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Eco-friendly and simple synthesis of some non-natural flavones through chalcones

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ABSTRACT

A distinctive feature of polyphenolics is the possession of biological properties such as antioxidant and antimicrobial activities. Simple synthesis and study about such important class of compounds and their analogs are very important to enhance the understanding of their role in human health and diseases. Accordingly, a series of chalcones (2a-f) have been synthesized by Claisen-Schmidt condensation reaction with required acetophenones and aromatic aldehydes in high yields. The conversion of chalcones to the corresponding flavones (1a-g) taking minimal amount of dimethyl sulfoxide with iodine in presence of sulfuric acid was carried out under microwave conditions in high yields.

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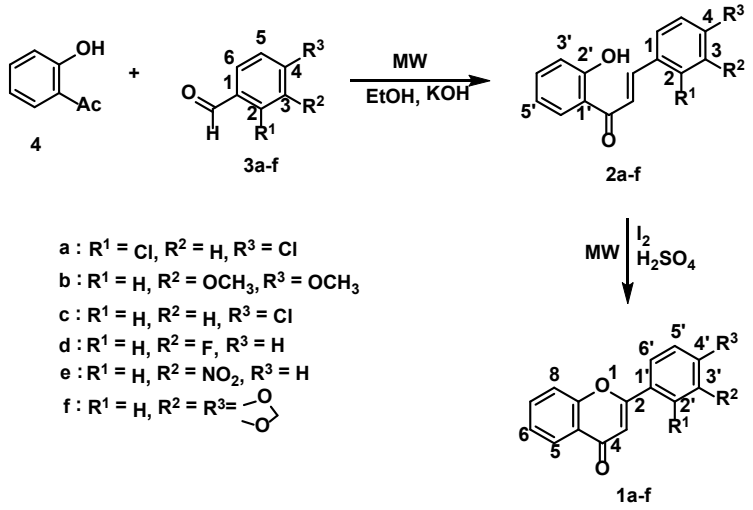
1. Introduction

The chromone ring system, 1-benzopyran-4-one, is the core fragment in flavonoids, such as flavones, flavonols and isoflavones [1]. From a chemical perspective, flavonoids are phenolic compounds that comprise of two benzene rings (A and B) attached with an oxygen-containing heterocyclic benzopyran ring (C) [2,3]. In both rings, the structural difference comes from the various oxidation levels and similarly from the number as well as substituents complexity [4,5]. Beneficial effects of flavonoids on human health have gained increasing interest among researchers over the last few years. Nonetheless, flavonoids have been shown to possess remarkable physiological activities in mammalian system [6,7]. Recently, researches on flavonoids have extensively been reported from the dietary sources, because of its sign of versatile health benefits through epidemiological findings [8]. From the bioactivity claims in the literature, flavonoids are considered to be one of the widely studied natural compounds [9]. Therefore, in the field of anti-infective, flavonoids have been reported to display antibacterial, antiviral, antiprotozoan and antifungal properties [10,11]. Moreover, chalcones, flavones, flavanones, flavonols, and flavan-3-ols are the most effective flavonoids against bacterial infections on suspended cells [12,13].

Lately, there has been a significant research concern in the development of polyphenolics and related compounds as important biomolecules, which is presently observed in the field of medicinal organic chemistry. Above observations clarify that, the synthesis and applications of flavones and their related compounds emerge as valuable and versatile class of compounds. In this regards, the nucleophilic reaction mode of carbonyl moieties at the β-position of different chalcones proved to be very important in the field of synthetic organic chemistry. Over the past two decades, the outstanding research efforts for organic syntheses using microwave (MW) irradiation technique has gained much attention [14-16].



Scheme 1

Because microwave (MW) technique not only reduces the undesirable by-products formation but also it decreases the demand for solvents to a lowest volume or even without the use of solvents [15,16].

Note worthily, chemical transformations under MW-irradiation with minimum or solvent-free condition has been a recommended tool by Green Chemistry [17]. Having in view these aspects, we focused on the design of microwave assisted syntheses and characterizations of numerous non-natural chalcones and their transformations to flavones using the mixture of iodine and sulfuric acid under minimal solvent condition.

