Three New Limonoids from *Cipadessa cinerascens*

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Three new limonoids, cipadesins D—F (1—3), together with 8,15-dihydroxy-13E-labdane, β-sitosterol and β-daucosterol, were isolated from the leaves and bark of *Cipadessa cinerascens*. Their structures were elucidated by spectral evidence. X-Ray crystallographic analysis confirmed the structure of 1.

**Key words** Meliaceae; *Cipadessa cinerascens*; limonoid; cipadesin D; cipadesin E; cipadesin F

The leaves and roots of *Cipadessa cinerascens* (PELL.) HAN-D-MAZZ (Meliaceae), a shrub distributed in Southwest China, are used for the treatment of rheumatism, malaria, scald and skin itch.1) From the leaves of *C. cinerascens* flavonoids and their glucosides were isolated.2—4) From the leaves and bark of *C. cinerascens*, novel limonoids, cipadesins A—C, were obtained during our study.5) The continued study led to the isolation of three new limonoids, cipadesins D—F (1—3), together with 8,15-dihydroxy-13E-labdane,6) β-sitosterol and β-daucosterol.

Cipadesin D (1) was isolated as colorless crystal (MeOH). Its molecular formula C_{31}H_{40}O_{13} was established from the quasi-molecular ion peak at m/z 667.2330 [M+Na]^+ in the HR-ESI-MS. The IR peaks at 1749 and 1738 cm^{-1}, and 13C-NMR signals at δ 205.3, 173.7, 170.8, 170.4, 168.8 and 168.1 revealed the presence of a ketonic carbonyl group and four ester carbonyl groups as well as the HMBC correlations of H-12 (δ 1.14) and H-19 (δ 1.55), OAc (δ 4.72), and three acetyl groups (δ 2.09, 2.11; 1.87, 5.20; 168.8, 170.4, 170.8). The hydroxyl group resonated at δ 108.8, 121.1, 140.4, 143.4 and four tertiary methyl groups as well as the HMBC experiment (Fig. 2) showed that 1 may be a limonoid. The presence of β-substituted furan ring (δC 6.42, 7.44, 7.59; 108.8, 121.1, 140.4, 143.4) and 13C-NMR signals indicated that 1 may be a limonoid. The relative stereochemistry of 1 was determined by NMR data in DMSO-d_6. The hydroxyl group resonated at δ 4.72 was assigned as α.

Cipadesin E (2) was isolated as white powder. Its molecular formula C_{33}H_{40}O_{13} was determined by NMR data in DMSO-d_6. The IR peaks at 1750, 1707, 1702, 1699 cm^{-1} and 13C-NMR signals at δ 175.0, 170.7, 170.2 and 169.9. HMBC experiment (Fig. 2) showed that 3 was methyl angolensate type limonoid (Fig. 2). A hydroxyl group resonated at δ 4.72 gave HMBC correlations with C-9 and C-11, and NOESY correlation with H-12 showing it to be assigned to C-11. The remaining structure was confirmed by HMBC and NOESY experiments (Fig. 2). The UV, IR, 1H- and 13C-NMR spectral data of cipadesins E, F (2, 3) were similar to those of 1, suggesting they are all limonoids.

Cipadesin F (3) was isolated as white powder. Its molecular formula C_{31}H_{40}O_{11} was concluded from the quasi-molecular ion peak at m/z 625.2283 [M+Na]^+ in the HR-ESI-MS. The presence of a ketonic carbonyl group and four ester carbonyl groups were recognized from the IR peak at 1746 cm^{-1}, and 13C-NMR signals at δ 210.7, 173.9, 170.8, 170.4 and 168.4. The HMBC correlations of H-12 (δ 1.55), H-19 (δ 1.14) and H-30 (δ 5.58, 5.28) with C-9 (δ 210.7) showed that 2 was trijugin type limonoid (Fig. 2). A hydroxyl group resonated at δ 4.72 gave HMBC correlations with C-9 and C-11, and NOESY correlation with H-12 allowing it to be assigned to C-11. The remaining structure was confirmed by HMBC and NOESY experiments (Fig. 2).

