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TWO FLAVONOLS FROM *EUODIA GLABRA**

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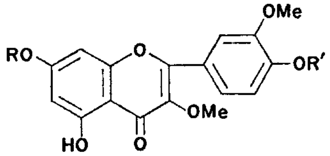
Key Word Index—*Euodia glabra*; Rutaceae; 7-isopentenyl and 7-methyl ethers of 3,3′-dimethylquercetin.

Abstract—Two flavonols in *Euodia glabra* have been characterized as 3,7,3′-trimethylquercetin (I) and 7-isopentenyl-3,3′-dimethylquercetin (II).

INTRODUCTION

We are currently examining species of the Rutaceae of S.E. Asia and in particular those from Malaysia and Ceylon. In Malaya, Stone[1] has found 19 genera and 60 species belonging to this family and we wish to report on the structure of two flavonols isolated from the bark of *Euodia glabra*.



(I) R = Me ; R′ = H
(II) R = $CH_2-CH=CMe_2$; R′ = H
(III) R = H; R′ = H
(IV) R = $CH_2-CH=CMe_2$; R′ = Me

RESULTS

The isolation of two flavonols, 5,4′-dihydroxy-3,-7,3′-trimethoxyflavone (I) and 5-4′-dihydroxy-3,3′-dimethoxy-7-isopentenyloxyflavone (II) from *E. glabra* is reported; (I) has recently been found in *Larrea cuneifolia*[2] (Zygophyllaceae). The isopentenylated compound (II) conforms to a pattern already established in the Rutaceae where many of its phenolic constituents are alkylated on oxygen or carbon.

Table 1. NMR spectra of *Euodia glabra flavonol* (II)*

H-2′	H-5′	H-6′	H-6	H-8	$-CH_2$	$-CH=$	Me= C=
7·60 7·70 *m*	7·04*d* (*J* 9Hz)	7·60 7·70 *m*	6·35*d* (*J* 2Hz)	6·44*d* (*J* 2Hz)	4·58*d* (*J* 7Hz)	5·50*m*	1·78*s* 1·82*s*

* Spectra were recorded in $CDCl_3$ on a varian H-100 spectrophotometer. Signals are designated *s*—singlet; *d*—doublet; *m*—multiplet. Values are given in ppm (δ scale) relative to TMS and the number in parenthesis indicates the coupling constants.

The structure of I was suggested by comparison with the spectral data of Mabry[2] and confirmed by direct comparison with a synthetic sample. Meanwhile the similarity in

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* Part I in the projected series "Rutaceous Constituents".

[1] Stone, B. C. (1972) *Tree Flora of Malaya* (Whitmore, T. C., ed.), Vol. 1, Longmans, London.

[2] Valesi, A. G., Rodriquez, E., Velde, G. V. and Mabry, T. J. (1972) *Phytochemistry* **11,** 2821.

spectral characteristics, with and without shift reagents, indicated that I and II were similar in structure. In the NMR spectrum of II, comparison with I indicated the loss of a methoxyl absorption at δ 3·85 and its replacement by absorption from an isopentenyl group. The similarity in UV maxima indicated that the isopentenyl group was located at C-7. Interpretation of the NMR signals (Table 1) showed that the C_5 alkyl group was of the conventional $Me_2C{=}CH{-}CH_2{-}$ type connected to the flavone nucleus through oxygen.

The occurrence of isopentenyl ethers in flavones is comparatively rare. In the Rutaceae, 7,3′-dimethoxy-5-hydroxy-4′-isopentenyloxy flavone has been found in *Melicope sarcococca*[3] and archangelenone (4′-isopentenylnaringenin) has been found together with 7,4′-di-isopentenylnaringenin in *Angelica archangelica*.[4]

The MS of these two flavon-3-methyl ethers showed some typical features consistent with data already reported for 3-methoxyflavones.[5] Loss of H, Me, MeCO, OH, H_2O and MeO fragments being typical while a retro-Diels–Alder reaction was relatively insignificant due to the oxygen rich character of ring A. With compound II (see Experimental) the molecular ion appeared at *m/e* 398 followed by an equally intense ion at *m/e* 330, indicating the easy loss of 2-methylbutadiene from ring A, hydrogen transfer occurring *via* an intermolecular McLafferty rearrangement.[6] The loss of the isopentenyl radical itself was confirmed by the presence of an ion at *m/e* 329 while a number of ions derived from the parent molecule also showed a related peak at M-58 corresponding to the loss of methylbutadiene at all stages in the molecular fragmentation processes.