2. Experimental

2.1. General

The melting points measured on a Fisher-John's electrothermal melting point apparatus by thin disc method were uncorrected. The ^{1}H NMR spectra were obtained with an Bruker AVANCE NMR spectrometer (400 MHz) using an internal standard of tetramethylsilane (TMS). The IR spectra were recorded on (FT-IR-plus/Shimadzu) spectrophotometer using KBr pellets. Elemental analyses were carried out on the Vario EL Cube V2.0.7 elemental analyzer. Column chromatography and thin-layer chromatography (TLC) were performed with Kieselgel 60G_{254} and Kieselgel 60 (70-230 mesh) (Merck). A microwave oven (ranging 0-650 W at 2.45 GHz, temperature range 60-250 °C) modified by fitting with a condenser unit, was employed as reaction apparatus and the temperature gradient was taken at 2-5 °C/sec.

2.2. General procedure for the synthesis of compound 2a-f

An equimolar mixture of 2-hydroxyacetophenone and substituted benzaldehyde was prepared in a round bottom flask. Afterward, this mixture was dissolved in minimal volume (~15 mL) of an alcoholic 30% KOH solution added dropwise with stirring. The obtained solution was exposed to MW irradiation at 60 °C (except **2e**, 40 °C) for 5-7 min, and monitored by TLC to complete the reaction. The reaction mixture was neutralized with 10% HCl followed by extraction with ethyl acetate. Afterward, the solvent was removed under reduced pressure to give a semisolid mass of 2'-hydroxychalcone, which was purified by recrystallization from a mixture of ethyl acetate:petroleum ether (1:4, *v*:*v*) or chloroform:petroleum ether (3:5, *v*:*v*) or using silica gel column chromatography (Scheme 1).

2'-Hydroxy-2,4-dichlorochalcone (**2a**): Color: Yellow crystalline solid. Yield: 74% (1.85 g). M.p.: 169-170 °C. FT-IR (KBr, ν, cm^{-1}): 1581 (C=C), 1697 (C=O), 3052 (C-H, aromatic), 3525 (OH) (br, alcohol). ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 6.96 (m, 1H, C5′-H), 7.05 (d, 1H, *J* = 8.2 Hz, C3′-H), 7.33 (dd, 1H, *J* = 6.8 Hz and 2 Hz, C5-H), 7.49 (d, 1H, *J* = 2 Hz, C3-H), 7.52 (m, 1H, C4′-H), 7.63 (d, 1H, *J* = 12.8 Hz, Ha), 7.71 (d, 1H, *J* = 7.2 Hz, C6-H), 8.9 (dd, 1H, *J* = 6.5 Hz and 2 Hz, C6′-H), 8.23 (d, 1H, *J* = 12.8 Hz, Hb), 13.41 (s, 1H, OH). Anal. calcd. for $C_{15}H_{10}Cl_2O_2$: C, 61.46; H, 3.44. Found: C, 60.98; H, 3.34%.

2'-Hydroxy-3,4-dimethoxychalcone (**2b**): Color: Deep orange crystalline solid. Yield: 86% (0.912 g). M.p.: 108-110 °C. FT-IR (KBr, ν, cm^{-1}): 1599 (C=C), 1692 (C=O), 2871, 2931 (C-H, aliphatic), 3525 (OH) (br, alcohol). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 3.97 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.96 (m, 2H, C3′-H and C5′-H), 7.05 (d, 1H, *J* = 8.4 Hz, C5-H), 7.18 (d, 1H, *J* = 1.5 Hz, C2-H), 7.28 (dd, 1H, *J* = 7.3 Hz and 1.5 Hz, C6-H), 7.53 (m, 1H, C4′-H), 7.54 (d, 1H, *J* = 15.3 Hz, H_a), 7.88 (d, 1H, *J* = 15.3 Hz, H_b), 7.96 (dd, 1H, *J* = 9.6 Hz, C6′-H), 13.33 (s, 1H, OH). Anal. calcd. for $C_{17}H_{16}O_4$: C, 71.82; H, 5.65. Found: C, 70.12; H, 5.26%.

