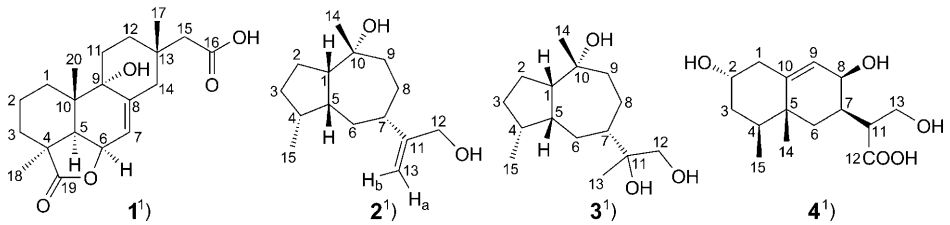
Four New Terpenoids from *Xylaria* sp. 101

by **Yao-Yao Li**, **Zhi-Yu Hu**, **Chun-Hua Lu**, and **Yue-Mao Shen***

Key Laboratory of the Ministry of Education for Cell Biology and Tumor Cell Engineering; Xiamen Engineering Research Center of Marine Microbial Drug Discovery; Fujian Engineering Laboratory of Pharmaceuticals; School of Life Sciences, Xiamen University, No. 422 South Siming Road, Xiamen 361005, P. R. China (phone: +86-592-2184180; fax: +86-592-2181722; e-mail: yshen@xmu.edu.cn)

One new diterpenoid, xylarenolide (**1**), and three new sesquiterpenoids, xylaranol A (**2**), xylaranol B (**3**), and xylaranic acid (**4**), were obtained from the fungal strain *Xylaria* sp. 101, which was isolated from the fruiting body of *Xylaria* sp. collected in Gaoligong Mountain, Yunnan Province. Their structures were elucidated by spectroscopic analyses, including 1D- and 2D-NMR experiments, and by HR-Q-TOF mass spectrometry. Their antimicrobial activities were evaluated.

Introduction. – Fungi of the genus *Xylaria* are very diverse with respect to their chemical constituents. Secondary metabolites of them are known to include terpenoids [1–4], cyclopeptides [5][6], polyketides [7][8], cytochalasins [9], xanthones [10][11], and unique unclassified xyloketals [12]. Recently, we have embarked on a research program of looking for new structural and bioactive metabolites from the strain 101, which was collected from Gaoligong Mountain of southwestern China, and identified as *Xylaria* sp. (family Xylariaceace). Here, we report the isolation, structure elucidation, and antimicrobial activities of four new terpenoids, namely xylarenolide (**1**), xylaranol A (**2**), xylaranol B (**3**), and xylaranic acid (**4**), from the fermentation products of the fungal strain *Xylaria* sp. 101.



Results and Discussion. – 1. *Structure Elucidation.* The morphological properties of the isolate 101 were examined after incubation for two months at 28° in potato–dextrose agar (PDA) medium. This organism was identified to be *Xylaria* sp. according to its ITS sequence of rDNA (ITS1-5.8S-ITS2). The fermentation culture was extracted successively with AcOEt. The AcOEt extract was purified by repeated column chromatography (*RP-18*, *Sephadex LH-20*, and silica gel) to afford compounds **1**–**4**.

