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SYNTHESIS OF RACEMIC 8-C-PRENYL-6",6"-DIMETHYLPYRANO(2",3":7,6)NARINGENIN

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Reaction of naringenin (1) with 2-methylbut-3-en-2-ol in the presence of BF_3-Et_2O gives a mixture of 6-C-prenyl-(5), 8-C-prenyl-(8) and 6,8-di-C,C-prenyl-(2) derivatives. The last compound (2) with DDQ afforded 8-C-prenyl-6",6"-dimethylpyrano(2",3":7,6)naringenin (11) along with its angular isomer (10) in racemic forms.

From the roots of *Tephrosia lupinifolia* Burch (DC), Smalberger et al.[1] isolated lupinifolin [m.p.117-9°,$[\alpha]_D$-8.7(C, 1.15, $CHCl_3$)] and assigned it the constitution of 8-C-prenyl-6",6"-dimethylpyrano(2",3":7,6)naringenin (11) on the basis of its spectral data. More recently, a compound of the same structure called flemichin-B [m.p.168°,$[\alpha]_D$-3.33°(C, 0.12, EtOH)] was isolated from the roots of *Flemingia wallichii* W. and A. by Rao et al.[2] Since their physical characterisatics such as m.p., optical rotation and UV data (see Table 1) differ, it was projected to synthesize unambiguously the racemic compound having structure (11).

Naringenin (1), on reaction with 2-methyl-but-3-en-2-ol in the presence of BF_3-Et_2O gave three products. The first column mobile but minor compound crystallised from benzene-light petroleum to give 6,8-di-C,C-prenylnaringenin (2) as light yellow crystals, m.p. 134-35°;[3] R_F 0.82 (solvent C);[4] dark brown ferric reaction; UV (see Table 1). Its diacetate (3) prepared by Ac_2O-py. method (in cold) crystallised from methanol as colourless flakes, m.p.112-13°; R_F 0.63 (solvent A), dark brown ferric reaction. NMR signals of the hydroxy compound (2) and the acetate (3) indicated that minor product has structure 2 which was further supported by formic acid treatment when 4'-hydroxy-6",6",6"',6"'-tetramethyl-4",5",4"',5"'-tetrahydrobispyrano(2",3":5,6; 2"',3"':7,8)flavanone (4) was obtained as colourless crystals, m.p.217-19°; R_F 0.53(solvent C), showing expected UV and NMR data(see Tables 1 & 2).

The second product crystallised from ethyl acetate-light petroleum mixture to yield 6-C-prenylnaringenin (5) as pale yellow crystals, m.p. 214-16°; R_F 0.66 (solvent C), intense brown ferric reaction; UV (see Table 1). The NMR data (see Table 2) indicated that it has one C-prenyl unit in the condensed benzene ring, the orientation of which was established by treatment with formic acid, when two mono-dihydropyrano derivatives having almost similar NMR

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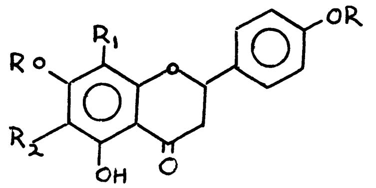
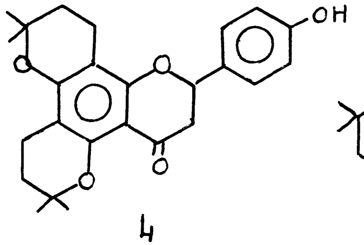


1, R = R_1 = R_2 = H
2, R = H; R_1 = R_2 = Pren
3, R = Ac, R_1 = R_2 = Pren
5, R = R_1 = H; R_2 = Pren
8, R = R_2 = H; R_1 = Pren
Pren stands for $Me_2C = CH-CH_2-$



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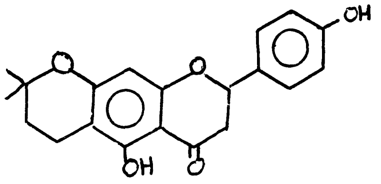

