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_3H): an efficient and practical catalyst

Mohammad Reza Naimi-Jamal *, Maryam karimi

Green Chemistry Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran 1684613114, Iran; Email: naimi@iust.ac.ir

Abstract: A simple and efficient synthesis of benzimidazolo-quinazolinones derivatives is achieved by three-component condensation of dimedone, different aldehydes with 2-amino benzimidazole as ammonia source using Silica-based sulfonic acid (MCM-41-SO_3H) 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_3H, Heterogeneous, Multi-component reaction, one-pot procedure, benzimidazolo- quinazolinones.

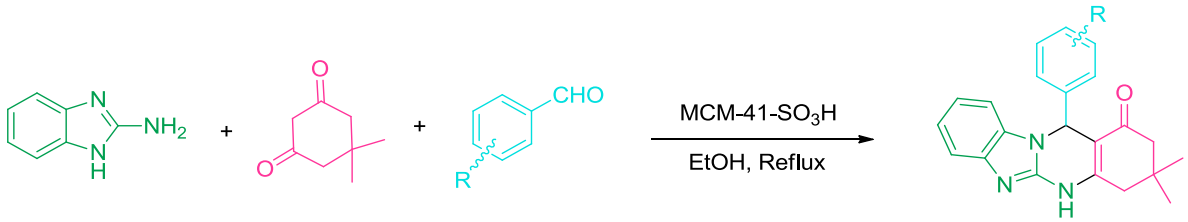
Introduction

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], antihypertensive [9], antihistaminic [10], antifertility [11] anti-inflammatory [12] and latent 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_3H as a recyclable heterogeneous catalyst under mild reaction conditions (Scheme 1).



Scheme 1. Synthesis of Scheme 1. Synthesis of benzimidazolo-quinazolinone derivatives catalyzed by MCM-41-SO_3H.

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_3H 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_3H 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_3H 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

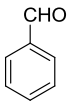
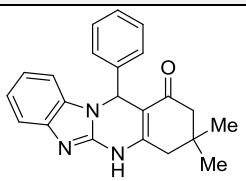
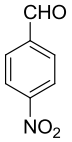
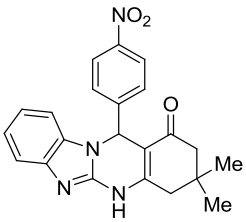
easily separated and the solid product was purified by recrystallization. The results are summarized in Table 2.

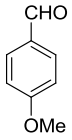
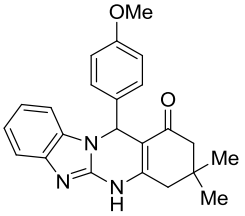
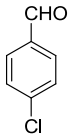
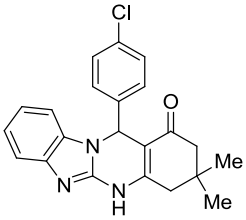
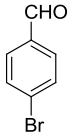
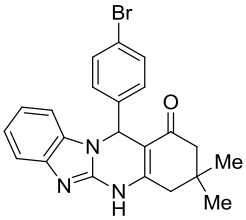
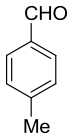
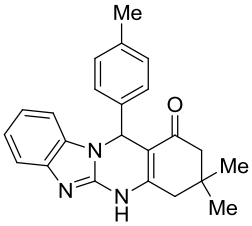
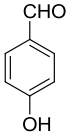
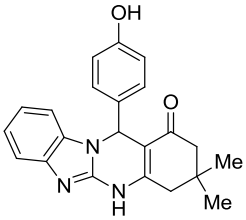
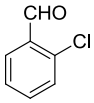
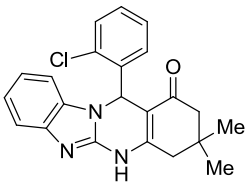
Table 1. Optimization of the amount of MCM-41-SO_3H.[a]

Entry	Catalyst (mol %)	Time (min)	Yield[b] (%)
1	-	120	20
2	0.005	60	20
3	0.01	60	55
4	0.015	60	75
5	0.02	40	90
6	0.025	60	92

[a]Reaction conditions: dimedone, (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_3H.[a]

Entry	Ar	Product [b]	Time(min)	Yield(%)[c]	MP (^oC)	
					Found	Reported
1			30	97	>300	>300[14]
2			20	95	>300	>300[15]

3			40	94	>300	>300[16]
4			20	93	>300	>300[17]
5			35	95	>300	>300[15]
6			30	95	>300	>300[18]
7			40	93	>300	>300[19]
8			25	93	>300	>300[20]

[a] Reaction conditions: dimedone (1 mmol), aldehyde (1 mmol), 2-aminobenzimidazole (1 mmol), EtOH (reflux) and MCM-41-SO_3H (0.02 gr). [b] All compounds were known and their structures were established from their spectral data and melting points as compared with literature values. [c] The yields refer to isolated products.

Conclusions

In summary, we have described a simple method for the synthesis of benzimidazolo-quinazolinone derivatives using MCM-41-SO_3H 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.

Acknowledgements

The authors gratefully acknowledge the partial support from the Research Council of the Iran University of Science and Technology.

References

[1] Domling A, Wang W (2012) Chem Rev 112: 3083

[2] Dekamin MG, Mokhtari Z (2012) Tetrahedron 68: 922

[3] Ganem B (2009) Acc Chem Res 42: 463

[4] Shaabani A, Maleki A, Rezayan AH, Sarvary A (2011) Mol Divers 15: 41

[5] Hagan DO (2000) Nat Prod Rep 17: 435

[6] Alagarsamy V, Murugananthan G, Venkateshperumal R (2003) Biol Pharm Bull 26: 1711

[7] Gujaral ML, Saxena PN, Tiwari RS (1955) Indian J Med Res 43:637

[8] Glasser AC, Diamond L, Combs G (1971) J Pharm Sci 60:127

[9] Alagarsamy V, Solomon VR, Murugan M (2007) Bioorg Med Chem 15: 4009

[10] Alagarsamy V (2004) Pharmazie 59: 3753

[11] Reif E, Ericson RJ (1972) 2-(1-Naphthyl)-2, 3-dihydro-4(1H)- quinazolinones. German Patent DE 2,118,683. Chem Abstr 76:72546

[12] Alagarsamy V, Murugananthan G, Venkateshperumal R (2003) Biol Pharm Bull 26:1711

[13] Ram VJ, Gael A, Verma M, Kanl IB, Kapil A (1994) Bioorg Med Chem Lett 4: 2087

[14] Puligoundla RG, Karnakanti S, Bantu R, Kommu N, Babu Kondra S, Nagarapu L (2013) Tetrahedron Lett 54: 2480

[15] Heravi MM, Ranjbar L, Derikvand F, Alimadadi B, Oskooie HA, Bamoharram FF (2008) Mol Divers 12:181

[16] Lipson VV, Desenko SM, Shishkina SV, Shirobokova MG, Shishkin OV, Orlov VD (2003) Chem Heterocycl Compd 39:1041

[17] Heravi MM, Derikvand F, Ranjbar L (2010) Synth Commun 40: 677

[18] Mourad AF, Aly A, Farag H, Beshr E (2007) Beilstein J Org Chem 3:1

[19] Ziarani GM, Badiei A, Aslani Z, Lashgari N (2011) Arab J Chem 8:54

[20] Shao Q, Tu S, Li C, Cao L, Zhou D, Wang Q, Jiang B, Zhang Y, Hao W (2008) J Heterocyclic Chem 45: 411