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GLECHOMANOLIDES AND EUDESMANOLIDES FROM *SMYRNIUM PERFOLIATUM*

NEZHUN GÖREN and AYHAN ULUBELEN

Faculty of Pharmacy, University of Istanbul, Istanbul, Turkey

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Key Word Index—*Smyrnium perfoliatum*; Umbelliferaea; glechomanolides; eudesmanolides.

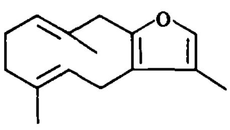
Abstract—In addition to five known sesquiterpenoids, six new compounds were isolated from *Smyrnium perfoliatum*. The new compounds were 1β-acetoxy-eudesma-3,7(11),8-trien-8,12-olide, 1β-acetoxyeudesma-4(15),7(11),8-trien-8,12-olide, 1β,10α;4α,5β-diepoxy-8β-isobutoxy-glechomanolide, 1β,10α;4α,5β-diepoxy-8α-isobutoxy-glechomanolide, 1β,4α-dihydroxy-2α,3α-epoxy-eudesma-7(11),8-dien-8,12-olide, 1β,4α-dihydroxy-2α,3α-epoxy-8β-methoxy-eudesma-7(11)-en-8α,12-olide.

INTRODUCTION

In addition to the known compounds furodiene (**1**) [1], 1β-acetoxy-8β-hydroxy-eudesma-4(15),7(11)-dien-8α,12-olide (**2**), 1β,10α;4α,5β-diepoxy-8β-hydroxy-glechomanolide (**3**) [2], germacron (**4**) [3], istanbulin A (**5**) [4] and stigmasterol (**6**) we have obtained six new sesquiterpenoids 1β-acetoxy-eudesma-3,7(11),8-trien-8,12-olide (**7**), 1β-acetoxy-eudesma-4(15),7(11),8-trien-8,12-olide (**8**), 1β,10α;4α,5β-diepoxy-8β-isobutoxy-glechomanolide (**9**), 1β,10α;4α,5β-diepoxy-8α-isobutoxy-glechomanolide (**10**) 1β,4α-dihydroxy-2α,3α-epoxy-eudesma-7(11), 8-dien-8,12-olide (**11**) and 1β,4α-dihydroxy-2α,3α-epoxy-8β-methoxy-eudesma-7(11)-en-8α,12-olide (**12**) from the roots and the fruits of *Smyrnium perfoliatum* L.

RESULTS AND DISCUSSION

Ether–petrol extracts of the roots of *Smyrnium perfoliatum* yielded the known compounds **1**, **3**, **6** while **2**–**5**



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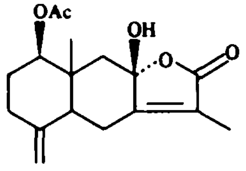

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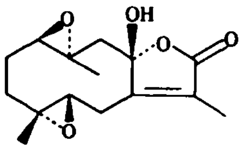

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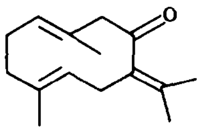

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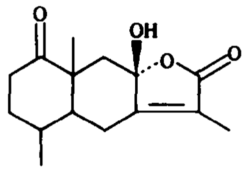

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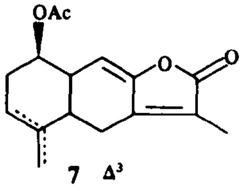
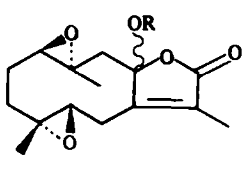
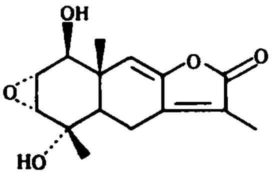


7 Δ^3
8 Δ^4



9 R = βiBu
10 R = αiBu



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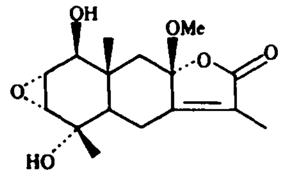

12

and the new compounds **7**–**12** were obtained from the fruits.

