A Possible Chemical Analogy for Coumestan Biosynthesis

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Summary 2′,4′,7-Trimethoxyisoflavanone has been converted into coumestrol by a route which might be analogous to the biosynthetic pathway.

FEEDING experiments have shown that the coumestans are biogenetically isoflavonoids and not coumarins.[1] 2′,4,4′-Trihydroxychalcone is a common intermediate in the biosynthesis of both coumestrol (II; R = H) and isoflavones.[2] Furthermore, 4′,7-dihydroxyisoflavone (daidzein) or dihydrodaidzein can act as precursors for coumestrol.[3,4] However, the later transformations in the biosynthetic pathway have not yet been elucidated. We report the chemical conversion of 2′,4′,7-trimethoxyisoflavanone (I) into coumestrol (II; R = H), a reaction which presumably proceeds *via* a 3,4-dehydropterocarpan (III) intermediate.† This reaction provides a possible chemical analogy for coumestan biosynthesis.

Fusion of 2′,4′,7-trimethoxyisoflavanone (I) at 180—200° with pyridine hydrochloride in the presence of atmospheric oxygen, an attempted synthesis of (III; R = H), produced among other compounds a small yield (0·2%) of coumestrol (II; R = H). This was characterised by its spectral properties and its chromatographic behaviour, all of which were identical to those of authentic coumestrol. Methylation with methyl iodide–potassium carbonate in acetone yielded dimethylcoumestrol (II; R = Me), also identical with authentic material. When the reaction was carried out *in vacuo* in a sealed tube, only faint traces of coumestrol were detected in the reaction mixture. Therefore, atmospheric oxygen must, at this temperature, be the oxidising species.

The reaction presumably involves an intermediate (III) which must be very susceptible to oxidation at the allylic position. [No compounds of type (III) were isolable from

the reaction mixture.] The conversion of (III; R = Me) into (II; R = Me) has been reported by Whalley and his co-workers,[5] who used chromium trioxide in acetic acid as oxidising agent. Our observations indicate that oxygen itself may effect the transformation. The reaction conditions would suggest that a free-radical mechanism must be involved; support for this postulate is obtained from the observation that demethylation of (I) with hydrogen iodide in acetic anhydride at 100° did not produce any coumestrol.

As a model for coumestan biosynthesis, the reaction described above may not be ideal. However, it illustrates the lability of 3,4-dehydropterocarpan derivatives towards oxidation, and it seems probable that these compounds could be intermediates in coumestan biosynthesis. Such compounds have been reported in Nature,[6] although it has been suggested[7] that these are artefacts of the extraction procedure. We feel, however, that the route isoflavanone →3,4-dehydropterocarpan → coumestan is a viable biosynthetic sequence.

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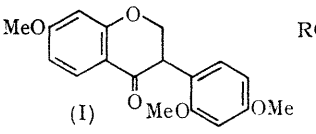
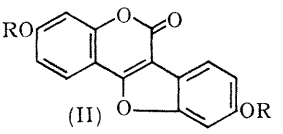
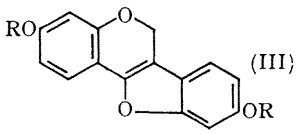


(I)



(II)



(III)

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† All nomenclature is based on the numbering system used for isoflavonoid compounds.

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