the mixture was treated with 5 mL of saturated ammonium chloride, and the product was isolated by ether extraction to give 1.05 g (94%) of colorless oil.

A 4.20-g sample of the above mixture of cyanohydrins was converted to the MTM ethers **14b** and **15b** by the procedure described above for **14b**. The resulting product (5.7 g, 97%), a yellow oil, was shown to be a 65:35 mixture by gas chromatography and NMR analysis. Separation was easily effected using preparative LC to afford the previously described trans isomer **14b** (major product) and the minor cis isomer **15b**: λ_{max}^{film} 3.35, 3.42, 3.48, 4.46, 6.84, 7.24, 8.95, 9.30, 9.60, 9.94 μm; $\delta_{Me_4Si}^{CCl_4}$ 4.47 (OCH_2), 2.17 (CH_3), 1.33 (CH_3), 1.27 (CH_3).

Anal. Calcd for $C_{11}H_{19}NOS$: C, 61.95; H, 8.98; N, 6.57; S, 15.03. Found: C, 61.78; H, 8.96; N, 6.49; S, 15.27.

***trans*-2-Cyano-1,2-dimethylcyclododecyl (Methanesulfonyl)methyl Ether (16a).** The procedure described for sulfone **8a** was employed, using 0.90 g (4.5 mmol) of *m*-chloroperoxybenzoic acid and 0.45 g (1.5 mmol) of cyano ether **14a** in 25 mL of chloroform. The sulfone **16a** (0.42 g, 85% yield) was secured as white needles: mp 105–106 °C from ethyl acetate–hexane; λ_{max}^{film} 3.29, 3.47, 4.48, 7.60, 8.78, 9.01, 10.7, 13.2 μm; $\delta_{Me_4Si}^{CDCl_3}$ 4.45 (OCH_2), 2.88 (CH_3), 2.55 (CH_3), 1.45 (CH_3 and CH_2 envelope).

Anal. Calcd for $C_{17}H_{31}NO_3S$: C, 61.97; H, 9.48; N, 4.25; S, 9.73. Found: C, 62.1; H, 9.5; N, 4.1; S, 9.9.

***cis*-2-Cyano-1,2-dimethylcyclododecyl (Methanesulfonyl)methyl Ether (17a).** The procedure described for sulfone **8a** was employed, using 0.30 g (1.5 mmol) of *m*-chloroperoxybenzoic acid and 0.14 g (0.47 mmol) of cyano ether **15a** in 10 mL of chloroform. The sulfone **17a** (0.093 g, 60% yield), mp 152–153 °C from ethyl acetate–hexane, was secured as a white solid: λ_{max}^{KBr} 3.49, 4.48, 7.58, 7.64, 8.84, 9.10 μm; $\delta_{Me_4Si}^{CDCl_3}$ 4.44 (OCH_2), 2.95 (CH_3), 1.39 (CH_3 and CH_2 envelope), 1.23 (CH_3).

Anal. Calcd for $C_{17}H_{31}NO_3$: C, 61.97; H, 9.48; N, 4.25; S, 9.73. Found: C, 62.1; H, 9.5; N, 4.1; S, 9.8.

Typical Procedures for Reduction–Elimination of Cyanohydrin Derivatives. A. Lithium in Ammonia. To a stirred solution of 84 mg (12 mg-atoms) of lithium in 20 mL of liquid ammonia and 5 mL of THF was added a solution of 0.31 g (1.05 mmol) of cyano ether **14a** in 3 mL of THF. After 1 min, the solution was cooled to −78 °C with a dry ice bath and solid ammonium chloride was added to discharge the blue color. The ammonia was allowed to evaporate and the product was isolated by hexane extraction, affording 0.22 g (100%) of a colorless oil. Distillation at 90–100 °C (bath temperature) at 0.15 torr afforded 0.17 g (83%) of a 35:65 mixture of (*E*)- and (*Z*)-1,2-dimethylcyclododecene (**22** and **21**) according to gas chromatographic analysis.[16]

B. Sodium Naphthalenide in Hexamethylphosphoramide. A mixture of sodium (0.45 g, 19.6 mg-atoms) and naphthalene (2.80 g, 22.0 mmol) in 15 mL of HMPA was stirred overnight. To the resulting green solution was added 0.165 g (0.50 mmol) of cyano ether **14a** in 2 mL of HMPA. After 24 h, water and aqueous HCl were added and the product was isolated by hexane extraction. Chromatography on silica gel, using hexane as the eluant, afforded 0.081 g (83%) of (*E*)-1,2-dimethylcyclododecene (**22**).[16]

Characteristics of the Cycloalkene Products. (*E*)-1-Methylcyclododecene (20):[14] λ_{max}^{film} 3.38, 3.48, 6.88, 6.95, 7.25 μm; $\delta_{Me_4Si}^{CCl_4}$ 5.28 (H-2, t, J = 8 Hz), 2.04 (allylic CH_2's, m), 1.60 (CH_3), 1.28 (CH_2 envelope).