The high resolution mass spectrum of **7** indicated the molecular formula $C_{17}H_{20}O_4$, *m/z* 288.13501. The ^1H NMR spectrum showed signals of an acetoxy methyl at δ2.10, two olefinic methyls at 1.90 (H-13, *d*) and 1.72 (H-15, *br s*) and a tertiary methyl at 0.96 (H-14, *br s*). The lack of a lactone proton as well as of isolated methylene protons at C-9 and the presence of an olefinic singlet at δ5.71 (H-9) indicated a double bond at Δ^8. The proton next to an acetyl group were at δ4.78 (1H, *dd*, H-1) and 2.74 (1H, *dd*, H-6). A multiplet at δ5.38 (H-3), together with the olefinic methyl (H-15), indicated another double bond at $\Delta^{3(4)}$ (Table 1). The stereochemistry at C-1 was decided by measuring the *J* values of H-1 ($J_{1a,2a} = 12$, $J_{1a,2e} = 5$ Hz) and by studying a Dreiding model. The high resolution mass spectrum of **8** indicated the molecular formula $C_{17}H_{20}O_4$, *m/z* 288.13501. The ^1H NMR spectrum was similar to that of **7** (Table 1), although signals at δ4.98 (1H, *br s*, H-15) and δ4.71 (1H, *br s*, H-15′) indicated the presence of an exocyclic methylene group at C-4, and the multiplet at δ5.38 (H-3) and the olefinic methyl at δ1.72 of **7** were lacking in **8**. The stereochemistry at C-1 was decided by measuring the *J* values of H-1 ($J_{1a,2a} = 11$, $J_{1a,2e} = 6.5$ Hz) and by studying a Dreiding model. The mass spectrum of **9** indicated the molecular formula $C_{19}H_{28}O_5$ *m/z* 336. Its structure was mainly determined by the ^1H NMR spectrum. Apart from signals arising from the substituent at C-8, which was established as an isobutoxyl group [δ3.96 (1H, *dd*), 3.87 (1H, *dd*), 1.96 (1H, *ddqq*), 0.93 (6H, *d*)], the spectrum of **9** was similar to that of **3** previously obtained from *Smyrnium cordifolium* [2], thus fixing the stereochemistry at C-8. ^1H NMR data are given in Table 2.

The mass spectrum of **10** indicated a molecular formula $C_{19}H_{28}O_5$, *m/z* 336. The ^1H NMR spectrum of **10** was similar to that of **9**, the differences consisting mainly in the chemical shifts of the methyl doublets of the isobutoxyl group (Table 2). Although **9** and **10** were epimers it was possible to separate them on TLC plates. The NOE experiments shown in Table 3, and inspection of Dreiding models, indicated that **9** and **10** were C-8 epimers.

Table 1. ^1H NMR spectral data of compounds **7**–**8** (400 MHz, $CDCl_3$)

	7	8
H-1	4.78 *dd*	4.87 *dd*
H-3	5.38 m	
H-6	2.74 *dd*	2.90 *dd*
H-9	5.71 *s*	5.80 *s*
H-13	1.90 *d*	1.92 *d*
H-14	0.96 *s br*	1.05 *s*
H-15		4.98 *s br*
H-15′	1.72 *s*	4.71 *s br*
OAc	2.10 *s*	2.11 *s*

J (Hz) **7**: 1,2 = 5; 1,2′ = 12; 5,6 = 4; 6,6′ = 17; 6,13 = 2. **8**: 1,2 = 6.5; 1,2′ = 11; 5,6 = 4; 6,6′ = 17; 6,13 = 2.

Table 2. ^1H NMR spectral data of compounds **3**, **9**, **10** (400 MHz, $CDCl_3$)

	3	9	10
H-1	2.69 *dd*	2.83 *d br*	2.80 *d br*
H-2	1.50 *dddd*	2.07 *dd br*	2.05 *d br*
H-2′	2.15 *d br*	1.46 *m*	1.40 *dddd*
H-3	2.25 *ddd*	2.23 *ddd*	2.25 *ddd*
H-3′	1.27 *ddd*	1.28 *ddd*	1.30 *ddd*
H-5	2.67 *d*	2.69 *dd*	3.24 *dd*
H-6	2.55 *dd*	2.35 *dd br*	2.50 *dd*
H-6′	2.82 *d*	2.96 *d br*	2.92 *ddq*
H-9	3.02 *d*	3.15 *d*	3.01 *d*
H-9′	1.37 *d*	2.38 *d*	1.92 *d*
H-13	1.90 *s*	2.05 *s br*	1.90 *d*
H-14	1.50 *s*	1.40 *s*	1.26 *s*
H-15	1.35 *s*	1.19 *s*	1.13 *s*
OH	4.78 *s br*	—	—
OR*	—	3.96 *dd*	3.14 *dd* H-1′$_1$
		3.87 *dd*	2.89 *dd* H-1′$_2$
		1.96 *ddqq*	1.81 *ddqq* H-2′
			0.89 *d* H-3′
		0.93 *d*	
			0.88 *d* H-4′

