

Two Novel Myrinsol Diterpenes from *Euphorbia prolifera*

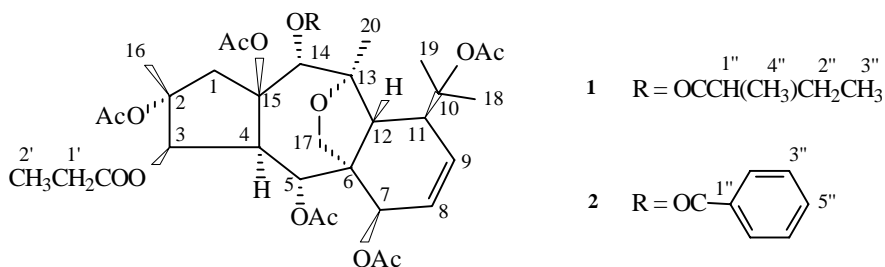
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Abstract: Two novel diterpenes, Euphorprolitherin **A** (**1**) and Euphorprolitherin **B** (**2**), were isolated from the roots of *Euphorbia prolifera*. Their structures were elucidated on the basis of spectroscopic methods.

Keywords: *Euphorbia prolifera*, Euphorbiaceae, myrinsol diterpenes, euphorprolitherin **A**, euphorprolitherin **B**.

Euphorbia prolifera (Euphorbiaceae) is used as a folk medicine for the treatment of inflammation and tumors in China¹. Previously, eight diterpenes and one steroid from this plant were isolated and characterized by other groups²⁻⁵. Our phytochemical investigation on this plant led to the isolation of two novel myrinsol diterpenes named euphorprolitherin **A** (**1**) and euphorprolitherin **B** (**2**). This paper deals with their structural elucidation.

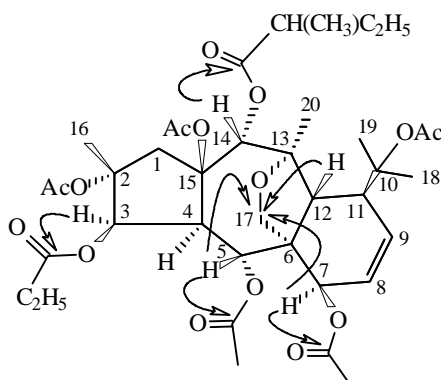


Euphorprolitherin **A** (**1**), was obtained as colorless cubes and gave prominent IR absorption (1714 cm⁻¹) of carbonyl groups. The ESI mass spectrum of **1** exhibited a quasi-molecular ion [M+Na]⁺ at *m/z* 773.4, indicating its molecular weight of 750. In conjunction with the analysis of the NMR spectra, the molecular formula was assigned as C₃₈H₅₄O₁₅, from which twelve degrees of unsaturation was deduced. The signals at δ 2.10, 2.08, 2.06, 1.98 and 1.96 in the ¹H NMR spectrum showed five 3H-singlets for acetate groups, respectively. The vicinal coupling signals between a quartet (δ 2.40, q, 2H, *J* = 7.0 Hz) and a triplet (δ 1.17, t, 3H, *J* = 7.0 Hz) indicated one propionate group. The existence of one 2-methylbutanoate group [δ 2.40 (m, 1H), 1.83 (m, 1H), 1.50 (m, 1H), 1.21 (d, 3H, *J* = 6.9 Hz) and 0.96 (t, 3H, *J* = 7.5 Hz)] was also evident.

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Accordingly, **1** was presumably substituted by seven ester groups. Four oxymethine protons geminal to ester functions [δ 5.89 (dd, $J = 11.0, 1.4$ Hz), 5.57 (s), 5.37 (d, $J = 4.0$ Hz) and 4.83 (d, $J = 6.5$ Hz)] suggested that the other three ester groups were located at quaternary carbons. Additionally, the signals of four tertiary methyl groups [δ 1.63, 1.52, 1.39 and 1.15 (each s, 3H)], two vicinal olefinic protons [δ 6.16 (ddd, $J = 10, 6.5, 1.4$ Hz) and 5.90 (dd, $J = 10, 6.0$ Hz)] and an oxygenated methylene group [δ 4.09 (d, $J = 8.8$ Hz) and 3.47 (dd, $J = 8.8, 1.4$ Hz)] were also observed in the ^1H NMR spectrum. In the ^{13}C NMR and DEPT spectra of **1**, twenty carbon signals were observed, which supported the result of ^1H NMR spectrum. With the consideration of 12 degrees of unsaturation, of which 7 resulted from ester residues, 5 degrees of unsaturation for a tetracyclic skeleton with one double bond were revealed. Comparison of the above data with those of myrsinol derivatives⁶ proposed that **1** was different from them by the absence of the typical bond between C-10 and C-18. This was verified by the chemical shifts of C-10 (δ 85.8, s) and C-18 (δ 25.3, q). Thus, **1** was a diterpene heptaester of a new parent alcohol related to myrsinol.

