The Identification of Lisetin as a Coumaronochromone and the Relation of Lisetin to the Isoflavone, Piscerythrone

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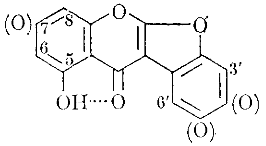
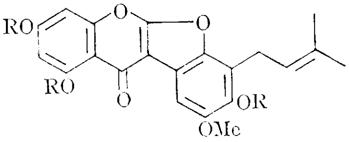
Lisetin was first isolated[1] from the root bark of Jamaican Dogwood, *Piscidia erythrina* L., and was tentatively formulated as $C_{25}H_{24}O_8$. In continuation of our studies[2,3] on this plant, we have re-examined lisetin and established its relation to a new isoflavone, piscerythrone,[4] also isolated from the same plant.

Lisetin $[C_{21}H_{18}O_7 \equiv C_{20}H_{12}O_3(OH)_3(OMe)]$ formed a triacetate and a trimethyl ether and the n.m.r. spectra of these derivatives clearly indicated the presence of a $\gamma\gamma$-dimethylallyl group[5] as an aromatic substituent, and three aromatic protons. Thus lisetin could be represented by the partial formula $[(C_{15}O_3)(H)_3(Me_2C{=}CH{\cdot}CH_2{-})(OMe)(OH)_3]$.

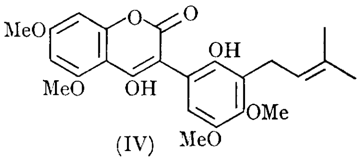
On empirical grounds, lisetin might have been a coumaronocoumarin (ν_{CO} 1700—1730 cm.$^{-1}$) of which several natural representatives are known,[6] but the infrared spectra of lisetin (ν_{CO} 1653 cm.$^{-1}$), its trimethyl ether (ν_{CO} 1660 cm.$^{-1}$), and its triacetate (ν_{CO} 1665 cm.$^{-1}$) excluded this. The infrared and ultraviolet spectra of lisetin and its derivatives indicated that it was isoflavonoid in type, but its oxidation level excluded its formulation as an isoflavone. However, the spectroscopic[6,7] evidence and biogenetic analogy[6,8] suggested that lisetin was a coumaronochromone with a hydrogen bonded carbonyl group and the oxygenation pattern shown in (I).



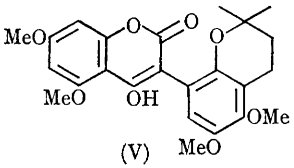
(I)*



(II) R=H
(III) R=Me



(IV)



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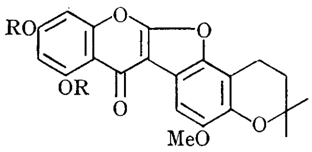
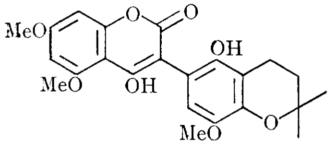
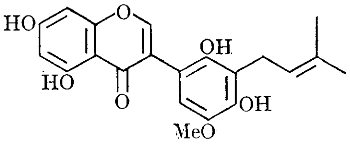


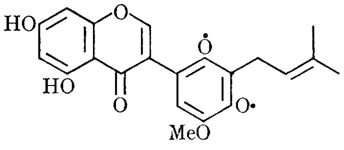
(VI) R=H
(VII) R=Me



(VIII)



(IX)



(X)

Of the three aromatic protons indicated by the n.m.r. spectra of lisetin and its derivatives, two formed an AB system (J = 2·5 c./sec.) characteristic of *meta*-related protons. Comparison of the chemical shifts of this pair of protons in lisetin triacetate (τ 3·08 and 2·64) and lisetin trimethyl ether (τ 3·59 and 3·42) with appropriate models[9] placed two hydroxyl groups in positions 5 and 7 (see I). It followed that the methoxyl group and

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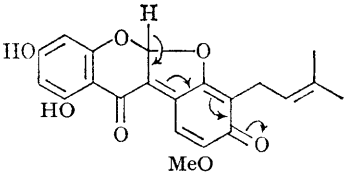
* The numbering used in this and subsequent formulae was adopted to conform with the usual numbering of the isoflavone skeleton.

