Journal of Chemical Reactivity and Synthesis 2025: 15(1) 41-49

Research Article

Nano mesoporous silica as an efficient catalyst for the preparation of 2H- indazolo[2,1-b]phthalazin-triones under solvent-free condition

Maryam Rezaei-Mirghaed, Haleh Sanaeishoar*

Department of Chemistry, Ahv.C., Islamic Azad University, Ahvaz, Iran

ABSTRACT

The KIT-1 is a nano mesoporous material featuring interconnecting wormlike channels in a three dimensional disordered network with uniform pore size and high surface area. The network like channel structure of the present material gives an advantage for preventing channel blockage over the linear channel in MCM-41. The KIT-1 has also remarkable hydrothermal stability. KIT-1 as an efficient and reusable heterogeneous catalyst have been used for the preparation of 2H-indazolo[2,1-b]phthalazin-1,6,11(13H)-trione derivatives from the three-component condensation reaction. The method involves the reaction of various aromatic aldehydes, phthalhydrazide and dimedone, under solvent-free conditions. High yields, short reaction times and easy work-up are some advantages of this work.

Keywords: Nano mesopotous silica, KIT-1, Heterogeneous catalyst, Solvent-free, 2H- indazolo[2,1-b]phthalazin-triones, phthalhydrazide

ARTICLE INFO

Received: 15 October 2025
Accepted: 10 November 2025
Available: 13 November 2025

: H. Sanaeishoar
hsanaei@iau.ac.ir

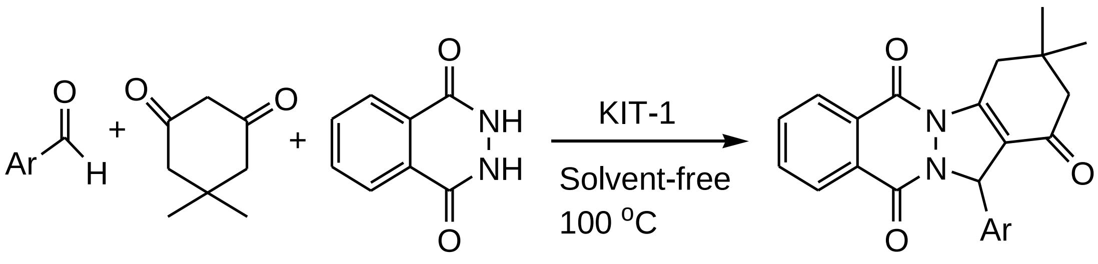
doi 10.82437/jcrs.2025.1221306

Introduction

The nano mesoporous silica material was discovered in 1992 [1]. Mesoporous silica is a porous amorphous silica material with diameter of controllable pores in the range 2-50 nm. The pores are arranged in a hexagonal pattern and separated by walls of amorphous silica. Nano mesoporous silica has large pore size which makes them very useful as miniature nano reaction container [2-4]. Investigation of the mesoporous systems resulted to discovery of several mesoporous materials with high surface area such as MCM-41, MCM-48, KIT-1, SBA, MSU and HMS [5, 6]. KIT-1 mesoporous system with three-dimensional disordered channel was prepared by Ryoo et al. using an electrostatic templating route using sodium silicate, HTACl, and ethylenediaminetetraacetic acid tetrasodium salt ($EDTANa_4$). Channel arrangements of KIT-1 coordinated in a three-dimensional disordered way. KIT-1 exhibit higher thermal and hydrothermal stability than the MCM-41. Also KIT-1 with branching channel structure shows remarkable adsorption and catalytic activities, comparing to the MCM-41 (hexagonal straight channels) [7].

The development of simple synthetic routes for complex organic molecules from readily available reagents is an important task in organic synthesis. Multi-component reactions (MCRs) are significant tools for the rapid and efficient synthesis of a wide variety of organic molecules [8]. These reactions have been investigated extensively in organic and diversely oriented synthesis; due to their ability to generate complex molecular functionality from simple starting materials via one-pot reaction. Organic reaction under solvent-free conditions has attracted much interest from chemists particularly from the viewpoint of green chemistry. Green chemistry approaches are significant due to the reduction in byproducts, wastes produced in a reaction, and costs of reaction energy. The possibility of performing multicomponent reaction under solvent-free conditions with a heterogeneous catalyst could enhance their efficiency from an economic as well as ecological point of view [9].

