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CONSTITUENTS OF LABIATAE—XIV[1]

VIEROL AND POWEROL, TWO NEW DITERPENES FROM *SIDERITIS CANARIENSIS*

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Abstract—The two new diterpenes, vierol (**1**) [(−)kaurane-16α,18-diol] and powerol (**3**) [(−)kaurane-7β,16α-diol] have been isolated from *Sideritis canariensis* Ait. **1** was obtained by partial synthesis from epicandicandiol (**7**), and **3** was related with (−)kauranol (**6**) and (−)kauren-7β-ol acetate (**11**). Reduction of the acetoxy-aldehyde **14** by the method of Huang-Minlon and posterior acetylation gave **11**, (−)isokauren-7β-ol acetate (**17**) and (−)kauran-7β-ol acetate (**18**).

From *Sideritis canariensis* Ait. we have previously obtained, besides the already known diterpenes (−)kaurene, dehydroabietane and epicandicandiol,[2] the four new ones trachilobane, trachinol, trachinodiol,[2] and tiganone.[3] The present work reports the isolation of two new diterpenes of the (−)kaurane series from the same plant, for which we propose the names vierol (**1**) and powerol (**3**).

RESULTS AND DISCUSSION

Vierol (**1**), m.p. 209–211° and empirical formula $C_{20}H_{34}O_2$ as determined by MS (M^+ 306), in the IR lacks carbonyl and double bond absorptions, showing a band at 3320 cm^{-1} (OH). Its NMR spectrum* presents signals corresponding to a $—CH_2OH$ group (6·55 and 6·90; each 1H, d, J 12 Hz), a methyl geminal to a hydroxyl at 8·60 and further two at 8·92 and 9·25. Mild acetylation gave the monoacetate **2**, the IR spectrum of which shows OH and OAc absorptions (3300 and 1740, 1250 cm^{-1}). In the NMR spectrum the $—CH_2OAc$ group appears as a quartet centred at 6·28. The position of these two protons in the acetate as well as in the alcohol indicates that the primary OH must be equatorial;[4] this is also deduced from comparing the chemical shifts of the Me groups at C_4 and C_{10} with the corresponding ones in epicandicandiol (**7**) and its diacetate (**12**).[5,6] On the basis of the aforesaid spectroscopic data, vierol is assigned structure **1** [(−)kaurane-16α,18-diol]. This was confirmed by synthesis from epicandicandiol as follows:

7 was oxidized with Jones reagent to give keto-aldehyde **8** and keto-acid **9**. Reduction of the latter to acid **10** by the method of Huang-Minlon and subsequent epoxidation with *m*-chloro-perbenzoic acid yielded **15** which would not crystallize. The epoxide was then reduced with LAH giving, besides starting material, two compounds. One, obtained in very small quantity, was identified as diol **16** by NMR, and the other proved to be identical in all respects with vierol. In structure **1** the configuration of the OH at C_{16} is shown as α taking into account that the epoxide **15** is always formed from the α side.[7]

The second diterpene powerol, $C_{20}H_{34}O_2$ (M^+ 306), m.p. 219–222°, $[\alpha]_D$ 3°, is assigned structure **3** [(−)kaurane-7β,16α-diol] based on the following considerations. Its NMR spectrum is similar to that of vierol except that it shows the presence of four methyl groups (8·62, 8·84, 9·12 and 9·15) and instead of a $—CH_2OH$ group a proton geminal to a secondary axial OH, the signal of which appears as a triplet at 6·30 ($W_{1/2}$ = 6 Hz). Mild acetylation of **3** gave monoacetate **4** which was dehydrated with $SOCl_2$ in pyridine to give a mixture of two compounds which were separated by dry column chromatography on silica gel impregnated with $AgNO_3$. One of them (m.p. 101–102°) has the characteristic IR and NMR absorptions of methylene groups (3025, 1640, 875 cm^{-1}; 5·16, 2H, s), therefore being attributed structure **11**. The other compound (m.p. 106–108°) is supposed to have structure **17** (NMR: 4·72, 1H, s, —CH=C<). The same dehydration products were also obtained by synthesis from epicandicandiol as follows: acetylation of **7** to **12** and subsequent partial hydrolysis gave the C_7-monoacetate **13** which was oxidized with Jones reagent to **14**. Upon Huang-Minlon reduction the aldehyde yielded a mixture of three alcohols which were acetylated and separated by dry column chromatorgraphy on silica gel with $AgNO_3$, thus affording the compounds **11**, **17** and **18**. The first two proved to be identical with those obtained from the dehydration of powerol monoacetate (**4**); the structure of **18** was determined on the basis of analytical and spectroscopical data. The configuration of the

*τ-scale.

tertiary hydroxyl in powerol (3) is shown as α because oxidation of 3 with chromic anhydride-pyridine complex to the keto-alcohol 5 followed by Huang-Minlon reduction gave (−)kauranol (6), identical with an authentic sample (m.m.p., TLC, IR and NMR spectra superimposable).

