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Some Constituents of *Austrobaileya scandens* (Austrobaileyaceae): Structures of Seven New Lignans

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Abstract

The aerial parts of *Austrobaileya scandens* C. T. White (Austrobaileyaceae) yielded the known substances β-sitosterol, its D-glucoside, the sesquiterpene, spathulenol, and the lignan, deoxypicropodophyllin. In addition, seven new lignans, austrobailignans-1 to -7, were isolated and their structures, including absolute stereochemistry, elucidated. Two are aryltetralin lactones, two are aryltetralins, two are bis-arylpropanes, and the last is a tetrahydrofuran derivative. A triterpene acid mixture, to be investigated further, was also obtained.

The family Austrobaileyaceae, which is confined to northern Australia, comprises only two species, *Austrobaileya scandens* C. T. White and *A. maculata* C. T. White, both of which are climbing shrubs. The relationship of this family to others remains uncertain. Thus Airy Shaw[1] remarks that its affinities are 'very obscure' and Hutchinson[2] states: 'The genus *Austrobaileya*, Austrobaileyaceae, with only two known species, has been something of a puzzle as to its true position in our system. Its author, the late C. T. White, suggested that it should be placed near Magnoliaceae but the free carpels with a bilobed style coupled with the opposite leaves, the sepals and petals graded into each other and the numerous petaloid introrse stamens exclude it from the alliance; for want of a better place I have it near Monimiacea. . . . .' In the hope of obtaining information that might be helpful in deciding the affinities of the family, a chemical examination of *A. scandens* has been undertaken.

The aerial parts of the plant were extracted in turn with light petroleum, ether and methanol and the extracts fractionated in the usual manner by extraction with dilute acid, 2% sodium bicarbonate, 2% sodium carbonate and 2% sodium hydroxide; the neutral fractions were further separated into 'oxygenated' and 'non-oxygenated' portions by partitioning between aqueous methanol and benzene–light petroleum. Two of the substances isolated, although phenolic, appeared in neutral fractions. All of the fractions were very dark and separation and purification of them required extensive column chromatography, thin-layer chromatography and fractional crystallization.

Alkaloids were absent. Fractions consisting of higher paraffins, alcohols, acids and esters which were identified as such by i.r. and n.m.r. spectroscopy were not further

[1] Airy Shaw, H. K., in 'A Dictionary of Flowering Plants and Ferns' By J. C. Willis revised by H. K. Airy Shaw, 7th Edn, p. 108 (Cambridge University Press 1966).

[2] Hutchinson, J., 'Evolution and Phylogeny of Flowering Plants' p. 27 (Academic Press: London 1969).

examined, and a mixture of triterpene acids was reserved for further study. Known substances isolated were β-sitosterol, its D-glucoside, the sesquiterpene spathulenol,[3] and the lignan deoxypicropodophyllin (1).[4] In addition, seven new lignans, austrobailignans-1 to -7, were isolated, and the present work is concerned with their structure determination. Since the amounts available were quite small, extensive use of spectroscopic methods was made.

The Lignans

Deoxypicropodophyllin (1)

The structure of this substance was readily apparent from its spectral properties. Its identity was confirmed by direct comparison with an authentic sample which was prepared by the base-catalysed isomerization of deoxypodophyllotoxin (2) under the mild conditions of Hartwell, Schrecker and Johnson.[4] Since in all cases where deoxypicropodophyllin has been isolated from natural sources it has been shown to be an artefact[5] arising from the extraction procedures employed, it is probable that in the present instance also (1) is an artefact produced from the undetected (2) by the alkaline fractionation used.

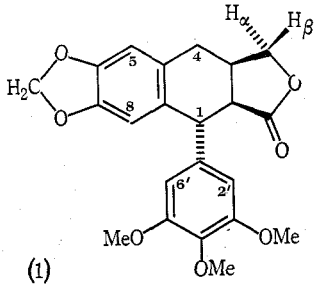
Austrobailignan-1 (3) and Austrobailignan-2 (4)

The structures of these two compounds were also readily apparent from their spectral properties. Austrobailignan-1 exhibited carbonyl absorption at 1780 cm^{-1} in the solution i.r. spectrum, which value is in accord with the presence of a strained *trans*-fused five-membered lactone. Austrobailignan-2 with the less strained *cis*-fused lactone ring had a carbonyl absorption band at a lower frequency, 1767 cm^{-1}. The aliphatic regions of the n.m.r. spectra of (3) and (4) were superimposable on those of deoxypodophyllotoxin (2) and deoxypicropodophyllin (1) respectively. Also since the signs of the rotations of (3) and (4) are the same as those of (2) and (1) respectively, the absolute stereochemistry of austrobailignan-1 and of austrobailignan-2 are assigned as shown in (3) and (4) respectively.

