

NOVEL WITHANOLIDES FROM *JABOROSA SATIVA*

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ABSTRACT.—Four new withanolides [**1**–**4**] have been isolated from the aerial parts of *Jaborosa sativa*. Jaborosalactones R [**1**], S [**2**], and T [**3**] contain a hemiketal (or ketal) ring formed between a 21-hydroxyl and a 12-ketone and the characteristic δ -lactone side-chain of the withanolides. Jaborosalactone U [**4**] possesses an epoxy- γ -lactone side-chain and was identified as the 24,25-epoxy analogue of trechonolide A [**5**].

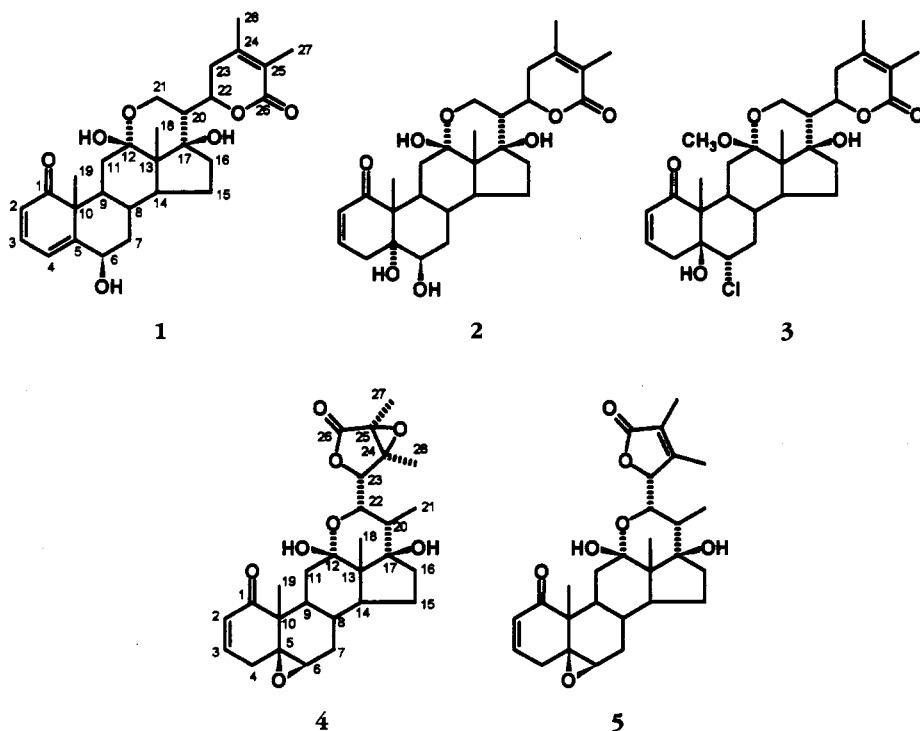
Jaborosa Miers is a South American genus belonging to the Solanaceae that comprises about 23 different species which grow mainly in Argentina (1). To date, six *Jaborosa* spp. have been reported to contain withanolides, namely, *J. integrifolia* (2–4), *J. leucotricha* (5–7), *J. bergii* (8), *J. odonelliana* (9), *J. laciniata* (formerly in the genus *Trechonaetes*) (10), and *J. magellanica* (11–14). These C_{28} steroidal lactones have been isolated from several genera of the Solanaceae and many of these compounds exhibit interesting biological activities, such as cytotoxic, immunosuppressive, anti-inflammatory, insecticidal, and antifeedant properties (15).

From *Jaborosa sativa* (Miers) A. T. Hunziker & G. Barbosa (*Trechonaetes sativa* Miers), we have isolated four new withanolides. Three of them, jaborosalactones R [**1**], S [**2**], and T [**3**] incorporate, in addition to the typical δ -lactone side-chain, a six-membered hemiketal (or ketal) ring involving what must have been originally a C-12 keto group and a C-21 hydroxyl functionality, a novel arrangement in the withanolide class of compounds. The fourth withanolide, jaborosalactone U [**4**] was characterized as the 24,25-epoxy analogue of trechonolide A [**5**] (10). The epoxy- γ -lactone side-chain found in **4** has no precedent among the withanolides, although epoxy- δ -lactones (and epoxy- δ -lactols) and unsaturated γ -lactones are commonly found among this group of compounds (8,13). Preliminary biological testing has shown that jaborosalactone S has strong antifeedant activity on larvae of *Tenebrio molitor* (R.D. Enriz and C.E. Tonn, Universidad Nacional de San Luis, Argentina, unpublished results).

