

SALVADORIAN COMPOSITAE. II. JUANISLAMIN AND
2,3-EPOXY-JUANISLAMIN, TWO NEW SESQUITERPENIC
LACTONES FROM *CALEA URTICIFOLIA*

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ABSTRACT.—From leaves of *Calea urticifolia*, two new sesquiterpene lactones were isolated and characterized as juanislamin (1) and 2,3-epoxyjuanislamin (2).

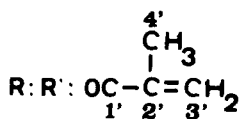
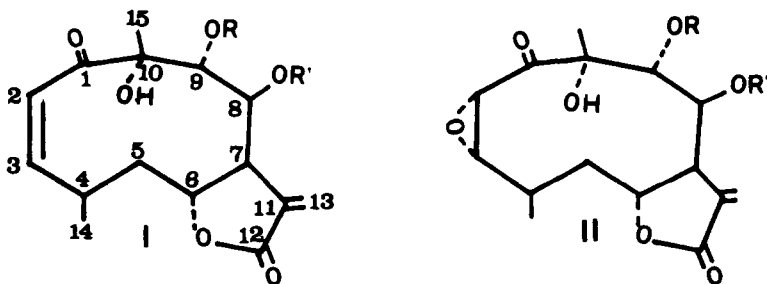
In continuation of our phytochemical studies of Salvadorian flora, we report in this paper the isolation of two new germacranolide sesquiterpene lactones which have not been previously described in the literature. They were isolated from *Calea urticifolia* (Compositae), collected in Sonsonate (El Salvador), where it is known as "juanislama". It is used in folk medicine as a topic bactericide as well as a treatment for gastric ulcers.

Previously we reported the isolation of the two germacranolides, caleine D and 2,3-epoxy-caleine D (1). Other research teams studying this species and *Calea zacatechichi* (2, 3) have also isolated lactones of the same type.

DISCUSSION

To carry out this work, 2.5 kg of dry leaves from *Calea urticifolia* were extracted and fractionated as indicated in the experimental section. In addition to caleine D and 2,3-epoxy-caleine D (1), two new compounds were isolated, and their structures were determined as 1 and 2. In view of the common name of the plant, we assigned the name juanislamin for 1 and 2,3-epoxy-juanislamin, for 2.

Juanislamin (1) when crystallized from ethyl ether afforded white crystals, mp=136-138°; $[\alpha]_D -320^\circ$. Its elementary analysis and ms are consistent with



an empirical formula, $C_{23}H_{28}O_8$. Its uv spectrum showed absorption at λ max 220 nm (ϵ , 15,250) and its ir spectrum absorption bands for hydroxyl and carbonyl groups as well as for an olefinic double bond. The corresponding proton signals of an α,β' -unsaturated γ -lactone group characteristic of sesquiterpene lactones appeared in the 1H -nmr spectrum; the C-13 exocyclic methylene signals appeared at δ , 6.32 (H, d, $J=1$ Hz) and 5.69 (H, d, $J=1$ Hz); the lactone C-6 proton appeared at δ , 4.62 (H, dd, $J=4$ and $J'=12$ Hz) and C-7 proton at δ , 2.66 (H, br s). At δ , 6.65 and 6.01 appeared two one-proton doublets, with a coupling constant of $J=12$ Hz, which were assigned to a *cis*, $\Delta^{2,3}$ olefinic system. The C-14 and C-15 methyl group signals appeared, the former as a doublet with $J=6.5$ Hz at 1.14 ppm and latter as a singlet at 1.33 ppm, due to the C_{15} -Me group on a totally substituted carbon. The C-8 and C-9 hydrogen signals appeared at δ , 5.70 as a broad singlet, owing to the overlap of their individual signals. In addition to the above-mentioned groups, the C-8 and C-9 are esterified as is usual in the genus *Calea* (1) and (2, 3), this time both by methacrylic acid. Their signals appear at δ , 1.88 (3H, dd, $J=1.5$ and $J'=1.5$ Hz) and at δ , 6.13 and 5.61 (2H, dq, $J=1.5$ and $J'=1.5$ Hz); at δ , 1.75 (3H, dd, $J=1.5$ and $J'=1.5$ Hz) and at δ , 5.95 and 5.47 (2H, dq, $J=1.5$ and $J'=1.5$ Hz). The presence of these two methacrylic acid esters was additionally confirmed by mass spectrometry, at M^+-69 (27%) (loss of $-CO-CMe=CH_2$), among others ions.

