Short Communication

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SYNTHESIS OF 3-METHOXY-4'-PRENYLOXY-FURANO (2'', 3'':7, 8) FLAVONE

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Flavonoids represent a group of phytochemicals exhibiting a wide range of biological activities such as anti-bacterial, anti-fungal, anti-inflammatory, antimicrobial, anti-cancer and insect antifeedant (Hodek *et al* 2002). A large number of natural products including flavonoids are being reported in the literature every year and their structures need to be confirmed by synthesis. In this paper, the synthesis of 3-methoxy-4'-prenyloxy-furano (2'',3'' :7,8) flavone (**8**) has been described starting from β-resacetophenone (Clarke 1955) (**1**), which may be used as synthetic markers. β-Resacetophenone (Clark 1955) (**1**) when refluxed with allyl bromide in presence of K_2CO_3 and acetone yielded 4-O-allylresacetophenone (Rangaswaqmi *et al* 1954) (**2**) which on Claisen migration gave 3-C-allylresacetophenone (Baker and Lothin 1935) (**3**).This was subjected to OsO_4/KIO_4 oxidation followed by orthophosphoric acid cyclization to 2-hydroxyfurano(2',3':4,3) acetophenone (Naik *et al* 1975) (**4**). p-Hydroxybenzaldehyde on treatment with prenyl bromide in the presence of K_2CO_3 and acetone gave 4-O-prenyloxybenzaldehyde (**5**). Alkaline condensation of **4** and **5** yield 2'-hydroxy-4-O-prenyloxy-furano(2'', 3'' :4', 3')chalcone (**6**). Compound **6** on treatment with H_2O_2 furnished 3-hydroxy-4'-O-prenyloxy-furano(2'', 3'' :7, 8)flavone (**7**) which upon methylation using dimethyl sulphate, K_2CO_3 and acetone afforded 3-methoxy-4'-O-prenyloxy-furano(2'', 3'' :7, 8) flavone (**8**).

Melting points were determined on an electrothermal melting point apparatus (Gallenkamp) and are uncorrected. IR spectra were recorded on KBr discs on a Pye-Unicam SP3-300 IR spectrophotometer (ν_{max} in cm^{-1}), ^{1}H-NMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) spectrophotometer in $CDCl_3$ with TMS as an internal standard (chemical shifts in δ values) and UV spectra were recorded on LKB 4053 Ultrospeck spectrophotometer in methanol (λ_{max} in nm). TLC was performed using silica gel GF_{254}. Satisfactory elemental analysis were obtained for all the compounds and structures are in accord with the UV, IR and ^{1}H-NMR data. Mass spectra were recorded on VG 7070E analytical mass spectrometer.

4-O-Allylresacetophenone (2). β-Resacetophenone (Clarke 1955) (10 g) in acetone (50 ml) was refluxed with allyl bromide (7.5 g) and anhydrous potassium carbonate (40 g) for 6 h. Inorganic salts were filtered off and washed with acetone. Acetone was removed by distillation. The residue was taken up in ether and extracted with 5% aq. Na_2CO_3 solution and then with 5% NaOH solution. Sodium hydroxide extract was acidified and again extracted with ether (2x50 ml), dried over anhydrous Na_2SO_4 and concentrated when a dark coloured oil (12 ml) was obtained, b.p. 156-157°C (9 mm) [Rangaswaqmi *et al* 1954, b.p. 156-157°C].

3-C-Allylresacetophenone (3). The above 4-O-allylresacetophenone (Rangaswaqmi *et al* 1954) was (4 g) heated in an oil-bath, cautiously. Rearrangement occurred at 180°C with evolution of heat and the test tube was raised for a few min. Then the temperature was maintained at 210-215°C for 2 h, when a pink coloured solid was obtained. The crude mixture was subjected to column chromatography over silica gel using benzene as eluent. Earlier fractions gave some oil and then pure 3-C-allylresacetophenone was obtained as colourless needles (1.3 g), m.p. 132-133°C (Baker and Lothin 1935, m.p. 131°C).

