

A FURTHER GUAIANOLIDE FROM *ARCTOTIS GRANDIS*\*

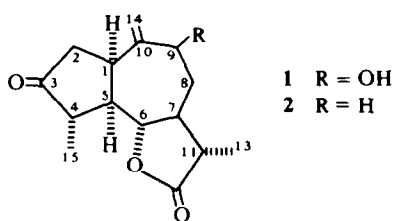
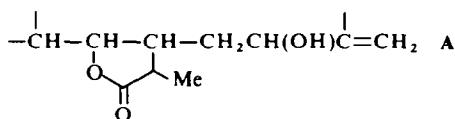
AHMED F. HALIM,† AHMED M. ZAGHLOUL† and FERDINAND BOHLMANN‡

† Faculty of Pharmacy, Mansoura University, Mansoura, Egypt; ‡ Institute for Organic Chemistry, Technical University Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, W. Germany

(Received 5 March 1980)

**Key Word Index** *Arctotis grandis*; Compositae; sesquiterpene lactone; new guaianolide.

In addition to simple polyacetylenes [1] and an unusual sesquiterpene [2], so far two guaianolides [3, 4] have been isolated from *Arctotis grandis* Thunb. We have now isolated a further sesquiterpene lactone,  $C_{15}H_{20}O_4$ , its  $^1H$  NMR data (see Table 1) clearly showing that it is the 6,12-lactone **1**, while the two other lactones are 8,12-lactones [2, 3]. Intensive decoupling experiments in  $CDCl_3$  and  $C_6D_6$ , as well as addition of  $Eu(fod)_3$ , clearly establish the configurations at all asymmetric centres. Irradiation at  $\delta$  3.95 ppm (in  $CDCl_3$ ) collapses the four-fold doublet at 2.05 to a three-fold one and changes the multiplet at 2.30, while irradiation at 2.05 collapses the three-fold doublet at 1.35 to a doublet of doublets and changes the multiplet at 2.54. The two corresponding protons are further coupled with the proton on the hydroxy group bearing carbon, which also show an allylic coupling with an exomethylene proton (5.44, *d*). The signal at 2.05 is further coupled with a multiplet at 2.30 (in  $C_6D_6$  1.52, *dq*,  $J = 11, 7$  Hz), which must be assigned to 11-H. These observations establish the sequence A:



Two double doublets at  $\delta$  2.61 and 2.48 obviously have to be assigned to a methylene group  $\alpha$  to a keto group: its presence also follows from the IR band at  $1730\text{ cm}^{-1}$ . These two hydrogens are coupled with a proton, which gives rise to a three-fold doublet at 2.97, as can be shown by irradiation at this frequency. Furthermore, the multiplet at 2.30 is changed, indicating that these two signals can only be assigned to 1- and 5-H. Irradiation of the 5-H signal

Table 1.  $^1H$  NMR data of **1** (270 MHz, TMS as internal standard)

	$CDCl_3$	$C_6D_6$	$\Delta$
1 $\alpha$ -H	2.97 <i>ddd</i>	1.97 <i>m</i>	0.53
2 $\alpha$ -H	2.61 <i>dd</i>	2.03 <i>dd</i> *	0.51
2 $\beta$ -H	2.48 <i>dd</i>	2.18 <i>dd</i> *	0.53
4 $\beta$ -H	2.22 <i>m</i>	1.96 <i>m</i>	0.50
5 $\alpha$ -H	2.30 <i>m</i>	1.33 <i>m</i>	0.43
5 $\beta$ -H	3.95 <i>dd</i>	2.99 <i>dd</i>	0.59
7 $\alpha$ -H	2.05 <i>dddd</i>	1.20 <i>dddd</i>	0.45
8 $\alpha$ -H	2.54 <i>m</i>	1.87 <i>ddd</i>	0.85
8 $\beta$ -H	1.35 <i>ddd</i>	0.67 <i>ddd</i>	0.98
9 $\alpha$ -H	4.23 <i>ddd</i>	3.36 <i>dd(br)</i>	1.28
11 $\beta$ -H	2.3 <i>m</i>	1.52 <i>dq</i>	0.46
13-H	1.25 <i>d</i>	1.00 <i>d</i>	0.25
14-H	5.44 <i>d</i>	5.08 <i>d</i>	1.03
14'-H	4.83 <i>s(br)</i>	4.43 <i>s(br)</i>	1.57
15-H	1.30 <i>d</i>	1.30 <i>d</i>	0.35
OH	1.81 <i>d</i>	0.95 <i>s(br)</i>	

\* Not first order.

