

SHORT COMMUNICATION

THE SYNTHESIS OF 2-IMINOCHROMENES USING MESOPOROUS MOLECULAR SIEVE MCM-41 AS A HETEROGENEOUS AND RECYCLABLE CATALYST

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ABSTRACT. A highly efficient procedure for the synthesis of 2-iminochromenes via condensation of *o*-hydroxybenzaldehydes and malononitrile using a catalytic amount of mesoporous molecular sieve MCM-41 in good yields is achieved.

KEY WORDS: 2-Iminochromenes, Recyclable catalyst, MCM-41, *o*-Hydroxybenzaldehydes

INTRODUCTION

Chromene derivatives are an important class of compounds, widely present in plants, including edible vegetables and fruits [1]. Numerous bioactive natural products have been identified, and the presence of the chromene-based structure has been associated with the capacity to prevent disease [2]. Synthetic analogues were developed over the years, some of them displaying remarkable effects as pharmaceuticals [3], including antifungal [4] and antimicrobial activity [5]. Chromenes have been widely employed as important intermediates in the synthesis of many natural products and medicinal agents [6]. Thus, various synthetic methods for the formation of these compounds have been reported [6, 7].

Among them synthesis from salicylaldehydes is most common [7]. The classic method for the synthesis of 2-iminochromenes is the Knoevenagel condensation of salicylic aldehydes with active methylene compounds [8]. These methods have unfavourable properties such as operating corrosion problems, difficulties in workup, not to mention the production of toxic wastes that damage the environment and some cases gave low yields. The present drive therefore is towards the development of more effective, non-stoichiometric, preferably heterogeneous catalysts for the synthesis of 2-iminochromenes.

In continuation of our interest in using solid catalysts in organic reactions [9], here we wish to report an efficient and environmentally benign procedure for the synthesis of 2-iminochromenes via condensation of *o*-hydroxybenzaldehydes and malononitrile in the presence of catalytic amounts of mesoporous molecular sieve MCM-41 in high yields (Scheme 1).



Scheme 1

RESULTS AND DISCUSSION

In recent years, great interest of many researchers has been focused on the heterogenization of homogeneous catalysts [10-13]. This is important because while some advantages of

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homogeneous catalysts such as catalytic activities and selectivities are retained, other properties like easier work-up, recyclability and stability of heterogeneous systems will be obtained. Different approaches like encapsulation or immobilization of homogeneous catalysts in solid supports such as faujasite zeolites [14, 15] and covalent grafting of homogeneous catalysts on reactive polymer surfaces [16] or inorganic solids [17, 18] have been used. The latter is of great importance especially after discovery of mesoporous molecular sieves such as MCM-41 by Mobil [19, 20] in 1992 containing reactive silanol groups which offer large pores and great surface area to accommodate the guest molecules. MCM-41 have attracted the attention of many researchers. These materials possess well-defined mesopores the diameters of which can be tailored to the desired value (18-100 Å) by the proper choice of surfactants, auxiliary organics and synthesis parameter [19]. Mesoporous silica of the MCM-41 type is an important class of a hexagonal arrangement of cylindrical pores between which an amorphous SiO₂ network is interposed [20, 21]. The most interesting feature of MCM-41 is its regular pore system, which consists of a hexagonal array of one-dimensional, hexagonally shaped pores. Other interesting physical properties of MCM-41 include a highly specific surface area up to 1500 m²/g, a specific pore volume up to 1.3 mL/g and a high thermal stability. All the above properties make it suitable for many catalytic applications. Molecular sieves are widely used in acid catalyzed reactions for the production of petrochemicals and fine chemicals.

In this investigation, we decided to synthesize of 2-iminochromenes via condensation of *o*-hydroxybenzaldehydes and malononitrile using MCM-41 as a heterogeneous and recyclable catalyst at room temperature. The experimental procedure with this catalyst is very simple and the catalyst can be removed easily by filtration. The scope and the generality of the present method were then further demonstrated by reaction of various *o*-hydroxybenzaldehydes with malononitrile. In all cases good yields and selectivity were obtained. In each reaction, the yield is a function of the reaction time and the best time for all reactions was optimized to be 2 h. The reaction proceeds very cleanly at room temperature and free of side products. In the absence of the catalyst, the reaction did not complete even after 12 h and the yield was 22%.