Figure 1 The key HMBC correlations of **1**



On the basis of 2D-NMR spectra (^1H - ^1H COSY, HMQC and HMBC) of **1**, the unambiguous assignment of all protons and carbons were achieved, which also clarified the positions of the ester groups. The following HMBC cross peaks: H-3 (δ 5.37, d, $J = 4.0$ Hz) with the signal of propionyloxy group (δ 173.6, s); H-5 (δ 5.89, dd, $J = 11.0, 1.4$ Hz) with the acetoxy signal at δ 169.2 (s); H-7 (δ 4.83, d, $J = 6.5$ Hz) with the acetoxy signal at δ 170.4 (s); and H-14 (δ 5.57, s) with the carbonyl carbon of 2-methylbutanoate (δ 175.4, s) disclosed that the propionyloxy, two acetoxy, and the 2-methylbutanoate groups were located at C-3, C-5, C-7, and C-14, respectively. Three quaternary carbon signals at δ 87.0 (C-2), 85.8 (C-10), and 90.2 (C-15) directed the other three acetoxy groups at C-2, C-10, and C-15, respectively.

The relative stereochemistry of **1** was decided by the NOESY experiment. The NOE effects: H-4 α with H-3; H-7 with H-17a, b and H-11 α with Me-20 supported the α -orientations for H-3, H-7 and Me-20. The NOE correlations: H-1 β with Me-16; H-12 β with H-5 and H-12 β with H-14 assigned the β -orientations for M-16, H-5, and H-14. Consequently, compound **1** was identified as 14-desoxo-2 α , 5 α , 7 β , 10,

15 β -O-pentaacetyl-3 β -O-propionyl-14 α -O-(2-methylbutryl)-10, 18-dihydromyrinsol.

Table 1 ^{13}C NMR Data for Compounds **1** and **2** (100 MHz, CDCl_3 , δ in ppm)

C	1	2	C	1	2
1	46.6 (t)	47.1 (t)	2-OAc	169.8 (s)	169.4 (s)
2	87.0 (s)	87.0 (s)		22.4 (q)	22.4 (q)
3	78.3 (d)	78.1 (d)	5-OAc	169.2 (s)	169.3 (s)
4	47.6 (d)	47.5 (d)		20.9 (q)	20.9 (q)
5	68.6 (d)	68.6 (d)	7-OAc	170.4 (s)	170.4 (s)
6	53.3 (s)	53.6 (s)		21.0 (q)	21.0 (q)
7	62.8 (d)	63.0 (d)	10-OAc	170.8 (s)	170.7 (s)
8	125.9 (d)	125.9 (d)		22.5 (q)	22.5 (q)
9	129.9 (d)	130.0 (d)	15-OAc	168.5 (s)	168.5 (s)
10	85.8 (s)	85.9 (s)		22.3 (q)	22.3 (q)
11	44.7 (d)	44.7 (d)	3-OPr	173.6 (s)	173.7 (s)
12	37.1 (d)	37.1 (d)	1'	28.0 (t)	28.0 (t)
13	90.1 (s)	89.9 (s)	2'	8.8 (q)	8.8 (q)
14	72.5 (d)	73.2 (d)	14-OMeBu	175.4 (s)	
15	90.2 (s)	90.1 (s)	1''	40.6 (d)	
16	18.9 (q)	18.8 (q)	2''	26.9 (t)	
17	70.0 (t)	69.8 (t)	3''	11.7 (q)	
18	25.3 (q)	25.2 (q)	4''	15.7 (q)	
19	21.4 (q)	21.3 (q)	14-OBz		165.8 (s)
20	24.2 (q)	24.4 (q)	1''		130.0 (s)
			2'', 6''		130.1 (d)
			3'', 5''		128.4 (d)
			4''		133.4 (d)

Euphorprolitherin **B** (**2**) was obtained as colorless needles from petroleum ether–acetone. The ESI mass spectrum of **2** produced a quasi-molecular ion $[\text{M}+\text{Na}]^+$ at m/z 793.4, suggesting the molecular weight of 770. In combination with the analysis of the NMR spectra, the molecular formula was deduced to be $\text{C}_{40}\text{H}_{50}\text{O}_{15}$. The comparison of the NMR spectra of **1** and **2** disclosed that the 2-methylbutyryloxy group of **1** was replaced by a benzoyloxy group in **2**. Thus, **2** was characterized as 14-desoxo-2 α ,5 α ,7 β ,10,15 β -O-pentaacetyl-3 β -O-propionyl-14 α -O-benzoyl-10,18-dihydromyrinsol.

