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# EXTRACTIVES OF <u>HELIOPSIS SCABRA</u>: STRUCTURE AND STEREOCHEMISTRY OF TWO NEW LIGNANS

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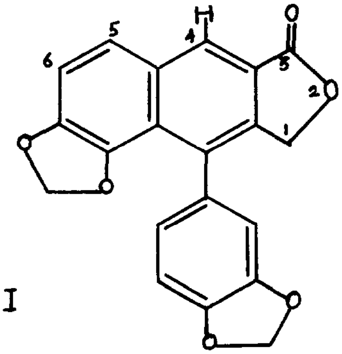
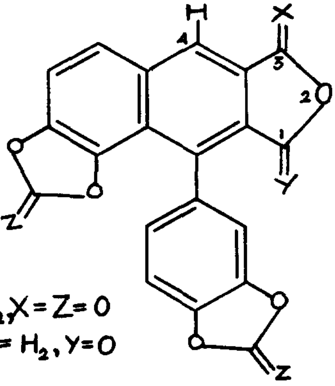
The roots of *Heliopsis scabra* have been investigated by Jacobson[1], who reported the occurrence of insecticidal isobutylamides. In addition, two non-toxic crystalline substances were discovered, but no structural assignments were made. In this communication we set out evidence for the formulation of these products as the lignans (I) and (VII) which we call helioxanthin and helianthoidin respectively.

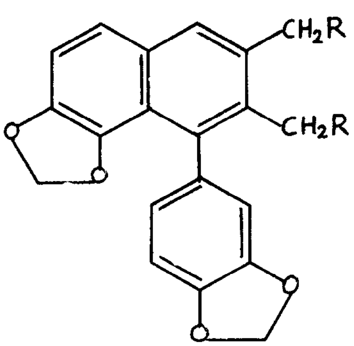
Helioxanthin, m.p. 240-241°, $C_{20}H_{12}O_6$, a yellow substance with a strong blue fluorescence, had $\nu_{max.}$ 1765 (γ-lactone), $\lambda_{max.}$ (EtOH) 267 (4,66), 290 (3.70), and 354 (3.88) mμ, formed mononitro- and monobromo- derivatives m.p. 280 and 283° respectively, and gave a positive Labat test. The presence of two methylenedioxyaryl groups was indicated by the n.m.r. resonances at τ 3.99 (2H) and 4.08 (2H), and confirmed by the formation of the cyclic carbonate (II), $C_{20}H_8O_8$, m.p. 330° (decomp.), $\nu_{max.}$ 1830 cm.$^{-1}$, on treatment with phosphorus pentachloride followed by aqueous sodium carbonate. In addition to methylenedioxy absorption, helioxanthin (I) showed n.m.r. signals assigned to an isolated aromatic proton (1.61 s), an *ortho* aromatic pair (2.33 d, 2.74 d, J = 8.5 c/s), three other aromatic protons (*ca.* 3.2 m), and a strongly deshielded methylene (4.84 s).



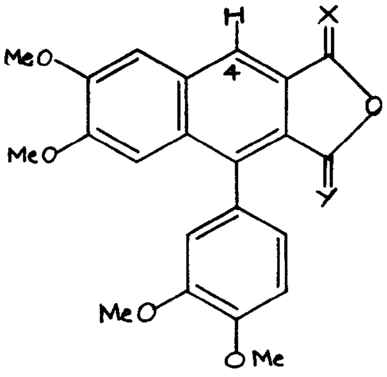
I



II; Y = $H_2$, X = Z = O
III; X = Z = $H_2$, Y = O



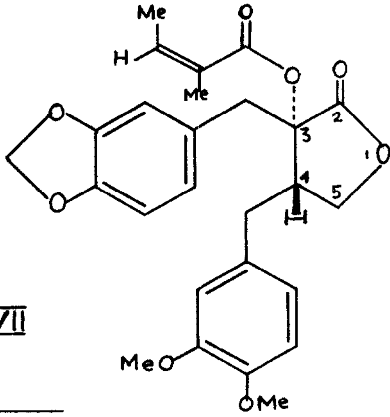
IV



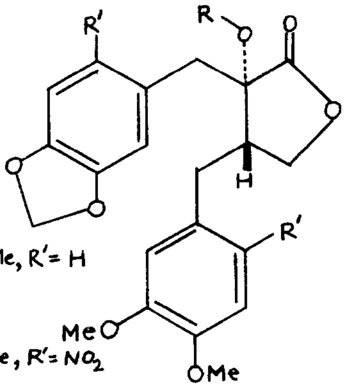
V; X = O, Y = $H_2$
VI; X = $H_2$, Y = O

Reduction of helioxanthin with lithium aluminium hydride gave the diol (IV; R = OH), $C_{20}H_{16}O_6$, m.p. 201-202°, forming a diacetate (IV; R = OAc) m.p. 134-135°. The diol (IV; R = OH) was identical (mixed m.p. and i.r. comparison) with the synthetic diol prepared by Brown and Stevenson*[2] during their tetradehydro-otobain synthesis. Hydrogenolysis of the diol yielded tetradehydro-otobain (IV; R = H).

