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TWO DERIVATIVES OF COSTIC ACID FROM *CENTAUREA ARGUTA*

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Key Word Index—*Centaurea arguta*; Compositae; costic acid derivatives; sesquiterpene lactones; guaianolides; flavonoids.

Abstract—The aerial parts of *Centaurea arguta* afforded, in addition to four known flavonoids and two known guaianolides, two new derivatives of costic acid.

INTRODUCTION

Phytochemical studies on species of *Centaurea* (Compositae, tribe: Cynareae) have shown sesquiterpene lactones to be common chemical constituents of this genus [1, 2]. Earlier investigations [3, 4] of *Centaurea arguta* Ness, an endemism of the Canary Islands, led to the isolation of four flavonoid compounds but no sesquiterpene lactones were described. Our reinvestigation of this plant afforded two new derivatives of costic acid, 3-oxo-1,2-dehydrocostic acid methyl ester (**1**) and 3-hydroxy-1,2-dehydrocostic acid methyl ester (**2**), besides the known compounds hispidulin (**4**) [4, 5], jaceosidin (**5**) [6], eupafolin (**6**) [5, 7], aguerin B (**7**) [8], cynaropicrin (**8**) [9] and 7-rutinosyl-3-methoxykaempferol (**9**) [3]. Compounds **4**, **5** and **9** were found previously in the same plant.

RESULTS AND DISCUSSION

The presence in the ^{1}H NMR spectrum (Table 1) of a pair of sharp doublets at δ6.85 and 6.01 together with two signals at δ6.08 (*dd*) and 5.18 (*t*) revealed that **1** possessed a ring A cross-conjugated dienone system identical with those of gerin [10], encelin [11] and 3-oxo-1,2-dehydrocostic acid [12]. The rest of the more significant signals, two three-proton singlets at δ0.98 and 3.77 and two broad singlets at δ6.23 and 5.63, confirmed that **1** was a methyl ester derivative of costic acid, the structure of which can be depicted as **1**. This compound was obtained by Bohlmann *et al.* [13] after methylation and further oxidation of the natural sesquiterpene **3**.

The ^{1}H NMR spectrum of **2** (Table 1) revealed two vinylic protons at δ5.52 and 5.64 assigned to H-1 and H-2, respectively. The signal of the proton attached to the carbon bearing the hydroxyl appeared at δ4.70, superimposed to one of the C-4 exocyclic olefinic protons. Inspection of Dreiding models indicated that the configuration of the hydroxy group is difficult to establish from the coupling constant $J_{2,3}$. Nevertheless, this configuration was established from the chemical shift changes of H-3 and H-15 in going from **2** to **2a** which are parallel to those in the epiisotelekin series (3β-hydroxyl), but not those in the isotelekin series (3α-hydroxyl) [14–16].

EXPERIMENTAL

C. arguta Ness was collected in Boca Tauce (2000 m), Tenerife, Canary Islands (Spain) at August 1985 (Z. D. Jorge, E. Gadeschi).

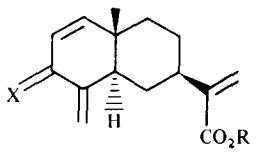
Isolation and characterization of compounds. Air-dried and

Table 1. ^{1}H NMR spectra of compounds from *Centaurea arguta*†

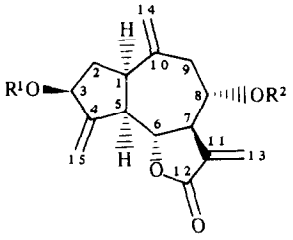
H	1	2	2a*
1	6.85 *d* (10.0)	5.52 *dd* (9.9, 0.9)	5.42 *br d* (10.0)
2	6.01 *d* (10.0)	5.64 *d* (9.7)	5.70 *br d* (10.0)
3	—	4.70 *br s*	5.88 *br s*
5	2.67 *dc* (11.7, 2.3)	2.22 *br d* (12.0)	—
6	1.49 *q* (12.0)	1.72–1.42 *m*	—
6′	1.88 *br dt* (12.0, 3.5)		
7	2.63 *tt* (11.7, 3.5)	2.56 *tt* (12, 3)†	—
8 and 8′	1.54–1.82 *m*	1.72–1.42 *m*	—
9 and 9′	1.54–1.82 *m*	1.72–1.42 *m*	—
13	6.23 *br s*	6.18 *d* (0.6)	6.24 *br s*
13′	5.63 *br s*	5.60 *t* (0.7)	5.65 *br s*
C_{10}-Me	0.98 *s*	0.84 *s*	0.89 *s*
15	6.08 *dd* (2.21, 1.35)	5.20 *d* (0.9)	4.97 *br s*
15′	5.18 *t* (1.2)	4.70 *br s*	4.70 *br s*
MeO	3.77 *s*	3.76 *s*	3.78 *s*
AcO	—	—	2.17 *s*

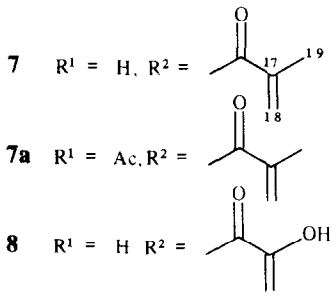
†Run in $CDCl_3$ at 200 MHz. Frequencies in ppm downfield from TMS as internal standard. Coupling constants (in parentheses) in Hz.

*Run in $CDCl_3$ at 60 MHz.

