116.2, 65.7, 57.1, 56.4, 56.3, 31.8, 32.9 ppm; $^1$H NMR ($CDCl_3$) δ 2.56–2.61 (t, $J$ = 7.2 Hz, 2 H), 3.27–3.22 (t, $J$ = 7.2 Hz, 2 H), 4.01 (s, 3 H), 4.07 (s, 3 H), 4.10 (s, 3 H), 6.78–6.80 (s, 1 H), 6.87 (s, 1 H), 7.04–7.09 (t, 1 H), 7.18–7.23 (t, 1 H), 7.31–7.33 (d, 1 H), 10.40 (br, 1 H), 10.70 (s, 1 H); IR (KBr) 3372, 3069, 3020, 2925, 2856, 1709 (s), 1688 (vs), 1620, 1478, 1470, 1322 (s), 1260, 1253, 1208 (s), 1197 (s), 1172 (vs), 1012 (s), 789, 749 cm$^{-1}$; MS (70 eV) calcd for $C_{24}H_{20}O_7$ 420.1203, found 420.1199.

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**Registry No.** 1, 80455-68-1; **2**, 105365-18-2; **3**, 17082-61-0; **4**, 100020-34-6; 4 (ketone), 83-33-0; **5**, 116664-59-6; **6**, 116664-60-9; (±)-**7**, 116698-30-7; (±)-**8**, 116698-31-8; (±)-**9a**, 116664-61-0; (±)-**9b**, 116698-32-9; (±)-**10** (isomer 1), 116664-62-1; (±)-**10** (isomer 2), 116698-33-0; **14**, 526-86-3; **15**, 5091-02-1; **16**, 116664-63-2; **18**, 116664-64-3; (±)-**19**, 116664-65-4; (±)-**22**, 116664-66-5; **23**, 116664-67-6; **26**, 70103-17-2; (±)-**28**, 116664-68-7; (±)-**29**, 116669-32-0; **30**, 2237-36-7; **31**, 5981-37-3; **32**, 490-64-2; **32** (Me ester), 20029-76-9; **32** (acid chloride), 42833-66-9; **33**, 105518-12-5; **33** (6-formyl deriv), 105518-13-6; (±)-**34**, 116664-69-8; (±)-**35**, 116664-70-1; (±)-**38**, 116664-71-2; $CH_2$=CHCH=$CH_2$, 106-99-0; 2,4-$(OH)_2C_6H_3CO_2H$, 89-86-1; Danishefsky diene, 54125-02-9.

# Acid-Catalyzed Transformations of the Heliangolide 15-Hydroxyacetylleptocarpin[1]

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Acid-catalyzed transformations of the natural heliangolide 15-hydroxyacetylleptocarpin (1) were carried out. Treatment with perchloric acid afforded three elimination products: the dihydropyran **2**, its acetate **3**, and the germacratrienolide **4**. $BF_3$·$OEt_2$ catalysis gave **5**, derived from a pinacolic rearrangement followed of hemiketalization. In all these cases, the 1(10)-epoxide promoted the reaction. Allylic chloride **7** was obtained by treatment of **1** with $SOCl_2$. Mechanisms explaining the characterized reaction products are proposed.

The acid-catalyzed cyclizations of germacrolides (*trans,trans*-1(10),4-germacradienolides) and their 1(10)- and 4(5)-epoxy derivatives have been extensively investigated because of interest in their biogenesis, the reaction mechanisms and the transformation products.[2] The reactions afford eudesmanolides, elemanolides, and guaianolides as the main products, and in some cases xanthanolides[3,4] and cyclobutane derivatives[3] have also been obtained. Few acid-catalyzed studies have been performed on the geometric isomers of germacranolides.[5] However, cyclization of heliangolides (1(10)-*trans*,4-cis-germacradienolides) gave cadinanolides[6,7] and eudesmanolides[7] in low yield.[8]

The present work deals with the acid-catalyzed transformations of the heliangolide 15-hydroxyacetylleptocarpin (**1**),[9] which yields products of functional groups transformations and rearrangements. The expected cadinanolides or eudesmanolides were not observed.

