Cadinane and Eudesmane Sesquiterpenoids from *Chloranthus henryi*

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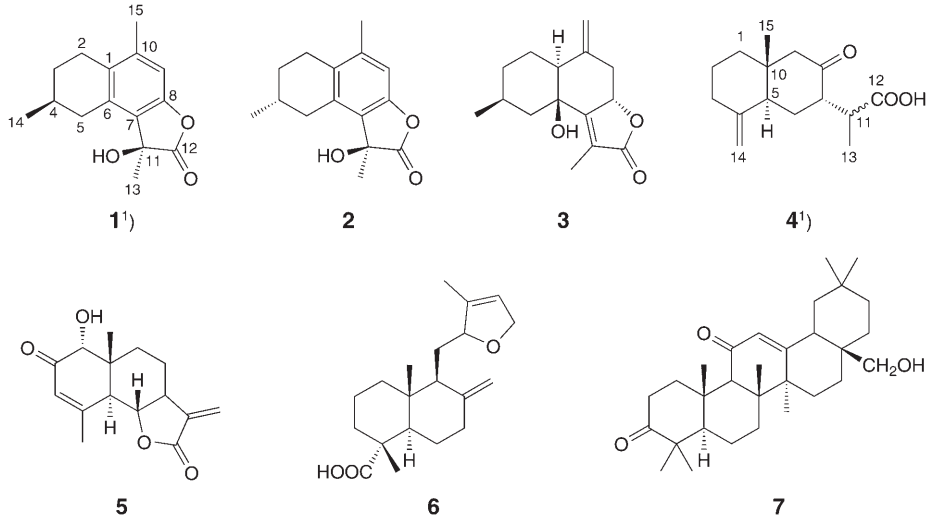
Chemical investigation of the leaves and stems of *Chloranthus henryi* resulted in the isolation and characterization of the three new cadinane-type sesquiterpenes **1**–**3** and of the new eudesmane-type sesquiterpene **4**, together with three known compounds. Among the new compounds, the two cadinane-type sesquiterpenes **1** and **2** possess an unusual aromatic ring B in their molecule. These structures were established on the basis of spectroscopic evidence. In addition, antitumor activities of the isolates were also evaluated.

Introduction. – *Chloranthus henryi* HEMSL., with the Chinese name 'dayejiji' and belonging to the Chloranthaceae family, has long been used as a folk medicine in mainland China for removing the toxic substances from the body [1]. Species of the genus *Chloranthus* are known to be rich in sesquiterpenes of the lindenane and eudesmane-type [2–9] including sesquiterpenoid dimers and trimers [10–15]. Other constituents like flavonoids and amides have also been reported [5][16]. Previous phytochemical investigations of *C. henryi* have shown the presence of diterpenes, sesquiterpenes, and coumarins [17–19]. The present phytochemical study of this species resulted in the isolation of three new cadinane-type sesquiterpenes, (11β)-8,11-dihydroxycadina-6,8,10-trien-12-oic acid γ-lactone[1]) (**1**), (4α,11β)-8,11-dihydroxycadina-6,8,10-trien-12-oic acid γ-lactone[1]) (**2**), (8α)-6,8-dihydroxycadina-7(11),10(15)-dien-12-oic acid γ-lactone[1]) (**3**), and one new eudesmane-type sesquiterpene, (7α)-8-oxoeudesm-4(14)-en-12-oic acid[1]) (**4**), together with three known compounds, tanapraetenolide (**5**), 12,15-epoxylabda-8(20),13-dien-18-oic acid (**6**), and 28-hydroxyolean-12-ene-3,11-dione (**7**). Compound **3** showed cytotoxicity against the Hela, A549, MCF, and K562 human-tumor cell lines.

Results and Discussion. – Compound **1** was obtained as a yellowish oil. The HR-FT-ICR-MS exhibited a molecular-ion peak at m/z 269.1150 ($[M+Na]^+$), indicating that the molecular formula is $C_{15}H_{18}O_3$. The IR spectrum revealed the presence of OH, benzyl, and lactone groups characterized by absorptions at 3444, 1772, 1618, 1494, and 1350 cm^{-1}. The ^{1}H- and ^{13}C-NMR (*Table 1*), COSY, HMQC, HMBC, and NOESY data allowed to elucidate the structure of **1** as (11β)-8,11-dihydroxycadina-6,8,10-trien-12-oic acid γ-lactone.

