Diterpenes from *Xylopia langsdorffiana*

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The phytochemical investigation of *Xylopia langsdorffiana* A.ST.-HIL. & TUL. led to the isolation of eight diterpenes, *i.e.*, of the four new compounds (5β,7β,8α,9β,10α,12α)-atisane-7,16-diol 7-acetate (**1**), named xylodiol 7-acetate, (5β,8α,9β,10α,12α)-16-hydroxyatisan-7-one (**2**), named xylopinone, (3α,12*Z*)-3-hydroxy-*ent*-labda-8(20),12,14-trien-18-oic acid (**3**), named labdorffianic acid A, and 8,20-epoxy-13-hydroxy-*ent*-labd-14-en-18-oic acid (**4**), named labdorffianic acid B, and of the four known compounds **5**–**8**, *i.e.*, *ent*-kauran-16-ol, *ent*-kaur-16-en-19-oic acid, *ent*-kaur-16-en-19-ol, and *ent*-trachyloban-18-oic acid. The structures were established by IR, HR-ESI-MS, and NMR data analysis with the aid of 2D techniques.

Introduction. – The Annonaceae family comprises *ca.* 2′300 species, which are distributed across approximately 130 genera [1]. *Xylopia* is composed of 160 species, of which various are used in folk medicine for rheumatism [2] and as antimicrobial agents [3]. Previous studies with this genus have reported isolations of kaurane diterpenes [4][5], labdanes [6], trachylobanes [7], atisanes [8], and dimeric diterpenes [9–11].

Xylopia langsdorffiana A.ST.-HIL. & TUL. is a 5–7-m tall tree popularly known in northeastern Brazil as 'pimenteira da terra' [3]. Isolations from this species include alkaloids [12], labdane diterpenes [13], atisane, and trachylobane [14]. Labdane and trachylobane diterpenes have demonstrated cytotoxic activity towards different cell lines [15–17]. Atisane diterpenes exhibit cytotoxic [18] and anti-inflammatory activity [19]. In this paper, we report the isolation from *X. langsdorffiana* and structure determination of eight diterpenes, *i.e.*, of the four new compounds: (5β,7β,8α,9β,10α,12α)-atisane-7,16-diol 7-acetate, named xylodiol acetate (**1**), (5β,8α,9β,10α,12α)-16-hydroxyatisan-7-one, named xylopinone (**2**), (3α,12*Z*)-3-hydroxy-*ent*-labda-8(20),12,14-trien-18-oic acid, named labdorffianic acid A (**3**), and 8,20-epoxy-13-hydroxy-*ent*-labd-14-en-18-oic acid, named labdorffianic acid B (**4**), and of the four known compounds *ent*-kauran-16-ol (**5**), *ent*-kaur-16-en-19-oic acid (**6**), *ent*-kaur-16-en-19-ol (**7**), and *ent*-trachyloban-18-oic acid (**8**) (*Fig.*).

Results and Discussion. – Compound **1** was isolated as optically active colorless crystals. The HR-ESI-MS showed the molecular ion peak at *m*/*z* 371.2553 ($[M+Na]^+$), corresponding to the molecular formula $C_{22}H_{36}NaO_3$. The IR absorptions at 3650 and 1735 cm^{-1} were related to the OH and ester carbonyl group, respectively. In the

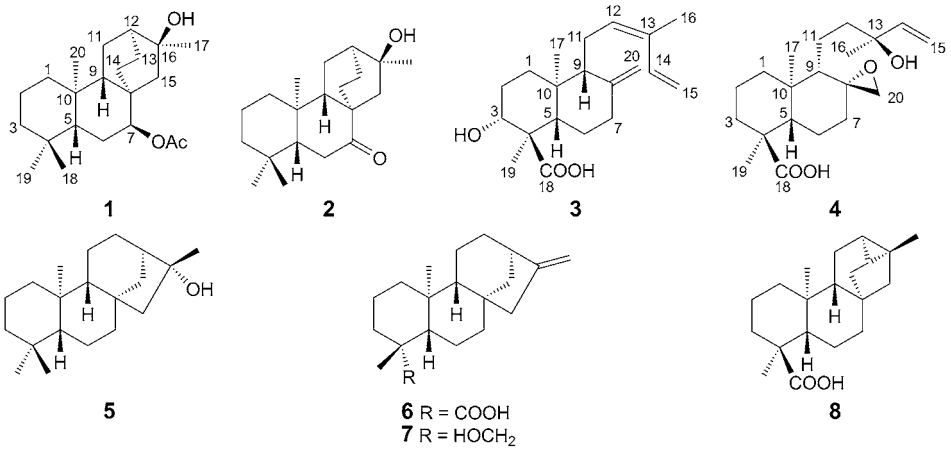

Figure. *Diterpenes* **1**–**8**, *isolated from the roots and fruits of* X. langsdorffiana

