

*dt*,  $J = 15.0$  and  $5.8$  Hz),  $4.18$  (2H, *d*,  $J = 5.8$  Hz),  $2.85$ – $2.80$  (1H, *m*),  $1.75$ – $1.50$  (2H, *m*),  $1.30$  (3H, *d*,  $J = 6.6$  Hz),  $0.99$  (3H, *t*,  $J = 7.3$  Hz)  $\nu_{\text{max}}^{\text{CHCl}_3}$   $3616$ ,  $1622$   $\text{cm}^{-1}$

**Asacoumarin A (2)** Colourless oil,  $[\alpha]_D + 7.0^\circ$  ( $\text{CHCl}_3$ ;  $c$  0.7).  $\nu_{\text{max}}^{\text{CHCl}_3}$   $3616$ ,  $3448$ ,  $1728$ ,  $1614$   $\text{cm}^{-1}$ .  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$   $161.9$  (s),  $161.2$  (s),  $155.8$  (s),  $143.4$  (d),  $139.7$  (s),  $138.5$  (s),  $134.8$  (s),  $128.7$  (d),  $128.4$  (d),  $121.8$  (d),  $119.8$  (d),  $113.1$  (d),  $112.9$  (d),  $112.5$  (s),  $101.5$  (d),  $76.6$  (d),  $66.1$  (d),  $65.2$  (t),  $47.3$  (t),  $34.0$  (t),  $25.8$  (q),  $17.9$  (q),  $17.1$  (q),  $14.0$  (q).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$   $7.64$  (1H, *d*,  $J = 9.5$  Hz, 4'-H),  $7.36$  (1H, *d*,  $J = 8.4$  Hz, 5'-H),  $6.83$  (1H, *dd*,  $J = 8.4$  and  $2.6$  Hz, 6'-H),  $6.80$  (1H, *d*,  $J = 2.6$  Hz, 8'-H),  $6.24$  (1H, *d*,  $J = 9.5$  Hz, 3'-H),  $5.57$  (1H, *t*,  $J = 6.2$  Hz, 11-H),  $5.44$  (1H, *d*,  $J = 8.4$  Hz, 7-H),  $5.07$  (1H, *t*,  $J = 7.0$  Hz, 3-H),  $4.58$  (3H, *m*, 8-H and 12-H<sub>2</sub>),  $3.99$  (1H, *t*,  $J = 6.7$  Hz, 5-H),  $1.82$ ,  $1.71$ ,  $1.70$ ,  $1.63$  (each 3H, *s*,  $4 \times \text{Me}$ ). MS  $m/z$   $329$ ,  $162$ ,  $69$

**Diacetate of 2.** Colourless oil  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$   $7.63$  (1H, *d*,  $J = 9.5$  Hz),  $7.36$  (1H, *d*,  $J = 8.5$  Hz),  $6.82$  (1H, *dd*,  $J = 2.5$  and  $8.5$  Hz),  $6.79$  (1H, *d*,  $J = 2.5$  Hz),  $6.24$  (1H, *d*,  $J = 9.5$  Hz),  $5.68$  (1H, *dt*,  $J = 8.5$  and  $5.9$  Hz),  $5.48$  (1H, *t*,  $J = 6.2$  Hz),  $5.36$  (1H, *d*,  $J = 8.5$  Hz),  $5.07$  (1H, *t*,  $J = 6.5$  Hz),  $4.98$  (1H, *t*,  $J = 7.0$  Hz),  $4.56$  (2H, *d*,  $J = 6.2$  Hz),  $2.44$ – $2.20$  (4H, *m*),  $2.04$ ,  $1.99$  (each 3H, *s*,  $2 \times \text{MeCO}$ ),  $1.79$ ,  $1.74$ ,  $1.67$ ,  $1.60$  (each 3H, *s*,  $4 \times \text{Me}$ ).

**Asacoumarin B (3).** Colourless amorphous powder,  $[\alpha]_D - 13.3^\circ$  ( $\text{CHCl}_3$ ,  $c$  0.4)  $\nu_{\text{max}}^{\text{CHCl}_3}$   $3700$ ,  $1728$ ,  $1712$ ,  $1616$   $\text{cm}^{-1}$ .  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$   $180.1$  (s),  $162.9$  (s),  $161.4$  (s),  $155.9$  (s),  $143.5$  (d),  $129.6$  (s),  $128.6$  (d),  $126.2$  (s),  $113.1$  (d),  $112.8$  (d),  $112.3$  (s),  $101.2$  (d),  $71.7$  (t),  $42.7$  (d),  $40.8$  (s),  $34.9$  (d),  $32.1$  (t),  $31.9$  (t),  $24.5$  (t),  $22.4$  (q),  $22.1$  (t),  $20.2$  (q)  $\times 2$ ,  $16.0$  (q).  $^1\text{H}$  NMR  $\delta$   $7.63$  (1H, *d*,  $J = 9.5$  Hz),  $7.34$  (1H, *d*,  $J = 8.8$  Hz),  $6.82$  (1H, *dd*,  $J = 8.8$  and  $2.5$  Hz),  $6.75$  (1H, *d*,  $J = 2.5$  Hz),  $6.24$  (1H, *d*,  $J = 9.5$  Hz),  $3.88$  (1H, *d*, A part of AB,  $J = 8.1$  Hz),  $3.70$  (1H, *d*, B part AB,  $J = 8.1$  Hz),

