Labdanes and Withanolides from *Physalis coztomatl*

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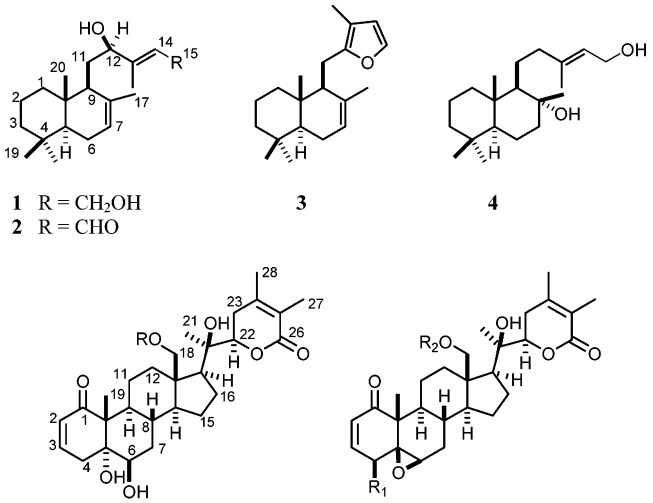
Aerial parts of *Physalis coztomatl* afforded a new labdane diterpene, physacoztomatin (**1**), and five new withanolides, physacoztolides A−E (**5**−**9**). Six known compounds were also isolated. The structures of the new compounds were established after analyses of their spectroscopic data and by means of chemical transformations. X-ray diffraction analyses of 15-dehydrophysacoztomatin (**2**) and **5** confirmed the structures of **1** and **5**. Labd-13(*E*)-ene-8α,15-diol (**4**) and physacoztomatin (**1**) represent the first labdane diterpenes isolated from the genus *Physalis*.

The genus *Physalis* (Solanaceae) is represented in Mexico by ca. 70 species, most of them endemic.[1] This genus is known as a source of withasteroids,[2] mainly withanolides and physalins. Many of these compounds show anti-inflammatory, antitumor, hepatoprotective, immunomodulatory, cytotoxic, and insect antifeedant activities.[2,3] The fruits of *P. philadelphica* and *P. coztomatl* are used in the preparation of sauces and other dishes, mainly in Mexico. Furthermore, the use of *P. coztomatl* (Tomate agrio or Tomate amarillo) in Mexican folk medicine has been described in the Florentine codex since the sixteenth century. This document tells us that the plant was used as an antidiarrheic, antipyretic, and diuretic and in the treatment of cataracts, nose abscess, liver spots on the face, flatulence, asthma, and stomach pains.[4] In the state of Oaxaca, *P. coztomatl* is still used in the treatment of pulpitis and stomach pains and as an antidiarrheic.

In continuation of our systematic study of Mexican *Physalis* species,[5] we undertook the chemical investigation of the aerial parts of *P. coztomatl* (Mociño & Sessé) Ex Dunal. The present paper details the structural elucidation of the new labdane physacoztomatin (**1**) and of five new withanolides, physacoztolides A−E (**5**−**9**), which were isolated from the EtOAc extract together with six known compounds. To our knowledge this is the first report of labdanes from the genus *Physalis*.



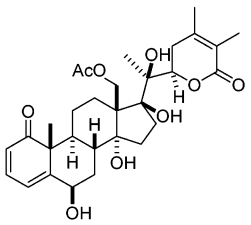
1 R = CH_2OH
2 R = CHO

3

4

5 R = Ac
6 R = H

7 R_1 = H R_2 = Ac
11 R_1 = OH R_2 = Ac
12 R_1 = OH R_2 = H



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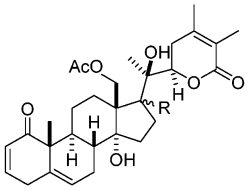

9 R = αH
10 R = βOH

Results and Discussion

Physacoztomatin (**1**) presented the molecular formula $C_{20}H_{34}O_2$ obtained by HRMS. Its ^{1}H NMR spectrum showed five signals (δ 1.71, 1.69, 0.86, 0.88, and 0.74) attributed to the methyl groups of a labdane diterpene (CH_3-16, CH_3-17, CH_3-18, CH_3-19, and CH_3-20, respectively) with double bonds at C-7 and C-13.[6,7] The positions of unsaturations were corroborated in the HMBC spectrum, which showed correlations of C-7 (δ 122.9) with H-5 (δ 1.25), H-9 (δ 2.02), and CH_3-17 and of C-14 (δ 123.5) with CH_2-15, CH_3-16, and H-12 (δ 4.13). The chemical shift of the last proton indicated that it was geminal to an OH group. A second alcohol was proposed at C-15 on the basis of the chemical shifts of H-15a (δ 4.23) and H-15b (δ 4.20). The fragments of *m*/*z* 205 $[M - C_5H_9O_2]^+$ and 191 $[M - C_6H_{11}O_2]^+$, observed in the mass spectrum, supported the presence of two alcohols and an unsaturation in the side chain.

To establish the stereochemistry of **1**, 15-dehydrophysacoztomatin (**2**), suitable for esterification with Mosher reagents, was obtained by means of selective oxidation with quinolinium chlorochromate. The γ-hydroxy-α,β-unsaturated aldehyde group in compound **2** was evidenced by the chemical shifts of the H-14 (δ 6.18), H-15 (δ 10.06), CH_3-16 (δ 2.20), C-12 (δ 76.4), C-13 (δ 164.5), and C-15 (δ 191.4) signals in the ^{1}H and ^{13}C NMR spectra. Compound **2** was submitted to the Mosher conditions;[8,9] however, instead of the expected 12-O-esterified derivative, furan diterpene **3** was obtained. The presence of a furan ring was deduced from the chemical shifts of H-15 (δ 7.22), C-12 (δ 151.6), C-13 (δ 113.0), C-14 (δ 113.0), and C-15 (δ 139.2) signals in the ^{1}H and ^{13}C NMR spectra. On the basis of the above, the structure of physacoztomatin was established as **1**. This structure was confirmed by X-ray analysis of its derivative **2** (Figure 1). If it is assumed that **1** belongs to the labdane series such as labd-13(*E*)-ene-8α,15-diol (**4**),[6,10] a diterpene also present in the plant, then the C-12 configuration must be *R*.