2'-Hydroxy-4-chlorochalcone (**2c**): Color: Bright yellow crystalline solid. Yield: 86.9% (1.85 g). M.p.: 152-154 °C. FT-IR (KBr, ν, cm^{-1}): 1564 (C=C), 1687 (C=O), 3548 (OH) (br, alcohol). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 12.76 (s, 1H, C2′-H), 6.9-7.9 (m, 4H, C3′-6′-H, 4× Ar-H), 7.43 (dd, 2H, J_o = 8.53Hz and J_m = 2Hz, C3,5-H), 7.68 (d, 1H, *J* = 15.7 Hz, =C-H), 6.90 (dd, 1H, J_o = 8.53 Hz and J_m = 2Hz, C2,6-H), 7.76 (d, 1H, *J* = 15.7 Hz, = C-H), 13.29 (s, 1H, OH). Anal. calcd. for $C_{15}H_{11}ClO_2$: C, 69.64; H, 4.28. Found: C, 68.98; H, 4.04%.

2'-Hydroxy-3-fluorochalcone (**2d**): Color: Yellow crystalline solid. Yield: 83% (1.67 g). M.p.: 87-89 °C. FT-IR (KBr, ν, cm^{-1}): 1605 (C=C), 1700 (C=O), 3510 (OH) (br, alcohol). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 6.97 (t, 1H, *J* = 6.5 Hz and *J* = 7.2 Hz, C5-H), 7.05 (dd, 1H, *J* = 8 Hz and 1.5 Hz, C4-H), 7.15 (m, 1H, C3′-H), 7.37 (d, 1H, *J* = 8.9 Hz, C6-H), 7.41 (s, 1H, OH), 7.44 (m, 1H, C2-H), 7.45 (m, 1H, C5′-H), 7.53 (m, 1H, C4′-H), 7.65 (d, 1H, *J* = 15.3 Hz, H_a), 7.78 (d, 1H, *J* = 15.3 Hz, H_b), 7.92 (dd, 1H, *J* = 7.0 Hz and *J* = 1.5 Hz, C6′-H). Anal. calcd. for $C_{15}H_{11}FO_2$: C, 74.37; H, 4.58. Found: C, 74.19; H, 4.30%.

2'-Hydroxy-3-nitrochalcone (**2e**): Color: Yellow crystalline solid. Yield: 82% (1.53 g). M.p.: 169-170 °C. FT-IR (KBr, ν, cm^{-1}): 1589 (C=C), 1697 (C=O), 1437 (N=O), 3505 (OH) (br, alcohol). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 6.98 (t, 1H, *J* = 8

Hz and *J* = 7.5 Hz, C5′-H), 7.06 (dd, 1H, *J* = 8.4 Hz and 1.6 Hz, C3′-H), 7.54 (m, 1H, C4′-H), 7.56 (m, 1H, C6-H), 7.65 (t, 1H, *J* = 8.5 Hz and *J* = 8.1 Hz, C5-H), 7.87 (d, 1H, *J* = 12.0 Hz, H_a), 7.93 (d, 1H, *J* = 12.0 Hz, H_b), 7.95 (s, 1H, C6-H), 8.30 (d, 1H, *J* = 6.8 Hz, C6′-H), 8.57 (s, 1H, C2-H), 8.57 (s, 1H, OH). Anal. calcd. for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12. Found: C, 66.58; H, 3.96%.

