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SESQUITERPENE LACTONES FROM *AMBROSIA MARITIMA* (DAMSSISSA)

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Key Word Index—*Ambrosia maritima* (Damssissa); Compositae; sesquiterpene lactones; pseudoguaianolides.

Abstract—Six sesquiterpene lactones were isolated from the aerial parts of *Ambrosia maritima*. Four pseudoguaianolides were isolated for the first time in addition to parthenin and neoambrosin.

INTRODUCTION

Ambrosia maritima L. is a common Egyptian plant used in folk medicine in treatment of renal colic and calculi [1–3]. The plant has been studied for its molluscicidal activity for the control of Bilharziasis and was proved to have lethal effect on snails, miracidiae and cercariae [4, 5]. From the genus *Ambrosia* (Compositae, Heliantheae, subtribe Ambrosiinae) several species have been studied chemically. Nearly all species contain ambrosanolides [6]. From *A. maritima* two pseudoguaianolides, damsin and ambrosin, were reported [7–10].

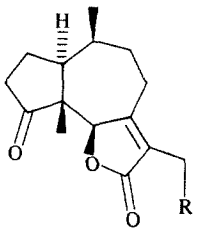
RESULTS AND DISCUSSION

The polar fractions of the aerial parts of *Ambrosia maritima* afforded in addition to damsin and ambrosin isolated previously from this species [7–10], parthenin (**7**) [11], neoambrosin (**8**) [12] and four minor lactones, the pseudoguaianolides **1**, **2**, **4** and **5**. The structure of **1** followed from the ^{1}H NMR spectrum (Table 1) and all data agreed with those reported for a lactone which has been prepared from anhydro parthenin by hydrogenation [9]. The structure of **2** which on acetylation afforded the acetate **3** also followed from the molecular formula and

Table 1. ^{1}H NMR spectral data of compounds **1–6** (400 MHz, $CDCl_3$, TMS as internal standard)

	1	**2**	**3**	**4**	**5**	**6**
H-1	2.30 *m*	2.35 *m*	2.33 *m*	1.55 *dd*	1.85 *m*	1.87 *m*
H-2	1.93 *m* 2.00 *m*	1.93 *m* 1.97 *m*	1.94 *m* 1.99 *m*	2.87 *dd* 2.47 *dd*	2.05 *m*	2.07 *m*
H-3	2.51 *ddd*	2.48 *ddd*	2.51 *ddd*	—	2.42 *dd br*	2.50 *ddd*
H-3′	2.33 *m*	2.34 *m*	2.30 *m*	—	2.18 *m*	2.21 *ddd*
H-6	4.63 *s br*	4.70 *s br*	4.69 *s br*	4.24 *d*	4.57 *d*	4.60 *d*
H-7	—	—	—	3.12 *ddddd*	2.55 *m*	2.53 *ddd*
H-8	2.79 *ddd* 2.30 *m*	2.94 *ddd* 2.38 *m*	3.01 *ddd* 2.38 *m*	1.65	2.05 *m* 1.74 *m*	2.07 *m* 1.74 *m*
H-9	1.55 *ddd* 2.13 *m*	1.36 *dddd* 2.17 *m*	1.36 *dddd* 2.17 *m*		1.56 *m* 1.85 *m*	1.58 *ddd* 1.93 *d br*
H-10	2.25 *m*	2.25 *m*	2.27 *m*	1.78 *m*	2.18 *m*	2.21 *m*
H-13	1.84 *s br*	4.36 *s br*	4.80 *s br*	6.32 *d* 5.59 *d*	3.79 *d br* 3.68 *d br*	4.29 *d* 4.18 *d*
H-14	1.02 *d*	1.00 *d*	1.02 *d*	1.17 *d*	1.06 *d*	1.10 *d*
H-15	0.85 *s*	0.85 *s*	0.86 *s*	0.87 *s*	1.13 *s*	1.19 *s*
OAc	—	—	2.06 *s*	—	—	2.11 *s*

J (Hz): Compounds **1–3**: 2, 3 = 8; 2′, 3 = 1.5; 3, 3′ = 18; 8, 8′ = 15; 8, 9 = 8; 8, 9′ = 1.5; 9, 9′ = 13; 9, 10 = 10; 10, 14 = 7; compound **4**: 1, 2 = 7.5; 1, 2′ = 0.8; 2, 2′ = 19; 6, 7 = 9; 7, 8 = 10; 7, 8′ ~ 3; 7, 13 = 3.5; 7, 13′ = 3; 10, 14 = 7; compounds **5**/**6**: 2, 3 = 8.5; 2′, 3 = 1.5; 2, 3′ = 10; 2′, 3′ ~ 10; 3, 3′ = 17; 6, 7 = 7.5; 7, 8 = 10; 7, 8′ = 2.5; 8, 8′ = 14; 8′, 9 = 12; 10, 14 = 7.5; 13, 13′ = 12.

