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High-efficient synthesis of 2-imino-2*H*-chromenes and dihydropyrano[*c*]chromenes using novel and green catalyst ($CaO@SiO_2@AIL$)

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Abstract

In this work, 1,3,5,7-tetraazaadamantan-1-ium chloride (AIL) functionalized silica-coated calcium oxide hybrid nanocatalyst ($CaO@SiO_2@AIL$) as a novel, efficient, green and recyclable heterogeneous ionic liquid catalyst was synthesized. Catalytic activity of the $CaO@SiO_2@AIL$ hybrid nanoparticles was investigated for synthesis of the pharmaceutically valuable 2-imino-2*H*-chromene and dihydropyrano[*c*]chromene derivatives. A wide range of amines and aromatic aldehydes containing either electron-withdrawing or electron-donating substituent were examined using optimized conditions to produce the desired products. 2-Imino-2*H*-chromenes were synthesized under solvent-free condition, and dihydropyrano[*c*]chromenes were prepared in aqueous medium as green conditions within short reaction times, high yields and using easy workup procedures. Structure confirmation and surface properties of the core/shell hybrid nanoparticles were considered via Fourier transform infrared spectroscopy, X-ray powder diffraction, scanning electron microscope, energy-dispersive X-ray spectroscopy, WDS map scan, thermogravimetric and elemental analyses. This IL-supported heterogeneous nanocatalyst can be reused at least six times without considerable loss of its performance.

Keywords Ionic liquid · Eggshells waste · Biocatalyst · 2-Imino-2*H*-chromenes · Dihydropyrano[*c*]chromenes

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Introduction

Heterocyclic motifs with anticancer and anti-HIV properties play a notable role in design and synthesis of bioactive molecules [1, 2]. The chromene derivatives are an important type of heterocyclic compounds, which have received considerable attention due to their biological and pharmacological properties and critical intermediates in the synthesis of many natural products and medicinal agents [3], such as anticancer, antibacterial [4], antiviral [5], antimicrobial [6] and anti-HIV [7] activities. They have also been widely employed as cosmetics, pigments, potent biodegradable agrochemicals [8] and are found in several natural tocopherols, alkaloids, anthocyanins and flavonoids [9].

In this sense, chromene's structural matter exists in several significant biologically active compounds like 2-imino-2*H*-chromenes. Functionalized 2-imino-2*H*-chromenes have attracted widespread attention due to their different applications, including tyrosine kinase (PTK) inhibitors [9], as well as anti-Alzheimer, anticancer and antimicrobial [10] agents. Despite these properties, there are a few reports for synthesis of 2-imino-2*H*-chromenes. Previous methods for the synthesis of these compounds are the Knoevenagel condensation of salicylaldehydes with methylene compounds [11] operated by catalysts like $NaHCO_3$ or Na_2CO_3 [12], potassium phthalimide [13], piperidine in the presence [14] or absence [15] of microwave irradiation and polyethylene polyamine [16]. Dihydropyrano[*c*]chromenes are also another vital class of chromenes structural motif which have attracted much attention due to their wide range of diverse pharmacological and biological properties such as spasmolytic [17], diuretic [18], anticoagulant [19], anticancer [20, 21] and anti-anaphylactic activity [6]. The most reported procedures for the synthesis of dihydropyrano[*c*]chromenes employ different catalytic systems including sodium dodecyl sulfate (SDS) [22], CuO nanoparticles [23], 4-(dimethylamino)pyridine (DMAP) [24], diammonium hydrogen phosphate (DAHP) [25].

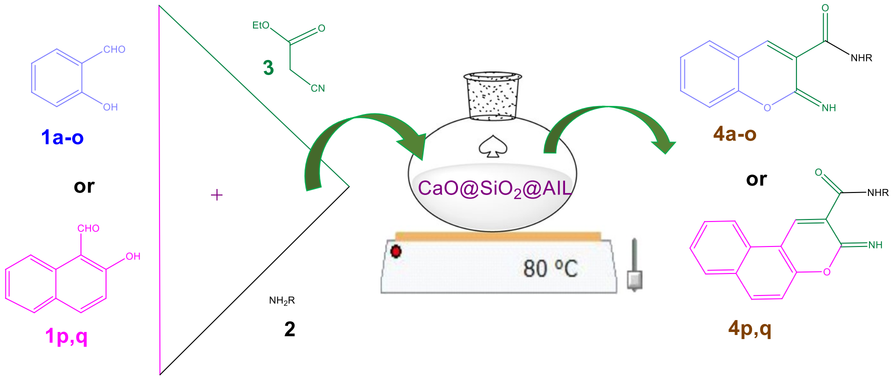
The green chemistry can be regarded as an attractive field in the development of clean and sustainable technology to replace the use of hazardous reagents and catalysts with relatively environmentally benign compounds [26]. Also, "green chemistry" emphasizes the optimization of synthetic methodologies to reduce pollution, costs and tedious workup procedures [27]. Furthermore, new challenges are leading to the use of natural and biocompounds for organic and inorganic applications.

Recently, immobilization of different catalysts onto various nanosized solid supports has emerged as the most promising alternative strategy to improve their stability and catalytic activity in the field of organo-catalysis [28]. The organic–inorganic nanohybrid materials can be regarded as attractive heterogeneous catalysts in organic synthesis, since these materials feature the functional variety and flexibility of organic structures combined with easy production and thermal and mechanical stability of inorganic solids [29, 30]. Also, the nanoheterogeneous catalysts offer larger surface area which is responsible for the higher catalytic activity [31].

