Triterpenes from Brazilian Medicinal Plant "Chuchuhuasi" (*Maytenus krukovii*)

Osamu Shirota, Toshihiko Tamemura, Hiroshi Morita, Koichi Takeya, and Hideji Itokawa*

Department of Pharmacognosy, School of Pharmacy, Tokyo University of Pharmacy & Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-03, Japan

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The isolation and structure elucidation of five novel triterpenes (**1**−**5**) from a South American medicinal plant "chuchuhuasi" (*Maytenus krukovii*) are described. The structures of these oleanane and ursane triterpenes, each containing an α,β-unsaturated ketone in the C ring, were elucidated by interpretation of their spectral data.

In continuing chemical studies on medicinal plants belonging to the genus *Maytenus* of the family Celastraceae,[1−11] which are widely used as folk medicines in South America,[12,13] we have previously examined the Paraguayan medicinal plant "cangorosa" (*Maytenus ilicifolia*),[1,2,5−7] the Peruvian "chuchuhuasi" (*M. ebenifolia*),[3,4] and the Brazilian "xuxuá" (*M. chuchuhuasca*).[8−11] Their constituents were determined to be oligo-nicotinated sesquiterpene polyesters,[5,7] sesquiterpene pyridine alkaloids,[3,4,6,8] quinoid and aromatic triterpenes,[2,9] and triterpene dimers.[1,10,11]

Herein, we report the result of a chemical study on the Brazilian species, *M. krukovii* A. C. Smith (local name "chuchuhuasi"), which is used for the treatment of skin cancer. By chromatographic purification of an extract of the bark, five novel triterpenes named krukovines A−E (**1**−**5**) were isolated. All of these structures have an α,β-unsaturated ketone system in the C ring and are triterpenoids based on either a 3-oxooleanane or a 3-oxoursane skeleton.

A CH_2Cl_2-soluble portion (27.6 g) obtained from the MeOH extract (250 g) of *M. krukovii* bark (1.3 kg) was subjected to Si gel column chromatography. The fractions eluted by 40% EtOAc in CH_2Cl_2 obtained were further separated by Si gel and ODS (octadecyl Si gel) medium-pressure liquid chromatography (MPLC) and HPLC to give five triterpenes named krukovines A (**1**; 0.000 84%), B (**2**; 0.00 26%), C (**3**; 0.000 85%), D (**4**; 0.000 96%), and E (**5**; 0.000 77%).