J (Hz) **3**: 1,2 = 11; 1,2′ = 1.5; 2,2 = 14; 2,3 = 2′, 3 = 3; 2,3′ = 13; 2′,3′ = 4; 5,6 = 8; 6,6′ = 14; 9,9′ = 14.5. **9**: 1,2 = 4; 1,2′ = 1; 2,2′ = 14; 3,3′ = 13; 2,3 = 4.5; 2,3′ = 3; 2′,3 = 2; 5,6 = 5; 5,6′ = 11; 6,6′ = 14; 9,9′ = 12; 1′$_1$,1′$_2$ = 10.5; 1′$_2$,2′ = 6.5; 2′,3′ = 2′,4′ = 7. **10**: 1,2 = 10; 1,2′ = 1.5; 2,2′ = 3,3′ = 14; 2,3′ = 2′,3 = 3; 2′,3′ = 13; 5,6 = 5.5; 5,6′ = 9; 6,6′ = 15; 9,9′ = 15; 1′$_1$,1′$_2$ = 8.5; 1′$_2$,2′ = 6.5; 2′,3′ = 2′,4′ = 7.

*R = $-CH_2-CH-(Me)_2$

1′ 2′ 3′,4′

Table 3. NOE experiments of compounds **9** and **10**

Irradiated protons	Effected protons in 9	Irradiated protons	Effected protons in 10
15	6, 14	15 (3′)*	6, 14, (1,5)*
14	9, 15	14	9, 15
13 (2′)*	6, (5)*	13 (9′)*	6, (1)*
6	13, 15	6	13, 15
5	1, 3′	5	1, 3′
1	5, 9′	1	5, 9′

*Overlapped signals.

The A rings of **11** and **12** were identical, the differences are only the presence of a methoxyl group at C-8 in **12** and a double bond at $\Delta^{8(9)}$ in **11**. The high resolution mass spectrum of **11**, *m/z* 278.1154, indicated the molecular formula $C_{15}H_{18}O_5$ and that of **12**, *m/z* 310.142, indicated the molecular formula $C_{16}H_{22}O_6$. The ^1H NMR spectrum for both compounds exhibited three methyl signals. The lack of a lactone proton as well as of isolated methylene protons and a singlet at δ5.83 (H-9) indicated a double bond at $\Delta^{8(9)}$ for **11**, while in **12** the lack of the lactone proton and the presence of an isolated methylene at C-9 (δ2.67 *d*, *J* = 13.5 Hz, H-9 and 1.25 *d*, *J* = 13.5 Hz, H-9′), as well as the presence of a methoxyl group at δ3.14, indicated the methoxyl should be situated at C-8. Both compounds showed a broadened one proton singlet at δ3.70 (for **11**) and δ3.47 (for **12**) which indicated an

Table 4. ^{1}H NMR spectral data of compounds 11–12 (400 MHz, $CDCl_3$)

	11	12
H-1	3.70 *s br*	3.47 *s br*
H-2	3.38 *d*	3.31 *d*
H-3	3.23 *d*	3.19 *d*
H-5	1.61 *dd*	1.23 *dd*
H-6	2.98 *dd*	2.88 *dd*
H-6′	2.46 *dd br*	2.20 *dd br*
H-9	5.83 *s*	1.25 *d*
H-9′		2.67 *d*
H-13	1.90 *d*	1.85 *s br*
H-14	1.04 *s*	1.07 *s*
H-15	1.41 *s*	1.38 *s*
OMe	—	3.14 *s*
OH	—	2.49 *s br*

J (Hz) **11**: 2,3 = 3.5; 5,6′ = 4; 5,6 = 14; 6,6′ = 17; 6,13 = 1.5. **12**: 2,3 = 3.5; 5,6′ = 4; 5,6 = 13.5; 6,6′ = 15; 9,9′ = 13.5.

Table 5. NOE experiments of compound **12**

Irradiated protons	Effected protons
H-14	H-15, H-6β, H-9β, OMe, H-2β
H-15	H-14, H-6β, H-3β
OH	H-2β, H-3β, H-1α, H-5α
H-5	H-1α
H-3	H-15
H-1	H-9α, H-5α, H-2β

oxygen function at C-1. Two, one-hydrogen doublets, with $J = 3.5$ Hz for each, at δ3.38 and 3.23 (for **11**) and δ3.31 and 3.19 (for **12**) indicated an epoxy group between C-2 and C-3. Since H-6, H-6′ and H-5 were present as double doublets for both compounds the fifth oxygen function (for **11**) and the sixth oxygen function (for **12**) could only be situated at C-4 as hydroxyl groups (Table 4). The stereochemistry at C-1 was decided by comparing $W_{1/2}$ of H-1 (3 Hz) with the value of 3 Hz obtained from a Dreiding model for $J_{1a,2e}$. The stereochemistry at C-2 and C-3 was decided by measuring the *J* values of H-2 ($J_{2e,3e}$ = 3.5 Hz) and H-3 ($J_{3e,2e}$ = 3.5 Hz) and by studying Dreiding models. NOE experiments with **12** showed the configuration (Table 5).

