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GUAIANOLIDE α-ARABINOPYRANOSIDES FROM *HELENIUM AMARUM*

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Key Word Index—*Helenium amarum*; Compositae; sesquiterpene lactones; pseudoguaianolides; guaianolide-α-arabinopyranosides; sesquiterpenes; seco-caryophyllenes; phenylpropane derivatives.

Abstract—The aerial parts of *Helenium amarum* afforded, in addition to compounds reported previously, several known sesquiterpene lactones as well as some new ones, two pseudoguaianolides and a complex mixture of guaianolide α-arabinopyranosides, which differed in the position of the double bond, the configuration at C-8 and the position of an acetate group in the sugar moiety. Furthermore seco-caryophyllenes and phenylpropane derivatives were isolated. The structures were elucidated by spectroscopic methods and few chemical transformations.

INTRODUCTION

Helenium amarum (Raf.) H. Rock (= *H. tenuifolium* Nutt.) has been investigated previously. While from the aerial parts three pseudoguaianolides were reported [1, 2] the roots contain characteristic acetylenic compounds [3]. We now have studied again the aerial parts. The results will be discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *Helenium amarum*, collected in North Carolina, afforded the known sesquiterpene lactones aromatin [4], balduilin [5], aromaticin [4], amarilin [6], 4-H-carabrone [7], florilenalin [8], baileyin acetate [9, 10], helenalin and tenulin, most isolated from the same species [1, 2], and several new ones, the pseudoguaianolides **1** and **2**, as well as a complex mixture of arabinopyranosides, which could not be separated completely. Only **3a**–**5a**, **5b** and **6b** could be obtained pure and the remaining mixture gave the corresponding three triacetates **3e**, **4e** and **5e**. Furthermore in addition to the seco-caryophyllene derivative **7** [11] the corresponding aldehyde **8**, already prepared by partial synthesis from caryophyllene [11] and inseparable phenylpropane derivatives [12].

The structure of **1** followed from careful ^{1}H NMR investigations (Table 1). While the stereochemistry at C-6–C-8 directly could be deduced from the couplings and the chemical shifts, especially if compared with those of compounds with known configurations, the stereochemistry at C-2–C-4 only could be established by NOE difference spectroscopy which showed clear effects between H-15 and H-8, OH, H-2 and H-10, between H-14 and H-2, between H-4 and H-1 and H-6 as well as between H-1 and H-7. These results clearly established the whole stereochemistry at all asymmetric centres. Thus **1** is 6β-acetoxyamarilin.

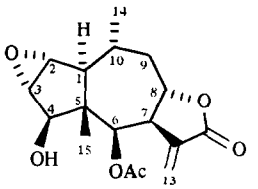
The ^{1}H NMR spectrum of **2** was close to that of balduilin (Table 1); only the H-6 signal was as expected shifted upfield, indicating that the acetoxy in the latter was replaced by a hydroxy group. Accordingly, 6β-hydroxyaromatin was present.

The structure of **5e**, obtained by acetylation of **5a** and **5b**, could be deduced from the ^{1}H NMR spectrum (Table 2) which was in part close to that of florilenalin. However, the low field signal of H-2 was missing and several additional low field signals indicated the presence of a glycoside. Careful spin decoupling and comparison of

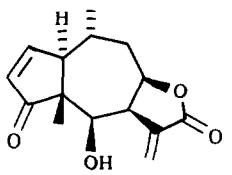
Table 1. ^{1}H NMR spectral data of **1** and **2** (400 MHz, $CDCl_3$, TMS as internal standard)

	1	**2**
H-1	1.80 *d*	2.33 *ddd*
H-2	3.43 *d*	7.63 *dd*
H-3	3.40 *d*	6.13 *dd*
H-4	4.00 *d*	—
H-6	5.32 *d*	4.40 *dd*
H-7	3.06 *dddd*	3.64 *dddd*
H-8	4.55 *ddd*	4.81 *ddd*
H-9	2.49 *ddd*	2.41 *ddd*
H-9′	1.36 *ddd*	1.71 *ddd*
H-10	2.10 *dddq*	2.10 *dddq*
H-13	6.26 *d*	6.40 *dd*
H-13′	5.33 *d*	6.17 *dd*
H-14	1.26 *d*	1.22 *d*
H-15	1.01 *s*	1.13 *s*
OAc	2.05 *s*	—
OH	3.04 *d*	4.74 *d*

