Three New Diterpenoids Based on the Novel Sarcopetalane Skeleton from *Croton sarcopetalus*

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The roots of *Croton sarcopetalus* afforded three new diterpenoids (**2**−**4**) with a novel carbon skeleton that seems to be derived biosynthetically from a pimarane precursor. The essential oil of the roots gave *trans*-methylisoeugenol as the main constituent, along with 22 further compounds.

The large phanerogamous family Euphorbiaceae has 317 genera with about 7500 species.[1] From these genera, the genus *Croton*, containing some 700 species, is distributed widely in the warm regions, less frequently in the temperate regions, and rarely in the cold regions of the Earth. Most of the species of this genus produce a variety of diterpenes, some of them with antitumor activity[2] and others produce skin inflammation characterized by an intense erythema followed by edema and hyperplasia and eye conjunctivitis.[3] Ingestion of some of these toxic diterpenes produces mouth mucous-membrane irritation, abundant salivary secretion, intestinal pain, and, in some cases, diarrhea.[4] *Croton sarcopetalus* Muell., commonly known as "lecherón" is a shrub that grows in northwestern and central Argentina, and its pubescence, leaf size, color, and indumentum vary with seasonal and altitudinal changes, edaphic factors, and so forth.[5]

In previous work of *C. sarcopetalus*[6] we have described the complete ^{13}C NMR assignments and conformational evaluation of junceic acid and of three yucalexins, including yucalexin B-6[7] and yucalexin P-4 (**1**).[7] Continuing our study on the roots of this species, we now report the isolation and structure elucidation of the three new diterpenoids **2**−**4** having a novel carbon skeleton that we name sarcopetalane. The structures of these new diterpenoids were determined using 1D and 2D NMR techniques. In addition, we analyzed the essential oil of the roots by GC−MS, which allowed the identification of *trans*-methylisoeugenol as the main constituent, together with 22 other compounds.

Results and Discussion

The positive-ion HRFABMS of sarcopetalolide (**2**) showed a quasimolecular ion peak $[M + H]^+$ at *m/z* 317.2123 (calcd for $C_{20}H_{29}O_3$, 317.2117 $[M + H]^+$), corresponding to the molecular formula $C_{20}H_{28}O_3$. According to a DEPT experiment, the 16 sp^3 carbon atoms are distributed as four CH_3, six CH_2, three CH, and three C, while the sp^2 region shows a keto carbonyl, an ester carbonyl, and a trisubstituted double bond. The ^1H and ^{13}C NMR signals for the A and B rings are similar to those observed for yucalexin B-6 and yucalexin P-4 (**1**),[6,7] also isolated from the plant material.

Table 1. ^{13}C NMR Spectral Data of Compounds **2** and **4** (75.4 MHz, in $CDCl_3$, TMS as Internal Standard)

	2		
C		HMBC[a]	**4**
1	38.4	H-2, H-5, H-9, H-20	37.7
2	34.2	H-1	34.1
3	215.9	H-1, H-2	216.7
4	47.2	H-5, H-6, H-18, H-19	47.4
5	53.8	H-1, H-6, H-7, H-9, H-18, H-19, H-20	54.8
6	19.8	H-5, H-7	22.7
7	37.7	H-5, H-9, H-14, H-16	33.4
8	41.4	H-6, H-7, H-9, H-11, H-14, H-15, H-16	60.4
9	49.0	H-1, H-5, H-7, H-11, H-14, H-20	49.3
10	37.5	H-1, H-2, H-5, H-6, H-9, H-11, H-20	37.6
11	27.7	H-9	29.8
12	171.5	H-9, H-11, H-16	179.7
13	147.2	H-14, H-15, H-16, H-17	139.4
14	52.4	H-7, H-9, H-15, H-16, H-17	135.8[b]
15	123.9	H-14, H-16, H-17	140.5[b]
16	90.3	H-7, H-9, H-14, H-15	139.6[b]
17	16.7	H-14, H-15	16.0
18	26.7	H-5, H-19	26.4
19	22.0	H-5, H-18	21.3
20	15.3	H-1, H-5, H-9	14.8

[a] At 500 MHz. [b] May be interchanged.

