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RESEARCH ARTICLE

Boehmite Silylpropyl Amine Sulfamic Acid as an Efficient and Recyclable Catalyst for the Synthesis of some Pyrazole Derivatives

Rahele Doosti[1], Mohammad Bakherad[1,*], Mahdi Mirzaee[1,*] and Khosrow Jadidi[2]

[1]*School of Chemistry, Shahrood University of Technology, Shahrood 3619995161, Iran;* [2]*Department of Chemistry, Shahid Beheshti University, Tehran 1983963113, Iran*

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Abstract: ***Background***: The design of biologically-active compounds is a challenging viewpoint in medicinal chemistry, and pyrazoles play a crucial role as biologically-active molecules.

Methods: Up to now, a few examples have been reported for the synthesis of pyrazoles catalyzed by heterogeneous catalysts. In this work, a new boehmite silylpropyl amine sulfamic (m-SABNPs) was applied as a catalyst for one-pot synthesis of pyrazole derivatives.

Results: It was found that this heterogeneous sulfamic acid is a highly efficient catalyst for the syntheses of 5-amino-1,3-aryl-1*H*-pyrazole-4-carbonitriles and pyrazolopyranopyrimidines in good to excellent yields and can be recovered by a simple filtration of the reaction solution and reused for five consecutive runs without significant loss of catalytic activity. Moreover, its structure was characterized by FT-IR spectroscopy, TGA, XRD, TEM and SEM techniques.

Conclusion: An efficient, and convenient method was proposed for the synthesis of pyrazole derivatives catalyzed by heterogeneous sulfamic acid in high-to-excellent yields. This method offers several advantages like milder reaction condition, shorter reaction time, cleaner reaction, and reusability of the catalyst.

Keywords: Boehmite nanoparticle, reusable catalyst, sulfamic acid, pyrazoles.

1. INTRODUCTION

Sulfamic acid (NH_2SO_3H, SA) is an odorless, non-volatile, non-hygroscopic, incorrodible, crystalline solid acid with outstanding catalytic properties in the heterocyclic synthesis. Moreover, the catalytic activity of solid acids could be efficiently increased by their immobilization onto a nanomaterial solid support with a high surface area. When the size of such a support decreases to a nanometer scale, surface area considerably increases, and the support can be evenly dispersed in solution to form a homogenous emulsion [1].

Boehmite is aluminum oxide hydroxide (γ-AlOOH), comprising additional hydroxyl groups on its surface. Among the various techniques utilized for the production of BNPs, the hydrothermal-assisted sol-gel hydrolysis of aluminum alkoxides, which is a one-pot procedure at low temperature, was used in this work. The most encouraging property of this method is the development of a crystalline single-phase product with no organic residues [2, 3]. Mirzaee *et al*. have recently reported the epoxidation of different olefins using oxosulfate vanadium(IV) and hexacarbonyl molybdenum complexes anchored onto the amine and/or Schiff base functionalized BNPs [4-6].

Pyrazoles and their derivatives are extensively used as pharmaceuticals and agrochemicals, the earliest example, antipyrine, dating from 1884 [7, 8]. Literature survey has revealed that a number of methods have been reported for the synthesis of pyrazole nucleus [9-11]. On the other hand, only a few examples of the synthesis of pyrazoles in the presence of heterogeneous catalysts such as $CsF\text{-}Al_2O_3$ [12], silica chloride [13], and CuO/ZrO_2 [14] have been mentioned in the literature. In continuation of our studies on the application of BNPs in organic synthesis [15, 16], herein we wish to report a simple, rapid, and green synthetic method for the syntheses of 5-amino-1,3-aryl-1*H*-pyrazole-4-carbonitriles, dihydropyrano[2,3-*c*]pyrazoles, and pyrazolopyranopyrimidines, catalyzed by BNPs -sulfamic acid (m-SABNPs) (Scheme **1**).

2. RESULTS AND DISCUSSION

2.1. Catalyst Preparation

m-SABNPs was prepared as shown in Scheme **2**. Initially, BNPs were prepared according to a reported procedure [2]. Then it was refluxed with trimethoxysilylpropyl amine

*Address correspondence to these author at the School of Chemistry, Shahrood University of Technology, Shahrood 3619995161, Iran;
Tel: +982332395441; E-mails: m.bakherad@yahoo.com;
mmirzaee@shahroodut.ac.ir

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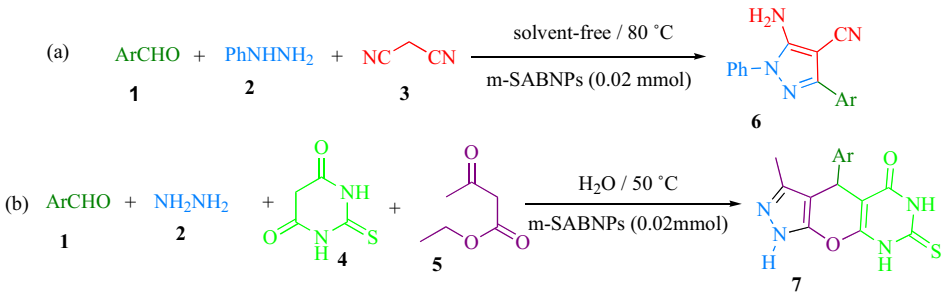
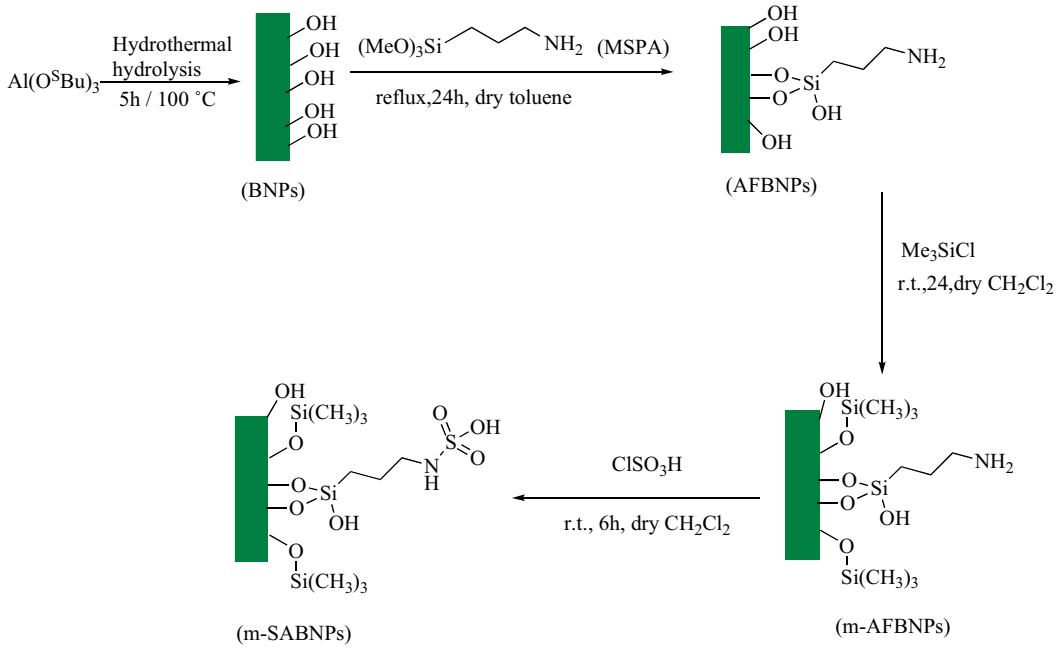


Scheme (1). Synthesis of 5-amino-pyrazole-4-carbonitrile derivatives (**a**), pyrazolopyranopyrimidine derivatives (**b**) in the presence of BNPs -sulfamic acid catalyst.



