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TWO PENTACYCLIC DITERPENE ESTERS FROM *EUPHORBIA DECIPIENS*

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Key Word Index—*Euphorbia decipiens*; Euphorbiaceae; diterpene esters; pentacyclic diterpenes; karajinone A and B.

Abstract—Two new diterpene esters, karajinone A and B, with a lathyrane skeleton have been isolated from the whole plant of *Euphorbia decipiens*, collected from Iran. Their structures have been characterized by spectroscopic methods. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Plants of the genus *Euphorbia* are known to contain a large number of biologically active compounds, in particular skin-irritant, tumour-promoting and anti-tumour diterpene esters [1, 2]. Some of them like *E. fischeriana* are used in Chinese folk medicine and some diterpene esters isolated from it exhibited anti-tumour activities [3].

As a part of our programme to characterize the chemical constituents of the Iranian *Euphorbia* plants we have investigated the chloroform-methanol extract of whole plants of *E. decipiens* Boiss and Buhse, a plant endemic to Iran. We now report on the isolation and structure elucidation of two new diterpene ester with a pentacyclic lathyrane or myrsinol type skeleton, karajinone A (**1**) and B (**2**) from this source [4].

RESULTS AND DISCUSSION

A methanol-chloroform extract of the whole plant of *E. decipiens* was subjected to CC on silica gel. Repeated CC and PTLC afforded two new polyester diterpenoids **1** and **2**. Compound **1** was obtained as a white powder. Its molecular formula was assigned as $C_{35}H_{42}O_{12}$ on the basis of the CI mass spectrum which showed the $[M]^+$ peak at *m/z* 654 (10%) and two peaks at *m/z* 594 $[M\text{-}HOAc]^+$ (100%) and 534 $[M\text{-}2xHOAc]^+$ (98%). The peak at *m/z* 105 (94%) $(C_6H_5CO)^+$ in the EIMS spectrum indicated the presence of benzoate ester in the molecule. The IR spectrum exhibited intense peaks for carbonyl groups (1740, 1730 cm^{-1}) and unsaturation (1605 cm^{-1}). The ^1H NMR spectrum of **1** (Table 1) showed five downfield signals due to the protons geminal to oxygen-bearing groups; three due to oxymethine groups [δ 5.16 (*t*, $J=3.9$ Hz, H-3), 5.93 (*dd*, $J=0.8$, 10.9 Hz, H-5) and 4.94 (*dd*, $J=4.4$, 7.2 Hz, H-7)], and two due to oxymethylene groups [δ 3.97 (*dd*, $J=1.0$, 9.7 Hz, H-17), 4.17 (*d*, $J=9.7$ Hz, H-17′) and AB signal at δ 3.78 (*d*, $J=11.2$ Hz, H-18), 3.83 (*d*, $J=11.2$ Hz, H-18′)]. The long range W coupling ($J=1.0$ Hz) between H-17 and H-5 together with a geminal coupling of $J=9.7$ Hz for H-17/H-17′ established a saturated furan ring through C-17 and C-13 which is also observed in ^1H NMR spectra of myrsinol esters [5]. One secondary methyl at δ 0.87 (*d*, $J=6.8$ Hz, H-16), and two tertiary methyls at δ 1.55 (*s*, H-20) and 1.17 (*s*, H-19), together with four acetyl methyl singlets at δ 2.18, 2.03, 1.96 and 1.54 were observed in the ^1H NMR spectra of **1**. The upfield shift of the last acetyl signal may be related to the anisotropic effect of other ester groups and is common in poly and macrocyclic diterpene esters [6, 7].

The ^{13}C NMR spectra for **1** (Table 1) displayed six CH_3, four CH_2, 11 CH and 11 quaternary carbon atoms. The upfield signals at δ 19.72 *d* (C-9), 22.12 *s* (C-10) and 15.49 *d* (C-11), suggested a cyclopropane ring which was substituted at C-10 with a methyl [δ 11.98 *q* (C-19)] and one acetoxy methylene [δ 73.6 *t* (C-18)]. The ^1H - ^1H- and ^1H - ^{13}C connectivities were supported by the ^1H-^1H COSY (Table 2) and HMQC spectra.

The assignment of the carbon skeleton and the ester groups locations were established by HMBC (Table 3) as well as by comparison of the ^1H and ^{13}C NMR chemical shifts and coupling constants observed for myrsinol esters [5, 8], aleppicatines A and B [9], and the pentacyclic diterpenes, euphoppins A–D (Fig. 1) [10], isolated from *E. allepica*.

