The Four Racemates of Leucocyanidin Tetramethyl Ether (5,7,3′,4′-Tetramethoxyflavan-3,4-diol)

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Summary The set of four racemic 5,7,3′,4′-tetramethoxyflavan-3-ols is completed by synthesis of the 2,3-*trans*-3,4-*cis*-isomer, and n.m.r. data for all four racemates are tabulated.

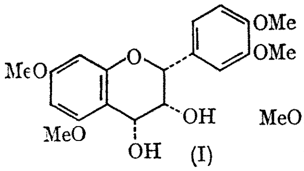
THE reported occurrence[1] in Nature of more than the theoretically possible number of dextrorotatory monomeric flavan-3,4-diol leucocyanidins led us to characterise the four possible racemic tetramethyl ethers of 5,7,3′,4′-tetrahydroxyflavan-3,4-diol which are shown with the 2*R*-configuration in the formulae (I), (II; R = H), (III), and (IV). The n.m.r. data (Table) for these racemates define their geometrical configurations and provide a basis for unequivocal assignment to the methyl ethers of natural leucocyanidins.

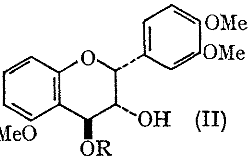
The 2,3-*cis*-racemates (I) and (II; R = H) were obtained

TABLE

Configuration of racemate	$J_{2,3}$ (c./sec.)	$J_{3,4}$ (c./sec.)	Chemical shifts ($CDCl_3$,τ) 2H (*ax*)	3H (*ax*)	3H (*eq*)	4H (*ax*)	4H (*eq*)	M.p. Diol	Diacetate
cis–cis (I)	*ca.* 1·0	4·8	5·07	—	5·78	4·82	—	161—162°	166—167°
2,3-*cis*-3,4-*trans* (II; R = H)	*ca.* 0·9	2·5	4·89	—	5·98	—	5·15	182—184°	169—170°
trans–trans (III)	10·1	7·3	5·30	5·91	—	4·98	—	205—207°	132—132·5°
2,3-*trans*-3,4-*cis* (IV) ..	10·1	4·1	5·09	6·07	—	—	4·99	165—167°	155—157°

from 5,7,3'4'-tetramethoxyflavanol (prepared from rutin), which gave the *cis–cis*-racemate (I) when hydrogenated over a nickel boride catalyst[2] prepared in aqueous ethanol (50%). The *cis–cis*-diol (I) was converted by boiling methanolic acetic acid (1%) during 62 hr. into 2,3-*cis*-3,4-*trans*-4,5,7,3',4'-pentamethoxyflavan-3-ol (II; R = Me).


(I)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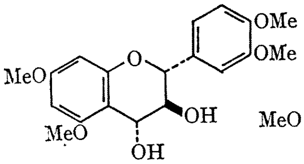
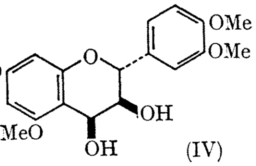

(III)


(IV)

Hydrolysis of this methyl ether with 1% acetic acid in aqueous dioxan (50%) during 4 min. gave the previously unknown 2,3-*cis*-3,4-*trans*-racemate (II; R = H). The 2,3-*trans*-racemates (III) and (IV)[3] were prepared from (±)-*trans*-3-hydroxy-5,7,3',4'-tetramethoxyflavanone by reduction with sodium borohydride in methanol. Dilution with water gave the *trans–trans*-diol (III) and acidification of the filtrate gave the 2,3-*trans*-3,4-*cis*-diol (IV); their configurations have already been assigned from n.m.r. data.[4] The dextrorotatory isomer of the *trans–cis*-diol (IV), prepared from (+)-catechin tetramethyl ether, is also known.[5]

Analysis of the n.m.r. spectra of these linear ABX systems by first-order procedures readily yields the vicinal coupling constants and chemical shifts for the heterocyclic ring protons (Table). These parameters permit unequivocal assignment of geometrical configurations to the four racemates, and hence also to the corresponding enantiomers.

Satisfactory analytical data have been obtained for all the compounds mentioned and for the set of four racemic diacetates.

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