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EUDESMANE DERIVATIVES FROM *IVA FRUTESCENS*

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Key Word Index—*Iva frutescens*; Asteraceae; sesquiterpenes; eudesmane derivatives.

Abstract—Re-investigation of the aerial parts of *Iva frutescens* resulted in the isolation of three sesquiterpenes, two of which are new natural products, and their structures were established by spectral data. © 1997 Published by Elsevier Science Ltd. All rights reserved

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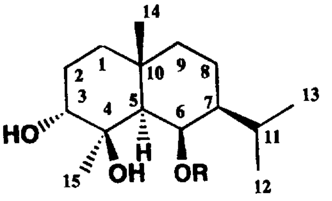
INTRODUCTION

As a part of our biochemical systematic study of the family Asteraceae, we re-investigated the terpenoid constituents of *Iva frutescens* L. ssp. *frutescens*. The genus *Iva* consists of annual and perennial herbs and shrubs with 15 species distributed in North America [1]. Morphological and cytological characters established three sections for the genus [2]. However, cpDNA investigations suggested that some taxonomic adjustments should be made [3, 4].

RESULTS AND DISCUSSION

Fractionation of the dichloromethane–methanol extract of the aerial parts of *Iva frutescens* by column chromatography on silica gel, then Sephadex LH-20 gave 5-methoxy-eriodictyol, ilicic acid [5] and two new sesquiterpenes **1** and **2**, in addition to the known melampolide, frutescin.



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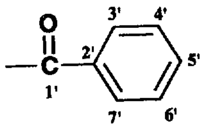

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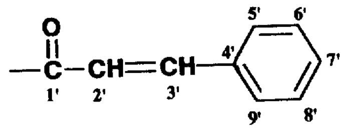

The structure of **1** was established from mass, ^1H and ^{13}C NMR spectral data. In the ^{13}C spectrum of **1**, 22 carbon signals were observed, of which seven represented an aromatic moiety and a carbonyl group. While DEPT experiments showed that the other 15 carbon signals included four methyl, four methylene, five methine and two quaternary carbons. The carbon signals were assigned from HMQC. The ^1H NMR spectrum suggested a eudesmane skeleton for **1**: four methyl signals at δ 0.88, 0.90, 1.13 and 1.21. Moreover, two protons geminal to hydroxyl groups were observed at δ 5.90 and 3.50. The downfield shift of the δ 5.90 signal suggested that the hydroxyl group must be acylated; its geminal proton exhibited correlation with a narrow doublet at δ 1.99 for H-5, detected in the ^1H-^1H COSY. However, in the same experiment, the signal at δ 3.50 correlated with a multiplet signal at δ 1.74 for H-2. Therefore, the acyl group is located at C-6. Additionally, the pair of doublets at δ 0.88 and 0.90 were coupled to a multiplet at δ 1.44, confirming the presence of an isopropyl group. The signal pattern of the aromatic protons, together with a carbonyl carbon signal at δ 167.89 established that the acyl group was benzoate. The stereochemistry of the chiral centres at C-3 and C-6 were assigned from comparison of the coupling constants with similar compounds [6, 7]. Furthermore, a NOESY experiment showed a correlation of H-3 with H-14, H-6 with H-15. The Cl-mass spectrum supported the proposed

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Table 1. ^{1}H NMR Spectral data of compounds **1** and **2** (500 MHz, $CDCl_3$, δ values)

	1*‡	**1**†	**2**‡§
H-1α	1.13 *m*		1.1
H-1β	1.65 *m*		1.62
H-2	1.74 *m*	1.69	1.62
H-3β	3.50 *t*(J = 1, 1 Hz)	3.48	3.58
H-5α	1.99 *d* (J = 1.5 Hz)	1.85	1.95
H-6α	5.90 *br s*	6.16	5.80
H-7α	1.21 *m*	1.25	1.23
H-8α	1.36 *m*	1.38	1.31
H-8β	1.71 *m*	1.64	1.69
H-9α	1.42 *m*	1.36	1.40
H-9β	1.62 *m*	1.60	1.59
H-11	1.44 *m*	1.37	1.42
H-12	0.88 *d* (J = 8 Hz)	0.82	0.87
H-13	0.90 *d* (J = 8 Hz)	0.95	0.88
H-14	1.13 *s*	1.09	1.19
H-15	1.21 *s*	1.26	1.19

* OR, H-3′,7′, 8.06 *d* (J = 7.5 Hz), H-4′,6′, 7.48 *t* (J = 7.5 Hz), H-5′ *t* (J = 7.5 Hz).

† In Acetone-d_6.

