Synthesis of (±)-Peltogynol Trimethyl Ether and its *cis,cis*-Stereoisomer

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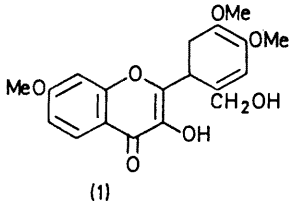
Summary Racemic peltogynol trimethyl ether has been synthesised from (±)-peltogynone trimethyl ether, obtained indirectly from 2'-hydroxymethyl-7,4',5'-trimethoxyflavonol; the flavonol has also been converted into the racemic *cis,cis*-isomer of peltogynol trimethyl ether.

RACEMIC peltogynol trimethyl ether, m.p. 185—188°, and its *cis,cis*-stereoisomer, m.p. 195—197° (decomp.), have been synthesised from 2'-hydroxymethyl-7,4',5'-trimethoxyflavonol (1), obtained by reduction of the chromenoisocoumarin (2)[1] with sodium borohydride. Acid-catalysed cyclisation of the flavonol (1) gave the isochromenochromone (3) which was converted into the racemic *cis,cis* isomer of peltogynol trimethyl ether (4) by catalytic hydrogenation over nickel boride. The *cis,cis* peltogynan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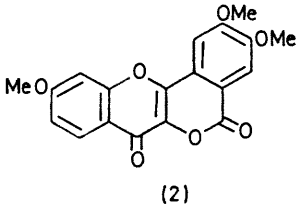
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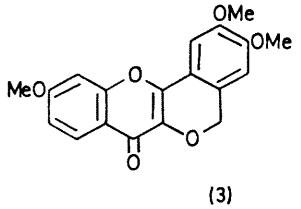
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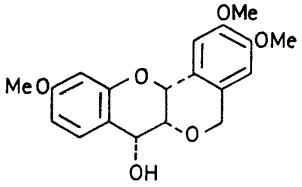
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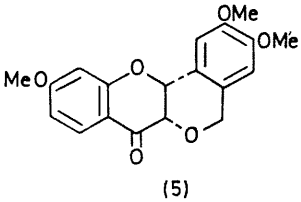
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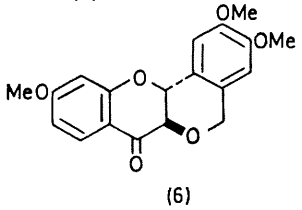
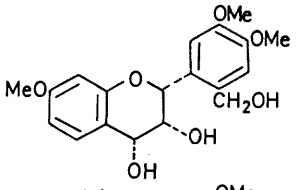

(6)

derivative (4) ($J_{2,3}$ 1·2, $J_{3,4}$ 4·6 Hz) was oxidised by manganese dioxide in chloroform to the (±)-*cis*-isomer of peltogynone trimethyl ether (5) ($J_{2,3}$ 3·4 Hz). Epimerisation of this compound to racemic peltogynone trimethyl ether (6) proved impossible owing to ready ring fission to give the known chalcone,[2] which was induced thermally and also under mild conditions of acid or base catalysis.

Catalytic hydrogenation of the flavonol (1) over nickel boride gave the *cis,cis*-flavan-3,4-diol (7), oxidised by manganese dioxide in chloroform to the hemiacetal (8) which is thought to arise *via* the enediol, the 4-hydroxy-3-oxoflavan, and the 4-hydroxyhemiacetal. Reduction of the hemiacetal (8) with sodium borohydride gave the *trans,trans*-triol (9), previously prepared by another method.[3] Attempts to cyclise the triol (9) directly to (±)-peltogynol trimethyl ether were discouraging and the triol was therefore oxidised with manganese dioxide in chloroform to the *trans*-3-hydroxyflavanone and cyclised to (±)-peltogynone trimethyl ether (6), as reported by Brown and Lewis.[4] Reduction of racemic peltogynone trimethyl ether (6) with sodium borohydride, as with the (+)-isomer,[2] gave (±)-peltogynol trimethyl ether (10). This had an n.m.r. spectrum indistinguishable[1,5] from that of the dextrorotatory enantiomer first prepared by Robinson and Robinson.[6]

Oxidation of the *trans,trans*-triol (9) gave the hemiacetal (8) as a minor by-product, whereas this hemiacetal was the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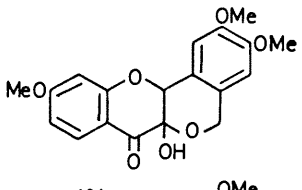
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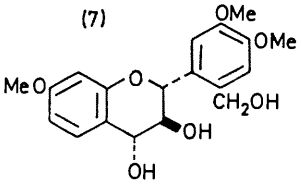
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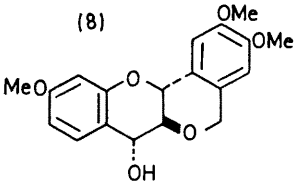
(10)

main product isolated from a similar oxidation of the *cis,cis*-triol (7). This indicates that the 3_{eq}-hydrogen atom in the intermediate *cis*-3-hydroxyflavanone is more favourably placed for conversion of the α-ketol into the enediol than is the 3_{ax}-hydrogen atom in the isomeric *trans*-3-hydroxyflavanone. Also the chromenoisocoumarin (2) is resistant to catalytic hydrogenation whereas the methylene analogue (3) undergoes hydrogenation normally, and the chalcone-flavanone equilibrium which normally favours flavanones is greatly displaced in favour of the chalcone in the case of the cyclic flavanones, (5) and (6), which cannot therefore be obtained by cyclisation of the chalcone.

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