17** (38 mg, 66%) as an oil: IR ($CHCl_3$) 3475, 1768, 1710, 1600, 1265 cm^{-1}; NMR ($CDCl_3$) δ 0.98 (3 H, s, C_{10}-CH_3), 1.13 (3 H, d, J = 6.0 Hz, C_4-CH_3), 1.22 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 3.70 (1 H, dd, J = 5.5, 12.0 Hz, C_1-H), 3.93 (1 H, t, J = ca. 10 Hz, C_6-H), 5.23 (1 H, ddd, J = 3.0, 3.0, 3.0 Hz, C_3-H), 7.40–7.70 (3 H, m, aromatic H), 7.90–8.17 (2 H, m, aromatic H); MS, m/e 372 (M^+).

Oxidation of 16. Chromic anhydride (340 mg, 3.4 mmol) was added in small portions into a mixture of dry pyridine (550 μL, 6.80 mmol) and dry methylene chloride (4 mL) at 0 °C and the mixture was stirred for 10 min. Then **16** (64 mg, 0.17 mmol) dissolved in dry methylene chloride (2 mL) was added to the mixture. The mixture was stirred at 0 °C for 6 h and then allowed to stand at room temperature overnight. Methylene chloride (20 mL) was added, and the precipitate was filtered. The filtrate was washed successively with saturated $NaHCO_3$ aqueous solution (20 mL × 3), 2 M HCl (20 mL × 3), and saturated NaCl aqueous solution, dried (Na_2SO_4 + silica gel, 1 g), and concentrated to give spectroscopically pure **15** (60 mg, 94%) as a crystalline material.

(11*S*)-3α-(Benzoyloxy)-1β-(mesyloxy)eudesmano-13,6α-lactone (18). To a stirred solution of **17** (74 mg, 0.20 mmol) in anhydrous pyridine (1 mL) was added methanesulfonyl chloride (45 μL, 0.6 mmol). The mixture was allowed to stand at room temperature for 2.5 h, poured into a saturated NaCl aqueous solution (20 mL) and extracted with ethyl acetate (10 mL × 2). The combined extracts were washed successively with 2 M HCl (10 mL) and a saturated NaCl aqueous solution (100 mL × 3), dried (Na_2SO_4), and concentrated to give an oil (92 mg). This was then purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9). The R_f band at 0.38 gave **18** (82 mg, 91%) as an oil: IR ($CHCl_3$) 1768, 1710, 1330 cm^{-1}; NMR ($CDCl_3$) δ 1.08 (3 H, s, C_{10}-CH_3), 1.15 (3 H, d, J = 7.5 Hz, C_4-Me), 1.23 (3 H, d, J = 6.5 Hz, C_{11}-Me), 2.96 (3 H, s, OSO_2CH_3), 3.93 (1 H, t, J = ca. 10 Hz, C_6-H), 4.80 (1 H, dd, J = 5.5, 11.5 Hz, C_1-H), 5.33 (1 H, ddd, J = 3.0, 3.0, 3.0 Hz, C_3-H), 7.43–7.67 (3 H, m, aromatic H), 7.93–8.13 (2 H, m, aromatic H); MS, m/e 450 (M^+).

Solvolysis Reaction of 18. Formation of (11*S*)-3α-(Benzoyloxy)-4β*H*-guai-1(10)-eno-13,6α-lactone (19) and (11*S*)-3α-(Benzoyloxy)-4β*H*-guai-10(14)-eno-13,6α-lactone (20). A mixture of **18** (154 mg, 0.34 mmol) and 0.5 M potassium acetate in acetic acid (7 mL) was stirred at the refluxing temperature for 21 h under N_2, cooled, poured into a saturated NaCl aqueous solution (40 mL), and extracted with ethyl acetate (30 mL, 20 mL, 10 mL). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution (50 mL × 3) and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude material. This was then chromatographed over silica gel (Merck, finner than 230 mesh, 7.5 g). The fractions that were eluted with a mixture of chloroform and carbon tetrachloride (1:1) gave a mixture of **19** and **20** (87 mg, 72% ca. 2:1). The fractions that were eluted with ethyl acetate gave 20 mg of oily material. This was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9) to give recovered **18** (12 mg, 8%).

