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A SESQUITERPENE LACTONE FROM *ARTEMISIA ARBORESCENS**

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Key Word Index—*Artemisia arborescens*, Compositae, sesquiterpene lactone, guaianolide

Abstract—A new sesquiterpene lactone has been isolated from the aerial parts of *Artemisia arborescens* By high-field two-dimensional NMR methods, its constitution and relative stereochemistries at the eight chiral centres have been determined

INTRODUCTION

Following our studies on the Italian Flora [1] we have now reinvestigated the components of *Artemisia arborescens* L, a plant used for contraceptive purposes by the ancient Greeks and Arabs [2] It is known that the genus *Artemisia* contains a variety of sesquiterpene lactones and various other compounds. The reinvestigation of the plant's aerial parts has afforded, besides the known products [3–8], the new sesquiterpene lactone **1**.

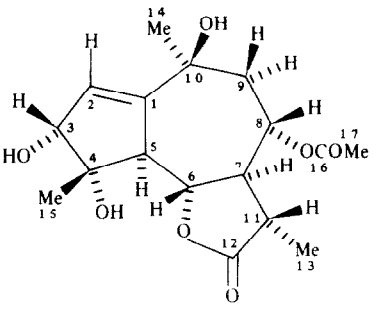
The mass spectrum of **1** (*m/z* 322 $[M-H_2O]^+$ gave the elemental composition, $C_{17}H_{24}O_7$, while IR absorptions indicated the presence of a five-membered lactone ring (ν_{max}^{KBr} 1760 cm^{-1}), an *O*-acyl function (ν_{max}^{KBr} 1735 cm^{-1}) and hydroxy groups (ν_{max}^{KBr} 3400–3200 cm^{-1}) The number of the latter functions followed from the ^1H NMR spectrum exhibiting 3 H/D-exchangeable proton signals. The inventory (C-17), multiplicity and chemical shift values of carbon atoms, as shown by the ^{13}C NMR spectrum, gave the number of unsaturated bonds as three, which, along with the gross structure, required that the constitution of **1** must be represented by a three-ring backbone. The actual structure and relative stereo-chemistry of the new product as portrayed in **1** were inferred from high-field ^1H NMR (400 MHz) and ^{13}C (100 MHz) NMR spectra. The assignments of the resonances in terms of proton and carbon-13 chemical shifts, δ_H, δ_C, ^{13}C-multiplicities and interproton coupling constants, J_{HH}, were performed by means of standard one- and two-dimensional (1D, 2D) FT NMR techniques and the assigned spectral parameters are collected in Table 1.

First, a proton–proton chemical shift correlation (COSY) experiment [9] was run to establish ^1H–^1H connectivities within the molecular framework and then, these pieces of information, combined with the results of a carbon–proton chemical shift correlation experiment (mediated by one-bond C-H couplings) [9], served as the starting point for the determination of the carbon–carbon connectivities Carbon–carbon sequences involving quaternary ^{13}C atoms were inferred from a series of carbon–proton chemical shift correlation experiments in which the relevant time periods were systematically varied such as to obtain observable ^1H–^{13}C magnetization transfer for the expected range (1 5–12 Hz) of long-range $^nJ_{CH}$ ($n=2$, 3, 4) couplings. The multiple bond correlations thus detected are also reported in Table 1 and labelled by the pertinent coupling pathways

Examination of the data in Table 1 shows that these are best accommodated within the proposed formula **1** Uncertainties due to regioisomerism resulting from the interchange of substituents at C-6 and C-8 were readily eliminated by means of selective ^1H–$\{^1H\}$ NOE experiments. pre-irradiation of the resonance due to OAc protons gave rise to signal enhancement at the chemical shift of the C-8 proton

Selective proton NOE experiments were also run in order to define the relative stereochemistries at chiral centres C-3, C-4 and C-10 while those at C-5, C-6, C-7, C-8 and C-11, as shown in **1**, followed directly from the observed interproton coupling data.