RESULTS AND DISCUSSION

Jaborosalactone R [**1**], $C_{28}H_{36}O_7$, showed a small molecular ion at m/z 484 in its mass spectrum (1.4%); the base peak at m/z 125 ($C_7H_9O_2$) corresponded to the δ -lactone ring, due to scission of the C-20–C-22 bond. The 1H -nmr spectrum of **1** exhibited, in the low-field region, signals at δ 6.97, 6.18, 6.03, and 4.56 ppm, which were assigned to H-3, -4, -2, and -6, respectively, of a 1-oxo-2,4-diene-6 β -hydroxywithanolide (8). The presence of two methyl signals at δ 1.86 and 1.94 indicated an α,β -unsaturated δ -lactone bearing methyl groups at positions C-24 and C-25, which were confirmed by the spin-spin couplings and 1H - 1H correlations (COSY-45) between H-22, H-23 α , and H-23 β .

The absence of a high-field methyl-21 doublet and the appearance of signals at δ 3.59 and 3.79 suggested an oxygenated function at C-21 which was consistent with the double double doublet observed for H-20. The COSY-45 spectrum showed the expected



correlations among both hydrogens at position C-21 and H-20. Furthermore, the spin-spin couplings observed between H-20 and each of the hydrogens at C-21 ($J=11.2$ and 5.5 Hz) strongly suggested that carbons 20 and 21 were part of a ring. The methyl-18 singlet at 1.07 ppm was in agreement with the presence of a β -oriented hydroxyl substituent at C-17; thus, this compound belongs to the α -oriented side-chain group of withanolides (8).

The ^{13}C -nmr and DEPT spectral data for jaborosalactone R [**1**] were in agreement with the proposed structure. Only four methyl carbons were observed and the carbonyl carbons C-1 and C-26 appeared at δ 205.46 and 165.89, respectively; six sp^2 carbons were evident in the 117–158 ppm range. The ^{13}C -nmr spectrum showed clear evidence for a hemiketal bridge between what must have originally been a C-12 ketone function and a C-21 alcohol, resulting in a 6-membered ring with a β -oriented 12-hydroxyl group (C-12 at δ 102.86). Molecular modeling calculations using the AM1 semiempirical method predicted a pseudo-boat conformation for the hemiketal ring. Table 1 summarizes the calculated coupling constants for relevant protons applying the Altona equation (16) on the calculated structures, which showed good consistency with the observed values. The coupling constant between H-20 and H-22 (7.6 Hz) suggested a preference for the rotamer with anti-orientation of these hydrogens (Figure 1).

TABLE 1. Calculated Coupling Constants (16) of H-20 for the Minimum Energy Conformers (AM1) Around the C-20–C-22 Bond of Jaborosalactone R [**1**].

Conformation	Relative energy (kcal/mol)	H-20–C–C–H-22 (degrees)	$J_{20,21\alpha}$ (Hz)	$J_{20,21\beta}$ (Hz)	$J_{20,22}$ (Hz)
anti	3.7	153.2	11.35	3.73	9.84
gauche 1	0.9	103.8	11.29	3.75	0.97
gauche 2	0.0	–47.4	11.26	3.54	3.62
observed	—	—	11.2	5.5	7.6

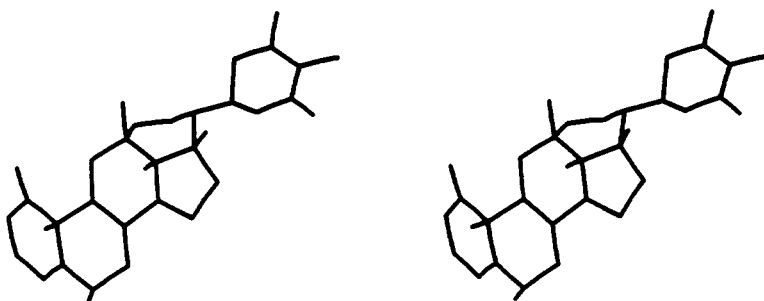


FIGURE 1. Stereoscopic views of the predominant conformer of jaborosalactone R [1] as predicted by AM1 calculations and ^1H - ^1H couplings.

