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GUAIANOLIDES AND OTHER CONSTITUENTS OF *ACHILLEA LIGUSTICA*

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Key Word Index—*Achillea ligustica*; Compositae; Anthemideae; sesquiterpene lactones; guaianolides; flavones; monoterpene.

Abstract—Extraction of the aerial parts of *Achillea ligustica* furnished the known guaianolides matricarin, chrysartemin A and chrysartemin B, a new guaianolide isoapressin, the flavones nevadensin, 3,6-dimethoxy-5,7,4′-trihydroxyflavone and quercetagetin 3,6,7-trimethyl ether and (+)-*E*-2,6-dihydroxy-2,6-dimethylocta-3,7-diene.

Representatives of the genus *Achillea* (Compositae. Anthemideae) chracteristically furnish sesquiterpene lactones of the guaianolide type. Our recent work on *Achillea ligustica* All., a species which occurs in the Mediterranean region, tends to confirm this generalization. Isolated were the known guaianolides matricarin (**1**), chrysartemin A (**2**) and chrysartemin B (**3**) as well as nevadensin (5,7-dihydroxy-6,8,4′-trimethoxyflavone), 3,6-dimethoxy-5,7,4′-trihydroxy flavone and quercetagetin 3,6,7-trimethyl ether. A new guaianolide was **4a** which, because of its relationship to **4b** (apressin) from *Achillea depressa* [1] we have named isoapressin. The monoterpene (+)-*E*-2,6-dihydroxy-2,6-dimethylocta-3,7-diene (**5**) of uncertain absolute configuration was also found.

Structure and stereochemistry of **4a** were established from the ^{1}H NMR spectrum (Table 1) using extensive decoupling which will not be described in detail and NOE studies. (Table 2). Most chemical shifts, coupling constants and the facile loss of oxygen in the CIMS paralleled earlier observations in the case of apressin (**4b**) [1] with one exception—the presence of a doublet at δ2.30 (J = 1.5 Hz) coupled to H-9 (*ddd* at δ5.02). After exchange with D_2O the signal at δ2.30 disappeared and the H-9 signal collapsed to a doublet. Hence the acetate function was attached to C-10, as is also indicated by the downfield shift of H-14, and the free hydroxyl was at C-9. Irradiation of H-6, H-9 and H-15 caused enhancements in the signals of H-2 and H-3, hence the olefinic bridge was β-orientated; the significant NOEs observed between H-6 and H-9, between H-9 and H-15 and between H-5 and H-7 showed that the protons involved were *syn*-related. The negative Cotton effect ($[\theta]_{257}$ −2350) shows that the relative configuration shown in formula **4a** represents the absolute configuration as well. Finally, the data provided in the Experimental established the structure of (+)-**5**, although the absolute configuration remains unknown.

Table 1. ^{1}H NMR spectrum of compound **4a** (270 MHz)

H	$CDCl_3$	C_6D_6
2	6.40 *br d* (5.5)	6.08 *br d*
3	6.38 *br d* (5.5)	5.94 *br d*
5	2.68 *d* (10.5)	2.28 *br d*
6	3.82 *t* (10)	3.22 *t*
7	3.47 *m*	3.05 *m*
8a	2.36 *ddd* (13, 9, 7)	2.05 *ddd*
8b	2.00 *ddd* (13, 10, 8)	1.60 *ddd*
9	5.02 *ddd* (9, 8, 1.5)	4.78 *ddd*
13a	5.45 *d* (3.2)	4.95 *d*
13b	6.20 *d* (3.5)	5.93 *d*
14*	1.34 *s*	1.10 *s*
15*	1.72 *s*	1.57 *s*
Ac*	2.16 *s*	1.83 *s*
OH	2.30 *d* (1.5)	1.90 *d*

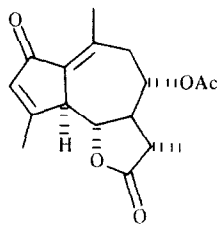
*Intensity three protons.

EXPERIMENTAL

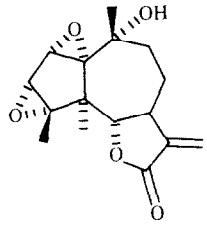
Above-ground parts (310 g) of *Achillea ligustica* All., collected near Piano degli Albanesi, Palermo, Sicily, in July 1986 (voucher

Table 2. NOE difference spectrum of compound **4a**

Saturation	Observed (% increase)
H-9	H-2+H-3 (9) H-6 (13) H-15 (10)
H-6	H-2+H-3 (14) H-9 (12)
H-7	H-5 (14)
H-5	H-7 (13)
H-15	H-2+H-3 (16) H-9 (15)



1



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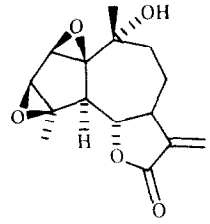

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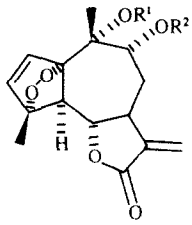
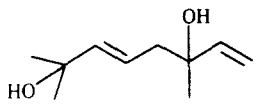


4a R^1 = Ac, R^2 = H
4b R^1 = H, R^2 = Ac



5

specimen deposited in herbarium of Botanical Garden of Palermo), were extracted with $CHCl_3$. Work-up in the usual manner [2] gave 10 g of crude gum which was adsorbed on 20 g of Si gel (Merck No. 7734 deactivated with 15% H_2O) and chromatographed over 400 g of the same adsorbent, 250 ml fractions being collected as follows. Frs 1–4 (petrol), 5–8 (petrol–EtOAc 4:1), 9–12 (petrol–EtOAc 3:2), 13–16 (petrol–EtOAc 2:3), 17–20 (petrol–EtOAc 1:4), 21–24 (EtOAc), 25–28 (EtOAc–MeOH 9:1).

