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SYNTHESIS OF LUPINIFOLIN

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Lupinifolin was isolated from the roots of Tephrosia lupinifolia Burch[1] (DC). Elucidation of its structure was mainly based on spectral data. The present communication describes its synthesis and confirms the structure earlier arrived at. For the synthesis of lupinifolin, prenylation of naringenin led to the formation of the key intermediate 6,8-di-C-prenyl naringenin (Major) and a number of minor products. In order to provide structural confirmations to the minor products condensation of naringenin with 2-methyl but-3-en-2-ol has also been carried out and the products compared.

Condensation of naringenin (I) with prenyl bromide[2] yielded a mixture comprising of diprenyl and unreacted flavanone along with small quantities of mono prenyl compounds. II, IIa, IIb & IIc, were obtained as single entities chromatographically and the major product was identified as di-C-prenyl derivative.

5,7,4'-Trihydroxy-6,8-di-C-prenyl flavanone (II), a viscous liquid (100 mg) gave brown ferric reaction (Found: C, 73.2; H, 7.0. $C_{25}H_{28}O_5$ requires C, 73.5; H, 6.8%). λ_{max}^{MeOH} 225, 295, 302sh nm. ν_{max}^{KBr} 1620 cm^{-1} (>C=O), NMR (δ, $CDCl_3$): 1.64, 1.71(2s, 12H, four methyl of two prenyl groups), 2.89(m, 2H, C_3 protons), 3.37(m, 4H, CH_2-Ar)$_2$, 5.30(m, 3H, C_2 proton and 2H of two olefinic protons of two prenyl groups), 6.85(d, 2H, J=10 Hz, 3',5' protons), 7.36(d, 2H, J=10 Hz, 2',6' protons), 12.1(s, 1H, chelated OH).

II was oxidatively cyclised by treating with DDQ in dry toluene. Column chromatography of the reaction mixture gave two products A & B which were further purified by preparative TLC.

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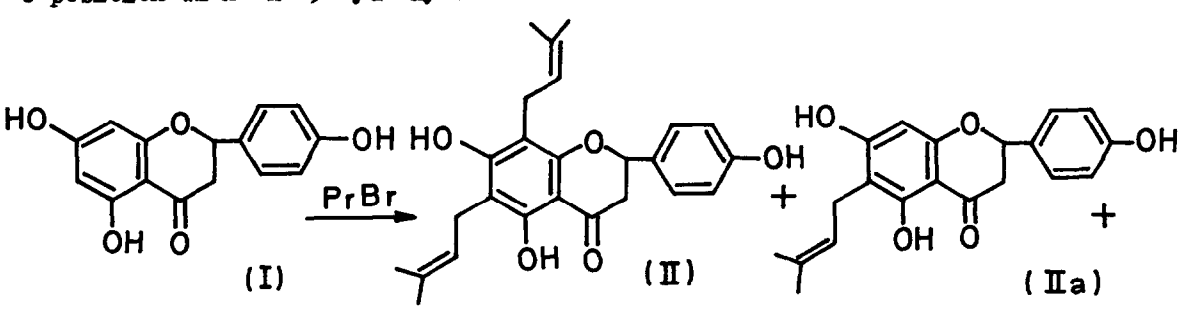
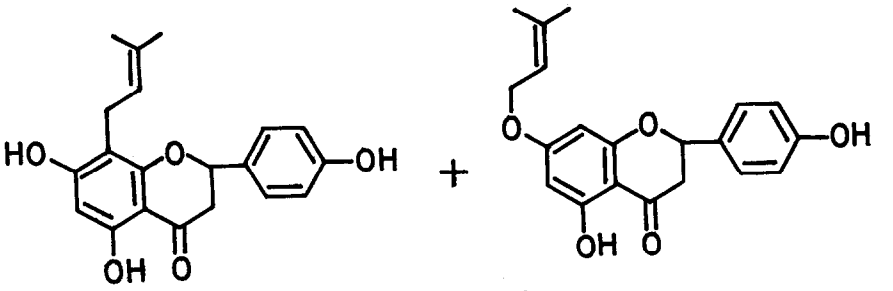
Compound **A** (8-prenyl 4',5-dihydroxy-2",2"-dimethyl pyrano(5",6",6,7)flavanone (III) separated from benzene - n-hexane mixture as pale yellow solid (50 mg), m.p. 112-13° (lit. 117-119°) (Found: C, 73.4; H, 6.7. $C_{25}H_{26}O_5$ requires C, 73.8; H, 6.4%). λ_{max}^{MeOH} 220, 275, 295sh, 300, 315 nm. ν_{max}^{KBr} 3250 (OH) and 1620(>C=O) cm^{-1}. NMR(δ, $CDCl_3$): 1.45(s, 6H, 2" gem dimethyl), 1.63(s, 6H, gem dimethyl of prenyl group), 2.86(m, 2H, two C_3 protons), 3.20(d, 2H, J=7.0 Hz, CH_2-Ar), 5.14(t, 1H, -CH= of prenyl group), 5.28(m, 1H, C_2-H), 5.50(d, 1H, J=10 Hz, 3"-H), 6.31(s, 4'-OH group), 6.65(d, J=10 Hz, 4"-H),6.85 (d, J=8.5 Hz, 3',5'-protons of B ring) and 7.30(d, J=8.5 Hz, 2',6'-protons), 12.3(s, 1H, chelated OH). It was identical (co-TLC and superimposable IR) with the natural sample of lupinifolin[1]. III (4 mg) was heated with formic acid. The product gave positive ferric reaction indicating the presence of free -OH group at 5-position and thus providing evidence that the prenyl group at position 6 was already involved in the formation of a chromene ring with -OH group at 7-position. Thus structure III could be assigned to A.