Table 1. Synthesis of 2-iminochromenes in the presence of MCM-41 as a catalyst.

Entry	R	Product	Time (h)	M.p. (°C)		Yield (%) ^a
				Observed	Reported [22]	
1	H	3a	2	184	183	94
2	3-Hydroxy	3b	2	>260	>260	94
3	4-Hydroxy	3c	2	>260	>260	93
4	5-Hydroxy	3d	2	>260	>260	92
5	4-Methoxy	3e	2	178	176-177	93
6	5-Bromo	3f	2	178	176-177	94

^aYields of isolated products.

Reusability of MCM-41. Next, we investigated the reusability and recycling of MCM-41. At the end of the reaction, the catalyst could be recovered by a simple filtration. The recycled catalyst could be washed with methanol and subjected to a second run of the reaction process. To assure that catalysts were not dissolved in acetonitrile, the catalysts were weighted after filtration and before using and reusing for the next reaction. The results show that these catalysts are not soluble in acetonitrile. In Table 2, the comparison of efficiency of MCM-41 in synthesis of **3a** after five times is reported. As it is shown in Table 1 the first reaction using recovered MCM-41 afforded similar yield to those obtained in the first run. In the second, third, fourth and fifth runs, the yield were gradually decreased.

Table 2. Reuse of the MCM-41 for synthesis of **3a**.

Entry	1	2	3	4	5
Time (h)	2	2.5	3	4	4.5
Yield (%) ^a	94	90	85	80	80

^a Isolated yields.

In conclusion, we developed an efficient and simple alternative for the preparation of 2-iminochromenes via the MCM-41-catalyzed condensation reaction under mild conditions at room temperature. Prominent among the advantages of this new method are operational simplicity, good yields, short reaction times, the low cost of the catalyst, low toxicity of the catalyst, recyclability of the catalyst and an easy work-up procedure.

EXPERIMENTAL

Chemical and apparatus. All products are known compounds and were characterized by m.p., IR, ¹H NMR and GC/MS. Melting points (uncorrected) were measured using Electro-thermal IA 9100 digital melting point apparatus. ¹H NMR spectra were recorded on a Bruker AQS AVANCE-300 MHz spectrometer using TMS as an internal standard (CDCl₃ solution) (Tehran, Iran). IR spectra were recorded from KBr disk on the FT-IR Bruker Tensor 27 (Tehran, Iran). Yields are based on GC/MS analysis using an Agilent (Denver, CO, USA) 6890 GC system Hp-5 capillary 30 m × 530 μm × 1.5 μm nominal (Tehran, Iran).

Preparation of MCM-41. MCM-41 was prepared according to the procedure described previously [23]. A typical procedure was as follow: 1.8 g of fumed silica was added to a solution prepared from dissolving 0.6 g of NaOH in 25 mL of water. The resultant mixture was stirred for 2 h, and then 1.9 g of cetyltrimethylammonium bromide (CTABr) in 20 mL of water was added to this solution and stirred for one more hour. The resulting reaction mixture which has the molar composition of 1 SiO₂, 7.5 Na₂O, 5.2 CTABr, 2500 H₂O was kept over night and poured into the teflon lined stainless steel autoclave to make crystallization under static condition at 100 °C. The product was filtered, washed with distilled water, dried at 70 °C and calcined in air at 540 °C for 4 h.

General procedure for the synthesis of 2-iminochromenes. A mixture of *o*-hydroxybenzaldehydes (1 mmol) and malononitrile (1 mmol) and MCM-41 (0.01 g) in acetonitrile (5 mL) was stirred at room temperature for 2 h. The progress of the reaction was monitored by TLC using EtOAc:hexane (1:3) as eluents. After completion of the reaction, the catalyst was filtered and the solvent was evaporated. The residue was recrystallized from ethanol to give the pure product. **3a**. M.p. 184 °C (Lit. [22] 183 °C); IR (KBr) (ν_{\max} , cm⁻¹): 2250 (CN), 3300 (NH); ¹H NMR (CDCl₃, 300 MHz) δ_{H} (ppm): 6.72 (1H, s, NH), 7.24-7.49 (m, 5H), 7.79 (1H, s).

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