

A facile synthesis of 3-chloro-2-phenyl-4*H*-chromen-4-ones using grinding technique at room temperature

D.K. Sharma^{*1}, S. Kumar²

¹Department of Chemistry, Kishan Lal Public (P. G.) College, Rewari, Haryana, 123401, India

²Department of Chemistry, Technological Institute of Textile and Sciences, Bhiwani, Haryana, 127021, India

Received June 15, 2014; Revised February 26, 2016

An efficient procedure for the synthesis of 3-chloro-2-phenyl-4*H*-chromen-4-ones by selective chlorination of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones with potassium chloride and ammonium persulfate gave 2-chloro-1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones which on cyclisation with phosphorus pentoxide yielded 3-chloro-2-phenyl-4*H*-chromen-4-ones under grinding conditions.

Keywords: 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones; 3-chloro-2-phenyl-4*H*-chromen-4-ones; grinding technique; chlorination.

INTRODUCTION

3-Chloro-2-phenyl-4*H*-chromen-4-ones constitute an important class of compounds in flavanoid chemistry due to their significant biological properties [1-4] and also act as important intermediates for the synthesis of 2-aryl coumaranones [5]. These compounds are generally obtained by direct chlorination of 2-phenyl-4*H*-chromen-4-ones [6,7] or by selective chlorination of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones followed by cyclisation of α -chloro derivatives [5,8]. However, selective chlorination of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones followed by cyclisation remains the most practical method for their preparation. Chlorination of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones has generally been carried out using sulfuryl chloride [5] or by oxidative chlorination using phase transfer catalysis [8].

But all the existing methods make use of highly toxic chemicals and organic solvents causing extreme damage to our environment.

The grinding technique has been considered to be an important tool to carry out reactions under solvent-free conditions, with maximum yield and minimum cost, and it also got much attention due to its operational simplicity [9,10]. In continuation of our work to develop efficient and ecological procedures for the synthesis of organic compounds avoiding hazardous chemicals and organic solvents [11] at any stage of the reaction, we report an efficient procedure for the synthesis of 3-chloro-2-phenyl-4*H*-chromen-4-ones using aqueous grinding

technique which avoids the use of hazardous chemicals and organic solvents during work-up.

EXPERIMENTAL

All the chemicals were obtained from commercial sources. Melting points were determined in open capillary tubes. IR (KBr) spectra were recorded on a Perkin-Elmer spectrum BX series FT-IR spectrophotometer; ¹H NMR and ¹³C NMR spectra were recorded on a Bruker 400 MHz and 100 MHz spectrometer, respectively, using TMS as the internal standard. The elemental analyses were performed on a Perkin Elmer 2400 elemental analyzer. Silica gel (100-200 mesh) was used for column chromatography. 1-(2-Hydroxyphenyl)-3-phenylpropane-1,3-diones 1a-1f, required for the present study, were prepared by Baker-Venkataraman rearrangement using grinding technique as reported previously [12].

General procedure for the synthesis of 3-chloro-2-phenyl-4H-chromen-4-ones (3a-3f)

A mixture of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones 1a-1f (1 mmol), potassium chloride (2 mmol) and ammonium persulfate (2.5 mmol) moistened with 10 drops of water was ground in a mortar by a pestle at room temperature for 10 min. The reaction mixture was diluted with ice-cold water and the separated solid was filtered, washed with water and dried in vacuum over anhydrous calcium chloride. The mixture of the dry solid and phosphorous pentoxide (1 mmol) was ground together in a mortar by pestle for 10-15 min, when formation of a single product was observed by thin layer chromatography. The reaction mixture was diluted with ice-cold water; the solid that separated out was filtered, washed

* To whom all correspondence should be sent:
E-mail: dksharma_84@rediffmail.com

with water and crystallized from ethanol to afford 3-chloro-2-phenyl-4*H*-chromen-4-ones 3a-3f.

3-Chloro-2-phenyl-4*H*-chromen-4-one (3a). IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 1667, 752; ^1H NMR (400 MHz, CDCl_3 , δ/ppm): 8.35-8.37 (dd, 1H, $J=8.0$ Hz & $J=2.0$ Hz), 7.72-8.05 (m, 3H), 7.25-7.65 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3 , δ/ppm): 179.8, 157.1, 155.5, 134.5, 131.6, 129.8, 129.8, 129.5, 127.2, 127.1, 127.1, 124.8, 121.1, 119.7, 104.8; Anal. calcd for $\text{C}_{15}\text{H}_9\text{ClO}_2$: C, 70.59; H, 3.53; Cl, 13.84. Found: C, 70.47; H, 3.53; Cl, 13.75.

