Phytochemistry, Vol. 23, No. 3, pp. 675–678, 1984.
Printed in Great Britain.

0031–9422/84 $3.00 + 0.00

TERPENOIDS AND A FLAVAN-3-OL FROM *VIGUIERA QUINQUERADIATA*

GUILLERMO DELGADO, LAURA ALVAREZ and ALFONSO ROMO DE VIVAR

Instituto de Química de la Universidad Nacional Autónoma de México*, Circuito Exterior Ciudad Universitaria, Coyoacán 04510, México D. F.

(*Revised received* 9 *August* 1983)

Key Word Index—*Viguiera quinqueradiata*; Compositae; Heliantheae; sesquiterpene lactones; *ent*-kaurenoic acids; *trans*-flavan-3-ol.

Abstract—The isolation is reported of the new natural products from *Viguiera quinqueradiata*, acetylleptocarpin and (2*R*,3*S*)-4′-hydroxy-3′,5,7-tri-*O*-methyl-flavan-3-ol. The diterpenes 15α-angeloyloxy-*ent*-kaur-16-en-19-oic acid, 15α-tigloyloxy-*ent*-kaur-16-en-19-oic acid and the sesquiterpene lactones leptocarpin and budlein A were also found.

INTRODUCTION

In the course of our systematic chemical investigation of the large genus *Viguiera*, we previously reported the major constituents in *V. stenoloba*, *V. pinnatilobata* [1], *V. buddleiaeformis* [2], *V. linearis* [3], *V. eriophora*, *V. hemsleyana*, *V. schultzii* [4] and *V. insignis* [5]. Sesquiterpene lactones [germacrolides, heliangolides and 3(2H)-furanoheliangolides] and diterpenes (stachene and *ent*-kaurene type) have been found to be the major terpenoid constituents of *Viguiera*. In this paper we describe the structure determination of the constituents of *V. quinqueradiata* (Cav.) A. Gray, the new flavan-3-ol (**4**) and the new heliangolide acetylleptocarpin (**7**).

RESULTS AND DISCUSSION

A chloroform extract of aerial parts of *Viguiera quinqueradiata* was extensively chromatographed affording two diterpene carboxylic acids, a flavan-3-ol and three sesquiterpene lactones. The diterpene carboxylic acids were identified as 15α-angeloyloxy-*ent*-kaur-16-en-19-oic acid (**1**) and 15α-tigloyloxy-*ent*-kaur-16-en-19-oic acid (**2**) by comparison of the mp, IR and ^{1}H NMR data with those published [6]. Upon hydrolysis, both acids afforded the same alcohol (**3**) [7].

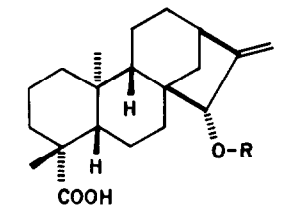
A minor constituent of *V. quinqueradiata* was the flavan-3-ol (**4**), $C_{18}H_{20}O_6$, mp 158–159°. Both the UV (204, 228, 278 nm) and the IR (3500, 1616, 1585 cm^{-1}) absorptions were typical for this type of compound [8]. The ^{1}H NMR spectrum showed an ABMX system with signals centred at δ 4.62, 4.05, 3.01 and 2.53 due to H-2, H-3, H-4a and H-4b respectively, thus confirming the flavan-3-ol nucleus. The coupling constant between H-2 and H-3 (8 Hz) indicates a *quasi-antiperiplanar* disposition between these protons. Therefore, the subtitution of the dihydropyran ring must be *trans*. The singlets at δ3.87 (3H), 3.78 (3H) and 3.73 (3H) indicated the presence of three methoxyl groups. An AB system centred at δ6.11 (*d*, 3 Hz) and 6.09 (*d*, 3 Hz) were assigned to H-6 and H-8 protons and the remaining protons of the C ring were observed at 6.80–7.00 with a typical pattern for a 3′-methoxyl and 4′-hydroxyl substitution [8]. The fragment at *m/z* 167 in the mass spectrum ($C_9H_{11}O_3$, 100%) indicated the dimethoxyl substitution of the B ring [9]. Methylation of **4** afforded (+)-catechin-5,7,3′,4′-tetramethyl ether (**5**), identified by its physical constants [10]. Therefore, the structure of the flavan-3-ol isolated from *V. quinqueradiata* should be repressented by (2*R*,3*S*)-4′-hydroxy-3′,5,7-tri-*O*-methyl-flavan-3-ol (**4**).

