Aerograph A90-P instrument using the 0.25-in. columns listed: (D) 10 ft, 5% KOH-5% Carbowax 4000 on Chromosorb W, (E) 10 ft, 5% UCONLB550X on Chromosorb G.

Preparation of the *cis*-Bicyclo[6.1.0]nonane-9-methanols (*syn*-3 and *anti*-3).—To 165 g (1.5 mol) of cyclooctene was added 4.0 g of anhydrous cupric sulfate. The mixture was heated and stirred at 70–80° under nitrogen while 28.5 g (0.25 mol) of ethyl diazoacetate[6] was added dropwise (*ca.* 1 hr for addition). The solution was heated and stirred at 55–60° overnight. The cupric sulfate was removed by filtration. Analysis by gc on column B at 110° showed essentially two volatile products in a ratio of 34:66.

To 140 ml of Vitride in 100 ml of dry ether was slowly added (*ca.* 2 hr) the crude reaction mixture at reflux. The mixture was allowed to cool to room temperature and stir overnight. To the crude reaction solution was added dropwise 100 ml of saturated sodium carbonate solution. The organic and aqueous layers were separated, and the organic layer was washed with two 50-ml portions of saturated sodium carbonate solution, four 50-ml portions of water, and one 50-ml portion of saturated salt solution. The organic layer was dried over anhydrous magnesium sulfate and filtered, and all of the volatile solvent was removed on a rotary evaporator. The crude, dark mixture was vacuum distilled to give 18.6 g (48.3%) of light yellow liquid, bp 96–100° (0.6 mm). Gc analysis on column C at 135° showed essentially two components in a ratio of 66:34 which were separated by gc using column D at 140°. Collection of the first component gave *anti*-3 (100% pure by gc): ir (neat) 3325, 3000, 2920, 2870, 1470, 1440, 1140, 1103, 1075, 1030, 1020 cm^{-1}; nmr (CCl_4, 100 MHz) δ 0.31–0.68 (m, 3), 0.75–2.23 (m, 13), 3.35 (d, $J = 6$ Hz, 2).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.66. Found: C, 77.72; H, 11.88.

Collection of the second peak gave 35% *anti*-3 and 65% *syn*-3. A more effective separation was obtained by converting the 66:34 *syn*- and *anti*-3 mixture to trimethylsilyl ethers and separating the mixture on column E at 115°. Hydrolysis[7] of the second gc fraction gave *syn*-3 (still contained 12% *anti*-3): ir (neat) 3375, 3000, 2920, 2870, 1470, 1440, 1160, 1145, 1105, 1090, 1015 cm^{-1}; nmr (CCl_4, 100 MHz) δ 0.57–2.30 (m, 16), 3.57 (d, $J = 7$ Hz, 2).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.66. Found: C, 77.68; H, 11.74.

The trimethylsilyl derivative was prepared by shaking for 10 min a mixture of 100 μl of **3**, 200 μl of Tri-sil,[8] and 400 μl of dimethyl sulfoxide. The mixture was extracted twice with 2-ml portions of pentane. The pentane solution was washed with 10% sulfuric acid and water and dried over sodium sulfate.

Acid-Catalyzed Rearrangement of *anti*-3.—To 0.11 g (0.73 mmol) of *anti*-3 was added 0.84 ml of 0.23 *M* perchloric acid and 4 ml of dioxane. The mixture was heated and stirred at 80° for 15 hr, whereupon all of the starting material was shown to be gone by gc on column C. To the mixture was added 30 ml of ether. The ether solution was washed with two 20-ml portions of 10% sodium carbonate, one 20-ml portion of water, and one 20-ml portion of saturated salt solution. The organic layer was dried over anhydrous magnesium sulfate and filtered, and the ether was removed on a rotary evaporator to yield 0.10 g (95%) of clear, viscous **4** (>95% pure on column C at 135°): ir (neat) 3320, 2900, 2700, 1450, 1350, 1260, 1170, 1120, 1053, 1015, 985, 860, 705 cm^{-1}; nmr (CCl_4, 100 MHz) δ 1.06–1.83 (m, 10), 1.83–2.28 (m, 3), 2.32–2.69 (m, 1), 3.21 (OH, 1), 3.73, (m, 1), 5.45 (m, 2). The ir and nmr spectra of an authentic sample of *trans*-cyclodec-3-en-1-ol and those of the major component were identical.

