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SO_3H-Functionalized Mesoporous Silica Materials as Solid Acid Catalyst for Facile and Solvent-free Synthesis of 2*H*-Indazolo[2,1-*b*]phthalazine-1,6,11-trione Derivatives

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Ali Alinasab Amiri, Shahrzad Javanshir,*[a] Zahra Dolatkhah and Mohammad G. Dekamin

SO_3H-Functionalized Mesoporous Silica Materials (SO_3H-FMSM), as an efficient, mild, recoverable and environmentally friendly heterogeneous mesoporous nanocatalyst has been used to synthesize 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives in a one-pot three-component condensation reaction of 2,3-dihydriphthalazine-1,4-dione, dimedone, and benzaldehyde derivatives under thermal solvent-free (SF) conditions in excellent yields and short reaction times.

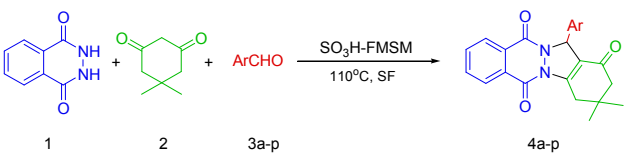
Introduction

During recent years, multicomponent Reactions (MCRs) have become progressively popular tools to assure sufficient molecular diversity and complexity, and simultaneously ensure an atom-economy and straightforward reaction design for substantial minimization of waste, labor, time, and cost, thus leading to useful heterocyclic scaffold for the construction of various chemical libraries of 'drug like' molecules.[1-3]

The preparation and synthesis of new heterocyclic compound has always been a topic of great interest owing to their wide applicability.[4] Aza heterocycles are an important class of compound that have many usage in pharmaceutical, agrochemical, and functional materials.[5] Among a large diversity of aza heterocyclic compounds, heterocycles containing phthalazine portion are of interest because of their several pharmacological and biological activities[4,6] such as cytotoxic, anti-inflammatory,[7] anticancer, anticonvulsant, antifungal,[8] antimicrobial, vasorelaxant,[9] cardiotonic, and also unique electrical and optical properties.[10] Despite many methods being available for the synthesis of phthalazine derivatives, their broad utility has accentuated the need to develop new synthetic routes for N-heterocycles containing the phthalazine moiety.[11]

In recent years, several three-component reactions (3-CRs) have been reported for the preparation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-triones in the presence of an acid or base such as TMSCl,[12] H_2SO_4,[13] phosphomolybdic acid (PMA)-SiO_2,[14] I_2,[15] *S*-Camphorsulfunic acid (*S*-CSA),[16] poly(*N*-bromo-*N*-ethylbenzene-1,3-disulfonamid) (PBBS),[17] ceric ammonium nitrate (CAN),[18] magnetic nanoparticle immobilized *N*-propylsulfamic acid (MNPs-PSA),[19] $ZrOCl_2.8H_2O$,[20] Fe_3O_4@silica sulfuric acid nanoparticles[21] and SBA-15/2,2,2-trifluoroethanole adduct (SBA-15/TFE)[22] via condensation of an aldehyde, 2,3-dihydrophthalazine-1,4-dione, and dimedone. Nevertheless, many of these methods have disadvantages such as low yields of products, long reaction times, harsh reactions conditions, exhausting work-ups leading to the generation of large amount of toxic metal- or halogen-containing waste, the requirement for an inert atmosphere and the use of stoichiometric or relativity expensive reagents.[22,23] As a result, offering novel synthetic methods or improving them for the preparation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives could be of considerable importance.

The point of this presented protocol is to highlight the synergistic effects of the combined use of MCRs and reactions under solvent-free conditions with an efficient heterogeneous nanocatalyst for the development of a new eco-compatible for the synthesis of heterocycles. Regarding the fact that solvent-free reactions and preventing the formation of by-products and also raising the rate of reactions could provide a large number of factors needed for green chemistry, we have decided to synthesize 2*H*-Indazolo[2,1-*b*]phthalazinetrione derivatives using phthalhydrazide, dimedone and benzaldehyde derivatives with the exploitation of SO_3H-FMSM, as a recyclable heterogeneous mesoporous nanaocatalyst in a one-pot multicomponent reaction in order to obtain more eligible efficiency and short reaction time (Scheme 1).



Scheme 1 Synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-triones by SO_3H-FMSM.

[a] *Heterocyclic Compounds Research Laboratory, Department of Chemistry, Iran University of Science and Technology, Tehran 16846-13114, Iran. E-mail: shjavan@iust.ac.ir*
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Results and Discussion

The synthesis and Characterisation of SO_3H-FMSM

MCM-41 is a family member of M41S mesoporous molecular silicates that has a regular hexagonal arrangement and is introduced as a solid substrate. Much attention to this substrate is due to its high surface area (1000-1300 m^2g^{-1}), specific pore size (15-100 A°) and mechanical, thermal and hydrothermal (over 800 °C) stability. For as much as MCM-41 is a neutral catalyst, its surface can be modified by SO_3H functional group. The MCM-41 nanotube was modified by the SO_3H acidic group to create acidic sites on its surface. MCM-41 and SO_3H-FMSM were synthesized according to previously reported methods.[24,25] The SO_3H-FMSM was characterized by SEM (Scanning Electron Microscopy), EDX (Energy Dispersive X-ray) and FT-IR spectroscopy. In FT-IR spectroscopy (Fig. 1), the bands at 1250 cm^{-1} and 1321 cm^{-1} are due to the symmetric and asymmetric stretching vibrations of S=O of the sulfonic acid group. The broad band in the region of 3200-3400 cm^{-1} is assigned to the O-H stretching vibration of hydroxyl groups. Moreover, a strong band at 1174 cm^{-1} is assigned to the Si–O–Si asymmetric stretching vibrations and a band at 850 cm^{-1} related to its symmetric stretching vibrations (Fig. 1).