Jaborosalactone S [2], $\text{C}_{28}\text{H}_{38}\text{O}_8$, did not show a molecular ion in its mass spectrum, but a peak at m/z 484 (6.0%) corresponding to the $[\text{M}-\text{H}_2\text{O}]^+$ ion was observed. Another significant peak was at m/z 125 (37.4%) which represented the δ -lactone side-chain. The fabms (thioglycerol, KCl) showed a $[\text{M}+\text{K}]^+$ ion at m/z 541, which was consistent with the proposed formula. The ^1H - and ^{13}C -nmr spectra were closely related to those of compound 1, the main difference being the absence of the signals due to the C-4, C-5 double bond in ring A and the presence of an additional tertiary hydroxyl group, inferred from the non-protonated carbon signal at 77.45 ppm in the ^{13}C -nmr spectrum (assigned to C-5). These data were consistent with a 1-oxo-2-en-5 α ,6 β -dihydroxy-withanolide (13). The COSY-45 spectrum of 2 confirmed the proton-proton connectivities for the proposed structure.

Jaborosalactone T [3], $\text{C}_{29}\text{H}_{39}\text{ClO}_7$, showed an ion at m/z 498 (33.4%) in its mass spectrum corresponding to the loss of HCl, and a strong peak at m/z 125 (70.6%), which represented the δ -lactone side-chain. The fabms (*m*-nitrobenzylalcohol, KCl) showed $[\text{M}+\text{K}]^+$ ions at m/z 573 (19.0%) and 575 (6.3%) that were consistent with the proposed formula. The ^1H - and ^{13}C -nmr data of rings C and D and the side-chain of 3 were closely related to those of the two previous withanolides indicating that they differed in the substitution pattern of rings A/B. A 1-keto- Δ^2 arrangement was evident from the ^1H -nmr signals between 6.07 and 6.80 ppm; however, a downfield shift of the H-2 and H-3 signals and an upfield shift of methyl-19 (compared with compound 2) was observed. Highly diagnostic for this structure was the strong upfield shift of the carbon resonance of methyl-19 (from 15.61 ppm in 2 to 9.16 ppm in 3) typical of a 5 β -hydroxy-6 α -chloro arrangement (17). Analysis of the COSY-45 and HETCOR spectra allowed a correlation of the H-6 signal at δ 4.33 ppm with the hydrogens at position 7 (1.55 and 2.32 ppm) and C-6 at 66.05 ppm, respectively. The spin-spin coupling pattern of H-6 (double doublet, $J=11.9$ and 4.0 Hz) indicated an equatorial (α) orientation of the substituent at this position. Compound 3 thus is one of the few examples of chlorinated withanolides found in a species of the Solanaceae (13,15,17,18). Finally, the ^1H -nmr spectrum of 3 also showed a sharp three-proton singlet at δ 3.14 assigned to a methoxy group, which correlated (HETCOR) with the methyl signal at 47.86 ppm in the ^{13}C -nmr spectrum and was assigned to a methyl ketal arrangement at C-12 (10). It is not clear if 3 is a natural product or an artifact of the extraction procedure, with the natural compound being the corresponding hemiketal. The 12-*O*-methyl derivative of trechonolide A [5] isolated by Lavie *et al.* (10) was considered by the authors an artifact originating from the extraction with boiling MeOH; however, in the present study several facts support the natural origin of 3. Our extraction procedure did not involve heating with MeOH at any stage, and was carried out entirely at room temperature. Furthermore, no traces of the methylated derivatives of jaborosalactones R [1] and S [2] were detected, and neither was

the hypothetical demethylated hemiketal of **3**. It appears unlikely that only one of these closely related compounds would react with MeOH.