[1]) Trivial atom numbering; for systematic names, see *Exper. Part.*



An aromatic-proton signal appeared at δ(H) 6.79 (*s*, H–(9)) in the ^{1}H-NMR spectrum of **1**, which, along with the signals at δ(C) 110.1 (*d*, C(9)), 123.1 (*s*, C(7)), 131.8 (*s*, C(1)), 135.6 (*s*, C(6)), 139.4 (*s*, C(10)), and 150.6 (*s*, C(8)) in the ^{13}C-NMR spectrum, confirmed the presence of a benzene ring in the molecule. The HMBC data established the presence of a cadinane-type backbone with an unusual aromatic ring B [20]. The long-range correlations from the signals at δ(H) 2.52–2.57 (*m*, H_α–C(2)) and 2.74–2.76 (H_β–C(2)) to the signals at δ(C) 28.2 (C(4)), 135.6 (C(6)), and 131.8 (C(1)), and the correlations from the signal at δ(H) 1.11 (*d*, J = 6.5 Hz, Me(14)) to the signals at δ(C) 31.5 (C(3)), 28.2 (C(4)), and 33.9 (C(5)), indicated the presence of a ring A moiety with the Me group attached to C(4). The ring-B moiety was suggested by the long-range correlations from the signals at δ(H) 2.52–2.57 (H_α–C(2)) and 2.74–2.76 (*m*, H_β–C(2)) to the signals at δ(C) 135.6 (C(6)), 139.4 (C(10)), and 131.8 (C(1)), and the correlations from the signals at δ(H) 3.21–3.25 (*m*, H_α–C(5)) and 2.35–2.37 (*m*, H_β–C(5)) to the signals at δ(C) 135.6 (C(6)), 123.1 (C(7)), and 131.8 (C(1)), as well as the correlations from the signal at δ(H) 2.33 (*s*, Me(15)) to the signals at δ(C) 110.1 (C(9)), 139.4 (C(10)), and 131.8 (C(1)). The OH group was located at C(11) (*s* at δ(C) 73.8) due to the long-range correlations from the signal at δ(H) 1.76 (*s*, Me(13)) to the signals at δ(C) 73.8 (C(11)), 177.8 (C(12)), and 123.1 (C(7)) in the HMBC plot. The relative configuration of **1** was determined on the basis of the NOESY experiment. The observation of NOESY correlations δ(H) 1.79–1.81 (*m*, H–C(4))/δ(H) 1.98–2.02 (*m*, H_α–C(3)) and 3.21–3.25 (*m*, H_α–C(5)), and δ(H) 1.11 (*d*, J = 6.5 Hz, Me(14))/δ(H) 2.74–2.76 (*m*, H_β–C(2)), 1.37–1.43 (*m*, H_β–C(3)), and 2.35–2.37 (*m*, H_β–C(5)) suggested that H–C(4), H_α–C(2), H_α–C(3), and H_α–C(5) are on the same face of the molecule, while Me(14) is in the β-configuration. The strong NOESY correlation δ(H) 1.76 (*s*, Me(13))/δ(H) 3.21–3.25 (*m*, H_α–C(5)) indicated that OH–C(11) is in a β-configuration, as shown.

Compound **2** was obtained as yellowish oil. The HR-FT-ICR-MS exhibited a molecular-ion peak at *m*/*z* 247.1327 ($[M+H]^+$), corresponding to the same molecular formula, $C_{15}H_{18}O_3$, as that of compound **1**. The UV and IR spectra of **2** exhibited the same general patterns as those of **1**. Based on the ^{1}H- and ^{13}C-NMR (*Table 1*) and NOESY data, the structure of **2** was determined as (4α,11β)-8,11-dihydroxycadina-6,8,10-trien-12-oic acid γ-lactone.

Table 1. *NMR Data* ((D$_6$)DMSO) *of* **1**–**3**[1]). δ in ppm, J in Hz.

