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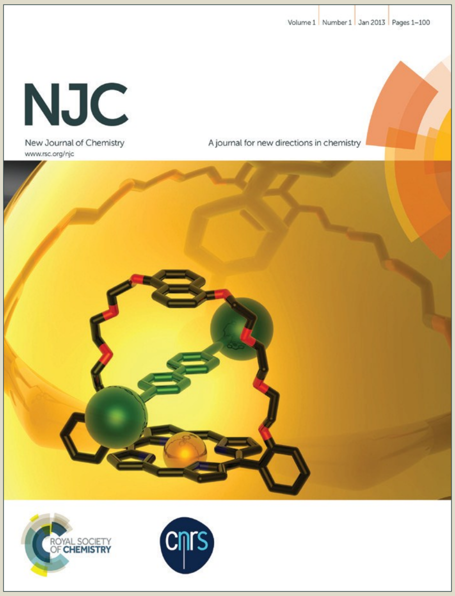

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ARTICLE

The First Report on the Preparation of Boehmite Silica Sulfuric Acid and Its Application in Some Multicomponent Organic Reactions

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Boehmite silica sulfuric acid (Boehmite-SSA) has been prepared for the first time *via* efficient sequential synthetic procedure. Initially, boehmite nanoparticles was prepared, coated by silica, then reacted with chlorosulfunic acid to obtain Boehmite-SSA. A simple, inexpensive, environmentally friendly and efficient procedure for the synthesis of polyhydroquinoline and 2,3-dihydroquinazolin-4(1*H*)-one derivatives using this compound as an efficient and novel nanocatalyst. Boehmite-SSA is stable, heterogeneous, cost-effective, easy to handle, recoverable catalyst and can be reused for several consecutive runs without significant loss of catalytic activity. Its structure was characterized by FT-IR spectroscopy, thermogravimetric analysis (TGA), powder X-ray diffraction (XRD) and scanning electron microscopy (SEM).

1 Introduction

Recently, separation and recycling of heterogeneous catalysts is employed in the various area of research [1]. However, immobilization of homogeneous catalysts usually decreases the catalytic activity or selectivity [2]. This drawback can be overcome using nanomaterials as heterogeneous supports. Since, when the size of the support is decreased to the nanometre scale, the surface area is substantially increased, which is combined with excellent accessibility of the surface-bound catalytic sites [3]. Among the various nanomaterials, nanoboehmite is oxide hydroxide (γ-AlOOH) particles of aluminum which has recently been used as an absorbent, opticalmmaterial, coatings, composite reinforcement material in ceramics, cosmetic products, vaccine adjuvants, pillared clays and sweep-flocculation for fresh water treatment, and also rarely used as heterogeneous supports in the isolation and recycling of expensive homogeneous catalysts [4, 5]. Also boehmite was used as the precursor material for the synthesis of alumoxanes [4]. Numerous methods have been reported for preparation of boehmite nanoparticles; but, most of them have focused on the morphologies, chemical and physical properties of the prepared particles; meanwhile, modification of nanoboehmite surface has been rarely reported as heterogeneous catalysts [5-7]. Boehmite nanoparticles has several advantages, such as non-toxic, easily and readily available, thermal and mechanical stability, high-surface-area [8, 9] and also the surface of nanoboehmite covered with hydroxyl groups, which presence of many OH on the nanoboehmite surface leads to reaction with tetraethyl orthosilicate (TEOS), dopamine, alkoxysilane and other reagents for the immobilization of other substances [9, 10].

2,3-Dihydro-4(1*H*)-quinazolinone and their polycyclic derivatives are a very important class of heterocycles that attracted much attention because they possess their potential biological and pharmaceutical activities including antifertility, antibacterial, antitumor, antifungal, and mono amine oxidase inhibition [11–15]. For example, altanserin and nitro altanserin are drugs for 5-HT2A receptor antagonists [16], also 2-(2-hydroxyphenyl)-4(3*H*)-quinazolinone was utilized in the detection of metal ions [17]. 2,3-Dihydro-4(1*H*)-quinazolinones are also reported to possess the ability to inhibit enzymes of biological importance [18]. Furthermore, 2,3-dihydro-4(1*H*)-quinazolinones derivatives are the key intermediate for the synthesis of 4-(3*H*)-quinazolinones compounds [19].

Besides, polyhydroquinoline derivatives have been reported to possess a wide range of biological properties and pharmaceutical activities such as vasodilator, hepatoprotective, antiatherosclerotic, bronchodilator, antitumor, geroprotective, antidiabetic activity and also their ability to modulate calcium channels [20-24]. Thus the synthesis of these heterocycles has become an area of great interest.