From the several types of C-21-functionalized withanolides known (15,19), those containing an oxygen function at this position have been isolated from *Datura* spp. and comprise eight 21-hydroxywithanolides (15,20,21) and eleven 21,24-oxidewithanolides (15, 22–24). The three withanolides described above, which share the unusual feature of a hemiketal or ketal ring involving C-21 and C-12, add a new type to the amazing diversity of withanolide structures.

Jaborosalactone U [**4**] had ¹H- and ¹³C-nmr data markedly different from the previous compounds but closely resembling those of trechonolide A [**5**] for rings A–D (10). The ¹³C-nmr spectra showed the presence of only two sp² carbons which corresponded to C-2 and C-3. The non-conjugated lactone carbonyl at δ 173.65 ppm and the C-27 and C-28 methyl hydrogens at 1.56 and 1.62 ppm, respectively, indicated a 24,25-epoxy-γ-lactone side-chain, a novel arrangement among the withanolides. The quaternary carbons at δ 60.83 and 66.41 in the ¹³C-nmr spectrum assigned to C-24 and C-25 confirmed the proposed structure. Spectral assignments were confirmed by COSY-45, DQF-COSY, and HETCOR spectra. Mass measurements were in accordance with structure **4**, C₂₈H₃₆O₈. In the low-resolution mass spectrum, a small peak was observed for the molecular ion at *m/z* 500 (1.1%). Loss of the side-chain upon cleavage of the C-17–C-20 and C-22–O bonds gave rise to the ion at *m/z* 332 (5.7%).

The stereochemistry at positions C-23, C-24, and C-25 of jaborosalactone U [**4**] was tentatively assigned based on spectroscopic and molecular modeling considerations. Two orientations are possible for the epoxide, either 24*R*,25*R* or 24*S*,25*S*, which, combined with the two possible configurations at C-23 (23*R* or 23*S*), led to four possible stereochemical arrangements for the lactone side-chain. Further, three rotamers around the C-22–C-23 bond are possible in each case; thus, the twelve structures were generated and their geometry optimized by molecular modeling using the AM1 semiempirical method. NOESY experiments carried out on jaborosalactone U [**4**], showed that at short mixing times (0.7 sec) extremely weak or no nOe cross-peaks were observed between protons over 3.0 Å apart. Under these conditions, strong cross-peaks were observed for the pairs H-28/H-23, H-21/H-23, H-28/H-22, and H-21/H-22 (Table 2). An extremely weak nOe cross-peak was barely detected for the pair H-20/H-23. Conformers corresponding to the configurations 23*S*,24*S*,25*S* and 23*R*,24*R*,25*R* were predicted to have H-28/H-23 distances larger than 3.1 Å for which almost no nOes should be

TABLE 2. Correlations Displayed by Jaborosalactone U [**4**] in the NOESY Nmr Spectrum.^a

Proton	δ	NOESY correlations
4α	1.94	3.15 (H-6)
4β	2.98	1.22 (H-19)
6	3.15	1.94 (H-4α)
8	1.66	1.22 (H-19)
11β	1.75	1.03 (H-18), 1.22 (H-19)
18	1.03	1.75 (H-11β), 2.70 (OH-12/OH-17)
19	1.22	1.75 (H-11β), 2.98 (H-4β)
20	2.01	1.82 (H-14)
21	0.98	4.26 (H-22), 4.60 (H-23)
22	4.26	0.98 (H-21), 1.62 (H-28)
23	4.60	1.62 (H-28)
28	1.62	4.26 (H-22), 4.60 (H-23)

^aInteractions between vicinal and geminal hydrogens are not included.