Treatment of **1** with perchloric acid in acetone for 1 h gave a mixture of compounds **2–4**. The major product **2**, mp 162–164 °C, analyzed for $C_{20}H_{24}O_6$ (elemental analysis and mass spectrometry), indicated that a $C_2H_4O_2$ unit was lost in the reaction. Its IR spectrum showed the presence of hydroxyl (3540 cm$^{-1}$), an α,β-unsaturated γ-lactone (1755 cm$^{-1}$), and double bonds (1640 cm$^{-1}$). $^1$H NMR spin decoupling experiments established the sequence from H-5 to H-9 and corresponded to the arrangement in **1**. Major differences are (a) the one-proton multiplet at δ 5.85, (b) an additional AB system of an oxymethylene group, overlapping with the AB system corresponding to H-15, and (c) the C-10 methyl resonance of the starting material was no longer present. The $^{13}$C NMR spectrum of **2** confirmed the presence of an additional trisubstituted double bond and the additional oxymethylene group, indicating the presence of a $\Delta^3$-dihydropyran ring. Addition of trichloroacetyl isocyanate (TAI) induced a paramagnetic shift (Δδ 1.16) in the signal of H-15, thus establishing that C-15 beared the primary allylic alcohol.[10] These data led to the deduction of structure **2**.

X-ray crystallographic analysis of **2** confirmed the proposed structure. Figure 1 is a computer-perspective drawing of the solved structure, and details of this analysis are included in the Experimental Section. The tricyclic structure **2** adopts the chair–boat conformation representative of the heliangolides,[11] although it is qualitatively more rigid than that of the starting material.

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(1) Contribution No. 903 from the Instituto de Química de la Universidad Nacional Autónoma de México. This work was presented in part at the Third Chemical Congress of North America, Toronto, Ontario, Canada, June 1988.

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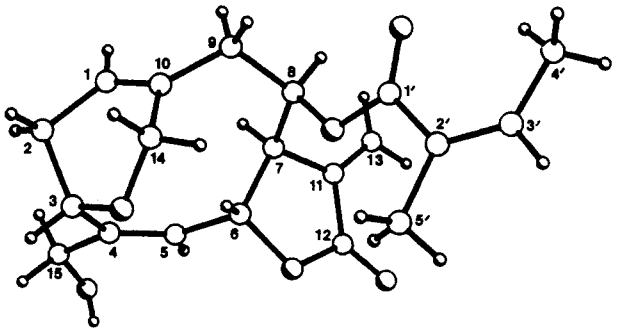


**Figure 1.** Computer-perspective drawing of **2**.

The less polar product **3**, analyzed for $C_{22}H_{26}O_7$ and its $^1H$ NMR spectrum, is superimposable upon that of **2** if allowance is made for the additional acetyl group at C(15). This was confirmed by acetylation of **2**, which gave a product identical in all respects with that of **3**.

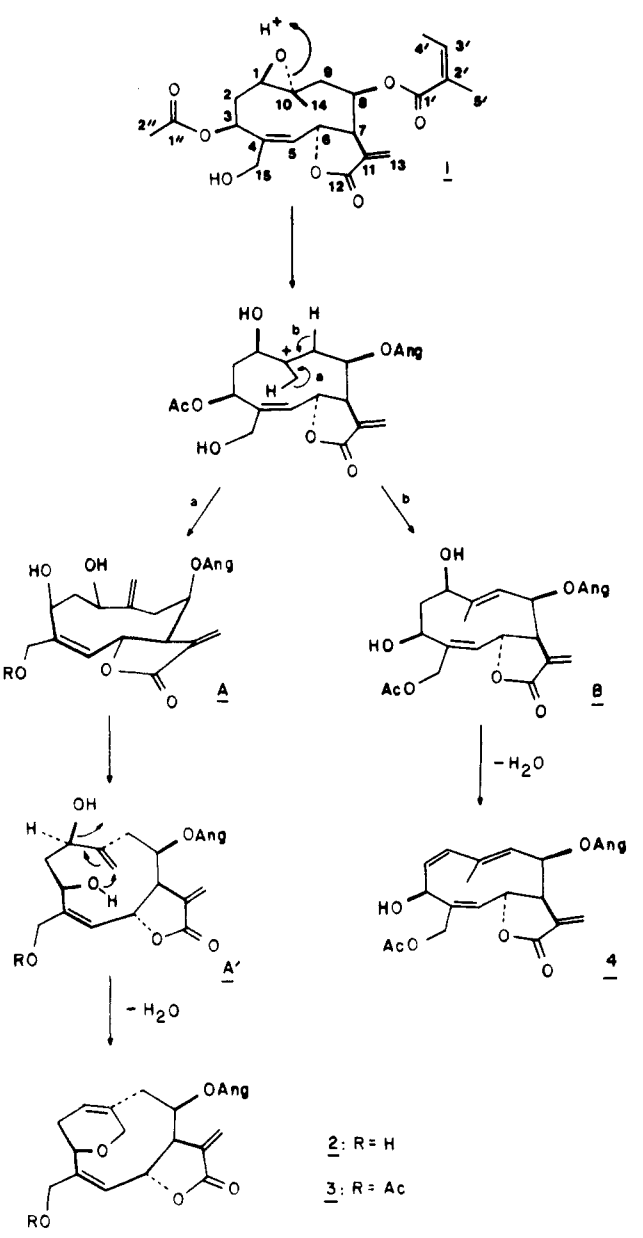
Compound **4**, $C_{22}H_{26}O_7$, is isomeric with **3**. The low-field chemical shift of H-15 in the $^1H$ NMR spectrum indicates a transfer of the acetyl group from C(3) to C(15). The $^1H$ NMR spectrum of **4** in $CDCl_3$ exhibits the typical pattern for H-5 and H-6 in the heliangolides.[12] However, the chemical shift of H-6 ($\delta$ 4.83) in **4** is considerably upfield with respect to the chemical shift of H-6 of the starting material ($\delta$ 6.09), thus indicating that the C(1)–C(10) epoxide was lost in the reaction. The signals for the vinyl protons (resolved in the $C_6D_6$ spectrum) indicate the C-(2)–C(1)–C(10)–C(9) carbon sequence of the germacrane system. The additional vinylic methyl group ($\delta$ 1.94) located at C-10 confirms this structural fragment. All these data are consistent with structure **4**.