Of special interest is the fact that upon reduction of the acetoxy-aldehyde 14 by the method of Huang-Minlon the double bond is isomerized from position 16–17 to 15–16. On the contrary, the reduction of the keto-acid 9 produces no such migration. Recently, Fujita *et al.*[8] reported an example for the reverse isomerization: when reducing the keto-aldehyde 19 by the same method they obtain (−)kaurene, (−)isokaurene and (−)kaurane.

EXPERIMENTAL

The m.ps, determined on a Kofler block, are uncorrected. The recrystallization solvent was MeOH unless otherwise stated. Optical rotations were measured in $CHCl_3$ on a Perkin-Elmer 141 polarimeter and the IR spectra on a Perkin-Elmer 237 spectrophotometer. NMR spectra were run on a Perkin-Elmer R-10 instrument (60 MHz) in $CDCl_3$ with TMS as internal reference, except where otherwise indicated. The mass spectra were recorded on a Hitachi Perkin-Elmer RMU-7. The chromatographic adsorbents were Merck products, the spray reagent for TLC being H_2SO_4-AcOH-H_2O (4:80:16). Column chromatography was performed on silica gel 0·2–0·5 mm and dry column chromatography on silica gel 0·05–0·2 mm. Acetylations were realized with Ac_2O in pyridine leaving the reaction at room temp overnight.

Isolation of the diterpene diols. The air-dried aerial part of the plant, collected on the Monte de las Mercedes (Tenerife), was finely cut and extracted several times with EtOH in a soxhlet. The combined and filtered cold ethanolic extracts were concentrated *in vacuo* and chromatographed on a column. Elution with benzene and benzene-EtOAc gave first hydrocarbons, then a mixture of monoalcohols, and last the diols which were rechromatographed on a dry column eluting with benzene-EtOAc (95:5). Thus were separated vierol (1), a mixture of trachinodiol and epicandicandiol, and powerol (3). Epicandicandiol (7) was obtained in pure form by dry column chromatography of the above mixture on silica gel impregnated with 20% $AgNO_3$.

Vierol. [(−)kaurane-16α,18-diol] **1**, m.p. 209–211°; M^+ *m/e* 306 ($C_{20}H_{34}O_2$ requires 306); IR (KBr): 3320, 1015 cm^{-1}; NMR: 6·55 and 6·90 (each 1H, d, *J* 12 Hz; $—CH_2$-OH), 8·62, 8·92 and 9·25 (each 3H, s; 3 Me). *18-Acetate* **2**, m.p. 133–135°, $[\alpha]_D$ −37° (*c*, 1·94); IR (nujol): 3300, 1740, 1250, 1040 cm^{-1}; NMR: 6·28 (2H, q, *J* 12 Hz; $—CH_2$-OAc), 8·68, 8·94 and 9·18 (each 3H, s; 3 Me).

Powerol. [(−)kaurane-7β,16α-diol] **3**, m.p. 219–222°, $[\alpha]_D$ 3° (*c*, 1·60); M^+ *m/e* 306 ($C_{20}H_{34}O_2$ requires 306); IR (KBr): 3380, 1400, 1390, 1095 cm^{-1}; NMR: 6·30 (1H, t, $W_{1/2}$ = 6 Hz; >C<u>H</u>OH), 8·62, 8·94, 9·12 and 9·15 (each 3H, s; 4 Me). *7β-Acetate* **4**, m.p. 192–194°, $[\alpha]_D$ 20° (*c*, 1·80); IR (KBr): 3255, 1710, 1380, 1370, 1270 cm^{-1}; NMR: 5·08 (1H, t, $W_{1/2}$ = 6 Hz; >C<u>H</u>OAc), 7·94 (3H, s, OAc), 8·62 and 8·93 (each 3H, s; 2 Me), 9·22 (6H, s; 2 Me).

Epicandicandiol. [(−)kaurene-7β,18-diol] **7**, m.p. 142–144°, $[\alpha]_D$ −41° (*c*, 1·57) (lit[5] m.p. 141°, $[\alpha]_D$ −39·5°); IR (KBr): 3380, 3020, 1660, 875 cm^{-1}; NMR: 5·21 (2H, s, $W_{1/2}$ = 6 Hz; $=CH_2$), 6·50 (1H, t, $W_{1/2}$ = 6 Hz; >C<u>H</u>OH), 6·80 (2H, q, *J* 12 Hz; $—CH_2OH$), 8·94 and 9·30 (each 3 H, s; 2 Me). *Diacetate* **12**, m.p. 122–124° (lit.[5] 120–121°), $[\alpha]_D$ −19° (*c*, 1·77).