Position	**1**		**2**		**3**	
	δ(C)[a])[b])	δ(H)[c])	δ(C)[a])[b])	δ(H)[c])	δ(C)[a])[b])	δ(H)[c])
C(1) or H–C(1)	131.8 (*s*)		131.8 (*s*)		49.5 (*s*)	2.04–2.08 (overlap)
CH_2(2)	26.9 (*t*)	2.52–2.57 (*m*, H_α), 2.74–2.76 (*m*, H_β)	26.2 (*t*)	2.52–2.57 (overlap, H_α), 2.73 (*d*, J = 13.3, H_β)	24.1 (*d*)	1.74–1.78 (*m*, H_α), 1.79–1.81 (*m*, H_β)
CH_2(3)	31.5 (*t*)	1.98–2.02 (*m*, H_α), 1.37–1.43 (*m*, H_β)	30.8 (*t*)	1.90–1.94 (*m*, H_α), 1.49–1.54 (*m*, H_β)	34.2 (*t*)	1.82–1.87 (*m*, H_α), 1.07–1.10 (*m*, H_β)
H–C(4)	28.2 (*d*)	1.79–1.81 (*m*)	27.8 (*d*)	1.81–1.85 (*m*)	27.4 (*t*)	1.89–1.93 (*m*)
CH_2(5)	33.9 (*t*)	3.21–3.25 (*m*, H_α), 2.35–2.37 (*m*, H_β)	33.7 (*t*)	3.01 (*d*, J = 17.2, H_α), 2.52–2.57 (overlap)	44.8 (*s*)	2.25 (*d*, J = 9.0, H_α), 1.74–1.76 (*m*, H_β)
C(6)	135.6 (*s*)		135.3 (*s*)		73.2 (*s*)	
C(7)	123.1 (*s*)		123.1 (*s*)		162.8 (*s*)	
C(8) or H–C(8)	150.6 (*s*)		150.5 (*s*)		79.3 (*s*)	4.86–4.92 (*m*)
H–C(9) or CH_2(9)	110.1 (*s*)	6.79 (*s*)	110.1 (*s*)	6.78 (*s*)	44.1 (*s*)	3.11–3.15 (*m*, H_α), 1.95–2.01 (*m*, H_β)
C(10)	139.4 (*s*)		139.3 (*s*)		142.6 (*s*)	
C(11)	73.8 (*s*)		74.0 (*s*)		120.2 (*s*)	
C(12)	177.8 (*s*)		178.3 (*s*)		174.2 (*s*)	
Me(13)	24.1 (*q*)	1.76 (*s*)	24.3 (*q*)	1.76 (*s*)	10.7 (*q*)	2.05 (*s*)
Me(14)	22.0 (*q*)	1.11 (*d*, J = 6.5)	22.0 (*q*)	1.07 (*d*, J = 8.7)	22.6 (*q*)	1.01 (*d*, J = 6.6)
Me(15) or CH_2(15)	20.3 (*q*)	2.33 (*s*)	21.3 (*q*)	2.23 (*s*)	114.9 (*q*)	4.99, 5.20 (2*s*)

[a]) Recorded at 125 MHz. [b]) Multiplicities from DEPT and HMQC experiments. [c]) Recorded at 500 MHz.

The ^{1}H- and ^{13}C-NMR spectra of **2** showed similar chemical shifts and the same multiplicities of all C-atoms as in **1**, with minor differences, indicating the presence of a cadinane-type backbone with an aromatic ring B and an OH group in **2**. The minor differences of the δ(H) and δ(C) of CH_2(3), H–C(4), and CH_2(5) suggested that the configuration of Me(14) was different from that of **1**. This inference was confirmed by a detailed NOESY experiment. The observation of the NOESY correlations δ(H) 1.81–1.85 (*m*, H–C(4))/δ(H) 2.73 (*d*, J = 13.3 Hz, H_β–C(2)), 1.49–1.54 (*m*, H_β–C(3)), and 2.52–2.57 (*m*, H_β–C(5)), suggested that Me(14) is in an α-configuration. The NOESY correlations δ(H) 1.76 (*s*, Me(13))/δ(H) 3.01 (*d*, J = 17.2 Hz, H_α–C(5)) indicated that OH–C(11) is in a β-configuration, as for **1**.

Compound **3** was obtained as yellowish oil. The HR-FT-ICR-MS exhibited a molecular-ion peak at m/z 271.1308 ($[M+Na]^+$), corresponding to the molecular formula $C_{15}H_{20}O_3$. Detailed analysis of the 1D-NMR data of **3** (*Table 1*), aided by COSY, HMQC, and HMBC experiments, led to the assignment of a cadinane-type backbone with an exocyclic CH_2 and an OH group, and the structure of **3** was elucidated as (8α)-6,8-dihydroxycadina-7(11),10(15)-dien-12-oic acid γ-lactone.