Further gc analysis was conducted on the trimethylsilyl ether of the reaction product (prepared as above). Analysis by gc on column A at 130° showed essentially one peak (>98%, 6.8 min). Coinjection of this major component with the trimethylsilyl derivative of *trans*-cyclodec-3-en-1-ol on two different columns gave one peak. The minor component (<2%, 10.0 min) was shown not to be the trimethylsilyl ether of *cis*-cyclodec-3-en-1-ol by coinjection with an authentic sample.

Acid-Catalyzed Rearrangement of *syn*-3.—A solution of 0.011 g of *syn*-3 (containing 12% *anti*-3), 2 ml of dioxane, and 84 μl of 0.23 *M* perchloric acid was heated at 80–85° for 20.5 hr and then worked up as described above. A portion of the reaction products was converted to trimethylsilyl derivative (as above) and analyzed on column A at 130° which showed four products in a ratio of 9:4:46:40. The latter two components were shown to be *trans*-4 and *cis*-4, respectively, by coinjection on columns A and C with authentic samples and by mass spectral comparison with these samples.

Acid-Catalyzed Rearrangement of a Mixture of *syn*-3 and *anti*-3.—To 6.5 g (0.042 mol) of **3** (66:34 mixture of *anti*-3 and *syn*-3) was added 220 ml of dioxane, 48 ml of water, and 1.6 g of 70% perchloric acid. The mixture was stirred, heated for 12 hr at 85–90°, and worked up as described above, which gave 6.2 g (95%) of products. A portion was converted to the trimethylsilyl derivative (as above) and analyzed on column A at 130° which gave four peaks in a ratio of 6:64:16:14. The first peak corresponds to the 9% unknown component observed from rearrangement of *syn*-3. The next two peaks correspond to *trans*-4 and *cis*-4; the last peak is unreacted *syn*-3 (coinjection on column A and C and mass spectral comparison).

Bicyclo[6.2.0]decan-9-ols (6).—The method of Wiberg and Nakihara[2] was used to produce bicyclo[6.2.0]decan-9-one (C=O at 1760 cm^{-1}), which was reduced with lithium aluminum hydride to give a mixture of alcohols (6): ir (neat) 3430, 2980, 2860, 1465, 1440, 1325, 1190, 1135, 1095, 1065, 870, 810 cm^{-1}; nmr (CCl_4, 100 MHz) δ 1.07–2.10 (m, 16), 3.23–4.02 (m, 1), 4.93 (s, OH).

Anal. Calcd for $C_{10}H_{18}O$: C, 77.88; H, 11.66. Found: C, 77.78; H, 11.82.

Analysis of the trimethylsilyl derivative of the above mixture (column A) indicated four overlapping peaks in an approximate ratio of 5:50:40:5. Coinjection of this mixture with the trimethylsilylated mixture from **3** gave no enhancement of peaks.

Registry No.—*syn*-3, 38858-51-4; *anti*-3, 38858-52-5; *trans*-4, 29971-50-4; *cis*-4, 29746-36-9; 6, 38868-39-2; cyclooctene, 931-88-4; bicyclo[6.2.0]decan-9-one, 38868-40-5.

Acknowledgment.—We thank the Research Corporation for their support of this work.

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(8) Pierce Chemical Co.

Christinine, a New Epoxyguaianolide from *Stevia Serrata* Cav.

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Contribution No. 367 from the Instituto de Química de la Universidad Nacional Autónoma de México, México 20, D. F.

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Very few sesquiterpene lactones had been isolated from *Stevia* genera.[1] We now describe the structure determination of a new guaianolide from *Stevia serrata* Cav.[2] which we have named *christinine*.

Fractionation of the methanol extract with chloroform and chromatographic separation involving silica gel and alumina yielded christinine ($C_{19}H_{24}O_7$).[3] The ion *m/e* 304 [$M^+ - (CH_3COOH)$] was observed by mass spectrometry: mp 164–165°; $[\alpha]D$ + 19.72° (*c* 3.65, $CHCl_3$); uv max (95% EtOH) 215 nm (ϵ 2270); ir ($CHCl_3$) 1775 (lactone), 1730 cm^{-1} (acetate).

