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SIX ADDITIONAL SESQUITERPENE LACTONES FROM *LIRIODENDRON TULIPIFERA*

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ABSTRACT.—The leaves of *Liriodendron tulipifera* yielded four sesquiterpene lactones: dihydrochrysanolide (**1**), β-cyclolipiferolide (**5**), 11,13-dehydrolanuginolide (**7**), and laurenobiolide (**3**), of which the first two are new compounds. β-Cyclolipiferolide (**5**), was prepared by acid cyclization of lipiferolide (**6**), and the stereochemistry at C-1, C-4, and C-5 was determined by nuclear Overhauser effect studies. Dihydrochrysanolide (**1**) was converted to chrysanolide (**2**) by MnO_2 oxidation, and the stereochemistry of the hydroxyl-bearing carbon, C-1, was established as *S* by the Horeau procedure. 11,13-Dehydrolanuginolide (**7**) was identified from physical data and by conversion to tulipinolide diepoxide (**8**), a derivative of tulipinolide (**9**) and a well-characterized lactone. Tulipinolide 1,10-epoxide, a product of partial oxidation of tulipinolide with *m*-chloroperoxybenzoic acid, was characterized by spectral data. The root bark afforded α-(**11**) and β-liriodenolide (**12**), which were identified by direct comparison with products from the cyclization of epitulipinolide 1,10-epoxide, and are new natural products.

The leaves and root bark of *Liriodendron tulipifera* L. (Fam. Magnoliaceae), commonly called yellow or tulip poplar, have reported for them nine sesquiterpene lactones (1-6), some of which possess cytotoxic and insect antifeeding activity (7). Further studies have yielded six additional members, four of which are new natural products, and are the subject of this report.

Dihydrochrysanolide (**1**) was isolated from a partition fraction of the ethanolic extract residue of the leaves by repeated chromatography and crystallization. High resolution ms supported the formula $C_{17}H_{22}O_5$, and the ir spectrum suggested hydroxyl, ester, lactonic, and olefinic functions. The ^{1}H-nmr spectrum (table 1) contained a pair of one-proton split doublets at 5.83 and 6.14 ppm, characteristic of methylene protons of α,β′-unsaturated γ-lactones. The extra splitting (J=0.9 Hz) of the typical doublets, which is caused by geminal coupling, is observed with *trans* lactones bearing an oxygen function with α-stereochemistry at the carbon adjacent to the lactonic carbon C-7 for either C-7 to C-6 or C-7 to C-8 lactones (2,6,8,9). ^{1}H-nmr peaks for an acetate, an olefinic methyl, and another exocyclic methylene were also present. Double irradiation experiments beginning at H-13 identified H-7, from which the protons on C-5 through C-9 were located, and from the multiplicities and chemical shifts the substituents were likewise assigned.

The stereochemistry of H-7 was assigned as α, as in the case for the lactones of established structure from this source. The cd spectrum with a negative Cotton effect peak at 252 nm for the $n\mapsto\pi^*$ transition of the lactone carbonyl was in conflict, according to Geissman and co-workers (10), with the ^{1}H-nmr data for the 7,8-*trans* lactone. However, it was of the same sign as observed for laurenobiolide (**3**) (11), pyrethrosin (1,10-epoxide of **3**), and chrysanolide (**2**) (8), three other 7,8-*trans* lactones that disobey the generality. The remaining substituent, a hydroxyl, was placed at C-1, because the broadened triplet at 3.93 ppm (which sharpened with D_2O) upon irradiation shar-

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TABLE 1. ^{1}H-nmr spectral data of *Liriodendron tulipifera* constituents.[a]

