Fast synthesis of some flavones under microwave irradiation^ψ

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Manuscript received 8 June 2005, revised 7 February 2006, accepted 10 May 2006

Abstract : Reactions under microwave irradiation occur under solvent free conditions. Such reactions occur in much shorter time than the usual ones. Fast synthesis of flavone from *o*-hydroxyacetophenone has been achieved in three steps under microwave irradiation.

Keywords : Flavone, microwave irradiation.

Some flavones have been synthesised by Baker-Venkataraman method under microwave irradiation. MW irradiation is an efficient and environmentally-benign method to activate various organic transformations to afford products in higher yields in shorter reaction periods and involving a very small amount of solvent^{1,2}.

Fast synthesis of flavones (**4a-d**) from *o*-hydroxyacetophenones has been achieved by us in three steps under microwave irradiation according to Scheme 1.

Results and discussion

The literature method³ of benzoylation of *o*-hydroxyacetophenone (**1a**) uses pyridine as base and the reaction mixture requires pouring into large volume of hydrochloric acid to get the benzoyl derivative precipitated. However, benzoylation has been achieved in step 1 of the Scheme 1 by simply shaking (**1**) with sodium hydroxide solution (and benzoyl chloride) without the need to pour the reaction mixture into hydrochloric acid. Hence, the use of both pyridine and hydrochloric acid has been avoided. In step 2, methanol in very small volume was used instead of pyridine in large volume according to the literature method³. Use of methanol instead of pyridine obviates the disadvantages of the use of the latter. In the step 3, microwave irradiation for only 3 min was required instead of 1 h of heating under normal heating. The yield in each step is also increased considerably.

The method reported here leads to a notable improvement in reaction conditions for flavone synthesis : the reaction time is reduced to only a few minutes in the

third step by using microwave dielectric heating, yield is improved, and the procedure is simplified by doing away with the large volume of pyridine.

Experimental

Reactions were carried out under atmospheric pressure in an open vessel adapted to a microwave oven. Compounds were identified by melting points which were found to be in good agreement with literature data. Flavones (**4a-d**) were also identified by IR, ¹H NMR and mass spectra.

M.ps. were taken in open capillaries and are uncorrected. Purity of the compound was checked by TLC. IR spectra were recorded on Perkin-Elmer 157 spectrometer in KBr. ¹H NMR spectra were recorded in CDCl₃ on a Bruker WM 400 MHz spectrometer, using TMS as an internal reference. Mass spectra were measured on Jeol JMS-300 spectrometer at 70 eV.

o-Benzoyloxyacetophenones (**2a-d**). *General procedure*: 0.025 mol of *o*-hydroxyacetophenone (**1a-d**) was suspended in 40 ml of 2 N NaOH solution in a well-corked conical flask followed by the addition of 4.9 g (4 ml, 0.035 mol) of benzoyl chloride with constant shaking for about 20 min. The solid benzoyl derivative (**2a-d**) was filtered off, washed with 5 ml of ice-cold methanol and then with 5 ml of water and recrystallised from methanol.

2a : Yield 80%, m.p. 87–88°

2b : Yield 75%, m.p. 102–103°

^ψPaper presented at 41st Annual Convention of Chemists, 2004 held at University of Delhi, Delhi, India.

2c : Yield 78%, m.p. 98–99°

2d : Yield 76%, m.p. 96–97°

o-Hydroxydibenzoylmethanes (**3a-d**). *General procedure* : 5 ml of CH₃OH was added to *o*-benzoyloxyacetophenone (**2a-d**) in a flask and the mixture heated to 50° to dissolve the later. To this solution was added with stirring 1.7 g (0.03 mol) of potassium hydroxide which had been powdered rapidly in a mortar

1a R₁ = H, R₂ = H, R₃ = H

1b R₁ = CH₃, R₂ = H, R₃ = H

1c R₁ = H, R₂ = CH₃, R₃ = H

1d R₁ = H, R₂ = H, R₃ = CH₃

4a R₁ = H, R₂ = H, R₃ = H

4b R₁ = CH₃, R₂ = H, R₃ = H

4c R₁ = H, R₂ = CH₃, R₃ = H

4d R₁ = H, R₂ = H, R₃ = CH₃

Scheme 1

preheated in an oven at 100°. Stirring was continued for 15 min resulting in the separation of the yellow potassium salt of the product. The reaction mixture was cooled to room temperature and acidified by adding with stirring 25 ml of 10 percent aqueous acetic acid. The pale yellow precipitate so obtained was dried and recrystallised from

methanol.