For this reason, many methods including a variety of supports have been developed over the years to find efficient these multicomponent reactions. However, the mesoporouse silicas such as MCM-41 [25], SBA-15 [26] or some nanoparticles such as TiO_2 NPs [27] and iron oxide [28] have been used as catalyst supports for organic synthesis, which requires high temperature for calcination or inert atmosphere and a lot of time and tedious conditions to prepare. Also some of previously reported catalysts such as heteropolyacids [29],

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carbon nanotubes [30] ionic liquids [31-33] or some polymers [33] are more expensive. While preparation of nanoboehmite was not air or moisture sensitive, more importance nanoboehmite was prepared in water at room temperature without inert atmosphere using commercial materials such as $Al(NO_3)_3.9H_2O$ and NaOH. Therefore herein Boehmite-SSA as a new nano heterogeneous catalyst has been reported for the synthesis of polyhydroquinoline and 2,3-dihydroquinazolin-4(1*H*)-one derivatives.

2 Experimental

2.1. Preparation of the boehmite-SSA

The solutions of 6.490 g NaOH in 50 ml of distilled water was added to solutions of 20 g $Al(NO_3)3.9H_2O$ in 30 ml distilled water as drop to drop under vigorous stirring. The resulting milky mixture was subjected to mixing in the ultrasonic bath for 3 h at 25 ºC. The resulted nanoboehmite was filtered and washed by distilled water and were kept in the oven at 220 ºC for 4 h.

The obtained boehmite nanoparticles (1 g) was dispersed in water (10 mL) and ethanol (50 mL) by sonication for 30 min. Under continuous stirring, PEG (5.36 g), ammonia solution (10 mL) and TEOS (2 mL) were respectively added into the suspension, and continuously reacted for 38 h at room temperature. Then, the product (boehmite-silica) was filtered and washed with ethanol and distilled water, the obtained boehmite-silica was dried at room temperature.

The obtained boehmite-silica (0.5 g) were dispersed in dry n-hexane (5 mL) by ultrasonic bath for 30 min. Subsequently, chlorosulfunic acid (0.75 mL) was added drop wise over a period of 30 min and the mixture was stirred for 4h at room temperature. Then, the final product was filtered and washed by dry n-hexane, ethanol and n-hexane respectively to remove the unattached substrates. The product (boehmite-SSA) dried at room temperature and stored in a refrigerator to use.

2.2 General procedure for the synthesis of polyhydroquinoline derivatives in the presence of boehmite-SSA

A mixture of aldehyde (1 mmol), dimedon (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1 mmol) and boehmite-SSA (0.03 g) was stirred in ethanol under reflux conditions and the progress of the reaction was monitored by TLC. After completion of the reaction, catalyst was separated by simple filtration and washed with ethyl acetate. Then, the solvent was evaporated and all products was recrystallized in ethanol, which the pure polyhydroquinoline derivatives were obtained in good to excellent yields.

2.3 General procedure for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones derivatives in the presence of boehmite-SSA

A mixture of boehmite-SSA (0.03 g), anthranilamide (1 mmol) and aldehyde (1 mmol) was stirred at 80 ºC in ethanol (2 mL). The progress was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. CH_2Cl_2 (2 ×5 mL) was added and the catalyst was separated using simple filtration. CH_2Cl_2 was evaporated and all products was recrystallized in ethanol for further purification.

2.4 Selected spectral data

2-(4-chlorophenyl)-2,3-dihydoquinazolin-4(1*H*)-one (entry 1, table 3): Mp: 202-204 °C. IR (KBr) cm^{-1}: 3309, 1655, 1611, 1435. 1H NMR (400 MHz, DMSO-d6): δH= 8.29 (s, 1H), 7.61-7.43 (m, 5H), 7.26-7.20 (t, J=7.5, 1H), 7.12 (s, 1H), 6.75-6.63 (m, 2H), 5.75 (s, 1H) ppm.

2-(4-ethoxyphenyl)-2,3-dihydoquinazolin-4(1*H*)-one (entry 3, table 3): Mp: 168-170 °C. IR (KBr) cm^{-1}: 3301, 1650, 1613, 1443. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 7.95-7.94 (b, 1H), 7.52-7.50 (m, 2H), 7.34 (s, 1H), 7.26 (s, 1H), 6.95-6.90 (m, 3H), 6.68-6.67 (m, 1H), 5.85 (s, 1H), 5.75 (s, 1H), 4.07-4.05 (q, *J*=4, 2H), 1.46-1.44 (s, 3H) ppm.

2-(4-methylphenyl)-2,3-dihydroquinazolin-4(1*H*)-one (entry 6, table 3): Mp: 230-232 °C. IR (KBr) cm^{-1}: 3313, 1658, 1611, 1439. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 8.21 (s, 1H), 7.62-7.59 (d, *J*=7.5, 1H), 7.38-7.35 (d, *J*=7.5, 2H), 7.26-7.14 (m, 3H), 7.03 (s, 1H), 6.75-6.64 (m, 2H), 5.71 (s, 1H), 2.49-2.42 (s, 3H) ppm.

