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An Expeditious Synthesis of Flavones on Montmorillonite K 10 Clay with Microwaves†‡

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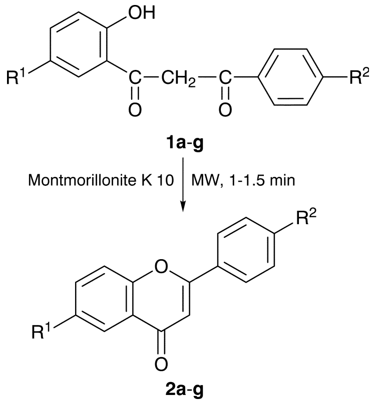
A manipulatively simple and rapid method for the synthesis of flavones is described *via* a solid-state dehydrative cyclization of *o*-hydroxydibenzoylmethanes on a clay surface using microwaves.

Flavonoids are a group of naturally occurring phenolic compounds widely distributed in the plant kingdom, the most abundant being the flavones. Members of this class have been shown to display a wide variety of biological activities[1] and have proven useful in the treatment of various diseases.[2] There are number of methods available for the synthesis of flavones and their analogues,[3a–e] including the Allan–Robinson synthesis,[3c] synthesis from chalcones[4] and *via* an intramolecular Wittig strategy.[5] The most common method, however, involves the Baker–Venkataraman rearrangement[6,7] wherein *o*-hydroxyacetophenone is benzoylated to form the benzoyl ester which is treated with base (pyridine/KOH) to effect an acyl group migration, forming a 1,3-diketone. The ensuing diketone is then cyclized under strongly acidic conditions using acetic acid and sulfuric acid to deliver the flavone. Consequently, there is a need for the development of a milder protocol for the cyclization process.

Clay-catalysed organic reactions have generated considerable interest in recent years in view of their inexpensive nature and special catalytic attributes under heterogeneous reaction conditions.[7] Microwave (MW) heating is used for a wide variety of organic reactions and has found application in rapid and cleaner synthesis of organic compounds.[8–11] More recently, the emphasis has shifted in favor of microwave-assisted methods under solvent-free conditions[9–11] which have special appeal as they provide an opportunity to work with open vessels, thus avoiding the risk of high pressure development. Further, this approach enhances the possibility of upscaling the reactions on a preparative scale. In continuation of our studies on microwave-accelerated solvent-free reactions on mineral solid supports,[10] we now report a manipulatively simple and rapid microwave protocol for the solid-state cyclodehydration of *o*-hydroxydibenzoylmethanes to flavones on a clay surface.

The method in its entirety involves the microwave irradiation of *o*-hydroxydibenzoylmethanes adsorbed on montmorillonite K 10 clay for 1–1.5 min (bulk temperature of alumina bath reaches 80–120 °C). The exclusive formation of cyclized flavones **2a**–**g** occurs which are easily extractable in good yields from the support (Table 1). The alumina bath, in addition to being a container for the reaction vessel, also serves as a heat sink for the microwaves in view of the small amount of reactants normally employed. Among the various other mineral supports explored, namely silica gel, neutral or basic alumina, the formation of flavone is ideally accomplished on K 10 clay; some reaction does occur on neutral alumina and silica surfaces but it is not complete.



Scheme

In conclusion, we have developed a simple and mild method for the solid-state cyclodehydration of *o*-hydroxydibenzoylmethanes to flavones on a clay surface using microwave irradiation.

Experimental

Mps are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ solutions at 60 MHz, using TMS as an internal standard. *o*-Hydroxydibenzoylmethanes **1a**–**g** were obtained by rearrangement of the corresponding *o*-benzoyloxyacetophenones.[13] A Sears Kenmore household microwave oven operating at 2450 MHz was used at its full power, 900 W, for all the experiments. Products were identified by comparison of their mp, IR and NMR spectra with those of authentic samples.

Typical Procedure: 4′-Methyl-6-methoxyflavone **2f**.—1-(2-Hydroxy-5-methoxyphenyl)-3-(4-methylphenyl)propane-1,3-dione **1f** (0.2 g, 0.70 mmol) was dissolved in a small amount of dichloromethane (1 ml) and adsorbed on montmorillonite K 10 clay (1.0 g). The contents, in a test-tube, were placed in an alumina bath inside the microwave oven and irradiated for 1.5 min. The crude product was extracted in dichloromethane (2 × 15 ml) and then crystallized from methanol to afford **2f** in 80% yield, mp 161–162 °C; ^{1}H NMR ($CDCl_3$) δ 2.26 (3 H, s, C4′-CH_3), 3.36 (3 H, s, C6-OCH_3), 6.26 (1 H, s, C3–H), 6.53–7.33 (7 H, m, aromatic H); *m/z* 266 (100%).

That the effect may not be purely thermal[14] is supported by the fact that the reaction could not be completed (65%) in 24 h at the same bulk temperature of 80 °C using an alternate mode of

Table 1 Synthesis of flavones from *o*-hydroxydibenzoylmethanes on clay[a]

Entry	R^1	R^2	Yield (%)	mp (°C) Observed	mp (°C) Reported
2a	H	H	75	96	95[3b]
2b	H	CH_3	77	108–109	110[3d]
2c	H	OCH_3	76	155–157	156–157[3d]
2d	H	NO_2	78	244–245	246–247[3d]
2e	OCH_3	H	73	161	163–164[3e]
2f	OCH_3	CH_3	80	161–162	–
2g	OCH_3	OCH_3	72	193–194	195[12]

[a] MW irradiated for 1 min (the bulk temperature of the alumina bath reached 80 °C at full power of the MW oven, 900 W).

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heating (oil-bath). The temperature of the reaction mixture inside the alumina bath reached ≈80 °C after 1 min of irradiation in a MW oven operating at full power of 900 W.

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