The oxygenation pattern of the pendant aromatic ring at C 1 in (3) and (4) was deduced from the n.m.r. spectra. Thus the coupling between C 2′–H and C 6′–H was 1·5 Hz, typical of a *meta* coupling; this value is too large for a *para* coupling and hence the possible substitution pattern (5) is eliminated. Irradiation of the methoxyl group signal caused the intensity of only one aromatic proton to be enhanced (14% and 15% in (3) and (4) respectively) so that the pattern (6) is also eliminated. In addition, in (6) the coupling constant between the aromatic protons would be expected to be larger than the observed value of 1·5 Hz. Detection of benzylic coupling between C 1–H and C 8–H allowed the assignment of signals for C 5–H and C 8–H. It should be noted that the signal for C 8–H is always upfield from the C 5–H signal because of the shielding effect of the out-of-plane pendant aromatic ring. The remaining assignments in the n.m.r. spectra which are set out in the Experimental section, are based on a recent report by Ayres *et al.*[6] All assignments were confirmed by double irradiation experiments.

[3] Bowyer, R. D., and Jefferies, P. R., *Chem. Ind.* (London), 1963, 1245.
[4] Hartwell, J. L., Schrecker, A. W., and Johnson, J. M., *J. Amer. Chem. Soc.*, 1953, **75**, 2138.
[5] Hartwell, J. L., and Schrecker, A. W., *Fortschr. Chem. Org. Naturst.*, 1958, **15**, 83.
[6] Ayres, D. C., Harris, J. A., Jenkins, P. N., and Phillips, L., *J. Chem. Soc., Perkin Trans. 1*, 1972, 1343.

For the same reasons stated above, austrobailignan-2 also is probably an artefact derived from austrobailignan-1. The latter was readily converted into the former under mild basic conditions.[4]



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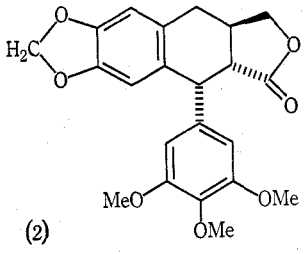

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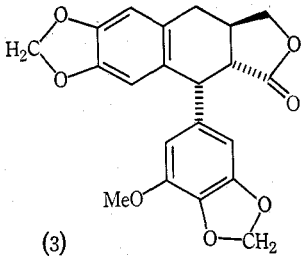

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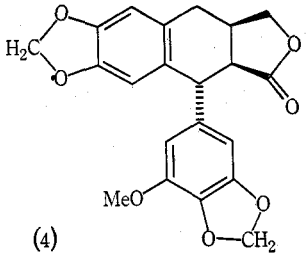

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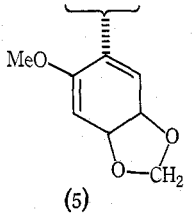

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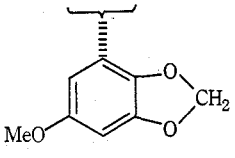

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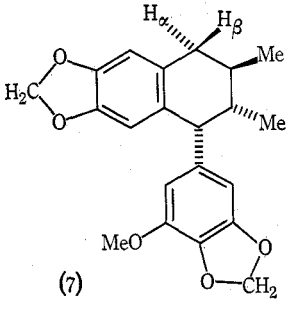

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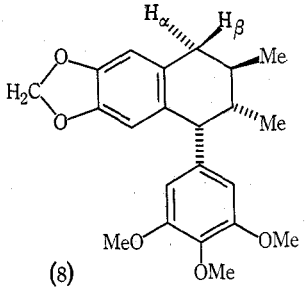


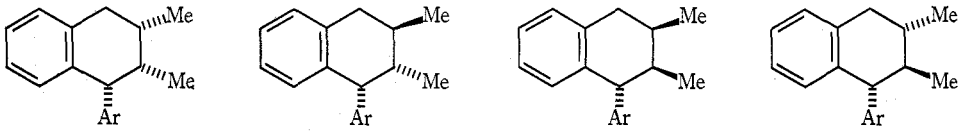
(8)

Austrobailignan-3 (*7*) *and Austrobailignan-4* (*8*)

The spectral properties of these two lignans also indicated their gross structures. The assignments for the n.m.r. spectra set out in the Experimental section were confirmed by double irradiation experiments (decoupling and n.O.e. experiments). In particular, the spectra gave the following stereochemically significant data for (7) and (8) respectively: $J_{1,2}$ 4·5 in both; $J_{3,4}$ 9·8 and 9·2; $J_{3,4}$ 5·0 and 4·5. The aliphatic regions of the spectra were virtually superimposable and the optical rotations were of the same sign and similar magnitude.

Four diastereoisomers, (A), (B), (C) and (D) (as well as another four enantiomers), are possible for a 1-aryl-2,3-dimethyltetralin structure. In view of the established absolute configuration of austrobailignan-1 (3) and of the absolute configurations of

austrobailignans-5, -6 and -7 in all of which the methyl groups have a *trans* relationship as discussed below, it seemed likely at the outset that austrobailignans-3 and -4 would have the configuration (B) or (D).



(A) (B) (C) (D)

The lignans (−)-galbulin (9) and (−)-galcatin (10) have known absolute configurations which are enantiomeric to configuration (D). Their n.m.r. spectra,[7] also now measured at 100 MHz, are significantly different from those of (7) and (8). In particular in (9) and (10), $J_{1,2}$ is 9 Hz, which is a consequence of the *trans* 1,2-substitution. Hence configuration (D) for (7) and (8) could be excluded.

