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SESQUITERPENE LACTONES FROM *SMYRNIUM CORDIFOLIUM*

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Key Word Index—*Smyrnium cordifolium*; Umbelliferae; eudesmanolides; glechomanolides.

Abstract—In addition to previously obtained furanosesquiterpenes, two new eudesmanolides and a new glechomanolide were isolated from the fruits of *Smyrnium cordifolium*, while the roots gave two new eudesmanolides. The new compounds from the fruits were 1β-acetoxy-eudesman-4(15),7(11)-dien-8,12-olide, 1β-acetoxy-8β-hydroxy-eudesman-4(15),7(11)-dien-8,12-olide, 1β,10α;4α,5β-diepoxy-8-hydroxy-glechomanolide, those obtained from the roots were smyrnicordiolide and the corresponding 8β-hydroxy derivative belonging to a new type of oxepine derivative.

INTRODUCTION

In a previous study of the fruits of *Smyrnium cordifolium* Boiss. [1] furanogermacranes and a highly unstable furanoeremophilane were isolated and their structures were established by spectral methods. In a further study of the fruits as well as the roots of *S. cordifolium*, in addition to the known compounds furodien (**1**) [2], glechomafuran (**2**) [3] and glechomanolide (**3**), we have obtained new eudesmanolide and glechomanolide type compounds, all closely related to **1** and **2** (Scheme 1).

RESULTS AND DISCUSSION

Chloroform extracts of the fruits and the roots of *S. cordifolium* yielded four new eudesmanolides and a new glechomanolide. By using spectral data the structures of the new compounds from the fruits were established as 1β-acetoxy-8β-hydroxy-eudesman-4(15),7(11)-dien-8α,12-olide (**4**), 1β-acetoxy-eudesman-4(15),7(11)-dien-8α,12-olide (**5**), 1β,10α;4α,5β-diepoxy-8β-hydroxy-glechoman-8α,12-olide (**6**) and those from the roots were smyrnicordiolide (**7**), 8β-hydroxysmyrnicordiolide (**8**).

The high resolution mass spectrum of **4** indicated the molecular formula $C_{17}H_{22}O_5$ and the IR (KBr) spectrum showed the presence of a γ-lactone (1760 cm^{-1}) (sh), acetate (1725, 1240 cm^{-1}) and hydroxyl (3400 cm^{-1}) groups. The structure of **4** was established by ^1H and ^{13}C NMR spectroscopy and by spin-decoupling experiments with its acetyl derivative (**4a**). The ^1H NMR spectrum of **4** showed the presence of an acetoxy methyl (δ2.06), a vinylic methyl (δ1.80, H-13), a tertiary methyl (δ1.09, *s* (*br*), H-14) and exocyclic methylene protons (δ4.69 and 4.94, each *s* (*br*), H-15, H-15′) (Table 1). Irradiation of the methyl protons at δ0.98 of compound **4a** sharpened the signal of H-1 and H-9′ (W-coupling). Irradiation of H-6 collapsed the signal of H-5 and H-6′ to doublets respectively, while irradiation of H-3′ collapsed the signal of H-3 to a doublet. Geminally coupled broad doublets at δ1.39 (H-9′) and at δ2.93 (H-9) indicated the presence of an isolated methylene group. The stereochemistry at C-1 was decided from the observed coupling constants between H-1 and H-2, H-2′ and a study of the Dreiding model. In the ^{13}C NMR spectrum of **4** all signals were in agreement with the given structure (Table 2).

The mass spectrum of **5** led to the molecular formula $C_{17}H_{22}O_4$. The IR (KBr) spectrum exhibited bands for γ-lactone (1755 cm^{-1}) and for acetate (1725, 1235 cm^{-1}), but no hydroxyl band was present. The ^1H NMR spectrum of **5** showed the presence of an acetoxy methyl (δ2.07), a vinylic methyl (δ1.83, H-13), a tertiary methyl (δ0.94, H-14) and exocyclic methylene protons (δ4.95 and 4.70, H-15, H-15′). A broad double doublet at δ4.77 (H-8) was coupled with the double doublets for H-9 at δ2.59 and H-9′ at 1.05. The stereochemistry at C-8 followed the observed coupling constants between H-8 and H-9, H-9′ and a study of the Dreiding model. All other signals were in agreement with the given structure (Table 1).

