the five components was obtained as an oil.

Analysis of **14** and **15** by ^{13}C NMR revealed that this fraction is a mixture of isomers which proved inseparable by both normal and reverse-phase high-pressure LC under a variety of solvent conditions. Separate control experiments (see below) revealed that the mixture of **14** and **15** is stable to the reaction conditions and results from the further rearrangement of **3c**, that **16** and **17** are interconvertible, but otherwise stable to the conditions, and that **18** is unchanged under the conditions.

Thermolysis of 6*S* Ketone 2c. As described in the preceding experiment, thermolysis of **2c** (25 mg, 0.06 mmol; 6 mL of isooctane, 100 °C, 3 h, Ar) and then a similar workup followed by semipreparative high-pressure LC afforded **3c** (4.0 mg, 16%), **14** and **15** (3.0 mg, 12%), **18** (4.0 mg, 16%), **16** (6.0 mg, 24%), and **17** (6.0 mg, 24%)

Thermal Control Experiments of Ketones 3c, 14, 15, and 18. In side-by-side experiments, the vitamin ketone **3c** (1 mg), a mixture of cyclized isomers **14** and **15** (1 mg), and *trans*-tachysterone **18** (1.5 mg) were individually heated in refluxing isooctane (8 mL, freshly distilled from $LiAlH_4$, 100 °C, Ar atmosphere). Monitoring by high-pressure LC (3% ethyl acetate/Skellysolve B) revealed that the vitamin ketone was completely consumed in 21 h, affording only a mixture of cyclized products **14** and **15** (LC comigration with the cyclized isomers; the ^1H NMR spectrum including the integration of the signals due to the C_{18}-methyls; UV spectral comparisons). The cyclized isomers **14** and **15** were stable to the thermolysis conditions (analytical high-pressure LC using the UV detector and ^1H NMR and UV spectra). The *trans*-tachysterone **18** was also stable to the thermolysis conditions (^1H NMR and UV spectra).

Thermal Equilibration of Ketones 16 and 17. In side-by-side experiments, isomer **16** (1 mg) and the methyl epimer **17** (1 mg) were heated for 3 h in refluxing isooctane (8 mL, freshly distilled from $LiAlH_4$, 100 °C, Ar atmosphere). Separation by high-pressure LC (3% ethyl acetate/Skellysolve B, recycle) afforded equilibrium ratios of the two isomers **16** and **17**. The ratio resulting from **16** was 46% and 54%, respectively, while that obtained from **17** was 48% and 52%, respectively. Ratios obtained by ^1H NMR were carried out by integrating the signals due to the C_{18}-methyl groups. High-pressure LC values were obtained by integration of the UV detector traces. The overall average equilibrium product distribution for the two thermolyses was 47 ± 2% **16** and 53 ± 1% **17**.

A similar control experiment where ketone **17** (6 mg) was heated (100 °C) in *n*-butanol-*d* (2 mL) for 3 h afforded an equilibrium mixture of **16** and **17**. Analysis of this mixture or the individually separated isomers revealed no deuterium incorporation at C_{10} in either **16** or **17** (^1H NMR integration of the signals attributed to the C_{10} hydrogens relative to the C_{15}-vinyl hydrogens).

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Registry No. **1a**, 79421-01-5; **1b**, 74398-26-8; **1c**, 87190-97-4; **2a**, 79421-04-8; **2b**, 74398-27-9; **2c**, 87190-98-5; **3c**, 87190-99-6; **9**, 74398-28-0; **12**, 5601-78-5; **13**, 83788-28-7; **14**, 87191-00-2; **15**, 87247-58-3; **16**, 87191-01-3; **17**, 87247-59-4; **18**, 87191-02-4.

Supplementary Material Available: Spectral and analytical data (5 pages). Ordering information is given on any current masthead page.

Structure of the Antibiotic Cyanobacterin, a Chlorine-Containing γ-Lactone from the Freshwater Cyanobacterium *Scytonema hofmanni*

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The structure of cyanobacterin, an allelopathic substance, has been determined by MS, IR, and ^1H and ^{13}C NMR experiments. Nuclear Overhauser effect (NOE) enhancements have been used to determine the relative stereochemistry, the substitution pattern in the chlorinated aromatic ring, and the geometry of the exocyclic double bonds in cyanobacterin and its anhydro isomers.