Configuration (C) could also be excluded by the following evidence. The moderate quantity of deoxypicropodophyllin (1) available from the present work was reduced by lithium aluminium hydride to the diol (11).[8] The ditosyl derivative of this substance on reduction by the same reagent afforded (12) (2-epiaustrobailignan-4), which was not the same as austrobailignan-4. Also in the n.m.r. spectrum of (12), $J_{1,2}$ was 5·8 Hz and the coupling constants between C3–H and C4–H_2 were 5·0 and 6·9 Hz.

To distinguish between configurations (A) and (B), an attempt was made to convert deoxypodophyllotoxin (2) (a small amount of which had been kindly made available by Dr J. L. Hartwell) into austrobailignan-4 (8). Reduction of (2) by lithium aluminium hydride gave a mixture of the anhydro compound (13) and the diol (14), in which the former unfortunately predominated. The ditosylate of (14) was reduced by lithium aluminium hydride to give an overall yield of a very small amount of a compound which had the same retention times as austrobailignan-4 (8) (but different times from (12)) on two different g.l.c. columns. Also the n.m.r. spectrum of the compound had signals from aromatic and methoxyl protons which were superimposable on the corresponding signals in the n.m.r. spectrum of a dilute solution of (8).

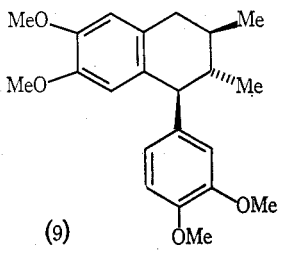
The above evidence is taken to be almost conclusive that austrobailignan-3 and austrobailignan-4 are (7) and (8) respectively. It should be noted that while the n.m.r. parameters support structures (7) and (8), the configuration (A) cannot be rigorously excluded on these grounds alone since one of its possible conformations would have similar n.m.r. parameters.*

Austrobailignan-5 (15) and Austrobailignan-6 (16)

The structures of these two compounds were readily deduced from their n.m.r. spectra (see Experimental). Since austrobailignan-6 gave a negative Gibbs test (spectrophotometric)[9] it was assigned the 4′-hydroxy-3′-methoxyphenyl substitution pattern. Both lignans have negative rotations and hence probably have the same absolute configurations as (−)-dihydroguaiaretic acid dimethyl ether (17).[8] Neither

* Further work on this problem by n.m.r. spectral techniques is in progress.

[7] Adjangba, M. S., *Bull. Soc. Chim. Fr.*, 1963, 1007.
[8] Schrecker, A. W., and Hartwell, J. L., *J. Amer. Chem. Soc.*, 1955, **77**, 432.
[9] Dacre, J. C., *Anal. Chem.*, 1971, **43**, 589.



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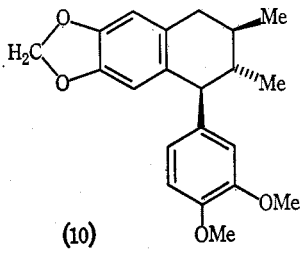

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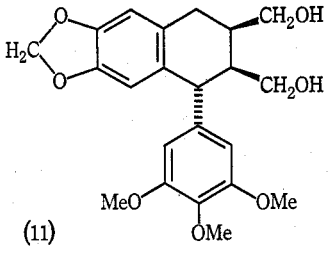

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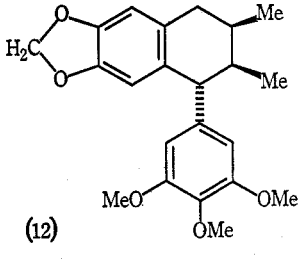

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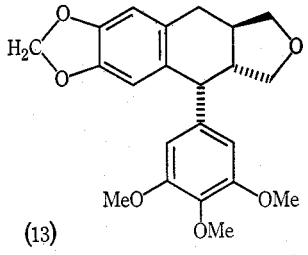

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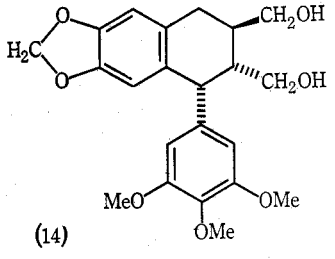

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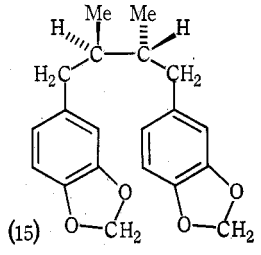

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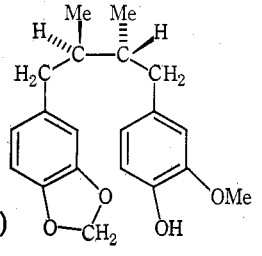

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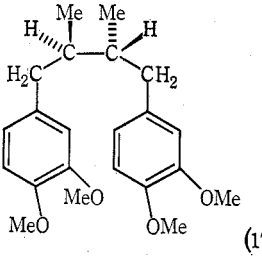

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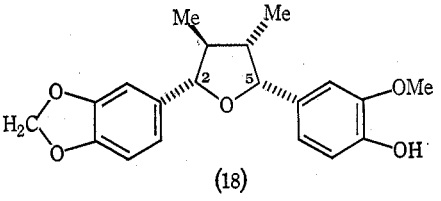

(18)

(15) or (16) was crystalline nor was the methyl ether of (16). A substance of the gross structure (15) has been previously synthesized[10] in presumably the *meso* form (m.p. 66°), but the structure has not been reported previously from a natural source.

