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Spiranoid Withanolides from *Jaborosa runcinata* and *Jaborosa araucana*

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From the aerial parts of *Jaborosa runcinata* six new withanolides were isolated and named jaborosalactones 1−6 (**1**−**6**). All contain a side chain with a carbon−carbon bond between C-12 of the intact steroid nucleus and C-23 and a spiranoid γ-lactone at the latter position. The additional ring thus formed has a 17(20)-ene-22-keto system. Jaborosalactones 4−6 (**4**−**6**) also contain a hydroxyl group at C-21. From the aerial parts of *Jaborosa araucana* were isolated the known withanolides trechonolide A (**8**), its 5α,6β-dihydroxy analogue jaborosotetrol (**9**), and the spiranoid withanolide jaborosalactone 2 (**2**), also isolated from *J. runcinata*. The stereochemistry of the spiranoid center at C-23 was determined as 23*R* based on NOESY NMR spectra and molecular modeling using the AM1 semiempirical method.

The withanolides are a group of C-28 steroids built on an ergostane skeleton in which C-22 and C-26 are appropriately oxidized in order to form a δ-lactone ring. Biogenetic transformations can produce highly modified compounds both in the steroid nucleus and in the side chain, including formation of additional rings. Such compounds are closely related to the withanolides and, by extension, are considered within this group of compounds.[1] Withanolides have been isolated from several genera of the Solanaceae, and many of them exhibit a variety of biological activities, including insecticidal and antifeedant properties.[1,2]

Jaborosa Miers is a South American genus belonging to the Solanaceae that comprises about 23 different species;[3] to date, seven have been studied and reported to contain withanolides: *J. bergii*, *J. integrifolia*, *J. laciniata* (ex *Trechonaetes*), *J. leucotricha*, *J. magellanica*, *J. odonelliana*, and *J. sativa*.[4,5] Continuing with our investigations of the withanolides of the Solanaceae growing in Argentina, we now report our findings on the withanolides present in the species *J. runcinata* Lam. and *J. araucana* Phil.

From *J. runcinata* we have isolated six spiranoid withanolides named jaborosalactones 1−6 (**1**−**6**) related structurally to jaborosalactone P (**7**) isolated from *J. odonelliana*,[6] but with a 17(20)-ene-22-keto system, resulting in a novel arrangement within the withanolides. The structures of the new compounds were elucidated by spectroscopic methods and with the aid of molecular modeling.

Results and Discussion

The Et_2O and EtOH extracts of the aerial parts of *J. runcinata* were pooled and fractionated by a combination of flash chromatography on normal and octadecyl-functionalized Si gel followed by final purification of the crude withanolides by preparative TLC, which rendered pure jaborosalactones **1**−**6**. Jaborosalactone 2 (**2**) was the first of these compounds isolated and characterized from the EtOH extract of the aerial part of *J. araucana*, but it was found only as a minor component in *J. runcinata*. This extract also contained the known

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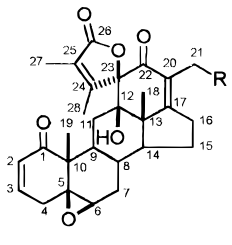

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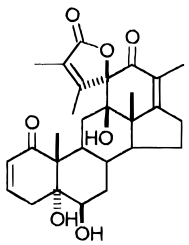
4 R=OH



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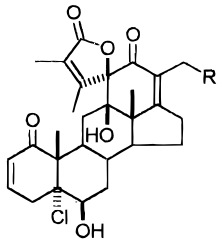

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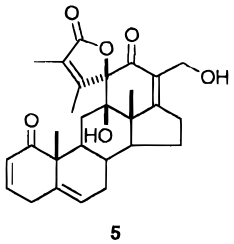
6 R=OH



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trechonolide A (**8**) and jaborosotetrol (**9**), which have been reported previously from *J. laciniata*[7] and *J. magellanica*,[8] respectively.

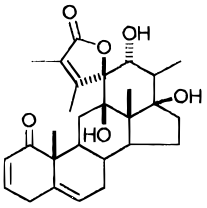
The molecular formula of the major component of *J. runcinata* was determined by HREIMS as $C_{28}H_{32}O_6$. The EIMS of jaborosalactone 1 (**1**) showed a small molecular ion peak at *m/z* 464 (2%) and a peak at 339 (26%) corresponding to the cleavage between C-23 and C-22 followed by the loss of CO and a fragment $C_5H_5O_2$ (C-24−C-28 of the γ-lactone ring); the latter fragmentation was present in the six spiranoid withanolides isolated and appears to be characteristic of this type of structure.

