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ACID CATALYSED REARRANGEMENTS OF ARBOREOL: A BIOMIMETIC SYNTHESIS OF GMELANONE

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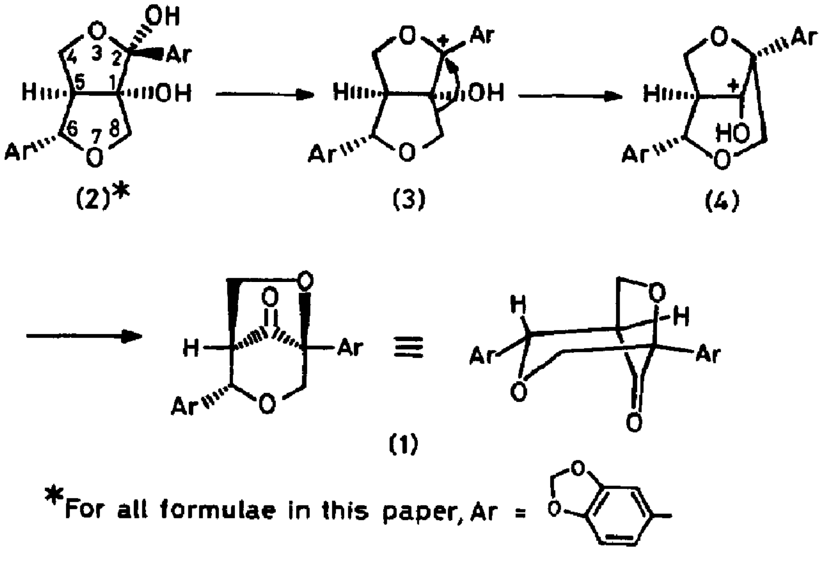
Arboreol rearranges under acid conditions to yield gmelanone, a reaction related to the possible biosynthesis of gmelanone, and one which confirms the absolute configuration of gmelanone. Gmelanone itself is unstable to acid and on exposure undergoes a ring opening reaction to give a new class of lignan.

To our knowledge gmelanone (1)[1] is the only naturally occurring lignan with a rearranged carbon skeleton[2], and as such its biosynthesis is of interest. Its co-occurrence with arboreol (2) caused us to speculate[1] that (2), or a suitable derivative in which the benzylic 2-hydroxyl group had been converted into an even better leaving group, could be a biological precursor of gmelanone. The rearrangement would proceed via the cation (2) (Scheme 1) which is stablised both by an adjacent oxygen atom and the 4-alkoxy group of the C-2 aryl ring.



*For all formulae in this paper, Ar =

Scheme 1

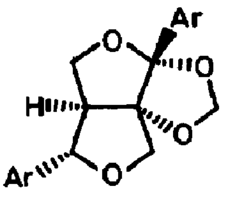
It is emphasised that experiments detailed in ref 1 show that gmelanone is a true natural product and is not an artefact produced from arboreol by the extraction process.

We now report that when arboreol (120 mg) dissolved in ethyl acetate was treated with a mixture of conc. H_2SO_4 and glacial acetic acid (1:1) under reflux for 1h. a residue (85 mg) was obtained from which by column chromatography followed by crystallisation from ethyl acetate, gmelanone (40 mg) m.p. 184 - 186° (lit. 190°)[1] was isolated. The m.p. of the 'synthetic' sample was not depressed by admixture with the natural product, and the two samples had identical i.r., ^{1}H and ^{13}C n.m.r. spectra. Most significantly the synthetic sample had $[\alpha]_D$ - 72° as compared with an $[\alpha]_D$ - 78° for the natural product. Thus the absolute configuration of gmelanone, which previously had been tentatively assigned on the basis of its presumed relationship with arboreol and the sterochemical restrictions inherent in the rearrangement process leading to the rigid bicyclic system of (1), is now put on a firm footing. We assume that this acid catalysed rearrangement follows the pathway of Scheme 1.

When arboreol (540 mg) was heated with glacial acetic acid containing some sulphuric acid a series of compounds AS1 -AS5 were isolated.

AS1 (ca 60 mg.), m.p. 174°, $[\alpha]_D$ + 50° was shown by analysis and spectroscopic means to be arboreol-1,2-methylene ether (5).* It was identical in all respects with an authentic sample prepared by treatment of arboreol with formalin. The introduction of the additional methylene group of (5) was surprising as the acetic acid used had been distilled from potassium permanganate immediately before use. Neither paulownin nor piperonylic acid yield formaldehyde under the rearrangement conditions but AS2 (6) (vide infra) does so within 10 min., presumably by a reverse aldol reaction, and is therefore the likely source of the methylene group of (5).

