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STRUCTURE OF MESUAFERRONE-B A NEW BIFLAVANONE FROM THE STAMENS OF MESUA FERREA LINN.

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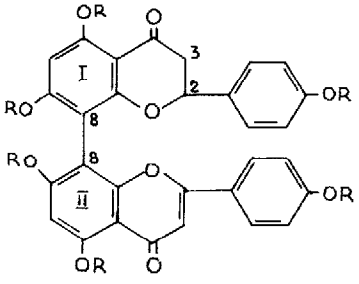
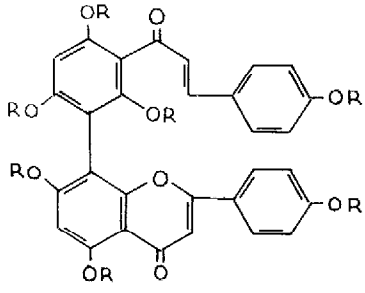
The stamens of Mesua ferrea linn. are valuable in Indian Medicine in the treatment of bleeding piles. The petroleum ether extract of the stamens (collected from Kanikhet, North India) yielded α-amyrin, β-amyrin and β-sitosterol. The subsequent acetone extraction and chromatographic separation of the resulting mixture led to the isolation of Mesuaferrone-B[1] besides mesuanic acid[2] and mesuaferrone -A[1].

Mesuaferrone-B, pale yellow needles, m.p. 255-56° (decomp.) had $[\alpha]_D^{25}$ -222.3° (c. 1.07, methanol) and calculated for $C_{30}H_{20}O_{10}\ \frac{1}{2}\ H_2O$ C, 65.57; H, 3.82. Found C, 65.41; H, 3.90. mass spectrum M^+ 540. Its phenolic nature is indicated by its solubility in sodium hydroxide, to give a yellow coloured solution. It gave red colour with magnesium-hydrochloric acid and brownish colour with alcoholic ferric chloride. Its ir.spectrum (nujol) showed the presence of hydroxy groups(3400-3300 cm^{-1}) and two chelated carbonyl groups (1640 and 1620 cm^{-1}). The u.v. absorption data λ_{max}^{EtOH} 275, 298 and 342(sh) nm(log ϵ 4.45, 4.48 and 4.32 respectively) were similar to those expected for a combination of naringenin [λ_{max}^{MeOH} 289 and 326(sh) nm] [3] and apigenin[λ_{max}^{MeOH} 267, 296(sh), 336 nm][3]. The longer wavelength band of mesuaferrone-B(I) underwent bathochromic shifts of the order 23 & 8 nm in the presence of ethanol/sodium acetate and ethanol/aluminium chloride respectively, suggesting a 5,7-dihydroxy flavanoid system[3,4].

Mesuaferrone-B forms a hexaacetate(2) $C_{42}H_{32}O_{16}$ m.p. 159° with pyridine/acetic anhydride indicating the presence of six hydroxy groups. It forms a heptamethyl ether (3) $C_{37}H_{34}O_{10}$ m.p. 219-22° $[\alpha]_D^{25}$ -146.6°($CHCl_3$) with dimethyl sulphate, acetone and potassium carbonate. The methyl ether on oxidation with hydrogen peroxide yielded anisic acid. Therefore the presence of a p-hydroxy phenyl group in mesuaferrone-B could be inferred. During the methylation of mesuaferrone-B(1), formation of the hexamethyl ether (4) was not observed.

The analytical and spectral data, and degradative reactions suggest that mesuaferrone-B may be a biflavanoid composed of naringenin and apigenin as components. The nature of linkage has now been determined by n.m.r and mass spectral measurements, and by dehydrogenation studies. Recently Scheinmann[5] has made an attempt to systematise and simplify the nomenclature of polyflavanoids. We propose an improvement by numbering each C_{15} flavanoid unit as I & II, the numbering within each of the C_{15} units being the same as that normally used in flavanoids.





