Coriaheptocins A and B, the First Heptahydroxylated Acetogenins, Isolated from the Roots of *Annona coriacea*[1]

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Two new annonaceous acetogenins, coriaheptocin A **(1)** and coriaheptocin B **(2)**, have been isolated from the roots of *Annona coriacea* Mart. (Annonaceae). Heptahydroxylated, they present an unusual 1,3,6,7-tetrol arrangement. Determination of their structures required an original MS and NMR strategy.

The large number of research works on acetogenins from the Annonaceae is due to their broad range of potential biological roles, for example, cytotoxic, antitumor, antiparasitic, pesticidal, antimicrobial, and immunosuppressive activities. Currently, their number is more than 220.[2,3]

The acetogenins of *Annona coriaceae* Mart. (Annonaceae) have been little studied to date. Only one bis-THF acetogenin, gigantecin, was previously described from this species.[4] In our preceding papers, we have reported from this species three cytotoxic mono-THF acetogenins and coriadienin, another acetogenin with two double bonds, which is considered a biogenetic precursor.[5,6]

The acetogenins from Annonaceae usually possess between two and five hydroxy groups, two of them generally flanking the THF ring and the others being distributed along the fatty acid chain. Recently, acetogenins possessing six hydroxyls, annohexocin[7] with a 1,3,5-triol arrangement, murihexocins A and B[8] with two diols along the hydrocarbon chain, and muricatin B[9] with an interesting 1,2,3-triol arrangement, have been isolated from the Annonaceae.

In this paper, we describe coriaheptocins A (**1**) and B (**2**) (Chart 1), the first acetogenins with seven hydroxyls that present an unusual 1,3,6,7-tetrol arrangement. The determination of their structures was achieved through an original MS and NMR strategy, both on native and derivatized acetogenins.

Coriaheptocin A (**1**) and coriaheptocin B (**2**) are white waxes concentrated by column chromatography of the more polar fractions of a CH_2Cl_2 extract and isolated by reversed-phase HPLC. The molecular formula of **1** and **2** was established to be $C_{35}H_{64}O_{10}$ from the exact mass measurements, 651.4664 for **1** and 651.4684 for **2**, of the $[M + Li]^+$ ion in the HRFABMS. The CIMS (NH_4^+) of **1** and **2** gave the same peak at *m/z* 645 $[M + H]^+$, which confirmed the molecular weight of both compounds.

Spectral characteristics, including ^{1}H and ^{13}C NMR of **1** and **2**, indicated the presence of an α,α′-dihydroxylated mono-THF acetogenin hydroxylated at C-4.[10] The formation of the heptaacetyl derivatives **1b** and **2b**, clearly identified by their ^{1}H-NMR spectra (seven acetoxy groups between δ 2.01 and 2.08), demonstrated the presence of four other hydroxy groups along the aliphatic chain. The bis-acetonide derivatives **1a** and **2a** further evidenced an unusual arrangement of these hydroxyls.

The proton resonances at δ 7.26 (H-33), 5.06 (H-34), 3.85 (H-4), 2.45 (H-3), and 1.42 (H-35) in **1**, correlated to the carbon signals at δ 152.4 (C-33), 78.2 (C-34), 69.1 (C-4), 33.0 (C-33), and 18.5 (C-35), were consistent with an α,β-unsaturated γ-methyl γ-lactone fragment.[10] Very similar signals were obtained from **2** (Table 1).

The presence of a C-4 OH group was indicated by the usual deshielding of the two C-3 protons in the ^{1}H-NMR spectra of **1** (δ 2.45) and **2** (δ 2.44),[10] further confirmed by the COSY and HOHAHA correlation spectra. However, the resonances of H-3a and H-3b at the same chemical shift indicated a lack of hydrogen bonding between the OH-4 and the lactone carbonyl group, suggesting interference from another OH group located near the C-4 position. The occurrence of this hydroxyl at C-7 was confirmed by MS measurements and HOHAHA correlations. The magnetic inequivalence of both protons in each C-5 and C-6 methylene group (Table 1) was consistent with hydrogen bonding between the C-4 and C-7 hydroxy groups, which has never been reported before. Hydrogen bonding between the C-7 hydroxy group and the lactone carbonyl, resulting in an unbonded hydroxyl at C-4, could also explain the spectral data observed for **1** and **2**.

