Three New Limonoids from the Leaves of *Cipadessa cinerascens*

by **Zhi-Guo Zhang***[a]), **Kai Yao**[b]), **Gui-Lin Hu**[a]), and **Ji Zhang**[a])

[a]) School of Light Industry, Zhejiang University of Science and Technology, Hangzhou 310023, P. R.China (phone: +86-571-85070788; fax: +86-571-85070785; e-mail: zhangzhiguo@zust.edu.cn)

[b]) Jiangsu Yuxiang Pharmaceutical Technology Co., Ltd., Yancheng 224500, P. R. China

Three new limonoids, cipadesins G–I (**1**–**3**), together with four known ones, were isolated from the leaves of *Cipadessa cinerascens*. Their structures were elucidated on the basis of 1D- and 2D-NMR data.

Introduction. – *Cipadessa cinerascens* (PELL.) HAND.–MAZZ. (Meliaceae) is a shrub mainly distributed in the Chinese southwest provinces such as Sichuan, Yunnan, Guizhou, and Guangxi [1]. Its leaves, barks, and roots have been used in Chinese folk medicine for the treatment of stomachache, dysentery, rheumatism, malaria, scald, and skin itch [2]. Previously, flavonoids and their glucosides were isolated from its leaves [3–5], and several structural novel limonoids were also reported [6–13]. This article reports the isolation and structural elucidation of the three new tetranortriterpenoids cipadesins G–I[1]) (**1**–**3**), together with cipadesin B (**4**) [6], cipadesin D (**5**) [7], cineracipadesin E (**6**) [8], and cipadesin C (**7**) [6] from the leaves of *C. cinerascens*.

Results and Discussion. – Cipadesin G (**1**) was isolated as white powder. Its molecular formula was deduced as $C_{29}H_{38}O_9$ from the HR-ESI-MS (*m*/*z* 553.2432 ($[M+Na]^+$)). The IR spectrum showed absorption bands for ketone C=O (1743 cm^{-1}) and ester C=O (1735 cm^{-1}) moieties. The ^{1}H-NMR data (*Table 1*) of **1** exhibited six Me *s* at δ(H) 1.04 (*s*, Me(18)), 0.91 (*s*, Me(19)), 1.05 (*s*, Me(28)), 0.86 (*s*, Me(29)), 2.06 (*s*, AcO–C(3)), and 3.71 (*s*, MeO) and a Me *d* at δ(H) 1.29 (*d*, J = 7.0 Hz, Me(30)), five of which were skeletal Me groups, besides three olefinic H-atoms at δ(H) 8.16 (*s*, H–C(21)), 6.66 (*s*, H–C(22)), and 7.47 (*s*, H–C(23)), suggesting the presence of a furan ring. The ^{13}C-NMR and DEPT spectra (*Table 2*) supported the existence of a furan ring by δ(C) 121.1 (*s*, C(20)), 142.2 (*d*, C(21)), 110.5 (*d*, C(22)), and 143.5 (*d*, C(23)), and also revealed a C=O group at δ(C) 212.9 (*s*, C(9)). All of these were characteristic of a cipadesin-type limonoid, in which rings *A* and *C* were connected *via* C(10) and C(11) [6]. HMBCs of H–C(5) with C(10) and C(11), and Me(19) with C(11) supported the connection. Further detailed 2D-NMR analysis confirmed the cipadesin-type limonoid skeleton as shown in *Fig. 1*. An AcO group was located at C(3) by a HMBC cross-peak H–C(3)/C=O of the AcO group, and a ROESY correlation H–C(3)/Me(19) indicated β-configuration of the AcO group. Therefore, the structure of **1** was established.

