Limonoids from the Leaves of *Cipadessa baccifera*

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Eight new limonoids with four different structural frameworks, including gedunin (**1**, **2**), havanensin (**3**, **4**), mexicanolide (**5**, **6**), and methyl angolensate types (**7**, **8**), together with six known limonoids, were isolated from the leaves of *Cipadessa baccifera.* Compounds **2** and **5** exhibited moderate cytotoxicity against the HL-60 cell line with an IC_{50} value of 20 μM.

Limonoids have attracted much attention because of their structural diversity and broad range of bioactivities, such as anticancer, antimalarial, and antimicrobial.[1−4] Previous investigations of the genus *Cipadessa* have shown that it is a rich source of limonoids with diverse skeletons.[5−14] *Cipadessa baccifera* (Roth.) Miq. (Meliaceae) is widely distributed in southwest China and has been used in folk medicine for the treatment of rheum, dysentery, and pruritus.[15,16] Until now, few chemical studies have analyzed its leaves, and this prompted us to conduct this project, in which we identified eight new limonoids, designated cipadesins J−Q (**1**−**8**), together with six known limonoids. In this paper, we describe the isolation, structural elucidation, and biological activities of the new limonoids.

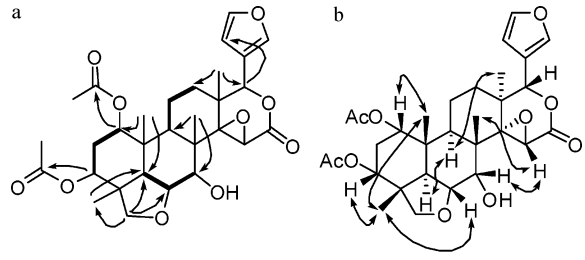
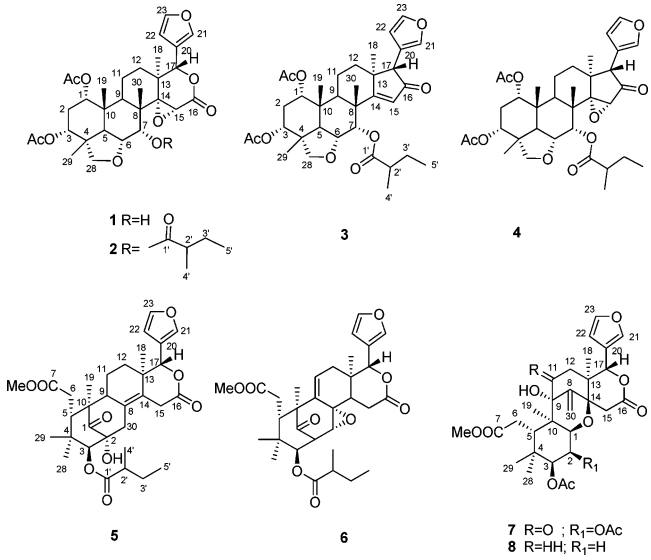


Figure 1. ^{1}H−^{1}H COSY (−) and selected HMBC (→) correlations of **1** (a) and selected ROESY (↔) correlations of **1** (b).



Results and Discussion

Cipadesin J (**1**) was assigned the molecular formula $C_{30}H_{38}O_{10}$ on the basis of its HR-ESIMS peak at *m*/*z* 581.2376 $[M + Na]^+$ (calcd 581.2362). The IR absorption bands at 3441, 1736, and 1255 cm^{-1} indicate the presence of hydroxy, carbonyl, and ether functionalities, respectively. The ^{1}H and ^{13}C NMR data of **1** show its structure to be closely related to that of piscidofuran, except for the presence of one more acetoxy group in **1**, replacing the tigloyl moiety at C-1 in piscidofuran.[17] This conclusion was confirmed with 2D NMR experiments. Specifically, the HMBC correlation of H-1 (δ 4.68 [s]) with C-1-OAc (δ 169.8) indicates an acetyl group at C-1. The relative configuration of **1** is also analogous to that of piscidofuran on the basis of ^{13}C NMR shifts and NOE data. Therefore, the structure of cipadesin J (**1**) was established as shown in Figure 1.