The ^{1}H-NMR spectrum of compound **1** exhibited in the lowfield region signals at δ 5.94 and 6.79 typical of a 2-en-1-one system without substituents at C-4. A 5β,6β-epoxide was inferred from the presence of a doublet at 3.13 ppm (J = 2.7 Hz) corresponding to H-6; the small coupling to H-7β observed in the latter signal confirmed the β stereochemistry of the substituent. The two methyl signals at δ 1.97 and 2.23 and the absence of a lactone hydrogen in the 4−5 ppm region indicated a spiranoid dimethyl-substituted α,β-unsaturated γ-lactone ring comprising C-23 to C-28; a similar arrangement has been described for jaborosalactone P (**7**) isolated from *J. odonelliana*.[6] A long-range homoallylic coupling of ca. 1 Hz could be observed between methyls 27 and 28, which appeared as quartets; this characteristic coupling was also present in the five jaborosalactones described below. The singlet for the 21-methyl at 1.71 ppm indicated the absence of a hydrogen at C-20, and the chemical shift value suggested the presence of a double bond involving the latter carbon.

The ^{13}C-NMR spectrum of jaborosalactone 1 (**1**) (Table 1) showed three carbonyl carbons, of which two corresponded to C-1 (202.6 ppm) and C-26 (173.1 ppm) and the third carbonyl at 192.9 ppm was assigned to C-22. Besides the signals of C-10 and C-13 at δ 47.7 and 48.3, three other nonprotonated carbons were evident in the δ 61−92 range. The signal at 91.4 ppm was assigned to the spiranoid lactone carbon C-23 and those at 61.8 and 75.3 to C-5 and C-12, respectively. Also evident from the ^{13}C-NMR spectrum were six olefinic carbon resonances between 123 and 164 ppm, and four of these

Table 1. ^{1}H- and ^{13}C-NMR Correlations Displayed by Jaborosalactone 1 (**1**) in the HETCOR Spectrum

		[δ_H]				[δ_H]	
C	δ_C	α	β	C	δ_C	α	β
1	202.6			15	23.3	1.65	1.65
2	128.9	5.94		16	25.8	2.48	2.48
3	144.2	6.79		17	162.8		
4	32.9	1.94	2.94	18	14.5	1.05	
5	61.8			19	15.0	1.18	
6	63.6	3.13		20	124.4		
7	29.6	1.44	2.07	21	12.3	1.71	
8	29.3		1.60	22	192.9		
9	42.1	1.44		23	91.4		
10	47.7			24	160.5		
11	35.0	2.33	1.50	25	127.8		
12	75.3			26	173.1		
13	48.3			27	8.9	1.97	
14	46.8	2.20		28	16.0	2.23	



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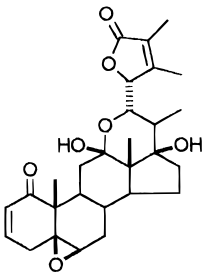

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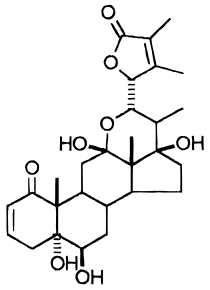

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corresponded to the expected signals of a 2-en-1-one system in ring A and an α,β-unsaturated γ-lactone ring; the signals at 124.4 and 162.8 ppm were assigned to C-20 and C-17. The presence of this double bond was in agreement with the chemical shift and multiplicity observed for the 21-methyl in the ^{1}H-NMR spectrum (Table 1).

Spectral assignments were confirmed by COSY-45, delayed-COSY, HETCOR, and NOESY NMR spectra. The HETCOR spectrum (Table 1) allowed unequivocal assignment of the five methyls in the ^{1}H- and ^{13}C-NMR spectra and correlation of the signal at δ 25.8 (C-16) with the multiplet at δ 2.48 assigned to both H-16. The delayed-COSY experiment revealed a long-range connectivity between H-21 (1.71 ppm) and H-16 (2.48 ppm) supporting the presence of a 17(20)-ene-22-keto functionality.

The stereochemistry at the spiranoid center (C-23) was deduced from the NOESY spectrum and molecular modeling calculations (AM1, AMPAC 5.0), considering that the stereochemistry at the B/C and C/D ring junctions is that of a standard steroidal skeleton. Table 2 shows the relevant correlations observed in the NOESY spectrum together with the calculated distances between the corresponding hydrogens. The strong correlations observed for the pairs H-28/H-9α and H-28/

Table 2. Correlations Displayed by Jaborosalactones 1 (**1**) and 4 (**4**) in the NOESY NMR Spectrum[a]