The presence of the mono-THF ring with a flanking OH group on each side in **1** and **2** was suggested by the HMQC spectra, showing proton signals at δ 3.74 (H-7), 3.90 (H-8), 3.88 (H-11), and 3.45 (H-12) correlated to the signals at δ 71.0 (C-7), 82.2 (C-8), 83.0 (C-11), and 74.0 (C-12) for **1**. Similar correlations were observed between the resonances at δ 3.45 (H-7), 3.78 (H-8), 3.81 (H-11), and 3.40 (H-12) and the signals at δ 74.3 (C-7), 82.9 (C-8), 82.5 (C-11), and 74.3 (C-12) for **2**. Further correlation peaks were seen between H-7 and H-8, and between H-11 and H-12, in the ^{1}H−^{1}H COSY spectrum of **1** and **2**. By comparison with a series of model compounds of known relative stereochemistry,[11,12] these NMR data indicated that the relative stereochemistry of the THF subunits was *erythro/trans/threo* in **1** and *threo/trans/threo* in **2**. The ^{1}H-NMR chemical shift of H-7 (δ 3.74) in **1** was indicative of the *erythro* configuration at C-7/C-8.

The seven hydroxylated carbons were characterized in the ^{13}C-NMR spectra of **1** and **2** by signals observed at δ 67.7, 68.0, 69.1, 71.0 (2C), 71.6, and 74.0

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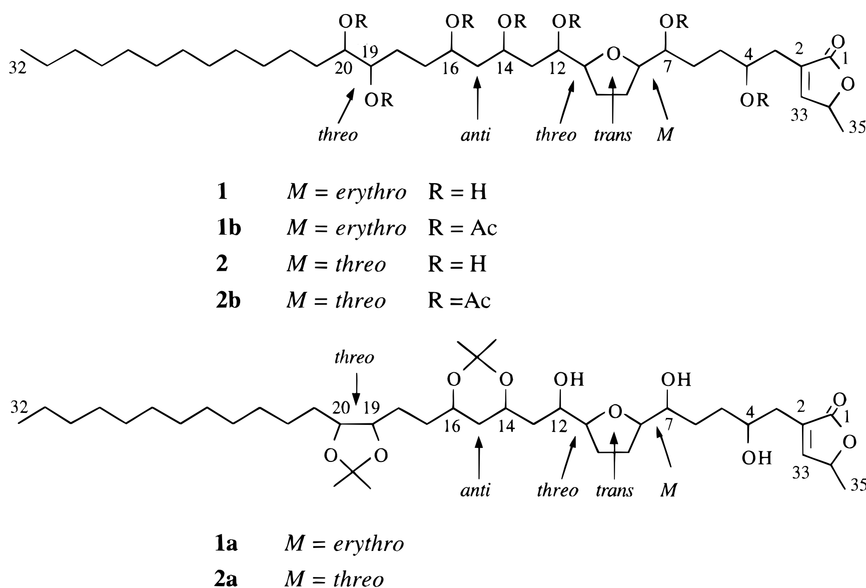
Table 1. ^{1}H- ($CDCl_3$, 400 MHz) and ^{13}C- ($CDCl_3$ + CD_3OD, 50 MHz) NMR Data of **1**, **2**, **1a**, and **2a**