Cipadesin K (**2**) has the molecular formula $C_{35}H_{46}O_{11}$ on the basis of the $[M + Na]^+$ ion peak at *m*/*z* 665.2932 in the HR-ESIMS. Its IR spectrum implies the presence of carbonyl and ether functionalities on the basis of the absorption bands at 1737 and 1252 cm^{-1}, respectively. The ^{1}H and ^{13}C NMR data are similar to those of **1**, with the only difference being the presence of a 2-methylbutyryloxy moiety at C-7 (δ_H 1.29 [d, J = 7.5 Hz, H_3-4′], 1.00 [t, J = 7.5 Hz, H_3-5′]; δ 174.6 [C-1′]) in **2** instead of the hydroxy group in **1**. This structural variation was confirmed by HMBC correlation of H-7 (δ 5.01 [d, J = 2.5 Hz]) to the carbonyl group (δ_C 174.6) of the 2-methylbutyryloxy group. Therefore, cipadesin K was assigned as **2**.

Cipadesin L (**3**) has the molecular formula $C_{35}H_{46}O_9$ (*m*/*z* 633.3044 $[M + Na]^+$). The ^{13}C NMR spectrum of **3** displays 35 carbon resonances assignable to eight methyl, five methylene (one oxygenated), 12 methine (four olefinic and four oxygenated), and 10 quaternary carbons (two olefinic and four carbonyls). The ^{1}H and ^{13}C NMR spectra further reveal the presence of two acetyl units, one 2-methylbutyryl unit, one carbonyl group, and one β-furan ring moiety. Apart from the seven degrees of unsaturation occupied by four carbonyls and three double bonds, the remaining five degrees of unsaturation require **3** to contain a pentacyclic core ring system. The aforementioned data support the assignment of **3** as a havanensin-type limonoid.

Analysis of its 2D NMR data, especially HMBC, also indicates that rings A−C of **3** are identical to those of **2**. Furthermore, HMBC correlations of H-7, H-15, H-17, and H_3-18 with C-14 (δ_C 190.8) and of H-17 with C-15 (δ_C 124.4) indicate the presence of a $\Delta^{14(15)}$ double bond, and the carbonyl group is assigned at C-16 (δ_C 204.6) on the basis of its strong HMBC correlations with H-15 and H-17. The relative configuration of

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Table 1. ^{1}H NMR Data of Compounds **1**−**4** in $CDCl_3$

no.	1	2	3	4
1	4.68, br s	4.93, d (2.5)	4.73, br s	4.76, br s
2α (a)	2.13, d (2.4)	2.21, d (2.5)	2.17, d (2.6)	2.17, d (17.0)
2*β* (b)	2.20, d (3.2)	2.17, m	2.21, m	2.23, d (17.0)
3	4.92, dd (2.4, 3.2)	4.72, br s	4.94, br s	4.93, br s
5	2.62, d (12.0)	2.59, d (12.5)	2.59, d (12.4)	2.56, d (12.5)
6	3.93, dd (12.0, 2.5)	4.01, dd (2.5, 12.5)	4.19, dd (2.8, 12.4)	4.10, dd (2.5, 12.5)
7	3.63, d (2.5)	5.01, d (2.5)	5.69, d (2.8)	5.11, d (2.5)
9	2.85, dd (7.5, 12.5)	2.89, dd (8.0, 15.5)	2.89, dd (7.6, 12.0)	3.06, dd (4.0, 11.5)
11α (a)	1.41[a]	1.40, m	1.47, m	1.44[a]
11*β* (b)	1.64[a]	1.73[a]	1.73[a]	1.80[a]
12α (a)	1.41[a]	1.47, m	2.00, s	1.68, m
12*β* (b)	1.64[a]	1.71[a]	1.75[a]	2.07, s
15	3.95	3.73, s	6.01, s	3.52[a]
17	5.57, s	5.56, s	3.40, s	3.85, s
18	1.26, s (3H)	1.24, s (3H)	1.03, s (3H)	1.06, s (3H)
19	1.00, s (3H)	1.05, s (3H)	1.08, s (3H)	1.06, s (3H)
21	7.40, s	7.40, d (3.0)	7.41, s	7.40, s
22	6.32, s	6.32, s	6.23, s	6.21, s
23	7.40, s	7.41, d (3.0)	7.44, s	7.53, s
28α (a)	3.59, s (2H)	3.52, s (2H)	3.48, d (7.6)	3.52[a], (2H)
28*β* (b)			3.54, d (7.6)	
29	1.19, s (3H)	1.18, s (3H)	1.21, s (3H)	1.18, s (3H)
30	1.00, s (3H)	1.12, s (3H)	1.30, s (3H)	1.18, s (3H)
1-OAc	2.06, s (3H)	2.01, s (3H)	2.02, s (3H)	2.02, s (3H)
3-OAc	2.01, s (3H)	2.04, s (3H)	1.99, s (3H)	2.00, s (3H)
2′		2.42, q (10.0)	2.28, m	2.32, q (8.0)
3′a		1.52, m	1.73[a]	1.44[a]
3′b		1.86, m	1.41, m	1.80[a]
4′		1.29, d (7.5) (3H)	1.15, d (7.6) (3H)	1.25, d (7.5) (3H)
5′		1.00, t (7.5) (3H)	0.89, t (7.2) (3H)	0.93, t (7.5) (3H)