Compound	H-1	H-5	H-6	H-7	H-8	H-9	H-13	H-14	H-15	Miscellaneous
1[b]	3.93 br t (~8.5)	5.01 br d (9.9, 1.2)	5.36 bdd (9.9, 9.9)	3.12 m (9.9, 8.3, 3.1, 2.7)	4.18 m (9.8, 8.3, 2.9)	2.85 m (14.1, 2.9, 1.8) eq 2.50 dd (14.1, 9.8) ax	6.14 dd (3.1, 0.9) 5.83 dd (2.7, 0.9)	5.13 m (2H)	1.81 d (1.2)	2.03 s (Ac) 3.6 br (OH)
5[b,c]	3.17 m	2.39 dd (11.2, 11.1)	4.47 dd (11.1, 9.1)	3.30 dq (9.1, 3.5, 2.9, 2.0)	5.53 m (4.3, 4.1, 2.0)	2.70 dd (14.3, 4.3) eq 2.41 dd (14.3, 4.1) ax	6.14 d (3.5) 5.56 d (2.9)	5.14 s 4.93 s	1.33 s	1.99 s (Ac)
7[d]	5.29 m	2.64 d (9.2)	4.26 dd (9.2, 6.7)	3.25 m (6.7, 4.4, 3.5, 3.2)	4.54 m (~8, 4.4, ~4)	2.5-2.1 m	6.38 dd (3.5, 0.6) 5.75 dd (3.2, 0.6)	1.80 s	1.28 s	2.03 s (Ac)
8[d]		2.81 d (9.5)	4.52 dd (9.5, 8.3)	3.16 m (8.3, 3.8, 3.2, 2.2)	4.67 dd (10.2, 2.2)		6.39 d (3.8) 5.71 d (3.2)	1.44 s	1.44 s	2.03 s (Ac)
10[d]	2.71 dd (11.1, 2.2)	5.25 dq (9.7, 1.6)	4.88 dd (9.7, 8.7)	2.99 tt (8.7, 7.8, 3.5, 3.2)	5.01 ddd (10.3, 7.8, 1.6)		6.35 dd (3.5, 0.8) 5.82 dd (3.2, 0.8)	1.24 s	1.85 d (1.6)	2.10 s (Ac)

[a]Taken at 90 MHz or as stated in given solvent with TMS as internal standard. Chemical shifts are in ppm (δ); coupling constants *J*, in Hz given in parentheses and multiplicities designated by the symbols; s=singlet, d=doublet, m=multiplet, q=quartet, t=triplet and br=broadened signal.

[b]In acetone-d_6.

[c]At 300 MHz.

[d]In $CDCl_3$.

pened the H-14 resonances. After accommodation of the functional groups, the molecular formula still required one double-bond equivalent, which suggested a ten-membered ring.

TABLE 2. ^{13}C-nmr spectral data of *Liriodendron tulipifera* constituents.[a]

Carbon Atoms	1[b]	5[d]	7[d,e]
1	70.1d	44.2d	127.4d
2	35.2t	26.4t	24.3t
3	31.7t	40.4t	35.9t
4	148.1	79.8	61.0
5	127.8d	56.4d	66.5d
6	73.2d	77.9d	72.5d
7	49.5d	50.2d	49.6d
8	79.3d	66.6d	80.1d
9	42.2t	43.7t	47.3t
10	138.9[c]	141.8	129.6
11	138.2[c]	134.8	133.9
12	169.4	169.0	169.0
13	123.8t	122.0t	125.2t
14	114.2t	116.2t	18.3q
15	17.4q	24.2q	17.3q
*Me*CO	20.9q	20.9q	21.0q
MEC*O*	169.9	170.3	170.2

[a]Taken at 20.12 MHz, or as stated in indicated solvent. Unmarked signals are singlets.
[b]In acetone-d_6 at 22.63 MHz.
[c]Assignments may be interchanged.
[d]In $CDCl_3$.
[e]Assignments made by comparison with lipiferolide (5) and related compound (21).

The spectral data, including ^{13}C-nmr (table 2), supported a structure related to chrysanolide (**2**), from *Chrysanthemum cinerariaefolium* (8), which would contain an allylic alcohol instead of the α,β-unsaturated ketone. Oxidation of dihydrochrysanolide (**1**) with MnO_2 formed a product identical with chrysanolide (**2**). Furthermore, the reduction product[5] of a hydroperoxide (**4**) prepared by photooxygenation of laurenobiolide (**3**) was identical with dihydrochrysanolide (**1**). Because laurenobiolide had been converted to pyrethrosin (11), and the latter was analyzed by X-ray diffraction (12), dihydrochrysanolide has its entire stereochemical structure confirmed except for C-1. This was determined by the Horeau procedure (13) with α-phenylbutyric anhydride. The acid remaining after esterification was (−)α-phenylbutyric acid in an optical yield of 20%, which corresponds to α-stereochemistry for the hydroxyl (or *S*-configuration for C-1).

