

861. *The Chemistry of Extractives from Hardwoods. Part XXVIII.**
The Occurrence of 3:4:3':5'-Tetrahydroxy- and 3:4:5:3':5'-
Pentahydroxy-stilbene in Vouacapoua species.

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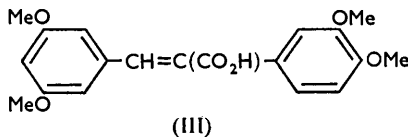
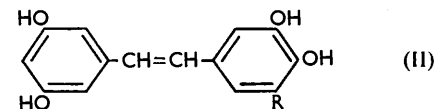
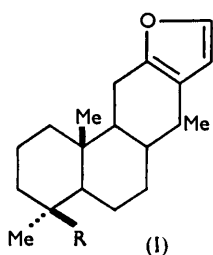
The heartwood of *Vouacapoua macropetala* and of *V. americana* contains 3:4:3':5'-tetrahydroxystilbene, which was isolated by ether-extraction. Also present in *V. macropetala* is the 3:4:5:3':5'-pentahydroxystilbene. The structures of these new products were deduced from the hydroxybenzoic acids obtained on oxidation of the fully acetylated compounds, and the constitution attributed to the tetrahydroxystilbene was confirmed by a synthesis of the tetramethyl ether from 3:5-dimethoxybenzaldehyde and 3:4-dimethoxyphenylacetic acid.

THE principal petroleum-soluble constituent of the wood from the South American *Vouacapoua americana* and *V. macropetala* consists of a diterpene ester, methyl vouacapenate (I; R = CO₂Me), and it occurs in the latter species together with vouapenyl acetate (I; R = CH₂·OAc).¹ The composition of the products obtained by

* Part XXVII, preceding paper.

¹ King, Godson, and King, *J.*, 1955, **1**, 117.

continuing the extraction with ether has now been examined and it has been shown that both species contain the hitherto unknown 3 : 4 : 3' : 5'-tetrahydroxystilbene (II; R = H). The ether extract of *V. macropetala* contains also 3 : 4 : 5 : 3' : 5'-pentahydroxystilbene (II; R = OH), the most fully substituted natural stilbene so far encountered. It is of interest that 3 : 5-dihydroxystilbene (pinosylvin) together with its methyl ethers constitutes



the sole example of this series found in the coniferous woods in which it is strictly confined to *Pinus* species.² On the other hand, the more heavily substituted compounds, e.g., 4'-hydroxy-3 : 5-dimethoxystilbene (pterostilbene),³ 2 : 4 : 3' : 5'-tetrahydroxystilbene,⁴ and its 4-substituted derivative chlorophorin,⁵ occur in various unrelated genera of dicotyledonous trees, although all examples so far recorded are derivatives of 3 : 5-dihydroxystilbene, a fact denoting a common phytochemical origin.

3 : 4 : 3' : 5'-Tetrahydroxystilbene was isolated from the brown resin extracted by ether from the light petroleum-exhausted wood by leaching it with hot water. The compound $C_{24}H_{12}O_4$ obtained by concentrating the aqueous solution and further crystallisation exhibited reducing properties and the usual colour reactions, e.g., transient blue violet with ferric chloride, characteristic of a polyhydric phenol. It formed a crystalline tetra-acetate, tetrabenzoate, and tetramethyl ether all of which retained the reactivity to aqueous bromine and potassium permanganate of the parent compound. Light absorption of the phenol and of its methyl ether in the ultraviolet region denoted a stilbene structure.