[a] Overlapped, without denoting multiplicity.

Table 2. ^{1}H NMR Data of Compounds **5**−**8** in $CDCl_3$

no.	5	6	7	8
1			3.73, d (4.3)	3.23, dd (1.6, 4.8)
2α (a)		3.64, dd (3.0, 9.5)	5.22, dd (3.2, 4.3)	1.88, m
2*β* (b)				2.12, m
3	5.06, s	5.06, d (9.5)	5.08, d (3.2)	4.72, t (2.4)
5	3.13, dd (5.0, 14.5)	3.04, t (5.0)	2.73[a]	2.95, d (9.6)
6α (a)	2.35, d (14.5) (2H)	2.16, dd (5.0, 24.5)	2.62, t (6.5, 18.0)	2.45[a]
6*β* (b)		2.54[a]	2.28, q (6.5)	3.08, d (9.6)
9	2.03, s			
11α (a)	1.79, m (2H)	5.82, t (5.0)		1.35[a]
11*β* (b)				2.74, dd (9.2, 14.0)
12α (a)	1.10, d (2.5)	2.33, d (5.0) (2H)	2.46, d (14.3)	1.35[a]
12*β* (b)	1.75[a]		3.52, d (14.3)	2.42[a]
14		1.81, m		
15α (a)	3.47, d (22.0)	2.73, dd (5.0, 19.5)	2.95, d (17.5)	2.93, d (18.0)
15*β* (b)	3.84, d (22.0)	3.18, dd (14.5, 19.5)	2.71, d (17.5)	2.59, d (18.0)
17	5.62, s	5.16, s	5.97, s	5.71, s
18	1.06, s (3H)	1.06, s (3H)	0.77, s (3H)	0.81, s (3H)
19	1.24[a], (3H)	1.20, s (3H)	0.97, s (3H)	0.81, s (3H)
21	7.40, s	7.42, s	7.46, s	7.39, d (1.6)
22	6.47, s	6.27, s	6.39, d (1.3)	6.38, s
23	7.54, s	7.36, s	7.44, t (1.3)	7.40, d (1.6)
28	0.77, s (3H)	0.82, s (3H)	1.06, s (3H)	0.99, s (3H)
29	0.69, s (3H)	0.86, s (3H)	0.76, s (3H)	0.82, s (3H)
30α (a)	1.77[a]	3.29, d (3.0)	5.12, s	5.01, s
30*β* (b)	3.23, d (14.0)		5.68, s	5.35, s
7-OMe	3.69, s	3.70, s	3.65, s (3H)	3.69, s
2-OAc (OH)	4.18, s		2.02, s (3H)	
3-OAc			2.15, s (3H)	2.09, s (3H)
9-OH			4.19, s	
2′	2.48, m	2.53[a]		
3′a	1.51, m	1.58, s		
3′b	1.76[a]	1.76, m		
4′	1.24[a], (3H)	1.24, d (7.0) (3H)		
5′	0.90, t (7.0) (3H)	0.96, t (7.5) (3H)		

[a] Overlapped, without denoting multiplicity.