Krukovines A (**1**) and B (**2**) were obtained as colorless amorphous solids with the same molecular formula $C_{30}H_{46}O_3$, as confirmed by HRMS. Analysis of their ^{1}H-NMR (Table 1) and ^{13}C-NMR (Table 2) spectra, and MS spectral data permitted their initial assignment as triterpenoids. It was found that the chemical shifts of the NMR signals of both compounds, especially in the region δ_H 2.3−5.7 of the ^{1}H-NMR spectra and δ_C 65−220 of the ^{13}C-NMR spectra, were very similar, and significant differences between **1** and **2** were detected only in certain signals [δ_H 0.90 (s) and 0.92 (s) for **1**, and δ_H 0.81 (d, J = 6.4 Hz) and 0.95 (br s) for **2**]. Therefore, it was suggested that these two compounds had the same substituents at similar regions of their respective triterpene skeletons. The following characteristic groups of **1** and **2** were deduced: an α,β-unsaturated ketone system [δ_H 5.60 (1H, s), δ_C 128.2 (d), 169.9 (s), 199.3 (s), ν max ($CHCl_3$) 1655 cm^{-1}, and λ max (MeOH) 250 nm for **1**; δ_H 5.54 (1H, s), δ_C 130.4 (d), 164.2 (s), 198.9 (s), ν max ($CHCl_3$) 1657 cm^{-1}, and λ max (MeOH) 250 nm for **2**], a hydroxymethyl group [δ_H 3.23, 3.48 (each 1H, d, J = 10.9 Hz), δ_C 69.6 (t), and ν max ($CHCl_3$) 3627 cm^{-1} for **1**; δ_H 3.16, 3.45 (each 1H, d, J = 11.0 Hz), δ_C 69.7 (t), and ν max ($CHCl_3$) 3627 cm^{-1} for **2**], and also a six-membered-ring ketone [δ_C 217.1 (s) and ν max ($CHCl_3$) 1700 cm^{-1} for **1** and **2**]. By means of careful integration of the ^{1}H-NMR signals and analysis of the HMQC spectrum of **2**, it became clear that the signal at δ_H 0.95, which seemed to be a broadened signal of a primary methyl group at first glance, was a secondary methyl group overlapped with a coupled methine proton. Johns *et al.*[14] reported that in the ^{1}H-NMR spectrum of an urs-12-ene derivative a secondary methyl group at C-30 was observed as a complex signal, which resulted from the close proximity in chemical shifts of the methyl protons at C-30 and the methine proton at C-20, to which the former protons were strongly coupled. In the view of this observation, **2** was suggested to have an urs-12-ene skeleton, and **1** was assumed to have an olean-12-ene skeleton, with the α,β-unsaturated ketone system being in ring C of each triterpenoid. By considering the MS fragmentations at m/z 289 and 248 (Figure 2), each cleaving at the α,β-unsaturated ketone system in ring C, the hydroxymethyl group seemed to be located in rings D or E, and the six-membered-ring ketone was in ring A or B of the respective triterpene structures. These assumptions were confirmed by means of the HMBC and NOESY spectra of **1** and **2**. For **1**, the H-12 olefinic proton (δ_H 5.60) gave ^{1}H−^{13}C long-range correlations with the methine carbons C-9 (δ_C 61.1), C-14 (δ_C 43.6), and C-18 (δ_C 42.7); the H-9 proton (δ_H 2.43) with C-1 (δ_C 39.8), C-5 (δ_C 55.5), and C-14 (δ_C 43.6); the H-18 proton (δ_H 2.18) with C-28 (δ_C 69.6); and the H-1 proton (δ_H 2.94) with C-3 (δ_C 217.1), in the HMBC spectrum (Figure 1). Furthermore, NOE correlations between H-12 and H-26, H-12 and H-18, H-18 and H-30, H-18 and H-28, H-26 and H-28, H-26 and H-25, H-9 and H-5, and H-9 and H-27 in the NOESY spectrum confirmed the stereochemistry of **1**. Similar ^{1}H−^{13}C long range (Figure 1) and NOE correlations were observed for **2**, except for ring E. The assigned functionalities for ring E of **2** were confirmed by observed ^{1}H−^{13}C long-range correlations between H-18 and C-19, H-29 and C-20, and H-30 and C-20, also by NOE correlations between H-18 and H-29, and H-12 and H-29. These spectroscopic data corroborated the structures of krukovines A (**1**) and B (**2**)

* To whom correspondence should be addressed. Phone: +81-426-76-3007. FAX: +81-426-77-1436.

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Table 1. ^{1}H-NMR Data of Krukovines A−E (**1**−**5**)[a]

	compound				
proton	**1**	**2**	**3**	**4**	**5**
H-1β	2.94 1H, ddd, 4.1, 7.1, 13.6	2.90 1H, ddd, 4.1, 7.1, 13.6	3.03 1H, ddd, 3.0, 6.3, 13.4	2.98 1H, ddd, 2.9, 6.3, 13.2	2.97 1H, ddd, 4.1, 7.2, 13.6
H-2α	2.36 1H, ddd, 4.1, 6.5, 15.9	2.34 1H, ddd, 4.1, 6.5, 15.9	2.24 1H, ddd, 3.1, 4.8, 15.2	2.25 1H, ddd, 2.9, 4.7, 15.2	2.37 1H, ddd, 4.1, 6.6, 15.9
H-2β	2.62 1H, ddd, 7.1, 11.1, 15.9	2.63 1H, ddd, 7.1, 11.1, 15.9	2.87 1H, ddd, 6.3, 13.8, 15.2	2.87 1H, ddd, 6.3, 13.7, 15.2	2.63 1H, ddd, 7.2, 11.1, 15.9
H-6α			4.52 1H, br s 1H ddd 6.3, 13.8, 15.2	4.51 1H, br s	
H-9	2.43 1H, s	2.40 1H, s	2.45 1H s	2.44 1H, s	2.41 1H, s
H-12	5.60 1H, s	5.54 1H, s	5.65 1H, s	5.60 1H, s	5.60 1H, s
H-18	2.18 1H, br dd, 3.4, 13.4	1.59 1H, br d, 10.8	2.20 1H, br dd, 4.1, 13.8	1.62 1H, br d, 9.9	1.77 1H, dd, 2.0, 10.9
H_3-23	1.06 3H, s	1.05 3H, s	1.17 3H, s	1.17 3H, s	1.10 3H, s
H_3-24	1.10 3H, s	1.09 3H, s	1.43 3H, s	1.43 3H, s	1.07 3H, s
H_3-25	1.26 3H, s	1.28 3H, s	1.70 3H, s	1.73 3H, s	1.27 3H, s
H_3-26	1.14 3H, s	1.17 3H, s	1.48 3H, s	1.51 3H, s	1.21 3H, s
H_3-27	1.39 3H, s	1.32 3H, s	1.34 3H, s	1.27 3H, s	1.29 3H, s
H-28a	3.23 1H, d, 10.9	3.16 1H, d, 10.9	3.23 1H, d, 10.9	3.19 1H, d, 11.0	
H-28b	3.48 1H, d, 10.9	3.45 1H, d, 10.9	3.49 1H, d, 10.9	3.47 1H, d, 11.0	
H_3-29	0.90 3H, s	0.81 3H, d, 6.4	0.90 3H, s	0.82 3H, d, 6.4	0.85 3H, d, 6.5
H_3-30	0.92 3H, s	0.95 3H, br s	0.91 3H, s	0.96 3H, br s	0.96 3H, d, 6.2