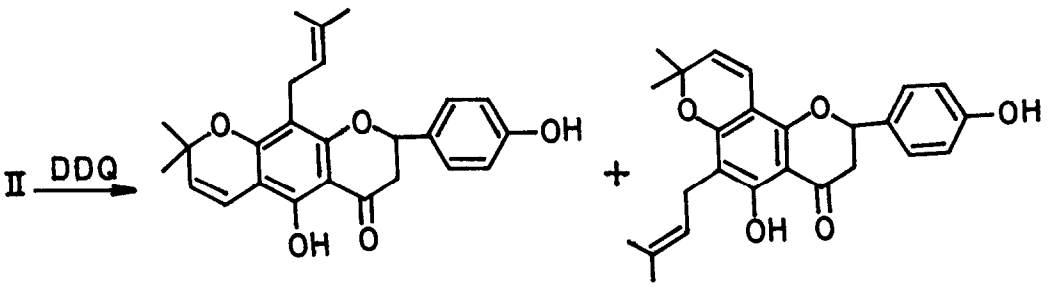
Compound B (6-prenyl-4',5-dihydroxy-(2",2"-dimethylpyrano-5",6",7,8)flavanone (IV) separated from benzene - n-hexane (40 mg) (Found: C, 73.5; H, 6.7. $C_{25}H_{26}O_5$ requires C, 73.8; H, 6.4%). λ_{max}^{MeOH} 220, 275, 295 nm. ν_{max}^{KBr} 3250(OH) and 1621(>C=O) cm^{-1}. NMR (δ, $CDCl_3$): 1.40(s, 6H, 2"-gem dimethyl), 1.64(s, 6H, gem dimethyl of prenyl group), 2.84(m, 2H, C_3-protons), 3.18(d, J=7.0 Hz, CH_2-Ar), 5.2(m, 1H, -CH= of prenyl group), 5.3(m, 1H, C_2-proton), 5.52(d, J=10 Hz, 3"-H), 6.3(s, 4'-OH group), 6.68(d, J=10 Hz, 4"-H), 6.86(d, J=8.5 Hz, 3',5' protons), 7.31(d, J=8.5, 2',6'-protons). Further confirmation of the structure (IV) for compound B was provided by its formic acid treatment. The negative ferric reaction of the product suggested the involvement of prenyl group at 6-position with the 5-hydroxyl.