J (Hz): Compound **1** 1,10 = 11.5; 2,3 = 4, OH = 6, 7 = 7, 13 = 7, 13′ = 3; 7,8 = 9; 8,9 = 3; 8,9′ = 12; 9,9′ = 13; 9,10 = 5; 9′,10 = 11; 10,14 = 6; compound **2** 1,2 = 3; 2,3 = 2; 1,10 = 12; 2,3 = 6; 6,7 = 6.5; 6,OH = 1.5; 7,8 = 8; 7,13 = 7,13′ = 2.5; 8,9 = 9; 8,9′ = 2.5; 9,9′ = 15; 9,10 = 4.5; 9′,10 = 6; 10,14 = 7; 13,13′ = 1.



1



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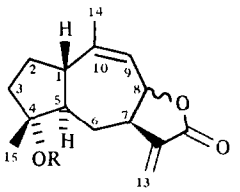
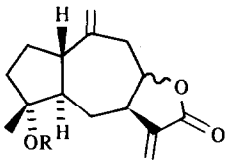
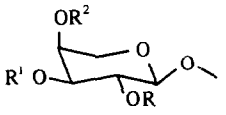


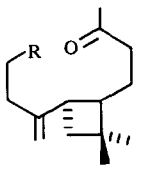
R	A	B	C	D	E
8α H	**3a**	**3b**			**3e**
8β H	**4a**	**4b**	**4c**	**4d**	**4e**



R	A	B	E
8αH	**5a**	**5b**	**5e**
8βH		**6b**	



	A	B	C	D	E
R	H	Ac	H	H	Ac
R^1	H	H	Ac	H	Ac
R^2	H	H	H	Ac	Ac



7 R = CHO

8 R = CH_2OH

the signals with those of ribopyranose tetra-acetate showed that the triacetate **5e** was present. Accordingly, the coupling $J_{3',4'}$ and $J_{4',5'}$ were small, while the coupling $J_{1',2'}$ was 7.5 Hz which agreed with those of an α-glycoside [13]. The stereochemistry of the chiral centres of the lactone moiety followed the couplings and chemical shifts, especially when compared with those of florilenalin, where the configuration is established by X-ray analysis [8].

The structure of **5a**, which showed no signals of acetate methyls, was clear as the acetylation gave **5e**. The structure of **5b**, which also could be transformed to **5e**, followed from the down field shifted double doublet at δ4.85 which was coupled with H-1'. Accordingly the acetoxy group was at C-2'.

If the ^{1}H NMR spectrum of **6b** was compared with that of **5b** (Table 2) it was obvious that these two lactones only differed in the stereochemistry at C-8. As in the spectra of other *trans*-8,12-guaianolides the H-7 signal of **6b** was shifted upfield. The acetoxy group was at C-2' as followed from decoupling of the low field signal (δ4.84 *dd*).

The ^{1}H NMR spectrum of **3e** (Table 2) was in part close to that of pleniradin [10, 14] and similar guaianolides with a 9,10-double bond. Furthermore the characteristic ^{1}H NMR signals of the sugar moiety showed that again an acetylated α-arabinopyranoside was present. All data therefore agreed with the proposed structure. Acetylation of **3a** afforded **3e**; accordingly, the structure of **3a** also was settled.

Comparison of the ^{1}H NMR spectral data (Table 2) of **3e** and **4e** showed that these compounds again only differed in the configuration at C-8. As usual the H-7 and H-8 signals were shifted upfield in the spectrum of the *trans*-lactone. The signals of the sugar moiety were nearly identical with that of **5e**. Accordingly, the same glycoside residue was present.

Acid catalysed hydrolysis of a mixture of the arabinosides followed by acetylation gave L-α-arabinopyranose-tetra-acetate as could be deduced from the ^{1}H NMR spectral data which agreed nicely with those expected (see Experimental).