[a] Measurements were performed in $CDCl_3$ at 400 MHz; the data shown chemical shifts (ppm), number of protons, multiplicity, and *J* values in Hz.

Table 2. ^{13}C-NMR Data of Krukovines A−E (**1**−**5**)[a]

	compound				
carbon	**1**	**2**	**3**	**4**	**5**
C-1	39.79 t	39.81 t	41.74 t	41.79 t	39.75 t
C-2	34.22 t	34.21 t	34.41 t	34.42 t	34.27 t
C-3	217.12 s	217.06 s	216.08 s	216.45 s	217.23 s
C-4	47.78 s	47.77 s	49.21 s	49.20 s	47.76 s
C-5	55.47 d	55.47 d	56.78 d	56.68 d	55.51 d
C-6	18.84 t	18.85 t	68.31 d	68.31 d	18.87 t
C-7	32.10 t	32.18 t	40.27 t	40.27 t	32.76 t
C-8	45.27 s	44.96 s	44.49 s	44.24 s	44.60 s
C-9	61.05 d	60.78 d	61.27 d	61.02 d	60.98 d
C-10	36.73 s	36.59 s	36.60 s	36.46 s	36.92 s
C-11	199.33 s	198.85 s	198.92 s	198.75 s	198.86 s
C-12	128.20 d	130.45 d	128.42 d	130.64 d	131.13 d
C-13	168.95 s	164.19 s	169.22 s	163.64 s	164.97 s
C-14	43.58 s	43.74 s	44.00 s	44.13 s	43.80 s
C-15	25.92 t	26.68 t	25.90 t	26.68 t	27.11 t
C-16	30.64 t	22.70 t	30.64 t	22.70 t	28.01 t
C-17	37.02 s	38.42 s	37.00 s	38.43 s	72.37 s
C-18	42.73 d	54.02 d	42.69 d	53.95 d	60.30 d
C-19	45.04 t	39.00 d	45.03 t	39.04 d	41.43 d
C-20	31.08 s	39.24 d	31.08 s	39.23 d	39.07 d
C-21	33.88 t	30.29 t	33.87 t	30.29 t	32.36 t
C-22	21.58 t	34.82 t	21.56 t	34.79 t	41.64 t
C-23	21.42 q	21.48 q	23.84 q	23.86 q	21.48 q
C-24	26.45 q	26.37 q	25.63 q	25.67 q	26.56 q
C-25	15.69 q	15.75 q	16.91 q	16.98 q	15.48 q
C-26	18.48 q	18.25 q	19.69 q	19.58 q	19.45 q
C-27	23.43 q	20.54 q	23.41 q	20.63 q	20.65 q
C-28	69.63 t	69.68 t	69.51 t	69.60 t	
C-29	23.33 q	17.36 q	23.43 q	17.34 q	17.37 q
C-30	32.91 q	21.09 q	32.91 q	21.09 q	20.50 q

[a] Measurements were performed in $CDCl_3$ at 100MHz, and assigned by HMQC and HMBC experiments.

