Synthesis of triazolo-quinazolinones employing MCM- 41-SO_3H: A mild, reusable and highly efficient heterogeneous catalyst

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Abstract: A multicomponent reaction (MCR) can create highly complex molecules from readily available starting materials without the complicated purification operations; thus, MCRs are resource and time-effective and economically favorable processes in diversity generation. A wide variety of quinazolinone derivatives have been synthesized by condensation of 3-amino- 1, 2, 4-triazole as amine source, with dimedone and aromatic aldehydes in the presence of 20 mol % of MCM-41-SO_3H as effective catalyst in green and reusable catalyst in refluxing DMF conditions through one-pot reactions. Triazoloquinazolinone are important because of their wide range of biological activities, application in medicinal chemistry, pharmaceutical industry and agrochemicals as herbicides and active pharmaceuticals.

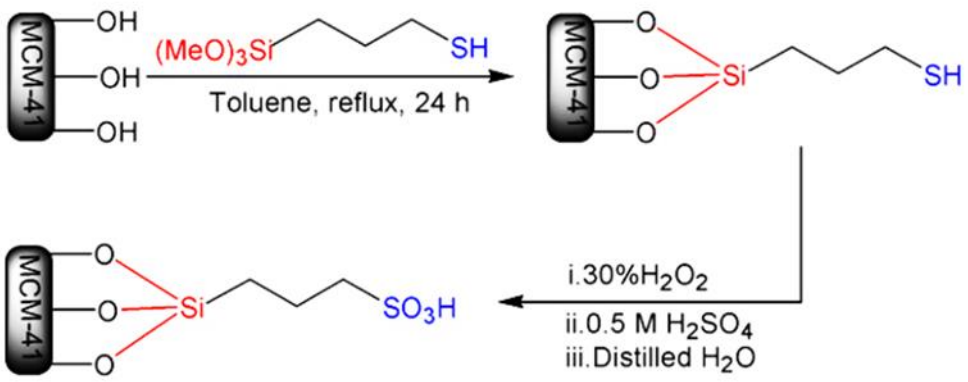
Keywords: Triazoloquinazolinone derivatives, MCM-41-SO_3H, heterogeneous catalyst

Introduction

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 [1]. Therefore, industrial and academic research teams have focused on the use of MCRs to synthesize a broad range of products [2]. Hence, MCRs are considered as a pivotal theme in the synthesis of many heterocyclic compounds such as quinazolinone derivatives nowadays.

In recent years, there has been an increasing interest in developing greener processes [3]. In this context, heterogeneous [4] catalysis is emerging as an alternative to homogeneous processes since catalysts can be recovered after the reaction and reused several times to achieve very high turn-over numbers. One strategy to transform a homogeneous into heterogeneous process is to anchor the active site onto a large surface solid carrier provided that the anchoring methodology maintains the intrinsic activity and selectivity of the catalytic centre [5].

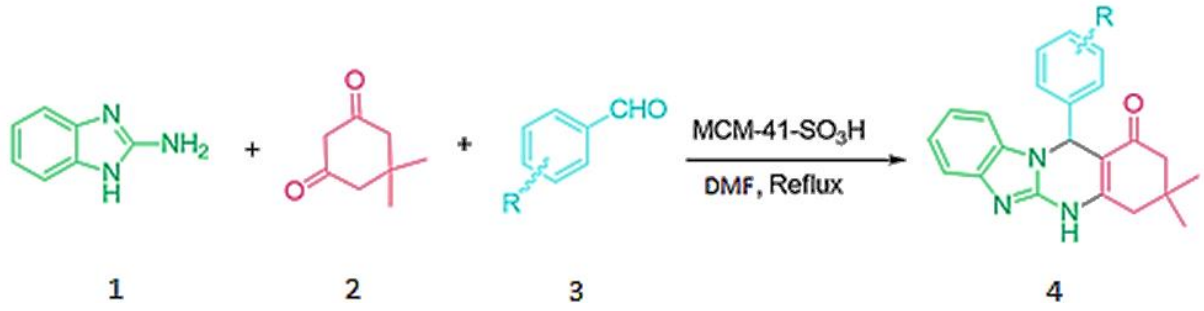
Among various solid supports, silica is usually preferred since it displays many advantageous properties including excellent stability (chemical and thermal), high surface area, good accessibility. Organic groups can also be robustly anchored to the surface; to provide catalytic centres [6]. Based on this idea, several types of sulfonic acid functionalized silica have been synthesized and applied as alternatives to traditional sulfonic resins in catalyzing chemical transformations [7]. Among the different types of silica-based sulfonic acids, Stein and co-workers prepared a novel sulfonic functionalized ordered microporous silicate, which shows a high loading and stability, and yet a uniform nanostructure. Recently, MCM-41 functionalized sulfonic acid as heterogeneous solid acid catalyst has been used to catalyze a variety of reactions [8].