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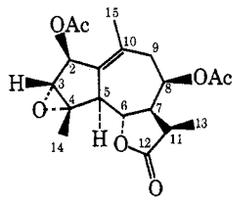
(2) We are indebted to Mr. H. Quero-Rico from the Instituto de Biología, UNAM, for the classification of the plant.

(3) Cited empirical formula was supported by satisfactory analysis and/or mass spectral molecular weight. We thank Mr. Cortés for the mass spectral data.

The proposed structure and stereochemistry of christinine (**1**) are based on the evidence gained from



1

the chemical shifts and coupling constants of its HA-100 nmr spectra (Table I) and verified by spin-decoupling experiments. Confirmations of the various assignments and pertinent coupling constants were sought using Eu(DPM)$_3$ as a chemical shift reagent.

TABLE I

NMR DATA FOR CHRISTININE

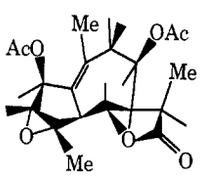
Proton	Multiplicity	Chemical shifts[a] C_6D_6	Chemical shifts[a] $CDCl_3$	Coupling constants
H_2	c	5.58	5.82	$J_{2,3} = 2.0$ $J_{2,5} = 1.0$ $J_{2,9} = J_{2,9'} = 1.75$ $J_{2,15} = 1.75$
H_8	ddd	4.73	5.29	$J_{8,7} = 1.5$ $J_{8,9} = 6.0$ $J_{8,9'} = 1.5$
H_6	dd	3.72	4.3	$J_{6,5} = 10$ $J_{6,7} = 9.5$
H_3	dd	3.45	3.64	$J_{3,5} = 1.0$
H_5	br d	2.74	3.17	$J_{5,15} = 1.75$
H_{11}	quintet	2.13	2.74	$J_{11,13} = 7.5$
H_7	ddd	2.25	2.58	$J_{7,11} = 7.0$
OAc	s	1.69	2.11	
OAc	s	1.57	2.01	
H_{14}	s	1.55	1.62	
H_{15}	t	1.41	1.61	
H_{13}	d	0.86	1.16	
H_9[b]	dd	4.7		$J_{9,8} = 7$; $J_{9,9'} = 15$
H_9[b]	br d	3.4		$J_{9',8} = 2$
OAc in C_2[b]	s	5.86		
OAc in C_3[b]	s	3.46		

[a] Chemical shifts are given in parts per million (δ scale) relative to TMS as internal standard. The coupling constants are in hertz. Singlets are marked as s. Multiplets are described as follows: d = doublet, t = triplet, br = broad, c = complex signal whose center is given. [b] Assignments of these signals were made using 30 mg of Eu(DPM)$_3$.

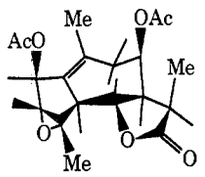
The trans diaxial positions between protons H_5 and H_6 and H_6 and H_7 were assigned based on $J_{5,6}$ and $J_{6,7}$ values, confirming firmly the trans ring attachment of the γ-lactone, H_5 and H_7 being α as has been proposed for globicin,[4] achillin,[5] and hydroxyachillin.[6] Decoupling of the methyl doublet at 1.16 ppm caused the quintet at 2.74 ppm corresponding to H_{11} to collapse to a doublet ($J_{7,11}$ = 7 Hz). Quintets with these characteristics have been observed[6,7] in compounds with the stereochemistry of H_{11} α and a dihedral angle H_{11}–H_7 of *ca.* 30°.

