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VIGUILENIN, A GERMACRANOLIDE FROM *VIGUIERA LINEARIS*

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Key Word Index—*Viguiera linearis*; Compositae; Heliantheae; new germacranolide; viguilenin.

Abstract—The new germacranolide, viguilenin, was isolated from *Viguiera linearis* and its structure was established by chemical and spectroscopic means.

INTRODUCTION

The species belonging to the genus *Viguiera* (Compositae, Heliantheae) elaborate sesquiterpene lactones with the same carbon skeleton as that found in the genus *Tithonia*. Both genera contain typical heliangolides [1] such as desacetylviguiestenin (**1**) found in *Viguiera stenoloba* and *V. pinnatilobata* [2]. Tagitinin E [3,4] isolated from *Tithonia tagitiflora* was found to be identical with desacetylviguiestenin.

The *Viguiera* species also elaborate germacranolides with an oxygen bridge between C-3 and C-10 such as budlein A (**2a**) [5] and viguiepinin (**2b**) [2]. This kind of compound has also been isolated from the genus *Tithonia* since tagitinin A (**3c**) [4], a constituent of *T. tagitiflora*, differs from **3a** only in the ester side chain.

Taking into consideration the above-mentioned facts we initiated a study of *Viguiera linearis*. The methanolic extract upon chromatography afforded a white crystalline compound which we named viguilenin.

RESULTS

Viguilenin (**3a**) $C_{20}H_{30}O_7$, mp 174–175°, $[\alpha]_D$ − 107° (MeOH), contained a γ-lactone function conjugated with an exocyclic methylene group as indicated by the IR band at 1760 cm^{-1}, the UV absorption at 220 nm, ε 8700, and the typical low-field doublets shown in its ^1H NMR spectrum. Compound **3a** also possessed an isovaleric ester side chain since its MS showed the base peak at *m/e* 85. Other important peaks were at *m/e* 382 ($M^+ - H_2O$) and 346 ($M^+ - 2H_2O$).

Viguilenin contained two hydroxyl groups (IR bands at 3400, 1150 and 1100 cm^{-1}), one of them was secondary since upon acetylation it yielded a monoacetate (**3b**) which still contained a free hydroxyl group. The ^1H NMR signal attributed to the proton at the carbon atom bearing the secondary OH group was shifted from δ 4.2 in **3a** to 5.0 in the acetate (**3b**). The seventh oxygen atom was present as an oxygen bridge between C-3 and C-10 which is frequently found in sesquiterpene lactones isolated from *Viguiera* species [2, 5]. This was proved by treatment of viguilenin with Jones' reagent at 0° which afforded dehydroviguilenin (**4**). The IR spectrum of **4** showed a band at 1740 cm^{-1} indicating the newly formed carbonyl group. The high frequency absorption of this carbonyl function suggested the presence of a tetrahydrofuranone moiety. Compound **4** still showed bands at 3400 and 1150 cm^{-1} in the IR spectrum for the tertiary hydroxyl group.

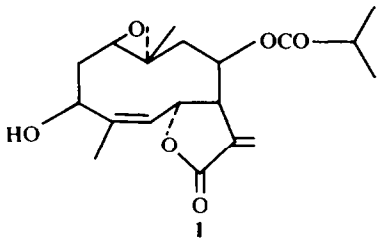
The presence of the carbonyl function at C-1 and the tertiary hydroxyl group at C-3 was established by the appearence of two AB doublets (δ 2.80, J = 15 Hz) in the ^1H NMR spectrum of **4**. This resonance represented the isolated distereotopic methylene group at C-2.

Confirmation of the relative position of the hydroxyl groups was obtained when viguilenin was treated with Jones' reagent at room temperature, thus affording the α,β-unsaturated ketone **5**. Similar behaviour was observed also in the hemiacetalic sesquiterpene lactone orizabin [6]. The IR spectrum of **5** showed strong bands at 1705 and 1605 cm^{-1} typical of this system. The vinylic proton at C-2 was shown in the ^1H NMR spectrum as a singlet (1 H) at δ 5.53 giving further support for the presence of a heterocyclic ring system of the type previously found in zexbrevin [7].

In viguilenin (**3a**) the lactone must be closed at position C-6 as observed in all sesquiterpene lactones previously isolated from the genus *Viguiera* [2, 5].

In the ^1H NMR spectra of compounds **3a**, **3b**, **4** and **5** the signal corresponding to H-7 had an abnormally low chemical shift (δ 4.02–4.1) due to the anisotropic effect of the ethereal oxygen atom upon the closely α-oriented H-7. This proximity requires a β-configuration for the C-3, C-10 oxygen bridge as previously pointed out [5, 7] and recently confirmed in woodhousin [8] and other hemiacetalic heliangolides with known stereochemistry [9].

