1745 (γ-lactone), 1695 (conj. ester), 1650 (double bond); EIMS (probe) *m/z* (rel. int.): 362 $[M]^+$ (2.6), 262 $[M-A]^+$ (41.1), 244 $[M-A-H_2O]^+$ (12.5), 200 $[M-A-CO_2]^+$ (10.6), 83 $[A']^+$ (100), 55 $[A'']^+$ (39.8); ^{13}C NMR (50.32 MHz, $CDCl_3$, TMS as internal standard): 76.8 *d* (C-1), 31.2 *t* (C-2), 33.7 *t* (C-3), 142.3 (C-4), 55.3 *d* (C-5), 78.6 *d* (C-6), 157.1 *s* (C-7), 65.5 *d* (C-8), 41.4 *t* (C-9), 41.1 *s* (C-10), 128.1 *s* (C-11), 172.4 *s* (C-12), 56.9 *t* (C-13), 12.2 *q* (C-14), 110.8 *t* (C-15), 168.2 *s* (C-1'), 128.2 *s* (C-2'), 140.0 *d* (C-3'), 14.8 *q* (C-2'-Me), 13.0 *q* (C-3'-Me). (Calc. for $C_{20}H_{26}O_6$: 362.1693. Found: MS 362.1675.)

Trichomatolide A diacetate (**6**). Acetylation of 10 mg **5** in pyridine–Ac_2O for 20 hr, followed by usual work-up, gave the diacetate (**6**), $C_{24}H_{32}O_8$, gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1735 (acetate, ester), 1720 (conj. ester), 1655 (double bond); EIMS (probe) *m/z* (rel. int.): 446 $[M]^+$ (4), 386 $[M-HOAc]^+$ (4), 304 $[M-A-C_2H_2O]^+$ (4.0), 286 $[M-A-HOAc]^+$ (4.3), 244 $[M-HOAc-A-C_2H_2O]^+$ (21.5), 226 $[M-2HOAc-A]^+$ (35.3), 211 $[M-HOAc-A-Me]^+$ (17.1), 83 $[A']^+$ (100), 55 $[A'']^+$ (28.4), 43 $[Ac]^+$ (43.4).

Acknowledgement—We thank Helga D. Fischer for technical assistance.

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Phytochemistry, Vol. 23, No. 4, pp. 912–913, 1984.
Printed in Great Britain.

0031-9422/84 $3.00 + 0.00

INTEGRIFOLIN, A GUAIANOLIDE FROM *ANDRYALA INTEGRIFOLIA**

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(*Revised received* 9 *June* 1983)

Key Word Index—*Andryala integrifolia*; Compositae; Lactuceae; sesquiterpene lactones; guaianolide; integrifolin.

Abstract—Integrifolin, the major constituent of *Andryala integrifolia*, has been isolated and characterized as 3β,8β-dihydroxy-4(15),10(14),11(13)-trien-(1αH), (5αH) guaian-6,12-olide (8-epi-desacylcynaropicrin).

INTRODUCTION

Only one species of the genus Andryala (tribe Lactuceae) has been investigated chemically [1, 2]. We have now initiated the study of the constituents of *A. integrifolia* L., a species found in mediterranean Europe [3]. The main constituent in this plant is a sesquiterpene lactone of the guaiane series, which has been named integrifolin (**1a**). In addition, the flavonoids luteolin [4] and apigenin [5] were isolated.

RESULTS AND DISCUSSION

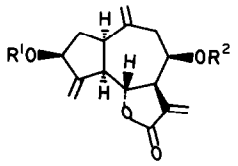
Integrifolin, mp 206–208°, $[\alpha]_D$ −17.5°, IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1750 (α,β-unsaturated-γ-lactone ring), 1655, 1630 (double bonds); MS *m/z*: 262.120 $[M]^+$, was obtained from the medium polar fractions. Its ^1H NMR data (Table 1) showed it was 3β,8β-dihydroxy-4(15), 10(14),11(13)-trien-(1α-H,5α-H)-guaian-6,12-olide (**1a**). The most characteristic features of this spectrum are signals of the α-methylene-γ-lactone grouping, two exocyclic methylenes (C-14 and C-15), and the C-6 lactonic

Table 1. ^1H NMR spectral data for integrifolin **1a** (ppm from TMS)

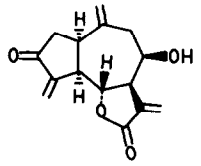
H-1	2.66	*ddd*	H-9	2.38	*dd*
H-2	1.52	*ddd*	H-9'	2.11	*dd*
H-2'	1.98	*ddd*	H-13	5.42	*d*
H-3	4.28	*dddd*	H-13'	6.14	*d*
H-5	2.53	*dd*	H-14	4.71	*br s*
H-6	4.32	*dd*	H-14'	4.83	*br s*
H-7	2.78	*dddd*	H-15	5.09	*br s*
H-8	4.08	*ddd*	H-15'	5.20	*br s*

J (Hz): 1,2 = 7.5; 1,2' = 9.5; 1,5 = 9.5; 2,2' = 13; 2,3 = 9; 2',3 = 7.5; 3,15 = 1.5; 5,6 = 10; 6,7 = 9; 7,8 = 3; 7,13' = 3.5; 7,13 = 3; 8,9 = 8, 9' = 6 and 9,9' = 13.5.

*Part 1 in the series "Structure and Chemistry of Secondary Metabolites from Compositae".