$J$  (Hz): 1 $\alpha$ , 2 $\alpha$  = 8.5; 1 $\alpha$ , 2 $\beta$  = 2; 1 $\alpha$ , 5 $\alpha$  = 8.5; 2 $\alpha$ , 2 $\beta$  = 18.5; 4 $\beta$ , 5 $\alpha$  ~ 10; 4 $\beta$ , 15 = 7; 5 $\alpha$ , 6 $\beta$  = 10; 6 $\beta$ , 7 $\alpha$  = 9; 7 $\alpha$ , 8 $\alpha$  = 2; 7 $\alpha$ , 8 $\beta$  = 10; 7 $\alpha$ , 11 $\beta$  = 11; 8 $\alpha$ , 8 $\beta$  = 12; 8 $\alpha$ , 9 $\alpha$  = 5.5; 8 $\beta$ , 9 $\alpha$  = 11; 9 $\alpha$ , 14 = 1.5; 11 $\beta$ , 13 = 7; 9 $\alpha$ , OH = 3.

changes a multiplet at 1.33 (in  $C_6D_6$ ), which itself is coupled with the second methyl doublet. These experiments show that sequence A can be extended to **1**. The observed couplings clearly establish the given configurations. If we look at a corresponding Dreiding model,  $J_{4,5}$  and  $J_{7,11}$  are both large. This is only in agreement with an  $\alpha$ -orientation of the methyl groups. Also the  $\alpha$ -orientation of 1- and 5-H, the presence of a 6,12-trans-lactone and the  $\beta$ -orientation of the 8-OH-group follow from the observed couplings. In addition to kaurane derivatives, we have already isolated from *A. revoluta* Jacq. the corresponding 8-desoxy compound **2** [5] and further guaianolides with a 6,12-lactone ring, while *A. repens* Jacq. afforded the germacranolide parthenolide [5]. The chemotaxonomic situation is still therefore complicated.

\* Part 291 in the series "Naturally Occurring Terpene Derivatives". For Part 290 see Bohlmann, F., Abraham, W.-R., Robinson, H. and King, R. M. (1980) *Phytochemistry* **19**, 2475.

## EXPERIMENTAL

The air-dried plant material (2 kg) was extracted with  $CHCl_3$ . In addition to the earlier described guaianolides [3, 4], a further

one was isolated by column chromatography ( $\text{SiO}_2$ ,  $\text{C}_6\text{H}_6$ - $\text{Et}_2\text{O}$ , 3:1). Colourless crystals, mp 143–144°: IR  $\nu_{\text{max}}^{\text{KBr}}$   $\text{cm}^{-1}$ : 3470 (OH), 1788 ( $\gamma$ -lactone), 1730 ( $\text{C}=\text{O}$ ), 1645, 908 ( $\text{C}=\text{CH}_2$ ); MS (70 eV, direct inlet)  $m/e$  (rel. int.): 264.136 (3) ( $\text{M}^+$ ,  $\text{C}_{15}\text{H}_{20}\text{O}_4$ ), 246 (30) ( $\text{M} - \text{H}_2\text{O}$ ), 218 (16) ( $246 - \text{CO}$ ), 203 (15) ( $218 - \text{Me}$ ), 41 (100) ( $\text{C}_3\text{H}_5^+$ ).

$\lambda_{\text{max}}^{\text{Et}_2\text{O}}$  =  $\frac{589}{+50}$   $\frac{578}{+53}$   $\frac{546}{+62}$   $\frac{436 \text{ nm}}{+131}$  ( $c = 0.1$ ,  $\text{CHCl}_3$ ).

**Acknowledgement**— We thank the Deutsche Forschungsgemeinschaft for financial support.

# REFERENCES

1. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*. Academic Press, London and New York.
2. Bohlmann, F. and Le Van, N. (1978) *Phytochemistry* **17**, 1666.
3. Samek, Z., Holub, M., Drozd, B. and Grabarczyk, H. (1977) *Collect. Czech. Chem. Commun.* **42**, 2217.
4. Halim, A. and Zaghloul, A. (1980) *Planta Medica* (in press).
5. Bohlmann, F. and Le Van, N. (1977) *Phytochemistry* **16**, 487.