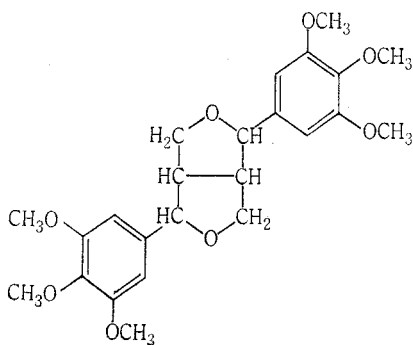


THE OCCURRENCE OF LIRIORESINOL-B DIMETHYL ETHER IN
EREMOPHILA GLABRA R.Br.*

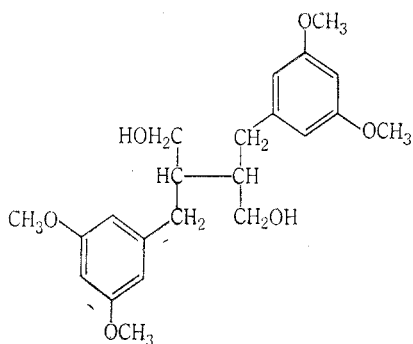
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Extraction of the leaves of *Eremophila glabra* R.Br. collected from Rottnest I. consistently afforded a colourless crystalline compound, $C_{24}H_{30}O_8$, which formed a dibromide, $C_{24}H_{28}O_8Br_2$. Only a trace of the same substance was obtained from the plant collected on the sand dunes of Rockingham, south of Perth. Six of the oxygen atoms were identified as methoxyl groups and the compound showed no infrared absorption corresponding to the presence of hydroxyl or carbonyl groups. Hence, it was considered likely that the remaining two oxygen atoms were attached by cyclic ether linkages, probably in a lignan of the 3,7-dioxabicyclo[3.3.0]octane type.

This has been confirmed by the well-established degradation technique used on this group of compounds, namely, the action of nitric acid on the dibromides (Erdtman and Gripenberg 1947; Hearon and McGregor 1955). The product in this case, 4-bromo-5,6-dinitropyrogallol trimethyl ether, indicated the structure (I) for the compound $C_{24}H_{30}O_8$.



(I)



(II)

The presence of benzyl ether linkages was demonstrated by hydrogenolysis, with sodium in ethanol, which afforded the diol (II). The loss of the central methoxyl groups would be expected for a pyrogallol trimethyl ether under these conditions as illustrated by the behaviour of elemicin (Semmler 1908), pyrogallol trimethyl ether (Thoms and Siebeling 1911) and 5-propylpyrogallol trimethyl ether (Sonn and Scheffler 1924). Permanganate oxidation of (II) yielded the expected 3,5-dimethoxybenzoic acid.

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At the time the structure of the lignan became clear, Dickey (1958) described the isolation of a diglucoside, liriiodendrin, from *Liriiodendrin tulipifera* L. Dependent on the methods used, three isomeric aglycones liriioresinol A, B, and C were obtained by hydrolysis of the glucoside. Dickey concluded on the basis of infrared comparison with synthetic (\pm)-syringaresinol (Freudenberg and Dietrich 1953) that the aglycones were stereoisomeric with the synthetic compound. Further degradation was shown to be analogous to that of syringaresinol although comparison with authentic samples was not made. Since then Pearl, Beyer, and Dickey (1958) have isolated from the spent sulphite liquor of aspen, three compounds of which one appears to be a further isomer of liriioresinol.

The identity of our material with liriioresinol-B dimethyl ether has been established by comparison with an authentic sample provided by Dickey.

The *cis*-fusion of the tetrahydrofuran rings is established by the optical activity of the diol (II). The alternative *trans*-fusion would be expected to lead to a *meso*-diol. Equilibration under the hydrogenolysis conditions would lead to racemization.

Experimental

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory at the University of Melbourne.

Melting points were determined in open Pyrex capillaries and are uncorrected.

Optical rotations were measured in chloroform in 1 dm tubes at room temperature unless otherwise stated.

