New Geometric and Stereoisomeric Triterpene Dimers from *Maytenus chuchuhuasca*

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New geometric and stereoisomeric triterpene dimers, 7,8-dihydroisoxuxuarine Eα (2), xuxuarines Fβ (3), Gα (4) and Gβ (5), along with a known compound, scutidin αA (1), were isolated from the South American medicinal plant "xuxuá" (*Maytenus chuchuhuasca* RAYMOND-HAMET *et* COLAS). Their structures were determined on the basis of spectroscopic evidence including CD spectral studies.

Key words *Maytenus chuchuhuasca*; Celastraceae; xuxuá; triterpene dimer; xuxuarine

During the course of our studies on the medicinal plants belonging to the genus *Maytenus* (Celastraceae),[2] which are widely used as folk medicines in South America,[3,4] we previously reported fourteen novel geometric and stereoisomeric triterpene dimers, called xuxuarines and isoxuxuarines,[2j,k,n] from the Brazilian plant "xuxuá" (*Maytenus chuchuhuasca* RAYMOND-HAMET *et* COLAS).[4,5] These triterpene dimers were found to be composed of one quinoid type and one aromatic type of triterpene derived from pristimerin, tingenone and/or their congeners joined together by two ether linkages formed between the two A rings.[2j,k,n] Up to now, a total of 29 triterpene dimers of this class have been isolated and their structures have been determined by González *et al.*[6] and us.[2a,j,k,n] These triterpene dimers have been isolated from only five Celastraceae plants, *Rzedowskia tolantonguensis*,[6b] *Maytenus ilicifolia*,[2a,m] *M. umbellata*,[6c] *M. chuchuhuasca*,[2j,k,n] and *M. scutiodes*.[6a]

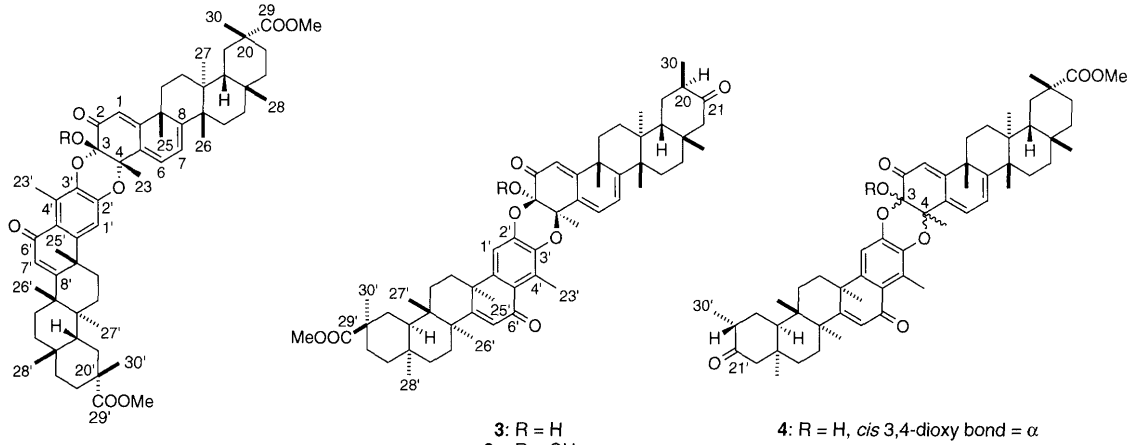
To obtain more triterpene dimers, we further investigated the remaining fractions containing minor triterpene dimers on *M. chuchuhuasca*, which resulted in the isolation of scutidin αA (**1**) and four new triterpene dimers, 7,8-dihydroisoxuxuarine Eα (**2**), xuxuarines Fβ (**3**), Gα (**4**) and Gβ (**5**).

In the present paper, we report the isolation and the structural elucidation of these five triterpene dimers containing geometrical and stereoisomerical isomers by several spectroscopic analyses.

Results and Discussion

From the methylene chloride soluble portion of a methanolic extract of *Maytenus chuchuhuasca* RAYMOND-HAMET *et* COLAS (bark; 5 kg), twelve fractions were derived by silica gel column chromatography using a CH_2Cl_2–EtOAc gradient system (1 : 0—0 : 1).[2k] Fraction IV was separated by silica gel medium-pressure liquid chromatography (MPLC), and the derived fractions were further purified by octadecyl silica gel (ODS) HPLC to obtain five triterpene dimers, scutidin αA (isoxuxuarine Eα; **1**: 0.0006%), 7,8-dihydroisoxuxuarine Eα (**2**: 0.0009%), xuxuarines Fβ (**3**: 0.0002%), Gα (**4**: 0.0003%) and Gβ (**5**: 0.0003%).