In the mass spectrum of **6** no mass peak was observed, but a peak at *m/z* 262 corresponded to $[M - H_2O]^+$. The molecular formula therefore was $C_{15}H_{20}O_5$. The IR (KBr) spectrum had a hydroxyl band at 3250 cm^{-1} and a γ-lactone band at 1740 cm^{-1}. The ^1H NMR spectrum of **6** exhibited signals for three methyl groups (δ1.90, H-13); 1.50, H-15); and 1.35, H-14). One proton doublets at δ3.02 (H-9) and 1.37 (H-9′) indicated an isolated methylene at C-9. Irradiation of the signal of H-1 collapsed the signals of H-2 and H-2′ to a triple doublet and double triplet respectively. Irradiation of the signal of H-2 collapsed the signals of H-1 and H-2′ to broad singlets and of H-3, H-3′ to double doublets. Irradiation of the signal of H-6 collapsed the signal of H-6′ and irradiation of the signal of H-9 collapsed the signal of H-9′ to broad singlets respectively. The lack of a lactone proton (H-8) and the isolated methylene group at C-9 confirmed with the suggested structure.

The mass spectrum of **7** which we have named smyrnicordiolide indicated the molecular formula $C_{15}H_{18}O_3$. The IR ($CHCl_3$) spectrum showed γ-lactone (1745 cm^{-1}). The structure was established by ^1H and ^{13}C NMR spectroscopy and by NOE experiments. The low field signals of two vinylic protons at δ6.2 (*q*, $J = 1.5$ Hz, H-3) and 6.15 (*d*, $J = 8$ Hz, H-2) indicated the presence of an enol ether linkage between C-2 and C-3. The third vinylic

Table 1. ^{1}H NMR data of compounds **4–8** (400 MHz, $CDCl_3$, TMS as int. standard)

H	**4**	**4a**	**5**	**6**	**7**	**8**
1	4.61 *dd*	4.62 *dd*	4.65 *dd*	2.69 *dd*	4.41 *dd*	4.67 *dd*
2	1.63 *dddd*	1.63 *dddd*	1.60 *dddd*	1.50 *dddd*	6.1 *d*	6.1 *d*
2′	1.87 *m*	1.88 *m*	1.81 *m*	2.15 *d* (*br*)		
3	2.38 *ddd*	2.38 *m*	2.39 *ddd*	2.25 *ddd*	6.2 *q*	6.2 *q*
3′	2.14 *ddd* (*br*)	2.15 *ddd* (*br*)	2.15 *ddd* (*br*)	1.27 *ddd*		
5	1.90 *dd* (*br*)	1.92 *dd* (*br*)	1.93 *dd* (*br*)	2.67 *d*	1.80 *dddd*	1.81 *d* (*br*)
6	2.66 *dd*	2.72 *dd*	2.78 *dd*	2.55 *dd*	2.79 *dd*	2.68 *m*
6′	2.51 *dd* (*br*)	2.38 *dd* (*br*)	2.37 *dd* (*br*)	2.82 *d*	2.59 *dd* (*br*)	
8	—	—	4.77 *dd* (*br*)	—	4.77 *dd* (*br*)	—
9	2.44 *d*	2.92 *d*	2.50 *dd*	3.02 *d*	2.34 *dd*	2.35 *d*
9′	1.48 *d* (*br*)	1.39 *d* (*br*)	1.05 *dd*	1.37 *d*	1.05 *t*	1.46 *d*
13	1.80 *d*	1.87 *d*	1.83 *t*	1.90 *s* (*br*)	1.82 *t*	1.83 *d*
14	1.09 *s* (*br*)	0.98 *s* (*br*)	0.94 *s*	1.50 *s*	1.23 *s*	1.21 *s*
15	4.94 *s* (*br*)	4.94 *s* (*br*)	4.95 *s* (*br*)	1.35 *s*	1.71 *d*	1.71 *d*
15′	4.69 *s* (*br*)	4.69 *s* (*br*)	4.70 *s* (*br*)			
OAc	2.06 *s*	2.07 *s*	2.07 *s*	—	—	—
OAc	—	2.06 *s*	—	—	—	—
OH	3.94 *s* (*br*)	—	—	4.78 *s* (*br*)	—	2.89 *s* (*br*)