(a) *Extraction*.—The leaves and terminal branches (4.4 kg) collected at Rottneest I. were extracted with methanol (4 × 8 l.) and the methanol evaporated. The oily residue was extracted with ether and the solution washed successively with dil. HCl, 2.5% NaOH, and water. Evaporation of the solvent gave a green tar which was washed with light petroleum and crystallized from methanol yielding prisms, m.p. 122–123 °C (18.8 g), $[\alpha]_D +45.8^\circ$ (c, 2.00 in 2 dm tube) (Found: C, 64.6; H, 6.8; O, 28.4; mol. wt., 423 (Rast); OCH₃, 40.8%. Calc. for C₂₄H₃₀O₈: C, 64.6; H, 6.8; O, 28.7; mol. wt., 446.5; 6 × OCH₃, 41.7%). There was no depression of melting point on admixture with a sample of liriioresinol-B dimethyl ether and the samples showed identical infrared spectra.

(b) *Bromination*.—The neutral material (I) (516 mg) was dissolved in carbon tetrachloride (22 g) and cooled to -4 °C. Bromine (330 mg) was added portionwise and the solution stood at 0 °C for 24 hr. After washing with saturated bicarbonate solution and evaporating to dryness a yellow solid was obtained which crystallized from methanol as needles, m.p. 157–157.5 °C, $[\alpha]_D -52.9^\circ$ (c, 1.93) (Found: C, 47.6; H, 4.6; Br, 26.6%. Calc. for C₂₄H₂₈O₈Br₂: C, 47.7; H, 4.7; Br, 26.5%).

(c) *Nitration*.—The dibromide (5.0 g) was added in small portions to nitric acid (50 ml) in a flask which was vigorously shaken. The solution became a deep violet colour which after shaking for 24 hr had turned green and precipitated a solid. The mixture was heated on a steam bath for 1½ hr and cooled before water (200 ml) was added. Recrystallization of the precipitate from methanol gave 4-bromo-5,6-dinitropyrogallol trimethyl ether, m.p. 134–135 °C, alone or mixed with an authentic sample prepared by the method of Kohn and Grün (1925).

The filtrate was carefully neutralized with sodium bicarbonate to pH 6, and then evaporated to dryness under reduced pressure. A very small amount of oil was obtained from the residue by continuous ether extraction but failed to crystallize.

(d) *Hydrogenolysis of Liriioresinol-B Dimethyl Ether*.—The dimethyl ether (1.58 g) was dissolved in ethanol (25 ml) and sodium (7 g) added in small portions to the solution on a steam-bath over a period of 7 hr. The mixture was cooled, excess ethanol added, and the solution steam distilled before extracting with ether (3 × 30 ml). Evaporation of the extract gave a yellow oil (1.28 g)

which partially crystallized. The oil was washed with a little ether and the insoluble residue recrystallized from light petroleum/chloroform giving needles, m.p. 97.5–98.5 °C, $[\alpha]_D -20.4^\circ$ (c, 0.85) (Found: C, 67.7; H, 7.7; O, 24.6; OCH_3 , 31.5%. Calc. for $\text{C}_{22}\text{H}_{30}\text{O}_6$: C, 67.7; H, 7.7; O, 24.6; $4 \times \text{OCH}_3$, 32.0%).

The infrared spectrum measured in carbon tetrachloride using a calcium fluoride prism showed absorption at 3638 cm^{-1} (ϵ_{max} , 110) due to two primary hydroxyls.

(e) *Oxidation of the Diol (II)*.—The diol (870 mg) was dissolved in acetone (40 ml) and treated with finely powdered potassium permanganate (4.0 g) with stirring. The mixture was allowed to stand for 16 hr and refluxed for a further 3.5 hr. The acetone was evaporated and the residue treated with excess sodium bisulphite solution. The solution was extracted with ether and the ether washed with 2.5% NaOH. The alkaline extract after acidification, extraction with ether, and evaporation of the solvent gave a red solid (300 mg) which recrystallized from aqueous methanol as prisms, m.p. 181–182 °C. There was no depression of melting point on admixture with an authentic sample of 3,5-dimethoxybenzoic acid and the infrared spectra were identical.

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