β-Cyclolipiferolide (**5**) was isolated by careful chromatography of fractions from which epitulipinolide diepoxide was originally isolated (4). Elemental and ms analyses supported formula $C_{17}H_{22}O_5$, and the ^{1}H-nmr, uv, and ir spectra suggested the presence of an α,β′-unsaturated γ-lactone, an acetate, an hydroxyl, and an exocyclic olefin. The doublets at 6.14 and 5.56 ppm (J=3.5 and 2.9 Hz), common for the lactonic exocyclic methylene, when irradiated in a double resonance nmr experiment located H-7 from which the protons of C-1 and C-5 through C-9 and their functional groups were assigned. The two one-proton singlets at 5.14 and 4.93 ppm are characteristic of an exocyclic olefin, and the three-proton singlet at 1.33 ppm of a methyl on a hydroxyl-

[5]One of us (F.S.E.) has prepared **1** in an independent study, the results of which will be published separately.

bearing quaternary carbon (14,15). Inasmuch as the formula still required two double-bond equivalents, a bicyclic guaianolide ring with retention of a normal sesquiterpene skeleton appeared best supported by the data. The stereochemistry at carbons 5 through 8, as assigned from proton *J* values, corresponded to that of lipiferolide (**6**) and resulted in a possible structure for the sesquiterpene lactone as one of its cyclization product. Indeed, cyclization of lipiferolide (**6**) by several acidic reagents (16) afforded β-cyclolipiferolide (**5**), identical with the natural product.

Although the mechanism of cyclization would be expected to yield a *cis* ring junction and unaltered stereochemistry at C-4, the large vicinal coupling constant $J_{1,5}=11.2$ Hz would also fit a *trans* ring junction. However, a series of nOe difference experiments (17,18) showed H-1 and H-5 to be *cis*. For example, irradiation at 2.39 ppm (H-5) showed an enhancement for the H-1 and H-7 signals of 10.4 and 10.1%, respectively. This also confirmed the placement of H-1 and H-5 on the α-face of the molecule and the Me(15) on the opposite side, since the last group showed no nOe. Conversely, irradiation of the H-1 proton gave a 14.5% increase in the H-5 signal, while irradiation at Me(15) showed a 16.5% increase for H-6. These results supported the final structure of β-cyclolipiferolide as **5**.

11,13-Dehydrolanuginolide (**7**), mp 168°, gave spectral (^{1}H-nmr, ^{13}C-nmr, ir, uv, and ms) evidence for the formula $C_{17}H_{22}O_5$, and the presence of α,β′-unsaturated γ-lactone, acetate, and olefin functions. The literature (19) records the isolation of this substance from the trunk bark of *Michelia lanuginosa* and the physical properties appeared comparable.[6] Confirmation of this assignment was obtained by epoxidation of 11,13-dehydrolanuginolide (**7**) to tulipinolide diepoxide (**8**) (2). Because the work on lipiferolide (**6**) (4) allows, by analogy, the presentation of the complete structure of tulipinolide diepoxide as **8**, that of 11,13-dehydrolanuginolide must be **7**. As a by-product from the incomplete epoxidation of tulipinoliode (**9**), the 1,10-epoxide (**10**) was also characterized.

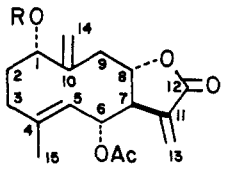
The last product isolated from the leaves was identified as laurenobiolide (**3**) by physical data and comparison with an authentic sample. Two lactones, α-(**11**) and β-liriodenolide (**12**), were isolated from the root bark after extensive chromatography and identifiied by direct comparison with known samples, prepared (4) by acid cyclization of epitulipinolide 1,10-epoxide (**13**). γ-Liriodenolide (double bond between C-4 and C-5) was previously reported from this source (4).