3 is deduced to be the same as those of **1** and **2** from their similar chemical shifts and ROESY correlations. Thus, the structure of **3** was fully established as shown.

The molecular formula of cipadesin M (**4**) was established as $C_{35}H_{46}O_{10}$ according to the ion peak at *m/z* 649.2987 $[M + Na]^+$ in the HR-ESIMS, one oxygen more than that observed for **3**.

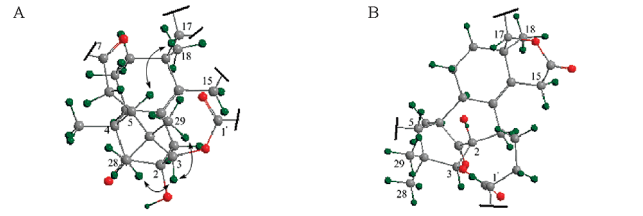
Table 3. ^{13}C NMR Data of Compounds (**1**−**8**)

no.	1	2	3	4	5	6	7	8
1	72.0	71.6	72.1	72.4	217.4	210.3	74.9	74.3
2	27.6	27.6	27.5	27.5	78.2	49.7	66.1	27.8
3	71.5	72.2	71.6	71.7	85.3	77.1	75.7	76.2
4	42.2	42.0	42.1	42.1	38.9	38.6	39.4	37.8
5	39.8	41.1	41.3	41.7	40.7	47.4	37.0	36.3
6	74.0	72.5	72.1	72.7	33.2	31.9	29.6	31.6
7	70.2	71.3	72.4	71.9	173.9	173.2	173.8	175.3
8	44.8	44.6	46.2	44.4	125.7	58.7	144.5	149.4
9	34.4	35.5	34.4	35.5	51.8	138.2	87.7	78.4
10	39.1	39.3	39.1	39.4	52.1	51.2	54.4	49.0
11	14.0	14.1	14.6	15.0	18.7	126.5	208.3	34.6
12	26.4	25.9	30.2	28.3	28.9	31.4	46.9	30.0
13	38.5	39.0	47.9	42.7	38.3	35.6	42.6	41.1
14	69.8	69.6	190.8	72.4	132.9	39.6	81.1	81.0
15	57.4	56.2	124.4	57.2	33.2	29.5	33.6	34.2
16	170.1	167.0	204.6	207.8	169.6	169.7	168.8	170.2
17	78.3	78.0	60.5	57.2	80.5	81.8	78.6	79.7
18	17.7	17.8	26.7	24.6	17.6	23.5	14.8	13.4
19	15.9	15.9	15.3	16.2	16.7	14.0	16.1	16.7
20	120.7	120.4	118.4	116.6	120.5	121.9	120.2	121.2
21	142.9	143.0	142.7	142.4	142.8	143.6	140.2	142.9
22	109.9	109.8	111.1	110.9	109.9	109.5	109.1	108.5
23	141.1	141.1	141.6	141.5	141.7	140.6	143.5	140.1
28	78.1	77.6	77.7	77.4	20.1	20.9	21.3	21.6
29	19.6	19.7	19.5	19.4	22.8	24.3	26.3	27.1
30	17.8	18.5	25.4	19.1	43.8	60.0	115.1	114.6
OMe					52.1	52.2	52.0	51.8
1-OAc	169.8	169.7	169.5	169.3				
	21.1	20.9	21.0	21.2				
2-OAc							170.6	
							20.7	
3-OAc	168.0	169.4	169.7	169.8			169.9	170.2
	21.3	21.2	20.8	20.9			21.6	21.6
1′		174.6	174.3	175.9	175.9	175.5		
2′		41.3	41.6	41.6	41.1	41.2		
3′		25.8	26.2	25.7	26.9	26.9		
4′		11.7	11.9	12.0	16.1	16.8		
5′		16.9	17.1	17.5	11.4	11.6		