2′-Hydroxy-3,4-methylenedioxychalcone (**2f**): Color: Pale yellow crystalline solid. Yield: 82% (1.53 g). M.p.: 121-122 °C. FT-IR (KBr, ν, cm^{-1}): 1580 (C=C), 1694 (C=O), 2777, 2910 (O-CH-O), 3550 (OH) (br, alcohol). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 5.75 (s, 2H, O-CH_2-O), 6.65 (d, 1H, *J* = 8.5 Hz, C5-H), 6.77 (d, 1H, *J* = 8.5 Hz, C6-H), 6.81 (s, 1H, C2-H), 7.79-7.38 (m, 4H, Ar-H), 7.68 (d, 1H, *J* = 15.0 Hz, H, vinylic proton), 7.96 (d, 1H, *J* = 15.0 Hz, H, vinylic), 13.30 (s, 1H, OH). Anal. calcd. for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51. Found: C, 71.58; H, 4.66%.

2.3. General procedure for the synthesis of flavones from 2′-hydroxychalcones (1a-g)

2.3.1. Synthesis of 2′,4′-dichloroflavone (1a)

Compound **2a** (0.402 g, 1.37 mmol) was dissolved in 4 mL of DMSO, followed by the successive addition of 2-3 drops of conc. H_2SO_4. After 15 min. of stirring a little crystal of I_2 was added carefully. Then the mixture was subjected to microwave irradiation for 2 min. 45 sec. each 15 sec. irradiation with a time interval 30 sec. The completion of the reaction was monitored by TLC. After cooling to room temperature, the reaction mixture was diluted with water (excess) and extracted with $CHCl_3$ (3 × 20 mL). The organic layer was washed with aqueous 20% sodium thiosulphate and water and dried over anhydrous sodium sulphate. The crude mass obtained was recrystallized from ethyl acetate to give pure 2′,4′-dichloroflavone, **1a** (Scheme 1). Color: White crystalline solid. Yield: 85% (0.339 g). M.p.: 120-122 °C. FT-IR (KBr, ν, cm^{-1}): 1587 (C=C), 1655 (C=O), 1574 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.56 (d, 1H, *J* = 2 Hz, C3′-H), 7.41 (dd, 1H, *J* = 8.3 Hz and 2 Hz, C5′-H), 7.60 (d, 1H, *J* = 9.2 Hz, C6′-H), 6.66 (s, 1H, C3-H), 8.25 (dd, 1H, *J* = 8.5 Hz and 2 Hz, C5-H), 7.45 (m, 1H, C6-H), 7.52 (d, 1H, *J* = 8.5 Hz, C8-H), 7.71 (m, 1H, C7-H). Anal. calcd. for $C_{15}H_8Cl_2O_2$: C, 61.88; H, 2.77. Found: C, 61.18; H, 2.76%.

2.3.2. Synthesis of 3′,4′-dimethoxyflavone (1b)

Compound **2b** (0.506 g, 1.78 mmol) was dissolved in 4 mL of DMSO and was added 2-3 drops of conc. H_2SO_4. After 15 min. of stirring a little crystal of I_2 was added carefully. Then the mixture was subjected to microwave irradiation for 2.5 min., each 30 sec. irradiation with a time interval 20 sec. and monitored by TLC to establish completion. After attaining the room temperature, the reaction mixture was extracted with ethyl acetate. The organic layer was washed with aqueous 20% sodium thiosulphate and water and dried over anhydrous sodium sulphate. The crude mass obtained was purified by silica gel column chromatography using ethyl acetate:*n*-hexane (1:4, *v*:*v*) as eluent which gave pure 3′,4′-dimethoxyflavone, **1b** (Scheme 1). Color: Off-white fluffy crystalline solid. Yield: 94% (0.474 g). M.p.: 150-152 °C. FT-IR (KBr, ν, cm^{-1}): 1601 (C=C), 1645 (C=O), 2871, 2931 (C-H, aliphatic). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 3.97 (s, 3H, OCH_3), 3.99 (s, 3H, OCH_3), 6.77 (s, 1H, C3-H), 7.00 (d, 1H, *J* = 8.5 Hz, C5′-H), 7.41 (d, 1H, *J* = 2 Hz, C2′-H), 7.44 (d, 1H, *J* = 8.5 Hz, C6′-H), 7.57 (d, 1H, *J* = 7.5 Hz, C8-H), 7.59 (d, 1H, *J* = 7.4 Hz, C5-H), 7.70 (m, 1H, C6-H), 8.40 (dd, 1H, *J* =7.2 Hz and 1.5 Hz, C7-H). Anal. calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.00; H, 4.72%.