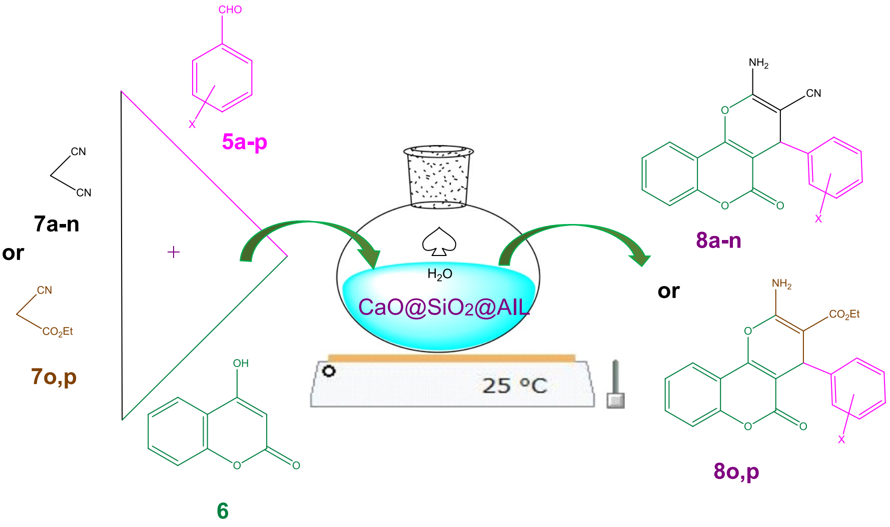
With attention to the outstanding biologically and therapeutically significance of chromene derivatives and their involvement as useful materials in synthetic organic and medicinal chemistry, increasing interest for preparation of these compounds by development of environmentally friendly and selective approaches using heterogeneous ionic liquid is still in high demand. Although previous methods for preparation of these chromenes are useful, some of them suffer from different limitations including long reaction times, multiple-step reactions, unsatisfactory yields, harsh reaction conditions and the use of relatively expensive catalysts. To avoid these limitations, attempts have focused on simple reactions under solvent-free conditions or use of water as a green and suitable solvent, and use of heterogeneous catalysts with high recyclability and reusability.

Calcium oxide (CaO) as a heterogeneous catalyst has a high stability, high catalytic efficiency, facile synthesis and functionalization along with highly specific surface. The eggshell waste has been used as raw material, and so the CaO particles are low cost, biodegradable, recyclable and biocompatible [32–34]. The CaO nanocatalyst has been synthesized by calcination–hydration–dehydration technique. The high surface area of CaO nanoparticles can be kept by SiO_2 until it improves its functionality [35]. Hexamethylenetetramine (HMT) is a white crystalline compound with a cage-like structure. This compound is easily accessible, has a low price and is highly soluble in water and polar organic solvents [36]. This polycyclic tertiary amine has applications in plastics, production of explosives, chemical synthesis and pharmacology. In several studies, HMT was used for reduction of graphene oxide and doping nitrogen into the graphene sheets to increase nitrogen content and its stability, and also promote the formation of zinc oxide [37] and ceria nanoparticles [38] where it seems to play a role in controlling the nanosizes and shapes.

By emphasizing the development of novel versatile and benign catalysts for the synthesis of various heterocyclic compounds, we were encouraged to prepare $CaO@SiO_2@AIL$ as a new core–shell hybrid nanocatalyst. The hexamethylenetetramine (HMT) with an ionic tag was grafted on silica-coated CaO nanoparticles, and its catalytic performance for the ecofriendly synthesis of 2-imino-2*H*-chromenes (Scheme 1) and dihydropyrano[*c*]chromenes (Scheme 2) was properly investigated.



Scheme 1 $CaO@SiO_2@AIL$ catalyzed synthesis of 2-imino-2*H*-chromenes



Scheme 2 CaO@SiO_2@AIL catalyzed synthesis of dihydropyrano[*c*]chromenes

Experimental

Materials and physicochemical characterization techniques

Chemicals were purchased from Merck chemical company. NMR spectra were recorded on 300 and 400 MHz Bruker Avance spectrometer using TMS as an internal standard. Fourier transform infrared (FT-IR) spectra were recorded on an ALPHA-Bruker and PerkinElmer spectrophotometer from KBr pellets. The structure of CaO@SiO_2@AIL MNPs was characterized by X-ray powder diffraction (XRD), EDX, IR, scanning electron microscope (SEM), elemental analyses (CHN) and thermogravimetric (TGA) analyses. The X-ray powder diffraction (XRD) was performed on the X'Pert-MPD PRO-PW3040/60 instrument. Energy-dispersive X-ray (EDX) and scanning electron microscopy (SEM) analysis of the prepared catalyst were carried out on a MIRA III instrument. Thermogravimetric analysis (TGA) was performed on a Q600TA instrument.

Synthesis of 1,3,5,7-tetraazaadamantan-1-ium chloride (AIL)

The AIL was synthesized according to previously reported method [36]. Accordingly, (3-chloropropyl)trimethoxysilane (1.8 mL, 10 mmol) was added to a solution of hexamethylenetetramine (1.4 g, 10 mmol) in dry toluene (20 mL) and refluxed for 48 h under nitrogen atmosphere. The resulted yellowish solid was filtered and washed with ethanol and dried at 90 °C for 2 h.

Synthesis of nano-CaO particles

The nano-CaO particles were prepared using eggshells according to the literature procedure [39]. Briefly, the household waste eggshells were washed with warm water to remove sand, tissue and other impurities. These clean eggshells were washed with distilled water and dried at 120 °C for 24 h, which then milled by a planetary ball mill. As the catalytic activity of particles increased with decreasing of their size, the milling time process was optimized (5 h) with the average size of 8 nm. Subsequently, nano-CaO particles obtained by eggshells were calcinated in a muffle furnace at 900 °C for 3 h and refluxed in water for 6 h, and dried in oven at 100 °C for overnight. The soiled nano-CaO particles were dehydrated by calcination at 870 °C for 3 h to convert the hydroxide groups to oxide form.