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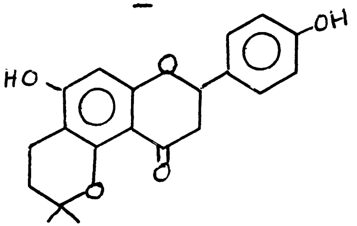

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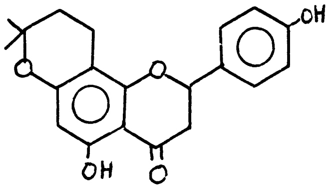

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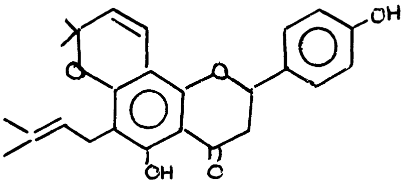

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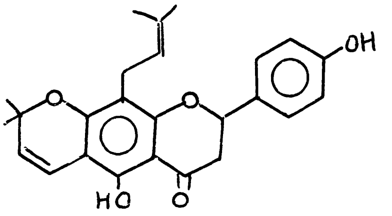

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spectra were obtained; one (6, m.p. 152-53°) has chelated OH and the other (7, m.p. 265-68°) not. Had it been 8-C-prenyl derivative, it would have formed only one such derivative.

The third main fraction of the nuclear prenylation reaction crystallised from ethyl acetate-light petroleum to afford 8-C-prenylnaringenin (8) as colourless crystals, m.p. 183-84°, R_F 0.59 (solvent C); dark brown ferric reaction; UV (see Table 1). Its NMR spectrum (see Table 1) showed the presence of one C-prenyl unit in the ring A, and the formation of only one dihydropyrano derivative (9), m.p. 157-58° during acid treatment located the prenyl unit in 8 position .

Reaction of the 6,8-diprenyl derivative (2) with DDQ gave two products which were separated by column chromatography and subsequent fractional crystallisation. The major product crystallised from benzene-light petroleum mixture to give 6-C-prenyl-6'',6''-dimethylpyrano (2'',3'':7,8) naringenin (10) as light yellow crystals, m.p. 138-40°; R_F 0.65 (solvent B); dark brown ferric reaction; UV (see Table 1). As expected, its NMR spectrum showed resonance signals of one C-prenyl unit and one condensed 2,2-dimethyl pyrano unit (see Table 2). The orientation of the pyran and prenyl units were established by its mass spectrum which showed a peak corresponding to the loss of C_4H_8 (56 mass unit) as established in similar cases earlier [7,8]. The minor product after two crystallisations from benzene-light petroleum mixture yielded racemic

8-C-prenyl-6",6"-dimethylpyrano(2",3":7,6)naringenin (11) as pale yellow needles, m.p. 124-25°; R_F 0.63 (solvent B); dark brown ferric reaction; UV and NMR data (see Tables 1 and 2). The linear character of the pyran ring was supported by its MS which showed $(M-55)^+$ peak at 351. The comparisons of the UV and the NMR spectral data of the synthetic compound (11) with those of lupinifolin and flemichin-B showed some deviations (Tables 1 and 2). Thus, a problem of whether three compounds have an identical structure with the exception of the stereochemistry, is left until more precise comparisons are made on these three compounds.

REFERENCES AND NOTES

1. T.M. Smalberger, R. Vleggaar and J.C. Weber, *Tetrahedron* **30**, 3927 (1974).
2. J. Madhusudhana Rao, K. Subrahmanyam, K.V. Jagannadha Rao and M. Gopala Rao, *Indian J. Chem.* **13**, 775 (1975).
3. All new compounds reported here gave correct analysis of C and H.
4. All R_F values refer to TLC carried out on silica gel G chromoplates using (A) benzene:ethyl acetate (9:1), (B) benzene:ethyl acetate (17:3) or (C) benzene:ethyl acetate (4:1) as the solvent. TLC plates were sprayed with 1% alcoholic $FeCl_3$ or 10% aq.H_2SO_4.
5. All UV spectra were reported in methanol; bands indicate absorption maxima and figures within parenthesis refer to log ϵ values.
6. Unless stated otherwise, all NMR spectra were run on 80MHz BS487C spectrometer using $CDCl_3$ as solvent and TMS as internal standard and the chemical shifts are expressed in δ values.
7. E. Ritchie, W.C. Taylor and J.C. Shannon, *Tetrahedron Letters*, 1437 (1964).
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Table 1 - UV data[5]