The HRMS of physacoztolide A (**5**) indicated a molecular formula of $C_{30}H_{42}O_8$. The IR spectrum showed bands at 3592, 3512, and 1705 cm^{-1} attributed to hydroxyl and carbonyl groups. Its ^{1}H

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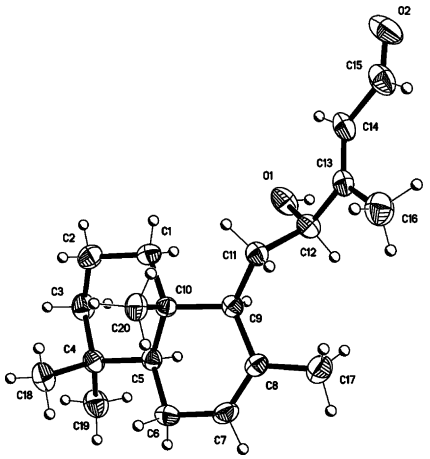

Figure 1. ORTEP projection of **2** (crystallographic numbering).

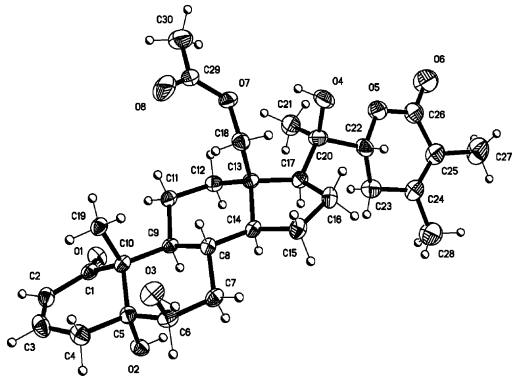

Figure 2. ORTEP projection of **5** (crystallographic numbering).

and ^{13}C NMR spectra showed the signals of the enone system in the A-ring and those of the δ-lactone side chain of a withanolide.[2] The presence of OH groups at C-5 and C-6 was evident by the chemical shifts of H-6 (δ 3.39), C-5 (δ 76.3), and C-6 (δ 72.8) and supported by the correlations of OH-5 (δ 4.27) with C-4 (δ 35.1), C-5, and C-10 (δ 50.9) and of OH-6 (δ 4.79) with C-5, C-6, and C-7 (δ 33.0), in the HMBC spectrum.

The ^{1}H and ^{13}C NMR spectra showed signals of an acetoxy group, which was proposed at CH_2-18 (δ 61.8) since, in the HMBC spectrum, the methylene correlated with C-12 (δ 35.0), C-13 (δ 44.7), C-17 (δ 54.3), and the acetate carbonyl (δ 170.5). In terms of the δ-lactone, the chemical shift and coupling constants of the H-22 signal (δ 4.09, dd, J = 13, 4 Hz) supported its axial orientation. Correlations of a third OH (δ 4.37) with C-17, C-20 (δ 73.8), and C-21 (δ 19.5) in the HMBC spectrum suggested an OH group at C-20. The NOESY spectrum of **5** showed NOE effects between H-4a and CH_3-19 and between H-4b and H-6; therefore, β-orientation of OH-6 was proposed. The NOE effects of H-14 with H-9 and H-17 were consistent with a β-side chain. Finally, the X-ray diffraction analysis of **5** (Figure 2) confirmed its structure.

Physacoztolide B (**6**) presented spectroscopic features very similar to those of **5**. The ^{1}H and ^{13}C NMR spectra of **6** did not show signals attributable to an acetyl group, in agreement with the molecular formula $C_{28}H_{40}O_7$ obtained by HRMS. Other differences were the upfield shifts of the H-18a (δ 3.56) and H-18b (δ 3.34) signals and the presence of a signal at δ 5.13, which was assigned to OH-18 by its coupling with that of C-18 in the HMBC spectrum. The structural relationship between **5** and **6** was proved when saponification of **5** produced **6**.

Physacoztolide C (**7**) was isolated as an amorphous solid. Its molecular formula, $C_{30}H_{40}O_7$ obtained by HRMS, contained two hydrogens and one oxygen less than **5**. The ^{1}H NMR spectrum showed the H-6 signal as a doublet at δ 3.18 (J = 2 Hz), which together with the chemical shifts of C-5 (δ 61.6) and C-6 (δ 61.9) led us to propose an epoxide. The coupling constant of H-6 was in agreement with those reported for 5β,6β-epoxides.[11−13] The remaining spectroscopic features of **7** were very similar to those of **5**; therefore, the structure of physacoztolide C is that depicted as **7**.

Physacoztolide D (**8**), $C_{30}H_{40}O_9$, exhibited signals at δ 5.99, 6.92, and 6.12 in the ^{1}H NMR spectrum, which were assigned to olefinic hydrogens of the A-ring dienone system (H-2, H-3, and H-4, respectively). In the ^{13}C NMR spectrum, the chemical shifts of C-1, C-2, C-3, C-4, and C-5 (δ 204.7, 116.8, 139.6, 125.8, and 157.8, respectively), and the UV (λ_{max} 314 nm) spectrum, corroborated the dienone function. An OH group attached to C-6 was proposed because the H-6 signal (δ 4.60) showed a coupling with that of its gem OH group (δ 3.20) in the ^{1}H−^{1}H COSY spectrum. The NOESY spectrum of **8** exhibited a NOE effect between H-4 and H-6, which indicated quasi-equatorial orientation of H-6 and β-orientation of the hydroxyl group. The ^{13}C NMR spectrum showed signals at δ 81.4 (C-14) and 87.1 (C-17), which indicated linkage of these carbon atoms to OH groups. The low-field shift of H-22 (δ 4.85) was justified by the deshielding effect of a hydroxyl group at C-17.[2] The chemical shifts of C-13, C-15, and C-16 (δ 56.9, 32.4, and 36.9, respectively) agreed with those reported for withanolides with 14α-OH and 17β-OH groups,[5c,14] then the structure of physacoztolide D was formulated as **8**.

The mass spectrum of physacoztolide E (**9**) did not show the molecular ion, but fragments at m/z 169 ($C_9H_{13}O_3$), 125 ($C_7H_9O_2$), and 43 (C_2H_3O) indicated the presence of the α,β-unsaturated δ-lactone side chain and of an acetoxy group. The ^{1}H and ^{13}C NMR spectra were similar to those of **5** and **7**, but in compound **9** the chemical shifts of H-6 (δ 5.60), C-5 (δ 135.1), and C-6 (δ 124.4) indicated a C-5 double bond. The chemical shift of C-14 (δ 83.4) suggested an OH group at this position. The side chain orientation was deduced by comparison of the ^{1}H NMR data of **9** with those of **7** obtained in $CDCl_3$. In both compounds the chemical shifts of CH_2-18 were very similar (**7**: δ 4.15, s; **9**: δ 4.19, s), but the H-17 signal of **9** was at low field (δ 2.2 m) compared with that of **7** (δ 1.45). Therefore, OH-14 and H-17 of physacoztolide E (**9**) should have an α-orientation, and the side chain should be β-oriented.

