

Limonoids and phytol derivatives from *Cedrela sinensis*

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Abstract

Two new compounds, cedrellin (**1**) and 2,6,10,15-phytatetraene-14-ol (**2**), together with five known compounds, 7 α -obacunyl acetate, 6-acetoxyobacunol acetate, 7 α -acetoxydihydronomilin, 2,6,10-phytatriene-1,14,15-triol and phytol were isolated from leaves of *Cedrela sinensis*. Their structures were elucidated on the basis of combined one- and two-dimensional spectral techniques. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: *Cedrela sinensis*; Limonoids; Phytol derivatives

1. Introduction

Cedrela sinensis A. Juss (Meliaceae), syn. *Toona sinensis* A. Juss, is widely cultivated in China. Its tender leaf containing carotene and vitamins B and C is edible [1]. Many flavonoids and phenolic compounds were also isolated from it [2,3]. *C. sinensis* was used for treating enteritis, dysentery, and skin itch in China and Korea [1–3]. Bioactivity against pests was also reported [4]. In our continual searching for bioactive compounds from Meliaceae [5], a new limonoid and a new

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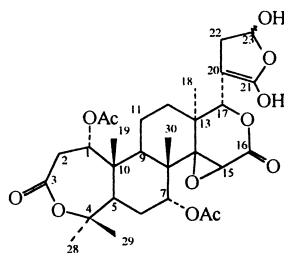
phytol derivative were isolated from the leaves of *C. sinensis* along with five known compounds, 7 α -obacunyl acetate [6], 6-acetoxyobacunol acetate [7], 7 α -acetoxydihydronomilin [8], phytol [9] and 2,6,10-phytatriene-1,14,15-triol [10].

2. Results and discussion

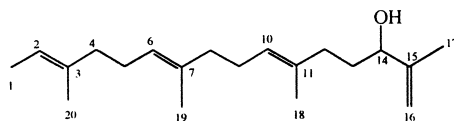
Compound **1**, from its negative-ion HRFAB-MS at m/z 591.2502 [M-H]⁻, together with the ¹³C-NMR and DEPT spectra, possessed a molecular formula of C₃₀H₄₀O₁₂. The IR spectrum showed absorption bands for hydroxyl at 3459 cm⁻¹, carbonyl group at 1739 cm⁻¹ and olefinic linkage at 1646 cm⁻¹. The ¹H-NMR spectrum indicated the presence of five tertiary methyls and two acetate groups. Therefore, the molecular formula suggested **1** to be a tetranortriterpenoid, as 7 α -obacunyl acetate, 6-acetoxyobacunol acetate and 7 α -acetoxydihydronomilin [6–8].

The ¹³C-NMR spectrum of **1** exhibited signals due to four ester carbonyl groups at δ_C 167.1, 169.7, 169.8, 170.3. In a HMBC experiment, cross-signals between δ_C 170.3 to δ_H 4.78 (H-1), and δ_C 169.8 to δ_H 4.45 (H-7) placed the two acetates at C-1 and C-7, both with α -orientation as determined by coupling constants for H-1 ($J = 7.3$ Hz) and H-7 (*br s*) [11,12]. In the HMBC spectrum, cross-signals between δ_C 167.1 to δ_H 5.41 (*s*, H-17) and the former to δ_H 3.46 (*s*, H-15) revealed that the D-ring of **1** was in the form of a δ -lactone with a C-14,15 epoxy substitution. Cross-signals between δ_C 169.7 (C-3), δ_C 85.4 (C-4), and δ_C 23.3 (C-29) to δ_H 1.29 (H-28) indicated the presence of a lactone system in a seven-membered A ring.

The ¹H- and ¹³C-NMR spectra of **1** were very similar to those of 7 α -acetoxydi-



1



2

hydnomilin [8], except for side chain data. Instead of signals for the β -substituted furan ring in ^{13}C and ^1H -NMR spectra of 7 α -acetoxydihydromilin, δ_{C} 150.6 (*s*, C-21), 132.9 (*s*, C-20), 97.6 (*d*, C-23), and 25.4 (*t*, C-22) were present in the ^{13}C -NMR spectrum of **1**, and corresponding δ_{H} 6.18 (1H, H-23) in ^1H -NMR spectrum of **1**. Taking these data and molecular formula ($\text{C}_{30}\text{H}_{40}\text{O}_{12}$) into account, the side chain of **1** was assumed to be a 3,4-dihydro-1,4-dihydroxyfuran group. The assumption was further confirmed by the HMBC spectrum, with a cross peak between δ_{H} 5.41 (*s*, H-17) to δ_{C} 132.9 (*s*, C-20). Therefore, compound **1**, named cedrellin, was deduced to be 22,23-dihydro-21,23-dihydroxy-7 α -acetoxyl-dihydromilin.