^{1}H-NMR spectrum (*Table 1*), an envelope of signals was observed in the region δ(H) 0.75–2.0 with resolved and unresolved multiplicities. Also five *s* were present at δ(H) 1.26, 0.75, 0.77, 0.94, and 2.0, the first one arising from a Me group at an oxygenated quaternary C-atom, and the last one being characteristic of an AcO group. Comparing the ^{1}H- and ^{13}C-NMR data of **1** (*Table 1*) with those of *xylodiol* (=(5β,7β,8α,9β,10α,12α)-atisane-7,16-diol) [13], it was possible to identify it as its acetylated derivative (5β,7β,8α,9β,10α,12α)-atisane-7,16-diol 7-acetate whose trivial name was given as xylodiol 7-acetate (**1**). The signal at δ(C) 72.0 was attributed to C(16), a characterictic signal of diterpenes of this type, which differed from the C(16) signal of kaurane-type diterpenes at δ(C) 77.6 [20]. The signals at δ(C) 76.2, 170.5, and 21.2 confirmed the presence of an AcO group. The chemical shifts at δ(C) 48.1 (CH), 46.8 (CH), and 50.4 (CH_2) compared to those of xylodiol (isolated from the leaves of *X. langsdorffiana* [13]) inferred the location of the AcO group at C(7), and allowed to assign these chemical shifts to C(5), C(9), and C(15), respectively. In the ^{1}H,^{13}C-HMQC spectrum, we observed direct correlations of δ(H) 1.26, 0.75, 0.77, 0.94, and 2.0 with δ(C) 30.5, 33.0, 21.4, 13.4, and 21.2, respectively, which were assigned to Me(17), Me(18), Me(19), Me(20), and *Me*CO, respectively. We also observed correlations of δ(H) 1.30, 4.6, 1.59, and 1.52 with δ(C) 48.1, 76.2, 46.8, and 37.8, respectively, which were assigned to CH(5), CH(7), CH(9), and CH(12), respectively. In the ^{1}H,^{13}C-gHMBC spectrum and its expansions, we noted the correlations δ(H) 4.6 (H–C(7))/δ(C) 48.1 (C(5)) and 46.8 (C(9)) confirming the insertion of the AcO group at C(7), besides the correlations δ(H) 0.75 (Me(18))/δ(C) 42.0 (C(3)), 32.4 (C(4)), 48.1 (C(5)), and 21.4 (C(19)), and δ(H) 1.26 (Me(17))/δ(C) 50.4 (C(15)) and 37.8 (C(12)). In the ^{1}H,^{1}H-gCOSY plot, we observed correlations of δ(H) 1.30 (H–C(5)) with δ(H) 1.58 which was assigned to H–C(6), and of δ(H) 1.59 (H–C(9)) with δ(H) 2.0 which was assigned to H–C(11). The ^{1}H,^{1}H-NOESY plot showed the correlations δ(H) 0.77 (Me(19))/δ(H) 0.94 (Me(20)) and δ(H) 0.94 (Me(20))/δ(H) 4.6 (H–C(7)), determining the relative configuraion of the stereogenic center at C(7). After analyis of all 1D

Table 1. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$; 500 and 125 MHz, resp.) *of Compounds* **1** *and* **2**. δ in ppm, J in Hz.