In another experiment was obtained 161 mg of an oily crude product starting from 181 mg (0.40 mmol) of **18** by the analogous procedure mentioned above. This was subsequently chromatographed over silica gel (Merck, finner than 230 mesh, 8 g) pregnant with 10% $AgNO_3$ and eluted with a 1:1 mixture of chloroform and carbon tetrachloride.

The first fraction gave spectroscopically pure **19** (25 mg), which was recrystallized from a mixture of ether and hexane to give colorless needles: mp 80–81 °C; IR (KBr) 1772, 1708, 1600 cm^{-1}; NMR ($CDCl_3$) δ 1.25 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.31 (3 H, d, J = 7.0 Hz, C_4-CH_3), 1.72 (3 H, d, J = 1.8 Hz, C_{10}-CH_3), 3.68 (1 H, t, J = 10.0 Hz, C_6-H), 5.38 (1 H, ddd, J = 3.2, 3.2, 3.2 Hz, C_3-H), 7.31–7.66 (3 H, m, aromatic H), 7.95–8.07 (2 H, m, aromatic H).

Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.50; H, 7.66.

The second fraction gave a mixture of **19** and **20** (50 mg).

The third fraction gave spectroscopically pure **20** (26 mg), which was recrystallized from a mixture of ether and hexane to give colorless needles: mp 120–121 °C; IR (KBr) 1760, 1724, 1634, 1602, 886 cm^{-1}; NMR ($CDCl_3$) δ 1.25 (6 H, d, J = 6.5 Hz, C_4, C_{11}-CH_3), 3.18 (1 H, ddd, J = ca. 9, 9, 9 Hz, C_1-H), 3.91 (1 H, t, J = 9.5 Hz, C_6-H), 4.84 and 4.94 (each, 1 H, m, =CH_2), 5.49 (1 H, ddd, J = 2.2, 2.2, 2.2 Hz, C_3-H), 7.31–7.66 (3 H, m, aromatic H), 7.96–8.09 (2 H, m, aromatic H); MS, m/e 354 (M^+); $[\alpha]^{20}_D$ −32.9° (c 1.38, $CHCl_3$).

Epoxidation of a Mixture of 19 and 20 by Adding Excess *m*-Chloroperoxybenzoic Acid. Formation of (11*S*)-3α-(Benzoyloxy)-1β,10β-epoxy-4β*H*-guaiano-13,6α-lactone (21), (11*S*)-3α-(Benzoyloxy)-1α,10α-epoxy-4β*H*-guaiano-13,6α-lactone (22), and (11*S*)-3α-(Benzoyloxy)-10α,14-epoxy-4β*H*-guaiano-13,6α-lactone (23). A mixture of **19** and **20** (61 mg, 0.17 mmol), which was obtained by the solvolysis reaction of **18**, was allowed to stand with *m*-chloroperoxybenzoic acid (61 mg, purity 80%, 0.28 mmol) in dichloromethane at room temperature for 72 h. The mixture was then poured into the stirred aqueous solution of KI and extracted with ethyl acetate (15 mL × 4). The combined extracts were washed successively with 0.2 M $Na_2S_2O_3$ aqueous solution, a saturated $NaHCO_3$ aqueous solution, and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give 60 mg of an oily crude product, which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOH–$CHCl_3$, 1:9).

The first band (R_f 0.41) gave **21** (19 mg, 30%) as an oil: IR ($CHCl_3$) 1770, 1713, 1268 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20 (3 H, d, J = 6.7 Hz, C_{11}-CH_3), 1.30 (3 H, s, C_{10}-CH_3), 1.30 (3 H, d, J = 7.8 Hz, C_4-CH_3), 3.97 (1 H, t, J = 9.5 Hz, C_6-H), 5.46 (1 H, ddd, J = 3.5, 5.1, 5.1 Hz, C_3-H), 7.32–7.64 (3 H, m, aromatic H), 7.92–8.07 (2 H, m, aromatic H); ^{13}C NMR ($CDCl_3$) δ 12.5 (q), 14.6 (q), 23.2 (t), 23.6 (q), 33.5 (t), 40.6 (t), 41.2 (d), 43.6 (d), 49.8 (d), 53.7 (d), 63.0 (s), 71.3 (s), 76.2 (d), 83.8 (d), 128.4 (d), 129.5 (d), 130.3 (s), 133.1 (d) 166.1 (s), 178.7 (s); MS, m/e 370 (M^+); $[\alpha]^{20}_D$ −43.7° (c 0.98, $CHCl_3$).