The most outstanding feature of the ^{13}C -nmr spectrum was the high chemical shift of the C-1 ketone group, which appeared at δ , 204. This high δ value indicated that the carbonyl group does not lie in the plane of the $\Delta^{2,3}$ double bond. Other interesting structural features were the relative positions and configurations of the ester groups and the C-15 methyl group of this compound whose values have been compared with those of caleine D (1) and of the neurolenines (4).

The *2,3-epoxy-juanislamin* (2), which crystallized from ethyl ether, had a mp of 146–148° and $[\alpha]_D -221^\circ$. Its elementary analysis and ms were consistent with an empirical formula of $C_{23}H_{28}O_9$. Its uv spectrum showed absorption at λ max 210 nm (ϵ , 15,780). Its ir spectrum was similar to that of juanislamin (1), except for the fingerprint zone. Its 1H -nmr spectrum was analogous to that of 1, but the two $\Delta^{2,3}$ olefinic proton signals were substituted by the signal of two oxiranic protons on the same positions; chemical shifts appeared at δ , 4.3 (H, d, $J=4$ Hz) and at 3.35 (H, dd, $J=4$ and $J'=8.5$ Hz), respectively. Its ^{13}C -nmr spectrum showed the substitution of the C-3 and C-2 olefinic carbon atom signals by two new ones at δ , 62.85 and 55.93, which indicated the oxiranic character of these two carbon atoms. Its ms spectrum showed a fragmentation pattern similar to that of 1.

EXPERIMENTAL¹

PLANT MATERIAL.—The leaves of *Calea urticifolia* (Compositae) were collected in Sonsonate, El Salvador, in July 1978.

EXTRACTION PROCEDURE.—Dried and milled leaves (2.5 kg) were extracted to exhaustion with ethanol. The ethanol extract was evaporated under reduced pressure to dryness. The ethanolic residue was dissolved in 600 ml of an aqueous solution of 25 g of lead acetate and 6 ml of acetic acid. After two days the suspension was filtered and evaporated. The residue was extracted with chloroform. When the washed and dried chloroform extract was evaporated, 17 g of residue was obtained.

ISOLATION.—The extract was chromatographed over a silica gel column with benzene-ethyl acetate (8:2) and (7:3) as the eluant. Elution was monitored by tlc. Elution with

¹All mp's are uncorrected. Ir spectra were recorded in nujol, uv spectra in EtOH, and 100 MHz spectra in $CDCl_3$ with TMS as an internal reference.