TABLE 3. Geometrical Data from AM1 Calculations for the Possible Configurations of **4**.^a

Configuration	Conformer	Relative energy ^b	H-22-C-C-H-23 (degrees)	$J_{22,23}$ (Hz)	D23,28 ^c (Å)	D23,21 ^c (Å)	D23,20 ^c (Å)	D22,28 ^c (Å)
23S,24R,25R ...	a1	2.21	59.7	2.4	2.55	2.19	3.19	4.37
	a2	0.0	160.8	8.4	2.58	2.59	2.44	3.90
	a3	1.25	-101.9	1.4	2.59	3.98	3.47	2.48
23R,24S,25S ...	b1	0.0	60.1	0.8	2.57	2.14	3.11	2.62
	b2	1.09	137.1	7.4	2.52	2.23	2.46	3.06
	b3	1.38	-78.9	1.7	2.64	3.90	3.68	4.19
Observed ^d ...	—	—	—	1.0	<3.0 ^a	<<3.0	>3.0	<3.0

^aDiastereomers with the configurations 23S,24S,25S and 23R,24R,25R had D23,28 larger than 3.1 Å and are not tabulated.

^bRelative energies are given within each set of rotamers around the C-22-C-23 bond.

^cDistances between hydrogens at the specified positions. When more than one hydrogen is present, the shortest distance is indicated.

^dNOESY spectrum with mixing time 0.7 sec showed measurable nOes only between pairs of hydrogens separated by less than 2.9-3.0 Å.

observed, and thus were discarded. Table 3 summarizes the relative energies of the six remaining structures, relevant geometrical data, and the predicted coupling between H-22 and H-23 using the Altona equation (16). The small coupling observed between H-22 and H-23 ($J=1.0$ Hz) allowed us to discard those structures where H-22 and H-23 have an anti arrangement. Considering the relative interproton distances in Table 3, only the lowest energy conformer in the 23R,24S,25S combination (indicated as b1) can account for the observed nOes (Figure 2). These results indicate the same absolute configuration at position 23 for trechonolide A [**5**] and jaborosalactone U [**4**], with the 24,25-epoxide having also the same absolute configuration as in all known withanolides containing 24,25-epoxy- δ -lactones or lactols (15).

It should be noted that trechonolide A [**5**] was isolated for the first time by Lavie *et al.* from *J. laciniata* that was formerly classified, as was the case for *J. sativa*, in the now disregarded genus *Trechonaetes* (10). It was later isolated by Parvez *et al.* from *J. magellanica* and renamed jaborosalactone M (12). To avoid confusion with the structurally different jaborosalactone M isolated from *J. bergii* (8) we have retained the original name for **5**.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—¹H- and ¹³C-nmr spectra were recorded on a Bruker AC-200 spectrometer at 200.13 and 50.32 MHz, respectively, except where indicated. Multiplicity determinations (DEPT) and 2D spectra (COSY-45, DQF COSY, HETCOR, NOESY) were obtained using standard Bruker software. Chemical shifts are given in ppm downfield from TMS as internal standard, and assignments were confirmed by COSY-45, DQF COSY, and HETCOR spectra. Low-resolution eims were measured on a VG

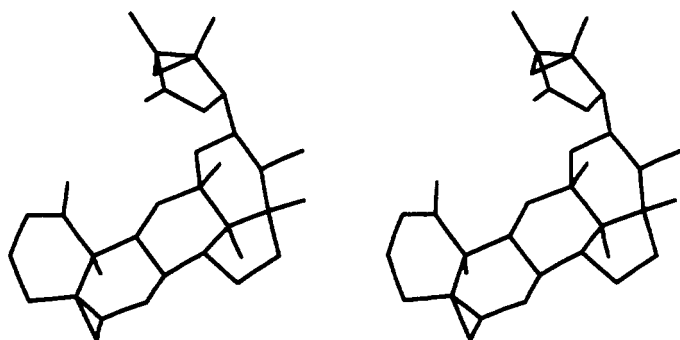


FIGURE 2. Stereoscopic views of the predominant conformer of jaborosalactone U [**4**] as predicted by AM1 calculations and nmr data (nOe and ¹H-¹H couplings).

Trio-2 at 70 eV by direct inlet; *fabms* and *hreims* were measured on a VG ZAB-BEQQ mass spectrometer. AM1 molecular modeling calculations were performed with Hyperchem 3.0 (Autodesk Inc.). Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Cc was performed on Kieselgel S 0.032–0.063 mm; tlc was performed on Si gel 60 F254, 0.2 mm thick.