COMPOUND	
Natural lupinifolin	224(4.38), 267sh(4.68), 275(4.72), 297sh(4.17), 314(4.15) and 364 nm (3.55)
Natural flemichin-B	214, 280, 300 and 320 nm
2	289(4.23) and 340 nm (3.48)
4	224(3.84), 272(4.23) and 322 nm (3.63)
5	285(4.27) and 340 nm (3.75)
8	292(4.23) and 324 nm (3.85)
10	282(4.53), 296(4.23) and 322 nm (3.87)
11	278(4.48), 298(4.24) and 318 nm (3.98)

TABLE 2 - NMR DATA[6]

COMPOUND or STRUCTURE	H-2	H-3	H-2',6' (see footnote a)	H-3',5'	H4" (see footnote b)	H5"	$(CH_3)_2C$	$ArC\underline{H}_2$-CH=	-C$\underline{H}$=	5-O$\underline{H}$	H of other groups
Natural Lupinifolin[1]	5.30[+] (dd)	3.03 2.78[#] (each dd)	7.28 (d, J= 8.5Hz)	6.84 (d, J= 8.5Hz)	6.63(d)	5.48(d)	1.44,1.64 (2,S,12H)	3.20 (d, J= 7Hz)	5.14 (t, J= 7Hz)	12.20	-
Natural Flemichin-B[2]	5.20 (m)	2.85 (m)	7.30 (d)	6.85 (d)	6.63 (d)	5.47 (d)	1.40(S,6H) 1.60(d, J= 1Hz, 6H)	3.20 (d, J=8Hz)	5.05 (m,1H)	12.25	-
2	5.20-5.50 (m)	2.50-3.15 (m)	7.33(d)	6.90(d)	-	-	1.45,1.62, 1.75 (3S,12H)	2.50-3.15 (m,4H)	5.20-5.50 (m,2H)	12.47	-
3	5.05-5.62 (m)	2.62-3.38 (m)	7.52(d)	7.21(d)	-	-	1.40,1.62, 1.75 (3S,12H)	2.62-3.38 (m,4H)	5.05-5.62 (m,2H)	-	2.35,2.40 (2S,6H,OAC)
4	5.07-5.35 (m)	2.40-2.95 (m)	7.25(d)	6.85(d)	-	-	1.25,1.30 (2S,12H)	-	-	-	1.52-1.90 2.40-2.95 (2m,8H, H4",5" .)
5	5.05-5.52 (m)	2.73-3.23 (m)	7.35(d)	6.85(d)	-	-	1.62,1.75 (2S,6H)	2.73-3.23 (m,)	5.05-5.52 (m,1H)	11.85	6.01 (S, H-8)
8	5.08-5.41 (m)	2.68-2.92 (m)	7.25(d)	7.00(d)	-	-	1.70,1.77 (2S,6H)	3.30 (d, J=7.5Hz)	5.08-5.41 (m,1H)	12.31	5.93 (S,H-6)
10	5.05-5.37 (m)	2.62-2.87 (m)	7.23(d)	6.83(d)	6.48(d)	5.46(d)	1.40,1.62 (2S,12H)	3.25 (d, J=8Hz)	5.05-5.37 (m,1H)	12.23	-
11	5.05-5.35 (m)	2.69-2.98 (m)	7.27(d)	6.84(d)	6.46(d)	5.47(d)	1.42,1.62 (2S,12H)	3.18 (d, J=8Hz)	5.05-5.35 (m,1H)	12.20	-

Unless otherwise stated, doublets have (a) J=9Hz ; (b) J=10Hz. [+] $J_{2,3ax}$ 12.7Hz, $J_{2,3eq}$ 3.3Hz.

[#] $J_{3ax,eq}$ 17.3Hz, $J_{2,3ax}$ 12.7Hz, $J_{2,3eq}$ 3.3Hz.

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