Signal enhancements observed upon selectively pre-irradiating the resonances due to 14-Me and 15-Me protons (see Table 1) proved distinctive for the relative steric disposition of substituents at C-3, C-4 and C-10.



1

*Preliminary results were presented at the 1st Princess Chulabhorn Science Congress 1987–International Congress on Natural Products, Bangkok, Thailand, December 1987

Table 1. NMR spectral data of compund **1***

C	δ_C	$^nJ_{C,H}$	δ_H	$^nJ_{H,H}$
1	151 18 (*s*)	$^3J_{H_3}$, $^3J_{H_{9\beta}}$, $^3J_{H_{14}}$; $^2J_{H_5}$; $^2J_{H_2}$	—	—
2	126.51 (*d*)	—	6 046	$^3J_{2,3}$ 2 9, $^4J_{2,5}$: 2 9
3	78 77 (*d*)	$^3J_{H_{15}}$, $^2J_{H_2}$, $^2J_{3\text{-OH}}$	4 055	$^3J_{3\,3\text{-OH}} \leqq 1$
4	79 74 (*s*)	$^2J_{H_{15}}$, $^3J_{H_2}$; $^2J_{H_5}$	—	—
5	56 85 (*d*)	$^3J_{H_2}$, $^3J_{H_{15}}$, $^3J_{H_3}$; $^3J_{H_7}$	3.194	$^3J_{5,6}$: 11.5
6	76 45 (*d*)	$^2J_{H_5}$	4 532	$^3J_{6,7}$: 10 1
7	56 81 (*d*)	$^3J_{H_{13}}$, $^3J_{H_5}$	2 123	$^3J_{7,8}$: 10.6, $^3J_{7\,11}$ 11.6
8	70 86 (*d*)	$^2J_{H_7}$, $^2J_{H_{9\beta}}$; $^2J_{H_{9\alpha}}$	5.387	$^3J_{8,9\beta}$. 3 3, $^3J_{8,9\alpha}$: 10.1
9	44 99 (*t*)	$^3J_{H_{14}}$	2.111 1.882	$^2J_{9\alpha,\,9\beta}$ −14.2
10	69 31 (*s*)	$^2J_{H_{14}}$, $^2J_{H_{9\beta}}$, $^3J_{H_2}$	—	—
11	40 71 (*d*)	$^2J_{H_{13}}$	2.570	$^3J_{11\,13}$ 7.0
12	177 53 (*s*)	$^3J_{H_{13}}$	—	—
13	14 96 (*q*)	$^3J_{H_7}$	1.285	—
14	29 79 (*q*)	$^3J_{H_{9\beta}}$	1 554	—
15	21 23 (*q*)	$^3J_{H_3}$	1 355	—
16	169.60 (*s*)	$^2J_{H_{17}}$	—	—
17	21 20 (*q*)	—	2.093	—
3-OH	—	—	3 115	—
4-OH	—	—	3 115†	—
10-OH	—	—	2 015†	—

Selective ^1H–{^1H} NOE data [Irradiated resonance enhanced resonance (% enhancement)]
15-Me 6-H (5%), 3-H (5%), 5-H (2%)
14-Me 2-H (8%), 9-Hβ (2 5%)
17-Me 8-H (2%)

* In $CDCl_3$ soln at ambient temp Chemical shifts are relative to internal TMS, ^1H–^1H coupling constants in Hz. Mutual interproton couplings are given only once, at their first occurrence in the Table. $^nJ_{C,H}$ indicate detected cross-peaks in the multiple-bond carbon–proton chemical shift correlation maps.

