Synthesis of amoradicin

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Amoradicin 6, a constituent of the stems of Paranigyna griffithii (Rutaceae) has been synthesised following an unambiguous route. All the new products have been characterised on the basis of spectral data and microanalysis.

Chalcones constitute an important group of natural products and some of them possess a wide range of biological activities such as antibacterial1,4, antifungal5,7, anti-inflammatory8,9, anti-microbial10,13, anti-tumour14, anti-cancer15, prostaglandin binding16, and insect antifeedant17 activities. Waterman et al.18 isolated amoradicin from the stems of Paranigyna griffithii and formulated it as 5, 3', 4'-trihydroxy-7-methoxy-6,8-di-C-prenylflavone 6. The structure for amoradicin 6, was assigned on the basis of spectral data but no chemical synthetic proof was provided. In this note we describe the synthesis of 6 starting from phloroacetophenone. Methylation of phloroacetophenone using dimethyl sulphate/potassium carbonate/acetonitrile afforded 2, 6-dihydroxy-4-methoxyacetophenone19 1 which on nuclear prenylation20 gave 2,6-dihydroxy-4-methoxy-3,5-di-C-prenylflavone 2 and several other minor products (Scheme 1). Alkaline condensation of 2 and 3, 4-dihydroxybenzaldehyde gave 2',6',3',4-tetrahydroxy-4'-methoxy-3',5'-di-C-prenylchalcone 5, whose on treatment with NaOAc/EtOH furnished 6, which m.p. and spectral data agreed with those reported values6 for the natural sample. A direct comparison was not possible owing to non-availability of the authentic sample.

Experimental Section

Melting points were determined using an electrothermal melting point apparatus (Gallenkamp) and are uncorrected. IR spectra were recorded (KBr discs) on a Pye-Unicam SP3-300 IR spectrophotometer (v_max in cm⁻¹), ¹H NMR spectra on a Varian 300 MHz instrument in CDCl₃ with TMS as an internal standard (chemical shifts in δ, ppm); and UV spectra on Milton-Roy UV-visible spectrophotometer

Ultrspecck in methanol (λ_max in nm). TLC was performed using silica gel 60G. Satisfactory elemental analyses were obtained for all the compounds and structures are in accord with the UV, IR and ¹H NMR data. Mass spectra were recorded on Jeol-300 analytical mass spectrometer.

Nuclear prenylation of 1. Compound 1 (4.5 g) was added to a well cooled solution KOH (3.1 g) in absolute methanol (60 mL) and the solution treated with prenyl bromide (2.8 mL) slowly with shaking. After keeping the reaction mixture for about 40 hr at room temperature, it was diluted with cold water, acidified and extracted with ether, washed twice with water and dried over Na₂SO₄ and evaporated to dryness. The ether extract on silica gel (60-120 mesh) column chromatography using petrol (40-60°C), petrol-benzene-n-hexane (12:5:4), petrol-benzene-n-hexane (15:7:5) and petrol-benzene-n-hexane (5:1:3) as eluents gave compounds A-D as the major products and several other minor products.

Compound A: Obtained from column chromatography was further purified by preparative TLC over silica gel GF₂₅₄ using petrol (40-60°C) as developing solvent. It was identified (m m p, co-IR, co-TLC) as the starting material (0.18 g).

Compound B: It was purified by preparative TLC over silica gel GF₂₅₄ using petrol-benzene-n-hexane (12:5:4) as developing solvent to give 2 as a white semi-solid (1.5 g) which could not be crystallised from any solvent. Rf 0.71 (petrol-benzene-n-hexane; 12:5:4); (M* 318); UV: 228, 235, 250, 355 nm; IR: 3540, 2810, 2800, 2470, 1645, 1600, 1590, 1470, 1365, 1050, 998 cm⁻¹; ¹H NMR: 1.81 [s, J 2H , 12H , 3H ]; 2.41 (s, 3H, -OH x3). 2.15 (s, 3H, -OH x3), 3.57 (d, 4H, J=7Hz, -CH₂-CH=CH=CH₂), 3.98 (s, 3H, -OCH₃), 5.43 (t, 2H, J=7Hz, -CH₂-CH=CH=CH₂), 12.15 (s, 3H, -OH x3). It was identified as 2, 6-dihydroxy-4-methoxy-3,5-di-C-prenylacetophenone.

