SHORT PAPER

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Synthesis of maritimin, a chromone from *Pancratium maritimum*

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The synthesis of maritimin (**1**), a chromone from *Pancratium maritimum* L., is described

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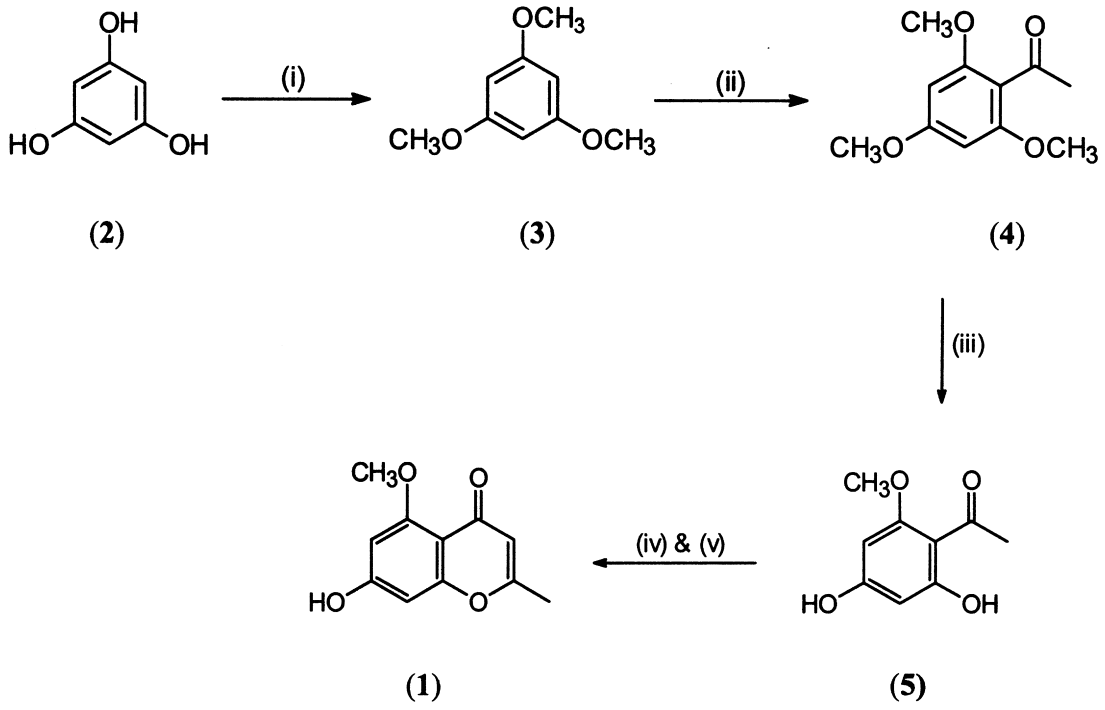
Oxygenated 2-methylchromones are widespread in nature.[1] The crude extracts of the plant-material containing such constituents are used in Indian folk medicine for a variety of ailments.[2] In a recent communication, Youssef *et al.*[3], reported the isolation and structure elucidation of a number of constituents from the ethanolic extract of the fresh flowering bulbs of *Pancratium maritimum* L (family Amaryllidaceae, subfamily Amaryllidoidae). Among these constituents was a new compound, designated as maritimin and shown by spectral analysis to be 7-hydroxy-5-methoxy-2-methylchromone (**1**). Since its synthesis has not been reported and the structure **1** was based only on spectral data, synthetic support to confirm the assigned structure seemed desirable. Herein, we report a short synthesis of maritimin (**1**) (Scheme 1).

The easily available starting material, phloroglucinol (**2**) was converted into its trimethyl ether (**3**), which on acylation[4] using $AcCl/AlCl_3$ furnished the crystalline acyltrimethyl ether (**4**). Partial demethylation of **4** employing the procedure reported by Gulati and Venkataraman[5] afforded 2,4-dihydroxy-6-methoxyacetophenone (**5**). Finally, **5** on reaction with Na and EtOAc followed by acid-catalysed cyclisation of the resulting β-diketone[6], gave a product which was found to be 7-hydroxy-5-methoxy-2-methylchromone (**1**). The melting point and spectral data (IR, ^1H NMR and MS) measured on our synthetic sample were in good agreement with the reported data on maritimin.[3] The ^{13}C NMR spectrum, not measured earlier on natural maritimin, has now been recorded on our synthetic sample and is fully consistent with the structure **1** (see experimental). This is the first report of the synthesis of maritimin.

Experimental

Melting points were determined by the capillary method and are uncorrected. Column chromatography was performed on silica gel 60–120 mesh size and TLC on precoated plastic sheets Polygram SIL G $_{uv\ 254}$ (Macherey Nagel & Co, Duren, Germany). IR spectra were recorded on a Shimadzu FTIR-8001 (KBr pellet). ^1H NMR and ^{13}C NMR spectra were measured on a Varian 300 MHz instrument and Bruker WM 300 MHz FT NMR spectrometer in $CDCl_3$ or DMSO-d_6 solution and chemical shifts were recorded in ppm units using $SiMe_4$



Scheme 1

Reagents and conditions: (i) DMS, acetone, K_2CO_3, reflux, (ii) CH_3COCl, anhydrous $AlCl_3$, –5°C to –10°C, (iii) anhydrous $AlCl_3$, chlorobenzene, reflux 1 h , (iv) Na, EtOAc, N_2 atmosphere, (v) MeOH, H_2SO_4, reflux 30 min.

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

as internal standard. Mass spectra were recorded on Jeol D-300 mass spectrometer at 70 eV. Petroleum ether refers to the fraction with b.p. 60–80°C.