The second band (R_f 0.33) gave spectroscopically pure **22** (24 mg, 38%) as a crystalline material, which was recrystallized from a mixture of ether and chloroform to give colorless prisms: mp 178–179 °C; IR ($CHCl_3$) 1772, 1710, 1268 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.27 (3 H, d, J = 6.5 Hz, C_4-CH_3), 1.35 (3 H, s, C_{10}-CH_3), 3.78 (1 H, dd, J = 9.5, 11.5 Hz, C_6-H), 5.48 (1 H, ddd, J = 2.5, 5.3, 5.5 Hz, C_3-H), 7.33–7.64 (3 H, m, aromatic H), 7.95–8.13 (2 H, m, aromatic H); ^{13}C NMR ($CDCl_3$) δ 12.5 (q), 15.2 (q), 20.9 (q), 25.0 (t), 38.0 (t), 38.1 (t), 42.2 (d), 42.2 (d), 54.1 (d), 55.0 (d), 61.5 (s), 71.4 (s), 76.3 (d), 84.6 (d), 128.4 (d), 129.7 (d), 130.3 (s), 133.0 (d), 162.2 (s), 177.8 (s); MS, m/e 370 (M^+); $[\alpha]^{20}_D$ −25.1° (c 1.12, $CHCl_3$).

The third band (R_f 0.23) gave spectroscopically pure **23** (13 mg, 20%) as a crystalline material, which was recrystallized from ether and chloroform to give colorless plates: mp 202–203 °C; IR ($CHCl_3$) 1765, 1710, 1268, 1600, 1582 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.27 (3 H, d, J = 6.5 Hz, C_4-CH_3), 1.89 (1 H, dd, J = 1.2, 8.7 Hz, C_2-H), 2.58 (1 H, dd, J = 1.0, 4.0 Hz, C_{14}-H_a), 2.74 (1 H, dd, J = 1.7, 4.0 Hz, C_{14}-H_b), 3.04 (1 H, ddd, J = 8.7, 8.7, 8.7 Hz, C_1-H), 4.06 (1 H, dd, J = 9.0, 9.5 Hz, C_6-H), 5.38 (1 H, ddd, J = 1.2, 3.0, 3.0 Hz, C_3-H), 7.33–7.63 (3 H, m, aromatic H), 7.94–8.05 (2 H, m, aromatic H); MS, m/e 370 (M^+); $[\alpha]^{20}_D$ −36.7° (c 0.83, $CHCl_3$).

Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08. Found: C, 71.41; H, 7.25.

Epoxidation of a Mixture of 19 and 20 with 0.5 Molar Equiv of *m*-Chloroperoxybenzoic Acid. Selective Epoxidation of 19 in a Mixture of 19 and 20. A mixture of **19** and **20** (569 mg, 1.61 mmol), which was obtained by the solvolytic rearrangement of **18**, was allowed to stand with *m*-chloroperoxybenzoic acid (ca. 80% purity, 173 mg, ca. 0.8 mmol) in dichloromethane (19 mL) at −1 °C for 22 h. The mixture was then poured into the stirred aqueous solution of a mixture of KI and NaCl and extracted with ethyl acetate (100 mL × 4). The combined extracts were washed successively with 0.2 M $Na_2S_2O_3$ aqueous solution (60 mL × 2), a saturated $NaHCO_3$ aqueous solution (60 mL × 2), and a saturated NaCl aqueous solution (60 mL × 2), dried (Na_2SO_4), and concentrated to give 621 mg of an oily crude product, which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9).

The first band (R_f 0.52) gave **20** (225 mg, 40%). The second band (R_f 0.41) gave **21** (131 mg, 22%). The third band (R_f 0.33) gave **22** (174 mg, 29%). The fourth band (R_f 0.23) gave **23** (18 mg, 3%).