AS2, the major product of the reaction (ca 250 mg.), λ_{max} 358 (20, 600), $[\alpha]_D$-70° was characterised as (6) on the basis of a detailed analysis of its mass spectrum and its ^{1}H and ^{13}C n.m.r. spectra. Some of the relevant n.m.r. signals are given in the Table.



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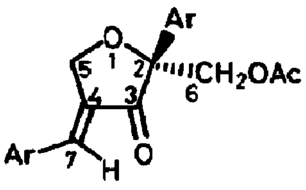

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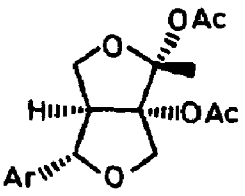

(7)

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* Full experimental details of the preparation, isolation and characterisation of all compounds mentioned in this note will be presented in the full paper.

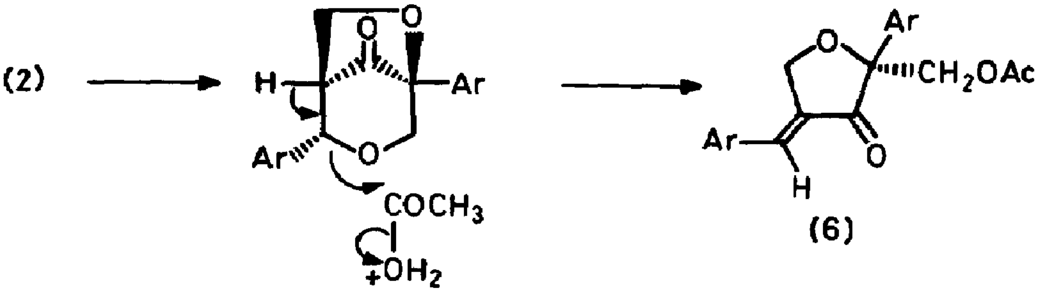
Table

Some ^1H and ^{13}C n.m.r. signals of AS2[a]

		^{13}C		^1H
	C-2	84.5s		
	C-3	200s		
	C-4	128.4s or 128.4s or 129.1s		
	C-5	68.0t[b]	H-5(2H)	4.88dd (14,3) 5.06dd (14,3)
	C-6	67.7t[b]	H-6(2H)	5.22d (12) 5.38d (12)
	C-7	134.9d	H-7(1H)	7.43t J3
Acetate	C=O	170.5s		
Acetate	CH_3	20.8q	Acetate CH_3	1.96s

a) All signals in δ b) Interchangeable assignments

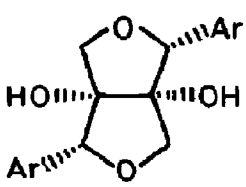
The carbon skeleton of (6) is new in lignan chemistry,[2] but its provenance is readily understood, if arboreol is first rearranged to gmelanone which undergoes attack as in Scheme 2. If this is correct then gmelanone should also produce (6) when submitted to the same reaction conditions as arboreol, and indeed gmelanone (20 mg) gave AS2 (15 mg) in these conditions.



Scheme 2

AS3 (ca 40 mg.) was shown to be arboreol diacetate (7), AS4 (50 mg.) was piperonylic acid whilst AS5 (50 mg.) was unchanged arboreol.

It was interesting to examine the action of acetic acid/sulphuric acid on another lignan 1,2-diol, wodeshiol[3] (8). In this case there was no rearrangement, but instead 5,6-dehydropaulownin acetate (9) was obtained. This compound is of interest as a prototype of intermediates to be expected from the phenolic ocidation of lignans.[1] Reaction of wodeshiol with phosphorus oxychloride in pyridine on work up merely gave the propellane (10).



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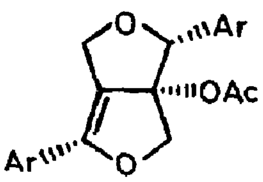

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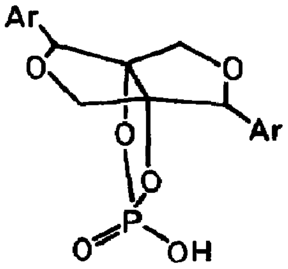

(10)

Thus in the wodeshiol system migration of an aromatic ring, a not uncommon organic process,[4] particularly when the resulting cation can be stabilised, could not be accomplished. The facile migration of a methylene group in arboreol would seem to be due both to the ready production of cation (3) and to the stabilisation of the rearranged cation (4) as the oxonium ion.

References.

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