carbon	^{1}H of **1**	^{13}C of **1**	^{1}H of **2**	^{13}C of **2**	^{1}H of **1a**	^{13}C of **1a**[a]	^{1}H of **2a**	^{13}C of **2a**[a]
1		174.9		174.9		*b*		*b*
2		130.3		130.4		*b*		*b*
3	2.45 br s	33.0	2.44 br s	33.3	2.42 dd (15.0; 8.0 Hz)	33.3	2.42 (dd) 15.1; 8.2 Hz)	33.2
					2.48 dd (15.0; 3.8 Hz)		2.48 dd (15.1; 3.8 Hz)	
4	3.85 m	69.1	3.85 m	69.3	3.88 m	69.7	3.87 m	69.7
5	1.63 m; 1.65 m	33.7	1.60; 1.63 m	33.8	1.60 m; 1.70 m	35.0	1.60; 1.75 m	33.5
6	1.60 m; 1.62 m	33.7	1.60; 1.63 m	33.8	1.37 m; 1.42 m	32.0	1.40 m	33.5
7	3.74 m	71.0	3.45 m	74.3	3.80 m	71.3	3.42 m	74.2
8	3.90 m	82.2	3.78 m	82.9	3.87 m	82.1	3.80 m	82.5
9	1.60 m; 1.91 m	25.1	1.62 m; 1.96 m	28.6	1.82 m; 1.88 m		1.68 m; 1.99 m	28.5
10	1.83 m; 1.98 m	28.2	1.57 m; 1.99 m	28.8	1.67 m; 1.96 m		1.71 m; 1.99 m	28.8
11	3.88 m	83.0	3.81 m	82.5	3.80 m	83.4	3.75 m	82.9
12	3.45 m	74.0	3.40 m	74.3	3.57 m	70.5	3.60 m	70.3
13	1.56 m	32.8	1.36 m	32.9	1.46 m; 1.50 m	40.0	1.47 m; 1.50 m	40.6
14	3.86 m	68.0	3.90 m	67.8	4.14 m	68.0	4.13 m	68.0
15	1.50 m	39.6	1.45 m	39.9	1.43 m; 1.46 m	40.0	1.44 m; 1.46 m	40.0
16	3.87 m	67.7	3.90 m	67.4	4.03 t (9.5 Hz)	68.3	4.03 t (9.8 Hz)	68.3
17	1.56 m	39.6	1.55 m	39.9	1.44 m; 1.65 m	35.0	1.45 m; 1.64 m	35.0
18	1.52 m	31.6	1.50 m	31.7	1.55 m; 1.60 m	35.0	1.55 m; 1.60 m	35.0
19	3.75 m	71.6	3.74 m	71.3	3.54 m	81.1	3.55 m	81.2
20	3.80 m	71.0	3.79 m	70.9	3.73 td (8.5; 1.0 Hz)	76.9	3.72 m	76.9
21	1.34 m	32.2	1.34 m	32.9	1.48 m	35.5	1.48 m	35.0
31	1.28 m	22.4	1.31 m	22.5	1.28 m	22.0	1.28 m	22.8
32	0.88 t (6.6 Hz)	13.7	0.87 t (6.5 Hz)	139.0	0.87 t (9.5 Hz)	13.9	0.87 t (6.5 Hz)	13.9
33	7.26 d (1.0 Hz)	152.4	7.26 s	152.4	7.20 d (1.2 Hz)	151.8	7.20 s	151.2
34	5.06 qd (6.7; 1.2 Hz)	78.2	5.05 q (7.5 Hz)	78.2	5.05 qd (6.6; 1.5 Hz)	78.1	5.05 q (7.7 Hz)	77.8
35	1.42 d (6.8 Hz)	18.5	1.41 d (5.8 Hz)	18.8	1.42 d (6.8 Hz)	19.0	1.43 d (6.8 Hz)	19.0
		acetal carbon				100.5		100.4
1,3-dioxane ring[c]		acetal methyl protons			1.33 s	25.2	1.33 s	25.2
					1.37 s	25.2	1.37 s	25.2
		acetal carbon				108.0		108.0
1,3-dioxolane ring[c]		acetal methyl protons			1.33 s	27.6	1.33 s	27.3
					1.37 s	27.6	1.37 s	27.7

[a] Assignments were made on the basis of HMQC ($CDCl_3$ 400 MHz) chemical shifts correlation method. [b] Signal not observed. [c] Assignments were made on the basis of HMBC ($CDCl_3$, 400 MHz) chemical shifts correlation method.

Chart 1



in **1**, and at δ 67.4, 67.8, 69.3, 70.9, 71.3, and 74.3 (2C) in **2**. The ^{13}C-NMR upfield positions of the carbinol carbons at δ 68.0 (C-14) and 67.7 (C-16) in **1** and δ 67.8 (C-14) and 67.4 (C-16) in **2** were correlated to protons at δ 3.86 (H-14) and 3.87 (H-16) in **1** and at δ 3.90 (H-14, H-16) in **2**. The carbinolic protons at δ 3.75 (H-19) and 3.80 (H-20) were correlated to the carbon signals at δ 71.6 (C-19) and 71.0 (C-20) in **1**, and the protons signals at δ 3.74 (H-19) and 3.79 (H-20) were correlated to the carbons signals at δ 71.3 (C-19) and 70.9 (C-20) in **2**.

The respective positions of the THF and OH groups along the hydrocarbon chain in **1** and **2** were determined using HOHAHA NMR correlations and tandem mass spectrometry (MS/MS). For the MS/MS measurements, high-energy collision-induced dissociation of $[M + Li]^{+}$ complexes (precursor ions selected at *m/z* 651) was used.