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

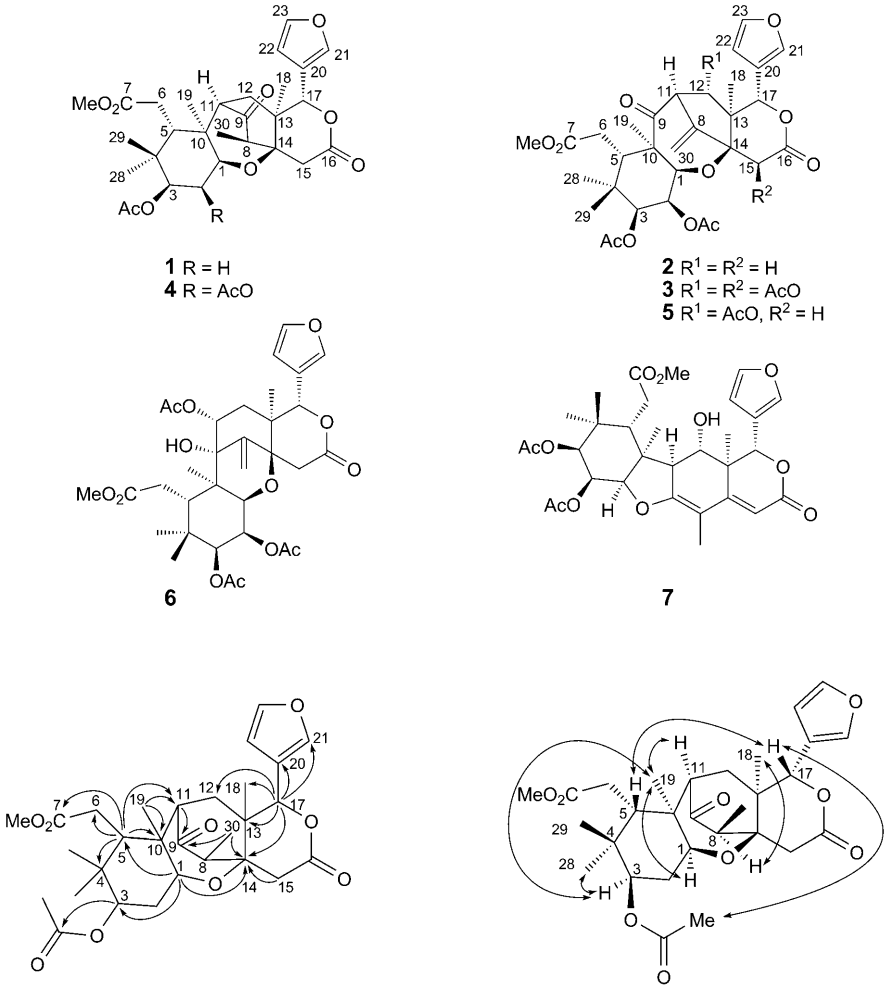

Fig. 1. *Important HMBCs* (H → C) *and ROESY* (H ↔ H) *correlations of compound* **1**

Cipadesin H (**2**) had a molecular formula $C_{31}H_{38}O_{11}$ as determined by the HR-ESI-MS (*m/z* 609.2284 ($[M+Na]^+$)). The IR peaks at 1746 and 1737 cm^{-1} suggested the presence of ketone C=O and ester C=O groups, respectively. The 1D-NMR spectra (*Tables 1* and *2*) showed four skeletal Me groups at δ(H) 0.87 (*s*, Me(18)), 1.09 (*s*, Me(19)), 1.05 (*s*, Me(28)), and 0.81 (*s*, Me(29)) and δ(C) 17.6 (*q*, Me(18)), 19.3 (*q*, Me(19)), 22.8 (*q*, Me(28)), and 27.5 (*q*, Me(19)), and an exocyclic C=C group at δ(H) 5.40 (*s*, H_a−C(30)) and 5.18 (*s*, H_b−C(30)) and δ(C) 114.2 (*t*, C(30)) and 143.5 (*s*, C(8)), together with a furan ring at δ(H) 7.55 (*s*, H−C(21)), 6.45 (*t*, $J = 1.0$ Hz, H−C(22)), and 7.46 (*t*, $J = 1.0$ Hz, H−C(23)) and δ(C) 121.8 (*s*, C(20)), 139.7 (*d*, C(21)), 108.5 (*d*, C(22)), and 144.2 (*d*, C(23)). Besides, a C=O group at δ(C) 209.2 (*s*, C(9)) was observed in the ^{13}C-NMR spectra. The above signals suggested that

