Phytochemistry Letters 6 (2013) 26–30

Contents lists available at SciVerse ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Panamonon A and B, a pair of novel tetrahydrobenzofuran derivatives from *Litsea panamonja* (Nees) Hook. f.

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ARTICLE INFO

Article history:
Received 14 May 2012
Received in revised form 17 September 2012
Accepted 12 October 2012
Available online 3 November 2012

Keywords:
Litsea panamonja (Nees) Hook. f.
Lauraceae
Panamonon
Tetrahydrobenzofuran-2,5-dione
Homogentisic acid

ABSTRACTS

A pair of novel tetrahydrobenzofuran-2,5-dione derivatives with a unique C_{18} carbon skeleton, panamonon A (**1**) and B (**2**), was isolated from the leaves and twigs of *Litsea panamonja* (Nees) Hook. f. These new compounds contain an unprecedented C_{18} carbon skeleton consisting of a characteristic tetrahydrobenzofuran-2,5(3H,6H)-dione core with a biosynthetically extended geranyl side chain, designated as "panamonane". Their structures were elucidated by comprehensive spectroscopic analyses. A plausible biosynthetic pathway for **1** and **2** is discussed. The isolates were evaluated for cytotoxic activities against human tumor cell lines HL-60, SMMC-7721, A-549, MCF-7, and SW480.

1. Introduction

The genus *Litsea* contains structurally diverse and biologically active aporphine alkaloids (Hart et al., 1969; Bhakuni and Gupta, 1983; Holloway and Scheinmann, 1973; Yang et al., 2005), butanolides (Chen et al., 1998; Cheng et al., 2001), flavonoids (Wang et al., 2010), and sesquiterpenes (Hoang et al., 2002; Zhang et al., 2001, 2003, 2003; Wang et al., 2011). *Litsea panamonja* (Nees) Hook. f., an evergreen tree, is found in southern Asia including Vietnam, India, and Southern China at altitudes of 800–1600 m (Li, 1979). No phytochemical studies on the species *L. panamonja* have been reported to date. As part of our continuing research on plants of the genus *Litsea*, the chemical constituents of the leaves and twigs of *L. panamonja* were investigated. Herein, we report the isolation, structural elucidation, the possible biosynthetic pathway, and evaluation for cytotoxic activities against five human tumor cell lines, of a pair of novel tetrahydrobenzofuran-2,5-dione derivatives with a unique C_{18} carbon skeleton, panamonon A and B (**1** and **2**).

2. Results and discussion

The ethanol extraction of the powdered leaves and twigs of *L. panamonja* was partitioned into diethyl ether. The ether soluble fraction was first chromatographed on a silica gel column, followed by separation on a reversed-phase silica gel column, and finally on a Sephadex LH-20 column, to give two compounds, **1** and **2**.

Compound **1**, $[\alpha]_D^{20}$ −30.8 (*c* 2.34, $CHCl_3$), was isolated as a colorless gum. High resolution electrospray ionization mass spectrometry (HRESIMS), *m/z* 327.1575 ($[M+Na]^+$), allowed the determination of the molecular formula, $C_{18}H_{24}O_4$. The molecular formula indicates seven degrees of unsaturation. The bands at 1784, 1712 and 1617 cm^{-1} in the IR spectrum revealed the presence of one γ-lactone, a conjugated ketone, and olefinic groups, respectively. For compound **1**, the signals of methylene protons overlapped heavily when ^1H NMR spectrum was measured in $CDCl_3$. The resolution of methylene signals was improved when DMSO-d_6 was used as the solvent. Thus, the NMR spectra of compound **1** were recorded in DMSO-d_6.