Oxidation of epicandicandiol. **7** (1·6 g) dissolved in acetone (minimum quantity) was treated dropwise with Jones reagent and left at room temp for 24 hr, upon which MeOH was added to destroy excess reagent. The mixture was poured into water and extracted as usual. Dry column chromatography of the resulting product, with benzene-EtOAc (95:5) as eluent, gave first the keto-aldehyde **8** (210 mg), m.p. 101–106°, $[\alpha]_D$ −50° (*c*, 1·07) (lit.[5] m.p. 100–107°, $[\alpha]_D$ −45·5°) and afterwards the keto-acid **9** (810 mg), m.p. 162–164°, $[\alpha]_D$ −43° (*c*, 0·96) (lit.[5] m.p. 163–164°, $[\alpha]_D$ −43·2°).

Huang-Minlon reduction of (−)kauren-7-on-18-oic acid. To a soln of **9** (650 mg) in diethyleneglycol (23 ml) hydrazine hydrate (5·2 ml) was added and the mixture refluxed for 2 hr (temp 145°). After addition of KOH pellets (780 mg) refluxing was continued for 45 min. Cooling was removed and the temp reached to 200° after which refluxing was continued for 3 hr. Usual work-up afforded acid **10** (530 mg), m.p. 158–161°, $[\alpha]_D$ −79° (*c*, 1·14) (lit.[5] m.p. 156–160°, $[\alpha]_D$ −80·5°); IR (KBr): 3500–2500 (br), 3070, 1695, 1660, 877 cm^{-1}; NMR: 5·23 (2H, s, $=CH_2$), 8·85 and 8·93 (each 3H, s; 2 Me).

Epoxidation of (−)kauren-18-oic acid. A mixture of **10** (310 mg) and *m*-chloroperbenzoic acid (145 mg), each dissolved in $CHCl_3$ (16 ml), was left at room temp in the dark for 6 hr and washed with 10% Na_2CO_3 aq. Usual work-up gave the epoxy-acid **15** which did not crystallize; IR ($CHCl_3$): 3600–2500 (br), 1700, 1270, 1110 cm^{-1}; NMR (CCl_4): 7·32 (2H, s; epoxide protons), 8·88 and 8·97 (each 3H, s; 2 Me).

Reduction of 16,17-epoxy-(−)kauran-18-oic acid. A soln of **15** (130 mg) in dry ether (10 ml) was added dropwise to a suspension of LAH (540 mg) in the same solvent (15 ml). After refluxing for 12 hr the excess reagent was destroyed by adding EtOAc and the mixture washed with 10% HCl aq and ether extracted. Dry column chromatography of the residue, eluting with benzene-EtOAc (7:3), yielded first starting material (50 mg), then diol **16** [NMR: 6·50–6·95 (4H, m; 2 $—CH_2OH$), 8·96 and 9·29 (each 3H, s; 2 Me)], and last vierol **1** (30 mg), m.p. 209–210°, which proved to be identical with the natural product (m.m.p., TLC, IR and NMR spectra superimposable).

Dehydration of powerol 7β-acetate. **4** (98 mg) dissolved in dry pyridine (19·6 ml) was treated with a soln of freshly distilled $SOCl_2$ (1·6 ml) in the same solvent (19 ml) at 0° and left at this temp for 1 hr. After pouring onto crushed ice and usual work-up the mixture consisting of two compounds was acetylated and separated by dry column chromatography on silica gel impregnated with $AgNO_3$. Elution with light petroleum-benzene (1:1) gave first compound **11** (40 mg) and then **17** (20 mg).

(−)Kauren-7β-ol acetate **11**, m.p. 101–103° $[\alpha]_D$ −22° (*c*, 1·18). (Found: C, 79·95; H, 10·51. $C_{22}H_{34}O_2$ requires: C, 79·95; H, 10·37%). IR (nujol): 3025, 1715, 1640, 1400, 1385, 1240, 875 cm^{-1}; NMR: 5·16 (3H, complex signal; $=CH_2$, >C<u>H</u>OAc), 7·93 (3H, s; OAc), 8·95 (3H, s; Me), 9·21 (6H, s; 2 Me).