(*Z*)-1-Methylcyclododecene (19):[14] λ_{max}^{film} 3.40, 3.48, 6.82, 6.90, 7.25 μm; $\delta_{Me_4Si}^{CCl_4}$ 5.05 (H-2, t, J = 8 Hz), 2.05 (allylic CH_2's), 1.64 (CH_3), 1.34 (CH_2 envelope).

(*E*)-1,2-Dimethylcyclododecene (22): λ_{max}^{film} 3.40, 3.46, 6.84, 6.90, 7.25 μm; $\delta_{Me_4Si}^{CCl_4}$ 2.72–2.02 (allylic CH_2's), 1.67 (CH_3's), 1.21 (CH_2 envelope).

(*Z*)-1,2-Dimethylcyclododecene (21): λ_{max}^{film} 3.40, 3.48, 6.80, 6.91, 7.15 μm; $\delta_{Me_4Si}^{CCl_4}$ 2.17–1.75 (allylic CH_2's), 1.54 (CH_3's), 1.32 (CH_2 envelope).

Acknowledgments. We are grateful to the National Science Foundation for support of this work through a research grant (MPS75-07777).

(16) The analysis was performed by using a 6 ft × 1/8 in. column of 5% (w/w) 1:10 silver nitrate–Carbowax 20M on 80–100 mesh Chromosorb W.

Tetracyclic Analogues of the Rosane Lactones from *Eupatorium album*[1]

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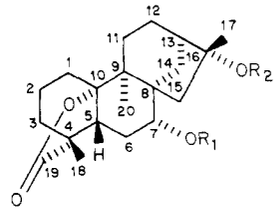
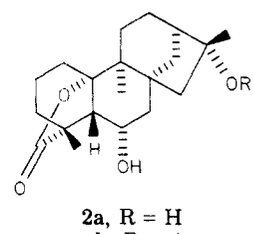
Isolation and structure determination of eupatalbin and eupatoralbin, two tetracyclic diterpenoids of a new skeletal type, from *Eupatorium album* L. are reported. Eupatalbin, details of whose structure and stereochemistry were established by X-ray crystallography, is *ent*-7β-hydroxy-9,10-friedokauran-19,10β-olide **1a**. Eupatoralbin is the *ent*-6β-hydroxy analogue **2a**. Comments are offered on the biogenesis. An earlier study (ref 2) dealt with *E. petaloideum* Britt., not *E. album*.

In an earlier article[2] we described isolation and structure determination of several new hydroxylated *ent*-kauranoic acids from what was presumed to be *Eupatorium album* L. Subsequent examination of the vouchers showed that the collection actually represented the morphologically very similar but geographically highly restricted *E. petaloideum* Britt. We now report isolation and structure determination from authentic *E. album* of eupatalbin (**1a**) and eupatoralbin (**2a**), two tetracyclic diterpenoids of a new skeletal type.[3] Eupatorin (3′,5-dihydroxy-4′,6,7-trimethoxyflavone) was also found.[5]



1a, $R_1 = R_2 = H$
b, R_1 = Ac; R_2 = H
c, $R_1 = R_2$ = Ac



2a, R = H
b, R = Ac

(1) Work at Florida State University supported in part by U.S. Public Health Service Grant CA-1312 through the National Cancer Institute.
(2) W. Herz and R. P. Sharma, *J. Org. Chem.*, 41, 1021 (1976).

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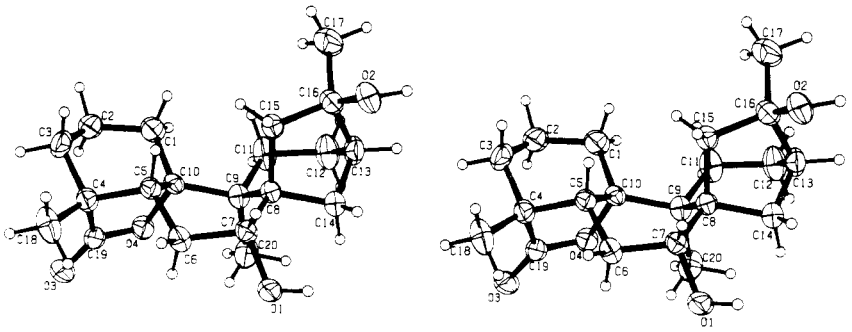
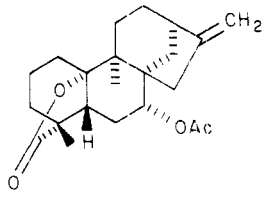


Figure 1. Stereoscopic view of eupatalbin (**1a**).