(11*S*)-1β,10β-Epoxy-3α-hydroxy-4β*H*-guaiano-13,6α-lactone (24). A mixture of **21** (34.9 mg, 0.094 mmol), 1 M K_2CO_3 aqueous solution (1 mL), and methanol (1 mL) was refluxed for 2.5 h under N_2 and then concentrated under reduced pressure. The residue was poured into a saturated NaCl aqueous solution and extracted with ethyl acetate (10 mL × 3). The aqueous layer was neutralized with 2 M HCl and further extracted with ethyl acetate (10 mL × 7). The combined extracts were washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give **24** (19.1 mg, 76%) as an oily material: IR ($CHCl_3$) 3590, 1768 cm^{-1}; NMR ($CDCl_3$) δ 1.16 (6 H, d, J = 6.5 Hz, C_4-, C_{11}-CH_3), 1.31 (3 H, s, C_{10}-CH_3), 3.93 (1 H, t, J = 10.0 Hz, C_6-H), 4.13–4.37 (1 H, m, C_3-H); MS, m/e 266 (M^+).

(11*S*)-1β,10β-Epoxy-3α-(mesyloxy)-4β*H*-guaiano-13,6α-lactone (25). To a solution of **24** (16.0 mg, 0.060 mmol) in anhydrous pyridine (1 mL) was added methanesulfonyl chloride (20 μL, 0.256 mmol). The mixture was allowed to stand at room temperature for 1 h and 15 min, poured into a saturated NaCl aqueous solution (10 mL), and extracted with ethyl acetate (10 mL × 2). The combined extracts were washed successively with 2 M HCl (10 ml) and a saturated NaCl aqueous solution (50 mL × 3), dried (Na_2SO_4), and concentrated to give **25** as a crystalline material (17.4 mg, 84%): NMR ($CDCl_3$) δ 1.18 (3 H, d, J = 7.0 Hz, C_{11}-CH_3), 1.31 (3 H, s, C_{10}-CH_3), 1.32 (3 H, d, J = 6.0 Hz, C_4-CH_3), 3.00 (3 H, s, CH_3SO_3), 3.89 (1 H, br t, J = 9.0 Hz, C_6-H), 5.10 (1 H, ddd, J = 2.0, 5.0, 5.0 Hz, C_3-H).

Arborescin (2). A mixture of **25** (17.4 mg, 0.051 mmol), Li_2CO_3 (9.7 mg, 0.131 mmol), and LiBr (8.5 mg, 0.098 mmol) in anhydrous DMF (1 mL) was stirred at 118–129 °C (bath temperature) for 2 h under N_2, cooled, poured into a saturated NaCl aqueous solution (10 mL), and extracted with ethyl acetate (10 mL × 2). The combined extracts were washed successively with 2 M HCl (10 mL) and a saturated NaCl aqueous solution (50 mL × 3), dried, and concentrated to give a crude oily product (12.2 mg), which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9). The band whose R_f value was 0.55 gave spectroscopically pure **2** (6.1 mg, 49%) as a crystalline material, which was recrystallized from a mixture of chloroform and ether to give colorles prisms, mp 140 °C (lit. mp[14,15] 145 °C, 140 °C). This material was identical with natural arborescin in NMR ($CDCl_3$, 60 MHz) spectra[8] and optical rotation.[14]

(11*S*)-1α,10α-Epoxy-3α-hydroxy-4β*H*-guaiano-13,6α-lactone (26). A mixture of **22** (31 mg, 0.084 mmol), 1 M K_2CO_3 aqueous solution (1 mL), and methanol (1 mL) was refluxed for 2.5 h under N_2 and then concentrated under reduced pressure. The residue was poured into a mixture of 2 M HCl (1 mL) and a saturated NaCl aqueous solution (10 mL) and extracted with ethyl acetate (5 mL × 6). The combined extracts were washed with a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily crude product (28 mg), which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9). The band whose R_f value was 0.073 gave spectroscopically pure **26** (18 mg, 77%) as an oily material: IR ($CHCl_3$) 3620, 1765 cm^{-1}; NMR ($CDCl_3$) δ 1.20 (3 H, d, J = 6.5 Hz), 1.21 (3 H, d, J = 6.5 Hz), 1.33 (3 H, s, C_{10}-CH_3), 3.73 (1 H, dd, J = 9.0, 10.0 Hz, C_6-H), 4.03–4.37 (1 H, m, C_3-H).