Compound **1** is a yellow amorphous solid with $[\alpha]_D$ +566.8° (c=0.41, $CHCl_3$). The FAB-MS spectrum of **1** gave an $[M+H]^+$ ion peak at m/z 943, and the molecular formula was determined to be $C_{60}H_{78}O_9$ based on the high resolution FAB-MS analysis (found m/z 943.5713 $[M+H]^+$, calcd 943.5724). The IR absorption at 3434 cm^{-1} was attributed to one free hydroxyl group. The NMR spectra revealed that **1** was a triterpene dimer



1: R = H
1a: R = CH_3
2: R = H, 7,8α-dihydro
2a: R = CH_3, 7,8α-dihydro

3: R = H
3a: R = CH_3

4: R = H, *cis* 3,4-dioxy bond = α
4a: R = CH_3, *cis* 3,4-dioxy bond = α
5: R = H, *cis* 3,4-dioxy bond = β
5a: R = CH_3, *cis* 3,4-dioxy bond = β

Chart 1

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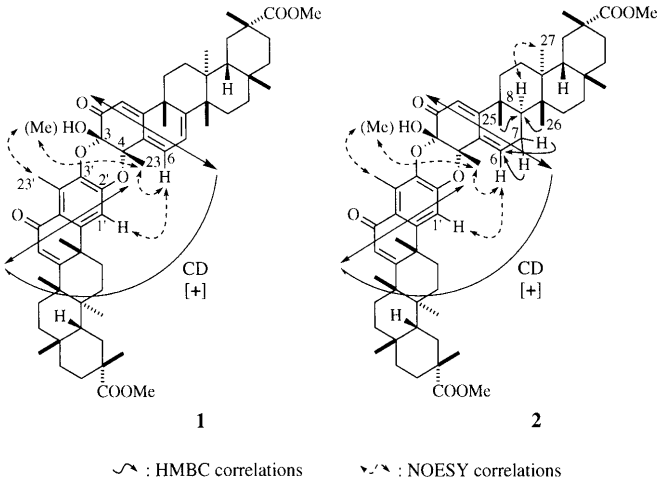

Fig. 1. HMBC and NOESY Correlations and CD Exciton Couplings of **1** and **2**

composed of two pristimerin type triterpenes, one in the quinoid form and the other in the aromatic form like xuxuarine Eβ,[2n] and most of the chemical shift values of **1** resembled those of scutidin αA, which had been isolated from *M. scutioides* by González *et al.*[6a] The CD spectrum of **1** showed a positive Cotton effect at 340 nm similar to that of the α type xuxuarines and scutidin αA.[2j,k,6a,7] The nuclear Overhauser enhancement and exchange spectroscopy (NOESY) spectrum of the 3-*O*-methyl derivative (**1a**), which showed nuclear Overhauser effect (NOE) correlations between the introduced *O*-methyl protons on C-3 and H-23′ and between the *O*-methyl protons and H-23, confirmed that the iso-type conjugation about the *cis* 3,4-dioxy bonds consisted of C-3—C-3′ and C-4—C-2′ linkages (Fig. 1). These data and the comparison with those described in the literature certified the structure of **1** to be scutidin αA (iso-type of xuxuarine Eα).[6a] The NMR signal assignments for **1**, which had not previously been reported, were based on the heteronuclear multiple quantum coherence (HMQC) and heteronuclear multiple bond correlation (HMBC) experiments shown in Tables 1 and 2.

