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Phytochemistry, 1980, Vol. 19, pp. 1230–1232. © Pergamon Press Ltd. Printed in England. 0031-9422/80/0601-1230 $02.00/0

GERMACRANOLIDES FROM *ERLANGEA CORDIFOLIA**

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(*Revised received* 8 *October* 1979)

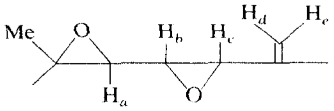
Key Word Index—*Erlangea cordifolia*; Compositae; Vernonieae; new sesquiterpene lactones; germacranolides; triepoxide.

INTRODUCTION

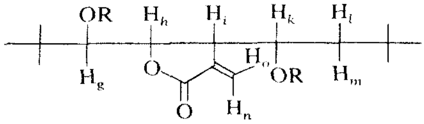
So far only 3 members of the large African genus *Erlangea* (Compositae, tribe Vernonieae) have been investigated. In addition to simple sesquiterpenes, one species contains two guaianolides [1], while in a second one germacranolide of the glaucolide type was found [2]. The third species only contains special 5-methylcoumarins [3] also present in *Bothriocline* [4] and *Ethulia* [5], both being African genera belonging to the Vernonieae. A germacranolide is reported in a patent application from *E. cordifolia* [6], however, no stereochemistry was given. We now report the isolation and structure elucidation of two highly oxygenated germacranolides from the same plant, which are named cordifene and 4,15-epoxy-4,15-dihydrocordifene.

RESULTS AND DISCUSSION

The polar fractions of the aerial parts of *E. cordifolia* afforded, as the main constituent, a crystalline compound with the molecular formula $C_{20}H_{24}O_7$. The ^1H NMR spectrum (Table 1) was very similar to the spectrum reported by Mugo [6]. The 270 MHz ^1H NMR spectrum displayed typical signals for a methylene lactone (*s*(*br*), 6.31 and 5.67) and those for an angelic acid ester (*qq*, 6.08; *dq*, 1.93 and *dq*, 1.79). Extensive double resonance experiments lead to the sequences *A* and *B*.



A



B

Irradiation of the signal for H_b (*dd*, 3.00) collapsed the doublet at 2.60 and the triplet doublet at 3.97 to singlets. Irradiation at 3.97 sharpened the signals of the methylene protons at 5.53 and 5.39. The coupling J_{H_a,H_b} was 7.5 Hz indicating a *cis* configuration of 1- and 2-H as in mikanolide [7, 8]. As the signal at 3.60 showed no further couplings and as there was a downfield methyl singlet at 1.58, the position of this group seems to be established. On irradiation of H_h (*d*(*br*), 4.38), a doublet at 4.12 H_g changes to a singlet, while irradiation of H_i sharpened the broadened singlets at 6.31 and 5.67 (13-H), and the *ddd* 5.11 became a *dd*. This clearly showed that the signal at 2.92 must be assigned to 7-H. Further irradiation of H_k (*ddd*, 5.11) collapsed the two double-doublets at 2.57 and 1.34 to doublets. These results are only in agreement with part *B*. However, the relative positions of the oxygen functions remained to be elucidated. On acetylation a monoacetate was obtained. In the ^1H NMR spectrum (Table 1) the signal

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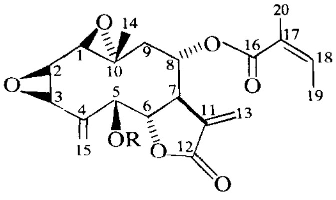
*Part 267 in the series: "Naturally Occurring Terpene Derivatives". For Part 266 see: Balbaa, S. I., Halim, A. F., Halaweish, F. T. and Bohlmann, F. *Phytochemistry* **19**, (in press).