Scheme (2). Synthesis of m-SABNPs catalyst.

(MSPA) in dry toluene for 24 h in order to graft the $-O_3Si(CH_2)_3NH_2$ group on the hydroxyl-covered surface of BNPs, affording amino functional boehmit nanoparticles (AFBNPs). Then some of the unreacted surface hydroxyl groups in AFBNPs were blocked using trimethylsilyl chloride in order to stabilize the catalyst in acidic media. The amine groups in the methylated product (m-AFBNPs) were then changed to sulfamic acid by reaction with chlorosulfunic acid, which led to the formation of m-SABNPs. The catalyst produced was characterized by FT-IR spectroscopy, and the TGA, DTA, XRD, BET, TEM, SEM, and EDX techniques.

2.2. Catalyst Characterization

The FT-IR spectra for BNPs (a), AFBNPs (b), m-AFBNPs (c), and m-SABNPs (d) are showed in Fig. (**1**). A broad band was observed in the range of 3400-3300 cm^{-1} in the BNPs and AFBNPs samples, which was assigned to the ν(O-H) stretching of their surface hydroxyl groups. BNPs also showed its characteristic bands in 1076, 756, and 493 cm^{-1}, which were assigned to the ν (O-H) stretching and δ (Al-OH) groups. The IR spectrum for AFBNPs (Fig. **1b**), in addition to the BNPs characteristic bands, showed new bands at 2939 and 1566 cm^{-1}, which were assigned to the ν(C-H) and ν(N-H) stretching of the grafted n-propyl amine groups, respectively. Partial blocking the surface hydroxyl groups in AFBNPs was confirmed by significant reductions in the ν(O-H) stretching of both the m-AFBNPs and m-SABNPs samples in the range of 3300-3400 cm^{-1} (Figs. **1c** and **d**). Elimination of some surface hydroxyl groups also clearly reduced the Al-OH-related vibrations in the FT-IR spectrum of m-AFBNPs (Fig. **1c**). Anew growth of the eliminated band in the range of 940-1080 cm^{-1} in the FT-IR spectrum of m-SABNPs, which was assigned to the SO_3-H moiety, confirmed the support of sulfamid acid onto the surface of BNPs.

Fig. (**2**) shows the XRD patterns for the BNPs, AFBNPs, m-AFBPNs, and m-SABNPs samples. The PXRD pattern for BNPs (Fig. **2a**) confirmed crystallization of the single-phased boehmite [2]. The PXRD patterns for AFBNPs, m-AFBNPs and m-SABNPs (Figs. **2b**, **2c** and **2d**) clearly showed the retention of the boehmite structure during functionalization, partial hydroxyl group blocking and preparation of the

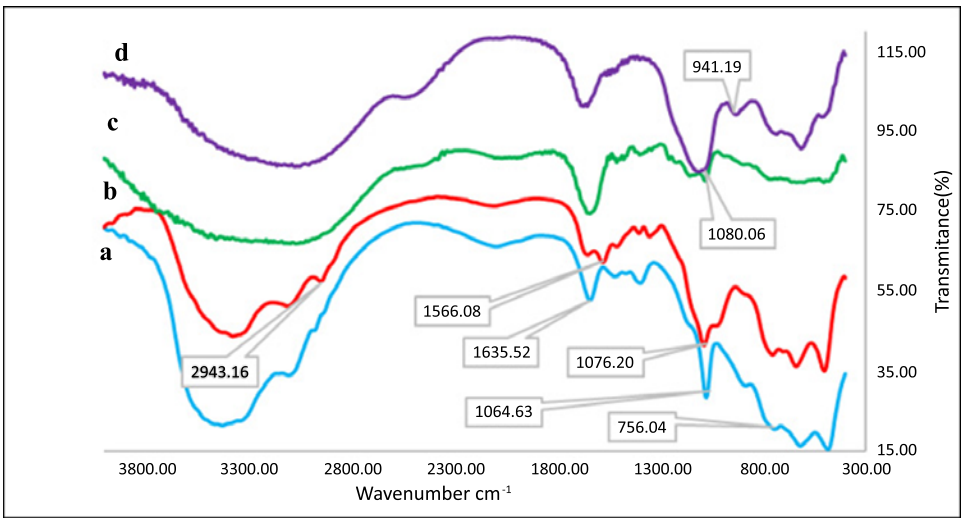


Fig. (1). FT-IR spectra for BNPs (**a**), AFBNPs (**b**), m-AFBNPs (**c**), and m-SABNPs (**d**).

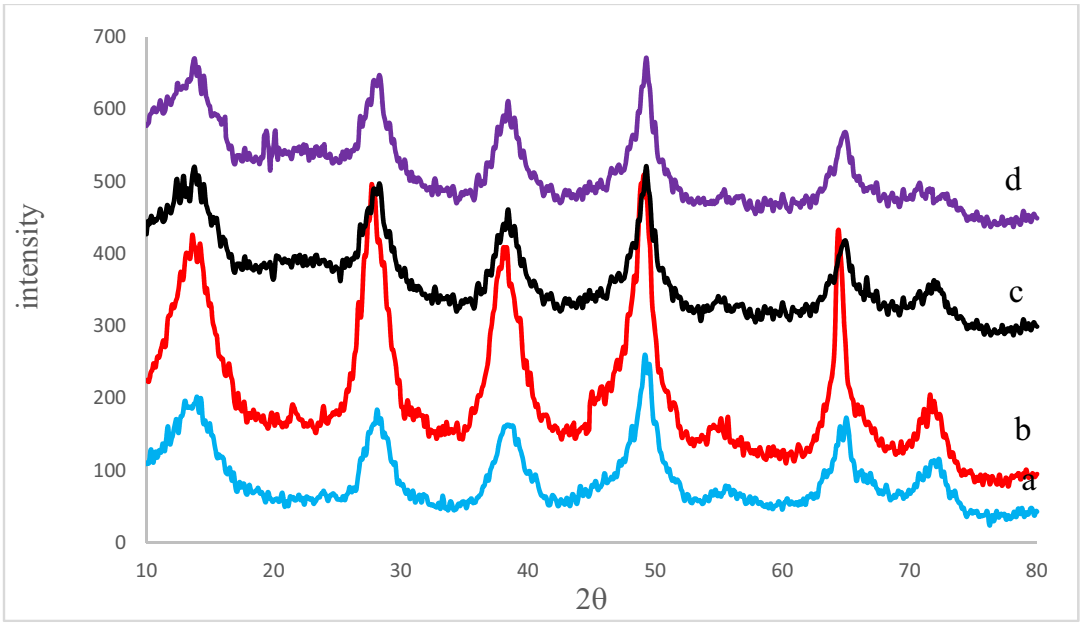


Fig. (2). XRD patterns for BNPs (**a**), AFBNPs (**b**), m-AFBPNs (**c**), and m-SABPNs (**d**).

