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THE STRUCTURES OF LIGNANS FROM *GMELINA ARBOREA* LINN

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Abstract—Five new lignans isolated from *Gmelina arborea* Linn have been characterised. The parent compound arboreol, is 2a,6e-dipiperonyl-1e,2e-dihydroxy-3,7-dioxabicyclo-[3,3,0]-octane. It is accompanied by its 2-O-methyl ether, the 2-O-ethyl ether and its 2-epimer, isoarboreol,. The fifth substance, gmelanone, is the first reported example of a lignan derived from 3,6-dioxabicyclo-[3,2,1]-octane.

The important commercial timber, *Gmelina arborea* Linn, is found in almost all the rain forests of India.[1] Its chemical constituents have only recently been examined and the isolation of luteolin[2] and alkaloids[3] from the leaves has been reported. The occurrence of octacosanol,[4] cluytyl ferulate[5] and furofurans[6] in the heartwood has also been noted. We have published two notes[7,8] describing some results of our examination of the heartwood and this paper contains full details of these investigations.

Extraction of the heartwood powder (for details see Experimental section) yielded a mixture of at least eight compounds which were separated by column chromatography and fractional crystallisation. The compounds, together with their physical constants and chromatographic data are listed in Table 1. Three of them, gmelinol **1**, paulownin **2** (see Fig.1) and β-sitosterol are known compounds, and were identified by means of their physical constants, spectral data, chemical reactions and comparison with authentic samples. Gmelinol **1** was first isolated from the Australian plant, *Gmelina leichhardtii*[9] and its structure and chemistry have been the subject of intensive studies.[10-14] More recently a similar lignan, paulownin **2** has been characterised.[15-17]

Arboreol, $C_{20}H_{18}O_8$, gave a positive Labat test and in the mass spectrum gave ions at *m/e* 121, 135 and 149 characteristic of the presence of methylenedioxyphenyl substituents (see Fig. 2). Furthermore many ions corresponding to those observed in the spectra of eudesmin and gmelinol[18] are found in the spectrum of arboreol. In particular abundant ions at *m/e* 164 and *m/e* 161 due to "sideways" and "lengthwise" degradation[18] of the bicyclo[3,3,0]-octane lignan skeleton are evidenced (Table 2), indicating that arboreol is a modified member of this series. The special relationship to gmelinol is shown by the ion at *m/e* 220, of a type characteristic of gmelinol and its isomers.[14] However, the presence of an ion at *m/e* 338 is characteristic of the arboreol series and corresponds to a loss of HOR′ followed by formaldehyde; this could involve rearrangement to gmelanone with loss of ROH, followed by the loss of the carbon fragment. Gmelanone itself does show an ion at *m/e* 338 as an important species.

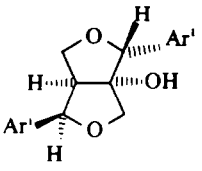
The ^{1}H NMR spectrum of arboreol (Table 3) confirms and amplifies the conclusions drawn. Signals of the correct τ value and multiplicity for those at C-4, C-5 and C-6 of gmelinol are clearly present, as are the two isolated protons at C-8, which appear as a simple doublet. However the signal characteristic of H-2 in gmelinol is absent and therefore this proton must be replaced in arboreol by another group, which in view of the molecular formula, must be a hydroxyl group. Arboreol is thus a hemi-ketal and the first member of a class with a hitherto unknown modification of the basic furofuran skeleton. Two separate piperonyl-residues are also demonstrated.

A closer examination of the spectrum, using criteria introduced by Pelter and his colleagues[14,19] to identify the

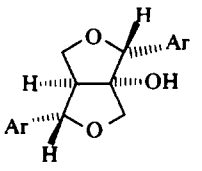
Table 1.

Compound	Formula	m.p.	$(\alpha)_D^{30}$	R_f^*	Yield%
β-Sitosterol	$C_{29}H_{50}O$	134°	−37°	0·61	0·003
Gmelinol **1**	$C_{22}H_{26}O_7$	124°	+129°	0·13	1·15
Paulownin **2**	$C_{20}H_{18}O_7$	105–6°	+29°	0·53	0·01
Arboreol **3**	$C_{20}H_{18}O_8$	162°	+76°	0·25	0·02
Isoarboreol **4**	$C_{20}H_{18}O_8$	162°	+39°	0·25	0.005
2-O-methyl arboreol **5**	$C_{21}H_{20}O_8$	134°	+84·5°	0·67	0·07
2-O-ethyl arboreol **6**	$C_{22}H_{22}O_8$	164°	+136°	0·71	0·02
Gmelanone **13**	$C_{20}H_{16}O_7$	190°	−78°	0·83	0·003

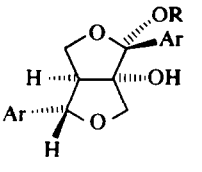
*Solvent system, benzene-ethyl acetate (9:1).



