^{1}H NMR: δ2.29 (3H, *s*), 2.52 (3H, *s*), 5.03 (1H, J = 3.3, 5.0 Hz, H-2), 3.44 (1H, *dd*) 3.34 (1H, *dd*) 6.89 (1H, *d*, J = 8 Hz) 7.81 (2H, *m*); MS *m/z*: 204 $[M]^+$, 189, 161, 145, 118, 89, 63, 43 (100%).

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SESQUITERPENE LACTONES FROM *CENTAUREA CORONOPIFOLIA*

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Key Word Index—*Centaurea coronopifolia*; Compositae; sesquiterpene lactones; germacranolides; flavonoids.

Abstract—The aerial parts of *Centaurea coronopifolia* afforded three new germacronolides, two of which are closely related to balsamin. The third is a new derivative of stizolicin, which is also present. The aerial parts also yielded four 6-methoxylated flavonoids and the triterpene, α-amyrin. The structures of the compounds were determined by spectroscopic methods.

INTRODUCTION

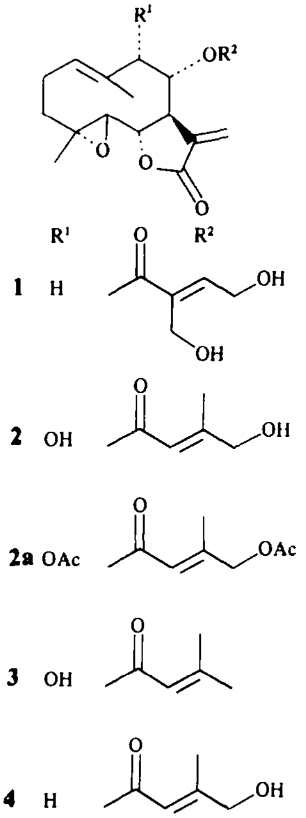
In the course of our investigation on the genus *Centaurea* [1–4], we have isolated four sesquiterpene lactones from the leaves of *Centaurea coronopifolia* Lam. Although one of the lactones, stizolicin, was isolated from *C. coronopifolia* [5] under the syn. *Stizolophus coronopifolius*, the other three are new: 1(10)en-4α-5β-epoxy-9α-hydroxy germacranolides with 8α-(4-hydroxy senecioate) (**2**), 8α-senecioate (**3**) and 1(10)en-4α,5β-epoxy-8α-(4-hydroxy senecioate) (**4**) side chains.

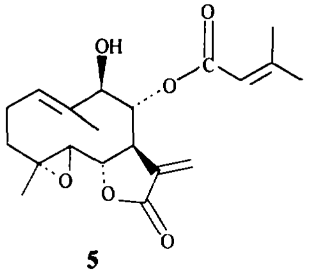
In addition, we also isolated the 6-methoxylated flavonoids 6-methoxyapigenin (**6**), 6-methoxyluteolin (**7**), quercetagetin 3,6-dimethyl ether (**8**) and quercetagetin 3,6-dimethyl ether 7-*O*-glucoside (**9**). The last two flavonoids were isolated from a *Centaurea* species for the first time. The leaves also yielded large amounts of the well known triterpene, α-amyrin.

RESULTS AND DISCUSSION

Compound **2** had the molecular formula $C_{20}H_{26}O_7$ (EIMS). Its IR spectrum showed the presence of a γ-lactone (1745 and 1140 cm^{-1}), an α,β-unsaturated ester function (1705 and 1280 cm^{-1}) and hydroxyl groups (3400 cm^{-1}). Its structure was established by ^{1}H NMR spectroscopy.

The ^{1}H NMR spectrum of **2** (Table 1) contained doublets for an exocyclic methylene conjugated with a γ-lactone at δ6.29 and 5.76 (^4J = 3.5, 3 Hz). A doublet at δ2.62 (J = 9 Hz) for H-5 supported an epoxide group between C-4/C-5. This doublet collapsed to a singlet when the double doublet at δ4.33 (J = 6.5, 9 Hz) (H-6) was irradiated and, in addition, the signal at δ3.82 (*dddd*, H-7) was simplified. However, irradiation of H-7 did not affect the double doublet at δ2.62 (H-5) but converted the double doublet at δ4.33 to a doublet (J = 9 Hz), the





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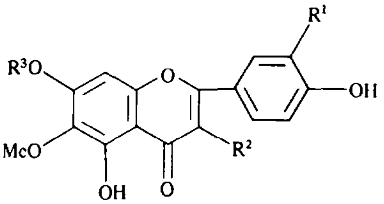