Position	**1**				**2**				
	δ(H)	δ(C)	HMBC	COSY	δ(H)	δ(C)	HMBC	COSY	NOESY
CH_2(1)	0.85 (*m*), 1.52 (*m*)	39.1		H–C(1)	1.63 (*m*), 0.85 (*m*)	38.7	C(10), C(20)	H–C(2)	
CH_2(2)	1.40, 1.58 (2*m*)	18.0			1.41 (*m*)	17.8			
CH_2(3)	1.17 (*m*), 1.40 (*m*)	42.0		H–C(3)	1.41 (*m*), 1.18 (*m*)	41.7			
C(4)	–	32.4			–	33.1			
H–C(5)	1.30 (*m*)	48.1	C(4), C(19)	H–C(6)	1.26 (*m*)	53.2			
CH_2(6)	1.58 (*m*), 1.66 (*m*)	24.0			2.36 (*dd*, J = 29, 15, H_{ax}), 2.31 (*dd*, J = 3, 16, H_{eq})	36.9	C(7), C(5), C(10)	H–C(5)	
H–C(7) or C(7)	4.6 (br. *s*)	76.2	C(5), C(9)	H–C(6)	–	215.9			
C(8)	–	37.9			–	47.2			
H–C(9)	1.59 (*m*)	46.8		H–C(11)	1.63 (*m*)	50.6	C(11), C(14), C(12), C(20)	H–C(11)	H–C(9)
C(10)	–	37.6			–	37.2			
CH_2(11)	2.0 (*m*)	22.5	C(8)	H–C(11)	1.23 (*m*)	22.9			
H–C(12)	1.52 (*m*)	37.8			1.61 (*m*)	37.2			
CH_2(13)	1.51 (*m*)	23.4			1.61 (*m*), 1.56 (*m*)	23.2		H–C(14)	
CH_2(14)	0.98 (*m*), 1.70 (*m*)	26.5		H–C(14)	1.84 (*m*), 1.10 (*m*)	26.7	C(16), C(9), C(8), C(14)	H–C(14)	Me(20)
CH_2(15)	1.17 (*m*), 1.59 (*m*)	50.4	C(9), C(17), C(14)	H–C(15)	1.93 (*d*, J = 14, H_{ax}), 1.41 (*d*, J = 3, H_{eq})	48.6		H–C(15)	
C(16)	–	72.0			–	71.7			
Me(17)	1.26 (*s*)	30.5	C(15), C(12)		1.29 (*s*)	30.1	C(16), C(15), C(12)		H_{ax}–C(15)
Me(18)	0.75 (*s*)	33.0	C(3), C(4), C(5), C(19)		0.81 (*s*)	32.6			H_{ax}–C(6)
Me(19)	0.77 (*s*)	21.4			0.81 (*s*)	20.9	C(5), C(3), C(4), C(18)		H–C(5)
Me(20)	0.94 (*s*)	13.4	C(1), C(5), C(9), C(10)		1.07 (*s*)	13.4	C(5), C(9), C(1), C(10)		H_{ax}–C(6)
AcO	2.0 (*s*)	170.5, 21.2							

and 2D NMR data, the structure of **1** was confirmed as (5β,7β,8α,9β,10α,12α)-atisane-7,16-diol 7-acetate (= xylodiol 7-acetate) which is the first report of this substance in the literature.

Compound **2** was isolated as optically active colorless crystals. The HR-ESI-MS showed the molecular-ion peak at *m/z* 305.2480 ($[M+H]^+$), corresponding to the molecular formula $C_{20}H_{36}O_3$. The IR spectrum in (KBr) showed absorptions at 3448 and 1678 cm^{-1}, characteristic of an OH and a keto C=O group, respectively. In the ^{13}C-NMR (APT) spectrum (*Table 1*), we observed the presence of 19 signals corresponding to 20 C-atoms. Of these, five were attributed to quaternary C-atoms and three to CH, eight to CH_2, and four to Me groups. The signals at δ(C) 53.2 (C(5)), 50.6 (C(9)), and 37.2 (C(10)), compared with those of **1** also suggested the presence of a tetracyclic C-atom skeleton of the atisane type. The signal at δ(C) 215.9 confirmed the presence of a keto C=O, and comparison with the ^{13}C-NMR data of **1** and xylodiol, suggested the position of this C=O group at C(7). In the ^{1}H-NMR spectrum (*Table 1*), an envelope of signal was observed in the region δ(H) 0.75–2.36 with resolved and unresolved multiplicities. Four *s* were present at δ(H) 1.29, 0.81, 0.81, and 1.07, the first one arising from a Me group at an oxygenated quaternary C-atom. The two *dd* at δ(H) 2.36 and 2.31 were assigned to H_{ax}–C(6) and H_{eq}–C(6), respectively. Comparing the ^{1}H- and ^{13}C-NMR data of **2** to those of **1** and xylodiol [13], it was possible to identify **2** as (5β,8α,9β,10α,12α)-16-hydroxyatisan-7-one, which was assigned the trivial name xylopinone. The ^{1}H,^{13}C-gHMQC spectrum showed the direct correlations of δ(H) 1.29, 0.81, 0.81, and 1.07 with δ(C) 30.1, 32.6, 20.9, and 13.4, respectively, which were assigned to Me(17), Me(18), Me(19), and Me(20), respectively. We also observed correlations of δ(H) 1.26, 1.63, 1.61 with δ(C) 53.2, 50.6, and 37.2, respectively, which were assigned to C(5), C(9), and C(12), respectively. The ^{1}H,^{13}C-HMBC spectrum and its expansions exhibited the correlation at δ(H) 0.81 (Me(19))/δ(C) 53.2 (C(5)). In the COSY plot, there was a correlation δ(H) 1.26 (H–C(5))/δ(H) 2.36 (1 H–C(6)). Returning to the HMBC, the cross-peaks δ(H) 2.36 (H–C(6))/δ(C) 215.9 (C(7)), δ(H) 1.07 (Me(20))/δ(C) 53.2 (C(5)), 50.6 (C(9)), 38.7 (C(1)), and 37.2 (C(10)), and δ(H) 1.93 (H_{ax}–C(15))/δ(C) 71.7 (C(16)), 50.6 (C(9)), 47.2 (C(8)), and 26.7 (C(14)) were observed. The ^{1}H,^{1}H-NOESY plot revealed the correlations δ(H) 1.93 (H_{ax}–C(15))/1.07 (Me(20)) and 2.36 (H_{ax}–C(6)). After analyis of all 1D- and 2D NMR data, the structure of **2** was confirmed as (5β,8α,9β,10α,12α)-16-hydroxyatisan-7-one (= xylopinone). Which is the first report of this substance.