The products **2**–**4**, obtained from perchloric acid treatment of **1**, can be rationalized as arising from cleavage of the C(10)–O bond and the cationic center at C(10) is stabilized by loss of a proton from C(14) (Scheme I, pathway a) or C(9) (pathway b), to form the intermediates A and B, respectively. The conformational change (A → A′) allows an intramolecular addition–elimination reaction to form the dihydropyran ring via a favored 6-*endo-trig* cyclization[13] (Scheme I), to form **2** and **3**. Elimination of the oxygenated function at C(1) of B affords the germacratrienolide **4**.

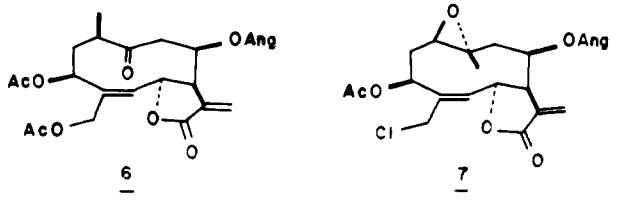
It is interesting to note that although to date no natural heliangolide derivatives incorporating a dihydropyran ring have been isolated, structural analogues of the intermediates A and B have been reported as natural[14] or reaction products.[15]

Treatment of **1** with boron trifluoride etherate in nitromethane afforded a leess polar isomer **5**. Its IR spectrum shows absorptions for an $\alpha,\beta$-unsaturated $\gamma$-lactone (1772 $cm^{-1}$), ester (1740 $cm^{-1}$), and hydroxyl group (3590 $cm^{-1}$). Comparative analysis of the $^1H$ NMR spectrum of the reaction product with the starting material **1**, as well as spin decoupling experiments, indicate that the protons in the sequence H-5 through H-9 remained unchanged. The chemical shift of H-15 ($\delta$ 4.76) established the above

**Scheme I**



described C(3) → C(15) acetyl transfer. The $^{13}C$ NMR spectrum shows resonances from three carbonyls, two trisubstituted double bonds, four carbons bearing oxygen (one primary and three secondary), one quaternary carbon linked to two oxygens, two methylenes, two methines, and four methyl groups. The upfield shift of the H-3 resonance ($\delta$ 3.50) in the $^1H$ NMR spectrum of **5** with respect to H-3 in the starting material ($\delta$ 5.35) suggests a C(3)–C(10) oxygen bridge. This surmise is strengthened by the presence of an hemiketal function at C(10) ($\delta_C$ 115.53), and hence the methyl group has shifted from C(10) to C(1) ($\delta_{H\text{-}15}$ 1.02, 3 H, $J$ = 7 Hz), thus establishing formula **5** for this compound. The presence of a masked ketone in **5** was demonstrated by acetylation to give the expected diacetyl derivative **6**.



