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Cipadesins A–C: Novel Tetranortriterpenoids from *Cipadessa cinerascens*

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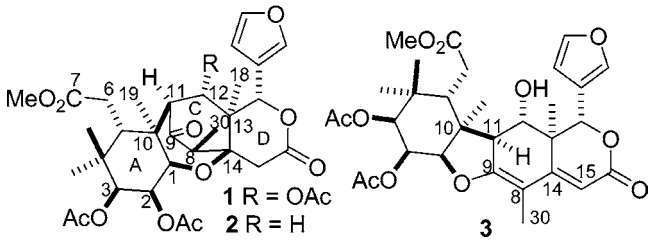
ABSTRACT



Three novel tetranortriterpenoids, cipadesins A–C (1–3), were isolated from the aerial parts of *Cipadessa cinerascens*. They possess a novel carbon skeleton, in which rings A and C were joined via C-10 and C-11. Their structures were elucidated by spectral evidence. X-ray crystallographic analysis confirmed the structure of 1.

Limonoids, a class of tetranortriterpenoids, are mainly found in plants belonging to the families Rutaceae and Meliaceae. They exhibit various biological effects, such as insect antifeedant and growth regulating activities,[1] antimicrobial activity[2], and potent cell adhesion inhibitory effects.[3] Several types of rings B,D-seco limonoids represented by methyl angolensate,[4] mexicanolide,[5] swietenin,[6] and trijugin[7] were reported.

From the genus *Cipadessa*, three diterpenoids,[8] three tetranortriterpenoids, two sterols, and two heneicosenes[9] have been isolated previously. The leaves and roots of *C. cinerascens* (Pell.) Hand-Mazz (Meliaceae), a shrub distributed in Southwest China, are used for the treatment of rheumatism, malaria, scald, and skin itch.[10] The leaves of *C. cinerascens* contain flavonoids and their glucosides.[11] The

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present study on the leaves and bark of *C. cinerascens* led to the isolation of three novel tetranortriterpenoids, cipadesins A−C (**1**−**3**), in which rings A and C were connected via C-10 and C-11. The carbon skeleton was different from that of either methyl angolensate-type tetranortriterpenoids,[4] with a six-membered ring C connected with ring A by C-9 and C-10, or from trijugin-type tetranortriterpenoids,[7] characterized by a five-membered ring C with an exocyclic carbonyl at C-9. To the best of our knowledge, they were tetranortriterpenoids with a novel carbon skeleton.

Cipadesin A (**1**) was isolated as a colorless crystal (MeOH). Its molecular formula, $C_{33}H_{42}O_{13}$, was established from the quasi-molecular ion peak at *m*/*z* 669.2517 $[M + Na]^+$ in the HRESIMS spectrum. IR peak at 1744 cm^{-1} and ^{13}C NMR signals at δ 209.5, 173.8, 170.9, 170.7, 169.1, and 168.1 revealed a ketonic carbonyl group and five ester carbonyl groups. Besides a methoxy group (δ_H 3.77; δ_C 52.3) and three acetyl groups (δ_H 1.88, 2.05, 2.11; δ_C 169.1, 170.7, 170.9), **1** contained 26 carbons, including a β-substituted furan ring (δ_H 6.60, 7.44, 8.10; δ_C 109.7, 121.0, 141.8, 143.2), four tertiary methyl groups (δ_H 0.87, 0.97, 1.01; 1.14), and one methyl group (δ_H 1.27, 3 H, d, 7.3) attached to methine (2.76, 1 H, q, 7.3). The above evidence suggested a tetranortriterpenoid.[9] HMBC correlations (Figure 1) H-11/C-8, H-12 and H-30/C-9, H-18/C-12 and C-14, H-30/C-14, and H-19/C-11 showed a six-membered ring C connected with ring A by C-11 and C-10. Three acetoxy groups were located at C-2, C-3, and C-12 by the HMBC cross signals H-2 (δ 5.10)/C-2-OAc (δ 170.4), H-3 (δ 5.08)/C-3-OAc (δ 170.8), and H-12 (δ 5.52)/C-12-OAc (δ 168.8). The relative stereochemistry of **1** was determined by NOESY experiments (Figure 1). X-ray crystallographic analysis of **1** (Figure 2) confirmed the proposed structure.[12]

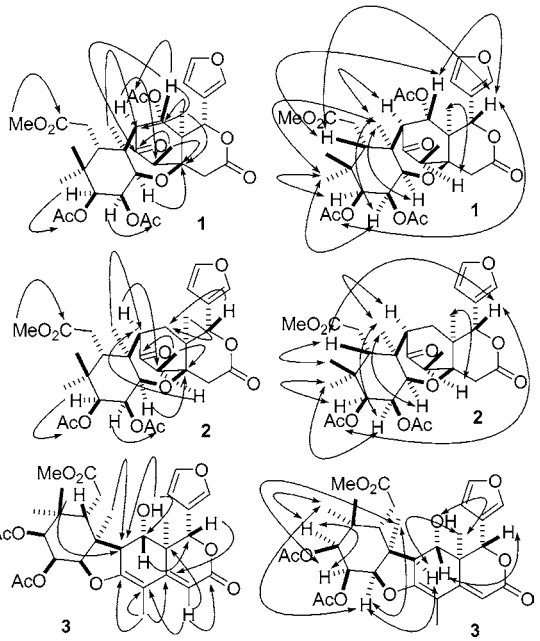

Figure 1. Important HMBC and NOESY correlations of **1**−**3** (HMBC: →; NOESY: ↔).