2-Hydroxy-furano(2',3':4,3)acetophenone (4). 3-C-Allylresacetophenone (Baker and Lothin 1935) (1 g) was dissolved in ethyl acetate (400 ml), an equal volume of water and osmium tetroxide (200 mg) was added. The mixture was stirred on a magnetic stirrer for 1.5 h during which period potassium periodate (6 g) was added in small quantities and the mixture was stirred for two more hours. The ethyl acetate layer was separated and the aqueous solution was further extracted with ethyl acetate (2x25 ml). The combined ethyl acetate extract was washed well with water, dried over anhydrous Na_2SO_4 and the solvent was distilled off. The residue obtained as dark coloured oil was heated on a water-bath with orthophosphoric acid (40 ml) for 20 min and then poured over crushed ice. The solid that separated was taken up in ether and the ether solution was washed successively with 5% Na_2CO_3 solution, water and dried (Na_2SO_4). The solvent was distilled off and the residue was taken up in benzene and passed through a column of neutral alumina when colourless flakes (230 mg) were obtained. m.p. 85°C (Naik *et al* 1975), m.p. 86°C); (M^+, 176); UV : 235, 275, 325; IR : 3440, 1630, 1585, 1500, 1440, 1375; ^{1}H-NMR: 2.45 (s, 3H, - $COCH_3$), 6.98 (d, 1H, J = 2 Hz, H-4'), 7.05 (d, 1H, J = 9 Hz, H-5), 7.55 (d, 1H, J = 2 Hz, H-5'), 7.65 (d, 1H, J = 9 Hz, H-6), 13.90 (s, 1H, - OH); [Anal. Calc. for $C_{10}H_8O_3$: C, 68.2 ; H, 4.5. Found: C, 67.9; H, 4.9%].

4-O-Prenyloxybenzaldehyde (5). A solution of p-hydroxybenzaldehyde (10 g) in acetone (50 ml) was refluxed with prenyl bromide (12.5 g) and anhydrous potassium carbonate (30 g) for 4 h. Acetone was distilled off and water was added to the residue. It was extracted with ether and ether solution was then extracted with 5% aq. NaOH. Aq. NaOH extract was

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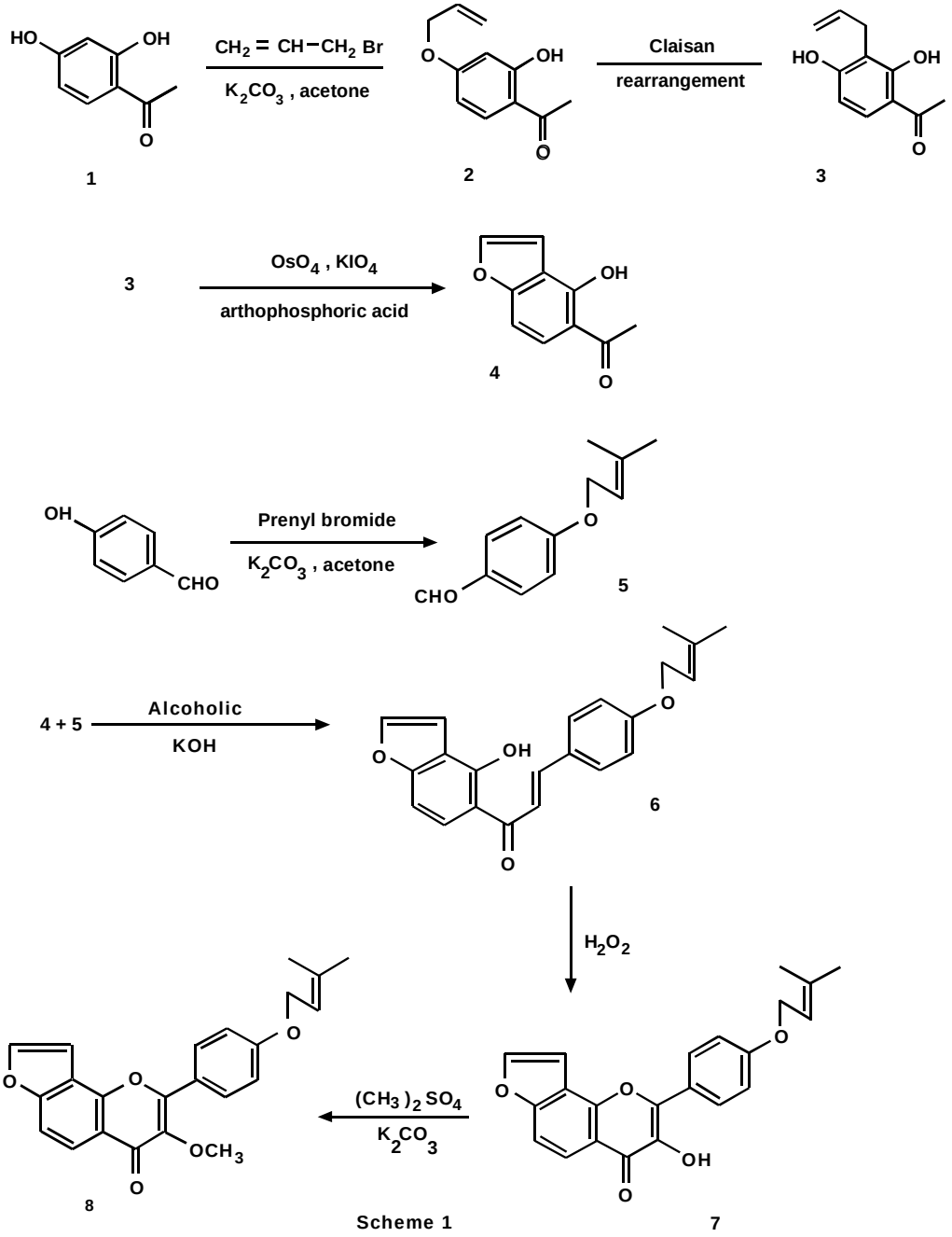
acidified and extracted with ether. Ether extract on column chromatography with petroleum spirit gave an oily liquid which on cooling gave colourless needles (6 g), m.p. 61°C; (M^+, 190); IR **:** 2980, 1640, 1500, 1375, 1330, 1250, 1190, 1130, 1065, 1000, 800, 605 cm^{-1}; ^{1}H-NMR : 1.72 [s, 6H, >C(CH_3)$_2$], 4.48 (d, 2H, J = 7 Hz, -O-C$\underline{H}_2$ - CH=), 5.43 (t, 1H, -O-CH_2 - C$\underline{H}$ =), 6.73 (d, 2H, J = 9 Hz, H-3 and 5), 7.55 (d, 1H, J = 9 Hz, H-2 and H-6), 9.40 (s, 1H, - CHO); [Anal. Calc. for $C_{12}H_{14}O_2$: C, 75.7 ; H, 7.4 . Found : C, 75.9; H, 7.5%].

