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SPHAEROCEPHALIN, A GERMACRANOLIDE ISOLATED FROM *VIGUIERA SPHAEROCEPHALA**

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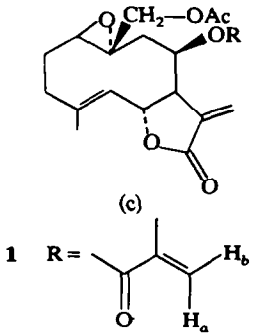
INTRODUCTION

In the course of our phytochemical investigations of different genera of the Compositae family found distributed throughout Mexico, we undertook the study of *Viguiera sphaerocephala* (DC.) Hemsl. A new germacranolide to which we propose the name sphaerocephalin (**1**) was isolated from the flowering aerial part of the plant.



RESULTS AND DISCUSSION

Sphaerocephalin (**1**) $C_{21}H_{26}O_7$, mp 223–225°; $[\alpha]_D^{20}$ + 50°. Common structural features with the previously isolated germacranes from *Viguiera* species [1–7] were evident from the spectroscopic data. The IR (1775 cm^{-1}) and UV (λ_{max} 214 nm, ε 13 435) spectra indicated the presence of a conjugated exocyclic methylene γ-lactone ring; the ^1H NMR spectrum exhibited the characteristic two doublets at δ 6.21 and 5.50 (1H each, J_{7-13} = 3.5 Hz, $J_{7-13'}$ = 3 Hz) of the methylene and a double doublet in 5.08 assigned to the H-6 proton under the lactone closure (J_{5-6} = 10, J_{6-7} = 9). The broad doublet at 5.72 corresponded to H-8 and the other one at 5.43 (J_{5-6} = 10 Hz) to H-5. The spectrum also showed four signals of an AB pattern (δ_A = 4.04, δ_B = 3.84, J_{AB} = 11.5 Hz) corresponding to the C-14 methylene protons.

The upfield region of the ^1H NMR spectrum of sphaerocephalin (**1**), exhibited a singlet at 1.98 (3H) of the methyl of an acetate group; a broad singlet at 1.86 (6H) which could be assigned to two vinylic methyl groups and, in addition, a broad doublet at 1.16 ppm ($J_{9-9'}$ = 15.5 Hz, J_{8-9} = 1 Hz) as part of an AMX pattern. The M part was localized at 3.19 as a double doublet ($J_{8-9'}$ = 6, $J_{9-9'}$ = 15.5 Hz, 1H), these signals were attributed to the C-9 methylene protons, the corresponding X part of the system appeared at 5.72. These considerations were corroborated by double and triple resonance experiments. On irradiation at 1.16 (H-9), the higher field doublet of the AB system at 3.84 was sharpened. Irradiation at 5.72 (H-8) collapsed the double doublet at 3.19 (H-9') into a doublet ($J_{9-9'}$ = 15.5 Hz) and it also resolved the broad doublet at 1.16 (H-9) and clearly simplified the signal at 3.0 (H-7). Simultaneous irradiation at 1.16 (H-9) and 5.72 (H-8) transformed the double doublets at

Table 1. ^1H NMR chemical shifts of sphaerocephalin (**1**)*

H	δ	Multiplicity	J(Hz)
H-1	2.86	*dd*	J_{1-2} = 2.5 J_{1-2} = 11.5
H-2	~2.30	*m*	
H-3	~2.30	*m*	
H-5	5.43	*br, d*	J_{5-6} = 10 J_{15-5} ~ 1
H-6	5.08	*dd*	J_{6-7} = 9
H-7	3.00	*m*	J_{7-8} ~ 1
H-8	5.72	*br, d*	J_{8-9} ~ 1 $J_{8-9'}$ = 6
H-9†	1.16	*br, d*	$J_{9-9'}$ = 15.5
H-9'	3.19	*dd*	
H-13	6.21	*d*	J_{7-13} = 3.5
H-13'	5.50	*d*	$J_{7-13'}$ = 3
H-14	3.84	*br, d*	$J_{14-14'}$ = 11.5
H-14'	4.04	*d*	
H-15	1.86	*br, s*	
Ha	6.00	*m*	J_{a1} = 1.5
Hb	5.58	*m*	J_{a1} = 1.3
Me(c)	1.86	*br, s*	
OAc	1.98	*s*	

* Carried out at 100 MHz with $CDCl_3$ as solvent and TMS as reference.