The ^1H NMR spectra displayed the presence of three methyl groups δ 1.46, 1.85, and 2.05), a 2H singlet at δ 3.13 (s), one oxygen-bearing methine proton (δ 4.69, dd, J = 12.7, 4.2 Hz, H-7a), and two trisubstituted olefinic protons at δ 5.25 (t) and 6.16 (s). Two pair of characteristic mutually coupling methylene doublets protons were also observed at δ 2.67 and 2.41 (d, ^2J = 16.1 Hz), and at δ 2.60 and 2.47 (d, ^2J = 15 Hz). The ^{13}C NMR spectrum of **1** exhibited 18 carbon signals and confirmed the presence of three vinylic methyl carbons; six methylene carbons; three methine, including an oxygen-bearing carbon at δ 82.6, and two olefinic methine carbons at δ 122.4 and 123.4; six quaternary carbons, including two olefinic carbons at δ 134.5 and 155.0, one ketone carbonyl at δ 207.5 (C-5),

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http://dx.doi.org/10.1016/j.phytol.2012.10.008

Table 1
^{1}H and ^{13}C NMR data, ^{1}H-^{1}H COSY, and HMBC correlations for **1**.

Position	δ_H[a] (J in Hz)	δ_C,[b] type	^{1}H–^{1}H COSY	HMBC
2		176.5[d] s		
3α	2.67 (1H, *d*, 16.1)[c]	40.1 t		C-7a, C-2, C-1′, C-4, C-3a
β	2.41 (1H, *d*, 16.2)			C-7a, C-1′, C-4
3a		47.7 s		
4α	2.60 (1H, *d*, 15)	45.1 t		C-3, C-1′, C-3a, C-5, C-7a
β	2.47 (1H, *d*, 14.7)			C-3, C-1′, C-3a, C-5, C-7a
5		207.5 s		
6	2.50 (2H, *m*)	38.1 t	H-7	C-4, C-7, C-7a, C-5
7α	2.21 (1H, *m*, overlap)	21.9 t	H-6, H-7a	C-3a, C-5, C-6, C-7a
β	2.29 (1H, *m*)			C-3a, C-5, C-6, C-7a
7a	4.69 (1H, *dd*, 12.7, 4.2)	82.6 d	H-7α,	C-3, C-3a, C-7, C-1′,
1′	2.08 (1H, *m*, overlap)	28.5 t	H-2′, H_3-10′	C-2′, C-3′
	1.90 (1H, *m*, overlap)			C-7a, C-4
2′	5.25 (1H, *t*, 7.1)	122.4 d	H-1′, H_3-10′ (w), H-4′ (w),	C-4′, C-1′, C-10′
3′		134.5 s		
4′	3.13 (2H, *s*)	55.1 t	H-6′, H-2′	C-2′, C-3′, C-5′, C-10′
5′		198.4 s		
6′	6.16 (1H, *s*)	123.4 d	H-8′, H-9′	C-5′, C-8′, C-9′
7′		155.0 s		
8′	2.05 (3H, *s*)	20.6 q	H-6′	C-5′, C-6′, C-7′, C-9′
9′	1.85 (3H, *s*)	27.5 q	H-6′	C-6′, C-7′, C-8′
10′	1.46 (3H, *s*)	16.8 q	H-2′	C-2′, C-3′, C-4′

[a] Spectra recorded at 500 MHz in DMSO-d_6.
[b] Spectra recorded at 125 MHz in DMSO-d_6.
[c] J values (in Hz) in parentheses.
[d] Multiplicities deduced by DEPT. (w) = weak.

one α, β-conjugated keto carbonyl at δ 198.4, and one lactone carbonyl carbon at δ 176.5. Strong UV absorption at 242 nm confirmed the presence of an α, β-conjugated ketone. Five of the seven degrees of unsaturation inherent in the formula were accounted for by the 2 double bonds and 3 carbonyl groups.