The MS/MS spectra of **1** and **2** were fully identical (Figure 1). They displayed a number of fragment ion peaks, among which two different ion series were distinguished, depending on whether or not they possess

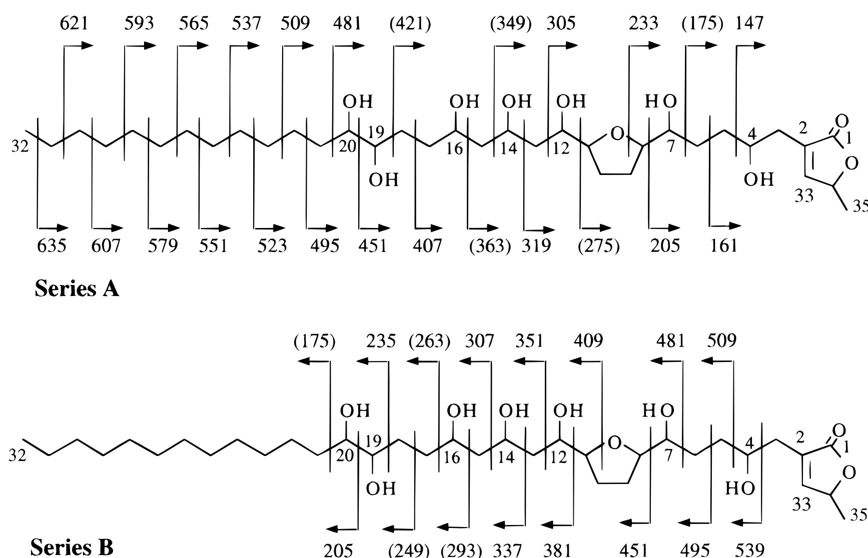


Figure 1. CID−MS/MS fragmentations of the $[M + Li]^+$ ion at *m/z* 651 from coriaheptocin A (**1**) and B (**2**); weak intensity peaks are given in parentheses.

the terminal lactone ring. The first ion series (series A), containing the lactone moiety, was formed by remote-charge fragmentations of the aliphatic chain leading to the typical pattern of successive ion peaks separated by 14 mass units (Figure 1). This ion series was interrupted at the substitution sites, thus allowing their location on the alkyl chain. The second ion series (series B) was attributed to ions containing the methyl-terminal side chain of the lithiated molecule. The loss of the lactone ring occurred by a β-cleavage, with loss of 112 amu from the precursor $[M + Li]^+$ ion, thus giving the fragment-ion peak at *m/z* 539.[13]

The presence of the fragment ions at *m/z* 305, 233, and 205 in the ion series A suggested the location of the THF ring between C-8 and C-11 on the alkyl chain. Furthermore, the fragment ions at *m/z* 481, 451, and 421 indicated the position of the 1,2-diol at C-19/C-20. The location of the 1,3-diol system at C-14/C-16 was ambiguous, because of the low intensity of daughter ions at *m/z* 319, 349, and 363 (series A), indicative of OH-14. However, the intense fragment ions at *m/z* 337 and 307 in the ion series B clearly indicated the presence of an OH group at C-14, and subsequently the location of the 1,3-diol system at C-14/C-16. Small but significant fragment ions at *m/z* 293 and 263 confirmed this hypothesis.

The positions of the seven hydroxy groups were confirmed by the HOHAHA spectrum of **2**, which demonstrated the correlations of H-7 (δ 3.45) to H-4 (δ 3.85), H-5, and H-6 (δ 1.63, 1.60). In turn, H-4 showed correlations with H-3 (δ 2.44), H-5, H-6, and H-7. On the other hand, H-12 (δ 3.40) was correlated to H-11 (δ 3.81), H-10 (δ 1.99, 1.57), H-8 (δ 3.78), and H-13 (δ 1.36). All these data confirmed the location of the THF ring with respect to the C-4 OH group. However, the HOHAHA spectra of the native compounds **1** and **2** did not allow the unambiguous positioning of the four remaining hydroxy groups. For this reason, the acetonide derivatives (**1a**, **2a**) were prepared from **1** and **2** and further purified by HPLC.

The major products **1a** and **2a** presented similar ion peaks at *m/z* 742 $[M + NH_4]^+$ in the CIMS (NH_4^+). The FABMS (*m*-NBA + LiCl) demonstrated ion peaks at *m/z* 731 $[M + Li]^+$, which were in agreement with the molecular formula $C_{41}H_{72}O_{10}$ of the diacetonide derivatives.

The $^1H-^1H$ COSY spectra showed correlation spots between the vicinal methines at δ 3.54 and 3.73 in **1a** (δ 3.55 and 3.72 in **2a**), indicating the presence of a dioxolane ring. On another hand, the absence of direct correlations between methines at δ 4.14 and 4.03 in **1a** (δ 4.13 and 4.03 in **2a**) indicated the presence of a 1,3-dioxane ring in both products (Table 1). These diacetonide derivatives were also investigated by CID−MS/MS (Figure 2).