(I) (II) (IIa)



(IIb) (IIc)



(III) (IV)

Condensation of naringenin (I) (3 g) with 2-methyl-but-3-en-2-ol (1.1 g)[3] in presence of boron trifluoride etherate in dry dioxan medium yielded a mixture which on column chromatography (silica gel) furnished P_1, P_2, P_3 as three main fractions.

Fraction P_1 (6-C-prenyl naringenin) was a syrupy liquid which failed to crystallise; positive ferric reaction (Found: C, 70.55; H, 5.82. $C_{20}H_{20}O_5$ requires C, 70.5; H, 5.8%). λ_{max}^{MeOH} 225, 290, 320sh nm; ν_{max}^{KBr} 1622 cm^{-1} (>C=O). NMR(δ, $CDCl_3$): 1.61(s, 6H, gem dimethyl), 2.88(m, 2H, C_3-protons), 3.12(d, 2H, $-CH_2-Ar$), 5.3(m, 2H, C_2-proton and 1H of one olefinic proton of one prenyl group), 6.13(s, 1H, C_8-protons), 6.85(d, 2H, J=10 Hz, 3',5'-protons), 7.35(d, 2H, J=10 Hz, 2',6' protons). P_1 (15 mg) was methylated at 7-position by dimethyl sulphate/K_2CO_3/acetone. Treatment of the product with formic acid gave a product different from the starting material (TLC). Its negative ferric reaction showed the involvement of 6-C-prenyl group with 5-hydroxy in cyclisation confirming the presence of prenyl group at 6-position in P_1. IIa was identical with P_1.

Fraction P_2 (8-C-prenyl naringenin) gave positive ferric reaction (Found: C, 70.6; H, 5.9. $C_{20}H_{20}O_5$ requires C, 70.5; H, 5.8%). λ_{max}^{MeOH} 225, 290, 320sh nm. ν_{max}^{KBr} 1624 cm^{-1} (>C=O). NMR(δ, $CDCl_3$) 1.6(s, 6H, gem dimethyl), 2.88(m, 2H, C_3 protons), 3.1(d, 2H, $-CH_2-Ar$), 5.3(m, 2H, C_2 proton and 1H of one olefinic proton of one prenyl group), 6.1(s, 1H, C_6-proton), 6.85(d, 2H, J=10 Hz, 3',5' protons), 7.35(d, 2H, J=10 Hz, 2',6'-protons). P_2 (15 mg) was methylated at 7-position by dimethyl sulphate/K_2CO_3/acetone. Treatment with formic acid did not cause cyclisation thus confirming the presence of prenyl group at 8 position in P_2. IIb was identical with P_2.

Fraction P_3 was identical with II.

7-Prenyloxy naringenin, obtained by partial C-prenylation of naringenin using one mole of prenyl bromide/K_2CO_3/acetone, crystallised from ethyl acetate - pet. ether as colourless needles m.p. 84-85°; positive ferric reaction (Found: C, 70.41; H, 5.5. $C_{20}H_{20}O_5$ requires C, 70.5; H, 5.8%). λ_{max}^{MeOH} 235, 295, 332sh nm. ν_{max}^{KBr} 1621 cm^{-1} (>C=O). NMR(δ, $CDCl_3$) 1.62(s, 6H, of $C(CH_3)_2$), 2.89(m, 2H, C_3- protons), 3.12(d, 2H, $-CH_2-Ar$), 4.48(d, J=7.5 Hz, 2H of $-O-CH_2$ group), 5.32(m, 2H, C_2-proton & olefinic proton of one prenyl group), 6.85(d, 2H, J=10 Hz, 3',5' protons), 7.36(d, 2H, J=10 Hz, 2',6' protons), 12.1(s, 1H, chelated OH). It was identical with IIc.

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