3a : Yield 83%, m.p. 120–121°

3b : Yield 76%, m.p. 138–139°

3c : Yield 80%, m.p. 130–131°

3d : Yield 78%, m.p. 125–126°

Flavones (4a-d). *General procedure* : 20 ml of glacial acetic acid was added to *o*-hydroxydibenzoylmethane (**3a-d**) (0.015 mol) taken in a flask followed by the addition of 1 ml of concentrated sulphuric acid with shaking. The mixture was irradiated with microwaves for 3 min at 40% (320 W) level in a Kenstar OM-20 ESP (800 W) unmodified domestic oven operating at 2450 MHz. The reaction mixture was poured with stirring on to about 100 g of crushed ice. The separated flavones (**4a-d**) were filtered off, washed with water until the washings were no longer acidic and dried. The crude compounds were recrystallised from appropriate solvents.

Flavone (4a) : White needles from light petroleum (b.p. 60–80°), yield 95%, m.p. 97–98° (lit.³ 98°) (Found : C, 81.12; H, 4.66; O, 14.38. C₁₅H₁₀O₂ requires : C, 81.08; H, 4.50; O, 14.41%); IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$ 1660 (C=O), 1610, 1382, 1312, 770; ¹H NMR (δ_{H}) (CDCl₃, TMS) 6.7 (3H, s), 7.1–7.2 (Ar 5-, 6-, 7-, 8-H, m), 7.5 (Ar 3'-, 4'- and 5'-H, m), 7.8 (Ar 2'-H and 6'-H, m); MS (m/z) 222 (M⁺, 100), 194 (M⁺-CO), 120, 102.

8-Methylflavone (4b) : White needles from EtOH, yield 88%, m.p. 169–170° (lit.⁴ 170°) (Found : C, 81.28; H, 5.02; O, 13.61. C₁₆H₁₂O₂ requires : C, 81.35; H, 5.08; O, 13.55%); IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$ 1658 (C=O), 1607, 1379, 1310, 768; ¹H NMR (δ_{H}) (CDCl₃, TMS) 2.5 (3H, s, Ar-CH₃), 6.7 (3H, s), 7.2–7.3 (Ar 5-, 6-, 7-H, m), 7.5 (Ar 3'-, 4'- and 5'-H, m), 7.8 (Ar 2'-H and 6'-H, m); MS (m/z) 236 (M⁺, 100), 208 (M⁺-CO), 134, 102.

7-Methylflavone (4c) : Yellow prisms from EtOH, yield 90%, m.p. 119–120° (lit.⁴ 120°) (Found : C, 81.38; H, 5.06; O, 13.53. C₁₆H₁₂O₂ requires : C, 81.35; H, 5.08; O, 13.55%); IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$ 1657 (C=O), 1606, 1379, 1308, 769; ¹H NMR (δ_{H}) (CDCl₃, TMS) 2.4 (3H, s, Ar-CH₃), 6.6 (3H, s), 7.2–7.3 (Ar 5-, 6-, 8-H, m), 7.4 (Ar 3'-, 4'- and 5'-H, m), 7.7 (Ar 2'-H and 6'-H, m); MS (m/z) 236 (M⁺, 100), 208 (M⁺-CO), 134, 102.

6-Methylflavone (4d) : Needles from light petroleum (b.p. 60–80°), yield 92%, m.p. 122–123° (lit.⁴ 122–123°)

Note

(Found : C, 81.32; H, 5.11; O, 13.53. $C_{16}H_{12}O_2$ requires : C, 81.35; H, 5.08; O, 13.55%); IR (KBr) $\nu_{\max}/\text{cm}^{-1}$ 1655 (C=O), 1608, 1378, 1310, 768; ^1H NMR (δ_{H}) (CDCl_3 , TMS) 2.3 (3H, s, Ar- CH_3), 6.7 (3-H, s), 7.1–7.2 (Ar 5-, 7-, 8-H, m), 7.5 (Ar 3'-, 4'- and 5'-H, m), 7.8 (Ar 2'-H and 6'-H, m); MS (m/z) 236 (M^+ , 100), 208 ($\text{M}^+ - \text{CO}$), 134, 102.

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