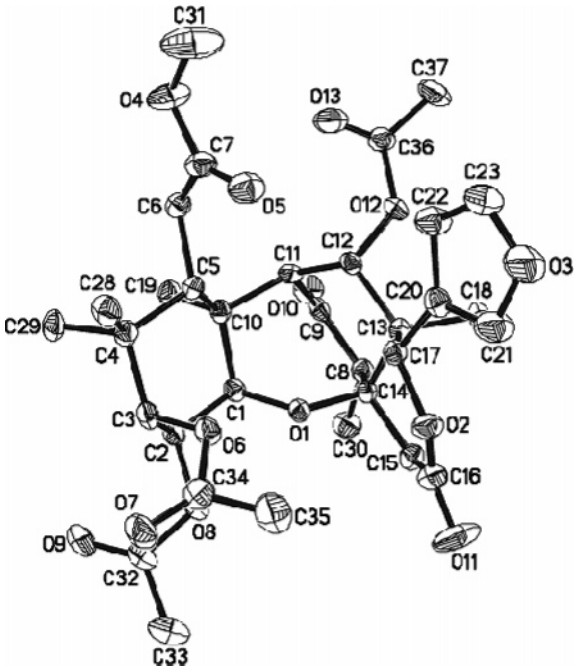

Figure 2. ORTEP diagrams of **1**.

The UV, IR, ^1H NMR, and ^{13}C NMR spectral data of cipadesins B and C (**2** and **3**) were similar to those of **1**, indicating that these compounds are all tetranortriterpenoids.

Cipadesin B (**2**) was isolated as a white powder. The quasi-molecular ion peak at *m*/*z* 611.2469 $[M + Na]^+$ in the HRESIMS spectrum provided the molecular formula $C_{31}H_{40}O_{11}$. A ketonic carbonyl group and four ester carbonyl groups were recognized from the IR peak at 1739 cm^{-1} and from the ^{13}C NMR signals at δ 212.0, 174.0, 170.8, 170.6, and 168.9. The ^1H and ^{13}C NMR spectral data of **2** showed close similarity to those of **1**, except for the absence of an acetyl group and an oxygenated methine, as well as the presence of an additional methylene (δ_H 1.30, dd, 16.4, 6.4;

(12) Crystal structure analysis: the structure was solved by direct method with SHELX 97[15] and refined by full-matrix least-squares on F^2. The H coordinates were determined by calculated geometry.

(13) Crystal data for **1**: $C_{34}H_{46}O_{14}$; M_W = 678.71; dimensions 0.56 × 0.46 × 0.26 mm; monoclinic system, space group $P2_12_12_1$, a =9.745 (4) Å, b = 15.562 (6) Å, c = 11.779 (4) Å, $\alpha = \beta = \gamma = 90°$, V = 1717.4 (13) Å^3, Z = 2, d = 1.312 g/cm^{-3}, λ = 0.71073 Å, μ (Mo KR) = 0.102 mm^{-1}, F (000) = 724, T = 298 (2) K. Of the 4300 reflections collected, 3894 were unique (R_{int} = 0.0315). Final refinement: data/restraints/parameters = 3894/1/445; $R1$ = 0.0827 (all data), $wR2$ = 0.0966 (all data); the Flack absolute structure parameter = 0 (10), and GOF = 0.984. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.202 and −0.260 e$^-$/Å^3, respectively.

(14) Crystallographic data (excluding the structure factor tables) have been deposited with the Cambridge Crystallographic Data Center, deposition no. 278634. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK, fax: +44 1223 336033.

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δ_H 2.62, d, 16.6). The ^{13}C NMR signals for C-11, C-12, and C-13 shifted to high field obviously, which indicated that C-12 was methylene. This assumption and the remaining structure were supported by HMBC and NOESY experiments (Figure 1).