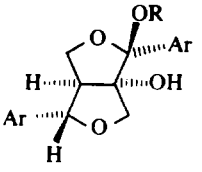
1
Gmelinol



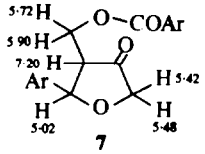
2
Paulownin



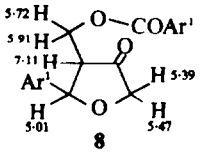
3
Arboreol **3**, R = H
2-O-Methyl arboreol **5**, R = CH_3
2-O-Ethyl arboreol **6**, R = CH_2CH_3



4
Isoarboreol **4**, R = H
2-O-Methyl isoarboreol **10**, R = CH_3
2-O-Ethyl isoarboreol **12**, R = CH_2CH_3



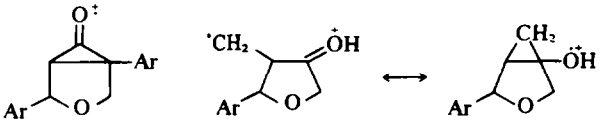
7
ν_{max} 1758, 1722 cm^{-1}



8
ν_{max} 1756, 1708 cm^{-1}

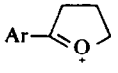
Ar = 3,4-methylenedioxyphenyl
Ar' = 3,4-dimethoxyphenyl

Fig. 1.

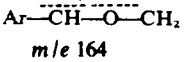


m/e 338

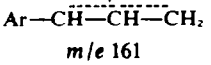
m/e 220



m/e 191



m/e 164



m/e 161

$ArC^{+}O$
m/e 149

$ArC^{+}H_2$
m/e 135

Ar^{+}
m/e 121

Ar = 3,4-methylenedioxyphenyl
All peaks have been accurately mass measured

Fig. 2. Fragments in the mass spectra of arboreol and its derivatives.

stereochemistry of C-2 and C-6 of the bicyclo[3,3,0]-octane lignans indicates that the aryl group at C-6 is equatorially disposed as the protons appear at relatively low field. Such criteria cannot be used to decide upon the stereochemistry at C-2, as the axial-proton at C-8 will always be under the influence of a polar group, be it aryl or hydroxyl, a situation peculiar to the arboreol series.

If the above conclusions are correct then arboreol is a 1,2-diol and should cleave with periodate. In fact arboreol **3** itself consumed one mole equivalent of sodium periodate in 4 hr whilst its isomer isoarboreol **4** (*vide infra*) took 12 hr in the same conditions. Arboreol is thus a *cis*-1,2-diol and, assuming the normal *cis*-fusion of the two five-membered rings, must be represented as **3**. The product of the oxidation of either arboreol or isoarboreol was the keto-ester **7** which corresponds closely to the keto-ester **8**, isolated as an oxidation product of gmelinol. Hydrolysis of **7** gave an equivalent of piperonylic acid (also obtained in 61% yield by the direct oxidation of methyl arboreol with chromium trioxide in pyridine.)

Further strong supporting evidence for structure **3** comes from the ^{13}C NMR* (Table 4). The two piperonyl residues are clearly seen with values close to those of paulownin. This is also true for all the aliphatic carbon atoms except C-2, which in arboreol is at *ca.* δ 102·85 (*ca.*

*An extensive study of the ^{13}C spectra of lignans has been made and will be reported in detail elsewhere. It suffices here to say that all the assignments are supported by off-resonance decoupling experiments and by analogies with reported data.

Table 2. Mass spectra of arboreol and related compounds

	Relative abundance (%)				
m/e	Arboreol **3**	Isoarboreol **4**	2-O-Methyl arboreol **5**	2-O-Ethyl arboreol **6**	Gmelanone **13**
414				0·5 (M^+)	
400			1·7 (M^+)		
386	0·3 (M^+)	0·4 (M^+)			
370	0·4	0·4	0·4	0·4	
369			1·4	1·5	
368	0·4	0·3	0·7	0·6	0·33 (M^+)
338	30	26	27	25	25
310	2	1	1	1	1
220	1	1	8	9	
191			2	2	
164	10	10	11	11	9
161	40	42	42	40	61
150	10	12	15	14	10
149	100	100	100	100	100
135	8	8	10	10	8
131	43	43	46	45	47
121	7	7	8	8	7
103	17	17	20	19	17

Table 3. ^{1}H NMR spectra

	τ-values (coupling constants in Hz in brackets)			
Assignment*	Arboreol **3** ($CDCl_3$)	Iso-arboreol **4** ($CDCl_3$-($CDCl_3$)	2-O-methyl arboreol **5** ($CDCl_3$)	2-O-ethyl arboreol **6** ($CDCl_3$)
4a	6.21 dd (2, 9)	6·14 dd (2, 8)	6·23 dd (9, 2)	6·16 dd (9, 2)
4e	5·66 dd (7, 9)	5·60 dd (7, 8)	5·90 dd (9, 7)	5·83 dd (9, 7)
5	7·38 m	7·31 m	7·40 m	7·35 m
6	5·53 d (7)	5·47 d (6)	5·55 d (7)	5·50 d (7)
8a	6·65 d (10)	6·66 d (10)	6·76 dd (10, 1·5)	6·75 d (10)
8e	6·34 d (10)	6·28 d (10)	6·35 d (10)	6·32 d (10)
OCH_2O	4·12, 4·15	4·08, 4·12	4·12, 4·17	4·07, 4·11
arom.	2·9–3·4	2·8–3·4	2·9–3·4	2·9–3·4
OH	6·80, 6·60	1·96, 6·63	6·45 d (1·5)	6·40
OCH_3			7·03	
$O\underline{CH_2}CH_3$				6·6–6·9
$OCH_2\underline{CH_3}$				8·88 t (7)

*All assignments are supported by appropriate spin-decoupling experiments.

35 ppm to lower field than C-2 of paulownin) and in a position to be expected for a cyclic hemi-ketal.[20] Optical rotation arguments supporting structure **3** are presented below.