However, the ^1H NMR signals of the ABX system corresponding to the $CH_2(11)$−CH(9) fragment appeared downfield when compared with those of yucalexin B-6.[7] The presence of a broad singlet at 4.98 ppm, ascribed to H-16, which, in the COSY experiment, showed correlation with the broad singlet at 5.47 ppm, assigned to H-15, together with the presence of a lactone carbonyl group signal at 171.5 ppm, instead of the ketone (C-12) at 211.5 ppm for yucalexin B-6,[6] as well as the HETCOR correlation of the methine signal at 90.3 ppm with the H-16 signal, indicated that the lactone ring closes at C-16. Furthermore, irradiation of H-16 at 4.98 ppm gave an 8% NOE effect of the H-15 signal at 5.47 ppm. In addition, the COSY experiment showed correlations of the H-14 signal at 2.69 ppm with the H-15, H-16, and $CH_3(17)$ signals at 5.47, 4.98, and 1.79 ppm, respectively, while the other H-14 signal, at 2.03 ppm, has correlations only with H-15 and $CH_3(17)$. To confirm the structure of sarcopetalolide (**2**), HMBC and NOESY experiments were performed, whose data are given in Table 1 and Table 2, respectively. All the above data, as well as the MMX calculations discussed below, are in agreement with structure **2**.

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Table 2. NOESY Correlations of Compound **2** (500 MHz, in $CDCl_3$, TMS as Internal Standard)

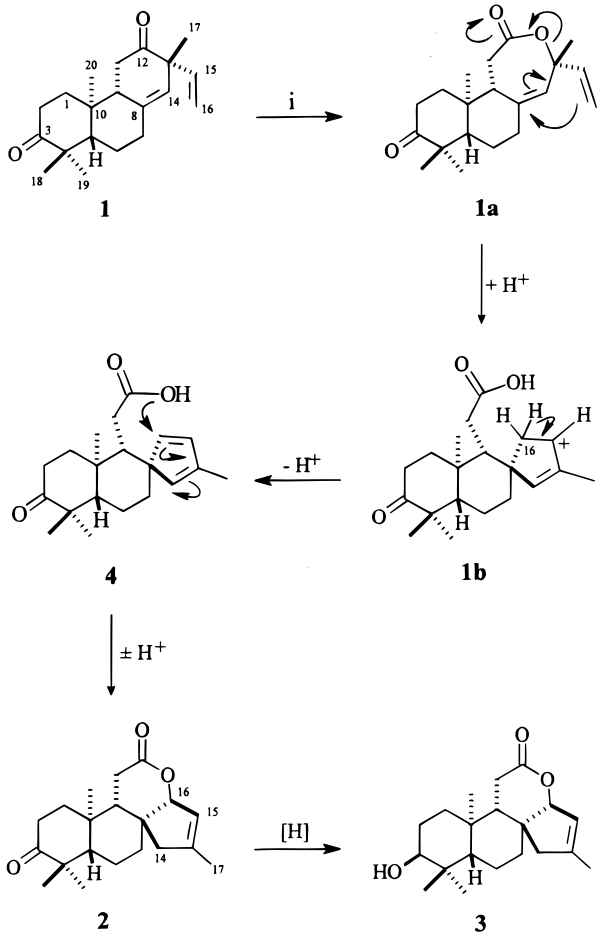
H	NOESY
1α	1*β*, 2*β*, 11α, 20
1*β*	1α, 2*β*, 9*β*
2α	2*β*, 20
2*β*	1α, 1*β*, 2α
5*β*	6*β*, 9*β*, 18
6α	6*β*, 7α, 16
6*β*	5*β*, 6α, 7α, 19
7α	6α, 6*β*, 7*β*, 16
7*β*	7α, 9*β*
9*β*	1*β*, 5*β*, 7*β*, 11α, 11*β*, 14α
11α	1α, 9*β*, 11*β*
11*β*	9*β*, 11α, 14α
14α	9*β*, 11*β*, 14*β*
14*β*	14α, 17
15	16, 17
16	6α, 7α, 15
17	14*β*, 15
18	5*β*
19	6*β*
20	1α, 2α

