Synthesis of 6-prenylpyranoflavanones:
Total synthesis of (±)-maxima flavanone A

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First total synthesis of (±)-maxima flavanone A (1) and the synthes is of other 6-prenylpyranoflavanones 2 and 7 has been described from pyranacetophenone 10. The acetophenone 10 on reaction with prenylbromide in DMF solution, in presence of K₂CO₃ gives the prenyl ether 11 which on heating in N,N-dimethylaniline at 160-170 °C undergoes Claisen and Cope rearrangements providing the pyranacetophenone 12. Condensation of 12 with aryl aldehydes using methanolic KOH as base in the presence of CTAB gives the chalcones 13a-c, which on cyclisation using KF-Celite in refluxing methanol yield the angular pyranoflavanones 1, 2 and 7, respectively.

Several naturally occurring pyranoflavanones like maxima flavanone A 1, fulvinervin A 3, erythrigenaline 4, fleminone 6 and euchrene s a₉, a₁₅ and a₁₂ 5, 8 and 9 possess a prenyl substituent at C-6 position. Some 6-prenylflavanones are reported to have biological activities.

Though various methods are available for the synthesis of flavanones, there is only one method reported for the synthesis of pyranoflavanones, such as 3, which has a prenyl group at C-6 position. This method involves nuclear prenylation of 5,7-dihydroxyflavanone (naringenin) and provides a mixture of products. Therefore, there was a need for a convenient and general method for the synthesis of 6-prenylpyranoflavanones of this type 1-9.

Recently we have reported a short and high yielding method for the synthesis of 6-prenylcoumarins. The highlight of this synthesis is Claisen and Cope rearrangements to provide 6-prenylcoumarins. The presence of Wittig reagent further leads to Wittig reaction, followed by isomerization of double bond and cyclisation, all occurring in one step. In this paper we report a convenient approach for the synthesis of (±)-maxima flavanone A (1) and the related 6-prenylpyranoflavanones 2 and 7 (Scheme 1).

In our approach (cf. Scheme I), the prenylated pyranacetophenone 12 was obtained by Claisen and Cope rearrangements and then converted to the chalcone and finally to the flavanone. Thus, the prenyl ether 11 was obtained in 87% yield by the reaction of pyranacetophenone 10 with γ,γ-dimethylallyl bromide (prenyl bromide) in DMF solution in the presence of K₂CO₃ at room temperature. The prenyl ether 11 on heating in N, N-dimethylaniline solution at 160-170 °C underwent Claisen and Cope rearrangements to give the prenylated pyranacetophenone 12 in 75% yield. Condensation of 12 with benzaldehyde, anisaldehyde and 6-formyl-2,2-dimethylchromene, using KOH-MeOH in the presence of CTAB [cetyl(trimethyl)ammonium bromide] provided the chalcones 13a-c. These chalcones 13a-c on cyclization, using KF-Celite in refluxing methanol, gave (±)-maxima flavanone A (1), 4'-methoxymaxima flavanone A (2) and 5-deoxy-euchrene a₁₅ (7) in 62, 61 and 60% yields, respectively.

Experimental Section

General. All mps are uncorrected. ¹H NMR spectra were recorded on JEOL FX 90 Q, Bruker AC 200 and Varian GEMINI 300 MHz instruments in CDCl₃ using TMS as internal standard (chemical shifts in 8 ppm downfield from TMS, and coupling constants in Hz). IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrophotometer. Elemental analyses were performed on a Hosli’s rapid Carbon-Hydrogen analyzer. Hexane refers to light petroleum with boiling point in the range 40-60 °C.
Preparation of 6-acetyl-5-prenyloxy-2,2-dimethylchromene 11. A mixture of 6-acetyl-5-hydroxy-2,2-dimethylchromene 10 (2 g, 9 mmoles), anhydrous potassium carbonate (3 g, 22 mmoles) and prenyl bromide (3 mL, 26 mmoles) in N,N-dimethylformamide (15 mL) was stirred at room temperature for 12 hr. It was poured into ice-cold water (50 mL) and extracted with ether (3x15 mL). The ether layer was washed first with 2N NaOH (2x10 mL) and then with water. It was dried (Na2SO4) and evaporated to give an oily product which was purified by chromatography over silica gel using hexane-ethyl acetate (95:5) as an eluent to provide the prenyl ether 11 (2.3 g, 87%) as a pale yellow liquid. Anal. Calcd for C13H22O3: C, 75.49; H, 7.74%. Found: C, 75.33; H, 7.99%; IR (neat): 1672 (CO) cm⁻¹; ¹H NMR (90 MHz): 1.44 (6H, bs, 2 x CH₃), 1.61 (3H, s, CH₃), 1.75 (3H, s, CH₃), 2.6 (3H, s, -COCH₃), 4.37 (2H, d, J = 7.7 Hz, -OCH₂-), 5.4 (1H, m, -OCH₂CH₂-), 5.65 (1H, d, J = 10 Hz, 3-H), 6.58 (1H, d, J = 8 Hz, 8-H), 6.61 (1H, d, J = 10 Hz, 4-H), 7.51 (1H, d, J = 8 Hz 7-H).

