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A NEW LIGNAN FROM GMELINA ARBOREA LINN.

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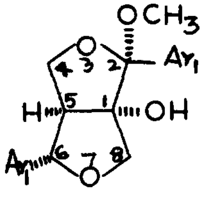
Our examination of the heartwood of Gmelina arborea Linn.(Verbanaceae), resulted in the isolation of a new lignan now named arboreol (I), besides gmelinol (II) isolated earlier by Birch et al.[1] from Gmelina leichhardtii. Arboreol (I), $C_{21}H_{20}O_8$, M^+ 400, m.p. 135°, $(\alpha)_D^{31°}$ + 84.5° (C, 1.0, $CHCl_3$), $\nu_{max}^{CHCl_3}$ 3537 (OH), 2829 (OCH_3), 2769, 936 ($O-CH_2-O$) and 1602 cm^{-1}, on oxidation with CrO_3/HOAc, afforded piperonylic acid in an yield of 61% suggesting two piperonyl units in the molecule. Further, arboreol (I) contained a tertiary hydroxyl resistant to acetylation.

The NMR spectrum of arboreol (I) (Table-I) is characteristically similar to gmelinol (II) and confirms a furofuran nucleus in this lignan. The aromatic region together with the methylenedioxy signals at τ 3.92s, 3.97s, also confirms the presence of two non-equivalent piperonyl nuclei in the molecule. The sharp singlet at τ 6.87 integrates for one methoxyl suggesting an alkyl methoxyl. This upfield signal for a methoxyl can be satisfactorily explained if it is located at C-2 to which the piperonyl ring is also attached. The only one benzylic hydrogen appears as a doublet at τ 5.40, J=7cps, which is taken to confirm its β -axial position at C-6 trans to the bridgehead hydrogen at C-5. The resonances of methylene hydrogens at C-8 and C-4 are significantly influenced by the two aryl substituents at C-2 and C-6[2]. The methylene hydrogens at C-4 appear as a pair of quartets at τ 6.02 and τ 5.72, similar to those noticed in iso- and neogmelinols[2]. It is, therefore, inferred that the C-6 aryl group must be equatorial as in iso- and neogmelinols. Similar considerations on the interaction between the C-2 piperonyl group and C-8 methylene hydrogens (τ 6.60 and 6.12) will suggest an axial position for this aryl group. The hydroxyl is noticed at τ 6.35d,J=1.5cps and when exchanged with deuterium, the C-8 axial hydrogen clearly comes out as a neat doublet at τ 6.60d, J=10cps.

TABLE - I

All the spectra were taken at 60MHz in $CDCl_3$ except (V) which was taken in $CDCl_3$+CD_3SOCD_3. All values are given in τ units with TMS as the internal standard.

Protons	Arboreol (I)	Isoarboreol (IV)	Desmethyl arboreol(V)	Keto-ester (VI)
O$\underline{H}$	6.35d,J=1.5	6.82br,s	5.90s(2 OH)	---
H_5	7.28t/d	7.34t/d	7.34m	7.20m
H_6	5.40d,J=7	5.45d,J=6	5.45d,J=6	5.02d,J=10
H_{4a}	6.02dd,J=10,2.5	6.12dd,J=9,2	5.60-6.20 m	5.72 and 5.90d
H_{4e}	5.72dd,J=10,7.5	5.78dd,J=9,7		
H_{8a}	6.60dd,J=10,1.5	6.68d,J=10	6.65d,J=10	5.42 and 5.48d
H_{8e}	6.12d,J=10	6.27d,J=10	6.32d,J=10	
$OC\underline{H}_3$	6.87s	6.93s	---	---
O-C$\underline{H}_2$-O	3.92s,3.97s	4.02s,4.03s	4.02s,4.04s	4.00s,4.08s
Aromatic (6H)	2.70-3.17m	2.79-3.34m	2.79-3.30m	2.47-2.82m (2H) 3.08-3.35m (4H)



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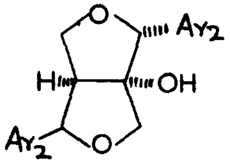

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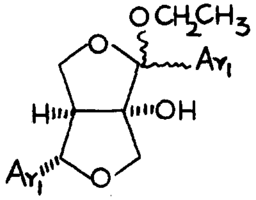

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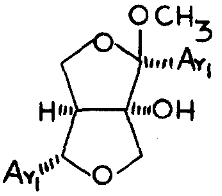

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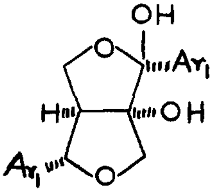

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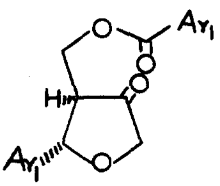

