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DITERPENES FROM *SIDERITIS SICULA* UCRIA

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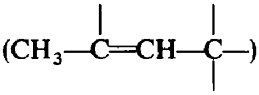
Abstract—Two new diterpenes, *sideridiol* $C_{20}H_{32}O_2$ and *siderol* $C_{22}H_{34}O_3$ were extracted from the corols of *Sideritis sicula* Ucria (Fam. Labiatae). Their structures were elucidated as I and IX, respectively, and the absolute configuration was proved to be related to (−)-isokaurene.

Sideritis sicula Ucria (Fam. Labiatae) is a perennial herbaceous shrub growing in barren, stony sites on the mountains of southern Italy and Sicily. The stems and leaves are covered with a whitish, felty toment and the flowers (from June to July) have a yellow corol. The species was once misnamed *Stachys italica* Mill.: but the present name *Sideritis sicula* Ucria was currently accepted for the shrub we studied.* The material used for this work was collected on the high summits of Madonie Mounts (Sicily) at 1500–1900 m.s.l.

From the petrol ether extract of the petals we obtained two crystalline products, having formula $C_{20}H_{32}O_2$ (*sideridiol*) and $C_{22}H_{34}O_3$ (*siderol*) respectively.†

Sideridiol $C_{20}H_{32}O_2$ (I) gave a positive test with TNM. Its IR spectrum has no band for CO, but has absorption maxima for an OH and for a trisubstituted double bond.

The NMR spectrum shows two tertiary Me's at 0·68 δ and 1·08 δ,‡ one Me on a double bond (D, 1·72 δ, J = 1·5 Hz) coupled to a vinyl proton with allylic interaction  ($CH_3—C=CH—C—$); the vinyl proton (5·50 δ) is not a well resolved quartet, but the width of the signal (5·0 Hz) excludes further vicinal couplings. The hydrogenation of the double bond does not affect the shifts of both Me's. There are, therefore: 2 hydroxyls (2H, 3·23 δ), an AB quartet with J = 11·0 Hz (geminal) and shifts 2·90 and 3·49 δ, partially overlapped to another proton (3·60 δ). The latter signals are shifted downfield on acetylation, and do not change on hydrogenation. These results

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* We thank Dr. A. Di Martino (Botanical Institute, University of Palermo) for identification of this species.

† A preliminary announcement of the isolation of these two products was published some years ago.[1]

‡ On C-4 and C-10 respectively. This assignment follows from the comparison of the angular Me in 18-hydroxy-atractylane (0·95 δ) and atractylanic acid methyl ester (0·95 δ).[2] The 4β-substituents do not influence the angular 10α-CH_3. See also the behaviour on acetylation. Angular methyls were found to be broader than tertiary methyls on C-4 in all the derivatives studied, because of stronger long-range interaction.

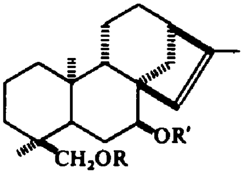
prove the presence of the $-\overset{|}{\underset{|}{C}}-CH_2OH$ and $\overset{|}{\underset{|}{C}}H-OH$ groups: the primary alcohol has to be near a quaternary, probably asymmetric carbon, as suggested by the non-equivalence of the two protons of the methylene group. As the signal of CH–OAc in diacetyl-sideridiol (II) is a small triplet (4·75 $\delta \cdot W_{\frac{1}{2}}$ = 6·0 Hz), i.e. the X part of an ABX spectrum, it follows that this hydrogen is coupled with only two adjacent protons; moreover it must be equatorial, any diaxial interaction being excluded by the small width of the signal.

The ease with which *diacetyl-sideridiol* $C_{24}H_{36}O_4$ (II) is obtained confirms the presence of two OH functions especially as alkaline hydrolysis restores sideridiol.

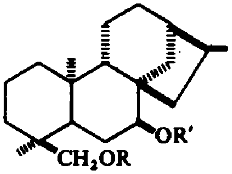
Catalytic hydrogenation required one mole of H_2 and yields *dihydro-sideridiol* $C_{20}H_{34}O_2$ (III)* [negative TNM test; IR: no C=C band; NMR: no vinyl proton, disappearance of the allylic Me, occurrence of a secondary Me, clearly visible in the diacetate (X): D, 0·99 δ, J_{obs} = 6 Hz, benzene-d6].

Also the titrations of sideridiol and diacetyl-sideridiol with perbenzoic acid indicate that only one double bond is present: hence the substance must have a tetracyclic skeleton.

Selenium dehydrogenation of sideridiol gives a complex mixture of 1-methyl-phenanthrene, 1,7-dimethyl-phenanthrene (pimanthrene), 1-methyl-7-ethyl-phenanthrene and 1-methyl-7-isopropyl-phenanthrene (retene) identified by VPC.† These and the above results suggest a tetracyclic isokaurene system.



