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5[1]. AGATHARESINOL

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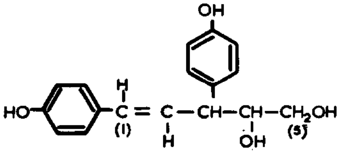
A previous paper in this series described the isolation from the heartwood of the New Zealand kauri (Agathis australis (Lamb. ex. D. Don) Steud.) of a phenolic compound which was named agatharesinol[3]. This compound is the most important constituent of the acidic fraction and forms about 5 per cent of the total resin and about 0.3 per cent of the heartwood. The present paper describes evidence that agatharesinol has structure 1.



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Thin layer chromatograms of the crude acid fraction from heartwood resin show a prominent spot at low R_F and the corresponding fraction after purification by chromatography gave agatharesinol. It readily gives a tetraacetate[4], $C_{25}H_{26}O_8$, and an acetonide, $C_{20}H_{22}O_4 \cdot H_2O$, but although soluble in bicarbonate agatharesinol contains no carboxyl group since its R_F on a thin layer plate is unchanged on brief treatment with diazomethane and since it lacks carbonyl absorption in the infrared.

The nmr spectra (60 Mc) of agatharesinol and its acetate and acetonide show an aromatic multiplet made up of two overlapping AB systems with coupling constants of approximately 8 cps. From the integrals it is clear that eight protons are involved in this multiplet indicating that there are two para-substituted aromatic rings in slightly different environments. The six-proton peak at 136 cps in the nmr spectrum of the tetra-acetate and the similar separation of the A and B protons in the two AB systems show that both aromatic rings have a para-hydroxyl group.

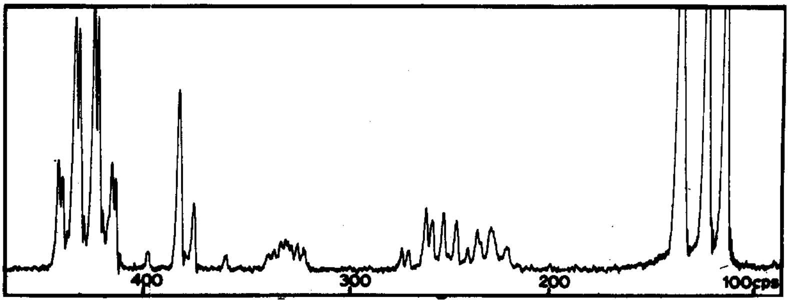
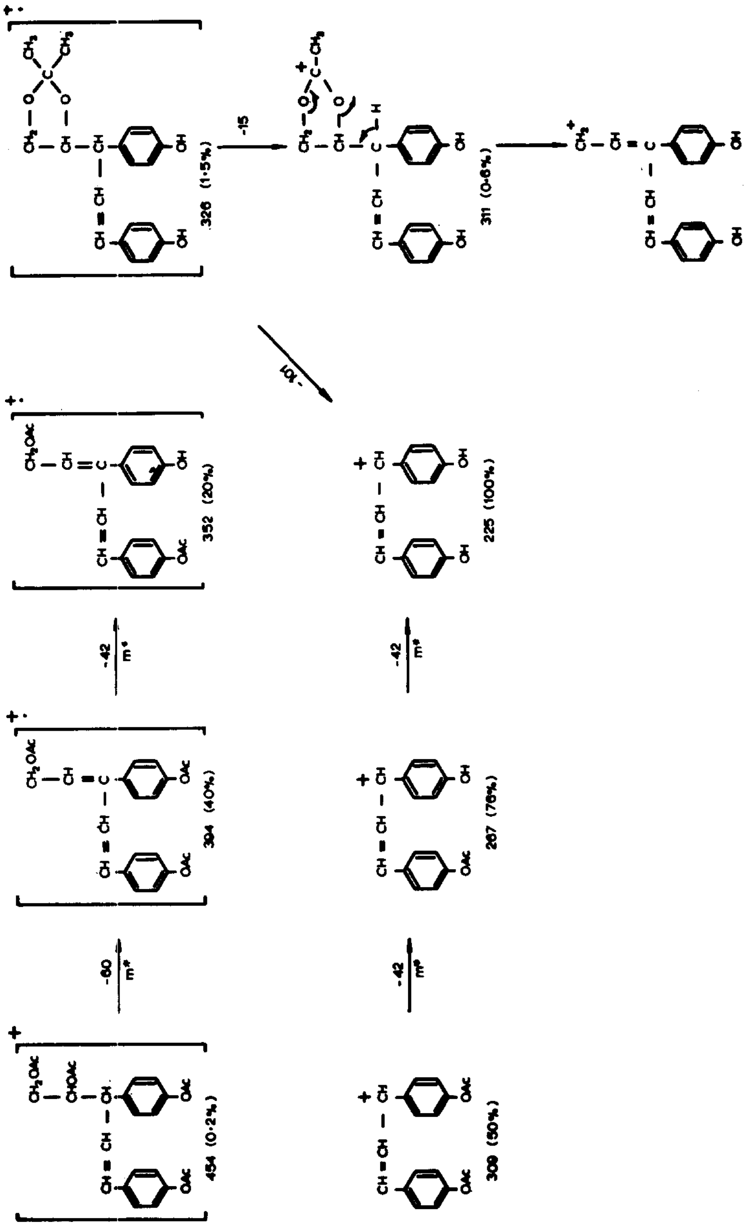