Compound **2** possessed a molecular formula of $\text{C}_{20}\text{H}_{34}\text{O}$ as indicated by EI-MS, ^{13}C -NMR and DEPT spectra, which was also supported from negative-ion HRFAB-MS. Its IR spectrum showed OH (3420 cm^{-1}) and C=C (1672 cm^{-1}) absorption bands. The ^1H and ^{13}C -NMR spectra showed signals for five methyl groups (four singlets and a doublet) attached to olefinic bonds, eight olefinic carbons [δ_{C} 109.5 (*t*), 124.0 (*d*), 124.2 (*d*), 124.5 (*d*), 135.0 (*s*), 135.8 (*s*), 136.0 (*s*), 151.9 (*s*)], six methylene groups (δ_{C} 39.8, 39.8, 35.7, 31.6, 26.8, 26.7), and an oxymethine (δ_{C} 75.2). Four olefinic bonds accounted for all degrees of unsaturation required by the molecular formula $\text{C}_{20}\text{H}_{34}\text{O}$, which suggesting the absence of ring in **2**. Inspection of one- and two-dimensional NMR spectra suggested that compound **2** possessed phytol derivative skeleton (linear chain diterpene) having four olefinic linkages and a hydroxyl substitution.

The secondary methyl at δ_{H} 1.60 (*d*, $J = 7.8\text{ Hz}$), showing correlation with an olefinic proton [δ_{H} 5.14 (*m*)] in ^1H - ^1H COSY experiment, suggested the presence of a double bond between C-2 and C-3. Two double bonds were assigned between C-6 and C-7, C-10 and C-11, respectively, based on almost identical chemical shift values with related compounds [13], as well as HMBC spectral evidences. In the HMBC spectrum, cross-signals between δ_{H} 1.63 (3H, *s*, H-17) and δ_{C} 75.2 (*d*, C-14), H-17 and δ_{C} 151.9 (*s*, C-15), and δ_{H} 5.07, 4.91 (each 1H, *s*, H-16) and δ_{C} 75.2 (*d*, C-14) not only assigned an olefinic linkage between C-15 and C-16, but also placed a hydroxyl at C-14 position. Accordingly, compound **2** was determined as 2,6,10,15-phytatetraen-14-ol.

3. Experimental

3.1. Plant material

The leaves of *C. sinensis* were collected from Kunming, Yunnan Province, P.R. China, in July 1996 and authenticated by Dr. Meng SW, Kunming Institute of Botany, *Academia Sinica*, where a voucher specimen (no. 5114) was deposited.

3.2. Extraction and isolation

The air-dried and powdered leaves (5.0 kg) were extracted with EtOH three

times at room temperature and the solvent was removed in vacuo. The residue, suspended in water, was extracted with petroleum ether and CHCl_3 . The petroleum ether fraction provided a residue (58 g) which was Si-gel CC eluting with petroleum ether–EtOAc mixts and then with petroleum ether– Me_2CO mixts to afford 3 mg 2,6,10,15-phytatetraene-14-ol (**2**). The CHCl_3 layer afforded a residue (86 g) which was Si-gel CC on silica gel using CHCl_3 – Me_2CO mixts and then purified on RP C_{18} Si-gel column using CH_3OH –water (8:2–7:3) as an eluent to yield compound **1** (32 mg), 7 α -obacunyl acetate (1.86 g), 6-acetoxycobacunol acetate (320 mg), 7 α -acetoxidihydronomilin (18 mg), 2,6,10-phytatriene-1,14,15-triol (180 mg) and phytol (8 mg).