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Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2***

Position	^{1}H		^{13}C	
	1	**2**	**1**	**2**
1α	3.41 (*dd*, *J*=9.5, 14.9 Hz)	2.71 (*dd*, *J*=11.2, 15.6 Hz)	42.16	46.29
1β	1.47 (*dd*, *J*=10.0, 14.9 Hz)	1.72 (*dd*, *J*=7.7, 15.6 Hz)		
2	2.1 (*m*)	2.1 (*m*)	36.15	34.07
3	5.16 (*t*, *J*=3.9 Hz)	5.24 (*dd*, *J*=3.7, 4.8 Hz)	77.60	79.33
4	2.48 (*dd*, *J*=3.6, 10.9 Hz)	2.99 (*dd*, *J*=3.7, 10.9 Hz)	53.32	52.40
5	5.93 (*dd*, *J*=0.8, 10.9 Hz)	5.74 (*dd*, *J*=1.5, 10.9 Hz)	68.30	68.09
6	-	-	54.18	54.38
7	4.94 (*dd*, *J*=4.4, 7.2 Hz)	4.88 (*dd*, *J*=3.2, 10.7 Hz)	73.46	76.30
8	1.85 (*m*)	1.7 (*dd*, *J*=8.0, 14.3 Hz)	23.34	24.22
8′	2.2 (*m*)	2.1 (*m*)		
9	1.13 (*m*)	1.2 (*m*)	19.72	21.65
10	-	-	22.12	23.76
11	1.18 (*t*, *J*=7.0 Hz)	0.98 (*dd*, *J*=6.7, 9.9 Hz)	15.49	14.81
12	2.82 (*br. d*, *J*=4.5 Hz)	3.08 (*d*, *J*=6.7 Hz)	39.19	41.06
13	-	-	89.90	88.06
14	-	-	201.40	-
15	-	-	88.94	83.05
16	0.87 (*d*, *J*=6.8 Hz)	0.92 (*d*, *J*=7.1 Hz)	14.53	15.41
17	3.97 (*dd*, *J*=1.0, 9.7 Hz)	4.04 (*dd*, *J*=1.5, 9.9 Hz)	71.65	74.41
17′	4.17 (*d*, *J*=9.7 Hz)	4.46 (*d*, *J*=9.9 Hz)		
18	3.78 (*d*, *J*=11.2 Hz)	3.73 (*d*, *J*=11.2 Hz)	73.60	73.28
18′	3.83 (*d*, *J*=11.2 Hz)	3.91 (*d*, *J*=11.2 Hz)		
19	1.17 (*s*)	1.13 (*s*)	11.98	11.63
20	1.55 (*s*)[a]	1.39 (*s*)	20.49	19.25
OCOCH_3 [b]	1.54 (*s*)[a]	1.34 (*s*)	20.49	20.84
	1.96 (*s*)	2.05 (*s*)	20.84	21.03
	2.03 (*s*)	2.07 (*s*)	21.01	21.21
	2.18 (*s*)	-	21.56	-
O$COCH_3$	-	-	169.14	169.97
	-	-	170.69	169.80
	-	-	170.95	169.80
	-	-	169.65	-
Benzoyl				
1′	-	-	130.40	-
2′,6′	7.95 (*br. dd*, *J*=1.0, 8.0 Hz)	7.95 (*br. dd*, *J*=1.3, 8.2 Hz)	129.71	129.90
3′,5′	7.41 (*br. t*, *J*=8.0 Hz)	7.43 (*br. t*, *J*=8.0 Hz)	128.30	128.49
4′	7.54 (*br. tt*, *J*=1.0, 7.5 Hz)	7.55 (*br. tt*, *J*=1.3, 7.5 Hz)	133.11	133.33
7′	-	-	166.01	166.41

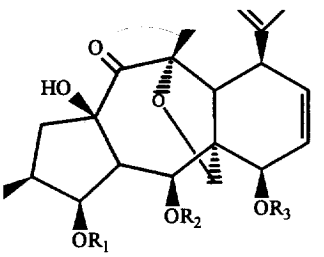
* All ^{1}H-^{13}C connectivities were assigned by HMQC; [a,b] Assignments may be interchanged.

