Phytochemistry of the Gum Copal Tree, *Trachylobium verrucosum* (Gaertn.) Oliv. The First Natural α-Hydroxychalcone and 2,3-*cis*- and 2,3-*trans*-3-Methoxyflavanones

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Besides high concentrations of (+)-2,3-*trans*-3,4-*trans*- and (+)-2,3-*trans*-3,4-*cis*-mopanols and -peltogynols, the heartwood of *Trachylobium verrucosum* contains α,2',3,4,4'-pentahydroxychalcone and 3-*O*-methyl-2,3-*cis*- and -2,3-*trans*-fustins, representing the first natural α-hydroxychalcone and also the first 3-methoxyflavanones and 3-oxygenated-2,3-*cis*-flavanone, as prominent metabolites. They are associated with low concentrations of 2-benzyl-2-hydroxybenzo[*b*]furan-3(2*H*)-one and 3-hydroxyflavone analogues.

Mechanistic aspects of the synthesis of 2'-hydroxy-α,3,4,4'-tetramethoxy-*trans*-chalcone from (±)-3,3',4',7-tetra-*O*-methyl-2,3-*trans*-fustin and *via* the crossed aldol condensation, and its novel conversion into both 3,3',4',7-tetra-*O*-methyl-2,3-*cis*- and -2,3-*trans*-fustins are discussed. Fisetin tetramethyl ether is converted by photolysis into both mopanin and peltogynin trimethyl ethers.

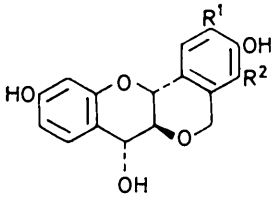
THE gum copal tree [*Trachylobium verrucosum* (Gaertn.) Oliv., syn. *T. hornemanniarium*] which populates the coastal rain forests of East Africa and North-Eastern Malagasy, is widely known for its exudate, Gum (Copal) Animi, and also for its timber[1]—the clear cylindrical bole exibiting a 6—7 cm wide sapwood surrounding a pale to red-brown heartwood. The latter was examined by Robinson and Robinson[2] some forty years ago and shown to contain a leucoanthocyanidin with properties resembling peltogynol.[2]

The present re-investigation not only confirms the predominance of (+)-peltogynol (I; $R^1 = OH$, $R^2 = H$)[2-5] with lesser amounts of (+)-peltogynol B (II; $R^1 = OH$, $R^2 = H$),[3-5] but also the presence of similar proportions of the isomeric pair (+)-mopanol and (+)-mopanol B (I and II; $R^1 = H$, $R^2 = OH$).[5] Their derivatives are compared with those of identical compounds from the mopane (*Colophospermum mopane*).[5] In *T. verrucosum* the peltogynoids are accompanied by flavonoids of the same phenolic substitution pattern (III—VII; $R = R^1 = R^2 = H$), many of them novel.

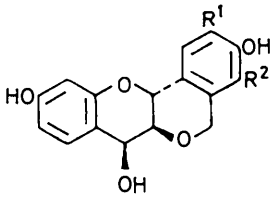
2-Benzyl-2,3',4',6-tetrahydroxybenzo[*b*]furan-3(2*H*)-one (III; R = H), present in trace amounts, shows the same high mobility on two-dimensional chromatograms as the α-hydroxychalcone. The n.m.r. spectrum of its tetramethyl ether (III; R = Me) showed chemical shifts of the 2-methoxy and methylene functions (τ

[1] I. R. Dale and P. J. Greenway, 'Kenya Trees and Shrubs,' Hatchards, London, 1961, p. 109.
[2] G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 1935, 744.
[3] W. R. Chan, W. G. C. Forsyth, and C. H. Hassall, *J. Chem. Soc.*, 1958, 3174.
[4] C. H. Hassall and J. Weatherston, *J. Chem. Soc.*, 1965, 2844.
[5] S. E. Drewes and D. G. Roux, *J. Chem. Soc.* (*C*), 1966, 1644.

6·75 and 6·83 respectively) which are characteristic [6,7] of related compounds. Its mass spectrum exhibited peaks which correlate with the anticipated fragments



(I)



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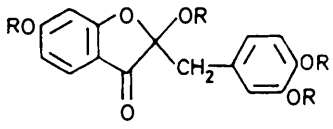

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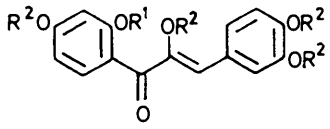
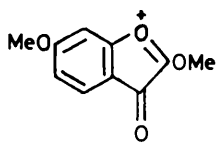
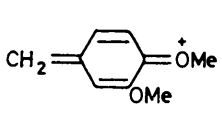


(IV)

(IIIa) and (IIIb), while i.r. absorption at 1715 cm^{-1} is indicative of a carbonyl group in a five-membered ring. Treatment with acetic anhydride–sulphuric acid gave an intense purple colour ascribed [8] to aurone formation. The structure of the methyl ether was confirmed by synthesis. The compound is similar to a 2-benzyl-2-hydroxybenzo[*b*]furan-3(2*H*)-one isolated by King *et al.*[9] from *Schinopsis* spp.

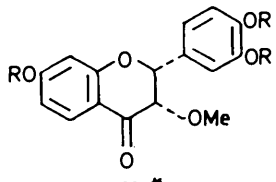


m/e 193 (29·2%)
(III a)

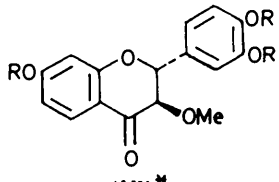


m/e 151 (100%)
(III b)

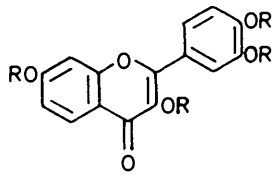
A very prominent metabolite, α,2′,3,4,4′-penta-hydroxychalcone [represented as the *trans* *-enolic form (IV; $R^1 = R^2 = H$)] showed significantly high mobility on paper (R_F 0·60) in 2% acetic acid compared



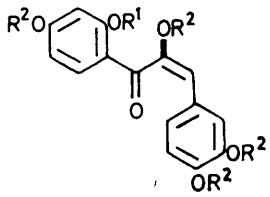
(V) *



(VI) *



(VII)



