

ARBORONE AND 7-OXO-DIHYDROGMELINOL: TWO NEW KETO-LIGNANS FROM *Gmelina arborea*¹

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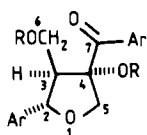
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ABSTRACT.—The structures of two new 2,3,4-trisubstituted tetrahydrofuran lignans **1a** and **2a**, isolated from the heartwood of *Gmelina arborea*, have been determined. In addition, two known furofuran lignans, paulownin acetate and epieudesmin, were isolated along with methyl *trans-p*-methoxycinnamate and *trans-p*-hydroxycinnamic acid. The conversion of **1a** into arboreol is also reported.

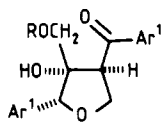
Extraction of the heartwood of *Gmelina arborea* L. (1) has yielded a number of novel lignans, including arboreol, isoarboreol, methyl arboreol, gummadiol, and gmelanone (2,3), the latter having a rearranged carbon skeleton derivable by acid-catalyzed rearrangement of arboreol (4). The present paper describes the isolation of six additional compounds of which two, arborone (**1a**) and 7-oxo-dihydrogmelinol (**2a**), are new. They are members of a relatively small group of lignans having aroyl-substituted tetrahydrofuran structures (5-7). The remaining four compounds comprise two known furofurans, paulownin acetate (8) and epieudesmin (9, 10), in addition to methyl *trans-p*-methoxycinnamate and *trans-p*-hydroxycinnamic acid.

RESULTS AND DISCUSSION

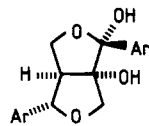
Arborone (**1a**), C₂₀H₁₈O₈, mp 216-218°, [α]_D²⁸+81.48 (CHCl₃), exhibited uv maxima at 206, 234, and 285 nm (log ϵ 4.44, 4.17, and 4.01). It formed a 2,4-dinitrophenylhydrazone, mp 268-270°, and on treatment with Ac₂O and pyridine gave a diacetate (**1b**). Arborone gave a positive Labat test and in its ¹H nmr and ms gave a clear indication of the presence of two 3,4-methylenedioxyphenyl groups. In its ir spectrum it gave a strong absorption at 1640 cm⁻¹ and this, coupled with the appearance of two low field aromatic protons at δ 7.73 dd (2,8) and δ 7.55 d (2) in the ¹H-nmr spectrum, suggested the presence of an aroyl residue. This was supported by the ms, which gave as the base peak an ion having *m/z* 149 (ArCO⁺). The two-proton signal at δ 3.60 in the ¹H-nmr spectrum of arborone, which was shifted downfield to δ 4.03 dd (6.8, 11.7) and 4.09 dd (7.5, 11.7) in the spectrum of the acetate, was consistent with the presence



1a Ar=piperonyl
R=H



2a Ar¹=veratryl
R=H



3 Ar=piperonyl

1b Ar=piperonyl
R=Ac

2b Ar¹=veratryl
R=Ac

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of a primary CH_2OH group. Further analysis of the ^1H -nmr spectra (Table 1) led to structure **1a** for arborone, and this was supported by the ms, which contained a number of ions at m/z 338, 192, 176, 164, and 161 that are characteristic of the arboreol series (2,3). Indeed, treatment of arborone with HCl in EtOAc gave a product, mp 162° , which was identical in all respects with arboreol (**3**) (2), thus confirming the structure and stereochemistry of **1a**. It seems likely that arborone arises in nature by hydrolytic cleavage of arboreol. The close relationship between the structures of the two compounds is confirmed by this experiment which thereby establishes the structure of arborone on a firm basis.

TABLE 1. ^1H -nmr Spectra^a

Proton	Compounds			
	Arborone (1a) $\text{CDCl}_3 + \text{DMSO}-d_6$ (100 MHz)	Arborone diacetate (1b) CDCl_3 (360 MHz)	7-Oxo-dihydro-gmelinol (2a) CDCl_3 (100 MHz)	7-Oxo-dihydro-gmelinol acetate (2b) CDCl_3 (360 MHz)
2	4.67 d (5) ^b	4.65 d (5.0)	5.09 s	4.91 s
3	2.7-2.9 m	3.01 q (6.8)	—	—
4	—	—	4.29 t (7.1)	4.31 t (7.3)
5	3.96-4.6 m	4.52 d (11.0)	4.19 dd (7.1, 6.1)	4.19 dd (7.3, 8.5)
CH_2	3.60 m	4.03 dd (6.8, 11.7) 4.09 dd (7.5, 11.7)	4.42 d (7.1) 3.64 br.s ^c	4.45 dd (7.3, 8.5) 4.14 s
arom	6.63 d (8), 6.75-7.15 m, 7.55 d (2) 7.73 dd (8, 2)	7.38 d (2), 7.54 dd (2, 8) 6.98 d (2), 6.86 dd (2, 8) 6.77-6.81	6.86-7.01 m 7.62 d (2) 7.47 dd (8.5, 2)	6.83-7.00 m 7.60 d (2) 7.73 dd (2, 8.5)
OCH_2O or OCH_3	5.96, 6.04 d (1.2)	5.96, 6.04 d (1.2)	3.81, 3.91, 3.94, 3.95 s	3.89, 3.91, 3.94, 3.95 s
OAc	—	1.65, 2.00 s	—	1.70 s
OH	Obscured	—	1.56, 1.96	2.2

^aAll the assignments are supported by appropriate spin decoupling experiments.

