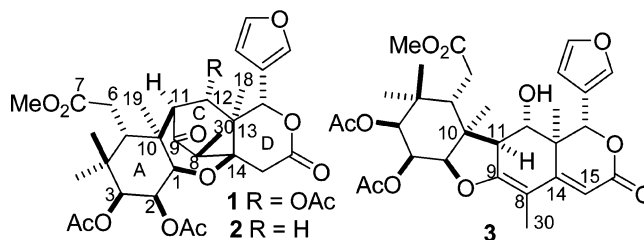


Cipadesins A–C: Novel  
Tetanortriterpenoids from *Cipadessa  
cinerascens*Xiao-Hong Yuan,<sup>†‡</sup> Bo-Gang Li,<sup>†</sup> Min Zhou,<sup>†</sup> Hua-Yi Qi,<sup>†</sup> and Guo-Lin Zhang<sup>\*†</sup>Chengdu Institute of Biology, Chinese Academy of Sciences, 610041, PR China, and  
Graduate School of Chinese Academy of Sciences, Beijing 100039, PR China

zhanggl@cib.ac.cn

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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 anti-feedant and growth regulating activities,<sup>1</sup> antimicrobial activity<sup>2</sup>, and potent cell adhesion inhibitory effects.<sup>3</sup> Several types of rings B,D-seco limonoids represented by methyl angolensate,<sup>4</sup> mexicanolide,<sup>5</sup> swietenin,<sup>6</sup> and trijugin<sup>7</sup> were reported.

From the genus *Cipadessa*, three diterpenoids,<sup>8</sup> three tetranortriterpenoids, two sterols, and two heneicosenes<sup>9</sup> 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.<sup>10</sup> The leaves of *C. cinerascens* contain flavonoids and their glucosides.<sup>11</sup> The

\* Corresponding author. Tel/Fax: +86-28-85225401. E-mail: zhanggl@cib.ac.cn.

<sup>†</sup> Chengdu Institute of Biology, Chinese Academy of Sciences.

<sup>‡</sup> Graduate School of Chinese Academy of Sciences.

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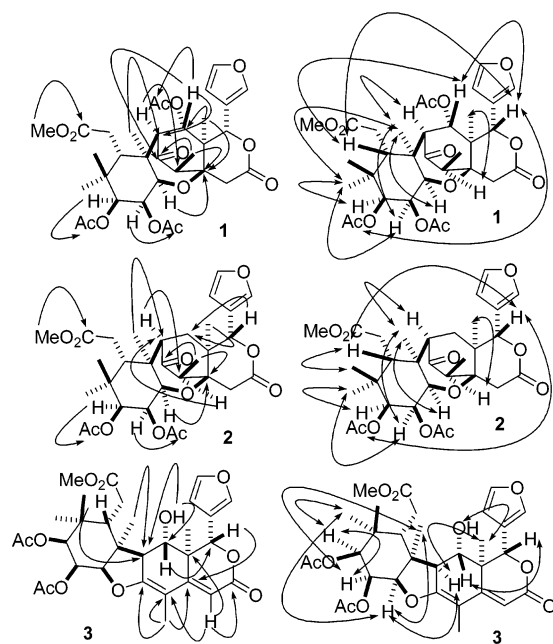
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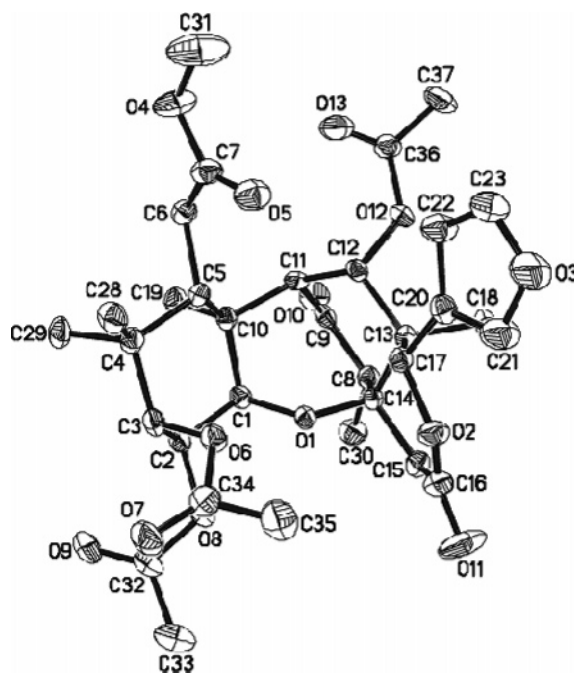
present study on the leaves and bark of *C. cinerascens* led to the isolation of three novel tetranortriterpenoids, cipadesins A–C (**1**–**3**), in which rings A and C were connected via C-10 and C-11. The carbon skeleton was different from that of either methyl angolensate-type tetranortriterpenoids,<sup>4</sup> with a six-membered ring C connected with ring A by C-9 and C-10, or from trijugin-type tetranortriterpenoids,<sup>7</sup> 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 [ $M + Na$ ]<sup>+</sup> in the HRESIMS spectrum. IR peak at  $1744\text{ cm}^{-1}$  and  $^{13}\text{C}$  NMR signals at  $\delta$  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 ( $\delta_H$  3.77;  $\delta_C$  52.3) and three acetyl groups ( $\delta_H$  1.88, 2.05, 2.11;  $\delta_C$  169.1, 170.7, 170.9), **1** contained 26 carbons, including a  $\beta$ -substituted furan ring ( $\delta_H$  6.60, 7.44, 8.10;  $\delta_C$  109.7, 121.0, 141.8, 143.2), four tertiary methyl groups ( $\delta_H$  0.87, 0.97, 1.01; 1.14), and one methyl group ( $\delta_H$  1.27, 3 H, d, 7.3) attached to methine (2.76, 1 H, q, 7.3). The above evidence suggested a tetranortriterpenoid.<sup>9</sup> HMBC correlations (Figure 1) H-11/