The three vinyl methyls together with the two trisubstituted double bonds suggested the presence of a geranyl side chain in **1**. Combined analysis of ^{1}H–^{1}H COSY, HMQC, and HMBC spectra (Table 1) provided further support for the geranyl side chain. In the ^{1}H–^{1}H COSY spectrum, the methyl groups at δ 1.85 (H-9′) and 2.05 (H-8′) showed a long-range allyl coupling with the C-6′ methine. Other correlations H-1′/H-2′, H-2′/H-10′, H-2′/H-4′, H-4′/H-6′ and the HMBC long-range correlations: between H-4′ and C-2′, C-3′, C-5′, and C-10′; between H-6′ and C-5′, C-8′, and C-9′; and between H-10′ and C-2′and C-3′ were observed. All these were consistent with the presence of a geranyl side chain in **1**. Further analysis of the ^{1}H–^{1}H COSY spectrum revealed that the oxygen-bearing methine proton signal at δ 4.69 (H-7a) was coupled with H-7, which, in turn, was coupled with H-6. Taken together, this suggested that C-7a was connected to C-7, which was then connected to C-6 (Fig. 2). The HMBC correlations between: H_2-4 and C-3, C-3a, C-1′, C-5, and C-7a; between H_2-6 and C-4, C-5, C-7a, and C-7; between H-7a and C-3, C-3a, C-7, and C-1′; and between H_2-3 and C-2, C-3a, C-4, and C-7a established the presence of a tetrahydrobenzofuran-2, 5 (3H, 6H)-dione subunit. The characteristic IR band for a γ-lactone at 1784 cm^{-1} confirmed the presence of the γ-lactone moiety, which was fused to the six-member ring at C-3a and C-7a. The position of the geranyl side chain at C-3a was determined by the HMBC correlations between: H_2-1′ and C-4 and C-7a; H_2-4 and C-1′; H-7a and C-1′; and H_2-3 and C-1′. Thus, the final planar structure of **1** was demonstrated as depicted in Fig. 2. Compound **1** possesses an unprecedented C_{18} skeleton with a tetrahydrobenzofuran-2,5(3H,6H)-dione framework and a biosynthetically extended geranyl side chain at C-3a.

The relative stereochemistry of **1** was obtained through an analysis of the ROESY spectrum and consideration of coupling constants (Fig. 3). The large coupling constants of H-7a (dd, J = 12.7, 4.2 Hz) suggested that H-7a was in an α-axial position, i.e. the 7a-O-atom was in a β-equatorial position (Takeda et al., 1992; Xie et al., 2012), which was further supported by the NOESY correlation. The NOESY correlations between H-7a and H-7α, H-4α and H-3 confirmed an axial orientation of H-7a. H_2-1′ showed NOEs with H-4β and H-7β, which established the axial orientation of the geranyl group at C-3a (Fig. 3). The *E* configuration of the $\Delta^{1'}$ geranyl double bond at C-2′ follows from the observation of an additional NOE between H-1′ with Me-10′. Thus, the relative stereochemistry of **1** was assigned as (3a*R**, 7a*S**). Accordingly, **1** was established to be 3*a*-((*E*)-3,7-dimethyl-5-oxoocta-2,6-dienyl)tetrahydrobenzofuran-2,5(3H,6H)-dione and given the trivial name of panamonon A (Fig. 1). This represents a unique C_{18} structural skeleton that has not previously been reported in nature.

Compound **2** was isolated as light yellow gum and has the same molecular formula as **1,** as determined by HRESIMS ([M+Na]$^{+}$ m/z

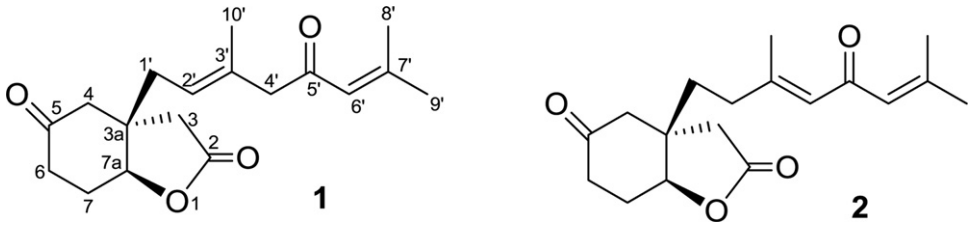

Fig. 1. The structures of compounds **1** and **2**.