(VIII)

* Racemates: (2*R*)-enantiomers are illustrated

with conventional chalcones (0·0) and was characterized as the 2-hydroxy-α,3,4,4′-tetramethyl ether (IV; $R^1 = H$, $R^2 = Me$) and its acetate (IV; $R^1 = Ac$, $R^2 = Me$), and as the penta-acetate (IV; $R^1 = R^2 = Ac$). The i.r. spectrum of the tetramethyl ether showed H-bonded carbonyl absorption (1635 cm^{-1}), which correlates with the deshielded proton (τ −2·62) in its n.m.r. spectrum (Table 1). Confirmation of structure was provided by complete synthesis of the tetramethyl ether; by its formation through alkaline ring opening of (±)-3,3′,4′,7-tetra-*O*-methyl-2,3-*trans*-fustin derived from other natural sources (see below), and by its

TABLE 1

N.m.r. spectra of α,2′,3,4,4′-pentasubstituted-*trans*- and -*cis*-chalcones

Chalcone	Solvent	τ Values												
		—H							—OMe				—OH	—OCOMe
trans-Methyl ethers		β	2	5	6	3′	5′	6′	α	2′	3,4	4′	2′	2′
2′-hydroxy-α,3,4,4′-tetramethoxy	$CDCl_3$	3·59s	2·51d	3·12d	2·68q	3·51d	3·53q	1·95d	6·26s		6·06s	6·13s	−2·57s	
2′-hydroxy-α,3,4,4′-tetramethoxy	C_6D_6	3·48s	2·53d	3·37d	2·67q	3·45d	3·63q	1·93d	6·47s		6·57s 6·60s	6·79s	−3·67s	
2′-acetoxy-α,3,4,4′-tetramethoxy	$CDCl_3$	3·50s	2·50d	3·15d	2·66q	3·26d	3·15q	2·32d	6·23s		6·08s	6·13s		7·80s
α,2′,3,4,4′-pentamethoxy	$CDCl_3$	3·57s	2·80d	3·13d	2·56q	3·44d	3·42q	2·58d	6·20s	6·13s	6·10s	6·17s		
cis-Methyl ethers														
2′-hydroxy-α,3,4,4′-tetramethoxy	$CDCl_3$	3·95s	3·23—3·33			3·57d	3·65q	2·45d	6·30s		6·18s	6·18s	−2·37s	
α,2′,3,4,4′-pentamethoxy	$CDCl_3$	4·09s	3·17—3·30			3·60d	3·52q	2·25d		6·17—6·27				
trans-*O*-Acetates										-OCOMe				
α,2′,3,4,4′-penta-acetoxy	$CDCl_3$	3·17s	2·47d	2·77d	2·50q	2·93d	2·87q	2·33d	7·67s (12H), 7·80s					
α,2′,3,4,4′-penta-acetoxy	C_6D_6	3·17s	2·52d	3·00d	3·02q	3·12d	3·19q	2·41d	8·07s, 8·12s, 8·20s (6H), 8·28s					

* The term *trans* used with chalcones refers to the relationship between the benzoyl and phenyl substituents on the olefinic double bond.

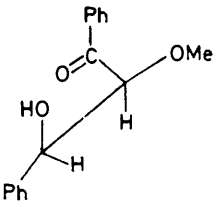
[6] F. du R. Volsteedt and D. G. Roux, *Tetrahedron Letters*, 1971, 1647.
[7] T. G. Fourie, I. C. du Preez, and D. G. Roux, *Phytochemistry*, 1971, **11**, 1763.
[8] H. G. C. King and T. White, *J. Chem. Soc.*, 1961, 3539.
[9] H. G. C. King, T. White, and R. B. Hughes, *J. Chem. Soc.*, 1961, 3234.

novel cyclization to the full methyl ethers of 2,3-*cis*- and 2,3-*trans*-fustins (V and VI; R = Me). The *trans*-configuration of the 2'-hydroxy-α,3,4,4'-tetramethoxychalcone (IV; R^1 = H, R^2 = Me) was confirmed by its photolysis to the *cis*-isomer (VIII; R^1 = H, R^2 = Me).

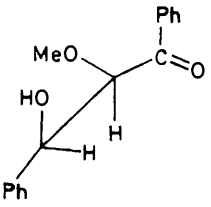
Racemic 3-*O*-methyl-2,3-*cis*- and 3-*O*-methyl-2,3-*trans*-fustins (V and VI; R = H) are likewise prominent metabolites in the heartwood of *T. verrucosum*. They were similarly characterized by n.m.r. and mass spectrometry of the trimethyl ethers (V and VI; R = Me) and tri-acetates (V and VI; R = Ac). Confirmation of structure was by the aforementioned cyclization of 2'-hydroxy-α,3,4,4'-tetramethoxy-*trans*-chalcone. The relative configurations of the 2,3-*cis*- and 2,3-*trans*-fustins were evident from the coupling constants ($J_{2,3}$ 2·0 and 10·4 Hz, respectively) and chemical shifts of the 2- and 3-protons of their derivatives, in comparison with those of synthetic 3-methoxy-2,3-*cis*- and 3-methoxy-2,3-*trans*-flavan-4-ones ($J_{2,3}$ 1·8—2·5 and 9·4—10·4 Hz, respectively).[10] Mass spectral fragmentations were also consistent with the proposed structures.

Synthesis of 2'-Hydroxy-α,3,4,4'-tetramethoxy-trans-chalcone, (±)-3,3',4',7-Tetra-O-methyl-2,3-cis- and -2,3-trans-fustin, and 2-Benzyl-2,3',4',6-tetramethoxybenzo[b]-furan-3(2H)-one.—Confirmation of structure of the foregoing α-hydroxychalcone, 2-benzyl-2-hydroxybenzofuranone, and 2,3-*cis*- and 2,3-*trans*-fustins was provided by synthesis of their methyl ethers.

