Tetrahedron Vol. 34, pp. 3563–3567
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0040-4020/78/1215-3563/$02.00/0

SYNTHESIS OF (±) LUPINIFOLIN, DI-O-METHYL XANTHOHUMOL AND ISOXANTHOHUMOL AND RELATED COMPOUNDS

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(*Received in UK 9 May 1978; accepted for publication 22 June 1978*)

Abstract—Nuclear prenylation of naringenin (7) with 2-methylbut-3-en-2-ol in the presence of boron trifluoride etherate gives a mixture of 6-C-prenyl-(11), 8-C-prenyl-(15) and 6,8-di-C-prenyl-(8) derivatives. On formic acid cyclisation, 11 yielded two monodihydropyrans (12 and 13), but 15 afforded only one *viz* 16; similarly 8 formed the bisdihydropyran 10. Methylation of 8-C-prenyl naringenin (15) with Me_2SO_4 resulted in the formation of di-O-methyl derivatives of xanthohumol (22) and isoxanthohumol (23).

Cyclodehydrogenation of 6,8-di-C-prenyl-naringenin (8) with DDQ gave a mono-C-prenyl-2,2-dimethylpyran (1) corresponding to (±) lupinifolin. The angular isomer (2) was also formed. The structure of natural flemichin-B therefore needs further consideration. Similarly, cyclodehydrogenation of 6-C-(11)- and 8-C-prenyl-(15) naringenins afforded the corresponding linear (24) and angular (25) derivatives which have been characterized by conversion into known chalcones 26 and 27 by O-methylation.

Lupinifolin was isolated recently from the aerial parts and the roots of *Tephrosia Lupinifolia* Burch (DC) by Smalberger *et al.*[1] who regarded it as 8-C-prenyl-6″,6″-dimethypyrano (2″,3″: 7,6) naringenin (1) on the basis of UV, IR and NMR spectra. Since its mass spectrum showed a peak at 351 corresponding to the loss of 55 mass units, it was considered as the linear rather than the angular isomer (2). A perusal of literature showed the occurrence of four more natural chalcones and flavanones having the same oxygenation pattern as lupinifolin. Flemichin-B isolated by Rao *et al.*[2] from the hexane extract of the roots of *Flemingia wallichii* W. and A. was ascribed the same structure as that of lupinifolin. Although the NMR spectral data are very close for both these compounds and the main mass fragments are identical, the m.ps of the two natural samples differ very much (flemichin-B, m.p. 168°, lupinifolin, m.p. 117–9°). Although both are laevorotatory, lupinifolin has a slightly higher rotation (−8.7°) than flemichin-B (−3.33°). Hence synthetical evidence is needed to establish which natural compound has the structure 1.

7,4′-Di-O-glucosylnaringenin having a C-prenyl unit in the 6-position (3) or in the 8-position (4) was isolated from the leaves of *Evodia rutaecarpa* by Grimshaw *et al.*[3] Here no aglucone was prepared and the structure was deduced only on the basis of the UV, NMR and mass spectra of the di-glucoside itself. Earlier, isoxanthohumol had been isolated from *Sophoro angustifolia* by Komatsu *et al.*[4] and identified as 8-C-prenylnaringenin 5-methyl ether (5). The corresponding naturally occurring chalcone is xanthohumol (6).[5,6] Since the above compounds could be derived in nature by nuclear prenylation of naringenin (7), similar *in vitro* reactions have now been carried out to synthesize some of them and establish their constitutions.

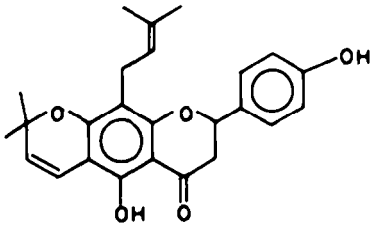
Nuclear prenylation of naringenin (7) under alkaline conditions proved to be difficult because the product was a complex mixture of a large number of compounds. However, when it was carried out with 2-methylbut-3-en-2-ol in the presence of boron trifluoride etherate, a mixture of three products was isolated. One minor product was identified as 6,8-di-C-prenylnaringenin (8) because it formed a diacetate (9) possessing one chelated OH group (δ 12.47) and two acetate groups singlets (δ 2.35 and 2.40). Further the NMR spectra of both the hydroxy compound and its acetate showed resonance signals of two C-prenyl units but no ring A aromatic protons. In confirmation, treatment of 8 with formic acid gave the bisdihydropyran (10) which possessed no chelated OH group but showed two singlets at δ 1.25 and 1.30 (*gem*-dimethyl groups) and two multiplets at δ 1.52–1.90 and 2.40–2.65 ppm ($2Ar-CH_2-CH_2$).