In addition to the above, from the aerial parts of *P. coztomatl*, the known physachenolide D (**10**),[5a] 18-acetoxywithanolide D (**11**),[15] and 18-hydroxywithanolide D (**12**)[16] were obtained. All the isolated withanolides (**5**−**12**) have oxidized C-18 as a structural characteristic and differed mainly in the A- and B-rings. The proposed pathway for the genesis of withanolides[2,17] suggests compounds with the 2,5-dien-1-one system, like **9** and **10**, as the key intermediaries, which generate the different functionalizations of the A- and B-rings. Compounds **5**−**12**, which coexist in *P. coztomatl*, can fit well into the proposed biosynthetic pathway. Thus, **9** could form **7** and **11**, the first by epoxidation and the second by C-4 hydroxylation followed by an epoxidation of the unconjugated double bond. Alternately, **11** could be obtained by C-4 hydroxylation of **7**. On the other hand, the opening of the epoxide group of **7** could form the 5,6-dihydroxy compound **5**, which by dehydration could afford **8**.

The flavonoids pachypodol[18,19] and retusine[20,21] and the diterpene labd-13(*E*)-ene-8α,15-diol (**4**)[6,10] were also isolated form *P. coztomatl*. Compound **4** and physacoztomatin (**1**) represent the first diterpenes isolated from the genus *Physalis*, although related diterpenes have been reported as constituents of other Solanaceae genera, such as *Nicotiana*[22] and *Fabiana*.[23]

Experimental Section

General Experimental Procedures. Melting points were determined on a Fisher-Johns melting points apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 343 polarimeter. UV and IR spectra were recorded on Shimadzu UV 160U and Bruker Tensor 27 spectrophotometers, respectively. 1D and 2D NMR spectra were obtained on an Eclipse JEOL 300 MHz, a Bruker Avance 300 MHz, or a Varian-Unity Inova 500 MHz spectrometer with tetramethylsilane

(TMS) as internal standard. EIMS (70 eV) and CIMS (CH_4) were obtained on a JEOL JMS-AX505HA mass spectrometer. ESIMS was obtained on a Bruker Daltonics Analysis 3.2 mass spectrometer, and HRFABMS data were measured with a JEOL JMS-SX102A mass spectrometer. Vacuum column chromatography (VCC) was carried out with Merck silica gel G60 and flash chromatography with silica gel 60 (230−400 mesh, Macherey-Nagel). Analytical thin-layer chromatography (TLC) was performed on precoated 0.25 mm thick Sil G UV_{254} aluminum plates (Macherey-Nagel), while preparative TLC was carried out using precoated Sil G-100UV_{254} plates (Macherey-Nagel). X-ray crystallographic analyses were carried out on a Bruker Smart Apex CCD diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods using the program SHELXS. Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms, except for those bonded to oxygen atoms, were included at calculated positions and were not refined.

Plant Material. Aerial parts, with flowers and fruits, of *Physalis coztomatl* (Mociño & Sessé) Ex Dunal were collected in the Parque Nacional Desierto de los Leones, D. F. México, in March 2001. A voucher specimen (No. 101081) was deposited at the Herbario Nacional, Instituto de Biología, UNAM.

Extraction and Isolation. Aerial parts (without fruits) were dried at room temperature for two weeks. After that, they were ground and the powder (1.28 kg) was exhaustively extracted with MeOH. The solvent was eliminated under reduced pressure until the volume reached 1 L and partitioned with hexane to yield 31 g of hexane residue and 148 g of MeOH residue. This last was suspended in H_2O and extracted with EtOAc to afford 55 g of organic residue, which was left at −13 °C until it was analyzed. The hexane residue (31 g) was purified by VCC (hexane−EtOAc polarity gradient system) to afford a mixture (212 mg) of *β*-sitosterol and stigmasterol. The EtOAc residue (55 g) was subjected to a VCC eluted with a polarity gradient system of hexane−EtOAc. Five fractions (I−V) were obtained. Fraction II was purified by VCC (hexane−EtOAc, 7:3, hexane−Me_2CO 4:1) to yield 14 mg of pachypodol[18,19] as yellow crystals (hexane−Me_2CO), mp 175−180 °C. Fractions I and III were combined and purified by VCC (CH_2Cl_2−Me_2CO gradient system) to give fractions IIIA−IIIC. Purification of fraction IIIA (VCC, hexane−EtOAc 3:1) gave 3 mg of retusine[20,21] as yellow crystals (hexane−Me_2CO), mp 158−160 °C, and 12 mg of pachypodol. Fraction IIIB was purified by VCC (CH_2Cl_2−Me_2CO, 9:1) to give a mixture (352 mg) of physacoztomatin (**1**) and labd-13(*E*)-ene-8α,15-diol (**4**). Fraction IIIC was purified by VCC (C_6H_6−EtOAc, 4:1) and preparative TLC (C_6H_6−EtOAc, 3:2, × 2) to afford 117 mg of **4**[6,10] as white crystals (hexane−C_6H_6), mp 125−126 °C, $[\alpha]_D$ −3.23 (*c* 0.34, $CHCl_3$), and 113 mg of **1**. Fraction IV was subjected to VCC (hexane−EtOAc gradient system) to yield fractions IVA−IVD. Fraction IVA was purified by VCC (hexane−Me_2CO, 4:1), flash CC (hexane−Me_2CO, 4:1), and preparative TLC (CH_2Cl_2−EtOAc, 4:1, × 2) to obtain 14 mg of physacoztolide C (**7**). Fraction IVB was submitted to VCC (CH_2Cl_2−EtOAc gradient system) and flash CC (CH_2Cl_2−Me_2CO, 97:3) to afford 43 mg of **7** and 34 mg of physacoztolide E (**9**). Fraction IVC was purified by VCC ($CHCl_3$−MeOH, 49:1) to give 1.7 g of physachenolide D (**10**)[5a] as white crystals (hexane−EtOAc), mp 162−169 °C, and 38 mg of physacoztolide D (**8**). Fraction IVD yielded 51 mg of physacoztolide B (**6**). VCC of fraction V ($CHCl_3$−MeOH gradient system) afforded fractions VA−VC. Fraction VA yielded 96 mg of 18-acetoxywithanolide D (**11**)[15] as white crystals (Et_2O−EtOAc), mp 147−158 °C, and 43 mg of 18-hydroxywithanolide D (**12**)[16] as white crystals (EtOAc), mp 178−181 °C. Physacoztolide A (**5**) (179 mg) was obtained from fraction VB. The purification of its mother liquors gave 117 mg of **12** and 74 mg of **5**. Fraction VC was submitted to flash CC (hexane−Me_2CO, 3:2, hexanes−EtOAc, 7:3) and preparative TLC (CH_2Cl_2−Me_2CO, 4:1, × 2) to afford 29 mg of **6** and 22 mg of **12**.

