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DITERPENOIDS FROM *VIGUIERA INSIGNIS*

GUILLERMO DELGADO, ALFONSO ROMO DE VIVAR, ALFREDO ORTEGA, JORGE CÁRDENAS and ELMER O. SCHLEMPER†

Instituto de Química de la Universidad Nacional Autónoma de México,* Circuito Exterior, Ciudad Universitaria, Delegación de Coyoacán 04510, México, D. F., Mexico; †Department of Chemistry, University of Missouri-Columbia, Columbia, MO 65211, U.S.A.

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Key Word Index—*Viguiera insignis*; Compositae, Heliantheae, diterpene acids; stach-15-en-3α,12β-diol.

Abstract—The isolation of several known diterpenoids and one new diterpene diol from aerial parts of *Viguiera insignis* is reported.

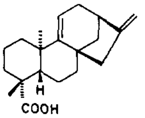
INTRODUCTION

Several *Viguiera* species have yielded sesquiterpene lactones [1–6], diterpenoids [7] or both [8]. In continuation of our chemical investigation on this and related genera, we now report the isolation and characterization of the diterpenes from *Viguiera insignis* Miranda.

RESULTS AND DISCUSSION

The less polar fractions of the chromatography of the chloroform extract of *V. insignis* contained several acidic compounds. This mixture of acids was methylated and separated into its components by Si gel chromatography. The components, in order of increasing polarity, were: *ent*-kaur-9(11)-16-dien-19-oic acid (**1**) [9], stach-15-en-19-oic acid (**3**) [8] and *ent*-kaur-16-en-19-oic acid (**2**) [10]. The identification of these compounds was carried out by physical constants, spectroscopic methods and direct comparison with authentic samples. The diterpene alcohol, stach-15-en-3α-ol (**4**) was isolated from these fractions and was identified by its spectroscopic characteristics [11].

The more polar fractions afforded two isomeric diols derived from stach-15-ene. One of these displayed physical and spectroscopic data identical with those reported for (+)-stach-15-en-3α,19-diol (**5**). This was converted into the known keto-aldehyde (**6**) and the ethylidene derivative (**7**) [12], thus confirming its structure. The second diol (**8**) $C_{20}H_{32}O_2$ (elemental analysis and mass spectrometry) also had features characteristic of a stachene derivative: a *cis* disubstituted double bond shown in ^{1}H NMR as an AB system (δ 5.70, 5.53; J = 5.7 Hz) which shifted upfield on epoxidation in **9** and **10**, and four quaternary methyl groups (see Table 1). The signals at δ 0.98 and 0.79 are in good agreement with a 4,4′-*gem*-dimethyl group adjacent to a 3-equatorial hydroxyl group [13] and the paramagnetic shift of Me-10 in the dihydro derivatives on hydrogenation in **11** and **12** indicates that the C-20 methyl group is present as such [14]. The presence of the second hydroxyl function on ring C was confirmed by the transformation of **8** to the derivatives **13–15**. The absence of a large coupling constant of the signal in ^{1}H NMR of the second carbinolic proton ($W_{1/2}$ = 7 Hz) suggests an axial orientation of the hydroxyl group. The experiments with Eu(fod)$_3$ *d* demonstrated that the C-17 methyl showed a remarkable downfield shift concordant only with a 12-β-ol (see Table 1). The structure and stereochemistry proposed for this diol was confirmed by X-ray diffraction and the stereostructure is depicted in Fig. 1. A complete list of refined coordinates is deposited at the Cambridge Crystallographic Data Centre.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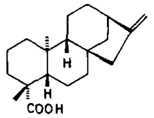
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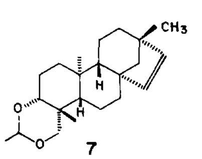
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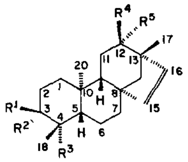