The second product was characterized as 6-C-prenylnaringenin (11) by its NMR spectrum which showed only one singlet of ring A (6.01) and peaks of one C-prenyl unit. The orientation of this unit was established by treatment with formic acid when two mono-dihydropyrans having almost similar NMR spectra were obtained; one (12) had chelated OH and the other (13) not. Had it been an 8-C-prenyl derivative, it could have formed only one isomer.

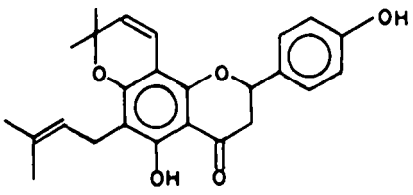
The third product was identified as 8-C-prenylnaringenin (15) because it was isomeric with 11 and had a similar NMR spectrum but gave on acid cyclisation only a single dihydropyran characterized as 6″,6″-dimethyl-4″,5″-dihydropyrano (2″,3″: 7,8) naringenin (16) by formation of its diacetate (17) and by NMR spectroscopy.

6-C-Prenylnaringenin (11) when acetylated gave the corresponding chalcone tetraacetate (18). But on methylation with two moles of dimethylsulphate, it gave a mixture of 2′-hydroxy-4,4′,6′-trimethoxy-5′-C-prenylchalcone (19) and 6-C-prenyl-7,4′-di-O-methylnaringenin (20). The structures of 18, 19 and 20 were supported by their UV and NMR spectra.

Methylation of 8-C-prenylnaringenin (15) with two moles of dimethylsulphate in the presence of K_2CO_3 and acetone afforded a mixture of 8-C-prenyl-7,4′-di-O-methylnaringenin (21) and 2′-hydroxy-3′-C-prenyl-4,4′,6′-



1: Lupinifolin



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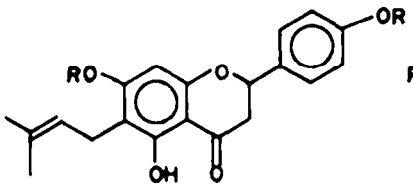
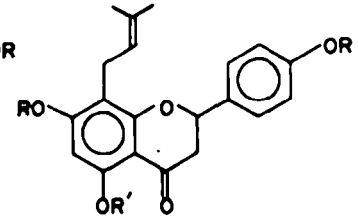
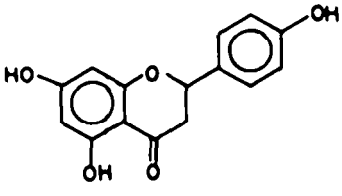


3: R = Glucosyl
11: R = H
20: R = Me



4: R = Glucosyl, R' = H
5: R = H, R' = Me, Isoxanthohumol
15: R = R' = H
21: R = Me, R' = H
23: R = R' = Me



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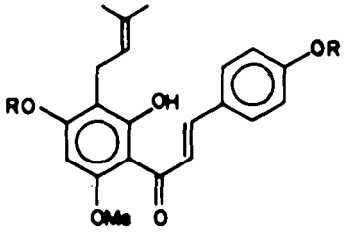
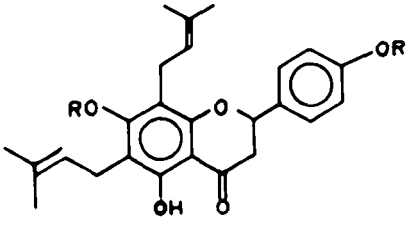
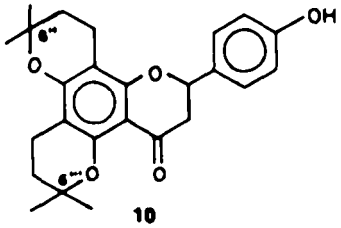


6: R = H, Xanthohumol
22: R = Me



8: R = H
9: R = Ac



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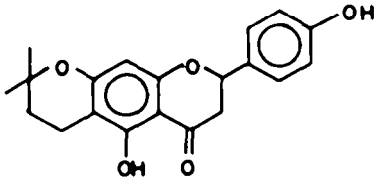

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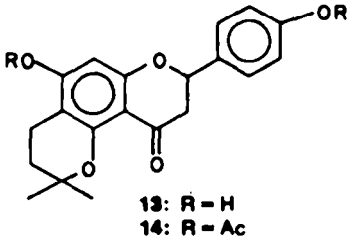
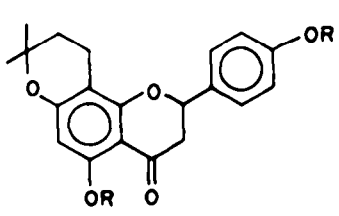
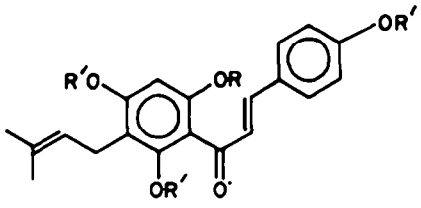