† Assignments of these OH protons may be interchanged

EXPERIMENTAL

General. Mass spectra.70 eV. IR: KBr. All NMR spectra were run on a dilute (8 mg/0 6 ml) $CDCl_3$ soln at 25°. Selective ^1H–{^1H} NOE experiments were performed in the difference mode Merck's DC-Alufolien kieselgel 60 F_{254} and Merck's kieselgel 60 (230–400 mesh ASTM) were used for TLC and CC The HPLC separations were performed using a LiChrosorb Si 60, 5 mμ, semiprep. column (25 cm × 10 mm) under isocratic conditions (CH_2Cl_2–hexane–*i*-PrOH, 14 6 1) with a flow rate of 3 ml/min and detection at 254 nm

A arborescens *L* Was collected from the Calabria (Italy) mountains during July 1985 and authenticated by Prof. D Puntillo, University of Calabria, a voucher specimen has been deposited at the Botanical Garden of the same University

Extraction and isolation The plant material was air-dried in the shade at room temp and then powdered, this material (550 g) was exhaustively percolated with Me_2CO The solvent was then evapd *in vacuo* and the residue (32 g) dissolved in MeOH–H_2O (1 1)

The soln, washed first with hexane, was then extracted with $CHCl_3$. The $CHCl_3$ soluble fraction (16 g) was flash-chromatographed on a silica gel column Elution with $CHCl_3$ containing increasing amounts of MeOH (up to 5%) yielded four main fractions

The first fraction contained only fats and sterols and has not been further examined The more complicated second fraction, chromatographed on HPLC, eluent CH_2Cl_2–hexane–*i*-PrOH, afforded 7 mg of (+)sesamin [4] and 6 mg of (+)fargesin [4]. The third fraction furnished, after crystallization from EtOAc, 72 mg of arthemetin [3]. From the mother liquor by HPLC on the previously described conditions were obtained 18 mg of (+)yangambin [4] and 15 mg of (+)sesartemin [4]. The fourth fraction rechromatographed on a silica gel column, eluent $CHCl_3$–MeOH (19:1), afforded 20 mg of **1** as a foam The identification of the known compounds was made by direct comparison with authentic samples.

3α,4α-10β-Trihydroxy-8α-acetyloxyguaian-12,6α-olide (**1**). White prisms from EtOH, mp 140–145° IR ν_{max}^{KBr} cm^{-1}. 3400–3200, 1760, 1735, 1390–1280, 1140–1090. MS, *m/z* (rel. int.): 322 $[M-18]^+$ (20), 262 (73), 219 (87), 189 (54), 147 (100) ^1H NMR and ^{13}C NMR see Table 1

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SESQUITERPENE LACTONES FROM *LEUZEA LONGIFOLIA*

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Key Word Index—*Leuzea longıfolıa*, Compositae; sesquiterpene lactones, guaianolides

Abstract—From aerıal parts of *Leuzea longıfolıa*, three new natural products, 11α,13-dıhydro-8α-methacryloyloxyzaluzanıne C, 11α-13-dıhydro-3β-(2-hydroxymethyl)acryloyloxyzaluzanıne C, 11α-13-dıhydro-3β-methacryloyloxyzaluzanıne C and a previously reported one, 11α-13-dıhydro-8α-(2-hydroxymethyl) acryloyloxyzaluzanıne C were isolated

INTRODUCTION

In continuation of our research interests about Portuguese endemic plants, we have studied the aerial parts of *Leuzea longıfolıa*. From the acetone extract, dewaxed with hexane, three major compounds were ısolated and identified as 11α,13-dihydro-8α-methacryloyloxyzaluzanine C (**1**), 11α,13-dihydro-8α-(2-hydroxymethyl) acryloyloxyzaluzanıne C (**2**), and 11α,13-dihydro-3β-(2-hydroxymethyl)acryloyloxyzaluzanıne C (**3**) Although compound **2** has been descrıbed in the lıterature [1] as a gum, we have obtaıned ıt as a crystallıne solid. A mınor lactone, whıch we were not able to purify, was identıfied as 11α,13-dihydro-3β-methacryloyloxyzaluzanine C (**4**)