Compound **3** was isolated as an optically active colorless oil. The HR-ESI-MS showed the molecular-ion peak at *m/z* 353.2113 ($[M+Cl]^-$), consistent with the molecular formula $C_{20}H_{30}O_3$. The IR spectrum showed absorptions at 3650 (OH) and 1690 cm^{-1} (COOH). In the ^{13}C-NMR spectrum (*Table 2*), we observed the presence of 20 C-atoms, *i.e.*, five quaternary C-atoms and five CH, seven CH_2, and three Me groups. The signals at δ(C) 49.9 and 56.9 were characteristic of labdane diterpene C-atoms C(5) and C(9), respectively, with a C=C bond between C(8) and C(20) which resonated at δ(C) 147.1 and 108.7. The signals at δ(C) 14.7, 10.5, and 182.1 were assigned to Me(17), Me(19), and C(18), respectively. These data corroborated the axial *cis* position of me(17) and Me(19). The Me(19) was more protected (δ(C) 10.5) suffering a γ-effect of an OH group at C(3). The chemical shift of the Me group at δ(C) 19.7 was assigned to Me(16), consistent with (12*Z*) configuration. In the ^{1}H-NMR spectrum (*Table 2*) and

Table 2. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$; 500 and 125 MHz, resp.) *of Compounds* **3** *and* **4**. δ in ppm, J in Hz.