J (Hz): **4**: **4a**: 1,2 = 12; 1,2′ = 4.5; 2,2′ = 13; 2,3 = 5; 2,3′ = 13; 2′,3 = 2; 2′,3′ = 5; 3,3′ = 14; 5,6 = 3.5; 5,6′ = 12; 6,6′ = 13.5; 9,9′ = 14; 6,13 = 1. **5**: 8,9 = 12; 8,9′ = 12; 6,13 = 8,13 = 1. **6**: 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. **7**: 1,2 = 8; 1,8 = 1.2; 3,15 = 1.5; 6,6′ = 15; 5,6 = 14; 5,6′ = 4.5; 6,8 = 1.5; 8,9 = 6; 8,9′ = 12.5. **8**: 1,2 = 7.5; 1,5 = 1; 3,15 = 1.5; 9,9′ = 14.

Table 2. ^{13}C NMR data of compounds **4** and **7** (100.6 MHz, $CDCl_3$, TMS as int. standard)

C	**4**	**7**
1	79.80 *d*	110.80 *d*
2	23.70 *t*	141.50 *d*
3	27.03 *t*	139.40 *d*
4	145.96 *s*	119.40 *s*
5	49.50 *d*	52.30 *d*
6	33.20 *t*	28.30 *t*
7	159.90 *s*	161.50 *s*
8	103.10 *s*	76.50 *d*
9	47.19 *t*	47.80 *t*
10	39.90 *s*	39.30 *s*
11	122.43 *s*	119.76 *s*
12	170.60 *s*	174.79 *s*
13	8.18 *q*	8.20 *q*
14	11.70 *q*	30.84 *q*
15	108.65 *t*	21.30 *q*
OCO$\underline{Me}$	21.04 *q*	—
O$\underline{C}$OMe	172.06 *s*	—

proton at δ4.41 (*dd*, *J* = 7.5 Hz and 1.2 Hz, H-1) showed long range coupling with H-8. NOE experiments with H-8 enhanced H-1 and with H-14 enhanced H-9, H-9′, H-1 and H-5. The lactone proton (H-8) showed a typical signal at δ4.77 (*dd*, *J* = 6 and 12 Hz), other signals and the ^{13}C NMR spectrum confirmed the given structure. The stereochemistry at C-8 followed from the observed coupling constants between H-8 and H-9, H-9′ and a study of the Dreiding model.

The mass spectrum of **8** indicated the molecular formula $C_{15}H_{18}O_4$. The IR ($CHCl_3$) spectrum contained hydroxyl bands at 3560, 3350 cm^{-1} and a γ-lactone band at 1755 cm^{-1}. The structure of **8** was determined by comparing the ^{1}H NMR spectrum with that of **7**. Vinylic protons at δ6.2 (1H, *q*, *J* = 1 Hz, H-3), 6.1 (1H, *d*, *J* = 7.5 Hz, H-2) and at 4.67 (1H, *dd*, *J* = 1.5 and 7.5 Hz, H-1) indicated the same ring A structure. The lack of the lactone proton and the presence of an isolated methylene group at C-9 showed that the hydroxyl group was situated at C-8. The hydroxyl signal was at δ2.89 (1H, *br s*) and all other signals were similar to that of **7** (Table 1).

As shown in Scheme 1 all the compounds are probably formed from **1**. The formation of **7** and **8** requires a 2,3-dehydro derivative of **3** which then will be transformed to the epoxide **9**, obviously the precursor of **7**, which itself is formed by an electrocyclic reaction similar to that invoked for the biogenesis of miscandenin [4]. The eudesmanolides **4** and **5** are most likely formed through **3a**, the epoxide of glechomanolide **3**, as shown in Scheme 1.