Physacoztomatin (1): colorless oil; $[\alpha]^{25}_D$ +12.5 (*c* 0.24, MeOH); IR ($CHCl_3$) ν_{max} 3610, 1664, 1602, 1456, 1387, 1366, 1044, 996 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.66 (1H, tdq, $J = 6.5, 1, 1$ Hz, H-14), 5.42 (1H, br s, H-7), 4.23, 4.20 (each 1H, dd, $J = 12.5, 6.5$ Hz, CH_2-15), 4.13 (1H, dd, $J = 10, 2$ Hz, H-12), 2.02 (1H, m, H-9), 2.00 (1H, m, H-6a), 1.88 (1H, m, H-6b), 1.85 (1H, br d, $J = 13$ Hz, H-1a), 1.71 (3H, br s, CH_3-16), 1.69 (3H, s, CH_3-17), 1.54 (2H, m, H-2a and H-11a), 1.48 (1H, m, H-2b), 1.42 (1H, m, H-11b), 1.41 (1H, br d, $J = 13$ Hz, H-3a), 1.25 (1H, dd, $J = 12, 5$ Hz, H-5), 1.18 (1H, ddd, $J = 13, 13, 4$ Hz, H-3b), 1.04 (1H, ddd, $J = 13, 13, 4$ Hz, H-1b), 0.88 (3H, s, CH_3-19), 0.86 (3H, s, CH_3-18), 0.74 (3H, s, CH_3-20); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.0 (C, C-13), 134.8 (C, C-8), 123.5 (CH, C-14), 122.9 (CH, C-7), 77.1 (CH, C-12), 59.1 (CH_2, C-15), 50.5 (CH, C-9), 50.1 (CH, C-5), 42.3 (CH_2, C-3), 39.3 (CH_2, C-1), 36.4 (C, C-10), 33.7 (CH_2, C-11), 33.1 (CH_3, C-18), 33.0 (C C-4), 23.9 (CH_2, C-6), 22.5 (CH_3, C-17), 21.8 (CH_3, C-19), 18.8 (CH_2, C-2), 13.6 (CH_3, C-20), 12.3 (CH_3, C-16); EIMS *m/z* (%) 307 $[M + H]^+$ (3), 288 (16), 270 (15), 257 (13), 245 (19), 205 (100), 191 (60), 190 (68), 175 (19), 164 (55), 133 (33), 109 (60), 95 (20), 82 (36), 81 (31), 69 (20), 55 (31); HRFABMS *m/z* 307.2633 (calcd for $C_{20}H_{35}O_2$, 307.2637).

Physacoztolide A (5): white crystals (Me_2CO−EtOAc); mp 303−305 °C; $[\alpha]^{25}_D$ +65.0 (*c* 0.28, MeOH); UV (MeOH) λ_{max} (log ϵ) 226 (4.17) nm; IR ($CHCl_3$) ν_{max} 3592, 3512, 1706, 1447, 1427, 1382, 1252, 1131, 1049, 1028, 951, 919 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 6.59 (1H, ddd, $J = 10, 5, 2.5$ Hz, H-3), 5.65 (1H, dd, $J = 10, 2.5$ Hz, H-2), 4.79 (1H, d, $J = 4.5$ Hz, OH-6), 4.37 (1H, s, OH-20), 4.27 (1H, s, OH-5), 4.09 (1H, dd, $J = 13, 4$ Hz, H-22), 4.03, 3.98 (each 1H, d, $J = 11$ Hz, CH_2-18), 3.39 (1H, dd, $J = 6, 2$ Hz, H-6), 3.09 (1H, dt, $J = 20, 2.5$ Hz, H-4a), 2.37 (1H, br t, $J = 17$ Hz, H-23a), 2.31 (1H, m, H-12a), 2.27 (1H, m, H-23b), 2.13 (1H, br d, $J = 13.5$ Hz, H-11a), 1.98 (3H, s, $COOCH_3$), 1.94 (1H, dd, $J = 20, 5$ Hz, H-4b), 1.92 (3H, br s, CH_3-28), 1.76 (1H, m, H-8), 1.76 (1H, br dd, $J = 19, 11$ Hz, H-16a), 1.76 (3H, br s, CH_3-27), 1.72 (1H, ddd, $J = 11, 11, 2.5$ Hz, H-9), 1.61 (1H, br dd, $J = 19, 9$ Hz, H-16b), 1.60 (1H, m, H-17), 1.58 (1H, m, H-15a), 1.55 (1H, m, H-7a), 1.38 (1H, br td, $J = 13, 2.5$ Hz, H-7b), 1.28 (1H, m, H-14), 1.23 (3H, s, CH_3-21), 1.17 (1H, td, $J = 12, 4.5$ Hz, H-12b), 1.12 (3H, s, CH_3-19), 1.06 (1H, br t, $J = 13.5$ Hz, H-11b), 0.99 (1H, ddd, $J = 18, 5, 5$ Hz, H-15b); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 204.0 (C, C-1), 170.5 (C, $COOCH_3$), 165.8 (C, C-26), 150.2 (C, C-24), 142.3 (CH, C-3), 127.5 (CH, C-2), 120.1 (C, C-25), 81.0 (CH, C-22), 76.3 (C, C-5), 73.8 (C, C-20), 72.8 (CH, C-6), 61.8 (CH_2, C-18), 55.5 (CH, C-14), 54.3 (CH, C-17), 50.9 (C, C-10), 44.7 (C, C-13), 40.7 (CH, C-9), 35.1 (CH_2, C-4), 35.0 (CH_2, C-12), 33.0 (CH_2, C-7), 31.0 (CH_2, C-23), 29.4 (CH, C-8), 23.3 (CH_2, C-15), 22.5 (CH_2, C-11), 21.0 (CH_3, $COOCH_3$), 20.9 (CH_2, C-16), 20.0 (CH_3, C-28), 19.5 (CH_3, C-21), 15.1 (CH_3, C-19), 12.1 (CH_3, C-27); FABMS *m/z* (%) 531 $[M + H]^+$ (9), 471 (2), 417 (8), 391 (6), 345 (6), 83 (53), 55 (100), 43 (71); HRFABMS *m/z* 531.2968 (calcd for $C_{30}H_{43}O_8$, 531.2958).