Cedrellin (1). M.p. 192–195°C (from acetone); $[\alpha]_{\text{D}}^{27}$: -28.3° (*c* 0.40, CH_3OH); UVmax (MeOH): 201 (log ϵ 3.15) nm; IR bands (KBr): 3459, 2986, 2950 1739, 1646, 1454, 1433, 1377, 1321, 1229, 1124, 1026, 931, 883 cm^{-1} ; $^1\text{H-NMR}$ [400 MHz, CDCl_3 + $(\text{CD}_3)_2\text{CO}$]: δ 6.18 (1H, *br s*, H-23), 5.41 (1H, *s*, H-17), 4.78 (1H, *d*, *J* 7.3Hz, H-1), 4.45 (1H, *br s*, H-7), 3.46 (1H, *s*, H-15), 3.45, 3.02 (each 1H, *m*, H-2), 2.81 (1H, *dd*, *J* 12.4, 6.4Hz, H-9), 2.43 (1H, *d*, *J* 12.8Hz, H-5), 2.05 (3H, *s*, OAc), 2.00 (3H, *s*, OAc), 2.02, 1.90 (each 1H, *m*, H-6), 1.80, 1.65 (each 1H, *m*, H-12), 1.80, 1.55 (each 1H, *m*, H-11), 1.51, 1.29, 1.29, 1.19, 1.14 (each 3H, *s*, Me); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3 + CD_3OD): 170.3 (OAc), 169.8 (OAc), 169.7 (C-3), 167.1 (C-16), 150.6 (C-21), 132.9 (C-20), 97.6 (C-23), 85.4 (C-4), 76.0 (C-17), 73.0 (C-7), 70.7 (C-1), 69.4 (C-14), 56.4 (C-15), 44.7 (C-10), 43.7 (C-5), 41.9 (C-8), 39.2 (C-13), 36.5 (C-9), 34.8 (C-2), 34.1 (C-28), 25.6 (C-6), 25.4 (C-22), 25.1 (C-12), 23.3 (C-29), 20.7 (OAc), 20.5 (OAc), 18.1 (C-30), 16.0 (C-30), 15.5 (C-19), 14.7 (C-11); EI-MS (70 eV) *m/z*: 592 $[\text{M}]^+$ (0.3), 546 (18), 531 (5), 503 (4), 486 (17), 472 (26), 430 (18), 412 (75), 397 (15), 369 (13), 353 (20), 341 (14), 317 (17), 299 (20), 273 (24), 255 (30), 227 (43), 185 (57), 173 (64), 145 (80), 133 (70), 119 (92), 105 (94), 91 (100); HRFAB-MS *m/z*: 591.2502 $[\text{M-H}]^-$ (calculated for $\text{C}_{30}\text{H}_{39}\text{O}_{12}$, 591.2442).

2,6,10,15-Phytatetraen-14-ol (2). Viscous oil; IR bands (KBr): 3420, 2929, 1672, 1453, 1379, 1073, 901 cm^{-1} ; $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 5.17 (1H, *m*, H-6), 5.14 (1H, *m*, H-2), 5.12 (1H, *m*, H-10), 5.07, 4.91 (each 1H, *s*, H-16), 4.06 (1H, *dd*, *J* 6.8, 5.2Hz, H-14), 1.70 (3H, *s*, H-20), 1.66 (3H, *s*, H-19), 1.63 (6H, *s*, H-17, H-18), 1.60 (3H, *d*, *J* 7.8Hz, H-1); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): 151.9 (C-15), 136.0 (C-3), 135.8 (C-11), 135.0 (C-7), 124.5 (C-6), 124.2 (C-2), 124.0 (C-10), 109.5 (C-16), 75.2 (C-14), 39.8 (C-8 and C-4), 35.7 (C-12), 31.6 (C-13), 26.8 (C-9), 26.7 (C-5), 25.6 (C-20), 17.7 (C-1 and C-18), 16.0 (C-17 and C-19); EI-MS (70eV) *m/z*: 290 $[\text{M}]^+$ (2), 203 (8), 187 (8), 175 (8), 161 (10), 147 (14), 135 (21), 123 (19), 109 (25), 95 (33), 81 (50), 69 (100); HRFAB-MS *m/z*: 289.2454 $[\text{M-H}]^-$ (calculated for $\text{C}_{20}\text{H}_{33}\text{O}$, 289.2531).

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