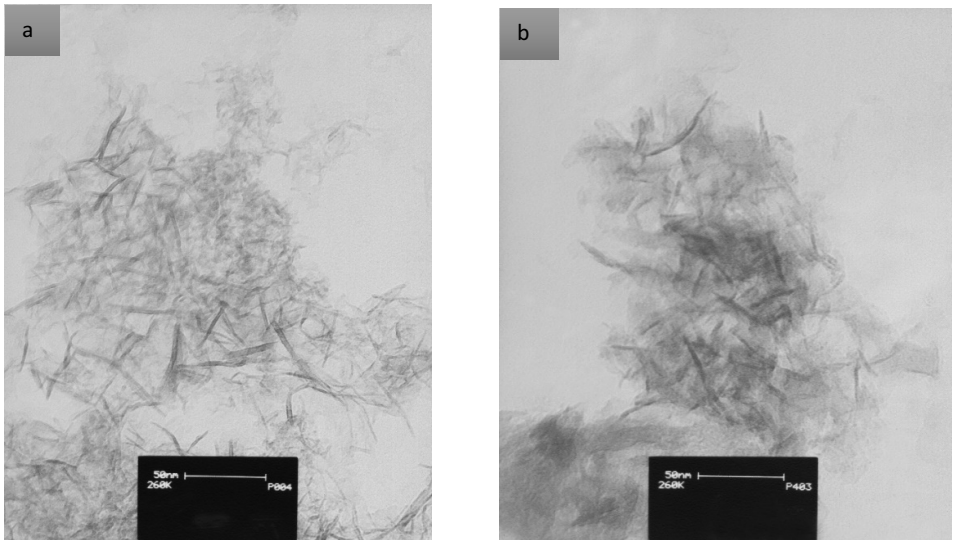


Fig. (3). Transmission electron microscopy images for BNPs (**a**) and m-SABNPs (**b**).

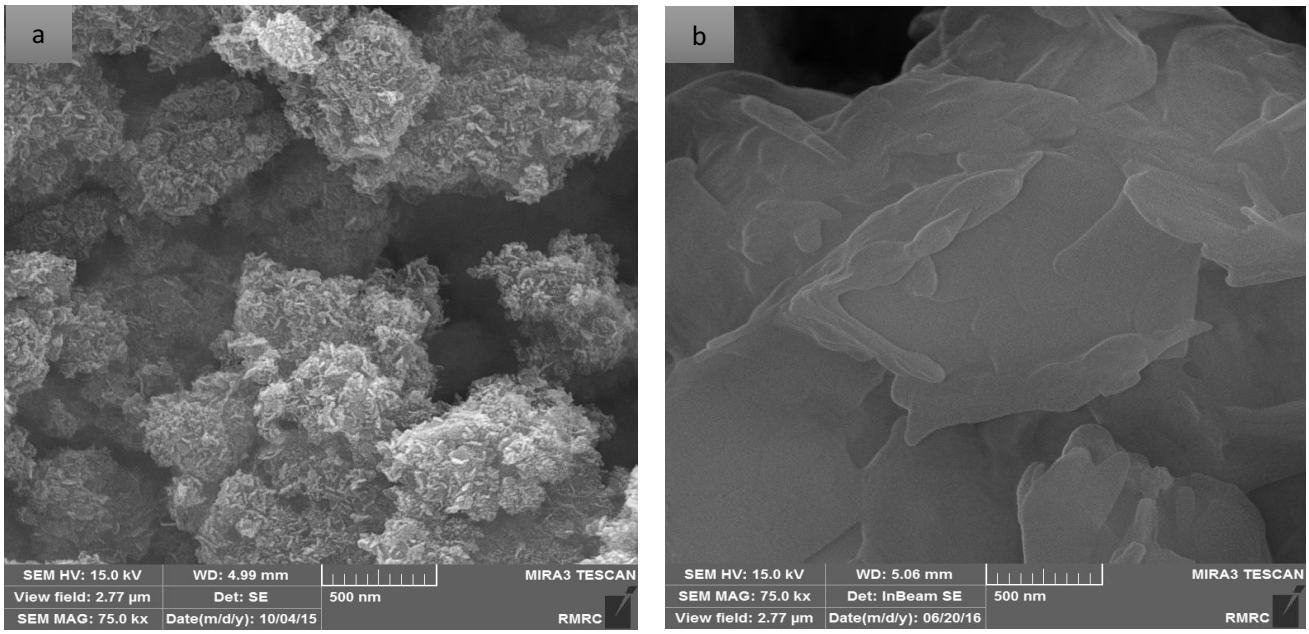


Fig. (4). Scanning electron micrographs for BNPs (**a**) and m-SABPNs (**b**).

m-SABNPs catalyst. Calculation of the average particle size using the PXRD pattern according to the Scherer equation showed 10-nm particles for BNPs. This was confirmed by the transmission electron microscopy (TEM) images for BNPs and m-SABNPs (Figs. **3a** and **3b**). In these images, needle-shaped BNPs can be seen over 50-nm long and up to 10-nm wide.

The surface morphology of the BNPs and m-SABNPs samples were also investigated by scanning electron microscopy (Fig. **4**). These micrographs showed that the surface morphology of BNPs changed completely during the preparation of the m-SABNPs catalyst, and that its surface porosity was wiped out. This was also confirmed by comparison of the BET surface areas of the samples at different stages during the catalyst preparation. The BET results showed that the surface area of this sample decreased dramatically by amine functionalization of BNPs from 326 to 27 m^2/g. The BET decrease was continued by changing the amine group to sulfamic acid with a slower rate, and the BET surface area of the m-SABNPs catalyst reached only 6 m^2/g.

EDX analysis (Fig. **5**) also confirmed the presence of sulfur atoms on the surface of m-SABNPs in addition to the carbon, oxygen, nitrogen, aluminum, and silicon atoms.

Furthermore, elemental analysis showed that the nitrogen content of AFBNPs was 0.93%, which meant that 0.66 mmol of the pendant amine groups were covalently bounded to the surface of 1.00 g of AFBNPs. According to this analysis, the carbon content of m-AFBNPs was 18.8 mmol that by considering of those related to amine groups, it showed that 5.6 mmol trimethylsilane were covalently bounded to the surface of 1.00 g of m-AFBNPs for partial blocking of surface hydroxyl groups. This is the minimum amount of this blocking agent which could protect the catalyst from dissolving in acidic medium of the next step of catalyst preparation. Also, this analysis showed that the sulfur content of m-SABNPs was 1.95%, which confirmed that 92.4% of the amine groups were changed to sulfamid acid, and it contained 0.61 mmol of covalently grafted sulfamid acid onto the surface of 1.00 g of m-SABNPs.

Fig. (**6**) shows the TG/DTG thermogram of the m-SABPNs catalyst. There are two important weight loss regions in the TG curve. The first one is in the temperature range of 110-360ºC, accompanied by an endothermic peak in DTG curve, which could be related to the decomposition of the organic residue onto the surface of BNPs. The other weight loss was observed in the temperature range of 470-560ºC, accompanied by other endothermic peaks in the DTG curve, which could be related to the dehydroxylation of boehmite and the crystallization of γ-alumina.

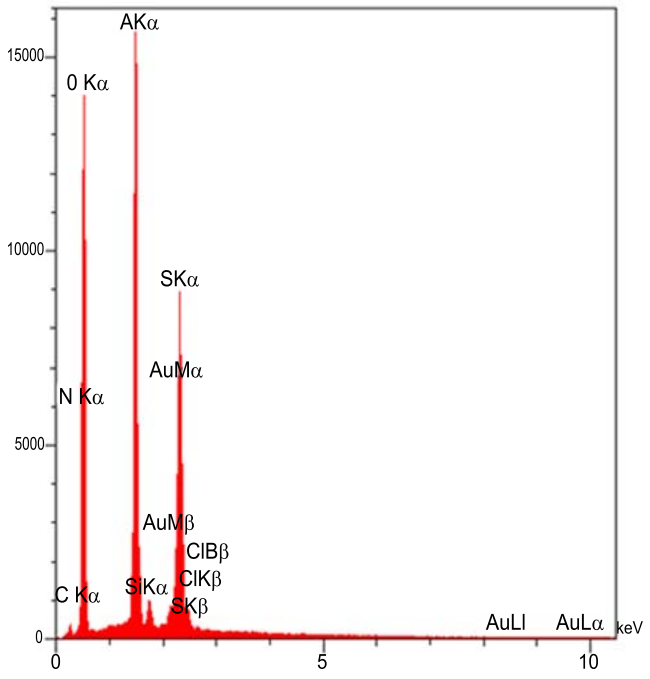


Fig. (5). EDX analysis of m-SABPNs.

