

STRUCTURE AND STEREOCHEMISTRY OF PSIADIOL, A NEW DITERPENOID

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The leaves of *Psiadia altissima* (Compositae) (1) contain diterpenoids and flavonoid products.

From the leaves of *Psiadia altissima*, among other products, we isolated a crystalline substance, we named Psiadiol (I). It is the most abundant terpenoid constituent. Its molecular formula is  $C_{20}H_{30}O_3$ , m.p. 138-140° (ethyl ether-petroleum ether),  $[\alpha]_D^{25} -58^\circ$ .

Although Psiadiol did not exhibit an ultraviolet absorption maximum above 210 m $\mu$ , the end absorption in the 210 m $\mu$  region was of a magnitude comparable to those of  $\beta$ -substituted furan derivatives (2,3).

Its spectral features were:  $\nu_{max}$  (CHCl<sub>3</sub>) 3400, 1750, 1640, 1498, 835, 872  $cm^{-1}$ ; N.M.R.: 0,80 (3H, s,  $\geq C-CH_3$ ), 1,26 (3H, s,  $\geq C-CH_3$ ), 3,39 and 4,11 (2H, AB quartet, J=10 cps,  $-CH_2-OH$ ), 4,76 (1H, b.s.,  $-C=CH_2$ ), 5,04 (1H, b.s.,  $-C=CH_2$ ), 6,36, 7,30 and 7,44 (1H, m, H $_{\beta}$ , H $_{\alpha}$ , H $_{\alpha}$  furan); M.S. 318, 300, 237, 223.

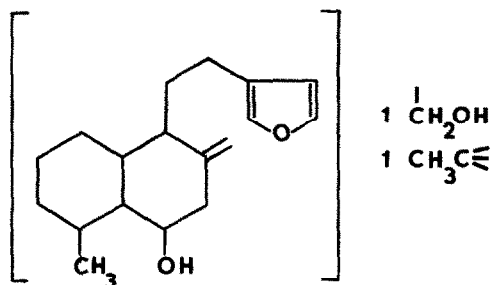
The I.R., N.M.R., U.V. and Mass spectra indicate the presence in the molecule of a  $\beta$ -substituted furan, also confirmed by a purple colour in the Ehrlich test.

Acetylation of I yielded a diacetate (II),  $C_{24}H_{34}O_5$ , m.p. 89-90°,  $[\alpha]_D^{23} -57^\circ$ ;  $\nu_{max}$  (CHCl<sub>3</sub>) 1725, 1650, 1505, 1250, 898, 872  $cm^{-1}$ ; N.M.R.: 0,79 (3H, s,  $\geq C-CH_3$ ), 1,14 (3H, s,  $\geq C-CH_3$ ), 2,06 (3H, s,  $CH_3-COO-$ ), 2,09 (3H, s,  $CH_3-COO-$ ), 4,14 (2H, s,  $\geq C-CH_2-OCOCH_3$ ), 4,80 (1H, b.s.,  $-C=CH_2$ ), 5,10 (1H, b.s.,  $-C=CH_2$ ), 5,11 (1H, six lines 1:1:2:2:1:1, J<sub>5,6</sub>=J<sub>6,7</sub>=11 cps and J<sub>6,7</sub>=5,5 cps,  $\geq C-CH-CH-CH_2-C\equiv$ ), 6,37, 7,31 and 7,48 (1H, m, H $_{\beta}$ , H $_{\alpha}$ , H $_{\alpha}$  furan).

Psiadiol (I), oxidized at 0° with Jones reagent (4) over a period of 10', yielded a ketoaldehyde (III),  $C_{20}H_{26}O_3$ , m.p. 58-60°,  $[\alpha]_D^{23} -87^\circ$ ;  $\nu_{max}$  (CHCl<sub>3</sub>)

1720, 1653, 1503, 902, 874  $\text{cm}^{-1}$ ; N.M.R.: 0,61 (3H, s,  $\text{>C-CH}_3$ ), 1,17 (3H, s,  $\text{>C-CH}_3$ ), 3,2 (2H, s,  $-\text{CO-CH}_2-\text{C}=\text{C}$ ), 4,88 (1H, b.s.,  $-\text{C}=\text{CH}_2$ ), 5,10 (1H, b.s.,  $-\text{C}=\text{CH}_2$ ), 6.37, 7,32 and 7,48 (1H, m,  $\text{H}_\beta$ ,  $\text{H}_\alpha$ ,  $\text{H}_\alpha$  furan), 10,4 (1H, s,  $\text{>C-CHO}$ ).

