chromatography gave epoxyparvinolide (**2**) (0.235 g, 0.008 %); mp 180–182° (petrol–C_6H_6); $[\alpha]_D + 37.59°$ ($CHCl_3$, *c* 0.47). (Found: C, 71.70; H, 8.79. Calc. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86 %) IR ν_{max}^{nujol} cm^{-1}: 2940, 1775, 1475, 1390, 1150, 985, 955, 880; ^1H NMR: δ1.12 (6H, *s*), 1.18 (3H, *s*), 1.62–2.37 (9H, *m*), 2.92 (1H, *dd*, $J = 2.5$ and 10 Hz), 4.43 (1H, *d*, $J = 10$ Hz), 5.28 (1H), 5.46 (1H). ^{13}C NMR (C-1–C-15 rsp.): δ47.74 (*d*), 21.60 (*t*), 24.21 (*t*), 58.76 (*s*), 64.06 (*d*), 28.55 (*t*), 38.39 (*t*), 143.03 (*s*), 88.78 (*d*), 180.45 (*s*), 43.55 (*s*), 18.07 (*q*)*, 17.34 (*q*)*, 22.75 (*q*)*, 123.50 (*t*) (*assignments may be interchanged). MS *m/z* (rel. int.): 250 $[M]^+$ (6.6), 235 (12), 222 (25), 207 (17.6), 206 (42), 194 (36), 192 (44), 177 (33), 163 (55.5), 152 (50.6), 125 (55.5), 69 (100).

REFERENCES

1. Patwardhan, S. A. and Gupta, A. S. (1981) *Phytochemistry* **20**, 1458.
2. Phadnis, A. P., Patwardhan, S. A., Gupta, A. S., Acharya, K. R., Tavale, S. S. and Guru Row, T. N. (1984) *J. Chem. Soc. Perkin Trans.* 1, 937.
3. Nanda, B., Patwardhan, S. A., Gupta, A. S., Acharya, K. R., Dhaneshwar, N. N., Tavale, S. S. and Guru Row, T. N. (1984) *J. Chem. Res.* (*S*) 394; (*M*) 3721.
4. Betancor, C., Freire, R., Gonzalez, A. G., Salazar, J. A., Pascard, C. and Prange, T. (1980) *Phytochemistry* **19**, 198.
5. Sims, J. J. and Pettus, J. A., Jr. (1976) *Phytochemistry* **15**, 1076.

Phytochemistry, Vol. 24, No. 11, pp. 2736–2738, 1985.
Printed in Great Britain.

0031-9422/85 $3.00 + 0.00

15-HYDROXY-ACETYLERIOFLORIN AND OTHER CONSTITUENTS FROM *VIGUIERA LINEARIS**

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(*Received* 25 *January* 1985)

Key Word Index—*Viguiera linearis*; Compositae; sesquiterpene lactones; diterpene carboxylic acid; 15-hydroxy-acetylerioflorin; heliangolides.

Abstract—Aerial parts of *Viguiera linearis* afforded 16α-hydroxy-*ent*-kauranoic acid, viguiestenin, leptocarpin, acetylleptocarpin, budlein B, clovandiol and the new heliangolide 15-hydroxy-acetylerioflorin.

INTRODUCTION

Several species of the large genus *Viguiera* (tribe Heliantheae, subtribe Helianthineae) have been investigated. Sesquiterpene lactones (germacrolides, heliangolides and furano-heliangolides) [1–8], diterpenes (*ent*-kaurenes [9, 10], modified *ent*-kaurenes [11], *ent*-beyerenes [12–14], *ent*-atisenes [12], *ent*-labdanes [2], and trachylobanes [15]), flavanol compounds [16] as well as cadinadienes [17] have been found as the major constituents of the species belonging to this genus. Here we report the isolation and structure determination of the new heliangolide 15-hydroxy-acetylerioflorin (**2**), and the previously identified compounds 16α-hydroxy-*ent*-kauranoic acid (**1**), viguiestenin (**3**), acetylleptocarpin (**4**), leptocarpin (**5**), budlein B (**6**), and clovandiol (**7**) from a collection of *Viguiera linearis*.

