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# THE ISOLATION AND CHARACTERISATION OF A NEW TYPE OF BIFLAVAN DERIVATIVE FROM A XANTHORRHOEA.

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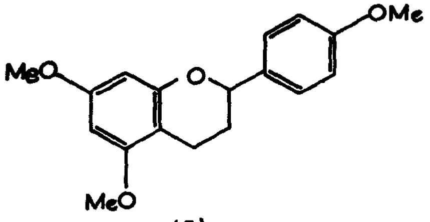
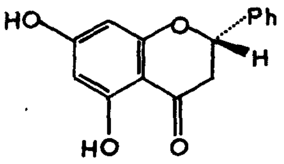
The phenolic resins of Australian Xanthorrhoea ("grass-trees") have so far yielded only minor proportions of crystalline flavonoids and several naphthalenes.(1) Among them are (-)-5,7-dimethoxyflavanone and the first flavan with no oxygen attached to the central ring, 4',5,7-trimethoxyflavan (I), isolated from a methylated fraction.(2) The nature of the bulk of the resin remains unknown, with the possible exception of X.hastile where it may consist chiefly of a polymer of cinnamyl-p-coumarate.(3)

From the carbonate-soluble fraction of a "red" Xanthorrhoea (preissii ?) was obtained by chromatography, 20% (-)-pinocembrin (II) identical with a specimen provided by Professor H.Erdtman. Exhaustive chromatography of the carbonate-insoluble fraction yielded, among many other compounds, xanthorrhone (III), m.p.193-196°, $[M]_D^{20}+ 550°$ and 14-hydroxyxanthorrhone (IV), m.p.190-193°, $[M]_D^{20}+ 1320°$. Owing to the small amounts available (35 mg. and 140 mg.) and our experience with mass spectrometry, (4,5,6,7) structure elucidation chiefly employed this technique. Preliminary results indicated that neither compound had a para-position to a hydroxyl unoccupied (negative Gibb's test) and the U.V.spectra (see table) showed great similarities of (III) and (IV) to each other and to pinocembrin. However if a value of $\varepsilon_{max.}$ 17,800 is used for the pinocembrin chromophore, the molecular weights appear as $\approx$570 and $\approx$600 respectively, indicating a dimeric structure and supported by osmometric measurements for (IV) which gave 520-560.

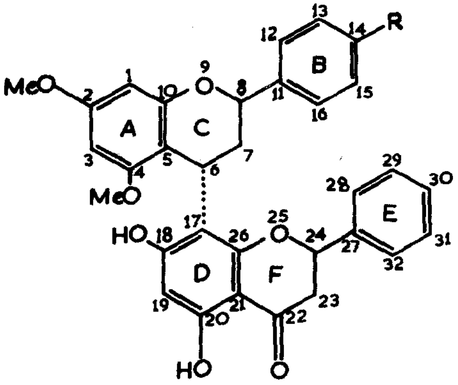
| | $\lambda_{max.}$ mμ (EtOH) | $\lambda_{min.}$ (EtOH) | $\lambda_{max.}$ (EtOH/KOH) | $\lambda_{max.}$ (EtOH/$AlCl_3$) |
|---|---|---|---|---|
| Xanthorrhone | 295, 336(s) | 255 | 250(s), 336 | 270, 313, 355 |
| Hydroxyxanthorrhone | 296, 336(s) | 255 | 245, 336 | 267, 316, 368 |
| Pinocembrin | 290, 325(s) | 247 | 247, 328 | 311, 370 |



(I)



(II)

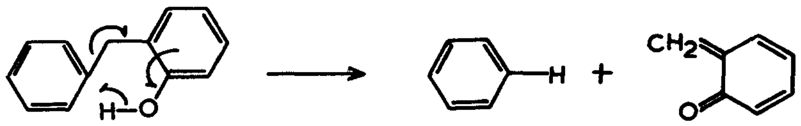


(III) R = H

(IV) R = OH

The molecular ions of (III) and (IV) were at 524.18686 ($C_{32}H_{28}O_7$) and 540.17842 ($C_{32}H_{28}O_8$). All the formulae given in Figs.I and II are supported by accurate mass measurements. Fig.I shows the results of splitting at the $C_6$-$C_{17}$ bond, with and without hydrogen transfer, the fragments behaving as expected.(5,7) Worthy of note is that the flavene fragment (a) differs by 16 mass units when produced from (IV) as compared with (III). Moreover, the highly favoured loss of an aryl group gives the common fragment (b), proving the extra hydroxyl group in (IV) to be on ring B.

