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SIDERONE, A DITERPENE FROM *SIDERITIS SYRIACA*

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Key Word Index—*Sideritis syriaca*; Labiatae; keto-diterpene; *ent*-7-oxo-kaur-15-en-18-ol.

ıbstract—Siderone, a new keto-diterpene, has been isolated from the petrol extract of the inflorescence of *Sideritis yriaca*. Its structure and stereochemistry have been established by spectroscopy and by chemical correlation with nown products to be *ent*-7-oxo-kaur-15-en-18-ol.

INTRODUCTION

ecently we reported [1] the isolation and structure lucidation of an epoxy-diterpene, ucriol (*ent*-15β,16β-poxykaurane-7β,18-dio) from the petrol extract of the ıflorescence of *Sideritis syriaca*. Further investigation of he petrol extract led us to the isolation of another new iterpenoid which was named siderone (**1**).

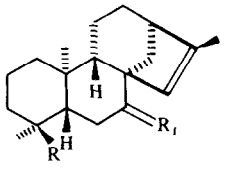
This paper reports the structure elucidation of **1** on he basis of spectroscopic evidence, by chemical correıtion with known products and by partial synthesis tarting from natural sideripol (**2**) [2].

RESULTS AND DISCUSSION

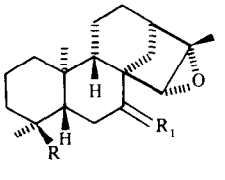
Siderone (**1**) mp 134–135°, $C_{20}H_{30}O_2$, (analytical and ıass spectra, m/z 302 $[M]^+$) gave a positive TNM test nd a negative Zimmermann test. Its IR spectrum showed haracteristic absorptions for a carbonyl function at 720 cm^{-1}, and a hydroxyl group at 3460 cm^{-1}.

The presence of the hydroxyl function was confirmed because acetic anhydride–pyridine treatment of compound **1** gave a monoacetyl derivate (**3**), $C_{22}H_{32}O_3$. The ^1H NMR spectrum of siderone showed two tertiary methyl groups (δ 0.78 and 1.21), one allylic methyl (δ 1.73, J = 1.5 Hz), an AB quartet (δ 3.06 and 3.37, J = 11.0 Hz) assigned to the C-18 equatorial $-CH_2OH$ and one vinyl proton (δ 5.49, $W_{1/2}$ = 6.0 Hz). The keto group on C-7 agrees with the deshielding ($\Delta = \delta$ 0.41) of the H-15 from **1** to **6** (δ 5.08). The ^{13}C NMR spectrum of **1** confirmed the proposed structure with the carbon resonances being in agreement with the assignment for *ent*-kaur-15-ene possessing a keto group at the C-7 position (δ 214.82) [3].

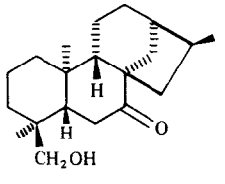
Catalytic hydrogenation of **1** yielded a 4:1 mixture of C-16 epimers in which the 16β-epimer (**4**) predominated. It is known that catalytic hydrogenation of *ent*-kaur-15-enes occurs exclusively from the less hindered α-face to give the 16β-methyl epimer. In this case partial addition from the β-side depends on the presence of the neighbouring carbonyl group at C-7 [4]. Jones oxidation of siderone (**1**) gave the keto-acid, $C_{20}H_{28}O_3$, which was identical



	R	R_1
1	CH_2OH	O
2	CH_2OAc	$\beta-OH$
3	CH_2OAc	O
5	COOH	O
6	CH_2OH	H_2
7	CH_2OH	$\alpha-OH$



	R	R_1
8	CH_2OAc	O
9	CH_2OH	O



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with the known *ent*-7-oxo-kaur-15-en-18-oic acid (**5**) [5]. Huang–Minlon reduction of siderone (**1**) yielded an alcohol, $C_{20}H_{32}O$, having physical constants in good agreement with the values described for *ent*-kaur-15-en-18-ol (**6**) [6]. The sodium borohydride reduction of **1** afforded episideridiol (*ent*-7β-18-dihydroxykaur-15-ene, **7**) of known absolute stereochemistry [4]. These results confirm the structure and the absolute configuration of **1** as *ent*-7-oxo-kaur-15-en-18-ol. The above structure was fully confirmed by partial synthesis of **1** starting from natural sideripol (**2**).

