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THE STRUCTURE OF GUMMADIOL - A LIGNAN HEMI-ACETAL

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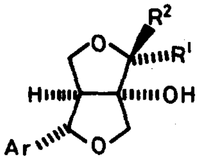
Summary

Gummadiol, a new lignan from Gmelina arborea, is shown to be 1,4-dihydroxy-2,6-dipiperonyl-3,7-dioxabicyclo-[3,3,0]-octane, the first member of a new series of dihydroxy lignans.

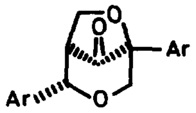
We have recently reported the isolation from Gmelina arborea of the new lignans arboreol (1) and isoarboreol (2) which are stereoisomeric 1,2-dihydroxy-2,6-dipiperonyl-3,7-dioxabicyclo-[3,3,0]-octanes, together with gmelanone (3) which may be formally derived from (1) and/or (2) by pinacolic rearrangement.[1,2] We now report the isolation, from the same source, of gummadiol (4), a structural isomer of the arboreols.

Gummadiol, $C_{20}H_{18}O_8$, m.p. 130°, $[\alpha]_D$ + 32°, has two hydroxyl groups (ν_{OH} 3580, 3400 cm^{-1}) and gave a diacetate (5), $C_{24}H_{22}O_{10}$, m.p. 140°, $[\alpha]_D$ + 31°. In the mass spectrum the ions at m/e 338 and 161, characteristic of the arboreols, were of low intensity (1% and 3% respectively). We have previously suggested that the peak at m/e 338 has structure (6) arising by rearrangement of arboreol to gmelanone followed by loss of formaldehyde.[2] Thus gummadiol should lack the 1,2-dihydroxy grouping characteristic of the arboreols, a suggestion confirmed in that unlike the arboreols, gummadiol did not undergo cleavage with periodate. The fact that the peak at m/e 161 ($Ar\,CH{=}CH\,\overset{+}{C}H_2$) was of little significance and that it was replaced by a peak at m/e 176 ($Ar\,CH{=}CH\,\overset{+\bullet}{CHO}$), relative intensity 88%, suggested that there was an oxygen at C-4.

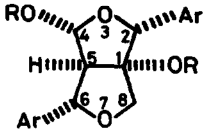
The ^{1}H n.m.r. spectra (Table 1) and also the ^{13}C n.m.r. spectra (Table 2) showed that gummadiol did in fact contain the 3,7-dioxabicyclo-[3,3,0]-octane skeleton and confirmed the structure (4). As in gmelinol and related compounds the H-8 protons each gave rise to a simple doublet, indicating that there was no hydrogen atom at C-1. The position of C-1 in the ^{13}C spectrum was at 91.99 p.p.m., closely similar to gmelinol, paulownin and the arboreols.[2] Thus a hydroxyl group is attached at C-1. The H-5 proton



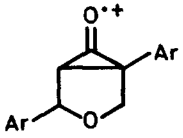
(1) $R^1 = OH, R^2 = Ar$
(2) $R^1 = Ar, R^2 = OH$
(8) $R^1 = Ar, R^2 = H$



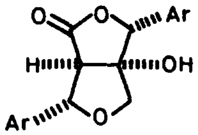
(3)



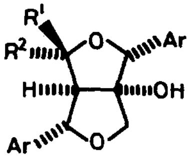
(4) R = H
(5) R = Ac*



(6)



(7)



(9) $R^1 = OMe, R^2 = H$
(10) $R^1 = H, R^2 = OMe$

Ar = 3,4-Methylenedioxyphenyl.
*The stereochemistry at C-4 not defined in this compound.

clearly seen at high field, was coupled to H-6 (J, 6 Hz) and also to one other proton (J, 2 Hz) at the atypical τ value of 4.85. It was almost certain therefore that the other hydroxyl group was attached to C-4, an inference verified both by the shift downfield of 1.11 p.p.m. of this proton in the diacetate (5) and by the fact that C-4 is at 96.47 p.p.m. as compared with 71.58 p.p.m. in paulownin (8). The rest of the ^1H and ^{13}C n.m.r. spectra were in complete accord with the assigned structures.