A most significant and prominent peak in the mass spectra of (III) and (IV) is at 154.062649 ($C_8H_{10}O_3$) assigned to phloroglucinol dimethyl ether, not normally found in the spectra of the monomers,(5) and therefore characteristic of the molecule as a whole. A possible model is the fission of an o-hydroxydiphenylmethane system, shown(8) to cleave by the cyclic process below.



Applied to (III) and (IV) the molecular ion takes the form (c) which undergoes normal ether cleavage with hydrogen transfer to yield dimethylphloroglucinol (e) and fragment (d) the latter breaking down by a reverse Diels-Alder(5) reaction to (g) and (f). Direct ether cleavage gives (h) and (i) which yields (j). Dimethylphloroglucinol can only arise if there is a linkage from $C_6$ to either $C_{17}$ or $C_{19}$. The $C_{16}$-fragments (g), (f) and (j) contain ring B joined by the carbon atoms of the flavan ring to ring D, as substantiated by the appropriate differences in the fragments when derived from (III) or (IV). The fragmentations of Fig.I ("horizontal") confirm the nature of the basic units and those of Fig.II ("diagonal") the nature of their linkage. The Gibb's test is, so far, the only evidence for the position of the linkage to ring D.

A study of the 100Mc N.M.R.spectra confirmed and extended these conclusions. The main difference between (III) and (IV) was in the $A_2B_2$ doublet at τ 3.19, 2.79 (J = 9 c/s.) in the latter, showing the extra hydroxyl group in ring B to be para (i.e. at $C_{14}$). Only the spectrum of (III) will be discussed in detail. Two methoxyl groups show at τ 6.25 and τ 6.32 and two hydroxyl groups at τ 3.38 and τ -2.63 (hydrogen bonded). Only three aromatic protons are at high field, two are meta-coupled at τ 3.92d(1H), τ 3.80d.(1H), (J = 2 c/s.), establishing the meta-substitution of ring A, and the other a singlet at τ 4.08.(1H) due to a proton between two carbon atoms bearing oxygen substituents. Since one hydroxyl is hydrogen bonded it must be at $C_{20}$ and the other, therefore, is placed at $C_{18}$. There are definitely only three aromatic protons in this region showing that linkage is through the phloroglucinol ring; the other aromatic protons are at τ 2.60-2.82.

In accord with the postulated linkage there are seven aliphatic protons at τ 4.65q.(1H) ($J_1$= 13 c/s., $J_2$= 4 c/s.), τ 4.99q.(1H) ($J_1$= 9 c/s., $J_2$ = 5 c/s.), τ 5.40t.(1H) (J = 4 c/s), τ 6.76-7.40m.(2H) and τ 7.64-7.88.m(2H). Comparison spectra of trimethoxyflavan (I), pinocembrin (II) and bileucofisetinidin(9) were available. Irradiation at τ 7.7 caused the quartet at τ 4.99 to collapse to a broad singlet, the triplet at τ 5.4 to become a sharp singlet, and left the quartet at τ 4.65 unchanged. Thus a $-\overset{|}{C}H-CH_2-\overset{|}{C}H-$ system is present,