Assuming that Psiadiol possesses the normal diterpene labdane skeleton, the U.V., I.R. and N.M.R. spectral features of I, II, III agree well with the following partial structure:



That the hydroxymethyl group was at  $\text{C}_4$  and not at  $\text{C}_{10}$  was indicated by both the reaction of I with acetone and  $\text{CuSO}_4$  to give an acetonide (IV),  $\text{C}_{23}\text{H}_{34}\text{O}_3$  and by the configuration of  $\text{C}_6$  hydroxyl group.

The six-line pattern at 5,11  $\delta$  in the N.M.R. spectrum of II and the coupling constants between the protons at  $\text{C}_5$ ,  $\text{C}_6$  and  $\text{C}_7$  establish the equatorial configuration of hydroxyl group at  $\text{C}_6$ .

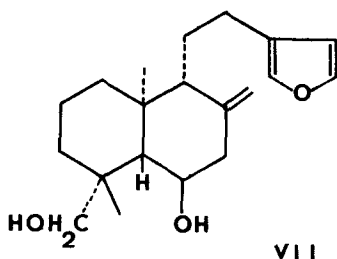
More direct evidence concerning the configuration at  $\text{C}_6$  was obtained as follows. The ketoaldehyde (III) on sodium borohydride reduction afforded an amorphous dihydroxy compound (V),  $\text{C}_{20}\text{H}_{30}\text{O}_3$ , different from I,  $[\alpha]_D^{24} -38^\circ$ ,  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3360, 1645, 1502, 897, 883, 873  $\text{cm}^{-1}$ . Acetylation of V gave a monoacetate (VI),  $\text{C}_{22}\text{H}_{32}\text{O}_4$ , with a free  $\text{C}_6$  hydroxyl group, m.p. 45-47°,  $\nu_{\text{max}}$  (nujol) 3460, 1730, 1650, 1245, 897, 880  $\text{cm}^{-1}$ ; N.M.R.: 1,02 (3H, s,  $\text{>C-CH}_3$ ), 1,08 (3H, s,  $\text{>C-CH}_3$ ), 2,09 (3H, s,  $\text{CH}_3-\text{COO-}$ ), 4,50 (1H, m,  $-\text{OH}$ ), 4,60 (2H, s,  $\text{>C-CH}_2-\text{OCOCH}_3$ ), 4,97 (1H, b.s.,  $-\text{C}=\text{CH}_2$ ), 5,17 (1H, b.s.,  $-\text{C}=\text{CH}_2$ ), 6,42, 7,38 and 7,52 (1H, m,  $\text{H}_\beta$ ,  $\text{H}_\alpha$ ,  $\text{H}_\alpha$  furan).

The conclusion is drawn, therefore, that the  $\text{C}_6$  hydroxyl group in V must have the axial configuration since the complex hydride reduction of III is sterically controlled by the 1,3 axial substituents in  $\text{C}_4$  and in  $\text{C}_{10}$ .

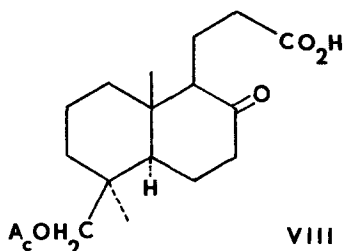
The assignment of configuration to the hydroxymethyl group at  $\text{C}_4$  in I rests upon N.M.R. data. In a study of the N.M.R. spectra of diterpenes (5,6,7) containing both a  $\text{C}_4$  methyl and a  $\text{C}_4$  hydroxymethyl (or acetoxymethyl) group, it was found that the protons of the oxygenated methylene appear as a quartet or a singlet at significantly lower field when the function has the axial configuration

than when it has the equatorial configuration. By comparison with the model acetates the axial configuration must be assigned to the C<sub>4</sub> acetoxymethyl group of Psiadiol derivative (II).