The simultaneous presence of the fragment ions at *m/z* 305, 275, 233, and 205 on the ion series A of **1** and **2** (Figure 1), and of **1a** and **2a** (Figure 2), confirmed the placement of the bis-hydroxy flanked THF ring between C-7 and C-12. The sequence of fragment ions at *m/z* 561/461 and 447/433/319 in the ion series A, in addition to the fragments at *m/z* 373/417/303 and 231/275/175 in the ion series B, confirmed the location of the 1,3-dioxane and 1,3-dioxolane rings in the aliphatic chain of **1a** and **2a**, and subsequently the position of the 1,2- and 1,3-diol arrangements at C19/20 and at C-14/16, respectively, for **1** and **2**. Consecutive losses of Me_2CO (58 mass units) were also observed from fragments containing the acetonide moieties.

Finally, the HOHAHA spectrum of **1a** demonstrated the correlation of H-3 (δ 2.42, 2.48) to H-4 (δ 3.88), H-5 (δ 1.70, 1.60), H-6 (δ 1.42), H-33 (δ 7.20), and H-34 (δ 5.05). Further correlations were observed between H-6 and H-7 (δ 3.80) in the $^1H-^1H$ COSY spectrum. The chemical shift of H-7 (δ 3.80) was indicative of the *erythro* configuration at C-7−C-8 in **1a** and subsequently of the *threo* configuration at C-11−C-12.

On the other hand, H-12 (δ 3.57) was correlated with H-11 (δ 3.80), H-10 (δ 1.96, 1.67), H-9 (δ 1.88), H-8 (δ 3.87), and with H-13 (δ 1.50) and H-14 (δ 4.14), thus indicating the position of the 1,3-diol acetonide two carbons away from the THF ring. H-14 exhibited the expected correlations with H-11, H-12, and H-13 and with H-15 (δ 1.46, 1.43), H-16 (δ 4.03), and H-17 (δ 1.65, 1.44). The 1,2-diol acetonide was further located at C-19/20, according to the correlations of H-17 with H-18,

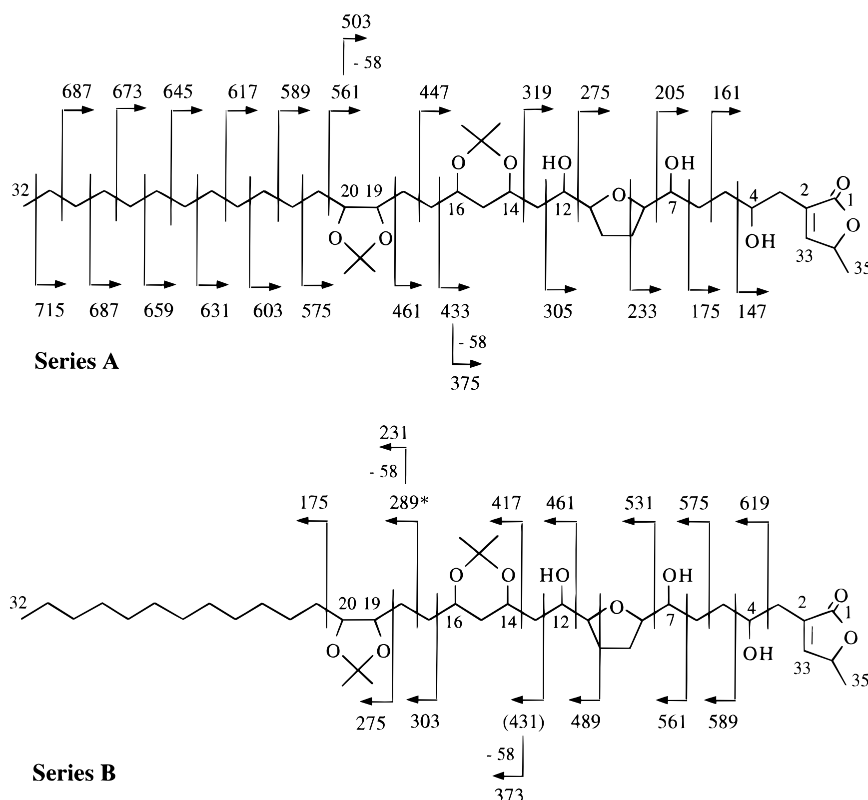


Figure 2. Diagnostic fragments in the CID–MS/MS of the $[M + Li]^+$ ions of the 14,16- and 19,20-diacetonides of coriaheptocins A (**1a**) and B (**1b**); weak intensity peaks are given in parentheses; *absence of peak.

H-19 (δ 3.54), and H-20 (δ 3.73). Similar observations were made in the HOHAHA correlation spectrum of **2a**.