Table 1. ^1H NMR data of compounds **1**, **2** and **5** (270 MHz, TMS as internal standard)

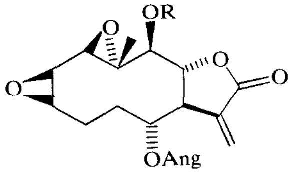
	1	Δ*	2	5
1-H	2.60 *d*	0.44	2.60 *d*	2.63 *d*
2-H	3.00 *dd*	0.37	3.05 *dd*	3.06 *dd*
3-H	3.97 *dt*	0.29	3.80 *d*(*br*)	3.83 *d*(*br*)
5α-H	4.12 *d*	0.25	5.39 *d*	3.23 *d*(*br*)
6β-H	4.38 *d*	0.31	4.46 *d*	4.53 *d*
7α-H	2.92 *d*(*br*)	0.21	2.95 *d*(*br*)	2.93 *d*(*br*)
8β-H	5.11 *ddd*	0.22	5.10 *ddd*	5.14 *ddd*
9α-H	1.34 *dd*	0.24	1.34 *dd*	1.43 *dd*
9β-H	2.57 *dd*	0.18	2.59 *dd*	2.63 *dd*
13-H	5.67 *s*(*br*)	0.10	5.70 *s*(*br*)	5.67 *s*(*br*)
13'-H	6.31 *s*(*br*)	0.14	6.37 *s*(*br*)	6.30 *s*(*br*)
15-H	5.29 *s*(*br*)	0.12	5.44 *s*(*br*)	3.29 *d*
15'-H	5.53 *s*(*br*)	0.24	5.63 *s*(*br*)	2.73 *d*(*br*)
14-H	1.58 *s*	0.16	1.60 *s*	1.64 *s*
18-H	6.08 *qq*	0.04	6.09 *qq*	6.11 *qq*
19-H	1.93 *dq*	0.04	1.93 *dq*	1.94 *dq*
20-H	1.79 *dq*	0.04	1.78 *dq*	1.80 *dq*
—OH	3.15 *s*(*br*)	0.22	—	3.14 *s*(*br*)
OAc	—	—	2.16 *s*	—

*Δ values after addition of Eu(fod)$_3$.

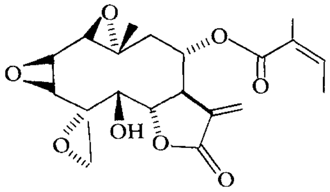
J (Hz): 1,2 = 7.5; 2,3 = 4.5; 3,15 ~ 1; 5,6 = 9.5; 7,8 = 10; 7,13 ~ 1; 8,9α = 12; 8,9β = 4; 9α,9β = 12.5; 18,19 = 7.5; 18,20 = 19,20 = 1.5; bei **5**: 15,15' = 5; 15',6 ~ 1.



1 R = H
2 R = Ac



3 R = H
4 R = Ac



5

for H_8 was shifted downfield. This indicated that we were dealing with a germacranolide. However, the stereochemistry and the relative position of the oxygen function still was not clear. It was obvious from the NMR data that the couplings $J_{6,7}$ and $J_{7,8}$ must be very small. Inspection of Dreiding-models showed that we were most probably dealing with a 6,12-*trans*-fused lactone in a conformation with C-14 and C-15 above the plane. The other observed couplings would be in agreement with **1**. However, the second possibility would be **3**. Considering the position of the signal for proton at the OH-bearing carbon, an allylic position as in **1** seemed to be more probable. Furthermore, the observed shifts on acetylation indicated this position as there was a pronounced shift of the signals of the methylene protons (15-H). All efforts to transform the alcohol to the corresponding ketone were unsuccessful. MnO_2 as well as pyridine chlorochromate gave no identifiable products. The stereochemistry at C-5, C-6 and C-8 followed from the observed couplings, while that at C-10 remained uncertain. We have assumed this configuration by analogy to similar lactones. All data therefore were in good agreement with the proposed structure **1**. Also the ^{13}C NMR data (Table 2) supported this assumption. The assignments of most of the signals were easy. However, some may be interchangeable. The unusual positions of the signal of C-8 is probably due to the shielding effect of the C-10 methyl, which support the configuration at C-10.