Compound **2**, a pale yellow amorphous solid with $[\alpha]_D$ +309.1° (c=0.56, $CHCl_3$), exhibited an $[M+H]^+$ ion peak at m/z 945 in the FAB-MS, and the molecular formula, $C_{60}H_{80}O_9$, was established by HRFAB-MS. The ^{1}H- and ^{13}C-NMR spectra of **2** showed its components to be two pristimerin type triterpene units, one in the quinoid form and the other in the aromatic form, but different from those of **1** and xuxuarine Eβ.[2n] The breadth of the signal assignable to the H-6 methine proton at δ_H 6.32 and the disappearance of the H-7 methine proton signal from the low field region were observed in the ^{1}H-NMR spectrum. Correspondingly, the disappearance of two olefinic carbons and the appearance of a methine and a methylene carbon signal were observed in the ^{13}C-NMR spectrum. These spectral changes suggested that the conjugated ketone system on the A and B rings of the quinoid triterpene unit in the molecule was partially saturated between C-7 and C-8. The structures of the triterpene units, including the C-7—C-8 saturated part in the quinoid triterpene unit, were finally confirmed by the analyses of the HMQC and HMBC spectra (Fig. 1). In the HMBC spectrum, H-C long-range correlations were observed between H-25 (δ_H 1.07) and C-8 methine carbon (δ_C 41.6), between H-26 (δ_H 0.98) and C-8 and between methylene protons (H-7; δ_H 2.07 and 2.21, each m) and C-6 olefinic methine carbon (δ_C 24.2). Furthermore, NOESY spectrum of **2** showed a NOE correlation between H-8 (δ_H 1.80, m) and H-27 (δ_H 0.74), confirming the configuration of C-8 as shown in Fig. 1. In a previous paper,[2n] we reported the characteristic chemical shift differences between the α and β types of xuxuarines, which were stereochemical isomers for the *cis* 3,4-dioxy bonds orientation, and between the xuxuarines and iso-type of the xuxuarines, which were geometrical isomers for the *cis* 3,4-dioxy bonds conjugation. That is, the chemical shift differences were observed at the signals of C-3 and C-4 (δ_C 92 and 79 for the α type of xuxuarines; δ_C 91 and 77 for the β type of the xuxuarines) in the 3-hydroxy-4-methyl-3,4-dioxy part of the quinoid unit, the signals of C-23 and H-6 (δ_C 22 and δ_H 6.3 for the α type; δ_C 24 and δ_H 6.5 for the β type), and the methyl group signals assignable to H-23′ (δ_H 2.7 for the xuxuarines, 2.5 for the isoxuxuarines). The chemical shifts of **2** assignable to H-6, H-23′, C-4 and C-23 (δ_H 6.32, 2.52, δ_C 79.5 and 22.7) suggested its linkage pattern to be the isoxuxuarine type conjugation with α orientation about the *cis* 3,4-dioxy bonds. These observations were confirmed by the NOESY and CD spectra. The NOESY spectrum of the 3-*O*-methyl derivative (**2a**), which showed NOE correlations between the introduced *O*-methyl protons on C-3 and H-23′ and between the *O*-methyl protons and H-23, and the CD spectrum of **2**, which showed a positive first Cotton effect at 324 nm similar to that of the α type xuxuarines and **1**,[7] confirmed the iso-type conjugation with α orientation about the *cis* 3,4-dioxy bonds as shown in Fig. 1. Therefore, the structure **2** was assigned as 7,8-dihydroisoxuxuarine Eα.

Compounds **3**, **4** and **5**, each a yellow amorphous solid with $[\alpha]_D$ −212.5° (c=0.10, $CHCl_3$) for **3**, $[\alpha]_D$ +325.6° (c=0.16, $CHCl_3$) for **4** and $[\alpha]_D$ −330.6° (c=0.11, $CHCl_3$) for **5**, had an identical molecular formula, $C_{58}H_{74}O_8$, which was established by HRFAB-MS. The NMR spectral data, which were similar to those of cangorosin B,[2m] suggested that each consisted of two different types of triterpene units, tingenone and pristimerin, one in the quinoid form and the other in the aromatic form. The chemical shifts of H-6, H-23′, C-4 and C-23 suggested the linkage pattern of each compound to be a β orientation about the *cis* 3,4-dioxy bond for **3** and **5**, an α orientation for **4**, and all of them formed the xuxuarine-type conjugation; these observations were confirmed by rotating frame nuclear Overhauser effect spectroscopy (ROESY) and CD spectral studies. In the ROESY spectra, all of 3-*O*-methyl derivatives showed rotating frame nuclear Overhauser effect (ROE) correlations between the introduced *O*-methyl protons on C-3 and H-1′ and between H-23′ and H-6, and in the CD spectra, **3** and **5** showed a negative first Cotton effect at 400 nm, while **4** showed a positive first Cotton effect at 356 nm. The FAB-MS data enabled us to determine whether the pristimerin and the tingenone type triterpene were in the quinoid form or in

Table 1. Typical ^{1}H-NMR Chemical Shifts (ppm, Multiplicity, and J/Hz) for Compounds **1**—**5**[a]