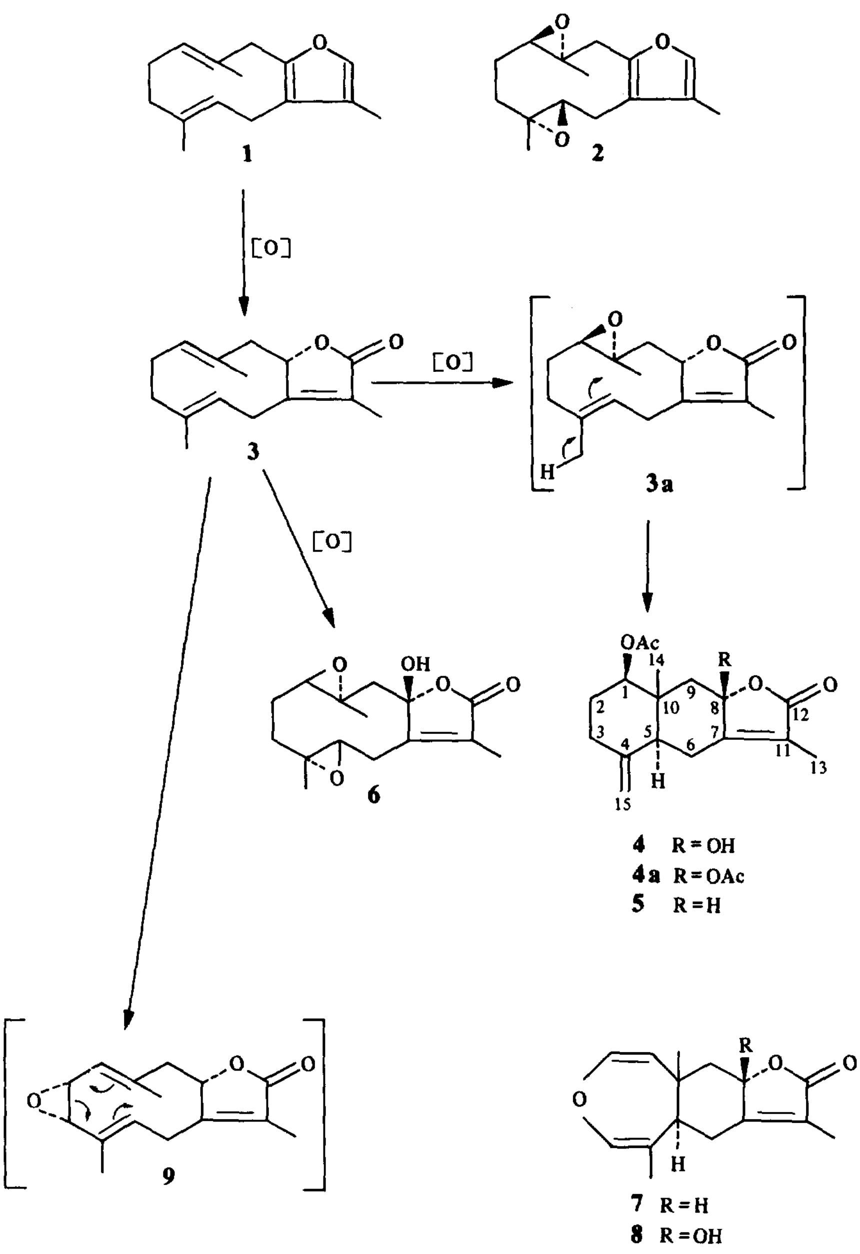
EXPERIMENTAL

Mp (Reichert-microscope instrument): uncorr.

The plant material collected for the previous study [1] was also used here.

Isolation of the compounds. Air dried and powdered fruits (150 g) and roots (300 g) were extracted with $CHCl_3$ in a Soxhlet separately. The extracts were evaporated under vacuum and the residues were fractioned by CC (silica gel) using $CHCl_3$ as eluting solvent, a gradient of MeOH was added up to 100%. The fractions were further separated and purified by prep. TLC (silica gel HF 254, petrol–Et_2O, 9:1) to give 120 mg **1**, 80 mg **2**, 15 mg **3**, 20 mg **4**, 20 mg **5**, 6 mg **6**, 15 mg **7** and 10 mg **8**.

1β-Acetoxy-8β-hydroxy-eudesman-4(15),7(11)-*dien*-8α,12-



Scheme 1.

olide (4). Colourless crystals, mp 212°. IR ν_{max}^{KBr} cm^{-1}: 3400, 2930, 2920, 1760 (sh), 1725, 1680, 1655, 1440, 1370, 1320, 1240, 1100, 1060, 1020, 950; ^{1}H NMR (400 MHz, CDCl$_3$): see Table 1; ^{13}C NMR (100.6 MHz, CDCl$_3$): see Table 2; EIMS, 70 eV, direct inlet, *m/z* (rel. int.): 306.1467 $[M]^+$ ($C_{17}H_{22}O_5$) (9), 288 $[M - H_2O]^+$ (3), 246 $[M - AcOH]^+$ (37), 228 $[M - H_2O - AcOH]^+$ (20), 218 $[M - AcOH - CO]^+$ (74), 173 (64), 145 (100).