In summary, the 15 sesquiterpene lactones isolated to date from *L. tulipifera* can be viewed as being derived biogenetically from the simplest germacranolide, costunolide (1) [the deacetoxy derivative of tulipinolide (**9**)]. Addition of an acetoxy group results in tulipinolide (**9**), epitulipinolide (2) (acetoxy α at C-8) and laurenobiolide (**3**) with the lactone now between C-7 and C-8. Tulipinolide would be converted to the 4,5-epoxide, 11,13-dehydrolanuginolide (**7**), while laurenobiolide would yield tulirinol (6) and dihydrochrysanolide (**1**). Epitulipinolide, which apparently affords the largest number of derivatives, would give lipiferolide (**6**), epitulipinolide diepoxide (4), and peroxyferolide (5), for a total of ten germacranolides from this plant. The remaining five products are three eudesmanolides, α-(**11**), β-(**12**), and γ-liriodenolide (**4**), a guaianolide, β-cyclolipiferolide (**5**), and the elemanolide, epitulipdienolide (4).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The instruments used, sources of materials, and general

[6]Although the specific rotation, melting point, and ^{1}H-nmr spectrum were the same for the isolated and authentic samples, the ir spectra taken in KBr were only similar. We assumed it was due to crystal polymorphism. Unfortunately, solution spectra were not available for comparison; however, the additional correlation of our compound to tulipinolide should dispel any doubt about its structure.



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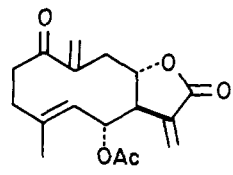

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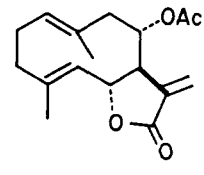

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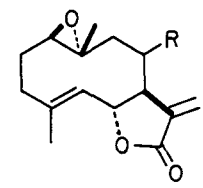

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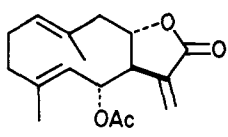
13 R = ▬OAc



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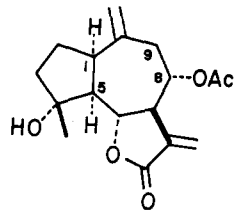

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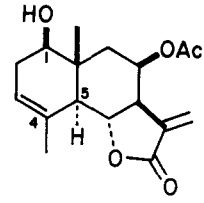

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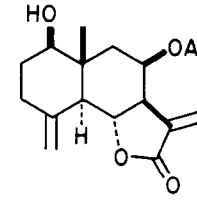

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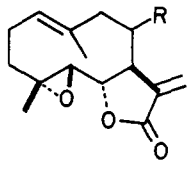
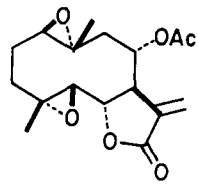


6 R = ▬OAc

7 R = ---OAc



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isolation sequences are given in reference (5). The tlc plates were sprayed with *p*-anisaldehyde-H_2SO_4-EtOH (1:1:13) and heated at 110° for color development.

ISOLATION OF DIHYDROCHRYSANOLIDE (**1**).—The 10% aqueous MeOH partition fraction (4) (405g) from 12 kg of dried leaves of *L. tulipifera* was taken up in 2 liters of MeOH-H_2O (7:3) and extracted successively five times with 2 liters of hexane and hexane-$CHCl_3$ mixures (4:1) and (1:1). The hexane-$CHCl_3$ (1:1) solubles (122 g) were separated on a column of silica gel 60 (1.65 kg) with PhMe-$CHCl_3$ (1:1, 2 liters) and (1:4, 22 liters), $CHCl_3$ (14 liters), $CHCl_3$-MeOH (49:1, 3 liters), (19:1, 8 liters), (9:1, 5 liters), and (3:1, 6 liters). Effluent fractions of 500 ml were collected, and fractions 74-82 (2.7 g), with a major tlc spot Rf 0.35 with EtOAc-hexane (3:2), were chromatographed on silica gel 60 (0.5 kg) with $CHCl_3$ (3.2 liters) and $CHCl_3$-MeOH (49:1, 1.8 liters) and (19:1, 1.8 liters). Fractions (40 ml) 42-99 and 114-166 were combined (1.8 g) and chromatographed first on 160 g of the same adsorbent with EtOAc-CCl_4 (2:3) and then by flash chromatography (20) with $CHCl_3$-MeCN (4:1). Crystallization from EtOAc or Et_2O-hexane gave 18 mg of dihydrochrysanolide (**1**): mp 163.0-163.5°; $[\alpha]^{24}D$ +8.6° (*c* 0.09, MeOH); cd (*C* 3.0×10^{-3}M, MeOH) $[\theta]_{300}$ 0, $[\theta]_{252}$ −3900, $[\theta]_{237}$ 0, $[\theta]_{220}$ +13400; uv λ max (MeOH) 205 nm (log ε 4.23); ir ν max ($CHCl_3$) 3595 (OH), 3495 (assoc. OH), 1765 (lactone C=O), 1739 (ester C=O) and 1660 cm^{-1} (C=C); and ms *m/z* 306 (0.4%, M^+), 288 (0.7, M-H_2O), 246 (16, M-AcOH), 228 (55, M-H_2O-AcOH), and 43 (100, Ac).