Cipadesin F (3) was isolated as white powder. Its molecular formula C_{33}H_{40}O_{11} was concluded from the quasi-molecular ion peak at m/z 611.2471 [M+Na]^+ in the HR-ESI-MS. Four ester carbonyl groups were revealed by the IR peak at 1739 cm^{-1} and 13C-NMR signals at δ 175.0, 170.7, 170.2 and 169.9. HMBC experiment (Fig. 2) showed that 3 was methyl angolensate type limonoid (11,11) characterized by a six-membered ring C connected with ring A by C-9 and C-10. The structure of 3 was determined by NMR data in DMSO-d_6. The hydroxyl group resonated at δ 4.72 was assigned as α.

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Fig. 1. Cipadesins D—F (1—3) Isolated from *Cipadessa cinerascens*

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signed as HO-9α on the basis of its correlations with C-8, C-9, C-10 and C-11 in HMBC experiment, and with H-11α in NOESY experiment (Fig. 2). Two acetyl groups were placed at C-2 and C-3 by the HMBC cross signals between H-2, OAc, and between H-3, OAc. The relative stereochemistry of 3 was determined by NOESY experiment.

**Experimental**

**General** Melting points were measured on an X-6 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 automatic polarimeter. UV and IR spectra were recorded on a Lambda 35 spectrometer and a Perkin-Elmer FT-IR spectrometer (KBr disk), respectively. Mass spectra were obtained on a Finnigan-LCQDECA mass spectrometer (ESI-MS) and a Bruker Daltonics Bio TOF-Q mass spectrometer (HR-ESI-MS). NMR spectra were carried out on a Bruker Avance 600 spectrometer with TMS as internal standard. Column chromatography was carried out on silica gel (200—300 mesh; Qingdao Haiyang Chemical Group Co., China), silica gel 60 (0.015—0.040 mm, Merck), MCI gel (75—150 μm, Mitsubishi) and RP-18 silica gel (Prepex 40—63 μm, Phenomenex). Semi-

![Fig. 3. ORTEP Diagram of 1](image-url)
preparative HPLC was carried out using a Perkin Elmer Series 200 HPLC system (Lichrocrop RP-C_{18}, column, 10.0×250 mm, 5 μm). Solvents were distilled prior to use.

**Plant Material** Leaves and bark of *Cipadesia cinerascens* were collected in May 2004 at Panzhihua City, Sichuan Province of China, and identified by Prof. Zuo-Cheng Zhao at Chengdu Institute of Biology of the Chinese Academy of Sciences (CAS). A voucher specimen (No. A-186) was deposited in the Natural Products Research Center at Chengdu Institute of Biology, CAS.

**Extraction and Isolation** Air-dried and powdered leaves and bark (4.8 kg) were percolated with 95% EtOH (40 l×2, each 7 d) at room temperature. After evaporation of the solvents in vacuo at 50 °C, a residue (310 g) was obtained. This residue was suspended in H_2O (1 l) and extracted with CHCl_3-MeOH soluble fraction from MeOH, and the remnant was then subjected to silica gel column (20 cm, 150 g) using petroleum ether (60—90 °C)–acetone (6 : 1) to give yellow oily residue (50 mg), from which 8,15-dihydroxy-13R,16S,17S-trihydroxy-13E,17E-labdane (20 mg) was obtained by crystallization from MeOH at 4 °C.

Cipadesin D (1): Colorless needles (MeOH). mp 208.1—209.0 °C. 1H-NMR data see Table 1. 13C-NMR data see Table 2. IR (KBr) cm\(^{-1}\): 3445, 2990, 1749, 1738, 1686, 1372, 1073, 1003, 875, 607. UV \( \lambda_{\text{max}} \) (CHCl_3) nm (log \( \varepsilon \)) 241 (2.87). HR-ESI-MS (positive mode) \( m/z \) 667.2330 (Calcd for C_{33}H_{40}O_{13}Na [M+Na]^+; 667.2361). \( \{\alpha\}^{25}_D -5.3°, \{\beta\}^{13C}_{\text{CHCl}_3} -5.3°, \{\alpha\}^{13C}_{\text{CHCl}_3} -7.2°, \{\beta\}^{13C}_{\text{CHCl}_3} -28.9°, \{\beta\}^{13C}_{\text{CHCl}_3} -157.9° (c=0.15, CHCl_3).