Table 2
NMR data of compound **2** [$CDCl_3$, 500 MHz (^1H), 125 MHz (^{13}C), δ (ppm)].

Position	δ_H (J in Hz)	δ_C, type	Position	δ_H (J in Hz)	δ_C, type
2	/	175.5 s	2′	2.00 (2H, *m*, overlap)	35.2 t
3α	2.56 (1H, *d*, 16.4)	41.6 t	3′	/	155.1 s
β	2.41 (1H, *d*, 15, overlap)				
3a	/	44.9 s	4′	5.94 (1H, *s*)	126.8 d
4α	2.37 (1H, *d*, 15.5)	48.7 t	5′	/	191.6 s
β	2.66 (1H, *d*, 15.5)				
5	/	205.9 s	6′	5.98 (1H, *s*)	126.4 d
6	2.59 (1H, *m*)	38.5 t	7′	/	155.5 s
	2.31 (1H, *m*)				
7α	2.07 (1H, *m*, overlap)	22.6 t	8′	2.09 (3H, *s*)	21.0 q
β	2.32 (1H, *m*, overlap)				
7a	4.45 (1H, *dd*, 13.2, 4.3)	84.0 d	9′	1.83 (3H, *s*)	28.1 q
1′	1.43 (1H, *ddd*, 15.1, 4.2, 4.6)	28.6 t	10′	2.05 (3H, *s*)	19.5 q
	1.31 (1H, *ddd*, 14.5, 4.2, 4.5)				

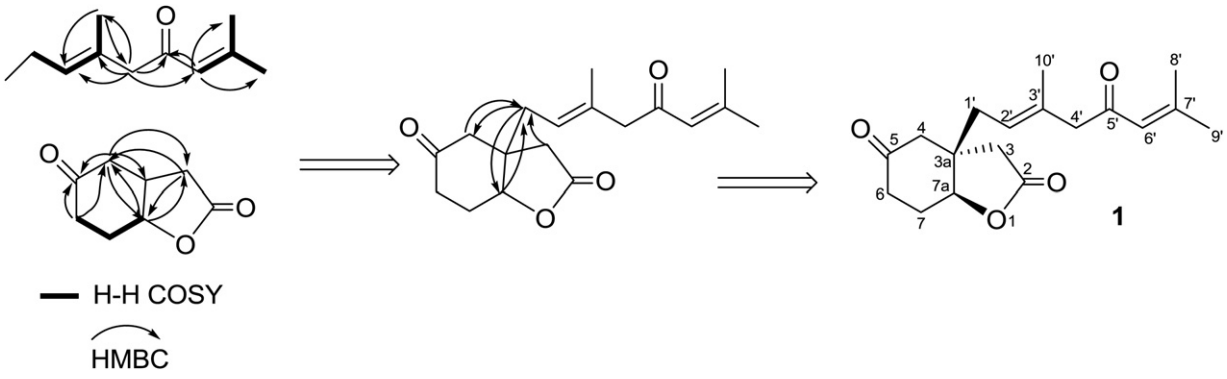

Fig. 2. The structure deduction of compound **1**.