^bCoupling constants in Hz.

^cSharpened after adding D_2O .

The second new compound (**2a**), $\text{C}_{22}\text{H}_{26}\text{O}_8$, mp 70° , $[\alpha]^{28}\text{D} + 63.05$ (CHCl_3), exhibited uv maxima at 231, 276, and 310 nm ($\log \epsilon$ 4.06, 3.80, and 3.47). It formed a 2,4-dinitrophenylhydrazone, mp $212\text{--}213^\circ$, but gave only a monoacetate (**2b**) on acetylation. However, the ir spectrum of **2b** still contained a prominent OH peak at 3450 cm^{-1} , indicating that **2a** contains two hydroxyl groups only one of which can be readily acetylated. The ir spectra of both **2a** and **2b** also contained a prominent $\text{C}=\text{O}$ peak at 1660 cm^{-1} , and the ^1H -nmr and mass spectra gave clear evidence for the presence of two 3,4-dimethoxyphenyl groups. The presence of two low field aromatic protons at δ 7.74 dd (8.5, 2) and δ 7.62 d (2) suggested that one of the aryl groups was again present as an aroyl unit, and this was supported by the ms, which gave as the base peak an ion having m/z 165 (Ar^1CO^+). In contrast to the ^1H -nmr spectrum of arborone (**1a**) and its acetate (**1b**), 7-oxo-dihydrogmelinol (**2a**) and its acetate (**2b**) did not display a high field signal corresponding to H-3 but instead gave a one-proton triplet at δ 4.30 corresponding to H-4. Both the multiplicity and the chemical shift of this signal place it unequivocally at C-4 adjacent to the $\text{C}=\text{O}$ and CH_2 groups. This observation together with the evidence for an isolated primary alcohol (CH_2OH) group lead to the assignment of the structure **2a**, which is again supported by the mass spectrum.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Ir spectra were recorded on a Shimadzu AR408 and uv spectra on a Beckman instrument. Mass spectra were recorded on an AEI MS9 spectrometer and 100 MHz

nmr spectra on an XL100 instrument. 360 MHz nmr spectra were provided by the Edinburgh University high field nmr service using a Bruker WH360 instrument.

ISOLATION OF LIGNANS.—The heartwood of *G. arborea* L. (2,3) was obtained from Berhampur, Orissa State. The wood shavings (10 kg) were powdered, and successively extracted with hexane and MeOH, and worked out following the procedure reported by Row *et al.* (2). The only operational modification was that no alkali was used at any stage.

The uncrystallizable gum (45 g) obtained from the MeOH extract was absorbed on silica gel (100 g, BDH, 200 mesh) and chromatographed using a column of silica gel (800 g) eluting successively with hexane (10 liters), hexane-C₆H₆ (9:1, 40 liters; 1:1, 30 liters), C₆H₆ (20 liters), and C₆H₆-EtOAc (9:1, 15 liters). The elution was monitored by tlc and 1-liter fractions collected. The compounds isolated are listed in Table 2. Methyl *trans-p*-methoxycinnamate, *trans-p*-hydroxycinnamic acid, paulownin acetate (8), and epieudesmin (9,10) were isolated and identified by mp, ir, and elemental analysis data.

TABLE 2. Data on Isolated Compounds

Eluent	Fractions	Weight	Isolated Compounds	
hexane	1-10	250 mg	oil	
hexane-C ₆ H ₆ (9:1)	11-13	30 mg	methyl <i>p</i> -methoxycinnamate	
	14-30	150 mg	oil	
	31-40	150 mg	2- <i>O</i> -ethylarborcol	
	41-50	240 mg	2- <i>O</i> -ethylarborcol	
hexane-C ₆ H ₆ (1:1)	51-60	800 mg	2- <i>O</i> -methylarborcol (350 mg)	
	61-65	600 mg		paulownin acetate (700 mg)
	66-70	350 mg	β-sitosterol	
	71-72	400 mg	paulownin	
	73-75	160 mg	epieudesmin (100 mg)	
	76-80	1 g		arborcol (560 mg)
	C ₆ H ₆	81-90	7 g	isoarborcol (400 mg)
		91-100	1.37 g	arborone (25 mg)
C ₆ H ₆ -EtOAc (9:1)	101-110	7.15 g	arborcol, isoarborcol	
	111-115	560 mg	gmelinol, arborcol, isoarborcol	
			gmelinol (7 g)	
			<i>p</i> -hydroxycinnamic acid (150 mg)	
			gmelinol (530 mg)	
			7-oxo-dihydrogmelinol (20 mg)	

