

THE FIRST CONDENSED TANNINS BASED ON A STILBENE

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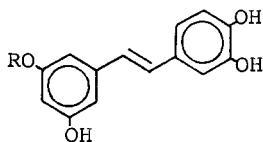
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Summary: In addition to 'conventional' proguibourtinidin condensed tannins, Rhodesian copalwood (*Guibourtia coleosperma*) contains significant concentrations of bi- and triflavanoid analogues uniquely based on nucleophilic *trans*-3,3',4',5-tetrahydroxystilbene and potentially electrophilic 2,3-*cis*- and 2,3-*trans*-4',7-dihydroxyflavan-3,4-diols (leucoguibourtinidins).

The occurrence of three diastereoisomeric leucoguibourtinidins (2,3-*cis*-3,4-*trans*-, 2,3-*trans*-3,4-*trans*- and 2,3-*trans*-3,4-*cis*-4',7-dihydroxyflavan-3,4-diols) in the proportions of 5:1:1 in Rhodesian copalwood (*Guibourtia coleosperma*) and their association with proguibourtinidin condensed tannins were demonstrated by Saayman and Roux.¹ Their study also involved the synthesis of the methyl ether acetates of all four possible racemates of the flavan-3,4-diols.

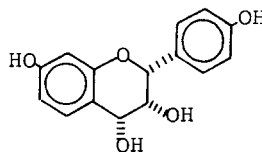
Our recent re-examination of the same material has shown that the sapwood contains a number of stilbene derivatives among which the 3-*O*-glucoside of 3,3',4',5-tetrahydroxystilbene (1) predominates, while the heartwood also contains the remaining 2,3-*cis*-3,4-*cis* diastereoisomer (3) of leucoguibourtinidin in excessively low (0.2 relative to the above ratio) concentration, together with five novel condensed tannin units derived from a combination of the nucleophilic stilbene aglycone (2) and the potentially electrophilic 2,3-*cis*- and 2,3-*trans*-leucoguibourtinidins [(3) and the predominant (2*R*)-diastereoisomers].

Examination of their methyl ether acetates by 80 MHz ¹H n.m.r. spectroscopy, mass spectrometry and circular dichroism has shown the presence of two 'dimeric' units in which the flavanyl substituents on the stilbene moiety possess 2,3-*cis*-3,4-*trans* (5) ($J_{2,3}$ 2.8, $J_{3,4}$ 5.1 Hz) and 2,3-*trans*-3,4-*trans* (7) ($J_{2,3} = J_{3,4} = 9.5$ Hz) configurations respectively. The 'unusual' coupling constants and chemical shifts (δ 5.81, 5.53 and 4.56 for 3-H, 2-H and 4-H respectively) of the heterocyclic protons of the former (5) are in general agreement with those of synthetic model compounds of identical configuration,² namely [4,8]- and [4,6]-2,3-*cis*-3,4-*trans*-(-)-teracacidin substituents on

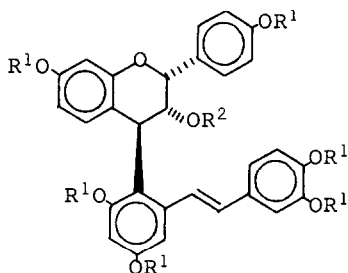


(1) R = glucosyl

(2) R = H



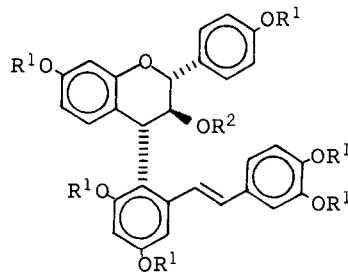
(3)



(4)

 $R^1 = R^2 = H$

(5)

 $R^1 = Me, R^2 = Ac$ 

(6)

(7)

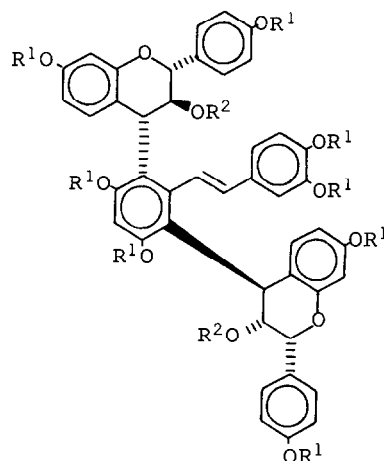
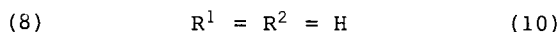
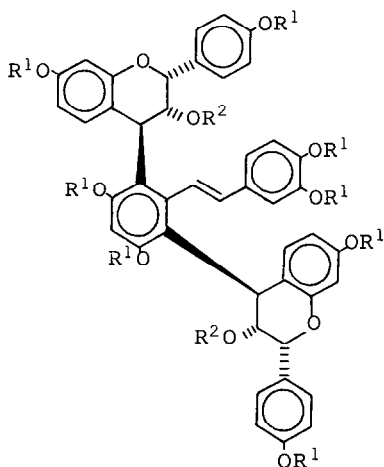
(+)-catechin [$J_{2,3}$ 2.5 and ~ 1.0 , $J_{3,4}$ 4.0 and 4.5 Hz; δ 5.55 and 5.61, 5.39 and 5.58, 4.55 and 4.50 respectively for 3-H, 2-H and 4-H respectively]. The coupling constants of the vinylic function ($J_{\alpha,\beta}$ 17.0 Hz) correlate with a *trans*-configuration of stilbene moieties. Temperature elevation to 100°C in $CDCl_3$ (pressure) was required at 80 MHz in order to obtain sharp spectra by overcoming the effects of dynamic rotational isomerism.³