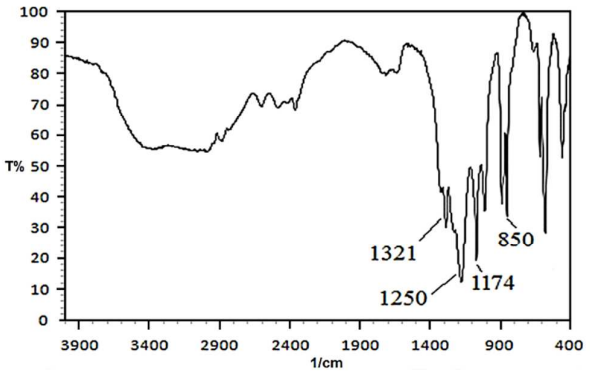


Fig. 1 FT-IR spectrum of SO3H-FMSM nanocatalyst.

In order to investigate the morphology of the catalyst structure, the SEM micrograph was used. As can be seen, nanoscale particles and pores of the catalyst is clearly evident (Fig. 2).

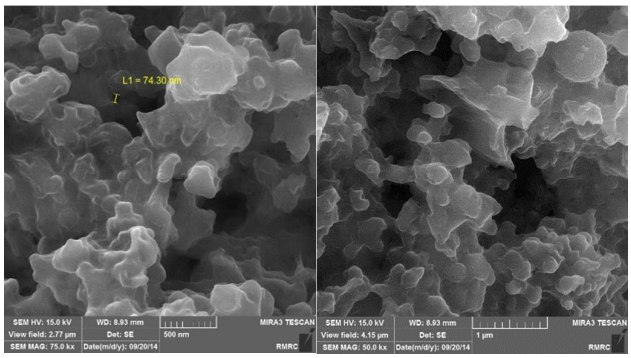
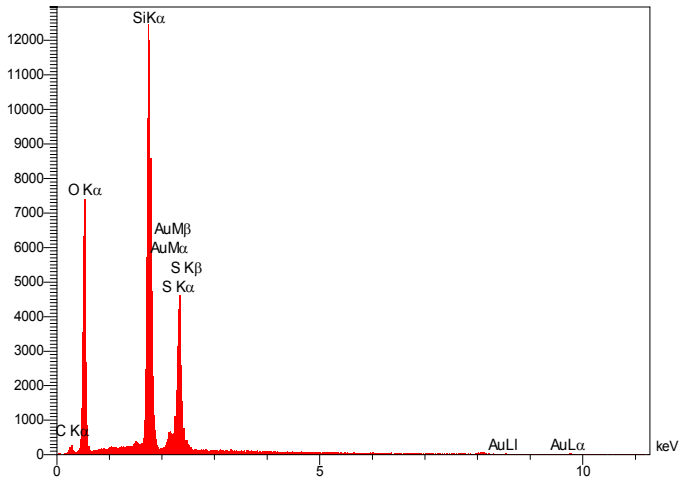


Fig. 2 The SEM micrographs of SO_3H-FMSM nanocatalyst.

EDX analysis is used to study the chemical composition and elemental analysis of solid samples. As shown in fig. 3, nanocatalyst contains the sulfur, silicon and oxygen. It shows that our catalyst is formed and functionalized. The low angle XRD and BET analysis of SO_3H-FMSM were also provided in supplementary data. The specific surface area, pore volume and average pore diameter were obtained by the N_2 adsorption isotherms calculated by the BET and BJH method and found 1078 $m^2\ g^{-1}$, 0.56 $cm^3\ g^{-1}$ and 2.5 nm respectively before functionalization and 71.7 $m^2\ g^{-1}$, 0.05$cm^3\ g^{-1}$ and 2.8 nm respectively after functionalization with SO_3H-groups. Pore volume are found lower than that of MCM-41 due to the functionalization. The results of N_2 adsorption isotherms also showed that SO_3H-FMSM exhibits typical type IV isotherm indicating that the mesoporous texture is largely maintained.

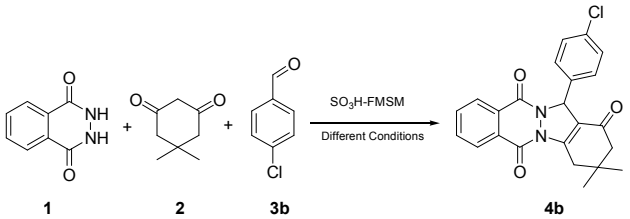
Fig. 3 EDX analysis of SO_3H-FMSM nanocatalyst.



Optimization of reaction conditions

2,3-dihydrophthalazine-1,4-dione **1** as an initial material in this reaction, was synthesized according to the reported method.[26] It was characterized with FT-IR and ^{1}H and ^{13}CNMR spectroscopy.

For gaining the optimum conditions, a model reaction was selected that involved a mixture of 2,3-dihydrophthalazine-1,4-dione (1.0 mmol, 162.1 mg), dimedone (1.0 mmol, 140.1 mg) and 4-chlorobenzaldehyde (1.0 mmol, 140.6 mg) under various conditions such as ball milling without heating; sonication in ethanol as solvent in room temperature and thermal solvent-free conditions in the presence of SO_3H-FMSM (20.0 mg) (Scheme 2).



Scheme 2 Model reaction for the synthesis of **4b**

The progress of the reaction monitored by thin-layer chromatography (TLC) indicated that the reaction was not completed and just the intermediate was formed after 30 minutes of ball milling and in the case of sonication the yield was low. However, under thermal condition, the reaction was completed after 30 min, and thus the thermal solvent-free conditions was selected as the best method (Table 1, Entry 3).