(12) The chemical shift of H-6 in 1(10)-epoxyheliangolides in abnormally deshielded by the oxirane and a 3$\beta$-O function, and this argument is diagnostic for structure assignment: (a) Herz, W.; Wahlberg, I. *J. Org. Chem.* **1973**, *38*, 2485. (b) Baruah, N. C.; Sharma, R. P.; Madhusudanan, K. P.; Thyagarajan, G.; Herz, W.; Murari, R. *J. Org. Chem.* **1979**, *44*, 1831.

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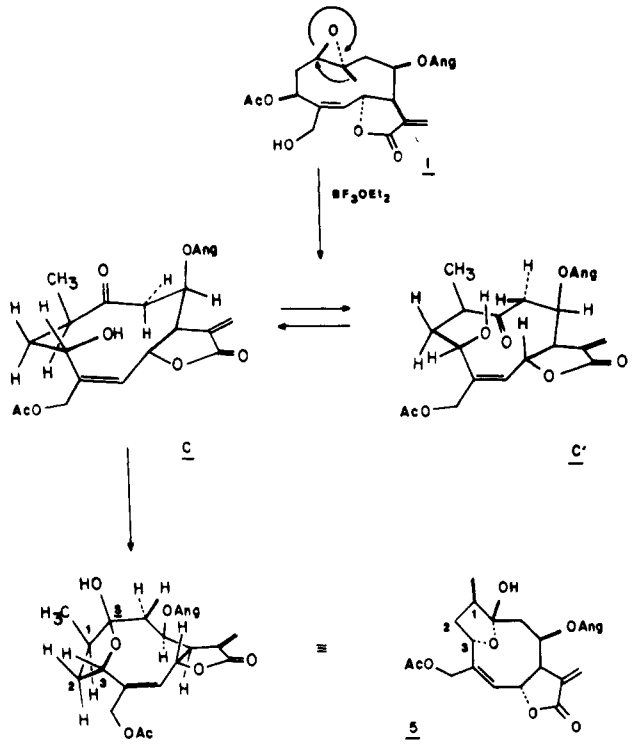
Scheme II



The configuration at C(1) and C(10) of **5** are assigned as follows: The methyl migration (due to pinacolic rearrangement of the epoxide[16]) should proceed with retention of configuration at C(1) to form the $\alpha$-methyl ketone (Scheme II, intermediates C and C'). Inspection of the Dreiding models reveals that C(3)-oxygen should approach the C(10)-carbonyl on the *si* face (intermediate C) via a favored 5-*exo*-*trig* ring closure,[13] since the *re* face presents steric hindrance with the *pro*-*S* C(9) proton (intermediate C'). Therefore the configuration at C(10) in **5** is *S*. This deduction is in accord with the observed chemical shift of H-7 in the spectrum of **5** ($\delta$ 3.50), since the *R* configuration at C(10) should produce an unusual lowfield shift of the H-7 resonance ($\delta \sim 4.10$) as previously reported,[17] owing to the proximity of this proton to the oxygen of the tetrahydrofuran ring.

Some oxirane cyclizations initiated by thionyl chloride treatment have been performed;[3,18] however, in this case, treatment of **1** with $SOCl_2$ afforded only the allylic chloride **7**.

The course of these acid-catalyzed reactions is dependent on the catalyst, conditions, and additional functionalities on the cyclodecadiene ring. The reactions observed in the present investigation are similar to those reported previously.[3,19] Thus, proton catalysis gave elimination products while boron trifluoride etherate promoted rearrangement.

(16) Pinacolic rearrangements with $CH_3$-migration similar to the one leading from **1** to **5** have been reported in the literature. See, inter alia: Lee, K. H.; Simpson, R. F.; Geissman, T. A. *Phytochemistry* **1969**, *8*, 1515. Niwa, M.; Iguchi, M.; Yamamura, Sh. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3137.

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## Experimental Section

Melting points were taken in a Fisher-Jones apparatus and are uncorrected. Column chromatography was carried out by using Merck Silica gel 60 (0.63–0.2 mm). The preparative TLC plates were of Merck (F-254, 20 × 20 × 0.2 cm). Mass spectra were recorded on a Hewlett-Packard 5985-B instrument at 70 eV.