Table 1. *^{1}H-NMR Data* (500 MHz, $CDCl_3$) *of Compounds* **1**–**3**. δ in ppm, J in Hz.

	1	**2**	**3**
H_α–C(1)	3.40 (*t*, *J* = 3.0)	4.18 (*d*, *J* = 2.8)	4.33 (*d*, *J* = 3.4)
CH_2(2) or H_α–C(2)	2.03–2.07 (*m*, 2 H)	5.21 (*t*, *J* = 2.8)	5.32 (*t*, *J* = 3.4)
H_α–C(3)	4.71 (*t*, *J* = 2.5)	5.11 (*d*, *J* = 2.8)	5.11 (*d*, *J* = 3.4)
H_α–C(5)	2.79 (*d*, *J* = 10.0)	2.94 (*t*, *J* = 4.5)	3.08 (*d*, *J* = 6.0)
H_α–C(6)	2.05–2.07 (*m*)	2.25 (*dd*, *J* = 18.5, 4.5)	2.25–2.27 (*m*)
H_β –C(6)	2.44 (*dd*, *J* = 17.5, 10.0)	2.89 (*dd*, *J* = 18.5, 4.5)	2.79 (*d*, *J* = 17.0)
H_α–C(8)	2.62 (*d*, *J* = 7.0)	–	–
H_α–C(11)	2.39 (*s*)	3.53 (*dd*, 11.0, 4.5)	3.36 (*d*, *J* = 2.5)
H_α–C(12)	1.25–1.30 (*m*)	1.70–1.76 (*m*)	–
H_β–C(12)	2.61–2.38 (*m*)	2.80–2.83 (*m*)	5.63 (*d*, *J* = 2.5)
H_α–C(15)	2.73 (*d*, *J* = 17.5)	2.79 (*d*, *J* = 18.0)	6.00 (*s*)
H_β–C(15)	2.56 (*d*, *J* = 17.5)	2.83 (*d*, *J* = 18.0)	–
H_β–C(17)	6.52 (*s*)	6.40 (*s*)	6.53 (*s*)
Me(18)	1.04 (*s*)	0.87 (*s*)	1.09 (*s*)
Me(19)	0.91 (*s*)	1.09 (*s*)	1.14 (*s*)
H–C(21)	8.16 (*s*)	7.55 (*s*)	7.56 (*s*)
H–C(22)	6.66 (*s*)	6.45 (*t*, *J* = 1.0)	6.41 (*s*)
H–C(23)	7.47 (*s*)	7.46 (*t*, *J* = 1.0)	7.43 (*s*)
Me(28)	1.05 (*s*)	1.05 (*s*)	1.07 (*s*)
Me(29)	0.86 (*s*)	0.81 (*s*)	0.85 (*s*)
Me(30) or CH_2(30)	1.29 (*d*, *J* = 7.0)	5.40 (*s*), 5.18 (*s*)	5.35 (*s*), 5.11 (*s*)
MeO	3.71 (*s*)	3.67 (*s*)	3.64 (*s*)
AcO–C(2)	–	2.11 (*s*)	2.12 (*s*)
AcO–C(3)	2.06 (*s*)	2.08 (*s*)	2.09 (*s*)
AcO–C(12)	–	–	1.86 (*s*)
AcO–C(15)	–	–	2.22 (*s*)

compound **2** was a trijugin-type limonoid characterized by a five-membered ring *C* with an exocyclic C=O group at C(9) [14]. By comprehensive 2D-NMR analysis, the trijugin-type limonoid framework was finally determined for compound **2** as shown in *Fig. 2*. Two AcO groups were placed at C(2) and C(3) by the HMBC cross-peaks H–C(2)/C=O of AcO–C(2), and H–C(3)/C=O of AcO–C(3). The ROESY correlations H–C(2)/H–C(1) and Me(19) and H–C(2)/Me(28) as well as H–C(3)/Me(28) indicated the relative β-configuration of these two AcO groups. Accordingly, the structure of compound **2** was identified.