PLANT MATERIAL.—Whole *Jaborosa sativa* plants were collected in Chulca, Departamento Trancas, Tucumán Province, Argentina. A voucher specimen is deposited at the Museo Botánico, Universidad Nacional de Córdoba under No. sp 24839.

EXTRACTION AND ISOLATION.—Dried and pulverized aerial parts (1 kg) were extracted with CHCl_3 . The residue obtained after evaporation of the CHCl_3 extract (48 g) was partitioned between hexane, MeOH, and H_2O (47:11:4). The aqueous MeOH layer was washed with hexane, concentrated, and extracted with CHCl_3 .

The residue (3.1 g) obtained after evaporation of the solvent was chromatographed on Si gel. Elution with $\text{C}_6\text{H}_6\text{-Me}_2\text{CO}$ (6:4) afforded fractions containing a partially resolved mixture of withanolides. The latter were pooled and fractionated by flash chromatography using hexane-EtOAc mixtures of increasing polarity (3:7 to 1:9) to yield four main fractions containing withanolides **1** (35 mg), **2** (35 mg), **3** (17 mg), and **4** (30 mg).

Jaborosalactone R [1].—White crystals, mp 263–264° (EtOAc/hexane); ^1H nmr (500 MHz) δ 6.97 (1H, dd, $J=9.5$ and 6.0 Hz, H-3), 6.18 (1H, d, $J=6.0$ Hz, H-4), 6.03 (1H, d, $J=9.5$ Hz, H-2), 4.56 (1H, dd, $J=3.4$ and 2.6 Hz, H-6), 4.36 (1H, ddd, $J=11.9$, 7.6, and 3.2 Hz, H-22), 3.79 (1H, dd, $J=11.2$ and 5.5 Hz, H-21 β), 3.59 (1H, t, $J=11.2$ Hz, H-21 α), 2.73 (1H, ddd, $J=11.2$, 7.6, and 5.5 Hz, H-20), 2.60 (1H, t, $J=11.9$ Hz, H-23 β), 2.28 (1H, dq, $J=12.7$ and 2.6 Hz, H-8), 1.94 (3H, s, H-28), 1.86 (3H, s, H-27), 1.66 (1H, dd, $J=14.5$ and 12.1 Hz, H-11 β), 1.48 (3H, s, H-19), 1.28 (1H, dt, $J=12.1$ and 4.3 Hz, H-9), 1.19 (1H, dt, $J=12.7$ and 3.4 Hz, H-7 α), 1.07 (3H, s, H-18); ^{13}C nmr δ 205.46 (C-1), 165.89 (C-26), 157.94 (C-5), 149.88 (C-24), 140.44 (C-3), 126.46 (C-2), 121.65 (C-25), 117.85 (C-4), 102.86 (C-12), 78.68 (C-17), 76.60 (C-22), 73.24 (C-6), 59.81 (C-21), 53.56 (C-10), 51.38 (C-13), 49.89 (C-14), 46.87 (C-20), 46.64 (C-9), 39.95 (C-11), 34.95 (C-16), 34.90 (C-23), 29.65 (C-7), 29.20 (C-8), 24.21 (C-15), 20.30 (C-28), 18.81 (C-19), 12.41 (C-27), 12.18 (C-18); eims m/z 484 $[\text{M}]^+$ (1), 466 $[\text{M}-\text{H}_2\text{O}]^+$ (27), 448 $[\text{M}-2\text{H}_2\text{O}]^+$ (23), 329 $[\text{M}-125-2\text{H}_2\text{O}]^+$ (14), 136 $[\text{C}_8\text{H}_8\text{O}_2]^+$ (33), 135 $[\text{C}_8\text{H}_7\text{O}_2]^+$ (52), 125 [lactone side-chain] $^+$ (100); *hreims* m/z found $[\text{M}]^+$ 484.2459 ($\text{C}_{28}\text{H}_{36}\text{O}$, requires 484.2461).