	R¹	R²	R³	R⁴	R⁵		
3	H	H	COOH	H	H		
4	H	OH	Me	H	H		
5	H	OH	CH_2OH	H	H		
6	=O		CH=O	H	H		
8	H	OH	Me	OH	H		
9	H	OH	Me	OH	H	15, 16	β-epoxy
10	H	OAc	Me	OAc	H	15, 16	β-epoxy
11	H	OH	Me	OH	H	15, 16	dihydro
12	H	OAc	Me	OAc	H	15, 16	dihydro
13	H	OAc	Me	OH	H		
14	H	OAc	Me	OAc	H		
15	=O		Me	=O			

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*Contribution No. 613.

Table 1 ^{1}H NMR data of compounds **8**–**15** (80 MHz, $CDCl_3$)*

	8	**8a**†	**8b**†	**8c**†	**9**	**10**	**11**	**12**	**13**	**14**	**15**
H-3	3.18 *dd* (10, 5.4)	4.05 *dd* (10, 5.4)	4.90 *dd* (10, 5.4)	5.72 *dd* (10, 5.4)	3.18 *dd* (10, 5.4)	4.46 *dd* (10, 5.4)	3.16 *dd* (10, 5.4)	4.45 *dd* (10, 5.4)	4.48 *dd* (10, 5.4)	4.48 *dd* (10, 5.4)	—
H-12	3.65 *m* ($W_{1/2}$ = 7)	4.30 *m* ($W_{1/2}$ = 7)	5.00 *m* ($W_{1/2}$ = 7)	5.68 *m* ($W_{1/2}$ = 7)	3.76 *m* ($W_{1/2}$ = 7)	4.95 *m* ($W_{1/2}$ = 7)	3.48 *m* ($W_{1/2}$ = 7)	4.67 *m* ($W_{1/2}$ = 7)	3.65 *m* ($W_{1/2}$ = 7)	4.83 *m* ($W_{1/2}$ = 7)	—
H-15	5.71 *d* (5.7)	5.90 *d* (5.7)	6.10 *d* (5.7)	6.25 *d* (5.7)	3.34 *d* (3.0)	3.37 *d*	—	—	5.72 *d* (5.7)	5.79 *d* (5.7)	6.10 *d* (5.7)
H-16	5.53 *d* (5.7)	5.70 *d* (5.7)	5.90 *d* (5.7)	6.05 *d* (5.7)	2.97 *d* (3.0)	3.04 *d* (3.0)	—	—	5.54 *d* (5.7)	5.55 *d* (5.7)	5.64 *d* (5.7)
H-17	1.05 *s*	1.39 *s*	1.7 *s*	2.10 *s*	1.10 *s*	1.00 *s*	1.02 *s*	0.93 *s*	1.05 *s*	0.95 *s*	1.11 *s*
H-18	0.99 *s*	1.39 *s*	1.70 *s*	2.10 *s*	1.00 *s*	0.88 *s*	0.99 *s*	0.86 *s*	0.86 *s*	0.86 *s*	1.11 *s*
H-19	0.79 *s*	1.22 *s*	1.65 *s*	2.04 *s*	0.81 *s*	0.88 *s*	0.79 *s*	0.86 *s*	0.86 *s*	0.86 *s*	1.06 *s*
H-20	0.69 *s*	0.93 *s*	1.18 *s*	1.40 *s*	0.91 *s*	0.93 *s*	0.91 *s*	0.93 *s*	0.71 *s*	0.71 *s*	0.95 *s*

*Coupling constants (Hz) in parentheses

†Addition of (**8a**) 0.105, (**8b**) 0.222 and (**8c**) 0.327 mol Eu $(fod)_3$ per mol substrate