2-(3,4-dimethoxyphenyl)-2,3-dihydoquinazolin-4(1*H*)-one (entry 7, table 3): Mp: 211-214 °C. IR (KBr) cm^{-1}: 3335, 1671, 1610, 1436. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 8.21 (s, 1H), 7.64-7.62 (d, *J*=7.6, 1H), 7.28-7.24 (t, *J*=0.8, 1H), 7.15 (d, *J*=1.6, 1H), 7.04-6.97 (m, 2H), 6.95 (s, 1H), 6.78-6.76 (d, *J*=8, 1H), 6.72-6.67 (t, *J*=1.2, 1H), 5.71 (s, 1H), 3.77 (s, 3H), 3.76 (s, 3H) ppm.

2-(4-bromophenyl)-2,3-dihydoquinazolin-4(1*H*)-one (entry 8, table 3): Mp: 196-198 °C. IR (KBr) cm^{-1}: 3310, 1656, 1608, 1433. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 8.17-8.14 (m, 1H), 7.80-7.78 (m, 1H), 7.63-7.59 (m, 3H), 7.47-7.44 (m, 2H), 7.30-7.24 (m, 1H), 6.77-6.72 (d, *J*=19.2, 1H), 6.71-6.68 (m, 1H), 5.76 (s, 1H) ppm.

Ethyl-4-(4-bromophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (entry 2, table 5): Mp: 251-253 °C. IR (KBr) cm^{-1}: 3276, 3243, 3207, 1703, 1649, 1421. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 9.14 (s, 1H), 7.41-7.39 (d, *J*=8.4, 2H), 7.13-7.11 (d, *J*=8, 2H), 4.84 (s, 1H), 4.01-3.96 (q, *J*=6.8, 2H), 2.52-2.46 (d, *J*=26.4 1H), 2.31-2.27 (m, 4H), 2.21-2.17 (d, *J*=16, 1H), 2.01-1.97 (d, *J*=16, 1H), 1.15-1.12 (t, *J*=7.2, 3H), 1.02 (s, 3H), 0.85 (s, 3H) ppm.

Ethyl-4-(4-methylphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (entry 4, table 5): Mp: 250-253 °C. IR (KBr) cm^{-1}: 3276, 3276, 3246, 3208, 1702, 1648, 1423. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 9.04 (s, 1H), 7.05-7.03 (d, *J*=8, 2H), 7.00-6.98 (d, *J*=8, 2H), 4.82 (s, 1H), 4.00-3.95 (q, *J*=7.2, 2H), 2.45-2.41 (d, *J*=16, 1H), 2.31-2.27 (m, 4H), 2.21-2.15 (m, 4H), 2.10-1.96 (d, *J*=16, 1H), 1.17-1.13 (t, *J*=6.8, 3H), 1.02 (s, 3H), 0.86 (s, 3H) ppm.

Ethyl-4-(4-ethoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3 carboxylate (entry 5, table 5): Mp: 172-174 °C. IR (KBr) cm^{-1}: 3446, 3276, 3198, 1684, 1607, 1494. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 7.28-7.19 (m, 2H), 6.74-6.72 (d, *J*=8, 2H), 5.80 (s, 1H), 4.99 (s, 1H), 4.07-4.05 (t, *J*=4, 2H), 3.97-3.96 (t, *J*=3.6 ,2H), 2.39-

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2.15 (m, 7H), 1.38-1.37 (m, 3H), 1.21-1.20 (m, 3H), 1.07 (s, 3H), 0.95 (s, 3H) ppm.

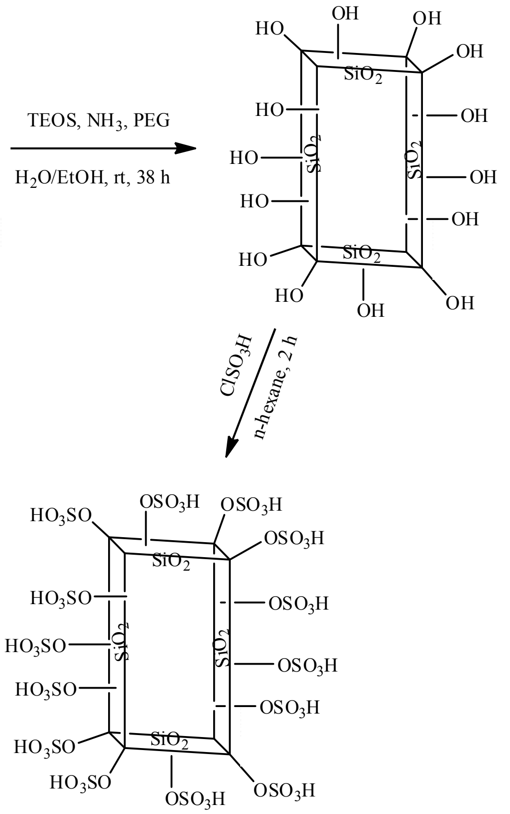
Ethyl-4-(3,4-dimethoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (entry 6, table 5): Mp: 204-206 °C. IR (KBr) cm^{-1}: 3280, 3213, 1696, 1645, 1452. ^1H NMR (400 MHz, DMSO-d_6): δ_H= 9.05 (s, 1H), 6.79-6.76 (m, 2H), 6.65-6.63 (d, *J*=8, 1H), 4.80 (s, 1H), 4.04-3.99 (q, *J*=7.2, 2H), 3.69-3.68 (d, *J*=4.4, 5H), 2.47-2.42 (d, *J*=17.2, 2H), 2.35-2.27 (m, 4H), 2.22-2.18 (d, *J*=16, 1H), 2.03-1.99 (d, *J*=16, 1H), 1.20-1.16 (t, *J*=6.8, 3H), 1.03 (s, 3H), 0.90 (s, 3H) ppm.