(11*S*)-1α,10α-Epoxy-3α-(mesyloxy)-4β*H*-guaiano-13,6α-lactone (27). To a solution of **26** (15.0 mg, 0.056 mmol) in anhydrous pyridine (1 mL) was added methanesulfonyl chloride (20.0 μL, 0.256 mmol). The mixture was allowed to stand at room temperature for 20 h, poured into a saturated NaCl aqueous solution (10 mL), and extracted with ethyl acetate (10 mL × 2). The combined extracts were washed successively with 2 M HCl (10 mL) and a saturated NaCl aqueous solution (50 mL × 3), dried (Na_2SO_4), and concentrated to give **27** (19.4 mg, 100%) as an oily material: NMR ($CDCl_3$) δ 1.21 (3 H, d, J = 6.5 Hz), 1.27 (3 H, d, J = 6.5 Hz), 1.35 (3 H, s, C_{10}-CH_3), 3.12 (3 H, s, CH_3SO_3), 3.77 (1 H, d, J = 10.0 Hz, C_6-H), 5.13 (1 H, m, C_3-H).

(11*S*)-1α,10α-Epoxyguai-3-eno-13,6α-lactone (1,10-Epiarborescin) (3) and (11*S*)-1α-Hydroxyguaia-3,10(14)-dieno-13,6α-lactone (28). A mixture of **27** (19.4 mg, 0.056 mmol), Li_2CO_3 (10.4 mg, 0.141 mmol), LiBr (7.6 mg, 0.087 mmol) in anhydrous DMF (1 mL) was stirred at 118–135 °C (bath temperature) for 3 h under N_2, cooled, poured into a saturated NaCl aqueous solution (10 mL), and extracted with ethyl acetate (10 mL × 2). The combined extracts were washed successively with 2 M HCl (10 mL) and a saturated NaCl aqueous solution (50 mL × 3), dried, and concentrated to give a crude oily product (16.7 mg), which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9). The first band (R_f 0.52) gave **3** (9.0 mg, 64%); NMR ($CDCl_3$) δ 1.23 (3 H, d, J = 6.5 Hz, C_{11}-CH_3), 1.34 (3 H, s,

C_{10}-CH_3), 1.95 (3 H, m, $W_{h/2}$ = 1.2 Hz, C_4-CH_3), 2.54 (1 H, dm, J = 11.0 Hz, C_5-H), 3.77 (1 H, dd, J = 9.5, 11.0 Hz, C_6-H), 5.57 (1 H, m, $W_{h/2}$ = 6.8 Hz, C_3-H); $[\alpha]^{20}_D$ + 38.7° (c 0.81, $CHCl_3$). The second band (R_f 0.24) gave **28** (4.3 mg, 31%): IR ($CHCl_3$) 3590, 1762, 1635 cm^{-1}; NMR ($CDCl_3$) δ 1.23 (3 H, d, J = 6.0 Hz, C_{11}-CH_3), 1.89 (3 H, br s, C_4-CH_3), 3.83 (1 H, t, J = 10.0 Hz, C_6-H), 5.03 (1 H, br s, C_{14}-H_a), 5.13 (1 H, br s, C_{14}-H_b), 5.53 (1 H, m, C_3-H).

In another experiment a mixture of **27** (18 mg, 0.052 mmol) Li_2CO_3 (18 mg, 0.243 mmol), and LiBr (17 mg, 0.195 mmol) in anhydrous DMF (1 mL) was stirred at the refluxing temperature for 3 h under N_2 and then treated as the above-mentioned manner to give 2.5 mg (19%) of **3** and 6 mg (45%) of **28**.