	1		**4**	
H	δ	correlates with δ[b]	δ	correlates with δ[b]
4α	1.94	3.13 (H-6, 2.3)	1.92	3.15 (H-6, 2.3)
4β	2.94	1.18 (H-19, 2.3)	2.95	1.19 (H-19, 2.3)
8β	1.60	1.05 (H-18, 2.2)	1.65	1.09 (H-18, 2.2)
9α	1.44	2.23 (H-28, 2.3)	1.44	2.23 (H-28, 2.2)
11β	1.50	1.05 (H-18, 2.4)	1.46	1.09 (H-18, 2.4)
		1.18 (H-19, 2.2)		1.19 (H-19, 2.2)
16	2.48	1.05 (H-18, 2.4)	2.60	1.09 (H-18, 2.4)
		1.71 (H-21, 2.4)		4.18 (H-21b, 2.1)
21	1.71	2.48 (H-16, 2.4)	4.18	2.60 (H-16, 2.1)
		2.23 (H-28, 2.8)		
27	1.97	2.23 (H-28, 2.4)	1.98	2.23 (H-28, 2.4)

[a] Interactions between vicinal and geminal hydrogens are not included. [b] Distances (Å) between interacting hydrogens from AM1 calculations are given in parentheses. When more than one hydrogen is present at a given position, the shortest distance is indicated.

H-21 indicated that the 28-methyl is positioned close to the α face of the steroid nucleus. The latter arrangement, only possible in the 23*R* stereoisomer (Figure 1), is coincident with that found in jaborosalactone P (**7**).[6] The other correlations shown confirm the assignments made and the structure of jaborosalactone 1.

^{1}H- and ^{13}C-NMR chemical shift values in compounds **2** and **3** were closely related to those of jaborosalactone 1 (**1**). A 2-en-1-one arrangement was evident from the signals between 5.8 and 6.7 ppm in the ^{1}H-NMR spectrum of each compound, but the upfield shift of the H-2 and H-3 signals and a downfield shift of methyl-19 (compared with compound **1**) indicated a different substitution pattern in ring B.

The molecular formula of jaborosalactone 2 (**2**) was established as $C_{28}H_{34}O_7$ from the HREIMS; the EIMS showed main fragments at *m/z* 482 (3%) and 357 (60%) corresponding to $[M]^+$ and $[M - CO - C_5H_5O_2]^+$, respectively. The main difference in the ^{1}H-NMR spectrum of **2** was the downfield shift of H-6, which appeared as a triplet at δ 3.68 ($J = 2.6$ Hz), as its small coupling with both hydrogens at position 7 indicated an equatorial orientation (α) of H-6; this observation is in combination with the presence in the ^{13}C-NMR spectrum of signals at δ 77.9 and 74.0 assigned to C-5 and C-6, respectively, and the molecular formula was consistent with hydroxyl groups at the 5α and 6β positions, a substitution pattern typical of many withanolides, which has been shown to derive biosynthetically from the corresponding 5β,6β-epoxide.[9]

The HREIMS of jaborosalactone 3 (**3**) showed a molecular ion at *m/z* 500.1965, consistent with the formula $C_{28}H_{33}O_6Cl$. In the EIMS, two significant peaks were at *m/z* 375 (47%) and 339 (20%), corresponding to the ions $[M - CO - C_5H_5O_2]^+$ and $[M - HCl - CO - C_5H_5O_2]^+$, respectively. Highly diagnostic for this structure was the downfield shift of the equatorial (α) H-6 resonance (from δ 3.68 in **2** to 4.03 in **3**), typical of a 5α-chloro-6β-hydroxy arrangement that has been found in several withanolides.[10] The substitution pattern in ring B was further corroborated by the signals at 78.8 and 74.4 ppm in the ^{13}C-NMR spectrum that were assigned to C-5 and C-6, respectively, and allow differentiation from isomeric 5-hydroxy-6-chloro arrangements.[10,11] The NMR spectral assignments for **2** and **3** were confirmed by DEPT and COSY-45 spectra.