Thus helioxanthin must be lactone (I), or the isomer (III). Support for the former proposition is obtained from the chemical shift of the aromatic 4-H, which appears at τ 1.61 in the lactone but shifts to τ 2.15 in the acetate (IV; R = OAc). Deshielding by an adjacent carbonyl group is indicated, as in (I). Klemm *et al.*[3] report τ 1.7 for the 4-H of lactone (V), compared with 2.24 for the corresponding proton in the isomer (VI).



VII



VIII ; R = CO.CHMeCH$_2$Me, R' = H
IX ; R = H , R' = H
X ; R = Ac , R' = H
XI ; R = COCMe:CHMe, R' = $NO_2$

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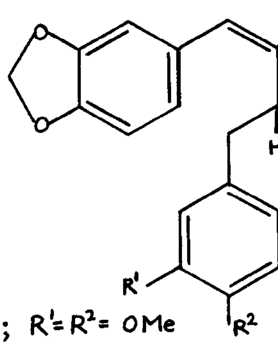
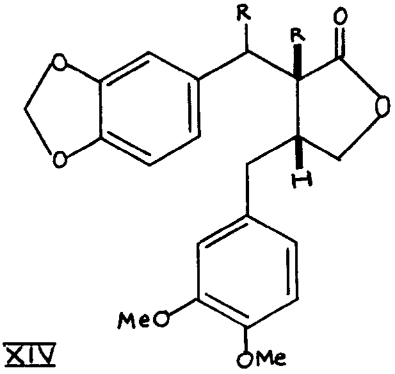
* We thank Professor Stevenson for a sample of this diol.

The substitution pattern of the aryl naphthalene system of helioxanthin is clearly shown in the n.m.r. spectrum of the diol (IV; R = OH), in $(CD_3)SO-D_2O$ solvent. The 4-H appears at $\tau$ 2.08 s, and the 5,6 pair as an AB quartet, centre $\tau$ 2.60, J = 10 c/s. The other ortho pair of protons are centred at $\tau$ 3.19, with J = 9 c/s; the higher field arm is coupled to the remaining proton ($\tau$ 3.18 d) with J = 2 c/s.

The second crystalline lignan from H. scabra, helianthoidin (VII), $C_{26}H_{28}O_8$, m.p. 134-135°, $[\alpha]_D^{25}$ - 145.4° (c, 1.52, $CHCl_3$), has $\nu_{max.}$ 1770, 1723 and 1648 $cm.^{-1}$, $\lambda_{max.}$ 227 (4.28) and 283 (3.80) mμ. It gives a positive Labat test, and yields acetaldehyde on ozonolysis (identified as its 2,4-dinitrophenylhydrazone). The n.m.r. spectrum of helianthoidin reveals the presence of six aromatic protons ($\tau$ 3.15 - 3.54), an olefinic proton ($\tau$ 3.65 - 3.84), one methylenedioxy group ($\tau$ 4.14 s) and two methoxy groups ($\tau$ 6.13 s). In addition, an isolated benzylic methylene ($\tau$ 6.92, J = 14 c/s), a methylene adjacent to oxygen (5.53 - 6.00, multiplet), and two unsaturated methyls (7.99 s, 7.96 broad doublet) were observed. The remaining three protons form a complex multiplet, $\tau$ 6.6 - 7.8. On hydrogenation, helianthoidin gives a dihydroderivative (VIII) m.p. 83-85°, $\nu_{max.}$ 1770, 1738 $cm.^{-1}$, $\tau$ 9.00t ($C\underline{H}_3CH_2$) and 8.7 d ($C\underline{H}_3C\underline{H}$ ). Alkaline hydrolysis of the lignan (VII) yields an amorphous alcohol (IX), which affords a crystalline acetate (X), m.p. 113°



XII; R¹= R²= OMe
XIII; R¹, R² = -OCH₂O-



XIV

On heating, helianthoidin produced a mixture of angelic and tiglic acids (identified as methyl esters by g.l.c.), the former being the major component. Thus, the natural lignan is the angelate ester, some cis → trans isomerisation taking place during pyrolysis. The olefin (XII), m.p. 129-130°, $[\alpha]_D^{26}$ - 83.3° (c 0.56, $CHCl_3$), $\nu_{max.}$ 1752, 1648 $cm.^{-1}$, $\lambda_{max.}$ 232.5 (4.22), 287 (4.02), 295 (4.01) and 332 (4.21) mμ was also formed in this reaction.

Oxidation of helianthoidin with potassium permanganate afforded veratric acid (mixed m.p. *and i.r. comparison with authentic material).* *Ozonolysis of the olefin (XII) yielded* piperonal (identified as its 2,4-dinitrophenylhydrazone). In agreement with the aromatic substitution pattern thus demonstrated, dinitrohelianthoidin (XI), m.p. 167-170°, displayed in its n.m.r. spectrum four aromatic singlets, at τ 2.45, 2.49 (both adjacent to $NO_2$), τ 3.11 and 3.46, none of which exhibited splitting from o or m neighbours.