When gummadiol was oxidised with either Jones' reagent or $CrO_3/AcOH$ only piperonylic acid was isolated. However CrO_3/pyridine gave as the major product the γ-lactone (7), $C_{20}H_{16}O_8$, m.p. 157°, ν_{OH} 3500 cm^{-1}, ν_{CO} 1770 cm^{-1}. The ^1H n.m.r. spectrum of this compound was simple and in agreement with structure (7). The peak assigned to C-4 in the ^{13}C n.m.r. spectrum now appeared at 174.90 p.p.m.

That one hydroxyl group in gummadiol was that of a hemi-acetal was clear in that when gummadiol was treated at room temperature with methanol containing a few drops of conc. hydrochloric acid a monomethyl ether (9), m.p. 176°, $[\alpha]_D$ - 22.5° was produced.

Table 1

^{1}H n.m.r. spectra[x] of gummadiol and derivatives.

Proton	Gummadiol (5) ($CDCl_3$)	Diacetate (6) ($CDCl_3$)	γ-Lactone (7) (d_6-DMSO)
2	4.86 s	4.63 s	4.46 s
4	4.85 d (2)	3.74 d (2)	-
5	7.15 dd (2, 6)	6.65 dd (2, 6)	6.64 d (5)
6	5.15 d (6)	5.02 d (6)	4.88 d (5)
8a	6.08 d (10)	5.72 d (10)	6.04 d (10)
8e	5.96 d (10)	5.48 d (10)	5.92 d (10)
OCH_2O	4.12 s, 4.14 s	4.09 s, 4.10 s	4.01 s
arom.	3.0 - 3.4 m	3.0 - 3.4 m	3.0 - 3.3 m
$O\underline{H}$	8.3 s	-	4.92 s
$OCOC\underline{H}_3$	-	7.94, 8.30	-

[x] 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 paulownin, gummadiol and derivatives.

Carbon	Paulownin (8) ($CDCl_3$)	Gummadiol (5) ($CDCl_3$)	Diacetate (6) ($CDCl_3$)	γ-Lactone (7) (d_6-DMSO)
1	91.74	91.99	94.63	86.20
2	87.48	88.00	88.79	85.58
4	71.58	96.47	100.20	174.90
5	60.58	64.92	64.70	58.79
6	85.88	83.39	83.67	82.63
8	74.98	75.10	75.81	77.20

[Ø] Signals due to aromatic, OCH_2O, and $COCH_3$ groups are not included.

Measurements are given as p.p.m. downfield from TMS as internal standard at zero.

All assignments are supported by off-resonance decoupling experiments.

The same reaction at reflux gave a different monomethyl ether, m.p. 182°, $[\alpha]_D$ + 36°, this presumably being the thermodynamically more stable product (10), with the alkoxyl group equatorial. The $[\alpha]_D$ of (9) compares favourably with that of gummadiol which therefore has the same stereochemistry.

The C-2 aryl group of gummadiol is clearly equatorial, since the H-8 protons come below 6.2 τ in the ^{1}H n.m.r. spectrum, as in eudesmin, gmelinol, etc.[3,4] The configuration at C-6 is less clear but so far all the lignans isolated from G. arborea have an equatorial aryl group at this position and the $[\alpha]_D$ of gummadiol would fit in very well with this assignment. The large positive rotation associated with an axial aryl group at C-6, as in gmelinol, is not exhibited by gummadiol and therefore the structure (4) with the stereochemistry shown is tentatively assigned to this compound. It is hoped that a thorough c.d. examination of 2,6-diaryl-3,7-dioxabicyclo-[3,3,0]-octane lignans will establish firm criteria for the determination of the absolute configuration at all centres.

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