Table 1 Study for selecting the best route for synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives.

Entry	Path of the reaction	Yield (%)
1	Ball milling	trace
2	))) [a], Ethanol, r.t.	30
3	Δ [b], Solvent-free	90

[a] Ultrasonic irradiation; [b] Thermal condition

In order to obtain the optimum reaction temperature, the model reaction was studied at different temperatures using constant amount of catalyst. According to the results 110°C was selected as optimum temperature (Table 2).

To put in evidence the role and effect of the catalyst in the rate of reaction, the model reaction was carried out in the absence of any catalyst (Entry1, table3). The results revealed that the yield of the reaction was very low and lapse of time hasn't had significant impact on efficiency of reaction.

To evaluate the appropriate catalyst loading, the model reaction was carried out using different amount of catalyst. It was found that 20 mg was the most effective amount (Table 3, entry 5) and larger amounts of catalyst do not increase the reaction yield. The reaction was also done in the presence of 20 mg of MCM-41-Propyl-SO_3H as a comparative acidic catalyst. The result suggests that SO_3H-FMSM is more suitable for this reaction (Table 3, entry 8).

Table 2 The temperature effect on efficiency and duration of synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives.

Entry	Temperature (°C)	Time (min)	Yield (%)*
1	50	70	20
2	70	55	50
3	85	30	88
4	100	25	93
5	110	18	95
6	120	18	94

*Isolated yields

To generalize the optimum conditions for the synthesis of 2H-indazolo[2,1-b]phthalazine-1,6,11-trione derivatives a one-pot reaction of 2,3-dihydrophthalazine-1,4-dione, dimedone and aromatic aldehydes (1:1:1) was carried out in the presence of 20 mg of SO_3H-FMSM at 110°C under solvent-free conditions for the appropriate time (Table 4). The results were excellent in terms of yields and product purity.

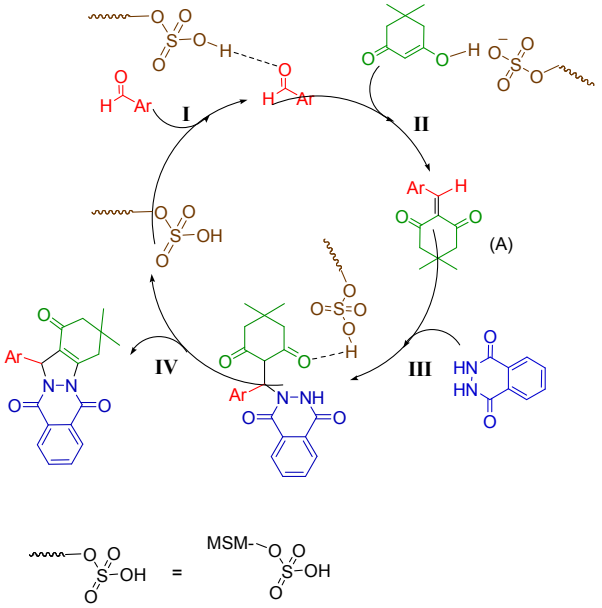
Table 3 The catalyst effect study and amount of it on efficiency and duration of synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives under thermal solvent-free conditions.

Entry	Catalyst	Amount catalyst (mg)	Time (min)	Yield (%)*
1	-	-	180	10
2	SO_3H-FMSM	5	80	70
3	SO_3H-FMSM	10	60	80
4	SO_3H-FMSM	15	40	88
5	SO_3H-FMSM	20	18	95
6	SO_3H-FMSM	25	20	95
7	SO_3H-FMSM	30	20	93
8	MCM-41-Pr-SO_3H	20	60	88

*Isolated yields

Proposed Mechanism

A plausible mechanism for the reaction is shown in Scheme 2. The formation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-triones involves initial formation of intermediate (**A**) via a Knoevenagel condensation of dimedone and aromatic aldehyde catalyzed by SO_3H-FMSM. Subsequent Michael-type addition of the phthalhydrazide followed by cyclization affords the corresponding product (Scheme 2).



Scheme 3 A plausible mechanism for the one-pot and three-component synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives catalyzed by SO_3H-FMSM.

Reusability of the catalyst

The reusability of the catalyst was also investigate, for this purpose it was filtered by nano-paper filter and washed by hot ethyl acetate and ethanol, then dried at 50°C. The recycled catalyst was used for 4 runs without considerable loss of activity (Figure 4). The FT-IR spectrum of SO_3H-FMSM after recycling are given in supporting information. In order to show the merit of this work in comparison with other work recently reported, we compared the results of the synthesis of 2H-indazolo [2,1-b] phthalazine-1,6,11-trione derivatives in the presence of various catalysts, regarding the reaction time, temperature, reaction conditions and product yields (Table 5).

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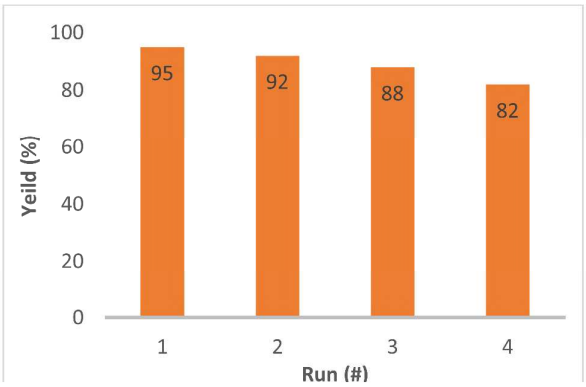
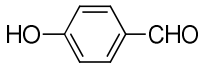
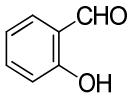
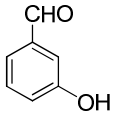
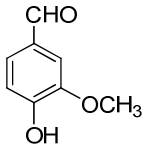
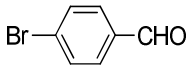
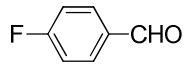


Fig. 4 Recyclability of SO_3H-FMSM as a nanocatalyst in this reaction.