Austrobailignan-7 (18)

The spectral properties of this lignan together with the fact that it gave a negative Gibbs test[9] suggested gross structure (18). The phenol was not crystalline although its acetyl and methyl ether derivatives were. The methyl ether was identical with calopiptin whose absolute stereochemistry is known.[11] Hence austrobailignan-7 has the structure (18).

Experimental

Melting points are uncorrected. Light petroleum had b.p. 50–70°. Analyses were carried out by the Australian Microanalytical Service, Melbourne. Ultraviolet spectra were measured on ethanol solutions and i.r. spectra on Nujol mulls unless stated otherwise. Mass spectra were determined with MS 902 or MS 30 instruments at 70 eV with the source temperature a few degrees below the m.p. of the compound. Analytical gas–liquid chromatography was carried out on Hewlett–Packard 400 and 402 gas chromatographs fitted with a flame ionization detector; helium was used as the carrier gas with a flow rate of 80 ml per min, and flow rates of hydrogen and air were 60 ml per min and 500 ml per min respectively. Retention times were taken from the time of appearance of the solvent peak. The columns used were: SE-30, a 1·1-m glass U-tube of 3 mm diameter packed with 3·8% SE-30 on 80–100 mesh Diatoport S, and OV-17, a 1·5-m glass U-tube of 3 mm diameter packed with 3% methylphenyl (1 : 1) silicone fluid on 100–120 mesh Gas-chrom Q. N.m.r. spectra were measured at 100 MHz on 5–10% solutions in deuterochloroform with tetramethylsilane as internal reference. Spectra were interpreted from first-order considerations; each signal as described in terms of multiplicity, intensity, chemical shift, assignment, and coupling constant in that order with the use of the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and (b) broad.

Extraction of A. scandens

The dried, milled aerial part of the plant (9·05 kg; SN 9004, collected at Boonjie in northern Queensland) was extracted at room temperature in turn with light petroleum, ether and methanol and each extract was then concentrated to a small volume.

The light petroleum concentrate was dissolved in ether and the solution kept for several days whereupon solid material deposited. This was collected and washed thoroughly with ether. From the ether washings crude austrobailignan-1 (0·26 g) was recovered. The residue was washed with chloroform to yield amorphous material (4·25 g), m.p. 200–250°, ν_{max} 3500–3200 cm^{-1}. Acetylation of a portion by refluxing with acetic anhydride–pyridine (3 : 2) for 2·5 h, followed by the usual workup and repeated recrystallization from ethanol, yielded colourless plates of the tetraacetyl derivative of β-sitosterol D-glucoside, m.p. 168°, $[\alpha]_D$ ($CHCl_3$) −32°; ν_{max} 1735 (b) cm^{-1} (lit.[11] 170–171°, $[\alpha]_D$ ($CHCl_3$) −33°). Acid hydrolysis of the acetyl derivative by Swift's method[12] gave β-sitosterol, m.p. 135–137°, identified by comparison with an authentic specimen.

The concentrated ether extract also gave a solid deposit which was collected and boiled several times with methanol until no more appeared to dissolve. The insoluble material (5·7 g) was identified as above as β-sitosterol D-glucoside. From the methanol filtrates a triterpene acid mixture (5·08 g) was recovered.

The concentrated methanol extract deposited dark intractable material (11·2 g) which was discarded. The filtrate was shaken with ether and a large volume of water. The aqueous layer was discarded and the ether layer worked up as described below.

[10] Blears, J. G., and Haworth, R. D., *J. Chem. Soc.*, 1958, 1985.
[11] McAlpine, J. B., Riggs, N. V., and Gordon, P. G., *Aust. J. Chem.*, 1968, **21**, 2095.
[12] Swift, L. J., *J. Amer. Chem. Soc.*, 1952, **74**, 1099.

Each of the extracts was extracted thoroughly with 2% hydrochloric acid, 2% sodium bicarbonate and 2% sodium hydroxide, and the extracts recycled. The neutral fractions were divided into 'oxygenated' and 'non-oxygenated' fractions by partitioning between methanol–water (9 : 1) and benzene–light petroleum (1 : 1).

The acid extracts gave negligible amounts of intractable basic material which was discarded.

The bicarbonate-soluble fractions (0·45 g, 3·27 g and 4·68 g respectively) were separately chromatographed on silica gel but yielded only fatty acids (i.r. and n.m.r. spectroscopy) which were not further examined.

The carbonate-soluble fraction (34 g) of the light petroleum extract also yielded only fatty acids. The corresponding ether fraction (19 g) was dissolved in a small volume of hot benzene. On standing crude triterpene acid mixture (5·74 g) separated. The residue was chromatographed on silica gel. Fractions eluted by benzene–ether (3 : 1) deposited more of triterpene acid mixture (1·76 g). The mother liquors of these fractions contained approximately equal amounts of the triterpene acid mixture and fatty acids which were separated by thin-layer chromatography of their methyl esters. All other fractions from the column chromatography appeared to contain only fatty acids. The carbonate-soluble fraction of the methanol extract (17 g) was dissolved in benzene (40 ml). After several days a solid separated which by several recrystallizations from methanol yielded crude triterpene acid mixture (0·5 g). All other fractions contained fatty acids only.