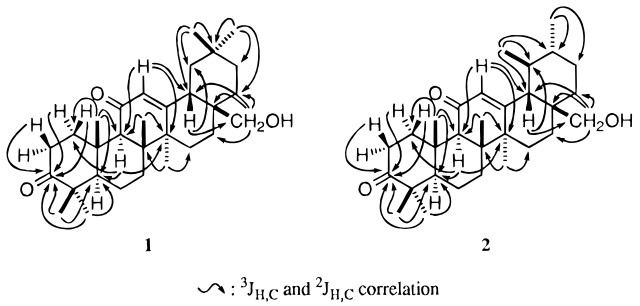


Figure 1. Fractional ^{1}H−^{13}C long-range correlations of krukovines A (**1**) and B (**2**).

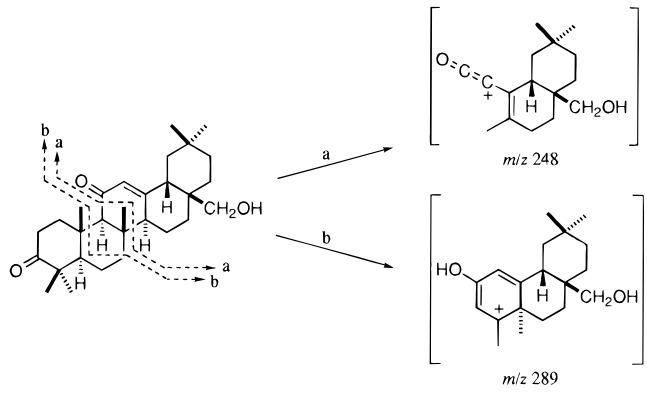


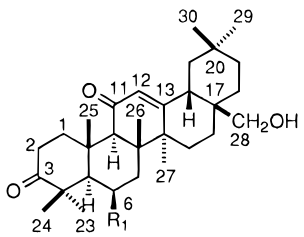
Figure 2. Mass spectral fragmentations of krukovine A (**1**).

as 28-hydroxyolean-12-ene-3,11-dione and 28-hydroxy-urs-12-ene-3,11-dione, respectively.

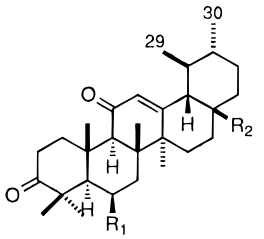
Krukovines C (**3**) and D (**4**), obtained as colorless crystals and an amorphous solid, respectively, and with the same molecular formula $C_{30}H_{46}O_4$, were in turn oleanane- and ursane-type triterpenoids having structures similar to **1** and **2**. Differences in the NMR spectra of **3** and **4** with respect to **1** and **2** (Tables 1 and 2) were the appearance of a broadened singlet proton signal around δ_H 4.5 and one methine carbon signal at δ_C 68.3 (d) instead of a methylene signal at δ_C 18.8 (t). These facts indicated the presence of a secondary hydroxyl group instead of a methylene on one of the rings. The MS spectra of **3** and **4** gave fragment ion peaks at both *m*/*z* 289 and 248, which were identical with both **1** and **2**, respectively, suggesting no modification in the rings C−E. Because the signals arising from ring A were not changed in the respective NMR spectra, the secondary hydroxyl group must be located in ring B of both **3** and **4**. The methine protons at δ_H 4.52 of **3** and δ_H 4.51 of **4** gave no ^{1}H−^{13}C long-range correlations in their HMBC spectra, however, these gave NOE correlations with the C-7 methylene protons (δ_H 1.67 and 1.90), the C-5 methine proton (δ_H 1.16), and the C-23 methyl protons (δ_H 1.17) in both cases. These facts were consistent with a β-hydroxyl group occurring at C-6. Therefore, the structures of krukovines C (**3**) and

D (**4**) were determined as 6β,28-dihydroxyolean-12-ene-3,11-dione and 6β,28-dihydroxyurs-12-ene-3,11-dione, respectively.

Krukovine E (**5**), a colorless amorphous solid possessing the molecular formula $C_{29}H_{44}O_3$, was assigned as an ursane-type triterpene in which the hydroxymethyl group at C-17 on **2** was substituted by a tertiary hydroxyl group, according to the NMR data obtained (Tables 1 and 2). The MS fragment ion peaks at *m/z* 275 and 234 also supported a C-17 substitution. The orientation of this tertiary hydroxyl group was assumed to be β, because of the observation of NOE correlations between H-20 and H-29, H-29 and H-18, H-18 and H-20, and H-19 and H-30 and no significant change of the ^{1}H- and the ^{13}C-NMR chemical shifts except for C-16, C-17, C-18, and C-22 with respect to compound **2**. Considering these spectroscopic observations, the structure of krukovine E (**5**) was determined as 17-hydroxy-28-norurs-12-ene-3,11-dione.



