

mol) was dissolved in 500 ml of benzene and sodium methoxide (5.4 g, 0.10 mol) was added. The mixture was stirred and solvent distilled out until all water and methanol had been removed. The mixture was then cooled to 35°, and allyl bromide (12.8 g, 0.106 mol) was added. After being stirred at room temperature for 3 days, the mixture was washed with water, diluted with twice its volume of petroleum ether, extracted with Claisen alkali, washed with water, dried over magnesium sulfate, and evaporated under vacuum to give 18.3 g of brown oil. Chromatography on Florisil (eluting with 20% methylene chloride in petroleum ether) gave 6.7 g (0.031 mol, 31%) of dienone 14, λ_{\max} 320 m μ (log ϵ 3.67).

Anal. Calcd for C₁₅H₂₀O: C, 82.5; H, 10.2. Found: C, 82.9; H, 10.4.

Its nmr spectrum had singlets (combined total 12 H) at τ 9.07 and 9.11, a doublet (3 H, $J = 0.5$ Hz) at τ 8.36, complex peaks (2 H and 3 H, respectively) at τ 7.5 to 8.0 and from τ 4.4 to 5.65, a doublet (1 H, $J = 2.0$ Hz) at τ 4.32, and a multiplet (1 H) at τ 3.23.

Rearrangement of Dienone 14.—Dienone 14 (0.75 g, 0.0034 mol) was heated at 120° for 3 hr. The carbonyl peak was then completely gone. Vpc analysis at 150° showed the presence of only one compound in the product. An analytical sample was isolated by vpc on a 20%, 5-ft SE-30 column at 200°.

Anal. Calcd for C₁₅H₂₀O: C, 82.5; H, 10.2. Found: C, 82.5; H, 9.98.

The product was identified as allyl 4-*tert*-butyl-2,6-dimethylphenyl ether (15) by its nmr spectrum: singlets (9 H and 6 H, respectively) at τ 8.75 and 7.80, a jagged doublet (2 H, $J = ca. 6$ Hz) at τ 5.77, a complex group of peaks (3 H) at τ 4.2–5.3, and a singlet (2 H) at τ 3.10.

Registry No.—4, 26319-90-4; 6, 26332-98-9; 7, 26319-92-6; 9, 20966-24-9; 11, 26319-93-7; 12, 26347-47-7; 13, 26347-39-7; 14, 26319-94-8; 15, 26319-95-9.

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Chihuahuin, a New Germacranolide from *Ambrosia confertiflora* DC. (*Compositae*)¹

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A continuation of our investigation² of the infra-specific variation of sesquiterpene lactones in *Ambrosia confertiflora* DC. led to the isolation and structure determination of a new germacranolide. Chloroform extraction of plant material collected north of

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(2) For recent investigations on the sesquiterpene lactones in this species, see (a) T. J. Mabry in "Phytochemical Phylogeny," J. B. Harborne, Ed., Academic Press, London, 1970, Chapter 13; (b) N. H. Fischer, and T. J. Mabry, *Tetrahedron*, **23**, 2529 (1967); (c) N. H. Fischer, and T. J. Mabry, *Chem. Commun.*, 1235 (1967); (d) N. H. Fischer, T. J. Mabry, and H. B. Kagan, *Tetrahedron*, **24**, 4091 (1968); (e) J. Romo, A. Romo de Vivar, A. Velez, and E. Urbina, *Can. J. Chem.*, **46**, 1535 (1968); (f) N. S. Bhacca and N. H. Fischer, *Chem. Commun.*, 68 (1969); (g) W. Herz, G. Anderson, S. Gibaja, and D. Raulais, *Phytochemistry*, **8**, 877 (1969); (h) H. Yoshioka, W. Renold, N. H. Fischer, A. Higo, and T. J. Mabry, *ibid.*, **9**, 823 (1970).