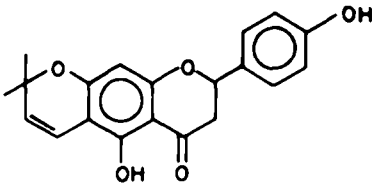
13: R = H
14: R = Ac



16: R = H
17: R = Ac



18: R = R' = Ac
19: R = H, R' = Me



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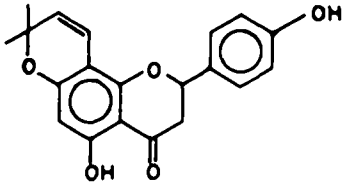

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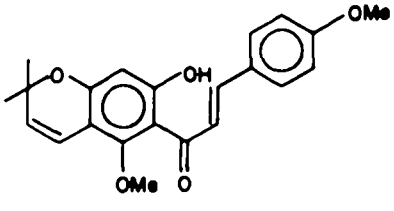

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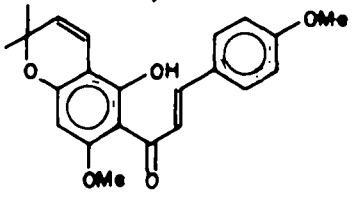

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trimethoxychalcone (22). The latter product was identical with di-O-methylxanthohumol.[6]

Methylation of 8-C-prenylnaringenin (15) with three moles of dimethylsulphate gave chalcone (22) along with 8-C-prenyl-trimethylnaringenin (23) which proved to be identical with di-O-methylisoxanthohumol.[4]

Finally, experiments on cyclodehydrogenation of 6-C-prenyl-(11), 8-C-prenyl-(15) and 6,8-di-C-prenyl-(8) naringenins with DDQ were carried out. Cyclodehydrogenation of 11 yielded 6",6"-dimethylpyrano (2",3": 7,6) naringenin (24) whereas 15 afforded the corresponding angular chromene (25). These chromenes were almost identical in their NMR spectra which showed characteristic resonance signals as two doublets at 5.4 and 6.5 (J = 10 Hz). They were characterized by methylation with dimethylsulphate to the corresponding (known) methylated chalcones (26[7] and 27[6]) respectively.

When 6,8-di-C-prenylnaringenin (8) was cyclodehydrogenated with DDQ, two products were obtained which were separated by column chromatography and fractional crystallization. The major product was identified as 6-C-prenyl-6",6"-dimethylpyrano (2",3": 7,8) naringenin (2) by its NMR spectrum which showed resonance signals appropriate to one condensed 2,2-dimethylpyran ring, and one C-prenyl unit, and one chalated OH group. The orientation of the prenyl unit was indicated by the mass spectrum which showed a peak corresponding to the loss of C_4H_8 (56 mass unit) characteristic of *O*-hydroxylprenyl residues. The minor cyclodehydrogenation product was proved to be the linear isomer (1) by its mass spectrum which showed $(M-55)^+$ peak at 351. The racemic linear chromene (1) was found closer to the m.p., UV and NMR data with natural optically active lupinifolin than with flemichin-B. Hence the structure of flemichin-B has to be studied further.

EXPERIMENTAL

All m.ps are uncorrected. Unless stated otherwise, UV spectra are recorded in MeOH and figure within parenthesis refer to log ε values; NMR spectra were determined by 80 MHz BS487C spectrometer using $CDCl_3$ as solvent and TMS as internal standard; the chemical shifts are given in δ values; light petroleum ether used has boiling range 60–80°; silica gel was used for column chromatography and silica gel G for TLC; R_f values recorded refer to TLC plates for which the solvent systems were: (A) benzene alone, (B) benzene:EtOAc (9:1), (C) benzene:EtOAc (17:3) and (D) benzene:EtOAc (4:1). Spraying of TLC plates was carried out with 10% H_2SO_4 aq and/or 1% ethanolic $FeCl_3$.

Nuclear prenylation of naringenin (7)

To a stirred soln of 7 (5.5 g) in dry dioxan (40 ml) was added gradually BF_3-etherate (5.4 ml) at room temp. during a course of 30 min. To this was added a soln of 2-methyl-but-3-en-2-ol (4 ml) in dry dioxan. The resulting soln was stirred for 6 hr, kept at room temp. for overnight, diluted with moist ether (150 ml), and the ethereal layer was washed with water (3 × 200 ml) and evaporated to dryness. The residue on column chromatography and elution successively with light petroleum:benzene (1:1), light petroleum:benzene (1:4), benzene alone and benzene:EtOAc (9:1) gave four fractions A–D.