The molecular formula of cipadesin I (**3**) was determined as $C_{35}H_{42}O_{15}$ from the HR-ESI-MS (*m*/*z* 725.2442 ($[M+Na]^+$)). Its IR spectrum showed absorption bands similar to those of **2**. The ^{1}H- and ^{13}C-NMR data (*Tables 1* and *2*) of **3** resemble those of **2**, except for the absence of two CH_2 groups and the presence of two additional CH–O groups at δ(H) 5.63 (*d*, *J* = 2.5 Hz, H–C(12)) and 6.00 (*s*, H–C(15)) and δ(C) 76.3 (*d*, C(12)) and 69.7 (*d*, C(15)), and two more AcO groups at δ(H) 1.86 (*s*, AcO–C(12)) and 2.22 (*s*, AcO–C(15)), and δ(C) 168.8 and 20.4 (*s* and *q*, AcO–C(12)), and 169.7 and 20.3 (*s* and *q*, AcO–C(15)). HMBC Cross-peaks H–C(12)/C=O of AcO–C(12), and H–C(15)/C=O of AcO–C(15) definitely positioned these two supplementary AcO groups at C(12) and C(15). The ROESY correlations H–C(12)/H–C(5) and H–C(17) and H–C(15)/H–C(1) assigned the

Table 2. *^{13}C-NMR Data* (125 MHz, $CDCl_3$) *of Compounds* **1**–**3**. δ in ppm.

	1	**2**	**3**		**1**	**2**	**3**
C(1)	75.5 (*d*)	73.7 (*d*)	75.7 (*d*)	C(19)	18.9 (*q*)	19.3 (*q*)	20.0 (*q*)
C(2)	27.5 (*t*)	65.4 (*d*)	65.8 (*d*)	C(20)	121.1 (*s*)	121.8 (*s*)	120.4 (*s*)
C(3)	75.4 (*d*)	74.4 (*d*)	75.2 (*d*)	C(21)	142.2 (*d*)	139.7 (*d*)	140.7 (*d*)
C(4)	37.8 (*s*)	39.0 (*s*)	39.1 (*s*)	C(22)	110.5 (*d*)	108.5 (*d*)	108.8 (*d*)
C(5)	37.0 (*d*)	37.6 (*d*)	35.2 (*d*)	C(23)	143.5 (*d*)	144.2 (*d*)	143.4 (*d*)
C(6)	30.7 (*t*)	29.1 (*t*)	28.7 (*t*)	C(28)	21.2 (*q*)	22.8 (*q*)	22.7 (*q*)
C(7)	174.2 (*s*)	174.2 (*s*)	173.7 (*s*)	C(29)	28.0 (*q*)	27.5 (*q*)	27.3 (*q*)
C(8)	44.4 (*d*)	143.5 (*s*)	139.6 (*s*)	C(30)	10.6 (*q*)	114.2 (*t*)	116.6 (*t*)
C(9)	212.9 (*s*)	209.2 (*s*)	204.4 (*s*)	MeO	52.2 (*q*)	51.8 (*q*)	51.9 (*q*)
C(10)	44.0 (*s*)	55.9 (*s*)	56.6 (*s*)	*Ac*O–C(2)		170.4 (*s*),	170.9 (*s*),
C(11)	57.5 (*d*)	58.5 (*d*)	69.4 (*d*)			20.8 (*q*)	21.2 (*q*)
C(12)	29.0 (*t*)	37.6 (*t*)	76.3 (*d*)	*Ac*O–C(3)	170.9 (*s*),	170.8 (*s*),	170.8 (*s*),
C(13)	40.3 (*s*)	45.5 (*s*)	53.3 (*s*)		21.0 (*q*)	20.4 (*q*)	20.6 (*q*)
C(14)	79.9 (*s*)	87.9 (*s*)	88.9 (*s*)	*Ac*O–C(12)			168.8 (*s*),
C(15)	38.7 (*t*)	33.5 (*t*)	69.7 (*d*)				20.4 (*q*)
C(16)	169.0 (*s*)	168.7 (*s*)	166.4 (*s*)	*Ac*O–C(15)			169.7 (*s*),
C(17)	79.6 (*d*)	79.4 (*d*)	79.3 (*d*)				20.3 (*q*)
C(18)	21.1 (*q*)	17.6 (*q*)	12.2 (*q*)				