Jaborosalactone S [2].—White crystals, mp 265–266° (EtOAc/hexane); ^1H nmr δ 6.62 (1H, ddd, $J=10.0$, 6.0, and 2.0 Hz, H-3), 5.91 (1H, dd, $J=10.0$ and 2.5 Hz, H-2), 4.37 (1H, ddd, $J=11.9$, 7.3, and 3.3 Hz, H-22), 3.98 (1H, dd, $J=11.5$ and 5.1 Hz, H-21 β), 3.69 (1H, br s, $W_{1/2}=3$ Hz, H-6), 3.64 (1H, t, $J=11.5$ Hz, H-21 α), 3.34 (1H, ddd, $J=17.9$, 2.5, and 2.0 Hz, H-4 β), 2.86 (1H, ddd, $J=11.5$, 7.3, and 5.1 Hz, H-20), 2.55 (2H, m, H-23 β and H-8), 2.20 (1H, dd, $J=14.5$ and 3.3 Hz, H-23 α), 2.15 (1H, dd, $J=17.9$ and 6.0 Hz, H-4 α), 1.95 (3H, s, H-28), 1.87 (3H, s, H-27), 1.33 (3H, s, H-19), 1.08 (3H, s, H-18); ^{13}C nmr δ 204.79 (C-1), 165.83 (C-26), 150.04 (C-24), 141.97 (C-3), 128.28 (C-2), 121.66 (C-15), 103.28 (C-12), 78.50 (C-17), 77.45 (C-5), 76.90 (C-22), 73.93 (C-6), 59.68 (C-21), 51.95 (C-10), 51.79 (C-13), 50.00 (C-14), 47.38 (C-20), 38.82 (C-9), 35.64 (C-11), 35.08 (C-16), 35.04 (C-4), 33.28 (C-23), 30.87 (C-7), 28.79 (C-8), 24.20 (C-15), 20.52 (C-28), 15.61 (C-19), 12.40 (C-18), 12.36 (C-27); eims m/z 484 $[\text{M}-\text{H}_2\text{O}]^+$ (6), 466 $[\text{M}-2\text{H}_2\text{O}]^+$ (5), 136 $[\text{C}_8\text{H}_8\text{O}_2]^+$ (15), 135 $[\text{C}_8\text{H}_7\text{O}_2]^+$ (27), 125 [lactone side-chain] $^+$ (37), 44 (100); *fabms* (thioglycerol, KCl) m/z 541 $[\text{M}+\text{K}]^+$ (44); *hreims* m/z found $[\text{M}-\text{H}_2\text{O}]^+$ 484.2460 ($\text{C}_{28}\text{H}_{36}\text{O}$, requires 484.2461).

Jaborosalactone T [3].—Amorphous solid, mp 234–235° (EtOAc/hexane); ^1H nmr δ 6.80 (1H, ddd, $J=10.0$, 6.0, and 2.0 Hz, H-3), 6.07 (1H, dd, $J=10.0$ and 2.0 Hz, H-2), 4.33 (1H, dd, $J=11.9$ and 4.0 Hz, H-6), 4.32 (1H, m, H-22), 3.74 (1H, dd, $J=11.5$ and 5.6 Hz, H-21 β), 3.62 (1H, t, $J=11.7$ Hz, H-21 α), 3.14 (3H, s, OMe), 2.80 (1H, m, H-20), 2.57 (1H, dd, $J=14.0$ and 11.9 Hz, H-23 β), 2.32 (1H, dt, $J=12.5$ and 4.0 Hz, H-7 β), 2.15 (1H, dd, $J=14.0$ and 4.1 Hz, H-23 α), 1.96 (3H, s, H-28), 1.88 (3H, s, H-27), 1.55 (1H, br q, $J=12.5$ Hz, H-7 α), 1.24 (3H, s, H-19), 0.96 (3H, s, H-18); ^{13}C nmr δ 200.28 (C-1), 165.16 (C-26), 149.31 (C-24), 143.02 (C-3), 127.50 (C-2), 121.94 (C-25), 102.44 (C-12), 78.52 (C-17), 77.37 (C-5), 76.33 (C-22), 66.05 (C-6), 60.37 (C-21), 55.04 (C-10), 51.99 (C-13), 50.15 (C-14), 47.86 (OMe), 46.84 (C-20), 42.37 (C-9), 38.54 (C-11), 35.43 (C-16), 35.17 (C-4), 33.74 (C-8), 31.74 (C-7), 31.50 (C-23), 24.00 (C-15), 20.45 (C-28), 12.39 (C-18 and C-27), 9.16 (C-19); eims m/z 498 $[\text{M}-\text{HCl}]^+$ (33), 173 (20), 136 $[\text{C}_8\text{H}_8\text{O}_2]^+$ (23), 135 $[\text{C}_8\text{H}_7\text{O}_2]^+$ (71), 125 [lactone side-chain] $^+$ (71), 97 (100); *fabms* m/z (*m*-nitrobenzylalcohol, KCl) 575 and 573 $[\text{M}+\text{K}]^+$ (7 and 19), 505 and 503 $[\text{M}-\text{OMe}]^+$ (35 and 100), 469 $[\text{M}-\text{CH}_2\text{O}-\text{Cl}]^+$ (25); *hreims* m/z found $[\text{M}-\text{MeOH}]^+$ 502.2119 ($\text{C}_{28}\text{H}_{35}\text{O}_6\text{Cl}$ requires 502.2122), $[\text{M}-\text{CH}_2\text{O}-\text{HCl}]^+$ 468.2518 ($\text{C}_{28}\text{H}_{36}\text{O}_6$ requires 468.2512).