The molecular weight of sarcopetalololide (**3**) was determined by a positive-ion HRFABMS to be 319.2285 for the $[M + H]^+$ ion (calcd for $C_{20}H_{31}O_3$, 319.2273 $[M+H]^+$). The structure of **3** was deduced by comparing its ^1H NMR spectrum with that of sarcopetalolide (**2**). The presence of a double doublet at 3.25 ppm along with an upfield shift of the A-ring signals, which produce an overlapping between 1.40 and 1.95 ppm with the signals of the B ring, is indicative of a C-3 hydroxyl group instead of the carbonyl group present in **2**. To determine the stereochemistry at C-3, the minimum energy conformation of the two C-3 epimers was calculated by the MMX method.[8] The calculated dihedral angles for the *β*-OH case were $H_\alpha C(2)-C(3)H_\alpha = 63°$ and $H_\beta C(2)-C(3)H_\alpha = 179°$. These angles allowed us to calculate the coupling constants by using a generalized Karplus-type equation,[9,10] which gave 3.7 and 11.5 Hz, respectively, in agreement with the observed (5.1 and 12.9 Hz) values. The alternate α-OH case gave coupling constants of 2.9 and 1.9 Hz for the angles $H_\alpha C(2)-C(3)H_\beta = 54°$ and $H_\beta C(2)-C(3)H_\beta = 60°$, respectively.

The structure of sarcopetaloic acid (**4**) was deduced from the ^1H and ^{13}C NMR spectra and its easy conversion, in $CDCl_3$ solution, into compound **2** during the NMR study. The ^{13}C NMR spectrum of **4** is very similar to that of **2**, except in the double bonds region with four carbon signals between 135.8 and 140.5 ppm and a carboxylic acid signal at 179.7 ppm instead of the lactone carbonyl signal at 171.5 ppm of **2**. In addition, the ^1H NMR spectrum showed three vinyl proton signals, whose coupling constants are indicative of a 2-methyl-1,3-butadiene fragment in a five-membered ring.

A possible biosynthetic route leading to the rearranged molecules is proposed to proceed via the pimarane **1**.[11] Formation of sarcopetaloic acid (**4**) might involve intermediates **1a** and **1b** as shown in Scheme 1. Intermediate **1a** could be formed by a biogenetic type Baeyer−Villiger oxidation, which is a common process in terpenoid biosynthesis.[12−14] Although the carboxylic acid of **4** might attack at C-14 or C-16, MMX calculations on both possible reaction products show significant differences in the dihedral angles for the $CH(9)-CH_2(11)$ fragment. The calculated dihedral angles for the C-16-lactonized isomer (**2**) are: $H\beta C(9)-C(11)H\alpha = -76°$ and $H\beta(9)-C(11)H\beta = 39°$, corresponding to coupling constants of 1.3 and 6.3 Hz, respectively, in reasonable agreement with the observed (3.0 and 6.1 Hz) values, while the alternate C-14-lactonized case gave coupling constants of 3.5 and 12.3 Hz for the angles $H\beta(9)-C(11)H\beta = -58°$ and $H\beta C(9)-C(11)H\alpha = -178°$, respectively. The observed cyclation product (**2**) is further in agreement with the direction of the electromeric effect, which generates a partial carbonium ion easier at C-16 than at C-14. The weak acidity, due to acid traces in the chloroform used as NMR solvent, probably catalyzed this reaction. A reduction of **2** might finally lead to **3**.