Fraction A crystallized from benzene-light petroleum and yielded 8 as light yellow crystals (300 mg), m.p. 134–35°; dark

brown ferric reaction; R_f 0.82 (solvent D) (Found: C, 73.2; H, 7.1. $C_{25}H_{28}O_5$ requires: C, 73.5; H, 6.9%); λ_{max} 289 and 340 nm (4.23 and 3.48 respectively); NMR spectrum: 1.45, 1.62, 1.75 (3s, 12H, two $(CH_3)_2C$=), 2.50–3.15 (m, 6H, two H-3 and two Ar-CH_2-CH=), 5.20–5.50 (m, 3H, two -CH_2-CH= and H-2), 6.90 (d, J = 9 Hz, 2H, H-3' and 5'), 7.33 (d, J = 9 Hz, 2H, H-2' and 6') and 12.47 (s, 1H, chelated OH). The diacetate (9) prepared by the Ac_2O–pyridine method in cold crystallized from MeOH as colourless flakes, m.p. 112–13°; dark brown ferric reaction; R_f 0.63 (solvent B) (Found: C, 70.9; H, 6.6. $C_{29}H_{32}O_7$ requires: C, 70.7; H, 6.5%); NMR spectrum: 1.40, 1.62, 1.75 (3s, 12H, two $(CH_3)_2C$=), 2.35, 2.40 (2s, 6H, two CH_3CO_2-), 2.62–3.38 (m, 6H two H-3 and two ArCH_2-CH=), 5.05–5.62 (m, 3H, two -CH_2-CH= and H-2), 7.21 (d, J = 9 Hz, 2H, H-3' and 5'), 7.52 (d, J = 9 Hz, 2H, H-2' and 6').

Fracture B was crystallized from EtOAc–light petroleum mixture when 11 formed as pale yellow crystals (600 mg), m.p. 214–16°; intense brown ferric reaction; R_f 0.66 (solvent D); (Found: C, 70.2; H, 5.8. $C_{20}H_{20}O_5$ requires: C, 70.6; H, 5.9%); λ_{max} 285 and 340 nm (4.27 and 3.75 respectively); NMR [$(CD_3)_2CO$] spectrum: 1.62, 1.75 (2s, 6H, $(CH_3)_2C$=), 2.73–3.23 (m, 4H, $ArCH_2$-CH= and two H-3), 5.05–5.52 (m, 2H, -CH_2-CH= and H-2), 6.01 (s, 1H, H-8), 6.85 (d, J = 9 Hz, 2H, H-3' and 5'), 7.35 (d, J = 9 Hz, 2H, H-2' and 6') and 11.85 (s, 1H, chelated OH).

When refluxed in Ac_2O–pyridine for 5 hr, 11 gave 18 which crystallized from MeOH as colourless flakes, m.p. 158–9°; R_f 0.43 (solvent B) (Found: C, 66.3; H, 5.8. $C_{28}H_{28}O_9$ requires: C, 66.1; H, 5.5%); NMR spectrum: 1.70, 1.75 (2s, 6H, $(CH_3)_2C$=), 2.12, 2.17, 2.36 (3s, 12H, four CH_3CO_2-), 3.21 (d, J = 8 Hz, 2H, $ArCH_2$-CH=), 5.10 (t, J = 7.5 Hz, 1H, -CH_2-CH=), 6.77 (s, 1H, H-3'), 7.07 (d, J_o = 9 Hz, J_m = 3 Hz, 2H, H-3 and 5), 7.12 (d, J = 16 Hz, 1H, H-α), 7.32 (d, J = 16 Hz, 1H, H-β), 7.62 (d, J_o = 9 Hz, J_m = 3 Hz, 2H, H-2 and 6).

Fraction C on crystallization from EtOAc–light petroleum mixture afforded 15 as colourless crystals (680 mg), m.p. 183–4°; dark brown ferric reaction; R_f 0.59 (solvent D) (Found: C, 70.7; H, 6.2. $C_{20}H_{20}O_5$ requires: C, 70.6; H. 5.9%); λ_{max} 292 and 324 nm (4.23 and 3.85 respectively); NMR spectrum: 1.70, 1.77 (2s, 6H, Me_2C=), 2.68–2.92 (m, 2H, H-3), 3.30 (d, J = 7.5 Hz, 2H, $ArCH_2$-CH=), 5.08–5.41 (m, 2H, -CH_2-CH= and H-2), 5.93 (s, 1H, H-6), 7.0 (d, J = 9 Hz, 2H, H-3' and 5'), 7.25 (d, J = 9 Hz, 2H, H-2' and 6') and 12.31 ppm (s, 1H, chelated OH).

Fraction D on crystallization from EtOAc–light petroleum mixture afforded the starting 7 (0.9 g).