Table 4 Three-components reaction for preparation of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives at 110°C catalyzed by SO_3H-FMSM.

Entry	Aromatic aldehyde	Product	Time (min)	Yield* (%)	m.p. Found (°C)	m.p. Reported (°C)
1		**4a**	20	93	202-204	204-206 [27]
2		**4b**	18	95	255-257	262-264 [27]
3		**4c**	22	95	265-267	264-266 [28]
4		**4d**	20	93	218-220	219-221 [29]
5		**4e**	15	95	224-227	223-225 [29]
6		**4f**	20	93	232-234	227-229 [28]
7		**4g**	20	93	264-266	270-272 [29]
8		**4h**	25	90	226-229	227-229 [29]
9		**4i**	22	92	214-216	218-220 [29]
10		**4j**	24	90	180-182	186-188 [19]

11		**4k**	24	90	225-227	225-227 [21]
12		**4l**	24	93	188-190	185-187 [30]
13		**4m**	22	95	252-255	257-258 [12]
14		**4n**	22	93	251-254	250-252 [31]
15		**4o**	20	95	265-267	265-267 [27]
16		**4p**	18	95	222-224	224-226 [31]

*Isolated yield.

Table 5 Comparison of the performance of SO_3H-FMSM with other catalysts in synthesis of *2H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives.

Entry	Catalyst	Condition	Temp. (°C)	Time (min)	Yield (%)	Ref.
1	TMSCl	(CH_3CN/DMF)	80	60	86.2	12
2	H_2SO_4	(Ethanol/H_2O)	80	30	88	13
3	H_2SO_4	[bmim]BF_4	80	35	90	13
4	PMA-SiO_2	Solvent free	80	40	91	14
5	I_2	Ethanol	80	25	90	15
6	(*S*)-CSA	Sonication	R.T.	40	82	16
7	PBBS	Solvent free	100	45	75	17
8	CAN	PEG-400[a]	50	120	94	18
9	MNPs-PSA	Solvent free	100	25	93	19
10	$ZrOCl_2.8H_2O$	Solvent free	80	60	89	20
11	Fe_3O_4@silica sulfuric acid	Solvent free	100	35	92	21
12	SBA-15/TFE	TFE[b]	65	150	94	22
13	SO_3H-FMSM	Solvent free	110	18	95	This work

[a]polyethylene glycol 400; [b] Trifluoroethanol

Conclusions

In summary, an efficient protocol for the one-step and one-pot synthesis of 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives has been described *via* a three-component condensation reaction of phthalhydrazide, dimedone and aromatic aldehydes in the presence of SO_3H-FMSM as a recoverable heterogeneous nanocatalyst under thermal solvent-free conditions. The products of the reaction were obtained in excellent yields and in short reaction times. SO_3H-FMSM could be successfully recovered and recycled for four runs without any important diminution of activity.

Experimental

Instruments and characterization

All chemicals were purchased from Merck, Fluka, and Sigma-Aldrich companies and were used without further purification. Thin layer chromatography (TLC) was performed by using aluminum plates coated with silica gel 60 F-254 plates (Merck) using ethyl acetate and *n*-hexane (1:2) as eluents. The spots were detected either under UV light or by placing in an iodine chamber. Melting points were determined in open capillaries using an Electrothermal 9100 instrument. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker Avance DPX-300 instrument. The spectra were measured in DMSO-d_6 relative to TMS as internal standard. FT-IR spectra were obtained with a shimadzu 8400S with spectroscopic grade KBr. CHN were recorded on a CHN-OS analyzer (Perkin Elmer 2400, series II). Scanning electron microscopy (SEM) was recorded on a VEG//TESCAN WITH GOLD COATING, and energy dispersive X-ray spectroscopy (EDX) was recorded on a VEG//TESCAN-XMU.

General procedure for preparation of MCM-41

2.7 g diethylamine was added to 42 mL deionized water in a 500 mL beaker at room temperature while the mixture was stirred. After 10 min, 1.47 g cetyltributylammonium bromide (CTAB) was inchmeal added to the mixture about 30 min, until a clear solution was obtained. In the following, 2.1 g Tetraethyl orthosilicate as a silica precursor was added drop-wise to the solution and the pH was adjusted to 8.5 by adding 1.0 M HCl solution slowly. After being stirred for 2 h, the white solid precipitate was filtered and washed with deionized water. The

obtained MCM-41 was dried at 45 °C for 12 h and then was calcined at 550 °C for 5 h to remove all the surfactant[24].

General procedure for preparation of SO_3H-FMSM

MCM-41 (1.0 g) and CH_2Cl_2 (5.0 mL) were transferred to 100 mL round bottom flask equipped with a gas outlet tube and a dropping funnel containing a solution of $ClSO_3H$ (1.5 mL) in CH_2Cl_2 (10 mL). The chlorosulfonic acid solution was added drop-wise to the flask containing over a period of 30 min at room temperature while the mixture was being stirred. Expulsion of evolved HCl gas from the reaction mixture was conducted via the gas outlet tube into a NaOH solution. After the completion of the reaction, the solvent was evaporated under reduced pressure and the SO_3H-FMSM was collected as a greyish white solid[25]. The amount of SO_3H groups is calculated by inverse acid–base titration of the catalyst. [32] The concentration of acid sites of catalyst was determined by titration: 0.5 g of the catalyst sample was added to 50 mL of NaCl solution (200 g/L) and stirred at room temperature. The ion exchange between H+ and Na+ was allowed to proceed for 24 h. The catalyst was filtered off and washed with distilled water, then the mixture was titrated with 0.01 N NaOH solution using phenolphthalein as pH indicator.