Acetyl derivative of 4 (4a). Compound 4 was acetylated in the usual way with Ac_2O in C_5H_5N. Amorphous powder. IR ν_{max}^{KBr} cm^{-1}: 2940, 1775, 1740, 1725, 1655, 1440, 1365, 1240, 1210, 1150, 1060, 1025, 970, 750; ^{1}H NMR (400 MHz, CDCl$_3$): see Table 1; EIMS, 70 eV, *m/z* (rel. int.): 348.1573 $[M]^+$ ($C_{19}H_{24}O_6$) (5), 288 $[M - AcOH]^+$ (20), 246 $[M - AcOH - MeOH + H]^+$ (36), 229 $[M - AcOH - AcO]$ (92), 228 $[M - 2 \times AcOH]$ (100), 218 $[M - AcOH - MeCO - CO]$ (48), 200 $[M - 2 \times AcOH - CO]^+$ (57), 173 (40), 121 (52), 105 (52).

*1β-Acetoxy-eudesman-*4(15),7(11)*-dien-*8α,12*-olide* (5). Colourless crystals, mp 140–142°. IR ν_{max}^{KBr} cm^{-1}: 2920, 1755, 1725, 1685, 1645, 1440, 1360, 1235, 1200, 1080, 1050, 1040, 900; ^{1}H NMR (400 MHz, CDCl$_3$): see Table 1; EIMS, 70 eV, *m/z* (rel. int.): 290.1518 $[M]^+$ ($C_{17}H_{22}O_4$) (26), 230 $[M - AcOH]^+$ (100), 202 $[M - AcOH - CO]^+$ (58), 187 $[M - AcOH - MeOH]^+$ (28), 159 (36), 119 (57).

1*β*,10*α*; *4α,5β-Diepoxy-8β-hydroxy-glechoman-*8*α*,12*-olide* (6). Colourless crystals, mp 207–208°. IR ν_{max}^{KBr} cm^{-1}: 3250, 2920, 1740, 1455, 1390, 1340, 1200, 1155, 1050, 950, 920, 800, 730; ^{1}H NMR (400 MHz, CDCl$_3$): see Table 1; EIMS, 70 eV, *m/z* (rel.

int.): 262.1205 $[M-H_2O]^+$ ($C_{15}H_{18}O_4$) (7), 220 (60), 177 (50), 149 (36), 109 (54).

Smyrnicordiolide (7). Amorphous. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 2930, 1745, 1680, 1650, 1455, 1440, 1410, 1385, 1375, 1350, 1320, 1300, 1285, 1270, 1195, 1160, 1115, 1045, 975, 950, 860; ^{1}H NMR (400 MHz, $CDCl_3$): see Table 1; ^{13}C NMR (100.6 MHz, $CDCl_3$): see Table 2; EIMS, 70 eV, m/z (rel. int.): 246.1256 $[M]^+$ ($C_{15}H_{18}O_3$) (42), 231 $[M-15]^+$ (20), 162 (52), 135 ($C_9H_{11}O$) (100), 95 (C_6H_7O) (80).

8β-Hydroxysmyrnicordiolide (**8**). Colourless crystals, mp 215°. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3560, 3300, 2920, 1755, 1690, 1670, 1650, 1435, 1370, 1320, 1250, 1195, 1125, 1075, 1020, 960; ^{1}H NMR (400 MHz, $CDCl_3$): see Table 1; EIMS, 70 eV, m/z (rel. int.); 262.1205 $[M]^+$ ($C_{15}H_{18}O_4$) (22), 244 $[M-H_2O]^+$ (4), 135 $[C_9H_{11}O]^+$ (100), 95 $[C_6H_7O]^+$ (70);

$$[\alpha]^{D}_{24^\circ} = \frac{589 \quad\; 578 \quad\; 546 \quad\; 434 \quad\; 365\,\mathrm{nm}}{+253.1 \quad +270.0 \quad +315.0 \quad +634.4 \quad +1257.5}.$$

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