Scheme 1. A Possible Biosynthetic Path for **2**−**4**



(i) "Biogenetic" Baeyer-Villiger

Experimental Section

General Experimental Procedure. Melting points were obtained on a Fisher−Johns melting point apparatus and are uncorrected. UV spectra were determined on a Perkin−Elmer UV/vis Lambda 12 spectrophotometer. IR spectra were recorded on a Perkin−Elmer 16F PC FT-IR spectrophotometer. Optical rotations were performed on a Perkin−Elmer 241 polarimeter. For separation of mixtures, HPLC with a differential refractometer detector was used. The column employed was a Beckman C_{18} (5 μ, 10 × 250 mm). Retention times (t_R) were measured from the solvent peak. The essential oil was analyzed using a Hewlett−Packard 6890 gas chromatograph with a selective mass detector HP-5973, equipped with a capillary column (HP-5, cross linked 5% phenylmethylsilicone, i.d. 32 μm, film thickness 0.17 μm, 25 m); gas carrier, He. NMR spectra were recorded on Varian XL-300GS or Unity-500 spectrometers. HRFABMS were obtained on a JEOL JMS SX 1021 spectrometer operated at an accelerating voltage of 10 kV. Samples were desorbed from a nitrobenzyl alcohol matrix using 6-kV positive xenon ions. Mass measurements are performed at a resolution of 10 000 using electric field scans and poly(ethylene glycol) ions as reference material. For

column chromatography, Si gel Merck 70−230 or 230−400 mesh ASTM was used.

Plant Material. Roots of *C. sarcopetalus* Muell. were collected in December 1994, at San Pedro de Colalao, Tucumán Province, Argentina. A voucher specimen (Catalán no. 623) is on deposit in the herbarium of the Fundación Miguel Lillo, Tucumán, Argentina.

Extraction and Isolation. Roots (500 g) of *Croton sarcopetalus* were extracted with petroleum ether (2 × 3 L) at room temperature for 6 days to give 12.9 g (yield 2.6%) of crude extract, which was chromatographed over Si gel (70−230 mesh, 650 g) using petroleum ether with increasing amounts of EtOAc (10−45%) and MeOH (1−10%) to give 249 fractions, which were monitored by TLC and IR.

Fractions 52−75 (3.5 g) from the mother column were combined, and a portion (300 mg) was processed by HPLC (MeOH−H_2O 95:5, 2.5 mL min^{-1}) to give 146 mg of a 75:25 mixture of *trans*-methylisoeugenol and veratraldehide, t_R 2.0 min, and 143 mg of junceic acid,[6] mp 47−49 °C, t_R 7.5 min.

Fractions 91−103 (250 mg) were combined and processed by HPLC (MeOH−H_2O 9:1, 2.5 mL min^{-1}) to give 19 mg of yucalexin P-4 (**1**),[7] mp 113−115 °C, t_R 5.7 min, and 6.1 mg of junceic acid[6] as a gum, t_R 17.5 min.

Fractions 127−151 (1.19 g) were combined and a portion (200 mg) processed by HPLC (MeOH−H_2O 85:15, 2.0 mL min^{-1}) to give 65.3 mg of yucalexin B-6,[7] mp 70−73 °C, t_R 9.7 min.

Fractions 203−223 (596 mg) were combined and a portion (300 mg) processed by HPLC (MeOH−H_2O 4:1, 2.0 mL min^{-1}) to give 5.5 mg of yucalexin B-6[7] and 9.7 mg of yucalexin A-16.[7]

Fractions 224−235 (401 mg) were combined and processed by HPLC as before to yield 41.3 mg of sarcopetalolide (**2**), t_R 4.0 min, and 10 mg of sarcopetaloic acid (**4**), t_R 11.0 min.

Fractions 236−248 (626 mg) were combined and a portion (500 mg) chromatographed over Si gel (230−400 mesh, 30 g) using $CHCl_3$ containing increasing amounts of EtOAc (12−50%), 122 fractions being collected. Fractions 20−30 (40 mg) were combined and processed by HPLC (MeOH−H_2O 7:3, 2.0 mL min^{-1}) to give 3.6 mg of **3**, t_R 11.5 min. Fractions 31−57 (47 mg) were combined and processed by HPLC (MeOH−H_2O 3:1, 2 mL min^{-1}) to give 5.6 mg of **4**, t_R 22.0 min.