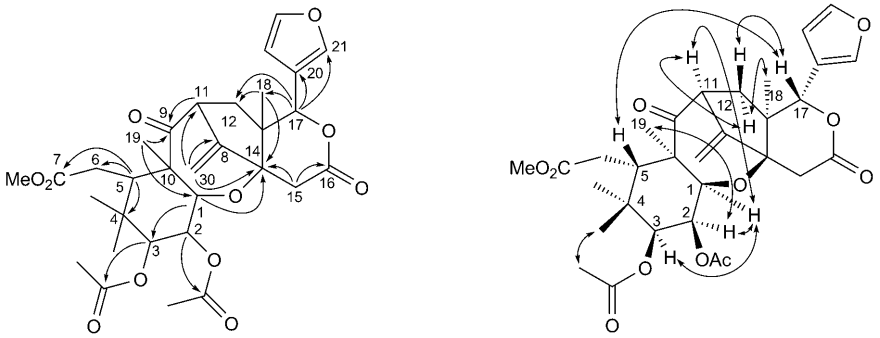

Fig. 2. *Important HMBCs* (H → C) *and ROESY* (H ↔ H) *correlations of compound* **2**

relative β- and α-configuration to H–C(12) and H–C(15), respectively. The structure of compound **3** was thus established.

The structures of the known compounds were identified by comparison of their physical data with those reported in the literature.

Experimental Part

General. TLC: visualization under UV or by heating at 110° after spraying with 98% H_2SO_4/EtOH 5:95. Column chromatography (CC): silica gel (SiO_2; 200–300 mesh; *Qingdao Marine Chemical Co., Ltd.*, P. R. China), *Lichroprep RP-18* (40–63 μm; *Merck*, Darmstadt, Germany), and *Kromasil RP-18* (5 μm, 10 × 250 mm; *Eka Chemicals*, Bohus, Sweden). HPLC: *Shimadzu* instrument (*LC-10A* pump, *SPD-10A* UV/VIS detector). Optical rotations: *WWZ-2S* polarimeter (*Shanghai Cany Precision*

Instrument Co., Shanghai, P. R. China). UV Spectra: *Shimadzu-UV-240* spectrophotometer; λ_{max} (log ε) in nm. IR Spectra: *Thermo-Nicolet-Nexus-670* FT-IR spectrometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. 1D- and 2D-NMR Spectra: *Bruker-500-Avance-III* spectrometer; at 500 (^{1}H) and 125 MHz (^{13}C); δ in ppm rel. to Me_4Si and solvent signals as internal references, *J* in Hz. HR-ESI-MS: *Bruker-Apex-III* mass spectrometer; in *m*/*z* (rel. %).

Plant Material. The leaves of *C. cinerascens* were collected in Guangxi Province of P. R. China and were purchased from the *Chinese Herb Transaction Center*, Anhui Province, P. R. China. The material was identified by Dr. *Gang Ren* (Zhejiang University, Hangzhou, P. R. China). A voucher specimen (No. CC 080703) is deposited with the School of Biological and Chemical Engineering, Zhejiang University of Science and Technology, P. R. China.

