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ZEYHERIN, A NATURAL 3,8-COUMARANONYLFLAVANONE FROM PHYLLOGEITON ZEYHERI SOND.

F. du R. Volsteedt and D.G. Roux

Department of Chemistry, University of the Orange Free State,
Bloemfontein, South Africa.

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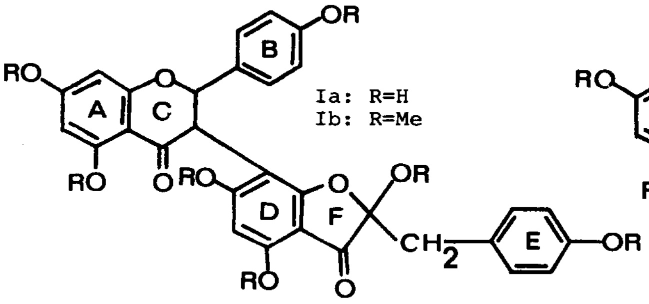
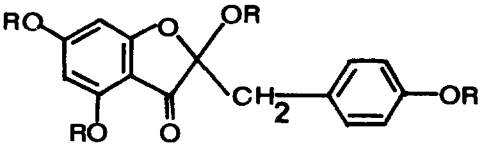
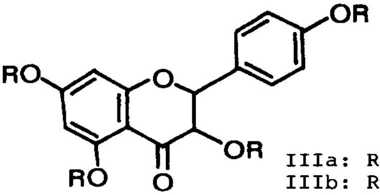
An extension of the series of natural 3,8-linked biflavonyls[1,2,3] is reflected by the characterization of a derivative of zeyherin (Ia), the first of this group to contain the relatively rare 2-hydroxy-2-benzylcoumaranone moiety. The biflavonyl together with the predominant maesopsin (IIa), aromadendrin (IIIa) and kaempferol (IVa), occurs in low concentration amongst the complex mixture of flavonoid analogues present in the red heartwood of Phyllogeiton zeyheri Sond. (formerly Rhamnus zeyheri Sond.) known as "red ivory". The above compounds were isolated as their methyl ethers (Ib-IVb respectively) after methylation of suitable fractions with dimethyl sulphate.



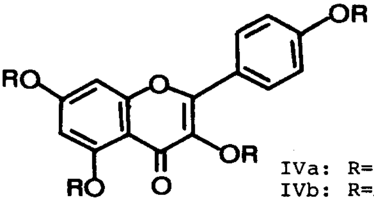
Ia: R=H
Ib: R=Me



IIa: R=H
IIb: R=Me



IIIa: R=H
IIIb: R=Me



IVa: R=H
IVb: R=Me

Thus, an enriched fraction of zeyherin, which yields phloroglucinol and p-hydroxybenzoic acid on alkali fusion, when methylated as above affords the crystalline heptamethylether (Ib), m.p.200.5-201.5°, $[\alpha]_D^{26}$+3.4°(c 0.9 in chloroform), M^+ 656, $\lambda_{max.}$ 289,333nm(shoulder), $\nu_{max.}$ 1700cm^{-1}. The infra red spectrum showed the absence of hydroxyl function. Low yields obtained from purification by t.l.c. necessitated characterization by spectrometric methods, particularly by n.m.r. spectrometry in a variety of solvent systems.

Conspicuous in the n.m.r. spectrum of zeyherin heptamethylether (Ib) in deuteriated chloroform are the elements of the spectrum of maesopsin tetramethylether, m.p.107° (IIb: τ values in parenthesis), particularly the characteristic singlets associated with the methylene τ 6.90(6.90), 2-methoxyl τ 6.73(6.75) and phenolic methoxyl groups τ 6.27(6.28) [6H and 3H resp.], 6.18(6.18) [6H each], and the A_2B_2 quartet τ 3.23(3.30), 2.79(2.85) [Δτ 0.44(0.45); J 8.6Hz] typical of the p-substituted 2-phenyl or "B"-ring 3',5'- and 2',6'-protons respectively.