Comparison of the ^1H and ^{13}C NMR data for **4** (Tables 1 and 3) with those of **3** shows many similarities, except that an epoxy ring between C-14 (δ 72.4) and C-15 (δ 57.2) replaces the double bond at this position in **3**. This deduction is confirmed by the HMBC correlations from H-15 to C-14, C-16, and C-17. The relative configurations of rings A−C in **4** are the same as those in **3** on the basis of their similar chemical shifts and ROESY data, and the 14,15-epoxide ring is assigned an α-orientation on the basis of the ROESY correlations of H-15 with H-7 and Me-30. Thus, the structure of **4** was fully identified as shown. Both **3** and **4** belong to the havanensin group, with intact rings A−D, and are usually thought to represent the earliest stage along the biosynthetic pathway of limonoids.

From a biogenetic point of view, compounds **1** and **2** are derived from compounds **3** and **4** by a Baeyer−Villiger-type oxidation. This is the first report of gedunin-type and havanensin-type limonoids in the genus *Cipadessa*.

Cipadesin N (**5**) has an HR-ESIMS molecular ion peak at *m*/*z* 593.2722 $[M + Na]^+$, corresponding to the molecular formula $C_{32}H_{42}O_9$. The IR spectrum implies the presence of hydroxy and carbonyl groups by the absorption bands at 3465 and 1736 cm^{-1}, respectively. The observation of proton signals for a β-substituted furan, four tertiary methyls, and a methoxy group in the ^1H NMR spectrum, as well as the characteristic carbonyl group at C-1 (δ_C 217.4) in the ^{13}C NMR spectrum, strongly implies that **5** is a mexicanolide-type limonoid.[13,18] Comparison of its spectroscopic data with those of 2′*R*-methylbutanoyl proceranolide identified a close similarity,[13] suggesting that **5** is a congener of the latter. A downfield resonance at δ_C 78.2 was shown by HMBC to correlate with the proton resonance at δ_H 4.18 of a hydroxy group, as distinguished by the HSQC spectrum, suggesting that the hydroxy group is located at C-2. The relative configuration of **5** was established with a ROESY experiment. However, because no ROE correlation of the 2-OH was observed, DFT calculations at the HF/6-31G* and then the B3LYP/6-31G* levels were used to examine the two possible structures of **5**, corresponding to the α (A) and β (B) orientations of 2-OH, shown in Figure 2 (for more details, see Supporting Information). Two optimized structures were obtained, in which the calculated distance of the proton pairs near the 2-OH in A was fully consistent with the corresponding ROESY data (Figure 2, A), and the 2-OH was determined to be α-oriented. Therefore, the structure of **5** was established as shown.



Proton Pairs	Distances Found in A	Distances Found in B	ROE Correlations
H-5/H-17	2.81Å	4.68Å	yes
H-3/H-28	2.27Å	2.39Å	yes
H-3/H-29	2.68Å	3.30Å	yes

Figure 2. Two density functional theory (DFT)-optimized possible structures (A and B) were found for cipadesin N (**5**). The calculated distances of the key proton pairs in the two structures are listed, and the major ROESY correlations (↔) used to define the relative stereochemistry of OH-2 are shown in A.

Cipadesin O (**6**) was isolated as a white powder. The molecular formula was determined to be $C_{32}H_{42}O_9$ by the $[M + Na]^+$ ion peak at *m*/*z* 591.2563 (calcd 591.2570) on HR-ESIMS. The ^1H and ^{13}C NMR data of **6** (Tables 2 and 3) show overall similarity to those of cineracipadesin A,[7] except that the double bond between C-9 (δ_C 138.2) and C-11 (δ_C 126.5) in **6** replaces the epoxy ring in cineracipadesin A.[7] The HMBC correlations of H-11 (δ 5.82 [t, J = 5.0 Hz]) with C-8, C-9, C-12, and C-13 confirm this deduction. ROESY experiments indicated that the relative configuration of **6** was the same as that of cineracipadesin A.[7] Thus, the structure of **6** was established as shown.