Crystal data of 5:[24] $C_{30}H_{42}O_8$, M_r 530.64, monoclinic, space group $P2_1$, $a = 10.8441(1)$ Å, $\alpha = 90.00°$, $b = 8.444(1)$ Å, $\beta = 91.221(2)°$, $c = 15.345(2)$ Å; $\gamma = 90.00°$, $V = 1394.5(3)$ Å^3, $Z = 2$, $D_c = 1.264$ g cm^{-3}, $F(000) = 572$; crystal dimensions 0.410 × 0.178 × 0.016 mm. Reflections collected 11 380, independent reflections 4877.

Physacoztolide B (6): amorphous solid; $[\alpha]^{25}_D$ +53.0 (*c* 0.29, MeOH); UV (MeOH) λ_{max} (log ϵ) 225 (3.95) nm; IR (Nujol) ν_{max} 3285, 1707, 1669, 1459, 1379, 1319, 1294, 1216, 1133, 1089, 1048, 1026, 954, 920 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 6.59 (1H, ddd, $J = 10, 5, 2$ Hz, H-3), 5.65 (1H, dd, $J = 10, 2.5$ Hz, H-2), 5.41 (1H, s, OH-20), 5.13 (1H, dd, $J = 7, 4$ Hz, OH-18), 4.77 (1H, d, $J = 4.5$ Hz, OH-6), 4.21 (1H, s, OH-5), 4.10 (1H, dd, $J = 13, 3$ Hz, H-22), 3.56 (1H, dd, $J = 11, 7$ Hz, H-18a), 3.38 (1H, dd, $J = 4, 3$ Hz, H-6), 3.34 (1H, m, H-18b), 3.10 (1H, dt, $J = 20, 2$ Hz, H-4a), 2.37 (1H, m, H-12a), 2.35 (1H, m, H-23a), 2.24 (1H, dd, $J = 17, 3$ Hz, H-23b), 2.12 (1H, br dd, $J = 13.5, 2.5$ Hz, H-11a), 1.93 (1H, dd, $J = 20, 5$ Hz, H-4b), 1.92 (3H, br s, CH_3-28), 1.79 (1H, m, H-16a), 1.75 (3H, br s, CH_3-27), 1.71 (1H, ddd, $J = 11, 11, 3$ Hz, H-9), 1.67 (1H, ddd, $J = 13, 11, 11, 3$ Hz, H-8), 1.56 (1H, m, H-16b), 1.55 (1H, m, H-15a), 1.53 (1H, m, H-17), 1.50 (1H, m, H-7a), 1.34 (1H, td, $J = 13, 3$ Hz, H-7b), 1.26 (3H, s, CH_3-21), 1.25 (1H, m, H-14), 1.22 (1H, m, H-11b), 1.16 (3H, s, CH_3-19), 1.06 (1H, m, H-12b), 1.06 (1H, m, H-15b); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 204.0 (C, C-1), 165.7 (C, C-26), 149.9 (C, C-24), 142.3 (CH, C-3), 127.5 (CH, C-2), 120.2 (C, C-25), 80.3 (CH, C-22), 76.3 (C, C-5), 73.9 (C, C-20), 72.8 (CH, C-6), 57.6 (CH_2, C-18), 55.5 (CH, C-17), 54.9 (CH, C-14), 51.0 (C, C-10), 47.0 (C, C-13), 40.8 (CH, C-9), 35.2 (CH_2, C-4), 34.4 (CH_2, C-12), 33.1 (CH_2, C-7), 31.0 (CH_2, C-23), 29.4 (CH, C-8), 23.3 (CH_2, C-15), 22.2 (CH_2, C-11), 20.9 (CH_2, C-16), 20.8 (CH_3, C-21), 20.0 (CH_3, C-28), 15.1 (CH_3, C-19), 12.1 (CH_3, C-27); FABMS *m/z* (%) 489 $[M + H]^+$ (19), 471 (25), 453 (9), 345 (9), 185 (73), 93 (100), 75 (26), 43 (25); HRFABMS *m/z* 489.2846 (calcd for $C_{28}H_{41}O_7$, 489.2852).

Physacoztolide C (7): amorphous solid; $[\alpha]^{25}_D$ +61.0 (*c* 0.21, MeOH); UV (MeOH) λ_{max} (log ϵ) 225 (3.02) nm; IR ($CHCl_3$) ν_{max} 3589, 1706, 1671, 1455, 1381, 1315, 1245, 1187, 1132, 1039, 962,

917 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 7.00 (1H, ddd, J = 10, 6.5, 2 Hz, H-3), 5.95 (1H, dd, J = 10, 3 Hz, H-2), 4.39 (1H, s, OH-20), 4.07 (1H, dd, J = 13, 3 Hz, H-22), 4.01, 3.91 (each 1H, d, J = 11.5 Hz, CH_2-18), 3.18 (1H, d, J = 2 Hz, H-6), 2.92 (1H, dt, J = 19, 2 Hz, H-4a), 2.34 (1H, br dd, J = 17.5, 13 Hz, H-23a), 2.28 (1H, dt, J = 13, 3.5 Hz, H-12a), 2.21 (1H, dd, J = 17.5, 3 Hz, H-23b), 2.00 (3H, s, $COOCH_3$), 1.95 (1H, m, H-11a), 1.94 (1H, m, H-7a), 1.93 (1H, m, H-4b), 1.90 (3H, s, CH_3-28), 1.82 (1H, dt, J = 11.5, 9.5 Hz, H-16a), 1.75 (3H, s, CH_3-27), 1.58 (2H, m, H-15a and H-16b), 1.56 (1H, m, H-17), 1.50 (1H, m, H-8), 1.27 (1H, m, H-7b), 1.25 (1H, m, H-11b), 1.22 (3H, s, CH_3-21), 1.15 (1H, br dt, J = 14, 5.5 Hz, H-14), 1.09 (3H, s, CH_3-19), 1.08 (1H, m, H-9), 1.07 (1H, m, H-12b), 1.00 (1H, m, H-15b); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 202.7 (C, C-1), 170.5 (C, $COOCH_3$), 165.8 (C, C-26), 150.2 (C, C-24), 146.2 (CH, C-3), 128.2 (CH, C-2), 120.1 (C, C-25), 80.9 (CH, C-22), 73.7 (C, C-20), 61.9 (CH, C-6), 61.6 (C, C-5), 61.4 (CH_2, C-18), 55.0 (CH, C-14), 54.1 (CH, C-17), 47.5 (C, C-10), 44.3 (C, C-13), 44.0 (CH, C-9), 34.6 (CH_2, C-12), 32.1 (CH_2, C-4), 31.0 (CH_2, C-23), 30.6 (CH_2, C-7), 29.2 (CH, C-8), 23.3 (CH_2, C-15), 22.9 (CH_2, C-11), 21.1 (CH_2, C-16), 20.1 (CH_3, $COOCH_3$), 20.0 (CH_3, C-28), 19.6 (CH_3, C-21), 14.6 (CH_3, C-19), 12.1 (CH_3, C-27); EIMS m/z (%) 512 $[M]^+$ (1), 452 (1), 434 (2), 327 (100), 309 (45), 169 (31), 126 (25), 43 (30); HRFABMS m/z 513.2855 (calcd for $C_{30}H_{41}O_7$, 513.2852).