$2.95$  (1H, *dd*,  $J = 5.5$  and  $11.0$  Hz),  $2.51$  (1H, *br d*,  $J = 13.9$  Hz),  $2.21$  (2H, *m*),  $1.90$  (4H, *m*),  $1.62$  (3H, *s*),  $1.61$  (1H, *d*, A part of AB,  $J = 13.1$  Hz),  $1.45$  (3H, *s*),  $1.20$  (1H, *dd*, B part of AB,  $J = 13.1$  and  $4.5$  Hz),  $1.15$  (3H, *s*),  $0.92$  (3H, *d*,  $J = 7.0$  Hz).

**Ozonolysis of 3** Into the MeOH (5.0 ml) soln of compound 3 (70 mg) was blown dry  $\text{O}_3$  at  $-72^\circ$  until the colour changed to pale violet. After the reaction, the excess  $\text{O}_3$  was blown out with air and small amount of  $\text{Me}_2\text{S}$  was added and stirred for 1 day at room temp., and evapd the solvent. The residue was purified by chromatography over a silica gel (*n*-hexane–AcOEt = 2:1) to afford two products, compound 4 (27 mg) and compound 5 (15 mg).

**Compound 4.** Colourless amorphous powder,  $^1\text{H}$  NMR  $\delta$   $7.64$  (1H, *d*,  $J = 9.5$  Hz),  $7.38$  (1H, *d*,  $J = 8.5$  Hz),  $6.84$  (1H, *dd*,  $J = 8.5$  and  $2.2$  Hz),  $6.81$  (1H, *d*,  $J = 2.2$  Hz),  $6.26$  (1H, *d*,  $J = 9.5$  Hz),  $3.88$  (1H, *d*, A part of AB,  $J = 9.0$  Hz),  $3.82$  (1H, *d*, B part of AB,  $J = 9.0$  Hz),  $1.35$ ,  $1.25$  (each 3H, *s*),  $0.96$  (3H, *d*,  $J = 7.0$  Hz)

**Compound 5** Colourless amorphous powder  $^1\text{H}$  NMR  $\delta$   $11.5$  (1H, *s*),  $9.72$  (1H, *s*),  $7.43$  (1H, *d*,  $J = 8.6$  Hz),  $6.54$  (1H, *dd*,  $J = 8.6$  and  $2.2$  Hz),  $6.42$  (1H, *d*,  $J = 2.2$  Hz),  $3.88$  (1H, *d*, A part of AB,  $J = 9.0$  Hz),  $3.81$  (1H, *d*, B part of AB,  $J = 9.0$  Hz),  $1.34$ ,  $1.23$  (each 3H, *s*),  $0.94$  (3H, *d*,  $J = 7.2$  Hz).

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## SESQUITERPENE LACTONES FROM *INULA HELENIUM*

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**Key Word Index**—*Inula helenium*, Compositae; 11(13)-dehydroeriolin; 2 $\alpha$ -hydroxyalantolactone; 4 $\alpha$ ,5 $\alpha$ -epoxy-10 $\alpha$ ,14-H-inuviscolide; carabrone.

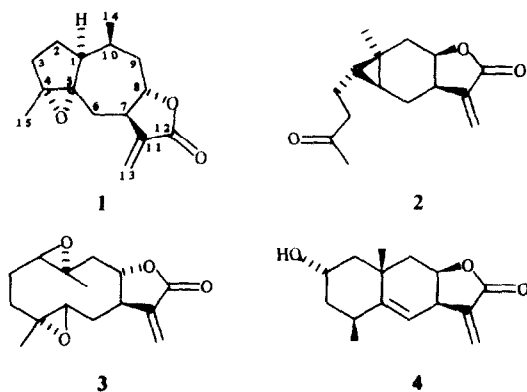
**Abstract**—The isolation of 11(13)-dehydroeriolin [a germacranolide also known as 11(13)-dehydroivaxillin], 2 $\alpha$ -hydroxyalantolactone, 4 $\alpha$ ,5 $\alpha$ -epoxy-10 $\alpha$ ,14-H-inuviscolide (the major component) and carabrone from the aerial parts of *Inula helenium* is reported. The first two lactones were isolated for the first time from this plant.

## INTRODUCTION

Extensive chemotaxonomic studies of *Inula* species [1], all grown from seeds originating from botanical gardens, revealed a variety of sesquiterpene lactones in *Inula helenium* (i.e. eudesmanolides, germacranolides, guaianolides and their 4,5-*seco*-analogues and one member of the pseudoguaianolide group). The main lactone constituents

in roots were eudesmanolides (alantolactone and isoalantolactone) whereas in the aerial parts, which contained a much smaller overall quantity of lactones, germacranolides were the major lactones together with smaller amounts of eudesmanolides.