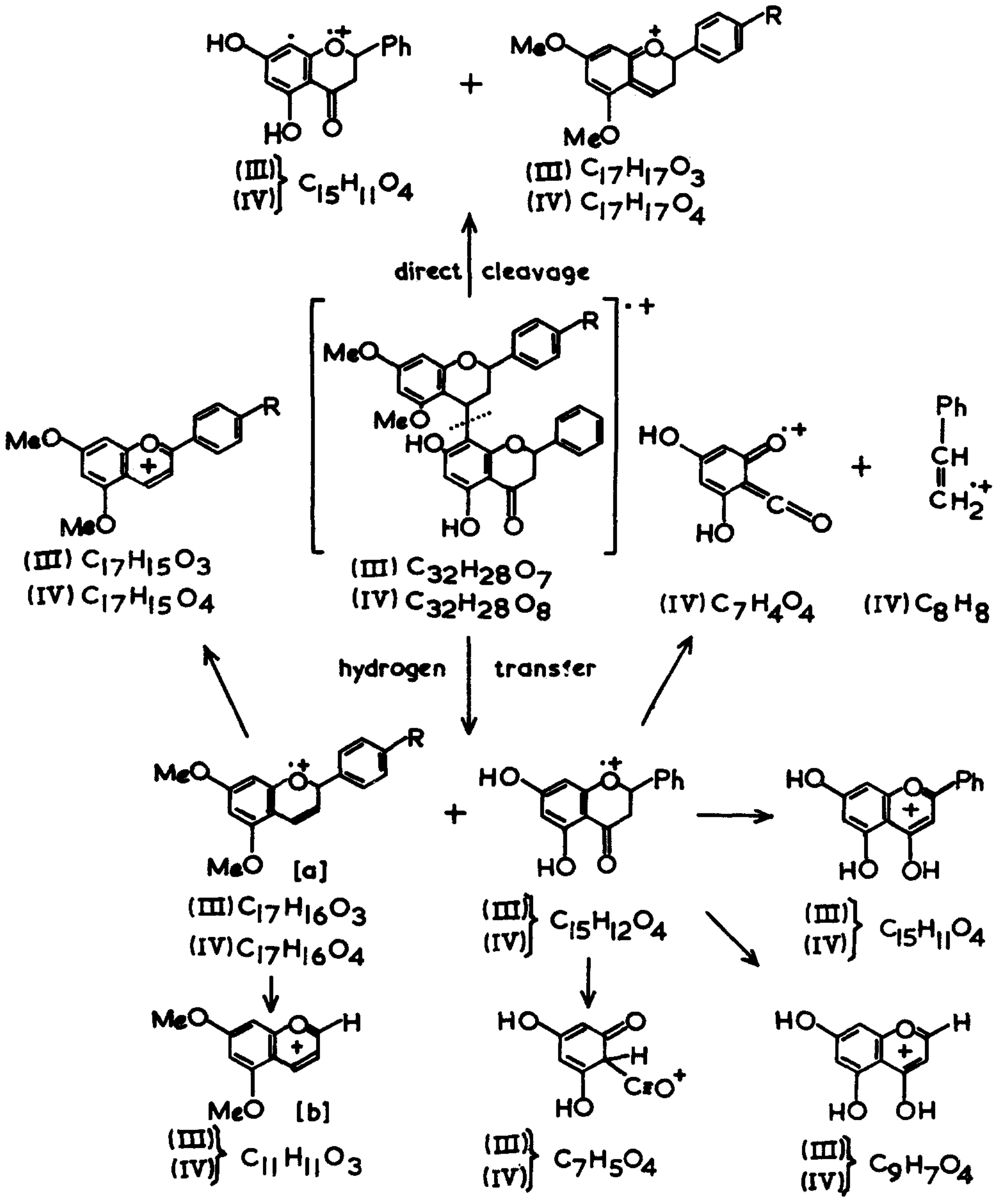

direct cleavage
(III) (IV) C15H11O4
(III) C17H17O3
(IV) C17H17O4
(III) C17H15O3
(IV) C17H15O4
(III) C32H28O7
(IV) C32H28O8
(IV) C7H4O4
(IV) C8H8
hydrogen transfer
[a]
(III)C17H16O3
(IV)C17H16O4
(III) (IV) C15H12O4
(III) (IV) C15H11O4
[b]
(III) (IV) C11H11O3
(III) (IV) C7H5O4
(III) (IV) C9H7O4