(11*S*)-10β-Hydroxy-3-oxo-4β*H*-guai-1-eno-13,6α-lactone (29). Chromic anhydride (74 mg, 0.74 mmol) was added in small portions to a mixture of anhydrous pyridine (115 mg, 118 μL, 1.47 mmol) and methylene chloride (1 mL). Then **24** (9.8 mg, 0.037 mmol) dissolved in methylene chloride (1 mL) was added into the mixture, which was stirred at room temperature for 14 h and filtered through Celite. The filtrate was diluted with ethyl acetate, washed successively with a saturated $NaHCO_3$ aqueous solution, 2 M HCl, and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily material (6.6 mg). TLC of silica gel (Merck GF_{254}, thickness 0.25 mm) was impregnated with the chloroform solution of this oxidation product, allowed to stand at room temperature for 43 h, and then developed by dipping in a mixture of ethyl acetate and chloroform (1:1). The black band monitored by an UV lamp was collected from TLC and extracted with acetone to give spectroscopically pure **29** (2.9 mg, 30%), which was recrystallized from ethanol to give colorless cubes: mp 189–190 °C; IR (KBr) 3475, 1760, 1693, 1600 cm^{-1}; NMR ($CDCl_3$) δ 1.26 (3 H, d, J = 6.7 Hz, C_{11}-CH_3), 1.28 (3 H, d, J = 7.3 Hz, C_4-CH_3), 1.54 (3 H, s, C_{10}-CH_3), 2.65 (1 H, ddd, J = 1.5, 2.9, 10.8 Hz, C_5-H), 3.90 (1 H, dd, J = 9.5, 10.8 Hz, C_6-H), 6.38 (1 H, d, J = 1.5 Hz, C_2-H); MS, m/e 264 (M^+).

(11*S*)-10α-Hydroxy-3-oxo-4β*H*-guai-1-eno-13,6α-lactone (30). Chromic anhydride (228 mg, 2.28 mmol) was added in small portions to a mixture of anhydrous pyridine (369 μL, 4.56 mmol) and methylene chloride (1.5 mL). Then **26** (30.1 mg, 0.114 mmol) dissolved in methylene chloride (1.5 mL) was added to the mixture at 0 °C. The mixture was stirred at 0 °C for 5.6 h and then at room temperature for 20 min, diluted with ethyl acetate, and filtered through Celite. The filtrate was washed successively with a saturated $NaHCO_3$ aqueous solution, 2 M HCl, and a saturated NaCl aqueous solution, dried (Na_2SO_4), and concentrated to give an oily material (20 mg). The column chromatography of silica gel (Merck, finner than 230 mesh, 1.5 g) was impregnated with the chloroform solution of this oxidation product, allowed to stand at room temperature for 68 h, and then eluted with chloroform to give **30** (16.4 mg, 54%) as an oily material: IR ($CHCl_3$) 1770, 1700, 1600 cm^{-1}; NMR ($CDCl_3$) δ 1.26 (3 H, d, J = 6.2 Hz, C_{11}-CH_3), 1.26 (3 H, d, J = 7.5 Hz, C_4-CH_3), 1.59 (3 H, s, C_{10}-CH_3), 2.49 (1 H, dq, J = 2.4, 7.5 Hz, C_4-H), 2.95 (1 H, ddd, J = 1.7, 2.4, 10.3 Hz, C_5-H), 3.69 (1 H, t, J = 10.3 Hz, C_6-H), 6.10 (1 H, d, J = 1.7 Hz, C_2-H).

(11*S*)-3α-Hydroxy-4β*H*-guai-10(14)-en-13,6α-lactone (31). A mixture of **20** (42 mg, 0.12 mmol), 1 M K_2CO_3 aqueous solution (1 mL), and methanol (3 mL) was refluxed for 3 h under N_2 and then concentrated under reduced pressure. The residue was poured into a mixture of 2 M HCl (3 mL) and a saturated NaCl aqueous solution (20 mL) and extracted with ethyl acetate (10 mL × 10). The combined extracts were washed successively with a saturated $NaHCO_3$ aqueous solution and a saturated NaCl aqueous solution (40 mL), dried (Na_2SO_4), and concentrated to give an oily crude product (32 mg), which was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9). The band whose R_f value was 0.08 gave spectroscopically pure **31** (28 mg, 95%) as an oily material: IR ($CHCl_3$) 3600, 1780, 1650 cm^{-1}; NMR ($CDCl_3$) δ 1.20 (3 H, d, J = 6.3 Hz), 1.22 (3 H, d, J = 6.8 Hz), 3.83 (1 H, t, J = 9.6 Hz, C_6-H), 4.05–4.24 (1 H, m, C_3-H), 4.77 (1 H, br s, $W_{h/2}$ = 3.3 Hz, C_{14}-H_a), 4.86 (1 H, br s, $W_{h/2}$ = 3.6 Hz, C_{14}-H_b); MS (13.6 eV), m/e 250 (M^+).