I: R = H, R′ = H
II: R = Ac, R′ = Ac
IX: R = H, R′ = Ac



III: R = H, R′ = H
X: R = Ac, R′ = Ac
XIII: R = H, R′ = Ac

The oxidation of sideridiol by Jones' reagent affords a *keto-acid* $C_{20}H_{28}O_3$ (IVa) (positive TNM test, negative Zimmermann test), whose IR spectrum accounts for a COOH, a C_6-ring CO and a trisubstituted double bond. Its *methyl ester* (IVb) $C_{21}H_{30}O_3$ has in the IR spectrum the typical band for an equatorial COOMe on C-4.[4] This is supported by the chemical shifts of the CH_2OH protons in the NMR spectrum of I: the values agree with the ones reported[5] for an equatorial CH_2OH on C-4 (compare especially the methylene shift in 18-hydroxy-(−)-kaurene: 3·42 and 3·09 δ). Moreover the shifts of tertiary Me's in the diacetate II (ang. 1·10 δ, tert 0·83 δ) agree with the 4-position and the equatorial orientation of the ester group:

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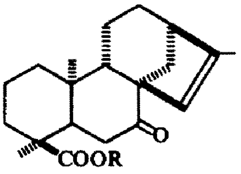
* The product was assigned the 16β-CH_3 configuration, as it is known that catalytic hydrogenation of a 15–16 double bond in a (−)-kaurane backbone yields only this epimer because of the easier attack from the less hindered α side.

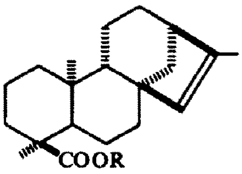
† Similar results in the VPC examination of a complex mixture of phenanthrenic hydrocarbons were reported in the case of the nor-diterpenoid atractyligenin.[3]

the angular 10α-Me is not affected, as expected, by the 4β-substituent, whereas the geminal 4α-Me is shifted slightly downfields on going from I to II.

Huang-Minlon reduction of the keto-acid (IVa) yields an *acid* $C_{20}H_{30}O_2$ (Va) whose *methyl ester* $C_{21}H_{32}O_2$ (Vb) has physical constants in good agreement with the values described[6] for *methyl* (−)-*kaur*-15-*en*-18-*oate*. Comparison of the IR spectra of the products prove their identity.

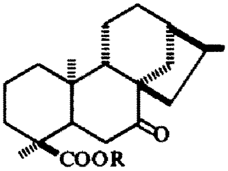


IVa: R = H
IVb: R = Me

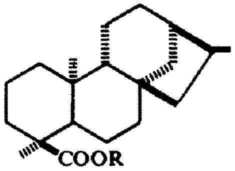


Va: R = H
Vb: R = Me

Jones oxidation of dihydro-sideridiol (III) gives the saturated *keto acid* $C_{20}H_{30}O_3$ (VIa), which on Huang–Minlon reduction affords an *acid* $C_{20}H_{32}O_2$ (VIIa) whose *methyl ester* $C_{21}H_{34}O_2$ (VIIb) is identical with the known[6] *methyl* 16β-(−)-*kauran*-18-*oate*.



VIa: R = H
VIb: R = Me



VIIa: R = H
VIIb: R = Me

These results prove the structure and the absolute configuration of sideridiol as I except for the position and the configuration of the secondary OH group. This was determined as follows.

The position 3 is excluded in accordance with the heat stability of the keto acids IVa and VIa; the negative Zimmermann test for both IVa and VIa also excludes the positions 1 and 2. Positions 6, 11, 12 and 2 are excluded because the proton near the oxygen (CH–OAc) is coupled with no more than two adjacent hydrogens. Taking into account that this proton must be equatorial, the positions 6-ax, 12-ax, 14-ax for the OH group are unlikely, because no appreciable shift of the tertiary Me's is observed in the monoacetyl derivative at the secondary alcoholic function (0·71 and 1·01 δ, see later: siderol), in comparison with I (0·68 and 1·08 δ). Position 7 is likely and supported by comparing the shifts of the H-15 vinyl proton in I (5·50 δ), II (5·24 δ), IX (5·30 δ) and Vb (5·06 δ): considering no influence at all on the vinyl proton by the substituents at C-4 which are too far away, it follows that the strong deshielding from Vb to I (Δ = 0·44 δ) may be due only to an axial 7β-OH, that lies nearly in the plane ($\vartheta \cong 30°$) of the double bond. This situation reproduces the 1,3-diaxial relationship in the cyclohexane ring. On acetylation of the OH group, the vinyl proton goes slightly upfield (5·30 δ): this behaviour is in agreement with the data reported by Okamoto and Kawazoe.[7]

The NMR spectrum of IVb shows the vinyl proton quartet (J_{allyl} = 1·5 Hz) at 5·50 δ, the allylic Me (D, J = 1·5 Hz) at 1·74 δ, a COOMe (3·66 δ) and the two tertiary Me's at 1·19 and 1·21 δ. The keto group on C-7 agrees with the deshielding (Δ = 0·44 δ) of H-15 from Vb to IVb; also the small deshielding of the angular Me on going from Vb (1·05 δ) to IVb can be explained because this Me lies, not near, but in the negative conical zone of the keto group.