**Treatment of 15-Hydroxyacetylleptocarpin (1) with $HClO_4$.** To a chilled solution of 593.1 mg of **1** in 10 mL of acetone was added 3.9 mL of $HClO_4$. The solution was stirred at ca. 5 °C for 6 h, diluted with 10 mL of $H_2O$, neutralized with solid $NaHCO_3$, and extracted with EtOAc (5 × 50 mL). The combined organic extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure. The residual pale yellow oil (420 mg) was chromatographed on 700 g of silica gel, with an *n*-hexane–EtOAc elution system. Some fractions eluted with *n*-hexane–EtOAc (4:1) showed a major spot on TLC and were combined to afford 73 mg of residue. Preparative TLC of this residual gum ($CHCl_3$–$Me_2CO$, 95:5) gave 22 mg (4%) of 15-acetoxy-3,14-epoxyheliangolide (**3**): mp 141–143 °C (from $Me_2CO$–*i*-$Pr_2O$); IR ($CHCl_3$) 2929, 1757, 1733, 1375, 1272, 1147, 1040, 992 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 6.35 (1 H, d, $J_{7,13a}$ = 3 Hz, H-13 cis), 6.10 (1 H, dd, $J_{5,6}$ = 10, $J_{6,7}$ = 4 Hz, H-6), 6.08 (1 H, qd, $J$ = 7, 1.2 Hz, H-3'), 5.83 (1 H, m, H-1), 5.72 (1 H, d, $J_{7,13b}$ = 3 Hz), 5.48 (1 H, br d, $J_{5,6}$ = 10 Hz, $J_{5,15}$ < 1 Hz, H-5), 5.35 (1 H, m, H-8), 4.68 (1 H, dd, $J$ = 8, 2 Hz, H-3), 4.50 (1 H, d, $J$ = 13 Hz, H-15a), 4.29 (1 H, d, $J$ = 13 Hz, H-15b), 4.35 (1 H, d, $J$ = 15 Hz, H-14a), 4.05 (1 H, d, $J$ = 15 Hz, H-14b), 2.93 (1 H, m, $W_{1/2}$ = 8 Hz, H-7), 2.10 (3 H, s, $CH_3CO$), 2.03 (3 H, dq, $J$ = 7, 1.2 Hz, H-4'), 1.85 (3 H, br s, $W_{1/2}$ = 8 Hz, H-5'); MS, *m/z* (relative intensity) 402 ($M^+$, 1), 342 (30), 302 (30), 242 (65), 100 (85), 99 (70), 83 (100), 60 (75), 55 (82), 43 (78), 42 (50). Anal. Calcd for $C_{22}H_{26}O_7$: C, 66.32; H, 5.57. Found: C, 66.29; H, 5.59.