The three 'phenolic' fractions (3·3 ,7·2 and 2·0 g) were combined and the total chromatographed on silica gel but only fatty acid mixtures could be recovered.

A portion (26·5 g) of the 'non-oxygenated' light petroleum fraction (120 g) was chromatographed on alumina. Light petroleum eluted a paraffin wax (11 g) and solvents up to light petroleum–benzene (1 : 1) long-chain esters (0·4 g). Light petroleum–benzene (1 : 2) eluted a mixture (3·0 g) of austrobailignan-3 and austrobailignan-5, which were separated by thin-layer chromatography. Elution with benzene–ether (4 : 1) gave austrobailignan-4 (0·4 g).

The 'non-oxygenated' fraction of the ether extract (34·5 g) on chromatography on alumina gave as recognizable products only paraffin wax (2·0 g) and β-sitosterol (0·1 g).

The corresponding fraction of the methanol extract (12·6 g) gave long-chain alcohols (0·9 g) and β-sitosterol (0·2 g).

The 'oxygenated' fractions of the ether and methanol extracts (8·8 g and 5·6 g) were combined and chromatographed on alumina deactivated by ethyl acetate. Elution with benzene gave a mixture of austrobailignan-1, austrobailignan-3 and austrobailignan-5 (4·4 g). Benzene–ether (99 : 1) eluted a mixture of austrobailignan-2 and β-sitosterol (1·8 g). Elution with benzene–ether (98 : 2) gave a mixture of austrobailignan-2, β-sitosterol and deoxypicropodophyllin (0·6 g). Individual compounds were separated by fractional crystallization and thin-layer chromatography (SiO_2, benzene–ether (9 : 1)). Elution with benzene–ether (1 : 1) to ether gave fractions containing austrobailignan-6 and austrobailignan-7 (3·8 g) which were combined with the corresponding fractions from the 'oxygenated' light petroleum fraction.

The 'oxygenated' light petroleum fraction (34·7 g) was chromatographed on alumina deactivated by ethyl acetate. Elution with benzene–light petroleum (1 : 3) gave crude austrobailignan-5 (1·8 g). Benzene–light petroleum (1 : 2) eluted crude austrobailignan-3 (3·0 g). A mixture of spathulenol and austrobailignan-4 (1·2 g) was eluted by benzene–light petroleum (1 : 1). Fractions eluted by benzene–light petroleum (2 : 1) to benzene–ether (19 : 1) contained austrobailignan-2, β-sitosterol and deoxypicropodophyllin (4·5 g). The above mixtures were separated by fractional crystallization and thin-layer chromatography. Elution with benzene–ether (1 : 1) to ether gave fractions containing austrobailignan-6 and austrobailignan-7 (10 g). These fractions were combined with corresponding fractions obtained above and chromatographed on silica gel. Austrobailignan-6 (0·5 g) was eluted by benzene–ether (96 : 4), and crude austrobailignan-7 (7·0 g) by benzene–ether (19 : 1) to benzene–ether (4 : 1).

Spathulenol

The sesquiterpene alcohol which was purified by thin-layer chromatography (yield 0·015%) was an oil (Found: mol. wt, 220. Calc. for $C_{15}H_{24}O$: mol. wt, 220); $[\alpha]_D^{20}$ +52° (*c*, 1·7 in $CHCl_3$) (lit.[3] +56°); n.m.r. spectrum: s, 2, 4·66, C=CH_2; s, 3, 1·27, CH_3COH; s, 6, 1·05, 2×CH_3. The 3,5-dinitrobenzoate crystallized from methanol in pale tan needles, m.p. 144–146°, undepressed by admixture with an authentic specimen of m.p. 148°.[3] The i.r. spectra of the two samples were also identical.

Deoxypicropodophyllin (1)

The substance (yield 0·02%) crystallized from methanol as fine colourless silky needles, m.p. and mixed m.p. 170–172° (lit.[4] 169–173°), $[\alpha]_D^{20}$ +36° (*c*, 1·1 in $CHCl_3$). An authentic specimen[4] prepared from deoxypodophyllotoxin had $[\alpha]_D^{20}$ +38° (*c*, 1·1 in $CHCl_3$). The i.r. and u.v. spectra of the two samples were also identical; n.m.r. specttum: s, 1, 6·66, C5–H, $W_{h/2}$ 1·6; s, 1, 6·58, C8–H, $W_{h/2}$ 1·6; s (b), 2, 6·34, C2′–H and C6′–H; ABq, 2, 5·92, OCH_2O, 1·4; d of d, 1, 4·43, CH_α, 9·0, 7·0; d, 1, 4·36, C1–H, 3·0; d of d, 1, 3·96, CH_β, 9·0, 2·9; s, 3, 3·84, C4′–OCH_3; s, 6, 3·80, 2 × OCH_3; d of d, 1, 3·34, C2–H, 3·0, 9·8; m, 1, 3·19–2·85, C3–H; d of d (distorted), 1, 2·85, C4–H_α, 6·0 (apparent); d of d (distorted), 1, 2·46, C4–H_β, 5·0, 15·1 (apparent).