Euphorprolitherin **A** (**1**): $\text{C}_{38}\text{H}_{54}\text{O}_{15}$, colorless cubes, mp 192–195°C; IR (KBr) $\nu(\text{cm}^{-1})$ 1741, 1370, 1246, 1131, 1098, 1019; EIMS m/z 649 (8), 630 (4), 589 (2), 570 (7), 529 (3), 510 (4), 497 (2), 451 (2), 437 (3), 377 (5), 293 (27), 43 (100); ESIMS m/z 773.4 (100) $[\text{M}+\text{Na}]^+$; ^1H NMR (400MHz, CDCl_3) δ 3.21 (d, 1H, $J = 17.3$ Hz, H-1 α), 2.40 (d, 1H, $J = 17.3$ Hz, H-1 β), 5.37 (d, 1H, $J = 4.0$ Hz, H-3), 3.70 (dd, 1H, $J = 11.0, 4.0$ Hz, H-4), 5.89 (dd, 1H, $J = 11.0, 1.4$ Hz, H-5), 4.83 (d, 1H, $J = 6.5$ Hz, H-7), 6.16 (ddd, 1H, $J = 10, 6.5, 1.4$ Hz, H-8), 5.90 (dd, 1H, $J = 10, 6.0$ Hz, H-9), 3.18 (m, 1H, H-11), 3.07 (d, 1H, $J = 3.0$ Hz, H-12), 5.57 (s, 1H, H-14), 1.39 (s, 3H, H-16), 4.09 (d, 1H, $J = 8.8$ Hz, H-17a), 3.47 (dd, 1H, $J = 8.8, 1.4$ Hz, H-17b), 1.63 (s, 3H, H-18), 1.52 (s, 3H, H-19), 1.15 (s, 3H, H-20), 2.10, 2.08, 2.06, 1.98, 1.96 (each s, 3H, 5 \times OAc), 2.40 (q, 2H, $J = 7.0$ Hz, H-1'), 1.17 (t, 3H, $J = 7.0$ Hz, H-2'), 2.40 (m, 1H, H-1''), 1.83 (m, 1H, H-2''), 1.50 (m,

1H, H-2''), 0.96 (t, 3H, $J = 7.4$ Hz, H-3''), 1.21 (d, 3H, $J = 6.9$ Hz, H-4'').

Euphorprolitherin **B** (**2**): $C_{40}H_{50}O_{15}$, colorless needles, mp 184-186°C; IR (KBr) ν (cm^{-1}) 1740, 1480, 1370, 1245, 1100, 1018, 714; EIMS m/z 710 (1), 669 (6), 650 (5), 609 (2), 590 (9), 530 (4), 470 (3), 456 (5), 105(85), 43(100); ESIMS m/z 793.4 (98) $[M+Na]^+$; 1H NMR (400MHz, $CDCl_3$) δ 3.31 (d, 1H, $J = 17.4$ Hz, H-1 α), 2.37 (d, 1H, $J = 17.4$ Hz, H-1 β), 5.41 (d, 1H, $J = 4.0$ Hz, H-3), 3.75 (dd, 1H, $J = 11.0, 4.0$ Hz, H-4), 5.96 (dd, 1H, $J = 11.0$ Hz, H-5), 4.85 (d, 1H, $J = 6.5$ Hz, H-7), 6.19 (ddd, 1H, $J = 9.8, 6.5, 1.4$ Hz, H-8), 5.91 (dd, 1H, $J = 9.8, 5.5$ Hz, H-9), 3.20 (m, 1H, H-11), 3.20 (m, 1H, H-12), 5.83 (s, 1H, H-14), 1.32 (s, 3H, H-16), 4.17 (d, 1H, $J = 8.8$ Hz, H-17a), 3.53 (dd, 1H, $J = 8.8, 0.8$ Hz, H-17b), 1.64 (s, 3H, H-18), 1.55 (s, 3H, H-19), 1.23 (s, 3H, H-20), 2.14, 2.10, 2.00, 1.98, 1.70 (s, each 3H, 5 \times OAc), 2.37 (q, 2H, $J = 7.5$ Hz, H-1'), 1.16 (t, 3H, $J = 7.5$ Hz, H-2'), 8.09 (d, 2H, $J = 7.6$ Hz, H-2'',6''), 7.59 (t, 1H, $J = 7.6$ Hz, H-4''), 7.45 (t, 2H, $J = 7.6$ Hz, H-3'',5'').

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