The synthesis of new heterocyclic compounds has always been a subject of great interest due to their wide applicability. Heterocyclic compounds occur very widely in nature and are essential to life. Amongst a large variety of heterocyclic compounds, heterocycles containing phthalazine moiety are of interest because they show some pharmacological and biological activities [10]. We reported an efficient method for the preparation of 2H-indazolo[2,1-b]phthalazin-trione derivatives **1** using KIT-1 as a catalyst under solvent-free conditions (Scheme 1).



Scheme. 1. The synthesis of 2H-indazolo[2,1-b]phthalazin-trione derivatives using KIT-1

Experimental

All chemicals were purchased from Merck or Fluka chemical Companies. KIT-1 was synthesized based on our previous report [11]. All compounds are known and their structures were identified by comparing their melting point and ^{1}H data with those reported in the literature. The ^{1}H NMR (250M Hz) was run on a Bruker Avance DPX-250, NMR spectrometer.

General procedure for the synthesis of 2H- indazolo[2,1-b]phthalazin-triones

Mixture of aldehyde (1 mmol), phthalhydrazide (1 mmol) and dimedone (1 mmol), KIT-1 (0.005 g) was heated at 100 ^{o}C for the appropriate time (Table 3). Completion of the reaction was indicated by TLC. After completion, the reaction mass was cooled to 25 ^{o}C, the solid residue was isolated and dissolved in ethyl acetate. KIT-1 was filtered; solvent was evaporated from the reaction mixture. The solid product was purified by recrystallization procedure in aqueous EtOH to give product in high yields. All of the 2H- indazolo[2,1-b]phthalazin-triones derivatives are known and were identified by comparison of their physical and spectroscopic data (NMR).

Spectral data

Spectral data of all unknown products are given in Table 3. Spectral data of compounds **1b** and **1d** were presented in below.

Compound 1b

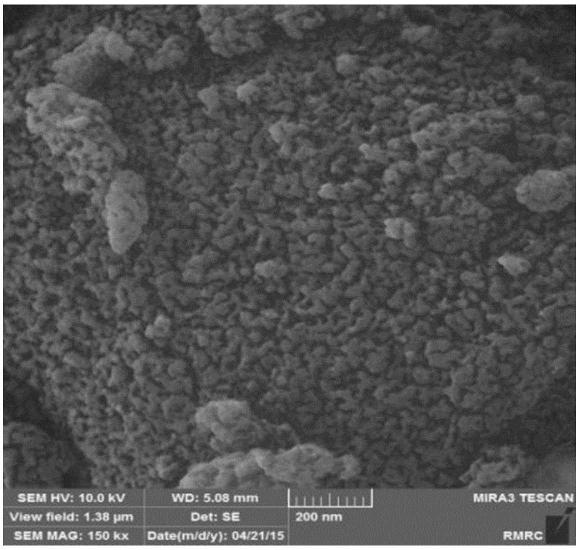
^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.25-8.35 (m, 2H), 7.82-7.85 (m, 2H), 6.84-7.35 (m, 4H), 6.42 (S, 1H),3.76 (s, 3H), 3.23 and 3.42 (AB system, J= 19.2 Hz, 2H), 2.34 (s, 2H), 1.21 (s, 6H). ^{13}C NMR (62.5MHz, $CDCl_3$): δ = 192.23, 159.74, 156.07, 154.28, 150.75, 134.47, 133.47, 129.18, 128.98, 128.51, 128.36, 127.93, 127.71, 118.58, 114.14, 64.59, 55.21, 50.99, 38.07, 34.65, 28.71, 28.51.

Compound 1d

^{1}H NMR (250 MHz, $CDCl_3$): δ =8.25-8.36 (m, 2H), 7.84-7.87(m, 2H), 7.39-7.43 (m, 2H), 6.99-7.04 (m, 2H), 6.43 (s, 1H), 3.27-3.62 (m, 2H), 2.45-2.53 (m, 2H), 2.24-2.33 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 192.37, 160.77, 155.74, 154.16, 152.49, 134.45, 133.53, 132.32, 132.27, 129.77, 129.06, 127.87, 127.38, 118.89, 115.49, 115.20, 64.06, 36.72, 24.29, 22.10.