Position	**1**	**2**	**3**	**4**	**5**
H-1	6.09 (d, 1.5)	5.97 (s)	6.11 (d, 1.7)	6.09 (d, 1.5)	6.08 (d, 1.5)
H-6	6.30 (dd, 1.5, 6.6)	6.32 (br s)	6.55 (dd, 1.7, 6.8)	6.25 (dd, 1.5, 6.5)	6.53 (dd, 1.5, 7.0)
H-7	5.95 (d, 6.6)	2.06 (m)	6.12 (d, 6.8)	5.95 (d, 6.5)	6.09 (d, 7.0)
		2.21 (m)			
H-19α	2.40 (d, 15.6)	2.34 (d, 13.0)		2.40 (d, 15.7)	2.39 (d, 15.8)
H-20			2.49 (m)		
H-22α			2.88 (d, 14.5)		
Me-23	1.57 (s)	1.47 (s)	1.60 (s)	1.59 (s)	1.59 (s)
Me-25	1.43 (s)	1.07 (s)	1.44 (s)	1.43 (s)	1.34(s)
Me-26	1.18 (s)	0.98 (s)	1.26 (s)	1.18 (s)	1.16 (s)
Me-27	0.54 (s)	0.75 (s)	0.97 (s)	0.55 (s)	0.53 (s)
Me-28	1.06 (s)	1.05 (s)	0.98 (s)	1.07 (s)	1.06 (s)
Me-30	1.16 (s)	1.17 (s)	1.00 (d, 6.2)	1.17 (s)	1.17 (s)
COOMe	3.58 (s)	3.64 (s)		3.60 (s)	3.59 (s)
H-1′	6.99 (s)	6.96 (s)	6.75 (s)	6.81 (s)	6.76 (s)
H-7′	6.22 (s)	6.22 (s)	6.22 (s)	6.28 (s)	6.25 (s)
H-19′α	2.45 (d, 15.6)	2.45 (d, 15.8)	2.40 (d, 15.7)		
H-20′				2.49 (m)	2.45 (m)
H-22′α				2.91 (d, 14.5)	2.89 (d, 14.5)
Me-23′	2.48 (s)	2.52 (s)	2.74 (s)	2.75 (s)	2.75 (s)
Me-25′	1.54 (s)	1.54 (s)	1.49 (s)	1.57 (s)	1.54 (s)
Me-26′	1.29 (s)	1.29 (s)	1.27 (s)	1.37 (s)	1.35 (s)
Me-27′	0.62 (s)	0.61 (s)	0.55 (s)	0.98 (s)	1.00 (s)
Me-28′	1.11 (s)	1.10 (s)	1.09 (s)	1.01 (s)	1.00 (s)
Me-30′	1.19 (s)	1.18 (s)	1.16 (s)	0.98 (d, 6.2)	0.96 (d, 6.4)
COOMe	3.58 (s)	3.55 (s)	3.49 (s)		

a) All measurements were made in $CDCl_3$ at 400 MHz, 300 K.

Table 2. ^{13}C-NMR Chemical Shifts (ppm and Multiplicity) for Compounds **1**—**5**[a]