Synthesis of CaO@SiO_2

CaO@SiO_2 was prepared according to the Stober method [40]. Typically, 1 g of the CaO nanoparticles was dispersed by ultrasonic vibration in a mixture of ethanol (40 mL), deionized water (6 mL) and 1.5 mL of aqueous ammonia solution (25 wt%) for 20 min. Subsequently, 1.4 mL of tetraethylorthosilicate (TEOS) was added dropwise and stirred for 22 h at room temperature under N_2 atmosphere. The product was filtered off and then washed several times with water and ethanol, and dried at 25 °C under vacuum for 24 h.

Synthesis of CaO@SiO_2@AIL

A mixture of CaO@SiO_2 (0.4 g) and dry toluene (10 mL) was stirred at 100 °C for 10 min. Then, 0.38 g (1 mmol) of AIL in dry toluene (10 mL) was added and the mixture stirred under reflux condition and nitrogen atmosphere for 24 h. Afterward, the crude product was filtered off and washed with ethanol three times and dried at 80 °C in vacuum for overnight.

General procedure for synthesis of 2-imino-2*H*-chromenes derivatives (4a–4q)

A mixture of alkyl or arylamine (1 mmol), ethyl cyanoacetate (1 mmol), 2-hydroxybenzaldehyde (1 mmol) or 2-hydroxy-1-naphthaldehyde (1 mmol) and 0.01 g of CaO@SiO_2@AIL as a catalyst was stirred at 80 °C under solvent-free conditions for an appropriate time (Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, hot EtOH was added (10 mL) and the catalyst separated out by centrifuge. After cooling the solution, the crude product was precipitated and isolated by filtration. The obtained product was recrystallized from ethanol to give pure compound.

General procedure for synthesis of dihydropyrano[*c*]chromene derivatives (8a–8p)

A mixture of aldehyde (1 mmol), 4-hydroxycoumarin (1 mmol), malononitrile or ethyl cyanoacetate (1 mmol) was added in a 25 mL round-bottomed flask containing 0.01 g of CaO@SiO_2@AIL in H_2O (5 mL). The resulting mixture was stirred at room temperature for an appropriate time (Table 4). Up on completion of reaction (TLC), the result mixture was diluted with hot ethanol (10 mL) and the solution filtered to remove the catalyst. The crude product was precipitated by cooling the solution, which was then isolated by filtration and recrystallized from ethanol to give the pure product.

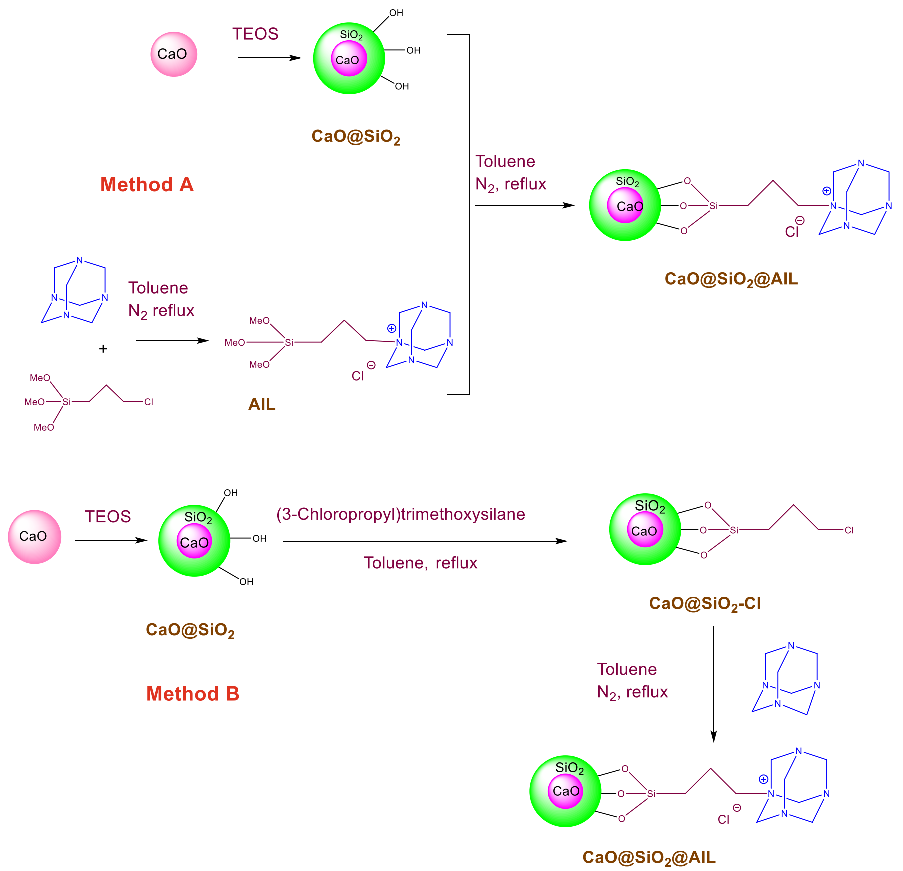
Results and discussion

Synthesis and structural characterization of CaO@SiO_2@AIL

Hexamethylenetetraamine-based ionic liquid stabilized onto silica-coated CaO nanoparticles was prepared as a novel nanosized, environmentally friendly and retrievable heterogeneous catalyst (Scheme 3). The ionic liquid (AIL) was prepared by previously reported method [36]. The prepared AIL was then grafted onto the surface of CaO@SiO_2 support to give the CaO@SiO_2@AIL as a novel hybrid nanomaterial. The structure of CaO@SiO_2@AIL was determined by Fourier transform infrared spectroscopy (FT-IR), SEM, CHN, energy-dispersive X-ray spectroscopy (EDS), WDS map scan, XRD and TGA analyses.

