Tetrahedron Letters No.51, pp. 5287-5288, 1968. Pergamon Press. Printed in Great Britain.

STEREOCHEMISTRY OF CYCLOLIGNANS - A REVISED STRUCTURE FOR THOMASIC ACID

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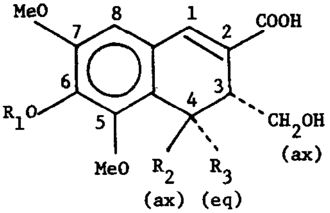
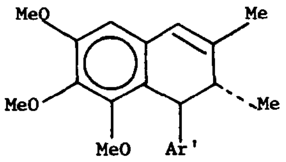
(Received in USA 7 June 1968; received in UK for publication 13 September 1968)

Recently, Seikel et al. (1) isolated from Ulmus thomasii Sarg. the new lignan thomasic acid, for which the structure Ia was postulated. The argument in favor of the cis arrangement of the C_3 and C_4 substituents (2) was based on (i) the failure of the acid to form a lactone whereby the C_2 methylol group is axial and (ii) the high-field methoxyl n.m.r. signal (6.37τ)* for the dimethyl derivative, assigned to the 5-OMe substituent shielded by the equatorial C_4 aryl group. We present here n.m.r. evidence for the trans diaxial disposition of the C3 and C4 moieties, and thus structure Ic for thomasic acid.





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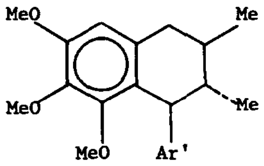
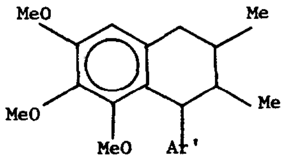


III

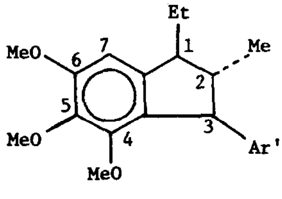
	R_1	R_2	R_3
Ia	H	H	Ar
Ib	Me	Ar'	H
Ic	H	Ar	H

Ar = 4-hydroxy-3,5-dimethoxyphenyl

Ar' = 3,4,5,-trimethoxyphenyl



IV



V

In connection with other studies we have prepared the compounds II - V. The n.m.r. signals of the high-field methoxyl groups are presented in Table I.

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*NMR spectra cited were recorded on a Varian A-60 NMR spectrometer in $CDCl_3$ solution using TMS as an internal standard.

TABLE I

N.M.R. Signals for 5-OMe (I-IV) and 4-OMe (V) Groups

Compound	Ib	II	III	IV	V
τ - values	6.37 $\pm$0.03	6.40	6.80	6.65	6.45

It may be seen from Table I that the 5-OMe group in III (6.80τ) is considerably more shielded by the 4-aryl group than that of II (6.40τ) and must therefore be in closer proximity to and above the plane of the aryl substituent.(3) This condition may be ratified if the 4-aryl group is equatorial in III and axial in II. In addition, the 4-OMe group in V, shielded by the *quasi* axial 3-aryl substituent, gives an n.m.r. signal (6.45τ) similar to II, and the naphthalene derivative (IV) has an n.m.r. signal for the 5-OMe group at 6.65τ.

The 5-OMe n.m.r. signal in dimethyl thomasic acid (6.37$\pm$0.03τ) has a value close to that of II but unlike the corresponding signal of III. Therefore, the 4-aryl group is axial, and as the C_3 methylol group is also axial(1), the C_3 and C_4 substituents are *trans* diaxially orientated, as in Ib. In support of this configuration, both Ib and II exhibit a broad singlet n.m.r. peak (5.33 and 5.92τ respectively) assigned to the C_4 dibenzilic proton which does not appreciably couple with the C_3 proton; the dihedral angle between the C_3-H and C_4-H bonds being 70°. Finally, examination of Dreiding models indicates that a diaxial arrangement of *trans* C_3 and C_4 substituents in Ib and II is preferable to the diequatorial conformation, allowing structure Ic for thomasic acid.

Acknowledgment. The author wishes to thank Dr. K. V. Sarkanen for his encouragement. The reported results form a part of work performed under a grant no. AP-00363-04 from the National Institutes of Health

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