Chemical Investigation of Ceylonese Plants. Part XII.[1] (+)-3,4′,5,7-Tetrahydroxy-3′-methoxyflavanone [(+)-Dihydroisorhamnetin] and 3,5,7-Trihydroxy-3′,4′-dimethoxyflavone (Dillenetin): Two New Natural Products from *Dillenia indica* L.

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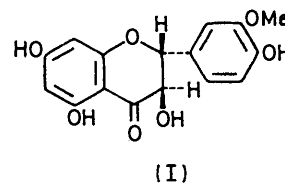
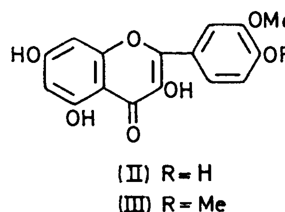
The title compounds [(I) and (III)] have been obtained from the bark and pericarp of *Dillenia indica* L., respectively.

As part of a programme of chemical studies on Ceylonese plants, extractives of the bark and pericarp of *Dillenia indica* L. (Dilleniaceae [2]) have been studied, and two new natural products have been isolated. The product from the bark was a pale yellow solid, $C_{16}H_{14}O_7$, giving the colour reactions of a flavanone and showing $\nu_{max.}$ 1640 (C:O) and 3340 and 3420 cm^{-1} (OH). In the n.m.r. spectrum, two doublets at τ 4·96 and 5·37 (each *J* 12 Hz) revealed that the compound was a 3-hydroxyflavanone. Signals at τ 2·90 (2′-H), 3·08 (6′-H), 3·22 (5′-H), 4·08 (6-H), and 4·12 (8-H) suggested a 3′,4′,5,7-oxygenation pattern [3] and the signal at τ 6·22 showed that one of the oxygen functions was present as a methoxy-group. Positions 5 and 7 were ruled out for the methoxy-group on the basis of u.v. spectral data: addition of aluminium chloride caused a bathochromic shift in band I of 50 nm (5-OH) and NaOAc effected a bathochromic shift in band II of 38 nm (7-OH).[4] Thus the methoxy-group was either at C-3′ or -4′. This fact was confirmed by diagnostically important mass spectral peaks at *m*/*e*



(I)



(II) R = H
(III) R = Me

318, 300, 166, 153, and 137.[5] The position of the methoxy-group was established by oxidation of the

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compound with air in acidic medium to the corresponding flavonol methyl ether,[6] which was identified as isorhamnetin (II) by comparison with an authentic sample. Hence the original compound was probably (+)-(2*R*,3*R*)-3,4′,5,7-tetrahydroxy-3′-methoxyflavanone [(+)-(2*R*,3*R*)-dihydroisorhamnetin] (I), in keeping with the absolute configuration of other naturally occurring 3-hydroxyflavanones.[7]

The product isolated from the ethyl acetate extract of the pericarp was a flavone, $C_{17}H_{14}O_7$, $\nu_{max.}$ 1650 (C:O) and 3290 and 3430 cm^{-1} (OH). The n.m.r. spectrum indicated that it was a flavonol with two methoxy-groups and a 3,3′,4′,5,7-oxygenation pattern.[3] Mass spectral peaks at *m/e* 330, 315, 300, 165, 153, and 137 showed that both methoxy-groups were in ring B.[5] From the above evidence, u.v. data, and its m.p.[8,9] (290—292°), the compound was identified as the known 3,5,7-trihydroxy-3′,4′-dimethoxyflavone (3′,4′-di-*O*-methylquercetin) (III). The structure was confirmed by conversion into the pentamethyl ether, which was identical with an authentic sample of quercetin pentamethyl ether. This new natural product has been named dillenetin.

Although the isolation of isorhamnetin (3′-*O*-methylquercetin) (II) from a large number of plants has been reported, this is the first report of the isolation of (+)-dihydroisorhamnetin (I)[10] and dillenetin (4′-*O*-methylisorhamnetin) (III) from natural sources.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. Microanalyses were carried out by the CSIRO Microanalytical Service, Melbourne.

Bark, timber, and fruits of *D. indica* L. were collected from Hanguranketha, Kandy. Bark was separated from the timber, dried, chipped, and powdered in a mill. The pericarp was separated from the fruit centre, chipped, and dried. The bark and pericarp were separately and successively extracted with hot light petroleum, benzene, and methanol.