Assessment of the bonding positions on the stilbene moiety was attempted by means of 500 MHz 1H n.m.r. spectroscopy in $DMSO-d_6$ at highly elevated temperatures (~ 453 K). The point of attachment for the methyl ether acetate (5) of one of the 'dimers', the 2,3-*cis*-3,4-*trans* isomer (4), was shown to be the 2-position of the resorcinol unit of the stilbene, since the lower field two-proton doublet [2-H + 6-H, δ 6.68, J 2.5 Hz ($CDCl_3$)] and higher field triplet [4-H, δ 6.41, J 2.5 Hz ($CDCl_3$)] characteristic of the parent stilbene tetramethyl ether are respectively replaced by two non-equivalent *meta*-coupled doublets [δ 6.87, 6.76 ($DMSO-d_6$)]. These resonances would have been equivalent under those dynamic conditions pertaining at high temperature had substitution occurred at the alternative C-4 position.

We presume that the derivative of the 2,3-*trans*-3,4-*trans* isomer (6), which is not amenable to 500 MHz spectroscopy due to persistence of considerable line-

broadening at the temperature limits (453 K), is attached at the same position, but this requires proof at lower magnetic field strengths.

Among the octamethyl ether diacetates of the three stilbene-based trimers, one (9) exhibits magnetic equivalence of all proton resonances contributed by the two 2,3-*cis*-3,4-*trans* flavanyl substituents, the coupling constants ($J_{2,3}$ 3.5, $J_{3,4}$ 6.0 Hz) and chemical shifts [δ 5.75, 5.55 and 4.55 for 3-H, 2-H and 4-H respectively (CDCl₃, 373 K, 80 MHz)] of heterocyclic protons closely resemble



ling those of the 'dimer' derivative (5). The remaining two with stereochemically 'mixed' 2,3-*trans*-3,4-*trans* ($J_{2,3} = J_{3,4} = 9.5$ and 9.7 Hz) and 2,3-*cis*-3,4-*trans* ($J_{2,3}$ both 3.7, $J_{3,4}$ both 6.7 Hz) substituents, although differing markedly in R_F values [t.l.c., 0.23, 0.30 in hexane-acetone-ethyl acetate (65:20:15 by vol.)] exhibit minor ¹H n.m.r. spectral differences at 80 MHz. Once again, only the all-2,3-*cis*-3,4-*trans*-isomer (9) exhibits sharp spectra under a combination of high magnetic field strength and high temperature (500 MHz, 480 K, DMSO-d₆), permitting unequivocal assignment of aromatic and vinylic protons. A singlet at δ 6.69 indicates a residual 4-proton, since the magnetic equivalence of protons of the two flavanyl substituents is consistent with 2 and 6 substitution on the resorcinol moiety of the stilbene. The vinylic system again shows the anticipated *trans* coupling ($J_{\alpha,\beta}$ 16.8 Hz). One of the derivatives of the stereochemically 'mixed' trimer appears to be in agreement with structure (11).

Mass spectral fragmentations of the methyl ether acetates of both 'dimers'

(5, 7) and the 'trimer' (9) (M^+ 626 and 952 respectively) are readily rationalised in terms of the proposed structure, the 'dimers' showing evidence of loss of 15 mass units and the equivalent of $C_{13}H_9^+$ ions characteristic of stilbenes.⁴

Circular dichroism of the same derivatives with positive, negative and positive Cotton effects (5, 7 and 9 respectively) at low wavelength, is consistent with their absolute stereochemistry at the point of attachment (4-C).⁵

The free phenolic forms of the 'dimers' (4) and (6) and the 'trimers' (8) and (10) readily give the single anthocyanidin, 3,4',7-trihydroxyppyrylium chloride (orange in visible, and bright yellow fluorescent under u.v. light).⁶

Synthesis of this novel series of compounds is in hand. However, an indication of the relative nucleophilicity of the 2 and 6 positions on 3,5-dihydroxyresorcinol moiety common to most natural stilbenes was obtained by Fourie⁷ through selective bromination of 3,3',4',5,5'-pentamethoxystilbene to give the 2,2',6-tribromo derivative.

Thanks are due to the Zimbabwe Forestry Commission, Bulawayo for a generous supply of the freshly-cut wood of *G. coleosperma*; and to Mr. I. Antonowitz, National Chemical Research Laboratory, C.S.I.R., Pretoria for recording 500 MHz n.m.r. spectra.

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(Received in UK 6 July 1983)