Austrobailignan-1 (3)

Austrobailignan-1 (0·008% yield) separated from methanol as fine colourless needles, m.p. 183–185°, $[\alpha]_D^{24}$ −110° (*c*, 1·2 in $CHCl_3$) (Found: C, 66·0; H, 4·7. $C_{21}H_{18}O_7$ requires C, 66·0; H, 4·7%). ν_{max} ($CHCl_3$) 1780, 1639, 1606 cm^{-1}; λ_{max} 244sh, 288, 293sh nm, ε 8250, 5050, 4800; ν_{max} 1770, 1632 cm^{-1}; n.m.r. spectrum: s, 1, 6·64, C5–H, $W_{h/2}$ 1·4; d (b), 1, 6·57, C6′–H, 1·6; s, 1, 6·49, C8–H, $W_{h/2}$ 1·4; d of d, 1, 6·07, C2′–H, 1·6, *J* (benzylic) 0·5; s, 2, 5·92, OCH_2O; ABq, 2, 5·88, OCH_2O, 1·4; d (b), 1, 4·55, C1–H, 3·0; m, 1, 4·38, CH_α; m, 1, 3·92, CH_β; s, 3, 3·89, OCH_3; m, 4, 3·25–2·60, C4–H_α, C4–H_β, C2–H, C3–H; mass spectrum: *m/e* 382 (100), 337 (14), 323 (12), 322 (8), 307 (7), 297 (14), 233 (17), 185 (26), 173 (23), 165 (37), 152 (11).

Austrobailignan-2 (4)

Austrobailignan-2 (0·02% yield) crystallized from methanol in fine colourless needles, m.p. 217–219°, $[\alpha]_D^{20}$ +88° (*c*, 2·5 in $CHCl_3$) (Found: C, 65·7; H, 4·9. $C_{21}H_{18}O_7$ requires C, 66·0; H, 4·7%). ν_{max} ($CHCl_3$) 1767, 1634, 1612sh cm^{-1}; ν_{max} (Nujol) 1770, 1757, 1635, 1612sh cm^{-1}; λ_{max} 204, 240sh, 287 nm, ε 51000, 8100, 5750; n.m.r. spectrum: s, 1, 6·64, C5–H, $W_{h/2}$ 1·5; s, 1, 6·58, C8–H, $W_{h/2}$ 1·5; d of d, 1, 6·34, C6′–H, 1·7, 0·8 (benzylic); d of d, 1, 6·26, C2′–H, 1·7, 0·7 (benzylic); s, 2, 5·92, OCH_2O; ABq, 2, 5·91, OCH_2O, 1·4; d of d, 1, 4·42, CH_α, 9·0, 7·0; d (b), 1, 4·33, C1–H, 2·8; d of d, 3·94, CH_β, 9·0, 2·9; s, 3, 3·86, OCH_3; d of d, 1, 3·29, C2–H, 2·8, 9·5; m, 1, 3·22–2·86, C3–H; d of d (distorted), 1, 2·86, C4–H_α, 15·2, 5·2 (apparent); mass spectrum: *m/e* 382 (100), 367 (5), 351 (5), 337 (16), 323 (14), 322 (11), 310 (18), 297 (18), 293 (5), 267 (10), 266 (6), 230 (12), 186 (5), 185 (8), 165 (11), 152 (6).

This substance was formed in 63% yield by refluxing a solution of austrobailignan-1 and anhydrous sodium acetate in absolute ethanol for 15 h according to the method of Hartwell, Schrecker and Johnson.[4]

Austrobailignan-3 (7)

Austrobailignan-3 (yield 0·1%) crystallized from light petroleum or methanol as colourless rods, m.p. 87–90°, $[\alpha]_D^{20}$ −120° (*c*, 2·5 in $CHCl_3$) (Found: C, 71·2; H, 6·4. $C_{21}H_{22}O_5$ requires C, 71·2; H, 6·3%). ν_{max} (CCl_4) 1637, 1616, 1506 cm^{-1}; λ_{max} 240sh, 289, 295sh nm, ε 8640, 5100, 4800; n.m.r. spectrum: s, 1, 6·57, C5–H, $W_{h/2}$ 2·1; s, 1, 6·37, C8–H, $W_{h/2}$ 1·7; d, 1, 6·22, C6′–H, 1·5; d, 1, 6·14, C2′–H, 1·5; s, 2, 5·89, OCH_2O; s, 2, 5·83, OCH_2O; s, 4, 3·84, C1–H and OCH_3; d of d, 1, 2·87, C4–H_α, 16·6, 5·0; d of d, 1, 2·38, C4–H_β, 16·6, 9·8; m, 2, 3·02–1·53, C2–H and C3–H; d, 3, 0·94, C3–CH_3, 6·0; d, 3, 0·79, C2–CH_3, 6·5 [addition of about 20% C_6D_6 to the sample caused C1–H to appear as doublet at δ 3·77 (*J* 4·5), unobscured by the methoxyl signal]; mass spectrum: *m/e* 354 (100), 298 (38), 297 (60), 268 (40), 267 (77), 253 (9), 239 (10), 225 (9), 209 (9), 202 (12), 187 (13), 165 (9), 148 (8), 139 (10).