Position	**3**				**4**		
	δ(H)	δ(C)	HMBC	COSY	δ(H)	δ(C)	HMBC
CH_2(1)	1.8 (*m*, H_{ax}), 1.3 (*m*, H_{eq})	36.7		H–C(3)	1.70 (*m*)	37.9	
CH_2(2)	1.7 (*m*, H_{ax}), 1.6 (*m*, H_{eq})	27.1			1.58 (*m*)	17.5	
H–C(3) or CH_2(3)	4.0 (*dd*, $^{1}J = 4.4$, $^{2}J = 12.0$)	74.5	C(19)	H–C(2)	1.59 (*m*)	36.9	
C(4)		53.6				47.1	
H–C(5)	1.8 (*m*)	49.9	C(4), C(10), C(6), C(17), C(19)	H–C(6)	1.81 (*m*)	50.6	C(5)
CH_2(6)	1.5 (*m*, H_{ax}), 1.3 (*m*, H_{eq})	26.1	C(5)		1.54 (*m*)	24.3	
CH_2(7)	2.1 (*m*, H_{ax}), 2.4 (*m*, H_{eq})	37.4	C(8), C(9), C(6)	H–C(7)	1.30 (*m*)	36.1	
C(8)		147.1				58.1	
H–C(9)	1.7 (*m*)	56.9			1.50 (*m*)	54.1	
C(10)		38.6				39.7	
CH_2(11)	2.2 (*m*, H_{ax}), 2.4 (*m*, H_{eq})	22.2		H–C(12), H–C(11), H–C(9)	0.83 (*m*)	15.8	
H–C(12) or CH_2(12)	5.2 (*br. t*)	130.8	C(14)		1.53 (*m*)	43.5	
C(13)		131.9				73.4	
H–C(14)	6.7 (*dd*, $^{1}J = 10.5$, $^{2}J = 17.0$)	133.7	C(15), C(13), C(16)	H–C(15)	5.87 (*dd*, $^{1}J = 11.0$, $^{2}J = 17.5$)	145.3	C(13)
CH_2(15)	5.0 (*dd*, $^{1}J = 4.0$, $^{2}J = 10.5$), 5.1 (*dd*, $^{1}J = 4.0$, $^{2}J = 17.0$)	113.4		H–C(14)	5.18 (*dd*, $^{1}J = 17.5$, $^{2}J = 1.0$), 5.01 (*dd*, $^{1}J = 11.0$, $^{2}J = 1.0$)	111.3	C(13)
Me(16)	1.7 (*s*)	19.7	C(12), C(13), C(14)		1.19 (*s*)	27.8	C(12), C(13), C(14)
Me(17)	0.73 (*s*)	14.7	C(9)		0.81 (*s*)	14.8	C(1), C(5), C(9), C(10)
C(18)		182.1				184.2	
Me(19)	1.12 (*s*)	10.5	C(18), C(3), C(4)		1.16 (*s*)	16.3	C(4), C(5), C(18)
CH_2(20)	4.5 (br. *s*), 4.8 (br. *s*)	108.7	C(9), C(7)		2.75 (*dd*, $^{1}J = 2.5$; $^{2}J = 4.5$), 2.46 (*d*, $J = 4.5$)	50.6	

its expansions, we observed two broad *s* at δ(H) 4.8 and 4.5 which were assigned the exocyclic CH_2(20)= group at C(8), and two *s* of quaternary Me groups at δ(H) 0.73 and 1.12 which are characteristic of *ent*-labdane-type diterpenes and which corroborated the equatorial orientation of the COOH group at C(4). The signal at δ(H) 4.0 (*dd*, ^1J = 4.4 Hz, ^2J = 12.0 Hz) was attributed to a CH–O group, located at position 3, those at δ(H) 5.0 (*dd*, ^1J = 4.0 Hz, ^2J = 10.5 Hz), 5.1 (*dd*, ^1J = 4.0 Hz, ^2J = 17 Hz), and 6.7 (*dd*, ^1J = 10.5 Hz, ^2J = 17.0 Hz) were characteristic of H–C(14) and CH_2(15) of a labda-12,14-diene, and the signal at δ(H) 1.7 (*s*, Me (16)) was characteristic of a Me group attached to a C=C bond. In the HMBC spectrum, we observed the following correlations: δ(H) 4.0 (H–(3))/δ(C) 10.5 (Me(19)) confirming the assignments of C(3) and Me(19) and corroborating the position of the OH group at C(3), δ(H) 1.8 (H–C(5))/δ(C) 10.5 (Me(19)) confirming the assignment of H–C(5), δ(H) 4.8 (1 H–C(20))/δ(C) 56.9 (C(9)) confirming the assignment of C(9), δ(H) 1.8 (H–C(5))/δ(C) 26.1 (C(6)) confirming the assignment of C(6), δ(H) 4.5 (1 H–C(20))/δ(C) 37.4 (C(7)) confirming the assignment of C(7), and δ(H) 1.7 (Me(16))/δ(C) 130.8 (C(12)), 131.9 (C(13)), and 133.7 (C(14)). After data analysis and comparison with the literature, one can conclude that **3** is (3α,12*Z*)-3-hydroxy-*ent*-labda-8(20)12,14-trien-18-oic acid, a new diterpene labdane named labdorffianic acid A.