The OH group of **3** was located at C(6) (*s*, δ(C) 73.2), due to the long-range correlations observed from δ(H) 1.89–1.93 (*m*, H–C(4)), 2.25 (*d*, J = 9.0 Hz, H_α–C(5)), 1.74–1.76 (*m*, H_β–C(5)), and 2.04–2.08 (*m*, H–C(1)), to δ(C) 73.2 (*s*, C(6)) in the HMBC plot. The NOESY correlations δ(H) 1.89–1.93 (*m*, H–C(4))/δ(H) 1.82–1.87 (*m*, H_α–C(3)) and 2.25 (*d*, J = 9.0 Hz, H_α–C(5)), and the correlations δ(H) 1.79–1.81 (*m*, H_β–C(2))/δ(H) 1.01 (*d*, J = 6.6 Hz, Me(14)), indicated that Me(14) is in a β-configuration. The correlations δ(H) 2.04–2.08 (*m*, H–C(1))/δ(H) 1.74–1.78 (*m*, H_α–C(2)) and 1.82–1.87 (*m*, H_α–C(3)) indicated that H–C(1) is in an α-configuration. The configuration at C(6) was determined by a methylation experiment with **3**. The obtained methoxy derivative showed the NOESY correlations δ(H) 3.38 (*s*, MeO–C(6))/δ(H) 1.85–1.90 (*m*, H_β–C(2)), 1.05 (*d*, J = 6.5 Hz, Me(14)), and 4.78–4.83 (*m*, H–C(8)), indicating that the two 6-membered rings are *trans*-fused and that H–C(8) is in the β-configuration.

Compound **4**, was obtained as a white powder, and the HR-FT-ICR-MS exhibited a molecular-ion peak at *m/z* 251.1675 ($[M+H]^+$), corresponding to the molecular formula $C_{15}H_{22}O_3$. The gross structure was elucidated by analysis of the 1D- and 2D-NMR data (*Table 2*) as 8-oxoeudesm-4(14)-en-12-oic acid, the same as that of an intermediate in the synthesis of natural (–)-artemisin [21]. The configuration at C(11) of **4** remains uncertain. Compound **4** was elucidated as (7α)-8-oxoeudesm-4(14)-en-12-oic acid.

The NOESY plot of **4** revealed that the relative configuration of **4** and the intermediate of the (–)-artemisin synthesis [21] were different. The NOESY correlations δ(H) 2.57–2.63 (*m*, H–C(7))/δ(H) 1.09–1.13 (*m*, H_β–C(6)) suggested that H–C(7) of **4** is in a β-configuration, differing from that of the intermediate [21].

Furthermore, a known eudesmane-type sesquiterpene, tanapraetenolide (**5**), a known labdane-type diterpene, 12,15-epoxylabda-8(20),13-dien-18-oic acid (**6**), and a known oleanane-type triterterpene, 28-hydroxyolean-12-ene-3,11-dione (**7**), were identified by comparison of their spectroscopic data with literature data [22–24].

All the compounds **1**–**7** were tested *in vitro* for antitumor activity against four human-tumor cell lines by using the MTT (= 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-1*H*-tetrazolium bromide) colorimetric method [25]. Only compound **3** showed antitumor activity against the Hela, A549, MCF, and K562 human-tumor cell lines, with IC_{50} values of 4.7, 8.9, 9.6, and 11.8 μg/ml, respectively.

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Experimental Part

General. TLC: *Merck* precoated plates (silica gel *60 F254*) of 0.25 mm thickness. HPLC: *Waters-600* prep. HPLC instrument, with a *Shim-pack PREP-ODS* (250 × 20 mm) column. Column chromatography (CC): silica gel (200–300 mesh), *Sephadex LH-20* (*Amersham*). M.p.: uncorrected; *Reichert* apparatus. Optical rotations: *Perkin-Elmer 341* polarimeter. UV Spectra: λ_{max} (log ε) in nm. IR Spectra: *Nicolet Avatar-360* FT-IR spectrometer; in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Bruker Avance-DMX-500* NMR spectrometer; at 500 (^{1}H) and 125 (^{13}C) MHz; δ in ppm rel. to $SiMe_4$ as internal standard (at 25°), J in Hz. MS: *Bruker Daltonics* mass spectrometer; ICR = ion cyclotron resonance; in *m/z*.