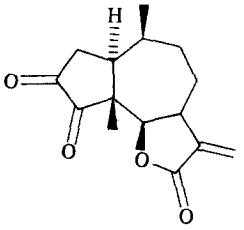


R

1 H

2 OH

3 OAc



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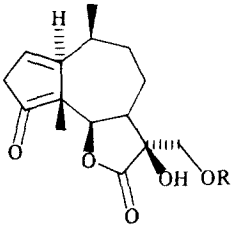
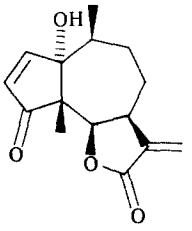


R

5 H

6 Ac



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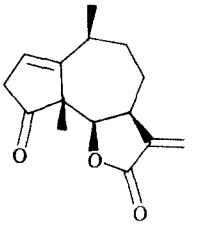

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from the ^{1}H NMR spectrum (Table 1) which was similar to that of **1**. However, the olefinic methyl signal was replaced by a broadened singlet at δ4.36 in the spectrum of **2** which was shifted down to 4.80 in that of **3**. Accordingly, the position of the hydroxyl group was settled. Spin decoupling allowed the assignment of all signals. NOE difference spectra further established the proposed stereochemistry. Thus irradiation of H-15 caused an NOE of H-9β and saturation of H-6 gave a clear effect with H-1.

The molecular formula of **4** indicated an additional oxygen function. Inspection of the ^{1}H NMR spectrum (Table 1) showed that this could be present only at C-3. In agreement with this in addition to the usual butyrolactone IR band a second one was visible and its frequency (1795 cm^{-1}) indicated an α,β-diketone in a five membered ring. Typical signals of a methylene lactone in the ^{1}H NMR spectrum and spin decoupling studies led to the structure **4** though some signals were overlapped multiplets.

The diol **5** was purified as its monoacetate **6**. The molecular formula ($C_{17}H_{24}O_6$) and the ^{1}H NMR spectrum (Table 1) indicated that in addition to the acetate group a hydroxyl, a keto and a γ-lactone grouping were present. Spin decoupling allowed the assignment of all signals though a few were overlapped multiplets. The stereochemistry could be deduced by NOE difference spectroscopy. Irradiation of the H-14 signal caused a clear NOE of H-8β and irradiation of H-15 showed effects of H-2β and H-8β. Saturation of the H-8β signal accordingly gave NOE with H-14 and H-15. Irradiation of the H-7 signal gave NOE with H-13 while H-6 gave NOE with H-13. Thus the β-orientation of the methyl groups and the α-orientation of the acetoxy methylene group was settled. The natural diol **5** is formed probably by hydrolysis of the corresponding epoxide. An epoxide of ambrosin (stramonin B) has been reported [13].

Parthenin and neoambrosin were identified by comparison of their NMR and IR spectra with those of authentic samples.

EXPERIMENTAL

The air-dried aerial parts (4 kg) (collected from Abies region near Alexandria in March 1982; Voucher specimen deposited in the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy, Alexandria, Egypt) were extracted with Et_2O–petrol (2:1) and the resulting extract was separated by CC (silica gel, Merck) starting elution with Et_2O saturated with H_2O, then adding increasing amounts of MeOH. Repeated TLC of the collected fractions (silica gel, PF 254, Et_2O saturated with H_2O, two developments, zones were visualized by UV light) resulting in isolation of 10 mg **1**, 10 mg **2**, 2 mg **4**, 10 mg **5**, 5 mg **7** and 10 mg **8**. All the isolated lactones were oils, attempts at crystallization from different solvents failed.

Lactone **1**. Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750 (γ-lactone); MS (CI, *i*-butane) *m/z* (rel. int.): 249 $[M+1]^+$ (100) ($C_{15}H_{20}O_3+1$).

Lactone **2**. Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone, C=O); MS *m/z* (rel. int.): 264.136 (11) $[M]^+$ (calc. for $C_{15}H_{20}O_4$: 264.136), 249 $[M-Me]^+$ (61), 246 $[M-H_2O]^+$ (24), 206 (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546\ nm}{+12 \quad +13 \quad +16}\ (CHCl_3;\ c\ 1.3).$$

Compound **2** (5 mg) was heated with 0.5 ml Ac_2O for 1 hr at 70°. TLC (Et_2O–petrol, 3:1) gave 4 mg **3**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1760 (γ-lactone, C=O); MS *m/z* (rel. int.): 306 $[M]^+$, 291 $[M-Me]^+$ (8), 246 [M – HOAc] (61), 206 (22), 55 (100); CI (*i*-butane): 307 $[M+1]^+$ (100).

Lactone **4**. Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1795, 1780 (γ-lactone, five membered ring α-diketone); MS *m/z* (rel. int.): 262.121 $[M]^+$ (12) (calc. for $C_{15}H_{18}O_4$: 262.121), 244 $[M-H_2O]^+$ (9), 234 $[M-CO]^+$ (10), 220 (24), 167 (50), 151 (51), 123 (67), 95 (96), 55 (100).

Lactone **5**. Colourless oil (^{1}H NMR see Table 1). The crude lactone **5** (10 mg) was acetylated (Ac_2O, 70°) and the acetate obtained (**6**) was purified by TLC (Et_2O–C_6H_6–$CHCl_3$, 1:1:1) and further by HPLC (MeOH–H_2O, 3:2, *R*, 3.5 min) to give 8 mg **6**, colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1775 (γ-lactone), 1745, 1220 (OAc); MS *m/z* (rel. int.): 324.17 $[M]^+$ (1) (calc. for $C_{17}H_{24}O_6$: 324.157), 309 $[M-Me]^+$ (7), 306 $[M-H_2O]^+$ (1), 246 $[406-HOAc]^+$ (11), 97 [methylcyclopentanone]$^+$ (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546\ nm}{+23 \quad +26 \quad +30}\ (CHCl_3;\ c\ 0.8).$$

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