Chihuahua, Mexico, yielded artemisiifolin³ (2), a germacranolide of known structure, and a new substance which we named chihuahuin (1), C₁₇H₂₂O₅. The spectral data suggested that the new sesquiterpene lactone was a germacranolide: λ_{\max} (EtOH) 209 nm (ϵ 17,200); ir bands (CHCl₃) at 3550 (hydroxyl), 1760 (γ -lactone), 1740 and 1210 (acetate), 1650 cm⁻¹ (double bonds). The 60-Mc nmr spectrum exhibited seven isolated and well-resolved signals which are characteristic for the germacranolides: two vinylic methyl doublets at 1.59⁴ ($J = 1$ Hz) and 1.63 ($J = 1.5$ Hz), a pair of double doublets for the C-11 methylene protons of the α,β -unsaturated γ -lactone at 5.79 ($J = 3$ and 1 Hz) and 6.30 ($J = 3.5$ and 1 Hz), a one-proton triplet at 4.42 ($J = 3$ Hz), a complex one-proton signal at 3.1, and an acetate methyl singlet at 2.07. The region between 4.6 and 5.5, integrating for 4 protons, was a complex set of signals that could only be resolved with a 100-Mc spectrum and extensive spin-decoupling experiments. Irradiation at the center of the complex one-proton signal at 3.1 altered the signals for the two C-11 methylene protons at 5.79 and 6.30 into a pair of broadened singlets; hence the C-7 proton could be ascribed to the 3.1 signal. Furthermore, the region around the C-6 and C-8 proton signals (4.9–5.0) was also affected. Indeed, irradiation at 4.98 changed the C-7 proton signal into a broad doublet and also changed the C-5 proton doublet at 5.37 ($J = 10$ Hz) into a broadened singlet, thus suggesting that the C-7 proton had only 2 adjacent protons. In reverse, irradiation at 5.37 altered the two vinyl methyl doublets into two singlets and also changed the C-6 proton double doublet at 4.95 ($J = 8$ and 10 Hz) into a doublet ($J = 8$ Hz) thus confirming the assignment for the C-6 proton. The position of the second vinyl proton became evident when irradiation was carried out at either 1.66 or 1.59, the resonance of the vinylic methyl groups: (a) a clearly resolved double doublet became evident for the first time at 5.18 ($J = 8$ and 10.5 Hz), hence establishing the position of the C-1 proton with respect to certain other groups to be as shown in 1; (b) the broad doublet at 5.37 for the C-5 proton became a sharp doublet ($J = 10$ Hz).

The data presented above left only the positions of the hydroxyl and acetate groups to be determined. That the one-proton triplet at 4.42 ($J = 3$ Hz) indeed belonged to a proton located on a carbon atom bearing a hydroxyl group became apparent when (a) acetylation of 1 yielded 3 and the triplet shifted, as expected, downfield to 5.27, and (b) irradiation of either 2.47 or 2.36 (the region of CH₂ resonance) changed the triplet at 4.42 into a singlet and irradiation at 4.44 had a marked effect upon the CH₂ region between 2.28 and 2.65. Thus, the hydroxyl group could either be placed at C-3 or C-9. The latter position was excluded when dihydrochihuahuin (4) was heated for 5 min at 205° to yield a compound which appeared from nmr data to be the expected Cope product 5; it was characterized

(3) The structure assigned to artemisiifolin was previously ascribed to salonitenolide, a germacranolide from *Centaurea salonitana* Vis.: cf. (a) T. H. Porter, T. J. Mabry, H. Yoshioka, and N. H. Fischer, *Phytochemistry*, **9**, 199 (1970); (b) H. Yoshioka, W. Renold, and T. J. Mabry, *Chem. Commun.*, 147 (1970).