Jones oxidation of **2** afforded a mixture of acetylsiderone (**3**) and *ent*-18-acetoxy-7-oxo-15β,16β-epoxykaurane (**8**). The structure of the latter was proved by the occurrence in its ^{1}H NMR spectrum of a typical signal for a proton (δ 3.08) and a methyl group (δ 1.46) on an epoxide ring. On alkaline hydrolysis compound **8** afforded *ent*-7-oxo-15β,16β-epoxykaurane-18-ol (**9**) while hydrolysis of **3** yielded a compound identical with the natural product, thus definitely establishing the structure and absolute configuration depicted for siderone in **1**. To our knowledge, this is the first report of the occurrence of a keto kaurenoid diterpene in a *Sideritis* species.

EXPERIMENTAL

Mps (Kofler block): uncorr. IR: nujol mull. ^{1}H NMR (360 MHz) $CDCl_3$, TMS as internal reference; ^{13}C NMR spectra (20.0 MHz) in $CDCl_3$ with TMS using the FT mode. All the assignments were confirmed by off-resonance experiments. MS: 75 eV. CC: silica gel Merck (0.063–0.200). TLC was run on chromatoplates of silica gel G Merck.

Plant material. Sideritis sytriaca L. (*S. sicula* Ucria) was collected from the high summits of Madonie Mount (Sicily) in the summer of 1981. A specimen is deposited in the Herbarium of the Orto Botanico, University of Palermo.

Isolation of the diterpene. General experimental details of extraction and separation of diterpenes from *S. syriaca* have been described previously [1, 2, 4]. The inflorescences (6 kg) were extracted for 75 hr with petrol (20 l.) in a Soxhlet. From the petrol extract the major diterpenic constituents were isolated by the procedure reported earlier. The mother-liquor gave a sticky residue which was repeatedly extracted with $CHCl_3$. Siderone (**1**) was isolated from this mother liquor by HPLC on Micropak MCH-5 developed with MeOH (flow 1.0 ml/min).

Crystallization from EtOAc gave **1** (25 mg) as needles, mp 133–135°, positive TNM test, negative Zimmermann test. IR ν_{max}^{Nujol} cm^{-1}: 3460 (OH), 1720 (CO) and 1650 (C=C). MS *m/z*: 302 [M]$^+$; ^{1}H NMR: δ 0.78 (3H, *s*, 4α-Me), 1.21 (3H, *s*, 10α-Me), 1.73 (3H, *d*, *J* = 1.5 Hz, 16-Me), 3.06 and 3.37 (2H, ABq, *J* = 11.0 Hz, 4β-CH_2–OH), 5.49 (1H, *br*, $W_{1/2}$ = 6.0 Hz, 15-H). ^{13}C NMR: δ 15.32 (*q*, C-20), 16.87 (2 × *q*, C-17, C-19), 17.76 (*t*, C-11), 18.09 (*t*, C-2), 24.33 (*t*, C-12), 37.08 (*t*, C-3), 37.08 (*t*, C-6), 38.06 (*s*, C-4), 38.71 (*s*, C-10), 39.73 (*t*, C-14), 42.51 (*t*, C-1), 43.46 (*d*, C-13), 46.54 (*d*, C-9), 49.42 (*d*, C-5), 62.35 (*s*, C-8), 71.02 (*t*, C-18), 129.12 (*d*, C-15) 144.71 (*s*, C-16), 214.82 (*s*, C-7).

Acetylsiderone (**3**). This was obtained as an oil by pyridine–Ac_2O treatment of **1** as usual; positive TNM test. IR ν_{max}^{Nujol} cm^{-1}: 1725 (broad CO and AcO), 1250 (AcO), 1650 (C=C), 3030 and 825 (trisubstituted C=C). ^{1}H NMR: δ 0.88 (3H, *s*, 4α-Me), 1.22 (3H, *s*, 10α-Me), 1.75 (3H, *d*, *J* = 1.5 Hz, 16-Me), 2.08 (3H, *s*, OAc), 3.78 (2H, *s*, 4β-CH_2OAc), 5.60 (1H, *br*, $W_{1/2}$ = 6.0 Hz, 15-H).