The chalcone (IV; R^1 = H, R^2 = Me) was obtained by condensation of 2'-hydroxy-2,4'-dimethoxyacetophenone with 3,4-dimethoxybenzaldehyde in the presence of alkali. According to t.l.c. evidence the thermodynamically less stable *cis*-chalcone, characterized by a blue colouration with H_2SO_4–HCHO spray and lower R_F than the *trans*-isomer, is formed first, followed by conversion into the *trans*-chalcone. Presuming that the α-methoxychalcone results from the base-induced dehydration of the aldol (*E*1cB mechanism), observation of the initial formation of the *cis*-isomer suggests that the free energy of the transition state[11] resulting from the *erythro*-isomer is lower than



erythro-Isomer (one enantiomer)

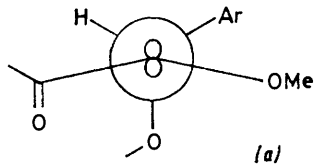


threo-Isomer (one enantiomer)

that from the *threo*-form. Subsequent and presumably base-catalysed conversion of the *cis*- into the *trans*-chalcone by reversible 1,4-addition of the elements of water provides a satisfactory explanation for the observed isomerization.

Cyclization of the chalcone (IV; R^1 = H, R^2 = Me) in acid medium[12] (3N-H_2SO_4 or -HCl in ethanol) yielded the benzofuranone (III; R = Me), while cyclization by using weakly basic conditions according to the method of Tominaga[13] yielded for the first time a 1 : 2 mixture of the 2,3-*cis*- and -2,3-*trans*-fustins (V and VI; R = Me). The latter reaction contrasts with the findings of Clark-Lewis *et al.*[10] who obtained only 3-hydroxy-2,3-*trans*-flavan-4-one derivatives under similar conditions. Cyclization under acidic conditions to give addition in the anti-Michael sense must be due to the inductive effect of the α-OMe function following protonation of the αβ-double bond, while cyclization under slightly alkaline conditions *via* a Michael 1,4-type addition to give a 1 : 2 ratio of 2,3-*cis*- and 2,3-*trans*-fustins probably reflects a 2,3-*cis*-fustin ⇌ chalcone ⇌ 2,3-*trans*-fustin equilibrium, these compounds being present in the reaction product. Clark-Lewis *et al.*[10] claimed the existence of a 1 : 2 2,3-*cis* ⇌ 2,3-*trans*-3-methoxyflavanone equilibrium under acidic conditions (trichloroacetic acid).

Ring opening of the tetra-*O*-methyl-2,3-*trans*-fustin (VI; R = Me) [prepared by complete methylation of natural (±)-fustin (VI; R = H) from *Rhus glabra*[14] with Me_2SO_4–anhydrous K_2CO_3 in dry acetone[15]] with alkali[3] yielded the anticipated *trans*-chalcone (IV; R^1 = H, R^2 = Me). This presumably proceeds *via* an *E*1cB-mechanism (*i.e.* initial abstracton of a 3-proton followed by ring opening).[16,17] Since the reaction, in contrast with the condensation step in the synthesis of the *trans*-chalcone, cannot be followed by t.l.c., the carbanion intermediate (*a*) resulting from the known



(*a*)

conformation of the C-ring of 3-oxygenated-2,3-*trans*-flavan-4-ones [2-*eq* : 3-*eq* substituents] is presumed to yield the *trans*-chalcone directly on ring opening.

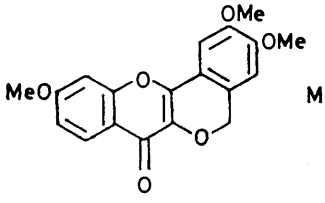
Although it was initially expected that complete methylation of (±)-fustin under the foregoing conditions would be accompanied to a large extent by oxidation to the 3-hydroxyflavone analogue,[18] the reaction was unexpectedly complicated in a different direction by the prominent production of the pentamethoxy-*trans*-chalcone (IV; R^1 = R^2 = Me)—a reaction which is not evident[15] during the methylation of (+)-taxifolin [(+)-3,3',4',5,7-pentahydroxy-2,3-*trans*-flavan-4-one]. Considering that the reaction was per-

[10] J. W. Clark-Lewis, R. W. Jemison, and V. Nair, *Austral. J. Chem.*, 1968, **21**, 3015.
[11] E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 151.
[12] J. Gripenberg, *Acta Chem. Scand.*, 1953, **7**, 1323.
[13] T. Tominaga, *J. Pharm. Soc. Japan*, 1960, **80**, 1202; 1962, **82**, 780.
[14] D. G. Roux and F. Freudenberg, *Annalen*, 1958, **613**, 56.
[15] E. V. Brandt, D. Ferreira, and D. G. Roux, *J.C.S. Chem. Comm.*, 1972, 392.
[16] J. March, 'Advanced Organic Chemistry. Reactions, Mechanisms and Structure,' McGraw-Hill, New York, 1968, p, 568.
[17] T. J. Houser, R. B. Bernstein, R. G. Miekka, and J. C. Angus, *J. Amer. Chem. Soc.*, 1955, **77**, 6201.
[18] T. R. Seshadri, *Tetrahedron*, 1959, **6**, 181.

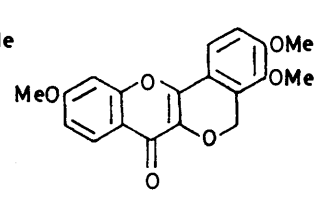
formed during abnormally damp atmospheric conditions, it is possible that despite stringent precautions for the exclusion of moisture, the chalcone originated either from the hydrolysis of the potassium carbonate and action of the resultant base on the 3-methoxyflavanone or from direct deprotonation of the latter by the carbonate ion.

Fisetin, and Photolytic Conversion of its Tetramethyl Ether into the Trimethyl Ethers of Peltogynin and Mopanin. Irradiation of α-Methoxychalcones.—The presence of fisetin (VII; R = H) in the wood extract of *T. verrucosum* was established by its brilliant yellow-green fluorescence and confirmed by the n.m.r. spectrum and m.p. of its tetra-*O*-methyl derivative in comparison with an authentic specimen.[19]

Furthermore, photolysis[20] of fisetin tetramethyl ether (VII; R = Me) under the improved conditions[21] devised for the cyclization of quercetin pentamethyl



(IX)



(X)

ether gave tri-*O*-methylpeltogynin (IX) and tri-*O*-methylmopanin (X) in good yields (18 and 16% respectively). The structures of these compounds were proved unequivocally by n.m.r. (Table 2) and mass spectrometry. The molecular ions (M^+ 340) of the trimethyl ethers of mopanin and peltogynin represent the base peaks in both cases, whereas fragmentation occurs through loss of CO and CH_3· following initial loss of H· from the D-ring. This represents the first synthesis of derivatives of mopanin and peltogynin, compounds which are absent from *T. verrucosum*, but present in the heartwood of the mopane (*C. mopane*).[19]