**Figure 1.** Important HMBC and NOESY correlations of **1**–**3** (HMBC:  $\rightarrow$ ; NOESY:  $\leftrightarrow$ ).

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 ( $\delta$  5.10)/C-2-OAc ( $\delta$  170.4), H-3 ( $\delta$  5.08)/C-3-OAc ( $\delta$  170.8), and H-12 ( $\delta$  5.52)/C-12-OAc ( $\delta$  168.8). The relative stereochemistry of **1** was determined by NOESY experiments



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

(Figure 1). X-ray crystallographic analysis of **1** (Figure 2) confirmed the proposed structure.<sup>12</sup>

The UV, IR,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  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 [ $M + Na$ ]<sup>+</sup> 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  $1739\text{ cm}^{-1}$  and from the  $^{13}\text{C}$  NMR signals at  $\delta$  212.0, 174.0, 170.8, 170.6, and 168.9. The  $^1\text{H}$  and  $^{13}\text{C}$  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 ( $\delta_H$  1.30, dd, 16.4, 6.4;

(12) Crystal structure analysis: the structure was solved by direct method with SHELX 97<sup>15</sup> 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  $0.56 \times 0.46 \times 0.26\text{ mm}$ ; monoclinic system, space group  $P2_12_12_1$ ,  $a = 9.745$  (4) Å,  $b = 15.562$  (6) Å,  $c = 11.779$  (4) Å,  $\alpha = \beta = \gamma = 90^\circ$ ,  $V = 1717.4$  (13) Å<sup>3</sup>,  $Z = 2$ ,  $d = 1.312\text{ g/cm}^3$ ,  $\lambda = 0.71073\text{ Å}$ ,  $\mu$  (Mo KR) =  $0.102\text{ mm}^{-1}$ ,  $F(000) = 724$ ,  $T = 298$  (2) K. Of the 4300 reflections collected, 3894 were unique ( $R_{\text{int}} = 0.0315$ ). 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  $-0.260\text{ e}^-/\text{Å}^3$ , 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](http://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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$\delta_{\text{H}}$  2.62, d, 16.6). The  $^{13}\text{C}$  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.**  $^1\text{H}$  NMR Data of Cipadesins A–C (**1–3**) in  $\text{CDCl}_3$  (600 MHz)<sup>a</sup>