Extraction and Isolation. The air-dried powder of the plant material (7.0 kg) was extracted with 95% EtOH. The EtOH extract was concentrated *in vacuo* to yield a residue (704 g). The residue was dissolved in H_2O and extracted with $CHCl_3$. The $CHCl_3$ extract (261 g) was partitioned between 95% aq. MeOH and petroleum ether (60–90°) to yield the MeOH-soluble fraction (53 g), which was then subjected to CC (SiO_2; $CHCl_3$/MeOH 1:0 → 1:1): *Fractions 1–5*. *Fr. 3* (17 g) was applied to CC (*RP-18* (40–63 μm); MeOH/H_2O 4:6 → 10:0), and then applied to CC (SiO_2; $CHCl_3$/acetone 10:1 → 8:2): **1** (35 mg), **3** (15 mg), and **4** (26 mg). *Fr. 4* (16 g) was applied to CC (SiO_2; $CHCl_3$/acetone 10:1 → 7:3), and then further purified by semi-prep. HPLC (MeOH/H_2O 65:35): **2** (3 mg), **5** (4 mg), **6** (4 mg), and **7** (4 mg).

Cipadesin G (=*(1*S*,4a*S*,5a*S*,7*R*,9*S*,9a*S*,10*S*,11a*S*,13*R*)-7-(Acetyloxy)-1-(furan-3-yl)dodecahydro-8,8,9a,11a,13-pentamethyl-3,12-dioxo-4a,10-ethano-4a*H*-pyrano[4,3-*b*][1]benzoxepin-9-acetic Acid Methyl Ester*; **1**): White amorphous solid. $[\alpha]_D^{25} = -10.7$ ($c = 0.075$, $CHCl_3$). IR: 3447, 2952, 1743, 1735, 1370, 1253, 1229, 1090, 1052. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 553.2432 ($[M+Na]^+$, $C_{29}H_{38}NaO_9^+$; calc. 553.2414).

Cipadesin H (=*(−)*-rel-*(4*R*,4a*R*,6*S*,7a*S*,8*R*,10*R*,11*S*,11a*S*,12a*R*)-10,11-Bis(acetyloxy)-4-(furan-3-yl)dodecahydro-4a,7a,9,9-tetramethyl-13-methylene-2,7-dioxo-6,12a-methano-4*H*,12a*H*-pyrano[4,3-*b*][1]benzoxocin-8-acetic Acid Methyl Ester*; **2**): White amorphous solid. $[\alpha]_D^{25} = -19.5$ ($c = 0.35$, $CHCl_3$). IR: 3439, 2962, 1746, 1737, 1378, 1248, 1160, 1083, 1048, 1025. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 609.2284 ($[M+Na]^+$, $C_{31}H_{38}NaO_{11}^+$; calc. 609.2311).

Cipadesin I (=*(−)*-rel-*(1*R*,4*R*,4a*R*,5*R*,6*R*,7a*S*,8*R*,10*R*,11*S*,11a*S*,12a*R*)-1,5,10,11-Tetrakis(acetyloxy)-4-(furan-3-yl)dodecahydro-4a,7a,9,9-tetramethyl-13-methylene-2,7-dioxo-6,12a-methano-4*H*,12a*H*-pyrano[4,3-*b*][1]benzoxocin-8-acetic Acid Methyl Ester*; **3**): White amorphous powder. $[\alpha]_D^{25} = -42.2$ ($c = 0.120$, $CHCl_3$). IR: 3437, 2961, 1744, 1735, 1433, 1385, 1227, 1176, 1081, 1060, 1029. ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. HR-ESI-MS: 725.2442 ($[M+Na]^+$, $C_{35}H_{42}NaO_{15}^+$; calc. 725.2421.

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