Jaborosalactone 4 (**4**) did not show a molecular ion in its HREIMS, but a peak at *m/z* 462.2041, corresponding to the loss of H_2O ($C_{28}H_{30}O_6$), was observed. The FABMS (thioglycerol, KCl) showed a $[M + K]^+$ ion at *m/z* 519, which was consistent with the proposed structure. EIMS showed main fragments at *m/z* 462 (5%), 337 (33%), and 319 (58%) corresponding to the ions $[M - H_2O]^+$, $[M - H_2O - CO - C_5H_5O_2]^+$, and $[M - 2H_2O - CO - C_5H_5O_2]^+$, respectively. The ^{1}H- and ^{13}C-NMR spectral data of **4** were very similar to those of compound **1**; however, the absence of a singlet for H-21 in the high-field end of the ^{1}H-NMR spectrum and the appearance of an AB quartet at 4.18−4.30 ppm suggested the presence of an isolated C-21 hydroxymethylene group. The ^{13}C-NMR spectrum showed only four methyl groups that were coincident with C-18, C-19, C-27, and C-28 of jaborosalactone 1 (**1**). The methylene signal at 58.5 ppm (C-21) confirmed the presence of a hydroxyl group at C-21. The substitution at this position also shifted the C-20 and C-17 resonances downfield, to 127.6 and 166.6 ppm, respectively. Spectral assignments were confirmed by HETCOR, COSY-45, delayed-COSY, and NOESY NMR spectra. The AB quartet at δ 4.18−4.30 assigned to CH_2-21 was correlated with the signal at 58.5 ppm (C-21) in the HETCOR spectrum and with the signal at 2.60 ppm (H-16) in the delayed-COSY experiment, supporting the presence of a 17(20)-ene-22-keto system and a 21-hydroxy substituent. As in the case of jaborosalactone 1 (**1**) a strong correlation was observed in the NOESY spectrum for the pair H-28/H-9α confirming the 23*R* stereochemistry; in this case no correlation was observed for the pair H-28/H-21 in accordance with the AM1 calculations, which predicted this distance to be larger than 3.6 Å (Table 2).

Jaborosalactone 5 (**5**) exhibited in the low-field end of the ^{1}H-NMR spectrum signals at δ 5.81, 6.73, and 5.53, which were assigned to H-2, H-3, and H-6, respectively, of a 1-oxo-2,5-dienewithanolide.[6] The corresponding olefinic signals at δ 135.4 and 124.1 assigned to C-5 and C-6 were observed in the ^{13}C-NMR spectrum. Signals due to hydrogens and carbons of rings C and D and the side chain were closely related to those of jaborosalactone 4 (**4**). The FABMS spectrum showed a quasi-molecular ion $[M + K]^+$ at *m/z* 503, and a peak at *m/z* 446.2095 was observed in the HREIMS, corresponding to the ion $[M - H_2O]^+$; the latter ions were consistent with the proposed structure. The EIMS showed peaks at *m/z* 446 (3%) and 321 (15%), which corresponded to the ions $[M - H_2O]^+$ and $[M - H_2O - CO - C_5H_5O_2]^+$, respectively.

Finally, jaborosalactone 6 (**6**) was isolated as a minor component of *J. runcinata*. The molecular ion was absent in the EIMS, but a peak at *m/z* 498 (0.6%), corresponding to the ion $[M - H_2O]^+$, was observed. Other significant peaks were at 462 (1%) and 373 (3%), corresponding to the ions $[M - H_2O - HCl]^+$ and $[M - H_2O - CO - C_5H_5O_2]^+$; the low abundance of these ions did not allow a high-resolution measurement, and the FABMS also showed a low abundance peak corresponding to the loss of H_2O. Comparison of the ^{1}H- and ^{13}C-NMR spectra with those of compound **3** showed almost identical signals for all carbons except for those corresponding to C-17, C-20, and C-21, which were shifted downfield, as in jaborosalactones 4 (**4**) and 5 (**5**). This similarity was evident in the ^{1}H-NMR spectra of **6** and

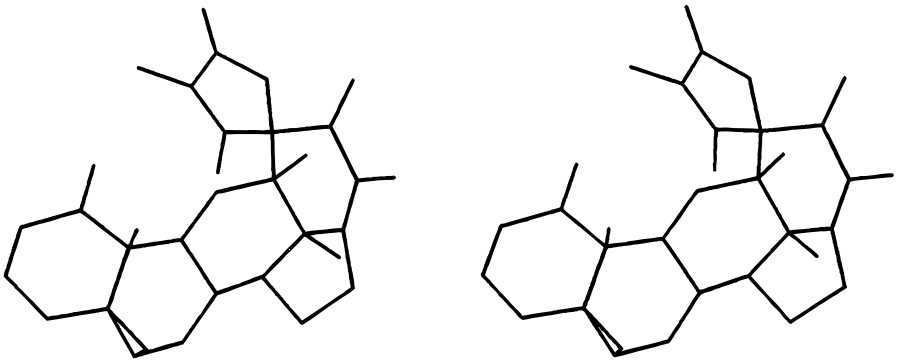

Figure 1. Stereoscopic view of jaborosalactone 1 (**1**) as predicted by AM1 calculations (AMPAC 5.0) and NMR data.

3, except for the AB quartet at 4.20/4.35 ppm assigned to H-21, which replaced the methyl-21 singlet in **3**. These data provided sufficient evidence to assign structure **6** to jaborosalactone 6.

In a previous publication we proposed the existence of closely related biosynthetic precursors for jaborosalactone P (**7**) and trechonolide A (**8**).[6] The cooccurrence of the latter compound and the spiranoid jaborosalactone 2 (**2**) in *J. araucana* supports this hypothesis.