Jaborosalactone U [4].—White crystals, mp 268–269° (EtOAc/hexane); ^1H nmr δ 6.85 (1H, ddd, $J=10.0$, 6.2, and 2.3 Hz, H-3), 5.97 (1H, dd, $J=10.0$ and 2.8 Hz, H-2), 4.60 (1H, br s, H-23), 4.26 (1H,

dd, $J=12.2$ and 1.0 Hz, H-22), 3.15 (1H, d, $J=2.6$ Hz, H-6), 2.98 (1H, ddd, $J=19.0$, 2.8, and 2.3 Hz, H-4 β), 2.22 (1H, dd, $J=13.3$ and 4.1 Hz, H-11 α), 2.10 (1H, ddd, $J=14.0$, 6.1, and 2.6 Hz, H-7 β), 2.01 (1H, m, H-20), 1.94 (1H, dd, $J=19.0$ and 6.2 Hz, H-4 α), 1.75 (1H, dd, $J=13.3$ and 11.5 Hz, H-11 β), 1.66 (1H, dt, $J=11.5$ and 6.1 Hz, H-8), 1.62 (3H, s, H-28), 1.56 (3H, s, H-27), 1.33 (1H, dt, $J=11.5$ and 4.1 Hz, H-9), 1.22 (3H, s, H-19), 1.21 (1H, dd, $J=14.0$ and 11.5 Hz, H-7 α), 1.03 (3H, s, H-18), 0.98 (3H, d, $J=6.8$ Hz, H-21); ^{13}C nmr δ 202.41 (C-1), 173.65 (C-26), 144.43 (C-3), 128.84 (C-2), 99.21 (C-12), 81.01 (C-23), 80.34 (C-17), 71.52 (C-22), 66.41 (C-24), 63.23 (C-6), 61.83 (C-5), 60.83 (C-25), 47.68 (C-10 and C-13), 46.85 (C-14), 42.33 (C-9), 37.22 (C-11), 35.67 (C-20), 33.45 (C-16), 32.91 (C-4), 30.49 (C-7), 29.37 (C-8), 22.69 (C-15), 15.36 (C-19), 13.75 (C-28), 12.00 (C-18), 10.02 (C-21), 8.46 (C-27); eims m/z 500 $[\text{M}]^+$ (1), 482 $[\text{M}-\text{H}_2\text{O}]^+$ (9), 464 $[\text{M}-2\text{H}_2\text{O}]^+$ (3), 332 (6), 314 (22), 109 [lactone side-chain $-\text{H}_2\text{O}]^+$ (20), 43 (100); hreims m/z , found $[\text{M}]^+$ 500.2390 ($\text{C}_{28}\text{H}_{36}\text{O}_8$, requires 500.2410), $[\text{M}-\text{H}_2\text{O}]^+$ 482.2309 ($\text{C}_{28}\text{H}_{34}\text{O}_8$, requires 482.2305).

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