Scheme 1. The preparation procedure for catalyst MCM-41-R-SO_3H

The preparation procedure for catalyst MCM-41-R-SO_3H is outlined in Scheme 1 with slight modification than the already reported method. The presence of covalently anchored organic functionality onto the surface of MCM-41 was determined by thermo gravimetric analysis (TGA). The TGA curve shows the initial weight loss below 100 ^oC, which is attributed to residual solvent or water molecules trapped into the MCM-41 framework, then the subsequent weight loss occurs between 260 and 550 ^oC, which is because of the loss of organic functionalities covalently anchored onto the surface of MCM-41 [9].

Quinazolinones derivatives are an important class of natural products and exhibit a wide range of spectrum of pharmacological and biological activities, such as analgesic [10], hypnotic [11], anticonvulsant [12], antihypertensive [13], antihistaminic[14], antifertility [15], anti-inflammatory [16] and latent leishmanicidal [17].



Scheme 2. Synthesis of triazoloquinazolinone derivatives catalyzed by MCM-41-SO_3H.

We report a highly efficient, convenient and simple approach for effecting one-pot three-component reaction of dimedone, various aldehydes and 3-Amino-1, 2, 4-triazole for preparation of quinazolinone derivatives using MCM-41-SO_3H as a recyclable heterogeneous catalyst under mild reaction conditions (Scheme 2).

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 triazoloquinazolinone derivatives: A mixture of dimedone (0.14 g, 1 mmol), benzaldehyde (0.11 g, 1 mmol) and 3-Amino-1, 2, 4-triazole (0.084 g, 1 mmol) in the presence 20 mol% MCM-41-SO3H in DMF (5 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_3H was evaluated in catalyzing a reaction for the efficient synthesis of triazoloquinazolinone derivatives by condensing dimedone, aryl aldehydes and 3-amino- 1, 2, 4-triazole in refluxing DMF (Table 1).

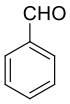
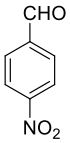
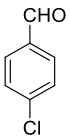
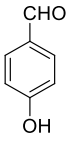
Table 1. Optimization of the amount of MCM-41-SO_3H.[a]

Entry	Catalyst (mol %)	Time (min)	Yield[b] (%)
1	-	80	20
2	5	60	20
3	10	50	55
4	15	40	75
5	**20**	**30**	**90**
6	25	40	90

[a]Reaction conditions: dimedone, (1 mmol), benzaldehyde (1 mmol), 3-Amino-1, 2, 4-triazole (1 mmol), refluxing DMF. [b]Yields of the isolated products.

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 DMF. MCM-41-SO_3H heterogeneous catalyst was tested for the synthesis of the triazoloquinazolinone derivatives from reaction of dimedone, wide range of aromatic aldehyde and 3-amino- 1, 2, 4-triazole in refluxing DMF. 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 2. Synthesis of triazoloquinazolinone derivatives in the presence of MCM-41-SO_3H.[a]

Entry	Amine source	Ar	Time(min)	Yield (%)	MP (°C)	
					Found	Reported
4a	3-Amino-1,2,4-triazole		30	97	248-250	248-250 [18]
4b	3-Amino-1,2,4-triazole		20	95	>300	307-309 [18]
4c	3-Amino-1,2,4-triazole		20	93	>300	303-305 [18]
4d	3-Amino-1,2,4-triazole		40	93	>300	>300 [18]

[a] Reaction conditions: dimedone (1 mmol), aldehyde (1 mmol), 3-Amino-1, 2, 4-triazole (1 mmol), DMF (reflux) and MCM-41-SO_3H (0.02 gr).

Conclusions

In this work, we have described a simple method for the synthesis of triazoloquinazolinone derivatives using MCM-41-SO_3H as a reusable and efficient heterogeneous catalyst in refluxing DMF under mild reaction conditions. Ease of catalyst recycling, excellent yields, short reaction times, green solvent, simple work up procedure and mild conditions are the advantages of this protocol.

Acknowledgements

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