4' - Hydroxy - 6",6",8",8" - tetramethyl - 4",5",4"",5"" - tetrahydro - bispyrano(2",3": 7,8; 2"",3"": 5,6)flavanone (10)

Compound 5 (50 mg) was heated with formic acid (10 ml) on a water bath for 2 hr, left at room temp. for 8 hr and finally poured on ice-cold water. The solid thus collected was crystallized from chloroform–light petroleum mixture when 10 formed as colourless crystals (30 mg), m.p. 217–19°; R_f 0.53 (solvent D) (Found: C, 73.4; H, 7.0. $C_{25}H_{28}O_5$ requires: C, 73.5; H, 6.9%); λ_{max} 224, 272 and 322 nm (3.84, 4.23 and 3.63 respectively); NMR spectrum: 1.25, 1.30 (2s, 12H, two Me_2C<), 1.52–1.90 (m, 4H, two $ArCH_2$-CH_2-), 2.40–2.95 (m, 6H, two $ArCH_2$-CH_2- and two H-3), 5.07–5.35 (m, 1H, H-2), 6.85 (d, J = 9 Hz, 2H, H-3' and 5') and 7.25 ppm (d, J = 9 Hz, 2H, H-2' and 6').

Acid cyclisation of 6-C-prenylnaringenin (11); *Formation of monodihydropyrans* 12 *and* 13

Compound 11 (100 mg) was heated with formic acid (20 ml) for 1 hr, left at room temp. for 4 hr and the soln poured on ice-cold water. The mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was evaporated to dryness and subjected to column chromatography. Successive elution with benzene alone and benzene:EtOAc (9:1) gave two fractions A and B.

Fraction A on crystallization from benzene–light petroleum mixture yielded 12 as colourless crystals (50 mg), m.p. 152–3°; green ferric reaction; R_f 0.64 (solvent C) (Found: C, 70.9; 6.3. $C_{20}H_{20}O_5$ requires: C, 70.6; H, 5.9%); λ_{max} 235 and 298 (4.18 and 4.19 respectively); NMR spectrum: 1.31 (s, 6H, Me_2C<), 1.75 and 2.55 (2t, J = 7 Hz, 4H, $ArCH_2$-CH_2-), 2.74–3.02 (m, 2H, H-3), 5.09–5.47 (m, 1H, H-2), 5.92 (s, 1H, H-8), 6.85 (d, J = 9 Hz, 2H, H-3' and 5'), 7.25 (d, J = 9 Hz, 2H, H-2' and 6') and 11.73 (s, 1H, chelated OH).

Fraction B when crystallized from EtOAc–light petroleum mixture afforded 13 as cream coloured crystals (20 mg), m.p. 266–8°; R_f 0.48 (solvent C) (Found: C, 70.1; H, 6.2. $C_{20}H_{20}O_5$ requires: C, 70.6; H, 5.9%); λ_{max} 272 and 328 (4.18 and 3.48 respectively); NMR spectrum: 1.32, 1.40 (2s, 6H, Me_2C<), 1.69, 2.57 (2t, J = 7 Hz, 4H, $ArCH_2$-CH_2-), 2.72–3.07 (m, 2H, H-3), 5.12–5.45 (m, 1H, H-2), 5.89 (s, 1H, H-8), 6.84 (d, J = 8 Hz, 2H, H-3' and 5'), 7.34 (d, J = 8 Hz, 2H, H-2' and 6'). The diacetate (14) prepared by Ac_2O-pyridine method (in cold) crystallized from MeOH as colourless flakes, m.p. 182–3°, R_f 0.58 (solvent B) (Found: C, 67.5; H, 5.8. $C_{24}H_{24}O_7$ requires: C, 67.9; H, 5.7%); NMR spectrum: 1.36 (s, 6H, Me_2C<), 1.77, 2.55 (2t, J = 7 Hz, 4H, $ArCH_2$-CH_2-), 2.29 (s, 6H, two CH_3CO_2-), 2.72–3.03 (m, 2H, H-3), 5.15–5.53 (m, 1H, H-2), 6.13 (s, 1H, H-8), 6.97 (d, J = 9 Hz, 2H, H-3' and 5'), 7.37 (d, J = 9 Hz, 2H, H-2' and 6').

Methylation of 6-C-prenylnaringenin (11) *and formation of* 19 *and* 20

An acetone soln of 11 (170 mg) was refluxed with dimethylsulphate (0.11 ml) and anhyd K_2CO_3 (1 g) for 4 hr. The solvent was distilled and the residue treated with water. The resulting viscous mass was dried and column chromatographed. Careful elution with benzene–light petroleum (1:9) gave two fractions A and B.

Fraction A crystallized from EtOAc and afforded 19 as yellow needles (30 mg), m.p. 137–8°; reddish brown ferric reaction; R_f 0.92 (solvent A) (Found: C, 72.1; H, 7.2. $C_{22}H_{26}O_5$ requires: C, 72.3; H, 6.8%); λ_{max} 225 and 363 nm (3.96 and 4.06 respectively); NMR spectrum: 1.72, 1.84 (2s, 6H, Me_2C=), 3.32 (d, J = 7 Hz, 2H, $ArCH_2$-CH=), 3.88, 3.93, 3.96 (3s, 9H, three OCH_3), 5.15 (t, J = 7 Hz, 1 H, -CH=), 6.04 (s, 1H, H-3'), 6.96 (d, J = 9 Hz, 2H, H-3 and 5), 7.40 (d, J = 18 Hz, 1 H, H-α), 7.60 (d, J = 9 Hz, 2H, H-2 and 6), 7.66 (d, J = 18 Hz, 1H, H-β) and 14.15 (s, 1H, chelated OH).