FT-IR spectra

Figure 1 shows FT-IR spectra of CaO, CaO@SiO_2, AIL and CaO@SiO_2@AIL. In Fig. 1a, b, and d, the broad absorption bands around 3400–3600 cm^{-1} are attributed to stretching vibration of –OH groups and physically adsorbed water (H_2O) [32]. The weak band at 1481 cm^{-1} typically corresponds to the asymmetric C=O stretching of carbonate ions. CaO@SiO_2 shows characteristic FT-IR absorption bands at around 968 cm^{-1} (symmetric stretching), 875 cm^{-1} (in plane bending) and 462 cm^{-1} (rocking mode) for the Si–O–Si groups and confirm the formation of SiO_2 shell. The twisting vibration mode of H–O–H in the silica shell is seen at 1641 cm^{-1}, and broad absorption bands in the range of 3200–3500 cm^{-1} attributed to stretching vibration mode of Si–OH bonds and adsorbed H_2O [41] (Fig. 1b, d). The presence of the attached alkyl groups is confirmed by the observed bands at 2936 and 2956 cm^{-1} related to the symmetric and asymmetric stretching modes of C–H bonds (Fig. 1c, d). The tertiary amine group is shown at 1467 cm^{-1} [36] (Fig. 1c, d). These spectra reveal the functional groups were successfully grafted onto the surface of the CaO nanoparticles.



Scheme 3 Preparation of CaO@SiO_2@AIL (methods A and B)

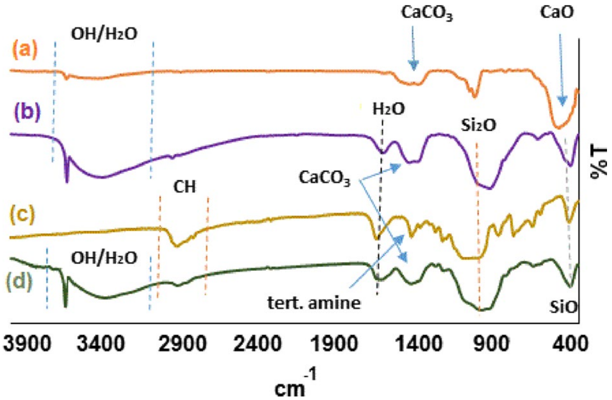


Fig. 1 FT-IR spectra of **a** nano CaO **b** nano-CaO@SiO_2, **c** AIL, **d** CaO@SiO_2@AIL catalyst

EDX analysis

For comparison, CaO@SiO$_2$@AIL was synthesized by two different procedures and their EDX spectra were properly compared. In method A, the AIL was prepared by employing the previously reported method [36]. The CaO@SiO$_2$ was separately synthesized and AIL grafted onto the CaO@SiO$_2$ core–shell surface to produce CaO@SiO$_2$@AIL (Scheme 3, method A). In method B, initially the CaO@SiO$_2$ was synthesized, and subsequently, the silanol groups on the surface of CaO@SiO$_2$ nanoparticles were treated with (3-chloropropyl)trimethoxysilane to produce CaO@SiO$_2$–Cl. Next, the resulted chloropropyl anchored CaO@SiO$_2$ was reacted with hexamethylenetetramine to give the final hybrid structure CaO@SiO$_2$@AIL (Scheme 3 method B).

The energy-dispersive X-ray spectrum (EDX) of CaO@SiO$_2$@AIL is shown in Fig. 2. This spectrum clearly indicates the expected elemental composition of N and Cl, which confirms the surface of CaO@SiO$_2$ was successfully coated with HMTA in two methods. The method A was more effective than B because the determined percentages of N and Cl are higher in method A. Thus, it indicates that AIL is more loaded on the CaO@SiO$_2$ surface (Fig. 2 method A).

SEM spectrum and histogram of CaO@SiO$_2$@AIL

The surface morphology and histogram of particle size distribution of the CaO@SiO$_2$@AIL were characterized by the scanning electronic microscopy (SEM) as presented in Fig. 3a and b, respectively. It can be seen that the particles of CaO@SiO$_2$@AIL are well dispersed with almost spherical morphology and the average size of about 8 nm, which matches well with XRD pattern. Furthermore, the mesoporous nature and the small size of these nanoparticles lead to the high specific surface area and high catalytic activity. The high surface area of these nanoparticles creates a certain degree of aggregation, which demonstrates the successful anchoring ionic liquid part on to CaO@SiO$_2$ nanoparticles (Fig. 3).

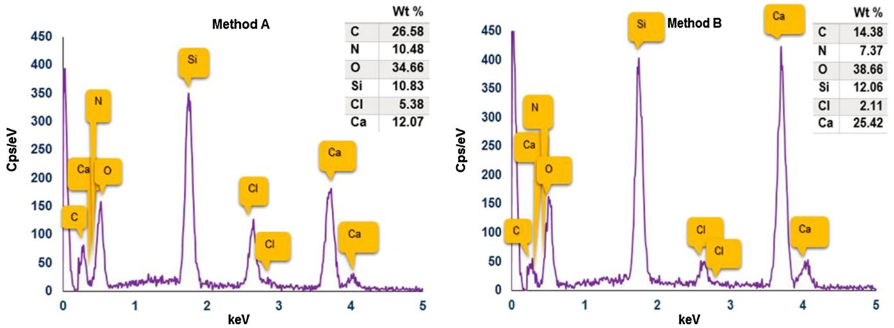


Fig. 2 EDX spectrum of CaO@SiO$_2$@AIL (papered by methods A and B)