Compound C: Obtained from column was further purified by preparative TLC over silica gel GF₂₅₄ using petrol-benzene-n-hexane (15:7:5) as developing solvent to give 3 as a white needles (0.52 g), mp 43°C; Rf 0.59 (petrol-benzene-n-hexane; 15:7:5), (M* 250); UV: 229, 265, 350 nm; IR: 3520, 2110, 1640, 1605, 1595, 1470, 1365, 1270, 1050 cm⁻¹; ¹H NMR:
1.79 (s, 6H, \( \text{CH}_2 \)); 2.45 (s, 3H, \( \text{COCH}_3 \)); 3.55 (d, 2H, \( J=7 \text{Hz}, \text{CH}_1=\text{CH} \)); 4.00 (s, 3H, \( \text{OCH}_3 \)); 5.44 (t, 1H, \( J=7 \text{Hz}, \text{CH}_2=\text{CH} \)); 6.98 (s, 1H, H-5); 12.15 (s, 2H, -OH\( \times 2 \)). It was identified as 2,6-dihydroxy-4-methoxy-3-C-prenylacetophenone.

**Compound D:** It was purified by preparative TLC over silica gel GF\(_{254}\) using petrol-benzene-n-hexane (5:1:3) as developing solvent. It was crystallised from xylene as colourless needles (0.29 g), mp 36°C; R\(_f\) 0.41 (petrol-benzene-n-hexane; 5:1:3); (M\(^+\) 250); UV: 229, 265, 350 nm; IR: 3540, 2080, 1645, 1600, 1590, 1475, 1360, 1271, 1055 cm\(^{-1}\); \(^1\)H NMR: 1.77 (s, 6H, \( >\text{C(\text{CH}_3)3} \)); 2.44 (s, 3H, \( \text{COCH}_3 \)); 3.56 (d, 2H, \( J=7 \text{Hz}, \text{CH}_1=\text{CH} \)); 4.00 (s, 3H, \( \text{OCH}_3 \)); 5.43 (t, 1H, \( J=7 \text{Hz}, \text{CH}_2=\text{CH} \)); 6.43 (s, 1H, H-3); 12.15 (s, 2H, -OH\( \times 2 \)). It was identified as 2,6-dihydroxy-4-methoxy-3-C-prenylacetophenone.

**3', 4', 5-Trihydroxy-7-methoxy-6,8-di-C-prenylflavanone (6, amoradilicin).** To a solution of 5 (0.5 g) in ethanol (20 mL), NaOAc (0.6 g) was added. The reaction mixture was left at room temperature for 3 days. It was diluted with water and extracted with ethyl acetate. The ethyl acetate layer was dried over anhydrous Na\(_2\)SO\(_4\) and concentrated. The product was purified by preparative TLC over silica gel GF\(_{254}\) using benzene as developing solvent. It crystallized from methanol as colourless needles (0.218 g), mp 64°C (lit.\(^{19}\) mp, 60-64°C); (M\(^+\) 438); \(^1\)H NMR: 1.78 (s, 12H, \( >\text{C(\text{CH}_3)3} \)); 3.56 (d, 4H, \( J=7 \text{Hz}, \text{CH}_1=\text{CH} \)); 3.99 (s, 3H, \( \text{OCH}_3 \)); 5.46 (t, 2H, \( J=7 \text{Hz}, \text{CH}_1=\text{CH} \)); 7.48 (m, 4H, H-\( \alpha \), H-2', H-5' and H-6'); 8.01 (d, 1H, \( J=9 \text{Hz}, \text{H-\( \beta \}) \)); 8.78 (s, 1H, -OH); 13.01 (s, 3H, -OH\( \times 3 \)) (Found: C, 72.3; H, 6.7. C\(_{29}\)H\(_{30}\)O\(_6\) requires C, 72.5; H, 6.4%)

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