A small long-range 4σ coupling between the allylic protons H_5 and H_2 was observed. This fact can only be made plausible when the two protons are α and a *M* or *W* coupling exists between them.[8] Irradiation of the C_{15} methyl signal at 1.61 ppm caused the multiplet at 5.82 ppm (assigned to H_2) to collapse, producing a quartet. Finally, triple irradiation at 1.61 and 3.17 ppm (attributed to H_5) eliminated the homoallylic and the 4σ coupling at 5.82 ppm, giving a triplet, suggesting similar angles for the homoallylic interaction,[9] H_2 with H_9 and $H_{9'}$, $J_{2,9} = J_{2,9'}$ = 1.75 Hz. This demonstrates that the eliminated second coupling constant, J = 1.0 Hz, was caused by the *M* interaction between H_2 and H_5, possible only when these protons are in the *M* path. Another confirming fact that H_2 is in the α position is the dihedral angle of about 60° between H_2 and H_3,[10] resulting from the largest coupling constant, $J_{2,3}$ = 2.0 Hz, thus establishing H_3 as β leaving the 3,4 epoxide in the α position as has been proposed by Kupchan and coworkers in a series of α-3,4-epoxy lactones.[11]

The stereochemistry of the C_8 acetate could be α or β and each isomer could exist in two conformations, these being the chair and boat forms of the seven-membered ring. One can eliminate the two conformations for the acetate in the α position because the coupling constant $J_{7,8}$ in the chair conformation should be larger. This has been observed in hydroxyachillin.[6] In case of a boat conformer, the signal for the homoallylic interaction of H_2 with H_9 and $H_{9'}$ would be a triplet, and not a quartet, as observed by irradiation of the C_{15} proton signals. From the other two possible conformations structure **1a** can be eliminated for the



1a



1b

following reasons. H_7 and H_8 should be in an α position with a dihedral angle of 15° and would show a larger coupling constant between them. In addition, the quartet for H_2 at 5.82 ppm formed by the homoallylic interactions with H_9 and H_9' would not be observable for this conformation. According to these results, we conclude that christinine must have the conformational structure **1b**.

Experimental Section

The uncorrected melting point was determined on a Culatti capillary melting point apparatus.

Infrared Spectra.—A Perkin-Elmer Model 521 infrared spectrophotometer was used. The sample was run in chloroform.

Optical Rotation.—A Perkin-Elmer Model 141 polarimeter was used.

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Mass Spectra.—An Hitachi Perkin-Elmer RMU-6D double focussing mass spectrometer was used, operating at 75 eV, with an inlet and source temperature of *ca.* 215°.

Nuclear Magnetic Resonance Spectra.—A Varian HA-100 spectrometer with Hewlett-Packard audio oscillator Models 200 CD and 200 AB was used. The samples were run in benzene-d_6 and deuterio chloroform, with tetramethylsilane as internal standard.

Isolation Procedure.—*Stevia serrata* was collected in September 1971 south of México City. A 4-kg portion of dried whole plant was extracted with 25 l. of warm methanol. The extract was filtered and concentrated to 2 l., then 1 l. of water was added and extracted, first with 1 l. of hexane, which was discarded, and then with 2 l. of chloroform. The chloroform extract was washed with water and concentrated to dryness, giving 200 g of a syrupy brown oil. The part soluble in AcOEt 10/B90, 180 g, was chromatographed on silica gel (packed in AcOEt 10/B90). The column was successively eluted, starting with 3 l. of AcOEt 10/B90, and increasing the amount of AcOEt in the solvent mixture in the following fashion: 3 l. (40/60), 4 l. (60/40), 2 l. (100); fractions close to 300 ml were taken. Fractions 20–40 were combined and evaporated to dryness, and the residue, 123 g of syrup, was redissolved in AcOEt 5/B95 and chromatographed in 2 kg of alumina. The column was packed in AcOEt 5/B95 and successively eluted, taking fractions of about 500 ml, first 5 l. (AcOEt 5/B95), 5 l. (AcOEt 10/B90), 20 l. (AcOEt 20/B80), 7 l. (AcOEt 40/B60), and finally 2 l. (AcOEt 90/MeOH 10). All fractions were monitored by tlc. Fractions 32–37 were joined and christinine, 250 mg, crystallized out in ethyl acetate–hexane. One recrystallization from acetone–diisopropyl ether yielded pure christinine (1): mp 164–165°; $[\alpha]_D$ + 19.72° (*c* 3.65, $CHCl_3$); ir ($CHCl_3$) 1775, 1730, 1360, 1000, 940 cm^{-1}; uv max (95% EtOH) 215 nm (ϵ 2270); mass spectrum (75 eV) *m/e* (rel intensity) 304 (M^+ − 60), 244 (45), 202 (64), 200 (74), 185 (47), 171 (77), 159 (100), 157 (63), 141 (70), 131 (85), 129 (77), 128 (82), 115 (71), 105 (24), 91 (39), 60 (31), 45 (20), 43 (30).

Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.62; H, 6.64; O, 30.76. Found: C, 62.54; H, 6.61; O, 30.47.

Registry No.—1, 38555-39-4.

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Total Synthesis of the Pavinane Alkaloid Platycerine[1]

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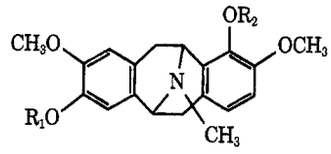
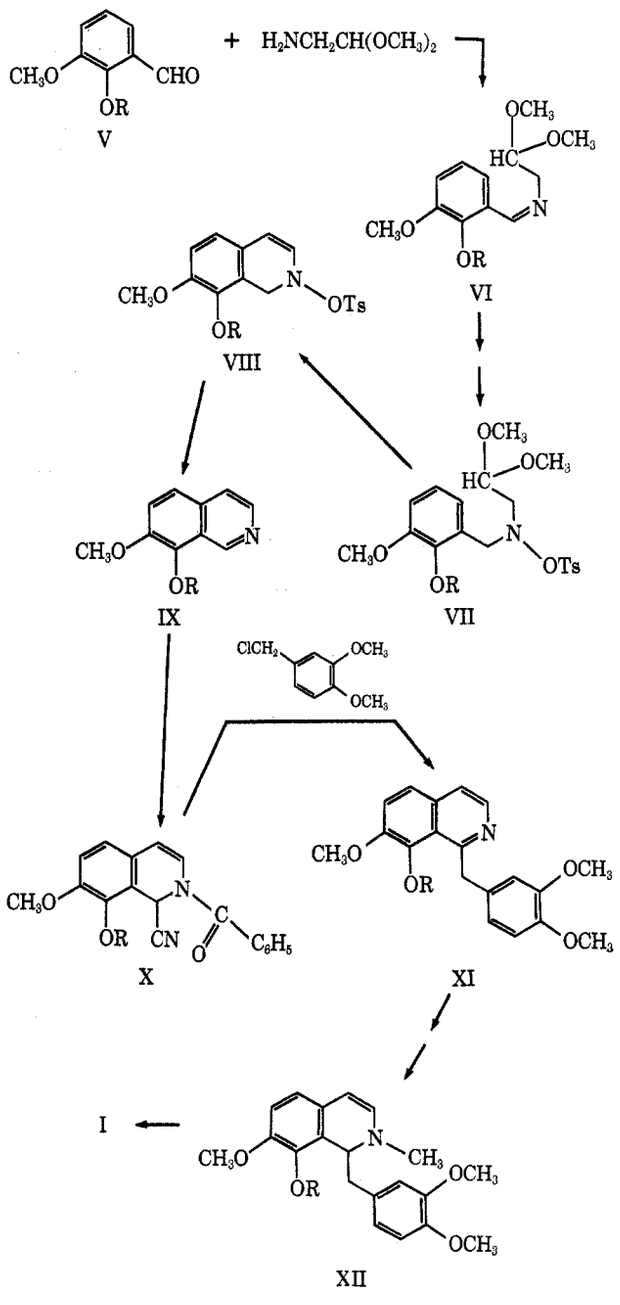
The alkaloid platycerine (I) was first isolated[2] from *Argemone platyceras* Link et Otto. and it was later shown[3] that methylation converted platycerine to *O,O*-dimethylmunitagine (II). II in turn had been prepared[4] by methylation of munitagine (III), whose structure rested[4] upon spectrographic and degradative evidence. Platycerine had also been isolated[5] from *A. gracilenta* Greene and structure I proposed[5] on the basis of its preparation by methylation of munitagine and its mass spectral fragmentation pattern. However, the alternate structure IV for platycerine remained an outside possibility and hence we have synthesized I as final proof of structure.



I, $R_1 = CH_3$; $R_2 = H$
II, $R_1 = R_2 = CH_3$
III, $R_1 = R_2 = H$
IV, $R_1 = H$; $R_2 = CH_3$

Our synthesis was accomplished by means of Scheme I and yielded (±)-platycerine identical with the natural

SCHEME I
(R = $CH_2C_6H_5$)



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