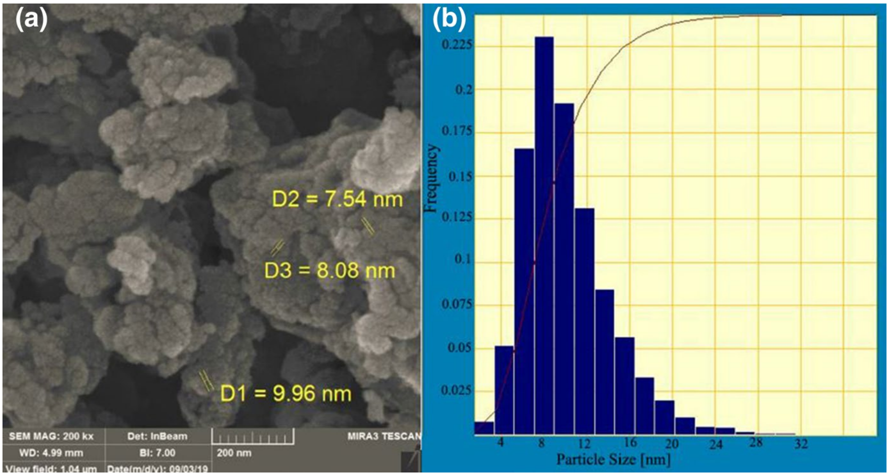


Fig. 3 **a** SEM image of CaO@SiO$_2$@AIL **b** histogram of CaO@SiO$_2$@AIL

WDX map scan of CaO@SiO$_2$@AIL

The projected distribution of N, O, Si, Ca, Cl and C elements in the catalyst via WDX images is shown in Fig. 4b–g, respectively, and can provide qualitative data on the distribution of various chemical elements in the catalyst matrix, coupled with

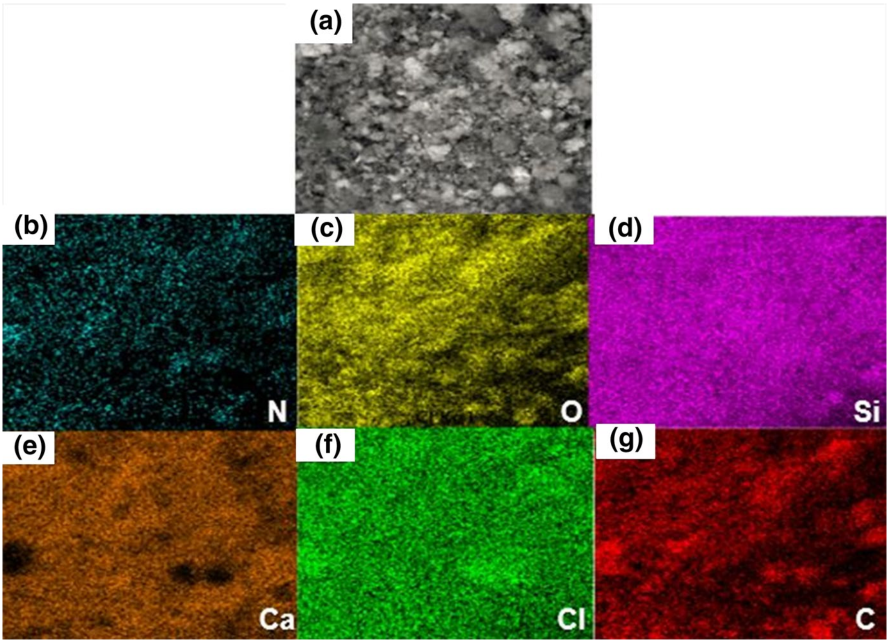


Fig. 4 **a** SEM image of CaO@SiO$_2$@AIL and elemental mapping of **b** N, **c** O, **d** Si, **e** Ca, **f** Cl and **g** C

SEM image presented in Fig. 4a. From these compositional maps, the homogeneous distribution of all the elements in the catalyst is clearly determined the regular uniformity of the catalyst. These analysis data clearly prove that the organic functional group is attached onto the surface of CaO@SiO_2.

XRD analysis

The XRD measurements were implemented to investigate the presence as well as the crystallinity degree of CaO, CaO@SiO_2 and CaO@SiO_2@AIL catalysts (Fig. 5). CaO nanoparticles appeared diffraction peaks at $2\theta = 32.50°$, 37.65°, 54,16°, 64.54° and 67.71° correspond to the Miller indices (*hkl*) at (111), (200), (202), (311) and (222) crystal planes, respectively [39]. These lattice parameters confirm the CaO nanoparticles are pure with a cubic structure and relative intensities. The results are in agreement with the standard values given in JCPDS card no.77-9574 for a calcite CaO powder sample. The broad peak around $2\theta = 18°$ to 28° is derived from amorphous silica phase of CaO@SiO_2 and CaO@SiO_2@AIL [35] (Fig. 5b, c). The average size of the crystallites can be estimated by applying Scherrer's formula ($D = 0.9\lambda/\beta \cos \theta$). In this formula, D is defined as the average crystalline size, where λ is the wavelength of the incident X-rays, β is the full width at half maximum height in radians and θ belongs to the Bragg angle. The peak at $2\theta = 37.65°$ (200) is selected to calculate the crystallite size. The crystallite size of the nanoparticle was obtained 8 nm by using Scherrer's equation, which is in the range of that determined by using SEM analysis. Besides, the XRD pattern indicates the retention of crystalline core structure of cubic CaO through the silica coating procedure.

TGA study

The thermal behavior of CaO@SiO_2@AIL reveals the mass loss of organic tags as they decompose upon heating (Fig. 6). The first step from room temperature to 150 °C is attributed to the removal of physically adsorbed water and remained

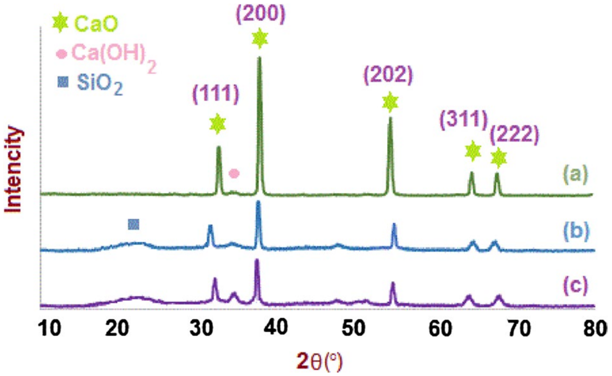


Fig. 5 XRD patterns of **a** CaO nanoparticles, **b** nano-CaO@SiO_2 and **c** nano-CaO@SiO_2@AIL