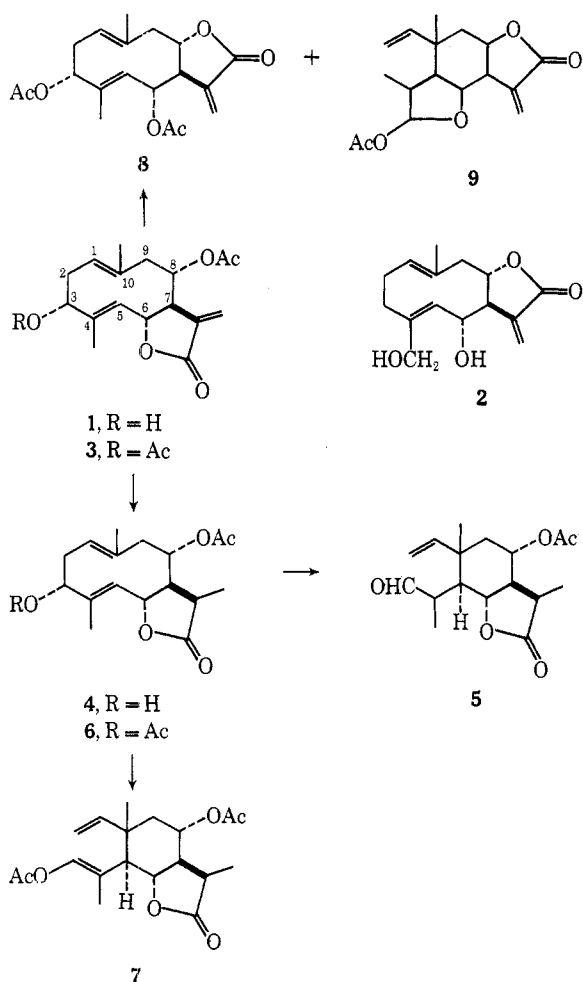
(4) All chemical shift values are reported in ppm (δ scale) relative to TMS as an internal standard. Numbers in parentheses denote coupling constants in hertz.

TABLE I
 NMR DATA FOR CHIHUAHUIN AND DERIVATIVES^a

Compd	H ₁ and H ₅	H ₂	H ₃	H ₈	C ₄ and C ₁₀ methyl groups	C ₁₁ CH ₂	C ₁₁ CH ₃	Miscellaneous
1	H ₁ , 5.18 dd ^b (8.0 + 10.5) H ₅ , 5.37 br dd ^b (10)	4.42 t (3.0)	4.95 dd ^b (8.0 + 10.0)	4.92c	1.63 d (1.5) 1.59 d (1.0)	6.30 dd (3.5 + 1.2) 5.79 dd (3.0 + 1.0)		Ac, 2.07 H ₇ , 3.10 c
3	... ^c	5.27 t (3.0)	... ^c	... ^c	1.72 d (1.0) 1.59 d (1.0)	6.30 dd (3.5 + 1.2) 5.79 dd (3.0 + 1.0)		Ac, 2.07 (6 H) H ₇ , 3.08 c
4	... ^d	4.42 t (3.0)	... ^d	... ^d	1.62 d (1.5) 1.54 d (1.0)		1.38 d (6.0)	Ac, 2.07
6	... ^e	5.27 t (3.0)	... ^e	... ^e	1.70 d (1.0) 1.56 d (1.0)		1.40 d (6.0)	Ac, 2.07 (6 H) H ₇ , 2.70 c
7	H ₁ , 5.74 dd (10.0 + 18.0) H ₅ , 2.83 d (12.0)	6.95 q (1.5)	4.27 dd (10.0 + 12.0)		1.70 d (1.5) 1.13 (C ₁₀ methyl)		1.22 d (7.0)	Ac, 2.05 (6 H) H _{2a} , 4.84 dd (18.0 + 1.2) H _{2b} , 4.86 dd (10.0 + 0.5) Ac, 2.08 H ₇ , 2.72 tt (12.0 + 3.0) H _{2a} , 5.05 d ^f (10.0) H _{2b} , 5.04 d (18.0)
9	H ₁ , 5.81 dd (10.0 + 18.0)	5.83 d (4.0)	3.90 t (12.0)	3.94 dd (10.0 + 0.5)	1.12 d (6.0) 1.17 (C ₁₀ methyl)	6.10 d (3.0) 5.75 d (3.0)		Ac, 2.08 H ₇ , 2.72 tt (12.0 + 3.0) H _{2a} , 5.05 d ^f (10.0) H _{2b} , 5.04 d (18.0)