Confirmation of these structures was obtained by their comparison with synthetic compounds. I was identical to a synthetic sample of 5,4′-dihydroxy-3,7,3′-trimethoxyflavone.[7] Compound II was hydrolysed under mild conditions to yield 4,7,3′-trihydroxy-3,4′-dimethoxyflavone (III) which was identical with synthetic material synthesized by King *et al.*[8] Direct introduction of the isopentenyl group was considered feasible since the hydroxyl group at C-7 had been shown to be more acidic than those at C-5 and C-3′,[9] and is ionized by sodium acetate solution. Monoisopentenylation of (III) gave low yields of (II) as an impure product, with the right spectral characteristics. However, comparison of the mono methyl ether of II with synthetic 3,3′,4′-trimethoxy-4-hydroxy-7-isopentenyloxyflavone (IV) showed complete agreement in physical and spectral properties.

EXPERIMENTAL

Euodia glabra bark was generously supplied by Mr. K. M. Kochummen of the Forest Research Institute, Kepong, Malaysia. This bark (1·7 kg) was milled and extracted with cold methylated spirits (98% EtOH) for 3 days, filtered and the solution evaporated to dryness under reduced pressure to give a dark syrup (140 g). This syrup was exhaustively extracted with hexane, $CHCl_3$ and finally MeOH, the $CHCl_3$-soluble material (31 g) showed two main components on TLC (silica gel, C_6H_6–EtOAc; 3:1). A portion of this extract (16 g) was separated on a silica gel column using C_6H_6 to C_6H_6–EtOAc (3:2) as eluant, the column eluants being monitored by TLC. Final purification of I was achieved by preparative TLC on silica gel with C_6H_6–EtOAc (9:1) and II was obtained by the same procedure using Et_2O–hexane (1:9) as eluant.

Compound I. Crystallized from C_6H_6 as yellow prisms m.p. 168–70° (131 mg). R_f ($CHCl_3$) 0·18, (C_6H_6–EtOAc; 3:1) 0·47 all on silica gel. Its spectral data corresponded to that reported by Mabry *et al.*[2] 5,4′-Dihydroxy-3,7,3′-trimethoxyflavone supplied by L. A. Briggs[7] had m.p. 166–7° and was undepressed on admixture with (I).

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Compound II. Crystallized from acetone–hexane as yellow needles, m.p. 101–2° (25 mg) λ_{max} (EtOH) 258, 269 sh, 362; (EtOH + NaOMe), 254, 270, 297sh, 404; (EtOH + $AlCl_3$), 272, 301sh, 370, 409; (EtOH + $AlCl_3$ + HCl), 273, 302, 365, 408; (EtOH + NaOMe), 257, 268 sh, 362. ν_{max} (KBr) 3340 (OH) and 1665 cm^{-1} (C=O). R_f ($CHCl_3$) 0·30 (C_6H_6–EtOAc, 3:1) 0·64. Found (MS) 398·1366. $C_{22}H_{22}O_7$ requires: 398·1365. Ms showed the following peaks, parent ion at *m/e* 398 (100), 383 (12), 331 (22), 330 (100), 329 (90), 316 (20), 315 (83), 313 (12), 312 (15), 311 (10), 301 (20), 299 (15), 287 (51), 151 (20), 69 (54), 41 (51). *m** 369·5 (398 → 383), 338·0 (330 → 329), 300·7 (330 → 315), 295·0 (330 → 312), 274·3 (398 → 330), 261·5 (315 → 287).

Hydrolysis of I. I (1 mg) was refluxed for 3 hr with HOAc (49 ml) containing 2 N HCl (1 ml), the mixture was diluted with H_2O and extracted with EtOAc. The organic layer was washed with $NaHCO_3$ repeatedly, H_2O (2x), dried and evaporated to give a product (~1 mg). The compound showed an identical UV spectrum to that of 3,3′-dimethoxy-5,7,4′-trihydroxyflavone (III)[10] and showed shift characteristics as expected for a 7-hydroxylated flavonol, λ_{max} (EtOH), 256, 268sh, and 360 nm, (EtOH + NaOAc–H_3BO_3) 256, 268 sh and 360 nm (EtOH + NaOAc) 260, 273 and 373 nm.