The ^{13}C-NMR chemical shifts of the acetal carbon atoms in the 1,3-dioxolanes are remarkably deshielded (δ 108.0 in **1a** and **2a**) in relation to those in the 1,3-dioxanes[14] (δ 100.5 in **1a** and δ 100.4 in **2a**). The stereochemistry of many alternating (1,3,5...) polyol chains can be determined by ^{13}C-NMR analysis of polyacetonide derivatives.[15] The stereochemistry of *syn*- and *anti*-1,3-diol acetonides can be assigned from the ^{13}C-NMR chemical shifts of the acetal methyl groups and of the acetal carbon.[15] Usually, the *syn*-1,3-diol acetonides display acetal methyl shifts at δ 19 and 30 and the acetal carbon shift at δ 98.5, while the *anti*-1,3-diol acetonides methyl groups are both observed at δ 25 and the acetal carbon at δ 100.5. The method using the ^{13}C NMR of acetonides has been widely employed to assign 1,3-diol stereochemistry.[16–19] Acetonides derived from *anti*-1,3-diols exist in a twist conformation in order to avoid the 1,3-diaxial interaction, which could be present in a chair conformation.[20,21] The ^{13}C-NMR chemical shifts observed for the dioxane ring of **1a** and **2a** (δ 25.2 for the acetal methyl groups and δ 100.5 or 100.4 for the acetal carbon) are in good agreement with an *anti* stereochemistry[14] for both 1,3-diol acetonides **1a** and **2a**. Thus, the relative *anti* stereochemistry was established for the 1,3-diol (C-14/16) in **1** and **2**.

The downfield chemical shifts at δ 3.75 (H-19) and 3.80 (H-20) in **1**, and at δ 3.74 (H-19) and 3.79 (H-20) in **2**, suggested an *erythro* stereochemistry[22] for the 1,2-diol arrangement of both compounds. However, the ^{1}H-NMR signals for the methine protons of the acetonide at δ 3.54 (H-19) and 3.73 (H-20) in **1a** (δ 3.55 and 3.72 in **2a**) indicated a *trans* assignment for the dioxolane ring. This configuration was confirmed by the very close singlet peaks for the acetonide methyl protons at δ 1.33 and 1.37. Thus, the configuration of the 1,2-diol was determined to be *threo*, because the *trans* configuration of C-19/C-20 in **1a** and **2a** could only arise from a vicinal diol with a *threo* configuration.[22] In addition, the coupling constant of 1.0 Hz between H-19 and H-20 in **1a** indicated a dihedral angle close to 90°, which is only possible with a *trans* configuration. Most of the relative configurations of coriaheptocins A and B were unambiguously assigned, but the relative stereochemistry between the asymmetric carbinol centers at C-16/19 and C-12/14 was not determined.

Compounds **1** and **2** show significant cytotoxicity towards a human tumor cell line, 9KB (nasopharyngeal carcinoma). The ED_{50} is 6.3×10^{-1} μg/mL for **1** and 1.8×10^{-1} μg/mL for **2**. Paclitaxel, used as a positive control, gives an ED_{50} value of 2.0×10^{-2} μg/mL. It is interesting to note that these polyhydroxylated acetogenins are less active than the tetra- or penta-hydroxylated mono-THF acetogenins (coriacin, 4-deoxycoriacin, and gigantetronenin) and the non-THF acetogenin with four hydroxyls (coriadienin), also isolated from this plant.[6] These weak activities, previously reported for the hexahydroxylated acetogenins,[7,8] could be related to an excessive degree of hydroxylation of the coriaheptocins A and B.

Experimental Section

General Experimental Procedures. Optical rotations were determined on a Schmidt-Haensch Polartronic E polarimeter at 25 °C. UV spectra were measured on a Perkin-Elmer 257 spectrometer. The ^{1}H- and ^{13}C-NMR spectra ($CDCl_3$) were obtained with Bruker ARX-400 and AC-200 instruments at 400 and 50 MHz, respectively. EIMS and CIMS $(NH_4)^+$ were performed

on a Nermag R10−10C spectrometer; FABMS (*m*-NBA + LiCl) spectra were obtained with a Kratos MS80RF mass spectrometer. MS/MS spectra were obtained using a ZabSpec-T five-sector tandem mass spectrometer (Fisons Instruments, VG organic, Manchester, UK). The first analyzer (MS1) comprises a Zabspec triple sector ($E_1B_1E_2$) instrument and the second mass spectrometer (MS2) consists of a double sector instrument (B_2E_3) of reverse Mattauch−Herzog geometry focusing the ion beam on a focal plane. $[M + Li]^+$ precursor ions were generated by cesium ion bombardment at 30 KeV (matrix: *m*-NBA + LiCl). The precursor ions submitted to MS/MS experiments were selected by MS1 set at appropriate E and B values and then focused in a collision cell in the fourth field-free region (between E_2 and B_2). Preparative HPLC was carried out with a Waters 590 pump system and a Millipore-Waters 484 (Milford, MA) spectrophotometer.

