Phytochemistry, Vol. 26, No. 7, pp. 2103–2104, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00

SESQUITERPENE LACTONES FROM *ARTEMISIA MARITIMA*

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(*Revised received* 18 *November* 1986)

Key Word Index—*Artemisia maritima*; Compositae; sesquiterpene lactones; 1-oxo-6β,7α,11βH,14β-methylgermacra-4(5)-ene-12,6-olide; 1-oxo-6β,7α,11βH-germacra-4(5),10(14)-dien-12,6-olide; vulgarin; santonin; gallicin.

Abstract—Two new sesquiterpene lactones have been isolated from *Artemisia maritima* and the structures have been assigned on the basis of their spectral properties as 1-oxo-6β,7α,11βH,14β-methylgermacra-4(5)-ene-12,6-olide and 1-oxo-6β, 7α, 11βH-germacra-4(5),10(14)-dien-12,6-olide.

The genus *Artemisia* has been shown to contain a variety of sesquiterpene lactones and other compounds [1–4]. The reinvestigation of *Artemisia maritima* afforded two new sesquiterpene lactones (**1** and **2**) in addition to the known compounds **3–5**, which are known constituents of the Spanish *Artemisia maritima* [2].

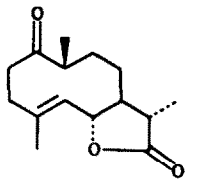
Compound **1** showed M^+ at *m/z* 250 and it was assigned the molecular formula $C_{15}H_{22}O_3$. It had an IR band at 1765 indicative of a γ-lactone. The absence of the hydroxyl absorption in the IR spectrum and the characteristic signals in the ^1H NMR (400 MHz) spectrum at δ2.83 and 2.60 for the α-methylene protons suggested the presence of a carbonyl group in addition to that of a lactone ring. A typical doublet of doublets at δ5.04, which broadened on irradiation of a triplet at 4.40, could be assigned to H-5 and indicated that the 4,5-double bond must be *trans*-oriented. The triplet at 4.40 was converted to a doublet on irradiation of a multiplet at 1.63 (assignable to H-7 with overlapping H-8/H-3 signals). From these spectral data compound **1** was assigned the structure 1-oxo-6β,7α,11βH,14β-methylgermacra-4(5)-ene-12,6-olide.

Compound **2** furnished M^+ at *m/z* 248 assignable to the molecular formula $C_{15}H_{20}O_3$. It showed a strong absorption at 1765 in the IR spectrum for γ-lactone and it showed characteristic singlets in the ^1H NMR spectrum at δ5.67 and 5.81 for exomethylene protons. In addition, a downfield doublet at 5.03 assigned to H-5 and a doublet at 1.75 for the H-15 methyl group were present. H-6 appeared as a doublet of doublets at 4.36. These spectral properties were comparable to the previous compound **1** except for the absence of a methyl group signal at 1.03 and its replacement by an exomethylene group signal. The position of the exomethylene group was concluded to be at C-10 resulting in the assignment of the structure as 1-oxo-6β,7α,11βH-germacra-4(5),10(14)-dien-12,6-olide. This was confirmed by comparison of the above data with the derivative of an oxidation product from gallicin [5].

Compound **3** was characterized as vulgarin which may be an artefact derived from **2** during the isolation process as the corresponding signals were missing in the ^1H NMR spectrum of the crude fraction. The known compounds, vulgarin (**3**), santonin (**4**), and gallicin (**5**), were characterized by comparison of their spectral data with those in the literature.

EXPERIMENTAL

Plant material. Aerial parts of *Artemisia maritima* (stem, leaves and flowers) were collected from the neighbourhood of Mussorie (India) in July–August 1985 and authenticated by Dr. A. K. Kashyap of the Botany Department, B. H. U., Varanasi 221 005, India. A voucher specimen is deposited in the Herbarium of the same department.



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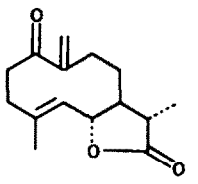

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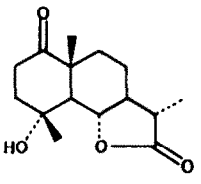

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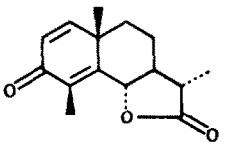

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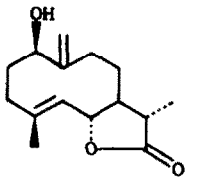

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Extraction and isolation. The plant material was air dried in the shade at room temp. and finally powdered. This material (260 g) was extracted at room temp. with Et_2O–MeOH (1:1) (1.5l. × 2) for 24 hr. The combined extracts were concd *in vacuo* and the residue defatted with MeOH. The residue (3.5 g) was chromatographed by CC on silica gel. The column was packed in petrol–Et_2O (1:1) and on elution with the same solvent gave fr 1 while fr 2 was eluted with petrol–Et_2O (1:3) and Et_2O.