Plant Material. The leaves and stems of *Chloranthus henryi* HEMSL. were collected in Suichang County, Zhejiang Province, People's Republic of China, in September 2003 and identified by Dr. *Hongxiang Sun* (Zhejiang University, Hangzhou, People's Republic of China). A voucher specimen

Table 2. *NMR Data* (500 MHz, (D_6)DMSO) of **4**[l]). δ in ppm, J in Hz.

Position	δ(C)[a])[b])	δ(H)[c])	^{1}H,^{1}H-COSY[d])	HMBC[e])
CH_2(1)	41.2 (*t*)	1.26–1.31 (*m*, H_α),	CH_2(2)	C(3), C(5), C(9), C(10), C(15)
		1.54–1.58 (*m*, H_β)	CH_2(2)	C(3), C(5), C(9), C(10), C(15)
CH_2(2)	23.6 (*t*)	1.80–1.83 (*m*, H_α),	CH_2(1), CH_2(3)	C(1), C(4), C(10)
		1.45–1.51 (*m*, H_β)	CH_2(1), CH_2(3)	C(1), C(4), C(10)
CH_2(3)	37.0 (*t*)	1.89–1.93 (*m*, H_α),	CH_2(2)	C(1), C(2), C(4), C(5), C(14)
		2.27–2.32 (*m*, H_β)	CH_2(2)	C(1), C(2), C(4), C(5), C(14)
C(4)	149.8 (*s*)			
H–C(5)	48.1 (*d*)	2.40–2.45 (*m*)	CH_2(6)	C(1), C(4), C(10), C(7), C(14), C(15)
CH_2(6)	29.1 (*t*)	1.23–1.25 (*m*, H_α),	H–C(5), H–C(7)	C(4), C(5), C(7), C(8), C(10), C(11)
		1.09–1.13 (*m*, H_β)	H–C(5), H–C(7)	C(4), C(5), C(7), C(8), C(10), C(11)
H–C(7)	38.9 (*d*)	2.57–2.63 (*m*)	CH_2(6), H–C(11)	C(5), C(12), C(13), C(8), C(9)
C(8)	210.2 (*s*)			
CH_2(9)	56.1 (*t*)	1.98 (*d*, J = 15.0, H_α),		C(1), C(5), C(7), C(8), C(15)
		2.24 (*d*, J = 15.0, H_β)		C(1), C(5), C(7), C(8), C(15)
C(10)	37.4 (*s*)			
H–C(11)	52.1 (*d*)	2.73–2.77 (*m*)	H–C(7)	C(6), C(8), C(12), C(13)
C(12)	177.0 (*s*)			
Me(13)	15.0 (*q*)	1.09 (*d*, J = 8.3)	H–C(11)	C(7), C(12)
CH_2(14)	107.8 (*t*)	4.47, 4.80 (2*s*)		C(3), C(4), C(5)
Me(15)	17.93 (*q*)	0.61 (*s*)		C(1), C(5), C(9), C(10)

[a]) Recorded at 125 MHz. [b]) Multiplicities inferred from DEPT and HMQC experiments. [c]) Recorded at 500 MHz. [d]) Proton showing correlation with indicated protons. [e]) Proton showing long-range correlation with indicated C-atoms.

(zju6985) was deposited at the College of Agriculture and Biotechnology, Zhejiang University, Hangzhou, People's Republic of China.

Extraction and Isolation. The shade-dried, powdered leaves and stems (3 kg) of *Chloranthus henryi* were extracted at r.t. with MeOH (3 × 5000 ml). The extracts were concentrated to afford a gummy residue (321 g). This residue was partitioned in H_2O (3 l) and extracted successively with petroleum ether (4 × 3 l) and AcOEt (4 × 3 l). The AcOEt extract (50 g) was adsorbed on silica gel (80 g) and subjected to CC (silica gel (2000 g) 9 × 100 cm column; hexane/AcOEt gradient): *Fractions 1–11*. Small samples of these main fractions were submitted to testing of cytotoxic activities, with the oils obtained from *Fr. 2*, *4*, and *5* showing bioactivities. *Fr. 2* was subjected to prep. HPLC (MeOH/H_2O 75:25, flow 8 ml/min, detection at 250 nm): **1** (13.8 mg; t_R 65.3 min) and **2** (12.7 mg; t_R 80.9 min). *Fr. 4* was applied to CC (*Sephadex LH-20* (300 g), 8 × 150 cm column, 70% MeOH at 15°). The collected fractions were purified by HPLC (MeOH/H_2O 72:28): **4** (12.6 mg) and **5** (12.9 mg). *Fr. 5* was applied to CC (*Sephadex*

LH-20 (300 g), 8 × 150 cm column, 70% MeOH at 15°). The collected fractions were purified by HPLC (MeOH/H_2O 70:30): **6** (11.5 mg) and **7** (12.3 mg).

