FOUR NEW LABDANE DITERPENE OXIDES FROM *SIDERITIS GOMERAE**

ANTONIO G. GONZÁLEZ, BRAULIO M. FRAGA, MELCHOR G. HERNÁNDEZ,
FRANCISCA LARRUGA and JAVIER G. LUIS

Department of Organic and Biochemistry, University of La Laguna, Instituto de
Investigaciones Químicas, C.S.I.C., Tenerife, Spain

(Received 13 May 1975)

Key Word Index—*Sideritis gomerae*; Labiatae; labdane diterpene oxides; gomerinaldehyde; 13-epigomerinaldehyde; gomic acid; 13-epigomic acid; eperu-13-ene-8 β ,15-diol.

Abstract—Four new labdane diterpene oxides gomerinaldehyde, 13-epigomerinaldehyde, gomic acid and 13-epigomic acid as well as eperu-13-ene-8 β ,15-diol were isolated from the aerial part of *Sideritis gomerae*.

INTRODUCTION

Continuing our work on the chemical components of the genus *Sideritis* [1, 2] we have studied *S. gomerae* Bolle, an endemic of Gomera (Canary Isles). In addition to eperu-13-ene-8 β ,15-diol [ent-labd-13(14)-ene-8 α ,15-diol; **5**] we isolated the new diterpenes gomerinaldehyde (ent-8,13-epoxylabdan-15-al; **1**), 13-epigomerinaldehyde (ent-8,13 β -epoxylabdan-15-al; **2**), gomic acid (ent-8,13-epoxylabdan-15-oic acid; **3**) and 13-epigomic acid (ent-8,13 β -epoxylabdan-15-oic acid; **4**).†

RESULTS AND DISCUSSION

Gomic acid (**3**) (C₂₀H₃₄O₃) showed IR bands indicative of an acid function (3300–2580, 1740 cm⁻¹). In the NMR spectrum characteristic signals of one CH₂COO and five methyl groups were observed. Two Me groups which appeared as a singlet at δ 1.41 must be situated on carbon atoms bearing oxygen. Treatment of (**3**) with CH₂N₂ gave the methyl ester (**7**) whose IR spectrum lacked OH absorption. Hence, the remaining oxygen must form an ether bridge. The acid

was reduced with LiAlH₄ to the primary alcohol (**9**) (δ 3.80, 2H). On the basis of the above data (**3**) was attributed the structure of a labdane oxide possessing an acid function at C-15. A compound analogous to (**7**) was obtained by Audier *et al.* [3] on oxidizing sclareol first with CrO₃–HOAc and then with Ag₂O in alkali, followed by treatment with CH₂N₂. Direct comparison of the resulting product with our ester (**7**) revealed that they had identical mp, IR and NMR spectra but opposite optical rotations, whence they must be enantiomers. Gomic acid was therefore assigned structure (**3**).

The NMR spectrum of 13-epigomic acid (**4**) differs from that of compound (**3**) only in the position of the C-8 and C-13 methyl and C-14 hydrogen signals, which indicates that (**4**) must be a C-13 epimer of gomic acid. Reduction of (**4**) with LiAlH₄ gave the alcohol (**10**) which was identical with that obtained by hydroboration of (–)-13-epimanoyl oxide (**11**) (mp, IR, NMR).

The unstable aldehydes gomerinaldehyde (**1**) and 13-epigomerinaldehyde (**2**) were also isolated from *Sideritis gomerae*. They were easily oxidized by air [4] and proved to be identical (TLC, NMR) with the oxidation products of the alcohols (**9**) and (**10**) respectively, which in turn had been prepared from the corresponding acids (**3**) and (**4**) as mentioned above. The co-occurrence of C-13 epimers has been reported before [5].

* Part 26 in the series "Constituents of the Labiatae". For Part 25 see González, A. G., Bretón, J. L., Fagundo, C. R. and Trujillo, J. M. (1975) *Anal. Quim.* (in press).

† Nomenclature is based on *The Common and Systematic Nomenclature of Cyclic Diterpenes*, 3rd revision, 1969, available from Dr. J. W. Rowe, U.S. Forest Products Laboratory, Madison, Wisc. 53705, U.S.A.

