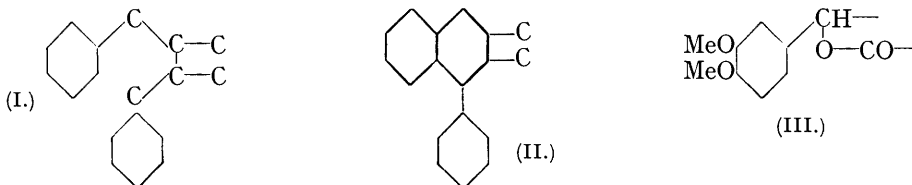


141. The Constituents of Natural Phenolic Resins. Part I.
Matairesinol.

By ROBERT D. HAWORTH and THOMAS RICHARDSON.

SINCE Schroeter, Lichtenstadt, and Irineu (*Ber.*, 1918, **51**, 1587) suggested that guaiaretic acid was an $\alpha\delta$ -diarylbutane derivative of skeletal formula (I), other naturally occurring compounds such as podophyllin (Borsche and collaborators, *Annalen*, 1932, **494**, 126; 1932, **499**, 59; 1933, **502**, 264; Spath and collaborators, *Ber.*, 1932, **65**, 1526, 1773; 1933, **66**, 125), sulphite-liquors lactone or tsugaresinol (Holmberg, *Ber.*, 1921, **54**, 2389, 2406; *Ann. Acad. Sci. Fennicæ*, 1927, *A*, **29**, No. 6; Erdtman, *Annalen*, 1934, **513**, 229; Kawamura, *Bull. Imp. Forestry Exp. Stat. Tokyo*, 1932, **31**, 73; Emde and Schartner, *Naturwiss.*, 1934, **44**, 734), and olivil (Vanzetti and Dreyfuss, *Gazzetta*, 1934, **64**, 381) have been recognised as belonging either to this class (I) or to its cyclised 1-phenyl-naphthalene form (II). It had been anticipated (see Meyer and Jacobson, "Lehrbuch der Organischen Chemie," vol. II, part IV, p. 166) that a reinvestigation of pinoresinol, lariciresinol, and matairesinol would probably reveal a close relationship between these compounds and guaiaretic acid, and while the present work was in progress Erdtman (*Svensk Kem. Tidskr.*, 1934, **46**, 229) showed that pinoresinol is a C_{20} compound of type (I) and not a C_{19} compound as earlier workers (Bamberger and co-workers, *Monatsh.*, 1894, **15**, 505; 1897, **18**, 481; 1900, **21**, 949; 1917, **39**, 474; Zincke, Erben, and Jele, *ibid.*, 1924, **44**, 571) suggested. Further Erdtman (*loc. cit.*) suggests that pinoresinol dimethyl ether and eudesmin (Robinson and Smith, *J. Proc. Roy. Soc. N.S. Wales*, 1915, **48**, 449) are optical antipodes.



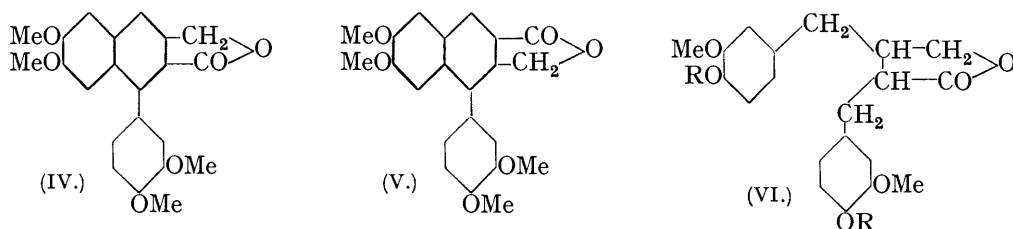
Structures (I) and (II) are derivable from two molecules of allylbenzene by dimerisation at the β -carbon atoms. With the exception of podophyllin, the natural products mentioned above are related to eugenol and it is probable that cubebin (Mameli, *Gazzetta*, 1907, **37**, ii, 483; 1909, **39**, i, 477, 494; 1912, **42**, ii, 546, 551; 1921, **51**, ii, 353), hinokinin (Yoshiki and Ishiguro, *J. Pharm. Soc. Japan*, 1933, **53**, 11), and sesamin (Bertram, Steur, and Watermann, *Biochem. Z.*, 1928, **197**, 1; Böeseken and Cohen, *ibid.*, 1928, **201**, 454) represent the safrole analogues.

The present communication describes an investigation on the structure of matairesinol, which was isolated by Easterfield and Bee (*J.*, 1910, **95**, 1028) from the heart-wood of the matai (*Podocarpus spicatus*), a tree growing in the forests of New Zealand. Easterfield

and Bee proposed the formula $C_{19}H_{20}O_6$, and suggested a relationship with pinoresinol and lariciresinol (Bamberger and co-workers, *Monatsh.*, 1897, **18**, 500; 1899, **20**, 647, 755; 1900, **21**, 564; 1903, **24**, 249; 1917, **38**, 470). They established the presence of a lactone group and two methoxyl groups, and the occurrence of two phenolic hydroxyl groups was indicated by the ferric reaction and the preparation of a dibenzoyl derivative. The matairesinol used in the present research was isolated and purified as described by Easterfield and Bee. No discrepancy in melting point was observed, but the specific rotation was -48.6° and not -4.89° as reported by the previous workers. The analytical figures now obtained suggest the formula $C_{20}H_{22}O_6$, and this is fully confirmed by an examination of the derivatives of matairesinol.