We have reported the isolation of an antibiotic, **1**, from a freshwater cyanobacterium (blue-green alga), *Scytonema hofmanni*, that is highly toxic toward other cyanobacteria and green algae.[1] Our studies suggest that **1** is an allelopathic substance, allowing a slow-growing organism like *S. hofmanni* to compete with more prolific species. Electron micrographs of cyanobacterin treated *Synechococcus* sp. and *Euglena gracilis* indicate that the primary target of the antibiotic is the thylakoid membranes.[2] Halogenated metabolites have not been previously isolated from freshwater algae, although marine species are known to produce a variety of chlorinated and brominated compounds.[3] The γ-ylidene-γ-butyrolactone structure is also unusual in that cyanobacterin does not contain any additional α,β-unsaturation as found in other natural products.[4] We report here the structural elucidation of cyanobacterin and anhydro isomers A and B.

Results and Discussion

The high-resolution mass spectrum of **1** has molecular ion peaks at m/z 430.1167 and 432.1128 which correspond to chlorine isotope peaks in the molecular formula $C_{23}H_{23}ClO_6$ (calcd m/z 430.1184 and 432.1154). Other fragments exhibiting characteristic chlorine isotope peaks are m/z 412/414 ($M^+ - H_2O$), 369/371 ($M^+ - H_2O - C_3H_7$), and 169/171 ($C_8H_6ClO_2^+$).

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(4) (a) Niwa, M.; Iguchi, M.; Yamamura, S. *Tetrahedron Lett.* **1975**, 1539. (b) Niwa, M.; Iguchi, M.; Yamamura, S. *Chem. Lett.* **1975**, 655. (c) Niwa, M.; Iguchi, M.; Yamamura, S. *Tetrahedron Lett.* **1975**, 4395. (d) Kazlauskas, R.; Murphy, P. T.; Quinn, R. J.; Wells, R. J. *Ibid.* **1977**, 37. (e) Petters, J. A., Jr.; Wing, R. M.; Sims, J. J. *Ibid.* **1977**, 41.

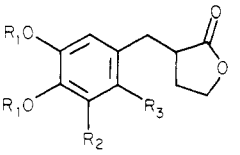
0022-3263/83/1948-4035$01.50/0

Table I. NMR Data[a] for Cyanobacterin and Its Anhydro Isomers

position	1 ^{13}C ($CDCl_3$)	1 ^1H ($CDCl_3$)	1 ^1H (benzene-d_6)	7,[b] ^1H ($CDCl_3$)	8,[b] ^1H ($CDCl_3$)
1	173.1 (s)				
2	53.0 (d)	2.90 (dd, 13.00, 5.42)	2.29 (dd, 7.02, 5.99)		
3	82.3 (S)	1.83-1.94 [OH]	1.36-1.48 [OH]		
4	143.0 (S)				
5a	28.9 (t)	3.10-3.20 (m)	2.85 (dd, 14.72, 7.02)	3.68 (br s)	3.77 (br s)
5b			2.53 (dd, 14.72, 5.99)		
6	133.7 (S)				
7	122.5 (d)[c]	6.83 (d, 1.63)†	6.73 (d, 1.56)†	6.64 (d, 1.59)†	6.63 (d, 1.60)†
8	113.7 (s)				
9	148.7 (s)†				
10	148.8 (s)†				
11	108.0 (d)[c]	6.78 (d, 1.63)†	6.64 (d, 1.56)†	6.68 (dt, 0.78, 1.59)†	6.66 (dt, 0.78, 1.60)†
12	101.8 (t)	6.03 (s)	5.23 (s)	5.99 (s)	6.00 (s)
13	33.4 (d)	2.19 (sep, 6.68)	1.83 (sep, 6.73)	3.12 (sep, 7.16)	2.80 (sep, 7.30)
14	15.7 (q)[c]	0.90 (d, 6.68)†	0.68 (d, 6.73)[d]	1.33 (d, 7.16)	1.08 (d, 7.30)
15	17.9 (q)[c]	1.09 (d, 6.68)†	0.97 (d, 6.73)[d]		
16	105.8 (d)[c]	5.72 (s)	5.66 (s)	6.15 (s)	6.88 (obscured)
17	125.9 (s)				
18, 22	130.1 (d)[c]	7.54 (d, 9.03)	7.61 (d, 8.92)	7.75 (d, 8.95)	7.21 (dd, 0.96, 8.92)
19, 21	114.0 (d)	6.89 (d, 9.03)	6.80 (d, 8.92)	6.91 (d, 8.95)	6.90 (d, 8.92)
20	158.9 (s)				
23	55.3 (q)	3.82 (s)	3.31 (s)	3.84 (s)	3.84 (s)