Hydrogenation of the olefin (XII) gave the dihydro derivative (XIV; R = H), m.p. 123°. The dideuterio analogue (XIV; R = D) was also prepared (using sodium borodeuteride, deuterioacetic acid, and palladium catalyst, in a Brown hydrogenator). In the mass spectrum of lactone *(XIV; R = H) two fragments, at m/e 135 (100%; from methylenedioxybenzyl) and 151 (68%;* from dimethoxybenzyl), were observed. In the deuteriated compound (XIV; R = D), only the former fragment is deuteriated *(m/e 136).* *Thus, in olefin (XII), the piperonyl residue is* attached to the double bond, rather than the veratyl.

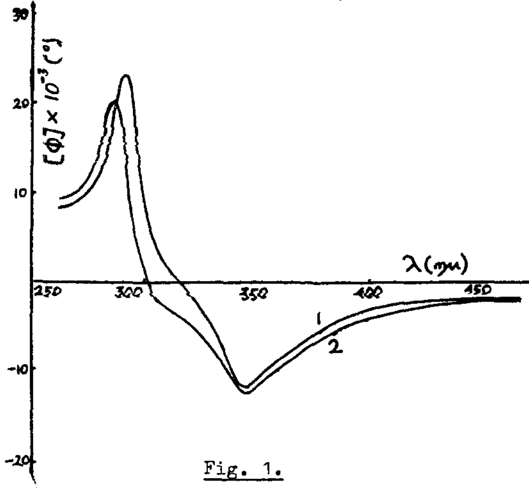


Fig. 1.

O.R.D. curves (dioxan, 25°) for:
(1) (-)-Hibalactone
(2) Olefin XII

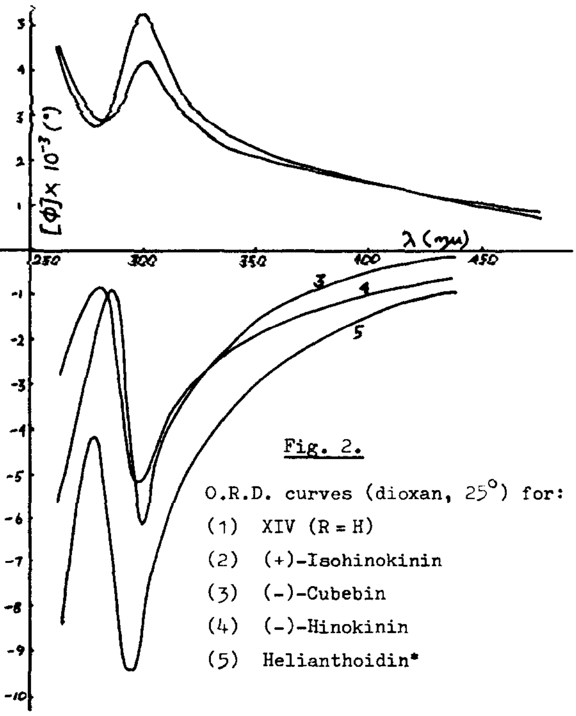
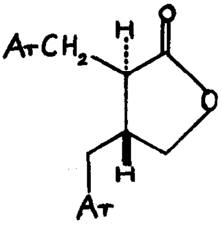


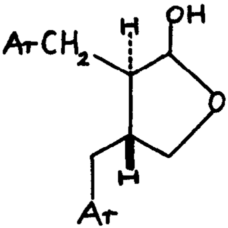
Fig. 2.

O.R.D. curves (dioxan, 25°) for:
(1) XIV (R = H)
(2) (+)-Isohinokinin
(3) (-)-Cubebin
(4) (-)-Hinokinin
(5) Helianthoidin*

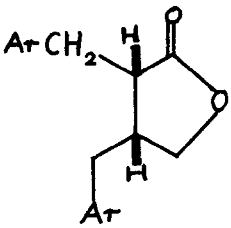
* Very similar curves were obtained for VIII and X



XV



XVI



XVII

Ar = Piperonyl

(-)-Hibalactone (XIII), of known absolute configuration,[4] and the olefin (XI) show very similar Cotton effect curves (Fig. 1). Thus the latter has the stereochemistry shown, and (-)-helianthoidin has the (S)-configuration at C-4 (VII). Helianthoidin itself shows a negative Cotton effect (Fig 2) as does (-)-hinokinin[5] (XV) and (-)-cubebin[5] (XVI). In contrast the <u>cis</u>-butyrolactone (XIV; R = H) shows a positive Cotton effect, in common with (+)-isohinokinin[5] (XVII). Thus, (-)-helianthoidin must have the <u>trans</u>-3(S), 4(S)- stereochemistry shown in cipher (VII).

## References

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