Ethyl-4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (entry 8, table 5): Mp: 248-250 °C. IR (KBr) cm^{-1}: 3278, 3246, 3208, 1701, 1649, 1423. 1^H NMR (400 MHz, DMSO-d_6): δ_H= 9.04 (s, 1H), 7.08-7.06 (d, *J*=8.4, 2H), 6.77-6.75 (d, *J*=8.4, 2H), 4.80 (s, 1H), 4.02-3.96 (q, *J*=7.2, 2H), 3.69 (s, 3H), 2.52-2.45 (d, *J*=29.2, 1H), 2.31-2.29 (m, 4H), 2.20-2.16 (d, *J*=16, 1H), 2.01-1.97 (d, *J*=16.4, 1H), 1.17-1.14 (t, *J*=7.2, 3H), 1.02 (s, 3H), 0.87 (s, 3H) ppm.

3 Results and discussion

3.1 Catalyst preparation

The boehmite-SSA was prepared by the concise route outlined in Scheme 1. Initially, boehmite nanoparticles have been prepared *via* addition of NaOH to the solution of $Al(NO_3)_3.9H_2O$ as the source of aluminum at room temperature. Ultimately, after coating of boehmite nanoparticles with silica using TEOS, the functionalization of terminal silanol groups with chlorosulfunic acid (The reaction of silanol group has been reported for the first time by Zolfigol [34]) led to the formation of boehmite silica sulfamic acid (boehmite-SSA). The catalyst has been characterized by scanning electron microscopy (SEM), X-ray diffraction (XRD) thermogravimetric analysis (TGA) and Fourier transform infrared spectroscopy (FT-IR).



Scheme 1. Synthesis of boehmite-SSA.

3.2 Catalyst characterization

The size of the catalyst was evaluated using SEM. The SEM image of boehmite-SSA was shown that the catalyst was formed of nanometer-sized particles (Figure 1). As shown in Figure 1a, the unit cells of boehmite were obtained in cubic orthorhombic structures.

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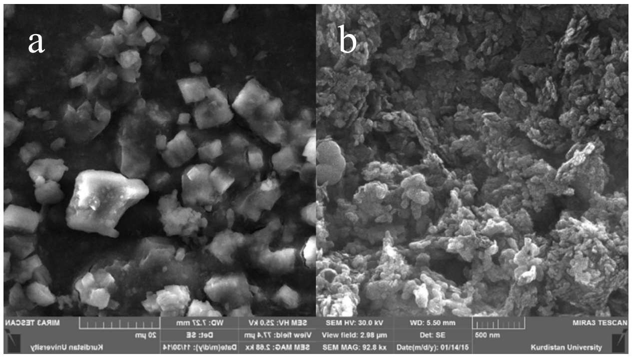

Figure 1. SEM image of boehmite (a) and boehmite-SSA (b).

The XRD patterns of boehmite nanoparticles was shown in Figure 2. As seen in Figure 2, the boehmite phase was identified from the XRD patterns by the peak positions at 14.40 (0 2 0), 28.41 (1 2 0), 38.55 (0 3 1), 46.45 (1 3 1), 49.55 (0 5 1), 51.94 (2 0 0), 56.02 (1 5 1), 59.35 (0 8 0), 65.04 (2 3 1), 65.56 (0 0 2), 68.09 (1 7 1), and 72.38 (2 5 1), which the main peaks of the XRD pattern are consistent with the characteristic peaks of the orthorhombic unit cell of the

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boehmite nanoparticles [5, 6]. The position and relative intensities of all peaks confirm well.

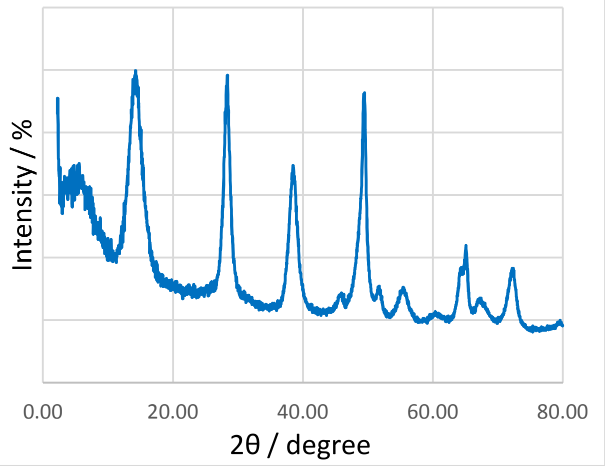

Figure 2. The XRD pattern of boehmite.