[a] s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, and m = multiplet. Chemical shifts are reported as parts per million downfield from internal Me_4Si, and coupling constants are in hertz. The ^1H NMR spectra were obtained at 360 MHz. Assignments followed by the same symbol in a column may be reversed. [b] Line-narrowed spectra by sine apodization. [c] Assignments confirmed by specific proton decoupling. [d] Confirmed by NOE enhancement experiments.

Table II. NOE Enhancements of Aromatic Proton Resonances during Benzylic Irradiation in $CDCl_3$

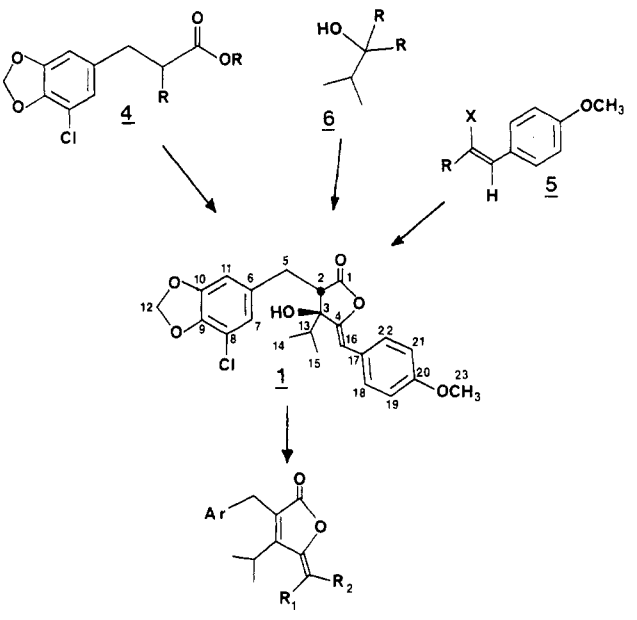


2, $R_1 = CH_2$; $R_2 = H$; $R_3 = Cl$
3, $R_1 = CH_3$; $R_2 = Cl$; $R_3 = H$

compd	irradiated H, ppm	% enhancement[a] downfield H_{Ar}	% enhancement[a] upfield H_{Ar}
1	2.83	4.5	2.1
	3.05	11.5	10.0
2	2.81	0	6.7
	3.33	0	7.7
3	2.71	11.9	12.5
	3.14	6.2	6.7

[a] Enhancements are observed in difference spectra and quantitated by measuring peak heights.

Scheme I



7) Isomer A, R_1=H, R_2=Ar
8) Isomer B, R_1=Ar, R_2=H

The fragment $C_8H_6ClO_2^+$ is obviously highly unsaturated and is associated with the aromatic resonances in the ^1H NMR spectrum at 6.83 (1 H) and 6.78 ppm (1 H); J = 1.63 Hz in $CDCl_3$ (see Table I). A benzo-1,3-dioxole system is indicated by characteristic absorbances, ^1H NMR (6.03 ppm, s) and ^{13}C NMR (101.8 ppm, t), which require chlorine and methylene substituents in the m/z 169/171 tropylium ion. The actual substitution pattern is determined by NOE enhancement experiments with 1–3. The results shown in Table II demonstrate that enhancement is observed only between benzylic and ortho protons. The positive correlation between 1 and 3 describes the substitution pattern. Substructure 4 (see Scheme I) is further described by homo- and heteronuclear decoupling experiments at H(2).