327.1581). The NMR data of **2** suggested that its structure was very similar to that of **1** (Table 2). It differs from **1** only by the shift of the double bond at $\Delta^{2',3'}$ in **1** to $\Delta^{3',4'}$ in **2** to form a 3′,6′-dien-5′-one conjugated structural subunit. The absence of a 2H singlet proton signal at δ 3.13 and the presence of a methylene proton signal at δ 2.00 is consistent with the shift of the double bond at $\Delta^{2',3'}$ in **1** to $\Delta^{3',4'}$ in **2**. This shift is further supported by the ^1H–^1H COSY correlation between the proton signal at δ 1.43 (1H, ddd, J = 15.1, 4.2, 4.6 Hz, H-1′) and the proton signal at δ 2.00 (2H, m, H-2′). The HMBC correlations between H-1′ (δ 1.43, 1.31) and C-2′, C-3′; between H-2′ (δ 2.00) and C-1′, C-3′, C-4′, C-10′; and between H-4′ (δ 5.94) and C-2′, C-3′, C-5′ and C-10′, confirmed the shift of the double bond ′ in **2**. The formation of a 3′,6′-dien-5′-one group results in significant upfield shift of the ^{13}C NMR signal of the carbonyl carbon C-5′ and downfield shifts of the signals of C-3′, C-4′and C-6′. A ROESY cross correlation between H-4′ and H-6′ established that **2** also has an *E* configuration of double bond at $\Delta^{3',4'}$. Compound **2** shared the same relative stereochemistry with **1** based on the analysis of NOE correlations and coupling constants (Fig. 3). Therefore, **2** was established as 3a-((*E*)-3,7-dimethyl-5-oxoocta-3,6-dienyl)-tetrahydrobenzofuran-2,5(3H,6H)-dione and named panamonon B (Fig. 1).

Panamonone A (**1**) and B (**2**) represent examples of a unique C_{18} structural skeleton that has not been previously reported in nature. They both possess an unprecedented skeleton with a tetrahydrobenzofuran-2,5(3H,6H)-dione framework and a biosynthetically extended geranyl side chain at C-3a. We have designated this structural type as "panamonane". Earlier studies reported a prototypic litsane sesquiterpene that was isolated from *L. verticillata* (Zhang et al., 2001, 2003). The similarity between panamonane and the litsane sesquiterpene was the presence of a geranyl side chain in their skeletons.

Panamonone A (**1**) and B (**2**) belong to a new structural type consisting of 18 carbons in its skeleton, by virtue of its novelty, a plausible biogenetic pathway for panamonone A and B is proposed as shown in Fig. 4. Panamonone A (**1**) must be generated first by an alkylation reaction between homogentisic acid and geranyl diphosphate to form compound **A**. Subsequent oxidation of compound **A** would produce compound **B**, the α, β-conjugated keto group in which, would in turn be reduced to a hydroxyl group to form compound **C**. Compound **C** then could be transformed to Panamonone A by the formation of a γ-lactone group through an esterification reaction. Panamonone B could be formed through an isomerization of the double bond from **1** (Zhang et al., 2006).

Compounds **1** and **2** were evaluated for cytotoxic activities against five human tumor cell lines: HL-60, SMMC-7721, A-549, MCF-7, and SW480, where they proved to be inactive ($IC_{50} > 40$ μM). Further bioassay studies are being pursued.

3. Experimental

3.1. General experimental procedures

Commercial silica-gel plates (Qing Dao Marine Chemical Group Co.) were used for TLC analyses. UV spectra was measured on a Shimadzu UV-2401PC spectrophotometer, λ_{max} in nm. Optical rotation was obtained on a Horiba SEAP-300 spectropolarimeter. IR spectra were measured on a Bio-Rad FTS-135 infrared spectrophotometer, ν_{max} in cm^{-1}. ^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) as well as 2D NMR spectra were recorded on a Brucker DRX-500 spectrometer, chemical shifts δ in ppm rel. to TMS, coupling