General procedure for preparation of MCM-41-Propyl-SO_3H

The MCM-41 (5 g) was added to a solution of 3-mercaptopropyl(trimethoxy)silane (10 mmol) in dry toluene and refluxed for 24 h. The 3-mercaptopropyl MCM-41 (MPMCM-41) was filtered off and washed with hot toluene and dried at 110 °C for 5 h to give the surface bound thiol (MPMCM-41) groups. Then, the mixture of MPMCM-41 (5 g), 30% H_2O_2 solution (50 mL) and conc. H_2SO_4 (0.078 g, 0.8 mmol) was stirred at room temperature for 20 h. The solid was filtered off at pump and washed with excess distilled water till the washings were neutral. In order to confirm that all the sulfonic acid groups are protonated, the solid material was further suspended in 0.05 M H_2SO_4(30 mL) for 5 h. The solid was then filtered off and washed with excess distilled water till the washings were neutral. Finally it was dried in air at 110 °C for 5 h.

A procedure for the synthesis of 2,3-dihydrophthalazine-1,4-dione

Hydrazine hydrate ($NH_2NH_2.H_2O$, 2.0 mmol) was added drop-wise to a stirred, cold (ice-bath) solution of Phthalimide (2.98 g, 2.0 mmol) in ethanol (30 mL) over a period of 30 min. The reaction mixture was stirred for 3 hours at 70°C and then allowed to cool to 0°C in an ice-water bath, causing the formation of a white precipitate. The precipitate was then collected by filtration, washed with ethanol, and dried under vacuum at room temperature to give the required compound[26].

General procedure for the synthesis of 2H-indazolo[2,1-b]phthalazine-1,6,11-triones catalyzed by the SO_3H-FMSM nanocatalyst

A pressurized seal tub equipped with a tiny magnetic stir bar was charged with a mixture of 2,3-dihydrophthalazine-1,4-dione **1** (1.0 mmol, 162.1 mg), dimedone **2** (1.0 mmol, 140.1 mg) and aldehyde **3a-p** (1.0 mmol) under solvent-free condition in the presence of nanocatalyst SO_3H-FMSM (20.0 mg) and heated at 110°C. The progress of the reaction was monitored by TLC. After completion of the reaction, the catalyst/product mixture was cooled to room temperature and the product was dissolved in ethyl acetate. The catalyst was removed by filtration, washed by hot ethanol and hot ethyl acetate and dried at 50 °C for reuse in recycling experiments. A totally pure product was obtained after recrystallization from ethyl acetate/*n*-hexane (1:3).

Spectral data for the selected compounds:

3,4-Dihydro-3,3-dimethyl-13-phenyl-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13H)-trione (*Table 4, entry 1, 4a*):

Yellow powder, m.p. 202-204 °C; IR (KBr): υ 2961, 1661, 1577 cm^{-1}; ^1H NMR (300.13 MHz, DMSO): δ 1.08 (s, 3H), 1.12 (s, 3H), 2.26 (s, 2H, CH_2C), 3.01-3.16 (AB system, 2H, CH_aH_bCO), 6.31 (s, 1H), 7.10-8.19 (m, 9H, aromatics) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.0, 28.2, 34.5, 37.9, 50.7, 64.9, 118.6, 127.0, 127.5, 127.8, 128.8, 129.3, 133.2, 134.2, 136.1, 150.9, 154.4, 156.0, 191.9 ppm; Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52%. Found: C, 74.22; H, 5.38; N, 7.49%.

3,4-Dihydro-3,3-dimethyl-13-(4-chlorophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13H)-trione (*Table 4, entry 2, 4b*):

Yellow powder, m.p. 255-257 °C; IR (KBr): υ 2963, 2935, 1689, 1654, 1632 cm^{-1}; ^1H NMR (300.13 MHz, DMSO): δ 1.08 (s, 3H), 1.11 (s, 3H), 2.24 (s, 2H, CH_2C), 3.04-3.19 (AB system, 2H, CH_aH_bCO), 6.28 (s, 1H), 7.34-7.49 (dd, 4H, ArCl), 7.96-8.28 (m, 4H, Ph) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.5, 28.6, 34.8, 38.2, 50.8, 64.1, 117.9, 127.4, 127.9, 128.3, 128.6, 128.8, 129.0, 133.5, 134.2, 134.6, 134.9, 150.9, 154.0, 156.1, 192.2 ppm; Anal. Calcd for $C_{23}H_{19}ClN_2O_3$: C, 67.92; H, 4.7; N, 6.85%. Found: C, 67.8; H, 4.62; N, 6.81%.

3,4-Dihydro-3,3-dimethyl-13-(4-nitrophenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13H)-trione (*Table 4, entry 5, 4e*):

Yellow powder, m.p. 224-227 °C; IR (KBr): υ 2970, 2955, 1689, 1694, 1662 cm^{-1}; ^1H NMR (300.13 MHz, DMSO): δ 1.06 (s, 3H), 1.15 (s, 3H), 2.25 (s, 2H, CH_2C), 3.02-3.16 (AB system, 2H, CH_aH_bCO), 6.35 (s, 1H), 7.27-8.20 (dd, 4H, $ArNO_2$), 7.85-7.90 (m, 4H, Ph) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.4, 28.8, 34.7, 37.9, 50.7, 64.3, 117.5, 123.8, 128.2, 128.3, 128.5, 128.8, 133.9, 134.7, 143.3, 148.0, 152.0, 154.4, 156.0, 192.1 ppm; Anal. Calcd for $C_{23}H_{19}N_3O_5$: C, 66.15; H, 4.59; N, 10.02%. Found: C, 66.21; H, 4.62; N, 9.99%.

