A Novel Sprio-Biflavonoid from *Larix gmelini*

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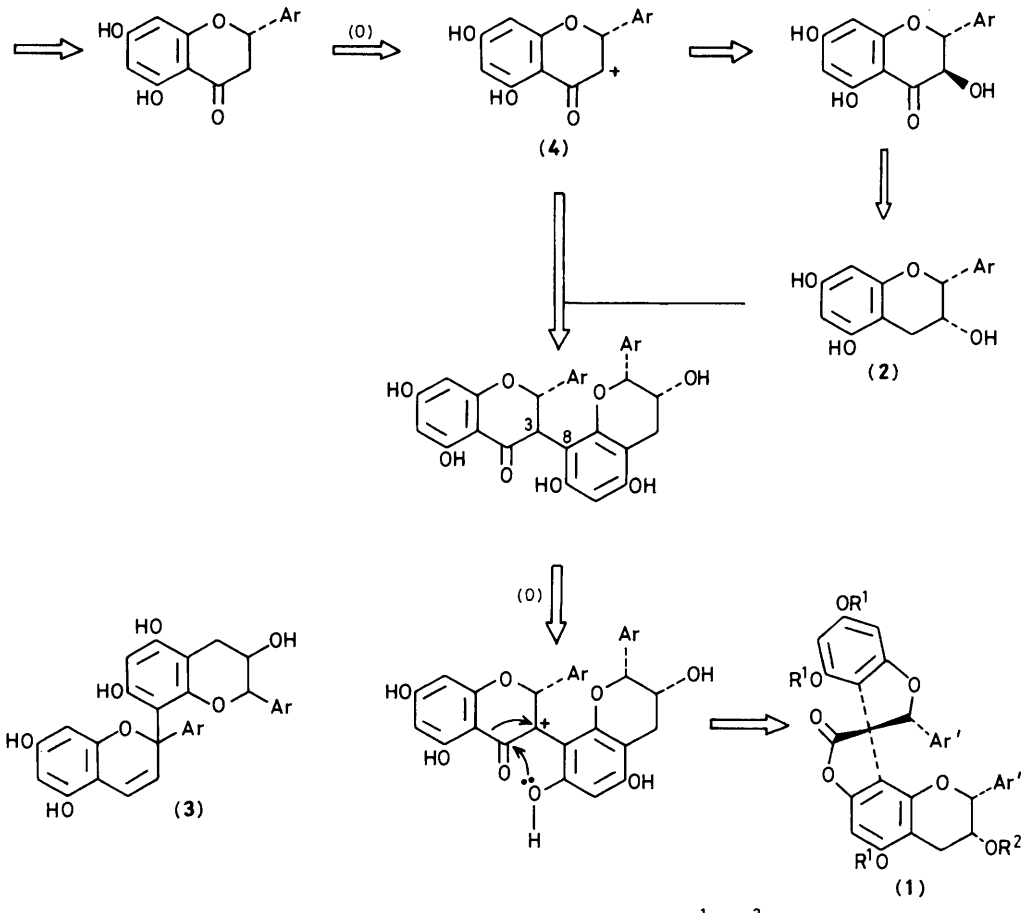
The unique spiro-biflavonoid structure of larixinol (**1a**) is described and a suggested pathway of biogenesis from dihydrokaempferol is proposed.

Larix gmelini (Rupr) Rupr is an important coniferous species of Northern China. During an investigation of the proanthocyanidins of the bark[1] a unique spiro-biflavonoid (**1a**) was isolated (0.15%) together with the flavan-3-ols, (−)-epicatechin, (+)-catechin, and (−)-epiafzelechin (**2**). The spiro compound was identical in all respects with the substance larixinol isolated from *Larix sibirica* by Chumbalov and his colleagues[2] and for which they proposed the structure (**3**). Larixinol, $C_{30}H_{22}O_{10}$,† m.p. 208—210 °C, $[\alpha]_D^{20}$ −151° (Me_2CO, *c* 1.0), R_F 0.83 (Bu^sOH–HOAc–H_2O, 14:1:5, Whatman No 2) formed a hexa-acetate (**1b**) on treatment with acetic anhydride–pyridine, m.p. 255—257 °C, $[\alpha]_D^{20}$ +33.3° ($CHCl_3$, *c* 0.9), a pentamethyl ether (**1c**) (Me_2SO_4–K_2CO_3), m.p. 183—186 °C, $[\alpha]_D^{20}$ −113.5°, and a hexamethyl ether (**1d**), (NaH–dimethyl sulphoxide–MeI). Larixinol and its derivatives all displayed a strong absorption at $\nu_{max.}$ *ca.* 1785 cm^{-1} indicative of a γ-lactone. Reduction with $LiAlH_4$ gave a triol (triacetate) supporting this assignment. The presence of the epiafzelechin (**2**) part structure in larixinol (**1a**) was confirmed by direct comparison of the ^1H and ^{13}C n.m.r. spectra. Of the remaining 15 carbon atoms in larixinol, six were similarly shown to be associated with a monosubstituted phloroglucinol ring and six to a second *para* (hydroxy) substituted phenyl ring. The remaining three carbon atoms in larixinol were attributed to a lactone carbonyl group δ 179.1, a methine carbon, benzylic and attached to oxygen, δ 91.0, and a quaternary carbon atom, δ 61.1. Larixinol was stable to acid, and catalytic hydrogenation (Pt–H_2) of its pentamethyl ether