(11β)-8,11-Dihydroxycadina-6,8,10-trien-12-oic Acid γ-Lactone (=*(1S,8S)-6,7,8,9-Tetrahydro-1-hydroxy-1,5,8-trimethylnaphtho[2,1-*b*]furan-2(1*H*)-one*; **1**): Yellowish oil. $[\alpha]_D^{24} = -22$ ($c = 0.001$, $CHCl_3$). UV (MeOH): 212 (4.31), 253 (2.32), 270 (3.12). IR: 3444, 1772, 1618, 1494, 1350, 1133, 1043, 949, 901. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS: 269 ($[M+Na]^+$), 245 ($[M-H]^-$). HR-FT-ICR-MS: 269.1150 ($[M+Na]^+$, $C_{15}H_{18}NaO_3^+$; calc. 269.1148).

(4α,11β)-8,11-Dihydroxycadina-6,8,10-trien-12-oic Acid γ-Lactone (=*(1S,8R)-6,7,8,9-Tetrahydro-1-hydroxy-1,5,8-trimethylnaphtho[2,1-*b*]furan-2(1*H*)-one*; **2**): Yellowish oil. $[\alpha]_D^{24} = -31$ ($c = 0.001$, MeOH). UV (MeOH): 211 (4.12), 255 (2.34), 270 (3.33). IR: 3446, 1768, 1614, 1490, 1355, 1130, 1046, 958, 898. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS: 247 ($[M+H]^+$), 245 ($[M-H]^-$). HR-FT-ICR-MS: 247.1327 ($[M+H]^+$, $C_{15}H_{19}O_3^+$; calc. 247.1329).

(8α)-6,8-Dihydroxycadina-7(11),10(15)-dien-12-oic Acid γ-Lactone (=*(3aS,5aS,8S,9aS)-4,5,5a,6,7,8,9,9a-Octahydro-9a-hydroxy-1,8-dimethyl-5-methylenenaphtho[2,1-*b*]furan-2(3a*H*)-one*; **3**): Yellowish oil. $[\alpha]_D^{24} = +42$ ($c = 0.001$, MeOH). UV (MeOH): 226 (4.32). IR: 3440, 3085, 1750, 1640, 1568, 1135, 895. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-MS: 271 ($[M+Na]^+$), 247 ($[M-H]^-$). HR-FT-ICR-MS: 271.1308 ($[M+Na]^+$, $C_{15}H_{20}NaO_3^+$; calc. 271.1305).

Methylation of **3**. Compound **3** (8 mg) was methylated by refluxing overnight with MeI/K_2CO_3 in acetone. The crude product was subjected to prep. HPLC (MeOH/H_2O 78:22, flow 8 ml/min, detection at 210 nm): *(3aS,5aS,8S,9aS)-4,5,5a,6,7,8,9,9a-Octahydro-9a-methoxy-1,8-dimethyl-5-methylenenaphtho[2,1-*b*]furan-2(3a*H*)-one* (2.0 mg; t_R 34.6 min). Gum. ^{1}H-NMR ((D$_6$)acetone, 500 MHz): 5.22 (*s*, 1 H–C(15)); 4.95 (*s*, 1 H–C(15)); 4.78–4.83 (*m*, H–C(8)); 3.38 (*s*, MeO–C(6)); 3.22–3.26 (*m*, H_α–C(9)); 2.29–2.31 (*m*, H_α–C(5)); 2.02–2.04 (*m*, H_β–C(9)); 2.01–2.02 (*m*, H–C(4)); 1.99–2.01 (*m*, H–C(1)); 2.01 (*s*, Me(13)); 1.85–1.90 (*m*, H_β–C(2)); 1.83–1.85 (*m*, H_α–C(3)); 1.70–1.73 (*m*, H_α–C(2)); 1.68–1.71 (*m*, H_β–C(5)); 1.12–1.16 (*m*, H_β–C(3)); 1.05 (*d*, $J = 6.5$, Me(14)).

