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A NEW MYRINSOL DITERPENOID ESTER FROM *Euphorbia dracunculoides*

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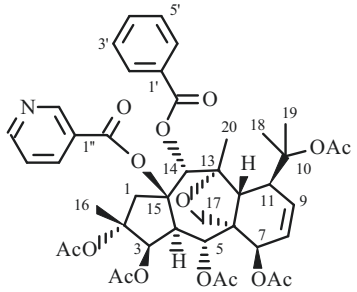
*A new myrinsol diterpenoid ester, 2α,3β,5α,7β,10-*O*-pentacetyl-14α-*O*-benzoyl-15β-*O*-nicotinoyl-10,18-dihydromyrsinol (**1**), along with a known analogue, proliferin C (**2**), were isolated from the aerial parts of* Euphorbia dracunculoides *Lam. Their structures were elucidated on the basis of spectroscopic evidence and comparison with literatures.*

Keywords: *Euphorbia dracunculoides,* myrinsol, diterpenoid ester.

Phytochemical investigations on *Euphorbia dracunculoides* are limited to the report of flavonoids [1–3], triterpenoids [3, 4], and coumarins [4]. To the best of our knowledge, diterpenoid constituents of this species have not been characterized. We reported previously that two compounds were isolated from the aerial part of *E. dracunculoides* [5]. Aiming to searching for more biologically active diterpenoids, we have investigated the aerial part of *E. dracunculoides*, collected in Xishuang Banna Prefecture, Yunnan Province, People′s Republic of China. As a result, a new myrinsol diterpenoid ester, 2*α*,3*β*,5*α*,7*β*,10-*O*-pentacetyl-14*α*-*O*-benzoyl-15*β*-*O*-nicotinoyl-10,18-dihydromyrsinol (**1**), and a known analogue, proliferin C (**2**), were obtained. We describe herein the isolation and structure elucidation of the new compound.

Compound **1**, $[\alpha]_D^{23.2}$ –119.5° (*c* 0.18, MeOH). UV (MeOH, λ_{max}, nm) (log ε): 224 (3.55) and 201 (3.47), obtained as a white powder from MeOH. Its molecular formula was determined to be $C_{43}H_{49}NO_{15}$ based on the HR-ESI-MS data (*m/z* 842.2994 $[M + Na]^+$, calcd 842.3000), corresponding to 20 degrees of unsaturation. Its IR spectrum showed absorption bands for carbonyl groups at 1740 cm^{-1}. The ^1H NMR spectrum (Table 1) showed nine 3H-singlets at δ 2.31, 2.13, 1.99, 1.80, 1.76, 1.65, 1.56, 1.37, and 1.26, of which five may be assigned to acetyls and four assigned to tertiary methyl groups. A mono-substituted benzene ring [δ 8.11 (2H, d, J = 7.4 Hz), 7.60 (1H, t, J = 7.4 Hz), 7.47 (2H, t, J = 7.4 Hz)] and a mono-substituted pyridine ring [δ 9.24 (1H, s), 8.80 (1H, br.s), 8.32 (1H, d, J = 7.4 Hz), 7.46 (1H, overlapped)] were also evident in the ^1H NMR spectrum. Additionally, the signals of two vicinal olefinic protons [δ 6.17 (1H, m), 5.92 (1H, dd, J = 10.0, 5.7 Hz)] and an oxygenated methylene group [δ 4.20 (1H, d, J = 8.8 Hz), 3.55 (1H, dd, J = 8.8, 1.4 Hz)] were also observed. Seven carbonyl signals at δ 170.8, 170.5, 169.6, 169.5, 168.7, 165.9, and 164.9 were obvious in the ^{13}C NMR spectrum of **1**.



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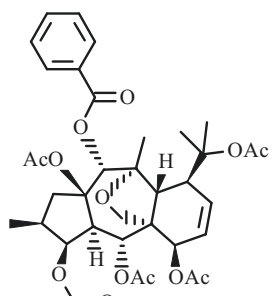

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TABLE 1. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR Data of **1** ($CDCl_3$, δ, ppm, J/Hz)

