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Microwave-assisted synthesis of functionalized flavones and chromones

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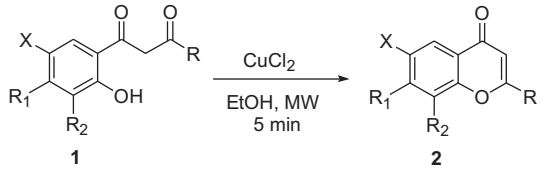
Abstract—A facile microwave synthesis of functionalized flavones and chromones via the cyclization of 1-(2-hydroxyaryl)-3-aryl-1,3-propanedione is described.

1. Introduction

Flavones and chromones are an important class of compounds belonging to the flavonoid group that occur naturally in fruits, vegetables, nuts, seeds, flowers, and barks.[1–3] They are an integral part of the human diet and have been reported to exhibit a wide range of biological effects.[4–11] They also demonstrate antioxidant,[12] antiinflammatory,[13] antibacterial,[14] and antitumor[15] properties. There are a number of methods available for preparing flavones, chromones, and their analogs,[16–20] including the Allan and Robinson synthesis.[17] The most common method, however, involves the Baker–Venkataraman rearrangement wherein an *o*-hydroxyacetophenone is benzoylated and the ester is treated with base (pyridine/KOH) to effect an acyl group migration, forming a 1,3-diketone.[21–24] The ensuing diketone is then cyclized under strongly acidic conditions using acetic acid and sulfuric acid to furnish flavones.

Microwave irradiation[25] offers a considerable advantage over conventional heating because it results in substantial rate enhancements in a wide range of organic reactions. Cleaner reactions are also commonly achieved, together with improvements in yield and selectivity.[26] The increasing demand for clean and 'green' chemical syntheses has resulted in increased use of microwave irradiation.



1 2

X= Br, Cl, CH_3, OH
R = Ar , CH_3, CF_3 ; R_1 = CH_3 OH; R_2 = OH

Scheme 1. Synthesis of flavone and chromones.

There have been several recent reports, describing the application of microwave irradiation to the synthesis of flavonoids[27–29] and nepflavonoids.[30] However, many of the reported methods require tedious procedures and produce relatively low yields.[16–20,24,27,28] Therefore, simpler and high yield approaches toward this valuable nucleus would be desirable.

We wish to report, a high yield synthesis of flavones and chromones (Scheme 1). In the present study, the intermediate 1,3-propanediones **1a**–**l** were synthesized in 5 min via dehydrative cyclization to the corresponding flavones and chromones **2a**–**l** in ethanol, in the presence of $CuCl_2$ under microwave irradiation. The results of the study are summarized in Table 1.

2. Flavones—general procedure

In a typical procedure, a mixture of 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanedione (1.0 mmol) and $CuCl_2$ (0.1 mmol or 10 mol%) was charged in a MW test tube

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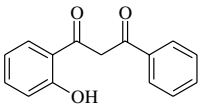
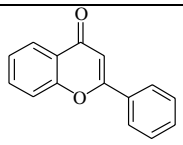
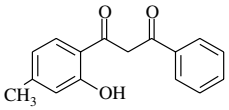
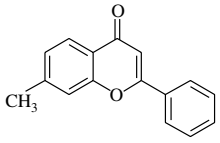
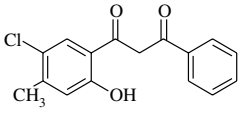
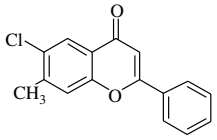
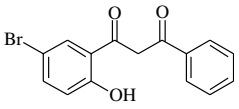
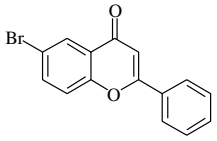
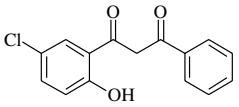
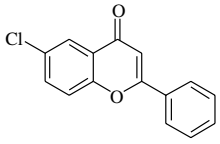
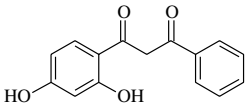
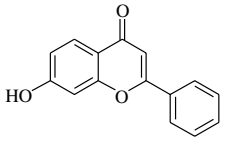
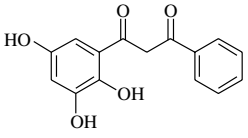
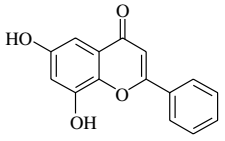
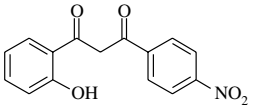
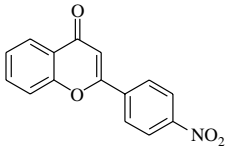
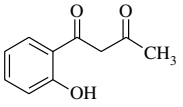
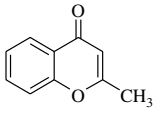
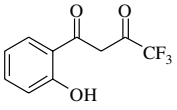
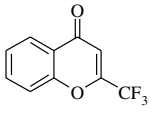
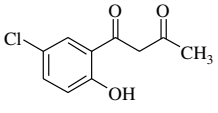
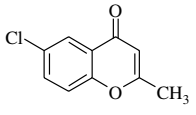
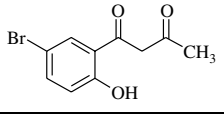
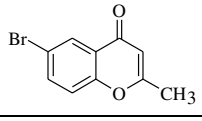
Table 1. Synthesis of flavones and chromones from 1,3-propanedines[a]

Entry	Substrate **1**	Product **2**	Yield[b] (%)
a			98
b			97
c			96
d			95
e			96
f			92
g			89
h			96
i			96
j			86
k			95
l			96

[a] All products were identified by ^{1}H, ^{13}C NMR, and comparison with authentic samples.
[b] Isolated yields.

(10 mL) containing a magnetic stirring bar and a rubber cap and 3 mL of ethanol. The test tube was placed in the microwave cavity (CEM, Discover). The tube was subjected to MW at 80 °C (power 100 W) for 5 min. After completion of the reaction, the tube was removed, cooled to room temperature, and the mixture added to water. The product was extracted with methylene chloride, which was filtered though a short silica column to afford flavone (98% yield).

In conclusion, we report a convenient procedure for preparing functionalized flavones and chromones from 1-(2-hydroxyaryl)-3-aryl-1,3-propanedione.

Acknowledgments

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