Deuterium exchange of the ester (VIb) gave 85% of d_2-product and 15% of d_1-product (mass spectrum).

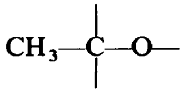
Determinations of ORD and CD on VIb gave a positive Cotton effect. Such evidence proves definitely the occurrence of the keto group at position 7.

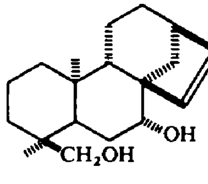
LAH reduction of IVb supported the configuration attributed to C-7: a mixture of sideridiol and its 7α-OH epimer (VIII) was obtained, in the approx 90:10 ratio, according to the easier attack from the less hindered α side.

Sideridiol therefore has the structure and the absolute configuration depicted in I.

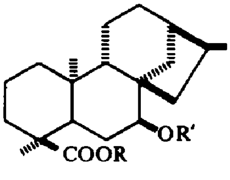
Siderol $C_{22}H_{34}O_3$, the second extractive from *Sideritis sicula*, on alkaline hydrolysis affords I. The structure of a monoacetyl derivative of sideridiol was proved to be IX with the acetyl group on the secondary OH function. This was easily shown by the presence of an acetyl group at 2·08 δ and by the downwards shift of the H-7 proton (4·72 δ) in the NMR spectrum of IX when compared with the NMR spectrum of I, while the signal of the CH_2OH protons remain unchanged (3·03 and 3·36 δ).

By acetylation, siderol (IX) gave diacetyl-sideridiol (II). Catalytic hydrogenation of IX gave *dihydro-siderol* (XIII), which was oxidized to 7β-*acetoxy*-16β-(–)-*kauran*-18-*oic acid* (XIa), from which 7β-*hydroxy*-16β-(–)-*kauran*-18-*oic acid* (XIIa) was obtained by alkaline hydrolysis. The latter was eventually oxidized to 7-keto-16β-(–)-kauran-18-oic acid (VIa); the same correlation was performed by oxidation of XIIb to VIb.

Jones oxidation of siderol (IX), followed by CH_2N_2 treatment, afforded a mixture of *methyl* 7β-*acetoxy*-(–)-*kaur*-15-*en*-18-*oate* (XIV) and *methyl* 7β-*acetoxy*-15,16α-*epoxy*-16β-(–)-*kauran*-18-*oate* (XVa):* the structure of the latter was proved by negative TNM test, molecular weight (mass spectrum) and by the occurrence in its NMR spectrum of a typical signal for a proton on an epoxy ring (S, 3·01 δ) and a  $CH_3{-}\overset{|}{\underset{|}{C}}{-}O{-}$ (S, 1·43 δ). On alkaline hydrolysis, XVa gave 7β-*hydroxy*-15,16α-*epoxy*-16β-(–)-*kauran*-18-*oic acid* (XVb).



VIII



XIa: R = H, R' = Ac
XIb: R = Me, R' = Ac
XIIa: R = H, R' = H
XIIb: R = Me, R' = H

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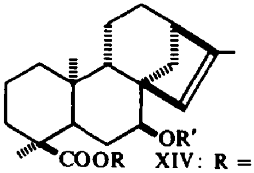
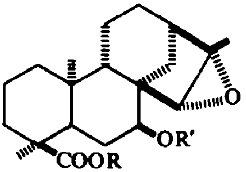
* The epoxide ring is assumed to have αα-orientation in accordance with the attack on the less hindered



XIV: R = Me; R′ = Ac



XVa: R = Me, R′ = Ac
XVb: R = H, R′ = H
XVc: R = Me, R′ = H

The structure of siderol is therefore 7-monoacetyl-sideridiol (IX).

To our knowledge, these diterpenes are the first examples of (−)-isokaurene derivatives with OH functions on C-7.

EXPERIMENTAL

M.ps (determined in capillary tubes) are uncorrected. Pet. ether refers to the 40–70° fraction (C. Erba pure reagent). TLC was run on chromatoplates of silica gel G Merck; for preparative chromatography on column, silica gel Merck (0·05–0·20 mm) and neutral aluminium oxide Merck was employed.

NMR spectra were run on a Varian A-60 spectrometer: the chemical shifts are expressed in ppm, taking TMS as internal standard with $\delta = 0$. IR spectra were recorded on a Perkin–Elmer Infracord 137 spectrophotometer. $[\alpha]_D^{20^\circ}$ measurements were performed in EtOH soln on a Perkin–Elmer 141 polarimeter.