Eupatalbin, mp 237.5–239 °C, and eupatoralbin, mp 257–258 °C, were isomeric lactones (IR bands at 1750 and 1740 cm^{-1}, respectively) of formula $C_{20}H_{30}O_4$ (elemental analyses and high-resolution mass spectra), each containing three methyl groups (^1H- and ^{13}C-NMR spectra). The two other oxygen atoms of eupatalbin were present in the form of two hydroxyl groups (IR spectrum) as evidenced by formation of a monoacetate (**1b**) and a diacetate (**1c**). One of the hydroxyl groups was secondary (downfield shift, on acetylation, of a one-proton triplet from 3.85 to 4.97 ppm), the second was tertiary and under a methyl group since the only notable further change in the ^1H-NMR spectrum of the diacetate was a downfield shift of one of the three methyl signals of **1a** from 1.40 to 1.62 ppm. The environment of the tertiary hydroxyl was further clarified by dehydration of **1b** ($POCl_3$–pyridine), which resulted in a mixture of double bond isomers **3** and **4**. The signal of



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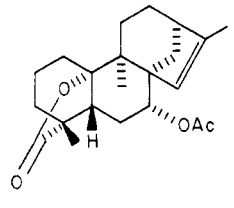

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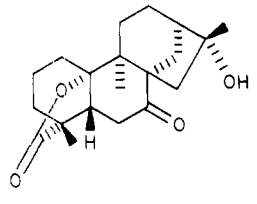
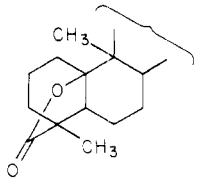


5

the vinylic proton of **4** exhibited only allylic coupling to the vinyl methyl, hence the corresponding carbon atom was attached to a quaternary center.

Oxidation of **1a** with Jones reagent yielded a hydroxy ketolactone **5** (new IR band at 1690 cm^{-1}). The ^{13}C-NMR spectra of **1a** and **1b** (Table I) exhibited one doublet and two singlets in the range characteristic of C–O, whereas that of **5** contained only two singlets near 80 and 88 ppm and a new C–O signal near 211 ppm. Therefore the lactone oxygen was attached to a tertiary center.

A structure incorporating partial structure A, fused to



A

two additional rings, would account for the above facts and the empirical formula. The hitherto unknown friedokaurane, friedophyllocladane, or friedoatisane with a tertiary hydroxyl on C-16 appeared likely possiblities. If so, multiplicity and coupling consonants of the proton under the secondary hydroxyl group required attachment of the hydroxyl to C-1, C-3, C-7, or C-11. To decide between the various possibilities and to establish the relative stereochemistry, an X-ray analysis was undertaken.

Crystal data for eupatalbin are listed in the Experimental Section. Figure 1 is a stereoscopic drawing of the molecule which also represents the absolute configuration (vide infra), i.e., eupatalbin is an *ent*-9,10-friedokauran-19,10β-olide.[6] Ring B is a somewhat distorted boat, the secondary hydroxyl group is attached to C-7 and α, and the tertiary hydroxyl group is also α. Tables II–IV containing final atomic and final anisotropic thermal parameters, bond lengths, bond angles, and torsion angles are available as supplementary material.

The absolute configuration was deduced from the CD curve of **5**, which exhibited a strong positive Cotton effect for the ketone ($[\theta]_{290}$ +8730) and a negative effect for the lactone group ($[\theta]_{210}$–7700). The signs are reversed from those displayed by rosenonolactone **8a** of enantiomeric absolute configuration[7] and are in accordance with the signs predicted on the basis of the octant and the lactone sector rules[8] using the model of Figure 1.

With the structure of eupatalbin securely established as **1a**, it was possible to attack the problem of the closely related minor isomer eupatoralbin. This also contained a secondary and a tertiary hydroxyl group as revealed by a ^1H-NMR multiplet at 4.17 ppm whose appearance indicated spin coupling to at least three adjacent protons, a ^{13}C-NMR doublet at 61.26 ppm and a singlet at 79.07 ppm in addition to the singlet at 86.83 ppm representing the terminus of the lactone function. However, in sharp contrast to **1a** acetylation of eupatoralbin was very sluggish, yielding only a small amount of a monoacetate

(3) *E. album* L. var. *album* is found in the coastal plain, the Piedmont, and the mountain provinces of the southeastern U. S., whereas *E. petaloideum* Britt. is restricted to five counties in North Florida.[4]

(4) V. I. Sullivan, *Can. J. Bot.*, **54**, 2907 (1976); V. I. Sullivan, Investigation of the Breeding System, Formation and Polyploids and the Reticulate Pattern of Hybridization in N.A. *Eupatorium*, Ph.D. Dissertation, Florida State University, August 1972.

(5) No sesquiterpene lactones or diterpenes were reported from a previous examination of *E. album*: F. Bohlmann, P. K. Mahanta, A. Suwita, A. Suwita, A. A. Natu, C. Zdero, W. Dorner, D. Ehlers, and M. Grenz, *Phytochemistry*, **16**, 1973 (1977). Identification of some of the species studied in this reference requires correction: W. Herz, R. Murari, and S. Govindan, *Phytochemistry*, in press.

(6) For nomenclature and numbering see the proposal by J. W. Rowe, "The Common and Systematic Nomenclature of Cyclic Diterpenes", Third revision, October 1968 and Addenda, February 1969.

(7) C. G. DeGrazia, W. Klyne, P. M. Scopes, D. R. Sparrow, and W. B. Whalley, *J. Chem. Soc.*, 896 (1966).