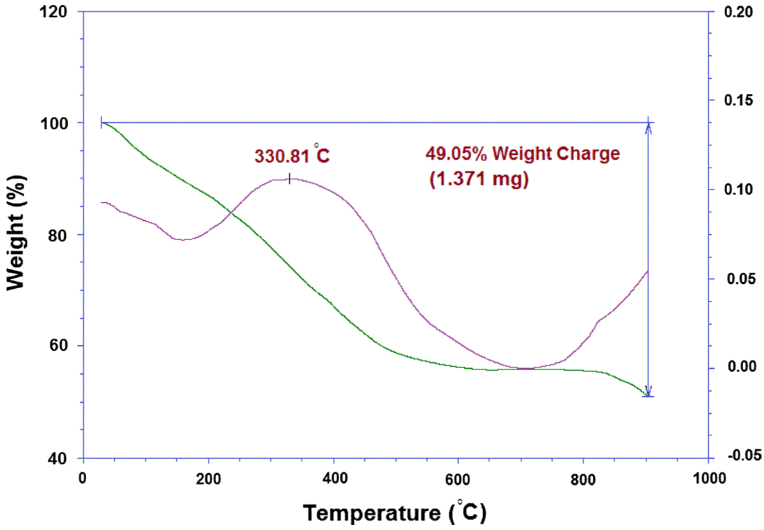


Fig. 6 TGA curve of CaO@SiO_2@AIL

organic solvents (weight loss 10%). The second step, in the region from 150 to 330 °C, is related to the loss of grafted AIL on the surface of CaO@SiO_2. The third step, the weight loss between 330 and 700 °C, is attributed to degradation of HMTA groups. Also the total loss weight between 150 and 700 °C is 35%, which can be related to the grafted organic tags. In accordance with this mass loss, 1.6 mmol of AIL was loaded on 1 g of CaO@SiO_2 catalyst.

Elemental analyses

In order to confirm the successful grafting of organic ionic liquid (AIL) onto surface of CaO@SiO_2, the elemental analysis was performed and revealed the percent of C (16.8%), H (3.8%), and N (8.6%). The percent of nitrogen was measured in organic moiety. Using the analytical data, and based on nitrogen content, the grafted organic moiety was calculated to be about 34% of AIL. It is nearly matched with thermal gravimetric (TGA) for CaO@SiO_2@AIL.

Synthesis of 2-imino-*2H*-chromenes catalyzed by CaO@SiO_2@AIL

After ensuring the successful fabrication of CaO@SiO_2@AIL, the catalytic activity of these nanomaterials for synthesis of 2-imino-*2H*-chromenes was investigated. To find out the optimized conditions, the reaction of 2-hydroxybenzaldehyde, phenylmethanamine and ethyl cyanoacetate was selected as a model. To investigate the effect of solvent, the model reaction was carried out by using different solvents including EtOH/H_2O, H_2O, MeOH, EtOH, CH_3CN and $CHCl_3$. Fortunately, solvent-free condition at 80 °C was found to be more applicable for this synthesis rather than using the organic solvents according to the principles of green chemistry. As shown in Table 1, the best result was obtained by using of 0.01 g of the catalyst among different amounts of catalyst. Therefore, the reaction was efficiently performed using 0.01 g of the catalyst at 80 °C under solvent-free conditions to give desired product in high yield over short reaction time (Table 1, entry 10). To study the scope and limitations of this procedure, a wide range of amines containing either electron-withdrawing or electron-donating substituent were used for preparation of 2-imino-2*H*-chromenes under optimized conditions (Table 2). The results show the corresponding 2-imino-2*H*-chromenes were synthesized with good to excellent yields. Thus, CaO@SiO_2@AIL was found to be superior and highly efficient catalyst for this reaction under green and mild conditions. A possible mechanism for synthesis of 2-imino-2*H*-chromenes in the presence of CaO@SiO_2@AIL is presented in Scheme 4. Firstly, a substitution reaction of amine and ethyl cyanoacetate gives *N*-alkyl-2-cyanoacetamide which is followed by a Knoevenagel condensation of *N*-alkyl-2-cyanoacetamide anion with 2-hydroxybenzaldehyde to produce intermediate A. The cyclization of intermediate A by OH nucleophilic attack on nitrile group resulted in the desired product.

Table 1 Optimization of reaction conditions for the synthesis of *N*-benzyl-2-imino-2*H*-chromene-3-carboxamide

Entry	Catalyst (g)	Solvent	Temp (°C)	Time (min)	Yield (%)
1	–	–	110	150	Trace
2	0.005	–	110	60	63
3	0.005	–	95	40	65
4	0.005	–	80	35	65
5	0.008	–	110	30	72
6	0.008	–	95	30	75
7	0.008	–	80	28	83
8	0.01	–	110	10	90
9	0.01	–	95	10	92
10	**0.01**	**–**	**80**	**10**	**98**
11	0.02	–	80	10	94
12	0.01	H_2O/EtOH	Reflux	40	83
13	0.01	H_2O	Reflux	55	82
14	0.01	MeOH	Reflux	30	80
15	0.01	EtOH	Reflux	20	88
16	0.01	$CHCl_3$	Reflux	65	72
17	0.01	CH_3CN	Reflux	45	75

Reaction conditions: 2-hydroxybenzaldehyde (1, 1 mmol), phenylmethanamine (2, 1 mmol), ethyl cyanoacetate (3, 1 mmol)

Bold values indicate the optimized reaction conditions

Table 2 Synthesis of 2-imino-2*H*-chromenes via three component condensation reactions in the presence of CaO@SiO$_2$@AIL

