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A new guaiane diterpenoid from *Euphorbia wallichii*

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A new guaiane-type diterpenoid, (1α,5β,7α)-3,10(18),11-dictytriene-19-acid, was obtained from the roots of *Euphorbia wallichii*. This is the first isolation of guaiane diterpene from this genus of *Euphorbia*. The structure was elucidated by spectral methods. And the compound was tested for the cytotoxicities on the cancer cell line P-388 and A-549 *in vitro*.

Keywords: *Euphorbia wallichii*; Euphorbiaceae; Guaiane diterpene; (1α,5β,7α)-3,10(18), 11-dictytriene-19-acid; Cytotoxicity

1. Introduction

Euphorbia wallichii hook. f. is a traditional Tibetan medicine used for curing furuncle, exanthema and cutaneous anthrax [1]. Our previous investigation on the species resulted in the isolation of three new abietane diterpenes [2]. In continuation of our studies, a new guaiane-type diterpene was obtained from the alcohol extract of the roots of this species. It is the first time that guaiane diterpene was isolated from the genus of *Euphorbia*. This article describes the structural elucidation of the new compound.

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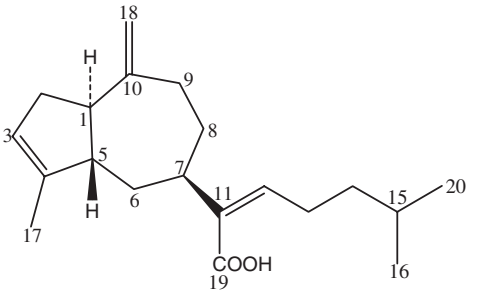
2. Results and discussion



1

Compound **1** had the molecular formula $C_{20}H_{30}O_2$ with six unsaturated degrees, as deduced from its HREI mass spectrum and the ^{1}H and ^{13}C NMR data. The NMR spectra (^{1}H NMR, ^{13}C NMR, DEPT-90 and DEPT-135) exhibited signals for two secondary methyls (C-16, 20), one tertiary methyl (C-17), an exomethylene group (C-10, 18), two trisubstituted olefin groups (C-3, 4, 11, 12), a carboxyl (C-19), six methylenes and four methines. These features are similar to those of dictytriene A [3]. The guaiane skeleton of **1** was established by the ^{1}H–^{1}H COSY, HMQC, HMBC and TOCSY (see table 1). Correlations in HMBC from H-18 to C-1, C-8, C-9 and C-10, H-12 to C-13 and C-19, H-16 to C-13, C-14, C-15 and C-20, H-17 to C-3, C-4, C-5 and C-6, and correlations in TOCSY from H-3 to H-1, H-2, H-5 and H-17 revealed

Table 1. 1D NMR data, ^{1}H–^{1}H COSY, TOCSY and HMBC of compound **1**[a].

	δ_H	δ_C	^{1}H–^{1}H COSY	TOCSY	HMBC
1	1.67 (t, 9.8)	49.7 (d)	H-5	H-2, 3, 5, 7, 8, 9, 18	C-2, 3, 5, 9, 10, 18
2	2.37 (m)	29.6 (t)	–	H-1, 3, 5	C-1, 10
3	5.14 (br d, 7.5)	129.8 (d)	H-5	H-1, 2, 5, 17	–
4	–	132.9 (s)	–	–	–
5	1.91 (m)	51.0 (d)	H-1, 3, 6	H-1, 2, 3, 6, 7, 8, 17	C-1, 2, 3, 4, 7, 10
6	1.75 (m, 6α); 2.59 (m, 6β)	35.0 (t)	H-5, 6, 7	H-5, 6, 7, 8	C-1, 5, 7, 17
7	2.21 (m)	28.5 (d)	H-6, 8, 9	H-1, 5, 6, 8, 9, 12	C-5, 6, 11, 12, 13, 19
8	1.73 (m, 8α); 1.08 (m, 8β)	26.5 (t)	H-7, 8, 9	H-1, 5, 6, 7, 8, 9	C-7, 9, 10
9	2.05 (m, 9α); 2.37 (m, 9β)	37.2 (t)	H-7, 8, 9	H-1, 7, 8, 9, 18	C-1, 8, 10, 18
10	–	153.6 (s)	–	–	–
11	–	135.6 (s)	–	–	–
12	6.90 (br s)	139.1 (d)	H-13	H-7, 13, 14	C-13, 19
13	2.59 (m); 2.21 (m)	29.4 (t)	H-12, 13, 14	H-12, 13, 14	C-7, 11, 12, 19
14	1.77 (m)	27.2 (t)	H-13, 16, 20	H-12, 13, 15, 16, 20	C-13, 16, 20
15	1.34 (br s)	48.1 (d)	–	H-14	–
16	0.85 (d, 7.0)	21.3 (q)	H-14, 20	H-14, 20	C-13, 14, 15, 20
17	1.55 (s)	21.3 (q)	–	H-3, 5	C-3, 4, 5, 6
18	4.68 (s); 4.60 (s)	104.0 (t)	H-18	H-1, 9, 18	C-1, 8, 9, 10
19	–	170.7 (s)	–	–	–
20	0.61 (d, 6.8)	15.4 (q)	H-14, 16	H-14, 16	C-13, 14, 15, 16