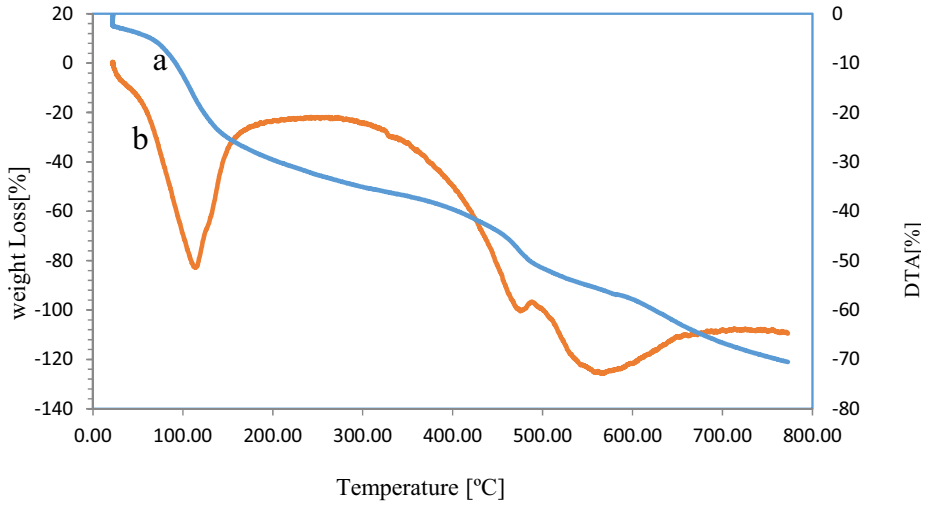
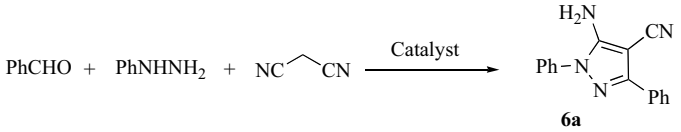


Fig. (6). TGA diagram of m-SABPNs catalyst (**a**) and DTA diagram of m-SABPNs catalyst (**b**).

Table 1. Optimization of reaction conditions for synthesis of 6a[a].



6a

Entry	Solvent	Catalyst (mg)	Temp. (ºC)	Time (min)	Yield (%)[b]
1	H_2O	30	Reflux	120	60
2	EtOH	30	Reflux	150	45
3	DMF	30	80	120	75
4	CH_3CN	30	Reflux	120	35
5	THF	30	Reflux	120	30
6	1,4-dioxane	30	Reflux	120	10
7	$CHCl_3$	30	Reflux	120	40
8	Solvent-free	30	80	45	95
9	Solvent-free	30	100	45	94
10	Solvent-free	50	80	45	92
11	Solvent-free	10	80	60	87
12	Solvent-free	----	80	180	20
13[c]	Solvent-free	30	80	45	49

[a]Reaction conditions: benzaldehyde (1.0 mmol), phenyl hydrazine (1.0 mmol), malononitrile (1.0 mmol), catalyst, solvent (3 mL).

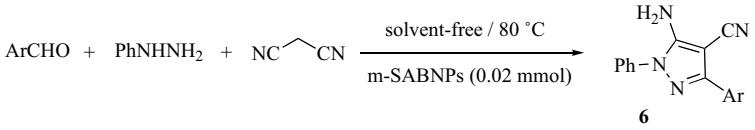
[b]Isolated yield.

[c]In the presence of BNPs.

2.3. Catalytic Activity

In our initial screening experiments, benzaldehyde, phenylhydrazine, and malononitrile were selected as the model substrates to optimize the reaction conditions, and the results obtained were tabulated in Table **1**. Firstly, several solvents were screened for the reaction in the presence of a catalytic amount of m-SABNPs. The results obtained showed that the efficiency and yield of the reaction under solvent-free conditions at 80ºC were higher than those obtained in solvents like H_2O, EtOH, DMF, CH_3CN, THF, 1,4-dioxane, and $CHCl_3$ (Table **1**, entries 1-7). Increasing the temperature did not improve the reaction yield (Table **1**, entry 9). Also the yield was reduced by increasing the amount of m-SABNPs (Table **1**, entry 10). When the reaction was carried out in the absence of a catalyst, only a low product yield was obtained, even after the reaction time was prolonged to 3 h (Table **1**,

Table 2. Synthesis of 5-amino-pyrazole-4-carbonitrile derivatives 6[a].



6

Entry	Ar	Product	Reaction Time (min)	Yield (%)[b]	M.p. (ºC) (Lit.) [Ref.]
1	C_6H_5	**6a**	45	95	160-162(159-160) [17]
2	4-Me-C_6H_4	**6b**	50	87	115-117(118-120) [18]
3	4-MeO-C_6H_4	**6c**	45	90	101-103(106-108) [18]
4	2-MeO-C_6H_4	**6d**	50	86	126-128(130-132) [17]
5	4-Me_2N-C_6H_4	**6e**	40	91	100-102(105-107) [17]
6	2-OH- C_6H_3	**6f**	35	91	160-161(160-161) [19]
7	2-OH-4-OMe- C_6H_3	**6g**	40	88	Oil
8	3,5-$(OMe)_2$-4-OH-C_6H_2	**6h**	45	94	175-177
9	2,3,4-$(OMe)_3$-C_6H_2	**6i**	50	93	146-148
10	4-Cl-C_6H_4	**6j**	30	90	128-130(128-130) [17]
11	2,4-$Cl_2C_6H_3$	**6k**	25	92	134-136(245-247) [20]
12	2,6-$Cl_2C_6H_3$	**6l**	35	90	150-152
13	2-F- C_6H_4	**6m**	25	93	93-95
14	3-F- C_6H_4	**6n**	25	86	110-112
15	4-F- C_6H_4	**6o**	20	94	Oil(oil) [21]
16	3-Br- C_6H_4	**6p**	35	93	80-82
17	4-Br- C_6H_4	**6q**	35	95	157-160(163-165) [21]
18	2-NO_2-C_6H_4	**6r**	25	85	160-162(160-161) [19]
19	3-NO_2-C_6H_4	**6s**	35	89	121-123(129-130) [19]
20	4-NO_2-C_6H_4	**6t**	30	95	163-165(164-166) [18]

[a]Reaction conditions: aldehyde (1.0 mmol), phenyl hydrazine (1.0 mmol), malononitrile (1.0 mmol), catalyst (0.02 mmol m-SABNPs), solvent free, 80ºC.

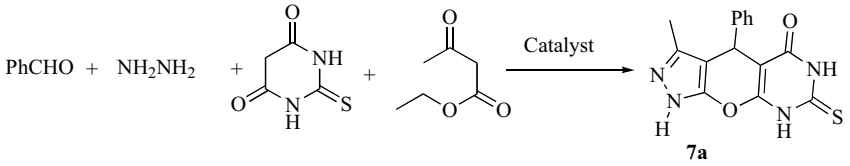
[b]Isolated yield.

entry 12). To find out the roles of BNPs and m-SABNPs during the reactions, synthesis of pyrazole **6a** was examined in the presence of BNPs. As shown in Table **1**, the products were obtained in 49% yield in the presence of BNPs. The generality of this three-component reaction was studied under the optimal reaction conditions by varying the structures of the aldehydes involved. The results obtained are summarized in Table **2**.