(11*S*)-3α-(Mesyloxy)-4β*H*-guai-10(14)-en-13,6α-lactone (32). A mixture of **31** (36 mg, 0.14 mmol) and methanesulfonyl chloride (56 μL, 0.72 mmol) in anhydrous pyridine (1 mL) was allowed to stand at room temperature for 27 h, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (20 mL × 5). The combined extracts were washed successively with 2 M HCl (20 mL) and a saturated NaCl aqueous solution (30 mL), dried (Na_2SO_4), and concentrated to give an oily crude product (63 mg), which was purified by TLC (silica gel GF_{254}, thickness 0.25 mm, EtOAc–$CHCl_3$, 1:9). The band whose R_f value was 0.41 gave spectroscopically pure **32** (46 mg, 97%) as an oily material: IR ($CHCl_3$) 1760, 1635, 1350 cm^{-1}; NMR ($CDCl_3$) δ 1.26 (3 H, d, J = 6.0 Hz), 1.27 (3 H, d, J = 6.6 Hz), 3.00 (3 H, s, OSO_2CH_3), 3.84 (1 H, t, J = 9.0 Hz, C_6-H), 4.76 (1 H, br s, $W_{h/2}$ = 4.5 Hz, C_{14}-H_a), 4.90 (1 H, br s, $W_{h/2}$ = 3.0 Hz, C_{14}-H_b), 4.93–5.10 (1 H, m, C_3-H); $[\alpha]^{20}_D$ −8.5° (c 0.87, $CHCl_3$).

(11*S*)-Guaia-3,10(14)-dieno-13,6α-lactone (33). A mixture of **32** (37 mg, 0.11 mmol), Li_2CO_3 (23 mg, 0.32 mmol), and LiBr (20 mg, 0.23 mmol) in anhydrous DMF (1 mL) was stirred at 110–115 °C (bath temperature) for 1.5 h under N_2, cooled, poured into a saturated NaCl aqueous solution (30 mL), and extracted with ethyl acetate (20 mL × 5). The combined extracts were washed successively with 2 M HCl (10 mL), a saturated NaCl aqueous solution (30 mL), dried (Na_2SO_4), and concentrated to give a crude oily product (29 mg). This was purified by TLC (Merck, silica gel GF_{254}, thickness 0.25 mm, $CHCl_3$–CCl_4, 1:1). The band whose R_f value was 0.36 gave spectroscopically pure **33** (19 mg, 72%) as an oily material: IR (neat) 1770, 1640 cm^{-1}; NMR (CCl_4) δ 1.16 (3 H, d, J = 6.0 Hz, C_{11}-CH_3), 1.83 (3 H, br s, $W_{h/2}$ = 5.1 Hz, C_4-CH_3), 3.85 (1 H, t, J = 9.0 Hz, C_6-H), 4.79 (2 H, br s, $W_{h/2}$ = 3.0 Hz, C_{14}-H), 5.42 (1 H, br s, $W_{h/2}$ = 5.4 Hz, C_3-H); NMR ($CDCl_3$) δ 1.23 (3 H, d, J = 6.0 Hz, C_{11}-CH_3), 1.83 (3 H, br s, $W_{h/2}$ = 5.4 Hz, C_4-CH_3), 3.10 (1 H, ddd, J = 7.0, 7.0, 7.0 Hz, C_1-H), 3.96 (1 H, t, J = 9.0 Hz, C_6-H), 4.82 (2 H, br s, $W_{h/2}$ = 5.7 Hz, C_{11}-H), 5.49 (1 H, br s, $W_{h/2}$ = 5.1 Hz, C_3-H); MS, m/e 232 (M^+).

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