Some fractions eluted with *n*-hexane–EtOAc (7:3) showed two spots on TLC. They were combined and concentrated to a yellow oil (85 mg) and purified by preparative TLC ($CHCl_3$–$Me_2CO$, 4:1). The faster moving band contained 13.2 mg of starting material **1**. The slower moving band contained 7 mg (1%) of gummy (1*Z*,4*Z*,9*E*)-15-acetoxy-8$\beta$-(angeloiloxy)-3$\beta$-hydroxygermacratrien-12,6$\alpha$-olide (**4**): IR ($CHCl_3$) 3580, 2920, 1760, 1730, 1710, 1640, 1120, 1030, 955 $cm^{-1}$; $^1H$ NMR (80 MHz, $C_6D_6$) $\delta$ 6.21 (1 H, d, $J_{7,13}$ = 3.4 Hz, H-13 cis), 5.83 (1 H, d, $J_{7,13'}$ = 3.1 Hz, H-13 trans), 6.05–5.55 (4 H, complex signal, H-2, H-5, H-8, H-3'), 5.44 (1 H, d, $J_{1,2}$ = 11.5 Hz, H-1), 5.25 (1 H, br d, $J_{8,9}$ = 11 Hz, $J_{9,14}$ < 1 Hz, H-9), 4.78 (1 H, dd, $J_{5,6}$ = 10 Hz, $J_{6,7}$ = 6 Hz, H-6), 4.27 (1 H, d, $J$ = 13 Hz, H-15a), 4.08 (1 H, d, $J$ = 13 Hz, H-15b), 4.01 (1 H, m, $W_{1/2}$ = 8 Hz, H-3), 2.82 (1 H, m, $W_{1/2}$ = 16 Hz, H-7), 2.00–1.55 (9 H, complex signals, H-14, H-4', H-5'), 1.75 (3 H, s, $CH_3CO$); $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 6.50 (1 H, d, $J$ = 3.5 Hz, H-13 cis), 5.76 (1 H, d, $J$ = 3.5 Hz, H-13 trans), 6.20–5.75 (4 H, complex signal, H-2, H-5, H-8, H-3'), 5.69 (1 H, d, $J_{1,2}$ = 11.5 Hz, H-1), 5.31 (1 H, br d, $J_{8,9}$ = 11 Hz, $J_{9,14}$ < 1 Hz, H-9), 4.80 (1 H, dd, $J_{5,6}$ = 10 Hz, $J_{6,7}$ = 6 Hz, H-6), 4.62 (1 H, m, H-3), 4.50 (2 H, br s, $W_{1/2}$ = 3 Hz, H-15a, H-15b), 3.20 (1 H, m, $W_{1/2}$ = 16 Hz, H-7), 2.10 (3 H, s, $CH_3CO$), 2.05–1.80 (9 H, complex signals, H-14, H-4', H-5'); MS, *m/z* (relative intensity) 402 ($M^+$, 1), 387 (1), 384 (5), 359 (12), 342 (15), 319 (5), 302 (10), 224 (60), 100 (80), 99 (72), 83 (100), 60 (45), 55 (80), 43 (80), 42 (35). Subsequent fractions of the main column, eluted with *n*-hexane–EtOAc, afforded a residue that crystallized when triturated with *i*-$Pr_2O$, gave 61 mg (12%) of 15-hydroxy-3,14-epoxyheliangolide (**2**): mp 155–156 °C (from $Me_2CO$–*i*-$Pr_2O$); $[\alpha]^{25}_D$ −93.6° (*c* 0.219, MeOH); UV $\lambda_{max}$ (MeOH) 203 nm ($\epsilon$ 4180); IR ($CHCl_3$) 3542, 2920, 1755, 1710, 1640, 1269, 1140, 1032 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 6.35 (1 H, d, $J_{7,13}$ = 2.9 Hz, H-13 cis), 6.11 (1 H, m, H-3'), 6.08 (1 H, dd, $J_{5,6}$ = 10 Hz, $J_{6,7}$ = 4 Hz, H-6), 5.83 (1 H, m, H-1), 5.74 (1 H, d, $J_{7,13'}$ = 2.8 Hz, H-13 trans), 5.49 (1 H, d, $J_{5,6}$ = 10 Hz, H-5), 5.35 (1 H, m, H-8), 4.77 (1 H, dd, $J$ = 2, 4 Hz, H-3), 4.27 (2 H, d, $J$ = 14 Hz, H-14 and H-15), 3.86 (2 H, d, H-14a and H-14b), 2.97 (1 H, m, $W_{1/2}$ = 7 Hz, H-7), 2.75–2.25 (4 H, complex signals, H-2, H-2', H-9 and H-9'), 2.05–1.85 (6 H, complex signals, H-4', H-5'); $^{13}C$ NMR (20 MHz, DMSO) $\delta$ 128.45 (d, C-1), 29.40 (t, C-2), 71.06 (d, C-3), 137.75 (s, C-4), 125.07 (d, C-5), 73.78 (d, C-6), 46.53 (d, C-7), 78.44 (d, C-8), 40.73 (t, C-9), 144.22 (s, C-10), 136.83 (s, C-11), 169.30 (s, C-12), 124.44 (t, C-13), 63.63 (t, C-14 or C-15), 63.13 (t, C-14 or C-15), 165.70 (s, C-1'), 126.69 (s, C-2'), 139.31 (d, C-3'),

15.38 (c, C-4'), 20.00 (c, C-5'); CIMS ($CH_4$), $m/z$ (relative intensity) 361 ($M^+ + 1$, 39), 343 (65), 325 (70), 307 (25), 243 (100), 225 (18).