2.3.3. Synthesis of 4′-chloroflavone (1c)

Compound **2c** (0.402 g, 1.55 mmol) was dissolved in 4 mL of DMSO in a two naked round bottom flask, followed by the successive addition of 2-3 drops of conc. H_2SO_4. After 15 min. of stirring, a little crystal of I_2 was added carefully. Then the mixture was subjected to microwave irradiation for 2 min 45 sec., each 15 sec. irradiation with a time interval 30 sec. and monitored by TLC to establish completion. A similar treatment of the reaction mixture (as in the case of compound **1a**) gave the titled compound **1c** (Scheme 1). Color: Yellow fluffy crystalline solid. Yield: 84.8% (0.34 g). M.p.: 193-195 °C. FT-IR (KBr, ν, cm^{-1}): 1606 (C=C), 1687 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.43-8.22 (m, 4H, 4× Ar-H), 6.79 (s, 1H, C3-H), 7.87 (dd, 2H, J_o = 9.2 Hz, J_m = 2 Hz, C3′, 5′-H, 2× Ar-H), 7.57 (dd, 2H, J_o = 9.5 Hz and J_m = 2 Hz, C2′,6′-H 2×Ar-H). Anal. calcd. for $C_{15}H_9ClO_2$: C, 70.19; H, 3.53. Found: C, 69.88; H, 3.26%.

2.3.4. Synthesis of 3′-fluoroflavone (1d)

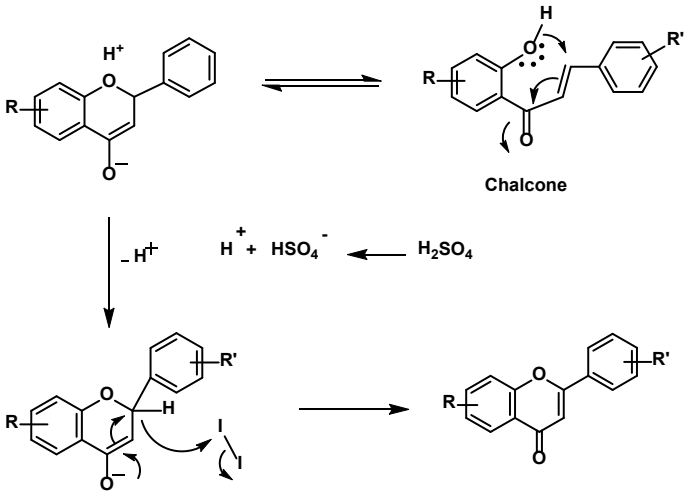
Compound **2d** (3.20 mmol, 0.724 g) was dissolved in 3 mL of DMSO. A few drops of conc. H_2SO_4 and a crystal of I_2 were added to it with stirring. The mixture was then subjected to microwave irradiation for 3 min 30 sec., each 30 sec. irradiation with a time interval 30 sec. and monitored by TLC to establish completion. A similar treatment of the reaction mixture (as in the case of compound **1a**) gave the titled compound **1d** (Scheme 1). Color: White crystalline solid. Yield: 80% (0.576 g). M.p.: 94-95 °C. FT-IR (KBr, ν, cm^{-1}): 1606 (C=C), 1662 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 6.82 (s, 1H, C3-H), 7.46 (t, 1H, *J* = 7.8 Hz and *J* = 8.0 Hz, C5′-H), 7.50 (m, 1H, C6-H), 7.53 (m, 1H, C7-H), 7.58 (d, 1H, *J* = 8.2 Hz, C6′-H), 7.67 (m, 1H, C4′-H), 7.73 (d, 1H, *J* = 8.3 Hz, C8-H), 7.76 (d, 1H, *J* = 1.5 Hz, C2′-H), 8.24 (dd, 1H, *J* = 7.6 Hz and *J* = 1.4 Hz, C5-H). Anal. calcd. for $C_{15}H_9FO_2$: C, 75.00; H, 3.78. Found: C, 74.5; H, 3.81%.