Position	**1**		**2**		**3**		**4**		**5**	
	Quinoid	Aromatic	Quinoid	Aromatic	Quinoid	Aromatic	Quinoid	Aromatic	Quinoid	Aromatic
C-1	115.8 (d)	110.5 (d)	113.0 (d)	110.5 (d)	115.0 (d)	110.7 (d)	115.2 (d)	111.4 (d)	114.6 (d)	110.5 (d)
C-2	190.4 (s)	144.4 (s)	191.5 (s)	144.5 (s)	189.5 (s)	145.1 (s)	190.2 (s)	144.7 (s)	189.4 (s)	145.2 (s)
C-3	91.8 (s)	138.3 (s)	91.3 (s)	138.3 (s)	91.0 (s)	137.5 (s)	92.0 (s)	137.7 (s)	91.1 (s)	137.6 (s)
C-4	79.3 (s)	129.3 (s)	79.5 (s)	129.4 (s)	76.9[i] (s)	128.3 (s)	79.4 (s)	127.8 (s)	76.9[i] (s)	128.5 (s)
C-5	130.5 (s)	123.3 (s)	134.1 (s)	123.3 (s)	132.1 (s)	123.9 (s)	129.8 (s)	124.4 (s)	131.8 (s)	123.8 (s)
C-6	126.3 (d)	187.2 (s)	134.1 (d)	187.2 (s)	128.6 (d)	187.3 (s)	126.8 (d)	187.7 (s)	128.9 (d)	187.2 (s)
C-7	116.1 (d)	126.3 (d)	24.2 (t)	126.3 (d)	117.2 (d)	126.1 (d)	116.1 (d)	126.1 (d)	117.2 (d)	126.2 (d)
C-8	161.2 (s)	170.9 (s)	41.6 (d)	171.0 (s)	163.3 (s)	171.2 (s)	161.5 (s)	170.7 (s)	164.4 (s)	170.2 (s)
C-9	41.8 (s)	40.1 (s)	37.4 (s)	40.1[b] (s)	43.7 (s)	40.0 (s)	42.0 (s)	39.8 (s)	43.9 (s)	39.8 (s)
C-10	173.4 (s)	151.7 (s)	170.2 (s)	151.8 (s)	173.0 (s)	151.2 (s)	174.2 (s)	150.4 (s)	173.2 (s)	151.1 (s)
C-11	33.0 (t)	34.3 (t)	30.7 (t)	34.2 (t)	33.1 (t)	34.0 (t)	32.9 (t)	34.3 (t)	32.7 (t)	34.1 (t)
C-12	29.5 (t)	30.0 (t)	29.4 (t)	29.7[c] (t)	29.9 (t)	29.9 (t)	29.5 (t)	30.2 (t)	29.5 (t)	30.1 (t)
C-13	38.2 (s)	39.0 (s)	38.9 (s)	39.0 (s)	39.8 (s)	39.0 (s)	38.1 (s)	40.2 (s)	38.7 (s)	40.2 (s)
C-14	44.6[b] (s)	44.7[b] (s)	40.1[b] (s)	44.7 (s)	44.0 (s)	44.7 (s)	44.7 (s)	44.3 (s)	44.4[b] (s)	44.3[b] (s)
C-15	28.4 (t)	28.5 (t)	28.3 (t)	28.5 (t)	28.5[b] (t)	28.5[b] (t)	28.4 (t)	28.4 (t)	28.6 (t)	28.4 (t)
C-16	36.4[c] (t)	36.4[c] (t)	36.0 (t)	36.4 (t)	35.5 (t)	36.4 (t)	36.3 (t)	35.6 (t)	36.4 (t)	35.5 (t)
C-17	30.5 (s)	30.5 (s)	30.2 (s)	30.5 (s)	38.2 (s)	30.5 (s)	30.5 (s)	38.2 (s)	30.8 (s)	38.2 (s)
C-18	44.2 (d)	44.3 (d)	44.6 (d)	44.3 (d)	43.5 (d)	44.2 (d)	44.1 (d)	43.5 (d)	44.2 (d)	43.4 (d)
C-19	31.0[d] (t)	31.1[d] (t)	30.5 (t)	31.0 (t)	31.9 (t)	30.9 (t)	30.9 (t)	32.0 (t)	30.5 (t)	31.9 (t)
C-20	40.5 (s)	40.6 (s)	40.5 (s)	40.6 (s)	41.9 (d)	40.5 (s)	40.4 (s)	41.9 (d)	40.4 (s)	41.9 (d)
C-21	29.7[e] (t)	29.8[e] (t)	29.9[c] (t)	29.9[c] (t)	213.5 (s)	29.8 (t)	29.9 (t)	213.7 (s)	29.8 (t)	213.7 (s)
C-22	34.8 (t)	35.0 (t)	36.0 (t)	35.0 (t)	52.4 (t)	35.0 (t)	34.7 (t)	52.6 (t)	34.7 (t)	52.7 (t)
C-23	22.2 (q)	13.3 (q)	22.7 (q)	13.4 (q)	24.6 (q)	13.2 (q)	22.2 (q)	13.0 (q)	24.6 (q)	13.2 (q)
C-25	35.0 (q)	37.6 (q)	22.1 (q)	37.7 (q)	40.0 (q)	37.7 (q)	34.9 (q)	38.6 (q)	39.1 (q)	38.6 (q)
C-26	22.5 (q)	20.8 (q)	16.0 (q)	20.9 (q)	22.3 (q)	20.9 (q)	22.5 (q)	20.8 (q)	22.4 (q)	20.8 (q)
C-27	18.4 (q)	18.5 (q)	16.9 (q)	18.6 (q)	19.6 (q)	18.4 (q)	18.7 (q)	19.7 (q)	18.2 (q)	19.8 (q)
C-28	31.6[f] (q)	31.6[f] (q)	31.7 (q)	31.6 (q)	32.5 (q)	31.6 (q)	31.6 (q)	32.6 (q)	31.5 (q)	32.6 (q)
C-29	178.8 (s)	179.3 (s)	179.0 (s)	179.2 (s)		179.1 (s)	178.9 (s)		178.8 (s)	
C-30	32.8[g] (q)	33.0[g] (q)	32.3 (q)	32.9 (q)	15.1 (q)	32.9 (q)	32.7 (q)	15.0 (q)	32.8 (q)	15.1 (q)
COOMe	51.6[h] (q)	51.8[h] (q)	51.7 (q)	51.6 (q)		51.4 (q)	51.7 (q)		51.6 (q)	

a) All measurements were made in $CDCl_3$ at 100 MHz, 300 K. *b*)—*h*) Assignments for values in each compound bearing the same superscript can be reversed. *i*) Signals bearing this superscript were superimposed on solvent signals.

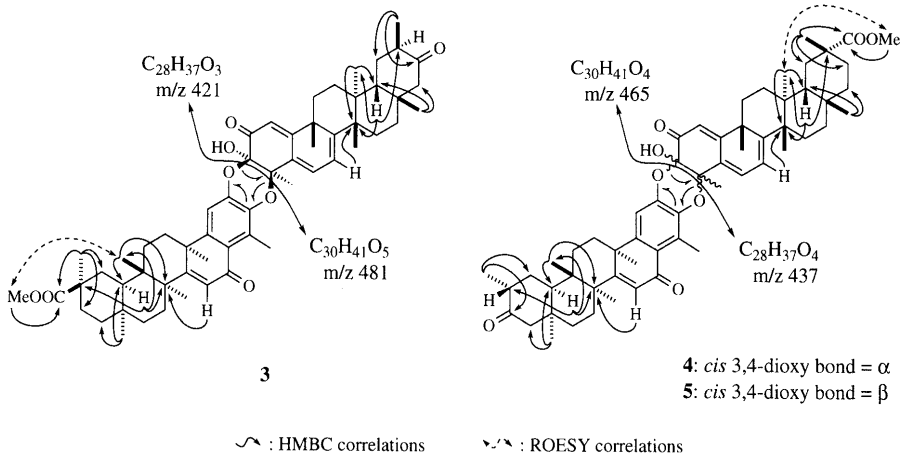

Fig. 2. MS Spectral Degradation Patterns and HMBC and ROESY Correlations of **3**—**5**