Cipadesin E (2): White powder. \( 1^3\)-NMR data see Table 1. \( 1^3\)-NMR data see Table 2. IR (KBr) cm\(^{-1}\): 3445, 2976, 1746, 1686, 1634, 1379, 1248, 1164, 1083, 1048, 1021, 876, 602. UV \( \lambda_{\text{max}} \) (CHCl_3) nm (log \( \varepsilon \)) 240 (2.03). HR-ESI-MS (positive mode) \( m/z \) 625.2283 (Calcd for C_{30}H_{36}O_{12}Na [M+Na]^+; 625.2255). \( \{\alpha\}^{25}_D -6.1°, \{\alpha\}^{13C}_{\text{CHCl}_3} -6.4°, \{\beta\}^{13C}_{\text{CHCl}_3} -7.4°, \{\alpha\}^{13C}_{\text{CHCl}_3} -10.2°, \{\beta\}^{13C}_{\text{CHCl}_3} -16.8° (c=0.39, CHCl_3).

Cipadesin F (3): White powder. \( 1^3\)-NMR data see Table 1. \( 1^3\)-NMR data see Table 2. IR (KBr) cm\(^{-1}\): 3451, 2953, 1739, 1635, 1384, 1250, 1198, 1168, 1049, 875, 602. UV \( \lambda_{\text{max}} \) (CHCl_3) nm (log \( \varepsilon \)) 240 (1.89). ESI-MS (positive mode) \( m/z \) 611 [M+Na]^+ (100). HR-ESI-MS (positive mode) \( m/z \) 611.2471 (Calcd for C_{30}H_{36}O_{12}Na [M+Na]^+; 611.2463). \( \{\alpha\}^{25}_D -36.5°, \{\alpha\}^{13C}_{\text{CHCl}_3} -38.2°, \{\alpha\}^{13C}_{\text{CHCl}_3} -43.5°, \{\alpha\}^{13C}_{\text{CHCl}_3} -74.8°, \{\beta\}^{13C}_{\text{CHCl}_3} -118.8° (c=0.42, CHCl_3).

**X-Ray Crystallography of 1** Crystal data: C_{33}H_{40}O_{13}Na; \( M_w \)=644.65; dimensions 0.48×0.48×0.46 mm; monoclinic system, space group P2_12_1; \( a=10.770(4) \, \text{Å}, b=11.174(3) \, \text{Å}, c=13.377(4) \, \text{Å}, \alpha=\beta=\gamma=90°, \gamma=169.6° \, (11) \, \text{Å} \); \( Z=2, d=1.330 \, \text{g/cm}^3, \lambda=0.71073 \, \text{Å}, \mu\, \text{(Mo Kα)}=0.089 \, \text{mm}^{-1}, F(000)=684, T=296(2) \, \text{K}. Of the 4231 reflections collected, 386 were unique (\( R_p \)=0.0064). The structure was solved by direct method with SHELX 97 [2] and refined by fullmatrix least-squares on \( F^2 \). Final refinement: data/restraints/parameters=3886/1442; \( R=0.0644 \) (all data), \( wR_2=0.1084 \) (all data); the Flack absolute structure parameter=0.18 (10), and GOF=0.945. The H coordinates were determined by calculated geometry. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.188 and --0.228 e/\( \text{Å}^3 \), respectively. CCDC 278633 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge \( \text{via} \) www.ccdc.cam.ac.uk or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K., fax: +44 1223 336033.

**Supporting Information Available** X-Ray data of 1; HR-ESI-MS spectra; 1D and 2D NMR diagrams of 1—3. This material is available free of charge \( \text{via} \) the Internet at http://cjb.pharm.or.jp.

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**References**