Leptocarpin (**6**), previously found in *Leptocarpha rivularis* [11] and *Calea hispida* [12], was isolated from this specimen and identified by direct comparison with an authentic sample. Acetylleptocarpin (**7**), $C_{22}H_{28}O_7$, mp 216–218°, now reported as a natural product, was identical with the acetylation product of leptocarpin (**6**). The ^{13}C NMR data of **6**, **7** and derivatives **10** and **11** (Table 1) are in agreement with the proposed structures. The previously unreported ^{13}C NMR spectrum of the heliangolides viguiestenin (**8**) and desacetylviguiestenin (**9**) [1] are included for comparison. The most polar sesquiterpene lactone isolated from this specimen was budlein A (**12**), previously found in several *Viguiera* [2, 4, 13], *Helianthus* [14] and *Calea* [15] species.

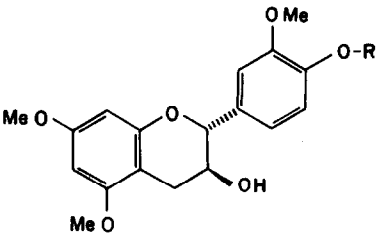
EXPERIMENTAL

Air dried and ground leaves (1.70 kg) of *Viguiera quinqueradiata* (Cav.) A. Gray (voucher on deposit in the National Herbarium MEXUARV 0022, Reg. No. 282551) were extracted with $CHCl_3$, affording 140.5 g syrup. This syrup (50 g) was chromatographed over a silica gel column (1.5 kg) which was eluted with a hexane–EtOAc gradient system. Fractions eluted with this mixture (7:3) giving a major spot on TLC were combined and evaporated. The residue (24 g) was rechromatographed on silica gel (720 g) using hexane–EtOAc (9:1) as constant eluent. From this column crystalline stigmasterol (50.3 mg) and an oily residue (2.1 g) with a major spot on TLC were obtained. This residue was further rechromatographed and gave 90.2 mg of 15α-tigloyloxy-*ent*-kaur-16-en-19-oic acid (**2**) mp 196–197° (lit: 198° [6]) and 70.5 mg of 15α-angeloyloxy-*ent*-kaur-16-en-19-oic acid (**1**) mp 189–190° (lit: 193–195° [6]). The hexane–EtOAc (7:3) fractions of the initial CC which showed the same spot on TLC were combined to yield 2.59 g residue which was further rechromatographed and afforded 72.2 mg of

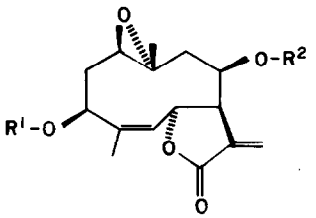
*Contribution No 638.



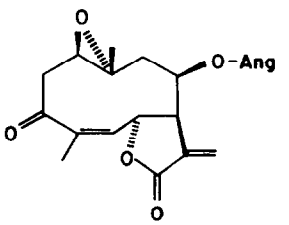
1 2 3
R Ang Tig H



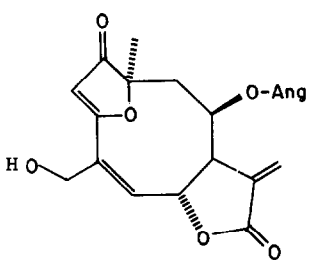
4 5
R H Me



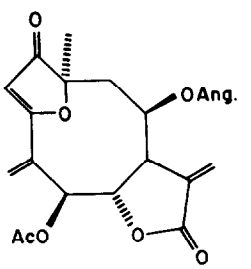
	6	7	8	9	10
R¹	H	Ac	Ac	H	Ac
R²	Ang	Ang	iBu	iBu	Epoxang.