Isoarboreol is indistinguishable from arboreol on TLC and was separated from it by fractional crystallisation. It is clear from the mass spectrum and ^{1}H NMR and ^{13}C NMR spectra that it is a stereoisomer of arboreol and the periodate oxidations show that it is epimeric at C-2. The optical rotation of isoarboreol is 37° lower than that of arboreol, in complete agreement with the conclusions drawn (see Table 5). The optical rotations also indicate that **3** is the absolute configuration of arboreol, and **4** that of isoarboreol.

Methyl arboreol contains a methoxyl group and a tertiary hydroxyl group giving a peak at 3335 cm^{-1} in the IR spectrum, exactly as does gmelinol, and resistant to acetylation. The ^{1}H NMR and ^{13}C NMR spectra closely resemble those of the arboreol isomers but show that one hydroxyl group has been replaced by a methoxyl group. The IR and chemical evidence indicate that the compound is 2-O-methyl arboreol or 2-O-methyl isoarboreol. The mass spectrum may only be interpreted in this fashion.

Similar arguments apply to a fourth substance whose properties can only be explained on the basis that it is 2-O-ethyl arboreol or its 2e-isomer.

For these ethers periodate oxidations cannot be used as a probe for the stereochemistry at the quaternary C-2 atom. The problem was solved by producing the isomers of the natural products by displacement reactions at C-2, which is the carbon of a ketal, and comparing the optical rotations of the natural products and their isomers.

When arboreol (**2a**, **6e**) or the natural 2-O-methyl ether were treated with aqueous acetone containing a small amount of hydrochloric acid then isoarboreol (**2e**, **6e**) resulted. When the natural 2-O-methyl ether was treated similarly with methanol containing a small amount of conc. sulphuric acid then an isomer m.p. 130, $[\alpha]_D + 10°$ was formed. Hence the natural ether $[\alpha]_D + 84·5°$ is 2-O-methylarboreol **3** and the synthetic substance is

Table 4. ^{13}C NMR spectra*

	1	5	4	8	2	6	1′1″	3′3″4′4″	2′2″5′5″6′6″		OCH_2O	OCH_3 OCH_2CH_3
Asarinin ae = ea	50·26 54·76		69·70 71·04		82·11 87·75		132·65 135·63	146·84 147·44 147·94 148·24	106·61 106·71 108·26	118·89 119·65	101·14	
Pinoresinol DME 2e, 6e	54·31		71·72		85·77		134·04	148·85 149·46	109·67 111·45 118·36			55·57 55·90
Gmelinol 2e, 6a	90·84	57·44	68·39	75·90	81·22	88·84	128·10 130·74	148·31 149·09 149·39	109·21 110·51 111·43	111·54 117·71 119·21		55·96
Neogmelinol 2a, 6e	93·89	62·69	69·72	76·78	88·66	85·20	129·68 132·86	148·68 149·02 149·16 149·47	108·82 109·71 111·28	111·38 117·49 118·70		56·02
Paulownin 2e, 6e	91·74	60·58	71·58	74·98	87·48	85·88	129·38 134·79	148·21 147·33	106·91 107·49 108·23	108·56 119·79 120·14	101·24 101·12	
Isoarboreol 2e, 6e	94·99	60·26	68·56	76·80	102·66	90·07	135·02	148·33 147·88	106·77 107·17 108·23	108·30 119·62 120·09	101·27 101·47	
Arboreol 2a, 6e	94·76	60·25	68·55	76·79	102·85	90·05	133·75 135·34	148·05 148·32	106·73 107·13 108·20	119·59 120·68	101·45 101·27	
Methyl arboreol 2a, 6e	95·62	60·40	68·47	76·61	105·20	90·01	129·97 135·23	147·60 147·94 148·14 148·29	107·18 107·42 108·08	108·23 120·05 120·55	101·23 101·34	49·01
Ethyl arboreol 2a,6e	95·53	60·51	68·49	76·61	105·00	89·97	130·60 135·20	147·50 147·81 147·97 148·20	107·13 107·23 107·98	108·17 119·98	101·15 101·27 120·28	15·32 57·44

	5	1	7	4	2	8	1′,1″	3′,3″,4′,4″	2′,2″,5′,5″,6′,6″	OCH_2O
Gmelanone	81·37	49·97	67·50	77·20	85·25	204·72	127·37 130·57	147·75 147·89 148·56	106·96, 107·12 108·28, 108·58 119·59, 120·17	101·23 101·43

*All assignments supported by off-resonance decoupling experiments. Measurements given as ppm downfield from TMS as internal standard at zero.

Table 5. Comparison of optical activities of stereoisomers of the 2,6-diaryl-3,7-dioxabicyclo-[3,3,0]-octane lignans

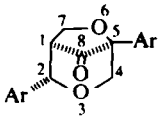
2a,* 6e isomer	$[\alpha]_D$	2e,* 6e isomer	$[\alpha]_D$	$\Delta(2a \rightarrow 2e)$
Epieudesmin	+119°	Eudesmin	+64	−55°
Asarinin	+120°	Sesamin	+71°	−49°
Neogmelinol	+60°	Isogmelinol	+30°	−30°
Arboreol	+76	Isoarboreol	+39°	−37°
Methyl arboreol	+84·5°	Methyl isoarboreol	+10°	−74·5°
Ethyl arboreol	+136°	Ethyl isoarboreol	+59·5°	−76·5°

*The configuration of the *aryl* group at C-2 is indicated.