Physacoztolide D (8): amorphous solid; $[\alpha]^{25}_D$ −48.0 (c 0.23, MeOH); UV (MeOH) λ_{max} (log ϵ) 210 (3.90), 224 (3.90), 314 (3.49) nm; IR ($CHCl_3$) ν_{max} 3607, 3576, 3390, 1706, 1659, 1627, 1603, 1573, 1453, 1382, 1322, 1133, 1090, 1046, 1000, 963 cm^{-1}; ^1H NMR ($CDCl_3$−DMSO-d_6, 500 MHz) δ 6.92 (1H, dd, J = 9.5, 6 Hz, H-3), 6.12 (1H, d, J = 6 Hz, H-4), 5.99 (1H, dd, J = 9.5, 0.5 Hz, H-2), 4.85 (1H, dd, J = 13.5, 4 Hz, H-22), 4.60 (1H, s, H-6), 4.50, 4.41 (each 1H, d, J = 11 Hz, CH_2-18), 3.20 (1H, s, OH-6), 2.64 (1H, dd, J = 19, 4 Hz, H-23a), 2.62 (1H, m, H-16a), 2.47 (1H, dd, J = 19, 13.5 Hz, H-23b), 2.41 (1H, ddd, J = 11, 11, 3 Hz, H-8), 2.16 (1H, m, H-12a), 2.10 (3H, s, $COOCH_3$), 1.94 (3H, s, CH_3-28), 1.93 (1H, m, H-7a), 1.90 (1H, m, H-9), 1.88 (3H, s, CH_3-27), 1.88 (1H, m, H-12b), 1.77 (1H, m, H-11a), 1.75 (1H, m, H-7b), 1.65 (2H, m, CH_2-15), 1.62 (1H, m, H-16b), 1.49 (1H, m, H-11b), 1.48 (3H, s, CH_3-19), 1.38 (3H, s, CH_3-21); ^{13}C NMR ($CDCl_3$−DMSO-d_6, 125 MHz) δ 204.7 (C, C-1), 169.7 (C, $COOCH_3$), 165.0 (C, C-26), 157.8 (C, C-5), 149.3 (C, C-24), 139.6 (CH, C-3), 125.8 (CH, C-4), 121.1 (C, C-25), 116.8 (CH, C-2), 87.1 (C, C-17), 81.4 (C, C-14), 79.5 (CH, C-22), 78.1 (C, C-20), 73.4 (CH, C-6), 64.6 (CH_2, C-18), 56.9 (C, C-13), 53.4 (C, C-10), 41.8 (CH, C-9), 36.9 (CH_2, C-16), 35.9 (CH_2, C-7), 34.2 (CH, C-8), 33.2 (CH_2, C-23), 32.4 (CH_2, C-15), 25.1 (CH_2, C-12), 20.8 (CH_3, $COOCH_3$), 20.7 (CH_2, C-11), 20.0 (CH_3, C-28), 18.3 (CH_3, C-21), 17.8 (CH_3, C-19), 11.7 (CH_3, C-27); CIMS m/z (%) 527 $[M - OH]^+$ (11), 509 (19), 491 (12), 467 (14), 449 (50), 431 (49), 419 (87), 401 (100), 375 (12), 357 (13), 297 (10), 279 (20), 251 (33), 169 (61), 125 (23); HRFABMS m/z 545.2744 (calcd for $C_{30}H_{41}O_9$, 545.2751).

Physacoztolide E (9): amorphous solid; $[\alpha]^{25}_D$ +62.0 (c 0.21, MeOH); UV (MeOH) λ_{max} (log ϵ) 226 (3.78) nm; IR ($CHCl_3$) ν_{max} 3590, 1705, 1666, 1466, 1453, 1383, 1320, 1131, 1097, 1038, 952, 933 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.80 (1H, ddd, J = 10, 5, 2 Hz, H-3), 5.89 (1H, br dd, J = 10, 1.8 Hz, H-2), 5.60 (1H, br d, J = 5.3 Hz, H-6), 4.24 (1H, dd, J = 13, 3.5 Hz, H-22), 4.19 (2H, br s, CH_2-18), 3.30 (1H, br d, J = 21 Hz, H-4a), 2.85 (1H, dd, J = 21, 5 Hz, H-4b), 2.35 (1H, br t, J = 16 Hz, H-23a), 2.25 (2H, m, H-15a and H-11a), 2.20 (1H, m, H-17), 2.15 (1H, m, H-23b), 2.06 (3H, s, $COOCH_3$), 2.05 (1H, m, H-8), 1.95 (3H, s, CH_3-28), 1.88 (3H, s, CH_3-27), 1.88 (3H, m, CH_2-7 and H-9), 1.77 (1H, m, H-15b), 1.60 (1H, m, H-12a), 1.40 (3H, s, CH_3-21), 1.40 (1H, m, H-12b), 1.38 (1H, m, H-11b), 1.23 (3H, s, CH_3-19); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.1 (C, C-1), 171.0 (C, $COOCH_3$), 166.1 (C, C-26), 148.9 (C, C-24), 145.5 (CH, C-3), 135.1 (C, C-5), 127.7 (CH, C-2), 124.4 (CH, C-6), 121.8 (C, C-25), 83.4 (C, C-14), 81.2 (CH, C-22), 74.9 (C, C-20), 62.8 (CH_2, C-18), 50.6 (C, C-13), 50.2 (C, C-10), 49.2 (CH, C-17), 36.2 (CH, C-8), 35.9 (CH, C-9), 33.3 (CH_2, C-4), 31.9 (CH_2, C-12), 31.5 (CH_2, C-23), 27.4 (CH_2, C-15), 25.2 (CH_2, C-7), 22.2 (CH_2, C-11), 21.2 (CH_3, $COOCH_3$), 20.5 (CH_2, C-16), 20.5 (CH_3, C-21), 20.4 (CH_3, C-28), 18.8 (CH_3, C-19), 12.3 (CH_3, C-27); EIMS m/z (%) 434 $[M - AcOH - H_2O]^+$ (71), 416 (10), 387 (9), 363 (24), 343 (14), 327 (42), 309 (81), 265 (85), 264 (46), 223 (41), 171 (66), 169 (76), 125 (89), 43 (100).