Oxidation of the tetra-acetate and the tetramethyl ether with chromic oxide gave inseparable products, but paper chromatography⁶ of the hydrolysed mixture from the acetate oxidation showed, by comparison with authentic specimens, the presence of 3 : 5- and of 3 : 4-dihydroxybenzoic acid. However, the method of identification made it desirable to seek further support for the structure, for example, by synthesis of the tetramethyl ether. A derivative of rhapontigenin (3 : 5 : 3'-trihydroxy-4'-methoxystilbene), isolated as a glycoside from the roots of *Rhus pontifica* and other species,⁷ has been synthesised⁸ by condensation of isovanillin with sodium 3 : 5-dihydroxyphenylacetate, but analogous condensations employing veratric or protocathechuic aldehyde failed to yield crystalline products. However, by the action of 3 : 5-dimethoxybenzaldehyde on sodium 3 : 4-dimethoxyphenylacetate, small quantities of the stilbene-carboxylic acid (III) were obtained, and decarboxylation of the product yielded the difficultly crystallisable 3 : 4 : 3' : 5'-tetramethoxystilbene, identical with the corresponding ether of the natural product. The well-characterised trinitrobenzene derivatives also were indistinguishable.

The ether extracts of *V. americana* gave no other purifiable compound, but by acetylation of the crude extract from *V. macropetala* a further crystalline product was isolated, which was unsaturated to bromine and permanganate, and corresponded in molecular formula with a penta-acetoxystilbene. Benzoylation of the crude extract gave a corresponding benzoate. Hydrolysis of the penta-acetate in an inert atmosphere gave the

² Erdtman, "Progress in Organic Chemistry," Butterworths, London, 1952, Vol. I, p. 22.

³ Spath and Schlager, *Ber.*, 1940, **73**, 881.

⁴ Barnes and Gerber, *J. Amer. Chem. Soc.*, 1955, **77**, 3259; Takaoka, *J. Fac. Sci., Hokkaido Imp. Univ.*, 1940, **3**, 1.

⁵ King and Grundon, *J.*, 1949, 3348; 1950, 3547.

⁶ Bate-Smith and Westall, *Biochem. Biophys. Acta*, 1950, **4**, 428.

⁷ Kawamura, *J. Pharm. Soc. Japan*, 1938, **58**, 83, 405.

⁸ Takaoka, *Proc. Imp. Acad. (Tokyo)*, 1940, **16**, 408.

pentahydroxystilbene in yellowish prisms, very readily oxidised in alkaline solution and giving an intense transient blue-black colour with ferric chloride.

Oxidation of the acetate with potassium permanganate, followed by mild hydrolysis, formed a mixture of acids which were separated by crystallisation into 3 : 5-dihydroxybenzoic acid and gallic acid, both of which were identified by m. p. and mixed m. p. They were converted into the methyl ethers which were also identified by comparison with authentic specimens. The structure of the parent phenol was thereby established as 3 : 4 : 5 : 3' : 5'-pentahydroxystilbene (II; R = OH).

EXPERIMENTAL

Light petroleum was of b. p. 60—80°.

3 : 4 : 3' : 5'-Tetrahydroxystilbene.—The powdered wood (3—3.2 kg.) which had previously been extracted with light petroleum was exhausted with boiling ether during 48 hr. The extracts were evaporated and the light petroleum-soluble part was removed with that solvent. Treated in this way *V. americana* gave 36 g. of a black gum and *V. macropetala* 56 g. of brown resin. The extract from *V. americana* was leached with boiling water (3 × 300 c.c.), and the extract filtered and concentrated (vacuum) to 50 c.c. After 24 hr. at 0° the *tetrahydroxystilbene* (1.6 g.) separated as a grey crystalline powder. Similar treatment of the extract from *V. macropetala* gave 7 g. of the phenol. Purification of the product from either water or methanol-benzene gave almost colourless plates, m. p. 229° (rapid heating, decomp.) (Found : C, 69.0; H, 4.9. C₁₄H₁₂O₄ requires C, 68.8; H, 4.95%), light absorption max. (in EtOH) at 330 mμ (ε 27,600). The ferric chloride colour was a transient blue-violet. The *tetra-acetate* obtained with acetic anhydride-pyridine separated from methanol in colourless needles, m. p. 114—115° [Found : C, 63.9; H, 4.5; OAc, 41.7%; M (Rast), 395. C₂₂H₂₀O₈ requires C, 64.1; H, 4.9; 4OAc, 42.5%; M, 412]. The *tetrabenzoate* crystallised from acetone-methanol as colourless needles, m. p. 123—124° [Found : C, 76.0; H, 4.6%; M (Rast), 675. C₄₂H₂₈O₈ requires C, 76.3; H, 4.3%; M, 660].