Irradiation at the frequency of H-7 (δ 4.02) caused the H-13 *cis* (J = 2.7 Hz) and H-13 *trans* (J = 3.4 Hz) doublets to become singlets; in addition it eliminated the 6.5 Hz splitting from the H-6 multiplet (δ 4.54) and the 3 Hz coupling from H-8 absorption at δ 5.60. From the above discussion we consider that the structure and stereochemistry for viguilenin should be as depicted in formula **3a**. Additional proof of the structure and stereochemistry of viguilenin (**3a**) and dehydroviguilenin (**4**) was obtained



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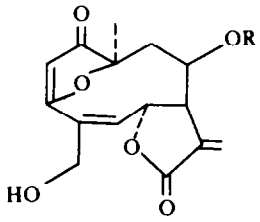
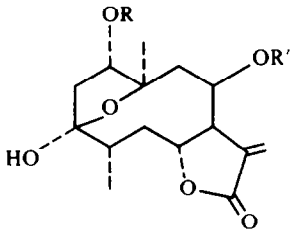
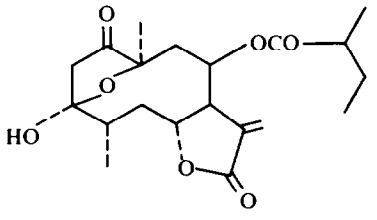


2a R = angeloyl
2b R = *iso*-butyroyl



3a R = H, R′ = COCH(Me)CH_2Me
3b R = Ac, R′ = COCH(Me)CH_2Me
3c R = H, R′ = $COCH(Me)_2$



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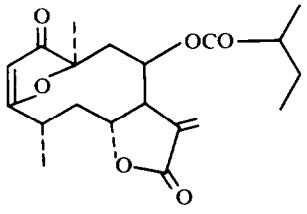

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Table 1. ^{13}C NMR spectra of viguilenin (**3a**) and dehydroviguilenin (**4**)

	3a	**4**
C-1	78.3 *d*	213.4 *s*
C-2	46.9 *t*	47.1 *t*
C-3	105.6 *s*	104.1 *s*
C-4	44.3 *d*	42.0 *d*
C-5	37.8 *t*	37.8 *t*
C-6	81.7 *d*	81.9 *d*
C-7	47.7 *d*	47.7 *d*
C-8	69.9 *d*	68.4 *d*
C-9	34.6 *t*	36.5 *t*
C-10	81.7 *s*	81.9 *s*
C-11	137.0 *s*	137.3 *s*
C-12	169.5 *s*	169.2 *s*
C-13	121.6 *t*	122.3 *t*
C-14	25.0 *q*	22.3 *q*
C-15	18.4 *q*	18.4 *q*
C-1′	175.0 *s*	175.4 *s*
C-2′	41.2 *d*	41.2 *d*
C-3′	26.5 *t*	26.5 *t*
C-4′	11.5 *q*	11.4 *q*
C-5′	16.5 *q*	16.5 *q*

Signal multiplicity obtained from single frequency off-centre decoupling. Assignment of signals confirmed by single frequency selective decoupling experiments.

from their ^{13}C NMR spectra (Table 1) which were identical to those of tagitinin A and its dehydroderivative [4] respectively.

EXPERIMENTAL

Mps are uncorr. IR spectra were recorded in $CHCl_3$ and UV in 95% EtOH unless otherwise stated. Chemical analyses were determined by Dr. Bernhard, Elbach, West Germany. Each sample for NMR investigation was dissolved in $CDCl_3$ containing 1% TMS. NMR spectra of viguilenin and dehydroviguilenin were recorded at 25.05 MHz (^{13}C) and 100 MHz (^1H).

Isolation of viguilenin (**3a**). Dried and ground material of *Viguiera linearis* (7 kg) was extracted 3 × with EtOH and worked up in the usual manner leaving an oily residue which was dissolved in hot C_6H_6 and chromatographed over Alcoa F-20 alumina. The fractions eluted with C_6H_6–EtOAc (3:1) were combined and evapd to dryness giving 7.3 g of crystalline viguilenin (**3a**); mp 168–169°, recrystallization from Et_2O *i*-PrOH raised the mp to 174–175°, $[\alpha]^{25}$ – 107° (MeOH); UV λ_{max}^{EtOH} nm 220 ε 8900; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1760, 1730, 1590 and 890; M^+ *m/e* 382 (Found: C, 62.89; H, 7.75; $C_{20}H_{30}O_7$ requires: C, 62.81; H, 7.91%).

Viguilenin acetate (**3b**). A soln of viguilenin (150 mg) in Ac_2O (1.5 ml) and Py (2 ml) was agitated for 4 hr at room temp. Work-up in the usual manner afforded viguilenin acetate (147 mg); mp 175–176°; $[\alpha]_D^{25}$ –97.86° (MeOH); UV λ_{max}^{EtOH} nm 222 ε 8700; M^+ *m/e* 424 (Found. C, 62.15, H, 7.48. $C_{22}H_{32}O_8$ requires: C, 62.25, H, 7.60%).

Dehydroviguilenin (**4**). To a soln of viguilenin (300 mg) in Me_2CO (25 ml) was added Jones' reagent (1.75 ml) at O°. Work-up in the usual manner afforded dehydroviguilenin (215 mg); mp

163–164°; $[\alpha]_D^{25}$ – 132° (MeOH); UV λ_{max}^{EtOH} nm:215 ε 8600; M^+ *m/e* 380 (Found: C, 63.10; H, 7.15; $C_{20}H_{28}O_7$ requires: C, 63.14; H, 7.42%).

Dehydroanhydroviguilenin (**5**). To a soln of viguilenin (300 mg) in Me_2CO (25 ml) was added at room temp. 1.75 ml of Jones' reagent. Work-up in the usual manner afforded a clear oil, dehydroanhydroviguilenin (50 mg); $[\alpha]_D^{25}$ + 63.3° (MeOH), UV λ_{max}^{EtOH} nm:215 (ε 8700) 258 (ε 15 800); M^+ *m/e* 364.

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