FIG. 1 Nmr spectrum of agatharesinol tetra-acetate

At slightly higher field in the nmr spectra there are two vinyl protons forming a third AB multiplet; this is most clearly seen in the spectrum of the acetate (383, 372 cps, J 16). The high field proton (H-2) of this pair has an additional 7 cps coupling and one peak coincides with the main peak of the low field proton (H-1). This multiplet accords well with a pair of protons on a <u>trans</u> double bond conjugated with an aromatic ring.

The ultraviolet (266 mμ, ε 26 000) and infrared spectra of agatharesinol confirm the presence of a p-hydroxystyrene grouping of <u>trans</u> configuration and show also that the second aromatic grouping is not involved in the conjugated system. The shift of the ultraviolet absorption of agatharesinol to shorter wavelength on acetylation (253 mμ, ε 22 000) provides further confirmation of a free hydroxyl on the aromatic ring conjugated with the double bond.

With the presence of the phenolic and p-hydroxystyrene groups firmly established, there remains the elucidation of the aliphatic three-carbon core carrying these and the two hydroxyl groups. The nmr spectrum of agatharesinol acetate shows, in addition to peaks due to four acetate groups, a one-proton multiplet at 327 cps and a complex multiplet at 220-270 cps. Examination of the complex multiplet with the aid of double resonance scans shows that the low field part is an AB system and that both protons of the AB pair are coupled with the proton at 327 cps. This system of couplings requires a $-CH-CH_2-$ grouping. Moreover, both carbons must carry hydroxyl groups since the 327 cps multiplet appears at the low field position only in the acetate and the positions of the $-CH_2-$protons cannot readily be explained by a single aromatic substituent. The difference in the positions of the low field proton (260 cps, J 12 and 3) and the high field proton (243 cps, J 12 and 6.5) of this AB



328 (1·5%)
-15
311 (0·6%)
251 (7%)
352 (20%)
225 (100%)
-42
m*
304 (40%)
267 (76%)
-60
454 (0·2%)
309 (50%)

FIGURE 2

pair (H_2-5) is not unexpected since the adjacent carbon is asymmetric but the difference in coupling constants seems less usual and may indicate that rotation is not completely free.

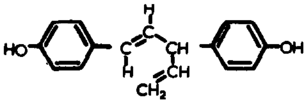
The C$\underline{H}$OAc proton at 327 cps (H-4) is coupled also to a proton in the high field part of the complex multiplet (226 cps, t, J 7). The position of this proton (H-3) shows that it must be attached to the same carbon as the p-hydroxyphenyl and p-hydroxystyrene groupings and double resonance scans show that the additional 7 cps coupling giving the 226 cps triplet is due to the B proton (H-2) of the AB vinyl pair. This is confirmed by the nmr spectrum of dihydroagatharesinol acetate in which the benzyl proton is shifted to 175 cps and appears as a quartet, which is reduced to a triplet in a double resonance scan removing the effect of the C$\underline{H}$OAc proton. The quartet must therefore be due to a benzyl proton (H-3) flanked by the CHOAc on one side and on the other by a CH_2 group formed in the hydrogenation.