Attempts at selective D-ring formation prior to C-ring closure by photolysis of the chalcones (IV; R^1 = H, R^2 = Me, and R^1 = R^2 = Me) resulted in the anticipated[22] and almost quantitative isomerization to the *cis*-isomers (VIII; R^1 = H, R^2 = Me, and R^1 = R^2 = Me), a configuration which is unfavourable for the desired cyclization. Maintenance of the *trans*–*cis* equilibrium[23] in the presence of iodine did not, however, yield the desired peltogynol- and mopanol-type chalcones. The *trans* ⟶ *cis* conversion nevertheless confirmed that the naturally derived chalcone tetramethyl ether (IV; R^1 = H, R^2 = Me), and the corresponding pentamethyl ether (IV; R^1 = R^2 = Me) derived from (±)-tetra-*O*-methylfustin during methylation, both represent the more stable *trans*-configuration.

In addition to differences in the n.m.r. spectra between *cis*- and *trans*-2′-hydroxy-α-methoxychalcones (Table 1), the *cis*-isomer shows lower mobility on kieselgel substrates during t.l.c. and develops an immediate blue colour with H_2SO_4–HCHO spray, compared with the more slowly developing red-brown given by the *trans*-form. These colourations may be linked with those resulting from similar treatment of 2-benzyl-2-hydroxybenzofuranones with H_2SO_4–HOAc, and attributed to aurone formations.[8]

Possible Significance of α-Hydroxychalcones and 3-Methoxyflavan-4-ones in the Biosynthesis of Peltogynoids.—Since the initial announcement of the presence in *T. verrucosum* of these novel metabolites,[24] the identical metabolites (α-hydroxychalcone, and 2,3-*cis*- and 2,3-*trans*-fustins) have been located in association with mopanols and peltogynols in *Peltogyne venosa* and *P. pubescens*,[25] albeit in low concentration. In spite of our inability to cyclisize α-methoxychalcones to their peltogynoid analogues (D-ring formation), these chalcones may represent key intermediates in the most likely biogenetic path leading to peltogynols and mopanols, owing to the advantage offered by their planarity during successive cyclizations. Peltogynoid chalcones and peltogynones have, for example, been

TABLE 2

N.m.r. spectra of derivatives of 2,3-*cis*- and 2,3-*trans*-fustins

	τ Values ($CDCl_3$) (J in Hz)											
	–H								–OMe			–OCOMe
	2	3	5	6	8	2′	5′	6′	3	3′,4′	7	3′,4′,7
(±)-2,3-*cis*-fustin												
3,3′,4′,7-tetra-*O*-methyl-	4·65d ($J_{2,3}$	6·27d 2·0)	2·07d	3·32q	3·45d	3·00d	3·07d	2·83q	6·62s	6·05s (6H)	6·15s	
3-*O*-methyl-3′,4′,7-tri-*O*-acetyl-	4·61d ($J_{2,3}$	6·24d 2·0)	2·01d	3·14q	3·12d	2·67d	2·62d	2·70q	6·67s			7·70s (9H)
(±)-2,3-*trans*-fustin												
3,3′,4′,7-tetra-*O*-methyl-	4·75d ($J_{2,3}$	5·92d 10·4)	2·13d	3·35q	3·52d	2·93d	3·10d	2·87q	6·59s	6·08s (6H)	6·17s	
3-*O*-methyl-3′,4′,7-tri-*O*-acetyl	4·64d ($J_{2,3}$	5·90d 10·4)	2·03d	3·13q	3·17d	2·50d	2·67d	2·62q	6·57s			7·70s (9H)

[19] S. E. Drewes and D. G. Roux, *J. Chem. Soc.* (*C*), 1967, 1407.
[20] A. C. Waiss, R. E. Lundin, and J. Corse, *J. Amer. Chem. Soc.*, 1967, **89**, 6213.
[21] E. V. Brandt, D. Ferreira, and D. G. Roux, unpublished work.
[22] G. J. Fonken, 'Organic Photochemistry,' ed. O. L. Chapman, Edward Arnold, London, 1967, p. 203.
[23] F. B. Mallory, C. S. Wood, and J. T. Gordon, *J. Amer. Chem. Soc.*, 1964, **86**, 3094.
[24] J. P. van der Merwe, D. Ferreira, E. V. Brandt, and D. G. Roux, *J.C.S. Chem. Comm.*, 1972, 521.
[25] E. Malan and D. G. Roux, *Phytochemistry*, in the press.

isolated recently from *Acacia carnei*,[21] *A. crombei*,[21,26] and *Gonniorrhacis marginata*.[27]

The mobility of the α-hydroxychalcone on cellulose in aqueous medium indicates that it exists naturally mainly in the colourless keto-form. This is supported by the isolation of both *cis*- and *trans*-enolic forms after methylation.[28] Evidence of the broader significance of α-hydroxychalcones as possible biogenetic precursors, stems from their isolation from a number of plant sources which were under study in these laboratories prior to their initial discovery, namely *Berchemia zeyheri* (2′,4,4′,6′-tetrahydroxy-),[28] *B. discolor* (2′,3,4,4′,6′-pentahydroxy-),[29] and *Peltogyne venosa* and *P. pubescens* (2′,3,4,4′-tetrahydroxy-).[25]

EXPERIMENTAL

Authenticated heartwood samples and freshly-cut sections of the trunk of *T. verrucosum* were kindly supplied respectively by Professor D. Normand, Centre Technique Forestier Tropical, Nogent-sur-Marne, France and Mons. J. M. Adriamampianina, Direction des Eaux et Florêts et de la Conservation des Sols, Ministére de l'Agriculture, Tananarive, Malagasy.