A second slightly more polar lactone, molecular formula $C_{20}H_{24}O_8$, showed a very similar ^1H NMR spectrum to **1**. The main difference was the absence of the vinylic proton signals for 15-H. They were replaced by a doublet at 3.29 and a broadened doublet at 2.73. The last signal showed a *W*-coupling with 5-H. The positions of these signals and the coupling constant indicated the presence of an epoxide of **1**. Though the configuration of this new group could not be established, the NMR data were in good agreement with the α-epoxide **5**. The observed shift of the signal for 6-H if compared with that in **1** again showed that the general structure **1** should be favoured, since it could not be explained by an epoxide of **3**. Therefore, most probably the second lactone was 4,15-epoxy-4,15-dihydrocoidifene (**5**).

The isolation of **1** and **5** from an *Erlangea* species again shows that highly oxygenated sesquiterpene lactones are characteristic for this genus. However, these compounds are also present in the large genus *Vernonia*. The chemotaxonomic situation in this tribe is

Table 2. ^{13}C NMR chemical shifts of compound **1** ($CDCl_3$)

C-1	52.4 *d**	C-11	134.0 *s*
C-2	54.2 *d**	C-12	167.8 *s*
C-3	62.4 *d*	C-13	127.1 *t*
C-4	139.5 *s*	C-14	118.6 *t*
C-5	80.6 *d*	C-15	17.8 *q*
C-6	77.8 *d*	C-16	166.0 *s*
C-7	47.9 *d*	C-17	127.0 *s*
C-8	67.9 *d*	C-18	140.0 *d*
C-9	45.4 *t*	C-19	15.8 *q*
C-10	55.2 *s*	C-20	20.1 *q*

*Possibly interchangeable.

still not very clear, but as pointed out by Jones [9] the systematic situation is also confused. Perhaps further chemical investigations may be helpful.

EXPERIMENTAL

IR: $CHCl_3$; ^1H NMR: 270 MHz, TMS as int. standard; MS: 70 eV; optical rotation: $CHCl_3$. The air-dried plant material (29 g aerial parts) was extracted with Et_2O at room temp. Saturated hydrocarbons were removed by treating with MeOH. The resulting extract was first separated by CC (Si gel, act. grade II). With Et_2O **1** and **5** were eluted, which could be separated by repeated TLC (Si gel GF 254) (Et_2O–petrol, 7:3) yielding *ca* 30 mg **1** and 15 mg **5**.

Cordifene (**1**). Colourless crystals from Et_2O–petrol, mp 183°. IR $\lambda_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1780 (γ-lactone), 1720 ($C{=}CCO_2R$); MS *m/e* (rel. int.): 376 (M^+ 0.6%) $C_{20}H_{24}O_4$); 361 ($-{}^{\cdot}Me$, 0.3); 358 ($-H_2O$, 1); 276 ($-C_4H_7CO_2H$, 2); 83 ($C_4H_7CO^+$, 100); 55 (83 − CO, 70).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436}{-127.1 \; -133.9 \; -154.8 \; -274.2} (c = 0.31).$$

5 mg **1** in 0.5 ml Ac_2O was heated for 30 min at 70°. After evapn the residue was purified by TLC (Et_2O–petrol, 7:3) yielding 3 mg of **2**, colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1800 (lactone), 1760, 1230 (OAc), 1730 ($C{=}CCO_2R$), MS (CI, isobutane *m/e* (rel. int.): M + 1 −; 391 (−CO, 100); 377 (−ketene, 49); 289 ($-{}^{\cdot}CHO$, $C_4H_7CO_2H$, 30); 229 (289 − HOAc, 17). Oxidation of **1** with MnO_2 or pyridine chlorochromate led to degradation of the lactone. Definite products could not be isolated.

4,15-*Epoxy*-4,15-*dihydrocordifene* (**5**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1780 (lactone), 1720 ($C{=}CCO_2R$); ^1H NMR see Table 1.

Acknowledgement—A. R. thanks the Ministry of Culture and Higher Education of Iran for financial support.

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