Phytochemistry, 1978, Vol. 17, pp. 955–956. © Pergamon Press Ltd Printed in England.

0031-9422/78/0501-0955 $02.00/0

TWO SESQUITERPENE LACTONES FROM *CENTAUREA CANARIENSIS**

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(*Revised received* 24 *November* 1977)

Key Word Index—*Centaurea canariensis*; Compositae; sesquiterpene lactones; aguerin A and B; cynaropicrin; deacylcynaropicrin; guaianolides.

Abstract—From the aerial part of *Centaurea canariensis* three sesquiterpene lactones were isolated: cynaropicrin, deacylcynaropicrin and aguerin A. The same species, grown from seed, yielded cynaropicrin, deacylcynaropicrin and aguerin B. The guaianolides aguerin A and B are reported for the first time. Aguerin B was subsequently found to be present in *Centaureana linifolia*, *C. canariensis* (var *subspinnata*) and *C. sventenii*.

INTRODUCTION

As part of our research into sesquiterpene lactones from the Compositae, we studied the composition of *Centaurea canariensis*, a plant endemic to the Canary Islands. Four sesquiterpene lactones were isolated from this plant, two of which were already known: cynaropicrin [1] and deacylcynaropicrin [2]; the other two were new guaianolides and were named aguerin A and B.

RESULTS AND DISCUSSION

Aguerin A (**1a**) was obtained as an oil: $C_{19}H_{24}O_5$; MS *m/e* 332 (M^+) $[\alpha]_D$ +89°; IR cm^{-1} 3470 (hydroxyl), 1760 (α-methylene-γ-lactone), 1720 (ester) and 1635 (methylene double bonds). The ^1H-NMR displays two doublets at δ 6.22 and 5.62 (2H, $J = 3$ Hz) characteristic of a $=CH_2$ group conjugated with the lactone CO, four signals at δ 5.12, 4.94 (2H, $J = 2$ Hz), 5.50 and 5.39 (2H, $J = 2$ Hz) due to two terminal methylene double bonds at C-10 and C-4 respectively. A signal at δ 1.20 (6H) was assigned to the methyls of an isopropyl group. The presence of this last group in the ester was confirmed by MS: *m/e* 244 (M^+-$C_4H_8O_2$) and *m/e* 71 (C_4H_7O). Compound **1a** was treated with Ac_2O–Py to give the monoacetate (**1b**) in the form of an oil: $C_{21}H_{26}O_6$; (no M^+) *m/e* 226 (M^+-148) (M^+-$C_4H_8O_2$-$C_2H_4O_2$), $[\alpha]_D$ +120°.

In order to relate aguerin A with a product of known structure, it was subjected to $NaBH_4$ reduction yielding **2**: mp 201–204°; $C_{19}H_{26}O_5$; MS *m/e* 334 (M^+), $[\alpha]_D$ +64°. Saturation of the double bond conjugated with the lactone group had taken place in this compound. This was reflected in its ^1H-NMR spectrum by the absence of signals characteristic of the olefinic proton of the α-methylene-γ-lactone group and the appearance of a doublet at δ 1.16 (3H, $J = 7$ Hz) due to a methyl group α to the lactone carbonyl group. Compound **2** was identical to 3β-hydroxy-8α-isobutyryloxyguaian-4(15), 10(14)-dien-6,12-olide obtained by zinc–copper couple reduction of chlorohyssopifolin A [3]; structure **1a** proposed for aguerin A was thus confirmed.

A second batch of *Centaurea canariensis*, grown from the seeds of the wild plant, showed no trace of aguerin A. However, together with cynaropicrin and deacylcynaropicrin, a new substance was isolated as an oil and called aguerin B.