3,4-Dihydro-3,3-dimethyl-13-(4-methylphenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13H)-trione (*Table 4, entry 8, 4h*):

Yellow powder, m.p. 226-229 °C; IR (KBr): υ 2958, 1667, 1628 cm^{-1}; ^1H NMR (300.13 MHz, DMSO): δ 1.08 (s, 3H), 1.10 (s, 3H), 2.2 (s, 3H, CH_3Ph), 2.26 (s, 2H, CH_2C), 3.03-3.20 (AB system, 2H, CH_aH_bCO), 6.28 (s, 1H), 7.22-7.38 (dd, 4H, ArMe), 7.92-8.25 (m, 4H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3, 28.6, 29.0, 34.6, 38.0, 60.0, 64.8, 118.5, 127.3, 127.7, 127.9, 128.8, 129.0, 129.4, 133.5, 133.6, 134.5, 138.4, 150.9, 154.1, 155.9, 192.3

ppm; Anal. Calcd for $C_{23}H_{22}N_2O_3$: C, 74.59; H, 5.77; N, 7.21%. Found: C, 74.61; H, 5.69; N, 7.31%.

3,4-Dihydro-3,3-dimethyl-13-(3-hydroxyphenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13H)-trione (*Table 4, entry 13, 4m*):

Yellow powder, m.p. 252-255 °C; IR (KBr): υ 3351, 2954, 2890, 1667 cm^{-1}; ^1H NMR (300.13 MHz, DMSO): δ 1.09 (s, 3H), 1.11 (s, 3H), 2.22 (s, 2H, CH_2C), 3.04-3.20 (AB system, 2H, CH_aH_bCO), 5.91 (b, 1H, OH), 6.27 (s, 1H), 6.66-7.19 (m, 4H, ArOH), 7.70-7.77 (m, 2H, Ph), 8.20-8.31 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.5, 28.6, 34.5, 37.9, 51.0, 64.6, 114.4, 115.8, 118.4, 118.6, 127.7, 127.9 (2), 128.9, 130.0, 133.5, 134.4, 138.0, 150.9, 154.1, 155.9, 192.2 ppm; Anal. Calcd for $C_{23}H_{20}N_2O_4$: C, 71.12; H, 5.22; N, 7.25%. Found: C, 71.13; H, 5.19; N, 7.28%.

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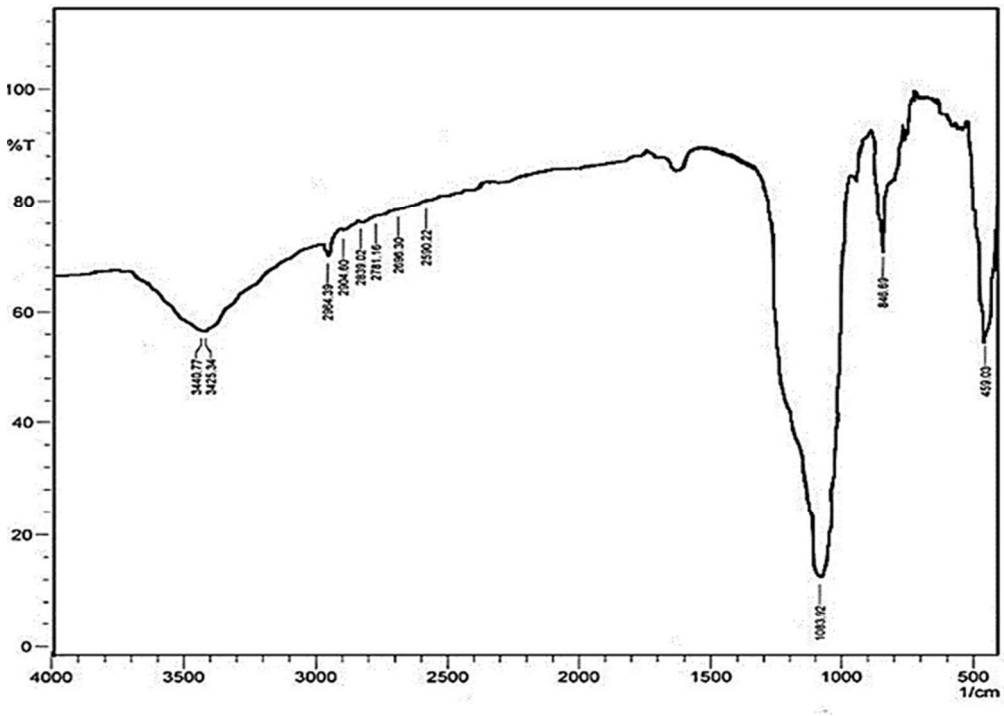
Supplementary data

Supplementary data associated with this article can be found, in the online version at http://dx.doi