**Treatment of 15-Hydroxyacetylleptocarpin (1) with $BF_3$·$Et_2O$.** To a solution of 370 mg of 1 in 10 mL of nitromethane chilled to 0 °C was added 0.35 mL of freshly distilled boron trifluoride etherate. The solution was stirred at room temperature for 1 h (the starting material had disappeared), diluted with 10 g of ice, and extracted with EtOAc (5 × 5 mL each). The combined organic extracts were washed with $NaHCO_3$ and $H_2O$, dried over $Na_2SO_4$, and concentrated under reduced pressure. The gummy residue (296 mg) was purified by column chromatography on 50 g of silica gel with $CHCl_3$ as constant eluent to afford 45 mg (12%) of 3,10-epoxyheliangolide (**5**): mp 123–125 °C ($Me_2CO$–*i*-$Pr_2O$); $[\alpha]^{25}_D$ 34.21 (*c* 0.038, MeOH); UV $\lambda_{max}$ (MeOH) 205 nm (9860); IR ($CHCl_3$) 3590, 2920, 1772, 1740, 1706, 1665, 1643, 1230, 1134, 930 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 6.31 (1 H, d, $J_{7,13}$ = 3 Hz, H-13 cis), 6.08 (1 H, qd, $J$ = 7, 1.2 Hz, H-3'), 5.86 (2 H, m, H-13 trans and H-5), 5.15 (2 H, m, $W_{1/2}$ = 10 Hz, H-6 and H-8), 4.76 (2 H, s, $W_{1/2}$ = 4 Hz, H-15a and H-15b), 3.50 (2 H, m, $W_{1/2}$ = 16 Hz, H-3 and H-7), 2.14 (3 H, s, $CH_3CO$), 2.06–1.85 (6 H, complex signals, H-4', H-5'), 1.02 (3 H, d, $J$ = 7 Hz, $CH_3$ at C-1); $^{13}C$ NMR (20 MHz, $CDCl_3$) $\delta$ 39.45 (d, C-1) 32.46 (t, C-2), 67.97 (d, C-3), 147.40 (s, C-4), 122.17 (d, C-5), 83.78 (d, C-6), 50.67 (d, C-7), 70.83 (d, C-8), 39.57 (t, C-9), 115.53 (s, C-10), 134.16 (s, C-11), 168.13 (s, C-12), 122.18 (t, C-13), 16.84 (q, C-14 or C-4'), 58.83 (t, C-15), 166.85 (s, C-1'), 127.46 (s, C-2'), 138.80 (d, C-3'), 15.72 (q, C-4' or C-14), 20.48 (q, C-5' or $CH_3CO$), 20.62 (q, C-5' or $CH_3CO$), 170.39 (s, $CH_3CO$); CIMS ($CH_4$), $m/z$ (relative intensity) 421 ($M^+ + 1$, 6), 403 (12), 343 (21), 321 (73), 303 (22), 216 (100), 243 (60), 215 (19). Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.84; H, 6.71. Found: C, 62.92; H, 6.65.

**Treatment of 15-Hydroxyacetylleptocarpin (1) with $SOCl_2$.** To a sample of 50 mg of 1 in 15 mL of $CHCl_3$ was added 1 mL of $SOCl_2$. The reaction mixture was stirred at 50 °C for 30 min. Evaporation of the solvent left a gummy residue, which was purified by column chromatography with *n*-hexane–EtOAc (9:1) as constant eluent. Several fractions showing a major spot on TLC were combined and further purified by preparative TLC ($CHCl_3$–$Me_2CO$, 95:5) to afford 28.2 mg of the chloro derivative 15-chloroacetylleptocarpin (**7**): mp 213–214 °C; $[\alpha]^{25}_D$ −20.5° (*c* 0.041, MeOH); IR ($CHCl_3$) 2910, 1755, 1735, 1712, 1640, 1450, 1385, 1360, 1140, 1120, 1030, 975, 950 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 6.37 (1 H, d, $J_{7,13}$ = 3 Hz, H-13 cis), 6.09 (1 H, qd, $J$ = 7, 1.2 Hz, H-3'), 6.07 (1 H, dd, $J_{5,6}$ = 11 Hz, $J_{6,7}$ = 2 Hz, H-6), 5.79 (1 H, d, $J_{7,13'}$ = 2.7 Hz, H-13 trans), 5.55 (1 H, d, $J$ = 11 Hz, H-5), 5.28 (2 H, m, H-3 and H-8), 4.30 (1 H, dd, $J$ = 11, 1 Hz, H-15a), 4.01 (1 H, dd, $J$ = 11, 0.9 Hz, H-15b), 2.95 (1 H, m, H-7), 2.11 (3 H, s, $CH_3CO$), 2.00 (3 H, dq, $J$ = 7, 1 Hz, H-4'), 1.88 (3 H, q, $J$ = 1 Hz, H-3'), 1.50 (3 H, s, H-14); CIMS ($CH_4$), $m/z$ (relative intensity) 442 (10), 441 (33), 440 (30), 439 (100, $M^+ + 1$), 339 (6), 321 (27), 279 (28), 261 (22), 243 (18). Anal. Calcd for $C_{22}H_{27}O_7Cl$: C, 60.27; H, 6.16; Cl, 7.99. Found: C, 60.05; H, 6.18; Cl, 8.03.