N.m.r. spectra were recorded in $CDCl_3$ with Me_4Si as internal standard, optical rotations in $CHCl_3$ on a Hilger and Watts M-412 polarimeter, and i.r. spectra also in $CHCl_3$. Two-dimensional chromatograms were run by ascent on Whatman No. 1 (28 × 46 cm) sheets in Bu^{s}OH saturated with water and in 2% HOAc. R_F values are indicated in this sequence. Preparative paper chromatography (p.p.c.) was run by ascent in 2% or 20% (v/v) HOAc, or by descent in Bu^{s}OH saturated with water on Whatman No. 3 paper (46 × 57 cm). Bands cut from these chromatograms were eluted with 70% (v/v) ethanol. T.l.c. was on Kieselgel PF_{254} (0·25 mm) and on a preparative scale (p.l.c.) on the same substrate (1·0 mm). Plates were air-dried and unactivated, and sprayed with H_2SO_4–40% HCHO (40 : 1). All evaporations of eluates from bands were under reduced pressure at 60°.

Unless otherwise specified, methylations were in methanol–ether solution with an excess of diazomethane at −15° for 24 h.

Extraction and Preliminary Separation.—Drillings (820 g) from the heartwood of *T. verrucosum* [after dewaxing with n-hexane (5 × 2·5 l) at room temperature] were extracted over 4 days with methanol (4 × 2·5 l) at ambient temperatures. After chromatographic confirmation of the identity of successive extracts, they were combined and concentrated under reduced pressure at 60° to a brown amorphous powder.

The solid extract (60 g) dissolved in acetone (1·5 l) was applied to Whatman No. 3 paper (300 sheets) and the chromatograms developed in 20% v/v acetic acid. Seven bands were differentiated under u.v. light or with spray reagents.[30] The bands were eluted and the solvent removed to give the following fractions.

Fraction	TV_1	TV_2	TV_3	TV_4	TV_5	TV_6	TV_7
R_F	0·71	0·64	0·58	0·51	0·42	0·32	0·11
Yield (g)	1·91	3·35	1·81	1·71	3·68	4·72	2·69

(±)-2-*Benzyl*-2,3′,4′,6-*tetrahydroxybenzo*[*b*]*furan*-3(2H)-*one* (III; R = H). Fraction TV_1 was purified by p.p.c. in 2% HOAc. Two bands, R_F 0·65 and 0·54, were eluted and recovered to give fractions TV_1a (0·56 g; R_F 0·81, 0·51) and TV_1b (0·96 g; R_F 0·80, 0·40) as brown amorphous powders.

(±)-2-*Benzyl*-2,3′,4′,6-*tetramethoxybenzo*[b]*furan*-3(2H)-*one* (III; R = Me). Methylation of fraction TV_1a (500 mg), followed by p.l.c. in benzene–acetone (9 : 1 v/v) yielded a yellow oil (57 mg), *m/e* 344(M^+, 9·0%), 194(5·1), 193(29), 178(8·5), 165(6·3), 163(9·3), 152(11·2), 151(100), and 150(9·8), $\nu_{max.}$ 1715 cm^{-1}, τ 2·52 (d, 4-H), 3·10—3·30 (m, 2′-, 5′-, and 6′-H), 3·43 (q, 5-H), 3·50 (d, 7-H), 6·12 (s, OMe), 6·19 (s, 2 × OMe), 6·75 (s, 2-OMe), and 6·83 (s, CH_2). The ABC system of the B-ring was resolved in C_6D_6. The compound gives a purple colour with H_2SO_4–40% HCHO (40 : 1) spray on t.l.c.

α,2′,3,4,4′-*Pentahydroxy*-trans-*chalcone* (IV; $R^1 = R^2$ = H), (±)-3-O-*methyl*-2,3-cis-*fustin* (V; R = H), *and* (±)-3-O-*methyl*-2,3-trans-*fustin* (VI; R = H). The fraction TV_2 (3·35 g) was purified by p.p.c. (50 mg per sheet) by upward development in 2% HOAc. The band, R_F 0·54, was eluted and evaporated to give a light brown amorphous powder (1·28 g). Two-way chromatograms showed this fraction as a single component (R_F 0·80, 0·40) and identical with fraction TV_1b (above). These fractions were accordingly combined (1·5 g), methylated, and the product separated by p.l.c. in benzene–acetone (8 : 2 v/v) to give three fractions [R_F 0·66 (173 mg), 0·56 (353 mg), and 0·49 (460 mg)].

2′-*Hydroxy*-α,3,4,4′-*tetramethoxy*-trans-*chalcone* (IV; R^1 = H, R^2 = Me). The R_F 0·66 fraction was purified by p.l.c. in benzene–acetone (9 : 1 v/v) (two developments). The resulting material (125 mg), having R_F 0·56 under these conditions, crystallized from methanol as clear *yellow plates*, m.p. 98·6°, *m/e* 344(M^+, 100%), 329(10·6), 313(41), 312(14·8), 297(5·0), 226(23), 207(35), 194(5·9), 193(8·5), 179(8·5), 165(9·1), 163(6·7), and 151(78) (Found: M^+, 344·123. $C_{19}H_{20}O_6$ requires M, 344·126), $\nu_{max.}$ 3040 (OH stretching, intramolecular H-bonded) and 1635 cm^{-1} (C=O stretching), n.m.r. spectrum (*cf.* Table 1).

2′-*Acetoxy*-α,3,4,4′-*tetramethoxy*-trans-*chalcone* (IV; R^1 = Ac, R^2 = Me). Acetylation of the 2′-hydroxychalcone (50 mg) in acetic anhydride–pyridine followed by purification on p.l.c. with benzene–acetone (9 : 1 v/v) gave a *yellow oil* (32 mg), *m/e* 386(M^+, 49%), 344(15), 343(13·4), 313(27), 312(16), 256(12·2), 207(22), 194(8·5), 193(27), 179(7·3), 178(12·2), 166(23), 165(33), 163(12·2), 152(13·4), 151(100), 150(18·3), and 149(22), $\nu_{max.}$ 1770 (C=O stretching, acetyl) and 1650 cm^{-1} (C=O stretching), n.m.r. spectrum (*cf.* Table 1).