[1]) Arbitrary atom numbering. For systematic names, see *Exper. Part.*

Xylarenolide (**1**) was obtained as a colorless oil. The HR-Q-TOF-MS showed the *quasi*-molecular-ion peak ($[M + Na]^+$) at *m/z* 371.2049, establishing the molecular formula $C_{20}H_{28}O_5$. The IR absorption at 3366 cm^{-1} indicated the presence of OH groups. The ^{13}C-NMR (DEPT) spectra of **1** (*Table 1*) displayed signals for seven quaternary C-atoms (one O-bearing, one olefinic, and two CO), and three CH (one O-bearing and one olefinic), seven CH_2, and three Me groups. The structure of fragment **1a**, a C_{13} moiety composed of $2 \times$ Me, $3 \times CH_2$, $3 \times$ CH groups, and five quaternary C-atoms, was determined on the basis of the ^{1}H,^{1}H-COSY correlations $H-C(1) \leftrightarrow H-C(2) \leftrightarrow H-C(3)$ and $H-C(5) \leftrightarrow H-C(6) \leftrightarrow H-C(7)$, along with the HMBCs from the H-atoms of Me(18) to C(3), C(4), C(5), and C(19), from those of Me(20) to C(1), C(5), C(9), and C(10), from $H-C(6)$ to C(8), and from $H-C(7)$ to C(9) (*Fig. 1*). Furthermore, the HMBC spectra showed correlations of the H-atoms of Me(17) with C(12), C(13), C(14), and C(15), and correlations from CH_2(15) to C(16) were observed. In combination with the ^{1}H,^{1}H-COSY $H-C(11) \leftrightarrow H-C(12)$, this led to the establishment of fragment **1b** (*Fig. 1*). Finally, the HMBCs from CH_2(12) to C(9) and from CH_2(14) to C(7) indicated that fragments **1a** and **1b** were linked together *via* C(9)–C(11) and C(8)–C(14), indicating a pimarane-type diterpene. The relative configuration of **1** was determined by the analysis of NOE spectrum. The presence of NOE correlations $H-C(18) \leftrightarrow H-C(5) \leftrightarrow H-C(6)$, and $H_{eq}-C(14) \leftrightarrow Me(17) \leftrightarrow H_{ax}-C(11) \leftrightarrow Me(20)$ (*Fig. 2*) indicated that **1** had the same relative configuration as that of hymatoxin E [13]. Indeed, **1** was the C(16) carboxylic derivative of hymatoxin E. Thus, from the above data, the structure of compound **1** was established to be 2-[(3a*R**,5a*S**,8*R**,10a*S**,10b*R**,10c*S**)-2,3,3a,4,5a,7,8,9,10,10a,10b,10c-dodecahydro-10a-hydroxy-3a,8,10b-trimethyl-4-oxo-1*H*-phenanthro[10,1-*bc*]furan-8-yl]acetic acid.

Table 1. *^{1}H- and ^{13}C-NMR Data of* **1**. At 600 and 150 MHz, resp., in $CDCl_3$; δ in ppm. *J* in Hz.

Position[1])	δ(H)	δ(C)	Position[1])	δ(H)	δ(C)
1	1.62–1.64 (*m*, H_{ax}), 1.29–1.34 (*m*, H_{eq})	27.3 (*t*)	11	1.91 (*dt*, *J* = 4.2, 14.0, H_{ax}), 1.52–1.54 (*m*, H_{eq})	27.0 (*t*)
2	1.77–1.79 (*m*, H_{ax}), 1.53–1.55 (*m*, H_{eq})	18.1 (*t*)	12	1.81 (*dt*, *J* = 4.2, 14.0, H_{ax}), 1.52–1.54 (*m*, H_{eq})	31.9 (*t*)
3	1.47 (*ddd*, *J* = 5.8, 8.5, 14.3, H_{ax}), 2.19–2.22 (*m*, H_{eq})	28.3 (*t*)	13		34.0 (*s*)
			14	2.46 (*d*, *J* = 11.0, H_{ax}), 2.18–2.20 (*m*, H_{eq})	43.2 (*t*)
4		42.4 (*s*)			
5	2.36 (*d*, *J* = 4.6, H_{ax})	43.9 (*d*)	15	2.31 (*s*)	48.1 (*t*)
6	4.81 (br. *d*, *J* = 2.5, H_{eq})	73.1 (*d*)	16		176.2 (*s*)
7	5.82 (br. *s*)	120.7 (*d*)	17	0.90 (*s*)	21.8 (*q*)
8		143.9 (*s*)	18	1.32 (*s*)	24.8 (*q*)
9		72.9 (*s*)	19		182.7 (*s*)
10		37.9 (*s*)	20	1.00 (*s*)	21.9 (*q*)

Xylaranol A (**2**) was obtained as a colorless oil. The molecular formula was determined as $C_{15}H_{26}O_2$ by its HR-Q-TOF-MS and NMR data. The IR spectrum exhibited the absorption at 3424 cm^{-1} typical for OH groups. The ^{1}H- and ^{13}C-NMR, and DEPT spectra (*Table 2*) indicated two Me, seven CH_2, four CH groups, and two