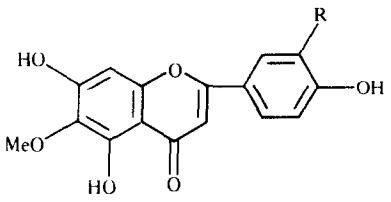


1 X = O R = Me
2 X = α-H, β-OH, R = Me
2a X = α-H, β-OAc, R = Me
3 X = α-H, β-OH, R = H

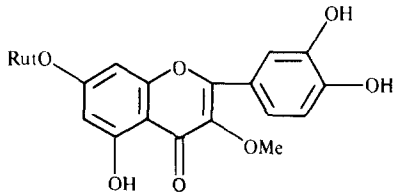




7 R^1 = H, R^2 =
7a R^1 = Ac, R^2 =
8 R^1 = H R^2 =



4 R = H
5 R = OMe
6 R = OH



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powdered aerial parts of the plant (667 g) were extracted first with CH_2Cl_2 and then with EtOH.

Study of the CH_2Cl_2 *extract.* After filtration, the extract was concd *in vacuo* at room temp. The residue (46.3 g) was subjected to CC over silica gel. Elution was started with petrol, a gradient of EtOAc was then added up to 100% EtOAc. Repeated sepn on a silica gel column with petrol–EtOAc mixtures gave the following compounds in order of elution: **1** (62 mg), **2** (24 mg), aguerin B (27 mg), hispidulin (136 mg), jaceosidin (193 mg), eupafolin (202 mg) and cynaropicrin (1047 mg). Compounds **4**–**9** were identified by comparison (IR, MS, ^{1}H NMR) with the literature.

3-*Oxo*-1,2-*dehydrocostic acid methyl ester* (**1**). Colourless oil. IR ν_{max}cm^{-1}: 1720 and 1665. MS *m/z*: 260 $[M]^+$ (4), 245 $[M-15]^+$ (4), 228 $[M-32]^+$ (6), 218 $[M-42]^+$ (6), 55 $[C_3H_3O]^+$ (69) and 43 (base peak).

3-*Hydroxy*-1,2-*dehydrocostic acid methyl ester* (**2**). Colourless oil, which suffered easy oxidation in contact with air to give **1**. IR ν_{max}cm^{-1}: 3585, 1720. MS *m/z*: 262 $[M]^+$ (5), 230 $[M-32]^+$ (3), 215 $[M-47]^+$ (4), 202 $[M-60]^+$ (5) and 78 (base peak). To **2** (16 mg) in pyridine (1 ml) was added Ac_2O (1 ml), extracted and CC (petrol–EtOAc, 8:2) afforded **2a** (9 mg), oily.

Study of the EtOH *extract.* After filtration, the EtOH extract was concentrated *in vacuo* at room temp. The residue (109 g) crystallized from EtOH gave **9** (27.4 g).

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A LUPEOL DERIVATIVE FROM *SALVIA PRATENSIS*

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Key Word Index—*Salvia pratensis*; Labiatae; triterpenoids; lupeol derivative; 7β-hydroxylup-20(29)-en-3-one.

Abstract—The aerial parts of *Salvia pratensis* afforded, in addition to the known triterpenoids β-amyrin, germanicol, lupeol and loranthol, a new related lupenol, 7β-hydroxylup-20(29)-en-3-one, whose structure was elucidated by spectroscopic methods and chemical transformations.

INTRODUCTION

A reinvestigation of the chemical constituents of *Salvia pratensis* L. [1, 2] has led to the isolation of one new derivative of lupeol, 7β-hydroxylup-20(29)-en-3-one (**1**). Furthermore the known compounds β-amyrin, germanicol, lupeol [3] and loranthol [4] were isolated.

RESULTS AND DISCUSSION

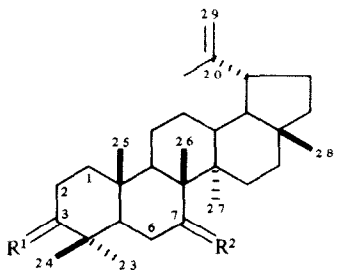
Chromatography of the neutral fraction from an extract of *Salvia pratensis* afforded a crystalline dextrorotatory material, which was identified as a mixture of β-amyrin, germanicol and lupeol by ^{13}C NMR spectral analysis which gave data coincident with those described by Bhattacharyya *et al.* [3].

Mass spectroscopy (M^+ at *m/z* 440) established the molecular formula of compound **1** as $C_{30}H_{48}O_2$. Its IR spectrum indicated a hydroxyl group (3.450 cm^{-1}), a carbonyl group (1.705 cm^{-1}) and an exocyclic methylene (1.645 and 885 cm^{-1}).

The ^1H NMR spectrum (Table 1) of **1** showed signals for six tertiary methyl groups, a vinylic methyl (δ1.64) which was shown to be coupled to two vinylic protons (δ4.65 and 4.53), thus indicating the presence of an isopropenyl group and also signals for a hydroxymethine group (δ3.83, 1H, *dd*, $J_1=6.8$ Hz, $J_2=8.8$ Hz) which must be axial and placed between a tetrasubtituted sp^3 carbon atom and a methylene grouping.

These data suggest a 20(29)-lupene structure with one β-hydroxy group and one keto group for the triterpenoid **1**. The functional groups were confirmed by the following reactions of this compound: the acetylation afforded a monoacetyl derivative **1a** and the Sarett oxidation gave the diketone **3**.

The carbonyl group of the compound **1** may be in any position with the exclusion of ring E (owing to its IR absorption), but it was located in position C-3 (the most likely on biosynthetic grounds) by comparison of the ^1H NMR data for H-3 in lupeol and acetoxylupeol at δ3.20 and 4.60, respectively [5, 6], with the ^1H NMR



	R^1	R^2
1	O	α-H; β-OH
1a	O	α-H; β-OAc
2	α-H; β-OH	α-H; β-OH
2a	α-H; β-OAc	α-H; β-OAc
3	O	O

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