(−)Isokauren-7β-ol acetate **17**, m.p. 106–108°, $[\alpha]_D$ 48° (*c*, 1·04). (Found: C, 80·00; H, 10·57. $C_{22}H_{34}O_2$ requires: C, 79·95; H, 10·37%). IR (KBr): 3025, 1720, 1650, 1395, 1385, 1245, 875 cm^{-1}; NMR: 4·72 (1H, broad s; —CH=C<), 5·30 (1H, t, $W_{1/2}$ = 6 Hz; >C<u>H</u>OAc), 7·99 (3H, s;

OAc), 8·29 (3H, d, *J* 2 Hz; —CH=Me), 8·95 (3H, s; Me), 9·21 (6H, s; 2 Me).

Partial hydrolysis of epicandicandiol diacetate. A soln of **12** (3 g) in benzene (minimum quantity) was saponified with 2% methanolic KOH (20 ml) leaving the mixture at room temp for 2 hr. Usual work-up and subsequent dry column chromatography with benzene-EtOAc (85:15) as eluent afforded, besides starting material (1·3 g), the 7β-monoacetate **13** (1·4 g), m.p. 138–140°, $[\alpha]_D$ −28° (*c*, 2·40). (Found: C, 76·24; H, 9·86. $C_{22}H_{34}O_3$ requires: C, 76·26; H, 9·89%). IR (KBr): 3550, 3020, 1710, 1650, 1240, 870 cm^{-1}; NMR (CCl_4): 5·21 (2H, s, $W_{1/2}$ = 6 Hz; $=CH_2$), 5·35 (1H, t, $W_{1/2}$ = 6 Hz; >CHOAc), 6·90 (2H, q, *J* 12 Hz; $—CH_2OH$), 8·00 (3H, s; OAc), 8·90 and 9·30 (each 3H, s; 2 Me).

Oxidation of epicandicandiol 7β-monoacetate. **13** (1·2 g) was treated dropwise with a slight excess of Jones reagent as mentioned above for **7** but leaving it at room temp for only 15 min. Dry column chromatography of the resulting mixture of products afforded the liquid aldehyde **14** (810 mg); IR (film): 3020, 2670, 1725, 1710, 1660, 880 cm^{-1}; NMR: 0·80 (1H, s; —CHO), 5·25 (3H, complex signal; $=CH_2$, >CHOAc), 8·92 and 8·97 (each 3H, s; 2 Me).

Huang-Minlon reduction of (−)kauren-18-al-7β-ol acetate. **14** (750 mg) in diethyleneglycol (65·6 ml) was treated with hydrazine hydrate (5·6 ml) as described above for **9** but at the end the temp rose to 220° and then refluxing continued for only 2 hr. Usual work-up afforded a product (710 mg) which by TLC (20% $AgNO_3$) was shown to consist of three compounds. The mixture was acetylated and chromatographed on a dry column impregnated with 20% $AgNO_3$, light petroleum-benzene (1:1) eluting the acetates **18** (180 mg), **11** (400 mg) and **17** (220 mg). The latter two were identical with the compounds obtained when dehydrating powerol-7β-acetate **4** (m.m.p., TLC, IR and NMR spectra superimposable).

(−)Kauran-7β-ol acetate **18**, m.p. 118–121°, $[\alpha]_D$ 19° (*c*, 0·20). (Found: C, 79·53; H, 11·03. $C_{22}H_{36}O_2$ requires: C, 79·46; H, 10·91%). IR (KBr): 1715, 1395, 1390, 1250 cm^{-1}; NMR: 5·26 (1H, t, $W_{1/2}$ = 6 Hz; >CHOAc), 8·02 (3H, s; OAc), 8·97 (3H, s; Me), 9·05 (3H, d, *J* 6 Hz; Me), 9·21 (6H, s; 2 Me).

Oxidation of powerol. A soln of **3** (130 mg) in dry CH_2Cl_2 (5 ml) was stirred at room temp for 1 hr with chromic anhydride-pyridine complex (10 ml) prepared by dissolving CrO_3 (1 g) in dry pyridine (1·58 g) and CH_2Cl_2 (25 ml). The mixture was then treated with 5% NaOH aq to dissolve the dark ppt, poured into water and $CHCl_3$ extracted. Usual work-up and recrystallization gave the keto-alcohol **5** (80 mg), m.p. 142–145°; IR (KBr): 3265, 1708, 1398, 1365 cm^{-1}; NMR: 8·63 and 8·82 (each 3H, s; 2 Me), 9·15 (6H, s; 2 Me).

Reduction of (−)kauran-7-on-16α-ol. **5** (65 mg) in diethyleneglycol (6·5 ml) was treated with hydrazine hydrate (0·5 ml) as described for **9**, except that at the end refluxing was continued for 2 hr. Thus (−)kauranol (**6**) was obtained (45 mg), m.p. 214–216°, which showed to be identical with an authentic sample (m.m.p., TLC, IR and NMR spectra superimposable).

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