Plant Material. Roots of *A. coriacea* were collected in July 1993, in Ceará, Brazil. The material was identified by Pr. Afranio Fernandes. A voucher specimen was deposited in the Herbarium of the Department of Biology of the Federal University of Ceará.

Extraction and Separation. The dried and pulverized roots (2.4 kg) were extracted with EtOH. The EtOH extract (320 g) was partitioned between H_2O−MeOH (90:10) and hexane. The aqueous MeOH fraction was concentrated and extracted with CH_2Cl_2 to yield 55 g of extract, 25 g of which were submitted to one fractionation by column chromatography (Si gel S, 230−400 mesh), eluting with a CH_2Cl_2−MeOH (99:1 to 80:20) gradient, which yielded 72 fractions (F001). Fractions 44−47 (1.3 g) from F001 were submitted to another column chromatography (Si gel S, 230−400 mesh) eluting with a EtOAc + MeOH (85:15 to 50:50) gradient, which furnished a partially purified fraction (F58−65) containing **1** and **2** (0.125 g). HPLC purification, using a μ Bondapack C18 prepacked column [10 μm, 25 × 100 mm], eluted with MeOH−H_2O (80:20) (flow rate 15 mL/min, UV detection at 214 nm) afforded **1** (18 mg, t_R = 17 min) and **2** (41 mg, t_R = 21 min).

Coriaheptocin A (1): white, waxy solid; $[\alpha]^{25}_D$ +19° (*c* 1.08, $CHCl_3$); UV (EtOH) λ max (log ϵ) 208.8 (4.6) nm; HRFABMS 651.4664 (calcd 651.46591 for $C_{35}H_{64}O_{10}Li$); CIMS (NH_4^+) *m/z* 645 (MH^+); ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR [$CDCl_3$ + CD_3OD (95:5), 50 MHz] see Table 1.

14,16,19,20-Diacetonide of Coriaheptocin A (1a). To **1** (10.6 mg) dissolved in C_6H_6 (2 mL) was added 2,2-dimethoxypropane (100 μL) and a trace of *p*-toluenesulfonic acid. The mixture was stirred under reflux for 1.5 h. K_2CO_3 (0.5 mg) was added, and the mixture was stirred for 4 h at room temperature (procedure a). The mixture was washed with H_2O, extracted with CH_2Cl_2, and concentrated to dryness to give a mixture of products, and the residue was washed with hexane (procedure b). The insoluble part (10 mg) was submitted to HPLC purification using a μ−Bondapack C18 prepacked column [10 μm, 25 × 100 mm], eluted with MeOH−H_2O (90:10) (flow rate 10 mL/min, UV detection at 214 nm), affording **1a** (4 mg) (procedure c); CID−MS/MS: *m/z* 731.6 $[M + Li]^+$, see Figure 2; EIMS (40 eV): *m/z* 321 (15%), 211 (19), 209 (23), 183 (17), 181 (21), 71 (88), 58 (100); CIMS (NH_4^+): *m/z* 742 $[M + NH_4]^+$ (85); ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR [$CDCl_3$ + CD_3OD (95:5), 50 MHz] see Table 1.

