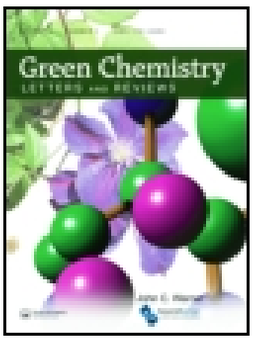

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RESEARCH LETTER

A green synthesis of 2-phenyl/2-styrylchromones under solvent-free conditions using grinding technique

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An efficient eco-friendly synthesis of flavones and 2-styrylchromones via cyclodehydration of corresponding 1-(2-hydroxyaryl)-3-aryl/styryl-1,3-propanediones is described under solvent-free conditions using grinding technique.

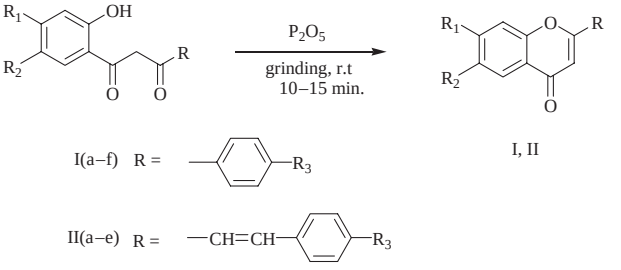
Keywords: flavones; 2-styrylchromones; cyclodehydration; grinding technique; eco-friendly reaction

Introduction

Flavones (2-phenylchromones) and 2-styrylchromones constitute an important class of naturally occurring compounds belonging to flavonoid group (*1–4*). These compounds have been reported to exhibit a variety of pharmacological properties (*5–10*) including anti-cancer (*1*) and antiHIV (*11*).

There are a number of methods available for the synthesis of chromone derivatives including the Allan–Robinson synthesis (*12*) and the oxidative cyclization of 2′-hydroxychalcones/2-hydroxycinnamylideneacetophenones (*13*). However, the cyclodehydration of 1-(2-hydroxyaryl)-3-aryl/styryl-1,3-propanediones obtained by the Baker–Venkataraman rearrangement of 2-aryloxy/cinammoyloxy acetophenones remains the most practical method for their preparation (*14*). The cyclodehydration of the ensuing 1,3-propanediones requires heating under strongly acidic conditions using acetic acid (*15*), hydrochloric acid (*16*), sulfuric acid (*17*), and p-toulenesulphonic acid (*18*). Recently, the cyclodehydration of these 1,3-propanediones has been reported with $CuCl_2$ in ethanol (*19*) under microwave irradiation.

Today much emphasis is on the development of synthetic procedures which avoid toxic and hazardous chemicals and solvents (*20*). In continuation of our work to develop simple and eco-friendly procedures for the synthesis of organic compounds, we wish to report a high yield synthesis of flavones and 2-styrylchromones which involves the grinding of the intermediate 1,3-propanediones with phosphorous pentoxide in a mortar and pestle at room temperature in the absence of any solvent (Scheme 1). The moisture absorbed by the reaction mixture during the grinding



Scheme 1. Synthesis of flavone and 2-styrylchromone.

seems to be sufficient for the formation of a homogeneous mixture and the product is isolated by diluting the reaction mixture with ice cold water.

The possibility of the cyclodehydration of 1,3-propanediones occurring by phosphoric acid which could have formed during the grinding by absorption of water by phosphorous pentoxide, was investigated by grinding the 1,3-propanediones with phosphoric acid alone. No reaction was found to have taken place even after grinding for 30 minutes.

The validity of the procedure was checked by preparing differently substituted flavones and 2-styrylchromones. The identity of the compounds (Table 1) was confirmed from their IR, H^1-NMR spectra and melting point comparison with literature value.

Experimental

All the chemicals were purchased from Aldrich and Fluka. Melting points were determined in open capillary tubes. IR (KBr) spectra were recorded in a Perkin–Elmer spectrum BX series FT-IR

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Table 1. Physical data of the compounds synthesized.

Compound	R_1	R_2	R_3	Time (min)[a]	Melting point (°C)	Literature melting point (°C)	Yield (%)[b]
Ia	H	H	H	10	98–100	97 (*21*)	80
Ib	H	CH_3	H	10	121	122 (*21*)	85
Ic	H	H	OCH_3	10	160	157–158 (*22*)	90
Id	H	CH_3	OCH_3	10	166–168	170 (*23*)	95
Ie	OCH_3	H	OCH_3	10	147	145 (*24*)	90
If	OCH_3	H	H	10	103	103–105 (*25*)	80
IIa	H	H	H	15	130	131 (*26*)	75
IIb	H	CH_3	H	15	135	137 (*27*)	80
IIc	H	H	OCH_3	15	170	167 (*27*)	95
IId	H	CH_3	OCH_3	15	157	160 (*27*)	85
IIe	OCH_3	H	H	15	187	189–190 (*28*)	90

[a]Grinding time.
[b]Yield after crystallization.

spectrophotometer and ^{1}H NMR on Bruker Avance II 400 MHz instrument using tetramethyl-silane as an internal standard.

General procedure

Synthesis of flavones/2-styrylchromones

The substituted 1-(2-hydroxyphenyl)-3-phenyl/styryl-1,3-propanedione (2.1 mmol) was ground with phosphorous pentoxide (2.1 mmol) by a pestle in a mortar for 10–15 minutes. The completion of the reaction was checked by thin layer chromatography (benzene). The reaction mixture was diluted with ice-cold water and the solid that separated out was filtered at vacuum, washed with water, and recrystallized from methanol to afford flavones/2-styrylchromones.

4′-Methoxyflavone (Table 1, Compound Ic)
IR (KBr) 1646 (C = O); ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3H, OCH_3); 6.75 (s, 1H, H-3); 7.0 (d, J = 9.0 Hz, 2H, H-3′, H-5′); 7.25–7.55 (m, 3H, H-6, H-7, H-8); 7.80 (d, J = 9.0 Hz, 2H, H-2′, H-6′); 8.20 (d, J = 9.0Hz, 1H, H-5).

4′-Methoxy-6-methylflavone (Table 1, Compound Id)
IR (KBr) 1640 (C = O); ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3H, CH_3); 3.75 (s, 3H, OCH_3); 6.60 (s, 1H, H-3); 6.70 (d, J = 9.0 Hz, 2H, H-3′, H-5′); 7.30 (s, 2H, H-7, H-8); 7.75 (d, J = 9.0 Hz, 2H, H-2′, H-6′); 7.90 (s, 1H, H-5).

6-Methyl-2-styrylchromone (Table 1, Compound IIb)
IR (KBr) 1629 (C = O); ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H, CH_3); 6.30 (s, 1H, H-3); 6.78 (d, J = 16.0 Hz, 1H, H-α); 6.82–7.42 (m, 8H, C_6H_5, H-β, H-7, H-8); 7.90 (s, 1H, H-5).

6-Methyl-2-(4-methoxystyryl)chromone (Table 1, Compound IId)
IR (KBr) 1640 (C = O); ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H, CH_3); 3.80 (s, 3H, OCH_3); 6.20 (s, 1H, H-3); 6.50 (d, J = 16.0 Hz, 1H, H-α); 6.70–7.80 (m, 8H, C_6H_5, H-β, H-7, H-8); 7.90 (s, 1H, H-5).

Conclusion

In conclusion, it can be said that the present method developed for the synthesis of flavones and 2-styrylchromones is simple, highly efficient and eco-friendly, and avoids the use of organic solvent during the reaction and working up of the reaction mixture.

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