Fraction B crystallized from benzene–light petroleum mixture to afford 20 as colourless crystals (20 mg), m.p. 162–3°; dark brown ferric reaction; R_f 0.75 (solvent A) (Found: C, 71.4; H, 6.8. $C_{22}H_{24}O_5$ requires: C, 71.7; H, 6.5%); λ_{max} 295 and 335 (4.30 and 3.67 respectively); NMR spectrum: 1.62, 1.75 (2s, 6H, Me_2C=), 2.50–2.75 (m, 2H, H-3), 3.22 (d, J = 8 Hz, 2H, $ArCH_2$-CH=), 3.92 (s, 6H, two OCH_3), 5.12–5.42 (m, 2H, -CH_2-CH= and H-2), 5.98 (s, 1H, H-8), 6.90 (d, J = 8 Hz, 2H, H-3' and 5'), 7.32 (d, J = 8 Hz, 2H, H-2' and 6') and 11.78 (s, 1H, chelated OH).

6",8" - Dimethyl - 4",5" - dihydropyrano(2",3": 7,8)naringenin (16)

Compound 15 (50 mg) was treated with formic acid. The product on crystallization from MeOH gave 16 as colourless flakes (40 mg), m.p. 157–8°; dark green ferric reaction; R_f 0.66 (solvent C) (Found: C, 70.5; H, 5.7. $C_{20}H_{20}O_5$ requires: C, 70.6; H, 5.9%); λ_{max} 297 (4.19); NMR spectrum: 1.29 (s, 6H, Me_2C<), 1.74, 2.58 (2t, J = 7 Hz, 4H, $ArCH_2$-CH_2-), 2.70–2.99 (m, 2H, H-3), 5.12–5.39 (m, 1H, H-2), 5.91 (s, 1H, H-6), 6.82 (d, J = 9 Hz, 2H, H-3' and 5'), 7.28 (d, J = 9 Hz, 2H, H-2' and 6'), 12.27 (s, 1H, chelated OH). The diacetate (17) prepared by the Ac_2O–pyridine crystallized from MeOH as colourless flakes, m.p. 142–3°; R_f 0.61 (solvent C) (Found: C, 67.8; H, 5.9. $C_{24}H_{24}O_7$ requires: C, 67.9; H, 5.7%); NMR spectrum: 1.35 (s, 6H, Me_2C<), 1.79, 2.57 (2t, J = 7 Hz, 4H, $ArCH_2$-CH_2), 2.27 (s, 6H, two CH_3CO_2-), 2.68–2.98 (m, 2H, H-3), 5.17–5.50 (m, 1H, H-2), 6.12 (s, 1H, H-6), 6.95 (d, J = 9 Hz, 2H, H-3' and 5') and 7.41 (d, J = 9 Hz, 2H, H-2' and 6').

Methylation of 8-C-prenylnaringenin (15) *with two moles of* Me_2SO_4; *formation of* 21 *and* 22

An acetone soln of 15 (170 mg) was refluxed with dimethyl sulphate (0.12 ml) and anhyd K_2CO_3 (1 g) for 4 hr. The product was found to be a mixture of two compounds on TLC. Fractional crystallization from benzene–light petroleum (mother liquor A) yielded 22 which crystallized from EtOH as orange yellow needles (30 mg), m.p. 131–32° (lit.[6] m.p. 133°); reddish brown ferric reaction; R_f 0.87 (solvent A) (Found: C, 72.8; H, 6.8. Calc. for $C_{25}H_{28}O_5$: C, 72.3; H, 6.8%); λ_{max} 223 and 362 nm (3.82 and 4.18 respectively); NMR spectrum: 1.64, 1.77 (2s, 6H, Me_2C=),

3.27 (d, J = 7 Hz, 2H, $ArCH_2$–CH=), 3.81, 3.87, 3.89 (3s, 9H, three OCH_3), 5.16 (t, J = 7 Hz, 1H, –CH_2–CH=), 5.96 (s, 1H, H-5'), 6.87 (d, J = 9 Hz, 2H, H-3 and 5), 7.37 (d, J = 18 Hz, 1H, H-α), 7.53 (d, J = 9 Hz, 2H, H-2 and 6), 7.64 (d, J = 18 Hz, 1H, H-β) and 14.07 ppm (s, 1H, chelated OH). The mother liquor A yielded a solid which after two crystallizations from benzene–light petroleum mixture gave 21 (20 mg), m.p. 165–6°; dark brown ferric reaction; R_f 0.69 (solvent A) (Found: C, 71.9; H, 6.8. $C_{22}H_{24}O_5$ requires: C, 71.7; H, 6.5%); λ_{max} 297 and 337 (4.31 and 3.78 respectively); NMR spectrum: 1.62, 1.70 (2s, 6H, Me_2C=), 2.62–2.82 (m, 2H, H-3), 3.38 (d, J = 8 Hz, 2H, $ArCH_2$–CH=), 3.73, 3.80 (2s, 6H, two OCH_3), 5.05–5.62 (m, 2H, –CH= and H-2), 6.18 (s, 1H, H-6), 6.82 (d, J = 9 Hz, 2H, H-3' and 5') and 7.43 (d, J = 9 Hz, 2H, H-2' and 6').