Table 1. ^1H NMR Data of Cipadesins A−C (**1**−**3**) in $CDCl_3$ (600 MHz)[a]

position	1	2	3
1α	3.69 (d, 4.0)	3.68 (d, 4.0)	4.24 (d, 3.5)
2α	5.10 (t, 3.7)	5.12 (t, 3.6)	5.31 (t, 3.4)
3α	5.06 (d, 3.1)	5.08 (d, 2.9)	5.04 (d, 2.5)
5*β*	2.85 (d, 9.6)	2.76 (d, 9.5)	2.24 (d, 9.5)
6α	2.55 (d, 17.4)	2.39 (m)	3.05 (d, 16.7)
6*β*	2.42 (dd, 17.4, 10.0)	2.03 (over- lapped)	2.36 (dd, 16.9, 9.4)
8α	2.76 (q, 7.3)	2.65 (q, 7.2)	
11α	2.45 (s)	2.39 (m)	2.60 (d, 9.5)
12α		1.30 (dd, 16.4, 6.4)	
12*β*	5.52 (m)	2.62 (d, 16.6)	4.38 (d, 10.0)
15α	2.70 (d, 5.5)	2.60 (d, 17.9)	5.67 (s)
15*β*	2.70 (d, 5.5)	2.70 (d, 17.9)	
17*β*	6.53 (s)	6.50 (s)	5.20 (s)
18	1.01 (s)	1.07 (s)	1.29 (s)
19	0.97 (s)	0.96 (s)	1.29 (s)
21	8.10 (s)	8.16 (s)	7.42 (s)
22	6.60 (d, 0.96)	6.67 (s)	6.55 (s)
23	7.44 (t, 1.6)	7.48 (s)	7.49 (s)
28	1.14 (s)	1.16 (s)	1.16 (s)
29	0.87 (s)	0.90 (s)	0.80 (s)
30	1.27 (d, 7.3)	1.25 (d, 7.2)	1.85 (s)
OMe	3.77 (s)	3.73 (s)	3.73 (s)
2*β*-OAc	2.05 (s)	2.05 (s)	2.10 (s)
3*β*-OAc	2.11 (s)	2.10 (s)	2.10 (s)
12α-OAc	1.88 (s)		

[a] Assignments were based on HSQC (or HMQC) and HMBC experiments.

Cipadesin C (**3**) was isolated as a white powder, with a molecular formula of $C_{31}H_{38}O_{11}$ from the quasi-molecular ion peak at *m*/*z* 609.2311 $[M + Na]^+$ in the HRESIMS spectrum. Four ester carbonyl groups were concluded from the IR peaks at 1740 and 1655 cm^{-1} and from the ^{13}C NMR signals at δ 175.2, 170.6, 170.4, and 165.8. HMBC correlations H-30 (δ 1.85, s)/C-8 (δ 101.9), C-9 (δ 160.1) and C-14 (δ 162.6), H-15 (δ 5.67, s)/C-8, C-13 (δ 44.2) and C-14, and H-17 (δ 5.20)/C-14 indicated a unsaturated system composed of C-9, C-8, C-14, C-15 (δ 105.4), and C-16 (δ 165.8). The ether bond between C-1 and C-9 was assumed by the fact that C-9 was a quaternary C-atom from HSQC experiment and that the ^{13}C NMR signal for C-1 was shifted from 76.6 in **1** to 86.3 in **3**. A hydroxyl group resonating at δ 1.52, from HSQC experiment, gave HMBC correlations (Figure 1) with C-11 and C-12 and exhibited NOESY correlation with H-18, allowing it to be assigned as 12α-OH. The HMBC cross signals of H-5, H-19, and H-12-OH/C-11 suggested the C-10 and C-11 connectivity. The remaining structure and relative stereochemistry of **3** was similar to that of **1** as determined by the HMBC and NOESY experiments (Figure 1).

Table 2. ^{13}C NMR Data of Cipadesins A−C (**1**−**3**) in $CDCl_3$ (150 MHz)[a]

C-atom	1	2	3
1	76.6	76.3	86.3
2	66.1	66.4	66.2
3	75.0	75.3	75.5
4	39.4	39.1	39.7
5	36.9	37.0	36.2
6	29.8	29.9	31.1
7	173.8	174.0	175.2
8	44.2	44.5	101.9
9	209.5	212.0	160.1
10	46.9	45.4	48.3
11	64.5	57.6	55.5
12	70.0	29.2	69.6
13	45.6	40.4	44.2
14	79.9	80.2	162.6
15	38.8	38.7	105.4
16	168.1	168.9	165.8
17	79.0	79.8	78.0
18	16.2	21.6	11.3
19	18.3	18.4	20.9
20	121.0	121.1	122.6
21	141.8	142.0	141.4
22	109.7	110.5	109.7
23	143.2	143.0	145.1
28	22.1	21.9	21.8
29	28.1	28.1	26.3
30	10.3	10.5	9.8
OCH_3	52.3	52.3	52.1
2*β*-$OCOCH_3$	170.7	170.6	170.4
2*β*-$OCOCH_3$	20.8	20.9	20.8
3*β*-$OCOCH_3$	170.9	170.8	170.6
3*β*-$OCOCH_3$	20.5	20.6	20.8
12α-$OCOCH_3$	169.1		
12α-$OCOCH_3$	20.7		

[a] Assignments were based on HSQC (or HMQC) and HMBC experiments.

Supporting Information Available: Experimental procedures; physical and spectral data; X-ray data of **1**; HRESIMS spectra; 1D and 2D NMR diagrams. This material is available free of charge via the Internet at http://pubs.acs.org.

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