1,3,5-Trimethoxybenzene **(3):** Anhydrous K_2CO_3 (11 g, 80 mmol) was added to a solution of 1,3,5-trihydroxybenzene (**2**, 3 g, 24 mmol) in dry acetone (22.5 ml). To this slurry was added dimethyl sulfate (7.8 ml, 80 mmol) while stirring with an overhead stirrer over a period of 1 h. The reaction mixture was then refluxed for 24 h, with simultaneous stirring. This was then cooled and filtered. The residual K_2CO_3 was washed with acetone and filtered. Evaporation of the solvent from the combined filtrate gave a brown solid. Chromatography on silica gel using petroleum ether : diethyl ether (9:1) gave a white solid. Recrystallisation from petroleum ether gave white needles of **3** (3.2 g, 80%) with m.p. 54°C (lit[7]. m.p. 54–55°C). IR $\nu/_{max}$ (KBr) 2900, 1630, 1615, 1475, 1450, 1210, 1200, 1160, 1075, 950 cm^{-1}.

2′,4′,6′-trimethoxyacetophenone **(4):** Anhydrous $AlCl_3$ (3.5 g) was added portionwise at –10°C to a solution of 1,3,5-trimethoxybenzene (**3**, 2.02 g, 12 mmol) in dichloromethane (150 ml). Then acetyl chloride (2 ml) was added dropwise maintaining the reaction temperature below –5°C. After stirring overnight, the mixture was poured into ice-water, and extracted with dichloromethane (3 × 40 ml). The combined organic layer was successively washed with saturated $NaHCO_3$ and brine, then dried over Na_2SO_4. Evaporation of the solvent gave a brown coloured residue which was further purified by silica gel column chromatography to give 2,4,6-trimethoxyacetophenone (**4**) as a light orange coloured solid (1.76 g, 70%) with m.p. 110°C (lit[5]. m.p. 110°C). IR $\nu/_{max}$ (KBr) 2900, 1700, 1620, 1600, 1475, 1450, 1415, 1275, 1210, 1175, 1125, 900 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.103 (s, 2 H, H-3, H-5), 3.80 (s, 3 H, OCH_3), 3.56 (s, 6 H, 2 × OCH_3), 2.45 (s, 3 H, CH_3); EIMS *m/z* (intensity %): 210.2 (M^+) (28), 195.1 ($M^+ - CH_3$) (100), 180.1 (8), 137 (8).

2′,4′-Dihydroxy-6-methoxyacetophenone **(5):** A mixture of 2′,4′,6′-trimethoxy-acetophenone (**4**, 1.5 g, 7.14 mmol), anhydrous $AlCl_3$ (3.5 g) and chlorobenzene (15 ml) was refluxed for 1 h. Chlorobenzene was then removed by steam distillation, and the residual solution cooled to give cream-coloured needles. Recrystallisation from ethanol gave **5** (0.5 g, 38.5%), m.p. 205°C (lit[5]. m.p. 205–207°C). IR $\nu/_{max}$ (KBr) 3450, 2900, 1645, 1620, 1610, 1475, 1450, 1280, 1210, 1160, 1110 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 13.78 (br s, exchangeable in D_2O, 1 H, –OH), 5.96 (d, *J* = 2.1 Hz, 1 H, H-5), 5.86 (d, *J* = 2.1 Hz, 1 H, H-3), 3.82 (s, 3 H, OCH_3), 2.52 (s, 3 H, CH_3). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 202.1 (C), 166.1 (C), 165.6 (C), 163.2 (C), 104 (C), 95.5 (CH), 91.2 (CH), 55.7 (OCH_3), 32.4 (CH_3); EIMS *m/z* (intensity %): 182.1 (M^+) (44), 167.1 ($M^+ - CH_3$) (100), 152.1 (10), 124.1 (8).

7-Hydroxy-5-methoxy-2-methylchromone **(*maritimin* 1):** A solution of **5** (0.1 g, 0.549 mmol) in dry ethyl acetate (1.2 ml) under N_2 atmosphere was added to pulverised sodium (0.12 g) with cooling. After 15 min, the reaction mixture was maintained at 0°C for 48 h. The excess ethyl acetate was removed under reduced pressure and the residue was treated with a mixture of crushed ice and HCl. The precipitated solid (β-diketone) was filtered, and dissolved in methanol containing a trace of sulfuric acid and heated under reflux for 30 min. The reaction mixture after cooling was diluted with water to give the brown coloured solid, which was further purified by silica gel column chromatography, eluent- petroleum ether : diethyl ether (4 : 1) to give a colourless crystalline solid (**1**, 0.018 g, 32 %) with m.p. 114°C (lit[3]. m.p. 112–113°C). IR $\nu/_{max}$ (KBr) 3450, 1665, 1610, 1565, 1200, 900 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.35 (d, *J* = 2.4 Hz, 1 H, H-8), 6.33 (d, *J* = 2.4 Hz, 1 H, H-6), 6.02 (s, 1 H, H-3), 3.84 (s, 3 H, OCH_3), 2.37 (s, 3 H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 180.5 (C), 167 (C), 163.3 (C), 160.8 (C), 158 (C), 108.7 (CH), 104.3 (C), 97.1 (CH), 94.9 (CH), 56.9 (OCH_3), 20.8 (CH_3); HRMS : found 206.0556, calculated for $C_{11}H_{10}O_4$: 206.0579; EIMS *m/z* (intensity %): 206 (M^+) (100), 178 (M^+ – CO) (16), 177(M^+ – [CO + H]) (90), 148 (30), 123 (20), 95 (30), 69 (40).

Further elution of the silica gel column with petroleum ether : diethyl ether (3 : 2) gave cream-coloured needles of recovered **5** (0.050 g).

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