2-O-methyl isoarboreol **10**. In the presence of methanolic hydrogen chloride isoarboreol **4** gave methyl arboreol **5** after 10 min, but if the reaction stood for 12 hr then only methyl isoarboreol resulted. It can be seen that initially reactions proceed with inversion at C-2, a surprising result as these displacement reactions are most unlikely to go *via* a simple S_N2 mechanism. As yet, however, the reaction conditions have not been standardised and further studies await larger quantities of the compounds. For our immediate purpose it sufficed that the isomeric compounds could be produced.

When methyl arboreol **5** was warmed with ethanol containing a few drops of conc. H_2SO_4, then crystals m.p. 154–6° resulted. The ^{1}H NMR spectrum of this sample indicated that it was a mixture of two isomeric ethyl arboreols in the ratio 1 : 1·7. On warming the crystals with acetic anhydride/pyridine the desired acetylation did not occur, but the recovered material m.p. 174°, $[\alpha]_D$ + 59·5° showed only single sets of signals in the ^{1}H NMR spectrum. A comparison of the optical rotations of this isomer and the natural product (Table 5) showed that the naturally occurring compound must be designated as 2-O-ethyl arboreol **6**.

It was rapidly obvious that the fifth substance isolated, gmelanone, $C_{20}H_{16}O_7$, was unusual in that it contained no hydroxyl groups. The molecular formula corresponded to that of arboreol minus water, but if such a relationship existed then a deep-seated rearrangement had occurred, as in the IR spectrum, gmelanone showed an absorption at 1765 cm^{-1} (KBr disc) characteristic of a γ-lactone or a ketone in a five-membered ring.



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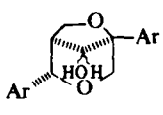


14

Arboreol equivalents to Gmelanone

C-2	C-5
C-4	C-7
C-5	C-1
C-6	C-2
C-8	C-4
C-1	C-8

Fig. 3.

The ^{13}C NMR spectrum of gmelanone (Table 4) showed a quaternary carbon atom at δ 204·7 characteristic of a ketone and quite outside the range for a cyclic or acyclic ester. The mass spectrum (Table 2) confirmed the relationship between gmelanone and the arboreol series, the resemblance in the lower mass range being quite striking.

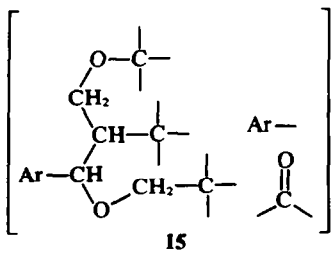
The ^{1}H NMR spectrum (Table 6) showed that one side of the molecule had a four proton system as in the arboreol series. It was remarkable however that *all* the aliphatic protons of gmelanone were moved downfield by up to 1 ppm relative to arboreol, suggesting that the carbonyl group was in a central position. An isolated methylene group was also present in gmelanone as were two methylenedioxyphenyl groups, and the part structure **15** can be written. Reduction of gmelanone with lithium aluminium hydride or sodium borohydride gave two epimeric dihydro-derivatives, which were secondary

Table 6. ^{1}H NMR data (τ), coupling constants (Hz) in brackets

	Gmelanone ($CDCl_3$-DMSO)	$LiAlH_4$ prodt. ($CDCl_3$)	$NaBH_4$ prodt. ($CDCl_3$)
7a	5·63 dd (8, 5)		6·17 dd (8, 5)
		5·88 d (2)	
7e	5·39 d (8)		5·86 d (8)
1	6.60 dd (3, 5)	7·03 m	7·56 br. t (5)
2	4·62 d (3)	5·14 d (2)	4·73 br. s
4a	6·17 d (11)	6·40 d (12)	6·37 d (11)
4e	5·95 d (11)	5·68 d (12)	5·60 d (11)
8	—	5·94[b]	5·80 d (5)
OCH_2O	4·07, 4·12	4·14, 4·20	4·16 (4 H)
arom.	3·0–3·4	2·7–3·4	2·7–3·4
OH	—	7·78[a]	7·56[a]

[a]Signals disappear on shaking with D_2O.
[b]Broad one-proton signal which becomes a sharp doublet (J = 4 Hz) after D_2O exchange.

alcohols. This confirmed that gmelanone was a ketone. Decoupling experiments showed conclusively that the proton α- to the hydroxyl groups was coupled to the proton central to the four proton systems present in gmelanone. The part structure **16** can be written for the dihydro-derivatives, and consideration of the molecular



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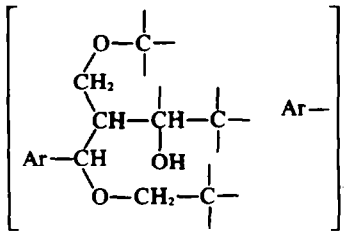


16

formula reduces this to **14**. From this the gross structure **13** for gmelanone follows. The ^{13}C NMR spectrum is in accord with this, there being a quaternary atom at 81·37 ppm corresponding to C-5, whilst C-1 has shifted to 49·97 ppm as compared with C-5 in arboreol which shows at 60·25 ppm. The carbon atoms C-7, C-4 and C-2 are found in the regions to be expected by comparison with the arboreol series.

Gmelanone is the first lignan derived from 3,6-dioxabicyclo-[3,2,1]-octane and indeed scelaranecic and sceleratinic dilactones[21,22] are the only natural products derived from this system. The question of the stereochemistry of gmelanone is deferred until the discussion.