C atom	δ_H	δ_C	C atom	δ_H	δ_C
1α	3.36 (1H, d, J = 17.2)	47.7 (t)	18	1.56 (3H, s)	21.5 (q)
1β	2.45 (1H, d, J = 17.2)		19	1.65 (3H, s)	25.4 (q)
2	–	87.1 (s)	20	1.26 (3H, s)	24.5 (q)
3	5.66 (1H, d, J = 3.7)	79.6 (d)	2-OAc	1.76 (3H, s)	169.6 (s); 22.5 (q)
4	3.91 (1H, dd, J = 11.1, 4.0)	47.9 (d)	3-OAc	2.31 (3H, s)	168.7(s); 22.8 (q)
5	6.08 (1H, dd, J = 11.1, 1.2)	68.8 (d)	5-OAc	1.99 (3H, s)	169.5 (s); 21.0 (q)
6	–	53.7 (s)	7-OAc	1.80 (3H, s)	170.5 (s); 21.0 (q)
7	4.85 (1H, d, J = 6.6)	62.9 (d)	10-OAc	2.13 (3H, s)	170.8 (s); 22.7 (q)
8	6.17 (1H, m)	125.7 (d)	14-OBz	–	165.9 (s)
9	5.92 (1H, dd, J = 10.0, 5.7)	130.1(d)	1′	–	130.0 (s)
10	–	86.0 (s)	2′, 6′	8.11 (2H, d, J = 7.4)	130.3 (d)
11	3.21 (1H, m)	44.8 (d)	3′, 5′	7.47 (2H, t, J = 7.4)	128.6 (d)
12	3.27 (1H, d, J = 3.3)	37.2 (d)	4′	7.60 (1H, t, J = 7.4)	133.6 (d)
13	–	90.2 (s)	15-*O*-nicotinoyl	–	164.9 (s)
14	5.90 (1H, s)	73.1 (d)	1′	–	127.0 (s)
15	–	90.2 (s)	2′	8.32 (1H, d, J = 7.4)	137.8 (d)
16	1.37 (3H, s)	19.2 (q)	3′	7.46 (1H, overlapped)	123.7 (d)
17a	4.20 (1H, d, J = 8.8)	69.9 (t)	4'	8.80 (1H, br.s)	153.1 (d)
17b	3.55 (1H, dd, J = 8.8, 1.4)		5′	9.24 (1H, s)	150.4 (d)

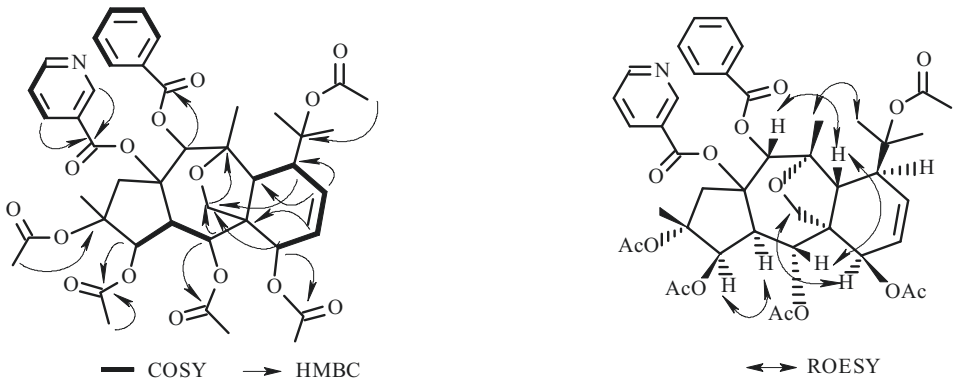

Fig. 1. Key COSY, HMBC, and ROESY correlations of **1**.

Accordingly, **1** was presumably a highly oxidized tetracyclic diterpenoid substituted by five acetoxy, one benzoyloxy, and one nicotinoyloxy groups. Four oxymethine protons geminal to ester functions [δ 6.08 (1H, dd, J = 11.1, 1.2 Hz), 5.90 (1H, s), 5.66 (1H, d, J = 3.7 Hz), 4.85 (1H, d, J = 6.6 Hz)] suggested that the other three ester groups were located at quaternary carbons. Comparison the above NMR data with those of euphorprolitherin B, a myrsinol diterpenoid [6] which was isolated from *Euphorbia prolifera*, indicated that they are quite structurally similar. The possible differences were that a propionyloxy group at C-3 and an acetoxy group at C-15 in euphorprolitherin B are replaced by an acetoxy group and a nicotinoyloxy group, respectively, in **1**. The hypothesis was further verified by the HMBC correlations (Fig. 1) from a methyl signal at δ_H 2.31 (3H, s) and an oxymethine proton signal at δ_H 5.66 (1H, d, J = 3.7 Hz, H-3) to a ester carbonyl signal at δ_C 168.7. Accurate assignments of all protons and carbons were preformed through the correlations in the 2D NMR spectra (^{1}H–^{1}H COSY, HSQC and HMBC) of **1** (Fig. 1), from which the positions of the ester groups were also clarified. The correlations of the protons at δ_H 6.08 (H-5), 4.85 (H-7), and 5.90 (H-14) with the carbonyl carbons at δ_C 169.5, 170.5, and 165.9 in the HMBC spectrum demonstrated that two acetoxy and one benzoyloxy groups were located at C-5, C-7, and C-14, respectively. In addition, two slightly weak correlations from methyl signals in the acetoxy groups at δ_H 1.76 (3H, s, 2-OAc) and 2.13 (3H, s, 10-OAc) to two quaternary carbons at δ_C 87.1 (s, C-2) and 86.0 (s, C-10), respectively, indicated that the two acetoxy groups were located at C-2 and C-10. Thus, the nicotinoyloxy group was only connected to C-15.