^a Spectra were determined in CDCl₃ with a Varian A-60 spectrometer. Chemical shifts are given in ppm (δ scale) relative to TMS as an internal standard. Number in parentheses denote coupling constants in hertz. Singlets are unmarked, multiplets are described as follows (or combinations thereof): d = doublet, t = triplet, c = complex signal whose center is given, brd = broad, q = quartet. ^b These chemical shifts were determined with a Varian HA-100 spectrometer and by spin decoupling. ^c A complex set of signals between 4.70 and 5.30 integrating for 5 protons. ^d A complex set of signals between 4.60 and 5.40. ^e Complex set of signals between 4.65 and 5.35. ^f Geminal coupling less than 0.5 hertz.

by the appearance of a doublet at 9.83 owing to the C-3 aldehyde proton. This latter result places the hydroxyl group at position 3; therefore the acetate group



must be attached at C-8. The C-8 proton signal overlapped the signals due to the C-1, C-5, and C-6 protons but decoupling experiments permitted assignment of the center of the C-8 signal to be at 4.92.

One final spin-decoupling experiment was carried out to demonstrate the presence of geminal coupling for the C-11 methylene protons in 1.⁵ Irradiation at 6.33 changed the double doublet at 5.79 (H trans to the carbonyl group of the γ -lactone) into a doublet ($J = 3$ Hz). In reverse, irradiation at 5.82 changed the double doublet at 6.3 (H cis to the carbonyl) into a doublet ($J = 3.5$ Hz).

Dihydrochihuahuin acetate (6) gave the expected enol acetate 7 upon pyrolysis. The Cope product was characterized by its nmr spectrum: quartet at 6.95 ($J = 1.5$ Hz) for the C-3 proton and a characteristic pattern for a monosubstituted vinyl group: a double doublet at 5.74 ($J = 10$ and 18 Hz) for the C-1 proton and a pair of double doublets at 4.84 ($J = 18$ and 1 Hz) and 4.86 ($J = 10$ and 0.5 Hz) for the C-2 protons.

The results described above suggested structure 1 (without stereochemistry) for chihuahuin. The structure proof, including stereochemistry, was provided by the conversion of 1 to chamissonin diacetate (8),⁶ a compound of known structure and stereochemistry.⁷ This conversion is in accord with a general relactonization rule for germacranolides containing both C-6 and C-8 lactonizable α -oxygen functions,^{3b} that is, they always relactonize to C-8 following strong alkaline treatment and subsequent acidification. In addition to chamissonin diacetate, a by-product, which was

(5) The detailed investigation of the geminal coupling phenomenon is presently underway by H. Yoshioka, T. J. Mabry, M. A. Irwin, T. A. Geissman, and Z. Samek.

(6) The isolation from this reaction of chamissonin itself was difficult to achieve as it tends to polymerize on work-up.

(7) M. F. L'Homme, T. A. Geissman, H. Yoshioka, T. H. Porter, W. Renold, and T. J. Mabry, *Tetrahedron Lett.*, 3161 (1969).

named neochihuahuin, $C_{17}H_{22}O_5$, was obtained in about equal yield; it was tentatively assigned structure 9 on the basis of spectral data (ir and nmr, Table I).