Austrobailignan-4 (8)

Austrobailignan-4 (0·02% yield) separated from methanol in colourless needles, m.p. 118–120°, $[\alpha]_D^{20}$ −124° (*c*, 2·4 in $CHCl_3$) (Found: C, 71·5; H, 7·3. $C_{22}H_{26}O_5$ requires C, 71·3; 7·1%). ν_{max} 1590, 1505 cm^{-1}; λ_{max} 235sh, 292 (b) nm, ε 11300, 4640; n.m.r. spectrum: s, 1, 6·57, C5–H, $W_{h/2}$ 2·4; s, 1, 6·38, C8–H, $W_{h/2}$ 1·9; s, 2, 6·20, C2′–H, C6′–H, $W_{h/2}$ 1·6; ABq, 2, 5·82, OCH_2O, 1·4; d, 1, 3·89, C1–H, 4·5; s, 3, 3·81, C4′–OCH_3; s, 6, 3·75, 2 OCH_3; d of d, 1, 2·90, C4–H_α, 16·7, 4·5; d of d, 1, 2·41, C4–H_β, 16·7, 9·2; m, 2, 2·06–1·58, C2–H, C3–H; d, 3, 0·96, C3–CH_3,

5·9; d, 3, 0·82, C2–CH_3; mass spectrum: 370 (100), 283 (42), 282 (5), 252 (5), 222 (5), 202 (8), 187 (7), 157 (7), 128 (5).

Reduction of deoxypicropodophyllin (1) with lithium aluminium hydride by the method of Schrecker and Hartwell[8] gave the diol (11), m.p. 232–236° (lit.[8] 237–238°), which (0·19 g) on treatment with tosyl chloride (4 g) in pyridine at 0° afforded the ditosylate (0·36 g) as a gum. Reduction of the latter with lithium aluminium hydride (5 g) in boiling tetrahydrofuran gave a crude product (0·09 g). Purification by thin-layer chromatography (silica gel, benzene–ether (19 : 1)), followed by crystallization from methanol, yielded *2-epiaustrobailignan-4* (12) (0·02 g), as colourless needles, m.p. 123–125°, $[\alpha]_D^{20}$ −40° (*c*, 0·4 in $CHCl_3$) (Found: C, 71·6; H, 7·0. $C_{22}H_{26}O_5$ requires C, 71·3; H, 7·1%). ν_{max} ($CHCl_3$) 1588, 1500 cm^{-1}; λ_{max} 225sh, 293 (b) nm, ε 20800, 4700; n.m.r. spectrum: s, 1, 6·57, C5–H, $W_{h/2}$ 1·8; s, 1, 6·33, C8–H, $W_{h/2}$ 1·6; s, 2, 6·24, C2′–H, C6′–H, $W_{h/2}$ 1·3; ABq, 2, 5·85, OCH_2O, 1·5; s, 3, 3·83, C4′–OCH_3; s, 6, 3·77, $2OCH_3$; d, 1, 3·59, C1–H, 5·8; d of d, 1, 2·88, C4–H_α (β), 16·3, 5·0; d of d, 1, 2·44, C4–H_β (α), 16·3, 6·9; m, 2, 2·18–1·78, C2–H, C3–H; d, 6, 0·90, C2–CH_3, C3–CH_3, 6·5; mass spectrum: *m/e* 370 (84), 313 (8), 283 (100), 282 (12), 268 (9), 267 (7), 252 (15), 239 (7), 222 (14), 202 (16), 187 (17).

Reduction of deoxypodophyllotoxin (0·17 g) with lithium aluminium hydride (0·15 g) in tetrahydrofuran (4 ml) as described by Schrecker and Hartwell[8] gave a crude product which was chromatographed on alumina. The less polar compound (0·08 g), apparently the anhydro compound (13), was not examined further. The more polar compound (0·03 g), apparently the diol (14), was converted into the crude tosyl derivative (0·08 g) in the usual manner. Reduction of this with lithium aluminium hydride in tetrahydrofuran gave a product which was purified by thin-layer chromatography (silica gel, benzene–ether (19 : 1) to yield a gum (0·005 g) (Found: mol. wt, 370. Calc. for $C_{22}H_{26}O_5$: mol. wt, 370). The product had the same retention times, 12·0 and 3·7 min, in the SE-30 (180°) and OV-17 (148°) columns respectively as austrobailignan-4; the corresponding times for 2-epiaustrobailignan-4 were 11·0 and 4·5 min. The n.m.r. spectrum of the gum (microcell, 150 scans with the CAT technique) clearly showed the aromatic and methoxyl proton signals of austrobailignan-4, and the spectrum was superimposable on that of the natural lignan run under the same conditions.

Austrobailignan-5 (*15*)

Austrobailignan-5 (0·1% yield) was a colourless oil which was purified by evaporative distillation at 100°/0·02 mm, $[\alpha]_D^{25}$ −37° (*c*, 2·5 in $CHCl_3$) (Found: C, 73·2; H, 7·0; mol. wt, 326·1511. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8%; mol. wt, 326·1517). ν_{max} (liquid film): 1610, 1502 cm^{-1}; λ_{max} 236, 288 nm, ε 8200, 7600; n.m.r. spectrum: d of d, 2, 6·70, 2×C6′–H, 0·8, 7·4; m, 4, 6·61–6·46, 2×C2′–H, 2×C5′–H; s, 4, 5·89, $2OCH_2O$; m, 4, 2·68–2·18, $2ArCH_2$; m, 2, 1·94–1·50, $CH_3CHCHCH_3$; d, 6, 0·80, $2CH_3$, 6·8; mass spectrum: *m/e* 326 (40), 190 (4), 163 (5), 161 (2), 149 (2), 135 (100), 105 (5).