2.3.5. Synthesis of 3′-nitroflavone (1e)

Compound **2e** (0.757 g, 2.80 mmol), dissolved in 4 mL of DMSO followed by the successive addition of 2-3 drops of conc. H_2SO_4. After 15 min. of stirring a little crystal of I_2 was added carefully. The mixture was subjected to microwave irradiation for 3 min, each 30 sec. irradiation with a time interval 30 sec. The reaction was monitored by TLC to establish completion. A similar treatment of the reaction mixture (as in the case of compound **1a**) gave the titled compound **1e** (Scheme 1). Color: Pale brown crystalline solid. Yield: 75% (0.564 g). M.p.: 199-201 °C. FT-IR (KBr, ν, cm^{-1}): 1571 (C=C), 1667 (C=O), 1489 (N=O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 6.91 (s, 1H, C3-H), 7.47 (t, 1H, *J* = 7.2 Hz and *J* = 7.6 Hz, C6-H), 7.64 (d, 1H, *J* = 7.2 Hz, C8-H), 7.73 (m, 1H, C7-H), 7.76 (m, 1H, C5′-H), 8.23 (m, 1H, C4′-H), 8.26 (m, 1H, C6′-H), 8.42 (d, 1H, *J* = 8.6 Hz, C_5-H), 8.83 (s, 1H, C2′-H). Anal. calcd. for $C_{15}H_9NO_4$: C, 67.42; H, 3.39. Found: C, 67.51; H, 3.76%.

2.3.6. Synthesis of 3′,4′-methylenedioxyflavone (1f)

Compound 2f (0.757 g, 2.80 mmol), dissolved in 4 mL of DMSO followed by the successive addition of 2-3 drops of conc. H_2SO_4. After 15 min. of stirring a little crystal of I_2 was added carefully. The mixture was subjected to microwave irradiation for 3 min; each 60 sec. irradiation with a time interval 30 sec. The reaction was monitored by TLC to establish completion. A similar treatment of the reaction mixture (as in the case of compound 1a) gave the titled compound **1f** (Scheme 1). Color: Pale yellow crystalline solid. Yield: 75% (0.564 g). M.p.: 199-201 °C. FT-IR (KBr, ν, cm^{-1}): 1602 (C=C), 1654 (C=O), 2746, 2924 (O-CH-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 5.88 (s, 2H, O-CHO-), 6.35 (s, 1H, C3-H), 6.75 (d, 2H, *J* = 7.8 Hz, C5′-H and C6′-H), 6.79 (d, 1H, *J* = 7.8 Hz, C2′-H), 7.65-7.95 (m, 4H, Ar-H × 4H). Anal. calcd. for $C_{16}H_{12}O_4$: C, 71.66; H, 4.49. Found: C, 71.51; H, 4.33%.



Scheme 2

2.3.7. Synthesis of 5,6,7,8,2',6'-Hexamethoxyflavone (1g)

In a solution of conc. H_2SO_4 (2-3 drops) and acetic acid (3 mL) the diketone (200 mg, 0.444 mmol) was added and the whole mixture was irradiated with stirring for 5 min. (30 sec. × 10 times, 30 sec. interval/irradiation) under MW exposure. The resulting semisolid mass was mixed with crushed ice and extracted with ethyl acetate followed by the addition of anhydrous $MgSO_4$. The crude solid was recrystallized from ethyl acetate and hexane to give the highly substituted flavones (165 mg, 85%). The compound was purified by a silica gel column chromatography (ethyl acetate:hexane, 1:1, *v*:*v*) (Scheme 1). Color: Colorless needles. M.p.: 99-100 °C. FT-IR (KBr, ν, cm^{-1}): 2874, 2934 (C-H, aliphatic), 1682 (C=O), 1605 (C=C), 1265 (C-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 3.88 (s, 9H, OCH_3×3), 3.90 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.64 (s, 1H, C3-H), 7.17 (s, 3H, Ar-H×3). Anal. calcd. for $C_{21}H_{22}O_8$: C, 62.68; H, 5.51. Found: C, 62.42; H, 5.52%.