The co-occurrence of *trans*-fused guaian-8,12-olides and the melampolide baileyin acetate again supports the proposed role of melampolides as precursors of helenandides and pseudoguaianolides [10]. Arabinopyranosides seem to be isolated for the first time. Though their

Table 2. ^{1}H NMR spectral data of **3a–6b*** (400 MHz, $CDCl_3$, TMS as internal standard)

	3a, b, e†	**4a–e**	**5a, b, e**	**6b‡**	
H-6	1.50 *m*	1.50 *m*	1.50 *m*	2.24 *ddd*	
H-6′				1.65 *m*	
H-7	3.07 *dddd*	2.52 *dddd*	3.02 *ddddd*	2.66 *dddd*	
H-8	5.23 *br d*	4.70 *br d*	4.53 *ddd*	4.30 *ddd*	
H-9	5.29 *br s*	5.85 *br s*	2.65 *ddd*	3.21 *dddd*	
H-9′			2.47 *dd*	2.56 *br dd*	
H-13	6.23 *d*	6.18 *d*	6.25 *d*	6.25 *d*	
H-13′	5.55 *d*	5.49 *d*	5.62 *d*	5.55 *d*	
H-14	1.73 *br s*	1.81 *br s*	4.99 *br s*	5.07 *br s*	
H-14′			4.90 *br s*	4.98 *br s*	
H-15	1.21 *s*	1.26 *s*	1.31 *s*	1.24 *s*	
	3a–5a	**3b–6b**	**4c**	**4d**	**3e–5e**
H-1′	4.40 *d*	4.72 *d*	4.40 *d*	4.38 *d*	4.56 *d*
H-2′	3.60 *m*	4.84 *dd*	3.78 *m*	3.78 *m*	5.16 *dd*
H-3′	3.75 *m*	3.78 *dd*	4.90 *dd*	4.03 *m*	5.04 *dd*
H-4′	3.90 *m*	3.90 *m*	4.00 *m*	5.12 *br s*	5.25 *ddd*
H-5_1′	3.96 *dd*	3.90 *m*	3.98 *dd*	4.03 *m*	4.00 *dd*
H-5_2′	3.55 *dd*	3.60 *m*	3.59 *br d*	3.58 *br d*	3.62 *dd*
OAc	—	2.13 *s*	2.18 *s*	2.15 *s*	2.15 *s*
					2.07 *s*
					2.02 *s*

*Signals of the single compounds in one of the series only differed in the range of 0.01–0.02 ppm; H-2, H-3 and H-5 overlapped multiplets; †H-1 3.30 *br dd*; ‡3.26 *br ddd*.

J (Hz): Compounds **3a, 3b, 3e, 4e–4e**: 6,7 ~ 10; 6′,7 ~ 3; 7,8 = 10; 7,13 = 3; 7,13′ = 2.8; 8,9 ~ 3; 8,14 = 9,14 ~ 1.5; compound **5a, 5b, 5e**: 1,2 = 1,2′ ~ 8; 1,5 ~ 10; 6,7 ~ 10; 6′,7 ~ 3; 7,8 = 8; 7,13 = 2; 7,13′ = 1.8; 8,9 = 5; 8,9′ = 11; 9,9′ = 13; compound **6b**: 6,7 = 10; 6,7′ = 7,13 = 7,13′ ~ 3; 7,8 = 9; 8,9 = 6; 8,9′ = 10; 9,9′ = 15; 9,14 = 9,14′ ~ 1.5; sugar moiety: 1′,2′ ~ 7.5; 2′,3′ ~ 10; 3′,4′ ~ 3.5; 4′,5_1′ ~ 2.5; 4′,5_2′ ~ 1.5; 5_1′,5_2′ ~ 13.

concentrations are very high the corresponding aglycones were not detected. Further investigations may show whether these glycosides are of chemotaxonomic interest.