	R¹	R²	R³
6	H	H	H
7	OH	H	H
8	OH	OMe	H
9	OH	OMe	glucose

Table 1. ^{1}H NMR spectral data of compounds **1–4** ($CHCl_3$, TMS as int. standard)

H	**1***	**2**†	**2a***	**3**†	**4***
1	5.32 *m*	5.67 *m*	5.45 *dm*	5.62 *m*	5.30 *m*
2α	—	1.26 *ddd*	—	1.36 *ddd*	—
2β	—	2.52 *dddd*	—	2.52 *dddd*	—
3α	—	2.22 *ddd*	—	2.22 *ddd*	—
3β	—	2.32 *m*	—	2.35 *m*	—
5	2.65 *d*	2.62 *d*	2.62 *d*	2.62 *d*	2.65 *d*
6	4.34 *dd*	4.33 *dd*	4.40 *dd*	4.35 *dd*	4.32 *dd*
7	3.31 *m*	3.82 *dddd*	3.70 *dddd*	3.81 *dddd*	3.25 *dddd*
8	4.58 *m*	4.57 *d*	4.55 *s* (*br*)	4.57 *d*	4.60 *m*
9	—	4.38 *s* (*br*)	5.20 *s* (*br*)	4.37 *s* (*br*)	—
13a	5.70 *d*	5.67 *d*	5.56 *d*	5.66 *d*	5.75 *d*
13b	6.32 *d*	6.29 *d*	6.30 *d*	6.29 *d*	6.33 *d*
14	1.82 *s*	1.80 *s*	1.87 *s*	1.83 *s*	1.82 *s*
15	1.30 *s*	1.23 *s*	1.30 *s*	1.31 *s*	1.30 *s*
OCOR	6.99 *t*	6.02 *sm*	5.58 *q*	5.68 *q*	5.99 *q*
	4.35 *s* (*br*)	4.16 *s* (*br*)	4.52 *s* (*br*)	1.94 *s*	4.17 *s* (*br*)
	4.80 *d*	2.02 *s*	2.07 *s*	2.13 *s*	2.03 *s*
OAc			2.17 *s*		
			2.19 *s*		

*200 MHz.

†400 MHz.

J (Hz) **2**, **2a**, **3**: 1, 2β = 7; 2α, 2β = 13; 2β, 3α = 6; 2β, 3β = 13; 3α, 2α = 1.5; 3α, 3β = 12; 6, 5 = 9; 6, 7 = 6.5; 7, 13a = 3; 7, 13b = 3.5; 7, 8 = 4.

J (Hz) **1** and **4**: 5, 6 = 9; 6, 7 = 6; ester CH_2–O = 6.

doublets of the exocyclic methylene at δ6.29 and 5.76 to sharp singlets and the doublet at δ4.57 (J = 4 Hz) to a broadened singlet, indicating that this signal must belong to H-8. The singlet (*br*) at δ4.34 and the multiplet at δ5.67 were assigned to H-9 which is adjacent to a hydroxyl group and the vinyl proton H-1 respectively. The protons of the ester side chain were accounted for by a one proton multiplet at δ6.02, a two proton singlet at δ4.16 and a three proton singlet at δ2.02. The chemical shifts of the multiplet and two proton singlet strongly suggested the presence of a 4-hydroxy senecioate moiety. This was confirmed by the presence in the mass spectrum of a base peak at *m/z* 99.

Acetylation of **2** (to form **2a**) gave rise to two sharp methyl signals at δ2.17 and 2.19 and caused downfield shifts at δ5.20 and 4.52 for H-9 and CH_2OH in the side chain, respectively.

The upfield chemical shift of H-8 was explained by the report in the literature [6] that in C-6-*trans*-fused germacranolides with C-8 α-esters, H-8β has a higher chemical shift than that of H-8α.

The stereochemistry at C-5 and C-9 followed the observed coupling constants ($J_{5\alpha,6\beta}$ = 9 Hz; $J_{8\beta,9\alpha}$ = 3 Hz; $J_{8\beta,9\beta}$ = 0–1 Hz) when the Dreiding model was inspected.

Compound **3**, $C_{20}H_{26}O_6$ (EIMS) exhibited IR absorption bands at 1740 and 1150 (γ-lactone), 3400 (hydroxyl), and 1708 and 1290 (ester) cm^{-1}. Its ^1H NMR spectrum (Table 1) exhibited the typical doublets of an exocyclic methylene at δ6.29 and 5.66 (^4J = 3.5, 3 Hz). The other signals were very similar to those of compound **2**, except for the side chain signals which consisted of two vinylic methyl singlets at δ1.94 and 2.13 and a vinylic proton quartet δ5.68. On the basis of the chemical shift of the vinyl proton, the ester side chain must be senecioate. This was confirmed by the presence in the mass spectrum of a base peak at *m/z* 83. Compound **3** was identified as the 9α-hydroxy isomer of balsamin (**5**) which was isolated from *Stizolophus balsamita* [7].