the third aromatic proton must be placed on ring B. The singlets due to this proton in lisetin trimethyl ether (τ 2·42) and lisetin triacetate (τ 2·48) are remarkably deshielded for a 1,2,4-trioxygenated benzene derivative and this suggested that this proton was in the deshielding cone of the carbonyl group.[10] This proton was therefore placed in position 6′ and the similar chemical shifts (τ 2·42 and 2·48) of this proton in lisetin trimethyl ether and the triacetate required the methoxyl group of lisetin to be placed in position 5′. The constitution (II) was then proposed for lisetin and this was confirmed by the following experiments. Alkaline hydrolysis of lisetin trimethyl ether (III) gave the 4-hydroxycoumarin (IV) which with acid gave the isomeric 4-hydroxycoumarin (V). Similarly the acid-catalysed cyclisation of lisetin (II) gave isolisetin (VI) and alkaline hydrolysis of isolisetin dimethyl ether (VII) gave the 4-hydroxycoumarin (VIII).

The new isoflavone, piscerythrone (IX), occurs in the same plant with lisetin (II) and the direct transformation (IX → II) has been achieved in good yield (35%) by oxidation with alkaline potassium ferricyanide.

Lisetin (II) is a new type of natural product which may be regarded as a further variant[6,8] upon the isoflavonoid theme; the occurrence of lisetin in other plants of the *Leguminosae* family has been established.[11] The ferricyanide oxidation of piscerythrone (IX) to give lisetin (II) may be regarded as a model for the biosynthesis[12] of natural coumaronochromones. This pathway presumably[13] involves the diradical (X), which by intramolecular coupling yields the quinone methide (XI), which is transformed (XI, see arrows) into lisetin (II).



(XI)

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[1] J. A. Moore and S. Eng, *J. Amer. Chem. Soc.*, 1956, **78**, 395.

[2] J. S. P. Schwarz, A. I. Cohen, W. D. Ollis, E. A. Kaczka, and L. M. Jackman, *Tetrahedron*, 1964, **20**, 1317.

[3] S. F. Dyke, W. D. Ollis, M. Sainsbury, and J. S. P. Schwarz, *Tetrahedron*, 1964, **20**, 1331.

[4] C. P. Falshaw, W. D. Ollis, J. A. Moore, and K. Magnus, forthcoming publication.

[5] B. F. Burrows, W. D. Ollis, and L. M. Jackman, *Proc. Chem. Soc.*, 1960, 177; R. B. Bates, R. H. Carnighan, R. O. Rakutis, and J. H. Schauble, *Chem. and Ind.*, 1962, 1020; R. B. Bates and D. M. Gale, *J. Amer. Chem. Soc.*, 1960, **82**, 5749; W. D. Ollis, M. V. J. Ramsay, I. O. Sutherland, and S. Mongkolsuk, *Tetrahedron*, 1965, **21**, 1453.

[6] W. D. Ollis, "The Chemistry of Flavonoid Compounds", ed. T. A. Geissman, Pergamon, Oxford, 1961, p. 353.

[7] L. Jurd, "The Chemistry of Flavonoid Compounds", ed. T. A. Geissman, Pergamon, Oxford, 1961, p. 107.

[8] H. Grisebach and W. D. Ollis, *Experientia*, 1961, **11**, 4.

[9] J. Massicot and J.-P. Marthe, *Bull. Soc. chim. France*, 1962, 1962; H. Erdtman and T. Norin, *Acta Chem. Scand.*, 1963, **17**, 1781; T. J. Batterham and R. J. Highet, *Austral. J. Chem.*, 1964, **17**, 428.

[10] L. Crombie and J. W. Lown, *J. Chem. Soc.*, 1962, 775.

[11] E. R. Crossley, C. P. Falshaw, W. D. Ollis, and I. O. Sutherland, forthcoming publication.

[12] A. I. Scott, *Quart. Rev.*, 1965, **19**, 1, and references there cited.

[13] For model experiments see C. A. Rhodes, Ph.D. thesis (University of Sheffield), 1965.