Extraction. Vacuum-dried corols (1 kg) were extracted in Soxhlet for 48 hr with 10 l. pet. ether. From the solvent, concentered to 500 ml, a white crystalline ppt (14·5 g) was collected: *siderol,* m.p. 152–153° (from pet. ether). After concentration of mother liquid, a white powder was collected (4·5 g): *sideridiol,* m.p. 196–197° (from aqueous MeOH). From the filtrate, a yellow sticky residue (23·5 g) was obtained after evaporation under vacuum: chromatography on Al_2O_3 act. 1 (eluent benzene–AcOEt 2:1) afforded 3 g of siderol.

Sideridiol (I). White needles, m.p. 196–197° (from aqueous MeOH), weak positive TNM test, $[\alpha]_D^{20^\circ} = +19^\circ$ (*c*, 0·87). (Found: C, 78·87; H, 10·47. $C_{20}H_{32}O_2$ requires: C, 78·89; H, 10·59. M.W.: Found* 297; $C_{20}H_{32}O_2$ requires: 304·46); IR spectrum (KBr): 3560 and 3460 cm^{-1} (OH), 1645 cm^{-1} (C═C), 830 and 3055 cm^{-1} (trisubstituted C═C);† NMR spectrum ($CDCl_3$): 0·68 δ (S, t-Me), 1·08 δ (S, ang-Me), 1·72 δ (D, J = 1·5 Hz, allylic Me), 2·90 and 3·49 δ (Q_{AB}, J_{gem} = 11·0 Hz, $-\overset{|}{\underset{|}{C}}-CH_2OH$), 3·60 δ (T, $W_{1/2}$ = 6 Hz, $>C\underline{H}-OH$), 5·50 δ (broad Q, $W_{1/2}$ = 5 Hz, $-CH=C<$), 3·23 δ (S, 2 OH).

Diacetyl-sideridiol (II). This was obtained by pyridine-Ac_2O treatment and had m.p. 128–129° (from aqueous EtOH); positive TNM test (yellow). $[\alpha]_D^{20^\circ} = +37^\circ$ (*c*, 1·90). (Found: C, 74·01; H, 9·58. $C_{24}H_{36}O_4$ requires: C, 74·19; H, 9·34); IR spectrum (nujol): 1735 and 1255 cm^{-1} (AcO), 822 cm^{-1} (trisubstituted C═C), no OH band; NMR spectrum ($CDCl_3$): 0·83 δ (S, t-Me), 1·10 δ (S, ang-Me), 1·71 δ (D, J = 1·5 Hz, allylic Me), 2·05 and 2·08 δ (S, 2 AcO), 3·68 δ (S, $C\underline{H}_2OAc$), 4·75 δ (T, $W_{1/2}$ = 6 Hz, $>C\underline{H}-OAc$), 5·24 δ (broad, $W_{1/2}$ = 5 Hz, $-C\underline{H}=C<$).

Refluxing 4 hr with 10% ethanolic KOH restored sideridiol, m.p. 196–197°, IR spectra superimposable.

Dihydro-sideridiol (III). By hydrogenation on 10% Pd-C in EtOH soln, sideridiol took up 1 mole H_2. The product had m.p. 155–156° (from EtOH), negative TNM test; $[\alpha]_D^{20^\circ} = +25^\circ$ ($CHCl_3$; *c*, 0·66). (Found: C, 78·29; H, 11·30. $C_{20}H_{34}O_2$ requires: C, 78·38; H, 11·18); IR spectrum (nujol): 3350–3400 cm^{-1} broad (OH), no C═C band; NMR spectrum ($CDCl_3$): 0·70 δ (S, t-Me), 1·07 δ (S, ang-Me, partially overlapped to other signals due to s-Me), 2·89 and 3·49 δ (Q_{AB}, J_{gem} = 11·5 Hz, $-\overset{|}{\underset{|}{C}}-C\underline{H}_2OH$), 3·56 δ (broad, $>C\underline{H}-OH$), 3·05 δ (S, 2 OH).

Diacetyl-dihydro-sideridiol (X). This was obtained by pyridine-Ac_2O treatment of III and had m.p. 159–160° (prismatic needles from EtOH), negative TNM test; $[\alpha]_D^{20^\circ} = +18^\circ$ (*c*, 1·09). (Found: C, 74·11; H, 9·69. $C_{24}H_{38}O_4$ requires: C, 73·80; H, 9·81); IR spectrum (nujol): 1735 and 1250 cm^{-1} (AcO), no OH

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* Vapor pressure osmometer Mechrolab 301 A, solvent dioxan.

† This last band was better observed on a Perkin Elmer Infracord 237 spectrophotometer.

and C═C band; NMR spectrum (CCl_4): 0·82 δ (S, t-Me), 1·07 δ (S, ang-Me), 1·95 and 1·97 δ (S, 2 AcO), 3·62 δ (S, CH_2OAc), 4·65 δ (T, $W_{\frac{1}{2}}$ = 5 Hz, C<u>H</u>—OAc); (benzene-d6): 0·68 δ (S, t-Me), 0·88 δ (S, t-Me), 0·99 δ (D, J_{obs} = 6 Hz, s-Me).