† Accurate analytical data (C,H) were obtained for all compounds described in the text.



Scheme 1. Suggested biosynthetic pathway to larixinol.

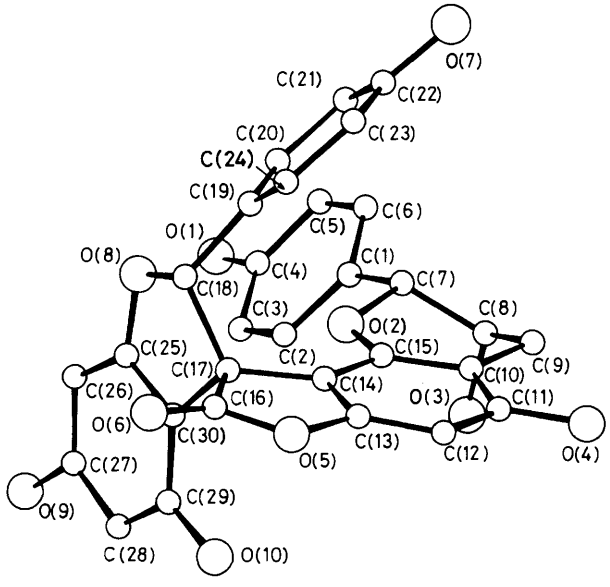


Figure 1. The molecular structure of larixinol showing the crystallographic numbering system.

gave products in which one, or both, of the *p*-methoxyphenyl rings was fully saturated. Of the various structures possible on the basis of the above evidence that of (**1a**) was finally confirmed by *X*-ray crystallography of its methanol solvate.‡ The structure was solved using the direct methods MULTAN-80[3] programme and refined with the CRYSTALS[4] package. All hydrogen atoms were located after several cycles of refinement. Hydroxy hydrogens were included in their final positions but the other hydrogen atoms were placed in calculated positions; they were not refined. Figure 1 shows a computer generated representation of the structure drawn from the final atomic co-ordinates. No attempt was made to define the absolute stereochemistry of (**1a**), but if, as suggested below (Scheme 1), the metabolite is derived from co-occurring flavanoids such as (−)-epiafzelechin (**2**) with the

‡ *Crystal data* for (**1a**): $C_{30}H_{22}O_{10} \cdot CH_3OH$, M = 574.5, orthorhombic, space group $P2_12_12_1$, a = 11.6426(11), b = 12.7589(16), c = 18.3476(17) Å, U = 2725.5 Å^3, D_c = 1.40 g cm^{-3}, Z = 4, R = 3.93, R_w = 5.42 for 2877 reflections $\theta < 76°$, $I > 3\sigma(I)$, crystal size 1.25 × 0.25 × 0.15 mm. Cu-K_α radiation λ = 1.5418 Å. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

2*R* stereochemistry then Figure 1 represents the absolute stereochemistry of larixinol.

Larixinol (**1a**) is representative of an entirely new class of biflavonoid. Its biosynthesis is presumed to be associated with that of the C-3–C-8[1] linked garcinia group of biflavonoids,[5] *e.g.* saharanflavone.[6] A plausible biogenetic pathway, incorporating the hypothesis that both larixinol (**1a**) and the garcinia biflavonoids are derived by interception of the putative intermediate (**4**) in the biosynthetic flavanone–flavanonol conversion,[7] is shown in Scheme 1.

Received, 7th May 1985; Com. 608

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