Heptaacetate of Coriaheptocin A (1b). To **1** (7 mg), dissolved in pyridine (0.5 mL), was added Ac_2O (0.5 mL). After 4 h at room temperature, the mixture was partitioned between H_2O and CH_2Cl_2 (procedure d). The CH_2Cl_2 extract was concentrated *in vacuo* affording **1b** (6.8 mg): CIMS (NH_4^+) *m/z* 758 (12) [M − 3 × (AcOH)], 698 (71) [M − 4 × (AcOH)], 311 (100); EIMS (38 eV) *m/z* 311 (15), 168 (16), 60 (100); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (3H, t, *J* = 6.5 Hz, H-32), 1.25 (2H, m, H-31), 1.40 (3H, d, *J* = 6.6 Hz, H-35), 1.55−1.58 (7H, m, H-21, H-6, H-5, H-10), 1.66 (1H, m, H-17), 1.68, 1.72 (2H, m, H-15), 1.73 (2H, m, H-18), 1.78 (1H, m, H-9), 1.85, 1.91 (2H, m, H-13), 1.95 (1H, m, H-10), 1.96 (1H, m, H-9), 2.01, 2.01, 2.02, 2.04, 2.05, 2.06, 2.08 (7 × 3H, CH_3CO), 2.51 (2H, d, *J* = 6.1 Hz, H-3), 3.90 (1H, m, H-11), 3.96 (1H, m, H-8), 4.88 (2H, m, H-14, H-16), 4.92 (1H, m, H-7), 4.93 (1H, m, H-20), 4.96 (1H, m, H-12), 5.04 (1H, m, H-34), 5.09 (1H, m, H-19), 5.10 (1H, m, H-4), and 7.09 (1H, d, *J* = 1.2 Hz, H-33); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0 (C-32), 18.9 (C-35), 21.0 (−CO*C*H_3), 22.8 (C-31), 26.6 (C-10), 29.3 (C-9), 30.0 (C-3, C-5, C-6), 35.0 (C-15), 35.2 (C-13), 69.0 (C-4, C-14, C-16), 70.3 (C-12), 71.3 (C-19), 73.5 (C-20), 75.0 (C-7), 77.5 (C-34), 80.0 (C-8), 80.4 (C-11), 130 (C-2), 151.0 (C-33), 170.0 (−*C*OCH_3), and 173.0 (C-1).

Coriaheptocin B (2). White, waxy solid; $[\alpha]_D$ +25° (*c* 1.00, $CHCl_3$); UV (EtOH) λ max (log ϵ) 207.2 (4.0) nm; HRFABMS 651.4684 (calcd 651.465 91 for $C_{35}H_{64}O_{10}$-Li); CIMS (NH_4^+) *m/z* 645 (MH^+); ^1H NMR ($CDCl_3$, 400 MHz), and ^{13}C NMR [$CDCl_3$ + MeOH (95:5), 50 MHz], see Table 1.

14,16,19,20-Diacetonide of Coriaheptocin B (2a). Compound **2** (10 mg) was converted into the acetonide **2a** by procedure a and purified by procedure b. The purified CH_2Cl_2 extract (8.4 mg) was treated by procedure c, affording **2a** (2.5 mg). CID−MS/MS: *m/z* 731.6 $[M + Li]^+$, see Figure 2; EIMS (40 eV) *m/z* 321 (15), 211 (19), 209 (23), 183 (17), 181 (21), 71 (88), 58 (100); CIMS (NH_4^+) *m/z* 742 $[M + NH_4]^+$ (85); ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR [$CDCl_3$ + CD_3OD (95:5), 50 MHz] see Table 1.

Heptaacetate of Coriaheptocin B (2b). Compound **2** (7 mg) was acetylated by procedure d. The CH_2Cl_2 extract was concentrated, affording **1b** (6.0 mg): CIMS (NH_4^+) *m/z* 698 (65) [M − 4 × (AcOH)], 311 (76) and 258 (74); EIMS (38 eV) *m/z* 311 (25), 168 (9), 45 (100); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (3H, t, *J* = 6.5 Hz, H-32), 1.29 (2H, m, H-31), 1.41 (3H, d, *J* = 6.7 Hz, H-35), 1.52−1.58 (9H, m, H-5, H-6, H-9, H-10, H-17, H-21), 1.67, 1.72 (2H, m, H-15), 1.73 (2H, m, H-18), 1.83, 1.86 (2H, m, H-13), 1.95 (2H, m, H-9, H-10), 2.01, 2.01, 2.02, 2.03, 2.05, 2.06, 2.08 (7 × 3H, C*H*$_3$CO), 2.51 (2H, d, *J* = 6.0 Hz, H-3), 3.90 (1H, m, H-11), 4.00 (1H, m, H-8), 4.89 (2H, m, H-14, H-16), 4.84 (1H, m, H-7), 4.93 (1H, m, H-20), 4.96 (1H, m, H-12), 5.02 (1H, m, H-34), 5.06 (1H, m, H-19), 5.10 (1H, m, H-4) and 7.09 (1H, d, H-33); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.1 (C-32), 18.8 (C-35), 21.1 (−CO*C*H_3), 23.0 (C-31), 27.8 (C-9, C-10), 29.7 (C-3), 30.0 (C-6, C-17, C-18), 30.5 (C-5), 35.0 (C-15), 35.3 (C-13), 69.0 (C-4, C-14, C-16), 70.0 (C-12), 71.2 (C-19), 73.5 (C-20), 75.0 (C-7), 77.5 (C-34), 80.0 (C-8, C-11), 130.0 (C-2), 151.6 (C-33), 170.8 (−*C*OCH_3), and 173.3 (C-1).

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References and Notes

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