Notes and references

1 G. Shukla, R. K. Verma, G. K. Verma, M. S. Singh, *Tetrahedron Lett.*, 2011, **52**, 7195.
2 (a) S. T. Staben, N. Blaquiere, *Angew. Chem., Int. Ed.* 2010, **49**, 325. (b) N. Ma, B. Jiang, G. Zhang, S.-J. Tu, W. Wever, G. Li, *Green Chem.*, 2010, **12**, 1357.
3 (a) C. Haurena, E. L. Gall, S. Sengmany, T. Martens, M. Troupel, *J. Org. Chem.*, 2010, **75**, 2645. (b) W.-B. Chen, Z.-J. Wu, Q.-L. Pei, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, *Org. Lett.*, 2010, **12**, 3132. (c) M. M. Heravi, B. Baghernejad, H. A. Oskooie, R. Hekmatshoar, *Tetrahedron Lett.*, 2008, **49**, 6101.
4 F. Al-Assar, K. N. Zelenin, E. E. Lesiovskaya, I. P. Bezhan, B. A. Chakchir, *Pharm. Chem. J.*, 2002, **36**, 598.
5 (a) A. R. Hasaninejed, M. Rasekhi Kazerooni, A. Zare, *Catal. Today* 2012, **196**, 148. (b) S. Nag, S. Batra, *Tetrahedron*, 2011, **67**, 8959. (c) Y. Xu, Q.-X. Guo, *Heterocycles*, 2004, **63**, 903.
6 (a) R. P. Jain, J. C. Vederas, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 3655. (b) R. W. Carling, K. W. Moore, L. J. Street, D. Wild, C. Isted, P. D. Leeson, S. Thomas, D. O'Conner, R. M. McKernan, K. Quirk, S. M. Cook, J. R. Atack, K. A. Wafford, S. A. Thompson, G. R. Dawson, P. Ferris, J. L. Castro, *J. Med. Chem.*, 2004, **47**, 1807.
7 J. S. Kim, H. K. Rhee, H. J. Park, S. K. Lee, C. O. Lee, H. Y. Park Choo, *Bioorg. Med. Chem.*, 2008, **16**, 4545.
8 (a) C. K. Ryu, R. E. Park, M. Y. Ma, J. H. Nho, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 2577. (b) J. Li, Y. F. Zhao, X. Y. Yuan, J. X. Xu, P. Gong, *Molecules*, 2006, **11**, 574.
9 El-Sakka, S. S.; Soliman, A. H.; Imam, A. M. *Afinidad*, 2009, **66**, 167.
10 (a) F. W. Lichtenthaler, *Acc. Chem. Res.* 2002, **35**, 728. (b) V. P. Litvinov, *Russ. Chem. Rev.*, 2003, **72**, 69.
11 (a) E. Mosaddegh, A. Hassankhani, *Tetrahedron Lett.*, 2011, **52**, 488. (b) M. Sayyafi, M. Seyyedhamzeh, H. R. Khavasi, V. Bazgir, *Tetrahedron*, 2008, **64**, 2375. (c) Y. K. Ramtohup, M. N. G. Jamse, J. C. Vederas, *J. Org. Chem.*, 2002, **67**, 3169.
12 L. Nagarapu, R. Bantu, H. B. Mereyala, *J. Heterocycl. Chem.*, 2009, **46**, 728.
13 J. M. Khurana, D. Magoo, *Tetrahedron Lett.*, 2009, **50**, 7300.
14 G. Sabitha, C. Srinivas, A. Raghavendar, J. S. Yadav, *Helv. Chim. Acta.*, 2010, **93**, 1375.
15 X. Wang, G. Lu, W. Ma, L. Wu, *E-J. Chem.* 2011, **8**, 1000.
16 G. Shukla, R. K. Verma, G. K. Verma, M. S. Singh, *Tetrahedron Lett.*, 2011, **52**, 7195.
17 R. Ghorbani-Vaghei, R. Karimi-Nami, Z. Toghraei-Semiromi, M. Amiri, M. Ghavidel, *Tetrahedron*, 2011, **67**, 1930.
18 M. Kidwai, R. Chauhan, A. Jahan, *Chin. Sci. Bull.*, 2012, **57**, 2273.
19 A. Rostami, B. Tahmasbi, A. Yari, *Bull. Korean Chem. Soc.*, 2013, **34**, 1521.
20 H. R. Tavakoli, S. M. Moosavi, A. Bazgir, *J. Korean Chem. Soc.*, 2013, **57**, 472.
21 J. Davarpanah, A. Kiasat, *J. Mol. Catal. A: Chem.*, 2013, **373**, 46.
22 S. Rostamnia, E. Doustkhah, *Tetrahedron Lett.*, 2014, **55**, 2508.
23 (a) M. Nabid, S. Tabatabaei, R. Ghahremanzadeh, A. Bazgir, *Ultrason. Sonochem.*, 2010, **17**, 159. (b) X. Wang, W. Ma, L. Wu, F. Yan, *J. Chin. Chem. Soc.*, 2010, **57**, 1341. (c) H. Shaterian, F. Khorami, A. Amirzadeh, R. Doost-M, M. J. Ghashang, *Iran. Chem. Soc.*, 2009, **2**, 57.
24 (a) M. A. Zanjanchi, Sh. Asgari, *Solid State Ionics*, 2004, **171**, 277.; (b) M. G. Dekamin, Z. Mokhtari, *Tetrahedron*, 2012, **68**, 922.
25 (a) S. Rostamizadeh, A. M. Amani, G. H. Mahdavinia, G. Amiri, H. Sepehrian, *Ultrason. Sonochem.*, 2010, **17**, 306. (b) E. Ali, M. R. Naimi-Jamal, M. G. Dekamin, *Sci. Iran.*, 2013, **20**, 592.
26 Y. Wu, L.-P. Sun, L.-X. Ma, J. Che, M.-X. Song, X. Cui, H.-R. Piao, *Chem. Biol. Drug. Des.*, 2013, **81**, 591.
27 B. Mombani-Godajdar, A. Kiasat, M. Mahmoodi-Hashemi, *Heterocycles*, 2013, **87**, 559.
28 A. Kiasat, S. Noorizadeh, M. Ghahremani, S. J. Saghanejad, *J. Mol. Struct.*, 2013, **1036**, 216.
29 A. R. Kiasat, A. Mouradzadegun, S. J. Saqganezhad, *J. Serb. Chem. Soc.*, 2013, **78**, 469.
30 M. Kidwai, A. Jahan, R. Chauhan, N. K. Mishra, *Tetrahedron Lett.*, 2012, **53**, 1728.
31 H. R. Shaterian, M. Aghakhanizadeh, *C. R. Chim.*, 2012, **15**, 1060.
32 S. Z.P. Xu, K.T. Chuang, Chem. Eng. Sci., 1997, 52, 3011.