Matairesinol dimethyl ether, $C_{22}H_{26}O_6$, is a saturated lævorotatory lactone, which is oxidised by potassium permanganate to veratric acid in yields exceeding 50% of the theoretical. This result suggests that matairesinol dimethyl ether contains two veratryl radicals, and this view is confirmed by the ready conversion of the ether into *dibromo-* and *dinitro-*derivatives, $C_{22}H_{24}O_6Br_2$ and $C_{22}H_{24}O_{10}N_2$ respectively. If one of the α -carbon atoms is involved in the lactone group as indicated by the partial formula (III), 4:5-dinitroveratrole and trinitroveratrole should be obtained from the dimethyl ether by the action of boiling 50% nitric acid and cold fuming nitric acid respectively. Actually, the former reagent yielded the dinitro-derivative, $C_{22}H_{24}O_{10}N_2$, mentioned above, and the latter reagent gave a strongly lævorotatory *tetranitro-*derivative, $C_{22}H_{22}O_{14}N_4$.

Oxidation of matairesinol dimethyl ether with lead tetra-acetate gave a crystalline oxidation product in yields varying between 10 and 15%. This was resolved by fractional crystallisation into the lactone of 6:7-dimethoxy-1-(3':4'-dimethoxyphenyl)-3-hydroxymethylnaphthalene-2-carboxylic acid (IV) and the isomeric lactone of 6:7-dimethoxy-1-(3':4'-dimethoxyphenyl)-2-hydroxymethylnaphthalene-3-carboxylic acid (V). The structure assigned to these lactones depends upon experiments described in the following communication, and the identification of these two oxidation products leads directly to the formula (VI; R = Me) for matairesinol dimethyl ether. This structure is in complete agreement with the observed properties of the ether. Dimroth and Schweizer (*Ber.*, 1923, **56**, 1375) showed that toluene was oxidised to benzyl alcohol by means of lead tetra-acetate, and this observation, together with the well-established reactivity of the 6-position of the veratrole nucleus, provides a reasonable explanation of the action of lead tetra-acetate on matairesinol dimethyl ether.



The positions of the phenolic hydroxyl groups in matairesinol have been determined by oxidising the *diethyl* ether with potassium permanganate. As 3-methoxy-4-ethoxybenzoic acid was isolated in yields greater than 50% of the theoretical, matairesinol must have the formula (VI; R = H).

Experiments concerned with the synthesis of matairesinol and similar compounds are in progress.

EXPERIMENTAL.

The resin (50 g.), obtained from heart shakes of adult matai trees growing on pumiceous soil at an altitude approximately 1800 feet above sea level, was boiled with methylated spirits (250 c.c.), and the hot solution filtered from chips of wood. On cooling, matairesinol (25 g.) separated in slender prisms, m. p. $74-76^\circ$, which contained alcohol of crystallisation. Recrystallisation from 30% acetic acid yielded the anhydrous form in stout prisms, m. p. $117-118^\circ$ (Found: C, 67.3, 67.1, 67.0; H, 6.3, 6.2, 6.3. Calc. for $C_{20}H_{22}O_6$: C, 67.0; H, 6.2%). In acetone (c , 2.409) $[\alpha]_D^{18} = -48.6^\circ$.

Matairesinol Dimethyl Ether.—Methyl sulphate (15 g.) was added to a solution of matairesinol (5 g.) in 4% methyl-alcoholic potassium hydroxide (50 c.c.). The solution was boiled and 50% aqueous potassium hydroxide was slowly added to maintain slight alkalinity. The methyl alcohol was removed, dilute sulphuric acid added to the residue, and the mixture boiled for 5 minutes. The *dimethyl ether* crystallised from methyl alcohol in stout prisms (4.8 g.), m. p. 127—128° (Found: C, 68.2, 68.1; H, 6.7, 6.8. $C_{22}H_{26}O_6$ requires C, 68.4; H, 6.7%). In chloroform (c , 3.740) it has $[\alpha]_D^{19} = 35.6^\circ$. The elevated temperature in the methylation did not induce racemisation and an identical product was obtained by methylating the resinol at 15°. The ether dissolved in concentrated sulphuric acid to a blue-green solution, which turned brown on the addition of a drop of concentrated nitric acid. The lactone ring was opened slowly on boiling with dilute sodium hydroxide solution, but rapid hydrolysis occurred with warm methyl-alcoholic potassium hydroxide. The methyl ether was recovered, unchanged in m. p. and specific rotation, after treatment with hydrogen in the presence of a palladised carbon catalyst which was capable of reducing guaiaretic acid dimethyl ether.