The evidence given above unequivocally links each carbon atom in the central aliphatic chain of the molecule and places each proton and substituent on the chain. Agatharesinol must therefore have structure 1. Agatharesinol is optically active and preliminary results indicate that it has a 3S:4S configuration.

Agatharesinol acetonide was present in the crude heartwood extract but must have been formed during acetone extraction. It is readily obtained on treatment of agatharesinol with p-toluene-sulphonic acid in acetone and also under mild methylation conditions with sodium bicarbonate and dimethyl sulphate in acetone. Its structure follows from the presence of two methyl peaks at 84 and 81 cps and the results discussed above.

The structure of agatharesinol is confirmed by analysis of the mass spectra of the acetate and the acetonide. The prominent peaks in these spectra are readily accounted for by the sequence of reactions summarised below[5] (FIG 2). The only ions of high stability expected to originate directly from the molecular ions are those produced by cleavage of the C(3)-C(4) bond and that formed from the acetate molecular ion by elimination of the C(4) acetate group together with the C(3) hydrogen; prominent peaks are accordingly present at m/e 225 in the acetonide spectrum and at m/e 309 and 394 in the acetate spectrum. The last two ions, due to the facile loss of aromatic acetate groups[6] can be expected to eliminate ketene and the presence of the corresponding ions is shown by prominent peaks at m/e 267, 225 and 352. In the upper part of these spectra there are only two further peaks of any intensity; at m/e 251 in the acetonide spectrum and at m/e 250 in the acetate spectrum. The former corresponds to an ion formed by elimination of a methyl group and acetic acid, a well established fragmentation of O-isopropylidene derivatives of diols[7], and the latter to an ion that may originate from either or both of the m/e 309 and 352 ions.

Agatharesinol represents a type of natural product of which no examples were known until the very recent isolation of hinokiresinol (2) from Chamaecyparis obtusa by Hirose and coworkers[8] and of sugiresinol (3)[9] from *Cryptomeria japonica*[10].



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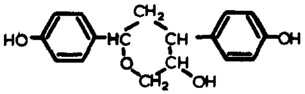

3

Agatharesinol has now also been isolated from *Athrotaxus selaginoides* by Erdtman and Nishimura[11]. Since Agatharesinol was not readily crystallised it seems possible that this type of compound may be of more frequent occurrence than is indicated by the number of compounds isolated so far[12]. Biogenetically the agatharesinol type compound can readily be accounted for by the coupling of two C_6-C_3 units similar to p-hydroxyphenylpyruvic acid, followed by dehydration, loss of the in-chain carboxyl and reduction.

Acknowledgement. We are indebted to Dr R Ryhage, Karolinska Institutet, Stockholm, for determination of the mass spectra.

REFERENCES AND FOOTNOTES

1 Part 1: B R Thomas, *Acta Chem Scand*, in the press

2 Present address: Research Department, Swedish Tobacco Company, Stockholm

3 C R Enzell and B R Thomas, *Acta Chem Scand*, **19**, 913 (1965)

4 Analytical samples of agatharesinol and its acetonide retained water and gave results that could be fitted to the preliminary C_{18} structure given in ref 3. However nmr and mass spectrometric results and analysis of the acetate show that these compounds have the compositions given here.

5 The figures for the intensities are given as a percentage of the intensity of the strongest peak in the spectrum, designated 100%. m^* indicates the presence of a diffuse peak due to the metastable ion involved in the reaction.

6 C R Enzell and R Ryhage, *Arkiv Kemi*, in the press

7 J A McCloskey and M J McClelland, *J Am Chem Soc*, **87**, 5090 (1965)

8 Y Hirose, N Oishi, H Nagaki and T Nakatsuka, *Tetrahedron Letters*, **1965**, 3665

9 Y Kai, *Mokuzai Gakkaishi*, **11**, 23 (1965)

10 K Funaoka, Y Kuroda, Y Kai and T Kondo, *ibid*, **9**, 139 (1963)

11 H Erdtman and K Nishimura, private communication

12 Although chromatographically and spectroscopically pure, agatharesinol from kauri crystallised (m.p. 105-108°) only after seeding with a sample of *Athrotaxus* material, kindly provided by Erdtman and Nishimura.