The remaining aromatic doublets in the ^1H NMR spectrum, H(18 + 22) and H(19 + 21), exhibit secondary structure indicative of an AA′BB′ system.[5] This spectral feature and the ortho coupling constant, J = 9.03 Hz, are consistent only with a para-disubstituted benzene. Comparison of the doublets show slightly broader lines in the downfield resonances, indicating long-range coupling. The presence of the *p*-methoxystyrene system is confirmed by ultraviolet absorbance (λ_{max} 266 nm) as well as ^1H (3.82 ppm, s) and ^{13}C (55.3 ppm, q) NMR resonances. The tropylium ion, $C_8H_9O^+$ (m/z 121.0665, calcd 121.0652), presumbly arises from an intramolecular hydrogen rearrangement similar to path A in Scheme II.

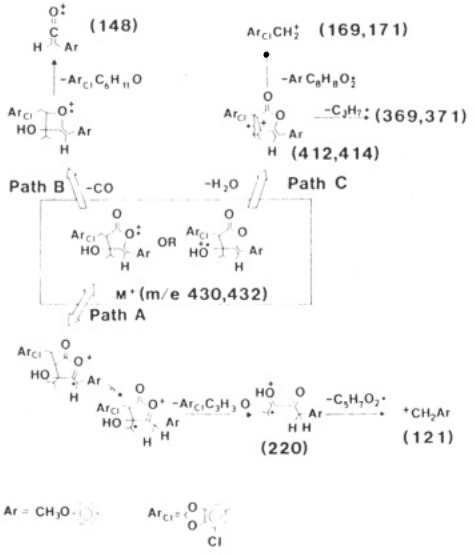
(5) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: New York, 1969; pp 134–136.

Table III. NOE Enhancement Experiments of Cyanobacterin and Anhydro Isomers[a]

irradiated H	enhanced protons (% enhancement)		
	1	7	8
2	7 (8), 11 (8)		
5a	2 (5), 7 (4), 11 (5), 14 (2), 5b (25)		11 (9), 7 (7), 14 + 15 (2)
5b	11 (4), 13 (7), 5a (23), 7 (5)		
7	2 (4), 5a (2), 5b (2)		
OH	2 (10), 16 (7)		
11	2 (4), 5a (2), 5b (2)		
13	14 (2), 15 (2), 7 (2), 5b (5), 11 (3)	16 (11), 14 + 15 (2)	18 + 22 (3), 14 + 15 (2)
14	5a (3), 5b (4), 13 (10)	7 (3), 5 (2), 11 (13), 16 (10), 13 (15)	18 + 22 (3), 5 (5), 7 (4), 11 (6), 13 (20)
15	13 (12), 16 (12)		
16	15 (1), 18 + 22 (9)	18 + 22 (9), 13 (12), 14 + 15 (1)	obscured
18 + 22	16 (15), 19 + 21 (14)	19 + 21 (13), 16 (12)	19 + 21 + 16 (9), 13 (6)
19 + 21	23 (5), 18 + 22 (13)		18 + 22 (8), 23 (10)
23	19 + 21 (9)		

[a] Percent enhancements are observed in difference spectra at 361 MHz and quantitated by peak heights (±10%). Compound **1** is in benzene-d_6, and the anhydro isomers **7** and **8** are in $CDCl_3$. H(5) and H(19 + 21) were not irradiated in anhydro isomer **7A**.

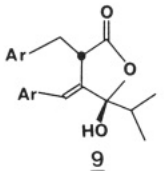
Scheme II. Mass Spectral Fragmentation of Cyanobacterin



The presence of an isolated isopropyl group is indicated in both the ^1H NMR and mass spectra (m/z 369/371). This data combined with the appearance of a sharp exchangeable (D_2O) singlet in anhydrous Me_2SO-d_6 defines the tertiary alcohol substructure **6**.