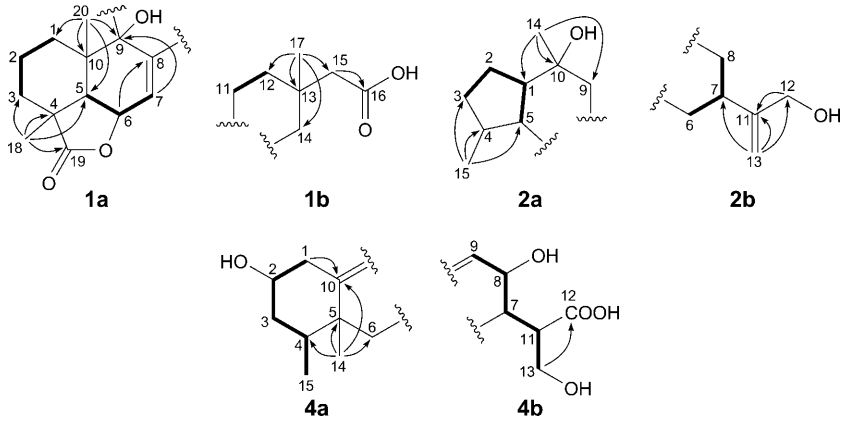


Fig. 1. *The structures of fragments* **1a** *and* **1b** *of compound* **1**, *fragments* **2a** *and* **2b** *of compound* **2**, *and fragments* **4a** *and* **4b** *of compound* **4**, *and selected HMBCs* (H → C) *and* ^{1}*H,*^{1}*H-COSY correlations* (bold line)

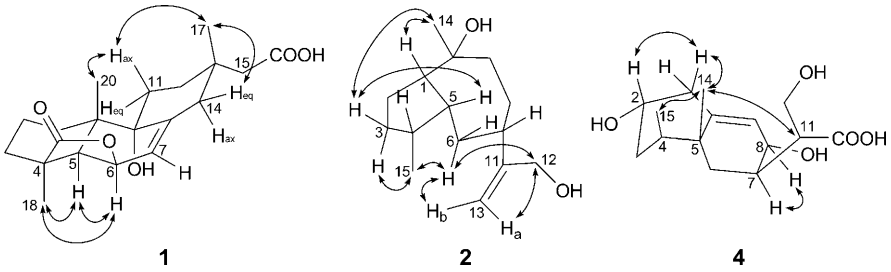


Fig. 2. *Selected NOE correlations for compounds* **1**, **2**, *and* **4** (H ↔ H)

quaternary C-atoms, of which a CH_2 group and a quaternary C-atom were O-bearing. Furthermore, the HSQC, HMBC, and ^{1}H,^{1}H-COSY spectra facilitated the assignments of all ^{1}H- and ^{13}C-NMR signals, indicating a simple guaiane-type structure [14]. The HMBCs from Me(14) to C(1), C(9), and C(10), and from Me(15) to C(3), C(4) and C(5), along with the ^{1}H,^{1}H-COSY correlations H−C(3) ↔ H−C(2) ↔ H−C(1) ↔ H−C(5) established the structure of fragment **2a** (*Fig. 1*). Meanwhile, the HMBCs from CH_2(13) to C(7), C(11), and C(12), in combination with the ^{1}H,^{1}H-COSY correlations H−C(6) ↔ H−C(7) ↔ H−C(8), led to the establishment of fragment **2b** (*Fig. 1*). Finally, the ^{1}H,^{1}H-COSY correlations H−C(5) ↔ CH_2(6) and CH_2(8) ↔ CH_2(9) connected the fragments **2a** and **2b**. The relative configuration of **2** was assigned on the basis of NOE spectrum (*Fig. 2*). Although the NOE correlations between H−C(1) and H−C(5) were not observed, as reported by *Fleischer et al.* [14], the fusion of ring *A* and ring *B* was determined to be *cis* based on the NOE correlations H−C(1) ↔ Me(14), Me(14) ↔ H_a−C(3) ↔ H−C(5), and H_b−C(3) ↔ Me(15) which determined the relative configurations at C(10) and C(4). The relative configuration of H−C(7) was determined to be β according to the NOE correlations H_α−C(6) ↔

Me(15) and H_α–C(6) ↔ CH_2(12). Therefore, the structure of compound **2** was established to be (1*R**,3a*S**,4*R**,7*S**,8a*R**)-decahydro-7-(1-hydroxyprop-2-en-2-yl)-1,4-dimethylazulen-4-ol.

Table 2. *^{1}H- and ^{13}C-NMR Data of* **2** ($CDCl_3$) *and* **3** ((D_6)DMSO). At 600/150 MHz, in $CDCl_3$; δ in ppm. *J* in Hz.

