Absolute Configuration of Mopanol, a New Leucoanthocyanidin from *Colophospermum mopane*

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EXAMINATION of the heartwood of *Colophospermum mopane* Kirk *ex* J. Leonard formerly *Copaifera mopane*) for compounds which are of potential interest in studies of the stereochemistry and reddening[1] of flavan-3,4-diols and their polymers (tannins), has shown the presence of a group of interrelated flavanoid compounds based on resorcinol A and catechol B nuclei. The mixture was resolved by conventional methods[2] and the components characterized as (−)-fisetinidol (I), (+)-epifisetinidol (II), (+)-3′,4′,7-trihydroxy-2,3-*trans*-flavan-3,4-*cis*-diol (III), polymeric leucofisetinidins, (+)-peltogynol (IV) and (+)-mopanol (V). The latter, (IV, V), both 4β-ols, are accompanied in low concentration by their epimers at C–4 (4α-ols).

The (−)-fisetinidol (2*R* : 3*S*-configuration of substituents) (I) was identical to the (−)-3′,4′,7-trihydroxy-2,3-*trans*-flavan-3-ol from the heartwood of black wattle (*Acacia mearnsii*)[2]. (+)-Epifisetinidol (II), m.p. 120—121° (decomp.), $[\alpha]_D$ +82° in acetone : water (1 : 1 v/v), trimethyl ether m.p. 124°, was shown to have the 2,3-*cis*-configuration by n.m.r. spectrometry of its amorphous trimethyl ether acetate, m.p. 50—55° ($J_{2,3} < 1$ c./sec.). (+)-Epifisetinidol (II) is formed in 40% yield by epimerization of (−)-fisetinidol (I) under conditions of autoclaving described by Drewes and Roux,[3,4] and has the absolute configuration indicated (II) [(2*S* : 3*S*)-3′,4′, 7-trihydroxyflavan-3-ol)].

The leucofisetinidin (III) gave a crystalline trimethyl ether, m.p. 186—187°, $[\alpha]_D$ +45° in acetone : water (9/5, v/v) identical with that formed by epimerization followed by methylation of (+)-3′,4′,7-trihydroxy-2,3-*trans*-flavan-3,4-*trans*-diol[3] and by the selective epimerization of the corresponding methyl ether at C–4 with BF_3 and $NaBH_4$ in diglyme.[5] The purity of the natural

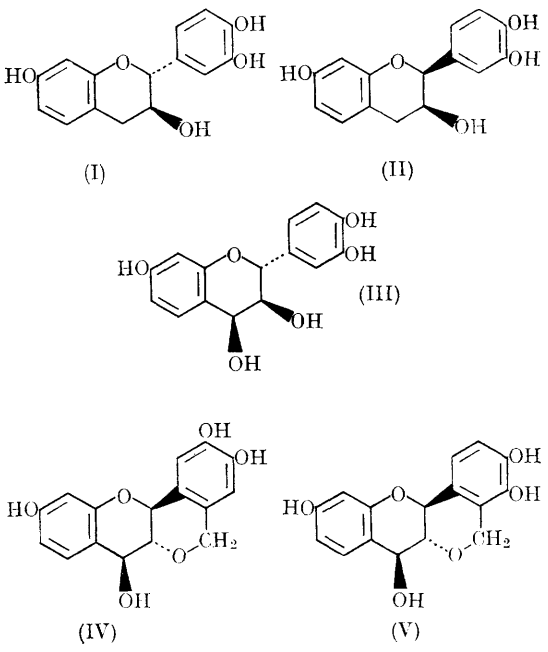
[1] D. G. Roux and S. E. Drewes, *Chem. and Ind.*, 1965, 1442.
[2] D. G. Roux and E. Paulus, *Biochem. J.*, 1961, **78**, 120.
[3] S. E. Drewes and D. G. Roux, *Biochem. J.*, 1965, **94**, 482.
[4] S. E. Drewes and D. G. Roux, *Biochem. J.*, 1965, in press.
[5] H. M. Saayman and D. G. Roux, *Chem. and Ind.*, 1964, 1761.

(+)-2,3-*trans*-3,4-*cis*-isomer was confirmed by paper ionophoresis in borate buffer[6] and by n.m.r. spectrometry[3] ($J_{2,3}$ = 10·0 c./sec.; $J_{3,4}$ = 3·4 c./sec.), and had the absolute configuration (III) [(2*R* : 3*S* : 4*S*)-3′,4′,7-trihydroxyflavan-3,4-diol)].