1: R_1 = H
3: R_1 = OH



2: R_1 = H, R_2 = CH_2OH
4: R_1 = OH, R_2 = CH_2OH
5: R_1 = H, R_2 = OH

Experimental Section

General Experimental Procedures. MPs were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. EIMS were obtained on a Hitachi M80 spectrometer, and HREIMS data were obtained on a VG Autospec spectrometer. UV and IR spectra were obtained with a Hitachi 557 spectrophotometer and on a Perkin-Elmer 1710 spectrophotometer, respectively. Medium-pressure liquid chromatography (MPLC) was performed with a CIG column system (22 mm i.d. × 300 mm, Kusano Scientific Co., Tokyo) packed with 10 μm Si gel or 20 μm ODS. HPLC was performed with an Inertsil PREP-ODS column (20 mm i.d. × 250 mm, GL Science Inc., Tokyo) packed with 10 μm ODS. TLC was conducted on precoated Kieselgel 60 F_{254} (Art. 5715; Merck) and the spots were detected by heating after spraying with 10% H_2SO_4. 1D and 2D ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker spectrometer (AM 400) or a Varian spectrometer (Unity Plus 400) at 300 K. NOESY experiments were made with a mixing time of 750 ms. The value of the delay to optimize one-bond correlation in HMQC spectra and suppress them in HMBC spectra was 150 ms, and the evolution delays for long-range couplings in HMBC spectra were set to 63 ms. The NMR coupling constants (*J*) are given in Hz.

Plant Material. The dark-brown stem bark of *M. krukovii* A. C. Smith (1.3 kg), known as "chuchuhuasi", was purchased at São Paulo, Brazil, in 1993. The botanical identification was carried out by Dr. William Antonio Rodrigues, Instituto Nacional de Pesquisas da Amazonia, São Paulo, Brazil. A voucher specimen has been deposited in the herbarium of Tokyo University of Pharmacy & Life Science.

Extraction and Isolation. The stem bark (1.3 kg) of *M. krukovii* was crushed and extracted with hot MeOH (12 L × 3) to give an extract (250 g), which was partitioned between CH_2Cl_2 and H_2O. The CH_2Cl_2-soluble fraction (27.6 g) was subjected to a Si gel column chromatography using a CH_2Cl_2−EtOAc gradient system (1:0−0:1), followed by a EtOAc−MeOH gradient system (9:1−0:1) to give 12 fractions (Fractions A−M). Fractions G and H were combined, then subjected to ODS MPLC with a MeOH−H_2O (8:2) solvent system, followed by Si gel MPLC with a *n*-hexane−EtOAc (6:4) solvent system to give **1**−**5**. These compounds were further purified by ODS HPLC with MeOH−H_2O (7:3) or MeCN−H_2O (6:4) solvent systems.

Krukovine A (28-hydroxyolean-12-ene-3,11-dione) (1) was obtained as a colorless amorphous solid (10.9 mg): mp 210−213 °C; $[\alpha]^{25}_D$ +98.2° (*c* 0.20, $CHCl_3$); UV (MeOH) λ max (log ϵ) 250 (3.95) nm; IR ($CHCl_3$) ν max 3627, 1700, 1655, 1617 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) data, see Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz) data, see Table 2; EIMS *m/z* [M]$^+$ 454 (55), 439 (15), 426 (22), 289 (54), 271 (26), 248 (98), 91 (100); HR-EIMS *m/z* [M]$^+$ 454.3459 (calcd for $C_{30}H_{46}O_3$, 454.3447).

Krukovine B (28-hydroxyurs-12-ene-3,11-dione) (2) was obtained as a colorless amorphous solid (34.3 mg): mp 239−241 °C; $[\alpha]^{25}_D$ +85.7° (*c* 0.65, $CHCl_3$); UV (MeOH) λ max (log ϵ) 250 (3.78) nm; IR ($CHCl_3$) ν max 3627, 1700, 1657, 1616 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) data, see Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz) data, see Table 2; EIMS *m/z* [M]$^+$ 454 (23), 439 (5), 420 (15), 289 (30), 248 (26), 234 (28), 91 (100); HREIMS *m/z* [M]$^+$ 454.3459 (calcd for $C_{30}H_{46}O_3$, 454.3447).

