Phytochemistry, Vol 23, No 11, pp 2674–2675, 1984
Printed in Great Britain

0031–9422/84 $3 00 + 0 00

15-OXO-ZOAPATLIN, A DITERPENE LACTONE FROM *VIGUIERA MACULATA*

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(*Received* 2 *February* 1984)

Key Word Index—*Viguiera maculata*, Compositae, Heliantheae, diterpenes, 15-oxo-zoapatlin

Abstract—The isolation of a new diterpene lactone and two known diterpenoid acids from the aerial parts of *Viguiera maculata* is reported

INTRODUCTION

Chemical examinations of the large genus *Viguiera* (Compositae, Heliantheae) have yielded diterpenes [1–3], sesquiterpene lactones [4–10] and flavonol compounds [11] We now report the isolation and structure determination of 15-oxo-zoapatlin (**1**), a new diterpene lactone found as a constituent of *Viguiera maculata* Blake This plant also contains the known diterpenoid acids, *ent*-kaur-16-en-19-oic (**2**) and 15α-hydroxy-*ent*-kaur-16-en-19-oic (**3**)

RESULTS AND DISCUSSION

Chromatographic separation of a chloroform extract of the aerial parts of *Viguiera maculata* afforded three diterpenoid compounds The two most abundant were identified as the known compounds *ent*-kaur-16-en-19-oic acid (**2**) [12] and 15α-hydroxy-*ent*-kaur-16-en-19-oic acid (**3**) [13] by their physical constants and direct comparison with authentic samples

The third diterpene, 15-oxo-zoapatlin (**1**) $C_{20}H_{26}O_3$, contained an α,β-unsaturated ketone (UV λ_{max} 233 nm, ε6083) conjugated with an exocyclic methylene group (^{1}H NMR δ5 95 *t*, *J* = 1 Hz, 5 20 *t*, *J* = 1 Hz) The ketone was located on a cyclopentane ring (IR 1718, 1639 cm^{-1}) These data clearly indicate the nature of the D ring of a tetracyclic diterpene Two methyl singlets at δ1 27 and 1 10 in the ^{1}H NMR spectrum suggested that this compound belonged to the kaurene or modified kaurene series Since a γ-lactone (IR 1755 cm^{-1}, ^{13}C NMR δ180 27 *s*) was closed to a quaternary carbon (^{13}C NMR δ87 64 *s*), this new substance was a modified *ent*-kauranoid with the C-10 methyl group shifted to C-9, similar to eupatalbin and eupatoralbin [14] It was therefore identified as the 15-oxo-derivative of zoapatlin (**4**) [15]

The ^{13}C NMR spectrum of 15-oxo-zoapatlin is in complete agreement with the proposed structure and the assignments were established by comparison with the spectra of various kauranoids [16] and closely related modified kauranoids [14, 17]

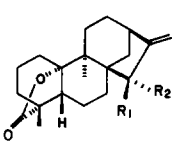
The fact that the new compound was indeed the 15-oxo-derivative of zoapatlin was confirmed by chemical correlation Zoapatlin (**4**), still available from earlier work, was transformed to **1** by treatment of **4** with SeO_2 yielding the 15α-hydroxy derivative **5**, which was treated with CrO_3–pyridine to afford 15-oxo-zoapatlin, identical in all respects with the natural product

Zoapatlin (**4**), first isolated from *Montanoa tomentosa* [15], was shown to be identical by direct comparison with the diterpene lactone tetrachyrin, isolated from *Tetrachyron orizabensis* var *websteri* and *Helianthus debilis* subsp *debilis* [17] Therefore the name tetrachyrin should be abandoned

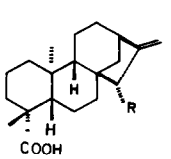
The results indicate a great similarity in chemical composition between *Viguiera* [1–11] and *Helianthus* [18–25] species since both genera of the subtribe Helianthineae elaborate closely related sesquiterpene lactones and diterpenoids

EXPERIMENTAL

$CHCl_3$ extraction of 960 g f the above ground parts of *Viguiera maculata* Blake (voucher on deposit in the National Herbarium of Mexico, Instituto de Biología de la UNAM, Reg No 282569), collected 125 km SSE Izúcar de Matamoros, Puebla, afforded 34 7 g of crude gum This was chromatographed over 1 2 kg of