The FT-IR spectrum for boehmite nanoparticles (a), boehmite-silica (b) and boehmite-SSA (c) are shown in Figure 3. In spectra of the IR boehmite nanoparticles, strong bands at 3086 and 3308 cm^{-1} which is assigned to the O-H bonds which are attached to the surface boehmite nanoparticles [8, 35]. Several peaks in FT-IR spectrum of boehmite nanoparticles at 480, 605 and 735 cm^{-1} can be attributed to the characteristic absorption of Al-O bonds [4]. Moreover, the band at 1650 cm^{-1} corresponding to the nitrate impurity vibration and the bands at 1164 and 1069 cm^{-1} corresponding to the hydrogen bands of OH…OH surface [4, 8]. In the FT-IR spectra of boehmite-silica and boehmite-SSA (Figure 3b and c): The band at 1072 and 770 cm^{-1} are due to Si–O–Si vibrations [36]. A broad bands is present at approximately 1070 and 770 cm^{-1} in boehmite-silica FTIR spectra , which can be attributed to the an overlap of the asymmetric and symmetric stretching vibration of the Si-O-Si bonds with Al-O and OH…OH stretching vibration leads to band broading. Reaction of boehmite-silica with chlorosulfunic acid produces boehmite-SSA in which the presence of SO_3H moiety is asserted with 938-1220 cm^{-1} and 3000-3400 cm^{-1} bands in FT-IR spectra.

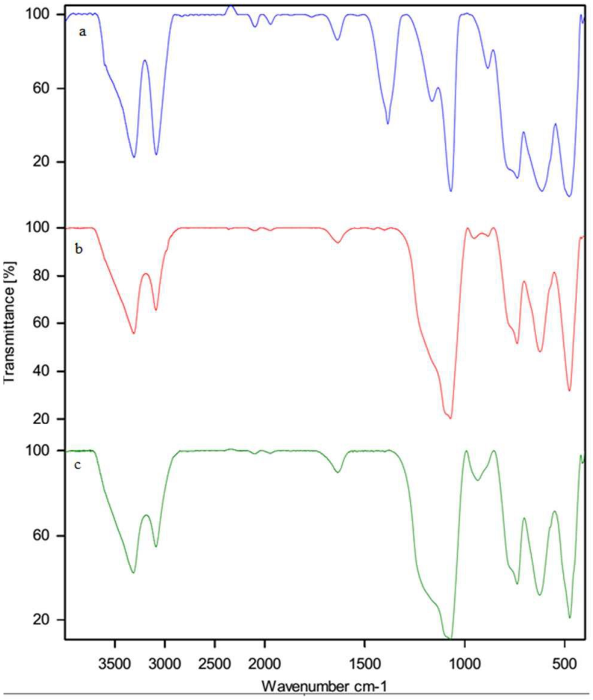

Figure 3. FT-IR spectra of (a) boehmite, (b) boehmite-silica and (c) boehmite-SSA.

The silica sulfuric acid loaded onto boehmite nanoparticles was quantified using TGA. Figure 4 shows the TGA curves for bare boehmite nanoparticles (blue curve), boehmite coated with silica (boehmite-silica) (red curve) and boehmite-SSA (green curve). In the TGA curves, adsorbed water mass loss occurred at temperatures below 250 ºC as well as the endothermic weight loss at 300 ºC is attributed to water loss from structural hydroxyl groups in the precursor [37]. After coating of silica on boehmite (Figure 4b), the TGA curves show loss of physically adsorbed water, residual solvent and hydroxyl groups decomposition. In the profile of boehmite-SSA, sulfonic groups have been reported to desorb at temperatures above 300 °C (about 25%). On the basis of this result, the well grafting of silica sulforic acid on the boehmite nanoparticles is verified.

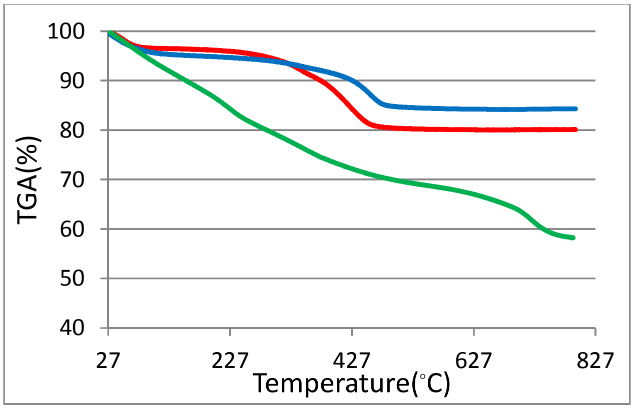

Figure 4. TGA diagram of boehmite (blue line), boehmite-silica (red line) and boehmite-SSA (green line).