Krukovine C (6β,28-dihydroxyolean-12-ene-3,11-dione) (3) was obtained as colorless needles (crystallized from MeOH; 11.0 mg): mp 256−258 °C; $[\alpha]^{25}_D$ +46.4° (*c* 0.21, $CHCl_3$); UV (MeOH) λ max (log ϵ) 250 (3.95) nm; IR ($CHCl_3$) ν max 3685, 3620, 1700, 1656, 1618 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) data, see Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz) data, see Table 2; EIMS *m/z* [M]$^+$ 470 (17), 455 (10), 442 (12), 289 (12), 248 (46), 123 (100); HREIMS *m/z* [M]$^+$ 470.3381 (calcd for $C_{30}H_{46}O_4$, 470.3396).

Krukovine D (6β,28-dihydroxyurs-12-ene-3,11-dione) (4) was obtained as a colorless amorphous solid (12.5 mg): mp 258−261 °C; $[\alpha]^{25}_D$ +39.6° (*c* 0.23, $CHCl_3$); UV (MeOH) λ max (log ϵ) 250 (4.08) nm; IR ($CHCl_3$) ν max 3684, 3620, 1701, 1657, 1616 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) data, see Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz) data, see Table 2; EIMS *m/z* [M]$^+$ 470 (37), 455 (13), 442 (12), 289 (44), 248 (100); HREIMS *m/z* [M]$^+$ 470.3394 (calcd for $C_{30}H_{46}O_4$, 470.3396).

Krukovine E (17-hydroxy-28-norurs-12-ene-3,11-dione) (5) was obtained as a colorless amorphous solid (7.5 mg): mp 210−214 °C; $[\alpha]^{25}_D$ +44.0° (*c* 0.17, $CHCl_3$); UV (MeOH) λ max (log ϵ) 250 (4.03) nm; IR (KBr) ν max 3450, 1701, 1655, 1618 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) data, see Table 1; ^{13}C-NMR ($CDCl_3$, 100 MHz) data, see Table 2; EIMS *m/z* [M]$^+$ 440 (43), 422 (50), 368 (59), 275 (87), 234 (100); HREIMS *m/z* [M]$^+$ 440.3309 (calcd for $C_{30}H_{46}O_4$, 440.3290).

References and Notes

(1) Itokawa, H.; Shirota, O.; Morita, H.; Takeya, K.; Tomioka, N.; Itai, A. *Tetrahedron Lett.* **1990**, *31*, 6881−6882.
(2) Itokawa, H.; Shirota, O.; Morita, H.; Takeya, K.; Iitaka, Y. *Phytochemistry* **1991**, *30*, 3713−3716.
(3) Itokawa, H.; Shirota, O.; Morita, H.; Takeya, K. *Heterocycles* **1992**, *34*, 885−889.
(4) Itokawa, H.; Shirota, O.; Morita, H.; Takeya, K.; Iitaka, Y. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1247−1254.
(5) Itokawa, H.; Shirota, O.; Ichitsuka, K.; Morita, H.; Takeya, K. *J. Nat. Prod.* **1993**, *56*, 1479−1485.
(6) Shirota, O.; Morita, H.; Takeya, K.; Itokawa, H. *Heterocycles* **1994**, *38*, 383−389.
(7) Itokawa, H.; Shirota, O.; Ichitsuka, K.; Morita, H.; Takeya, K. *J. Nat. Prod.* **1994**, *57*, 460−470.
(8) Shirota, O.; Otsuka, A.; Morita, H.; Takeya, K.; Itokawa, H. *Heterocycles* **1994**, *38*, 2219−2229.
(9) Shirota, O.; Morita, H.; Takeya, K.; Itokawa, H. *J. Nat. Prod.* **1994**, *57*, 1675−1681.
(10) Shirota, O.; Morita, H.; Takeya, K.; Itokawa, H. *Chem. Lett.* **1995**, 101−102.
(11) Shirota, O.; Morita, H.; Takeya, K.; Itokawa, H. *Tetrahedron* **1995**, *51*, 1107−1120.
(12) Flores, A. F. In *Advances in Economic Botany, Vol.1, Ethnobotany in the Neotropics*; Prance, G. T., Kallunti, J. A., Eds.; The New York Botanical Garden: New York, 1984; pp 1−8.
(13) Gonzalez, G. J.; Monache, D. G.; Monache, D. F.; Marini-Bettolo, B. G. *J. Ethnopharmacol.* **1982**, *5*, 73−77.
(14) Johns, R. S.; Lamberton, A. J.; Morton, C. T.; Suares, H.; Willing, I. R. *Aust. J. Chem.* **1983**, *36*, 2537−2547.

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