*2'-Hydroxy-4-prenyloxy-furano(2",3":4',3') chalcone (**6**).* A mixture of 2-hydroxy-furano(2',3':4,3) acetophenone (**4**, 1 g) and 4-prenyloxybenzaldehyde (**5**, 0.824 g) in ethanolic solution of KOH (50%, 10 ml) was kept at room temperature for about 75 h. The reaction mixture was diluted with ice-cold water, acidified with cold dil. HCl and extracted with ether. The ether layer was washed with water, dried over anhydrous Na_2SO_4 and evaporated to dryness. It was crystallized from benzene-petroleum spirit as yellow needles (400 mg), m.p. 102-104°C; (M^+, 348); R_f 0.64 (benzene-acetone-ethyl acetate ; 4:9:1); UV: 250, 275, 320 ; IR : 3450, 1645, 1600, 1590, 1470, 1420, 1375, 1325; ^{1}H-NMR : 1.74 [s, 6H, >C(CH_3)$_2$], 4.42 (d, 2H, J = 7 Hz, -O - C$\underline{H}_2$-CH =), 5.51(t, 1H, - O- CH_2- C$\underline{H}$ =), 6.79



Scheme 1

(d, 2H, J = 9 Hz, H-3 and 5), 6.99 (d, 2H, J = 9Hz, H-5' and H-6'), 7.18 (d, 1H, J = 2 Hz, H-4"), 7.43 (d, 1H, J = 9Hz, H-α), 7.58 (d, 1H, J = 9 Hz, H-2 and H - 6), 7.81 (d, 1H, J = 2Hz, H-5"), 8.03 (d, 1H, J = 9 Hz, Hβ), 12.71 (s, 1H, - OH); [Anal. Calc. for $C_{22}H_{20}O_4$: C, 75.8 ; H, 5.7 .Found: C, 75.9 ; H, 5.8%].