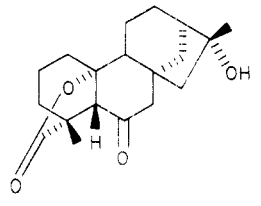
(8) P. M. Scopes, *Fortschr. Chem., Org. Naturst.*, **32**, 167 (1975).

Table I. ^{13}C-NMR Spectra[a]

	1a	1b[b]	5	2a	6	7
C-1	31.16 t	31.16 t	32.47 t	30.40 t	29.13 t	25.08 t
C-2	20.15 t	20.38 t	20.03 t	20.10 t	19.69 t	18.35 t
C-3	35.51 t	35.82 t	35.31 t	34.96 t	34.68 t	36.06 t
C-4	47.60	48.27	47.55	44.89[c]	45.73[d]	46.95[c]
C-5	48.15 d	48.87 d	48.13 d	53.47 d	61.29 d	135.15
C-6	29.57 t	26.78 t	29.08 t	61.21 d	208.84	195.37
C-7	74.43 d	77.79 d	211.22	44.62 t	50.48 t	50.39 t[d]
C-8	51.39	49.99	59.18	45.38[c]	47.46[d]	c,f
C-9	41.59	42.14	42.42	41.00	42.85	42.68
C-10	88.02	87.84	87.01	86.83	90.78	166.22
C-11	24.01 t	24.13 t	23.55 t	24.24 t	23.43 t	23.78 t
C-12	33.59 t[c]	34.78 t[c]	33.66 t[c]	34.19 t	31.19 t[c]	28.81 t
C-13	45.65 d	46.36 d	46.02 d	46.22 d	46.65 d	46.52 d
C-14	32.70 t[c]	33.42 t[c]	32.77 t[c]	40.32 d	38.31 t	37.04 t
C-15	53.14 t	53.52 t	48.65 t	53.93 t	52.36 t	47.36 t[d]
C-16	78.66	80.20	77.80	79.07	77.11	77.92
C-17	23.63 q	23.62 q	23.77 q	23.59 q	23.51 q	23.56 q
C-18	17.07 q	17.24 q	16.75 q	16.83 q	18.04 q[e]	24.72 q
C-19	179.29	179.69	178.29	179.58	177.50	178.75
C-20	19.69 q	19.80 q	20.03 q	17.84 q	17.86 q[e]	19.23 q
C-21		170.46				
C-22		21.14 q				

[a] Run in Me_2SO-d_6 at 67.90 MHz. Unmarked signals are singlets. [b] Run in $CDCl_3$. [c,d,e] Assignments may be interchangeable. [f] Not visible or obscured by solvent signals.

2b derived from the tertiary alcohol. On the other hand oxidation proceeded smoothly to give a product **6** whose



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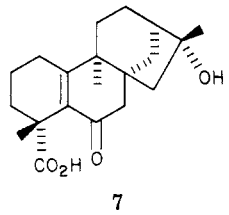

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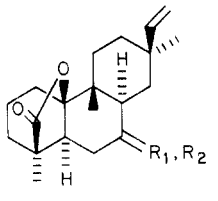


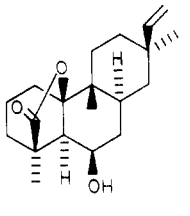
8a, R_1, R_2 = =O
b, R_1 = β-OH; R_2 = α-H

IR spectrum displayed a new band at 1710 cm^{-1} indicative of a ketone group in a six-membered ring.

The environment of the new carbonyl group in **6** and hence that of the secondary alcohol in **2a** was apparent from the ^{1}H-NMR spectrum which contained two signals newly emerged from the methylene and methinyl envelope, one a two-proton AB quartet centered at 2.45 ppm (J = 15 Hz) and the other a sharp singlet at 2.55 ppm. Hence the carbonyl group was located at either C-6 or C-12 if the carbon skeletons of eupatalbin and eupatoralbin were identical.

That this was so and that the hydroxyl group of eupatoralbin was attached to C-6 became clear on close examination of the ^{13}C-NMR spectra (Table I). Assignments for **1a**, **1b**, and **5** are based on comparison with signals exhibited by lactones of the rosane series[9] modified, for the carbons also included in ring C, by appropriate corrections required by the presence of ring D. As a first approximation these can be obtained by comparing the ^{13}C-NMR spectra of various kauranoids[10,11] with those of tricyclic diterpenes. For example C-11 is 6 ppm downfield from the C-11 of kauranoids because of the presence of the methyl group on C-9 (β effect) but upfield from C-11 of the rosane lactones because of the γ-gauche effects of C-15 and C-16. C-7 is deshielded relative to C-7 of rosenololactone (**8b**)[9] because of the two-carbon bridge attached to C-8, the effects of acetylation (in **1b**) and oxidation (in **5**) on the shifts of the α and β carbons being predictable.[12,13] The upfield shift of C-15 relative to the C-15 of *ent*-kauran-16β-ol (~5 ppm)[10] may be due to the change in stereochemistry and hence in conformation of ring B, which places that carbon in the flagpole position of a somewhat distorted boat since the shift does not depend on location of the hydroxyl group in ring B (compare **1a** with **2a**) and is enhanced to ca. 10 ppm on oxidation to **5**. The doublet at 48.15 ppm is assigned to C-5 rather than to C-13 by comparison with C-5 of **8a** and **8b**, an assignment supported by the invariance of the C-13 signal throughout the series.