(±)-3,3′,4′,7-*Tetra*-O-*methyl*-2,3-cis-*fustin* (V; R = Me). The R_F 0·56 fraction (353 mg; from methylation of combined fractions TV_1b and TV_2) after purification by p.l.c. with benzene–acetone (9 : 1 v/v) (two developments), gave an oil (214 mg), *m/e* 344(M^+, 55%), 195(12·3), 194(100), 193(19·2), 179(22), 152(5·7), and 151(58) (Found: M^+, 344·123. $C_{19}H_{20}O_6$ requires M, 344·126), $\nu_{max.}$ 1685 cm^{-1} (C=O stretching), n.m.r. spectrum (Table 2) indicates a 2,3-*cis*-configuration [10] ($J_{2,3}$ 2·0 Hz) and C(3)OMe group (τ 6·62).

(±)-3,3′,4′,7-*Tetra*-O-*methyl*-2,3-trans-*fustin* (VI; R =

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[27] O. R. Gottlieb and J. Régo de Sousa, *Phytochemistry*, 1972, **11**, 2841.
[28] F. du R. Volsteedt, G. J. H. Rall, and D. G. Roux, *Tetrahedron Letters*, 1973, 1001.
[29] F. du R. Volsteedt, G. J. H. Rall, D. Ferreira, and D. G. Roux, unpublished work.
[30] D. G. Roux and E. A. Maihs, *J. Chromatog.*, 1960, **4**, 65.

Me). The R_F 0·49 fraction (460 mg; from methylation of combined fractions TV_1b and TV_2), following purification as for the *cis*-isomer, crystallized from ethanol as *white needles* (340 mg), m.p. 143°, *m/e* 344(M^+, 24%), 195(13·1), 194(100), 179(22), and 151(12) (Found: M^+, 344·124. $C_{19}H_{20}O_6$ requires M, 344·126), $\nu_{max.}$ 1685 cm^{-1} (C=O stretching), n.m.r. spectrum (Table 2) confirmed the 2,3-*trans*-configuration [10] ($J_{2,3}$ 10·4 Hz) and C(3)OMe group (τ 6·59).

α,2′,3,4,4′-*Penta-acetoxy*-trans-*chalcone* (IV; $R^1 = R^2$ = Ac), (±)-3′,4′,7-*tri*-O-*acetyl*-3-O-*methyl*-2,3-cis-*fustin* (V; R = Ac), *and* (±)-3′,4′,7-*tri*-O-*acetyl*-3-O-*methyl*-2,3-trans-*fustin* (VI; R = Ac). Acetylation of the combined fraction TV_1b and TV_2 (400 mg) followed by p.l.c. with 1,2-dichloroethane–acetone (19 : 1 v/v) gave three fractions, R_F 0·54, 0·60, and 0·71.

The R_F 0·71 band gave the chalcone (IV; $R^1 = R^2$ = Ac) as a *yellow oil* (28 mg), *m/e* 498(M^+, 0·4%), 456(21), 414(25), 372(27), 330(12·0), 312(10·5), 250(8), 221(15), 208(31), 192(10·5), 179(46), 166(80), 150(16), 137(46), 136(14·5), and 123(100), n.m.r. spectrum (*cf.* Table 1).

The R_F 0·60 fraction gave the 2,3-*cis*-fustin (V; R = Ac) as a pale yellow oil (62 mg). The n.m.r. spectrum (Table 2) again correlated with a 2,3-*cis*-configuration ($J_{2,3}$ 2·0 Hz) and the presence of C(3)-methoxy (τ 6·67) and three aromatic acetoxy-functions (τ 7·70).

The R_F 0·54 fraction gave the 2,3-*trans*-fustin (VI; R = Ac) as an oil (82·4 mg). The n.m.r. spectrum (Table 2) correlated with a 2,3-*trans*-configuration ($J_{2,3}$ 10·4 Hz) and the presence of C(3)-methoxy (τ 6·57) and three aromatic acetoxy-functions (τ 7·70).

Synthesis of 2′-*Hydroxy*-α,3,4,4′-*tetramethoxy*-trans-*chalcone* (IV; R^1 = H, R^2 = Me) *and* (±)-2-*Benzyl*-2,3′,4′,6-*tetramethoxybenzo*[b]*furan*-3(2H)-*one* (III; R = Me) *from* (±)-2,3-trans-*Fustin*.—(±)-Fustin (400 mg) from *Rhus glabra* [14] in dry acetone (25 ml) was stirred with anhydrous K_2CO_3 (10 g) and dry Me_2SO_4 (1 ml) for 12 h at 60°. After removal of excess of K_2CO_3 by filtration and evaporation of the solvent, the product was separated into two bands R_F 0·58 and 0·62 by p.l.c. with benzene–acetone (8 : 2 v/v).

(±)-3,3′,4′,7-*Tetra*-O-*methyl*-2,3-trans-*fustin* (VI; R = Me). The R_F 0·58 band (144 mg) gave *white needles* (from ethanol) (91 mg), m.p. and mixed m.p. with the corresponding compound derived from *T. verrucosum*, 143°. The n.m.r. spectra of these compounds were identical.

α,2′,3,4,4′-*Pentamethoxy*-trans-*chalcone* (IV; $R^1 = R^2$ = Me). The R_F 0·62 band (120 mg) gave *yellow needles* (from methanol), m.p. 92°, *m/e* 358(M^+, 56), 344(8·5), 343(3·8), 327(5·4), 315(2·3), 287(3·1), 194(22), 193(2·3), 179(6·9), 165(100), and 151(13·8), $\nu_{max.}$ 1650 cm^{-1} (C=O stretching), n.m.r. spectrum (Table 1) correlated with the presence of five methoxy-groups (τ 6·10—6·20) and the β-proton (τ 3·57).

2′-*Hydroxy*-α,3,4,4′-*tetramethoxy*-trans-*chalcone* (IV; R^1 = R^2 = Me). (±)-3,3′,4′,7-Tetra-*O*-methyl-2,3-*trans*-fustin (100 mg) in a 10% (w/v) KOH solution (15 ml) was stirred for a 2 h at 96°. After filtration and acidification with 10% (v/v) HCl the solution was extracted with $CHCl_3$ (3 × 25 ml), and the extract dried and evaporated. Purification of the solid by p.l.c. in benzene–acetone (8 : 2 v/v) followed by crystallization from methanol gave clear yellow plates, m.p. (mixed m.p. 98°) and n.m.r. spectrum identical with those of the natural product.