EXPERIMENTAL

The air dried aerial parts (240 g, collected in North Carolina, voucher RMK 9310, deposited in the National Herbarium, Washington) was extracted with MeOH–Et_2O–petrol, 1:1:1, at room temp. and the resulting extract was worked-up in the usual fashion [15]. Column chromatography (SiO_2) afforded five crude fractions: 1 (petrol), 2 (Et_2O–petrol, 1:10), 3 (Et_2O–petrol, 1:1), 4 (Et_2O) and 5 (Et_2O–MeOH, 10:1–1:1). Fraction 1 contained nothing of interest. TLC of fraction 2 (SiO_2, PF 254, CH_2Cl_2–C_6H_6–Et_2O, 5:5:1) gave 5 mg **7** (R_f 0.7) and 7 mg **8** (R_f 0.45). TLC of fraction 3 (Et_2O–petrol, 3:2) gave 2 mg aromaticin, 4 mg aromatin [4], a mixture, which on repeated TLC (Et_2O–petrol, 4:1) gave a mixture of 2 mg baileyin acetate [9, 10] and 7 mg balduilin [5], as well as a mixture which gave on repeated TLC (Et_2O–petrol, 9:1, three developments) 3 mg 4-H-carabron, 1.5 mg **2** (R_f 0.45), 3.5 mg **1** (R_f 0.40) and 9 mg amarilin [6] (R_f 0.32) and a mixture which on repeated TLC (Et_2O, two developments) gave 2 mg amarilin, 10 mg helenalin, a mixture of helenalin and tenulin and 0.6 g tenulin. Fraction 4 gave 3 g tenulin by crystallization and fraction 5 gave 1.5 g of a crystalline mixture of **3a–6b** after treatment of the crude material with carbon in MeOH. One tenth of this material was separated by HPLC (RP 8, MeOH–H_2O, 11:9, always ~ 100 bar and flow rate ~ 3 ml/min) affording six fractions (I–VI). From fraction I nothing could be identified. II contained 60 mg florilenalin [8], III on repeated HPLC (RP 8, MeOH–H_2O, 9:11) gave 2 mg **5a** (R_t 7.5 min) and IV was separated again by TLC (Et_2O–MeOH, 9:1) affording 5 mg **5b** (R_f 0.35), 2 mg **4a** (R_f 0.19) and 2 mg **3a** (R_f 0.15). V on TLC (Et_2O–MeOH, 9:1) gave 6 mg **6b** (R_f 0.30) and VI could not be separated completely by TLC (Et_2O–MeOH, 9:1) or repeated HPLC (RP 8, MeOH–H_2O, 11:9). Known compounds were identified by comparing with authentic samples (400 MHz, ^{1}H NMR and co-TLC or, if no material was available, by comparing the ^{1}H NMR spectral data with those reported in the literature and by complete assignment of all signals by spin decoupling. Compounds **1**, **2**, **3a**, **4a**, **5a** and **6b** could not be induced to crystallize, but they were homogeneous by ^{1}H NMR and TLC in different solvents.

6β-Acetoxyamarilin (**1**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3520 (OH, hydrogen bonded), 1780 (γ-lactone), 1730, 1265 (OAc); MS *m/z* (rel. int.): 262.121 $[M-HOAc]^+$ (11) (calc. for $C_{15}H_{18}O_4$: 262.121), 233 $[262-CHO]^+$ (12), 215 $[233-H_2O]^+$ (19), 203 $[233-CH_2O]^+$ (44), 175 $[203-CO]^+$ (37), 161 $[203-C_2H_2O]^+$ (72), 133 $[161-CO]^+$ (100); $[\alpha]_D^{24°}$ +40 ($CHCl_3$; *c* 0.1).

6β-Hydroxyaromatin (**2**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1700 (C=CCO); MS *m/z* (rel. int.): 262.121 $[M]^+$ (3) (calc. for $C_{15}H_{18}O_4$: 262.121), 244 $[M-H_2O]^+$ (2), 216 $[244-CO]^+$ (2), 201 $[216-Me]^+$ (2), 124 (100), 96 (62); $[\alpha]_D^{24°}$ +32 ($CHCl_3$; *c* 0.1).