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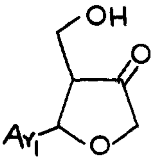


VII

Ar_1 = Piperonyl

Ar_2 = Veratryl

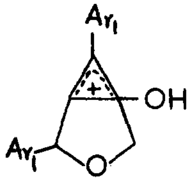
The position of the methoxyl at C-2 in arboreol (I) was conclusively established by the following series of reactions. When treated in ethanol solution with a few drops of Conc.H_2SO_4, arboreol (I) gave rise to a new compound (III) ($C_{22}H_{22}O_8$, m.p. 154-56°, $(\alpha)_D + 54.5^\circ$) in which the methoxyl was displaced by an ethoxyl. In the NMR spectrum of (III), the C-methyl appeared as two triplets centered at τ 8.72 and 8.82 (J=7cps) in the ratio of 1:1.7 suggesting a mixture of two isomeric compounds. When treated with Py/Ac_2O, no acetylation took place; but the resulting compound, m.p. 174°, $(\alpha)_D + 59.5^\circ$, gave a single methyl triplet at 8.82 (J=7cps) which is therefore the stabler isomer of the two.

The methoxyl in arboreol (I), is therefore labile and is likely to exchange with a hydroxyl or even isomerize under suitable conditions. These assumptions indeed came true. When treated at 30° with a few drops of Conc. H_2SO_4 in methanol, it was converted completely into an isomeric compound (IV), m.p. 130°, $(\alpha)_D^{31^\circ} + 10^\circ$, whose NMR spectrum contained the methoxyl at τ 6.93. Possibly, there was inversion at C-2 during this treatment and consequently, the equatorial-axial arboreol (I) isomerized to the more stable diequatorial isomer (IV). The optical rotation has fallen also to +10° which confirms this configuration at C-2 in isoarboreol (IV). A similar fall in optical rotation has been recorded between gmelinol (II) (ax-eq), $(\alpha)_D + 124^\circ$ and isogmelinol[3] (dieq), $(\alpha)_D + 30^\circ$ and also between asarinin (eq-ax), $(\alpha)_D + 120^\circ$ and sesamin (dieq)[4], $(\alpha)_D + 71^\circ$.

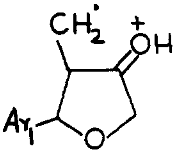
Final proof for structure (I) was obtained by the following reactions. When (I) was warmed with aqueous acetone (50%) containing 5% HCl, a desmethyl arboreol (V), m.p. 162°, $(\alpha)_D + 29.9^\circ$, $(\nu_{max}^{CHCl_3}$ 3557, 3325br cm^{-1} (OH), was obtained as colourless plates. Reconversion of (V) into (I) in presence of methanolic HCl was complete within 10 minutes; but after 12 hours, isoarboreol (IV) was formed. The desmethyl arboreol (V) contained a 1,2-glycol system which suffered periodate oxidation to the ketoester (VI) (obtained as a gum) $\nu_{max}^{CHCl_3}$ 1758 (for 5-membered cyclic ketone) and 1722 cm^{-1} (for ester). (VI) formed a 2:4 DNP derivative, m.p. 190-02°, $\nu_{max}^{CHCl_3}$ 1710 cm^{-1}. Mild alkaline hydrolysis of the ketoester (VI) furnished piperonylic acid and a keto alcohol (VII), m.p. 194-97°, ($\nu_{max}^{CHCl_3}$ 3460br, 1758 cm^{-1}), which was not uniform in TLC suggesting a probable mixture of keto-enol tautomers.

The mass spectrum of arboreol (I) conforms to the pattern of fragmentation recorded by Pelter[5] for gmelinol (II) and other ~~other~~ furofurans. The molecular ion M^+ 400 (75) is very prominent and the base peak is the diaryl cyclopropyl furan nucleus ($C_{19}H_{14}O_6$; m/e 338) which carried the hydroxyl as in gmelinol (II). Loss of a methoxyl (M^+ - 31) occurred producing the peak at m/e 369 and also m/e 370. Other peaks of considerable structural interest are m/e 220, 164, 150, 149 and 135.

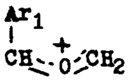
Arboreol (I) is the first furofuran with a methoxyl at C-2 to be discovered in nature. An oxygen function at C-2 has been frequently found in lignans, which in this case ended as a O-methylated hemiacetal.



m/e 338



m/e 220 (81)



$\overset{Ar_1}{\overset{|}{CH}}\cdots\overset{+}{O}\cdots CH_2$

m/e 164 (70)

$Ar_1.CHO^{\cdot +}$

m/e 150 (71)

$Ar_1.C\equiv O^+$

m/e 149 (78)

$Ar_1.CH_2^+$

m/e 135 (49)

Ar_1 = Piperonyl

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