† There is a J 4 σ between H-9 and one of the H-14 hydrogen atoms.

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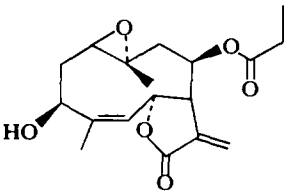
3.19 into a singlet, and the complex signal at 3.0 (H-7) was simplified and when this signal was decoupled, the doublets at 6.21 and 5.50 (H-13, H-13') collapsed into singlets, the broad doublet at 5.72 (H-8) was sharpened ($J_{8-9'} = 6$ Hz, $J_{8-9} = 1$ Hz). On irradiation at 1.86 (vinylic–methyl protons), the signal at 5.43 (H-5) appeared as a thin doublet and the multiple signals at 6.00 and 5.58 (vinylic proton of the methacrylic moiety) collapsed into two doublets ($J_{a1} = 1.5$ Hz, $J_{a1} = 1.3$ Hz). At this point only one oxygen atom from the molecular formula was missing and it was assigned to an epoxide ring based upon the presence in the ^{1}H NMR spectrum of sphaerocephalin of a double doublet centred at 2.86 ppm ($J_{1-2} = 2.5$ Hz, $J_{1-2'} = 11.5$ Hz, 1H).

On the other hand, the MS base peak (*m/e* 69), followed in intensity by peaks at *m/e* 43 and 41 together with the ^{1}H NMR data, corroborated the presence of a methacrylic ester in sphaerocephalin.

The stereochemistry of sphaerocephalin was supported by the coupling constant values across the protons at positions C-5 to C-8 ($J_{5-6} = 10$ Hz, $J_{6-7} = 9$ Hz, $J_{7-8} = 1$ Hz). In this case, the geometry of the double bond is *trans* [8] in contrast to the *cis* geometry of this double bond in erioflorin isolated from the same plant. The γ-lactone was also *trans*-fused and the metacrylic ester was β as indicated by the J_{7-8} value.

The observed coupling between H-1 with H-2α (11.5 Hz) and H-2β (2.5 Hz) is only possible with a dihedral angle of 180° in the former and 60° in the latter case. Similarly, one of the CH_2-14 protons must have a W or M arrangement with the 9α-proton to generate the observed 4 σ interaction. The difference in chemical shift between H-9α and H-9β (2.03 ppm) is indicative of a diamagnetic shielding of the epoxide ring to H-9α. All these features are evident from a Dreiding model of **1**.



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Erioflorin (**2**) previously isolated from *Eriophylum confertum* [9], was also obtained from *Viguiera sphaerocephala* and identified by comparison with an authentic sample.

EXPERIMENTAL

Viguiera sphaerocephala (DC.) Hemsl. was collected in September in Cacahuamilpa, State of Guerrero, Mexico. The dried stems, leaves and flowers (700 g) were milled and extracted 3× with hot MeOH (200 ml each time); the MeOH extracts were collected and concd, H_2O was added and the mixture extracted with hexane until a faint colour was observed in the hexane fraction. The *aq.* MeOH residue was extracted 3× with C_6H_6 (300 ml each time), the solvent was evapd and a deep green syrup (16 g) was obtained. Treatment of the residue with diisopropyl ether afforded 500 mg of sphaerocephalin (**1**); recrystallization from Me_2CO–diisopropyl ether yielded a pure compound mp 223–225°; $[\alpha]_D^{20}$ + 50°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775 (γ-lactone), 1749 (OAc), 1675 and 1649 (double bonds); UV λ_{max}^{EtOH} nm: 214 (ε 13 475). [Calc. for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71, O, 28.69. Found: C, 64.37; H, 6.70; O, 28.64%]. From the mother liquors, 25 mg of erioflorin (**2**) was obtained and was identified by direct comparison with an authentic sample.

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