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ISOLATION AND PARTIAL SYNTHESIS OF *ENT*-18-ACETOXYKAUR-16-ENE-3β,7α,15β-TRIOL FROM *SIDERITIS SCARDICA*

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Key Word Index—*Sideritis scardica*; Labiatae; tetracyclic diterpenes; 18-acetoxy-leucanthol.

Continuing our work on the diterpenes of the genus *Sideritis* [1] (family Labiatae), we have examined the petrol extract of *Sideritis scardica* Griseb, a species growing on the central part of the Balkan peninsula. By Si gel column chromatography the following previously known diterpenes were isolated: siderol (*ent*-7α-acetoxykaur-15-en-18-ol) [2], epoxysiderol (*ent*-7α-acetoxy-15β,16β-epossikaur-18-ol) [3], isolinearol (*ent*-18-acetoxy-3β,7α-dihydroxykaur-15-ene) [4, 5] (**1**), eubol (*ent*-7α-acetoxykaur-16-ene-15β,18-diol) [6], sideroxol (*ent*-15β,16β-epoxykaurane-7α,18-diol) [7]. A new diterpene, shown to be 18-acetoxy-leucanthol (**2**), was isolated. This compound has previously been quoted as a constituent of *Sideritis biflora* [8] but no physical or spectroscopic data were reported. We now report the structural elucidation and a partial synthesis of compound **2** whose molecular formula, $C_{22}H_{34}O_5$, was determined by MS. The IR spectrum showed the presence of a hydroxyl function (3330 and 3640 cm^{-1}), an ester group (1725 and 1252 cm^{-1}) and a typical absorption for an exocyclic methylene (1650 and 895 cm^{-1}). The ^1H NMR spectrum showed characteristic signals for two tertiary methyls, one acetyl, three —CHOH (δ 3.65, 3.95 and 4.15), one CH_2OAc in the equatorial configuration [2, 9] and two vinyl protons at δ 5.15 and 5.27. By treatment with Ac_2O–Py it gave the same tetracetate (**3**), $C_{28}H_{40}O_8$, previously obtained by acetylation of leucanthol (*ent*-3β,7α,15β,18-tetrahydroxykaur-16-ene) [10] from *Sideritis leucantha*. All these data were consistent with the structure **2** of *ent*-18-acetoxykaur-16-ene-3β,7α,15β-triol (18-acetoxy-leucanthol).

The above structure was fully confirmed by partial synthesis of **2** starting from natural isolinearol (**1**). This was transformed, as described previously, into epoxy-isolinearol (*ent*-18-acetoxy-15β,16β-epoxykaur-3β,7α-diol) (**4**) [4] from *Sideritis theezans*, and the epoxy ring of **4** was cleaved with BF_3–Et_2O complex in DMSO to yield compound **2** [11] identical to the natural product, thus definitely establishing the structure and stereochemistry at C-15 of compound **2**.

EXPERIMENTAL

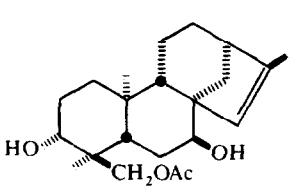
Mps were determined in a Kofler apparatus and are uncorr. IR: Nujol mull. NMR, $CDCl_3$ soln with TMS as an internal standard. MS were recorded at an ionization potential of 75 eV. CC was performed on Si gel (0.05–0.020 mm). All the products here reported gave satisfactory elemental analyses.

Plant material. Sideritis scardica Griseb was collected on the mountain of Xanti (Tracia) at 400–500 m in the summer of 1976 and identified by Prof. A. Di Martino, Botanical Institute, University of Palermo. A specimen is deposited in the herbarium of the Orto Botanico of this university.

Extraction and separation of the diterpenes. Powdered air-dried *S. scardica* (350 g) was Soxhlet-extracted with petrol for 48 hr. The conc extract was repeatedly chromatographed on a Si gel column with petrol–Et_2O (3:1), petrol–Et_2O (1:3), Et_2O–EtOAc (3:1) and Et_2O–EtOAc (1:1) as eluent, yielding the following compounds in order of elution: siderol (150 mg) (*ent*-7α-acetoxykaur-15-en-18-ol), epoxy-siderol (50 mg) (*ent*-7α-acetoxy-15β,16β-epossikaur-18-ol), isolinearol (30 mg) (*ent*-18-acetoxy-3β,7α-dihydrokaur-15-ene) (**1**), eubol (100 mg) (*ent*-7α-acetoxykaur-16-ene-15β,18-diol), sideroxol (80 mg) (*ent*-15β,16β-epoxykaurane-7α,18-diol) and 18-acetoxy-leucanthol (18 mg) (*ent*-18-acetoxykaur-16-ene-3β,7α,15β-triol) (**2**). The previously known diterpenes were identified by their physical and spectroscopic (mp, IR, NMR, MS) data and by comparison with authentic samples.