RESULTS AND DISCUSSION

The structure of compound 1 was deduced from spectral data, maınly ^{1}H (Table 1) and ^{13}C (Table 2) NMR, as well as δH/δH (COSY) and δH/δC (HCCORR) bi-dimensional correlations, which allowed unambıguous assignments of the signals. The ^{1}H NMR spectrum of compound **1** showed four sıgnals at δ5 12 (1H, *s*), 5 14 (1H, *s*) and 5 35 (1H, *t*), 5 44 (1H, *t*), characterıstıc of two exomethylene protons. The *trans* fusıon of the lactone ring is concluded from the coupling constant $J_{6,7}$ = 11 Hz, obtaıned from the peaks at δ4 20 (1H, *t*) and 2.70 (1H, *ddd*) assigned to H-6 and H-7, respectively. A doublet at δ 1.16 (3H) and a double quartet at δ2.80 (1H), $J_{11,13}$ = 7 5 Hz, showed the presence of the methyl group ın a posıtıon α to the lactonıc carbonyl The configuratıon of thıs methyl group was inferred from the coupling constant $J_{7,11}$ = 7.5 Hz.

Table 1 ^{1}H NMR spectra* of compounds **1–4**

H	1	2	3	4
1	2 90 *m*	2 90 *m*	3 00 *m*	2 93 *m*
2	1 78 *ddd*	1 72 *dt*	1 88 *dt*	1 85 *dt*
2	2 31 *ddd*	2 30 *dt*	2 46 *m*	2 45 *m*
3	4 53 *tt*	4 51 *tt*	5 60 *tt*	5 57 *m*
5	2 90 *m*	2 90 *m*	3 00 *m*	2 93 *m*
6	4 20 *br t*	4 19 *br t*	4 18 *dd*	4 16 *br t*
7	2 70 *ddd*	2 70 *dt*	2 80 *m*	2 80 *m*
8	4 90 *ddd*	4 93 *ddd*	3 71 *ddd*	3 70 *ddd*
9	2 87 *dd*	2 83 *dd*	2 74 *dd*	2 73 *dd*
9	2 17 *dd*	2 18 *dd*	2 19 *dd*	2 20 *dd*
11	2 80 *dq*	2 76 *qnt*	2 80 *m*	2 80 *m*
13	1 16 *d*	1 14 *d*	1 27 *d*	1 27 *d*
14a	5 14 *br s*	5 13 *br s*	5 03 *s*	5 02 *s*
14b	5 12 *br s*	5 09 *br s*		
15a	5 44 *t*	5 42 *t*	5 38 *t*	5 36 *t*
15b	5 35 *t*	5 33 *t*	5 28 *t*	5 26 *t*
3′a	6 11 *qnt*	6 23 *q*	6 25 *dt*	6 13 *s*
3′b	5 62 *qnt*	5 88 *q*	5 90 *dt*	5 60 *s*
4′	1 95 *t*	4 33 *br s*	1 28 *s*	1 94 *s*

*Measured ın $CDCl_3$ (**1**, **2**, **4**) at 200 MHz, ınt ref. $CHCl_3$ and CD_3CD (**3**), ınt ref. TMS

J(Hz) Compound **1** 2α,3 = 2β,3 = 7,4, 3,15 = 2, 6,7 = 7,8 = 11, 7,11 = 11,13 = 7 5, 8,9α = 4.5; 8,9β = 8 5; 9α,9β = 12 5 Compound **2** 2α,3 = 2β,3 = 7 4, 3,15 = 2, 6,7 = 7,8 = 10; 7,11 = 11,13 = 7 5, 8,9α = 4 5, 8,9β = 8.4, 9α,9β = 12 8 Compound **3** 2α,3 = 2β,3 = 7 3, 3,15 = 2, 11,13 = 8, 8,9α = 4 5, 8,9β = 9 2, 9α,9β = 12 2 Compound **4** 3,15 = 2, 11,13 = 7 5, 8,9α = 4 5, 8,9β = 8 5, 9α,9β = 13 4