Dibromomatairesinol dimethyl ether, prepared in 80% yield by the action of bromine (2.2 mols.) on a cold acetic acid solution (10 parts) of the ether, crystallised from alcohol in long prisms, m. p. 126—127° (Found: C, 48.6, 48.5; H, 4.7, 4.6. $C_{22}H_{24}O_6Br_2$ requires C, 48.5; H, 4.5%). The dibromo-compound, which does not decolorise bromine in chloroform solution, dissolves in concentrated sulphuric acid to a light brown solution, which becomes bright red on the addition of a drop of concentrated nitric acid. In chloroform (c , 3.540), it has $[\alpha]_D^{18} = 38.4^\circ$.

Dinitromatairesinol dimethyl ether, prepared quantitatively by the action of concentrated nitric acid (2.2 mols.) on a cold solution of the ether in glacial acetic acid (20 parts), crystallised from alcohol-chloroform in pale yellow needles, m. p. 179—180° (Found: C, 55.2, 55.1; H, 5.0, 5.1. $C_{22}H_{24}O_{10}N_2$ requires C, 55.4; H, 5.0%). In chloroform (c , 3.610) it has $[\alpha]_D^{18} = 126.6^\circ$. It gives with concentrated sulphuric acid a bright red solution, which darkens on the addition of a drop of concentrated nitric acid. The dinitro-compound was reduced in alcoholic suspension with zinc dust and concentrated hydrochloric acid; the filtered solution gave a deep blue-green coloration with ferric chloride. This dinitro-compound was also obtained in 50% yield by boiling matairesinol dimethyl ether (1 part) with a mixture of concentrated nitric acid (10 vols.) and water (10 vols.) for 12 hours. When matairesinol dimethyl ether (1 part) was treated either with cold fuming nitric acid (15 vols.) or with boiling concentrated nitric acid (10 vols.) for 10 minutes, it was converted into a *tetranitro-derivative*, which crystallised from alcohol-acetone in colourless needles, m. p. 202—203° (Found: C, 46.5; H, 4.2. $C_{22}H_{22}O_{14}N_4$ requires C, 46.5; H, 4.2%). In acetone (c , 0.5260) it has $[\alpha]_D^{19} = 161.6^\circ$.

Matairesinol diethyl ether, prepared by ethylating the resinol with ethyl sulphate in alcoholic solution as described in the preparation of the dimethyl ether, crystallised from methyl alcohol in colourless prisms, m. p. 97—98° (Found: C, 69.4; H, 7.6. $C_{24}H_{30}O_6$ requires C, 69.6; H, 7.3%).

Oxidation of the Ethers with Potassium Permanganate.—(a) A solution of matairesinol dimethyl ether (2 g.) in hot methyl alcohol (20 c.c.) was treated with 10% sodium hydroxide solution (4 c.c.). After boiling for 10 minutes, water (40 c.c.) was added, the alcohol removed, and the cooled solution subjected to a continuous stream of carbon dioxide during the gradual addition of 3% potassium permanganate solution (200 c.c.). The manganese dioxide was removed, and the concentrated filtrate acidified, boiled for 5 minutes, and extracted with chloroform. The extract, after being washed with sodium bicarbonate solution, yielded 0.2 g. of unchanged matairesinol dimethyl ether. Acidification of the bicarbonate solution gave a crude acid (1.3 g.), which yielded veratric acid (1.0 g.), m. p. 178—180° after crystallisation from hot water.

(b) A similar oxidation of the diethyl ether (2.0 g.) gave 0.2 g. of unchanged ether and 1.1 g. of 3-methoxy-4-ethoxybenzoic acid, m. p. 194°.

Oxidation of the Dimethyl Ether with Lead Tetra-acetate.—Matairesinol dimethyl ether (0.5 g.) in acetic acid (5 c.c.) was treated at 70° with lead tetra-acetate (1.2 g.) in acetic acid (15 c.c.). After heating for 10 minutes at 70°, water was added and the mixture was extracted with chloroform. The extract was washed with sodium bicarbonate solution, and the solvent removed; the residue solidified on trituration with a little methyl alcohol. The solid (0.5—0.8 g.), melting indefinitely between 190° and 215°, was dissolved in hot methyl alcohol-chloroform (7:3); the crystals, m. p. 237—241°, obtained on cooling were collected (A) and recrystallised several times from methyl alcohol-chloroform, giving colourless prisms, m. p. 250—252° (Found: C, 69.3; H, 5.5. $C_{22}H_{20}O_6$ requires C, 69.5; H, 5.3%), which were identified as (IV) by comparison with a specimen prepared as described in Part II. The chloroform was removed from the mother-liquors (A), and, on cooling, crystals, m. p. 200—203°, separated; after several

recrystallisations from methyl alcohol (carbon), slender prisms, m. p. 213—215° (Found : C, 69.4; H, 5.4. $C_{22}H_{20}O_6$ requires C, 69.5; H, 5.3%), were obtained, which were identified as (V) by comparison with a specimen prepared as described in Part II.

We are deeply indebted to Mr. A. J. Gibson of the London Shellac Research Bureau for obtaining a supply of matai resin from the Director of Forestry, State Forestry Service, Wellington, New Zealand. One of us (T. R.) thanks the Durham County Council Education Department for a scholarship.

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