Compound **4** was isolated as an optically active colorless oil. The HR-ESI-MS showed the molecular-ion peak at *m*/*z* 337.2373 ($[M+H]^+$), consistent with the molecular formula $C_{20}H_{32}O_4$. In the ^{13}C-NMR spectrum (*Table 2*) we observed the presence of 20 C-atom signals, *i.e.*, five quaternary C-atoms and three CH, nine CH_2, and three Me groups. As in **3**, the signals at δ(C) 184.2, 16.3, 14.8, and 50.6 were compatible with an *ent*-labdane diterpene and assigned to C(18) (equatorial COOH), Me(19), Me(17), and CH_2(20), respectively, Me(17) and Me(19) being *cis* and axially positioned, and with C(5) suffering a γ-gauche effect from the carbonyl O-atom of the COOH group. The signals at δ(C) 58.1 (quaternary C(8)) and 50.6 (CH_2(20)) corroborated the presence of an epoxy moiety at C(8) and C(20). In the ^{1}H-NMR spectrum (*Table 2*), the three *s* at δ(H) 0.81, 1.16, and 1.19 corresponded to quaternary Me groups. The two signals at δ(H) 2.46 (*d*, *J* = 4.5 Hz) and 2.75 (*dd*, ^1J = 2.5 Hz, ^2J = 4.50 Hz) replaced the two broad *s* at δ(H) 4.5 and 4.8 of **3**, compatible with the prescence of a labdane-type diterpene [21] epoxidated between C(8) and C(20). The signals at δ(H) 5.87 (*dd*, ^1J = 11.0 Hz, ^2J = 17.5 Hz), 5.18 (*dd*, ^1J = 17.5 Hz, ^2J = 1.0 Hz), and 5.01 (*dd*, ^1J = 11.0 Hz, ^2J = 1.0 Hz), for H–C(14) and CH_2(15) suggested the presence of a similar structure than that of the diterpene *ent*-13-epimanool (=(αR,1*R*,4a*R*,8a*R*)-α-ethenyldecahydro-α,5,5,8a-tetramethyl-2-methylenenaphthalene-1-propanol). The direct correlations between C- and H-atoms were observed in the HMQC spectrum and confirmed that δ(C) 47.1, 58.1, 39.7, 73.4, and 184.2 as were the signals of quaternary C-atoms. The HMBC spectrum showed the following correlations: δ(H) 5.18 (1 H–C(15))/δ(C) 73.4 (C(13)), confirming the assignment of C(13), δ(H) 1.19 (Me(16))/δ(C) 43.5 (C(12)), 73.4 (C(13)), and 145.3 (C(14)) confirming the assignments of Me(16), C(12), C(13), and C(14), δ(H) 1.16 (Me(19))/δ(C) 47.1 (C(4)), 50.6 (C(5)), and 184.2 (C(18)), confirming the assignments of Me(19), C(4), C(5), and C(18), and δ(H) 0.81 (Me(17))/δ(C) 37.9 (C(1)), 50.6 (C(5)), 54.1 (C(9)), and 39.7 (C(10)) confirming the assignments of Me(17), C(1), C(5), C(9), and C(10). After analyis of all NMR data and comparison with literature data [21], the structure of **4**

was determined as 8,20-epoxy-13-hydroxy-*ent*-labd-14-en-18-oic acid, a new natural product named labdorffianic acid B.

The compounds **5**–**8** were identified by comparison with the literature as *ent*-kauran-16-ol, *ent*-kaur-16-en-19-oic acid, *ent*-kaur-16-en-19-ol, and *ent*-trachyloban-18-oic acid, respectively.

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Experimental Part

General. Anal. TLC: silica gel plates PF_{254} *7749* (*Merck*); visualization under UV light (254 and 366 nm) or by exposure to I_2 vapor. Prep. TLC: silica gel *F 254 G* (*Vetec*). Column chromatography (CC): silica gel (SiO_2; 0.063–0.20 mm; *Merck*). M.p.: *Microquimica MQAPF-302*; uncorrected. Optical rotation: *Jasco-P-2000* polarimeter. IR Spectra: *Bomem-MB-100* spectrophotometer; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Varian* spectrometer; at 500 (^1H) and 125 MHz (^{13}C); in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-ESI-MS: *Bruker Daltonics MicfroTOF-II*; in *m*/*z*.

Plant Material. The roots and fruits of *X. langsdorffiana* were collected in the municipality of Cruz do Espírito Santo, Paraíba, Brazil, in June 2008 and were identified by *M. F. A.* A sample was deposited with the Herbarium *Lauro Pires Xavier*, Universidade Federal da Paraíba, under the voucher specimen number Agra 5541.