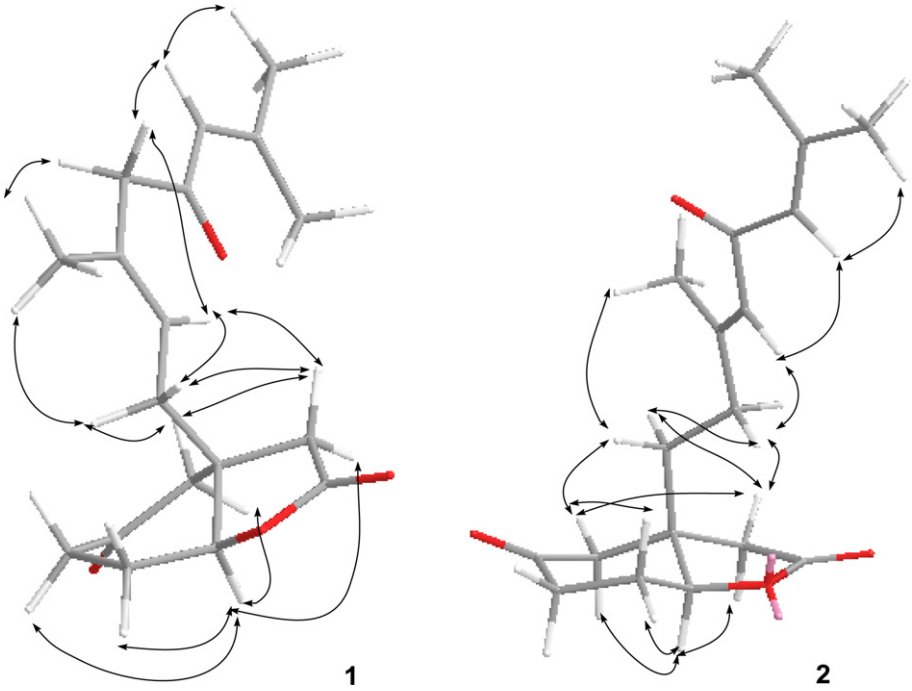

Fig. 3. The selected NOESY correlations of **1** and **2**.

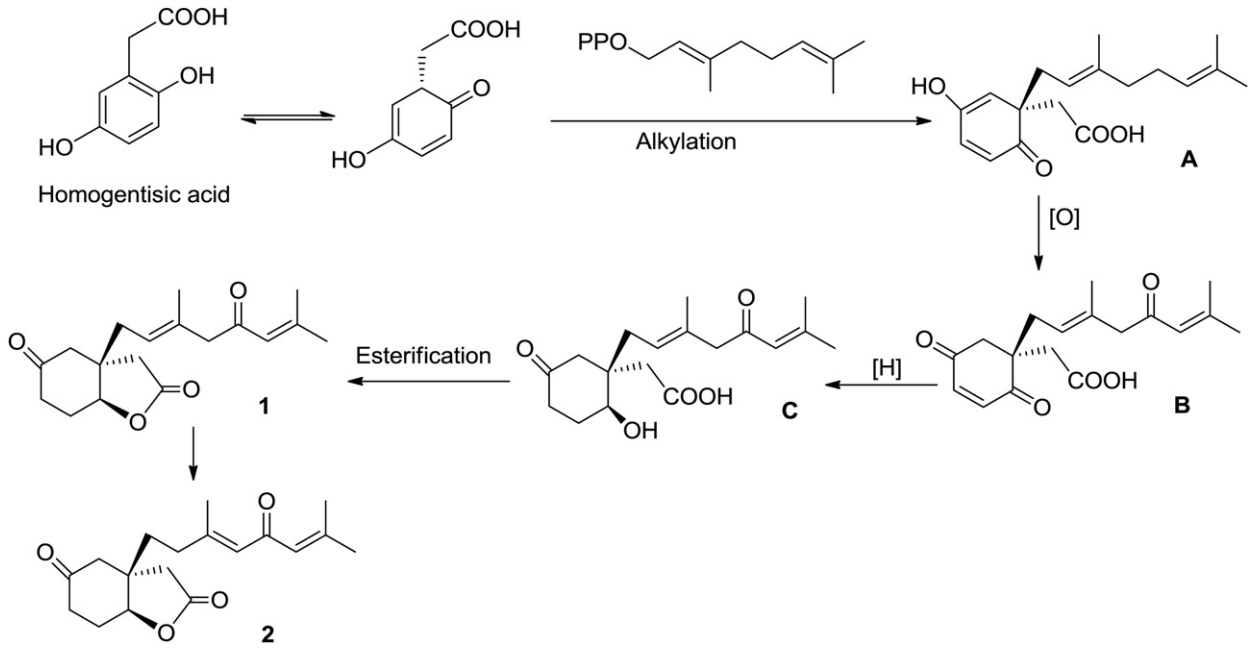

Fig. 4. Proposed biosynthetic pathway for panamonon A (**1**) and B (**2**).

constant *J* in Hz. ESI-MS spectra were acquired on a VG-Autospec 3000 mass spectrometer.