1a $R^1=R^2=H$
1b $R^1=H, R^2=Ac$
1c $R^1=Ac, R^2=H$
1d $R^1=R^2=Ac$



2

proton, which appeared as a typical triplet ($J_{5,6}$ = 10 Hz, $J_{6,7}$ = 9 Hz). The coupling of this proton indicated its *trans*-diaxial disposition to the hydrogens at C-5 and C-7. Chemical shifts and coupling constants of H-2, H-2′ and H-3 were similar to those of other 3β-hydroxyguaianolides [6]. The position at C-8 for the second hydroxy group of **1a** was selected on the following basis: (a) The signal of the proton on the carbon bearing this hydroxy group was clearly nonallylic, and (b) the product obtained by chromium trioxide oxidation showed a maximum at 263 nm [7, 8].

The β-orientation for the hydroxyl group at C-8 was deduced from the paramagnetic shift for H-13 [9], and the small coupling $J_{7,8}$. In spite of the difficulty in determining the stereochemistry of C-1 and C-5 [10], we presume integrifolin (**1a**) has that shown in the figure, based upon the preceding papers on lactones with similar relationships [11].

Integrifolin forms, under controlled conditions, the monoacetates **1b** and **1c**. The diacetate **1d** was obtained when integrifolin was acetylated in the usual manner. The foregoing assignations were confirmed by correlation of integrifolin with 8β-hydroxydehydrozaluzanin C (**2**) by selective oxidation of the allylic hydroxyl group with MnO_2 [12]. Compound **2** has been recently isolated from *A. pinnatifida* [2].

EXPERIMENTAL

Mps are uncorr. ^{1}H NMR 360 MHz, ($CDCl_3$–MeOD, 1:1). *A. integrifolia* was collected in May 1981, near Puerto Real (Cádiz). The air-dried whole plant (6 kg) was extracted with hot EtOH and the resulting extracts were separated by CC. Compound **1a** (0.110 g) was obtained by crystallization from EtOAc–petrol; mp 206–208°, $[\alpha]_D$ −17.5° (*c* 0.20), MS *m/z* (rel. int.): 262.120 $[M]^+$ (4) ($C_{15}H_{18}O_4$), 244 $[M-H_2O]^+$ (10), 226 $[M-2H_2O]^+$ (8), 198 $[226-CO]^+$ (7).

Chromium trioxide oxidation of **1a**. A soln of **1a** (6 mg) in Me_2CO (1.5 ml) was treated with 8 N CrO_3 at 5° until an orange colour persisted. After recovery as previously described [8] a colourless gum was obtained, λ_{max}^{EtOH} nm: 263.

Monoacetates **1b** *and* **1c**. Acetylation of **1a** with 4 ml Ac_2O–pyridine (3:1), 20 min, 0°, afforded **1b** and **1c** as colourless gums.

Compound **1b**. ^{1}H NMR (60 MHz, $CDCl_3$, TMS): δ6.30 (1H, *d*, *J* = 3.5 Hz, H-13′), 5.50 (1H, *d*, *J* = 3.5 Hz, H-13), 5.50 (1H, superimposed, H-8), 5.45 (1H, *br s*, H-15′), 5.35 (1H, *br s*, H-15), 5.12 (1H, *br s*, H-14′), 4.93 (1H, *br s*, H-14), 4.55 (1H, *t*, *J* = 10 Hz, H-6), 4.60 (1H, *m*, H-3), 2.03 (3H, *s*, C-8–OAc).

Compound **1c**. ^{1}H NMR (60 MHz, $CDCl_3$, TMS): δ6.35 (1H, *d*, *J* = 3.5 Hz, H-13′), 5.60 (1H, *d*, *J* = 3.5 Hz, H-13), 5.60 (1H, superimposed, H-3), 5.51 (1H, *br s*, H-15′), 5.30 (1H, *br s*, H-15), 5.09 (1H, *br s*, H-14′), 4.99 (1H, *br s*, H-14), 4.47 (1H, *t*, *J* = 10 Hz, H-6), 4.40 (1H, *m*, H-8), 2.11 (3H, *s*, C-3–OAc).

Diacetate **1d**. Acetylation of **1a** with 4 ml Ac_2O–pyridine (3:1), overnight, room temp, afforded **1d** (colourless gum); ^{1}H NMR (60 MHz, $CDCl_3$, TMS): δ6.25 (1H, *d*, *J* = 3.5 Hz, H-13′), 5.46 (4H, *m*, H-3, H-8, H-13, H-15′), 5.25 (1H, *br s*, H-15), 5.02 (1H, *br s*, H-14′), 4.88 (1H, *br s*, H-14), 4.46 (1H, *t*, *J* = 10 Hz, H-6), 2.11 (3H, *s*, C-3–OAc), 2.03 (3H, *s*, C-8–OAc).

8β-Hydroxydehydrozaluzanin C. A soln of **1a** (0.050 g) in CH_2Cl_2–EtOH (95:5) was treated with MnO_2 (0.750 g). The mixture, stirred for 2.5 hr, filtered through a dry column (silica gel) and concd yielded **2** (0.010 g), colourless gum, $[M]^+$ at *m/z* 260, ^{1}H NMR (60 MHz, $CDCl_3$, TMS): δ6.42 (1H, *d*, *J* = 3.5 Hz, H-13′), 6.27 (1H, *br s*, H-15′), 5.92 (1H, *br s*, H-15), 5.74 (1H, *d*, *J* = 3.5 Hz, H-13), 5.06 (1H, *br s*, H-14′), 4.75 (1H, *br s*, H-14), 4.50 (2H, *m*, H-6, H-8), 3.20 (2H, *m*, H-5, H-7), 3.10 (1H, *m*, H-1).

Acknowledgement—We thank Professor S. Silvestre Domingo, Departamento de Botanica, Facultad de Farmacia, Universidad de Sevilla (Spain) for the identification of the plant material.

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