RESULTS AND DISCUSSION

Air-dried and ground leaves and stems of *V. linearis* were extracted with dichloromethane–methanol (1:1). Extensive chromatography of this extract gave seven crystalline substances (**1a**–**7**). The less polar fractions afforded an hydroxy-diterpene carboxylic acid which was identified by its physical constants and methyl ester derivative as 16α-hydroxy-*ent*-kauranoic acid (**1a**) [18, 19]. The previously unreported ^{13}C NMR data agree with the structure and are included in the Experimental.

The new sesquiterpene lactone, 15-hydroxy-acetylerioflorin (**2**), $[\alpha]_D^{25} = -69.4$ (MeOH, *c* 0.167) had molecular formula $C_{21}H_{26}O_8$ (mass spectrometry and elemental analysis) and its IR spectrum showed hydroxyl (3550 cm^{-1}), α-methylene-γ-lactone (1755, 1660 cm^{-1}) and ester (1725 cm^{-1}, broad) absorption bands. The ^1H NMR spectrum of **2** exhibited typical signals of an heliangolide with a 3β-OR substitution similar to other heliangolides isolated from this species (*vide infra*). The

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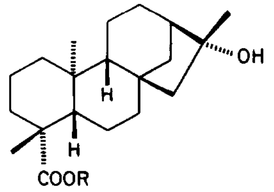
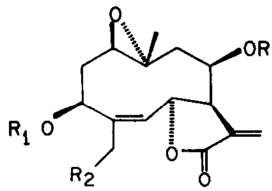
*Contribution No. 730 of the Instituto de Química de la Universidad Nacional Autónoma de México.



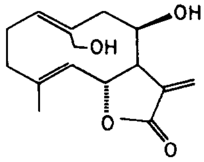
1a R = H

1b R = Me

TAC: OCONHCOCCl$_3$



	R_1	R_2	R_3
2	Ac	OH	Meacr
3	Ac	H	iBu
4	Ac	H	Ang
5	H	H	Ang
8	Ac	H	Meacr
9	Ac	TAC	Meacr



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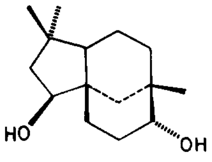

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presence of a 4(5)-*cis* double bond, a 6,12-*trans* lactone as well as an 8β-acyloxy residue vicinal to H-9 and H-9′ were determined by spin decoupling experiments (see Experimental). The ^{1}H NMR pattern resembles to that of acetylerioflorin (**8**), except for the signals of the C-15 methyl group. Instead, it showed a two-proton broad singlet which sharpened on addition of D_2O and shifted downfield ($\Delta\delta 0.63$) after *in situ* formation of the trichloroacetyl carbamate **9**, upon addition of TAI, indicating the presence of an hydroxymethylene group. Confirmation of the relative position of the 3β- and 8β-acyloxy groups was achieved by chemical correlation. Treatment of acetylerioflorin (**8**, a compound occurring in *V. eriophora* [1]), with selenium dioxide, gave a mixture of products from which **2** was identified. Therefore the new lactone is 15-hydroxy-acetylerioflorin (**2**).

The heliangolides viguiestenin (**3**), acetylleptocarpin (**4**), and leptocarpin (**5**) [16], as well as the cytotoxic germacrolide budlein B (**6**) and the tricyclic sesquiterpene clovandiol (**7**) [7, 20] were isolated from this species and their structures established by direct comparison with authentic samples.

These results along with the previous work on *V. linearis* [8] indicate that there is an infraspecific variation in the chemical constituents of this widespread species, since none of the secondary metabolites described in this work were reported from the previously studied collection. The investigation of other species of *Viguiera* and related genera is in progress.