Discussion

These result shows that the pore size of nano mesoporous silica is less than 20 nm (Scheme 2). It could be readily observed that KIT-1 shows a coral-like structure.



Scheme. 2. SEM photograph of nano mosoporous silica

The nano mesoporous silica catalyzed reaction was carried out using benzaldehyde, dimedone and phthalhydrazide as a model reaction to investigate different parameters, such as effect of solvent and concentration of the catalyst. Furthermore, we have screened several solvents for this reaction (Table 1). Therefore, some solvents have been tested (Table 1, entry 1-5). Finally, the target product was obtained in 87% yield in solvent free method at 100 ^{o}C is as green condition (Table 1, entry 6).

Table. 1. Optimization of solvent for the preparation of 2H- indazolo[2,1-b]phthalazin-triones using nano mesoporous silica as catalyst (0.005 g)[a]

Entry	**Solvent**	**Time (min)**	**Yield (%)**
1	THF	90	56
2	EtOH	80	45
3	MeOH	100	55
4	CH_2Cl_2	90	45
5	H_2O	120	-
6	Solvent-free	10	87

[a] The reaction was conducted with benzaldehyde (1 mmol), β-naphthol (1 mmol), phthalhydrazide (1 mmol), and 5 mg KIT-1 in 3 mL solvent

The quantity of the catalyst can improve the reaction yield and shorten reaction time (Table 2). First, reaction was carried out in absence of catalyst at ambient temperature; it was found 39% product formed after 300 min. Even though amount of the catalyst decreased from 0.01g to 0.005 g no change in the yields, whereas using 0.005g nano mesoporous silica in model reaction generated 87% product.

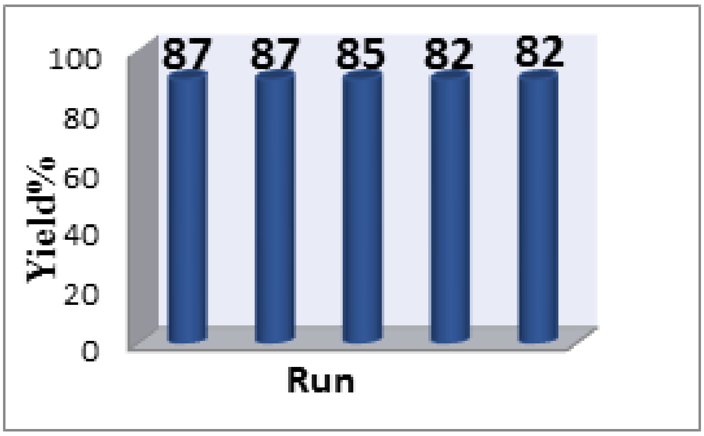
Table. 2. Comparison of the efficiencies of different catalyst for the synthesis of 2H- indazolo[2,1-b]phthalazin-triones[a]

Entry	Temperature (°C)	Amount of catalyst (g)	Time (min)	Yield[b](%)
1	Ambient	-	300	39
2	60	0.005	180	48
3	80	0.005	60	67
4	90	0.005	30	75
5	100	0.005	15	87
6	100	0.007	45	87
7	100	0.008	45	87
8	100	0.01	30	87

[a] The reaction was conducted with conducted with benzaldehyde (1 mmol), dimedone (1 mmol) and phthalhydrazide (1 mmol) under solvent free at 100 °C

[b] Yield of isolated product

To evaluate the stability of catalytic activity and the potential for recycling, we completed several catalytic cycles. After each cycle of the reaction, the catalyst was recovered by simple filtration, washed and subsequently dried at 50 °C to the reused. As shown in Scheme 3 KIT-1 could be reused for the next cycle without any appreciable loss of its activity even after five runs.



Scheme. 3. Catalytic reusability of KIT-1

These results encouraged us to investigate the scope and generality of this new protocol for various aromatic aldehydes under optimized conditions. As shown in Table 3, a series of aromatic aldehydes containing either electron-withdrawing or electron-donating substituents successfully react with phthalhydrazide and dimedone afforded good to high yields of products with high purity, at 100 ^oC under solvent-free conditions. The nature and electronic properties of the aldehyde substrates affect the conversion rate and yield.