Methylation of II. II (8 mg) was treated with excess CH_2N_2 in Et_2O–MeOH solution for 24 hr. Evaporation of the solvent gave 5-hydroxy-7-isopentenyloxy-3,3′,4′-trimethoxyflavone (IV) which crystallized from Et_2O–hexane as yellow needles, m.p. 105–6° (6 mg). R_f ($CHCl_3$) 0·27, C_6H_6–EtOAc; 3:1) 0·84. Found (MS) 412·1515. $C_{23}H_{24}O_F$ requires: 412·1521. λ_{max} (EtOH) 257 (log ϵ 4·12), 268 sh (4·11), 358 nm (4·11). ν_{max} (KBr) 3250 (OH), 1650 cm^{-1} (C=O). δ ($CDCl_3$) 1·70 and 1·75 (each 3H, s, =CMe_2), 3·79 (3H, *s*, OMe), 3·89 (6H, *s*, OMe), 4·51 (2H, *d*, *J* 2Hz, H-6), 6·37 (1H, *d*, *J* 2Hz, H-8), 6·92 (1H, *d*, *J* 9Hz, H-5), 7·56–7·68 (2H, complex, H-2′ and H-6′). 12·52 (1H, *s*, OH). MS showed the following peaks; parent peak at *m/e* 413 (25%), and other relevant peaks at *m/e* 412 (100), 358 (12), 357 (10), 345 (21), 344 (96), 343 (75), 330 (15), 329 (62), 315 (29), 313 (21), 301 (62), 283 (10), 165 (23), 149 (10), 123 (12), 69 (17).

3,3′-*Dimethoxy*-5,7,4′-*trihydroxyflavone* (III). 4′-Benzyloxy-3,3′dimethoxy-5,7-dihydroxyflavone (800 mg), prepared from benzylvanillic anhydride and 2,4,6-trihydroxy-ω-methoxy-acetophenone,[10] was debenzylated by reflux in conc. HCl (5 ml) and HOAc (25 ml) for 1 hr. Precipitation of the flavone with water and recrystallization from HOAc gave (III) m.p. 252–3°,[13] ν_{max} (KBr) 3140 (OH) 1655 cm^{-1} (C=O) δ_{CD_3OD} 3·80 (3H, *s*, OMe), 3·94 (3H, *s*, OMe), 6·21 and 6·41 (each 1H, *d*, *J* 2Hz; H-6 and H-8), 6·94 (1H, *d*, *J* 9Hz; H-5′ and 7·54–7·78 (2H, complex, H-2′ and H-6′).

3,3′-*Dimethoxy*-5,4′-*dihydroxy*-7-*isopentenyloxyflavone* (II). The flavonol (III; 75 mg), anhyd. NaOAc (300 mg) and dimethylallyl bromide[11] (0·1 ml) in anhyd. acetone (10 ml) was stirred at room temp. After 4 days (II) had been produced and an additional compound of higher R_f (on TLC) first appeared when the reaction was stopped by filtration and the solution evaporated and the residue purified by PLC (silica gel C_6H_6–EtOAc; 3:1) the band at R_f 0·64 being removed and the product isolated (12 mg). Crystallization from C_6H_6–hexane gave (II) as yellow needles m.p. 58–60° λ_{max} (EtOH) 257, 268sh and 362 nm. ν_{max} (KBr) 3340 (OH) and 1665 cm^{-1} (C=O). No improvement in m.p. could be obtained and m.m.p. with naturally occurring (II) gave 58–101°. R_f ($CHCl_3$) 0·30 C_6H_6–EtOAc; 3:1) 0·64.

3,3′,4′-*Trimethoxy*-5-*hydroxy*-7-*isopentenyloxyflavonone* (IV). 3,3′,4′-Trimethoxy-5,7-dihydroxyflavone (62 mg) [prepared by the Allan–Robinson method[12] m.p. 240–5°[13]] anhyd. K_2CO_3 (800 mg) and dimethylallyl bromide (0·1 ml) was stirred in anhyd. acetone (10 ml) at room temp. for 2 hr. Isolation of the product (56 mg) and purification by PLC (silica gel, Et_2O–petrol. (b.p. 30–40°); 1:1) gave (IV) which crystallized from acetone–hexane as yellow needles m.p. 107–8°. λ_{max} (EtOH) 257, 269 sh and 359 nm. ν_{max} (KBr) 3420 (OH) and 1660 cm^{-1} (C=O). R_f ($CHCl_3$) 0·23, (C_6H_6–EtOAc, 3:1) 0·83. A m.m.p. with the methyl ether of naturally occurring II was undepressed 105–8°.

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