the aromatic form. The fragmentation ion peaks at *m/z* 421 and 481, which showed the tingenone-type triterpene to be in the quinoid form and the pristimerin type in the aromatic form, were observed in **3**, and those at *m/z* 437 and 465, which suggested that the tingenone-type triterpene was in the aromatic form and the pristimerin-type in the quinoid form were observed in **4** and **5** (Fig. 2). Moreover, careful analyses of their HMQC, HMBC and ROESY spectra enabled the signal assignments of each compound, including the E ring parts, as shown in Tables 1 and 2. Considering this spectroscopic evidence, structures **3**, **4** and **5** were assigned to xuxuarines Fβ, Gα and Gβ, respectively.

Experimental

Silica gel (Si gel) open column chromatography (cc) was performed on silica gel 60 (Merck). MPLC was performed with a CIG column system (22 mm i.d. × 300 mm or 22 mm i.d. × 100 mm; Kusano Scientific Co., Tokyo) packed with 10 μm or 5 μm Si gel and/or ODS. HPLC was performed with an Inertsil PREP-ODS column (5 mm i.d. × 250 mm for analysis, 20 mm i.d. × 250 mm for preparative; GL Science Inc., Tokyo) packed with 10 μm ODS. TLC was conducted on precoated silica gel 60 F_{254} (Merck) and/or RP-18 F_{254}s (Merck) and the spots were detected by heating after spraying with 10% H_2SO_4. Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter and the $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. FAB-MS and HRFAB-MS spectra were obtained on a JEOL AX-505H spectrometer. UV and IR spectra were taken with a Hitachi U-2000 spectrophotometer and a JASCO FT/IR-5300 spectrophotometer, respectively. 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 using Bruker or Varian standard pulse sequences. NMR coupling constants (*J*) are given in Hz. Phase sensitive NOESY experiments were conducted with a mixing time of 500 ms, and phase sensitive ROESY experiments were conducted with a mixing time of 300 ms. A 150 ms delay was used to optimize one-bond correlation in HMQC and HSQC spectra and suppress them in HMBC spectra, and the evolution delay for long-range couplings in HMBC spectra was set to 63 ms.

Plant Material Dark reddish brown stem bark of *Maytenus chuchuhuasca* Raymond-Hamet *et* Colas (5 kg), commonly known as "xuxuá", was purchased in São Paulo, Brazil in 1992. The botanical identification was made by Dr. William Antonio Rodrigues (Instituto Nacional de Pesquisas da Amazonia). A voucher specimen has been deposited in the herbarium of the Tokyo University of Pharmacy and Life Science.

Extraction and Isolation Crushed bark (5 kg) of *Maytenus chuchuhuasca* Raymond-Hamet *et* Colas was extracted with hot MeOH (54 l) to give a MeOH extract (1.5 kg), which was partitioned between CH_2Cl_2 and H_2O. The CH_2Cl_2-soluble fraction (155 g) was subjected to silica gel cc using a CH_2Cl_2–EtOAc gradient system (1:0—0:1) following MeOH to give twelve fractions. Fraction IV was separated by Si-MPLC using a *n*-hex–EtOAc gradient system (8:2—7:3), and the fractions derived were further purified by ODS-HPLC (85%, 95% or 100% CH_3CN) to obtain five triterpene dimers, scutidin αA (**1**: 0.0006%), 7,8-dihydroisoxuxuarine Eα (**2**: 0.0009%), xuxuarines Fβ (**3**: 0.0002%), Gα (**4**: 0.0003%) and Gβ (**5**: 0.0003%).