3.2. Plant material

The leaves and twigs of *L. panamonja* (Nees) Hook. f. were collected in Xishuangbanna, Yunnan Province, PR China, in May 2008, and identified by Professor Jing-Rong Cui. A voucher specimen is deposited in Key Laboratory of Medicinal Chemistry for Natural Resource, Ministry of Education, School of Chemical Science and Technology, Yunnan University.

3.3. Extraction and Isolation

Powdered leaves and twigs of *L. panamonja* (10.0 kg) were repeatedly extracted with EtOH at room temperature. The extract was then concentrated under reduced pressure to give a brown syrup, which was then partitioned in H_2O with solvents of increasing polarity to yield an ether-fraction (120 g) and a n-BuOH-fraction (150 g) fraction. The ether-soluble fraction was subjected to silica gel column chromatography and eluted with petroleum ether-ethyl acetate (9:1–1:1), ethyl acetate to afford eighteen fractions (I–XVIII). Fraction XV (15 g) was further

separated by reversed-phase silica gel column chromatography eluted with H_2O–MeOH (7:3, 6:4, 5:5, 4:6, 3:7), and then followed by Sephadex LH-20 column chromatography ($CHCl_3$–MeOH elution) to give **1** (6 mg) and **2** (3 mg).

3.4. Panamonon A (1)

Colorless gum; $[\alpha]_D^{20}$ −30.8 (*c* 2.34, $CHCl_3$); IR (KBr) ν_{max} 2958, 2922, 1784, 1712, 1617, 1436, 1376, 1279, 1180, 1036; UV ($CHCl_3$) λ_{max} 242; for ^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectroscopic data see Table 1; ESI-MS: *m*/*z* (positive ions) 327 $[M+Na]^+$, 124; HRESIMS: *m*/*z* 327.1575 $[M+Na]^+$ (calcd for $C_{18}H_{24}O_4Na$, 327.1572).

3.5. Panamonon B (2)

Colorless gum; $[\alpha]_D^{20}$ −41.69 (*c* 0. 66, CH_3OH); IR (KBr) ν_{max} 2355, 1781, 1641, 1548, 1401, 1012; UV ($CHCl_3$) λ_{max} 278; for ^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectroscopic data see Table 2; ESI-MS: *m*/*z* (positive ions) 327 $[M+Na]^+$, 124; HRESIMS: *m*/*z* 327.1581 $[M+Na]^+$ (calcd for $C_{18}H_{24}O_4Na$, 327.1572).

3.6. Bioassays

Human cancer cell lines myeloid leukemia HL-60, hepatocellular carcinoma SMMC-7721, lung cancer A-549, breast cancer MCF-7, and colon cancer SW480 cells were used in the cytotoxic assay performed according to the MTT (3-(4,5-dimethylthiazol-2-yl)-3,5-di-phenytetrazoliumromide) method in 96-well microplates (Jiang et al., 2011). Cells were cultured in RPMI-1640 or DMEM medium (Hyclone, USA), supplemented with 10% fetal bovine serum (Hyclone, USA) in 5% CO_2 at 37 °C.

Acknowledgements

This work was supported by the National Nature Science Foundation of China (Nos. 21262040, 20862018, and 21162038), the Science Foundation of Yunnan University (Grant No. 2009B10Q), Open Fund of Key Laboratory of Medicinal Chemistry for Natural Resource (Grant No. X3109007), Ministry of Education, and the Yong Academic and Technical Leader Raising Foundation of Yunnan Province (Grant No. 2007PY01-23). We thank Dr. Michael W. Nee, Oberlin College, Ohio, USA for kind help.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.phytol.2012.10.008.