Dihydrosiderone (**4**). Catalytic hydrogenation of compound **1** on 10% Pd/C in EtOH soln required 1 mol of H_2 and gave a product as a syrup containing 80% of dihydro-siderone (**4**) and 20% of its 16α-epimer (GC), negative TNM test. IR ν_{max}^{Nujol} cm^{-1}: 3460 (OH), 1720 (C=O), no C=C band. ^{1}H NMR: δ 0.68 (3H, *s*, 4α-Me), 0.96 (3H, *s*, 10α-Me), 0.98 (3H, *d*, *J* = 6.0 Hz, 16-Me), 3.02 and 3.40 (2H, ABq, *J* = 11.0 Hz, 4β-CH_2OH).

Jones oxidation of siderone (**1**) Jones reagent (2 ml) was added to an ice-cooled soln of siderone (10 mg) in Me_2CO (5 ml); after 2 hr, the soln was diluted with H_2O (15 ml) and the ppt collected afforded 8 mg of *ent*-7-oxo-kaur-15-en-18-oic acid (**5**), mp 214–215° (from EtOH–H_2O) identified by comparison with an authentic marker (mmp, IR, ^{1}H NMR) [5].

Huang–Minlon reduction of **1** *to yield* ent-*kaur*-15-*en*-18-*ol* (**6**). Compound **1** (10 mg) was reduced with 98% N_2H_4 (2 ml) in a soln of diethylene glycol (6 ml) and dry EtOH (2 ml) according to the usual procedure. The alcohol (**6**) crystallized from petrol as needles mp 134–135°, and was identical (mmp, TLC, IR and NMR) with the product described previously [6].

$NaBH_4$ *reduction of* **1** *to yield* ent-*kaur*-15-*en*-7β,18-*diol* (*episideridiol*) (**7**). Siderone (5 mg) in dry MeOH (5 ml) was treated with $NaBH_4$ (15 mg) at room temp. for 12 hr and after normal work-up gave a diol identical in all respects with the episideriol (**7**), mp 197–198° from (MeOH–H_2O) previously reported [4]. IR spectra superimposable.

Partial synthesis of siderone (**1**). *Jones oxidation of* ent-18-*acetoxy-kaur*-15-*ene* (**2**) *to yield compounds* **3** *and* **8**. Oxidation of sideripol (**2**, 200 mg) was carried out using the same conditions described for **1**. The crude product gave two spots on TLC (cyclohexane–EtOAc, 3:7) with R_f = 0.60 and 0.75, therefore it was chromatographed on silica gel (deactivated with 15% H_2O). Elution with cyclohexane–EtOAc (1:1) gave the substance with R_f = 0.75, elution with cyclohexane–EtOAc (1:2) yielded the substance with R_f = 0.60. The first was identical with acetylsiderone (**3**) (TLC, IR, NMR), which by hydrolysis with 10% ethanolic KOH in the usual manner gave a compound identical (mmp, TLC, IR, NMR) with siderone (**1**). The second compound, mp 82–84° (spontaneously on cooling), negative TNM test. IR ν_{max}^{Nujol} cm^{-1}: no C=C band. ^{1}H NMR: δ 0.89 (3H, *s*, 4α-Me), 1.08 (3H, *s*, 10α-Me), 1.46 (3H, *s*, 16-Me, on epoxy ring), 2.05 (3H, *s*, OAc), 3.08 (1H, *s*, 15-H, on epoxy ring), 3.72 (2H, *s*, 4β-CH_2OAc). Hence the substance was *ent*-18-acetoxy-7-oxo-15β,16β-epoxykaurane (**9**). Hydrolysis with 10% ethanolic KOH gave *ent*-7-oxo-15β,16β-epoxykaurane-18-ol (**9**), mp 178° (from EtOAc), negative TNM test. IR ν_{max}^{Nujol} cm^{-1}: 3480 (OH), 1715 (C=O). MS *m/z*: 318 [M]$^+$. ^{1}H NMR: 0.78 (3H, *s*, 4α-Me), 1.10 (3H, *s*, 10α-Me), 1.45 (3H, *s*, 16-Me, on epoxy ring), 3.11 (1H, *s*, 15-H, on epoxy ring), 3.06 and 3.37 (2H, ABq, *J* = 11.0 Hz, 4β-CH_2–OH).

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