Scutidin αA (1) A yellow amorphous solid, mp 208—212 °C (lit. mp 193—194 °C), $[\alpha]_D$ +566.8° (*c*=0.41, $CHCl_3$), (lit. $[\alpha]_D$ +278.6 (*c*=4.1, $CHCl_3$)). UV λ_{max} (MeOH) nm (log ε): 252 (4.32), 299 (4.18), 381 (4.02), (lit. UV λ_{max} (MeOH) nm (log ε): 253.0 (4.12), 299.0 (4.01), 380.6 (3.80)). CD λ_{max} (MeOH) nm (Δε): 340 (+24.9), 302 (+25.7), 255 (−38.1), (lit. CD λ_{max} (MeOH) nm (Δε): 337.6 (+1.57), 299.0 (+1.53), 251.4 (−2.42)). IR (KBr) cm^{-1}: 3434, 2948, 1732, 1676, 1649, 1595, 1464, 1379, 1306, 1202, 1144, 1100, 1065, 1022, 872, (lit. IR (KBr) cm^{-1}: 3400, 3014, 2950, 1726, 1642, 1464, 1308, 1225, 1142, 750). ^{1}H-NMR ($CDCl_3$, 400 MHz): Table 1. ^{13}C-NMR ($CDCl_3$, 100 MHz): Table 2. FAB-MS *m/z* (rel. int. %): 943 (M^++H, 100), 479 (3), 464 (12), 450 (5). HRFAB-MS *m/z*: 943.5713 (Calcd for M^++H, $C_{60}H_{79}O_9$: 943.5724).

7,8-Dihydroisoxuxuarine Eα (2) A pale yellow amorphous solid, mp 218—222 °C, $[\alpha]_D$ +309.1° (*c*=0.56, $CHCl_3$). UV λ_{max} (MeOH) nm (log ε): 250 (4.25), 297 (4.32). CD λ_{max} (MeOH) nm (Δε), 324 (sh, +19.0), 294 (+29.6), 252 (−13.4). IR (KBr) cm^{-1}: 3463, 2946, 1732, 1684, 1649, 1595, 1464, 1381, 1306, 1204, 1140, 1028, 872. ^{1}H-NMR ($CDCl_3$, 400 MHz): Table 1. ^{13}C-NMR ($CDCl_3$, 100 MHz): Table 2. FAB-MS *m/z* (rel. int. %): 945 (M^++H, 100), 479 (7), 467 (10). HRFAB-MS *m/z*: 945.5886 (Calcd for M^++H, $C_{60}H_{81}O_9$: 945.5880).

Xuxuarine Fβ (3) A yellow amorphous solid, mp 215—219 °C, $[\alpha]_D$ −212.5° (*c*=0.10, $CHCl_3$). UV λ_{max} (MeOH) nm (log ε): 253 (4.21), 297 (4.09), 384 (4.02). CD λ_{max} (MeOH) nm (Δε): 400 (−4.6), 331 (+9.9), 261 (−34.9). IR (KBr) cm^{-1}: 3441, 2948, 1713, 1649, 1595, 1541, 1460, 1379, 1308, 1204, 1152, 1086, 1003, 872. ^{1}H-NMR ($CDCl_3$, 400 MHz): Table 1. ^{13}C-NMR ($CDCl_3$, 100 MHz): Table 2. FAB-MS *m/z* (rel. int. %): 899 (M^++H, 100), 481 (53), 421 (28). HRFAB-MS *m/z*: 899.5471 (Calcd for M^++H, $C_{58}H_{75}O_8$: 899.5462).

Xuxuarine Gα (4) A yellow amorphous solid, mp 219—223 °C, $[\alpha]_D$ +325.6° (*c*=0.16, $CHCl_3$). UV λ_{max} (MeOH) nm (log ε): 252 (4.26), 294 (4.13), 381 (3.99). CD λ_{max} (MeOH) nm (Δε): 356 (+14.9), 300 (+8.1), 246 (−24.0). IR (KBr) cm^{-1}: 3451, 2948, 1713, 1676, 1651, 1584, 1460, 1379, 1306, 1202, 1150, 1094, 1061, 1017, 872. ^{1}H-NMR ($CDCl_3$, 400 MHz): Table 1. ^{13}C-NMR ($CDCl_3$, 100 MHz): Table 2. FAB-MS *m/z* (rel. int. %): 899 (M^++H, 100), 465 (12), 437 (18). HRFAB-MS *m/z*: 899.5465 (Calcd for M^++H, $C_{58}H_{75}O_8$: 899.5462).

Xuxuarine Gβ (5) A yellow amorphous solid, mp 216—220 °C, $[\alpha]_D$ −330.6° (*c*=0.11, $CHCl_3$). UV λ_{max} (MeOH) nm (log ε): 252 (4.22), 298 (4.08), 384 (4.02). CD λ_{max} (MeOH) nm (Δε): 400 (−6.1), 333 (+7.9), 261 (−36.5). IR (KBr) cm^{-1}: 3443, 2946, 1711, 1651, 1458, 1379, 1306, 1204, 1154, 1094, 1017, 843. ^{1}H-NMR ($CDCl_3$, 400 MHz): Table 1. ^{13}C-NMR ($CDCl_3$, 100 MHz): Table 2. FAB-MS *m/z* (rel. int. %): 899 (M^++H, 100), 465 (40), 437 (41). HRFAB-MS *m/z*: 899.5480 (Calcd for M^++H, $C_{58}H_{75}O_8$: 899.5462).