Oxidation of the Tetra-acetoxystilbene.—The acetate (50 mg.) with acetic acid (30 c.c.) containing chromic oxide (35 mg., 1.1 mol.) was kept for 15 min. at room temperature and then poured into water. The products were extracted with ether, and the extract was evaporated; the residue was then warmed for a short time with excess of dilute aqueous sodium hydroxide and again acidified and extracted with ether (5 × 15 c.c.). The residues were examined by paper chromatography.⁶ The mobile phase first used was butanol-acetic acid-water (4 : 1 : 5), and development with ferric chloride showed a single green spot corresponding in *R_F* value to protocatechuic acid. Development of a similar chromatogram with diazotised benzidine gave a pink spot corresponding to that given by 3 : 5-dihydroxybenzoic acid. Direct chromatographic comparison of the degradation products with authentic samples of both dihydroxybenzoic acids in butanol-acetic acid-water and in *m*-cresol-water confirmed the identification of the oxidation products. No other spots could be detected.

3 : 4 : 3' : 5'-Tetramethoxystilbene-α-carboxylic Acid.—Sodium 3 : 4-dimethoxyphenylacetate⁹ (1.77 g.) and 3 : 5-dimethoxybenzaldehyde (1.4 g., 1.1 mol.) (prepared by oxidation of the corresponding alcohol¹⁰ with chromic oxide in pyridine) were heated with acetic anhydride (20 c.c.) at 175—180° (bath-temp.) for 8 hr. and then the acetic anhydride was removed *in vacuo*. The residual gum was dissolved in ether and washed with dilute acid. Removal of the solvent left a gum which crystallised when boiled with light petroleum. The acid was purified from methanol, from which it separated in yellow needles (1.3 g.), m. p. 167—168° (Found : C, 66.7; H, 6.1. C₁₉H₂₀O₆ requires C, 66.3; H, 5.85%).

3 : 4 : 3' : 5'-Tetramethoxystilbene.—(a) Methylation of the tetrahydroxystilbene (3 g.) with methyl sulphate (7.5 g.) and potassium carbonate (15 g.) in boiling acetone for 20 hr. gave, after filtration and removal of the acetone, a brown oil (3.6 g.). Repeated distillation of the residue gave a pale yellow oil, b. p. 180—190°/0.1 mm., which, after chromatography on alumina in light petroleum-benzene followed by refrigeration under light petroleum, gave the *tetramethoxystilbene* (1 g.) as colourless needles, m. p. 68—69° (Found : C, 72.0; H, 6.6; OMe, 41.2. C₁₈H₂₀O₄ requires C, 72.0; H, 6.7; 4OMe 41.2%), light absorption max. (in EtOH) at 325 mμ (ε 31,000).

(b) The pure stilbenecarboxylic acid above (0.65 g.) was heated in boiling quinoline (20 c.c.)

⁹ Julian and Sturgis, *J. Amer. Chem. Soc.*, 1935, **57**, 1126.

¹⁰ Adams, Harfenist, and Loewe, *ibid.*, 1949, **71**, 1627.

with copper bronze (2 g.) for 10 min. When cool the mixture was diluted with ether (100 c.c.) and filtered. The filtrate was exhaustively extracted with dilute hydrochloric acid and aqueous sodium hydroxide, dried, and distilled. Repeated distillation gave an oil which was covered with light petroleum and then, after some time, crystallised. Purification from methanol gave the stilbene as needles, m. p. and mixed m. p. 68—69° (Found: C, 72.0; H, 6.5%), light absorption max. (in EtOH) at 325 μ (ϵ 31,000).