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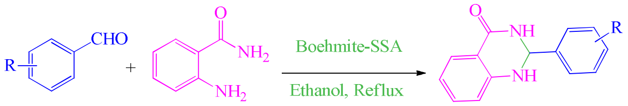
3.3 Catalytic studies

Herein we examined the catalytic activity of boehmite-SSA as an efficient, stable, recyclable and commercially viable catalyst for synthesis of Polyhydroquinoline and 2,3-dihydroquinazolin-4(1*H*)-one derivatives. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives using cyclocondensation reaction of aldehydes and anthranilamide in the present of boehmite-SSA was shown in Scheme 2. In our initial screening experiments, 4-chlorobenzaldehyde and anthranilamide were selected as model substrates to optimize the reaction conditions, and the results are shown in Table 1. At first, the solvent effect was examined. That good yields were obtained in ethanol as the solvent (Table 1,entry 6), whereas H_2O, ethyl acetate, CH_2Cl_2, n-hexane and acetone afforded low to moderate yields (Table 1, entries 1-5), therefore, ethanol was selected as the solvent. Finally, the amount of boehmite-SSA was also examined, and 30 mg of boehmite-SSA was found to be optimal, Meanwhile a lower yield was observed when the amount of the catalyst was decreased (Table 1, entries 6-8).



Scheme 2. Boehmite-SSA catalyzed the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one derivatives.

Table 1. Optimization of the synthesis 2,3-dihydroquinazolin-4(1H)-ones conditions for the condensation of 4-chlorobenzaldehyde whit anthranilamide as a model compound in ethanol for 50 min.

Entry	Solvent	Catalyst (mg)	Yield (%)[a]
1	H_2O	30	70
2	Ethyl acetate	30	62
3	CH_2Cl_2	30	29
4	n-Hexane	30	Trace
5	Acetone	30	Trace
6	Ethanol	30	98
7	Ethanol	25	76
8	Ethanol	20	61

[a] Isolated yield.

In order to show the role does boehmite or boehmite-silica and boehmite-SSA plays during the reactions, synthesis of 2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one was examined in the presence of boehmite-SSA compared to alone boehmite and boehmite-silica. The results of this comparison are shown in Table 2. As shown in Table 2, the products were obtained in 43 and 26% of yield in the presence of boehmite and boehmite-silica, respectively. Also, direct functionalization of the boehmite (in the absent of silica layer) by chlorosulfunic acid (boehmite-SA) has been done and its catalytic activity was compared with boehmite-SSA (Table 2, entry 4). As shown in Table 2, the products were obtained in 64 of yield in the presence of boehmite-SA. Therefore to increase the surface area of boehmite and make more efficient and effective acidic catalyst, boehmite surface coated with silica.

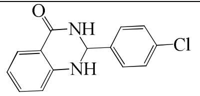
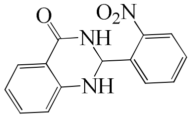
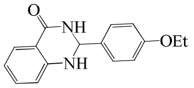
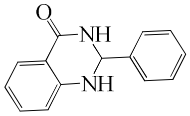
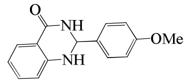
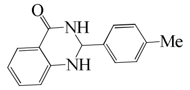
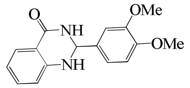
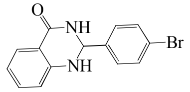
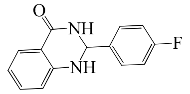
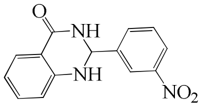
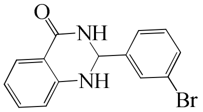
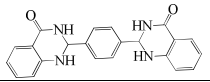
Table 2. The effect of boehmite or boehmite-silica and boehmite-SA in comparison with boehmite-SSA in the condensation of 4-chlorobenzaldehyde whit anthranilamide as a model compound under optimized conditions.

Entry	**Substrate**	**Catalyst**	**Yield (%)**[a]
1	4-chlorobenzaldehyde	-	Trace[b]
2	4-chlorobenzaldehyde	Boehmite nanoparticles	43[c]
3	4-chlorobenzaldehyde	Boehmite-silica	26[c]
4	4-chlorobenzaldehyde	boehmite-SA	64[c]
5	4-chlorobenzaldehyde	boehmite-SSA	98

[a] Isolated yield after 50 min, [b] Reaction proceeds in the absence of the catalyst, [c] Isolated yield was obtained by plate chromatography.

Then, a variety of aldehydes were described to explore the scope of substrates under the optimized reaction conditions and the results are shown in Table 3. Various electron-donating and electronwithdrawing substituents such as $-CH_3$, $-OCH_3$, $-OCH_2CH_3$, -Br, -Cl, -F, and $-NO_2$ on aldehydes were well tolerated.