Perbenzoic acid titration on sideridiol (I) *and diacetyl-sideridiol* (II). The oxidations were performed at 0–2° during 3 days on 0·5 mmoles of substance in $CHCl_3$ soln of perbenzoic acid;[8] 0·1 N $Na_2S_2O_3$ was used for titration. The results are tabulated as follows, reporting the number of oxidized double bonds:

	6 hr	24 hr	48 hr	72 hr
Sideridiol	0·90	1·06	1·06	1·06
Diacetyl-sideridiol	0·70	1·06	1·10	1·10
Blank	0·00	0·00	0·00	0·00

Selenium dehydrogenation of sideridiol (I). Sideridiol (1 g) and Se powder (2 g) were heated 8 hr at 280° and 3 hr at 300° in a long-necked flask; after elimination of Se, an oily residue was obtained and distilled (185–190°/0·4 mmHg): the distillate (320 mg) containing ~20% of phenanthrenic hydrocarbons (quantitative UV estimation) was treated with trinitrobenzene and the crystalline adduct decomposed on basic aluminium oxide (Merck). The hydrocarbons mixture submitted to VPC* revealed many peaks: 4 of them, accounting for ~75% of the total, were identified from their T_R as *1-methyl-phenanthrene* (40–42%), *pimanthrene* (7–8%), *1-methyl-7-ethyl-phenanthrene* (2–3%) and *retene* (24%); the identification was confirmed by crossed injection with authentic specimens. The other peaks were attributed to unidentified naphtalenic hydrocarbons (14–16%) and high boiling products (10%).

Jones oxidation of sideridiol (I): *7-keto-(−)-kaur-15-en-18-oic acid* (IVa). Jones' reagent (3 ml) was dropped into a soln of sideridiol (500 mg) in acetone (20 ml); after 3 hr, water (100 ml) was added and the ppt collected: m.p. 214–215° (from aqueous EtOH), weight 400 mg; positive TNM test (faint yellow), negative Zimmermann test;[9] $[\alpha]_D^{20^\circ} = -22^\circ$ (*c*, 1·98). (Found: C, 75·99; H, 8·99. $C_{20}H_{28}O_3$ requires: C, 75·91; H, 8·91%); IR spectrum (nujol): 1735 cm^{-1} (C_6-ring CO), 1705 cm^{-1} (COOH), 829 cm^{-1} (trisubstituted C═C).

Methyl 7-keto-(−)-kaur-15-en-18-oate (IVb). This was prepared by CH_2N_2 treatment of IVa: m.p. 94–95° (needles from aqueous EtOH); positive TNM test (yellow); $[\alpha]_D^{20^\circ} = -22^\circ$ (*c*, 2·02). (Found: C, 76·09; H, 9·51. $C_{21}H_{30}O_3$ requires: C, 76·32; H, 9·15); IR spectrum (nujol): 1720 cm^{-1} ($COOCH_3$), 1708 cm^{-1} (C_6-ring CO), 1245 cm^{-1} (equatorial COOMe on C-4), 826 cm^{-1} (trisubstituted C═C); NMR spectrum ($CDCl_3$): 1·19 and 1·21 δ (S, 2 t-Me), 1·74 δ (D, *J* = 1·5 Hz, allylic Me), 3·66 δ (S, COOMe), 5·50 δ (broad, $W_{\frac{1}{2}}$ = 5 Hz, $-CH{=}C\langle$).

Huang-Minlon reduction of IVa: *(−)-kaur-15-en-18-oic acid* (Va). The keto acid (300 mg) was reduced with 98% N_2H_4 (5 ml) in a soln of diethylene glycol (15 ml) and anhyd EtOH (5 ml) according to usual procedures. The product had m.p. 170–172° (from aqueous EtOH); positive TNM test (yellow); $[\alpha]_D^{20^\circ} = -4^\circ$ (*c*, 0·60). (Found: C, 79·16; H, 10·13. $C_{20}H_{30}O_2$ requires: C, 79·42; H, 10·00%); IR spectrum (nujol): 1725 cm^{-1} (COOH), 819 cm^{-1} (trisubstituted C═C).

Methyl (−)-kaur-15-en-18-oate (Vb). This was obtained by CH_2N_2 treatment of Va: m.p. 115–116°, $[\alpha]_D^{20^\circ} = -2^\circ$ ($CHCl_3$; *c*, 0·55).† (Found: C, 79·52; H, 10·25. $C_{21}H_{32}O_2$ requires: C, 79·70; H, 10·19); IR spectrum (nujol): 1725 cm^{-1} (COOMe), 1255 cm^{-1} (equatorial COOMe on C-4), 819 cm^{-1} (trisubstituted C═C)‡ NMR spectrum ($CDCl_3$): 1·05 δ (S, ang-Me), 1·14 δ (S, t-Me), 1·68 δ (D, *J* = 1 Hz, allylic Me), 3·65 δ (S, COOMe), 5·06 δ (broad Q, $W_{\frac{1}{2}}$ = 4·5 Hz, $-CH{=}C\langle$).