Experimental Section⁸

Isolation of Chihuahuin (1) and Artemisiifolin (2).—Dried ground stems and leaves (1.86 kg) of *Ambrosia confertiflora* DC. (voucher⁹ no. 257744; collection made on Aug 22, 1967, about 25 miles north of Chihuahua, Mexico) were extracted three times with a total of 15 l. of $CHCl_3$. Work-up of the extracts in the usual way¹⁰ afforded 3.5 g of crude syrup. A second extraction yielded 21.5 g of crude syrup after work-up and a third and final extraction gave an additional 5.6 g of crude syrup. Column chromatography on silica gel of the first 3.5 g of crude extract yielded 0.5 g of chihuahuin and 0.42 g of artemisiifolin. In a second column chromatographic run, 15.8 g of crude syrup (10 g of the second extract and all of the third extract, 5.6 g) were dissolved in CH_2Cl_2 and chromatographed over silica gel (packed in CH_2Cl_2). The column was successively eluted first with 500 ml of CH_2Cl_2 , followed by a CH_2Cl_2 -ethyl acetate solvent mixture containing an increasing amount of ethyl acetate [400 (9.5:0.5), 400 (9:1), 600 (8.5:1.5), 1000 (4:1), 400 (3:1), 400 (7:3), 200 (3:2), 1000 (1:1), 200 ml (1:3)], 200 ml of ethyl acetate, and finally 500 ml of methanol. For the first 1100 ml of eluent, 100-ml fractions were taken (fractions 1-11); then 20-30-ml fractions were collected (no. 12-58) for the next 1200 ml of eluent, and finally 60-ml fractions were taken (no. 59-120) for the last 3500 ml of eluent. All fractions were monitored by tlc. Fractions 45-56 were combined and evaporated to dryness; the residue was redissolved in CH_2Cl_2 . After the addition of a small amount of diisopropyl ether, the solution was allowed to stand at -20° for several days; chihuahuin crystallized out in long (5-6 mm) white rhombic needles (956 mg). The mother liquor gave an additional 725 mg of chihuahuin. One recrystallization from CH_2Cl_2 -diisopropyl ether yielded pure chihuahuin (1), mp $168-170^\circ$,¹¹ $[\alpha]^{25}_D +112^\circ$ ($CHCl_3$, c 4.85).

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24; O, 26.11. Found: C, 66.78; H, 7.40; O, 25.98.

Chihuahuin could be acetylated with Ac_2O and pyridine under standard conditions but the acetate 3 which was characterized by nmr (Table I), was not obtained crystalline.

Fractions 91-100 were combined and evaporated to dryness, and the residue was redissolved in CH_2Cl_2 . After some *n*-hexane and a few seed crystals were added to the solution, it afforded, at room temperature, 1.30 g of artemisiifolin (2), mp $128-130^\circ$; the material was identical (ir, nmr, mixture melting point and tlc) with an authentic sample.^{3a}

Dihydrochihuahuin (4).—To an ice-cooled solution of 405.4 mg of chihuahuin (1) (1.325 mmol) in 40 ml of methanol was added a freshly prepared solution of 105 mg of sodium borohydride (2.78 mmol) in 10 ml of methanol. After stirring the cold solution for 30 min, 20 ml of distilled water were added. The final solution was extracted with 200 ml of CH_2Cl_2 . The organic layer was washed twice with water, dried over anhydrous magnesium sulfate, filtered, and evaporated to dryness to yield a colorless oil. After redissolving the oil in CH_2Cl_2 , *n*-hexane was added until turbidity persisted. Dihydrochihuahuin (4) crystallized in needles at room temperature, 332 mg (81% of theory), mp $151-155^\circ$. The nmr spectrum of dihydrochihuahuin did not exhibit the characteristic pair of doublets for the C-11 methylene protons, but instead exhibited a new methyl doublet at 1.38 ($J = 6$ Hz).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85; O, 25.94. Found: C, 66.36; H, 7.98; O, 25.79.

