Tetrahedron Letters No.7, pp. 599-602, 1969. Pergamon Press. Printed in Great Britain.

CANDICANDIOL, A NEW DITERPENE FROM
"SIDERITIS CANDICANS" Ait., var. "ERIOCEPHALA" Webb.
(LABIATAE)

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(Received in UK 13 December 1968; accepted for publication 10 January 1969)

Sideritis candicans Ait. var. Eriocephala Webb. is a specie of the Labiatae family found only at the Canary Islands (1).

Ethanolic extraction of the aerial parts of this plant, and further chromatographic fractioning of the extract, led to the isolation of a compound, candicandiol (I) [$C_{20}H_{32}O_2$ ‡; m.p. 219-219.5ºC; $[\alpha]_D^{27º}$ -87.5º ($\bar{c}$ 1.1, MeOH)] . Candicandiol behaves like a pure product (t.l.c.; g.l.c.); its i.r. spectrum does not exhibit $>C=O$ bands; there is -OH (3340 cm^{-1}, broad) and $>C=CH_2$(3068, 1660, 880 and 870 cm^{-1}) absorptions; the n.m.r. spectrum (δ values) shows two tertiary methyls at 0.75 and 1.07, a signal at 4.75 assigned to the terminal methylene and an AB quartet at 3.12 and 3.55 partially superimposed to a 1H signal at 3.70.

Acetylation of I yields a diacetate (II) [$C_{24}H_{36}O_4$; m.p. 100-102ºC; $[\alpha]_D^{24º}$ -64.1º ($\bar{c}$ 1.7, $CHCl_3$)]. The n.m.r. spectrum of II shows an AB quartet centered at 3.68 (J=10 Hz, geminal) assigned to a grouping of the $-\overset{|}{\underset{|}{C}}-C\underline{H}_2-OCOCH_3$ type at equatorial configuration (2,3). In addition, a broad signal ($W_{\frac{1}{2}}$=16 Hz) at 4.63 ($>C\underline{H}-OCOCH_3$) can be observed, overlapping with the signal at 4.75 -

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‡ Correct elementary analysis have been obtained for all crystalline compounds described in this communication.

assigned to the terminal methylene. Judging from the width of the signal at 4.63 one could expect an equatorial -OH (4) coupled to two vicinal protons at least.

Oxidation of I with Py/CrO$_3$ affords a ketoaldehyde (III) [$C_{20}H_{28}O_2$; m.p. 100-107ºC; $[\alpha]_D^{27º}$ -45.5º ($\bar{c}$ 0.34, CHCl$_3$)] that gives a negative Zimmermann test; i.r. spectrum: -CHO (2752, 2690 and 1700 cm^{-1}), $>C{=}CH_2$ (3070, 1663, 890 and 873 cm^{-1}) $>C{=}O$ (1725 cm^{-1}); u.v. spectrum λ_{max}^{EtOH} 276 and 295 nm (ϵ_1 51; ϵ_2 72); the n.m.r. spectrum of III shows the aldehydic proton signal at 9.12, confirming thus the equatorial configuration of the primary hydroxyl group (5). Huang-Minlon reduction of III yields (-)-kaurene (IV)(6) [$C_{20}H_{32}$; m.p. 51ºC; $[\alpha]_D^{22º}$ -62º ($\bar{c}$ 0.4, CHCl$_3$)]. Likewise, oxidation of III with Jones' reagent affords a ketoacid (V) [$C_{20}H_{28}O_3$; m.p. 163-164ºC; $[\alpha]_D^{23º}$ -43.2º ($\bar{c}$ 0.43, EtOH)]; i.r. spectrum: -COOH (3500-2500, 1685 and 1253 cm^{-1}), $>C{=}O$ (1730 cm^{-1}) and $>C{=}CH_2$ (3075, 1658(sh) and 880 cm^{-1}). This ketoacid (V) when reduced by the Huang-Minlon procedure yields an acid (VI) the methyl ester of which is identical with methyl (-)-kaur-16-en-18-oate (VII)(6).

In this way we establish the structure and stereochemistry (I) assigned to candicandiol as far as the hydrocarbon skeleton, the position and configuration of the primary hydroxyl group and that of the exocyclic double bond are concerned.

The location of the secondary hydroxyl group can be inferred from the following data. Position 3 can be excluded on grounds of the stability of the ketoacid obtained; negative Zimmermann test would also exclude positions 1 and 2 (3). In the other hand, the n.m.r. spectrum of the ketoaldehyde (III) shows a signal at 3.34 (1H, quartet) that can be assigned, in principle, to the C-13 proton, allylic to the double bond and alfa to the carbonyl group. The proximity of the keto-group to the terminal methylene is also indicated by the fact that passing from the hydroxyl to the keto groups originates a down-field shift of the olefinic protons (Table 1). Position 15 is excluded because the u.v. spectrum of III does not correspond to an α,β-unsaturated ketone. Catalytic hydrogenation of I affords dihydrocandicandiol (VIII)(7) [m.p. 230-231ºC; $[\alpha]_D^{23º}$ -38.1º ($\bar{c}$ 0.42, MeOH)], i.r. and n.m.r. spectra confirming the dissappearance of the $>C{=}CH_2$ group. Oxidation (AcOH/CrO$_3$) of VIII leads to a ketoacid (IX)