Both specimens of the stilbene gave identical *adducts* with trinitrobenzene in ethanol, as maroon-coloured prisms, m. p. and mixed m. p. 109—110° (Found, for natural compound: C, 55.8; H, 4.6; for synthetic compound C, 56.3; H, 4.3. $C_{18}H_{20}O_4, C_6H_3O_6N_3$ requires C, 56.1; H, 4.5%).

3 : 4 : 5 : 3' : 5'-*Penta-acetoxystilbene*.—The crude ether extract of *V. macropetala* (56 g.) was acetylated in pyridine at 100° for 30 min. The solution was evaporated under reduced pressure, leaving a brown residue which crystallised when warmed with methanol. Recrystallisation from acetone-methanol (charcoal) gave the penta-acetate (16.9 g.) as colourless plates, m. p. 173—174° [Found: C, 61.4; H, 4.6; OAc, 44.4%; *M* (Rast), 441. $C_{24}H_{22}O_{10}$ requires C, 61.3; H, 4.7; 5 OAc, 45.7%; *M*, 470].

3 : 4 : 5 : 3' : 5'-*Pentahydroxystilbene*.—The penta-acetate (1 g.) was hydrolysed under nitrogen for 30 min. at room temperature with 2% methanolic potassium hydroxide (100 c.c.). The excess of alkali was then neutralised with acetic acid, and the solution evaporated. The residue was dissolved in water and extracted with ethyl acetate, and the extract was evaporated. The *pentahydroxystilbene* thus obtained crystallised from a small amount of water in pale yellow needles, m. p. ca. 245° (decomp., *evac. capillary*) (Found, on an air-dried sample: C, 57.0; H, 5.4. $C_{14}H_{12}O_5, 2H_2O$ requires C, 56.75; H, 5.4. On a sample dried at 100°: C, 64.2; H, 4.8. $C_{14}H_{12}O_5$ requires C, 64.6; H, 4.65%). The *pentabenzoate* prepared in pyridine crystallised from chloroform-methanol in needles, m. p. 165—166° (Found: C, 75.4; H, 4.3. $C_{49}H_{32}O_{10}$ requires C, 75.4; H, 4.1%). The same benzoate could also be obtained in small yield by benzoylation in pyridine of the crude timber extract.

Oxidation of the Penta-acetoxystilbene.—The penta-acetate (4.8 g.) in acetone (75 c.c.) was treated at room temperature with potassium permanganate (10 g.). When the permanganate had been destroyed the acetone was evaporated and the residue was warmed for a short time with dilute alkali to complete the hydrolysis of the acetoxy-group. The suspension was then acidified by the passage of excess of sulphur dioxide. Exhaustive extraction of the solution with ether followed by removal of the solvent afforded a brown acidic residue (2.5 g.). This residue was warmed with water (5 c.c.), and the solid which separated in the cold was recrystallised from water to give nearly colourless rods, m. p. 232—234° raised to 233—235° by admixture with authentic 3 : 5-dihydroxybenzoic acid (m. p. 236—238°). The water-soluble fraction of the crude oxidation product was isolated by evaporation and crystallised from ethyl acetate as light brown flat prisms, m. p. 245—250° (effervescence), giving colour reactions with ferric chloride and potassium cyanide identical with those shown by gallic acid.

Both acids were methylated with methyl sulphate in acetone in the presence of potassium carbonate and after hydrolysis of any ester produced gave respectively: 3 : 5-dimethoxybenzoic acid as colourless needles (from ethyl acetate), m. p. and mixed m. p. 185—186° (lit., 185—186°) (Found: C, 59.6; H, 5.7; OMe, 34.2. Calc. for $C_9H_{10}O_4$: C, 59.3; H, 5.5; 2OMe, 34.3%); and trimethylgallic acid as colourless needles (from ethyl acetate-light petroleum), m. p. and mixed m. p. 169—170° (lit., 168°) (Found: C, 56.1; H, 5.6; OMe, 43.8. Calc. for $C_{10}H_{12}O_5$: C, 56.6; H, 5.7; 3OMe, 43.8%).

One of the authors (D. H. G.) thanks the Department of Scientific and Industrial Research for a Maintenance Allowance.