Experimental Section

General Experimental Procedures. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AC-200 NMR spectrometer at 200.13 and 50.32 MHz, respectively. Multiplicity determinations (DEPT) and 2D spectra (COSY-45, delayed-COSY, HETCOR, NOESY) were obtained using standard Bruker software. Chemical shifts are given in ppm downfield from TMS as internal standard. EIMS were collected on a VG Trio-2 mass spectrometer at 70 eV by direct inlet; FABMS and HREIMS (70 eV) were measured on a VG ZAB-BEQQ mass spectrometer. IR and UV spectra were measured on a Nicolet Magna 560 FTIR and a Hewlett-Packard 8451A spectrophotometer, respectively. AM1 calculations were performed with AMPAC-5.0 (Semichem). Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Column chromatography was performed on Kieselgel 60-G (Merck), Kieselgel S 0.032−0.063 mm, or on octadecyl-functionalized Si gel (Aldrich). TLC analysis was performed on Si gel 60 F254 (0.2 mm thick).

Plant Material. Whole *J. araucana* plants were collected in December 1992 in Parque Saavedra, Comodoro Rivadavia, Chubut Province, Argentina. A voucher specimen is deposited at the Museo Botánico, Universidad Nacional de Córdoba under No. CORD 131. Whole *J. runcinata* plants were collected in March 1995 in El Jagüel, Departamento Paraná, Entre Ríos Province, Argentina. A voucher specimen is deposited at the Museo Botánico, Universidad Nacional de Córdoba under No. CORD 248.

Extraction and Isolation. The dried and pulverized aerial parts of *J. runcinata* (500 g) were extracted successively with Et_2O and EtOH at room temperature. The residue obtained after evaporation of the combined extracts (935 mg) was chromatographed on Kieselgel 60-G. Elution with hexane−EtOAc mixtures of increasing polarity (100:0−0:100) afforded four main fractions containing withanolides. These fractions were further fractionated on octadecyl-fuctionalized Si gel using MeOH−H_2O mixtures of increasing strength (60:40−100:0) as elution solvents. The fractions containing withanolides were purified by preparative TLC to yield withanolides **1** (25.6 mg), **2** (1.0 mg), **3** (3.4 mg), **4** (19.0 mg), **5** (6.8 mg), and **6** (1.0 mg).

The dried and pulverized aerial parts of *J. araucana* (668 g) were extracted with EtOH at room temperature, the solvent was evaporated, and the residue (200 g) was partitioned between hexane, MeOH, and H_2O (30:3:1). The aqueous MeOH layer was washed with hexane, concentrated, and extracted with $CHCl_3$. The residue (14.5 g) obtained after evaporation of the solvent was chromatographed on Si gel. Elution with hexane−Me_2CO mixtures of increasing polarity afforded fractions containing partially resolved mixtures of withanolides. The latter were pooled and fractionated by flash chromatography using hexane−EtOAc mixtures of increasing polarity (5:1−1:1) to yield a fraction containing trechonolide A (90 mg, identified by comparison of its ^{1}H- and ^{13}C-NMR spectra with those reported[7]) and two fractions that, after purification by preparative TLC, yielded jaborosotetrol (9 mg, identified by comparison of its ^{1}H- and ^{13}C-NMR spectra with those reported[8]) and jaborosalactone 2 (**2**) (3.8 mg).

Jaborosalactone 1 (1): white crystals (EtOAc−hexane); mp 269−270 °C; UV (MeOH) λ_{max} 224 nm; IR (dry film) ν_{max} 3480, 1746, 1673, 1254, 1008 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.79 (1 H, ddd, J = 10.1, 6.0, 2.4 Hz, H-3), 5.94 (1 H, dd, J = 10.1, 2.4 Hz, H-2), 3.13 (1 H, d, J = 2.7 Hz, H-6), 2.94 (1 H, dt, J = 19.2, 2.4 Hz, H-4β), 2.48 (2 H, m, H-16), 2.33 (1 H, m, H-11α), 2.23 (3 H, q, J = 1.0 Hz, H-28), 2.07 (1 H, m, H-7β), 1.97 (3 H, q, J = 1.0 Hz, H-27), 1.94 (1 H, dd, J = 19.2, 6.0, H-4α), 1.71 (3 H, s, H-21), 1.65 (2 H, m, H-15), 1.60 (1 H, m, H-8), 1.50 (1 H, m, H-11β), 1.44 (1 H, m, H-9), 1.44 (1 H, m, H-7α), 1.18 (3 H, s, H-19), 1.05 (3 H, s, H-18); ^{13}C NMR, see Table 1; EIMS m/z [M]$^+$ 464 (2), 339 (26), 321 (8), 295 (6), 277 (9), 107 (11), 91 (18), 43 (100); HREIMS m/z found [M]$^+$ 464.2197 ($C_{28}H_{32}O_6$ requires 464.2199).