3. Results and discussion

Substituted aromatic ketones are very useful compounds as starting material and/or synthetic intermediate in the field of synthetic organic chemistry. These compounds can be synthesized by Friedel-Crafts acylation of an aromatic nucleus in the presence of stoichiometric amount of a Lewis acid, such as $AlCl_3$ [18-20]. MW-assisted condensation of ketone 4 with 2,4-dichlorobenzaldehyde (**3a**) in minimal amount of alcoholic KOH solution gave 2'-hydroxy-2,4-dichloro-chalcone (**2a**) (Scheme 1). The structure of chalcone **2a** was determined by ^{1}H NMR. Two vinylic protons appeared at δ 7.63 and 8.23 ppm with the coupling value of 12.8 Hz conforming to *trans*-coupling interaction. The other main aromatic peaks were found to be at δ 6.98 and 7.38 ppm with coupling values of 7.2 Hz and 1.8 Hz, respectively. The same compound was synthesized by using the protection and deprotection strategy in which the hydroxyl group of the compound **4** was protected with methoxymethyl group. The 2'-methoxymethyl chalcone thus afforded was hydrolyzed with concentrated HCl in methanol and chloroform mixture to give compound **2a** in 74% yield (via two steps from compound **3a**). The yield of chalcone was found to be almost the same for both routes. Other chalcones were obtained (**2b**-**f**) in high yields using the microwave protocol.

The subsequent ring closure reaction of compound **2a** afforded the desired flavone **1a** in 85% yield. This reaction was carried out under microwave irradiation taking minimal volume of DMSO as solvent in presence of iodine and catalytic amount of sulfuric acid. The decisive singlet peak appeared at δ 6.66 ppm for the C3-H, a characteristic peak for flavones. Aromatic protons appeared for B ring at δ 7.45 and 7.63 ppm as doublets pattern. All other compounds **1b**-**f** were synthesized in a similar manner in high yields described in the experimental section (*vide ante*). The same ring closure was also achieved in AcOH and H_2SO_4 mixture. But, the latter method gave lower yields compared to the former. Oxidative cyclization of 2'-hydroxychalcone using catalytic amount of iodine in DMSO by conventional heating is very useful except for the large volume of DMSO required for it to occur successfully. The reaction of chalcone in the mixture with iodine was found to run smoothly possibly due to ease of the mode of reaction. We reckon that, the reaction follow a nucleophilic path with iodine. Using MW irradiation in the presence of iodine reagents not only can faster the reaction pathway but it is also valuable from economic and environmental standpoints. The catalytic path in the presence of H_2SO_4 comprises enhancement of the attack by OH of ring A on the beta (β) carbon to produce an intermediate, which would further convert into the targeted product. The following (Scheme 2) is a plausible pathway in favor of formation of the target molecule of flavone.

On the other hand, flavones are also achievable by the cyclization of diketones obtained from benzoyl esters presented in the experimental section (*vide ante*). This involves more steps compared to the direct cyclization but still is very useful for a planned synthesis. A simple and green pathway is described for the synthesis of highly substituted flavones using a diketone through a number of protection-deprotection steps [21].

4. Conclusion

For a planned chemical synthesis of polyphenolics and related compounds in order to evaluate their bioactivity, a series of chalcones (**2a**-**f**) were synthesized by Claisen-Schmidt condensation. Their subsequent cyclization afforded the corresponding flavones (**1a**-**g**) through Green Chemistry adopted synthetic procedure. The moderate to high yield syntheses of flavones taking minimal amount of DMSO with iodine in the presence of a trace amount of sulfuric acid was also carried out under both microwave conditions and conventional heating methods. All the synthesized compounds have been characterized by elemental analysis, IR and ^{1}H NMR spectroscopic measurements.

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Disclosure statement

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