Jones oxidation of dihydro-sideridiol (III):

7-Keto-16β-(−)-kauran-18-oic acid (VIa). Dihydro-sideridiol (500 mg) gave the keto-acid (400 mg), m.p. 206–207° (from aqueous EtOH); negative TNM test, negative Zimmermann test; $[\alpha]_D^{20^\circ} = -15^\circ$

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* A Wilkens Aerograph HyFi A-600 instrument with flame ionization detector was used, carrier gas N_2 1·2 atm, temp 220°; two different 5′ × ⅛″ columns were employed, the first packed with 10% Silicone Oil DC-710 on W-HMDS Chromosorb, the second packed with 10% Apiezon L on W-HMDS Chromosorb. T_R values for the identified hydrocarbons were, on the two columns resp., 1·61–1·66, 2·34–2·50, 3·20–3·46, 3·83–4·07 (phenanthrene, T_R = 1·00).

† Ourisson[6] reported m.p. 123° and $[\alpha]_D^{20^\circ} = 0^\circ$ ($CHCl_3$ soln).

‡ We thank Prof. G. Ourisson for the comparison of IR spectra of our product and his specimen.

(*c*, 1·83). (Found: C, 75·84; H, 9·59. $C_{20}H_{30}O_3$ requires: C, 75·45; H, 9·50%); IR spectrum (nujol): 1725 cm^{-1} (C_6-ring CO), 1695 cm^{-1} (COOH).

Methyl 7-keto-16β-(−)-kauran-18-oate (VIb). This was prepared by CH_2N_2 treatment of VIa: m.p. 82–83° (from aqueous EtOH); negative TNM test, negative Zimmermann test; $[\alpha]_D^{20^\circ} = -9°$ (*c*, 0·45). (Found: C, 75·82; H, 9·72. $C_{21}H_{32}O_3$ requires: C, 75·86; H, 9·70%); IR spectrum (nujol): 1725–1700 cm^{-1} broad (C_6-ring CO and COOMe), 1255 cm^{-1} (equatorial COOMe on C-4). ORD*: positive Cotton effect, $[\alpha]_{307} = +1305°$ (EtOH; *c*, 0·1). CD:** positive Cotton effect, $\Delta\varepsilon = +2·26$ (dioxan; *c*, 0·097).

Huang-Minlon reduction of VIa:

16β-(−)-*Kauran-18-oic acid* (VIIa). Compound VIa was reduced according to the conditions reported for the reduction of IVa. The product had m.p. 180–181° (from aqueous EtOH), $[\alpha]_D^{20^\circ} = -35°$ (*c*, 1·08). (Found: C, 79·11; H, 10·59. $C_{20}H_{32}O_2$ requires: C, 78·89; H, 10·59%); IR spectrum (nujol): 1700 cm^{-1} (COOH).

Methyl 16β-(−)-kauran-18-oate (VIIb). This was obtained by CH_2N_2 methylation of VIIa and by catalytic hydrogenation of IVb: m.p. 126–127° (long prisms from MeOH), $[\alpha]_D^{20^\circ} = -35°$ (*c*, 1·05).† (Found: C, 79·29; H, 10·77. $C_{21}H_{34}O_2$ requires: C, 79·19; H, 10·76%). IR spectrum (nujol): 1725 cm^{-1} (COOMe), 1250 cm^{-1} (equatorial COOMe on C-4).‡

Deuteherium exchange of methyl 7-keto-16β-(−)-kauran-18-oate (VIb). Sodium (50 mg) was dissolved in pure dioxan (1·5 ml) and D_2O (1·5 ml), then the keto-ester (30 mg) was added. The soln was kept at 70° under N_2 flow during 30 min then evaporated under reduced press; the residue was taken up with dil HCl, collected, dried and treated with CH_2N_2: m.p. 82–82·5° (from aqueous EtOH). MS†† *m/e* 332 absent, *m/e* 333 and 334 present in the 15:85 ratio.

LAH reduction of IVa

Sideridiol (I) *and 7-epi-sideridiol* (VIII). The keto-acid (250 mg) was reduced with excess LAH in Et_2O soln. The crude product gave two spots on TLC (eluent benzene–AcOEt 3:7) with R_f 0·60 and 0·45 and was repeatedly chromatographed on silica gel (20 g).

Elution with benzene–AcOEt (1:1) afforded the first substance, m.p. 196–197°, $R_f = 0·60$, identified as *sideridiol* (I) by comparison of IR spectra mixed m.p. and TLC: it accounted for the greater part of the product (≥ 90%).

Elution with benzene–AcOEt (1:2) yielded the second substance in very small quantity (4–5 mg), m.p. 197–198°, $R_f = 0·45$, positive TNM test. (Found: C, 78·84; H, 10·91. $C_{20}H_{32}O_2$ requires: C, 78·89; H, 10·59%); IR spectrum (KBr): 3350 cm^{-1} broad (OH), 1655 cm^{-1} (C═C), 817 cm^{-1} (trisubstituted C═C). The substance was assumed to be the 7α-OH epimer (VIII) of sideridiol.