DISCUSSION

The first question is whether methyl or ethyl arboreol or even gmelanone are genuine natural products or have been formed during the extraction process. This is particularly important as an ethyl ether is a most unusual

Table 7. Extraction of *Gmelina arborea* in layers

	Gmelinol	Paulownin	Arboreol	Me-Arboreol	Et-Arboreol	Gmelanone
Layer I	+	+	−	+	−	−
Layer II	+	+	+	+	+	−
Layer III	+	+	+	−	+	+

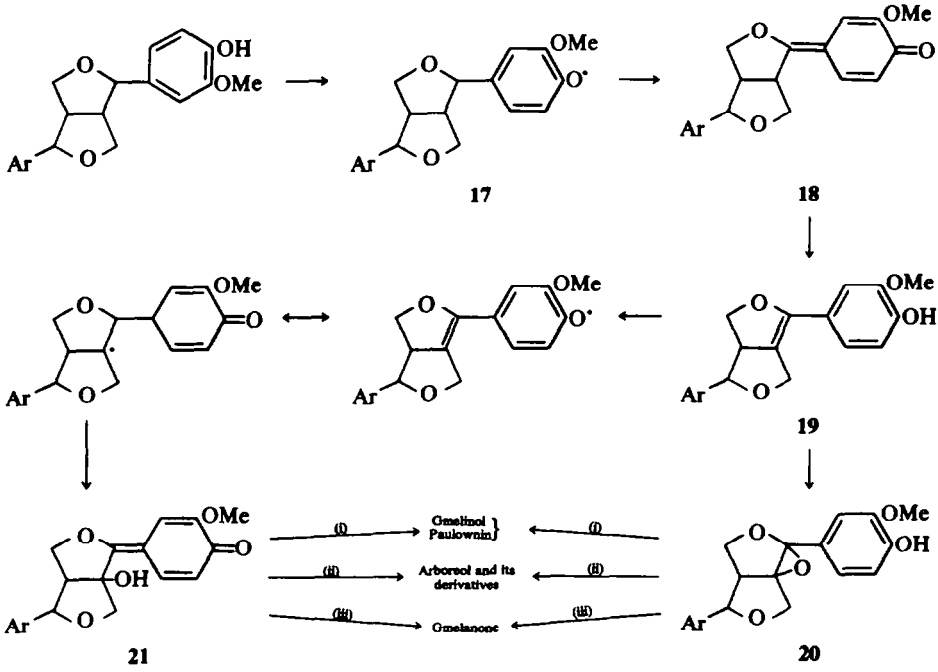
feature in a natural product (only very recently have any been characterised[23]), and also because of the unique nature of gmelanone. Ethanol was not used in the original extraction process, but methanol and ethyl acetate were. However, arboreol does not react with methanol alone even after 8 hr reflux. When arboreol was allowed to stand with ethyl acetate containing acetic acid or 5% sodium hydroxide, no change was observed. The extraction was repeated using only n-hexane and benzene and 2-O-ethyl arboreol was isolated as before. To further establish the point, the wood was planed in layers of 1″ to 3″ and each layer was extracted separately and in the same way. The results (Table 7) indicate that all the extractives are natural products. As yet gmelanone has not been obtained by acid treatment of arboreol or its derivatives.

The next question concerns the biosynthesis of these compounds. Whereas gmelanone may be formally derived from arboreol by a pinacol-pinacolone rearrangement, a hypothesis which would explain the production of all the known lignans of this plant may be proposed. Lignin itself is known to arise by the oxidative polymerisation of coniferyl alcohol, and the lignans are reasonably supposed to arise by a similar process, giving pinoresinol as the first product. Further phenolic oxidation must be instrumental in producing the methylenedioxy group, but equally the radical **17** could lose a hydrogen atom to yield the strained olefin **19**, which could give either the epoxide **20** or the quinone methide **21**. Both these compounds solve the interesting problem as to why in the further oxidation of the initially formed 2,6-diaryl-3,7-dioxabicyclo-[3,3,0]-octane lignans it is the tertiary, unactivated proton that is removed to yield gmelinol rather than the benzylic protons or the protons α- to an oxygen atom. Simple reduction of either **20** or **21** would give the gmelinol type structure, whilst the arboreol class would be produced by attack of OR^-. Attack by acids on either **20** or **21** could readily lead to isomerisation to give the gmelanone skeleton.

We are pursuing these ideas by searching for the epoxide **20**, whilst at the same time carrying out *in vitro* experiments designed to initiate the transformations shown. We have also examined the heartwood of *G. asiatica* Linn[24] and established the presence of cycloolivil, gmelinol and paulownin amongst the lignans produced, with gmelinol as the major component of this, as well as the other two *Gmelina* species examined. A re-examination of the heartwood of *G. leichhardtii* using modern methods of separation would seem to be justified.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer 237 spectrophotometer. Mass spectra were obtained on an AEI MS9 spectrometer and NMR spectra on Varian HA100 and XL100 instruments. ^{1}H NMR data are reported as τ-values relative to TMS as internal reference with coupling constants in Hz. Optical rotations were measured in 1% solution in chloroform at 30°, unless otherwise stated. All melting points are uncorrected. TLC data refer to silica gel C and benzene-ethyl acetate (9:1).



(i) $H^{(-)}$; $RO^{(-)}$; (iii) $H^{(+)}$. All followed by the appropriate reactions to yield veratryl or piperonyl residues.