Comparison of the spectra of **1a** and **2a** indicated significant changes in the signals attributable to C-3 through C-8 and to C-14 which parallel those in going from **8b** to **9**.[9] Hence the hydroxyl of eupatoralbin could be placed



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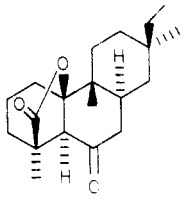

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on C-6. The large downfield shift of C-14 (ca. 8 ppm) can be ascribed to removal of a γ-gauche interaction present

(9) B. Dockerill, J. R. Hanson, and M. Siverns, *Phytochemistry*, **17**, 572 (1978).

(10) J. R. Hanson, M. Siverns, F. Piozzi, and G. Savona, *J. Chem. Soc., Perkin Trans. 1*, 114 (1976).

(11) For other leading references see F. W. Wehrli and T. Nishida, *Fortschr. Chem., Org. Naturst.*, **36**, 1 (1979).

(12) Just as in the case of **8b** the C-8 signal experiences a downfield shift of ~8 ppm on oxidation of **1a** to **5**, while the C-6 signal remains essentially constant.

(13) E. Wenkert, *Chem. Ind. (London)* 282 (1955).

in **1a** and **8b**. The ^{13}C-NMR spectrum of **6** is in agreement with this deduction as the signals attributed to C-5 and C-7 exhibited the expected paramagnetic shifts. Finally chemical proof for formula **6** of the ketone and hence formula **2a** for eupatoralbin exclusive of stereochemistry was provided by the discovery that preparative TLC of **6** over silica gel resulted in partial isomerization to an α,β-unsaturated keto acid which on the basis of spectroscopic evidence (IR bands at 1690 and 1660 cm^{-1}, UV λ_{max} 251 nm, ^{13}C-NMR spectrum in Table I) had to be formulated as **7**. Isomerization of **2a** to **7** also occurred on prolonged standing.

The stereochemistry of the hydroxyl group of **2a** was established in the following manner. Conversion of **2a** to **6** results in a paramagnetic shift (~4 ppm) of the C-10 signal which must be attributed to the removal of a γ-gauche interaction. This requires that the hydroxyl be quasi-axial and α, if the absolute stereochemistry of eupatalbin and eupatoralbin were the same. The relative stereochemistry assigned to **2a** is supported by the shape of the H-6 signal whose appearance (narrowly split multiplet, $W_{1/2}$ = 12 Hz) is consonant only with quasi-equatorial orientation of H-6 (model). The absolute stereochemistry of **2** can be deduced from the CD curve of **6**, which not only exhibits a negative ketone Cotton effect in agreement with the octant rule as well as a negative lactone Cotton effect in agreement with the lactone sector rule, but is enantiomeric with the CD curve of dihydrorosonolactone (**10**).[7]

The structures of the new lactones whose tetracyclic carbon skeleton cannot be formed by the conventional proton-triggered nonstop biocyclization–methyl shift path proceeding from geranylgeranyl pyrophosphate by way of copalyl pyrophosphate[13-15] suggest that their biosynthesis involves an intermediate stage, the backbone rearrangement of an *ent*-kaurene precursor such as an *ent*-9(11)-kaurene, *ent*-9-hydroxykaurane, or *ent*-11-hydroxykaurane. Kauranoids of this type appear to be widely distributed in Heliantheae;[16] especially noteworthy is the occurrence of *ent*-11-hydroxykauran-19-oic acids in the closely related *E. petaloideum*.[2] However even then the circumstance that the lactone ring lies on the same face as the methyl group which has migrated from C-10 to C-9 suggests that the processes of methyl migration and lactonization are not concerted, just as in the case of the tricyclic rosane lactones. In the biosynthesis of the latter the intervention of $\Delta^{1(10)}$, Δ^{5}, or $\Delta^{5(10)}$ intermediates has been excluded and alternatives to account for this have been suggested.[14,15,17] Whether this is necessary in the case of **1a** and **2a** remains to be seen.[18]

Experimental Section

Isolation of Eupatalbin and Eupatoralbin. Above ground parts of *Eupatorium album* L., weight 4.9 kg, collected by Dr. R. K. Godfrey on August 31, 1968 4.5 mi N of Crystal River, Citrus Co., Florida along U.S. Route 16 (Godfrey No. 68127 on deposit in herbarium of Florida State University) was extracted with $CHCl_3$ and worked up in the usual fashion.[19] The crude gum, weight 62 g, was adsorbed on 120 g of silicic acid (Mallinckrodt, 100 mesh) and chromatographed over 750 g of the same adsorbent packed in benzene, fractions of increasing polarity being collected as follows: 1–6 (Bz and Bz–$CHCl_3$, 4:1), 7–13 (Bz–$CHCl_3$, 1:1), 14–29 ($CHCl_3$), 30–35 ($CHCl_3$–MeOH, 39:1), 36–37 ($CHCl_3$–MeOH, 19:1), and 38–40 ($CHCl_3$–MeOH, 9:1).