‡ Assigned by ^{1}H-^{1}H COSY.

§ OR, H-2′, 6.42 *d* (J = 16.0 Hz), H-3′, 7.68 *d* (J = 16.0 Hz), H-5′,7′,8′, 7.40 *m*.

Table 2. ^{13}C NMR Spectral data of compounds **1** and **2** (500 MHz, $CDCl_3$, δ values)

	1*‡§	2†‡
C-1	36.02 *t*	36.05
C-2	24.63 *t*	24.65
C-3	75.69 *d*	75.74
C-4	72.83 *s*	72.90
C-5	48.99 *d*	49.03
C-6	70.44 *d*	69.95
C-7	50.20 *d*	50.04
C-8	21.24 *t*	21.33
C-9	44.91 *t*	44.97
C-10	34.22 *s*	34.28
C-11	28.85 *d*	28.83
C-12	20.29 *q*	20.70
C-13	20.75 *q*	21.10
C-14	23.79 *q*	23.81
C-15	21.10 *q*	21.10

* OR, C-1′, 167.80, C-2′, 130.39, C-3′,7′, 128.64, C-4′,6′, 129.78, C-5′, 133.50.

† OR, C-1′, 168.30, C-2′, 118.29, C-3′, 145.70, C-4′, 134.20, C-5′,9′, 128.93.

‡ Splitting assigned by DEPT.

§ Assigned by HMQC.

structure for **1** and revealed an $[M+H]^+$ peak at *m/z* 361 for $C_{22}H_{32}O_4$, followed by consecutive loss of a molecule of water and benzoic acid at *m/z* 343 and 221, respectively.

The ^{1}H and ^{13}C NMR spectral data of **2** showed an additional two olefinic carbons (Tables 1 and 2) with two *trans*-protons at δ 7.68 (J = 16 Hz) and 6.42 (J = 16 Hz) on two carbons at δ 145.70 and 118.29. DEPT experiments indicated that the two additional carbons in **2** relative to **1** were methines. Those two carbons, together with six aromatics at δ 134.20 (C-4′), 130.58 (C-7′), 128.93 (C-5′,9′), 128.25 (C-6′,8′) and a carbonyl carbon at δ 168.30, could be assigned to a cinnamate moiety. The other ^{1}H and ^{13}C NMR signals of **2** were almost identical with those of **1** (Tables 1 and 2). The Cl-mass spectrum gave a peak at *m/z* 387, $C_{24}H_{34}O_4$. These data indicated that in **2** a cinnamate moiety has replaced the benzoate in **1**.

Chemical investigation of some members of the genus *Iva* showed that most of the species were characterized by the accumulation of guaianolides [8–13], one species, *Iva frutescens* L. ssp. *frutescens* gave melampolide [14], and one species produced seco-eudesmanolide [15] while a few species produced eudesmanolide and eudesmane derivatives [16, 17].

EXPERIMENTAL

Plant material. I. frutescens was collected in Harris Co., Texas. Voucher specimens (Miao 61-7, 61-2) were deposited in The Plant Resources Centre, The University of Texas at Austin (TEX).

Extraction and isolation. The air-dried aerial parts (200 g) of the plant were extracted with CH_2Cl_2–MeOH (1:1) at room temp. (24 h). Evapn of the solvent afforded 0.8 g of a green gummy material. Sepn of this concentrate on a silica gel column using a hexane–ether step gradient gave five frs. The hexane–Et_2O (1:3) fr. was further chromatographed on a Sephadex LH-20 column to give 15 mg of **1**, 8 mg of **2**, 2 mg of ilicic acid and 4 mg 5-methoxyeriodictyol.

6$_\beta$-Benzoyloxy-3$_\beta$-hydroxyeudesmane (**1**). Gum; IR ν_{max} cm^{-1}: 3440, 1670, 1640, 1460. CIMS *m/z* (rel. int.): 361 $[M+H]^+$ (100), 343 $[M+H-H_2O]^+$ (77), 221 $[M+H-H_2O\text{-benzoic acid}]^+$ (17). ^{1}H and ^{13}C NMR, see Tables 1 and 2, respectively.

6$_\beta$-Cinnamoyloxy-3$_\beta$-hydroxyeudesmane (**2**). Gum; IR ν_{max} cm^{-1}: 3450, 1675, 1655, 1470. CIMS *m/z* (rel. int.): 387 $[M+H]^+$ (70), 369 $[M+H-H_2O]^+$ (34), 221 $[M+H-H_2O\text{-benzoic acid}]^+$ (11). ^{1}H and ^{13}C NMR, see Tables 1 and 2, respectively.

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