Scheme

Extraction of the heartwood of G. arborea Linn

The heartwood of *G. arborea* Linn, was secured from Berhampur, Orissa State. The wood shavings (10 kg) were powdered and successively extracted with n-hexane (b.p. 64–67°) and methanol in a large soxhlet extractor. The yellow, n-hexane extract (10 l) was distilled to remove the solvent. The residue (300 g) did not crystallise and so was not studied further. The dark brown methanol extract (10 l) was concentrated to one litre and kept overnight. Some waxy material was deposited and filtered off. The solvent from the dark brown filtrate was completely removed under reduced pressure. The residue (200 g) was warmed with several small lots of ethyl acetate and separated. The ethyl acetate soluble portion was washed thoroughly with 5% aq. NaOH solution to remove the phenolic bodies. The ethyl acetate layer was then diluted with 500 ml ether and left overnight. A thick mass of colourless plates separated out, m.p. 120–4° (Compound A, 100 g). The filtrate on further concentration deposited colourless needles, m.p. 128–32° (Compound E, 7 g).

Further concentration did not yield any crystalline material and so the solvent was completely removed under vacuum. The residual gum showed seven clear spots A to G on TLC in the increasing order of their R_f values. It was adsorbed upon silica gel (100 g) (finer than 200 mesh) and the dry powder placed on a column of silica gel (2′ × 2·5″) set in n-hexane. The column was eluted with n-hexane, n-hexane-benzene mixtures and finally benzene. The elution was monitored by TLC while collecting one litre fractions. The table below gives the fractions and their composition as indicated by TLC monitor.

Table 8.

Eluent	Fraction	Compounds present	Yield
Hexane	1–10	Oil	100 mg
Hexane : Benzene 9 : 1	11–20	G	300 mg
	21–25	G, F	300 mg
	26–40	F	1 g
	41–50	F, G, E	1 g
Hexane : Benzene 1 : 1	51–55	F,D	500 mg
	56–65	D, C	1 g
	66–70	C	300 mg
	71–80	C, B	1·5 g
	81–85	B, A	1 g
Benzene	86–100	A	15 g

The fractions 11–20 were mixed and crystallised from ethyl acetate when compound G came out as colourless needles, m.p. 190° (250 mg). From the fractions 21–25 and 41–50, some more of compound G was crystallised (100 mg). The residue from these fractions on further concentration yielded compound F, m.p. 162°, which was also obtained from fractions 26–40. Further concentration of the residual liquids gave compound E, m.p. 134° (100 mg).

The residue from fractions 51–55 and 56–65 crystallised from methanol to yield compound D, m.p. 134° (300 mg) as colourless plates as the first fraction and later compound C (m.p. 105–6°, 600 mg) came out as colourless needles from acetone. Compound C was also obtained from the mixed fractions 66–70 and 71–80. The residue from the latter crystallised from benzene to yield compound B as colourless needles, m.p. 162° (1·5 g).

Identification of Compound A: *Gmelinol* **1**:

The substance crystallised from ethyl acetate-ether as colourless hexagonal plates, m.p. 124°, $[\alpha]_D$ + 129·9° (lit.[5] m.p. 124°, $[\alpha]_D$ + 124°). Bromination with Br_2 in glac. acetic acid gave dibromoisogmelinol, m.p. 195° (lit.[5] 195°).

Examination of Compounds B_1 and B_2: *Arboreol* **3** *and Isoarboreol* **4**

Arboreol (B_1) (1 g) crystallised from benzene as colourless needles, m.p. 162°, $[\alpha]_D$ + 70°. R_f 0·25. (Found: C, 62·23; H, 4·98. $C_{20}H_{18}O_8$ requires: C, 62·78; H, 4·70%). IR (Nujol): 3400 (OH), 1610 (arom), 940 cm^{-1} (OCH_2O). Accurate mass measurements: *m/e* 338·0787 ($C_{19}H_{14}O_6$), 161·0603 ($C_{10}H_9O_2$), 149·0241 ($C_8H_5O_3$), 131·0499 (C_8H_7O), 121·0291 ($C_7H_5O_2$), 103·0549 (C_8H_7). From the mother liquors after the separation of arboreol, isoarboreol (B_2) (500 mg) separated, m.p. 162°, $[\alpha]_D$ + 30°, R_f 0·25. (Found: C, 62·68; H, 5·02. $C_{20}H_{18}O_8$ requires: C, 62·78; H, 4·70%). IR (Nujol): 3400 (OH), 1610 (arom), and 940 cm^{-1} (OCH_2O).

Identification of Compound C: *Paulownin* **2**

The substance crystallised from acetone as colourless needles, m.p. 105–6°, $[\alpha]_D$ + 29°, R_f 0·53, Labat test positive for OCH_2O. It was found to be identical with paulownin (m.m.p. and IR). (Lit.[15], m.p. 104–5°). With Ac_2O/NaOAc an acetate m.p. 144° (lit.,[15] 144–5°) was obtained.

Identification of Compound D: *β-sitosterol*:

The substance crystallised out from methanol as colourless flakes, m.p. 134°, $[\alpha]_D$ − 37°. The mixed melting point with an authentic sample was not depressed.[25]

Examination of Compound E: *Methyl arboreol* **5**

The substance crystallised from methanol as colourless needles, m.p. 134°, $[\alpha]_D$ + 84·5°, R_f 0·69, Labat test positive for OCH_2O. (Found: C, 63·11; H, 5·13. $C_{21}H_{20}O_8$ requires: C, 63·00; H, 5·03%). IR ($CHCl_3$): 3535 (OH), 2830 (OCH_3), 2766 and 930 (OCH_2O), 1604 cm^{-1} (arom.).