Fresh roots (1.39 kg) were cut in small pieces. A stream of steam at 98 °C was passed through until no oily material was condensed. The distillate afforded 3.03 g (yield 0.22%) of essential oil, which was analyzed by capillary GC−MS using an HP-5, 25-m column. The following compounds were tentatively identified by comparison with the spectra from the MS library of the used mass spectrometer: α-thujene (0.01%), α-pinene (0.02%), *β*-pinene (0.01%), camphene (0.15%), myrcene (0.05%), *p*-cymene (0.03%), sabinene (0.01%), 1,8-cineole (0.13%), limonene (0.13%), linalool oxide (0.08%), dihydrolinalool (0.03%), isoborneol (0.02%), borneol (0.9%), sabinene hydrate (0.03%), dihydro-*β*-ionone (1.0%), anethol (0.25%), methyleugenol (7.8%), *cis*-isoeugenol (0.10%), *trans*-isoeugenol (0.16%), *trans*-methylisoeugenol (74.7%), undecanoic acid (2.7%), myrcenyl formate (2.13%), and bisabolene (0.8%). In addition, the following constituents were further confirmed by co-injection with authentic samples: α-thujene, α-pinene, *β*-pinene, camphene, myrcene, *p*-cymene, sabinene, 1,8-cineole, limonene, isoborneol, borneol, anethol, methyleugenol, *cis*-isoeugenol, *trans*-isoeugenol, bisabolene, and *trans*-methylisoeugenol. The structure of this last was also verified by ^1H NMR spectroscopy of an isolated sample.

Sarcopetal-15-en-3-one-12,13-olide (sarcopetalolide) (2): solid, mp 149−151 °C; $[\alpha]^{26}_{589}$ +115°, $[\alpha]^{26}_{578}$ +120°, $[\alpha]^{26}_{546}$ +138°, $[\alpha]^{26}_{436}$ +255°, $[\alpha]^{26}_{365}$ +444° (*c* 1.29, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 201 (3.7) nm; IR ($CHCl_3$) ν_{max} 3028, 1726, 1706, 1386, 1228 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.47 (1H, m, H-15), 4.98 (1H, br s, H-16), 2.69 (1H, br d, J = 17.5 Hz, H-14α), 2.62 (1H, dd, $J_{9\beta,11\beta,}$ = 6.1 Hz, $J_{11\alpha,11\beta}$ = 18.0 Hz, H-11*β*), 2.59 (1H, ddd, $J_{1\alpha,2\alpha}$ = 6.8 Hz, $J_{1\beta,2\alpha}$ = 12.6 Hz, $J_{2\alpha,2\beta}$ =16.1 Hz, H-2α), 2.53 (1H, dd, $J_{9\beta,11\alpha}$ = 3.0 Hz, $J_{11\alpha,11\beta}$ = 18.0 Hz, H-11α), 2.41 (1H, ddd, $J_{1\alpha,2\beta}$ = 3.6 Hz, $J_{1\beta,2\beta}$ = 6.2 Hz, $J_{2\alpha,2\beta}$ = 16.1 Hz, H-2*β*), 2.07 (1H, ddd, $J_{1\alpha,1\beta}$= 13.3 Hz, $J_{1\alpha,2\alpha}$ = 6.8 Hz, $J_{1\alpha,2\beta}$ = 3.6 Hz, H-1α), 2.03 (1H, br d, J = 17.5 Hz, H-14*β*), 1.98 (1H, ddd, $J_{6\alpha,7\alpha}$ = 3.6 Hz, $J_{6\beta,7\alpha}$ = 3.5 Hz, $J_{7\alpha,7\beta}$ = 13.7 Hz, H-7α), 1.79 (3H, br s, H-17), 1.70 (1H, dd, $J_{9\beta,11\alpha}$ = 3.0 Hz, $J_{9\beta,11\beta}$ = 6.1 Hz, H-9*β*), 1.63 (1H, dddd, $J_{5\beta,6\beta}$ = 3.0 Hz, $J_{6\alpha,6\beta}$ = 12.3 Hz, $J_{6\beta,7\alpha}$ = 3.5 Hz, $J_{6\beta,7\beta}$ = 1.6 Hz, H-6*β*), 1.51 (1H, dd, $J_{5\beta,6\alpha}$ = 11.5 Hz, $J_{5\beta,6\beta}$ = 3.0 Hz, H-5*β*), 1.47 (1H, ddd, $J_{1\alpha,1\beta}$ = 13.3 Hz, $J_{1\beta,2\alpha}$ = 12.6 Hz, $J_{1\beta,2\beta}$ = 6.2 Hz, H-1*β*), 1.48−1.59 (2H, m, H-6α, H-7*β*), 1.12 (3H, s, H-18), 1.09 (3H, s, H-19), 1.08 (3H, s, H-20); ^{13}C NMR and HMBC, see Table 1; NOESY, see Table 2; EIMS *m/z* 316 $[M]^+$ (7), 272 (53), 257 (22), 191 (27), 121 (46), 106 (100), 93 (74), 80 (45), 43 (36); HRFABMS (methane) *m/z* 317.2123 (calcd for $C_{20}H_{29}O_3$, 317.2117).