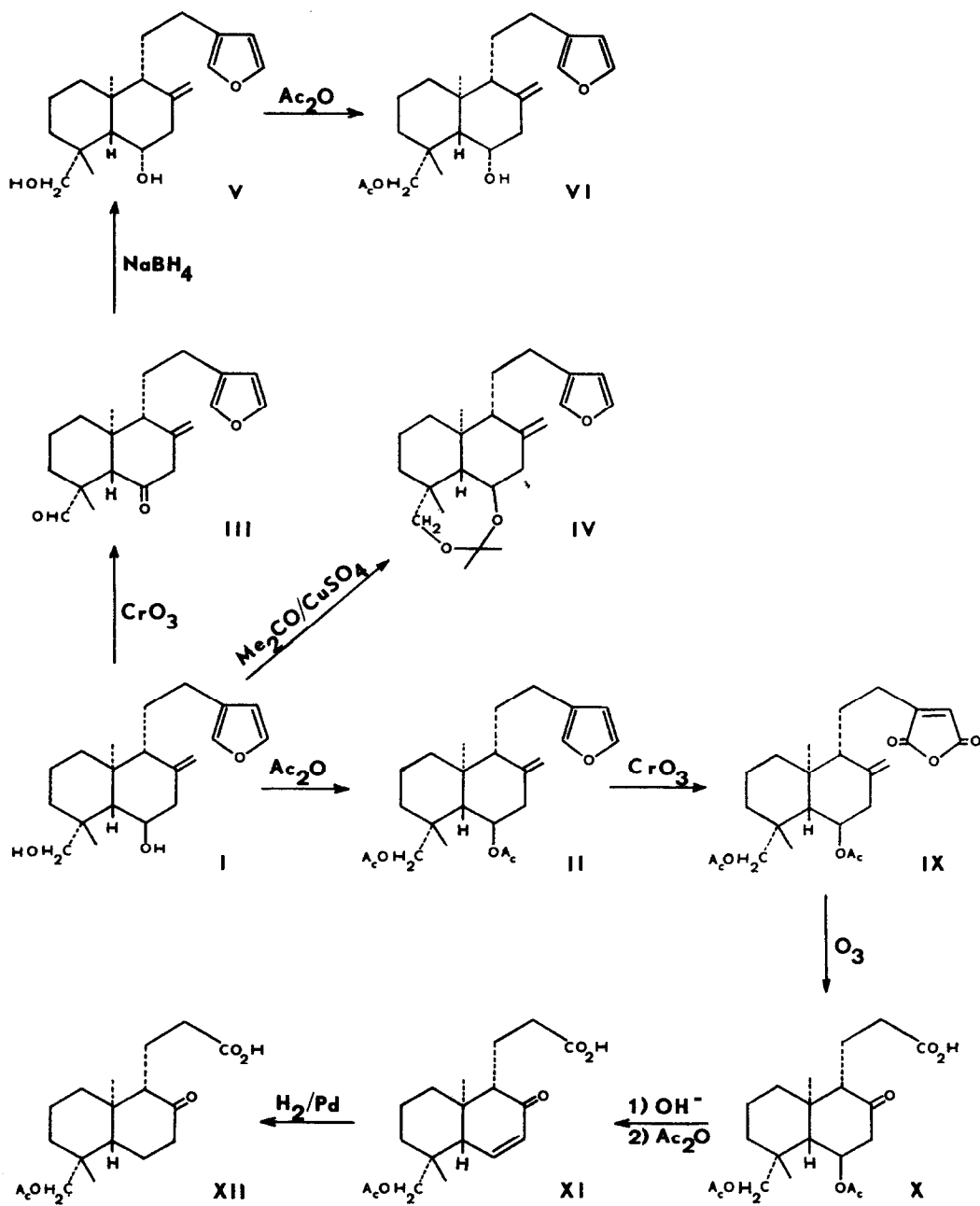
All these results can be rationalized in terms of the following structure (or its mirror image):



Confirmation of the correctness of this structure as well as proof for the stereochemistry indicated in formula VII was provided by a correlation with a Lambertianic acid derivative (VIII) of established structure and configuration (3):