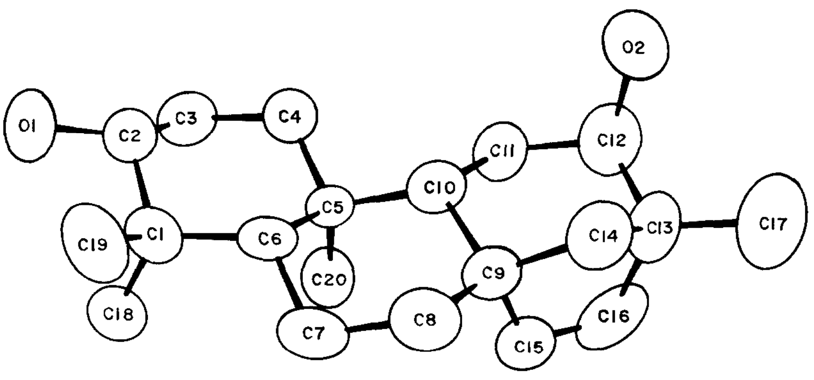

Fig 1

The results obtained are in agreement with the similarities observed in the terpenoids of some sections of *Viguiera* and *Helianthus* [15], which are placed in the same subtribe (Helianthineae) The diterpenoid acids are widespread in these genera

EXPERIMENTAL

Mps are uncorr

Aerial parts (3 1 kg) of *V insignis*, (collected on 19 November 1979, *ca* 16 km SSE of Izucar de Matamoros, Puebla, Hwy 190, voucher AOH 0022, MEXU 320489) were extracted with $CHCl_3$ affording 133 g residue This was fractionated over tonsil eluting with hexane–$CHCl_3$ (9 1) and with $CHCl_3$–EtOAc (8.2) yielding 72 3 and 42 1 g residue, respectively Part of the non-polar residue (20 g) was chromatographed on Si gel using hexane–EtOAc (9 1) The first fractions were combined and evaporated, leaving a residue (1 3 g) which was treated with CH_2N_2 The mixture containing the methyl esters was chromatographed on Si gel The fractions eluted with hexane–C_6H_6 (20 1) afforded **1**–**3** as methyl esters From the fractions eluted with hexane–EtOAc (9 2), was isolated **4**

The polar residue was chromatographed on Si gel and elution with $CHCl_3$–Me_2CO (20 1) gave (+)-stach-15-en-3α,19-diol (**5**) (1 21 g) Subsequent fractions eluted with $CHCl_3$–Me_2CO (4 1) gave 1 73 g (+)-stach-15-en-3α,12β-diol (**8**) Mp 204–205° $[\alpha]_D^{25}$ +8 73° (MeOH, *c* 0.126) IR ν_{max}^{nujol} cm^{-1} 3360, 1460, 1412, MS *m/z* (rel int) 304 $[M]^+$ (3 8), 286 (2 3) 110 (24 6), 119 (34 6), 107 (100), 105 (65 3), 93 (69 2), 91 (74 6), 81 (55 4), 43 (61 5). (Found. C, 78 71, H, 10 60, O, 10 53 $C_{20}H_{32}O_2$ requires C, 78 89, H, 10 59, O, 10 51 %) This substance was submitted to X-ray analysis, giving the following general parameters *a* (Å) = 12 221 (2), *b*(Å) = 15 166 (2), *c*(Å) = 19 471 (5) Space group $P2_12_12_1$ ρ_{calc} (mg/m^3) = 1 120 (1), wavelength, MoKα = 0 71073 Å

Derivatives of **5** 150 mg **5** in Me_2CO was treated with Jones reagent at 0° for 10 min Usual work-up gave **6** (130 mg), mp 108–109°, lit [12] 109–110° 180 mg **5** in Et_2O was shaken with paraldehyde (1 2 ml) and HCl (0 4 ml) to give, after usual work-up, 140 mg **7**, mp 120–121°, lit [12] 120–121°