Austrobailignan-6 (*16*)

Austrobailignan-6 (0·01% yield) was also an oil which was purified by evaporative distillation at 100–120°/0·02 mm, $[\alpha]_D^{25}$ −32° (*c*, 1·3 in $CHCl_3$) (Found: mol. wt, 328·1675. $C_{20}H_{24}O_4$ requires mol. wt, 328·1673). ν_{max} (liquid film) 3500 (b), 1604, 1510, 1500 cm^{-1}; λ_{max} 233, 286 nm, ε 19400, 7250; n.m.r. spectrum: m, 6, 6·90–6·40, 6ArH; s, 2, 5·99, OCH_2O; s, 1, 5·50, OH; s, 3, 3·81, OCH_3; m, 4, 2·68–2·19, $2ArCH_2$; m, 2, 1·92–1·53, $CH_3CHCHCH_3$; d, 6, 0·81, $2CH_3$, 6·7; mass spectrum: *m/e* 328 (50), 137 (100), 135 (70).

Methylation of the lignan (0·27 g) with dimethyl sulphate (0·5 g) and anhydrous potassium carbonate (0·55 g) in refluxing acetone for 15 h, followed by the usual workup, afforded the *methyl ether* (0·18 g), a gum which was purified by thin-layer chromatography (silica gel, benzene), $[\alpha]_D^{25}$ −22° (*c*, 1·6 in $CHCl_3$) (Found: mol. wt, 324·184. $C_{21}H_{26}O_4$ requires mol. wt, 324·183). ν_{max} (liquid film) 1608, 1590, 1513, 1502 cm^{-1}; λ_{max} 231, 284 nm, ε 12100, 5800; n.m.r. spectrum: m, 6, 6·76–6·34, 6ArH; s, 2, 5·88, OCH_2O; s, 3, 3·83, OCH_3; s, 3, 3·80, OCH_3; m, 4, 2·55–2·33, $2ArCH_2$; m, 2, 1·82–1·62, $CH_3CHCHCH_3$; d, 6, 0·81, $2CH_3$, 6·7; mass spectrum: *m/e* 342 (27), 151 (100), 135 (36).

Austrobailignan-7 (*18*)

Austrobailignan-7 (0·1% yield) was a pale yellow gum which was purified by evaporative distillation at 130°/0·02 mm, $[\alpha]_D^{25}$ +12° (*c*, 2·9 in $CHCl_3$) (Found: C, 70·4; H, 6·5; mol. wt, 342·1462.

$C_{20}H_{22}O_5$ requires C, 70·2; H, 6·8%; mol. wt, 342·1467). ν_{max} ($CHCl_3$) 3550, 1610, 1512, 1503 cm^{-1}; λ_{max} 234, 284 nm, ε 12300, 6750; n.m.r. spectrum: m, 6, 7·10–6·50, 6ArH; s, 2, 5·92, OCH_2O; s(br), 1, 5·68, OH; d, 1, 5·07, C2–H, 8·2; d, 1, 4·33, C5–H, 8·8; s, 3, 3·82, OCH_3; m, 2, 2·40–1·45, C3–H, C4–H; d, 3, 1·02, C4–CH_3, 6·1; d, 3, 0·63, C3–CH_3, 6·6; mass spectrum: *m/e* 342 (34), 257 (3), 192 (40), 190 (100), 177 (7), 175 (19), 145 (35).

The *acetyl derivative* prepared with acetic anhydride in pyridine in the usual manner crystallized from isopropyl alcohol as colourless plates, m.p. 81–82°, $[\alpha]_D^{20}$ +23° (*c*, 1·5 in $CHCl_3$) (Found: C, 68·6; H, 6·3. $C_{22}H_{24}O_6$ requires C, 68·7; H, 6·3%). ν_{max} (CCl_4) 1773, 1609, 1505 cm^{-1}; λ_{max} 220sh, 278sh, 282, 285sh nm, ε 11300, 5400, 6000, 5300; n.m.r. spectrum: m, 6, 7·16–6·66, 6ArH; s, 2, 5·95, OCH_2O; d, 1, 5·12, C2–H, 8·0; d, 1, 4·55, C5–H, 8·5; s, 3, 3·82, OCH_3; s, 3, 2·28, CH_3CO; d, 3, 1·04, C4–CH_3, 6·2; d, 3, 0·66, C3–CH_3, 6·8; mass spectrum: *m/e* 384, (22), 234 (12), 192 (87), 190 (100), 177 (10), 175 (26), 162 (10), 161 (8), 160 (10), 149 (10), 145 (39), 135 (9), 117 (10).

Methylation of the lignan (0·95 g) as above gave a crude product which was purified by thin-layer chromatography followed by crystallization from methanol. Calopiptin (0·34 g) was obtained as colourless plates, m.p. 93–94°, $[\alpha]_D^{20}$ +33° (*c*, 1·2 in $CHCl_3$) (lit.[11] m.p. 95·5°, $[\alpha]_D^{14}$ +28°). The mixed m.p. with an authentic sample was undepressed and the u.v., i.r., and n.m.r. spectra of the two samples were identical.

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