The fifth diterpene was identified with eperu-13-ene-8 β ,15-diol (5) by comparison with an authentic sample, previously obtained from a *Beyeria* species [6].

EXPERIMENTAL

Mp's are uncorr. Optical activities and IR spectra were taken in CHCl₃, NMR spectra on a 60-MHz instrument in CDCl₃ with TMS as internal standard. MS were measured at 70 eV (probe). Column and dry column chromatography was performed on Si gel 0.2–0.5 and 0.063–0.20 mm respectively.

Isolation of the diterpenes. The air-dried aerial part of the plant (2 kg), collected on Gomera (Canary Isles) beside the North Route at km 4 in July, was chopped and extracted several times with EtOH in a Soxhlet. The cold extract was filtered, concentrated *in vacuo* and chromatographed on a column. Petrol, petrol–EtOAc and EtOAc eluted mixtures of diterpenes and flavones which were rechromatographed on dry columns yielding the following diterpenes, in order of elution: gomeraldehyde (1), 13-epigomeraldehyde (2), gomic acid (3), 13-epigomeric acid (4), and eperu-13-ene-8 β ,15-diol (5).

Gomeraldehyde (ent-8,13-epoxylabdan-15-al; (1), unstable. NMR: δ 0.76 (6H, s, C-18, C-19), 0.85 (3H, s, C-20), 1.28 and 1.32 (each 3H, s, C-16, C-17), 2.46 (2H, t, J 4 Hz, C-14), 9.90 (1H, t, J 4 Hz, C-15).

13-Epigomeraldehyde (ent-8,13 β -epoxylabdan-15-al; (2), unstable. NMR: δ 0.80 (6H, s, C-18, C-19), 0.85 (3H, s, C-20), 1.25 and 1.31 (each 3H, s, C-16, C-17), 2.33 and 2.86 (1H each, q, J_{AX} 4 Hz, J_{AB} 15 Hz, C-14), 9.92 (1H, t, J 4 Hz, C-15).

Gomic acid (ent-8,13-epoxylabdan-15-oic acid; (3) (4 g). Mp 113–115° (petrol), $[\alpha]_D -34^\circ$ (c 0.13). (Found: C, 74.51; H, 10.42. C₂₀H₃₄O₃ requires: C, 74.49; H, 10.63%). IR $\nu_{\max}$ cm⁻¹: 3300–2580, 1740, 1430, 1385, 1379, 1250, 1100, 940. NMR: δ 0.84 (6H, s, C-18, C-19), 0.92 (3H, s, C-20), 1.41 (6H, s, C-16, C-17), 2.53 (2H, d, deformed AB system, C-14). MS *m/e* (%): 322 (M⁺; 1), 307 (100), 289, 261, 245, 191, 189, 175, 149, 137, 123. **Methyl ester** (7), obtained by treating (3) with CH₂N₂, mp 106–107° (MeOH), $[\alpha]_D -22^\circ$ (c 1.46). (Found: C, 75.18; H, 10.78. C₂₁H₃₆O₃ requires: C, 74.95; H, 10.78%). NMR: δ 0.82 (6H, s, C-18, C-19), 0.88 (3H, s, C-20), 1.32 and 1.36 (each 3H, s, C-16, C-17), 2.48 (2H, s, C-14), 3.70 (3H, s, OMe). MS *m/e* (%): 321 (M⁺ – 15; 23), 306 (100), 270, 245, 137, 109.

13-Epigomeric acid (ent-8,13 β -epoxylabdan-15-oic acid; (4) (0.6 g). Mp 127–129° (MeOH), $[\alpha]_D -20^\circ$ (c 0.60). IR $\nu_{\max}$ cm⁻¹: 3320–2600, 1745, 1390, 1380, 1075, 990. NMR: δ 0.85 (6H, s, C-18, C-19), 0.92 (3H, s, C-20), 1.36 and 1.40 (each 3H, s, C-16, C-17), 2.55 and 2.80 (each 1H, bs, deformed AB system, C-14). MS *m/e* (%): 306 (M⁺ – 15; 100), 288, 263, 261, 245, 230, 207, 177, 165, 163, 149, 137, 123. **Methyl ester** (8), obtained by treating (4) with CH₂N₂, would not crystallize. NMR: δ 0.78 (6H, s, C-18, C-19), 0.82 (3H, s, C-20), 1.22 (6H,

s, C-16, C-17), 2.61 (2H, d, deformed AB system, C-14), 3.61 (3H, s, OMe).