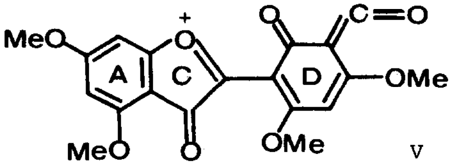
Residual signals, particularly the heterocyclic protons, are reminiscent of those of aromadendrin tetramethyl ether (IIIb), dihydroflavonol analogue of maesopsin tetramethyl ether (IIb).

The presence of a second A_2B_2 quartet at τ 3.37 and 2.83 [Δτ 0.54; J 8.8Hz] indicative of a second p-substituted "B"-ring, and a singlet (τ 4.08) overlapping an AB-quartet (τ 4.07,4.03, J 1.8Hz) upfield in the aromatic region and representing "A"-ring protons, indicate that the link between presumed flavonoid units is not through "B"-rings, but involves one of the phloroglucinol "A"-rings.

By subtraction, the residual methoxyl signals, one each at τ 6.10,6.27 and 6.40, and the only remaining signals which underlie these (AB-quartet, J_{AB} 14.4Hz, τ 5.90,6.43), together with the above data correlate with a flavanone unit substituted in the 3-position by a coumaranonyl moiety equivalent to maesopsin tetramethylether (IIb).

With progressive addition of C_6D_6 to the $CDCl_3$ over the range 10-80% ($^V/_V$) all the phenolic methoxyl groups undergo continued and ultimately very pronounced shifts (Δτ +0.51-0.61), while the aliphatic 4-methoxyl remains relatively stationary (Δτ +0.07). Shifts of this magnitude of all the phenolic methoxyls indicate[4] that the interflavonoid link is to the 8-position of the D-ring. This process also serves to uncover completely the unusually large AB-coupling of protons of the heterocyclic C-ring, and to confirm their trans-diaxial arrangement ($J_{2,3}$ 14.4Hz), while the singlet 6-H (D-ring) shifts sharply upfield (τ 4.08→4.65) and exposes the AB meta-coupling of the A-ring protons.

The above almost unambiguous structural assignments, based on n.m.r. spectrometry, correlate with the mass spectrum, where apart from the molecular ion M^+ 656(9.4), the only prominent peaks are at $^m/_e$ 535(30.6), 534(100),



V

372(6.7), 371(14.7) and 121(18.4). The latter, equivalent to $CH_2=C_6H_4=\overset{+}{O}CH_3$, reflects the loss of a benzylic radical involving the E-ring thus affording the prominent fragment $^m/_e$ 535, as well as the base peak $^m/_e$ 534 after further loss of a proton from the heterocyclic C-ring. Alternative loss of the equivalent of a benzylic radical from the flavanone moiety[5] to give $^m/_e$ 535, followed by loss of $CH_3\overset{+}{O}=\overset{-}{C}-CH_2-C_6H_4-CH_3$ ($^m/_e$ 164) by the equivalent of a RDA-fragmentation of the F-ring affords the fragment $^m/_e$ 371 (V). The latter together with minor fragments $^m/_e$ 311(1.6) and 355(1.3) reflecting double RDA fragmentations, or RDA fragmentation plus loss of a benzylic radical, correlates with a linkage through the 3-position to the D-ring.

The CD-curve of zeyherin shows a weak positive Π-Π^* Cotton effect (298nm) of lower intensity but similar to that afforded by maesopsin. The strong Cotton effects typical of flavanones and 3-hydroxyflavanones[6] are absent. No deductions regarding the absolute configuration of the apparently racemized flavanone, or 2-hydroxy-2-benzylcoumaranone moieties were accordingly possible from available data.

The 3,8-biflavonyl analogues first isolated by Locksley, Scheinmann *et al*[1]. and by Venkataraman *et al*[2], represent 4',5,7- trihydroxyflavanones substituted in the 3-position with the equivalent of the different oxidation states, and presently of a rearrangement, of a second flavanone unit.

Apart from the free radical mechanism proposed by Locksley, Scheinmann *et al*[1]. (cf. ref. [7]) for the biflavonyls, zeyherin (Ia) could also originate from electrophilic attack on maesopsin (IIa) by an unstable 3-carbonium ion originating from the associated dihydroflavonol, aromadendrin (IIIa). Formation of such carbonium ions is implied from the conversion of dihydroflavonols to flavanones under mildly acid but non-reductive conditions[8].

Acknowledgements.

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