Compound **4**, $C_{20}H_{26}O_6$ (EIMS) gave rise to IR bands at 3440 (hydroxyl), 1750 and 1140 (γ-lactone), and 1715 and 1280 (ester) cm^{-1}. Its ^1H NMR spectrum (Table 1) had the characteristic signals of an α-methylen-γ-lactone at δ5.75 and 6.33 (^4J = 3, 3.5 Hz), a H-5 epoxy proton at δ2.65 (*d*, J = 9 Hz) and a 4-hydroxy senecioic group at δ5.99 (*m*, vinylic proton), 2.03 (*s*, vinyl methyl) and 4.17 (*s*, $\underline{CH_2}OH$). The presence of this ester group was confirmed by the base peak at *m/z* 99. The spectral data indicated that compound **4** is a new derivative of stizolicin (**1**).

EXPERIMENTAL

Mps uncorr. Plant material was collected from Polatli (near Ankara, Turkey) in July 1980. A voucher specimen (No. 45502) is deposited in the Herbarium of the Faculty of Pharmacy, Istanbul.

Isolation and identification of compounds **1–4**. Air-dried and powdered aerial parts (1 kg) of *C. coronopifolia* was extracted with $CHCl_3$ in a Soxhlet, after evapn *in vacuo* the extract (21 g) was subjected to CC over silica gel and eluted with $CHCl_3$ by gradual addition of MeOH.

Compound **1**. Mp 141°, white crystals from MeOH (100 mg). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1760 and 1150 (γ-lactone), 1715 and 1276 (ester), 1649 (C=C), 840–800 (HC=CRR′). ^1H NMR: see Table 1. MS *m/z* (rel. int.): 378 $[M]^+$ $C_{20}H_{26}O_7$ (5), 360 $[M-18]^+$ (10), 263 $[M-C_5H_7O_3]^+$ (8), 246 $[M-C_5H_7O_4]^+$ (25), 188 $[C_{12}H_{12}O_2]^+$ (92), 97 $[C_5H_5O_2]^+$ (100). UV λ_{max}^{MeOH}: 225 nm.

Compound **2**. Mp 203°, white crystals from MeOH (20 mg). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1745 and 1140 (γ-lactone), 1705 and 1280 (ester), 1645 (C=C), 840–800 (HC=CRR′). ^1H NMR see Table 1. MS *m/z* (rel. int.): 378 $[M]^+$ $C_{20}H_{26}O_7$ (7), 279 $[M-C_5H_7O_2]^+$ (8), 262 $[M-C_5H_8O_3]^+$ (24), 115 $[C_3H_7O_3]^+$ (10), 99 $[C_5H_7O_2-CO]^+$ (68). UV λ_{max}^{MeOH}: 227 nm. *Diacetate of* **2**. A mixture of **2** (5 mg), C_5H_5N (1 ml) and Ac_2O (1 ml) was left at room temp. for 12 hr. ^1H NMR: see Table 1. MS *m/z* (rel. int.) 462 $[M]^+$ $C_{24}H_{30}O_9$ (4), 378 $[M-C_4H_4O_2]^+$ (6), 141 $[C_7H_9O_3]^+$ (40), 99 $[C_5H_7O_2]^+$ (100).

Compound **3**. Mp 225°, white crystals from MeOH (13 mg). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1740 and 1150 (γ-lactone), 1708 and 1290 (ester), 1645 (C=C), 850–818 (HC=CRR′). ^{1}NMR: see Table 1. MS *m/z* (rel. int.): 362 $[M]^+$ $C_{20}H_{26}O_6$ (5), 279 $[M-C_5H_7O]^+$ (23), 263 $[M-C_5H_7O_2]^+$ (5), 244 $[C_{15}H_{18}O_4-H_2O]^+$ (12), 83 $[C_5H_7O]^+$ (100), 55 $[C_5H_7O-CO]^+$ (64). UV λ_{max}^{MeOH}: 230 nm.

Compound **4**. Oily (5 mg). IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1750 and 1140 (γ-lactone), 1715 and 1280 (ester), 1655 (C=C). ^1H NMR see Table 1. MS *m/z* (rel. int.): 362 $[M]^+$ $C_{20}H_{26}O_6$ (5), 264 $[M-C_5H_6O_2]^+$ (5), 247 $[M-C_5H_8O_3]^+$ (9), 99 $[C_5H_7O_2]^+$ (100), 83 $[C_5H_7O]^+$ (92). UV λ_{max}^{MeOH}: 225 nm.

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