Eperu-13-ene-8 β ,15-diol (ent-labd-13(14)-ene-8 α ,15-diol; (5) (0.5 g). Mp 131–132° (petrol), $[\alpha]_D +0.6^\circ$ (c 1.40) (lit. [6] mp 130.5–131.5°, $[\alpha]_D +0.7^\circ$). NMR: δ 0.76 (6H, s, C-18, C-19), 0.82 (3H, s, C-20), 1.12 (3H, s, C-17), 1.68 (3H, s, C-16), 4.12 (2H, d, J 8 Hz, C-15), 5.42 (1H, t, J 8 Hz, C-14). MS *m/e* (%): 290 (M⁺ – 18; 7), 275, 257, 191, 177 (100), 149, 137, 123. **Acetate** (6), prepared as usual; NMR: δ 0.78 (6H, s, C-18, C-19), 0.84 (3H, s, C-20), 1.10 (3H, s, C-17), 1.69 (3H, s, C-16), 2.02 (3H, s, OAc), 4.55 (2H, d, J 8 Hz, C-15), 5.32 (1H, t, J 8 Hz, C-14).

Reduction of gomic acid. (3) (140 mg) in dry Et₂O (14 ml) was refluxed with LiAlH₄ (170 mg) for 8 hr. Excess reagent was destroyed by adding H₂O, the mixture was washed with 10% aq. HCl and extracted with Et₂O to give the alcohol (9) (130 mg), mp 45–47° (MeOH), $[\alpha]_D -3.5^\circ$ (c 0.60). NMR: δ 0.79 (6H, s, C-18, C-19), 0.83 (3H, s, C-20), 1.29 (6H, s, C-16, C-17), 3.80 (2H, t, C-15).

Reduction of epigomic acid. (4) (50 mg) in dry Et₂O (10 ml) was reduced as described above for (3), yielding the alcohol (10) (35 mg), mp 87–89° (petrol), $[\alpha]_D -13^\circ$ (c 1.50). NMR: δ 0.78 (6H, s, C-18, C-19), 0.84 (3H, s, C-20), 1.22 and 1.28 (each 3H, s, C-16, C-17), 3.80 (2H, m, C-15).

Hydroboration of (–)-13-epimanoyl oxide (ent-8,13 β -epoxy-14-labdene; (11). Through a soln of (11) (380 mg) in dry THF (20 ml) diborane was passed by applying a slight flow of dry N₂. Diborane was prepared by the dropwise addition of a soln of NaBH₄ (4 g) in diglyme (90 ml) to a stirred soln of BF₃ etherate (25 ml) in diglyme (20 ml). After completing the NaBH₄ addition the diborane generator was heated to boiling for 1 hr and the resulting organoborane oxidized by adding 3 N NaOH (20 ml) and 30% H₂O₂ (15 ml). The mixture was stirred for 1 hr and worked up as usual. Dry column chromatography (C₆H₆–EtOAc, 4:1) gave the alcohol (10) (190 mg), mp 88–90° (petrol), $[\alpha]_D -14^\circ$ (c 1.70). (Found: C, 78.10; H, 11.74. C₂₀H₃₆O₂ requires: C, 77.87; H, 11.76%). This compound was identical (mp, IR, NMR) with the compound obtained by reduction of (4).

Oxidation of (9) and (10). A soln of (9) (140 mg) in Me₂CO (10 ml) was treated dropwise with a slight excess of Jones reagent, poured into H₂O and worked up as usual, yielding the aldehyde (1) (90 mg) and the acid (3) (30 mg). Oxidation of (10) (160 mg) in the same way gave the aldehyde (2) (110 mg) and the acid (4) (30 mg).

Acknowledgements—We thank Prof. W. Wildpret (Department of Botany, University of La Laguna) for identifying the plant, M. Galván for collecting it, Prof. Primo and J. Sendra (Instituto de Agroquímica, Valencia) for the MS, and Prof. Fetizon (Université de Paris-Sud) and Prof. Jefferies (University of Western Australia) for samples of (3), (7) and (5) respectively.

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