Derivatives of **8** *Acetylation* 213 mg **8** was acetylated to give, after TLC (eluted with hexane-EtOAc, 4 1) the diacetate (**14**) (89 1 mg), mp 125–127°, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1731, 1370, 1250, MS *m/z* (rel int) 388 $[M]^+$ (4 7), 328 (25 1), 268 (4 2), 253 (6.2), 145 (23.9), 133 (92 3), 119 (44 1), 107 (38 2), 106 (50 9), 91 (57 7), 43 (100) (Found C, 73 95, H, 9 48, O, 16 70 $C_{24}H_{36}O_4$ requires C, 74 19, H, 9 34, O, 16 47 %) and the monoacetate (**13**) (57 5 mg), mp 137–139° IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600, 1730, 1350, 1250 MS *m/z* (rel int) 346 $[M]^+$ (1 0), 330 (5 1), 316 (0 5), 270 (20 1), 255 (12 5), 107 (25 0), 105 (26 4), 93 (34 6), 81 (25 0), 43 (100)

Epoxidation Treatment of **8** (110 mg) in CH_2Cl_2 with mcpba (100 mg) afforded 95 mg **9**, mp 194–196°, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3420, 1450, 1030, MS *m/z* (rel int) 320 $[M]^+$ (20 1), 302 (4 7), 287 (5 8), 250 (10 5), 249 (56 9), 161 (21 0), 159 (20 1), 147 (27.5), 145 (28 5), 135 (100), 123 (46 5), 107 (67 0), 105 (77 9), 93 (68 4), 91 (94 7), 79 (84 1)

Hydrogenation 139 mg **8** in MeOH was hydrogenated using Pd–C to afford 126 5 mg **11**, mp 198–199° $[\alpha]_D^{25}$ −24 53° (MeOH, *c* 0 163) IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600, 1448, 1380, 1362 MS *m/z* (rel. int.) 306 $[M]^+$ (13 9), 288 (21 7), 273 (20 0), 231 (18 0), 136 (73 2), 121 (82 9), 109 (54 0), 197 (100), 105 (65 1), 79 (78 9), 43 (40.0) (Found C, 78 67; H, 11 23, O, 10 20 $C_{20}H_{34}O_2$ requires C, 78 38, H, 11 18, O, 10 44 %)

Oxidation Jones oxidation of 121 1 mg **8** gave 74 3 mg **15** after TLC (eluted with $CHCl_3$–Me_2CO, 9 1), mp 92–94°, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1770, 1440, 1380, 1360 MS *m/z* (rel int) 300 $[M]^+$ (58 3), 272 (8.1), 148 (12 1), 145 (11 5), 119 (32 2), 107 (38 2), 106 (68 8), 105 (53 3), 93 (100), 91 (84 1), 79 (51 1), 77 (58 0), 67 (38 2)

Conversion of **14** *to* **10** 90 mg **14** in CH_2Cl_2 was oxidized with mcpba to give 70 mg **10**, mp 178–180°, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1740, 1460, 1372, 1250 MS *m/z* (rel int). 404 $[M]^+$ (2 6), 344 (4 8), 269 (5 5), 255 (6 0), 161 (7 6), 147 (10 0), 135 (26 4), 131 (10 9), 121 (19 3), 107 (15.7), 105 (20 1), 95 (23 7), 43 (100)

Conversion of **14** *to* **12**. Catalytic hydrogenation of **14** (95 1 mg) in EtOAc afforded **12** (87 3 mg), 135–136° IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1720, 1450, 1365, 1250 MS *m/z* (rel int.): 390 $[M]^+$ (0.5), 330 (9 3), 316 (1 8) 302 (1 0), 288 (1 0), 270 (43 4), 255 (47 9), 226 (20 0), 136 (30 1), 121 (39 8), 107 (40 0), 93 (35.2), 91 (35 0), 43 (100). (Found C, 73 56; H, 9 75, O, 16 30 $C_{24}H_{38}O_4$ requires C, 73 80, H, 9 81, O, 16 39 %)

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