EXPERIMENTAL

Mps are uncorr. Aerial parts of *Viguiera linearis* (Cav.) Sch. Bip. ex Hemsley were collected *ca* 4 km east of Nopala, Hidalgo, on August 19, 1982 (voucher deposited in the National Herbarium, Instituto de Biología de la Universidad Nacional Autónoma de México, G. Delgado, collection No. 1150). After drying, the plant material (1.7 kg) was extracted (×2) with CH_2Cl_2–MeOH (1:1) at room temp. The extract was taken to dryness under red. pres., affording 70 g residue as a syrup which was dissolved in a minimum amount of hexane–EtOAc (9:1) and applied to a silica gel column (1.35 kg) packed in the same solvent mixture. The column was eluted with a hexane–EtOAc gradient with increasing amounts of EtOAc. Several fractions eluted with hexane–EtOAc (4:1) were combined and the residue (7.9 g) was rechromatographed on a silica gel column (300 g) using hexane–EtOAc (9:1) as eluent. 78.9 mg of 16α-hydroxy-*ent*-kauranoic acid (**1a**), mp 275–279°, were obtained. The IR and ^{1}H NMR spectra of **1a** and **1b** (obtained by treatment with ethereal CH_2N_2, 100% yield) tallied exactly with those reported in the literature [18, 19]. The previously unreported ^{13}C NMR data of **1a** agrees with the structure: ^{13}C NMR ($CDCl_3$, 20 MHz): δ39.40 (*t*, C-1), 19.00 (*t*, C-2), 37.98 (*t*, C-3), 43.09 (*s*, C-4), 56.53 (*d*, C-5), 22.02 (*t*, C-6), 40.58 (*t*, C-7), 44.92 (*s*, C-8), 55.86 (*d*, C-9), 41.99 (*s*, C-10), 18.09 (*t*, C-11), 26.66 (*t*, C-12), 48.08 (*d*, C-13), 37.25 (*t*, C-14), 57.75 (*t*, C-15), 77.44 (*s*, C-16), 24.36 (*q*, C-17), 28.78 (*q*, C-18), 178.82 (*s*, C-19), 15.49 (*q*, C-20).

Several fractions eluted with hexane–EtOAc (1:1) from the main column were combined (11.4 g) and loaded on a silica gel column (350 g) which was then eluted with a CH_2Cl_2–Me_2CO gradient. From fractions eluted with the starting mixture (19:1), crystallized 45 mg of acetylleptocarpin (**4**), mp and mmp 216–218° [16], and 28 mg of viguiestenin (**3**), mp and mmp 207–209° [2]. From fractions eluted with CH_2Cl_2–Me_2CO (9:1), 33 mg of leptocarpin (**5**), mp 211–213° (lit. 192–195° [21], 213–215° [16]) were isolated. Fractions eluted with CH_2Cl_2–Me_2CO (4:1) were combined and purified by repeated prep. TLC, to give 12 mg of clovandiol (**7**), mp and mmp 152–153° [20].

Main column fractions eluted with hexane–EtOAc (3:7) contained principally **2** and **6**. These fractions were combined (15 g) and applied to a silica gel column (500 g) eluted with hexane–EtOAc (1:1). From this column, 180 mg of budlein B (**6**), mp and mmp 162–163° [3], were isolated. Several fractions which showed the same spot on TLC were combined and the residue (388 mg) rechromatographed on a column of silica gel (eluted with hexane–EtOAc, 4:5) affording a residue which was further purified by prep. TLC (hexane–EtOAc, 4:5, two developments). 17 mg of **2** were obtained, mp 244–248° (from *iso*-Pr_2O–Me_2CO, 1:1); $[\alpha]_D^{25}$ -69.4 (MeOH, *c* 0.167); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1755, 1725, 1660, 1600, 940, 890; ^1H NMR ($CDCl_3$, 80 MHz): δ6.37 (*d*, $J = 2.5$ Hz, H-13a), 6.13 (*s* (*br*), $W_{1/2} = 3$ Hz, H-18a), 6.11 (*dd*, $J = 2, 11$ Hz, H-6), 5.78 (*d*, $J = 2.5$ Hz, H-13b), 5.60 (*t* (*br*), $W_{1/2} = 3$ Hz, H-18b), 5.40 (2H, complex, H-5 and H-8), 5.22 (*dd*, $J = 2.5$ Hz, H-3), 4.20 (2H, *s* (*br*), H-15a, H-15b), 2.87 (*m*, H-7), 2.13 (3H, *s*, Ac), 1.89 (3H, *s* (*br*), 19-Me), 1.52 (3H, *s*, 14-Me). On treatment with TAI, all the signals remained unchanged, except H-15a and H-15b ($\Delta\delta = 0.63$) and H-5 ($\Delta\delta = 0.14$), which shifted downfield; EIMS (direct inlet, 75 eV) *m/z* (rel. int.): 406 $[M]^+$ (<1), 337 (25), 83 (70), 69 (100), 55 (85), 43 (79). (Found: C, 62.10; H, 6.66; O, 31.30%. $C_{21}H_{26}O_8$ requires: C, 62.06; H, 6.45; O, 31.49%.)