Examination of Compound F: *Ethyl Arboreol* **6**

The substance crystallised from ethyl acetate as colourless needles, m.p. 164°, $[\alpha]_D$ + 136°, R_f 0·71. (Found: C, 63·82; H, 5·61. $C_{22}H_{22}O_8$ requires: C, 63·76; H, 5·35%). (Found: M^+ 414·1315. $C_{22}H_{22}O_8$ requires: 414·1315). IR (Nujol): 3500 (OH), 1610 (arom.) and 940 (OCH_2O) cm^{-1}.

Examination of Compound G: *Gmelanone* **13**

The substance crystallised from ethyl acetate as colourless needles, m.p. 190°, $[\alpha]_D$ − 78°, R_f 0·83. (Found: C, 65·06; H, 4·71. $C_{20}H_{16}O_7$ requires: C, 65·22; H, 4·38%). (Found: M^+ 368·0896. $C_{20}H_{16}O_7$ requires: 368·0896). IR (KBr): 1765 (five membered C=O), 1610 (arom.), 1450, 1325, 1235, 1165, 1140, 1105, 1035, 935 cm^{-1}. Accurate mass measurements: *m/e* 338·0790 ($C_{19}H_{14}O_6$), 310·0841 ($C_{18}H_{14}O_5$), 164·0473 ($C_9H_8O_3$), 161·0603 ($C_{10}H_9O_2$), 149·0239 ($C_8H_5O_3$), 135·0446 ($C_8H_7O_2$), 131·0499 (C_9H_7O).

Reactions of Arboreol **3**

Periodate oxidation. Arboreol (100 mg) was dissolved in dioxan (10 ml) and an aqueous solution (5 ml) of potassium periodate (100 mg) was added. The reaction was complete in 4 hr at room temp. [change in R_f value 0·43 → 0·82, benzene-acetone (8:2)]. The contents were poured into water (200 ml) and thoroughly extracted with ether. The ether layer was washed with dilute $NaHCO_3$, water, dried over $MgSO_4$ and evaporated. The keto-ester **7** came out as a yellow gum (50 mg). (Found: C, 62·75; H, 4·46. $C_{20}H_{16}O_8$ requires: C, 62·50; H, 4·20%). IR ($CHCl_3$): 1772, 936 (OCH_2O), 1758 (five membered ketone), 1772 (aromatic ester), 1610 (arom) cm^{-1}. 2:4-DNP of the keto ester melted at 190–2°. In acidic medium, the reaction was complete in 30 min and the same keto-ester was obtained.

Alkaline hydrolysis of the keto ester **7**. A solution of the keto ester (300 mg) in 4% methanolic alkali (25 ml) was refluxed for 0·5 hr. Methanol was removed under vacuum and the contents extracted with ether. The ether layer deposited a colourless solid (200 mg), m.p. 194–198°, upon removal of the solvent, which could not be purified.

IR ($CHCl_3$): 3460 br. (OH), 2870, 936 (OCH_2O), 1760 (five membered C=O), 1600 (arom.) cm^{-1}.

The alkali layer was acidified with dilute HCl and extracted with ether. The ether was evaporated and the solid crystallised from benzene to give colourless needles (50 mg), m.p. 225–7°. The mixed melting point with an authentic sample of piperonylic acid was not depressed.

Reaction of Isoarboreol **4**

Periodate oxidation. Isoarboreol (100 mg) was dissolved in dioxan (100 ml) and an aqueous solution (5 ml) of potassium periodate (100 mg) was added. The reaction was complete in 12 hr at room temperature [change in R_f value 0·43→0·82 benzene-acetone (8:2)]. The product was the same keto-ester as obtained from arboreol (IR and TLC).

Reactions of Methyl arboreol **5**

Oxidation of methyl arboreol: isolation of piperonylic acid. Methyl arboreol (100 mg) was dissolved in glac. acetic acid (2 ml) and chromium trioxide (100 mg) was added. The mixture was left overnight at room temperature. Excess chromium trioxide was destroyed by methanol, the mixture diluted with water, and extracted with ether. Upon removal of the ether, colourless crystals were deposited which crystallised from benzene as needles (51 mg), m.p. 225–7°. The mixed melting point with an authentic sample of piperonylic acid was not depressed.

Action of aq-acetone-HCl on arboreol **3**: *formation of isoarboreol* **4**. When arboreol (100 mg) in aq. acetone (10 ml) was treated with conc. HCl (2·5 ml) for 2 hr, isoarboreol was obtained as colourless needles (90 mg), $[\alpha]_D$ + 30°.

Action of aq-acetone-HCl on Isoarboreol **4**: *Formation of Arboreol* **3**

Isoarboreol (100 mg) in aq. acetone (1:1) was refluxed with conc. HCl (2 drops) for 2 hr and left at room temperature overnight. On concentration arboreol crystallised out as colourless needles, (90 mg), m.p. 162°, $[\alpha]_D$ + 70°.