3-Hydroxy-4'-prenyloxy-furano(2",3":7,8) flavone (7). To the above hydroxychalcone (**6**, 1 g) in pyridine (10 ml) and NaOH (20%, in 20 ml) kept at 60 - 70°C. H_2O_2 (30%, 30 ml) was added with stirring during 15 min. The reaction mixture was acidified 20 min and the solid that separated was filtered. The solid was dissolved in benzene and crystallised from petroleum ether as yellow needles (0.34g) , m.p. 124-127°C ; (M^+, 362) ; R_f 0.74 (benzene-acetone-n-hexane: 4:3:1) ; UV: 225, 255, 355 ; IR : 3470, 2980, 2875, 1643, 1595, 1510, 1472, 1375, 1365 cm^{-1} ; ^{1}H-NMR: 1.69 [s, 6H, ›C(CH_3)$_2$], 4.44 (d, 2H, J = 7 Hz, - O - C<u>H</u>$_2$- CH =), 5.54 (t, 1H, - O- CH_2- C<u>H</u> =), 6.72 (d, 2H, J = 9 Hz, H-3 and 5), 6.95 (d, 2H, J = 9Hz, H-5' and H-6'), 7.12 (d, 1H, J = 2 Hz, H-4"), 7.58 (d, 1H, J = 9 Hz, H-2 and H-6), 7.81 (d, 1H, J = 2 Hz, H-5"), 13.21 (s, 1H, - OH); [Anal. Calc. for $C_{22}H_{18}O_5$: C, 72.9 ; H, 4.9 .Found: C, 72.5 ; H, 4.5%].

3-Methoxy-4'-prenyloxy-furano(2",3":7,8) flavone (8). A mixture of **7** (1.40g), dimethyl sulphate (0.228g) and anhydrous K_2CO_3 (10g) in acetone (25 ml) was refluxed for 2 h. Acetone was removed by distillation, water was added to the residue and extracted with ether. The ether layer was washed with water, dried over anhydrous Na_2SO_4 and evaporated to dryness. The product purified by preparative TLC over silica gel GF_{254} using methanol-chloroform (10:1) as developing solvent. It was crystallized from methanol to give yellow crystals (0.68g), m.p 147 - 149°C ; R_f 0.66 (methanol-chloroform; 10: 1), (M^+, 376), UV : 232, 255, 364; IR : 1645, 1605, 1590, 1470, 1372, 1365, 1147 cm^{-1}; ^{1}HNMR : 1.71 [s, 6H, ›C(CH_3)$_2$], 3.98 (s, 3H, - OCH_3), 4.41 (d, 2H, J = 7 Hz, - O- C<u>H</u>$_2$- CH =), 5.55(t, 1H, - O- CH_2- C<u>H</u> =), 6.73 (d, 2H, J = 9 Hz, H-3 and 5), 6.93 (d, 2H, J = 9Hz, H-5' and H-6'), 7.15 (d, 1H, J = 2 Hz, H-4"), 7.59 (d, 1H, J = 9 Hz, H-2 and H-6), 7.84 (d, 1H, J = 2Hz, H-5"). [Anal. Calc. for $C_{23}H_{20}O_5$: C, 73.4; H, 5.3 .Found: C, 73.6 ; H, 5.5%].

The compounds **1** (β-resacetophenone), **2** (4-O-allylresacetophenone), **3** (3-C-allylresacetophenone) and **4** (2-hydroxyfurano (2', 3':4,3) have been prepared by following literature procedures (Clarke 1955; Rangaswaqmi *et a1* 1954; Baker and Lothin 1935; Niak *et al* 1975). The formation of these products has been confirmed by comparing their melting points with the reported values (Clarke 1955; Rangaswaqmi *et a1* 1954; Baker and Lothin 1935; Niak *et al* 1975). p-Hydroxybenzaldehyde on treatment with prenyl bromide in the presence of K_2CO_3 and acetone gave 4-O-prenyloxybenzaldehyde **5**. The formation of which was ascertained by spectral studies. IR spectrum of **5** showed 1640 cm^{-1} indicating the presence of keto group in conjugation. The compound **4** on cross-aldol condensation with **5** afforded the compound **6** after dehydration of the initial product. The IR spectrum of compound **6** showed absorption frequencies at 3450, 1645 cm^{-1} indicating the presence of a hydroxyl, a conjugated carbonyl groups and the absorption peaks at 1600 and 1590 cm^{-1} .This indicated the presence of unsymmetric ethylenic double bond and aromatic rings respectively. The singlet for methyl protons of acetyl group disappeared while two new doublets at δ7.43 and 8.03 appeared showing the presence of two vinylic protons (α and β protons). The elemental analysis for C and H showed satisfactory results (within + 0.4%). The cyclized product **7** was obtained by H_2O_2/pyridine/NaOH treatment of its precusor **6**. The formation of **7** was confirmed by comparing its spectral data and elemental analysis. IR spectra of compound **7** showed 3470 cm^{-1} (phenolic - OH), 1643 cm^{-1} (C=O) and 1595 cm^{-1} (double bond/ aromatic ring). In the ^{1}H›NMR spectrum two doublets at δ7.43 and 8.03 for vinylic protons disappeared. The title compound **8** was finally obtained by methylation of its precursor.

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***Key words*:** Synthesis, Chalcone, Flavone

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