Cipadesin P (**7**) gave an HR-ESIMS molecular ion peak at *m*/*z* 625.2248 $[M + Na]^+$, corresponding to the molecular formula $C_{31}H_{38}O_{12}$. The IR spectrum implies the presence of hydroxy and carbonyl groups on the basis of the absorption bands at 3446 and 1746 cm^{-1}, respectively. The ^1H and ^{13}C NMR data (Tables 2 and 3) show the presence of four quaternary methyls, one β-substituted furan, one methoxy, and one ring-D lactone. Two acetyl groups (δ_H 2.02 [s, 3H], 2.15 [s, 3H]; δ_C 20.7, 21.6, 170.6, 169.9), one carbonyl (δ_C 208.3), and one exocyclic methylene group (δ_H 5.68 [s], 5.12 [s]) were also observed from the ^1H and ^{13}C NMR spectra. Those spectroscopic features, together with the characteristic chemical shift of C-14 (δ_C 81.1), suggest that **7** has a methyl angolensate-type skeleton.[7,9] Comparison of its 1D NMR data with those of cineracipadesin B indicates an overall similarity, except for the absence of an oxygenated methine in cineracipadesin B and the presence of an additional carbonyl group in **7**.[7] Extensive 2D NMR experiments confirmed the structure of **7** and located the ketone group at C-11 by its HMBC correlations with H-12 and OH-9. The relative configuration of **7** was also shown to be the same as that of cineracipadesin B by its similar chemical shifts and ROESY correlations. Thus, the structure of **7** was fully established.

Cipadesin Q (**8**) was obtained as a white, amorphous powder. The molecular formula, $C_{29}H_{38}O_9$, was inferred from its HR-ESIMS (*m*/*z* 553.2402 $[M + Na]^+$). The 1D NMR data of **8** (Tables 2 and

3) resemble those of **7**, except for the absence of the 2-*O*-acetyl and 11-carbonyl groups in **8**, as suggested by the presence of two additional methylenes and the apparent downshifted C-9 (Δ 9.3 ppm) and C-12 (Δ 16.9 ppm) in **8**. This conclusion was confirmed by 2D NMR experiments (HSQC, HMBC, ^{1}H−^{1}H COSY, and ROESY).

The six known compounds were identified as cipadesin E,[9] cipatrijugin A,[8] 2′*R*-methylbutanoylproceranolide,[13] cipadonoid B,[11] cipadesin A,[5] and cipadesin B[5] by comparison of their observed and reported 1D NMR data.

Previous studies of the limonoids from the seeds and stems of *C. baccifera* have revealed three kinds of structural frameworks: the mexicanolide,[12,13] prieurianin, and evodulone types.[14] However, our study of compounds **1**−**8** and other known compounds demonstrates seven different structural frameworks, which indicates that the limonoids from the leaves of *C. baccifera* differ greatly in their structural diversity from those reported from the stems and seeds. The hypothesis of a biogenetic relationship between the limonoids of *C. baccifera* is shown (see Supporting Information). The reported gedunin-type and havanensin-type limonoids in *C. baccifera* have not yet been found in *C. cinerascens*, which might be regarded as a chemotaxonomic difference between these two species.

Compounds **1**−**8** were evaluated for their cytotoxicity against five cancer cell lines, including HL-60, SMMC-7721, A-549, MCF-7, and SW480 (for more details, see Supporting Information). Cipadesin K (**2**) and cipadesin N (**5**) showed moderate cytotoxicity in HL-60 cells with an IC_{50} value of 20 μM. Cipadesin K (**2**) also showed weak cytotoxicity against the SMMC-7721 human tumor cells, with an IC_{50} value of 36.5 μM. However, the lack of cytotoxicity of cipadesin J (**1**) indicated that the 7-(2-methylbutyryloxy) moiety might be an influential factor in the cytotoxicity of the gedunin-type limonoids.