1 R = H

2 R = -CO.CH_3.

3 R = -CH_3

4 R = H; I 2,3 (double bond)

5 R = -CH_3; I 2,3 (double bond)

6 R = CH_3

N.m.r. data of mesuaferrone-B(1) was recorded on a Varian A-60D in $(CD_3)_2CO$ using TMS as internal standard. The aliphatic region showed a multiplet at δ 2.5 - 3.5(2H) assignable to the methylene protons of the flavanone moiety (H-3, I). Further, 2-H(I) appeared as double - doublet at δ 5.5(J=11 Hz, J=5 Hz)[6]. A sharp signal at δ 6.7 (H, 3, II) characteristic of the 3 proton of a flavone was observed. The highly shielded aromatic signals δ 6.36(s, 1H) and 6.46(s, 1H) suggested the presence of protons in an aromatic ring of the phloroglucinol type. Further, in the aromatic region, signals at δ 6.85 (J=9.0 Hz), 7.08(J=9.0 Hz), 7.43(J=9.0 Hz) and 7.76(J=9.0 Hz) are assignable to eight protons of the two p-hydroxy substituted phenyl rings of I and II[7]. In the low field region of the spectrum, the protons in the two chelated hydroxy groups appeared at δ 12.5(1H), 12.25(1H)(D_2O exchangeable) while the remaining four hydroxy groups those in appeared as a broad hump between δ 8.8 & 10.5(4H) (D_2O exchangeable).

Biflavanoids with C-3 of the flavanone linked to the C-8 of the flavone are known to occur in nature[8]. In the present case n.m.r. and mass spectral data ruled out the possibility of such linkage. The other possible modes of linkage are 8-8, 6-6 and 6-8. The easy methylation of the hydroxy groups at

the 5-positions suggested that the interflavanone-flavone linkage may be 8-8 or 6-8. The type of linkage was finally decided by dehydrogenation of mesuaferrone-B by 2,3-dichloro 5,6-dicyano 1,4-benzoquinone(d.d.q.) or with iodine and potassium acetate in acetic acid to give dehydromesuaferrone-B(4) $C_{30}H_{18}O_{10}$ m.p. > 300° $[\alpha]_D^{25}$ + 26.7°(c, 1.272, methanol). Its u.v. R_f and i.r. spectral data are in good agreement with the data of natural cupressuflavone, an extractive of Cupressus torulosa[9]. The optically active dehydromesuaferrone-B, (4) on methylation yielded hexamethyl ether(5) $C_{36}H_{30}O_{10}$ whose m.p. 159-61° is in good agreement with cupressuflavone hexamethyl ether, m.p. 161° obtained by methylation of optically active natural cupressuflavone 7,7", 4',4"' tetramethyl ether[10], but is at variance with the m.p. 296° of cupressuflavone hexamethyl ether[9] prepared from racemic and natural cupressuflavone as well as with that of purely synthetic cupressuflavone hexamethyl ether m.p. 294°[11]. Further, the i.r. spectrum of dehydromesuaferrone-B hexamethyl ether is indistinguishable from that of cupressuflavone hexamethyl ether derived from the natural and racemic cupressuflavone, obtained by extraction of Cupressus torulosa[9]. It is observed that different m.p.'s. were recorded for cupressuflavone hexamethyl ether[9,10,11] depending upon its origin.

The optical activity of mesuaferrone-B is largely due to atropisomerism relating to the biflavonyl system, though the flavanone structure may also contribute a share towards optical activity. The mass spectrum of mesuaferrone-B (1) revealed ions M^+ 540(100%),m/e 522(22), 422(18), 402(32), 302(8), 285(45), 120(48), 107(12) and 94(6). The fragmentation pathway is in agreement with the reported pattern for those of biflavanoids[8], and flavanones[8]. Based on the spectral and chemical evidence the structure of mesuaferrone-B is 8-(8-naringeninyl) apigenin i.e. structure(1). We have no evidence as regards the absolute configuration.

The n.m.r. spectrum of the heptamethyl ether (6) in $CDCl_3$ indicated the presence of 7-separate methoxy groups in the region of δ 3.45 to 4.10, and 13 protons in the region between δ 6.50 to 7.30 assignable to 10 aromatic protons, 3-H of the flavone (II) unit and the α & β (olefinic)-protons of the chalcone portion. The above data suggest that during methylation of mesuaferrone-B the ring opening of the flavanone unit of (1) took place leading to the formation of the heptamethyl ether. The optical activity of (6) as well as (1) is due to atropisomerism. Satisfactory combustion analysis were obtained for all the compounds.

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