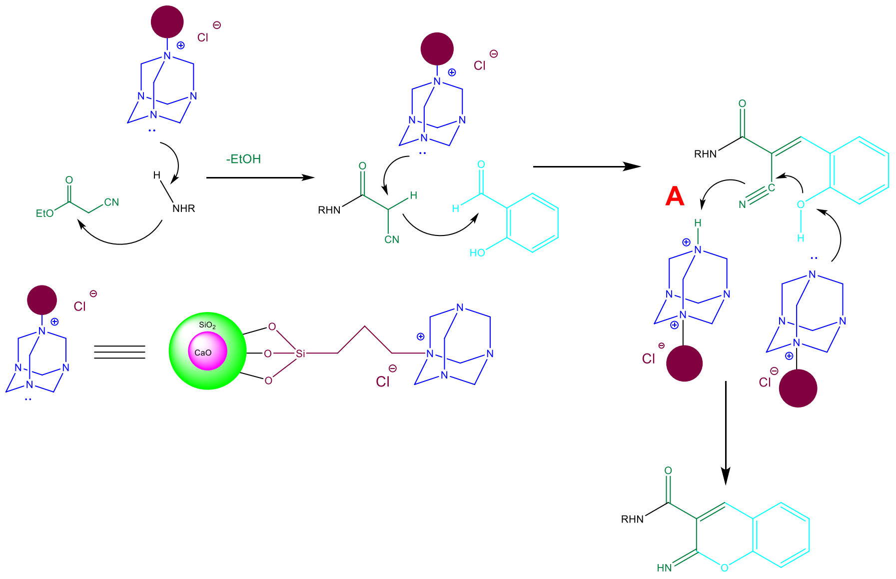
Entry	Amine	Product	Time (min)	Yield (%)	MP (°C)	
					Found	Reported Refs.
1	PhNHNH$_2$	4a	10	73	263–265	266–267 [15]
2	1,3-diaminopropane	4b	23	68	291–292	293–295 [42]
3	1,4-diaminobutane	4c	20	85	257–259	253–255 [42]
4	cyclopentylamine	4d	18	86	210–212	213–216 [43]
5	3,4-dimethoxyaniline	4e	30	80	158–160	157–159 [44]
6	4-nitroaniline	4f	10	90	138–141	146–147 [44]
7	4-bromoaniline	4g	15	79	160–162	164–165 [44]
8	3,4-dichloroaniline	4h	15	93	168–169	171–173 [44]
9	cyclohexylamine	4i	35	94	201–203	207–209 [45]
10	phenylmethanamine	4j	10	98	128–130	133 [14]
11	semicarbazide	4k	10	98	219–221	–
12	2,4-dinitrophenylhydrazine	4l	10	90	254–255	–
13	2-amino-4-methylpyrimidine	4 m	15	95	210–212	–
14	phormilhydrazine	4n	10	80	219–224	–
15	4-pyridinecarboxylic acid hydrazide	4o	10	92	230–232	–
16	semicarbazide	4p	10	83	255–257	–
17	4-pyridinecarboxylic acid hydrazide	4q	10	80	277–279	–

Reaction conditions: 2-hydroxybenzaldehyde (1a–o, 1 mmol) or 2-hydroxy-1-naphthaldehyde (1p,q, 1 mmol), alkyl or arylamine (2, 1 mmol), ethyl cyanoacetate (3, 1 mmol) and catalyst (0.01 g)

Synthesis of dihydropyrano[*c*]chromenes catalyzed by CaO@SiO$_2$@AIL

Preliminarily, the optimal reaction conditions for synthesis of dihydropyrano[*c*] chromenes in the presence of CaO@SiO$_2$@AIL were investigated. The reaction of 4-chlorobenzaldehyde, 4-hydroxycoumarin and malononitrile was selected as a model. The reaction was carried out in different solvents such as H$_2$O, EtOH, CHCl$_3$, THF, DMF, EtOAc and CH$_3$CN. As Table 3 shows, H$_2$O was found to be a suitable solvent for this reaction at room temperature. In addition, the crucial role of CaO@SiO$_2$@AIL as a catalyst in this reaction was approved by performing the reaction in the absence of catalyst, which gave only trace amount of the expected product after a prolonged reaction time (Table 3, entry 1). The best conditions along with high possible yield of product and short reaction time were obtained by 0.01 g of catalyst (Table 3, entry 10).

After optimization of reaction conditions, to examine the generality of this procedure, the reaction of several aromatic aldehydes bearing either electron-withdrawing or electron-donating substituent groups was examined using the optimized conditions to produce desired products (Table 4). This procedure for various substrates was very efficient, and the dihydropyrano[*c*]chromene



Scheme 4 Possible mechanism for one-pot synthesis of 2-imino-2*H*-chromenes using CaO@SiO$_2$@AIL as a catalyst

Table 3 Optimization of reaction conditions for synthesis of 2-amino-4-(4-chlorophenyl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile

Entry	Catalyst (g)	Solvent	Temp (°C)	Time (min)	Yield (%)
1	–	H_2O	25	240	Trace
2	0.005	H_2O	80	45	60
3	0.005	H_2O	50	40	62
4	0.005	H_2O	25	35	65
5	0.008	H_2O	80	35	85
6	0.008	H_2O	50	30	88
7	0.008	H_2O	25	30	90
8	0.01	H_2O	80	25	92
9	0.01	H_2O	50	25	93
10	**0.01**	**H_2O**	**25**	**20**	**96**
11	0.02	H_2O	25	20	94
12	0.01	THF	25	80	20
13	0.01	DMF	25	70	32
14	0.01	EtOAc	25	85	20
15	0.01	EtOH	25	35	80
16	0.01	$CHCl_3$	25	75	30
17	0.01	CH_3CN	25	50	70

Reaction conditions 4-chlorobenzaldehyde (5, 1 mmol), 4-hydroxycoumarin (6, 1 mmol) and malononitrile (7, 1 mmol)

