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EPOXY-*ISO*SIDOL: A NEW DITERPENOID FROM *SIDERITIS BIFLORA*[*]

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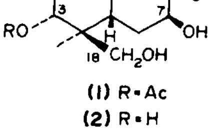
Key Word Index—*Sideritis biflora*; Labiatae; tetracyclic diterpenes; new *ent*-15β,16-epoxykaurane derivative.

Abstract—The new diterpenoid *ent*-3β-acetoxy-7α,18-dihydroxy-15β,16-epoxykaurane has been isolated from *Sideritis biflora*. Twelve previously known *ent*-kaurane derivatives have also been obtained from the same source.

Plant. Sideritis biflora Port. et Rig. = *S. bourgaeana* (Boiss. et Reut.) Font Quer = *S. leucantha* Cav. var. *paucidentata* Wk. *Source.* Low areas in the S.E. of the Iberian Peninsula (near Tobarra, Albacete). *Previous work.* None.

Present work. From the aerial parts of this plant have been isolated 12 diterpenoids previously described: *ent*-18-acetoxy-3β,7α-dihydroxykaur-16-ene (linearol), *ent*-18-acetoxy-3β,7α-dihydroxykaur-15-ene (*iso*linearol), *ent*-3β-acetoxy-7α,18-dihydroxykaur-16-ene (sidol), *ent*-3β-acetoxy-7α,18-hydroxykaur-15-ene (*iso*sidol), *ent*-3β,7α,18-trihydroxykaur-16-ene (foliol), *ent*-3β,7α,18-trihydroxykaur-15-ene (*iso*foliol) [1], *ent*-3β,7α,15β,18-tetrahydroxykaur-16-ene (leucanthol), *ent*-3β,7α,17,18-tetrahydroxykaur-15-ene (*iso*leucanthol) [2], *ent*-18-acetoxy-3β,7α,15β-trihydroxykaur-16-ene, *ent*-3β-acetoxy-7α,15β,18-trihydroxykaur-16-ene [3], *ent*-18-acetoxy-3β,7α-dihydroxy-15β,16-epoxykaurane (epoxy-*iso*linearol) [4] and *ent*-3β,7α,18-trihydroxy-15β,16-epoxykaurane (epoxy-*iso*foliol) [5], plus a new compound (**1**, $C_{22}H_{34}O_5$). The NMR spectrum of **1** showed signals for two tertiary methyls, one acetyl, one > C<u>H</u>OH and one methyl and one proton both on an epoxide ring. The chemical shifts and shapes of the above signals were identical with those previously observed for epoxy-*iso*linearol [4]; on the other hand, the signals for the C-3 and C-18 protons appeared at δ 5.00 and 3.18 respectively, indicating attachment of the acetoxyl group on C-3; this was also confirmed by the small diamagnetic shift (Δδ −0.07) undergone by the C-4 axial methyl group in compound **1** with respect to epoxy-*iso*linearol.



(**1**) R = Ac
(**2**) R = H

The new diterpenoid (**1**) is thus *ent*-3β-acetoxy-7α,18-dihydroxy-15β,16-epoxykaurane (epoxy-*iso*sidol). The above structure was confirmed by alkaline hydrolysis of **1** to give compound **2**, identical (physical and spectroscopic data) with epoxy-*iso*foliol [5].

EXPERIMENTAL

For general details on extraction and separation of diterpenes from *Sideritis*, see Ref. [4]; for most experimental details, see part 13 [6] of this series. The previously described compounds have been identified by their physical (mp $[\alpha]_D$) and spectroscopic (IR, NMR) data and by comparison with authentic samples. *Epoxy-*iso*sidol* (**1**). Mp 177–181° (Me_2CO–*n*-hexane); $[\alpha]_D^{20°}$ −3.6° (EtOH; *c* 0.74). IR ν_{max}^{KBr} cm^{-1}: 3450, 3300 (–OH); 1730, 1250 (–OAc). NMR (60 MHz, $CDCl_3$): δ 5.00 (1 H, *m*, $W_{\frac{1}{2}}$ = 18 Hz, C-3), 3.80 (1 H, *m*, $W_{\frac{1}{2}}$ = 6 Hz, C-7), 3.18 (2 H, AB *q*, *J* 12 Hz, C-18 methylene), 3.10 (1 H, *s*, C-15, epoxide ring), 2.06 (3 H, *s*, –OAc), 1.44 (3 H, *s*, Me on epoxide ring), C–Me singlets at 1.06 and 0.68. MS (70 eV) *m/e* rel. int.): 378 M^+ (13), 363 (3), 360 (5), 318 (5), 300 (16), 270 (100, base peak), 255 (56), 242 (17), 105 (60), 95 (64). (Found; C, 69.93; H, 9.03. $C_{22}H_{34}O_5$ requires: C, 69.81; H, 9.05%.

Alkaline hydrolysis of **1**. Treatment of compound **1** (30 mg) with 5% KOH–EtOH (15 ml) for 24 hr at room temp. gave **2** (23 mg): mp 248–250° (Me_2CO); $[\alpha]_D^{20°}$ +27.8° (EtOH; *c* 0.72). IR ν_{max}^{KBr} cm^{-1}: 3460, 3380 (–OH). MS: 336 *m/e* (M^+). (Found: C, 71.31; H, 9.37. Calc. for $C_{20}H_{32}O_4$: C, 71.39; H, 9.59%). Compound **2** was identical in all respects with epoxy-*iso*foliol [5].