Methylation of 8-C-prenylnaringenin (15) *with three moles of* Me_2SO_4; *formation of* 22 *and* 23

To a soln of 15 (100 mg) in acetone (20 ml) was added dimethylsulphate (0.09 ml) and anhyd K_2CO_3 (1 g) and the soln refluxed for 12 hr. The product on column chromatography and successive elution with benzene:light petroleum (1:9) and 100% benzene gave two main fractions A and B.

Fraction A crystallized from EtOH and yielded 22 as orange yellow needles (40 mg), m.p. and m.m.p. with the sample prepared earlier, 131–2°.

Fraction B crystallized from EtOAc-light petroleum mixture gave 23 as colourless crystals (10 mg), m.p. 172–3° (lit.,[6] m.p. 174–5°); R_f 0.52 (solvent C) (Found: C, 72.2; H, 6.6. Calc. for $C_{23}H_{26}O_5$: C, 72.3; H, 6.8%); λ_{max} 272, 285 and 328 nm (4.15, 4.23 and 3.81 respectively).

6",6"-Dimethylpyrano(2",3": 7,8)naringenin (24)

To a soln of 11 (85 mg) in dry, freshly distilled benzene (10 ml) was added DDQ (70 mg) and the resulting mixture refluxed for 3 hr on a boiling water bath. Hydroquinone was filtered off and the filtrate evaporated. The residue on column chromatography and elution with benzene:light petroleum (7:3) yielded 24 which crystallized from benzene–light petroleum mixture as shining light yellow crystals (70 mg), m.p. 147–48°; dark brown ferric reaction, R_f 0.62 (solvent C) (Found: C, 70.7; H, 5.5. $C_{20}H_{18}O_5$ requires: C, 71.0; H, 5.3%); λ_{max} 228, 297 and 338 nm (3.94, 4.28 and 3.10 respectively); NMR spectrum: 1.46 (s, 6H, Me_2C<), 2.82–3.07 (m, 2H, H-3), 5.18–5.59 (m, 1H, H-2), 5.45, 6.51 (2d, J = 10 Hz, 2H, H-5" and 4" respectively), 5.98 (s, 1H, H-8), 6.87 (d, J = 9 Hz, 2H, H-3' and 5'), 7.29 (d, J = 9 Hz, 2H, H-2' and 6') and 12.05 ppm (s, 1H, chelated OH).

4,6'-Dimethoxy - 2' - hydroxy - 6",6" - dimethylpyrano(2",3": 4",5')chalcone (26)

An acetone soln of 24 (50 mg) was refluxed with dimethyl sulphate (0.02 ml) in the presence of anhyd K_2CO_3 for 4 hr. The product on crystallization from EtOH gave mainly 26 as deep yellow needles (20 mg); m.p. 118–19° (lit.[7] m.p. 120°); dark brown ferric reaction, R_f 0.79 (solvent C); (Found: C, 71.8; H, 6.4. Calc. for $C_{22}H_{22}O_5$: C, 72.1; H, 6.0%); λ_{max} 232 and 368 (3.84 and 4.45 respectively); NMR spectrum: 1.40, 1.48 (2s, 6H, Me_2C<), 3.75, 3.82 (2s, 6H, two OCH_3), 5.51, 6.50 (2d, J = 10 Hz, 2H, H-5" and 4") 6.23 (s, 1H, H-3'), 6.87 (d, J = 9 Hz, 2H, H-3 and 5), 7.12, 7.38 (2d, J = 20 Hz, 2H, H-α and β), 7.32 (d, J = 9 Hz, 2H, H-2 and 6).

6",6"-Dimethylpyrano(2",3": 7,8)naringenin (25)

To a soln of 15 (100 mg) in dry benzene (20 ml) was added DDQ (80 mg) and the resulting soln refluxed for 2 hr. The product on column chromatography and elution with benzene–light petroleum (7:4) yielded 25 which crystallized from benzene-light petroleum mixture as pale yellow crystals (60 mg), m.p. 162–3°; dark brown ferric reaction; R_f 0.75 (solvent D) (Found: C, 71.2; H, 5.6. $C_{20}H_{18}O_5$ requires C, 71.0; H, 5.3%); λ_{max} 228, 288 and 337 nm (3.94, 4.08 and 3.72 respectively); NMR spectrum: 1.43 (s, 6H, Me_2C<), 2.78–2.98 (m, 2H, H-3), 5.15–5.58 (m, 1H, H-2), 5.47, 6.53 (2d, J = 10 Hz, 2H, H-5" and 4"), 6.00 (s, 1H, H-6), 6.87 (d, J = 9 Hz, 2H, H-3' and 5'), 7.33 (d, J = 9 Hz, 2H, H-2' and 6').