The relative stereochemistry at C(2)–C(3) in **1** and the configuration of the exocyclic olefin in **1**, **7**, and **8** are determined by NOE enhancement experiments as shown in Table III. Specifically, irradiation of H(13) results in enhancement of H(16) in **1** and **7** while the H(18,22) resonance is enhanced in **8**. In cyanobacterin, irradiation of the hydroxyl resonance produces significant enhancement of H(2). Corroborating data is obtained by using lanthanide shift reagents, $Ln^{III}(fod)_3$ (Ln = Eu, Pr, and Gd), with **1**. Induced chemical shifts decrease in the order OH > H-2 > H-5a > H-16 > H-5b in CCl_4.

The pseudoacid, structure **9**, is ruled out primarily on



9

the basis of the negative reaction of cyanobacterin with diazomethane. Furthermore, base- (CH_3O^- or aqueous OH^-) catalyzed dehydration of **1** in THF results in anhydro isomer **7A**. The infrared absorbances of **1** at 1812 and 1680 cm^{-1} in CCl_4 correlate well with γ-methylene-γ-butyrolactone.[6]

Anhydro isomers A and B are obtained from the algal extract as a 3:1 mixture. In the presence of light and solvent (benzene, MeOH, or $CDCl_3$) isomerization of **7** to **8** occurs. Equilibrium is reached after 7 days so that isomer B predominates, 72%.

The isopropyl methyl groups become equivalent in the ^1H NMR on dehydration of **1**, and in compound **8** they are 0.3 ppm upfield of the corresponding resonance in **7** due to ring-current shielding. In the conversion of **7** to **8**, resonance H(18,22) shifts upfield 0.5 ppm while the olefinic proton, H(16), moves downfield 0.7 ppm. This effect is presumably due to the close proximity of the lactone ring oxygen to H(18,22) in **7** and H(16) in **8**. Extended conjugation in both anhydro isomers is evident in their UV spectra: λ_{max} = 357–360 nm.

Attempts to produce crystals suitable for X-ray diffraction analysis are being made. The total chemical synthesis of cyanobacterin is currently in progress.

Experimental Section

General Methods. Infrared (IR) spectra were recorded on a Nicolet MX-1 spectrophotometer. Mass spectra were taken with a AEI MS-30 at the University of Minnesota Chemistry Department. NOE enhancement experiments were performed by Robert Thrift using a Nicolet NTC–360 nuclear magnetic resonance spectrometer. Sample irradiation (3 s) at a power sufficient for saturation was followed by data acquisition (16K) and transformed with 2-Hz line broadening. ^{13}C NMR spectra were obtained on a Nicolet NT-300 (75.5 MHz), and rotations were measured with a Perkin-Elmer 241 polarimeter. Ultraviolet spectra were recorded on a GCA McPherson EU-700-56. All reagents were obtained from the Aldrich Chemical Co. Fisher solvents were used as received with the exception of tetrahydrofuran (THF) which was distilled from Na/benzophenone under nitrogen. Analtech silica gel GF 1000-μm plates were used for preparative TLC. HPLC purifications were performed on a Hewlett-Packard 1084B with a Du Pont semipreparative Zorbax silica gel column (1.0 × 20 cm). Elemental analyses were carried out by Galbraith Laboratories, Knoxville, TN.

Isolation and Purification. *Scytonema hofmanni* (UTEX 1581) was grown and cell-free material prepared as previously described.[1] Sonicated cells are lyophilized and extracted several times with *tert*-butyl methyl ether (700 ml). The crude concentrate is applied to preparative TLC plates and developed with CCl_4/EtOAc (9:1). Two major fluorescence-quenching bands are

(6) Amos, R. A.; Katzenellenbogen, J. A. *J. Org. Chem.* **1978**, *43*, 560.