14 mg of **8** was treated with SeO_2 (10 mg) in dioxan (3 ml) and H_2O (1 ml) at room temp. for 15 hr. Usual work-up yielded a residue which was applied to a silica gel (1 g) column. By using hexane–EtOAc (1:1) as eluent, 8 mg **2** was isolated, identical by direct comparison with the natural product.

Acknowledgements—The authors thank M.Sc. José L. Villaseñor, National Herbarium, Instituto de Biología de la Universidad Nacional Autónoma de México, for the identification of plant material. This work was supported in part by the Consejo Nacional de Ciencia y Tecnología, México. Proyecto PCCBBNA-002049.

REFERENCES

1. Delgado, G., Romo de Vivar, A. and Herz, W. (1982) *Phytochemistry* **21**, 1305.
2. Romo de Vivar, A., Delgado, G., Guerrero, C., Reséndiz, J. and Ortega, A. (1978) *Rev. Latinoam. Quim.* **9**, 171.
3. Romo de Vivar, A., Guerrero, C., Díaz, E., Bratoeff, E. and Jiménez, L. (1976) *Phytochemistry* **15**, 525.
4. Guerrero, C., Santana, M. and Romo, J. (1976) *Rev. Latinoam. Quim.* **7**, 41.
5. Gershenzon, J., Liu, Y. L., Mabry, T. J., Korp, J. D. and Bernal, I. (1984) *Phytochemistry* **23**, 1281.
6. Liu, Y. L., Gershenzon, J. and Mabry, T. J. (1984) *Phytochemistry* **23**, 1967.
7. Delgado, G., Cárdenas, H., Peláez, G., Romo de Vivar, A. and Pereda-Miranda, R. (1984) *J. Nat. Prod.* **47**, 1042.
8. Romo de Vivar, A., Bratoeff, E., Ontiveros, E., Lankin, D. C. and Bhacca, N. S. (1980) *Phytochemistry* **19**, 1795.
9. Delgado, G., Romo de Vivar, A., Ortega, A., Cárdenas, J. and Schlemper, E. O. (1983) *Phytochemistry* **22**, 1227.
10. Delgado, G. and Romo de Vivar, A. (1984) *Chem. Letters* 1237.
11. Delgado, G., Alvarez, L. and Romo de Vivar, A. (1984) *Phytochemistry* **23**, 2674.
12. Delgado, G., Romo de Vivar, A., Cárdenas, J., Pereda-Miranda, R. and Huerta, E. (1984) *Phytochemistry* **23**, 2285.
13. Bohlmann, F., Zdero, C. and Mahanta, P. (1977) *Phytochemistry* **16**, 1073.
14. Bohlmann, F., Jakupovic, J., Ahmed, M., Grenz, M., Suding, H., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 113.
15. Bohlmann, F., Zdero, Ch., Schmeda-Hirschmann, G., Jakupovic, J., Castro, V., King, R. M. and Robinson, H. (1984) *Liebigs Ann. Chem.* 495.
16. Delgado, G., Alvarez, L. and Romo de Vivar, A. (1984) *Phytochemistry* **23**, 675.
17. Bohlmann, F., Gerke, T., Jakupovic, J., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1183.
18. Sebryakov, E. P., Kobrina, N. S., Simolin, A. V. and Kucherov, V. F. (1968) *Chem. Ind.* 770.
19. Krishnaswamy, N. R., Seshadri, T. R. and Vedanthan, T. N. C. (1970) *Indian J. Chem.* **8**, 375.
20. Gupta, S. and Dev, S. (1971) *Tetrahedron* **27**, 635.
21. Martínez, R., Ayamante, I. S., Núñez-Alarcón, J. A. and Romo de Vivar, A. (1979) *Phytochemistry* **18**, 1527.