Siderol (IX). White soft needles, m.p. 152–153° (from pet. ether), positive TNM test (faint yellow), $[\alpha]_D^{20^\circ} = +43°$ (*c*, 1·96). (Found: C, 76·24; H, 9·92. $C_{22}H_{34}O_3$ requires: C, 76·26; H, 9·89%); IR spectrum (KBr): 3500 cm^{-1} (OH), 1715 and 1265 cm^{-1} (AcO), 1648 cm^{-1} (C═C), 3060 and 820 cm^{-1} (trisubstituted C═C); NMR spectrum ($CDCl_3$): 0·71 δ (S, t-Me), 1·08 δ (S, ang-Me), 1·72 δ (D, $J = 1·5$ Hz, allylic Me), 2·08 δ (S, AcO), 3·03 and 3·35 δ (Q_{AB}, $J_{gem} = 11·0$ Hz, $-\overset{|}{\underset{|}{C}}-C\underline{H}_2OH$), 4·71 δ (T, $W_{\frac{1}{2}} = 6$Hz, $>CH-OAc$), 5·28 δ (broad, $W_{\frac{1}{2}} = 4·5$ Hz, $-CH{=}C<$).

Refluxing 4 hr with 10% ethanolic KOH gave *sideridiol* (I), m.p. 196–197°, IR spectra superimposable. Pyridine-Ac_2O treatment afforded *diacetyl-sideridiol* (II), m.p. 128–129°, IR spectra superimposable.

Dihydro-siderol (XIII). This was prepared by hydrogenation of siderol (IX) with 10% Pd-C in EtOH soln: 1 mole H_2 was absorbed. The product had m.p. 152–153° (from aqueous EtOH), negative TNM test, $[\alpha]_D^{20^\circ} = +16°$ (*c*, 1·92). (Found: C, 75·69; H, 10·55. $C_{22}H_{36}O_3$ requires: C, 75·81; H, 10·41%); IR spectrum (nujol): 3450 cm^{-1} (OH), 1718 and 1270 cm^{-1} (AcO).

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[**] By the courtesy of Prof. G. Ourisson (Institut de Chimie, Université de Strasbourg).

[†] Ourisson[6] reported m.p. 121° and $[\alpha]_D^{20^\circ} = -30°$.

[‡] We thank Prof. G. Ourisson for the comparison of IR spectra of our product and his specimen.

[††] Mass spectra were registered by Dr. A. Selva (Istituto di Chimica, Politecnico di Milano) to whom our thanks are due. An Hitachi Perkin Elmer RMU6D spectrometer was used, ionisation potential 70 eV, direct inlet into ionization chamber.

Refluxing 4 hr with 10% ethanolic KOH yieldel *dihydro-sideridiol* (III), m.p. 155–156°, IR spectra superimposable. Pyridine-Ac_2O treatment afforded *diacetyl-dihydro-sideridiol* (X), m.p. 159–160°, IR spectra superimposable.

Jones oxidation of siderol (IX)

Methyl 7β-acetoxy-(–)-kaur-15-en-18-oate (XIV) *and methyl 7β-acetoxy-15,16α-epoxy-16β-(–)-kauran-18-oate* (XVa). Jones' reagent (4 ml) was dropped into an ice-cooled soln of siderol (1 g) in acetone (20 ml): after 6 hr, water (100 ml) was added, the ppt collected, dried and treated with CH_2N_2. The crude methyl ester showed on TLC (eluent cyclohexane–AcOEt 3:1) two spots with R_f 0·85 and 0·55, therefore it was chromatographed on Al_2O_3 (act. 2): elution with cyclohexane–benzene (1:1) gave the substance with R_f = 0·85; elution with benzene yielded the substance with R_f = 0·55.

The first, m.p. 140–141° (from aqueous EtOH), positive TNM test, $[\alpha]_D^{20°} = +28°$ (*c*, 0·65), showed in its mass spectrum the peak of molecular ion at 374 *m/e*. (Found: C, 74·50; H, 9·27. $C_{23}H_{34}O_4$ requires: C, 73·76; H, 9·15%); IR spectrum (nujol): 1725–1720 cm^{-1} sl. broad (COOMe and AcO), 1250 cm^{-1} (AcO), 1245 cm^{-1} (equatorial COOMe on C-4); NMR spectrum ($CDCl_3$): 1·07 δ (S, ang-Me), 1·12 δ (S, t-Me), 1·69 δ (D, *J* = 1·5 Hz, allylic Me), 2·08 δ (S, AcO), 3·58 δ (S, COOMe), ~4·60 δ (T of 2·5 Hz, $>$CH—OAc), 5·30 δ (broad, —CH=C$<$). Hence the substance has the structure XIV of *methyl 7β-acetoxy-(–)-kaur-15-en-18-oate*.