Action of Methanol-H_2SO_4 on Arboreol **3**: *Formation of Methyl Isoarboreol* **9**

Arboreol (100 mg) in methanol (10 ml) was treated with 2 drops of conc. H_2SO_4 and left at room temp. overnight. On concentration, methyl isoarboreol crystallised out as colourless needles (85 mg), m.p. 134°, $[\alpha]_D$ + 10°. (Found: C, 63·11; H, 5·3. $C_{21}H_{20}O_8$ requires: C, 63·00; H, 5·00%). IR (Nujol): 3535 (OH), 2830 (OCH_3), 2766 and 930 (OCH_2O), 1604 (arom) cm^{-1}. ^1H NMR ($CDCl_3$) 4a-H, 6·12 (1 H, dd, J 2, 9), 4e-H, 5·78 (1 H, dd, J 7, 9), 5-H, 7·34 (1 H, dt), 6-H, 5·45 (1 H, d, J 6), 8a-H, 6·68 (1 H, d, J 10), 8e-H, 6·27 (1 H, d, J 10), OCH_2O, 4·02 (2 H, s) and 4·03 (2 H, s), arom 2·8–3·3, OH, 6·82, OCH_3, 6·93.

Action of Methanol-HCl on Isoarboreol **4**: *Formation of Methyl Arboreol* **5**

Isoarboreol (100 mg) in methanol (5 ml) was treated with conc. HCl (2 drops). After 1 hr the reaction mixture was poured into water and the product crystallised from methanol as colourless needles (90 mg), m.p. 134°, $[\alpha]_D$ + 84°. When the reaction mixture was left overnight, methyl isoarboreol crystallised out as colourless needles (70 mg), m.p. 134°, $[\alpha]_D$ + 10°.

Hydrolysis of Methyl Arboreol **5**: *Isolation of Isoarboreol* **4**

Methyl arboreol (500 mg) in aq. acetone (50 ml, 1:1) was treated with conc. HCl (2·5 ml) and kept at room temp. overnight. Isoarboreol crystallised out from aq. acetone as colourless shining plates (450 mg), m.p. 162°, $[\alpha]_D$ + 30°, R_f 0·25.

Hydrolysis of Methyl Isoarboreol **9** *to Arboreol* **3**

Upon refluxing a solution of methyl isoarboreol (100 mg) in aq. acetone (10 ml, 1:1) containing conc. HCl (0·75 ml) for 1·5 hr arboreol came out as colourless elongated plates (80 mg), m.p. 162°, $[\alpha]_D$ + 76°.

Action of conc. H_2SO_4 and Methanol on Methyl Arboreol **5**: *Formation of Methyl Isoarboreol* **9**

Methyl arboreol (100 mg) on treatment with methanol (10 ml) containing a few drops of conc. H_2SO_4 at room temp. gave methyl isoarboreol as colourless needles (90 mg), m.p. 130°, $[\alpha]_D$ + 10°, R_f 0·67.

Action of conc. H_2SO_4 and Ethanol on Methyl Arboreol **5**: *Formation of Ethyl Isoarboreol* **10**

Methyl arboreol (500 mg) in ethanol (20 ml) was treated with ten drops of conc. H_2SO_4 and within 10 min at room temp. colourless needles separated out. These were filtered and recrystallised from ethanol, when colourless shining needles (450 mg), m.p. 154–6°, R_f 0·71, were obtained.

This material (100 mg) was dissolved in pyridine (2 ml) and acetic anhydride (1 ml), kept for 2 hr at 100°, and left overnight at room temp. The reaction mixture was poured into water and the product recrystallised from ethanol to give ethyl isoarboreol as colourless needles, m.p. 174°, $[\alpha]_D$ + 59·5°, R_f 0·71. (Found: C, 63·51; H, 5·93. $C_{22}H_{22}O_8$ requires: C, 63·76; H, 5·35%). IR ($CHCl_3$) 3542 (OH), 2871 and 932 (OCH_2O), 1607 (arom) cm^{-1}. ^1H NMR ($CDCl_3$) 4a-H, 6·32 (1 H, dd, J 9,3), 4e-H, 5·95 (1 H, dd, J 9, 7), 5-H 7·40 (1 H, m), 6-H 5·63 (1 H, d, J 8), 8a-H, 8e-H, and OCH_2CH_3, 6·33–6·90 (4 H,m), OCH_2O, 4·15 (2 H, s) and 4·20 (2 H, s), OCH_2CH_3, 8·90 (3 H, t, J 7), arom, 3·08–3·50.

Reactions of Gmelanone **13**

Reduction with LAH. Gmelanone (100 mg) in anhydrous ether (10 ml) was added to a slurry of $LiAlH_4$ (50 mg) in anhydrous ether (10 ml) and the mixture refluxed for 1 hr. After work up, the product crystallised from benzene as colourless needles (50 mg), m.p. 117°, $[\alpha]_D$ + 73°, R_f 0·42. (Found: C, 64·31; H, 5·13. $C_{20}H_{18}O_7$ requires C, 64·86; H, 4·90%). IR (Nujol): 3560 s and 3420 br (OH). M^+ 370·1054 ($C_{20}H_{18}O_7$).

Reduction with $NaBH_4$. To a solution of gmelanone (100 mg) in absolute ethanol (20 ml), $NaBH_4$ (50 mg) was added slowly at room temperature. The reaction was complete in 15 min (change in R_f value 0·83→0·42). Ethanol was removed under vacuum, water (10 ml) added, and the mixture extracted with ether. The ether layer on evaporation gave a solid which crystallised from benzene as colourless needles (70 mg), m.p. 185°, R_f 0·42. (Found: C, 64·62; H, 4·82. $C_{20}H_{18}O_7$ requires: C, 64·86; H, 4·90%). M^+ 370·1048, $C_{20}H_{18}O_7$ requires: 370·1052.

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