Fraction 15 (2.6 g) showed one major spot on TLC. Crystallization of the material from $CHCl_3$–MeOH yielded 1.03 g of eupatorin (3′,5′-dihydroxy-4′,6,7-trimethoxyflavone), mp 196–197 °C, identical in all respects with authentic material by direct comparison.

Fractions 19 and 20 were combined (weight 2.7 g) and triturated with ethyl acetate, whereupon eupatoralbin (**2a**) (0.38 g) was deposited. Recrystallization from MeOH afforded material which had: mp 257–258 °C; $[\alpha]^{22}_D$ +30.14 (*c* 0.0146, MeOH); IR bands (KBr) at 3400, 3350, and 1750 cm^{-1}; NMR signals ($CDCl_3$) at 4.17 (m, $W_{1/2}$ = 12 Hz, H-6), methyl singlets at 1.55, 1.39, and 1.32 ppm. The high-resolution mass spectrum displayed significant peaks, in addition to the moleculear ion (18.6%), at *m/e* (composition, %) 316 ($C_{20}H_{28}O_3$), 301 ($C_{19}H_{25}O_3$, 2.3%), 298 ($C_{20}H_{26}O_2$, 7.7), 291 ($C_{17}H_{23}O_4$, 38.4), 290 ($C_{19}H_{30}O_2$, 8.6), 283 ($C_{19}H_{23}O_2$, 5.4), 273 ($C_{17}H_2O_3$, 34.8), 272 ($C_{19}H_{28}O$), and 237 ($C_{14}H_{21}O_3$, base peak).

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04; molecular weight, 334.2143. Found: C, 71.84; H, 9.10; molecular weight (MS), 334.2127.

Fractions 27–31 (weight 6.4 g) showed one major spot and were combined. Recrystallization of the material from ethyl acetate–methanol yielded eupatalbin (**1a**), weight 3.26 g. A further recrystallization from MeOH raised the melting point to 237.5–239 °C: $[\alpha]^{22}_D$ −40.24° (*c* 0.0418, MeOH); IR bands (KBr) at 3500, 3440, and 1750 cm^{-1}; NMR signals ($CDCl_3$) at 3.85 (t, J = 9 Hz, H-7), methyl singlets at 1.40, 1.30, and 1.13 ppm. The high-resolution mass spectrum had significant peaks in addition to the molecular ion (80%) at *m/e* 316 ($C_{20}H_{28}O_3$, 58.6), 298 ($C_{20}H_{26}O_2$, 18.1), 290 ($C_{19}H_{30}O_2$, 18.3), 283 ($C_{19}H_{23}O_2$, 18.1), 273 ($C_{17}H_{21}O_3$, base peak), 272 ($C_{19}H_{28}O$, 38.5).

Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04; molecular weight, 334.2143. Found: C, 71.77; H, 9.06; molecular weight (MS), 334.2148.

Acetylations. A mixture of 0.2 g of **1a**, 5 mL of acetic anhydride, and 3 mL of pyridine was allowed to stand at room temperature for 48 h and worked up as usual. Preparative TLC of the crude product ($CHCl_3$–MeOH, 47:3) furnished 0.14 g of **1b** and 0.04 g of **1c**. Monoacetate **1b**, recrystallized from $CHCl_3$–MeOH, had: mp 263–267 °C; $[\alpha]^{22}_D$ −64.41 (*c* 0.0428, $CHCl_3$); IR bands (KBr) at 3490, 1740, 1725, and 1250 cm^{-1}; NMR signals at 4.97 (dd, J = 8, 9 Hz, H-7), 2.07 (Ac), and methyl singlets at 1.39, 1.29, and 1.11 ppm. Besides the molecular ion (1.8%) the high-resolution mass spectrum exhibited significant peaks at *m/e* 358 ($C_{22}H_{30}O_4$, 3.2), 316 ($C_{20}H_{28}O_3$, base peak), 289 ($C_{20}H_{26}O_2$, 20), 283 ($C_{19}H_{23}O_2$, 5.3), and 272 ($C_{19}H_{28}O$, 54).

Anal. Calcd for $C_{22}H_{32}O_5$: C, 70.19; H, 8.57; O, 21,25; molecular weight, 376.2248. Found: C, 70.24; H, 8.59; O, 20.80; molecular weight (MS), 376.2245.

Diacetate **1c** melted at 147 °C and had IR bands (KBr) at 1780 and 1720 cm^{-1} (double intensity); NMR signals at 4.89 (t, J = 9 Hz, H-7), 2.05 and 1.99 (acetates), methyl singlets at 1.62, 1.29, and 1.09 ppm. The high-resolution mass spectrum did not exhibit the molecular ion; significant peaks were observed at *m/e* 358.1247 (calcd for $C_{22}H_{30}O_4$ 358.2143, 33.4), 330 ($C_{21}H_{30}O_3$, 12.9), 316 ($C_{20}H_{30}O_3$, 45.8), 314 ($C_{21}H_{30}O_2$, 16.0), 298 ($C_{20}H_{26}O_2$, base peak), 283 ($C_{19}H_{23}O_2$, 15.9), 270 ($C_{19}H_{26}O$, 23.7), 254 ($C_{19}H_{26}$, 36.8), and 238 ($C_{18}H_{23}O$, 26).

