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SECO-EREMOPHILANOLIDES FROM *SENECIO MACEDONICUS*

ANTOANETA B. TRENDAFILOVA, ELENA T. TSANKOVA and LJUBA N. EVSTATIEVA*

Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria; *Institute of Botany, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

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Key Word Index—*Senecio macedonicus*; Asteraceae; *seco*-eremophilanolides; secomacrotolides.

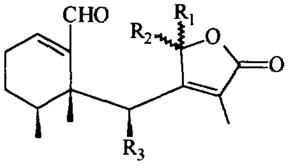
Abstract—Four sesquiterpene lactones with *seco*-eremophilane skeleton have been isolated from the leaves of *Senecio macedonicus*, two of which are new C-8 epimeric secomacrotolides. Their structures were elucidated by spectral analysis.

INTRODUCTION

Many species of the large genus *Senecio* have been investigated but nothing is known about the chemical constituents of *Senecio macedonicus* Griseb. This species is a perennial plant the distribution of which is restricted to the eastern part of the Balkan peninsula [1]. In this paper, we report on the isolation and structure of four sesquiterpene lactones (**1**–**4**) with the uncommon *seco*-eremophilane skeleton from the leaves of *S. macedonicus*. Two of the lactones, **2** and **4** are new representatives of the small group of secomacrotolides [2, 3].

RESULTS AND DISCUSSION

The leaves of the title plant afforded a mixture of lactones which could be further separated into two TLC spots (**A** and **B**) only after acetylation (see Experimental). The mass spectra (CI, isobutane) of **A** and **B** proved to be identical, each of them displaying two quasimolecular peaks at *m/z* 405 (0.2%) and 391 (36%). This indicated that each sample consisted of two lactones (**1** and **2** in **A**, **3** and **4** in **B**) with molecular formula $C_{22}H_{28}O_7$ and $C_{21}H_{26}O_7$, respectively. The mass spectra exhibited fragmentation peaks at *m/z* 345 (0.2%) and 331 (20%) due to the loss of acetic acid from each quasimolecular ion. Further, the single base peak at *m/z* 305, corresponding to elimination of two different acids ($C_5H_8O_2$ and $C_4H_6O_2$), suggested that the lactones possessed the same framework but differed in the nature of the ester group. This was confirmed by the ^{1}H NMR data (Table 1) which exhibited all the characteristic signals for angelate and methacrylate moieties in a ratio of 1:10. Furthermore, the ^{1}H NMR spectra showed three downfield shifted signals (δ 6.97–6.03) which were assigned to H-1, H-8 and H-6, while the most lowfield signals at δ 9.24–9.32 were attributed to the aldehyde group. In the methyl region, it showed signals corresponding to three different methyl groups (δ 1.33 *s*, 0.86 *d*, 2.10 *s*). All these data can be only accommodated by the *seco*-eremophilane skeleton of the secomacrotolides, recently isolated from *S. macrotis* [2] and *S. zoellneri* [3]. The ester groups at C-6 were assumed to be β-oriented by analogy with the known secomacrotolides [2, 3]. However, the stereochemistry at C-8 could not be determined, although the diastereomeric pairs **1**/**3** and **2**/**4** were successfully separated. The ^{1}H NMR data of the C-8 epimeric lactones **1** and **3** are identical with those published by Bohlmann [2] for 6β-angeloyloxy-secomacrotolide acetate and 8-epi-6β-angeloyloxy-secomacrotolide acetate. However, the other pair of epimeric lactones, **2** and **4** which contain methacrylate ester group, are new natural compounds.



	1	**2**	**3**	**4**
R_1	H	H	OAc	OAc
R_2	OAc	OAc	H	H
R_3	OAng	OMeacr	OAng	OMeacr

It is worth noting that no other eremophilane derivative could be detected in the plant extract. The isolation of secomacrotolides from *Senecio* species growing in Brazil [2], Chile [3] and Bulgaria illustrated that this taxonomically very diverse genus is also chemically diverse.

EXPERIMENTAL

The plant material was collected in June 1994 in West Stara Planina mountain (round Beledie Han) at blossom-time. A voucher specimen, SOM 151029, is deposited in

Table 1. ^{1}H NMR data of compounds **1**–**4** (250 MHz, $CDCl_3$)

H	**1**	**2**	**3**	**4**
1	6.97 *t*	6.97 *t*	6.97 *t*	6.97 *t*
2	2.42 *m*	2.42 *m*	2.40 *m*	2.40 *m*
6	6.06 *s*	6.05 *s*	6.04 *s*	6.03 *s*
8	6.67 *s*	6.67 *s*	6.68 *s*	6.68 *s*
9	9.24 *s*	9.30 *s*	9.24 *s*	9.32 *s*
13	2.13 *s*	2.13 *s*	2.10 *s*	2.10 *s*
14	1.33 *s*	1.34 *s*	1.33 *s*	1.33 *s*
15	0.86 *d*	0.86 *d*	0.86 *d*	0.86 *d*
OAc	2.16 *s*	2.16 *s*	2.19 *s*	2.19 *s*
OR	6.12 *qq*	6.14 *br s*	6.10 *qq*	6.14 *br s*
	1.98 *dq*	5.61 *dq*	1.98 *dq*	5.60 *dq*
	1.91 *dq*	1.94 *br s*	1.91 *br s*	1.93 *br s*

J(Hz): 1,2 = 1,2′ = 3.8; 4,15 = 6.9; OAng: 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5; OMeacr: 3′,3″ = 3′,4 = 3″,4′ = 1.5.

the herbarium of the Institute of Botany, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Air-dried leaves (200 g) of *S. macedonicus* were extracted with $CHCl_3$ (room temp) and the total extract (4 g) was fractionated as previously described [4] to give the crude lactone fraction (0.5 g). Subsequent CC sepn (silica gel, $CHCl_3$–Et_2O, 3:1) afforded a mixt. of lactones (77 mg) giving one TLC spot (R_f 0.5, $CHCl_3$–Et_2O, 2:1). After acetylation (Ac_2O, pyridine, room temp, 12 hr), the mixt. (60 mg) was subjected to CC (hexane–Et_2O, 1:1) and prep. TLC (hexane–Et_2O, 2:1, twice). This gave two spots **A** (25 mg) and **B** (10 mg) with R_f 0.26 and 0.18, respectively (hexane–Et_2O, 1:1), which could not be further separated.

6β-*Methacroyloxy-secomacrotolide acetate* (**2**). Gum, IR ν_{max}^{film} cm^{-1}: 1775 (γ-lactone), 1770, 1750, 1720, 1680, 1670, 1620; CIMS (isobutane) *m/z* (rel. int): 391 $[M + H]^+$, (36), 331 $[391–AcOH]^+$ (20), 305 $[391–MeacrOH]^+$ (100), 277 $[305–CO]^+$ (4), 245 $[305–AcOH]^+$ (16).

8-*epi*-6β-*Methacroyloxy-secomacrotolide acetate* (**4**). Gum, IR ν_{max}^{film} cm^{-1}: 1770 (γ-lactone), 1760, 1710, 1690, 1675, 1620, CIMS (isobutane) *m/z* (rel. int.): 391 $[M + H]^+$, (20), 331 $[391–AcOH]^+$ (4), 305 $[391–MeacrOH]^+$ (100), 277 $[305–CO]^+$ (2), 245 $[305–AcOH]^+$ (4).

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