(±)-2-*Benzyl*-2,3′,4′,6-*tetramethoxybenzo*[b]*furan*-3(2H)-*one* (III; R = Me). The 2′-hydroxychalcone (50 mg) in ethanol (5 ml) and 3N-H_2SO_4 (5 ml) was heated at 96° for 24 h. The solution was neutralized with saturated aqueous $NaHCO_3$ and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 and removal of the $CHCl_3$ the product was purified by p.l.c. in benzene–acetone (8 : 2 v/v). The band R_F 0·60 gave a pale yellow oil with n.m.r. spectrum identical with that of the natural derivative.

Complete Synthesis of (±)-3,3′,4′,7-*Tetra*-O-*methyl*-2,3-cis-*fustin* (V; R = Me) *and* (±)-3,3′,4′,7-*Tetra*-O-*methyl*-2,3-trans-*fustin* (VI; R = Me).—2′-*Hydroxy*-2,4′-*dimethoxyacetophenone*. *m*-Methoxyphenol (2·48 g), methoxyacetonitrile (2·82 g), and freshly fused $ZnCl_2$ (4·0 g) in dry ether (100 ml) were cooled to −10°.[31] Dry HCl gas was led through for 3 h while maintaining the temperature at −5 to −10°, and the mixture left for 48 h at −15°. After decanting the ether the orange precipitate was washed with dry ether (2 × 50 ml) and heated with water (250 ml) under reflux for 2 h. The white precipitate obtained on cooling was recrystallized from water as white needles (3·6 g), m.p. 132°, τ 1·58—1·90 (OH), 2·04 (d, 6′-H), 3·37 (q, 5′-H), 3·43 (d, 3′-H), 5·32 (s, CH_2), 6·10 (s, 4′-OMe), 6·47 (s, 2-OMe) ($J_{3',5'}$ 2·3 and $J_{5',6'}$ 9·0 Hz).

2′-*Hydroxy*-α,3,4,4′-*tetramethoxy*-trans-*chalcone* (IV; R^1 = H, R^2 = Me).[10] 2′-Hydroxy-2,4′-dimethoxyacetophenone (1·96 g) and 3,4-dimethoxybenzaldehyde (2·08 g) were dissolved in ethanol (50 ml) and after addition of 40% (w/v) KOH solution (20 ml) the mixture was stirred for 9 h at 60°. After acidification with 3N-H_2SO_4 and partial removal of ethanol under reduced pressure, the solution was extracted with $CHCl_3$ (3 × 50 ml). The extract was dried, and after evaporation the product purified by p.l.c. with benzene–acetone (17 : 3 v/v). The R_F 0·59 band crystallized from methanol as clear yellow plates, m.p. (mixed m.p. 98°) and n.m.r. spectrum identical with those of the corresponding naturally-derived compound.

(±)-3,3′,4′,7-*Tetra*-O-*methyl*-2,3-cis- (V; R = Me) *and* -2,3-trans-*fustin* (VI; R = Me). The 2′-hydroxychalcone (200 mg) with sodium acetate (800 mg) in 50% (v/v) ethanol (20 ml) was heated (96°) under reflux for 24 h.[13] The solution was taken to dryness under reduced pressure and the organic components extracted from the sodium acetate with dry acetone. P.l.c. in benzene–acetone (23 : 2 v/v) showed the presence of three components at R_F 0·51, 0·57, and 0·67.

The R_F 0·57 fraction (23·4 mg; light yellow oil) had a n.m.r. spectrum identical with that of the corresponding naturally-derived 2,3-*cis*-product.

The R_F 0·51 fraction (45 mg) crystallized as white needles (40 mg) from ethanol, m.p. (mixed m.p. 143°) and n.m.r. spectrum identical with those of the corresponding naturally-derived 2,3-*trans*-product.

The R_F 0·67 band (52·6 mg) was unchanged 2′-hydroxychalcone.

(+)-*Mopanol B and* (+)-*Peltogynol B* (II; R^1 = H, R^2 = OH *and* R^1 = OH, R^2 = H).—Fraction TV_5 (R_F 0·42) from *T. verrucosum* (3·68 g) was purified by p.p.c. on Whatman No. 3 (40 mg per sheet) by ascending development in 20% (v/v) acetic acid. The R_F 0·42 band (pink with toluene-*p*-sulphonic acid) was eluted, and the eluates were evaporated to give a brown amorphous powder (1·84 g). This was dissolved in acetone (300 ml), applied to Whatman No. 3 paper, and the chromatograms developed by descent in butan-2-ol saturated with water giving two bands, R_F 0·84 (mopanol B) and 0·73 (peltogynol B). Elution and evaporation gave (+)-mopanol B (384 mg; R_F 0·70,

[31] A. I. Vogel, 'A Textbook of Practical Organic Chemistry,' Longmans, London, 1967, p. 736.

0·15; wine-red with toluene-*p*-sulphonic acid) and (+)-peltogynol B (342 mg; R_F 0·60, 0·15; violet with toluene-*p*-sulphonic acid) as pale brown powders.

(+)-4,4′,5′,7-*Tetra*-O-*acetylmopanol B and* (+)-3′,4,4′,7-*Tetra*-O-*acetylpeltogynol B*.—Following acetylation with acetic anhydride–pyridine of (+)-mopanol B and (+)-peltogynol B (100 mg each), the individual acetates were purified by p.l.c. with benzene–acetone (9 : 1 v/v). The tetra-*O*-acetylmopanol B compound, R_F 0·63, was obtained as an amorphous white powder (48 mg), m.p. 132°, $[\alpha]_D^{25}$ +186° (*c* 0·5 in $CHCl_3$) {lit.,[5] m.p. 85—185°, $[\alpha]_D^{20}$ +214° (*c* 0·3)}. The n.m.r. spectrum was identical with that in the literature.[5] The tetra-*O*-acetylpeltogynol B, R_F 0·58, was obtained as an amorphous white powder (54 mg), m.p. 228°, $[\alpha]_D^{25}$ +193° (*c* 0·5 in $CHCl_3$) {lit.,[5] m.p. 240°, $[\alpha]_D^{20}$ +221° (*c* 0·3)}. The n.m.r. spectrum was identical with that in the literature.[5]

(+)-*Mopanol and* (+)-*Peltogynol* (I; R^1 = H, R^2 = OH and R^1 = OH, R^2 = H).—Fraction TV_6 (R_F 0·32) from *T. verrucosum* (4·72 g) was purified by ascending p.p.c. as for their B-epimers. The components, R_F 0·32, were resolved by descent in butan-2-ol saturated with water as described above (R_F 0·85, mopanol; and 0·74, peltogynol) to give light brown amorphous powders of (+)-mopanol (634 mg; R_F 0·69, 0·07; wine-red with toluene-*p*-sulphonic acid) and (+)-peltogynol (715 mg; R_F 0·60, 0·07; violet with toluene-*p*-sulphonic acid).