benzene-ethyl acetate (8:2) gave *juanislinamin* (1), mp 136–38° (ethyl ether), $[\alpha]_D -320^\circ$ (c, 0.25 in chloroform); uv, λ max (EtOH) 220 nm (15,250); ir, ν max (nujol) 3450, 1760, 1725, 1690, 1630, etc. cm^{-1} ; $^1\text{H-nmr}$ (CDCl_3) δ , 6.65 (H, d, $J=12$ Hz, H-3), 6.32 (H, d, $J=1$ Hz, H-13'), 6.13 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'a), 6.01 (H, d, $J=12$ Hz, H-2), 5.95 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'a), 5.70 (2H, br s, H-8 and H-9), 5.69 (H, d, $J=1$ Hz, H-13), 5.61 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'b), 5.47 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'b), 4.62 (H, dd, $J=4$ and $J'=12$ Hz, H-6), 4.15 (H, s, OH), 3.12 (H, m, H-4), 2.66 (H, br s, H-7), 1.88 (3H, dd, $J=1.5$ and $J'=1.5$ Hz, 2'-Me), 1.75 (3H, dd, $J=1.5$ and $J'=1.5$ Hz, 2'-Me), 1.33 (3H, s, 10-Me) and 1.14 (3H, d, $J=6.5$ Hz, 4-Me); $^{13}\text{C-nmr}$ (CDCl_3) δ , 204.9 (C-1), 168.74 (C-12), 166.64 (C-1'), 165.45 (C-1'), 148.01 (C-3), 134.99 (C-11), 134.81 (C-2'), 127.64 (C-2'), 127.24 (C-3'), 126.78 (C-13), 126.38 (C-3'), 125.61 (C-2), 79.49 (C-10), 76.41 (C-6), 74.39 (C-8), 74.13 (C-9), 41.31 (C-7), 40.38 (C-5), 28.36 (C-4), 23.66 (C-4'), 19.75 (C-14) and 18.08 (C-15) ppm; mass spectrum m/e (%) 432 (12, M⁺), 414 (20, M⁺-18), 364 (27, M⁺-69), 217 (100), 150 (91), etc.

Anal. Calcd. for $\text{C}_{23}\text{H}_{28}\text{O}_5$: C, 63.88%; H, 6.48%. Found: C, 63.01%; H, 6.55%.

Elution with benzene-ethyl acetate (7:3) gave *2,3-epoxy-juanislinamine* (2), mp 146–48° (ethyl ether); $[\alpha]_D -221^\circ$ (c, 0.5 in chloroform); uv, λ max (EtOH) 210 nm (15,780); ir, ν max (nujol) 3450, 1765, 1735, 1645, etc. cm^{-1} ; $^1\text{H-nmr}$ (CDCl_3) δ 6.34 (H, d, $J=1$ Hz, H-13'), 6.16 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'a), 5.96 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'a), 5.83 (2H, br s, H-8 and H-9), 5.78 (H, d, $J=1$ Hz, H-13), 5.65 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'b), 5.50 (H, dq, $J=1.5$ and $J'=1.5$ Hz, H-3'b), 4.84 (H, dd, $J=4$ and $J'=12$ Hz, H-6), 4.3 (H, d, $J=4$ Hz, H-2), 3.96 (H, s, OH), 3.35 (H, dd, $J=4$ and $J'=8.5$ Hz, H-3), 2.39 (H, br s, H-7), 1.9 (3H, dd, $J=1.5$ and $J'=1.5$ Hz, 2'-Me), 1.78 (3H, dd, $J=1.5$ and $J'=1.5$ Hz, 2'-Me), 1.25 (3H, s, 10-Me) and 1.16 (3H, d, $J=6$ Hz, 4-Me); $^{13}\text{C-nmr}$ (CDCl_3) δ 206.07 (C-1), 168.53 (C-12), 166.79 (C-1'), 165.50 (C-1'), 134.98 (C-11), 134.59 (C-2'), 128.05 (C-2'), 127.38 (C-3'), 126.94 (C-13), 126.64 (C-3'), 80.04 (C-10), 74.87 (C-6), 74.08 (C-8), 71.94 (C-9), 62.85 (C-3), 55.94 (C-2), 40.99 (C-7), 38.89 (C-5), 26.08 (C-4), 24.49 (C-4'), 18.58 (C-14) and 17.96 (C-15) ppm. Mass spectrum m/e (%) 448 (5, M⁺), 379 (7, M⁺-69), 224 (100), 207 (90), 146 (90), 118 (94), etc.

Anal. Calcd. for $\text{C}_{23}\text{H}_{28}\text{O}_5$: C, 61.60%; H, 6.25%. Found: C, 60.76%; H, 6.14%.

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