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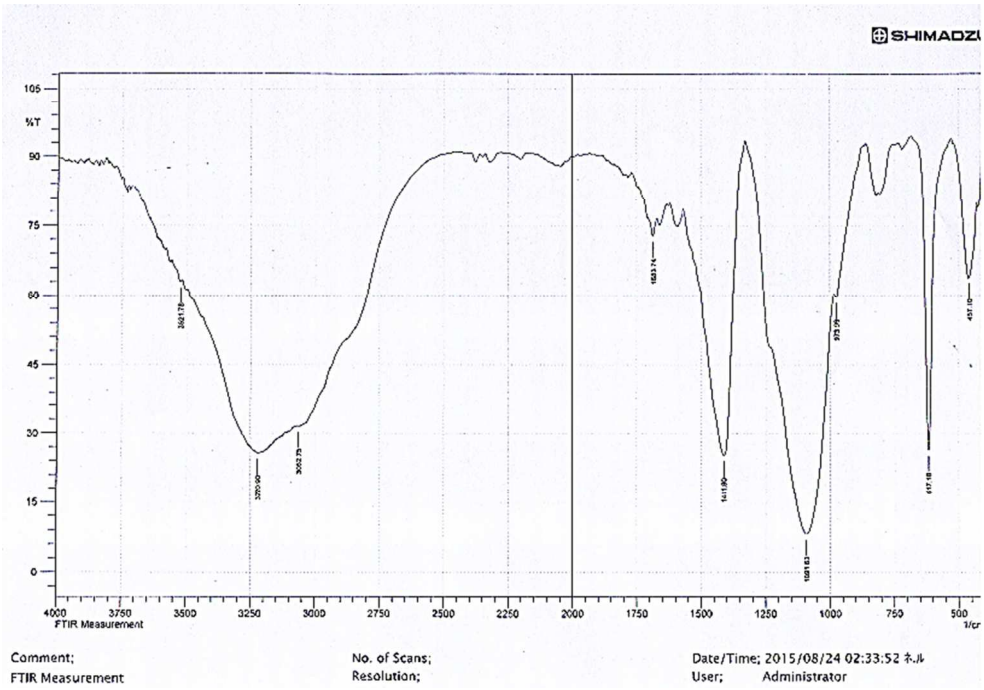

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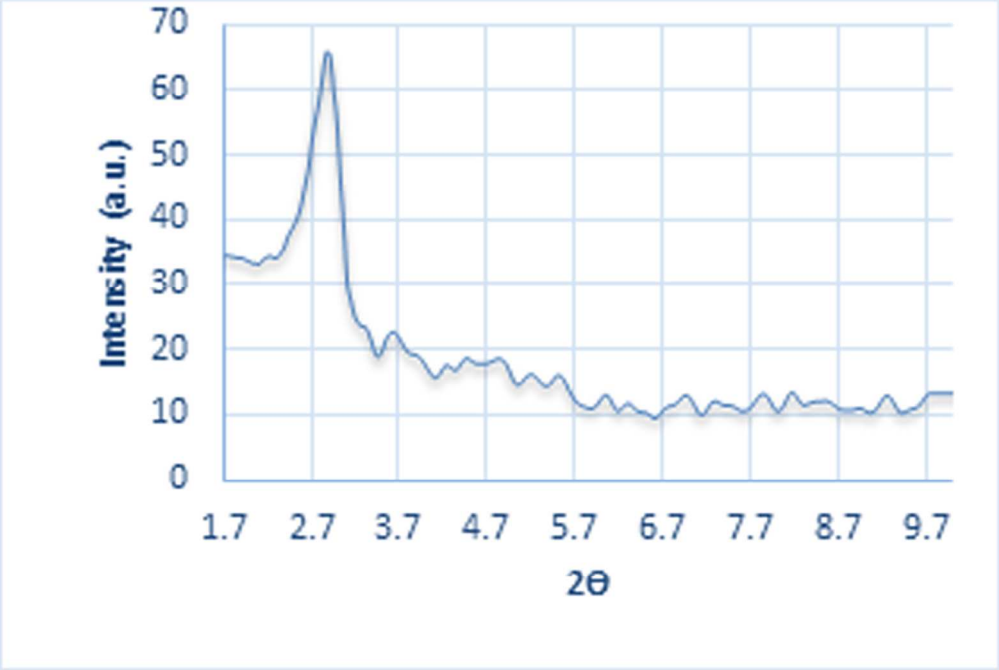

Graphical Abstract

SO_3H-Functionalized Mesoporous Silica Materials as Solid Acid Catalyst for Facile and Solvent-free Synthesis of 2*H*-Indazolo[2,1-*b*]phthalazine-1,6,11-trione Derivatives

Ali Alinasab Amiri, Shahrzad Javanshir,* Zahra Dolatkhah and Mohammad G. Dekamin

SO_3H-Functionalized Mesoporous Silica Materials (SO_3H-FMSM), as an efficient, recoverable and environmentally friendly heterogeneous mesoporous nanocatalyst has been used to synthesize 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11-trione derivatives in a one-pot three-component condensation reaction of 2,3-dihydriphthalazine-1,4-dione, dimedone, and benzaldehyde derivatives under thermal solvent-free (SF) conditions.