Table . 3. Preparation of 2H- indazolo[2,1-b]phthalazin-triones **1a-e** using nano mesoporous silica (KIT-1) (0.005 g) as catalyst[a]

Entry	Ar	Product	Time(min)	Yield[b] (%)	M.P (^oC)	Ref M.P (^oC)
1	C_6H_5	**1a**	10	87	200-202	(204-206)[12]
2	$4\text{-}CH_3OC_6H_4$	**1b**	20	85	216-218	(218-220)[12]
3	$3\text{-}NO_2C_6H_4$	**1c**	15	80	253-255	(254-255)[12]
4	$4\text{-}FC_6H_4$	**1d**	10	87	254-256	(258-260)[12]
5	2-Naphthyl	**1e**	35	79	250-252	(251-252)[12]

[a] The reaction was conducted with conducted with benzaldehyde (1 mmol), dimedone (1 mmol), phthalhydrazide (1 mmol) and KIT-1 (5 mg) under solvent free at 100 ^oC

[b] Yield of isolated product

Conclusion

In summary, an efficient protocol for the preparation of 2H- indazolo[2,1-b]phthalazin-trione derivatives was described. The reaction were carried out under thermal solvent-free conditions with short reaction time and produce the corresponding products in excellent yields. Also the catalyst could be successfully recovered and recycled at least for five runs without significant loss in activity.

References

[1] Kresge, C. T., Leonowicz, M.E., Roth, W. J., Vartuli, J. C., Beck, J. S. Nature (London), 359 (1992) 710-712.

[2] Beck, J. S., et al, A new family of mesoporous molecular sieves prepared with liquid crystal templates. Journal American Chemistry Society, 114 (1992) 10834-10843.

[3] Aronson, B. J. Blanford, C. F., Stern, A. Synthesis, characterization, and ion-exchange properties of zinc and magnesium manganese oxides confined within MCM-41 channels. The Journal Physics Chemistry B, 104 (2000) 449-459.

[4] Srdanov, V. L, Alxneit, I., Stucky, G. D., Reaves, C. M., Den Baars,S. P., Optical properties of GaAs confined in the pores of MCM-41. The Journal Physics Chemistry B, 102 (1998) 3341-3344.

[5] Linseen, T., Cassie, K., Cool, P., Vansat, E. F. Mesoporous templated silicates: an overview of their synthesis, catalytic activation and evaluation of the stability, Advances in Colloid and Interface Science. 103 (2003) 121-147.

[6] Soler-Illia, G.J. A., Sanchez, C., Lebeau, B., Chemical strategies to design textured materials: from microporous and mesoporous oxides to nanonetworks and hierarchical structures. Patarin, Journal Chemical Review. 102 (2002) 4093-4138.

[7] Ryoo, R., Kim, J. M., C. H. Ko, H., Shin, C. H. Disordered molecular sieve with branched mesoporous channel network, Journal of Physical Chemistry. 100 (1996) 17718-17721.

[8] Habibi, A., Seikhhosseini-Lori, E. Synthesis of novel furo-pyran derivatives via reaction between an isocyanide and alkylidene-substituted Meldrum's acid. Tetrahedron Letter. 50 (2009) 1075-1078.

[9] Kumar, A., Maurya, R. A. Synthesis of polyhydroquinoline derivatives through unsymmetric Hantzsch reaction using organocatalysts. Tetrahedron, 63 (2007)1946-1952.

[10] Al-Assar, F., Zelenin, K. N., Lesiovskaya, E., Bezhan, I. P., Chahchir, B. A. Synthesis and pharmacological activity of 1-hydroxy-, 1-amino-, and 1-hydrazino-substituted 2, 3-dihydro-1H-pyrazolo [1, 2-a] pyridazine-5, 8-diones and 2, 3-dihydro-1H-pyrazolo [1, 2-b] phthalazine-5,10-diones Pharmaceutical Chemistry Journal. 2002, 36, 598-603.

[11] Sanaeishoar, H., Sabbaghan, M., Mohave, F., Nazarpour, R. Disordered mesoporous KIT-1 synthesized by DABCO-based ionic liquid and its characterization, Microporous and Mesoporous Materials. 228 (2016) 305–309.

[12] Jitender, M., Devanshi, M. Efficient one-pot syntheses of 2H-indazolo [2, 1-b] phthalazine-triones by catalytic H_2SO_4 in water–ethanol or ionic liquid. Tetrahedron Letter. 50 (2009) 7300-7303.