An investigation of the chemical constituents of the aerial parts of *Inula helenium*, collected during flowering from the locality near Belgrade, is reported in this paper.



### RESULTS AND DISCUSSION

A silica gel column chromatography (using benzene-diethyl ether as eluent) of a chloroform extract of dried powdered aerial parts of *Inula helenium* afforded four  $\gamma$ -lactones (1–4), each belonging to a different skeletal type. Whereas lactones 1 and 2 have been previously isolated from *I. helenium* [1], a crystalline diepoxygermacranolide 3, named 11(13)-dehydroeriolin [2, 3] or 11(13)-dehydrovaxillin [4], and eudesmanolide 4 (i.e. 2 $\alpha$ -hydroxy alantolactone) have not been found in this plant before. Lactone 3 has been isolated from *Schkuhria* species [2] and also from *Carpesium abrotanoides* [4]. The antibacterial properties of 3 have been reported [4]. The IR and  $^1\text{H}$  NMR spectra of 3 from *I. helenium* were superimposable to the spectra of the same compound from the sources quoted above. The related monoepoxygermacranolides, such as 4 $\beta$ ,5 $\alpha$ -epoxy-4,5-*cis*-inunolide and 1 $\beta$ ,10 $\alpha$ -epoxy-1,10-*H-cis*-inunolide, previously isolated from *I. helenium* [1], have not been detected in this extract. Lactone 4, a colourless oil, exhibited the spectral data ( $^1\text{H}$  NMR, IR and MS) identical to those reported for 2 $\alpha$ -hydroxyalantolactone, originating from *Inula royleana* [1]. The  $^1\text{H}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ ) spectral data of the major lactone 1, assigned by means of 2D NMR techniques (such as  $^{13}\text{C}$ - $^1\text{H}$  HETCOR,  $^1\text{H}$  COSY and NOESY), were almost identical to those measured at 270 MHz for 4 $\alpha$ ,5 $\alpha$ -epoxy-10 $\alpha$ ,14-*H*-inviscolide, a minor lactone constituent of the aerial parts of the previously studied *I. helenium* [1]. The original spectral assignment [1] concerning protons attached to C-2 and C-3 in 1 should be partially changed. Thus, the previous assignment of a signal at  $\delta$ 0.85 as 3 $\alpha$ -H should be altered to 2 $\beta$ -H, whereas 3 $\alpha$ -H gave rise to the signal at  $\sim$ 1.7 (overlapped with a signal of the 2 $\alpha$ -H).  $^{13}\text{C}$  NMR chemical shifts of lactone 1, assigned by means of  $^{13}\text{C}$ - $^1\text{H}$  HETCOR, are presented in the Experimental.

The remaining lactone 2 was identified as carabrone by identity of its  $^1\text{H}$  NMR spectrum with that presented for this compound [5].

### EXPERIMENTAL

**Plant material.** *Inula helenium* L. (specimen No 150785, Institute of Chemistry, Faculty of Science, Belgrade) was collected in summer 1985, near Boleč (ca 10 km south-east from Belgrade), Yugoslavia.

**Isolation procedure.** A crude  $\text{CHCl}_3$  extract (22 g) obtained from powdered air-dried aerial parts of plant (2 kg) using the usual procedure [5], was chromatographed on a silica gel column. The elution was started with  $\text{C}_6\text{H}_6$  and the polarity of the eluent was gradually increased by addition of  $\text{Et}_2\text{O}$ . The lactones were eluted in the following order (the ratio of  $\text{C}_6\text{H}_6$ - $\text{Et}_2\text{O}$  is given in parentheses) 1 (19/1), 2 (19/1), 3 (9/1) and 4 (22/3). Compounds 1 (1.4 g), 2 (67 mg) and 4 (112 mg) were isolated from the crude fractions by rechromatography using the same procedure as above. 11(13)-Dehydroeriolin (3) (75 mg) was isolated from the crude fraction by crystallization from MeOH; mp (uncorr.) 168°.

4 $\alpha$ ,5 $\alpha$ -Epoxy-10 $\alpha$ -14-*H*-inviscolide (1), isolated as a viscous colourless oil (turning to solid after some time) exhibited the following  $^{13}\text{C}$  NMR (100.6 MHz in  $\text{C}_6\text{D}_6$ ) resonances:  $\delta$ 47.1 (C-1), 28.7 (C-2), 32.4 (C-3), 68.0, 68.7 (C-4, C-5), 30.0 (C-6), 43.7 (C-7), 81.1 (C-8), 40.0 (C-9), 34.2 (C-10), 139.6 (C-11), 168.8 (C-12), 117.9 (C-13), 13.9 (C-14) and 14.9 (C-15).

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