Jaborosalactone 2 (2): white crystals (EtOAc−hexane); mp 250−251 °C; UV (MeOH) λ_{max} 224 nm; IR (dry film) ν_{max} 3462, 1740, 1676, 1387, 1254, 1009 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.60 (1 H, ddd, J = 10.2, 5.0, 2.4 Hz, H-3), 5.84 (1 H, ddd, J = 10.2, 2.4, 1.0 Hz, H-2), 3.68 (1 H, t, J = 2.6 Hz, H-6), 3.25 (1 H, dt, J = 19.6, 2.4 Hz, H-4β), 2.50 (2 H, m, H-16), 2.25 (3 H, q, J = 1.0 Hz, H-28), 2.09 (1 H, ddd, J = 19.6, 5.0, 1.0 Hz, H-4α), 2.03 (3 H, q, J = 1.0 Hz, H-27), 1.85 (1 H, m, H-7β), 1.75 (3 H, s, H-21), 1.60 (1 H, m, H-7α), 1.26 (3 H, s, H-19), 1.11 (3 H, s, H-18); ^{13}C NMR ($CDCl_3$) δ 203.0 (C, C-1), 193.1 (C, C-22), 173.0 (C, C-26), 162.9 (C, C-17), 160.5 (C, C-24), 141.5 (CH, C-3), 128.5 (CH, C-2), 124.4

(C, C-20), 128.1 (C, C-25), 91.6 (C, C-22), 77.9 (C, C-5), 75.6 (C, C-12), 74.0 (CH, C-6), 51.7 (C, C-10), 48.7 (C, C-13), 46.7 (CH, C-14), 38.5 (CH, C-9), 35.6 (CH_2, C-11), 34.5 (CH_2, C-4), 32.1 (CH_2, C-7), 29.5 (CH, C-8), 25.8 (CH_2, C-16), 23.3 (CH_2, C-15), 16.0 (CH_3, C-28), 15.0 (CH_3, C-19), 14.8 (CH_3, C-18), 12.3 (CH_3, C-21), 9.0 (CH_3, C-27); EIMS *m/z* $[M]^+$ 482 (3), 465 (1), 358 (14), 357 (60), 125 (10), 105 (8), 91 (15), 43 (100); HREIMS *m/z* found $[M]^+$ 482.2308 ($C_{28}H_{34}O_7$ requires 482.2305).

Jaborosalactone 3 (3): white crystals (EtOAc–hexane); mp 262–264 °C; UV (MeOH) λ_{max} 224 nm; IR (dry film) ν_{max} 3439, 1738, 1683, 1255, 1173 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.63 (1 H, ddd, J = 10.0, 5.0, 2.1 Hz, H-3), 5.86 (1 H, dd, J = 10.0, 2.1 Hz, H-2), 4.03 (1 H, br s, H-6), 3.46 (1 H, dt, J = 20.0, 2.1 Hz, H-4β), 2.60 (2 H, m, H-16), 2.53 (1 H, dd, J = 20.0, 5.0 Hz, H-4α), 2.24 (3 H, q, J = 1.0 Hz, H-28), 2.17 (1 H, m, H-7β), 2.01 (3 H, q, J = 1.0 Hz, H-27), 1.73 (3 H, s, H-21), 1.73 (1 H, m, H-7α), 1.29 (3 H, s, H-19), 1.10 (3 H, s, H-18); ^{13}C NMR ($CDCl_3$) δ 203.0 (C, C-1), 193.0 (C, C-22), 173.0 (C, C-26), 162.5 (C, C-17), 161.0 (C, C-24), 141.2 (CH, C-3), 128.4 (CH, C-2), 124.5 (C, C-20), 128.0 (C, C-25), 91.4 (C, C-23), 78.8 (C, C-5), 75.5 (C, C-12), 74.4 (CH, C-6), 52.1 (C, C-10), 48.7 (C, C-13), 46.6 (CH, C-14), 39.1 (CH, C-9), 37.1 (CH_2, C-4), 34.4 (CH_2, C-11), 32.4 (CH_2, C-7), 29.7 (CH, C-8), 25.8 (CH_2, C-16), 23.4 (CH_2, C-15), 16.0 (CH_3, C-28), 15.6 (CH_3, C-19), 14.8 (CH_3, C-18), 12.3 (CH_3, C-21), 9.0 (CH_3, C-27); EIMS *m/z* $[M]^+$ 500 (2), 464 (2), 446 (14), 375 (47), 339 (20), 321 (35), 91 (24), 43 (100); HREIMS *m/z* found $[M]^+$ 500.1965 ($C_{28}H_{33}O_6Cl$ requires 500.1966).