Aguerin B (**3**), $C_{19}H_{22}O_5$, MS *m/e* 330 (M^+), $[\alpha]_D$ +96° displayed IR bands at cm^{-1} 3590 (hydroxyl), 1760 (α-methylene-γ-lactone), 1710 (α, β-unsaturated ester) and 1635 (methylene double bond). Its ^1H-NMR spectrum had signals characteristic of three methylene groups, δ 6.22 and 5.62 (C-13, $J = 3$ Hz), 5.12 and 4.94 (C-14, $J = 2$ Hz) and 5.40 (C-15, $J = 2$ Hz), and of methacrylic group protons, δ 6.22 and 5.65 plus a singlet at 1.95. The MS also showed this latter group, (prominent peaks at at MS *m/e* M^+-$C_4H_6O_2$ and *m/e* 69 (C_4H_5O). Oxidation of aguerin B gives a dehydroderivative, $C_{19}H_{20}O_5$, MS *m/e* 328 (M^+); $[\alpha]_D$ +91°; cm^{-1} 1725 (α,β-unsaturated cyclopentenone); UV λ_{max} 215 nm, which confirmed the presence of a secondary hydroxyl group at C-3.

$NaBH_4$ reduction of aguerin B led to the formation of the dihydroderivative **4** as an oil: $C_{19}H_{24}O_5$, MS *m/e* 332 (M^+); $[\alpha]_D$ +35°; identical to 3β-hydroxy-8α-methacryloyloxyguaian-4(15),10(14)-dien-6,12-olide [3], thus firmly establishing the structure of aguerin B as **3**.

Aguerin B was later isolated in this laboratory from *Centaurea linifolia* (0.008% yield) *C. canariensis* (var. *subspinnata*) (traces) and *C. sventenii* (0.025% yield).

EXPERIMENTAL

Mps were determined on a Kofler block and are uncorr. Optical activities were measured in $CHCl_3$, UV spectra in EtOH and ^1H-NMR spectra on a 60 MHz instrument in $CDCl_3$ with TMS as int. ref.

Extraction and isolation. The aerial part of *Centaurea canariensis* (3 kg), collected at La Laguna (Tenerife) in April–May 1977, was triturated, exhaustively extracted with hot EtOH and worked up in the usual manner [4]. The resulting extract (60 g) was first chromatographed on a column of Si gel then on Si gel impregnated with $AgNO_3$ (20%); both columns were eluted with C_6H_6-EtOAc (1:1).

Aguerin A (**1a**). This product was purified by PLC and eluted

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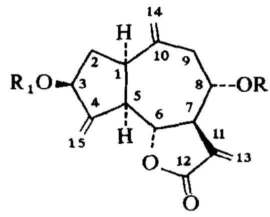
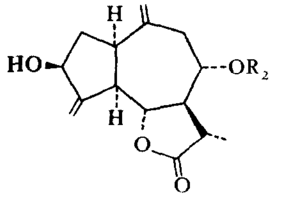
* Part 36 of the series 'Constituents of the Compositae'. For Part 35, see: González, A. G., Bermejo, J., Amaro, J. M., Massanet, G. M., Galindo, A. and Cabrera, I. (1978) *Can. J. Chem.* in press.



1a: R_1 = H R_2 = COPr^i
1b: R_1 = Ac R_2 = COPr^i



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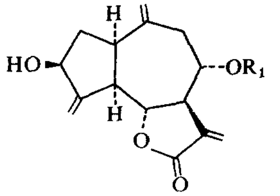

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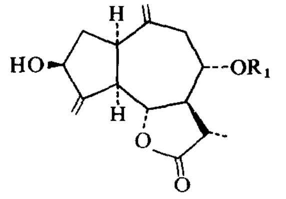

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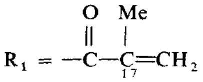

$$R_1 = -\overset{O}{\overset{\|}{C}}-\overset{Me}{\overset{|}{\underset{17}{C}}}=CH_2$$

with C_6H_6–EtOAc (1:1) giving 300 mg oil (0.01 % yield) which could not be crystallized: MS m/e 332 (M^+); $[\alpha]_D$ +89° (ca 0.14); IR ν_{max}^{film} cm^{-1}: 3470, 1760, 1720 and 1635; NMR: δ 6.22 and 5.62 (2H, dd, J = 3 Hz, C-13), 5.12 and 4.93 (2H, dd, J = 2 Hz, C-14), 5.50 and 5.39 (2H, dd, J = 2 Hz, C-15) and 1.20 (6H, s, —CH(Me)$_2$) (Calc for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28 Found: 68.37; H, 7.12%).