As shown in this table, the variation in the electronic properties and the position of the functional groups on the aromatic ring of the aldehyde did not show a clear effect on the reaction yields. Furthermore, the steric effects of the substituents at the ortho-position of the aromatic aldehyde did not have a clear effect on the reaction yields. On the other hand, benzaldehydes with electron-donating groups (Table **2**, entries 2-9) or electron-withdrawing groups (entries 10-20) were condensed into the corresponding 5-amino-1,3-aryl-1*H*-pyrazole-4-carbonitriles in high yields.

The excellent efficiency of m-SABNPs, as a catalyst, in the synthesis of pyrazoles motivated us to explore its efficacy for the synthesis of the pyranopyrazolopyrimidine derivatives. For this purpose, the condensation reaction of benzaldehyde, hydrazine hydrate, malononitrile, and thiobarbituric acid were taken into consideration using the catalyst 0.02 mmol (30 mg) in water (Table **3**). As shown in Table **3**, in the absence of the catalyst, low product yields were obtained after 1 h (Table **3**, entries1-2). Also the impact of the temperature on the conversion was studied, and the results obtained were tabulated in Table **3**. It is obvious that at room temperature, low yield of **7a** was formed (Table **3**, entry 2). With increase in the temperature from room temperature to 80ºC, the yield of **7a** was found to increase. We obtained the

Table 3. Effects of various solvents and temperature on synthesis of pyranopyrazolopyrimidine 7a[a].



7a

Entry	Solvent	Reaction Temp. (°C)	Time (min)	Yield (%)[c]
1[b]	H_2O	r.t	60	5
2	H_2O	r.t	60	35
3	H_2O	50	15	95
4	H_2O	80	15	95
5	Neat	50	60	48
6	EtOH	50	15	72
7	$CHCl_3$	50	15	43
8	DMF	50	15	83
9	THF	50	15	Trace
10	CH3CN	50	15	28
11	1,4-dioxane	50	15	15

[a]Reaction conditions: Ethyl acetoacetate (1.0 mmol), hydrazine hydrate (1.0 mmol), benzaldehyde (1.0 mmol), thiobarbituric acid (1.0 mmol), catalyst.

[b]Catalyst-free.

[c]Isolated yield.

best results at 50ºC (Table **3**, entry 3). When the reaction was carried out under solvent-free conditions, the target product was obtained in low yield (Table **3**, entry 5). Moreover, the model reaction was examined in the presence of m-SABNPs at 50ºC in several solvents including EtOH, $CHCl_3$, DMF, THF, CH_3CN, and 1,4-dioxane (Table **3**, entries 6-11). Among all these solvents, H_2O was found to be the best one, affording the highest product yield (Table **3**, entry 3).

Also various pyranopyrazolopyrimidine derivatives were synthesized *via* four-component condensation reactions of several aromatic aldehydes, hydrazine hydrate, malononitrile, and thiobarbituric acid under the same reaction conditions (Table **4**). As it is evident in this table, all reactions proceeded efficiently, and the desired products were produced in good-to-high yields in relatively short reaction times without the formation of any by-product. The reactions proceeded rapidly for the aromatic aldehydes with electron-withdrawing or electron-donating groups at different positions of the ring (Table **4**, entries 1-10) and heteroaryl aldehydes (Table **4**, entries 11-13), and the desired products were isolated in high yields without any side-product formation in short reaction times.

2.4. Catalyst Recyclability

The reusability of a catalyst is one of its most significant advantages, and makes it useful for industrial and commercial applications. Therefore, the reusability of the m-SABNPs catalyst was investigated for the reaction between benzaldehyde, phenylhydrazine, and malononitrile at 80ºC under solvent-free conditions. As shown in Fig. (**7**), the catalyst was recovered by a simple filtration, and reused over 5 runs without a substantial decrease in its activity even after 5 runs. The average yield for five successive runs was 93%, which obviously shows the practical recyclability of this catalyst.

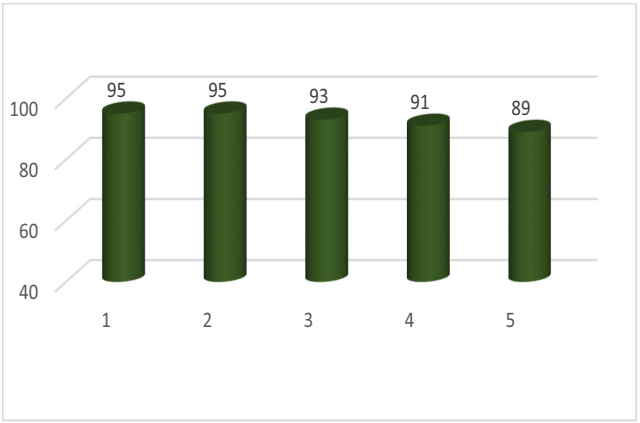
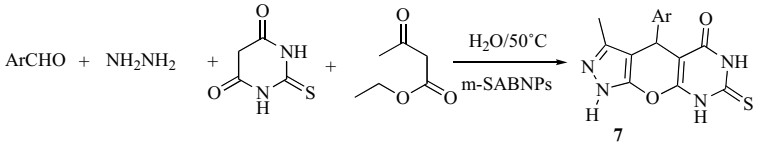


Fig. (7). Synthesis of product **6a** catalyzed by recycled catalyst.

3. EXPERIMENTAL

All the chemicals used were purchased from Merck or Fluka Chemical Companies. All the known compounds were identified by comparison of their melting points and ^1H

Table 4. Synthesis of pyranopyrazolopyrimidine derivatives[a].



Entry	Ar	Product	Reaction Time (min)	Yield (%)[b]	Mp (ºC) (Lit.) [Ref.]
1	Ph	**7a**	15	95	222-221 (220-221) [22]
2	2-OH-C_6H_4	**7b**	20	91	204-205
3	4-MeO-C_6H_4	**7c**	20	87	224-225
4	2-MeO-C_6H_4	**7d**	25	90	219-220
5	2-Cl-C_6H_4	**7e**	15	83	286-287
6	2,6-Cl_2-C_6H_3	**7f**	20	94	226-227
7	4-Br-C_6H_4	**7g**	20	87	216-217
8	3-NO_2-C_6H_4	**7h**	10	90	211-212 (212-213) [22]
9	4-NO_2-C_6H_4	**7i**	10	94	234-235
10	2, 3, 4 $(OMe)_3$-C_6H_2	**7j**	15	90	235-236
11	2'-Furanyl	**7k**	20	92	205-206
12	2'-Thiophenyl	**7l**	15	93	189-190
13	2'-Pyridinyl	**7m**	20	86	239-240

[a]Reaction conditions: Hydrazine hydrate (1.0 mmol), ethyl acetoacetate (1.0 mmol), thiobarbituric acid (1.0 mmol), aldehyde (1.0 mmol) in 4 mL water, catalyst (0.02mmol m-SABNPs), 50ºC.

[b]Isolated yield.