| position         | 1                        | 2                     | 3                       |
|------------------|--------------------------|-----------------------|-------------------------|
| 1 $\alpha$       | 3.69 (d, 4.0)            | 3.68 (d, 4.0)         | 4.24 (d, 3.5)           |
| 2 $\alpha$       | 5.10 (t, 3.7)            | 5.12 (t, 3.6)         | 5.31 (t, 3.4)           |
| 3 $\alpha$       | 5.06 (d, 3.1)            | 5.08 (d, 2.9)         | 5.04 (d, 2.5)           |
| 5 $\beta$        | 2.85 (d, 9.6)            | 2.76 (d, 9.5)         | 2.24 (d, 9.5)           |
| 6 $\alpha$       | 2.55 (d, 17.4)           | 2.39 (m)              | 3.05 (d, 16.7)          |
| 6 $\beta$        | 2.42<br>(dd, 17.4, 10.0) | 2.03<br>(over-lapped) | 2.36<br>(dd, 16.9, 9.4) |
| 8 $\alpha$       | 2.76 (q, 7.3)            | 2.65 (q, 7.2)         |                         |
| 11 $\alpha$      | 2.45 (s)                 | 2.39 (m)              | 2.60 (d, 9.5)           |
| 12 $\alpha$      |                          | 1.30 (dd, 16.4, 6.4)  |                         |
| 12 $\beta$       | 5.52 (m)                 | 2.62 (d, 16.6)        | 4.38 (d, 10.0)          |
| 15 $\alpha$      | 2.70 (d, 5.5)            | 2.60 (d, 17.9)        | 5.67 (s)                |
| 15 $\beta$       | 2.70 (d, 5.5)            | 2.70 (d, 17.9)        |                         |
| 17 $\beta$       | 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 $\beta$ -OAc   | 2.05 (s)                 | 2.05 (s)              | 2.10 (s)                |
| 3 $\beta$ -OAc   | 2.11 (s)                 | 2.10 (s)              | 2.10 (s)                |
| 12 $\alpha$ -OAc | 1.88 (s)                 |                       |                         |

<sup>a</sup> Assignments were based on HSQC (or HMQC) and HMBC experiments.

Cipadesin C (**3**) was isolated as a white powder, with a molecular formula of  $\text{C}_{31}\text{H}_{38}\text{O}_{11}$  from the quasi-molecular ion peak at  $m/z$  609.2311  $[\text{M} + \text{Na}]^+$  in the HRESIMS spectrum. Four ester carbonyl groups were concluded from the IR peaks at 1740 and  $1655\text{ cm}^{-1}$  and from the  $^{13}\text{C}$  NMR signals at  $\delta$  175.2, 170.6, 170.4, and 165.8. HMBC correlations H-30 ( $\delta$  1.85, s)/C-8 ( $\delta$  101.9), C-9 ( $\delta$  160.1) and C-14 ( $\delta$  162.6), H-15 ( $\delta$  5.67, s)/C-8, C-13 ( $\delta$  44.2) and C-14, and H-17 ( $\delta$  5.20)/C-14 indicated a unsaturated system composed of C-9, C-8, C-14, C-15 ( $\delta$  105.4), and C-16 ( $\delta$  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  $^{13}\text{C}$  NMR signal for C-1 was shifted from 76.6 in **1** to 86.3 in **3**. A hydroxyl group resonating at

$\delta$  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 12 $\alpha$ -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.**  $^{13}\text{C}$  NMR Data of Cipadesins A–C (**1–3**) in  $\text{CDCl}_3$  (150 MHz)<sup>a</sup>

| 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 <sub>3</sub>                | 52.3  | 52.3  | 52.1  |
| 2 $\beta$ -OCOCH <sub>3</sub>   | 170.7 | 170.6 | 170.4 |
| 2 $\beta$ -OCOCH <sub>3</sub>   | 20.8  | 20.9  | 20.8  |
| 3 $\beta$ -OCOCH <sub>3</sub>   | 170.9 | 170.8 | 170.6 |
| 3 $\beta$ -OCOCH <sub>3</sub>   | 20.5  | 20.6  | 20.8  |
| 12 $\alpha$ -OCOCH <sub>3</sub> | 169.1 |       |       |
| 12 $\alpha$ -OCOCH <sub>3</sub> | 20.7  |       |       |

<sup>a</sup> 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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