The relative configurations of **1** were determined by a ROESY experiment (Fig. 1) as well as from biosynthetic considerations. For the reported natural myrsinol diterpenoids, the three rings (5/7/6) forming the myrsinol diterpenoid skeleton are *trans*-fused, H-4 and H_2-17 are α-oriented, and Me-16, H-12, the side chain at C-11, and the C-15 acyloxy group are

β-oriented [7]. In addition, the ROESY correlations of H-4α with H-3 and H-7 with H_2-17 supported the α-orientations for H-3 and H-7, respectively, and the ROESY correlations between H-12β with H-5, H-12 and H-14, H-18 and Me-20, were in agreement with the β-orientations of H-5, H-14, and Me-20. Consequently, compound **1** was elucidated as 2α,3β,5α,7β,10-*O*-pentacetyl-14α-*O*-benzoyl-15β-*O*-nicotinoyl-10,18-dihydromyrsinol.

EXPERIMENTAL

General. Optical rotations were recorded in MeOH using a JASCO P-1020 Polarimeter. UV spectra were acquired in MeOH with a Shimadzu UV-2401PC UV-VIS spectrophotometer. IR spectra were measured on a Bruker Tensor 27 FTIR spectrometer with KBr disks. NMR spectra were recorded in $CDCl_3$, using a Bruker Avance III-600 spectrometer, and TMS was used as internal standard. ESI-MS spectra were recorded using a Waters Xevo TQ-S ultrahigh pressure liquid chromatography triple quadrupole mass spectrometer. HR-ESI-MS data were obtained using an Agilent G6230 Q-TOF mass instrument. Semipreparative HPLC was conducted on a Hitachi Chromaster system equipped with a DAD detector and a YMC-Triart C_{18} column (250 mm × 10 mm i.d., 5 μm).

Plant Material. The aerial parts of *Euphorbia dracunculoides* Lam. were collected in September 2012 from Xishuang Banna Prefecture, Yunnan Province, People′s Republic of China, and authenticated by Mr. Shun-Cheng Zhang, Xishuang Banna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen (No. Zhang20120927) was deposited at Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried and powdered aerial parts of *E. dracunculoides* (4.0 kg) were extracted with 70% aqueous acetone (10 L × 2 d × 3) at room temperature. The extracts were concentrated to remove organic solvent. The aqueous residue was then partitioned with petroleum ether, EtOAc, and *n*-BuOH sequentially. The petroleum ether-soluble part (48.0 g) was subjected to silica gel column chromatography (CC), eluting with petroleum ether–acetone (1:0–0:1), to afford six fractions (A–F). Fraction E (3.1 g) was firstly separated by MPLC (MCI gel CHP 20P, 90%MeOH) to give a subfraction Fr. E-1. Fraction E-1 was then subjected to Sephadex LH-20 CC and eluted by $CHCl_3$–MeOH, 1:1, followed by semipreparative HPLC (MeCN–H_2O, 64:36, 3.0 mL/min) to get compounds **1** (1.0 mg) and **2** (2.5 mg).

Compound 1. White powder; $[\alpha]_D^{23.2}$ –119.5° (*c* 0.18, MeOH). UV (MeOH, λ_{max}, nm) (log ε): 224 (3.55) and 201 (3.47). IR (KBr, ν, cm^{-1}): 3441, 1740, 1631, 1371, 1243. ESI-MS (positive mode) *m/z:* 820 $[M + H]^+$, 842 $[M + Na]^+$, 858 $[M + K]^+$; HR-ESI-MS (positive mode) *m/z* 842. 2994 $[M + Na]^+$ (calcd for $C_{43}H_{49}NO_{15}Na^+$, 842.3000). For ^1H and ^{13}C NMR data, see Table 1.

The known compound was identified as proliferin C (**2**) by comparison of experimental data with those previously reported [8].

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