Frs 8–10 dissolved in petrol–EtOAc on refrigeration (−20°, overnight) deposited 50 mg of matricarin [3–5]. Radial chromatography ($CHCl_3$–MeOH 49:1) of the mother liquor and further purification by CC gave 7 mg of nevadensin identical with an authentic sample [6, 7]. CC ($CHCl_3$) of fr. 11 gave two fractions. Radial chromatography of the first furnished 10 mg of **4a**, IR ($CHCl_3$ 3560, 1770, 1740, 1660 cm^{-1}; CD curve (MeOH) $[\theta]_{257}$ −2350; CIMS *m/z* (rel. int.) 337 ($[M+1]^+$, 100) 319 (4), 305 (3), 277 (8), 259 (8), 183 (22), 164 (11); ^1H NMR spectrum in Table 1. CC ($CHCl_3$–Et_2O 3:2) of the second fraction gave 20 mg of **5** as an oil, IR ($CHCl_3$) 3340, 3310, 1630, 985, 960; $[\alpha]_{546}^{24}$ +3.6° ($CHCl_3$; *c* 0.38); CIMS *m/z* (rel. int.) 171 ($[M+1]^+$, 1), 153 (47), 135 (11), 83 (100); ^1H NMR spectrum ($CHCl_3$, 270 MHz) H-1a δ5.20 *dd* (17, 1) H-1b δ5.05 *dd* (11, 1), H-2 δ5.92 *dd* (17, 11), H-4a δ2.30 *dd* (13, 6), H-4b δ2.22 *dd* (13, 6), H-5 δ5.60 *dt* (16, 6), H-6 δ5.72 (16), Me's at δ1.30 and 1.25 (all *s*).

Rechromatography of fr. 12 gave 17 mg of 3,6-dimethox-5,7,4′-trihydroxyflavone whose mp and spectroscopic properties corresponded to the literature data [8]. Rechromatography of the combined frs 14 and 15 gave two fractions. Radial chromatography ($CHCl_3$–MeOH 37:3) of the first fraction gave 17 mg of chrysartemin B (**3**) [9, 10]. Repurification of the second fraction by CC (petrol–EtOAc 3:2) gave 8 mg of quercetagetin 3,6,7-trimethyl ether identified by mp and spectroscopic properties [11, 12]. Frs 16 and 17 were combined and rechromatographed (CC, $CHCl_3$–MeOH 49:1) to give impure chrysartemin A (**2**) which was further purified by radial chromatography (petrol–EtOAc 1:1) to give 12 mg of pure **2** [13].

REFERENCES

1. Tsankova, E., Kempe, U. J., Norin, T. and Ognyanov, I. (1981) *Phytochemistry* **20**, 1436.
2. Herz, W. and Högenauer, G. (1962) *J. Org. Chem.* **27**, 905.
3. Herz, W. and Ueda, K. (1961) *J. Am. Chem. Soc.* **83**, 1139.
4. Lee, K., Simpson, R. F. and Geissman, T. A. (1969) *Phytochemistry* **8**, 1515.
5. Romo, J., Romo de Vivar, A. Teviño, R., Joseph-Nathan, J. and Diaz, E. (1970) *Phytochemistry* **3**, 1615.
6. Farkas, L., Nogradi, M., Sudarsanam, V. and Herz, W. (1966) *J. Org. Chem.* **31**, 3228.
7. Herz, W. and De Groote, R. (1977) *Phytochemistry* **16**, 1307.
8. Saleh, A. A., Cordell, G. A. and Farnsworth (1976) *J. Nat. Prod.* **29**, 456.
9. Osawa, T., Taylor, D., Suzuki, A. and Tamura, S. (1977) *Tetrahedron Letters*. 1169.
10. Ohno, N., Gershenzon, J., Roane, C. and Mabry, T. J. (1980) *Phytochemistry* **19**, 103.
11. Ghisalberti, E. L., Jeffreys, P. R. and Stacey, C. I. (1967) *Aust. J. Chem.* **20**, 1049.
12. Rodriguez, E., Carman, N. J., Van der Velde, G., McReynolds, J. H. and Mabry, T. J. (1972) *Phytochemistry* **11**, 3509.
13. Kelsey, R. G., Safizadeh, F., Campbell, J. A., Craig, A. C., Campana, C. F. and Craig, R. E. R. (1983) *J. Org. Chem.* **48**, 125.