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[*] Part 33 in the series "Studies on diterpenes from *Sideritis* genus". For part 32 see Carrascal, M. I., Rodriguez, B. and Valverde, S. *An. Quim.* in press.

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ISOPRENOID TRIETHER LIPIDS FROM *CALDARIELLA*

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Key Word Index—*Caldariella*; lipids; ether lipids; isoprenoids; tri-*O*-phytanylglycerol.

In the *Caldariella* group of extreme thermoacidophile bacteria [1], the major lipids [2,3] are macrocyclic sn-1,2-diethers of glycerol derived from a range of C_{40} diols with unique ω,ω′-biphytanyl structures. In the hope of shedding some light on their biosynthesis, we investigated minor lipid components, here shown to be triethers of glycerol with partly-or fully-saturated C_{20} (phytanyl) alcohols.

Separation of minor lipids

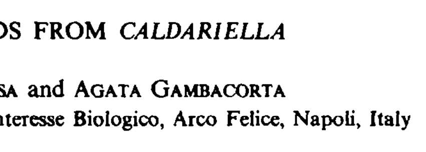
From *ca* 350 g of lyophilized cells of the MT-3 and MT-4 strains of *Caldariella acidophila*, some 25 g of total lipid was obtained, of which *ca* 0.5 g (accumulated over a series of experiments) was directly soluble in hexane and separated accordingly. Chromatography of this fraction afforded the thianaphthenequinone described elsewhere [4] as major component, a complex mixture of hydrocarbons, and some 30 mg of glycerol triethers. These on TLC (Si gel; hexane–Et_2O, 7:3) afforded two components, R_f 0.5 and 0.4; the former predominated in the triether fraction from MT-4.

Tri-O-phytanylglycerol (**1**)

The IR spectrum of the less polar triether showed only saturated alkyl and ether bands (ν_m 1110, 1375–1385, 1465, 2850–2950 cm^{-1}) and the ^1H NMR spectrum showed, per 11 CH_2–O and CH–O protons (δ 3.40, *br*) some 72 saturated CH_2 and CH protons (δ1.22–1.60, *br*) and 45 CH_3 protons (δ 0.86, *d*, $J = 9Hz$). Satisfactory MS were not obtained. Treatment with BCl_3 gave glycerol (TLC) and an alkyl chloride $C_{20}H_{41}Cl$ (by MS); similarly HI cleavage gave $C_{20}H_{41}I$. The ^1H NMR spectra of these halides showed, per 2 CH_2X protons (δ 3.15, *t*) 24 CH_2 and CH protons (δ 1.22–1.60) and 15 CH_3 protons (δ 0.86, *d*, $J = 9$ Hz) and their identification as phytanyl halides was confirmed by conversion into the acetate which was identical (MS, NMR, and GLC) with authentic phytanyl acetate. Thus structure (**1**) for the less polar triether is established.

The more polar component

The more polar triether component was very similar to (**1**) but contained some unsaturation (addition ν_m 1665 cm^{-1}; NMR data below). Hydrogenation gave a product identical with (**1**) which was similarly converted into authenticated phytanyl acetate. The extent and location of unsaturation in this component (which is probably a mixture) were in part established by ^1H NMR methods. If we regard (**1**) biogenetically as a tri-*O*-geranylgeranylglycerol which has been completely reduced, then in a partly-reduced analogue there are 12 possible double bond sites and these are of three distinguishable kinds: (i) in the α-residue, bearing allylic CH_2–O; (ii) in the β- and γ-residues; (iii) in the δ-residue, with terminal $=CMe_2$.



(**1**) (no unsaturation)
(**2**) (unsaturation as broken lines, see text)

The resolved signals, assignments, and approximate integrals (calibrated from the total of the $C\underline{H}_2$–O and $C\underline{H}O$ signals, δ 3.40 and 3.95; 11 protons) in the ^1H NMR spectrum of the more polar triether fraction are: δ 0.86 (21H, *d*, $J = 9$ Hz, $C\underline{H}_3$–CH sat); 1.10–1.40 (36H, *br*, $C\underline{H}_2$ and $C\underline{H}$, sat); 1.57 (6H, *s*, one $C\underline{H}_3$–CMe= in δ-residue); 1.66 (18H, *s*, $C\underline{H}_3$–C= in α, β, γ and one $C\underline{H}_3$–CMe= in δ-residue); 2.00 (18H, *br*, $C\underline{H}_2$–CH=); 3.40 (9H, *br*, sat $C\underline{H}_2$–O and $C\underline{H}$–O); 3.95 (2H,*d*, $J = 8$ Hz, =CH–$C\underline{H}_2$–O); 5.05 (5H, *br*, =$C\underline{H}$–CH_2); 5.35 (1H, *t*, $J = 8$ Hz, =$C\underline{H}$–CH_2O). The data are satisfied if in the more polar triethers there are (approximately) 6 double