NMR data with the corresponding data reported in the literature. NMR spectra were recorded on a Bruker Avance 300 MHz instrument. FT-IR spectra were obtained as potassium bromide pellets in the range of 400-4000 cm^{-1} on a Bomem MB series spectrometer. Powder X-ray diffraction (XRD) patterns were collected using a Philips PW-1800 or STOE diffractometer with Cu Kα radiation. Elemental analyses were performed using a Thermo Finnigan Flash EA micro-analyzer. Electron microscopy was performed with a JEOL JSM-6360LV transmission electron microscope (TEM). Scanning electron microscopy (SEM) studies were conducted on a MIRA3TESCAN-XMU instrument. Thermogravimetric (TG) analyses were carried out with a Rheometric Scientific STA-1500 or BAHR Thermo analyse GmbH with a heating rate of 10°C min^{-1} in air and used Brunauer-Emmett-Teller (BET).

3.1. Preparation of Boehmite Nanoparticles-supported Sulfamic Acid (m-SABNPs)

Aluminium 2-butoxide was prepared according to the general method reported for the synthesis of aluminium alkoxides. Then, it was used for the preparation of BNPs, as reported earlier [8]. Then, 1.0 g powder prepared was added to a 100-mL round-bottom flask, which contained 50 mL anhydrous toluene and 5 mmol (0.89 g) of (3-aminopropyl) trimethoxysilane. The solution was refluxed for 24 h, and the amine-functionalized BPNs powder (AFBNPs) obtained was filtered-off, washed with toluene (2 × 20 mL) and methanol (2 × 20 mL), and dried in vacuum at 100 ºC for 10 h. Then 1.0 g of AFBNPs was dispersed in 30 mL of dichloromethane, and 10 mmol (1.08 g) of trimethylsillyl chloride was added to this suspension. After stirring the mixture for 24 h at room temperature, the methylated AFBNPs powder (m-AFBNPs) obtained was filtered-off and washed for 3 times with dichloromethane, toluene, and acetone, and dried at 70ºC for 3 h. Then 1.0 g of m-AFBNPs was dispersed in dry dichloromethane in ultrasonic bath for 10 min. Subsequently, 5 mmol (0.58 g) chlorosulfonic acid was added dropwise over a period of 10 min, and the mixture was stirred for another 6 h at room temperature. Then, the final sulfamid-supported product (m-SABNPs) was filtered-off and washed with dichloromethane, ethanol, and acetone, respectively, to remove the unreacted compounds, and then dried at 50ºC overnight.

3.2. General Procedure for Preparation of 5-Amino-Pyrazole-4-carbonitrile Derivatives (6)

To a mixture of aromatic aldehyde (1.0 mmol), malononitrile 1.0 mmol (0.066 g), and phenyl hydrazine1.0 mmol (0.1g) in a test tube was added 0.02mmol (30 mg) of m-SABPNs.

The resulting mixture was heated with stirring at 80ºC for an appropriate time, and the reaction progress was monitored by TLC. At the end of the reaction, the mixture was cooled down, and then an excess amount of hot ethanol was added to it. Subsequently, it was filtered to remove the catalyst, and after evaporation of the solvent, the residue was crystalized from ethyl acetate to afford the pure product. The structures of the compounds were characterized by the spectroscopic data and elemental analysis, comparing them with their spectroscopic data and physical properties reported in the literature. In order to recover the catalyst, the separated catalyst was washed twice with ethanol (5 mL) and reused after drying.

3.3. General Procedure for Synthesis of Pyrazolopyranopyrimidine Derivatives (7)

Ethyl acetoacetate 1mmol (0.13g) and m-SABPNs 0.02mmol (30 mg) were added to a solution of hydrazine hydrate 1mmol (0.06g) in H_2O. Then, an aromatic aldehyde (1mmol) and thiobarbituric acid 1mmol (0.14g) were added to the mixture, and the mixture was refluxed for an appropriate time. The reaction progress was monitored by TLC. After completion of the reaction, the mixture was cooled, and the precipitate formed was filtered-off, dried, and dissolved in hot ethyl acetate to separate the catalyst. The pure product was obtained after recrystallization from ethyl acetate.

3.3.1. 5-Amino-3-(2-hydroxyphenyl)-1-phenyl-1H-pyrazole-4 carbonitrile (6f)

256 mg (91% yield); ^{1}HNMR ($CDCl_3$, 300 MHz) δ:6.79 (t,1H, *j*7.2 Hz, ArH), 6.86-7.00 (m,4H), 7.15-7.28 (m, 3H, ArH), 7.56 (dd, 1H, *J* 1.6Hz and 7.6Hz, ArH), 8.17(S, 2H, NH), 10.43(S, 1H, OH); ^{13}CNMR($CDCl_3$, 75 MHz) δ:111.83, 115.91, 119.81, 120.21, 121.65, 125.45, 129.20, 130.05, 130.25, 138.14, 145.73, 151.02, 152.30, 156.52. Anal. calcd for $C_{16}H_{12}N_4O$: C, 69.55; H, 4.38; N, 20.28; found: C: 69.36; H: 4.17; N: 20.37.

3.3.2. 5-Amino-3-(2, 3, 4-trimethoxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (6i)

325 mg (93% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.92 (s, 3H, OCH3), 3.94 (s, 3H, OCH3), 3.95 (s, 3H, OCH3), 6.77 (d, 1H, *j* 8.7, ArH), 6.89 (t, 1H, *j* 7.2, ArH) 7.15(d, 2H, *j* 7.8, ArH), 7.28-7.34(m, 1H, ArH), 7.73-7.76(m, 2H, ArH), 7.98 (S, 2H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ:56.21, 58.26, 60.21, 110.10, 115.17, 121.44, 124.43, 130.16, 131.15, 131.75, 139.18,141.39, 151.62, 152.57, 159.10; Anal. calcd for $C_{19}H_{18}N_4O_3$: C: 65.13; H: 5.18; N: 15.99; found: C: 65.24; H: 5.17; N: 15.80.

3.3.3. 5-Amino-3-(2, 6-dichlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (6l)

296 mg (90% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 6.95 (t, 1H, *j* 7.2, ArH), 7.13-7.19 (m, 3H, ArH), 7.29-7.40 (m, 4H, ArH), 7.91 (s, 2H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 57.1, 119.20, 123.6, 125.7, 126.3, 127.8, 128.9, 129.3, 130.7, 134.7, 136.4, 139.1, 149.1, 157.3; Anal. calcd for $C_{16}H_{10}Cl_2N_4$: C: 58.38; H: 3.06; N: 21.54; found: C: 58.26; H: 3.13; N: 21.69.

3.3.4. 5-Amino-3-(2-fluorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (6m)

258 mg (93% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 6.79-6.84 (m, 1H, ArH), 6.94-7.10 (m, 4H, ArH), 7.15-7.24 (m, 3H, ArH), 7.69 (s, 1H, ArH), 7.91 (s, 2H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ:67.2, 112.6, 116.8, 119.8, 123.3, 124.1, 126.6, 129.1, 130.1, 131.4, 141.2, 149.3, 156.2, 165.2; Anal. calcd for $C_{16}H_{11}FN_4$: C: 69.06; H: 3.98; N: 20.13; found: C: 69.63; H: 3.86; N: 20.24.

3.3.5. 5-Amino-3-(3-bromophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (6p)

308 mg (93% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 6.94 (m, 1H, ArH), 7.15-7.86 (m, 7H, ArH), 7.86 (s, 1H, ArH), 8.10 (S, 2H, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 57.2, 114.1, 119.3, 124.4, 128.2, 129.0, 130.6, 131.1, 132.9, 149.1, 153.7, 162.1; Anal. calcd for $C_{16}H_{11}BrN_4$: C: 56.66; H: 3.27; N: 16.52; found: C: 56.21; H: 3.24; N: 16.24.