Isolation of (+)-3,4′,5,7-*Tetrahydroxy*-3′-*methoxyflavanone* [(+)-*Dihydroisorhamnetin*] (I).—An ethyl acetate extract of the methanolic extract of the bark was separated on a silica gel column with diethyl ether–light petroleum (35 : 65) and furnished a solid (0·002%). It was recrystallised from aqueous ethanol to yield the *flavanone* (I) as pale yellow crystals, m.p. 230°, $[\alpha]_D^{27}$ +25° (in ethanol) (Found: C, 60·05; H, 4·4%; M^+, 318·0745. $C_{16}H_{14}O_7$ requires C, 60·4; H, 4·4%; *M*, 318·0739); $\lambda_{max.}$ (MeOH) 287 (log ε 4·23) and 320 (3·89); $\lambda_{max.}$ (MeOH–$AlCl_3$) 311 (4·34) and 370 (3·71); $\lambda_{max.}$ (MeOH–$AlCl_3$–HCl) 311 (4·28) and 370 (3·69); $\lambda_{max.}$ (MeOH–NaOMe) 250 (4·23) and 325 (3·80); $\lambda_{max.}$ (MeOH–NaOAc) 290 (3·87) and 325 (4·01); $\lambda_{max.}$ (MeOH–NaOAc–H_3BO_3) 290 (4·24) and 318 nm (3·95); τ [$(CD_3)_2SO$; 100 MHz] −2·87 (1H, s, 5-OH), 2·90 (1H, s, 2′-H); 3·08 (1H, d, *J* 8 Hz, 6′-H), 3·22 (1H, d, *J* 8 Hz, 5′-H), 4·08 (1H, d, *meta*-coupled, 6-H), 4·12 (1H, d, *meta*-coupled, 8-H), 4·96 (1H, d, *J* 12 Hz, 2-H), 5·37 (1H, d, *J* 12 Hz, 3-H), and 6·22 (3H, s, OMe); *m/e* 318 (60%), 300 (14), 289 (60), 166 (60), 153 (100), and 137 (50). Treatment with iron(III) chloride gave a brown colour and with magnesium–concentrated hydrochloric acid an orange-red colour.

Oxidation of (+)-*Dihydroisorhamnetin* (I).—(+)-Dihydroisorhamnetin (0·015 g) in aqueous 2N-sulphuric acid (5 ml) was refluxed on a steam-bath, while a gentle stream of air was passed over the liquid, for 24 h. After dilution with water, the mixture was extracted with ethyl acetate and worked up. Recrystallisation from aqueous ethanol furnished isorhamnetin as a bright yellow solid (0·010 g), m.p. 298° (lit.,[11] 305—307°), identical (mixed m.p., co-t.l.c., and i.r. and u.v. spectra) with an authentic sample.

Isolation of 3,5,7-*Trihydroxy*-3′,4′-*dimethoxyflavone* (*Dillenetin*) (III).—An ethyl acetate extract of the methanolic extract of the pericarp was triturated with cold methanol to remove betulinic acid. The filtrate was evaporated and the residue refluxed with ethyl acetate and cooled. The deposited solid (0·007%) was recrystallised from aqueous ethanol to give the flavone (III) as a bright yellow solid, m.p. 290—292° (lit.,[8,9] 291—292°) (Found: C, 61·6; H, 4·15%; M^+, 330. Calc. for $C_{17}H_{14}O_7$: C, 61·8; H, 4·25%; *M*, 330); $\lambda_{max.}$ (MeOH) 253 (log ε 4·11), 267 (4·01), and 365 (4·09); $\lambda_{max.}$ (MeOH–$AlCl_3$) 263 (4·20), 360 (3·87), and 420 (4·13); $\lambda_{max.}$ (MeOH–$AlCl_3$–HCl) 260 (4·15), 267 (4·14), 356 (3·87), and 420 (4·07); $\lambda_{max.}$ (MeOH–NaOMe) 280 (4·09), 325 (3·85), and 414 (4·04); $\lambda_{max.}$ (MeOH–NaOAc–H_3BO_3) 255 (4·09), 266 (3·99), and 366 nm (4·05); τ [$(CD_3)_2SO$; 100 MHz] 2·20 (1H, d, *J* 9 Hz, 6′-H), 2·26 (1H, s, 2′-H), 2·88 (1H, d, *J* 9 Hz, 5′-H), 3·52 (1H, d, *meta*-coupled, 6-H), 3·81 (1H, d, *meta*-coupled, 8-H), and 6·18 (2 × 3H, s, 2 × OMe); *m/e* 330 (100%), 315 (25), 300 (25), 287 (25), 259 (10), 244 (10), 165 (10), 153 (8), and 137 (5). Treatment with iron(III) chloride gave an olive-green colour and with magnesium–concentrated hydrochloric acid an orange colour.

Methylation of 3,5,7-*Trihydroxy*-3′,4′-*dimethoxyflavone* (III).—Compound (III) (0·05 g) in methanol (5 ml) was treated with an excess of ethereal diazomethane and left overnight. The residue obtained on evaporation was separated on a silica gel column with chloroform–benzene (1 : 1) and gave quercetin pentamethyl ether (0·025 g) as pale yellow needles (from methanol), m.p. 151—152° (lit.,[12] 150—151°), identical (mixed m.p., i.r., and n.m.r. spectra, and t.l.c.) with an authentic sample.

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