Sarcopetal-15-en-3*β*-ol-12,13-olide (sarcopetalololide) (3): solid, mp 88−90 °C; $[\alpha]^{26}_{589}$ +94.3°, $[\alpha]^{26}_{578}$ +94.3°, $[\alpha]^{26}_{546}$ +111.4°, $[\alpha]^{26}_{436}$ +205.7°, $[\alpha]^{26}_{365}$ +364.2° (*c* 0.12, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 201 (3.5) nm; IR ($CHCl_3$) ν_{max} 3444, 3028, 1715, 1386, 1228 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.47 (1H, m, H-15), 4.92 (1H, br s, H-16), 3.25 (1H, dd, $J_{2\alpha,3\alpha}$ = 5.1 Hz, $J_{2\beta,3\alpha}$ = 12.9 Hz, H-3α), 2.64 (1H, br d, $J_{14\alpha,14\beta}$ = 17.5 Hz, H-14α), 2.53 (1H, dd, $J_{9\beta,11\beta}$ = 6.0 Hz, $J_{11\alpha,11\beta}$ = 19.0 Hz, H-11*β*), 2.48 (1H, dd, $J_{9\beta,11\alpha}$ = 3.5 Hz, $J_{11\alpha,11\beta}$ = 19.0 Hz, H-11α), 2.00 (1H, br d, $J_{14\alpha,14\beta}$ = 17.5 Hz, H-14*β*), 1.79 (3H, br s, H-17), 1.48 (1H, dd, $J_{5\beta,6\alpha}$ = 9.8 Hz, $J_{5\beta,6\beta}$ = 4.0 Hz, H-5*β*), 1.45−1.95 (9H, m, CH_2-1, CH_2-2, CH_2-6, CH_2-7, H-9), 1.04 (3H, s, H-18), 0.87 (3H, s, H-19), 0.94 (3H, s, H-20); EIMS *m/z* 300 $[M - H_2O]^+$ (1), 274 (18), 257 (15), 256 (15), 175 (35), 150 (82), 106 (100), 93 (90), 80 (86), 69 (84), 57 (93), 43 (64); HRFABMS (methane) *m/z* 319.2285 (calcd for $C_{20}H_{31}O_3$, 319.2273).