Acetylation of 40 mg of **2a** for 48 h and purification of the crude product by preparative TLC resulted in recovery of 25 mg of **2a** and isolation of 8 mg of monoacetate **2b**, which decomposed gradually above 120 °C: IR bands (KBr) at 3480, 1760, and 1725 cm^{-1}; NMR signals at 4.16 (m, $W_{1/2}$ = 12 Hz, H-6), 1.99 (acetate), and methyl singlets at 1.62, 1.40 and 1.31 ppm. Significant peaks in the high-resolution mass spectrum were found at *m/e* 376 (M^+, 2%), 332 ($C_{21}H_{32}O_2$. 1.4), 316 ($C_{20}H_{28}O_3$, 47.5), 298 ($C_{20}H_{26}O_2$, 23.9), 283 ($C_{19}H_{23}O_2$, 8.1), 279 ($C_{16}H_{23}O_4$, 20.8), 273 ($C_{17}H_{21}O_3$, 53.3), 272

(14) J. R. Hanson, *Fortschr. Chem., Org. Naturst.*, **29**, 395 (1971).
(15) R. M. Coates, *Fortschr. Chem., Org. Naturst.*, **33**, 72 (1976).
(16) For some recent reports, see F. Bohlmann and C. Zdero, *Phytochemistry*, **15**, 1310 (1976); F. Bohlmann and N. Le Van, *ibid.*, **16**, 579 (1977); F. Bohlmann, P. Zitzkowski, A. Suwita, and L. Fiedler, *ibid.*, **17**, 2101 (1978).
(17) B. Dockerill and J. R. Hanson, *J. Chem. Soc., Perkin Trans. 1*, 324 (1977).
(18) **Note Added in Proof**: After acceptance of this article, we became aware of an earlier report of a friedokauranolide: Y. Caballero and F. Walls, *Bol. Inst. Quim. Univ. Nac. Auton. Mex.*, **22**, 79 (1979). The abstract in *Chem. Abstr.*, **74**, 136398w (1971), erroneously refers to this substance, zapoatlin, as a sesquiterpene lactone.
(19) W. Herz and G. Högenauer, *J. Org. Chem.*, **27**, 905 (1962).

($C_{19}H_{28}O$, 15.5), 270 ($C_{19}H_{26}O$, 6.9), 107 (C_8H_{11}, 100).

Dehydration of 1b. A solution of 10 mg of **1b** in 0.5 mL of anhydrous pyridine was mixed with 0.1 mL of $POCl_3$ under cooling, stirred at 0 °C for 15 min, and kept at room temperature for 6 h. The mixture was decomposed by ice water and extracted with $CHCl_3$. The washed and dried extract was evaporated; purification of the residue by preparative TLC ($CHCl_3$–MeOH, 19:1) gave 7 mg of a single fraction homogeneous by TLC criteria, which NMR analysis showed to be an 8:5 mixture of **3** and **4**. The major isomer **3** exhibited signals at 4.98 (t, J = 9 Hz, H-7), 4.83 and 4.78 (br, H-17a,b), 2.04 (acetate), and methyl singlets at 1.28 and 1.11 ppm. The signals of **4** appeared at 5.26 (br, H-15), 4.93 (t, J = 9 Hz, H-7), 2.03 (acetate), methyl singlets at 1.30 and 1.11 ppm.

Oxidations. (A) A solution of 0.1 g of **1a**, 15 mL of acetone, and 0.8 mL of Jones reagent was stirred at room temperature. After 15 min excess reagent was destroyed by adding 2-propanol. The mixture was diluted with water and extracted with $CHCl_3$. The washed and dried extract was evaporated and the residue was purified by preparative TLC ($CHCl_3$–MeOH 19:1) to give 90 mg of **5** which was recrystallized from $CHCl_3$–MeOH and then had: mp 249–251 °C; $[\alpha]^{22}_D$ +122.3° (c 0.0157, $CHCl_3$); CD curve $[\theta]_{290}$ +8730 (max), $[\theta]_{210}$ −7700 (min), $[\theta]_{206}$ −6980 (last reading); IR bands (KBr) 3450, 1750, and 1690 cm^{-1}; NMR signals at 1.42, 1.16 and 1.13 ppm (methyl singlets); significant peaks in the high-resolution mass spectrum at m/e 314 ($C_{20}H_{26}O_3$, 45.8), 299 ($C_{19}H_{23}O_3$, 9.1), 296 ($C_{20}H_{24}O_2$, 23.8), 289 ($C_{18}H_{25}O_3$, 32.2), 288 ($C_{19}H_{28}O_2$, 9.3), 286 ($C_{19}H_{26}O_2$, 12.1), 274 ($C_{17}H_{22}O_3$, 9.5) 271 ($C_{17}H_{19}O_3$, 28.1), 270 ($C_{19}H_{26}O$, 7.3), 268 ($C_{19}H_{24}O$, 35.4), and 79 (C_6H_7, base peak).