Anal. calcd for $C_{17}H_{22}O_5$: MW 306.1467. Found: MW (mass spectrum) 306.1474.

OXIDATION OF DIHYDROCHRYSANOLIDE (**1**) WITH MnO_2.—A 11.7-mg sample of **1** in 1.5 ml of CH_2Cl_2 was passed into a column of 1.5 g of MnO_2 (Winthrop)-diatomaceous earth (1:2) packed in CH_2Cl_2. After 1 h the column was washed with 25 ml of Me_2CO. The effluent, upon evaporation, left 11.6 mg of crystalline residue, which yielded from $CHCl_3$-MeOH 8.0 mg rosettes of fine needles, identified as chrysanolide (**2**) by direct comparison (uv, ir, ^{1}H-nmr, ms, [α]D, and mp] with an authentic sample (8).

HOREAU ESTERIFICATION OF DIHYDROCHRYSANOLIDE (**1**).—A 13.8-mg sample of **1** and 34.5 mg of α-phenylbutyric anhydride were stirred in 2.5 ml of C_5H_5N for 26 h under N_2. After stirring for 2 h with 2.5 ml of H_2O, the mixture was evaporated. The residue was mixed with 5 ml of 5% $NaHCO_3$ and

extracted four times with Et_2O. The combined Et_2O extract was washed with 5% $NaHCO_3$ and H_2O; and the total combined aqueous layer was acidified with 2 N H_2SO_4 to pH 2 and extracted with $CHCl_3$. The $CHCl_3$ residue of α-phenylbutyric acid, 24.5 mg, $[\alpha]D-3.65°$ (*c* 0.489, C_6H_6) corresponded to an optical yield of 20% [after substraction of 3.6 mg of unreacted starting alcohol isolated by chromatography on silica gel 60 and EtOAc-hexane (3:2)]. The configuration at C-1 must be *S*.

ISOLATION OF β-CYCLOLIPIFEROLIDE (**5**).—A hexane-$CHCl_3$ partition fraction (4) of 73 g was chromatographed on 500 g of silicic acid (Mallinckrodt) containing 5% H_2O and eluted with 2 liters of $CHCl_3$ and 1.5 liters each of 1% and 2% MeOH in $CHCl_3$. The last solvent gave 6.3 g of residue that was separated on 100 g of silicic acid containing 2.5% H_2O and eluted with 0.3 liter each of C_6H_6-$CHCl_3$ (1:1) and (1.3), 1.0 liter $CHCl_3$, and 0.3 liter of 1% MeOH in $CHCl_3$. The $CHCl_3$ fraction (3.6 g) was passed through 52 g of Sephadex LH-20 in MeOH to remove phenolics, and the material passing through was chromatographed on 120 g of silica gel 60 with 46% EtOAc in hexane to yield 153 mg (2.3×10^{-3}% of dry leaves) of β-cyclolipiferolide (**5**), tlc Rf 0.42 with MeCN-$CHCl_3$ (1:4) and 0.24 with EtOAc-hexane (3:2). Crystallization from ether gave needles of **5**: mp 161-2°; $[\theta]^{24}D-101.4°$ (*c* 0.5, MeOH); cd (*C* 4.7×10^{-3}M, MeOH) $[\theta]_{310}$ 0, $[\theta]_{260}$ −1100(shld), $[\theta]_{217}$ −20400; uv (MeOH) λ (end abs) 210 nm (log ε 3.97); ir ν max ($CHCl_3$) 3590 (OH), 1768 (lactone C=O), 1740 (ester C=O), 1665 and 1640 cm^{-1} (C=C); and ms (ci i-BuH) *m/z* 307 (22%, MH^+), 289 (20, MH-H_2O), 247 (28, MH-AcOH) and 229 (100, MH-H_2O-AcOH).