Experimental Section

General Experimental Procedures. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. IR spectra were recorded on a Bio-Rad FTS-135 spectrometer with a KBr disk. The ^{1}H NMR spectra of **3** and **8**, ^{13}C NMR spectra of **1**−**3**, **5**, **7**, and **8**, and 2D NMR spectra were recorded on a Bruker AM-400 spectrometer, while ^{1}H NMR spectra of **1**, **2**, and **4**−**7** and ^{13}C NMR spectra of **4** and **6** were recorded on a Bruker DRX-500 instrument. ESIMS and HR-ESIMS spectra were measured with a Finnigan MAT 90 instrument and VG Auto Spec-3000 spectrometer, respectively. Semipreparative HPLC was performed on a Merck column (i.d. 100−10 mm; Merck, Darmstadt, Germany), developed with CH_3OH/H_2O (50:50 to 58:42, 35 min) (flow rate, 3.0 mL/min, detection, UV 210 nm) at 30 °C. Column chromatography was performed on silica gel (90−150 μm; Qingdao Marine Chemical Inc.), MCI gel (CHP20P, 75−150 μm, Mitsubishi Chemical Industries Ltd.), C18 reversed-phase silica gel (20−45 μm; Merck, Darmstadt, Germany), and Sephadex LH-20 (40−70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden). TLC plates were precoated with silica gel GF_{254} and HF_{254} (Qingdao Haiyang Chemical Plant, Qingdao, People's Republic of China).

Plant Material. The leaves of *C. baccifera* were collected in Xishuangbanna, Yunnan Province, People's Republic of China, and were identified by Prof. Jing-Yun Cui of the Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen (KIB 080421) was deposited at the State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Science.

Extraction and Isolation. Powdered, dried leaves of *C. baccifera* (2.6 kg) were extracted three times with 95% EtOH. The extracts were combined, concentrated, and suspended in H_2O. The water layer was then extracted with PE and EtOAc. The EtOAc extracts (214 g) were subjected to silica gel column chromatography, eluted with PE/acetone (from 1:0 to 2:1), yielding four fractions (A1−A4), and then eluted with $CHCl_3$/MeOH (from 10:1 to 1:1), yielding three fractions (A5−A7). Fraction A3 (17 g) was first applied to MCI gel (eluted with MeOH/H_2O/acetone from 9:1:0 to 0:0:10) and then to a reversed C-18 column chromatograph (eluted with MeOH/H_2O from 5:5 to 10:0), yielding six fractions (B1−B6). Fraction B2 (181 mg) was first purified on Sephadex LH-20 and then applied to silica gel (eluted with $CHCl_3$/acetone from 20:1 to 8:1), yielding **1** (6 mg), **3** (4 mg), and **4** (5 mg). Fraction B3 (656 mg) was applied to Sephadex LH-20, yielding two fractions (C1, C2). C1 (67 mg) was purified by semipreparative HPLC to yield **2** (4 mg) and **7** (26 mg). Fraction B4 (908 mg) was further purified on Sephadex LH-20 and then applied to silica gel ($CHCl_3$/acetone from 80:1 to 10:1), yielding **5** (30 mg), **6** (5 mg), and **8** (25 mg).

Cipadesin J (1): white, amorphous power; $[\alpha]^{25}_D$ +4.9 (*c* 0.15, $CHCl_3$); IR (KBr) ν_{max} 3441, 2952, 1736, 1255, 1164, 1054 cm^{-1}; positive-ion ESIMS *m/z* 559.5 $[M + H]^+$; HR-ESIMS *m/z* 581.2376 $[M + Na]^+$, calcd 581.2362; ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 3.