Table 2. ^{1}H - ^{1}H COSY correlations for **1** and **2**

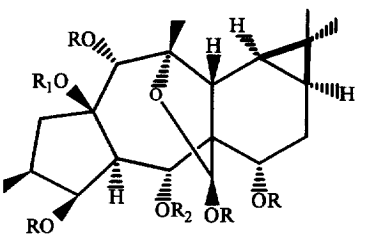
1	**2**
Hα-1 : Hβ-1, H-2	Hα-1 : Hβ-1, H-2
H-2 : Hβ-1, H-3, H-16	H-3 : H-4, H-2
H-3 : H-4	H-4 : H-5
H-4 : H-5	H-7 : H-8, H-8′
H-5 : H-17	H-8 : H-8′, H-9
H-7 : H-8, H-8′	H-8′ : H-9
H-8 : H-8′, H-9	H-9 : H-11
H-8′ : H-9	H-11 : H-12
H-11 : H-12	

Table 3. HMBC data for **1** and **2**

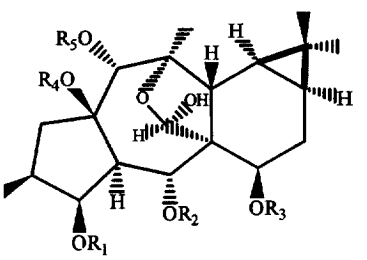
1	**2**
Hα-1 : C-2, C-3, C-14	Hα-1 : C-3
H-3 : C-1, C-15	Hβ-1 : C-15
H-4 : C-3, C-5	H-4 : C-5, C-15
H-5 : C-3, C-6, C-17, $OCOCH_3$	H-5 : C-4, C-7, $OCOCH_3$
H-12 : C-5, C-7, C-10, C-11, C-17	H-7 : C-5, C-6, C-12, C-13, OCOPh
H-16 : C-1, C-2, C-3	H-12 : C-5, C-6, C-7, C-10, C-11
H-17 : C-5, C-7, C-13	H-16 : C-1, C-2, C-3
H-17′ : C-5, C-6, C-12, C-13	H-17 : C-5, C-7
H-18 : C-9, C-10, C-11, C-19, $OCOCH_3$	H-17′ : C-5, C-6, C-12, C-13
H-19 : C-9, C-10, C-11, C-18	H-18 : C-9, C-10, C-11, $OCOCH_3$
H-20 : C-12, C-14	H-18′ : C-10, C-11, $OCOCH_3$
	H-19 : C-9, C-10, C-11, C-18
	H-20 : C-12, C-13



myrsinol ester



aleppicatine

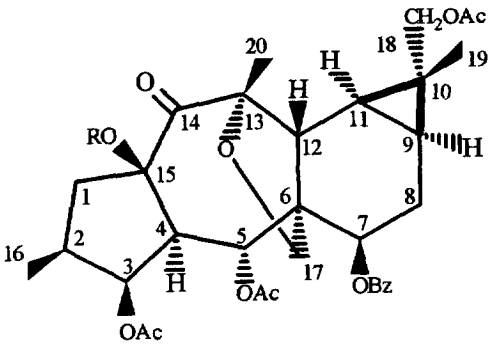


euphoppin

Fig. 1.

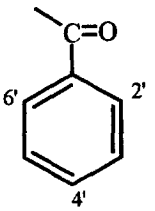
The stereochemistry of **1** was determined by comparison of the ^1H NMR coupling constants of **1** with those recorded for myrsinol esters [5, 8] and the diterpene esters isolated from *E. allepica* [9, 10] with similar structure as well as by NOE difference spectroscopy and NOESY spectra. The coupling constant of H-3 (*t*, $J = 3.9$ Hz) and H-4 (*dd*, $J = 3.6$, 10.9 Hz) indicated that H-2 to H-4 must lie on one face of the molecule with the same dihedral angle between H-2/H-3 and H-3/H-4. The J (10.9 Hz) between H-4 and H-5 showed the *trans* relationship between them. The NOESY cross peaks between H-3/H-4, H-5/H-12, H-12/H-19, established that H-5, H-12 and H-19 must be located on one face of the molecule. In NOE difference spectroscopy, irradiation of H-18 gave significant enhancement at H-19 and H-9. Irradiation of H-17 enhanced H-7 which confirmed H-7 as α.