visible, consisting of anhydro isomers (R_f 0.6) and cyanobacterin (R_f = 0.4). Each band is rechromatographed with CCl_4/acetone (9:1) on silica gel plates. Final purification is accomplished by normal-phase HPLC with gradient elution (2.5–6.3% EtOAc/CCl_4) and detection at 280 nm. Note: If hexane is used as the nonpolar solvent, partial dehydration of 1 occurs during rotary evaporation: For 1: yield ~200 mg/100 g wet weight of cells; UV (CH_3OH) 266 nm (ϵ 1.2 × 10^4); $[\alpha]_D^{30}$ ($CHCl_3$) +102°; IR (CCl_4) 3580, 2970, 1812, 1680, 1605, 1510, 1500, 1485, 1430, 1255, 1050, and 1040 cm^{-1}; IR (KBr) 3490, 2970, 1805, 1735, 1680, 1610, 1512, 1500, 1480, 1430, 1253, 1180, 1050 cm^{-1}; MS (20 eV), *m/z* (relative intensity) 432 (2.7) and 430 (10.8) (M^+), 414 (25), 412 (77), 371 (7.5), 369 (16), 220 (12), 171 (37), 169 (100), 148 (33), 135 (14), 121 (77). Anal. Calcd: C, 64.11; H, 5.38; Cl, 8.23. Found: C, 64.13; H, 5.51; Cl, 8.43.

The yield of the anhydro isomers is approximately 30 mg/100 g wet weight of cells. MS (20 eV), *m/z* (relative intensity) 412 (100) and 414 (36) (M^+), 369 (22), 371 (7), 148 (11), 121 (14). UV spectra are obtained as the separated isomers elute from an RP-8 analytical column in 85% MeOH/H_2O: isomer A 360 nm (λ_{max}), 243 (0.61 λ_{max}), 286 (0.39 λ_{max}); isomer B 357 nm (λ_{max}), 245 (0.64 λ_{max}), 276 (0.53 λ_{max}). Anal. Calcd: C, 66.91; H, 5.13; Cl, 8.59. Found: C, 66.70; H, 5.33; Cl, 8.80.

3-(6-Chloropiperonyl)dihydro-2(3*H*)-furanone (2). This compound was prepared according to a published procedure by condensation of γ-butyrolactone and 6-chloropiperonal in benzene with $NaOCH_3$.[7] Dehydration of the benzyl alcohol was accomplished with 10% H_2SO_4, and hydrogenation of the resulting olefin (PtO_2, 1 atm of H_2) yielded the desired product. The crude product was purified by preparative TLC on silica gel (ethyl ether; R_f 0.7) and crystallized from CCl_4 to give slightly yellow prisms; mp 103–104 °C (uncorrected); ^1H NMR (270 MHz, $CDCl_3$) δ 1.93–2.32 (m, 2 H, CH_2CH_2O), 2.81 (dd, 1 H, *J* = 18, 8.7 Hz, Ar–CH_a), 2.90 (m, 1 H, Ar–CH_2CH), 3.33 (dd, 1 H, *J* = 18, 5.4 Hz, Ar–CH_b), 4.09–4.37 (m, 2 H, CH_2OC=O), 5.97 (s, 2H, OCH_2O), 6.74 (s, 1 H, 2-Ar), 6.84 (s, 1 H, 5-Ar); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3 (s, C=O), 147.2 and 146.9 (2 s, 3- and 4-Ar), 125.7 (s, 6-Ar), 129.1 (s, 1-Ar), 110.3 and 109.9 (2 d, 2- and 4-Ar), 101.7 (t, OCH_2O), 66.3 (t, C–O), 40.0 (d, CH–C–O), 33.2 (t, Ar–CH_2), 28.0 (t, C–C–O); MS, *m/z* (relative intensity) 254 (21) and 256 (7), 219 (23), 191 (16), 171 (31), 169 (100). Anal. Calcd: C, 56.59; H, 4.35; Cl, 13.92. Found: C, 57.24; H, 4.44; Cl, 13.23.

