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THE ISOLATION AND STRUCTURE OF 6''-BROMO-ISOARBOREOL - THE FIRST BROMINE CONTAINING LIGNAN

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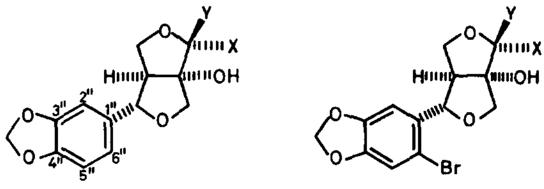
Summary

A new lignan from Gmelina arborea is shown to be 1, 2a-dihydroxy-2e-piperonyl-6e-(6''-bromopiperonyl)-3, 7-dioxabicyclo-[3, 3, 0]-octane, the first example of a bromine containing lignan.

We have recently reported the isolation of a number of new lignans including arboreol (1) and isoarboreol (2) from Gmelina arborea Linn.[1,2] We now report the isolation from the same source of 6''-bromo-isoarboreol (for brevity designated as GA6) (3), a rare example of a halogen containing product derived from a higher plant.

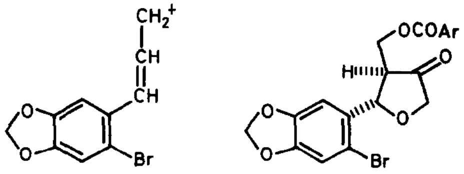
The substance, $C_{20}H_{17}BrO_8$, m.p. 190°, $[\alpha]_D$ -22° gave ^1H and ^{13}C n.m.r. spectra which were essentially similar to those of arboreol and isoarboreol (Tables 1 and 2) and established that the aliphatic moiety of the arboreol/isoarboreol molecule was completely intact. The bromine atom was therefore attached to one of the aromatic rings. Comparison of the ^{13}C spectra of GA6, dibromoisogmelinol and arboreol showed that one of the normal signals due to C-6' or C-6'' was missing and a new quaternary signal at δ 111.60 was present.

The fragmentation pattern of GA6 revealed by its mass spectrum was also very similar to that of the arboreols[2] involving sequential loss of H_2O and CH_2O from the molecular ion (see Scheme). The presence of an ion at m/e 239/241 (structure 4), losing $Br^{\bullet}$ to give m/e 160, and the absence of m/e 161 ($ArCH{=}CHCH_2^+$) suggested that the bromine atom was attached to the C-6'' aryl group. This was confirmed by periodate oxidation which gave a keto-ester (5), m.p. 122°, $\nu_{C=O}$ 1760 cm^{-1}, which could be hydrolysed to piperonylic acid and a keto-alcohol containing bromine. Furthermore periodate oxidation of GA6 required 10 hr. whereas periodate oxidation of its C-2 epimer (see below) required $4\frac{1}{2}$ hr. indicating that GA6 is a derivative of isoarboreol (2) rather than arboreol. The mass spectrum of the keto-ester (5) was also in complete accord with the proposed structure.



(1) X=OH, Y=Ar
(2) X=Ar, Y=OH
(6) X=Ar, Y=OMe
(7) X=OMe, Y=Ar
(3) X=Ar, Y=OH
(8) X=OH, Y=Ar

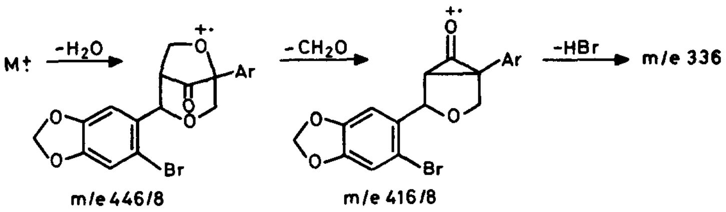
(Ar = 3,4 -methylenedioxyphenyl)



(4) (5)

Figure

6''-Bromo-isoarboreol could be prepared by treating methyl isoarboreol (6) with bromine in chloroform. When methyl arboreol (7) was treated with bromine in chloroform the isomer, 6''-bromo-arboreol, m.p. 162°, $[\alpha]_D$ -6°, was obtained which could be converted into the isoarboreol derivative, GA6, upon treatment with hydrogen chloride in acetone. The n.m.r., i.r., and mass spectra of GA6 and its isomer were superimposable and both gave the same keto-ester (5) upon periodate oxidation. However the times required for periodate oxidation clearly established that GA6 is a derivative of isoarboreol whereas the isomer (8) is a derivative of arboreol itself. Clearly the demethylation which accompanies bromination in anhydrous conditions proceeds with retention of configuration, presumably by direct attack of a bromide anion upon a methyl group.



Scheme

Table 1. ^{1}H n.m.r. spectra[*] of GA6, isoarboreol and derivatives.

Proton	GA6 (3) (d_6-acetone)	Isoarboreol (2) ($CDCl_3$)	Keto-ester (5) ($CDCl_3$)
4a	5.89 dd (9, 4)	6.14 dd (8, 2)	5.49 d (4, 5)
4e	5.53 dd (9, 9)	5.60 dd (8, 7)	
5	7.29 m	7.31 m	7.28 m
6	4.98 d (5)	5.47 d (6)	4.51 d (10)
8a	6.56 d (10)	6.66 d (10)	6.00 d (17)
8e	6.36 d (10)	6.28 d (10)	5.64 d (17)
OCH_2O	3.99, 4.05	4.08, 4.12	4.06, 4.09
arom.	2.8 - 3.4 m	2.8 - 3.4 m	2.5 - 3.4 m
OH	4.00, 4.33	6.96, 6.63	

[*] Values are given in τ, coupling constants (Hz) in brackets. All assignments are supported by appropriate spin decoupling experiments and correct integration.

Table 2. ^{13}C n.m.r. spectra[ø] of GA6, arboreol and isoarboreol.

Carbon	GA6 (3) ($CDCl_3$-DMSO)	Arboreol (1) ($CDCl_3$)	Isoarboreol (2) ($CDCl_3$)
1	94.09	94.76	94.99
2	101.53	102.85	102.66
4	69.03	68.55	68.56
5	59.60	60.25	60.26
6	87.73	90.05	90.07
8	76.33	76.79	76.80

[ø] Signals due to aromatic and OCH_2O groups not included. Measurements are given as p.p.m. downfield from TMS All assignments are supported by off-resonance decoupling experiments.

That the configuration of the C-6 aryl group is equatorial is confirmed by the ^{1}H n.m.r. spectrum of GA6 in which both H-4 protons come below 6τ.[3,4]

The change in $[\alpha]_D$ on going from GA6 to the corresponding bromoarboreol is +16°, fully in line with a change from isoarboreol to arboreol (2e→2a, aryl) of +37°.

Thus GA6 is 1,2a-dihydroxy-2e-piperonyl-6e-(6''-bromopiperonyl)-3,7-dioxabicyclo-[3,3,0]-octane, a monobromo derivative of isoarboreol, and the first example of a bromine containing lignan.

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