Compound **2** afforded a molecular ion peak at *m/z* 612 (CIMS) suggesting the molecular formula $C_{33}H_{40}O_{11}$. The IR spectrum showed, besides the peaks for carbonyl groups (1740, 1720 cm^{-1}) and unsaturation (1600, 1570 cm^{-1}), a broad peak at 3450 cm^{-1} indicating the presence of a hydroxyl group. In the ^1H NMR spectra there were three methyl singlets for acetyl groups at δ 2.05, 2.07 and 1.34 indicating that **2** was the desacetyl derivative of **1**. In the case of the other proton signals there were some small differences between the chemical shifts and coupling constants of **1** and **2**. In the ^{13}C NMR spectra, the ketonic carbonyl group at C-14 was absent which may be due to the low concentration of the compound. The upfield shift of C-15 toward δ 83.05 determined the position of free hydroxyl group in this compound which was confirmed by the HMBC cross peaks for H-5, H-18 and



Compound	R
1	Ac
2	H

Bz =



H-7 with the corresponding carbonyl esters at δ 169.97, 169.80 for acetyls and 166.41 for benzoyl group, respectively.

EXPERIMENTAL

General

NMR: $CDCl_3$, with TMS as int. standard. PTLC: precoated PTLC silica gel 60 F_{254}, detection under UV light.

Plant material

The whole plant of *Euphorbia decipiens* Boiss. and Buhse was collected from mount Kandovan, North of Karaj, Tehran, Iran, in July 1995 and identified by Dr. Fereydoon Terme at The Center for Plant Research Eveen, Tehran, Iran.

Extraction and isolation

The dried plant material, after grinding, was extracted with a mixture of $CHCl_3$-MeOH (1 : 1) for 24 hr. The extract was concentrated under reduced pressure, dissolved in a small amount of MeOH and kept in a freezer overnight.

The cold MeOH soln was filtered to remove long chain hydrocarbons and fatty acids. The extract (20 g) was subjected to CC over a silica gel column (400 g) using hexane with a gradient of $CHCl_3$ upto 100% and followed by MeOH. The $CHCl_3$ rich fractions were then subjected to flash chromatography on silica gel (230–400 mesh) and PTLC (precoated silica gel 60 F_{254}) using EtOAc - hexane (3:7) and $CHCl_3$-Me_2CO(47:3) as eluent and mobile phase respectively to give pure **1** and **2**.

Compound **1**

^1H and ^{13}C NMR: Table 1; IR λ_{max} ($CHCl_3$) cm^{-1}: 3000, 1740, 1730, 1605, 1460, 1380, 1320, 1280, 1120, 1080, 1030, 980, 610; UV λ_{max} (MeOH) nm: 198.2, 227.4, 270.8; CIMS *m/z*: 654 ($C_{35}H_{42}O_{12}$) $[M]^+$, 594 (100), 534, 474, 431, 371, 311, 173, 123, 105. HREIMS *m/z*: 626.2706 ($C_{34}H_{42}O_{11}$) $[M\text{-}CO]^+$, 594.2441 ($C_{33}H_{38}O_{10}$) $[M\text{-}HOAc]^+$; EIMS *m/z* (rel.int.): 626 (3), 594 (1), 566 (9), 233 (37), 173 (100), 145 (12), 133 (10), 131 (8), 121 (2), 125 (9), 105 (94), 77 (11).

Compound **2**

^1H and ^{13}C NMR: Table 1; IR λ_{max} (KBr) cm^{-1}: 3450, 2980, 1740, 1720, 1650, 1620, 1600, 1570, 1540, 1520, 1470, 1370, 1270, 1245, 1110, 1100, 1070, 1020, 710, 600; UV λ_{max} (MeOH)nm: 200.0, 227.6, 270.8; CIMS *m/z*: 612 ($C_{33}H_{40}O_{11}$) $[M]^+$, 583, 552 (100), 534, 492, 431, 371, 123, 105, 61, 41; HREIMS *m/z*: 584.2559 ($C_{32}H_{40}O_{10}$) $[M\text{-}CO]^+$, 552.2364 ($C_{31}H_{36}O_9$) $[M\text{-}HOAc]^+$; EIMS *m/z* (rel.int.): 584 (4), 524 (21), 342 (7), 282 (7), 239 (6), 233 (34), 175 (21), 173 (100), 145 (21), 133 (11), 105 (21), 60 (10).

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