3-(5-Chloro-3,4-dimethoxybenzyl)dihydro-2-(3*H*)-furanone (3). Vanillin was chlorinated according to the procedure of Raiford and Tichty to yield 5-chlorovanillin.[8] Reaction of this product (186 mg, 1.00 mmol) with excess diazomethane in ether produced the dimethoxy compound in quantitative yield. The carbanion of γ-butyrolactone (86.1 mg, 1.00 mmol) was preformed at -78 °C in dry THF (10 mL) under a nitrogen atmosphere by using lithium diisopropylamide (1.1 mmol of diisopropylamine and 1.0 mmol of *n*-butyllithium, 1.3 M in hexane). A solution of the aldehyde in THF (5 mL) was added via syringe over a 5-min period while the temperature was maintained at -78 °C. After 10 min, 25% H_2SO_4 (10 mL) was added and the reaction mixture allowed to warm to room temperature. The reaction mixture was extracted with ether (3 × 20 mL) and dried (Na_2SO_4), and the solvent was removed at reduced pressure. The residual oil was dissolved in ethyl acetate (25 mL) and reduced with PtO_2 (20 mg) under 1 atm of H_2. The reaction mixture was filtered and evaporated to yield a pale yellow oil. This mixture was purified by isochratic HPLC (35% ethyl acetate/hexane) on a preparative silica gel column (Du Pont, Zorbax, 1 × 20 cm, 5 mL/min): yield 163 mg (60%); colorless oil; t_R = 8.40 min; ^1H, NMR (361 MHz, $CDCl_3$) δ 1.99 (m, 1 H, CH_a–C–O), 2.29 (m, 1 H, CH_b–C–O), 2.71 (dd, 1 H, *J* = 13.81 8.90, Ar–CH_a), 2.83 (m, 1 H, CH–C=O), 3.14 (dd, 1 H, *J* = 13.81, 4.25, Ar–CH_b), 3.85 (s, 3 H, 4-OMe), 3.86 (s, 3 H, 3-OMe), 4.17 (dt, 1 H, *J* = 9.12, 6.63, CH_a–O), 4.23 (dt, 1 H, *J* = 9.12, 2.74, CH_b–O), 6.69 (d, 1 H, *J* = 1.93, 2-ArH), 6.80 (d, 1 H, *J* = 1.93, 6-ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.3 (s, C=O), 153.7 and 144.0 (2 s, 3- and 4-Ar), 134.9 (s, 1-Ar), 128.0 (s, 5-Ar), 121.9 (d, 6-Ar), 111.6 (d, 2-Ar), 66.5 (t, C–O), 60.6 and 56.1 (2 q, 3- and 4-OMe), 40.9 (d, C–C=O), 35.6 (t, Ar–C), 27.9 (t, C–C–O); MS (70 eV), *m/z* (relative intensity) 270 (35) and 272 (11), 185 (100) and 187 (31). Anal. Calcd: C, 57.68; H, 5.59; Cl, 13.10. Found: C, 57.50; H, 5.68; Cl, 13.31.

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Registry No. 1, 80902-00-7; 2, 87174-76-3; 3, 87174-77-4; 7, 87174-78-5; 8, 87183-65-1; 6-chloropiperonal, 15952-61-1; γ-butyrolactone, 96-48-0; 5-chlorovanillin, 19463-48-0; 3-chloro-4,5-dimethyoxybenzaldehyde, 18268-68-3; 3-[(3-chloro-4,5-dimethoxyphenyl)carbonyl]dihydro-2(3*H*)-furanone, 87174-79-6.

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Crystal Structure and Stereochemistry of Achalensolide, a New Guaianolide from *Stevia achalensis*[1]

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Structure and stereochemistry of achalensolide, a new guaianolide, and its 11,13-dihydro derivative, both isolated from *Stevia achalensis*, were deduced by a combination of NMR spectroscopy, X-ray diffraction, and chemical transformations.

Discovery of the intensely sweet diterpene glycoside stevioside in leaves of *Stevia rebaudiana* Bertoni some years ago[2] initiated a study of other representatives of this large American genus. Since then, sweet glycosides have been isolated only from *S. rebaudiana*, *S. paniculata*, and *S. ovata*,[3,4] while other diterpenoids and various sesqui-

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(2) For references to work on stevioside from *S. rebaudiana* prior to 1963, see: Högenauer, R. "Chemotaxonomie der Pflanzen"; Birkhäuser Verlag: Basel and Stuttgart, 1964; Vol. 3, p 483.

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