EXPERIMENTAL

Plant material. Smyrnium perfoliatum L. was collected from the European section of Turkey (Mahya Dag-Kirklareli), a voucher (ISTE 21008) is deposited in the Herbarium of the Faculty of Pharmacy, University of Istanbul. Dried and powdered roots of *S. perfoliatum* (3 kg) were extracted with Et_2O–petrol (1:2) and the extract was treated with MeOH to remove long chain saturated hydrocarbons. The residue was separated by CC (silica gel) and the fractions were further separated and/or purified on TLC plates to yield 5 mg **1**, 250 mg **2** and 2.5 g **6**. The dried and powdered fruits (2.4 kg) were extracted and treated in a similar way to yield 150 mg **2**, 10 mg **3**, 80 mg **4**, 4 mg **5**, 2.5 mg **7**, 2.5 mg **8**, 44 mg **9**, 146 mg **10**, 12 mg **11** and 2.5 mg **12**. The spectral data for compounds **1**–**5** were given in refs [1–4].

*1β-Acetoxy-eudesma-*3,7(11),8-*trien*-8,12-*olide*(**7**). Amorphous. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1740, 1650, 1235; ^{1}H NMR given in Table 1; MS *m/z* (rel. int.): 288. 13501 $[M]^+$ ($C_{17}H_{20}O_4$) (24), 245 $[M-COMe]^+$ (7), 228 $[M-AcOH]^+$ (79), 213 $[228-Me]^+$ (100), 185 (30), 105 (20), 91 (28).

1β-Acetoxy-eudesma-4(15),7(11),8-*trien*-8,12-*olide* (**8**). Amorphous. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1740, 1650, 1235; ^{1}H NMR given in Table 1; MS *m/z* (rel. int.): 288.13501 $[M]^+$ ($C_{17}H_{20}O_4$) (24), 245 $[M-COMe]^+$ (8), 228 $[M-AcOH]^+$ (82), 213 $[228-Me]^+$ (100), 185 (30), 105 (20), 91 (28), 57 (34).

1β,10α;4α,5β-Diepoxy-8β-isobutoxy-glechomanolide (**9**). Colourless crystals, mp 155°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1755, 1485, 1350, 1200, 1150; ^{1}H NMR given in Table 2; MS *m/z* (rel. int.): 336 $[M]^+$ ($C_{19}H_{28}O_5$) (0.1), 263 $[M-OC_4H_9]^+$ (3), 220 (27), 155 (22), 126 (38), 57 $[C_4H_9]^+$ (100).

1β,10α;4α,5β-Diepoxy-8α-isobutoxy-glechomanolide (**10**). Amorphous. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1755, 1480, 1350, 1195, 1150; ^{1}H NMR given in Table 2; MS *m/z* (rel. int.): 336 $[M]^+$ ($C_{19}H_{28}O_5$) (0.1), 321 $[M-Me]^+$ (81), 263 $[M-OC_4H_9]^+$ (1), 220 (5), 193 (6), 155 (17), 126 (22), 57 $[C_4H_9]^+$ (100).

1β,4α-Dihydroxy-2α,3α-epoxy-eudesma-7(11),8-*dien*-8,12-*olide* (**11**). Amorphous. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420, 1755, 1655, 1480, 1350, 1070; ^{1}H NMR given in Table 4; MS *m/z* (rel. int.): 278.1154 $[M]^+$ ($C_{15}H_{18}O_5$) (33), 231 (18), 164 $[C_{10}H_{12}O_2]^+$ (72), 163 $[C_{10}H_{11}O_2]^+$ (100), $[C_3H_3O]^+$ (19).

1β,4α-Dihydroxy-2α,3α-epoxy-8β-methoxy-eudesma-7(11)-*en*-8α, 12-*olide* (**12**). Amorphous. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3555, 1760, 1605, 1480, 1350, 1170, 1080; ^{1}H NMR given in Table 4; MS *m/z* (rel. int.): 310.142 $[M]^+$ ($C_{16}H_{22}O_6$) (61), 282 $[M-CO]^+$ (65), 251 $[282-OMe]^+$ (25), 164 $[C_{10}H_{12}O_2]^+$ (10), 163 $(C_{10}H_{11}O_2)^+$ (19), 61 (100). $[\alpha]_D^{24}$ − 33.6° (589 nm), − 35.4° (578 nm), − 42.5° (546 nm), − 92.9° (435 nm), − 204.0 (365 nm).

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