Preparation of Methyl Derivatives Each compound (5—10 mg) was

dissolved in 0.5 ml of CH_3CN–MeOH (9 : 1) and treated with 2 drops of TMS–CHN_2 (2.0 M, *n*-hexane solution) and 2 drops of *N,N*-diisopropylethylamine for 6—18 h at room temperature.[8] The reaction mixture was partitioned between CH_2Cl_2 and H_2O, and the organic layer was concentrated. Then, the residue was purified by HPLC eluted with 97% or 100% MeOH to give each methyl derivative (60—80% yield).

3-*O*-Methyl Scutidin αA (**1a**): A yellow amorphous solid. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.97 (1H, br s), 6.23 (1H, s), 6.21 (1H, dd, J=1.7, 6.6 Hz), 5.95 (1H, d, J=1.7 Hz), 5.90 (1H, d, J=6.6 Hz), 3.62 (3H, s), 3.58 (3H, s), 3.57 (3H, s), 2.58 (3H, s), 2.45 (1H, d, J=15.6 Hz), 2.40 (1H, d, J=15.9 Hz), 1.59 (3H, s), 1.55 (3H, s), 1.39 (3H, s), 1.30 (3H, s), 1.19 (3H, s), 1.17 (3H, s), 1.16 (3H, s), 1.11 (3H, s), 1.05 (3H, s), 0.62 (3H, s), 0.54 (3H, s). FAB-MS *m/z* (rel. int. %): 957 (M^++H, 55), 479 (7), 450 (9).

3-*O*-Methyl 7,8-Dihydroisoxuxuarine Eα (**2a**): A pale yellow amorphous solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.94 (1H, s), 6.23 (1H, s), 6.23 (1H, br s), 5.83 (1H, s), 3.64 (3H, s), 3.59 (3H, s), 3.54 (3H, s), 2.62 (3H, s), 2.45 (1H, d, J=15.5 Hz), 2.34 (1H, d, J=12.3 Hz), 1.54 (3H, s), 1.49 (3H, s), 1.29 (3H, s), 1.18 (3H, s), 1.17 (3H, s), 1.11 (3H, s), 1.05 (3H, s), 1.04 (3H, s), 0.96 (3H, s), 0.74 (3H, s), 0.61 (3H, s). FAB-MS *m/z* (rel. int. %): 959 (M^++H, 100), 481 (7), 452 (25).

3-*O*-Methyl Xuxuarine Fβ (**3a**): A yellow amorphous solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.03 (1H, br s), 6.55 (1H, br d, J=6.6 Hz), 6.22 (1H, s), 6.09 (1H, d, J=6.6 Hz), 5.88 (1H, s), 3.54 (3H×2, s), 2.91 (1H, d, J=14.5 Hz), 2.51 (1H, m), 2.51 (3H, br s), 2.44 (1H, d, J=15.8 Hz), 1.58 (3H, s), 1.53 (3H, s), 1.49 (3H, s), 1.29 (3H×2, s), 1.18 (3H, s), 1.10 (3H, s), 1.07 (3H, s), 1.01 (3H, d, J=6.2 Hz), 1.00 (3H, s), 0.56 (3H, s).

3-*O*-Methyl Xuxuarine Gα (**4a**): A yellow amorphous solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.91 (1H, s), 6.29 (1H, s), 6.13 (1H, dd, J=1.5, 6.6 Hz), 5.95 (1H, d, J=1.5 Hz), 5.89 (1H, d, J=6.6 Hz), 3.65 (3H, s), 3.60 (3H, s), 2.91 (1H, d, J=14.3 Hz), 2.73 (3H, s), 2.49 (1H, m), 2.40 (1H, d, J=15.7 Hz), 1.60 (3H, s), 1.58 (3H, s), 1.39 (3H, s), 1.38 (3H, s), 1.17 (3H×2, s), 1.06 (3H, s), 1.03 (3H, s), 1.01 (3H, s), 0.97 (3H, d, J=6.4 Hz), 0.54 (3H, s).

3-*O*-Methyl Xuxuarine Gβ (**5a**): A yellow amorphous solid. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.02 (1H, br s), 6.51 (1H, br d, J=6.8 Hz), 6.25 (1H, s), 6.05 (1H, d, J=6.8 Hz), 5.86 (1H, s), 3.60 (3H, s), 3.54 (3H, br s), 2.91 (1H, d, J=14.4 Hz), 2.53 (3H, br s), 2.49 (1H, m), 2.42 (1H, d, J=16.4 Hz), 1.58 (3H, s), 1.57 (3H, s), 1.41 (3H, br s), 1.37 (3H, s), 1.20 (3H, s), 1.18 (3H, s), 1.08 (3H, s), 1.01 (3H, s), 1.00 (3H, s), 1.00 (3H, d, J=6.4 Hz), 0.61 (3H, s).

References and Notes

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