Cipadesin K (2): white, amorphous power; $[\alpha]^{25}_D$ −2.4 (*c* 0.20, $CHCl_3$); IR (KBr) ν_{max} 2922, 1737, 1252 cm^{-1}; positive-ion ESIMS *m/z* 665 $[M + Na]^+$; HR-ESIMS *m/z* 665.2932 $[M + Na]^+$, calcd 665.2937; ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 3.

Cipadesin L (3): white, amorphous solid; $[\alpha]^{25}_D$ −47.8 (*c* 0.11, $CHCl_3$); IR (KBr) ν_{max} 2935, 1736, 1376, 1252, 1154, 1053 cm^{-1}; positive-ion ESIMS *m/z* 633 $[M + Na]^+$; HR-ESIMS *m/z* 633.3044 $[M + Na]^+$, calcd 633.3099; ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 3.

Cipadesin M (4): white, amorphous solid; $[\alpha]^{25}_D$ −21.6 (*c* 0.10, $CHCl_3$); IR (KBr) ν_{max} 2936, 1738, 1377, 1249, 1155, 1055 cm^{-1}; positive-ion ESIMS *m/z* 627.3 $[M + H]^+$ and 649.4 $[M + Na]^+$; HR-ESIMS *m/z* 649.2987 $[M + Na]^+$, calcd 649.2988; ^{1}H NMR data, see Table 1; ^{13}C NMR data, see Table 3.

Cipadesin N (5): white, amorphous power; $[\alpha]^{25}_D$ −72.3 (*c* 0.25, $CHCl_3$); IR (KBr) ν_{max} 3465, 2971, 1736, 1687, 1024 cm^{-1}; positive-ion ESIMS *m/z* 593.5 $[M + Na]^+$; HR-ESIMS *m/z* 593.2722 $[M + Na]^+$, calcd 593.2726; ^{1}H NMR data, see Table 2; ^{13}C NMR data, see Table 3.

Cipadesin O (6): white, amorphous power; $[\alpha]^{25}_D$ −106.1 (*c* 0.071 $CHCl_3$); IR (KBr) ν_{max} 1736, 1027 cm^{-1}; positive-ion ESIMS *m/z* 591.5 $[M + Na]^+$; HR-ESIMS *m/z* 591.2563 $[M + Na]^+$, calcd 591.2570; ^{1}H NMR data, see Table 2; ^{13}C NMR data, see Table 3.

Cipadesin P (7): white, amorphous power; $[\alpha]^{25}_D$ −157.4 (*c* 0.50, $CHCl_3$); IR (KBr) ν_{max} 3446, 2952, 1747, 1705, 1240, 1050 cm^{-1}; positive-ion ESIMS *m/z* 625.5 $[M + Na]^+$; HR-ESIMS *m/z* 625.2248 $[M + Na]^+$, calcd 625.2260; ^{1}H NMR data, see Table 2; ^{13}C NMR data, see Table 3.

Cipadesin Q (8): white, amorphous power; $[\alpha]^{25}_D$ −17.4 (*c* 0.30, $CHCl_3$); IR (KBr) ν_{max} 3467, 2952, 1736, 1249, 1171, 1056 cm^{-1}; positive-ion ESIMS *m/z* 553.5 $[M + Na]^+$; HR-ESIMS *m/z* 553.2402 $[M + Na]^+$, calcd 553.2413; ^{1}H NMR data, see Table 2; ^{13}C NMR data, see Table 3.

Cytotoxicity Bioassays. The cytotoxicity of the compounds against HL-60, SMMC-7721, A-549, MCF-7, and SW480 human tumor cells was determined by the MTT method,[19] and DDP (*cis*-diammineplatinum(II) dichloride) was used as the positive control (IC_{50} values of 2.8, 12.6, 10.7, 14.9, and 10.6 μM against HL-60, SMMC-7721, A-549, MCF-7, and SW480 cells, respectively). The cells were plated in 96-well plates 12 h before treatment and continuously exposed to different concentrations of the compounds for 72 h. The cell growth inhibition curve was graphed and the IC_{50} value of each compound was calculated by the Reed and Muench method.[20]

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Supporting Information Available: This material is available free of charge via the Internet at http://pubs.acs.org.

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