(+)-Peltogynol (IV), m.p. > 270°, $[\alpha]_D$ + 289° in ethyl acetate : ethanol (1 : 1, v/v), trimethyl ether m.p. 155—156° (sinter) and 196—200° (decomp.), is identical with the compound obtained from *Peltogyne porphyrocardia* by Robinson and Robinson.[7] The revised structure[8] and 2,3-*trans*-3,4-*trans*-configuration recently proposed for (IV) by Hassall and Weatherston[9] was confirmed by examination of the spin–spin coupling constants ($J_{2,3}$ = 10·0, $J_{3,4}$ = 8·8 c./sec.) of the 2-,3-, and 4-protons of the tetra-acetate, m.p. 178°. The substitution patterns of the benzenoid A- and B-rings were similarly confirmed by examination of the benzenoid protons of the methyl ether acetate, m.p. 154—155°, those of the B-ring showing *para*-coupling (AB system, singlets at τ2·90 and 3·54, $J_{2',5'}$ < 1 c./sec.).

(+)-Mopanol (V), m.p. > 270°, $[\alpha]_D$ + 209° in ethyl acetate, trimethyl ether, m.p. 196°, is a new leucoanthocyanidin which is isomeric with peltogynol (IV). The n.m.r. spectrum of the corresponding derivatives of (IV) and (V) are identical ($J_{2,3}$ = 10·0; $J_{3,4}$ = 8·8 c./sec.), except for the B-ring benzenoid protons of the trimethyl ether acetate m.p. 162—163°, and tetra-acetate, m.p. 220°, of (+)-mopanol which show *ortho*-coupling (AB system, quartet τ2·65 and 3·12, $J_{2',3'}$ = 8·5 c./sec.) for the methyl acetate. Consideration of the substitution patterns that are common to the above associated compounds (1′, 4′-disubstitution) leads to the tentative assignment of *ortho*-benzenoid protons in the 2′- and 3′-positions for mopanol. Also, the methylene protons which are apparently equivalent in (+)-peltogynol tetra-acetate (singlet, τ5·19), are unequally shielded in the corresponding (+)-mopanol derivative (τ 5·15 and 5·36) giving an AB quartet which shows geminal coupling (J = 16 c./sec.). The optical rotations of the tetra-acetates and trimethyl ethers of (+)-peltogynol (IV) and (+)-mopanol (V) are identical, proving their identical absolute configurations.

(+)-Epifisetinidol is the first natural epicatechin of the "resorcinol series", and also the first natural 2,3-*cis*-catechin with 2*S*-configuration. The mixture of (−)-fisetinidol and (+)-epifisetinidol represents the first natural association of 2,3-*trans*- and 2,3-*cis*-catechins of 2*R*- and 2*S*-configurations respectively. The (+)-2,3-*trans*-3,4-*cis*-leucofisetinidin (III) is the second compound of this configuration to be identified with certainty (*cf.* ref. 10). The compound (III) is enantiomeric at the three asymmetric centres with the 4-epimers of peltogynol (IV) and mopanol (V) indicating that in *C. mopane* it is the probable precursor of the



accompanying polymeric leucofisetinidin tannins, rather than of these epimeric compounds through reaction with formaldehyde (*cf.* refs. 8,9.) However, the association of the isomeric pairs (+)-mopanol and (+)-peltogynol (2*S* : 3*R* : 4*S*), and their 4-epimers (2*S* : 3*R* : 4*R*), supports the latter suggestion for the biogenesis of these specific compounds since free rotation of the phenyl nucleus of the corresponding (−)-leucofisetinidins could feasibly result in two groups of isomers during condensation with formaldehyde. (+)-Mopanol and (+)-peltogynol accordingly might have a common origin in (−)-3′,4′,7-trihydroxy-2,3-*trans*-flavan-3,4-*trans*-diol[11] (*cf.* Hassall *et al.*[8,9]).

[6] S. E. Drewes and D. G. Roux, *Biochem. J.*, 1964, **92**, 555.
[7] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 1935, 744.
[8] W. R. Chan, W. G. C. Forsyth, and C. H. Hassall, *J. Chem. Soc.*, 1958, 3174.
[9] C. H. Hassall and J. Weatherston, *J. Chem. Soc.*, 1965, 2844.
[10] S. E. Drewes and D. G. Roux, *Chem. and Ind.*, 1965, 1342.
[11] S. E. Drewes and D. G. Roux, *Biochem. J.*, 1964, **90**, 343.

Examination of Dreiding models of (+)-mopanol (V) and (+)-peltogynol (IV) shows that the heterocyclic ring-c exists in the "sofa" conformation as suggested[9]. The observed coupling constants for the protons of this ring (*cf.* above) correlate with their respective dihedral angles (173°, 150°) according to the Karplus relation.[12]

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[12] M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.