3.3.6. 5-Amino-3-(4-bromophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (6q)

322 mg (95% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 6.77 (t, 1H, *j* 7.2Hz, ArH), 7.10 (d, 2H, *j* 7.5, ArH), 7.21-7.26 (m, 2H, ArH), 7.55-7.63 (m, 4H, ArH), 7.84 (s, 2H, NH); ^{13}C NMR($CDCl_3$, 75 MHz) δ:58.1, 115.2, 119.1, 124.4, 128.2, 130.1, 131.6, 131.7, 132.4, 148.3, 153.4, 161.3; anal. calcd for $C_{16}H_{11}BrN_4$: C: 56.66; H: 3.27; N: 16.52; found: C: 56.06; H: 3.39; N: 16.35.

3.4. Spectral Data for Some Representative Pyrazolopyrano- Pyrimidine Derivatives

3.4.1. 3-Methyl-4-(2-hydroxyphenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7b)

298 mg (91% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 2.29 (s, 3H), 5.65 (s, 1H), 6.97 (t, J = 7.2 Hz), 7.41 (t, J = 7.5 Hz), 7.70 (d, J = 7.2 Hz), 11.65 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.4, 89.1, 113.1, 114.0, 118.1, 121.1, 126.6, 128.6, 134.9, 143.5, 144.59, 152.1, 161.6, 171.9 ppm; Anal. Calcd. for $C_{15}H_{12}N_4O_3S$: C, 54.87; H, 3.68; N, 17.06. Found: C, 54.66; H, 3.59; N, 17.25.

3.4.2. 3-Methyl-4-(4-methoxyphenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7c)

297 mg (87% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.21 (s, 3H), 3.68 (s, 3H), 5.36 (s, 1H), 6.76 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.4 Hz), 10.16 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.0, 30.3, 55.9, 91.4, 104.9, 125.1, 132.6, 132.7, 138.8, 143.3, 148.0, 150.5, 160.6, 171.3 ppm; Anal. Calcd. for $C_{16}H_{14}N_4O_3S$: C, 56.13; H, 4.12; N, 16.36. Found: C, 56.30; H, 4.20; N, 16.55.

3.4.3. 3-Methyl-4-(2-methoxyphenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7d)

307 mg (90% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.26 (s, 3H), 3.63 (s, 3H), 5.58 (s, 1H) 6.80 (d, J = 6.9 Hz,

1H), 7.07 (t, *J* = 6.9 Hz), 7.34 (d, *J* = 6.9 Hz), 11.14 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 9.9, 29.9, 56.1, 96.1, 105.3, 111.4, 111.7, 120.3, 127.6, 127.8, 130.1, 139.7, 143.5, 160.4, 172.8 ppm; Anal. Calcd. for $C_{16}H_{14}N_4O_3S$: C, 56.13; H, 4.12; N, 16.36. Found: C, 56.34; H, 4.22; N, 16.17.

3.4.4. 3-Methyl-4-(2-chlorophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7e)

287 mg (83% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.27 (s, 3H), 5.39 (s, 1H), 6.99 (d, *J* = 8.4 Hz), 7.03 (d, *J* = 8.4 Hz), 7.19-7.33 (m, 1H), 11.52 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 11.1, 30.3, 88.2, 127.8, 128.9, 129.2, 130.9, 131.2, 134.2, 151.8, 152.6, 156.6, 161.0 (C13), 172.2 ppm; Anal. Calcd. for $C_{15}H_{11}ClN_4O_2S$: C, 51.95; H, 3.20; N, 16.16. Found: C, 51.76; H, 3.29; N, 16.34.

3.4.5. 3-Methyl-4-(2,6-dichlorophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7f)

358 mg (94% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.13 (s, 3H), 5.63 (s, 1H), 7.16 (d, *J* = 7.8 Hz), 7.30 (d, *J* = 8.1 Hz), 7.39-7.45 (m, 1H), 11.38 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 11.2, 30.4, 88.8, 127.7, 128.9, 129.0, 129.6, 131.3, 132.0, 132.2, 151.4, 152.2, 167.7, 172.3 ppm; Anal. Calcd. for $C_{15}H_{10}Cl_2N_4O_2S$: C, 47.26; H, 2.64; N, 14.70. Found: C, 47.47; H, 2.73; N, 14.90.

3.4.6. 3-Methyl-4-(4-bromophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7g)

340 mg (87% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.24 (s, 3H), 5.67 (s, 1H), 6.98 (d, *J* = 8.4 Hz), 7.34 (d, *J* = 8.4 Hz), 11.53 (s, 1H), 11.61 (s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.0, 33.1, 88.7, 125.1, 126.3, 127.2, 130.9, 131.1, 138.6, 139.3, 149.7, 155.3, 163.0, 173.1 ppm; Anal. Calcd. for $C_{15}H_{11}BrN_4O_2S$: C, 46.05; H, 2.83; N, 14.32. Found: C, 46.24; H, 2.91; N, 14.50.

3.4.7. 3-Methyl-4-(4-nitrophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7i)

336 mg (94% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.24 (s, 3H), 5.48 (s, 1H), 7.30 (d, *J* = 8.4 Hz), 8.10 (d, *J* = 8.4 Hz), 11.50 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 9.9, 30.8, 96.0, 105.4, 126.1, 127.1, 128.1, 131.3, 139.0, 143.7, 154.6, 163.2, 172.9 ppm; Anal. Calcd. for $C_{15}H_{11}N_5O_4S$: C, 50.42; H, 3.10; N, 19.60. Found: C, 50.60; H, 3.01; N, 19.25.

3.4.8. 3-Methyl-4-(2,3,4-trimethoxyphenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5 (1H)-one(7j)

362 mg (90% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.03 (s, 3H), 3.88 (s, 3H), 3.94 (s, 6H), 4.94 (s, 1H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 11.42 (br, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.4, 27.2, 55.5, 59.7, 60.1, 91.6, 104.3, 106.6, 123.3, 129.2, 131.1, 139.7, 141.6, 143.5, 151.7, 161.5, 161.7, 172.1ppm; Anal. Calcd. for $C_{18}H_{18}N_4O_5S$: C, 53.72; H, 4.51; N, 13.92. Found: C, 53.91; H, 4.60; N, 14.10.

3.4.9. 3-Methyl-4-(2'-furanyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7k)

278 mg (92% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.08 (s, 3H), 5.41 (s, 1H), 6.46 (s, 1H), 6.85 (t, *J* = 4.2 Hz, 1H), 7.33 (d, *J* = 5.1 Hz, 1H), 10.01 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.0, 27.7, 80.1, 102.2, 105.9, 110.2, 138.8, 141.1, 155.5, 163.6, 174.1 ppm; Anal. Calcd. for $C_{13}H_{10}N_4O_3S$: C, 51.65; H, 3.33; N, 18.53. Found: C, 51.84; H, 3.42; N, 18.34.

3.4.10. 3-Methyl-4-(2'-thiophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7l)

296 mg (93% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.21 (s, 3H), 5.51 (s, 1H), 6.59 (d, *J* = 3.0 Hz, 1H), 6.80-6.88 (m, 1H), 7.25 (d, *J* = 5.1 Hz, 1H), 11.34 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.3, 30.9, 79.6, 95.4, 104.1, 112.6, 112.9, 127.5, 128.2, 136.2, 163.4, 173.0 ppm; Anal. Calcd. for $C_{13}H_{10}N_4O_2S_2$: C, 49.04; H, 3.17; N, 17.60. Found: C, 49.23; H, 3.09; N, 17.79.