Table 3. Synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones catalyzed by boehmite-SSA in ethanol and at 80 ºC.

Entry	Product	Time (min)	Yield (%)[a]	Melting point (ºC)	Reference
1		50	98	202-204	[11]
2		35	94	188-190	[19]
3		120	85	168-170	[12]
4		50	96	223-225	[11]
5		100	89	189-191	[14]
6		65	90	230-232	[19]
7		130	88	211-214	[12]
8		70	90	196-198	[14]
9		65	91	194-196	[19]
10		45	94	204-205	[19]
11		50	96	184-186	[12]
12		65	93	243-245	[14]

[a] Isolated yield.

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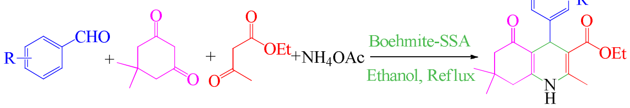
Also, we report the application of boehmite-SSA as catalysts for the synthesis of polyhydroquinoline derivatives using the condensation of aldehyde with dimedon, ethylacetoacetate and ammonium acetate (Scheme 3). In order to optimize the reaction conditions, the reaction of 4-chlorobenzaldehyde (1 mmol) with dimedon (1 mmol), ethyl acetoacetate (1 mmol) and ammonium acetate (1.2 mmol) was optimized using various solvents such as H_2O, EtOH and CH_3CN (Table 4, entries 1–3) in the presence of different amount of boehmite-SSA as the catalyst (Table 4, entries 3–5). The best results were obtained in ethanol at reflux for 180 min in the presence of 30 mg of catalyst (Table 4, entry 3). Therefore, ethanol was selected as a solvent for this reaction.



Scheme 3. Boehmite-SSA catalyzed the one-pot synthesis of polyhydroquinoline derivatives.

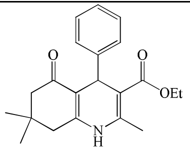
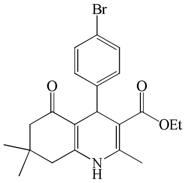
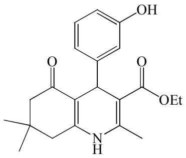
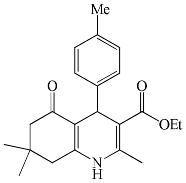
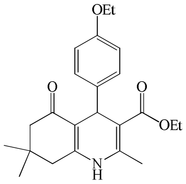
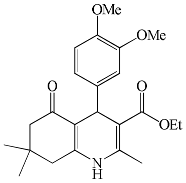
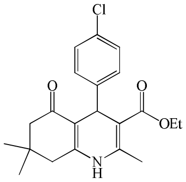
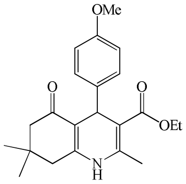
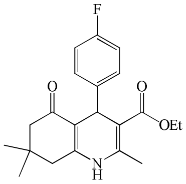
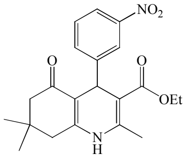
Table 4. Optimization of the synthesis polyhydroquinolines conditions for the condensation of 4-chlorobenzaldehyde, dimedon, ethyl acetoacetate and ammonium acetate as a model compound in ethanol at 80 ºC for 180 min.

Entry	Solvent	Catalyst (mg)	Yielde (%)[a]
1	H_2O	30	32
2	CH_3CN	30	41
3	Ethanol	30	95
4	Ethanol	20	68
5	Ethanol	15	52

[a] Isolated yield, [b]no reaction.

Using the optimized conditions, we extended the study with different aldehydes for the synthesis of various polyhydroquinoline derivatives using boehmite-SSA. The results of this study are depicted in Table 5. As shown, a variety of benzaldehydes bearing electron-donating and electron-withdrawing substituents were successfully employed to prepare the corresponding polyhydroquinoline derivatives in excellent yields.

Table 5. Synthesis of polyhydroquinolines catalyzed by boehmite-SSA in ethanol and at 80 ºC.

Entry	Product	Time (min)	Yield (%)[a]	Melting point (ºC)	Reference
1		215	94	217-219	[14]
2		270	94	251-253	[21]
3		210	88	228-230	[14]
4		250	96	250-253	[14]
5		250	90	172-174	[14]
6		215	95	204-206	[14]
7		180	95	237-239	[14]
8		230	96	248-250	[14]
9		200	90	183-185	[21]
10		320	91	176-179	[23]

[a]Isolated yield.

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3.4 Recyclability of the catalyst

The reusability of the boehmite-SSA catalyst was studied for the reaction between benzaldehyde with dimedon, ethyl acetoacetate and ammonium acetate in ethanol under reflux condition. As shown in figure 5, the catalyst was recovered by a simple filtration and reused over 5 runs without considerable decrease in activity even after 5 runs. The average isolated yield for five successive runs was 93%, which clearly demonstrates the practical recyclability of this catalyst.