Position[1])	**2**		**3**	
	δ(H)	δ(C)	δ(H)	δ(C)
1	2.09–2.16 (*m*)	55.3 (*d*)	1.99 (*dd*, *J* = 8.7, 18.1)	54.8 (*d*)
2	1.54–1.57 (*m*, H_α), 1.72–1.75 (*m*, H_β)	26.2 (*t*)	1.46 (*ddd*, *J* = 4.9, 10.6, 22.6, H_α), 1.52–1.58 (*m*, H_β)	25.6 (*t*)
3	1.72–1.74 (*m*, H_α), 1.22–1.25 (*m*, H_β)	31.1 (*t*)	1.63–1.65 (*m*, H_α), 1.12–1.19 (*m*, H_β)	30.6 (*t*)
4	2.03–2.05 (*m*)	38.9 (*d*)	1.89–1.99 (*m*)	38.6 (*d*)
5	2.02–2.04 (*m*)	45.9 (*d*)	1.79–1.82 (*m*)	46.1 (*d*)
6	1.45–1.50 (*m*, H_α), 1.91–1.94 (*m*, H_β)	29.2 (*t*)	0.82 (*dd*, *J* = 12.7, 23.1, H_α), 1.65 (br. *d*, *J* = 10.0)	21.3 (*t*)
7	2.32 (*td*, *J* = 8.5, 3.5)	41.8 (*d*)	1.73–1.76 (*m*)	43.0 (*d*)
8	1.28–1.31 (*m*, H_α), 1.48–1.52 (*m*, H_β)	29.4 (*t*)	1.05–1.08 (*m*, H_α), 1.74–1.77 (*m*, H_β)	23.9 (*t*)
9	1.94–1.96 (*m*, H_α), 1.58–1.61 (*m*, H_β)	36.2 (*t*)	1.73–1.75 (*m*, H_α), 1.30–1.33 (*m*, H_β)	33.8 (*t*)
10		75.0 (*s*)		72.4 (*s*)
11		156.3 (*s*)		74.5 (*s*)
12	4.13 (*s*)	65.0 (*t*)	3.21 (*s*)	67.8 (*t*)
13	4.88 (*s*, H_a), 4.97 (*s*, H_b)	106.9 (*t*)	0.87 (*s*)	19.4 (*q*)
14	1.21 (*s*)	29.7 (*q*)	1.01 (*s*)	30.9 (*q*)
15	0.89 (*d*, *J* = 5.5)	16.1 (*q*)	0.89 (*d*, *J* = 7.0)	16.3 (*q*)

Xylaranol B (**3**) showed a *quasi*-molecular-ion peak ($[M+H]^+$) at *m*/*z* 257.2969 in the positive-ion-mode HR-Q-TOF-MS, which was consistent with the molecular formula $C_{15}H_{28}O_3$. The IR spectrum exhibited the absorption at 3427 cm^{-1} for OH groups. The ^{1}H- and ^{13}C-NMR data of **3** (*Table 2*) were similar to those of **2**. The difference was at δ(C) 74.5 (C(11)) and 19.4 (C(13)) due to the hydration of the C(11)=C(13) bond, which was supported by the HMBCs from Me(13) to C(7), C(11), and C(12). The relative configuration of **3** was determined on the basis of the same NOE correlations as those of **2**. Therefore, compound **3** was determined to be 2-[(3*R**,3a*R**,5*S**,8*R**,8a*S**)-decahydro-8-hydroxy-3,8-dimethylazulen-5-yl]propane-1,2-diol.

Xylaranic acid (**4**) was deduced to have the molecular formula $C_{15}H_{24}O_5$ from the HR-Q-TOF-MS and NMR spectral data. The IR absorption at 3404 cm^{-1} indicated the presence of OH groups. The ^{1}H- and ^{13}C-NMR, and DEPT spectra (*Table 3*) exhibited 15 signals, which were assigned to two Me, four CH_2 (one O-bearing), six CH (one olefinic and two O-bearing) groups, and three quaternary C-atoms (one olefinic and one CO). Comparison of ^{1}H- and ^{13}C-NMR data of **4** (*Table 3*) with those of phomenone in literature [15] revealed that **4** had the same ring C-atom skeleton as a