18-Acetoxy-leucanthol (**2**). Mp 173–176° (from EtOAc); negative TNM test; IR ν_{max}^{Nujol} cm^{-1}: 3330–3640 (OH), 1725 and 1252 (OAc), 1650 and 895 (>C=CH_2); MS *m/e*: 378 (M^+); ^1H NMR: δ 0.77 (3H, *s*, 4-Me), 1.06 (3H, *s*, 10-Me), 2.12 (3H, *s*, COMe), 3.65 (1H, *m*, 3-H), 3.95 (1H, *m*, 7-H), 4.08 (2H, *s*, 4-CH_2OAc), 4.15 (1H, *m*, 15-H), 5.15 and 5.27 (2H, *br*, >C=CH_2).

Tetracetyl-leucanthol (**3**). Treatment of compound **2** (15 mg) with Py–Ac_2O (1–2 ml) gave the same tetracetate (**3**) obtained by acetylation of leucanthol [10], mp 200–202° (from EtOH–H_2O); IR ν_{max}^{Nujol} cm^{-1}: no OH absorption, 1725 and 1250 (OAc), 3080, 1650 and 890 (C=CH_2); ^1H NMR: δ 0.75 (3H, *s*, 4-Me), 1.12 (3H, *s*, 10-Me), 1.96 (12H, *s*, COMe), 4.80 (1H, *br*, 3-H), 4.95



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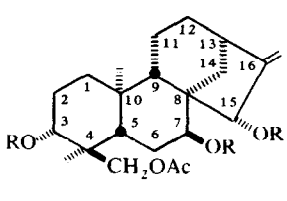

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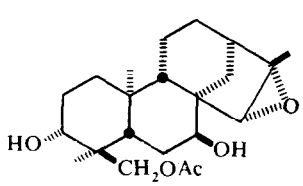

4

(1H, *br*, 7-H), 3.54 and 3.97 (2H, q_{AB}, J = 12 Hz, $-CH_2OAc$), 5.04 (1H, *br*, 15-H), 5.22 and 5.41 (2H, *br*, $C{=}CH_2$).

Partial synthesis of ent-18-*acetoxykaur*-16-*ene*-3β,7α,15β-*triol* (**2**). (a) Ent-18-*acetoxy*-15β,16β-*epoxykaur*-3β,7α-*diol* (*epoxy-isolinearol*) [4, 5] (**4**). *Ent*-18-acetoxy-3β,7α-dihydrokaur-15-ene (natural isolinearol) (**1**) (150 mg) in Et_2O (100 ml) was treated with *p*-nitroperbenzoic acid (150 mg) at room temp. for 24 hr. After conventional work-up, the epoxy-isolinearol was isolated in good yield; mp 218–220° by comparison with authentic samples, IR superimposable. (b) *Rearrangement of epoxy-isolinearol* (**4**). The epoxide (**4**) (100 mg), dissolved in dry DMSO (20 ml), was treated with freshly distilled BF_3–Et_2O complex (3 drops) and heated at 100° for 20 hr. The soln was then diluted with H_2O (80 ml) and extracted with Et_2O. Evapn of the solvent left a residue (65 mg) which was separated by chromatography on Si gel (cyclohexane–EtOAc, 1:1) giving pure **2** (40 mg) as needles, mp 174–176° (from EtOAc). The IR and ^1H NMR spectra were identical to natural 18-acetoxy-leucanthol isolated from *S. scardica* and then from *S. biflora*.

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STEROLS FROM SOME BASIDIOMYCETES

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Key Word Index—*Armillariella mellea*; *Boletus luridus*; *Pholiota aegerita*; Basidiomycetes; mushroom; sterols; ergosterol; ergost-7-en-3β-ol; ergosta-7,22-dien-3β-ol; ergosta-5,7-dien-3β-ol.

INTRODUCTION

In recent years the sterol mixtures from terrestrial sources have been reinvestigated in detail using modern techniques. Many early studies on sterols from fungal species resulted in the isolation of one or two sterols, but others present in low concentrations were often undetected. Ergosterol is often the major sterol of Basidiomycetes [1–3] which, however, have been examined by modern methods in only a few cases. As a continuation of our studies [4, 5], we have now examined the sterol contents of three species of Basidiomycetes, namely *Armillariella mellea*, *Boletus luridus* and *Pholiota aegerita*.

RESULTS

The unsaponified lipids were obtained by the usual procedure from the Basidiomycetes and the sterol fractions were separated by column chromatography over Si gel. After acetylation, the individual components were separated by column chromatography on Si gel impregnated with $AgNO_3$. The identification of each sterol was based on a comparison of the experimentally derived MS and NMR spectra with those reported in the literature [6, 7] and co-injection with standards. The results are summarized in Table 1. All fungi examined contained ergosterol as the predominant sterol accompanied by the other closely related sterols ergost-7-en-3β-ol, ergosta-7,22-dien-3β-ol and ergosta-5,7-dien-3β-ol. Cholesterol was found only in trace amounts.

Table 1. Sterol composition of Basidiomycetes (%)

Family and species	Sterol present 1	2	3	4
Agaricaceae				
P. aegerita	5.0	4.6	1.3	89.0
Trichelomataceae				
A. mellea	4.4	4.4	11.1	80.0
Polyporaceae				
B. luridus	3.9	9.8	1.2	85.0

1 = Ergost-7-en-3β-ol; **2** = ergosta-7,22-dien-3β-ol; **3** = ergosta-5,7-dien-3β-ol; **4** = ergosterol.