Fr 1 on crystallization with petrol–Et_2O afforded colourless crystals (25 mg) of santonin (**4**) [6]. Fr 2 afforded a semisolid which on prep. TLC in Et_2O–petrol (3:2) gave a band at R_f 0.45 which on further prep. TLC in CH_2Cl_2–C_6H_6–Et_2O (3:3:1) with two developments gave three bands (2/1–2/3). Band 2/1 on HPLC (RP 8, MeOH–H_2O, 7:3, flow rate *ca* 3 ml/min, 100 bar) afforded 9 mg of **1** as a colourless oil (R_t 5.9 min) and 7 mg of **2** as a colourless crystals (R_t 7.1 min). Band 2/2 afforded **3** as colourless crystals, mp 176–177° [3] and band 2/3 was gallicin (**5**), mp 115° (114–116° [5]).

Compound **1**. Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 (γ-lactone), 1610, 1460, 1385, 1130, 1100; MS *m/z* (rel. int.): 250.1579 $[M]^+$ (18), 235 $[M-Me]^+$ (17), 232 $[M-H_2O]^+$ (8), 217 $[235-CO]^+$ (6), 61 (100), 55 (74); ^1H NMR ($CDCl_3$): δ5.04 (*dd*, *J* = 10, 2 Hz, H-5), 4.40 (*dd*, *J* = 10, 9 Hz, H-6), 2.83 (*ddd*, *J* = 16, 12, 4.5 Hz, H-2), 2.60 (*dd*, *J* = 12, 4.5 Hz, H-2'), 1.94 (*d*, *J* = 2 Hz, 4-Me), 1.21 (*d*, *J* = 7 Hz, 13-Me) and 1.03 (*d*, *J* = 7.5 Hz, 14-Me).

Compound **2**. Colourless crystals, mp 132° (128–130° [5]), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 (γ-lactone), 1610, 1460, 1390, 1140, 1100; MS *m/z* (rel. int.): 248 $[M]^+$ (7), 230 $[M-H_2O]^+$ (5), 220 $[M-CO]^+$ 81 (100), 61 (65); ^1H NMR ($CDCl_3$): δ5.81 and 5.67 (2*s*, H-14), 5.03 (*dd*, *J* = 10, 2 Hz, H-5), 4.36 (*dd*, *J* = 10, 9 Hz, H-6), 1.77 (*d*, *J* = 2 Hz, 4-Me) and 1.24 (*d*, *J* = 7 Hz, 11-Me).

Acknowledgement—The authors are grateful to Professor F. Bohlmann, Director, Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G. for valuable discussions.

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Phytochemistry, Vol. 26, No. 7, pp. 2104–2106, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00

TWO CALEINES FROM *CALEA ZACATECHICHI**

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(*Revised received* 24 *October* 1986)

Key Word Index—*Calea zacatechichi*; Compositae; Asteraceae; sesquiterpene lactones; caleines.

Abstract—Caleine E and F, two new sesquiterpene lactones, were isolated from *Calea zacatechichi*. Their structures and stereochemistry were determined by spectroscopic means and chemical derivatization of caleine E.

INTRODUCTION

Calea zacatechichi Schldl. is a wild shrub which grows in southern Mexican fields and has been used in folk medicine for stomach disease and in magic treatments as a dream inducer [1, 2]. Previous chemical work on *Calea zacatechichi* revealed the presence of caleines A (**3**), B (**4**), C and D, cromenes, flavones and acetylenic compounds [1, 3, 4].

The present investigation led to the isolation and identification of the known compounds 5 hydroxy-7,4'-dimethoxyflavone [5], acetylerioflorine [6], zexbrevine [7] and two new sesquiterpene lactones that we name caleine E (**1**) and F (**2**).

RESULTS AND DISCUSSION

Two different collections of *C. zacatechichi* were investigated for sesquiterpene lactones and flavonoids. The first collection (November 1979) afforded acetyleriof-

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