**Acetylation of 15-Hydroxy-3,14-epoxyheliangolide (2).** A 15-mg portion of **2** was treated with 2 drops of pyridine and 0.3 mL of acetic anhydride at room temperature for 5 h. After this time, 300 mg of ice was added and the solution was extracted with EtOAc. The combined organic extracts were washed with HCl (5%), $NaHCO_3$, and $H_2O$, dried over $Na_2SO_4$, and concentrated under reduced pressure. Trituration of the residue with *i*-$Pr_2O$ afforded 9.2 mg (60%) of 15-acetoxy-3,14-epoxyheliangolide (**3**), Identical in all respects (melting point, mixture melting point, $[\alpha]_D$, IR, $^1H$ NMR) with the above described substance obtained by treatment of 1 with $HClO_4$.

**Acetylation of 3,10-Epoxyheliangolide (5).** A 24-mg sample of **5** in 2 mL of pyridine was treated with 0.8 mL of acetic anhydride at room temperature for 3 h. The above described workup of the reaction mixture gave 19 mg of a pale yellow oil, which was subjected to preparative TLC (*n*-hexane–EtOAc, 9:1) to afford 11 mg (50%) of the diacetyl derivative **6** as a colorless oil: IR ($CHCl_3$) 2924, 1775, 1728, 1370, 1240, 1044 $cm^{-1}$; $^1H$ NMR (80 MHz, $CDCl_3$) $\delta$ 6.28 (1 H, d, $J$ = 3.5 Hz, H-13 cis), 6.07 (1 H, dq, $J$ = 7, 1.2 Hz, H-3'), 5.94 (1 H, m, $W_{1/2}$ = 6 Hz, H-5), 5.83 (1 H, d, $J$ = 3.5 Hz, H-13 trans), 5.11 (2 H, m, $W_{1/2}$ = 10 Hz, H-6 and H-8), 4.90 (2 H, br s, $W_{1/2}$ = 6 Hz, H-15a and H-15b), 4.56 (1 H, t, $J$ = 9 Hz, H-3), 3.50 (1 H, m, $W_{1/2}$ = 8 Hz, H-7), 2.10 (3 H, s, $CH_3CO$), 2.02 (3 H, s, $CH_3CO$), 1.90–1.80 (6 H, complex signals, H-4' and H-5'), 0.91 (3 H, s, $J$ = 7 Hz, $CH_3$ at C-1); MS, $m/z$ (relative intensity) 462 ($M^+$, 1), 447 (3), 419 (5), 402 (10), 379 (8), 342 (10), 302 (12), 242 (15), 100 (85), 83 (95), 60 (72), 43 (100), 42 (75).

**X-ray Analysis of 15-Hydroxy-3,14-epoxyheliangolide (2).** Crystals of **2** suitable for analysis were obtained by slow crystallization from ethyl acetate. They were orthorhombic, space group $P2_12_12_1$, with $a$ = 7.757 (2) Å, $b$ = 13.855 (6) Å, $c$ = 17.619 (7) Å, and $d_{calcd}$ = 1.262 g $cm^{-3}$ for $Z$ = 4 ($C_{20}H_{26}O_7$). The intensity data were measured on a Nicolet R3m diffractometer (graphite monochromated Mo K$\alpha$ radiation). The size of the crystal used was approximately 0.18 × 0.16 × 0.40 mm, $\mu$ = 0.87 $cm^{-1}$. A total of 1453 accessible reflections were measured on $\omega$ scan mode for $3 < 2\theta < 45$ of which 1049 were considered to be observed $|F_o| \geq 3\sigma(F_o)$. The structure was solved by direct methods and refined by block diagonal least squares with anisotropic temperature factor for non-hydrogen atoms and fixed isotropic temperature factor $U$ = 0.045 $Å^2$ for H atoms. The final $R$ value was 0.0596 ($R_\omega$ = 0.0592). Atomic scattering factors were from the International Tables for X-ray crystallography. All calculations were performed on a NOVA 45 computer with the SHELXTL package program.[20]

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**Supplementary Material Available:** Tables of crystallographic data for compound **2** (5 pages). Ordering information is given on any current masthead page.

(20) (a) Sheldrick, G. M. SHELXTL Revision 3. An Integrated System for Solving, Refining and Displaying Structures from Diffraction Data; University of Göttingen: Federal Republic of Germany, 1981. (b) *International Tables for X-Ray Crystallography*; Kynoch: Birmingham, 1974; Vol. IV, pp 99–101.