A simple, convenient three component one-pot procedure for the synthesis of benzimidazolo-quinazolinone derivatives in the presence Silica-based sulfonic acid (MCM-41-SO$_3$H): an efficient and practical catalyst

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Abstract: A simple and efficient synthesis of benzimidazolo-quinazolinones derivatives is achieved by three-component condensation of dimesdone, different aldehydes with 2-amino benzimidazole as ammonia source using Silica-based sulfonic acid (MCM-41-SO$_3$H) as a green and reusable catalyst in refluxing ethanol. This procedure is a clean and environmentally benign approach that offers many advantages including short high to quantitative yields, reaction times, cost effectiveness of catalyst and straightforward workup.

Keywords: Silica-based sulfonic acid, MCM-41-SO$_3$H, Heterogeneous, Multi-component reaction, one-pot procedure, benzimidazolo-quinazolinones.

Introduction
Multicomponent reactions (MCRs), as an attractive and important strategy for organic synthesis, are one-pot processes, which a involve reaction of three or more accessible components to form a single product that incorporates essentially most or all the atoms of all the reactants. MCRs have showed a new dimension in the field of designing methods to produce of biologically active compounds and new molecular frameworks for potential drugs
with various pharmacological activities [1]. Development of MCRs can lead to highly
efficient synthetic methodologies to afford many small organic compounds in the field of
modern organic, bioorganic, and medicinal chemistry [2]. MCRs strategies grant remarkable
advantages over conventional bimolecular reactions due to a low number of reactions and
purification steps, operational simplicity, selectivity, high atom-economy, structural diversity,
synthetic efficiency [3]. Therefore, industrial and academic research teams have focused on
the use of MCRs to synthesize a broad range of products [4]. Hence, MCRs are considered as
a pivotal theme in the synthesis of many heterocyclic compounds such as quinazolinone
derivatives nowadays.

Nitrogen-containing heterocycles have always shown a significant role in the pharmaceutical
and agrochemical industries because of their potent physiological properties, which have
resulted in program applications [5]. Among them quinazolinones derivatives are an
important class of natural products and exhibit a wide range of spectrum of pharmacological
and biological activities, such as analgesic [6], hypnotic [7], anticonvulsant [8],
leishmanicidal [13].

We report a highly efficient, convenient and simple approach for effecting one-pot three-
component reaction of dimedone, various aldehydes and 2-aminobenzimidazole for
preparation of quinazolinone derivatives using MCM-41-SO$_3$H as a recyclable heterogeneous
catalyst under mild reaction conditions (Scheme 1).

Scheme 1. Synthesis of benzimidazolo-quinazolinone derivatives catalyzed
by MCM-41-SO$_3$H.
Experimental

*Instruments and characterization*

All chemicals were purchased from commercial sources Merck, Fluka and Sigma-Aldrich companies and were used without further purification. All reactions and the purity of benzimidazolo-quinazolinones derivaties were monitored by thin-layer chromatography using aluminum plates coated with silica gel F254 plates using n-hexane and ethyl acetate as eluents. The spots were detected either under UV light or by placing in an iodine chamber. Melting points were determined on an Electrothermal 9100 apparatus.

*General procedure for the synthesis of benzimidazolo-quinazolinone derivatives*

A mixture of dimedone (0.14 g, 1 mmol), benzaldehyde (0.11 g, 1 mmol) and 2-amino-benzimidazole (0.133 g, 1 mmol) in the presence 20 mol% MCM-41-SO$_3$H in ethanol (3 ml) was refluxed for 30 min until the formation of a crystalline precipitate. The progress of the reaction was monitored by TLC. After completion of the reaction, a thick precipitate was obtained. The reaction mixture was cooled and after removal of the catalyst, product was filtered off and recrystallized.

*Results and Discussion*

The catalytic ability of the MCM-41-SO$_3$H was evaluated in catalyzing a reaction for the efficient synthesis of benzimidazolo-quinazolinones by condensing dimedone, aryl aldehydes and 2-amino-benzimidazole in refluxing EtOH (Table 1). The results were evaluated qualitatively through TLC. It was found that the quantitative yield can be achieved when the reaction was carried out in the presence of 0.02 g catalyst for 30 min in refluxing EtOH.

MCM-41-SO$_3$H heterogeneous catalyst was tested for the synthesis of the benzimidazolo-quinazolinone derivatives from reaction of dimedone, wide range of aromatic aldehyde and 2-aminobenzimidazole in refluxing ethanol. After completion of the reaction, the catalyst was
easily separated and the solid product was purified by recrystallization. The results are summarized in Table 2.

Table 1. Optimization of the amount of MCM-41-SO$_3$H.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Time (min)</th>
<th>Yield$^b$ (%)</th>
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<tr>
<td>1</td>
<td>-</td>
<td>120</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
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<td>60</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>0.01</td>
<td>60</td>
<td>55</td>
</tr>
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<td>4</td>
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<td>60</td>
<td>75</td>
</tr>
<tr>
<td>5</td>
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<td>90</td>
</tr>
<tr>
<td>6</td>
<td>0.025</td>
<td>60</td>
<td>92</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: dinedone, (1 mmol), benzaldehyde (1 mmol), 2-amino-benzimidazole (1 mmol), refluxing EtOH. $^b$Yields of the isolated products.

Table 2. Synthesis of benzimidazolo-quinazolinone derivatives in the presence of MCM-41-SO$_3$H.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Product $^b$</th>
<th>Time(min)</th>
<th>Yield$^c$ (%)</th>
<th>MP (°C)</th>
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</thead>
<tbody>
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<td></td>
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<td><img src="N2.png" alt="Image" /></td>
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<td><img src="N3.png" alt="Image" /></td>
<td><img src="N4.png" alt="Image" /></td>
<td>20</td>
<td>95</td>
<td>&gt;300</td>
</tr>
</tbody>
</table>
Reaction conditions: dimedone (1 mmol), aldehyde (1 mmol), 2-aminobenzimidazole (1 mmol), EtOH (reflux) and MCM-41-SO₃H (0.02 gr).

All compounds were known and their structures were established from their spectral data and melting points as compared with literature values.

The yields refer to isolated products.

Conclusions
In summary, we have described a simple method for the synthesis of benzimidazolо-
quinoxalinone derivatives using MCM-41-SO3H as a reusable and efficient heterogeneous
catalyst in refluxing ethanol under mild reaction conditions. Excellent yields, short reaction
times, green solvent, ease of catalyst recycling, simple work up procedure and mild
conditions are the advantages of this protocol.

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References

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