4,6' - Dimethoxy - 2' - hydroxy - 6",6" - dimethylpyrano(2",3": 4",3')chalcone (27)

An acetone soln of 25 (50 mg) was refluxed with dimethyl sulphate (0.02 ml) in the presence of anhyd K_2CO_3 for 3.5 hr. The product on crystallization from EtOH gave mainly 27 as yellow crystals (25 mg), m.p. 112–14° (lit.[8] m.p. 114–15°); brown ferric reaction, R_f 0.83 (solvent C) (Found: C, 72.3; H, 6.3. Calc. for $C_{22}H_{22}O_5$: C, 72.1; H, 6.0%); λ_{max} 232 and 352 (3.82 and 4.23 respectively); NMR spectrum: 1.38, 1.44 (2s, 6H, Me_2C<), 3.74, 3.79 (2s, 6H, OCH_3), 5.53, 6.52 (2d, J = 10 Hz, 2H, H-5" and 4"), 6.24 (s, 1H, H-5'), 6.90 (d, J = 9 Hz, 2H, H-3 and 5), 6.92, 7.38 (2d, J = 20 Hz, 2H, H-α and β), 7.36 (d, J = 9 Hz, 2H, H-2 and 6).

Reaction of 6,8-di-C-C-prenylnaringenin (8) *with DDQ; formation of* 1 *and* 2

To a soln of 8 (200 mg) in dry benzene (40 ml) was added DDQ (140 mg) and the soln was refluxed for 3 hr. The product on column chromatography and elution with benzene:light petroleum (7:4) gave a solid which on TLC proved to be a mixture. Fractional crystallization from benzene–light petroleum (mother liquor A) yielded a solid which recrystallized from benzene–light petroleum mixture 2 as light yellow crystals (40 mg), m.p. 138–40°; dark brown ferric reaction; R_f 0.65 (solvent C) (Found: C, 73.7; H, 6.5. $C_{25}H_{26}O_5$ requires: C, 73.9; H, 6.4%); λ_{max} 282, 296 and 322 nm (4.53, 4.23 and 3.87 respectively); NMR spectrum: 1.40, 1.62 (2s, 12H, Me_2C< and Me_2C= respectively), 2.62–2.87 (m, 2H, H-3), 3.25 (d, J = 8 Hz, 2H, $ArCH_2$–CH=), 5.05–5.37 (m, 2H, –CH_2–CH= and H-2), 5.46, 6.48 (2d, J = 10 Hz, 2H, H-5" and 4"), 6.83 (d, J = 9 Hz, 2H, H-3' and 5'), 7.23 (d, J = 9 Hz, 2H, H-2' and 6') and 12.23 ppm (s, 1H, chelated OH). 406 (60%), 391 (100%), 350 (30%), 285 (30%), 271 (60%), 257 (5%), 242 (20%), 147 (30%) and 120 (80%).

The mother liquor A yielded a solid which after two crystallization from benzene:light petroleum mixture gave 1 as pale yellow needles (20 mg), m.p. 124–5° (lit.[1] m.p. 117–19°); dark brown ferric reaction; R_f 0.63 (solvent C) (Found: C, 74.3; H, 6.8. Calc. for $C_{25}H_{26}O_5$: C, 73.9; H, 6.4%); λ_{max} 278, 298 and 318 nm (4.48, 4.24 and 3.98 respectively); NMR spectrum: 1.42, 1.62 (2s, 12H, Me_2C< and Me_2C= respectively), 2.69–2.98 (m, 2H, H-3), 3.18 (d, J = 7.5 Hz, 2H, $ArCH_2$–CH=), 5.05–5.35 (m, 2H, –CH_2–CH= and H-2), 5.47, 6.46 (2d, J = 10 Hz, 2H, H-5" and 4"), 6.84 (d, J = 9 Hz, 2H, H-3' and 5'), 7.27 (d, J = 9 Hz, 2H, H-2' and 6'). 406 (70%), 391 (90%), 351 (35%), 286 (35%), 271 (25%), 243 (5%) and 148 (100%). In all these properties, it agrees with those of natural lupinfolin[1] but not with flemichin-B.[2]

Acknowledgements—The authors are indebted to the University Grants Commission, New Delhi, India for the award of NF to ACJ and the C.S.I.R. India for a JRF to R.C.G.

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