Extraction and Isolation. The roots of *X. langsdorffiana* (4 kg) were dried, crushed, and subjected to exhaustive maceration with EtOH (95%) at r.t. for 3 times, with solvent renewal every 72 h. After this process, the extraction soln. was concentrated at 40°: 70 g of crude EtOH extract. The EtOH extract (50 g) was subjected to vacuum chromatography through a fritted funnel (SiO_2, hexane, hexane/AcOEt 8:2 and 1:1, 2:8), AcOEt, AcOEt/MeOH 1:1, and MeOH): *Fractions I–VII*. *Fr. II* (4 g) was subjected to CC (SiO_2, hexane, hexane/AcOEt, AcOEt): *Frs. II1–II87. Frs. II6–II8* (93 mg) were subjected to CC (SiO_2, AcOEt/hexane 0 → 10%): **1** (15 mg) and **2** (12 mg). *Frs. II49–II52* (48 mg) were subjected to CC (SiO_2 impregnated with $AgNO_3$ [22], hexane and AcOEt/hexane 0 → 20%): **5** (21 mg) and **6** (8 mg). *Fr. IV* (1.83 g) was subjected to CC (SiO_2, hexane, hexane/AcOEt, AcOEt). *Frs. IV6–IV8* (88 mg) were resubjected to CC (SiO_2, AcOEt/hexane 0 → 15%): **7** (35 mg) and **8** (13 mg).

The fruits of *X. langsdorffiana* were dried, crushed, and subjected to exhaustive maceration with MeOH at r.t. for 3 times, with solvent renewal every 72 h. After this process, the soln. was concentrated at 40°: 150 g of crude MeOH extract. The MeOH extract (150 g) was suspended in MeOH/H_2O 7:3 and subjected to a liquid/liquid hexane fractionation (CH_2Cl_2, AcOEt): *Fractions VIII–X*. *Fr. VIII* (10 g) was subjected to CC (hexane, hexane/AcOEt, AcOEt): *Fractions VIII1–VIII210*. *Frs. VIII170–VIII179* were filtered through SiO_2 and eluted with hexane and AcOEt: **3**. *Frs. VIII180–VIII200* were also filtered through fresh SIO_2 and eluted in AcOEt/hexane: **4**.

(5β,7β,8α,9β,10α,12α)-Atisane-7,16-diol 7-Acetate (= *Xylodiol 7-Acetate*; **1**): Colorless crystals. M.p. 51–54°. $[\alpha]_D^{25} = -25$ ($c = 0.01$, $CHCl_3$). IR (KBr): 3650, 1735. ^1H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 371.2553 ($[M+Na]^+$, $C_{22}H_{36}NaO_3^+$; calc. 371.2557).

(5β,8α,9β,10α,12α)-16-Hydroxyatisan-7-one (= *Xylopinone*; **2**): Colorless crystals. M.p. 169–172°. $[\alpha]_D^{25} = -45$ ($c = 0.01$, $CHCl_3$). IR (KBr): 3448, 1678. ^1H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 305.2480 ($[M+H]^+$, $C_{20}H_{37}O_3^+$; calc. 305.2402).

(3α,12Z)-3-Hydroxy-ent-*labda-8(20),12,14-trien-18-oic Acid* (= *Labdorffianic Acid A* = *(1*R,*2*R,*4a*S,*5*R,*8a*S*)-Decahydro-2-hydroxy-1,4a-dimethyl-5-[(2Z)-3-methylpenta-2,4-dien-1-yl]-6-methylenenaphthalene-1-carboxylic Acid*; **3**): Colorless oil. $[\alpha]_D^{25} = -34$ ($c = 0.01$, $CHCl_3$). IR (KBr): 3650, 1690. ^1H- and ^{13}C-NMR: *Table 2*. HR-ESI-MS: 353.2113 ($[M+Cl]^-$, $C_{20}H_{30}ClO_3^-$; calc. 353.1889).

8,20-Epoxy-13-hydroxy-ent-*labda-14-en-18-oic Acid* (= *Labdorffianic Acid B* = *(1*S,*2*R,*4a*S,*5*S,*8a*R*)-Octahydro-1-[(3*S*)-3-hydroxy-3-methylpent-4-en-1-yl]-5,8a-dimethylspiro[naphthalene-2(1*H*),*

2′-oxirane]-5-carboxylic Acid; **4**): Colorless oil. $[\alpha]_D^{25} = -38$ ($c = 0.01$, $CHCl_3$). IR (KBr): 3405, 2980, 1690, 1266, 920. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-ESI-MS: 337.2373 ($[M+H]^+$, $C_{20}H_{33}O_4^+$; calc. 337.2373).

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