Jaborosalactone 4 (4): white crystals (EtOAc–hexane); mp 273–274 °C; UV (MeOH) λ_{max} 228 nm; IR (dry film) ν_{max} 3429, 1740, 1677, 1381, 1254, 1119 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.80 (1 H, ddd, J = 10.2, 6.0, 2.4 Hz, H-3), 5.94 (1 H, dd, J = 10.2, 2.4 Hz, H-2), 4.30 (1 H, d, J = 12.3 Hz, H-21a), 4.18 (1 H, d, J = 12.3 Hz, H-21b), 3.15 (1 H, d, J = 2.5 Hz, H-6), 2.95 (1 H, dt, J = 19.0, 2.4 Hz, H-4β), 2.60 (2 H, m, H-16), 2.36 (1 H, m, H-11α), 2.23 (3 H, q, J = 1.0 Hz, H-28), 2.05 (1 H, m, H-7β), 1.98 (3 H, q, J = 1.0 Hz, H-27), 1.92 (1 H, dd, J = 19.0, 6.0 Hz, 4α), 1.65 (1 H, m, H-8), 1.46 (1 H, m, H-11β), 1.45 (1 H, m, H-7α), 1.44 (1 H, m, H-9), 1.19 (3 H, s, H-19), 1.09 (3 H, s, H-18); ^{13}C NMR ($CDCl_3$) δ 202.7 (C, C-1), 193.0 (C, C-22), 173.0 (C, C-26), 166.6 (C, C-17), 159.9 (C, C-24), 144.4 (CH, C-3), 128.9 (CH, C-2), 127.6 (C, C-20)[12], 128.3 (C, C-25)[12], 91.2 (C, C-23), 75.3 (C, C-12), 63.6 (CH, C-6), 61.8 (C, C-5), 58.5 (CH_2, C-21), 48.7 (C, C-13), 47.8 (C, C-10), 46.6 (CH, C-14), 42.0 (CH, C-9), 35.9 (CH_2, C-11), 32.9 (CH_2, C-4), 29.6 (CH_2, C-7), 29.4 (CH, C-8), 25.3 (CH_2, C-16), 23.3 (CH_2, C-15), 16.0 (CH_3, C-28), 15.1 (CH_3, C-19), 14.5 (CH_3, C-18), 9.0 (CH_3, C-27); EIMS *m/z* $[M - H_2O]^+$ 462 (5), 446 (3), 429 (2), 416 (5), 398 (5), 337 (33), 319 (58), 293 (18), 107 (10), 91 (37), 43 (100); HREIMS *m/z* found $[M - H_2O]^+$ 462.2041 ($C_{28}H_{30}O_6$ requires 462.2042); FABMS (*m*-nitrobenzyl alcohol, KCl) *m/z* $[M + K]^+$ 519 (100).

Jaborosalactone 5 (5): white crystals (EtOAc–hexane); mp 234–235 °C; UV (MeOH) λ_{max} 226 nm; IR (dry film) ν_{max} 3477, 1754, 1672, 1387, 1260, 1014 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (1 H, ddd, J = 10.0, 5.0, 2.5 Hz, H-3), 5.81 (1 H, dd, J = 10.0, 2.0 Hz, H-2), 5.53 (1 H, m, H-6), 4.33 (1 H, d, J = 12.2 Hz, H-21a), 4.20 (1 H, d, J = 12.2 Hz, H-21b), 3.25 (1 H, ddd, J = 19.0, 2.5, 2.0 Hz, H-4β), 2.83 (1 H, dd, J = 19.0, 5.0 Hz, H-4α), 2.61 (2 H, m, H-16), 2.25 (3 H, q, J = 1.0 Hz, H-28), 2.05 (1 H, m, H-7β), 2.02 (3 H, q, J = 1 Hz, H-27), 1.70 (1 H, m, H-7α), 1.17 (3 H, s, H-19), 1.14 (1H, s, H-18); ^{13}C NMR ($CDCl_3$) δ 202.8 (C, C-1), 193.0 (C, C-22), 173.0 (C, C-23), 166.4 (C, C-17), 159.5 (C, C-24), 145.0 (CH, C-3), 135.4 (C, C-5), 127.6 (C, C-20)[12], 128.4 (C, C-25)[12], 127.7 (CH, C-2), 124.1 (CH, C-6), 91.2 (C, C-23), 75.6 (C, C-12), 58.7 (CH_2, C-21), 49.9 (C, C-10), 48.7 (C, C-13), 46.9 (CH, C-14), 40.7 (CH, C-9), 35.0 (CH_2, C-7), 33.3 (CH_2, C-4), 32.1 (CH, C-8), 29.7 (CH_2, C-11), 25.3 (CH_2, C-16), 23.3 (CH_2, C-15), 18.5 (CH_3, C-19), 15.9 (CH_3, C-28), 14.4 (CH_3, C-18), 9.0 (CH_3, C-27); EIMS *m/z* $[M - H_2O]^+$ 446 (3), 339 (1), 321 (15), 135 (13), 107 (6), 91 (18), 43 (100); HREIMS *m/z* found $[M - H_2O]^+$ 446.2095 ($C_{28}H_{30}O_5$ requires 446.2093); FABMS (*m*-nitrobenzyl alcohol, KCl) *m/z* $[M + K]^+$ 503 (63).