11



12



13

acetylleptocarpin (7). Mp 216–218° (lit. 180–182° [11]). Succesive recrystallizations from *iso*-Pr_2O–$CHCl_3$ raised the mp to 219–220°. $[\alpha]_D^{25} = -112.8°$ (MeOH, *c* 0.125); UV λ_{max}^{MeOH} nm (log ε): 205 (4.09); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1764, 1733, 1722, 1670, 1648; ^1H NMR (80 MHz, $CDCl_3$): δ1.49 (3H, *s*, H-14), 1.80 (3H, *br s*, H-15), 1.90 (3H, *dt*, H-19), 2.10 (3H, *s*, Ac), 2.83 (1H, *dd*, J = 4, 10 Hz, H-1), 2.85 (1H, *m*, H-7), 5.10–5.40 (3H, *m*, H-3, H-5, H-8), 5.72 (1H, *d*, J = 2 Hz, H-13a), 6.08 (1H, *m*, H-18), 6.12 (1H, *dd*, J = 2, 11 Hz, H-6), 6.34 (1H, *d*, J = 2 Hz, H-13b); ^{13}C NMR (20 MHz, $CDCl_3$): Table 1; MS *m/z* (rel. int.): 404 $[M]^+$ (1.0), 386 (1.0), 261 (28.2), 95 (20.6), 83 (100), 55 (34.0), 43 (36). (Found: C, 65.23; H, 6.95; O, 27.60%. $C_{22}H_{28}O_7$ requires: C, 65.33; H, 6.98; O, 27.69%.) Some fractions of the initial CC, eluted with hexane–EtOAc (3:2) were combined yielding 1.79 g residue. This residue was purified on a silica gel column (50 g) using a $CHCl_3$–Me_2CO gradient elution system and gave 28.6 mg of leptocarpin (6). Mp 213–215° (lit. 192–195° [11]). Some fractions of this chromatography showed a constant red spot on TLC, and

Table 1. ^{13}C NMR spectral data of *Viguiera* constituents and derivatives (20 MHz, $CDCl_3$)

	6	7	8	9	10	11
C-1	60.74 *d*	60.35 *d*	60.24 *d*	60.67 *d*	60.21 *d*	57.73 *d*
C-2	32.68 *t*	30.62 *t*	30.68 *t*	30.71 *t*	30.73 *t*	43.08 *t*
C-3	72.45 *d*	73.04 *d*	73.04 *d*	72.38 *d*	72.99 *d*	203.82 *s*
C-4	141.65 *s*	138.26 *s*	138.31 *s*	141.72 *s*	138.62 *s*	142.26 *s*
C-5	126.67 *d*	126.32 *d*	126.27 *d*	126.58 *d*	126.13 *d*	125.44 *d*
C-6	74.17 *d*	74.55 *d*	74.47 *d*	74.16 *d*	74.13 *d*	75.18 *d*
C-7	48.68 *d*	48.66 *d*	48.61 *d*	48.55 *d*	48.46 *d*	49.19 *d*
C-8	75.91 *d*	75.67 *d*	75.66 *d*	75.70 *d*	75.47 *d*	75.32 *d*
C-9	43.84 *t*	43.72 *t*	44.00 *t*	44.06 *t*	44.25 *t*	43.14 *t*
C-10	58.66 *s*	58.30 *s*	58.26 *s*	58.66 *s*	58.09 *s*	57.73 *s*
C-11	137.66 *s*	137.23 *s*	137.16 *s*	137.47 *s*	137.01 *s*	136.74 *s*
C-12	169.50 *s*	169.15 *s*	169.13 *s*	169.55 *s*	169.01 *s*	168.54 *s*
C-13	124.54 *t*	124.73 *t*	124.77 *t*	124.71 *t*	124.97 *t*	125.04 *t*
C-14	20.31 *q*	20.23 *q*	21.05 *q*	20.04 *q*	21.06 *q*	20.23 *q*
C-15	22.94 *q*	22.95 *q*	22.95 *q*	22.99 *q*	22.95 *q*	18.50 *q*
C-16	166.51 *s*	166.09 *s*	175.41 *s*	175.92 *s*	168.43 *s*	166.22 *s*
C-17	127.67 *s*	126.67 *s*	34.46 *d*	34.26 *d*	59.33 *s*	126.77 *s*
C-18	139.98 *d*	140.86 *d*	18.66 *q*	18.60 *q*	60.08 *d*	140.69 *d*
C-19	15.66 *q*	15.77 *q*	18.89 *q*	18.85 *q*	13.21 *q*	15.72 *q*
C-20	15.71 *q*	19.35 *q*	169.13 *s*		19.02 *q*	19.48 *q*
C-21		169.15 *s*	19.69 *q*		169.12 *s*	
C-22		21.01 *q*			19.80 *q*	