Anal. calcd for $C_{17}H_{22}O_5$ (306)·½H_2O. C, 64.74; H, 7.35. Found: C, 64.99; H, 7.18.

ISOLATION OF 11,13-DEHYDROLANUGINOLIDE (**7**).—A 58-g sample of the MeOH-H_2O (9:1) partition fraction (4) from 1.4 kg of leaves was chromatographed on 1.4 kg of silicic acid (Mallinckrodt) with $CHCl_3$ (9 liters), and $CHCl_3$-MeOH (19:1, 15 liters), (9:1, 5 liters), and (4:1, 10 liters). A fraction (6.0 g) appearing at the end of the $CHCl_3$ and beginning of $CHCl_3$-MeOH (19:1) effluent was rechromatographed on 200 g of silica gel with PhH-MeCOEt (9:1) to yield 0.627 g of material that crystallized from Et_2O-hexane to give 11,13-dehydrolanuginolide (**7**): mp 168°; $[\alpha]24D-97.5°$ (*c* 0.32, MeOH), $[\alpha]D-98.3°$ (*c* 0.865, $CHCl_3$) [Lit. (19) values: mp 168°; $[\alpha]D-96.5°$ (*c* 0.74, $CHCl_3$)]; cd (*C* 3.3×10^{-3}M, MeOH) $[\theta]_{300}$ 0, $[\theta]_{260}$ −337, $[\theta]_{242}$ −61, $[\theta]_{220}$ −7650, $[\theta]_{200}$ 0; tlc Rf 0.59 with EtOAc-$CHCl_3$ (1:1); uv (MeOH) λ (end abs) 210 nm (log ε 4.10); ir ν max ($CHCl_3$) 1770 (lactone C=O), 1740 (ester C=O), and 1655 (C=C) cm^{-1}. The ^{1}H-nmr and ^{13}C-nmr spectra are found in tables 1 and 2, respectively. Comparison of ^{1}H-nmr spectra (60 MHz, $CDCl_3$) of isolated and authentic 11,13-dehydrolanuginolide (**7**) showed them to be identical.[6] The ms (ci, i-BuH) showed peaks at *m/z* 307 (4%, MH^+), 289 (6, MH-H_2O), 247 (36, MH-AcOH), 229 (89, MH-AcOH-H_2O), 61 (100, $AcOH_2$).

EPOXIDATION OF 11,13-DEHYDROLANUGINOLIDE (**7**) TO TULIPINOLIDE DIEPOXIDE (**8**).—A 26 mg sample of **7** and 30 mg of *m*-chloroperoxybenzoic acid (85%) in 3 ml of $CHCl_3$ was allowed to react for 20 h. Extraction of the mixture with 5% aqueous Na_2SO_3, 5% aqueous $NaHCO_3$ and H_2O, followed by evaporation of the $CHCl_3$, left a residue that crystallized from $CHCl_3$-hexane as needles (22 mg) of **8**, mp 170-2°; $[\alpha]D-64.6°$ (*c* 0.26, MeOH).[7] The tlc, ^{1}H-nmr, ir, uv, and ms were the same as those from the diepoxide prepared from tulipinolide (2).

EPOXIDATION OF TULIPINOLIDE (**9**) TO THE DIEPOXIDE **8** AND THE 1,10-EPOXIDE **10**.—A 10-mg sample of tulipinolide in 0.8 ml of CH_2Cl_2 was treated with 15 mg of *m*-chloroperoxybenzoic acid, and after 8 h with 15 mg more. After 14 h, the reaction mixture, devoid of by-products by extraction, was separated on 3 g of silica gel 60 with EtOAc-$CHCl_3$ (1:4). The first eluted material crystallized as long needles of monoepoxide **10** from EtOAc-hexane: mp 145-7°; $[\alpha]D+66°$ (*c* 0.18, $CHCl_3$); ms (ci i-BuH) *m/z* 307 (19%, MH^+), 289 (6, MH-H_2O), 247 (96, MH-AcOH), 229 (100, MH-AcOH-H_2O). ^{1}H-nmr spectrum of **10** is in table 1. Later eluted fractions gave the diepoxide **10** (2). Tlc on silica gel G with EtOAc-$CHCl_3$ (1:1) showed Rf 0.52 for the 1,10-epoxide **10** and 0.42 for the diepoxide **8**.