(7α)-8-Oxoeudesm-4(14)-en-12-oic Acid (=*(2S,4aR,8aS)-Decahydro-α,4a-dimethyl-8-methylene-3-oxonaphthalene-2-acetic Acid*; **4**): White powder. M.p. 183–185°. $[\alpha]_D^{24} = +45$ ($c = 0.001$, $CHCl_3$). UV (MeOH): 228 (3.38). IR: 3490–2500, 1713, 1692, 1640, 1552, 1456, 1372, 897, 796. ^{1}H- and ^{13}C-NMR: *Table 2*. ESI-MS: 251 ($[M+H]^+$), 249 ($[M-H]^-$). HR-FT-ICR-MS: 251.1675 ($[M+H]^+$, $C_{15}H_{23}O_3^+$; calc. 251.1672).

Cytotoxity Bioassay. The cytotoxic activities of the compounds isolated were evaluated against Hela, A549, MCF, and K562 human-tumor cell lines by using the MTT method, according to a previously described procedure [25]. DDP (*Sigma*) was used as a positive control. All experiments were carried out in triplicate.

REFERENCES

[1] B.-T. Zhou, *Zhongyaocai* **2004**, *27*, 539.
[2] J. Kawabata, S. Tahara, J. Mizutani, *Agric. Biol. Chem.* **1981**, *46*, 1447.
[3] J. Kawabata, J. Mizutani, *Agric. Biol. Chem.* **1989**, *53*, 203.
[4] Y. Li, D.-M. Zhang, J.-B. Li, S.-S. Yu, Y. Li, Y.-M. Luo, *J. Nat. Prod*. **2006**, *69*, 616.
[5] W.-Y. Tsui, G. D. Brown, *Phytochemistry* **1996**, *43*, 819.
[6] Y. Takeda, H. Yamashita, T. Matsumoto, H. Terao, *Phytochemistry* **1993**, *33*, 713.
[7] G. Kusano, M. Abe, Y. Koike, M. Uchida, S. Nozoe, Z. Taira, *Yakugaku Zasshi* **1991**, *111*, 756.
[8] S. Tahara, Y. Fukushi, J. Kawabata, J. Mizutani, *Agric. Biol. Chem.* **1981**, *45*, 1511.
[9] T. Takemoto, M. Uchida, G. Kusano, *Chem. Pharm. Bull*. **1976**, *24*, 531.
[10] J. Kawabata, Y. Fukushi, S. Tahara, J. Mizutani, *Phytochemistry* **1990**, *29*, 2332.
[11] J. Kawabata, E. Fukushi, J. Mizutani, *Phytochemistry* **1995**, *39*, 121.
[12] S.-P. Yang, J.-M. Yue, *Tetrahedron Lett*. **2006**, *47*, 1129.
[13] J. Kawabata, E. Fukushi, J. Mizutani, *Phytochemistry* **1993**, *32*, 1347.
[14] J. Kawabata, E. Fukushi, J. Mizutani, *Phytochemistry* **1998**, *47*, 231.
[15] J. Kawabata, J. Mizutani, *Phytochemistry* **1992**, *31*, 1293.

[16] T. Takemoto, M. Uchida, K. Koike, *Chem. Pharm. Bull.* **1975**, *23*, 1161.
[17] C.-J. Li, D.-M. Zhang, Y.-M. Lou, *Acta Pharmacol. Sin.* **2005**, *40*, 525.
[18] B. Wu, S. He, Y. Pan, *Planta Med.* **2006**, *72*, 1334.
[19] B. Wu, S. He, Y. Pan, *Tetrahedron Lett*. **2007**, *48*, 453.
[20] B. Tomita, Y. Hirose, *Phytochemistry* **1972**, *11*, 3355.
[21] K. Naemura, M. O. Nakazaki, *Tetrahedron Lett.* **1969**, *10*, 33.
[22] G. Naemura, *Phytochemistry* **1996**, *42*, 747.
[23] Y. C. Li, Y. H. Kuo, *Chem. Pharm. Bull.* **2002**, *50*, 498.
[24] S. Osamu, T. Toshihiko, M. Hiroshi, T. Koichi, I. Hideji, *J. Nat. Prod.* **1996**, *59*, 1072.
[25] P. R. Tweentyman, M. Luscombe, *Br. J. Cancer* **1987**, *56*, 279.

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