were combined to give 155.6 mg of residue which was further purified by repeated prep. TLC, affording 18.5 mg of **4**, which crystallized from MeOH, mp 158–159°. $[\alpha]_D^{25} = -12.77°$ (MeOH, *c* 0.18); UV λ_{max}^{MeOH} nm (log ε): 204 (3.79), 228 (4.36), 278 (4.60); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1616, 1585, 1490, 1450; ^1H NMR (80 MHz, $CDCl_3$): δ 2.53 (1H, *dd*, *J* = 16, 10 Hz, H-4a), 3.01 (1H, *dd*, *J* = 16, 6 Hz, H-4b), 3.73 (3H, *s*, OMe), 3.78 (3H, *s*, OMe), 3.87 (3H, *s*, OMe), 4.05 (1H, *ddd*, *J* = 10, 8, 6 Hz, H-3), 4.62 (1H, *d*, *J* = 8 Hz, H-2), 5.62 (1H, *s*, OH), 6.09 (1H, *d*, *J* = 3 Hz, H-6), 6.11 (1H, *d*, *J* = 3 Hz, H-8), 6.87 (1H, *m*, H-2'), 6.93 (2H, *m*, H-5', H-6'); MS *m/z* (rel. int.): 332 $[M]^+$ (18), 301 (8.9), 167 (100), 137 (50.5). Some hexane–EtOAc (1:1) fractions of the initial CC were combined and concd affording crystals of budlein A (**12**), 989.9 mg, mp 103–104° (lit. 106–108° [2], 154–155° and 134–136° [14], identified by direct comparison.

Hydrolysis of **1**. Compound **1** (70.2 mg) was treated with 5% KOH–MeOH under reflux for 24 hr. Usual work-up afforded 36.9 mg of 15α-hydroxy-*ent*-kaur-16-en-19-oic acid (**3**), mp 229–231° (lit. 228–230° [7], 230–232° [16]).

Hydrolysis of **2**. Compound **2** (50.1 mg) was treated as described above furnishing 28.2 mg of **3**.

Methylation of **4**. A soln of **4** (5.3 mg) in MeOH was treated with excess ethereal CH_2N_2 at 5° for 24 hr. The crystalline material obtained from Et_2O upon evaporation was recrystallized to afford **5**, mp 142–144° (lit. 143–144°, [9], 144–146° [17]). $[\alpha]_D^{25} = -13.1°$ (CCl_4, *c* 0.11) (lit. $[\alpha]_D^{25} = -13.4°$ [9]).