Pyrolysis of Dihydrochihuahuin (4) and Its Acetate (6).—Dihydrochihuahuin (20 mg) was heated under a water pump vacuum at 205° in a sublimation tube. After 5 min, the tube was rapidly cooled with ice water. A colorless oily residue (19 mg)

was obtained and tlc (CH_2Cl_2 :ethyl acetate, 1:1) indicated the presence of one major compound; an nmr spectrum of the material showed a characteristic doublet for an aldehyde proton (as in 5) at 9.82. In a similar experiment 100 mg of dihydrochihuahuin acetate (6) afforded 95 mg of 7 as a crude oily residue (tlc, benzene:ethyl acetate, 3:1). An nmr spectrum (Table I) of the material was in agreement with structure 7.

Conversion of Chihuahuin (1) to Chamissonin Diacetate (8) and Neochihuahuin (9).—To 106 mg of finely powdered chihuahuin (1) were added 1.85 ml of a 10% aqueous sodium hydroxide solution. Since chihuahuin did not dissolve at room temperature, the mixture was heated for 10 min on a steam bath¹² to give a lightly yellow colored solution which was cooled in ice water and then rapidly evaporated under high vacuum without applying heat. To the viscous oil-like residue thus obtained was added 2 ml of pyridine and 10 ml of acetic anhydride. The solution was allowed to stand at room temperature for 17 hr and then it was filtered from the solid material (sodium acetate) and the salt was washed with a few milliliters of ethyl acetate. Washings and filtrate were evaporated under vacuum to dryness to yield 167 mg of a yellow oil which was dissolved in ethyl acetate; the solution was washed several times with water to remove the last traces of sodium acetate. After the ethyl acetate extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated, a crude yellow oil was obtained which contained two major constituents by tlc ($CHCl_3$:ether, 3:2), R_f values 0.56 and 0.40, the latter value was identical with that observed for a cochromatographed sample of chamissonin diacetate. Preparative thick layer chromatography of the crude oil (silica gel G; $CHCl_3$:ether, 3:2) yielded 28 mg of chamissonin diacetate (8) (23% of theory). After recrystallization of the crude material from 95% ethanol, 12.3 mg of 8, mp $175-176.5^\circ$, was obtained. The material was identical (ir, nmr, mixture melting point, and tlc) with an authentic sample of chamissonin diacetate.

The less polar fraction from the thick layer plates (corresponding to the material with an R_f of 0.56) gave 35 mg of a partially crystalline material which gave, after trituration with *n*-hexane, 22 mg of crystalline material, mp $112-119^\circ$. Recrystallization of the crude crystals from ether *n*-hexane yielded 18 mg, mp $119-120^\circ$, of neochihuahuin (9): ir bands ($CHCl_3$) 1770 and 1742 (carbonyls), 1670 and 1638 (double bonds), 1230 cm^{-1} (acetate).

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.43; H, 7.38.

Registry No.—1, 25739-42-8; 3, 25739-43-9; 4, 25739-44-0; 6, 25739-45-1; 7, 25739-46-2; 9, 25739-47-3.

(12) The Cope rearrangement required for the ultimate formation of neochihuahuin may have occurred during this step.

Isomerization of (–)-β-Pinene to High Optical Purity (–)-α-Pinene

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A recent publication¹ dealing with the isomerization of β-pinene to high optical purity α-pinene utilizing iron pentacarbonyl, has prompted us to disclose our method for carrying out this conversion.

(1) Philip A. Spaninger and J. L. Von Rosenberg, *J. Org. Chem.*, **34**, 3658 (1969).

(8) All melting points are uncorrected. Analyses were determined by Dr. Alfred Bernhardt, Mikroanalytisches Laboratorium Elbach über Engelskirchen, West Germany.

(9) This voucher is deposited in The University of Texas at Austin Herbarium.

(10) See, for example, T. J. Mabry, H. E. Miller, H. B. Kagan, and W. Renold, *Tetrahedron*, **22**, 1139 (1966).

(11) The melting point of chihuahuin was determined by placing crystals on a hot plate at different temperatures. If inserted below 168° , polymerization occurred, and, if inserted above 170° , chihuahuin melted immediately.