[a]NMR data were measured in $CDCl_3$ and Me_3OD at 125 MHz for carbon and 500 MHz for proton and 2D NMR data.

Table 2. Inhibition rates of compound **1** with different concentrations (in MeOH) against cancer cell line P-388[a] and A-549[b].

Concentration	10^{-4} mol/L	10^{-5} mol/L	10^{-6} mol/L	10^{-7} mol/L	10^{-8} mol/L
P-388	40.6%	7.5%	13.8%	7.5%	6.8%
A-549	91.6%	22.5%	0	0	0

[a]active time is 48 h; [b]active time is 72 h.

that the structure of **1** is 3,10(18),11-dictytriene-19-acid. The relative stereochemistry at C-1, C-5 and C-7 were finally determined by Roesy spectrum, in which NOE interaction between H-1 with H-7, H-1 with H-9α, H-5 with H-8β were observed. Thus **1** was elucidated to be (1α,5β,7α)-3,10(18),11-dictytriene-19-acid. The cytotoxicity bioassay indicated that compound **1** had moderate activity against cancer cell line P-388 and A-549 (see table 2).

3. Experimental

3.1. *General procedure*

Melting point was measured on an XRC-1 micromelting apparatus and was uncorrected. Optical rotation was measured with a Horbia SEAP-300 spectropolarimeter. IR spectrum was obtained on a Bio-Rad FTS-135 infrared spectrophotometer with KBr pellet. UV spectrum was taken on a Shimadzu double-beam 210A spectrophotometer. MS spectrum was obtained with a VG Auto Spec-3000 spectrometer, at 70 eV for EI. NMR spectra were recorded on a Bruker AM-400 and a DRX-500 MHz spectrometer with TMS as internal standard. Silica gel (200–300 mesh) for CC and GF254 for analytical TLC were from the Qindao Marine Chemical Factory, P.R. China.

3.2. *Plant material*

Euphorbia wallichii hook. f. was collected from Xinghai county, Qinghai province, P.R. China, in July 2001. It was identified by Prof. Zhang Xiao-Feng, Northwest Plateau Institute of Biology, *Academia Sinica*, Xining, Qinhai, P.R. China, where a voucher specimen (No. 1002) was deposited.

3.3. *Extraction and isolation*

The air-dried roots (10 kg) of *E. wallichii* were extracted with EtOH (95%) four times at room temperature, and the combined extracts were evaporated *in vacuo*. The residue was suspended in H_2O and then extracted with $CHCl_3$ three times. The $CHCl_3$ layer was concentrated *in vacuo* to give 200 g of residue, which was chromatographed over silica gel. The column was eluted with petroleum ether–EtOAc (from petroleum ether to petroleum–EtOAc 1 : 1). According to differences in composition monitored by TLC (GF_{254}), 17 fractions were obtained. Sediments from fraction 4 were washed intensively with petroleum ether, and recrystallized from MeOH to afford **1** (39 mg).

3,10(18)-11-dictytriene-19-acid (**1**), $C_{20}H_{30}O_2$, white powder, m.p. 128–130°C; $[\alpha]_D^{14.6}$ +54.46 (*C*, 0.10, MeOH); UV λ_{max} (log ε) 210.4 (2.97) nm; IR (KBr) ν: 3435, 2930, 2864, 1685, 1638, 1289, 1182, 883 cm^{-1}; EIMS *m*/*z*: 302 $[M]^+$ (49), 287 (9), 259 (65), 232 (7), 213 (15), 204 (11), 189 (19), 175 (11), 161 (74), 149 (12), 136 (82), 121 (58), 107 (48), 93 (100), 81 (57), 69 (35), 55 (20); HREIMS calcd. 302.2246, found 302.2249 (error: −0.9 ppm).

3.4. *Cytotoxicity assay*

Compound **1** was dissolved in MeOH at different concentrations. Methyl-thiazol-tetrozolium deoxidize method and sulforhodamine B protein dyeing were used in the tests against cancer cell line P-388 and A-549 respectively. The active time of the former was 48 h, and that of the latter was 72 h.

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