simple eremophilane-type sesquiterpene. The HMBCs from Me(14) to C(4), C(5), C(6), and C(10), and from CH_2(1) to C(10), in combination with the ^{1}H,^{1}H-COSY correlations $CH_2(1) \leftrightarrow H-C(2) \leftrightarrow CH_2(3) \leftrightarrow H-C(4) \leftrightarrow Me(15)$, established the structure of fragment **4a** (*Fig. 1*). Additionally, the HMBC spectrum showed that CH_2(13) were correlated with C(12), and the correlations $H-C(9) \leftrightarrow H-C(8) \leftrightarrow H-C(7) \leftrightarrow H-C(11) \leftrightarrow CH_2(13)$ were observed in ^{1}H,^{1}H-COSY spectrum, determining the structure of fragment **4b** (*Fig. 1*). Finally, the HMBCs from CH_2(1) to C(9), and from CH_2(6) to both C(7) and C(11), assigned the fragments **4a** and **4b** to be linked together *via* C(9) and C(10), and C(6) and C(7). The relative configuration of **4** was determined from the NOE spectrum. The presence of NOE correlations $H_\beta-C(1) \leftrightarrow H-C(2) \leftrightarrow Me(14) \leftrightarrow Me(15)$ as well as $H-C(7) \leftrightarrow H-C(8)$ indicated that H–C(2), Me(14), and Me(15) were β-oriented, while H–C(7) and H–C(8) were in α-orientation (*Fig. 2*). Thus, the structure of compound **4** was established to be 2-[(2*R**,3*S**,6*S**,8*S**,8a*R**)-1,2,3,5,6,7,8,8a-octahydro-3,6-dihydroxy-8,8a-dimethylnaphthalen-2-yl]-3-hydroxypropanoic acid.

Table 3. *^{1}H- and ^{13}C-NMR Data of* **4**. At 600/150 MHz, in $CDCl_3$; δ in ppm. *J* in Hz.

Position[1])	δ(H)	δ(C)	Position[1])	δ(H)	δ(C)
1	2.41 (br. *d*, *J* = 11.5, H_β),	41.9 (*t*)	7	2.66–2.69 (*m*)	34.3 (*d*)
	2.28 (*t*, *J* = 11.5, H_α)		8	4.93 (*dd*, *J* = 2.0, 7.0)	76.0 (*d*)
2	3.59–3.62 (*m*)	71.0 (*d*)	9	5.52 (br. *d*, *J* = 2.0)	118.0 (*d*)
3	1.41–1.45 (*m*, H_α),	39.7 (*t*)	10		148.1 (*s*)
	1.82–1.84 (*m*, H_β)		11	2.73–2.76 (*m*)	47.0 (*d*)
4	1.37–1.40 (*m*)	40.6 (*d*)	12		178.1 (*s*)
5		35.9 (*s*)	13	4.03 (*dd*, *J* = 5.5, 11.3),	60.5 (*t*)
				3.86 (*dd*, *J* = 5.5, 11.3)	
6	1.83 (*dd*, *J* = 6.1, 14.8, H_β),	35.5 (*t*)	14	1.08 (*s*)	20.1 (*q*)
	1.71 (*dd*, *J* = 4.9, 14.8, H_α)		15	0.91 (*d*, *J* = 6.6)	14.9 (*q*)

2. *Biological Study.* The antibacterial activities of compounds **1**–**4** were tested against bacteria (*Escherichia coli* (CMCC (B) 44103), *Bacillus subtilis* (CMCC (B) 63501), *Bacillus pumilus* (CMCC (B) 63202), and *Staphylococcus aureus* (CMCC (B) 26003)), and yeast (*Candida albicans* (AS 2.538)) using *Oxford* plate assay system. Two replicates were performed for each compound at a concentration 0.3 mg/ml with the loading volume 100 µl. The results showed that compounds **1**–**4** had no effects on the growth of tested bacteria or yeast at 30 µg/plate.

This work was financially supported by the *National Science Fund for Distinguished Young Scholars* to *Y.-M. Shen* (No. 30325044) and the *Key Grant of Chinese Ministry of Education* (No. 306010).

Experimental Part

General. Column chromatography (CC): silica gel (SiO_2; 200–300 mesh; *Qingdao Marine Chemical Factory*, Qingdao, P. R. China), silica gel GF_{254} (*Merck*), *RP-18* (*Merck*), and *Sephadex LH-20* (*Amersham Biosciences*). TLC: precoated silica-gel GF_{254} plates (0.20–0.25 mm; *Qingdao Marine Chemical Factory*, Qingdao, P. R. China). Optical rotations: *Perkin-Elmer 341* polarimeter, with $CHCl_3$ as solvent. IR Spectra: in KBr on a *Nicolet FT-IR 360* spectrophotometer. ^{1}H- and ^{13}C-NMR spectra:

Bruker DRX-600 spectrometer, at 600 and 150 MHz, resp., in $CDCl_3$ or (D_6)DMSO; δ in ppm rel. to Me_4Si, *J* in Hz.