FIG. I

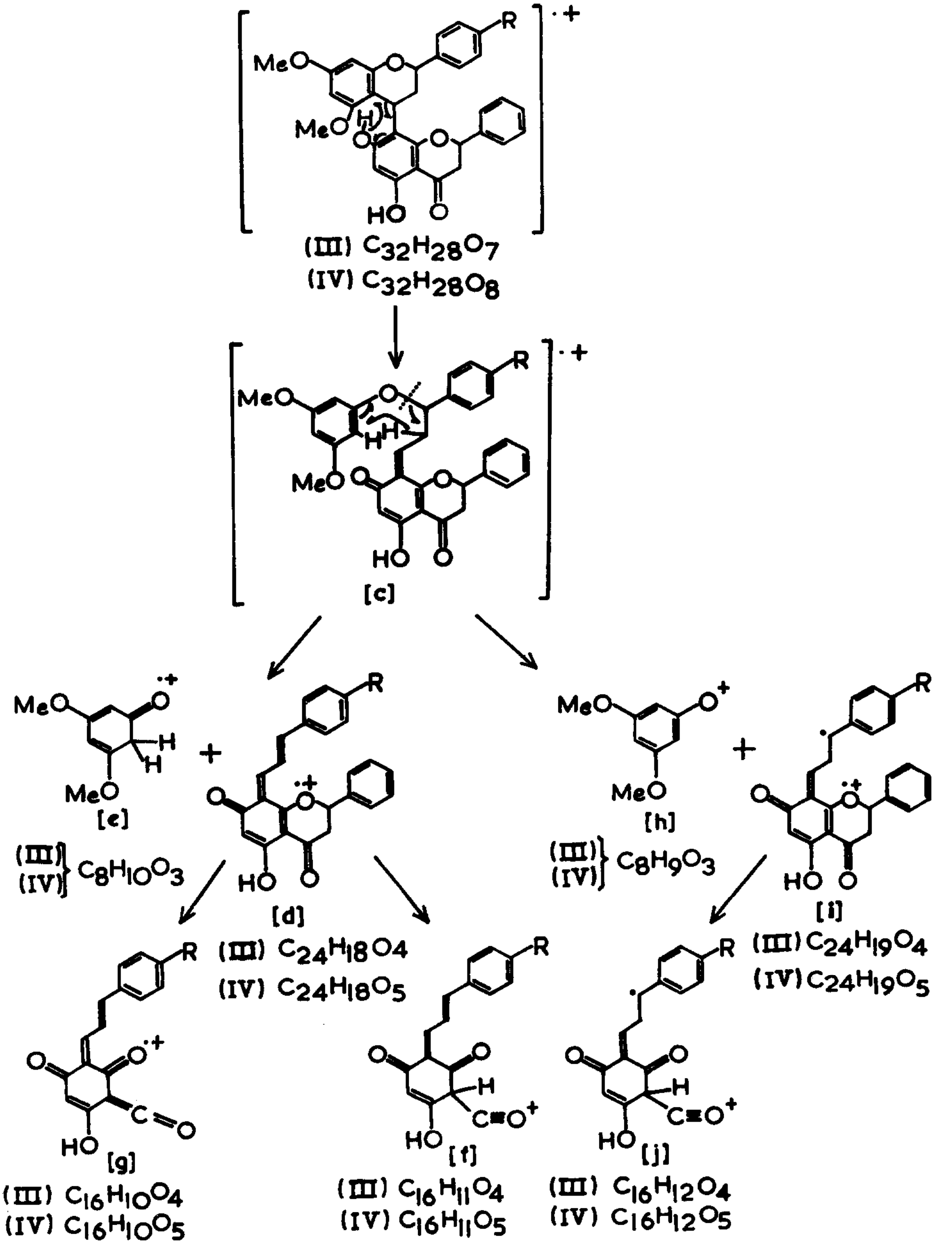

·+
MeO
R
H
O
HO
(III) $C_{32}H_{28}O_7$
(IV) $C_{32}H_{28}O_8$
[c]
[e]
(III) (IV) $C_8H_{10}O_3$
[d]
(III) $C_{24}H_{18}O_4$
(IV) $C_{24}H_{18}O_5$
[h]
(III) (IV) $C_8H_9O_3$
[i]
(III) $C_{24}H_{19}O_4$
(IV) $C_{24}H_{19}O_5$
C=O
C≡O⁺
[g]
(III) $C_{16}H_{10}O_4$
(IV) $C_{16}H_{10}O_5$
[f]
(III) $C_{16}H_{11}O_4$
(IV) $C_{16}H_{11}O_5$
[j]
(III) $C_{16}H_{12}O_4$
(IV) $C_{16}H_{12}O_5$

FIG. II

the high τ value for the $-CH_2-$ being in accord with the flavan system as is the position of the other protons. The quartet at τ 4.99 is due to $H_8$ (τ 5.1 in [I]) and the J values indicate a highly unsymmetrical coupling with the methylene protons. The coupling constants $J_{8,7e} = 5$ c/s, $J_{8,7a} = 9$ c/s would on the basis of the Karplus relationship be consistent with angles of 34° and 171° indicating a ψ-equatorial attachment of ring B. The triplet at τ 5.40 for $H_6$ is symmetrical, the small coupling constant indicating that $C_6-H_6$ approximately bisects the angle made by $H_{7e}-C_7-H_{7a}$. The mirror image relationships that satisfy these requirements are illustrated in Fig.III, again supporting the proposed linkage and indicating the relative stereochemistry.

FIG.III

Irradiation at τ 7.09 led to the quartet at τ 4.65 collapsing to a highly unsymmetrical doublet, whilst irradiation at τ 4.6 produced a quartet from the multiplet at τ 7.09. These protons are assigned to ring F. [cf. pinocembrin τ 4.60q.(1H), τ 7.1m.(2H)]. The coupling constants $J_{24,23e} = 4$ c/s, $J_{24,23a} = 13$ c/s, corresponding to dihedral angles of 45° and 180°, are identical with those in pinocembrin, and indicate that the phenyl group is attached to ring F in a ψ-equatorial position.

Work on the absolute configuration and the synthesis of these compounds is in hand.

The proanthocyanidin colour test with acid is extensively used in the search for reduced flavonoids but is not given by either (III) or (IV). Biogenetically they may represent nucleophilic attack by the readily available pinocembrin on the easily produced 4-carbonium ion of a flavan (possibly from the flavan-4-ol). The higher fractions of the resin may contain higher polymers of the same type. This may represent one example of a series where various nucleophiles are involved, hitherto undetected, as not bearing a 3-OH group they do not give an anthocyanidin with acid.

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