3.4.11. 3-Methyl-4-(2'-pyridinyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo-[4',3':5,6]pyrano[2,3-d]pyrimidin-5(1H)-one (7m)

269 mg (86% yield); ^{1}H NMR (DMSO-d_6, 300 MHz) δ = 2.01 (s, 3H), 4.99 (s, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.69-7.75 (m, 1H), 8.44 (d, *J* = 4.8 Hz, 1H), 11.35 (s, 2H) ppm; ^{13}C NMR (DMSO-d_6, 75 MHz) δ = 10.4, 36.4, 91.2, 103.2, 121.2, 122.4, 128.2, 137.0, 138.7, 141.8, 143.6, 162.4, 172.2 ppm; Anal. Calcd. for $C_{14}H_{11}N_5O_2S$: C, 53.66; H, 3.54; N, 22.35. Found: C, 53.45; H, 3.63; N, 22.52.

CONCLUSION

We demonstrated an environmentally friendly method for the syntheses of 5-amino-1, 3-aryl-1*H*-pyrazole-4-carbonitriles and pyrazolopyranopyrimidines using m-SABNPs as an efficient and reusable nanocatalyst. This method offers several advantages like milder reaction condition, shorter reaction time, cleaner reaction, green and reusability of the catalyst, and high reaction yield. Moreover, this novel heterogeneous catalyst could be easily separated and reused for at least 5 repeated cycles without an appreciable loss in its catalytic activity.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's web site along with the published article.

REFERENCES

[1] Zhu, Y.; Stubbs, L.P.; Ho, F.; Liu, R.; Ship, C.P.; Maguire, J.A.; Hosmane, N.S. Magnetic nanocomposites: A new perspective in catalysis. *Chem. Cat. Chem*., **2010**, *2*, 365-374.

[2] Amini, M.M.; Mirzaee, M. Effect of solution chemistry on preparation of boehmite by hydrothermal assisted sol-gel processing of aluminum alkoxides. *J. Solgel Sci. Tech*., **2005**, *36*, 19-23.

[3] Ashraf, D.A.; Rajabi, L. Review on applications of carboxylate–alumoxane nanostructures. *Powder Technol*., **2012**, *226*, 117-129.

[4] Mirzaee, M.; Bahramian, B.; Amoli, A. Schiff base-functionalized boehmite nanoparticle-supported molybdenum and vanadium complexes: efficient catalysts for the epoxidation of alkenes. *Appl. Organomet. Chem*., **2015**, *29*, 593-600.

[5] Mirzaee, M.; Bahramian, B.; Mirebrahimi, M. Amine-functionalized boehmite nanoparticle-supported molybdenum and vanadium complexes: Efficient catalyst for epoxidation of alkanes. *Chin. J. Catal*., **2016**, *37*, 1263-1274.

[6] Mirzaee, M.; Bahramian, B.; Gholizadeh, J.; Feizi, A.; Gholami, R. Acetylacetonate complexes of vanadium and molybdenum supported on functionalized boehmite nano-particles for the catalytic epoxidation of alkenes. *Chem. Engin. J*., **2017**, *308*, 160-168.

[7] Nagamallu, R.; Kariyappa, A.K. Synthesis and biological evaluation of novel formyl-pyrazoles bearing coumarin moiety as potent antimicrobial and antioxidant agents. *Bioorg. Med. Chem. Let*., **2013**, *23*, 6406-6409.

[8] Piyush, N.K.; Shailesh, P.S.; Dipak, K.R. Synthesis, identification and *in vitro* biological evaluation of some novel 5-imidazopyrazole incorporated pyrazoline and isoxazoline derivatives *New J. Chem*., **2014**, *38*, 2902-2910.

[9] Bhat, B.; Dhar, K.; Puri, S.; Saxena, A.; Shanmugavel, M.; Qazi, G. Synthesis and biological evaluation of chalcones and their derived pyrazoles as potential cytotoxic agents. *Bioorg. Med. Chem. Lett*., **2005**, *15*, 3177-3180.

[10] Zora, M.; Kivrak, A.; Yazici, C. Synthesis of pyrazoles via electrophilic cyclization. *J. Org. Chem*., **2011**, *76*, 6726-6742.

[11] Kalaria, P.N.; Satasia, S.P.; Raval, D.K. Synthesis, characterization and pharmacological screening of some novel 5-imidazopyrazole incorporated polyhydroquinoline derivatives. *Eur. J. Med. Chem*., **2014**, *78*, 207-216.

[12] Branco, M.; Cao, R.; Liu, L.; Ege, G. Regioselective benzylation of an indazolyl-substituted pyrazole under the influence of inorganic solid supported bases. *J. Chem. Res*., **1999**, *4*, 274-275.

[13] Jawale, D.V.; Pratap, U.R.; Mali, J.R.; Mane, R.A. Silica chloride catalyzed one-pot synthesis of fully substituted pyrazoles. *Chin. Chem. Lett*., **2011**, *22*, 1187-1190.

[14] Maddila, S.; Rana, S.; Pagadala, R.; Kankala, S.; Maddila, S.; Jonnalagadda, S.B. Synthesis of pyrazole-4-carbonitrile derivatives in aqueous media with CuO/ZrO_2 as recyclable catalyst. *Catal. Commun*., **2015**, *61*, 26-30.

[15] Keivanloo, A.; Bakherad, M.; Imanifar, E.; Mirzaee, M. Boehmite nanoparticles, an efficient green catalyst for the multi-component synthesis of highly substituted imidazoles. *Appl. Catal. A. Gen*., **2013**, *467*, 291-300.

[16] Keivanloo, A.; Mirzaee, M.; Bakherad, M.; Soozani, A. Boehmite nanoparticle catalyst for the one-pot multicomponent synthesis of 3, 4-dihydropyrimidin-2-(1H)-ones and thiones under solvent-free conditions. *Chin. J. Catal*., **2014**, *35*, 362-367.

[17] Srivastava, M.; Rai, P.; Singh, J.; Singh, J. An environmentally friendlier approach-ionic liquid catalysed, water promoted and grinding induced synthesis of highly functionalised pyrazole derivatives. *RSC Adv*., **2013**, *3*, 16994-16998.

[18] Hasaninejad, A.; Firoozi, S. Catalyst-free, one-pot, three-component synthesis of 5-amino-1, 3-aryl-1*H*-pyrazole-4-carbonitriles in green media. *Mol. Diver*., **2013**, *17*, 459-469.

[19] Guo, R.-Y.; An, Z.-M.; Mo, L.-P.; Yang, S.-T.; Liu, H.-X.; Wang, S.-X.; Zhang, Z.-H. Meglumine promoted one-pot, four-component synthesis of pyranopyrazole derivatives. *Tetrahedron*, **2013**, *69*, 9931-9938.

[20] Peng, Y.; Song, G.; Dou, R. Surface cleaning under combined microwave and ultrasound irradiation: Flash synthesis of 4 H-pyrano [2, 3-c]pyrazoles in aqueous media. *Green Chem*., **2006**, *8*, 573-575.

[21] Zolfigol, M. A.; Afsharnadery, F.; Baghery, S.; Salehzadeh, S.; Maleki, F. Catalytic applications of {[HMIM]C (NO 2) 3}: As a nano ionic liquid for the synthesis of pyrazole derivatives under green conditions and a mechanistic investigation with a new approach. *RSC Adv*., **2015**, *5*, 75555-75568.

[22] Li, X-T.; Zhao, A-D.; Mo, L-P.; Zhang, Z-H. Meglumine catalysed expeditious four-component domino protocol for synthesis of pyrazolopyranopyrimidines in aqueous medium. *RSC Adv*., **2014**, *4*, 51580-51588.