Arborone (1a).—Crystallized from EtOAc as colorless needles mp 216-218°; [α]^{28D}+81.48 (c, 0.054, CHCl₃) and gave a positive Labat test for the OCH₂O group; (Found: C, 62.10; H, 4.75. C₂₀H₁₈O₈ requires C, 62.18; H, 4.7%); uv λ MeOH 206, 234, 285 nm (log ε 4.44, 4.17, 4.09.); ir (KBr) 3515, 3400, 2900, 1640 (Ar-C=O), 1600 cm⁻¹; ms *m/z* 338 (8%, M-H₂O-CH₂O), 192 (2), 176 (13), 164 (5), 161 (18), 150 (11), 149 (100), 135 (7), 131 (12), 103 (4), 64 (15), 63 (17).

Arborone diacetate (1b).—Arborone (7 mg) was dissolved in 0.3 ml of dry pyridine, and 0.5 ml of dry Ac₂O was added. The reaction mixture was kept at room temperature for 24 h. After the usual work up, the acetate was obtained as a gum that was purified on a small column of silica gel by eluting with CHCl₃, when the acetate was obtained as a colorless oil (8 mg); Rf 0.64 (C₆H₆-EtOAc, 9:1); Found: C, 61.2; H, 4.8. C₂₄H₂₂O₁₀ requires C, 61.27; H, 4.72%; uv λ (MeOH) 234, 284, 313 nm (log ε 4.44, 4.17, 4.11); ir (CHCl₃) 1740 (acetate C=O), 1675, 1610, 1510 cm⁻¹; ms *m/z* 470 (1%, M⁺), 351 (7), 350 (18), 338 (3), 337 (15), 261 (3), 228 (3), 202 (3), 201 (3), 194 (3), 177 (4), 176 (6), 171 (2), 161 (2), 150 (11), 149 (100), 135 (6), 121 (13), 65 (14).

Conversion of Arborone to Arborcol (3).—Arborone (5 mg) was dissolved in EtOAc (1 ml), and to it HCl (0.5 ml) was added. The solution was kept at room temperature for 24 h and worked up in the usual manner. The light yellow residue on crystallization from C₆H₆ furnished colorless needles (80%), mp 162°, [α]^{28D}+75°, Rf 0.25 (C₆H₆-EtOAc, 9:1). The mmp was unchanged with an authentic sample of arborcol.

7-Oxo-dihydrogmelinol (2a).—Crystallized from C₆H₆/petroleum ether (40-60°) as colorless needles, mp 70°; [α]^{28D}+63.05 (1.134, CHCl₃); (Found C, 63.10; H, 6.36. C₂₂H₂₆O₈ requires C, 63.15; H, 6.27%); uv λ (MeOH) 231, 276, 310 nm (log ε 4.06, 3.8, 3.47); ir (KBr) 3500, 2950, 12660 (Ar-C=O),

1595, 1518 cm^{-1} ; *ms m/z* 382 (10%, M-2H₂O), 192 (30), 167 (35), 166 (14), 165 (100), 151 (7), 139 (29), 124 (11), 122 (11), 108 (10), 107 (10), 95 (10), 94 (10), 92 (12), 79 (38), 77 (32).

7-Oxo-dihydrogmelinol acetate (2b).—Treatment of **2a** with Ac₂O/pyridine gave a colorless oil (7 mg); R_f 0.37 (C₆H₆-EtOAc, 3:2); (Found: C, 62.54; H, 6.2. C₂₄H₂₈O₉ requires C, 62.6; H, 6.13%); *uv λ* (MeOH) 231, 281, 308 nm (log ϵ 4.47, 4.28, 4.11); *ir* (CHCl₃) 3450 (OH), 1735 (acetate C=O), 1655, 1590, 1510 cm^{-1} ; *ms m/z* 443 (3%, M-OH), 384 (8), 383 (13), 382 (46), 381 (9), 370 (6), 368 (9), 360 (7), 352 (7), 351 (28), 339 (6), 295 (6), 278 (24), 277 (84), 276 (7), 269 (8), 268 (36), 250 (9), 240 (28), 235 (10), 234 (13), 233 (13), 232 (17), 217 (18), 209 (22), 208 (67), 192 (35), 167 (60), 166 (18), 139 (44), 137 (13), 124 (11), 122 (14), 107 (12).

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