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.86; H. 8.49; molecular weight, 332.1986. Found: C, 72.55, H, 8.53; molecular weight (MS), 332.1979 (29.3%).

(B) Oxidation of 65 mg of **2a** in the manner described in the previous paragraph followed by the usual workup and purification by recrystallization from $CHCl_3$–MeOH furnished 62 mg of **6** which had mp 230–235 °C, the melting point of **7** to which it is converted on heating: IR bands ($CHCl_3$) at 3400, 1765, and 1710 cm^{-1}; NMR signals at 2.55 (H-5), 2.46 (center of AB quartet, J = 15 Hz, H-7a and H-7b), and methyl singlets at 1.39 and 1.2 ppm; CD curve (MeOH) $[\theta]_{294}$ -6220 (min), $[\theta]_{240}$ −820 (max), $[\theta]_{212}$ −9040 (min), $[\theta]_{206}$ −7630 (last reading); peaks in the high-resolution mass spectrum at m/e 314 ($C_{20}H_{26}O_3$, 26.2), 304 ($C_{18}H_{28}O_3$, 9.5), 290 ($C_{17}H_{22}O_4$, 64.7), 288 ($C_{19}H_{28}O_2$, 20.7), 286 ($C_{19}H_{26}O_2$, 12.9) 255 ($C_{18}H_{23}O$, 17.6), and 122 ($C_8H_{10}O$, base peak).

Anal. Calcd for $C_{20}H_{28}O_4$; molecular weight, 332.1986. Found: molecular weight (MS), 332.1998 (7.4%).

An attempt to purify **6** by preparative TLC (silica gel 60 PF: 254–366; EM reagents) resulted in partial conversion of **7** (NMR spectrum), although stirring of a solution of **6** in MeOH with silica gel used for column chromatography (silica gel powder, Baker) did not result in any change. At room temperature, **6** is only stable for 1–2 days and is gradually converted to **7** on standing. Purification of **7** by preparative TLC ($CHCl_3$–MeOH) and recrystallization from MeOH–$CHCl_3$ afforded crystals which melted at 233–235 °C dec and exhibited IR bands at 3360, 1690, and 1660 cm^{-1}; UV absorption at 251 nm (ϵ 8800); NMR signals (Me_2SO-d_6) at 4.21 (br, disappears on D_2O exchange) and methyl singlets at 1.21, 1.20, and 1.19 ppm. The high-resolution mass spectrum exhibited significant peaks at m/e 314 ($C_{20}H_{26}O_3$, 9.2), 296 ($C_{20}H_{24}O$, 7.5), 288 ($C_{19}H_{28}O_2$, 52.7), 286 ($C_{19}H_{26}O_2$, 83.2), 271 ($C_{18}H_{23}O_2$, 7.7), 270 ($C_{19}H_{26}O$, 18.0), 268 ($C_{19}H_{24}O$, 14.3), and 255 ($C_{18}H_{23}O$, base peak).

Anal. Calcd. for $C_{20}H_{28}O_4$: molecular weight 332.1986. Found: molecular weight (MS), 332.1979.

X-ray Analysis of Eupatalbin. Single crystals of **1a** (from ethyl acetate–methanol) were orthorhombic, space group $P2_12_12_1$, with a = 7.505 (1), b = 13.550 (2), c = 17.207 (2) Å, and d_{calcd} = 1.270 g cm^{-3} for Z = 4 ($C_{20}H_{30}O_4$, M = 334.46). The intensity data were measured on a Hilger–Watts diffractometer (Ni filtered Cu Kα radiation, θ–2θ scans, pulse height discrimination). A crystal measuring approximately 0.3 × 0.4 × 0.5 mm was used for data collection; the data were corrected for absorption. A total of 1373 reflections were measured for θ <57° of which 1340 were considered to be observed [$I > 2.5\sigma(I)$]. The structure was solved by a multiple solution procedure[20] and was refined by full-matrix least squares. Ten low θ reflections which were strongly affected by extinction were omitted from the final refinement. In the final refinement anisotropic thermal parameters were used for the heavier atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indices are R = 0.035 and R_W 0.049 for the remaining 1330 observed reflections. The final difference map has no peaks greater than ±0.2 $Å^{-3}$.

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Registry No. **1a**, 70775-63-2; **1b**, 70775-64-3; **1c**, 70775-65-4; **2a**, 70775-66-5; **2b**, 70775-67-6; **3**, 70775-68-7; **4**, 70775-69-8; **5**, 70775-70-1; **6**, 70775-71-2; **7**, 70775-72-3; eupatorin, 855-96-9.

Supplementary Material Available: Tables II–VI listing final atomic parameters, final anisotropic thermal parameters, bond lengths, bond angles, and torsion angles (5 pages). Ordering information is given on any current masthead page.

(20) G. Germain, P. Main, and M. Woolfson, *Acta Crystallogr., Sect. A.*, **27**, 368 (1971).