ISOLATION OF LAURENOBIOLIDE (**3**).—A 7 g sample of the hexane-$CHCl_3$ (4:1) partition fraction, as described in the section on the isolation of dihydrochrysanolide, was chromatographed on 200 g of silica gel with EtOAc-hexane (3:7). The effluent material with Rf 0.49 on tlc with EtOAc-hexane (2:3) was pooled (1.8 g) and rechromatographed twice on 100 g of silica gel, first with EtOAc-CCl_4 (1:4), then with i-Pr_2O-CCl_4 (1:1) employing the flash chromatographic method (20). The 0.36 g fraction crystallized from Et_2O-hexane to give 70 mg 0.006% yield of colorless crystals of **3**: mp 100-1°; $[\alpha]D+14.8°$ (*c* 0.15, MeOH) [Lit. (11) values: mp 101-3°; $[\alpha]D+17.1°$ (*c* 1, EtOH)]. The ^{1}H-nmr and ir spectra, and tlc mobility were identical with that of an authentic sample.

ISOLATION OF β-(**11**) AND β-LIRIODENOLIDE (**12**).—A finely ground sample (400 g) of root bark collected in Mississippi (5) during the summer of 1973 was percolated with EtOH to yield 49 g of residue.

[7]The value $[\alpha]D+81°$ reported earlier (2) for tulipinolide diepoxide is incorrect.

Partitioning between solvent pairs (4) gave 36.5 g of 10% aqueous MeOH solubles that were further divided between PhH and 30% aqueous MeOH. The PhH solubles (22.8 g) were chromatographed on 200 g of silicic acid (Mallinckrodt) containing 13% H_2O and developed with i-Pr_2O-hexane (1:1, 2 liters), i-Pr_2O (2 liters), and 2, 5, 10, and 20% MeOH in i-Pr_2O (each ~1.5 liters) to afford 20 fractions based on tlc. Fractions 9 and 10 [Rf 0.29 with MeOH-i-Pr_2O-$CHCl_3$ (8:41:41)] were combined (1.6 g) and chromatographed on 85 g of silica gel with PhH-$CHCl_3$ (1:1, 0.7 liter) $CHCl_3$ (1.4 liters), and 1% and 2% MeOH in $CHCl_3$ to give 217 mg from the 1% MeOH in $CHCl_3$ effluent, which was again separated on 5 g of silica gel with i-Pr_2O-$CHCl_3$-MeOH (18:6:1). The 94-mg fraction crystallized from Et_2O-i-Pr_2O to give β-liriodenolide (**11**), mp 72-3°, identical (mp, tlc, [α]D, ^{1}H-nmr and ir) with a known sample prepared (4) from epitulipinolide 1,10-epoxide (**13**).

Fractions 11-13 (2.9 g) from the first column were combined and separated on 170 g of silicic acid with $CHCl_3$ (2 liters) and 0.5% MeOH in $CHCl_3$ (2 liters) to give 771 mg of a fraction, that was purified first on 70 g of silica gel with Et_2O-PhH-$CHCl_3$ (0.3:1:1), then on 5 g of Sephadex LH-20 with MeOH to remove the phenolics, and finally on 25 g of silica gel impregnated with 5% $AgNO_3$ with Et_2O as solvent. A fraction (114 mg) was eluted, which crystallized from Et_2O-i-Pr_2O to give triangular plates of β-liriodenolide (**12**), mp 119-120°, tlc Rf 0.14 with 3.5% MeOH in i-Pr_2O-$CHCl_3$ (1:1). It was identical (mp, tlc, [α]D, ^{1}H-nmr, and ir) with a known sample prepared (4) from epitulipinolide 1,10-epoxide (**13**).

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