(+)-3′,4′,7-*Tri*-O-*methylmopanol and its Acetate*.—Methylation of (+)-mopanol (400 mg) and crystallization from ethanol gave white needles (280) mg), m.p. 194°, $[\alpha]_D^{25}$ +208° (*c* 1·0 in $CHCl_3$) {lit.,[5] m.p. 195°, $[\alpha]_D^{20}$ +235° (*c* 0·8)}. Acetylation of the methyl ether (100 mg) with acetic anhydride–pyridine, and crystallization from ethanol gave needles (84 mg), m.p. 162°, $[\alpha]_D^{25}$ +241° (*c* 0·5 in $CHCl_3$) (lit.,[5] m.p. 162—163°).

(+)-4′,5′,7-*Tri*-O-*methylpeltogynol and its Acetate*.—Similar treatment of (+)-peltogynol (400 mg) gave white needles (308 mg), m.p. 197°, $[\alpha]_D^{25}$ +203° (*c* 1·0 in $CHCl_3$) {lit.,[5] m.p. 196—200°, $[\alpha]_D^{20}$ +235° (*c* 0·8)}, and its acetate, m.p. 153°, $[\alpha]_D^{25}$ +235° (*c* 0·6 in $CHCl_3$) {lit.,[5] m.p. 154—155°, $[\alpha]_D^{20}$ +230° (*c* 0·8)}.

The n.m.r. spectra of the above derivatives were identical with those in the literature.[5]

3,3′,4′,7-*Tetra*-O-*methylfisetin* (VII; R = Me).—Fraction TV_7, R_F 0·11, from *T. verrucosum* (2·0 g) was methylated and the product purified by t.l.c. in benzene–acetone (8 : 2 v/v). The band, R_F 0·37, crystallised from ethanol in pale yellow needles (485 mg), m.p. 150° (lit.,[19,32] m.p. 150°). The n.m.r. spectrum was identical with that in the literature.[19]

Synthesis of Tri-O-*methylmopanin* (X) *and Tri*-O-*methylpeltogynin* (IX) *from Tetra*-O-*methylfisetin* (VII; R = Me).—Tetra-*O*-methylfisetin (300 mg) in methanol (400 ml) was irradiated for 6 h at 350 nm[20] (Rayonet Photochemical Reactor, New England Ultra-Violet Co., Middletown, Conn., U.S.A.) in a quartz vessel while nitrogen was led through for 5 min at half-hourly intervals.[21] After removal of solvent the product was separated by p.l.c. in benzene–acetone (9 : 1 v/v) by double development into two bands, R_F 0·26 and 0·39, both giving a bright yellow colour with toluene-*p*-sulphonic acid.

The R_F 0·39 band (48·5 mg) gave tri-*O*-methylmopanin (X) as yellow needles from ethanol (34·2 mg), m.p. 176° (lit.,[19] 190° for natural product derivative), *m/e* 340(M^+, 100%), 339(11·7), 312(26), 297(9·4), 211(4·6), 165(45), 150(36), and 122(27). The n.m.r. spectrum (Table 3) is identical with that of the natural derivative, but indicates a small amount of impurity in the methoxy-area (τ 6·30) which could not be removed, and probably accounts for the low m.p. The impurity probably reflects a small amount of autoxidation of the methylene function of the D-ring.

The R_F 0·26 band (54 mg) gave tri-*O*-methylpeltogynin (IX) as yellow needles from ethanol (42 mg), m.p. 256° (lit.,[19] 260° for natural derivative suspected to be peltogynin trimethyl ether), *m/e* 340(M^+, 100%), 339(56), 325(3·3), 312(1·8), 297(17·8), 269(3·3), 254(3·3), 239(1·8), 211(1·8), 165(5·5), and 150(4·1). The n.m.r. spectrum (Table 3) was consistent with the structure (IX).

TABLE 3

N.m.r. spectra of the methyl ethers of peltogynin, mopanin, and fisetin

	τ Values ($CDCl_3$)												
	–H							CH_2	–OMe				
	5	6	8	2′	3′	5′	6′		3	7′	3′	4′	5′
Tri-*O*-methylpeltogynin	1·82d	3·07q	3·05d		3·32s		2·72s	4·80s		5·97s		6·07s	6·07s
Tri-*O*-methylmopanin	1·81d	3·07q	3·15d			3·03d	2·47d	4·67s		6·13s	6·07s	6·07s	
Tetra-*O*-methylfisetin	1·78d	2·95q	3·03d	2·27d		3·07d	2·25q		6·07s	6·05s	6·00s	6·00s	

Photolysis of the Chalcones (IV; R^1 = H, R^2 = Me) *and* (IV; R^1 = R^2 = Me).—The 2′-hydroxy-α,3,4,4′-tetramethoxy- and α,2′,3,4,4′-pentamethoxy-*trans*-chalcones (100 mg each) were dissolved independently in methanol (140 ml) and each solution was irradiated for 9 h in quartz flasks at 350 nm as described for mopanin and peltogynin trimethyl ethers. After removal of methanol the individual products were purified by t.l.c. with benzene–acetone (8 : 2 v/v) to give 2′-hydroxy-α,3,4,4′-tetramethoxy-*cis*-chalcone (R_F 0·59) as a light yellow oil (48 mg), n.m.r. spectrum (Table 1), and α,2′,3,4,4′-pentamethoxy-*cis*-chalcone (R_F 0·55), respectively, as a light yellow oil (47 mg), n.m.r. spectrum (Table 1).

Similar irradiation at 300 nm led to the same products. Greater displacement of the *trans–cis* equilibrium towards the *trans*-isomer by addition of iodine crystals[23] during photolysis at different wavelengths (350, 300, and 285 nm) and for different times (9—45 h) failed to provide (t.l.c.) desired chalcones of the mopanol and peltogynol type.

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