Oxidation of Physacoztomatin (1). Compound **1** (102 mg) and QCC (131 mg) in anhydrous CH_2Cl_2 (10 mL) were stirred for 35 min at room temperature under nitrogen. Hexane (30 mL) was added, and the reaction mixture was filtered. The solvent was eliminated under reduced pressure and the residue submitted to preparative TLC (C_6H_6−EtOAc, 9:1) to afford 29 mg of **2** as white crystals (hexane), mp 127−133 °C; IR ($CHCl_3$) ν_{max} 3608, 2963, 2926, 2850, 1671, 1614, 1455, 1386, 1367, 1118, 1076, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 10.06 (1H, d, J = 8 Hz, H-15), 6.18 (1H, ddq, J = 8, 1.5, 1.5 Hz, H-14), 5.46 (1H, br s, H-7), 4.26 (1H, ddd, J = 8.5, 4.5, 4 Hz, H-12), 2.20 (3H, d, J = 1.5 Hz, CH_3-16), 2.07 (1H, br s, H-9), 2.00 (1H, br d, J = 17.5 Hz, H-6a), 1.88 (1H, dddd, J = 17.5, 12, 4, 2 Hz, H-6b), 1.82 (1H, dd, J = 13, 1.5 Hz, H-1a), 1.72 (3H, dd, J = 2, 1 Hz, CH_3-17), 1.54 (2H, m, CH_2-11), 1.52 (2H, m, CH_2-2), 1.42 (1H, ddd, J = 13, 3, 1.5 Hz, H-3a), 1.26 (1H, dd, J = 12, 5 Hz, H-5), 1.18 (1H, td, J = 13, 4 Hz, H-3b), 1.04 (1H, td, J = 13, 4.5 Hz, H-1b), 0.89 (3H, s, CH_3-19), 0.87 (3H, s, CH_3-18), 0.74 (3H, s, CH_3-20); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 191.4 (CH, C-15), 164.5 (C, C-13), 134.1 (C, C-8), 125.0 (CH, C-14), 123.5 (CH, C-7), 76.4 (CH, C-12), 50.4 (CH, C-9), 50.2 (CH, C-5), 42.2 (CH_2, C-3), 39.3 (CH_2, C-1), 36.4 (C, C-10), 33.8 (CH_2, C-11), 33.1 (CH_3, C-18), 33.0 (C C-4), 23.9 (CH_2, C-6), 22.5 (CH_3, C-17), 21.8 (CH_3, C-19), 18.7 (CH_2, C-2), 13.7 (CH_3, C-16), 13.6 (CH_3, C-20); EIMS m/z (%) 304 $[M]^+$ (1), 286 (5), 204 (40), 190 (12), 181 (14), 161 (8), 124 (39), 109 (100), 100 (75), 81 (69), 69 (24), 55 (19), 43 (14), 41 (22).

Crystal data of 2:[24] $C_{20}H_{32}O_2$, M_r 304.46, monoclinic, space group C2, a = 14.420(1) Å, α = 90.00°, b = 7.5903(7) Å, β = 97.056(3)°, c = 16.398(2) Å; γ = 90.00°, V = 1794.4(3) Å^3, Z = 4, D_c = 1.127 g cm^{-3}, $F(000)$ = 672; crystal dimensions 0.384 × 0.312 × 0.088 mm. Reflections collected 12 544, independent reflections 6392.

Formation of 3. 15-Dehydrophysacoztomatin (**2**, 6 mg) was treated with (*S*)-(+)-α-methoxy-α-trifluormethylphenylacetyl chloride (2.4 μL) and DMAP (1 mg) in anhydrous pyridine (0.3 mL). The mixture was stirred for 38 h, and then the pyridine was removed under reduced pressure. The residue was purified by VCC (hexane) to afford 3 mg of **3** as a colorless oil. A similar treatment of **2** (5 mg) with (*R*)-(−)-α-methoxy-α-trifluoromethylphenylacetyl chloride (2.3 μL) gave 2 mg of **3**: IR (film) ν_{max} 2923, 2851, 1671, 1624, 1559, 1511, 1450, 1388, 1366, 1261, 1227, 1210, 1149, 1085, 1048 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.22 (1H, d, J = 2 Hz, H-15), 6.13 (1H, d, J = 2 Hz, H-14), 5.41 (1H, br s, H-7), 2.65 (1H, d, J = 15 Hz, H-11a), 2.47 (1H, dd, J = 15, 9 Hz, H-11b), 2.42 (1H, br d, J = 9 Hz, H-9), 1.99 (1H, br d, J = 18 Hz, H-6a), 1.95 (3H, s, CH_3-16), 1.86 (1H, dddq, J = 18, 12, 2.5, 2.5 Hz, H-6b), 1.80 (1H, ddd, J = 13, 4.5, 3 Hz, H-1a), 1.53 (1H, m, H-2a), 1.48 (3H, br dd, J = 2.5, 1 Hz, CH_3-17), 1.47 (1H, m, H-2b), 1.41 (1H, ddd, J = 13, 3, 2 Hz, H-3a), 1.27 (1H, dd, J = 12, 4.5 Hz, H-5), 1.19 (1H, ddd, J = 13, 13, 4 Hz, H-3b), 1.11 (1H, ddd, J = 13, 13, 4 Hz, H-1b), 0.90 (3H, s, CH_3-19), 0.87 (3H, s, CH_3-18), 0.83 (3H, s, CH_3-20); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 151.6 (C, C-12), 139.2 (CH, C-15), 134.9 (C, C-8), 122.6 (CH, C-7), 113.0 (C, C-13), 113.0 (CH, C-14), 52.3 (CH, C-9), 50.1 (CH, C-5), 42.2 (CH_2, C-3), 39.2 (CH_2, C-1), 33.3 (CH_3, C-18), 33.0 (C C-4), 29.7 (C, C-10), 23.9 (CH_2, C-11), 23.8 (CH_2, C-6), 22.0 (CH_3, C-19), 21.8 (CH_3, C-17), 19.0 (CH_2, C-2), 13.7 (CH_3, C-20), 10.1 (CH_3, C-16); ESIMS m/z (%) 287 $[M + H]^+$ (100), 205 (4), 191 (19).