1 R_1, R_2 = O
4 R_1 = R_2 = H
5 R_1 = H, R_2 = OH



2 R = H
3 R = OH

*Contribution No 670

silica gel using a hexane–EtOAc gradient elution system All the fractions were monitored by TLC Some fractions eluted with hexane–EtOAc (7 3), which showed the same spot on TLC, were combined to yield 1 9 g residue This was rechromatographed over silica gel (60 g) and elution with hexane–EtOAc (9 1) afforded crude 15-oxo-zoapatlin (**1**), recrystallization from EtOAc–*iso*-Pr_2O yielded 347 3 mg of **1**, mp 164–165°, $[\alpha]_D^{25}$ −74 7° ($CHCl_3$, *c* 0 123), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1755, 1715, 1690, 880; ^1H NMR ($CDCl_3$, 80 MHz) δ5 94 (*dd*, *J* = 1 Hz, H-17a), 5 20 (*dd*, *J* = 1 Hz, H-17b), 2 87 (*m*, 1H, H-13), 1 27 (*s*, 3H, C-18), 1 10 (*s*, 3H, C-20), ^{13}C NMR ($CDCl_3$, 20 MHz) δ210 39 (*s*, C-15), 180 27 (*s*, C-19), 149 20 (*s*, C-16), 114 92 (*t*, C-17), 87 64 (*s*, C-10), 52 09 (*s*, C-8), 52 00 (*d*, C-5), 47 51 (*s*, C-9), 43 64 (*s*, C-4), 39 15 (*t*, C-1), 37 62 (*d*, C-13), 35 50 (*t*, C-14), 31 08 (*t*, C-7), 30 19 (*t*, C-3), 29 64 (*t*, C-12), 25 71 (*t*, C-11), 20 12 (*t*, C-6), 18 54 (*q*, C-20), 18 24 (*t*, C-2), 17 06 (*q*, C-18), MS (direct inlet) 75 eV, *m/z* (rel int) 314 $[M]^+$ (86), 271 (100), 270 (56), 255 (39), 237 (18), 212 (34), 199 (22) (Found C, 76 28, H, 8 36, O, 15 28% $C_{20}H_{26}O_3$ requires C, 76 40, H, 8 34, O, 15 27%)

Subsequent fractions of the initial CC were combined affording 6 17 g residue, which was rechromatographed on silica gel (180 g) using hexane–EtOAc (9 1) as constant eluent From this column, were isolated 1 6287 g of *ent*-kaur-16-en-19 oic acid (**2**), mp 178–180°, IR, ^1H NMR, ^{13}C NMR and MS identical with authentic material [1, 17] From the fractions eluted with hexane–EtOAc (3 2) of the initial CC, were isolated 17 4 mg of 15α-hydroxy-*ent*-kaur-16-en-19-oic acid (**3**), mp 230–231° (lit 229–231° [11], 230–232° [20]), identical by direct comparison with an authentic sample

Oxidation of zoapatlin Compound **4** (75 mg) was treated with SeO_2 (15 mg) in dioxan (5 ml) and H_2O (1 5 ml) at room temp for 5 hr Usual work-up yielded a residue which was chromatographed on silica gel (1 g) using hexane–EtOAc (4 1) as eluent, 44 mg of 15α-hydroxyzoapatlin (**5**) were obtained Mp 169–171°, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3500, 1756, 1680, ^1H NMR ($CDCl_3$, 80 MHz) δ5 21 (*br s*, $W_{1/2}$ = 3 Hz, H-17a), 5 06 (*br s*, $W_{1/2}$ = 3 Hz, H-17b), 4 08 (*br s*, $W_{1/2}$ = 3 Hz, H-15), 2 55 (*m*, H-13), 1 19 (*s*, 3H, C-18), 1 08 (*s*, 3H, C-20), MS (direct inlet) 75 eV *m/z* (rel int) 316 $[M]^+$ (91), 274 (53), 220 (69), 147 (39), 105 (62), 91 (100), 79 (68), 55 (48) Compound **5** (34 mg) was treated with CrO_3 (50 mg) in pyridine (1 ml) at 0° for 12 hr followed by the usual work-up, to yield, after purification through a small silica gel column (0 5 g), 25 mg of **1**, IR, ^1H NMR, ^{13}C NMR and MS identical with the natural product isolated from *Viguiera maculata*

Acknowledgements—The authors thank Prof A Cronquist (New York Botanical Garden) for the identification of plant material, Dr F Walls (Instituto de Química de la Universidad Nacional Autónoma de México), for a generous gift of zoapatlin and Dr T J Mabry (University of Texas at Austin) for spectral data of zoapatlin This work was supported in part by the Consejo Nacional de Ciencia y Tecnología Mexico (Proyecto PCCBBNA-002049)

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