3-Chloro-2-(4-methoxyphenyl)-4*H*-chromen-4-one (3b). IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 1660, 750; ^1H NMR (400 MHz, CDCl_3 , δ/ppm): 8.35-8.37 (dd, 1H, $J=8.0$ Hz & $J=2.0$ Hz), 8.05 (d, 2H, $J=8.0$ Hz), 7.71-7.85 (m, 1H), 7.30-7.60 (m, 2H), 7.10 (d, 2H, $J=8.0\text{Hz}$), 3.92 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , δ/ppm): 179.9, 163.2, 157.1, 155.5, 134.6, 127.7, 127.7, 127.2, 124.8, 123.3, 121.2, 119.8, 115.9, 115.9, 104.8, 56.1; Anal. calcd for $\text{C}_{16}\text{H}_{11}\text{ClO}_3$: C, 67.03; H, 3.87; Cl, 13.39. Found: C, 67.12; H, 3.75; Cl, 13.26.

3-Chloro-6-methyl-2-phenyl-4*H*-chromen-4-one (3c). IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 1665, 740; ^1H NMR (400 MHz, CDCl_3 , δ/ppm): 8.20 (d, 1H, $J=8.0$ Hz), 8.0-8.10 (m, 2H), 7.50-7.85 (m, 5H), 2.40 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CDCl_3 , δ/ppm): 180.1, 157.2, 152.8, 136.5, 135.5, 131.7, 129.9, 129.9, 129.5, 127.1, 127.1, 125.6, 119.1, 118.6, 104.8, 20.7; Anal. calcd for $\text{C}_{16}\text{H}_{11}\text{ClO}_2$: C, 70.99; H, 4.10; Cl, 13.12. Found: C, 67.12; H, 4.18; Cl, 13.03.

3-Chloro-2-(4-methoxyphenyl)-6-methyl-4*H*-chromen-4-one (3d). IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 1660, 745; ^1H NMR (400 MHz, CDCl_3 , δ/ppm): 8.15 (d, 1H, $J=8.0$ Hz), 7.98 (d, 2H, $J=8.0$ Hz), 7.90-7.95 (m, 2H), 6.85 (d, 2H, $J=8.0$ Hz), 3.90 (s, 3H, OCH_3), 2.25 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CDCl_3 , δ/ppm): 180.1, 163.2, 157.2, 152.8, 136.5,

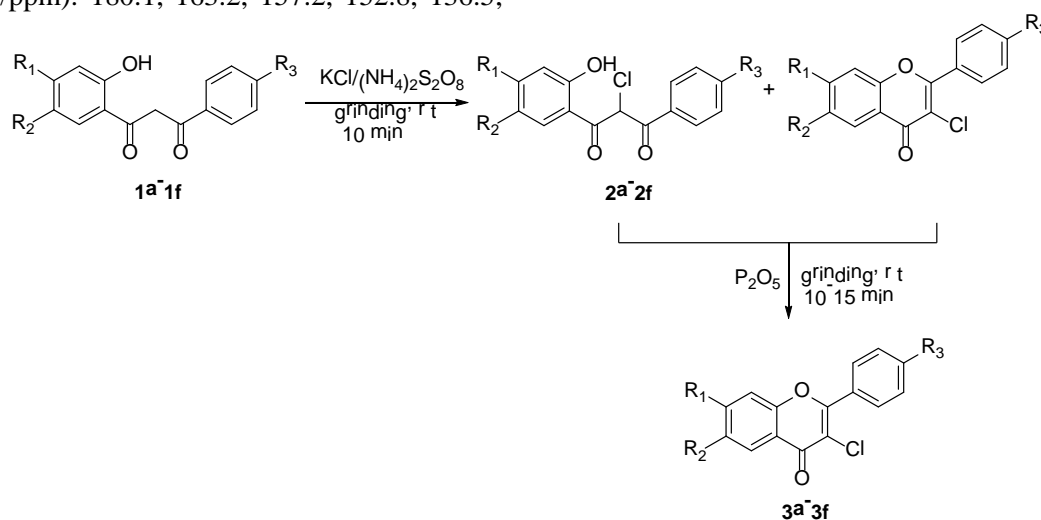
135.5, 127.7, 127.7, 125.6, 123.3, 119.1, 118.6, 116.0, 116.0, 104.9, 55.8, 20.7; Anal. calcd for $\text{C}_{17}\text{H}_{13}\text{ClO}_3$: C, 67.91; H, 4.36; Cl, 11.81. Found: C, 67.80; H, 4.39; Cl, 11.71.

3-Chloro-7-methyl-2-phenyl-4*H*-chromen-4-one (3e). IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 1664, 725; ^1H NMR (400 MHz, CDCl_3 , δ/ppm): 8.30 (d, 1H, $J=8.0$ Hz), 7.50-8.10 (m, 5H), 7.30 (dd, 1H, $J=8.0$ Hz & $J=2.0$ Hz), 6.92 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , δ/ppm): 179.9, 157.1, 155.1, 146.9, 131.7, 129.8, 129.8, 129.7, 128.5, 127.1, 127.1, 123.6, 121.0, 114.5, 104.8, 21.4; Anal. calcd for $\text{C}_{16}\text{H}_{11}\text{ClO}_2$: C, 70.99; H, 4.10; Cl, 13.12. Found: C, 70.85; H, 4.15; Cl, 13.03.