Saponification of Physacoztolide A (5). Compound **5** (50 mg) and K_2CO_3 (100 mg) in MeOH were stirred for 30 min at room temperature. After the reaction mixture was filtered, the solvent was eliminated using an air flux, the residue was suspended in H_2O, and the suspension was extracted with $CHCl_3$. The organic phase was dried over Na_2SO_4, and elimination of the solvent with an air flux afforded 26 mg of physacoztolide B (**6**).

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Supporting Information Available: ^1H NMR spectra of physacoztomatin (**1**) and physacoztolides A−E (**5**−**9**) are available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Martínez, M. *Anales del Instituto de Biología*; Universidad Nacional Autónoma de México, Serie Botánica, 1998; Vol. 69, pp 71−117.
(2) Ray, A. B.; Gupta, M. In *Progress in Chemistry of Organic Natural Products*; Hertz, W., Kirby, G. W., Moore, R. E., Steglich, W., Tamm, C., Eds.; Spring-Verlag: Austria, 1994; Vol. 63, pp 1−106.

(3) (a) Misico, R. I.; Song, L. L.; Veleiro, A. S.; Cirigliano, A. M.; Tettamanzi, M. C.; Burton, G.; Bonetto, G. M.; Nicotra, V. E.; Silva, G. L.; Gil, R. R.; Oberti, J. C.; Kinghorn, A. D.; Pezzuto, J. M. *J. Nat. Prod.* **2002**, *65*, 677−680. (b) Soares, M. B. P.; Bellintani, M. C.; Ribeiro, I. M.; Tomassini, T. C. B.; Ribeiro do Santos, R. *Eur. J. Pharmacol.* **2003**, *459*, 107−112. (c) Veras, M. L.; Bezerra, M. Z. B.; Braz-Filho, R.; Pessoa, O. D. L.; Carvalho, M. R.; Pessoa, C.; De Moraes, M. O.; Costa-Lotufo, L. V. *Planta Med.* **2004**, *70*, 551−555.

(4) *Atlas de las Plantas de la Medicina Tradicional Mexicana*; Argueta, V. A., Coordinador; Instituto Nacional Indigenista: México, 1994; Vol. I, p 543.

(5) (a) Maldonado, E.; Torres, F. R.; Martínez, M.; Pérez-Castorena, A. L. *Planta Med.* **2004**, *70*, 59−64. (b) Pérez-Castorena, A. L.; García, M.; Martínez, M.; Maldonado, E. *Biochem. Syst. Ecol.* **2004**, *32*, 1231−1234. (c) Maldonado, E.; Alvarado, V. E.; Torres, F. R.; Martínez, M.; Pérez-Castorena, A. L. *Planta Med.* **2005**, *71*, 548−553.

(6) Forster, P. G.; Ghisalberti, E. L.; Jefferies, P. R. *Phytochemistry* **1985**, *24*, 2991−2993.

(7) Francesca, F. C. L.; Castillo, M. *Phytochemistry* **1985**, *29*, 324−325.

(8) Seco, J. M.; Quiñoá, E.; Riguera, R. *Chem. Rev.* **2004**, *104*, 17−117.

(9) El-Gamal, A. A. H.; Chiu, E.-P.; Li, C.-H.; Cheng, S. Y.; Dai, C.-F.; Duh, C.-Y. *J. Nat. Prod.* **2005**, *68*, 1749−1753.

(10) Jefferies, P. R.; Payne, T. G. *Aust. J. Chem.* **1965**, *18*, 1441−1450.

(11) Lavie, D.; Bessalle, R.; Pestchanker, M. J.; Glottlieb, H. E.; Folow, F.; Giordana, O. S. *Phytochemistry* **1987**, *26*, 1791−1795.

(12) Kupchan, S. M.; Anderson, W. K.; Bollinger, P.; Doskotch, R. W.; Smith, R. M.; Saenz, R. J. A.; Schnoes, H. K.; Burlingame, A. L.; Smith, D. H. *J. Org. Chem.* **1969**, *34*, 3858−3866.

(13) Veleiro, A. S.; Cirigliano, A. M.; Oberti, J. C.; Burton, G. *J. Nat. Prod.* **1999**, *62*, 1010−1012.

(14) Kirson, I.; Gottlieb, H. E. *J. Chem. Res., Miniprint* **1990**, 4275−5293.

(15) Raffauf, R. F.; Shemluck, M. J.; Le Quesne, P. W. *J. Nat Prod.* **1991**, *54*, 1601−1606.

(16) Misico, R. I.; Gil, R. R.; Oberti, J. C.; Veleiro, A. S.; Burton, G. *J. Nat. Prod.* **2000**, *63*, 1329−1332.

(17) Veleiro, A. S.; Burton, G.; Gross, E. G. *Phytochemistry* **1985**, *24*, 2573−2575.

(18) *Dictionary of Natural Products*; Chapman & Hall, Chemical Database, 1994; Vol. 4, p 4530.

(19) Itokawa, H.; Suto, K.; Takeya, K. *Chem. Pharm. Bull.* **1981**, *29*, 254−256.

(20) Vidari, G.; Finzi, P. V.; De Bernarde, M. *Phytochemistry* **1971**, *10*, 3335−3339.

(21) Jurd, L. *J. Org. Chem.* **1962**, *27*, 1294−1297.

(22) Wahlberg, I.; Wallin, I.; Nordfors, K.; Nishida, T.; Enzell, C. R.; Reid, W. W. *Acta Chim. Scand. B* **1979**, *33*, 541−543.

(23) Erazo, S.; Zaldivar, M.; Delporte, C.; Backhouse, N.; Tapia, P.; Belmonte, E.; Monache, F. D.; Negrete, R. *Planta Med.* **2002**, *68*, 361−363.

(24) Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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