Isolation and Fermentation of the Fungal Strain. The fungus was isolated from the fruiting body of *Xylaria* sp., which was collected in 'Gaoligong Mountain National Natural conservation Area', Yunnan Province, P. R. China. Both a traditional morphological assessment and internal transcribed spaces (ITS) sequencing were performed to characterize it as *Xylaria* sp. 101. The fermentation was performed, and the mycelia of 101 grown on PDA plates were used to inoculate 1-l *Erlenmeyer* flasks containing 200 ml of PD medium (potato 200 g/l, glucose 20 g/l, pH-neutral). The flasks were incubated on a rotary shaker for 5 d at 28° with shaking at 160 rpm. The cultures were transferred into 4 20-l flasks containing PD medium (5 l) and cultivated for two months at 28° without agitation.

Extraction and Isolation. The culture filtrate was concentrated under vacuum at 45° to a volumn of 2 l and then extracted with AcOEt (3 ×). The combined org. layer, upon solvent removal, yielded a crude extract as a brown syrup (4.8 g). The extract was subjected to MPLC (145 g of *RP-18*; 30, 50, 70%, aq. acetone, and neat acetone; 2 l for each gradient) to yield 14 fractions: *Frs. a–m*.

Fr. b (828 mg) was subjected to *Sephadex LH-20* (in MeOH) twice, followed by CC (1. $CHCl_3$/MeOH 100 : 1; 2. MPLC (30 g *RP-18*, Me_2CO/H_2O 3 : 7)) to afford **4** (4 mg). *Fr. d* (300 mg) was subjected to *Sephadex LH-20* (in MeOH) to afford *Fr. d.1* (166 mg), which was then combined with *Fr.e.1* (44 mg) and purified by passage over *Sephadex LH-20* (in MeOH) again, and followed by purification on MPLC (30 g *RP-18*; Me_2CO/H_2O 3 : 7) to afford **3** (26 mg). *Fr. e* (214 mg) was subjected to *Sephadex LH-20* (in MeOH) to afford two subfractions, *Fr. e.1* and *Fr. e.2*. *Fr. e.2* (25 mg) was purified by repeated CC (1. $CHCl_3$/MeOH 10 : 1; 2. Petroleum ether (PE)/acetone 15 : 1) to afford **1** (6 mg). *Fr. g* (406 mg) was subjected to CC (1. *Sephadex LH-20:* MeOH; 2. PE/Me_2O 15 : 1; 3. MPLC: 30 g *RP-18*; 35% aq. acetone) to afford **2** (4 mg).

Xylarenolide (*=(6β,13α)-9-Hydroxy-18-oxo-6,18-epoxypimar-7-en-16-oic Acid = 2-[(3a*R,*5a*S**, *8*R**,10a*S**,10b*R**,10c*S**)-2,3,3a,4,5a,7,8,9,10,10a,10b,10c-Dodecahydro-10a-hydroxy-3a,8,10b-trimethyl-4-oxo-1*H*-phenanthro[10,1-*bc*]furan-8-yl]acetic Acid*; **1**). Colorless oil. $[\alpha]_D^{20} = -18.0$ ($c = 0.054$, $CHCl_3$). IR (KBr): 3366, 2917. ^{1}H- and ^{13}C-NMR: *Table 1*. HR-Q-TOF-MS: 371.2049 ($[M+Na]^+$, $C_{20}H_{28}NaO_5^+$; calc. 371.1834).

Xylaranol A (*=(1*R**,3a*S**,4*R**,7*S**,8a*R**)-Decahydro-7-(3-hydroxyprop-1-en-2-yl)-1,4-dimethyl-azulen-4-ol*; **2**). Colorless oil. $[\alpha]_D^{20} = -24.2$ ($c = 0.08$, $CHCl_3$). IR (KBr): 3424, 2928. ^{1}H- and ^{13}C-NMR: *Table 2*. ESI-MS (pos.): 238 ($[M+Na]^+$). HR-Q-TOF-MS: 261.1928 ($[M+Na]^+$, $C_{15}H_{26}NaO_2^+$; calc. 261.1825).