2-Desoxypleniradin-L-α-arabinopyranoside (**3a**). Colourless, viscous oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS (CI, isobutane) *m/z* (rel. int.): 381 $[M+1]^+$ (1), 231 $[381-C_5H_{10}O_5]^+$ (100), 133 $[C_5H_9O_4]^+$ (28), 115 $[133-H_2O]^+$ (41); $[\alpha]_D^{24°}$ −64 ($CHCl_3$; *c* 0.1). Acetylation (Ac_2O, 70°) gave **3e**, colourless crystals, mp 195–196°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone, OAc); MS *m/z* (rel. int.): 386 $[M-2HOAc]^+$ (1), 344 $[386-\text{ketene}]^+$ (1.5), 275.077 $[C_{11}H_{15}O_8]^+$ (12), 259.082 $[C_{11}H_{15}O_7]^+$ (82), 231.138 $[C_{15}H_{19}O_2]^+$ (64), 230.131 $[C_{15}H_{18}O_2]^+$ (44), 157 (63), 139 (100); $[\alpha]_D^{24°}$ −38 ($CHCl_3$; *c* 1.0).

2-Desacetoxygaillardin-L-α-arabinopyranoside (**4a**). Colourless, viscous oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS (CI, isobutane) *m/z* (rel. int.): 381 $[M+1]^+$ (1), 231 $[C_{15}H_{19}O_2]^+$ (100). Acetylation (s.a.) afforded **4e**, colourless crystals, mp 228–230°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (γ-lactone, OAc); MS *m/z* (rel. int.): 259.082 $[C_{11}H_{15}O_7]^+$ (42), 231 $[C_{15}H_{19}O_2]^+$ (58), 230.131 $[C_{15}H_{18}O_2]^+$ (82), 157 (64), 139 (100); $[\alpha]_D^{24°}$ −26 ($CHCl_3$; *c* 0.33).

2-Desoxyflorilenalin-L-α-arabinopyranoside (**5a**). Colourless, viscous oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS (CI, isobutane) *m/z* (rel. int.): 381 $[M+1]^+$ (0.5), 231 $[C_{15}H_{19}O_2]^+$ (100), 133 $[C_5H_9O_4]^+$ (17); $[\alpha]_D^{24°}$ −10.0 ($CHCl_3$; *c* 0.1). Acetylation (s.a.) afforded **5e**, colourless viscous oil; MS *m/z* (rel. int.): 231.138 $[C_{15}H_{19}O_2]^+$ (58), 230, 131 $[C_{15}H_{18}O_2]^+$ (42), 139 (100).

2-Desoxyflorilenalin-[2'-O-acetyl-L-α-arabinopyranoside] (**5b**). Colourless crystals, mp 96°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone, OAc); MS (CI, isobutane) *m/z* (rel. int.): 231 $[M-\text{sugar moiety}]^+$ (20), 175 $[C_5H_9O_3, OAc]^+$ (100), 115 $[175-HOAc]^+$ (7).

2-Desoxy-8-epi-florilenalin-[2'-O-acetyl-L-α-arabinopyranoside] (**6b**). Colourless viscous oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone, OAc); MS (CI, isobutane) *m/z* (rel. int.): 423 $[M+1]^+$ (1), 231 $[C_{15}H_{19}O_2]^+$ (28), 175 $[C_5H_9O_3OAc]^+$ (100); $[\alpha]_D^{24°}$ −16 ($CHCl_3$; *c* 0.4).

Preparation of L-α-arabinopyranose-tetraacetate. 50 mg of a mixture of the arabinosides **3a**/**3b** in 2 ml methanol were heated for 2 hr with 20 mg *p*-toluenesulfonic acid. After addition of $NaHCO_3$ and evaporation water was added and the lactones were extracted with $CHCl_3$. The aqueous solution was evapd and acetylated. The $CHCl_3$ extract gave by TLC (Et_2O–$CHCl_3$, 2:1) 6 mg L-α-arabinopyranose-tetraacetate; $[\alpha]_D^{24°}$ +48 ($CHCl_3$; *c* 0.6, lit. +42.5° [16]); ^{1}H NMR ($CDCl_3$, 400 MHz): 5.61 (*d*, H-1), 5.29 (*dd*, H-2), 5.10 (*dd*, H-3), 5.30 (*br s*, H-4), 4.04 (*dd*, H-5), 3.77 (*dd*, H-5'); (*J* [Hz]: 1, 2 = 7; 2, 3 = 9; 3, 4 = 4, 5 = 3.5; 4, 5' = 1.5; 5, 5' = 13).

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