The second, m.p. 171–172° (from cyclohexane), negative TNM tests, $[\alpha]_D^{20°} = +68°$ (*c*, 0·58), showed in its mass spectrum the peak of molecular ion at 390 *m/e*. (Found: C, 70·34; H, 8·90. $C_{23}H_{34}O_5$ requires: C, 70·74; H, 8·78%); IR spectrum (nujol): 1725 cm^{-1} (COOMe and AcO), 1245 cm^{-1} broad (AcO; equatorial COOMe; epoxyde band?); NMR spectrum ($CDCl_3$): 1·05 δ (S, ang-Me), 1·13 δ (S, t-Me), 1·43 δ (S, Me on epoxyde ring), 2·12 δ (S, AcO), 3·01 δ (S, H on epoxyde ring), 3·60 δ (S, COOMe), 4·70 δ (T of 2·5 Hz, $>$C<u>H</u>—OAc). Hence the substance has the structure XVa of *methyl 7β-acetoxy-15,16α-epoxy-16β-(–)-kauran-18-oate*.

7β-Hydroxy-15,16α-epoxy-16β-(–)-kauran-18-oic acid (XVb). A soln of 50 mg of XVa in 5 ml 5% ethanolic KOH was refluxed 3 hr; after evaporation of the solvent, the residue was taken up in water, acidified with dil HCl, collected and crystallized: m.p. 265–266° (from EtOH), negative TNM test. (Found: C, 71·35; H, 8·89. $C_{20}H_{30}O_4$ requires: C, 71·82; H, 9·04%): IR spectrum (nujol): 3450 cm^{-1} (OH), 1720 cm^{-1} (COOH).

Methyl 7β-hydroxy-15,16α-epoxy-16β-(–)-kauran-18-oate (XVc). This was obtained by CH_2N_2 treatment of XVb: m.p. 168–169° (brilliant scales, from EtOH), negative TNM test, $[\alpha]_D^{20°} = +28·5°$ (*c*, 0·10). (Found: C, 72·38; H, 9·29. $C_{21}H_{32}O_4$ requires: C, 72·38; H, 9·26%); IR spectrum (nujol): 3450 cm^{-1} (OH), (OH), 1725 cm^{-1} (COOMe), 1255 cm^{-1} (equatorial COOMe on C-4).

Jones oxidation of dihydro-siderol (XIII)

7β-Acetoxy-16β-(–)-kauran-18-oic acid (XIa). Jones' reagent (5 ml) was dropped in a soln of XIII (1 g) in acetone (20 ml); after 5 hr water (100 ml) was added and the ppt collected: m.p. 216–217° (soft needles, from aqueous EtOH), negative TNM test, $[\alpha]_D^{20°} = +25°$ (*c*, 0·89). (Found: C, 73·06; H, 9·61. $C_{22}H_{34}O_4$ requires: C, 72·89; H, 9·45%); IR spectrum (nujol): 1705 cm^{-1} (COOH), 1738 and 1265 cm^{-1} (AcO).

Methyl 7β-acetoxy-16β-(–)-kauran-18-oate (XIb). This was prepared by CH_2N_2 treatment of XIa: m.p. 171–172° (long needles, from EtOH), $[\alpha]_D^{20°} = +25°$ (*c*, 0·91). (Found: C, 73·61; H, 9·56. $C_{23}H_{36}O_4$ requires: C, 73·36; H, 9·64%); IR spectrum (nujol): 1725–1715 cm^{-1} broad (COOMe and AcO), 1255 cm^{-1} (AcO), 1245 cm^{-1} (equatorial COOMe on C-4).

7β-Hydroxy-16β-(–)-kauran-18-oic acid (XIIa). A soln of XIa (200 mg) in 10 ml 5% ethanolic KOH was refluxed 3 hr; after usual procedure, the product had m.p. 211–213° (little, soft needles, from aqueous EtOH), $[\alpha]_D^{20°} = +5°$ (*c*, 1·91). (Found: C, 74·93; H, 10·10. $C_{20}H_{32}O_3$ requires: C, 74·96; H, 10·06%); IR spectrum (nujol): 3400 cm^{-1} (OH), 1690 cm^{-1} (COOH).

Jones oxidation of XIIa gave VIa, m.p. 206–207°, no depression at mixed m.p., IR spectra superimposable.

Methyl 7β-hydroxy-16β-(–)-kauran-18-oate (XIIb). This was obtained by CH_2N_2 methylation of XIIa: m.p. 150–151° (thin needles, from aqueous EtOH), $[\alpha]_D^{20°} = +5°$ (*c*, 1·80). (Found: C, 75·88; H, 10·31. $C_{21}H_{34}O_3$ requires: C, 75·40; H, 10·25%); IR spectrum (nujol): 3400 cm^{-1} (OH), 1721 cm^{-1} (COOMe) 1245 cm^{-1} (equatorial COOMe on C-4).

Jones oxidation of XIIb yielded VIb, m.p. 82–83°, no depression at mixed m.p., IR spectra superimposable.

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