Xylaranol B (*=2-[(3*R**,3a*R**,5*S**,8*R**,8a*S**)-Decahydro-8-hydroxy-3,8-dimethylazulen-5-yl]propane-1,2-diol*; **3**). Colorless power. $[\alpha]_D^{20} = -3.6$ ($c = 0.018$, $CHCl_3$). IR (KBr): 3427. ^{1}H- and ^{13}C-NMR: *Table 2*. HR-Q-TOF-MS: 257.2969 ($[M+H]^+$, $C_{15}H_{29}O_3^+$; calc. 257.2117).

Xylaranic Acid (*=2-[(2*R**,3*S**,6*S**,8*S**,8a*R**)-1,2,3,5,6,7,8,8a-Octahydro-3,6-dihydroxy-8,8a-dimethylnaphthalen-2-yl]-3-hydroxypropanoic Acid*; **4**). Colorless oil. $[\alpha]_D^{20} = +23.4$ ($c = 0.096$, $CHCl_3$). IR (KBr): 3404, 2927, 1751. ^{1}H- and ^{13}C-NMR: *Table 3*. HR-Q-TOF-MS: 285.3016 ($[M+H]^+$, $C_{15}H_{25}O_5^+$; calc. 285.1702).

REFERENCES

[1] C. J. Smith, N. R. Morin, G. F. Bills, A. W. Dombrowski, G. M. Salituro, S. K. Smith, A. Zhao, D. J. MacNeil, *J. Org. Chem.* **2002**, *67*, 5001.

[2] S. J. Coval, M. S. Puar, D. W. Phife, J. S. Terracciano, M. Patel, *J. Antibiot.* **1995**, *48*, 1171.

[3] S. T. Deyrup, J. B. Gloer, K. O'Donnell, D. T. Wicklow, *J. Nat. Prod.* **2007**, *70*, 378.

[4] Z.-Y. Hu, Y.-Y. Li, Y.-J. Huang, W.-J. Su, Y.-M. Shen, *Helv. Chim. Acta* **2008**, *91*, 46.

[5] Y. Lin, X. Wu, S. Feng, G. Jiang, S. Zhou, L. L. P. Vrijmoed, E. B. G. Jones, *Tetrahedron Lett.* **2001**, *42*, 449.

[6] H. Huang, Z. She, Y. Lin, L. L. P. Vrijmoed, W. Lin, *J. Nat. Prod.* **2007**, *70*, 1696.

[7] S. Boonphong, P. Kittakoop, M. Isaka, D. Pittayakhajonwut, M. Tanticharoen, Y. Thebtaranonth, *J. Nat. Prod.* **2001**, *64*, 965.

[8] D. O' Hagana, S. V. Rogers, G. R. Duffin, R. L. Edwards, *Tetrahedron Lett.* **1992**, *33*, 5585.
[9] H. Jayasuriya, K. B. Herath, J. G. Ondeyka, J. D. Polishook, G. F. Bills, A. W. Dombrowski, M. S. Springer, S. Siciliano, L. Malkowitz, M. Sanchez, Z. Guan, S. Tiwari, D. W. Stevenson, R. P. Borris, S. B. Singh, *J. Nat. Prod.* **2004**, *67*, 1036.
[10] R. A. Davis, G. K. Pierens, *Magn. Reson. Chem.* **2006**, *44*, 966.
[11] P. C. Healy, A. Hocking, N. Tran-Dinh, J. I. Pitt, R. G. Shivas, J. K. Mitchell, M. Kotiw, R. A. Davis, *Phytochemistry* **2004**, *65*, 2373.
[12] Y. Lin, X. Wu, S. Feng, G. Jiang, J. Luo, S. Zhou, L. L. P. Vrijmoed, E. B. G. Jones, K. Krohn, K. Steingröver, F. Zsila, *J. Org. Chem.* **2001**, *66*, 6252.
[13] K. Borgschulte, S. Rebuffat, W. Trowitzsch-Kienast, D. Schomburg, J. Pinon, B. Bodo, *Tetrahedron* **1991**, *47*, 8351.
[14] T. C. Fleischer, R. D. Waigh, P. G. Waterman, *J. Nat. Prod.* **1997**, *60*, 1054.
[15] C. Riche, C. Pascard-Billy, M. Devys, A. Gaudemer, M. Barbier, J.-F. Bousquet, *Tetrahedron Lett.* **1974**, *15*, 2765.

Received August 11, 2009