3-Chloro-2-(4-methoxyphenyl)-7-methyl-4*H*-chromen-4-one (3f). IR (KBr, $\nu_{\max}/\text{cm}^{-1}$): 1680, 750; ^1H NMR (400 MHz, CDCl_3 , δ/ppm): 8.05 (d, 1H, $J=8.0$ Hz), 7.35-7.85 (m, 4H), 7.28 (dd, 1H, $J=8.0$ Hz & $J=2.0$ Hz), 7.05 (s, 1H), 3.85 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3 , δ/ppm): 179.8, 163.2, 157.2, 155.1, 146.9, 128.5, 127.7, 127.7, 123.6, 123.5, 121.0, 116.0, 116.0, 114.5, 104.8, 55.6, 21.4; Anal. calcd for $\text{C}_{17}\text{H}_{13}\text{ClO}_3$: C, 67.89; H, 4.36; Cl, 11.81. Found: C, 67.80; H, 4.41; Cl, 11.71.

RESULTS AND DISCUSSION

1-(2-Hydroxyphenyl)-3-phenylpropane-1,3-dione 1a was ground with potassium chloride and ammonium persulfate in a mortar using a pestle under slightly moist conditions. Formation of two compounds was observed by thin layer chromatography, which were separated by column chromatography and were identified as 2-chloro-1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (2a) and 3-chloro-2-phenyl-4*H*-chromen-4-one (3a) (Scheme 1).



Scheme 1. Synthesis of 3-chloro-2-phenyl-4*H*-chromen-4-ones using grinding technique

Table 1. Physical data of 3-chloro-2-phenyl-4H-chromen-4-ones.

Compound	R ₁	R ₂	R ₃	Time (min) (a+b)	Mp (°C)	Mp. (°C) ref. [5]	Yield (%) ^c
3 a	H	H	H	10+10	124-25	125	85
3 b	H	H	OCH ₃	10+10	131-33	135	95
3 c	H	CH ₃	H	10+10	137-39	139	85
3 d	H	CH ₃	OCH ₃	10+15	133	135	90
3 e	CH ₃	H	H	10+15	122-24	122	80
3 f	CH ₃	H	OCH ₃	10+15	150	152	92

a - time for grinding with KCl and (NH₄)₂S₂O₈b- time for grinding with P₂O₅

c- Purified isolated yields

It appears that 2-chloro-1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione **2a** formed at the initial stage undergoes cyclisation to some extent under these conditions to give 3-chloro-2-phenyl-4H-chromen-4-one **3a**. The mixture of the two products obtained in the above reaction on grinding with phosphorus pentoxide without any further purification gave only 3-chloro-2-phenyl-4H-chromen-4-one, involving the cyclisation of the remaining uncyclized 2-chloro-1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione. The reaction mixture on dilution with ice-cold water gave the product directly, thus avoiding the use of any organic solvent for extraction. Optimum conditions for the reaction were achieved by using varying amounts of potassium chloride and ammonium persulfate and best results were obtained with 2 mmol of potassium chloride and 2.5 mmol of ammonium persulfate. The presence of moisture was found essential, in the absence of which no reaction was found to take place. This was attributed to the fact that the formation of chloride and persulfate ions is being facilitated and the oxidation of the chloride ion produces chlorine *in situ* which is consumed there and then in the reaction. The HCl produced during the reaction is absorbed in the medium by the water present and does not spoil the atmosphere.

The validity of the reaction was established by converting differently substituted 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones **1a-1f** into 3-chloro-2-phenyl-4H-chromen-4-ones **3a-3f** (Scheme 1, Table 1) in high yield.

CONCLUSIONS

In conclusion it can be said that the present method developed for the selective chlorination of 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones and synthesis of 3-chloro-2-phenyl-4H-chromen-4-ones under solvent-free conditions using grinding technique is simple, clean, mild, highly efficient and ecological.

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ПРОСТА СИНТЕЗА НА 3-ХЛОРО-2-ФЕНИЛ-4H-ХРОМЕН-4-ОНИ С ИЗПОЛЗВАНЕТО НА СМИЛАНЕ ПРИ СТАЙНА ТЕМПЕРАТУРА

Д.К. Шарма^{*1}, С. Кумар²

¹Департамент по химия, Публичен колеж „Кишан Лал“, Реуардж, Харияна 123401, Индия

²Департамент по химия, Технологичен институт за наука и текстил, Бхвуани, Харияна 127021, Индия

Постъпила на 15 юни, 2014 г.; Коригирана на 26 февруари, 2016 г.

(Резюме)

Постигната е ефективна процедура за синтезата на 3-хлоро-2-фенил-4H-хромен-4-они чрез селективното хлориране на 1-(2-хидроксифенил)-3-фенилпропан-1,3-диони с калиев хлорид и амониев персулфат. Получени са 2-хлоро-1-(2-хидроксифенил)-3-фенилпропан-1,3-диони които след циклизация с дифосфорен пентоксид дава 3-хлоро-2-фенил-4H-хромен-4-они след смилане.