Jaborosalactone 6 (6): white amorphous solid; UV (MeOH) λ_{max} 226 nm; IR (dry film) ν_{max} 3450, 1749, 1683, 1376, 1255, 1096, 1019 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.65 (1 H, ddd, J = 12.0, 5.0, 2.0 Hz, H-3), 5.85 (1 H, dd, J = 12.0, 2.0 Hz, H-2), 4.35 (1 H, d, J = 12.2 Hz, H-21a), 4.20 (1 H, d, J = 12.2 Hz, H-21b), 4.03 (1 H, br s, H-6), 3.45 (1 H, dt, J = 20.0, 5.0 Hz, H-4β), 2.60 (2 H, m, H-16), 2.23 (3 H, q, J = 1.0 Hz, H-28), 2.02 (3 H, q, J = 1.0 Hz, H-27), 1.29 (3 H, s, H-19), 1.14 (3 H, s, H-18); ^{13}C NMR ($CDCl_3$) δ 193.0 (C, C-22), 165.8 (C, C-17), 159.9 (C, C-24), 141.3 (CH, C-3), 128.3 (CH, C-2), 128.0 (C, C-20), 128.0 (C, C-25), 78.2 (C, C-5), 77.0 (C, C-12), 74.3 (CH, C-6), 58.7 (CH_2, C-21), 52.0 (C, C-10), 48.5 (C, C-13), 46.3 (CH, C-14), 39.0 (CH, C-9), 37.1 (CH_2, C-4), 34.4 (CH_2, C-11), 32.3 (CH_2, C-7), 29.7 (CH, C-8), 25.2 (CH_2, C-16), 23.3 (CH_2, C-15), 15.9 (CH_3, C-28), 15.5 (CH_3, C-19), 14.7 (CH_3, C-18), 9.0 (CH_3, C-27); EIMS *m/z* $[M - H_2O]^+$ 498 (0.6), 462 (1), 444 (2), 426 (1), 373 (3), 107 (12), 105 (16), 91 (32), 43 (100); FABMS (*m*-nitrobenzyl alcohol, KCl) *m/z* $[M - H_2O + K]^+$ 537 (3).

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References and Notes

(1) For a review see Glotter, E. *Nat. Prod. Rep.* **1991**, *8*, 415–440.
(2) Baumann, T. W.; Meier, C. M. *Phytochemistry* **1993**, *33*, 317–321.
(3) Hunziker, A. T. *Linn. Soc. Symp. Ser.* **1979**, *7*, 60.
(4) Bonetto, G. M.; Gil, R. R.; Oberti, J. C.; Veleiro, A. S.; Burton, G. *J. Nat. Prod.* **1995**, *58*, 705–711 and references cited therein.
(5) Misico, R. I.; Oberti, J. C.; Veleiro, A. S.; Burton, G. *J. Nat. Prod.* **1996**, *59*, 66–68 and references cited therein.
(6) Monteagudo, E. S.; Oberti, J. C.; Gros, E. G.; Burton, G. *Phytochemistry* **1990**, *29*, 933–935.
(7) Lavie, D.; Besalle, R.; Pestchanker, M. J.; Gottlieb, H. E.; Frolow, F.; Giordano, O. S. *Phytochemistry* **1987**, *26*, 1791–1795.
(8) Fajardo, V.; Podesta, F.; Shamma, M.; Freyer, A. J. *J. Nat. Prod.* **1991**, *54*, 554–563.
(9) Veleiro, A. S.; Burton, G. and Gros, E. G. *Phytochemistry* **1985**, *24*, 2573–2575.
(10) Besalle, R.; Lavie, D. *Phytochemistry* **1992**, *31*, 3648–3651.
(11) Veleiro, A. S.; Oberti, J. C.; Burton, G. *Phytochemistry* **1992**, *31*, 935–937.
(12) ^{13}C-NMR assignments may be interchanged.

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