Preparation of 6-acetyl-5-hydroxy-8-prenyl-2,2-dimethylchromene 12. A solution of acetoephone 11 (1 g, 4.5 mmoles) in N,N-dimethylformamide (10 mL) was heated at 160-170 °C under N₂ atmosphere for 4 hr. The reaction mixture was cooled, poured into ice-cold water (20 mL), acidified with dil. HCl and extracted with ether (3x10 mL). The combined ether layer was dried (Na2SO4) and evaporated to give a brown oily product which was chromatographed over silica gel using hexane-ethyl acetate (98:2) as eluent to give the chromene 12 (0.75 g, 75%) as a pale yellow liquid. Anal. Calcd for C13H22O3: C, 75.49; H, 7.74. Found: C, 75.37; H, 7.94%; IR (neat): 1643 (C=O) cm⁻¹; ¹H NMR (200 MHz) 1.46 (3H, s, CH₃), 1.49 (3H, s, CH₃), 1.75 (6H, s, 2 x CH₃), 2.54 (3H, s, -COCH₃), 3.19 (2H, d, J = 7.3 Hz, ArCH₂), 5.24 (1H, m, ArCH₂CH₂), 5.59 (1H, d, J = 10 Hz, 3-H), 6.73 (1H, d, J = 10 Hz, 4-H), 7.35 (1H, s, 7-H).
C, AnaL C a LCD for mp 121-123 NMR silica gelising hex an e - ethyl acetate (98:2) as eluent from hexane-ethyl acetate while 7 was obtained as a thick liquid. The flavanones 1 and 2 were obtained as solids which were recrystallized evaporated and the co oled and filtered. The retu xe d for 38-42 py r anochalcone (13a, 13b or 13c; 1 mmole) and flavanones 1,2 and 7. A mixture of an appropriate KF-C c lite

\[ \text{\(J = 15.5 \text{ Hz}, \quad \text{CH}_3\)} \] 

5.67 (lH, d, \(J = 10 \text{ Hz}\), \(\text{ArCH}=\text{CH}\), 7.00-7.25 (4H, m, 3xAr-H, -COCH=CH-), 7.65 (lH, d, J = 10 Hz, ArCH=CH-), 6.85 (lH, d, J = 8 Hz, Ar-H), 7.05 (1H, d, J = 2 Hz, Ar-H), 7.2 (1H, dd, J = 8.2 Hz, Ar-H), 7.62 (1H, s, Ar-H).

4'-Methoxy maxima flavanone A (2). Pyranochalcone 13b yielded the flavanone 2, yield 61%, mp 96-98 °C. Anal. Calcd for C_{30}H_{32}O_4: C, 77.2; H, 6.98. Found: C, 77.28; H, 7.05%. IR (Nujol): 1674 (C=O) cm\(^{-1}\). \(^1H\) NMR (300MHz): 1.43 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.72 (6H, s, 2xCH_3), 2.97 (1H, dd, \(J = 17 \text{ and } 3 \text{ Hz}, \text{-COCH}_2\)) 3.03 (1H, dd, \(J = 17 \text{ and } 13 \text{ Hz}, \text{-COCH}_2\)), 3.22 (2H, d, \(J = 7.3 \text{ Hz}, \text{ArCH}_2\)). 3.83 (3H, s, OMe), 5.25 (1H, t, ArCH_2CH=), 5.40 (1H, dd, \(J = 13 \text{ and } 3 \text{ Hz}, \text{-COCH}_2\)), 5.56 (1H, d, \(J = 10 \text{ Hz}, \text{ArCH}=\text{CH}\)), 6.63 (1H, d, \(J = 10 \text{ Hz}, \text{ArCH}=\text{CH}\)), 6.95 (2H, d, \(J = 8.8 \text{ Hz}, \text{Ar-H}\)), 7.4 (2H, d, \(J = 8.8 \text{ Hz, Ar-H}, 7.6 (1H, s, Ar-H).

5-Deoxy euchreneqa_{5}(7). Pyranochalcone 13c provided the flavanone 7 as a thick liquid, yield 60%. Anal. Calcd for C_{30}H_{32}O_4: C, 78.92; H, 7.06. Found: C, 79.01; H, 6.81%. IR (Nujol): 1679 (C=O) cm\(^{-1}\). \(^1H\) NMR (300MHz): 1.45 (12H, s, 3xCH_3), 1.72 (6H, s, 2xCH_3), 2.78 (1H, dd, \(J = 17 \text{ Hz, COCH}_2\)), 3.01 (1H, dd, \(J = 17 \text{ and } 13 \text{ Hz, COCH}_2\)), 3.24 (1H, d, \(J = 7.3 \text{ Hz, ArCH}_2\)), 5.27 (1H, t, ArCH_2CH=), 5.35 (1H, dd, \(J = 13 \text{ and } 3 \text{ Hz, COCH}_2\)), 5.55 (1H, d, \(J = 10 \text{ Hz, ArCH}=\text{CH}\)), 6.65 (1H, d, \(J = 10 \text{ Hz, ArCH}=\text{CH}\)), 6.95 (2H, d, \(J = 8.8 \text{ Hz, Ar-H}\)), 7.4 (2H, d, \(J = 8.8 \text{ Hz, Ar-H}, 7.6 (1H, s, Ar-H).

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