Sarcopetal-13,15-dien-3-one-12-oic acid (sarcopetaloic acid) (4): gum; $[\alpha]^{26}_{589}$ −34.4°, $[\alpha]^{26}_{578}$ −38.7°, $[\alpha]^{26}_{546}$ −44.7°, $[\alpha]^{26}_{436}$ −78.2°, $[\alpha]^{26}_{365}$ −146.1° (*c* 0.33, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 200 (3.5), 252 (2.9) nm; IR ($CHCl_3$) ν_{max} 3215, 1711 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.51 (1H, dd, $J_{14,16}$ = 2.1 Hz, $J_{15,16}$ = 5.4 Hz, H-16), 6.27 (1H, dd, $J_{14,15}$ = 1.7 Hz, $J_{15,16}$ = 5.4 Hz, H-15), 5.67 (1H, m, H-14), 2.62 (1H, ddd, $J_{1\alpha,2\alpha}$ = 7.1 Hz, $J_{1\beta,2\alpha}$ = 10.9 Hz, $J_{2\alpha,2\beta}$ = 15.7 Hz, H-2α), 2.49 (1H, ddd, $J_{1\alpha,2\beta}$ = 4.2 Hz, $J_{1\beta,2\beta}$ = 6.8 Hz, $J_{2\alpha,2\beta}$ = 15.7 Hz, H-2*β*), 2.28 (1H, dd, $J_{9\beta,11\alpha}$ = 6.2 Hz, $J_{9\beta,11\beta}$ = 3.5 Hz, H-9*β*), 2.04 (1H, dd, $J_{9\beta,11\beta}$ = 3.5 Hz, $J_{11\alpha,11\beta}$ = 17.4 Hz, H-11*β*), 1.91 (3H, br d, 1.5 Hz, H-17), 1.87 (1H, ddd, $J_{1\alpha,1\beta}$= 12.0 Hz, $J_{1\alpha,2\alpha}$ = 7.1 Hz, $J_{1\alpha,2\beta}$ = 4.2 Hz, H-1α), 1.80 (1H, m, H-6*β*), 1.68 (1H, ddd, $J_{1\alpha,1\beta}$ = 12.0 Hz, $J_{1\beta,2\alpha}$ = 10.9 Hz, $J_{1\beta,2\beta}$ = 6.8 Hz, H-1*β*), 1.62−1.75 (2H, m, H6α, H7*β*), 1.58 (1H, dd, $J_{5\beta,6\alpha}$ = 10.4 Hz, $J_{5\beta,6\beta}$ = 4.2 Hz, H-5*β*), 1.55 (1H, dd, $J_{9\beta,11\alpha}$ = 6.2 Hz, $J_{11\alpha,11\beta}$ = 17.4 Hz, H-11α), 1.41 (1H, ddd, $J_{6\alpha,7\alpha}$ = 2.9 Hz, $J_{6\beta,7\alpha}$ = 2.9 Hz, $J_{7\alpha,7\beta}$ = 13.1 Hz, H-7α), 1.17 (3H, s, H-18), 1.12 (3H, s, H-19), 1.07 (3H, s, H-20); ^{13}C NMR, see Table 1. Sarcopetaloic acid (**4**) began to convert into sarcopetalolide (**2**) in the NMR sample tube after several hours, with the conversion being completed over the weekend.

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References and Notes

(1) Webster, G. L. *Ann. M. Bot. Gard.* **1994**, *81*, 33−35.
(2) Kupchan, S. M.; Uchida, I.; Branfman, A. R.; Dailey, R. G., Jr.; Fei, B. Y. *Science* **1976**, *191*, 571−572.
(3) Evans, F. J.; Taylor, S. E. *Prog. Chem. Org. Nat. Prod.* **1983**, *44*, 1−99.
(4) Forsyth, A. A. *British Poisonous Plants*. Ministry of Agriculture, Fisheries and Food, Her Majesty's Stationery Office: London, 1986; p 74.
(5) Croizat, L. *Darwiniana* **1941**, *5*, 421−428.
(6) De Heluani, C. S.; Catalán, C. A. N.; Hernández, L. R.; Burgueño-Tapia, E.; Joseph-Nathan, P. *Magn. Reson. Chem.* **1998**, *36*, 947−950.

(7) Sakai, T.; Nakagawa, Y. *Phytochemistry* **1988**, *27*, 3769−3779.
(8) Burket, U.; Allinger N. L. *Molecular Mechanics*. ACS monograph 177, American Chemical Society: Washington, DC, 1982.
(9) Hasnoot, C. A. G.; De Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783−2792.
(10) Cerda-García-Rojas, C. M.; Zepeda, L. G.; Joseph-Nathan, P. *Tetrahedron Comput. Methodol.* **1990**, *3*, 113−118.
(11) Manitto P. *Biosynthesis of Natural Products*. John Wiley and Sons: New York, 1981; p 259.
(12) Miller, H. E.; Kagan, H. B.; Renold, W.; Mabry, T. J. *Tetrahedron Lett.* **1965**, *38*, 3397−3403.
(13) Mabry, T. J.; Miller, H. E.; Kagan, H. B.; Renold, W. *Tetrahedron* **1966**, *22*, 1139−1146.
(14) Kagan, H. B.; Miller, H. E.; Renold, W.; Lakshmikantham, M. V.; Tether, L. R.; Herz, W.; Mabry, T. J. *J. Org. Chem*. **1966**, *31*, 1629−1632.

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