References

Bhakuni, D.S., Gupta, S., 1983. Alkaloids of *Litsea wightiana*. Planta Med. 48, 52–54.
Chen, I.S., Lai Yaun, I.L., Duh, C.Y., Tsai, I.L., 1998. Cytotoxic butanolides from *Litsea akoensis*. Phytochemistry 49, 745–750.
Cheng, H.I., Lin, W.Y., Duh, C.Y., Lee, K.H., Tsai, I.L., Chen, I.S., 2001. New cytotoxic butanolides from *Litsea acutivena*. J. Nat. Prod. 64, 1502–1505.
Hart, N.K., Johns, S.R., Lamberton, J.A., Loder, J.W., Moorhouse, A., Sioumis, A.A., Smith, T.K., 1969. Alkaloids of several *Litsea* species from new Guinea. Aust. J. Chem. 22, 2259–2262.
Hoang, V.D., Tan, G.T., Zhang, H.J., Tamez, P.A., Hung, N.V., Cuong, N.M., Soejarto, D.D., Fong, H.H.S., Pezzuto, J.M., 2002. Natural anti-HIV agents – Part 1: (+)-demethoxyepiexcelsin and verticillatol from *Litsea verticillata*. Phytochemistry 59, 325–329.
Holloway, D.W., Scheinmann, F., 1973. Co-occurrence of aporphine and biphenyl constituents in *Litsea turfosa*. Phytochemistry 12, 1503–1505.
Jiang, M.Y., Li, Y., Wang, F., Liu, J.K., 2011. Isoprenylated cyclohexanoids from the basidiomycete *Hexagonia speciosa*. Phytochemistry 72, 923–928.
Li, X.W., 1979. Flora Reipublicae Popularis Sinicae. Tomus 31. Science Press, Beijing, p. 305.
Takeda, Y., Ichihara, T., Yamasaki, K., Otsuka, H., Utsumi, H., 1992. Flexarabdonins I, J and K, ent-kaurenoids from *Rabdosia inflexa*. Phytochemistry 32, 145–150.
Xie, W.D., Li, X., Zhao, J.H., Liu, Y.H., Row, K.H., 2012. Abietane diterpenoids from *Isodon inflexus*. Phytochemistry 81, 153–158.
Wang, Y.S., Huang, R., Lu, H., Li, F.Y., Yang, J.H., 2010. A new 2′-oxygenated flavone glycoside from *Litsea glutinosa* (Lour.) C. B. Rob. Biosci. Biotech. Biochem. 74, 652–654.
Wang, Y.S., Liao, Z., Li, Y., Huang, R., Zhang, H.B., Yang, J.H., 2011. A new megastigmane diglycoside from *Litsea glutinosa* (Lour) C. B. Rob. J. Braz. Chem. Soc. 22, 2234–2238.
Yang, J.H., Li, L., Wang, Y.S., Huang, R., Zhao, J.F., Luo, S.D., 2005. Two new aporphine alkaloids from *Litsea glutinosa*. Helv. Chim. Acta 88, 2523–2526.
Zhang, H.J., Tan, G.T., Hoang, V.D., Hung, N.V., Cuong, N.M., Soejarto, D.D., Pezzuto, J.M., Fong, H.H.S., 2001. Litseaverticillol A a prototypic litseane sesquiterpene from *Litsea verticillata*. Tetrahedron Lett. 42, 8587–8591.
Zhang, H.J., Tan, G.T., Hoang, V.D., Hung, N.V., Cuong, N.M., Soejarto, D.D., Pezzuto, J.M., Fong, H.H.S., 2003. Natural anti-HIV agents – Part 3: Litseaverticillols A-H, novel sesquiterpene from *Litsea verticillata*. Tetrahedron 59, 141–148.
Zhang, H.J., Ma, C.Y., Hung, N.V., Cuong, N.M., Tan, G.T., Santarsiero, B.D., Mesecar, A.D., Soejarto, D.D., Pezzuto, J.M., Fong, H.H.S., 2006. Miliusanes, a class of cytotoxic agents from *Miliusa sinensis*. J. Med. Chem. 49, 693–708.