Monoacetylaguerin A (**1b**). A mixture of aguerin A (40 mg), C_5H_5N (2 ml) and Ac_2O (2.5 ml) was left for 12 hr and the monoacetate recovered as an oil: MS m/e (no M^+), 226 (M^+-$C_4H_8O_2$—$C_2H_4O_2$); $[\alpha]_D$ +120° (ca 0.1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770, 1730, 1640 and 1240; NMR. δ 6.22, 5.61 (2H, dd, J = 3 Hz, C-13), 5.60, 5.38 (2H, dd, J = 2 Hz, C-15), 5.11, 4.98 (2H, dd, J = 2 Hz, C-14) and 2.10 (3H, s, —COOMe).

$NaBH_4$ reduction. About 100 mg of aguerin A (**1a**) was dissolved in MeOH (5 ml), $NaBH_4$ (285 mg) being added, and the mixture was stirred at 0° for 10 min. The MeOH was then eliminated and the residue was acidified with 0.1 N HCl. It was extracted with EtOAc and crystallized with EtOAc–petrol: mp 201–204°; MS m/e: 334 (M^+); $[\alpha]_D$ +64° (ca 0.12); NMR: δ 5.30 (2H, d, J = 2 Hz, C-15), 5.12, 5.00 (2H, dd, J = 2 Hz, C-14), 1.22 (6H, s, CH(Me)$_2$) and 1.16 (3H, d, J = 7 Hz, C-15, Me).

Aguerin B (**3**). From a second batch of *C. canariensis*, treated in the same way as the first, an oil (0.02 % yield) was isolated identical with aguerin A by chromatography but with different physical constants and spectroscopic data: MS m/e: 330 (M^+); $[\alpha]_D$ +96° (ca 0.17); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 1760, 1710 and 1635; NMR: δ 6.22, 5.62 (2H, dd, J = 3 Hz, C-13), 6.22, 5.65 (2H, dd, J = 2 Hz, C-17 = CH$_2$), 5.40 (2H, d, J = 2 Hz, C-15), 5.12, 4.94 (2H, dd, J = 2 Hz, C-14) and 1.95 (3H, s, C-17-Me).

Dehydroaguerin B. Ca 200 mg of **3** was dissolved in Me_2CO (30 ml) and cooled in ice. While the mixture was continually stirred, Jones reagent was added in drops to slight excess and stirring continued for a further 15 min. The excess reagent was eliminated with MeOH and it was extracted as usual yielding an oily-looking residue: MS m/e 328 (M^+); $[\alpha]_D$ +91° (ca 0.75); UV λ_{max} nm: 215 (log ε = 4.16); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1725 and 1640; NMR; δ 6.30, 5.70 (2H, dd, J = 2 Hz, C-17=CH$_2$), 6.30, 5.70 (2H, dd, J = 3 Hz, C-13), 5.88 (2H, d, J = 2 Hz, C-15), 5.08, 4.90 (2H, dd, J = 2 Hz, C-14) and 2.01 (3H, s, C-17-Me).

$NaBH_4$ reduction. Aguerin B (120 mg) dissolved in MeOH (5 ml) was treated with $NaBH_4$ as for aguerin A above. A non-crystalline product was obtained: MS m/e 332 (M^+); $[\alpha]_D$ +35° (ca 0.18); NMR: δ 1.25 (3H, d, J = 8 Hz, C-15, Me).

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