Psiadiol diacetate (II) was oxidized at 0° over a period of 11h with Jones reagent and a maleic anhydride (IX), C<sub>24</sub>H<sub>32</sub>O<sub>7</sub>, was obtained, m.p. 110-115°,  $\nu_{\max}$  (nujol) 1840, 1780, 1730, 1640, 1250, 902 cm<sup>-1</sup>. The anhydride was ozonized in glacial acetic acid and ethyl acetate and the product worked oxidatively to yield X, C<sub>20</sub>H<sub>30</sub>O<sub>7</sub>, m.p. 110-112° (ethyl ether and petroleum ether),  $\nu_{\max}$  (CHCl<sub>3</sub>) 1725, 1250 cm<sup>-1</sup>; N.M.R.: 0,82 (3H, s, >C-CH<sub>3</sub>), 1,18 (3H, s, >C-CH<sub>3</sub>), 2,06 (3H, s, CH<sub>3</sub>-COO-), 2,08 (3H, s, CH<sub>3</sub>-COO-), 4,16 (2H, s, >C-CH<sub>2</sub>-OCOCH<sub>3</sub>), 5,27 (1H, six lines, 1:1:2:2:1:1, J<sub>5,6</sub>=J<sub>6,7</sub>=11 cps and J<sub>6,7</sub>=5,5 cps, >C-CH-CH-CH<sub>2</sub>-C<sub>3</sub>), 9,7 (1H, m, -COOH). This compound by treatment with KOH in CH<sub>3</sub>OH-H<sub>2</sub>O and reacylation yielded an  $\alpha,\beta$ -unsaturated ketone (XI), C<sub>18</sub>H<sub>26</sub>O<sub>5</sub>, m.p. 88-90° (isopropyl ether and ligroine),  $\lambda_{\max}$  230 m $\mu$  ( $\epsilon$ =5850),  $\nu_{\max}$  (CHCl<sub>3</sub>) 2650, 1735, 1710, 1678, 1620 cm<sup>-1</sup>; N.M.R.: 0,83 (3H,



s,  $\geq\text{C}-\text{CH}_3$ ), 1,16 (3H, s,  $\geq\text{C}-\text{CH}_3$ ), 2,07 (3H, s,  $\text{CH}_3-\text{COO}-$ ), 4,11 (2H, s,  $\geq\text{C}-\text{CH}_2-\text{OAc}$ ), 6,10 (1H, q,  $J_{6,7}=11\text{cps}$ ,  $J_{6,5}=3,7\text{cps}$ ,  $\geq\text{C}-\underset{|}{\text{CH}}-\text{CH}=\text{CH}-\text{CO}-$ ), 7,16 (1H, q,  $J_{7,6}=11\text{cps}$ ,  $J_{7,5}=1,5\text{cps}$ ,  $\geq\text{C}-\underset{|}{\text{CH}}-\text{CH}=\text{CH}-\text{CO}-$ ), 8,2 (1H, m,  $-\text{COOH}$ ). The catalytic reduction of XI in ethanol on Pd-C yielded XII,  $\text{C}_{18}\text{H}_{28}\text{O}_5$ , m.p. 129-131° (ethyl ether and petroleum ether,  $\nu_{\text{max}}$  (nujol) 3120, 2680, 1735, 1720, 1230  $\text{cm}^{-1}$ ; N.M.R.: 0,72 (3H, s,  $\geq\text{C}-\text{CH}_3$ ), 1,05 (3H, s,  $\geq\text{C}-\text{CH}_3$ ), 2,07 (3H, s,  $\text{CH}_3-\text{COO}-$ ), 3,82 and 4,23 (2H, AB quartet,  $J=11\text{cps}$ ,  $\geq\text{C}-\text{CH}_2-\text{OCOCH}_3$ ), 10,55 (1H, m,  $-\text{COOH}$ ). This acid melted as the acid VIII obtained from Lambertianic acid. The I.R. and N.M.R. spectra of the two acids were identical. The specific rotations measured at the Hg lines ( $[\alpha]^{24}_{578\text{m}\mu} +26^\circ$ ,  $[\alpha]^{24}_{365\text{m}\mu} +299^\circ$  (c=1% in 95% ethanol)) were of the same magnitude but opposite in sign, revealing an antipodal relationship between acids XII and VIII.

Therefore the absolute configuration depicted for Psiadiol in formula VII may be taken as proved.

I.R. spectra were measured with a Perkin-Elmer mod 21 instrument; U.V. spectra with a Perkin-Elmer mod 137 instrument in  $\text{CH}_3\text{OH}$  solution; optical rotation on a Perkin-Elmer mod 141 polarimeter in dioxane solution (c=1%) unless otherwise stated; mass spectra on a LKB gas chromatograph-mass spectrometer; N.M.R. spectra on a Perkin-Elmer mod R10 instrument in  $\text{CDCl}_3$  solution (TMS as internal standard; values are in  $\delta=\text{ppm}$ ; s=singlet, b.s.=broad singlet, q=quartet, m=multiplet).

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