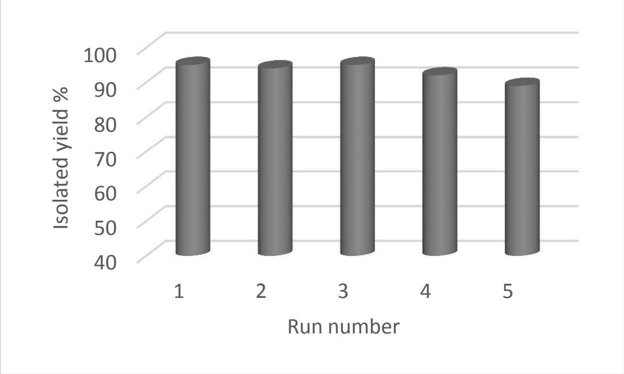

Figure 5. The recycling experiment of boehmite-SSA in condensation of 4-chlorobenzaldehyde, dimedon, ethylacetoacetate and ammonium acetate.

3.5 Comparison of the catalyst activity

The efficiency of this nanocatalyst is demonstrated by comparison our results on the synthesis of 2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one with the previous methods in the literatures (Table 6). As it can be seen from this Table the good reaction time and higher yield than the other reported catalysts has been achieved. Also this new catalyst is comparable or may be better in terms of price, non-toxicity, stability and easy separation than the reported ones. In addition, Boehmite-SSA can be reused over 5 runs. The recyclability and reusability of the prepared catalyst is another point, the Boehmite-SSA was reused over 5 runs without any significant loss of its activity. The average isolated yield for 5 successive runs was 93%, which clearly demonstrates the practical recyclability of this catalyst. Moreover, the mesoporous silica or some nanoparticles NPs have been used as catalyst supports, which require high temperature for calcination and a lot of time and tedious conditions to prepare. Also some of previously reported catalysts such as heteropolyacids, ionic liquids or some polymers are more expensive, while preparation of nanoboehmite was not air, or moisture sensitive. This nanomaterial was prepared in water at room temperature without inert atmosphere.

Table 6. Comparison of Boehmite-SSA for the synthesis of 2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1*H*)-one with previously reported procedure.

Entry	Substrate	Catalyst	Time (min)	Yield (%)[a] [Reference]
1	4-ClC_6H_4CHO	GSA@MNPs	50	99 [28]
2	4-ClC_6H_4CHO	$[Bmim]PF_6$	40	90 [32]
3	4-ClC_6H_4CHO	TBAB/100 ºC	60	75 [38]
4	4-ClC_6H_4CHO	SiO_2-$FeCl_3$	420	87[39]
5	4-ClC_6H_4CHO	2-(N-morpholino)ethanesulfonc acid	180	89 [40]
6	4-ClC_6H_4CHO	2-(N-morpholino)ethanesulfonc acid/ MW (600 W)	12	92 [40]
7	4-ClC_6H_4CHO	$ZrCl_4$	37	91 [41]
8	4-ClC_6H_4CHO	$[hnmp][HSO_4]$	28	83 [42]
9	4-ClC_6H_4CHO	$[NMP][HSO_4]$	22	84 [42]
10	4-ClC_6H_4CHO	$[NMP][H_2PO_4]$	38	79 [42]
11	4-ClC_6H_4CHO	Boehmite-SSA	50	98 [this work]

[a] Isolated yield.

4 Conclusions

In summary, we have developed a novel, practical and environmentally friendly method for synthesis of 2,3-dihydroquinazolin-4(1*H*)-one and polyhydroquinoline derivatives using boehmite-SSA as efficient and reusable nanocatalyst. This catalyst can be prepared by a simple procedure from commercially available and cheap materials. In addition, the catalyst can be easily recovered and reused for several times without any significant loss of activity.

Acknowledgements

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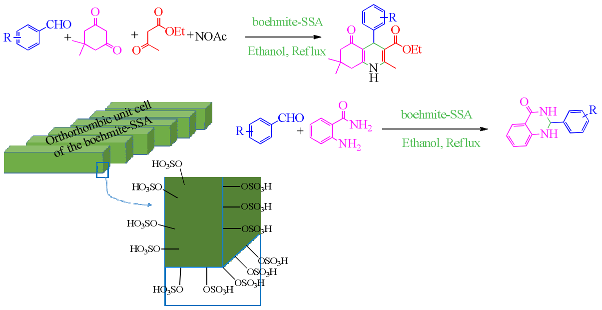
The First Report on the Preparation of Boehmite Silica Sulfuric Acid and Its Application in Some Multicomponent Organic Reactions

Arash Ghorbani-Choghamarani and Bahman Tahmasbi



Boehmite silica sulfuric acid was prepared at room temperature using commercially available materials and applied as nanocatalyst for preparation of DHQs and PHQs.

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