Epoxidation of leptocarpin (**7**). Treatment of 30.1 mg of **7** with MCPBA in CH_2Cl_2 afforded after usual work up, 26.4 mg of **10**. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1720, 1675, 965; ^1H NMR (80 MHz, $CDCl_3$): δ 1.22 (3H, *d*, *J* = 7 Hz, H-19), 1.55 (3H, *s*, H-14), 2.14 (3H, *s*, Ac), 5.10–5.35 (3H, *m*, H-3, H-5 and H-8), 5.74 (1H, *d*, *J* = 2.5, H-13a), 6.12 (1H, *dd*, *J* = 11, 2 Hz, H-6), 6.33 (1H, *d*, *J* = 2.5, H-13b); ^{13}C NMR (20 MHz, $CDCl_3$): Table 1; MS *m/z* (rel. int.): 420 $[M]^+$ (1.0), 404 (9.1), 378 (22.1), 377 (20.2), 345 (60.6), 95 (40), 43 (100).

Oxidation of leptocarpin (**6**). Jones oxidation of 117 mg of **6** gave 71.4 mg of **11** after purification by TLC; mp 136–138° (lit. 135.5–137° [11]). ^{13}C NMR (20 MHz, $CDCl_3$): Table 1.

Acetylation of budlein A (**12**). To a soln of 229 mg of **12** in 1 ml pyridine was added 2 ml Ac_2O. The reaction mixture was kept for 18 hr at room temp. After usual work-up, 159.3 mg of **13** were obtained. Mp 165–166° (lit. 168–172° [13]) identical by direct comparison with an authentic sample.

Acknowledgement—We are grateful to Professor Arthur Cronquist, New York Botanical Garden for the identification of the plant material and interesting discussions on the taxonomy of *Viguiera*.

REFERENCES

1. Romo de Vivar, A., Delgado, G., Guerrero, C., Reséndiz, J. and Ortega, A. (1978) *Rev. Latinoam. Quim.* **9**, 171.
2. Romo de Vivar, A., Guerrero, C., Díaz, E., Bratoeff, E. and Jiménez, L. (1976) *Phytochemistry* **15**, 525.
3. Romo de Vivar, A., Bratoeff, E., Ontiveros, E., Lankin, D. C. and Bhacca, N. S. (1980) *Phytochemistry* **19**, 1795.
4. Delgado, G., Romo de Vivar, A. and Herz, W. (1982) *Phytochemistry* **21**, 1305.
5. Delgado, G., Romo de Vivar, A., Ortega, A., Cárdenas, J. and Schlemper, E. O. (1983) *Phytochemistry* **22**, 1227.
6. Esahak Ali, P. P., Ghosh, D. and Pakrashi, C. (1974) *J. Indian Chem. Soc.* **51**, 409.
7. Piozzi, F., Spiro, V., Passannanti, S. and Mondelli, R. (1968) *Gazz. Chim. Ital.* **98**, 907.
8. Mabry, T. J., Markham, K. R. and Thomas, M. B. (1970) *The Systematic Identification of Flavonoids*. Springer, New York.
9. Drewes, S. E. (1968) *J. Chem. Soc.* (*C*) 1140.
10. Birch, A. J., Clark-Lewis, J. W. and Robertson, A. V. (1957) *J. Chem. Soc.* 3586.

11. Martínez, R., Ayamante, I. S., Núñez-Alarcón, J. A. and Romo de Vivar, A. (1979) *Phytochemistry* **18**, 1527.
12. Bohlmann, F., Gupta, R. K., Jakupovic, J., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 2899.
13. Guerrero, C., Santana, M. and Romo, J. (1976) *Rev. Latinoam. Quim.* **7**, 41.
14. Ohno, N., Gershenzon, J., Neuman, P. and Mabry, T. J. (1981) *Phytochemistry* **20**, 2393.
15. Bohlmann, F., Gupta, R. K., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 2593.
16. Ohno, N. and Mabry, T. J. (1980) *Phytochemistry* **19**, 609.
17. Kiatgrajai, P., Wellons, J. D., Gollob, L. and White, J. D. (1982) *J. Org. Chem.* **47**, 2910.