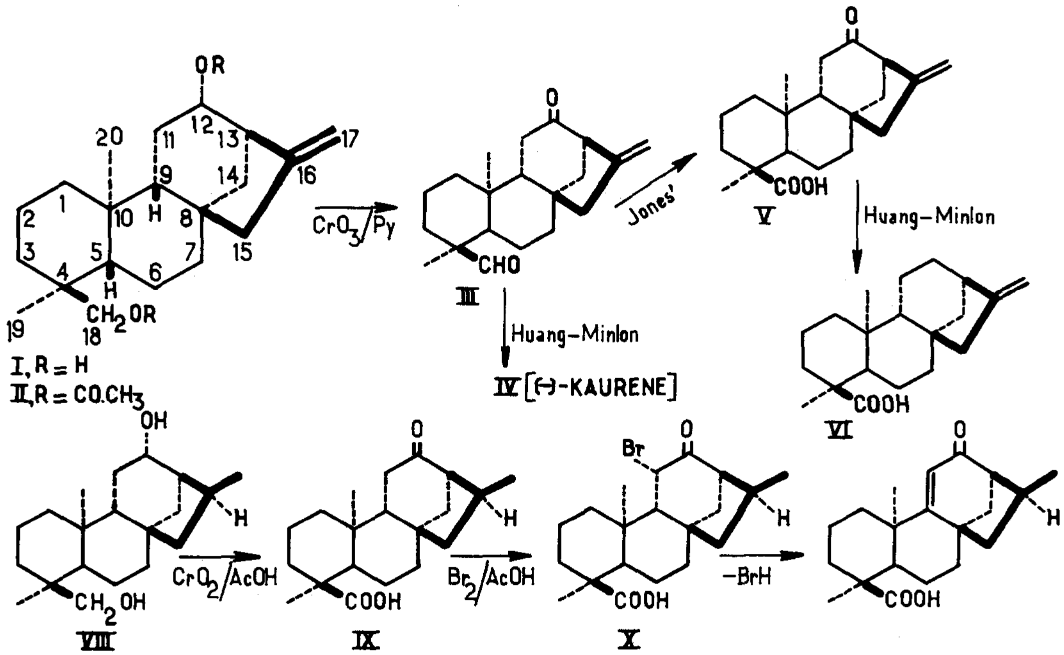
[$C_{20}H_{30}O_3$; m.p. 175–177ºC; $[\alpha]_D^{23º}$ −13.3 ($\bar{c}$ 0.8, EtOH); i.r. spectrum: $>$C=O at 1728 and 1685 cm^{-1}] that when treated with Br_2/AcOH (8) gives an α-bromoderivative. This compound (X) [$C_{20}H_{29}O_3Br$; m.p. 189–192ºC; $[\alpha]_D^{22º}$+56.5 ($\bar{c}$ 0.3, EtOH); i.r. spectrum: $>$C=O bands at 1725 and 1700 cm^{-1}; comparison with IX suggesting an axial configuration for the bromine atom] shows an n.m.r. spectrum with 1H doublet at 4.35 (J=4.5 Hz) that can be assigned to the equatorial proton of the −CHBr−CH$<$ grouping (8). The C-10 angular methyl (Table 1) undergoes an up-field shift ($\Delta\delta$ =0.36) with respect to IX, implying a shielding of this methyl group by the axial halogen. Only three positions of the keto-group could account for these results, positions: 12 (bromine at 11), 7 (bromine at 6) and, less probably, position 11 (bromine at 12). Position 7 for the keto-group can be excluded since IX is not identical with 7-keto-16β-(−)-kauran-18-oic acid (9). Furthermore, the bromoketoacid (X) eliminates readily HBr, originating a compound the u.v. spectrum of which corresponds to that of an α,β-unsaturated ketone [λ_{max}^{EtOH} 241 nm, ε 7.450]. The formation of this compound can be explained only if the keto-group is placed at C-12 and the bromine atom at C-11, excluding thus the reverse arrangement (8).

Accordingly X must posses the structure indicated (ring C in boat conformation, axial bromine) and candicandiol must be represented by I, that is, the 12α,18-dihydroxyl-derivative of (−)-kaurene, with ring C in boat conformation (10).

TABLE 1

Chemical shifts (δ units)

Compound	Me C-4	Me C-10	Me C-16	$>$C=CH_2	Solvent
I	0.75s	1.07s	-----	4.75m	C_5D_5N
II	0.84s	1.11s	-----	4.75m	$CDCl_3$
III	1.21s	1.10s	-----	4.85m	"
IV	0.84 and 0.81s	1.03s	-----	4.69m	CCl_4
V	1.22s	1.20s	-----	4.93m	$CDCl_3$
VIII	0.75s	1.06s	0.94d	-----	"
IX	1.22s	1.21s		-----	"
X	1.34s	0.84	1.00d	-----	"



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9.- We thank Prof. F. Piozzi (University of Palermo, Italy) for sending us a sample of this compound.

10.- A more detailed justification of the conformation assigned to ring C of candicandiol will be given in the full paper on the components of S. candicans.