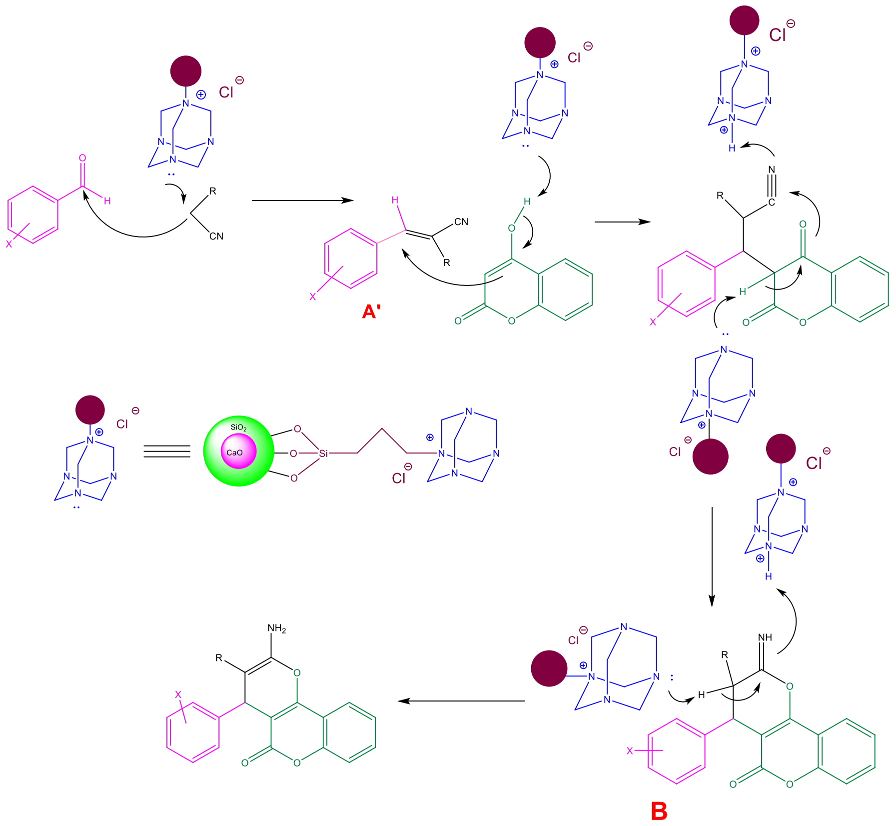
Bold values indicate the optimized reaction conditions

Table 4 Synthesis of dihydropyrano[*c*]chromenes via three component condensation reactions using $CaO@SiO_2@AIL$

Entry	Aldehyde	Product	Time (min)	Yield (%)	MP (°C)	
					Found	Reported Refs.
1	2,4-$(Cl)_2C_6H_3$	8a	7	93	280–281	283–284 [27]
2	4-ClC_6H_4	8b	20	96	255–257	256–258 [46]
3	3-$NO_2C_6H_4$	8c	10	90	230–232	229–231 [46]
4	2-ClC_6H_4	8d	16	80	269–271	273–274 [27]
5	2-BrC_6H_4	8e	10	93	288–290	293–296 [47]
6	3-OHC_6H_4	8f	25	75	258–260	262–263 [25]
7	4-$NO_2C_6H_4$	8g	9	95	260–262	263–264 [48]
8	2-$NO_2C_6H_4$	8h	10	90	250–252	255–256 [27]
9	2,5-$(MeO)_2C_6H_3$	8i	30	80	218–220	228–230 [23]
10	4-FC_6H_4	8j	10	96	244–246	245–247 [49]
11	3-EtO-4-OH-C_6H_3	8 k	15	85	240–242	248–250 [50]
12	3-Phenoxy-C_6H_4	8l	15	80	254–255	–
13	2,2′-(butane-1,4-diylbis(oxy)) dibenzaldehyde	8 m	60	88	210–212	–
14	4,4′,4″-((1,3,5-Triazine-2,4,6-triyl) tris(oxy))tribenzaldehyde	8n	45	93	219–224	–
15	4-FC_6H_4	8o	10	95	230–232	223–225 [51]
16	4-$NO_2C_6H_4$	8p	8	95	245–247	241–243 [24]

Reaction conditions: arylaldehyde (5a–p, 1 mmol), 4-hydroxycoumarin (6, 1 mmol), malononitrile (7a–n, 1 mmol) or ethyl cyanoacetate (7o, p, 1 mmol) and catalyst (0.01 g)

derivatives were obtained in good to excellent yields in relatively short reaction times, without formation of byproducts. A plausible mechanism, similar to that reported in literature, Ref. [32] is presented for the synthesis of dihydropyrano[*c*] chromenes (Scheme 5). As shown in Scheme 5, firstly, the formation of the products can be rationalized by initial standard Knoevenagel condensation reaction between an aldehyde and malononitrile anion to form arylidene malononitrile as intermediate A' under the catalytic effect of the $CaO@SiO_2@AIL$. Subsequently, 4-hydroxycumarin anion attacks catalyst-activated arylidene malononitrile via a Michael addition and the subsequent cyclization produce the intermediate B. At the last step, the H-abstraction by catalyst and following tautomerization gives the desired product. The efficiency of $CaO@SiO_2@AIL$ catalyst is comparable with that of other reported catalysts for the synthesis of 2-amino-4-(4-chlorophenyl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile under optimized conditions (Table 5). As shown in Table 5, the $CaO@SiO_2@AIL$ is an efficient catalyst for this reaction in terms of short reaction time, high yield, and green chemistry. This efficiency may be related to the inherent properties of CaO in inorganic part, the cage-like structure of HMTA in organic part, high active surface area and ionic liquid properties of $CaO@SiO_2@AIL$.



Scheme 5 Possible mechanism for one-pot synthesis of dihydropyrano[*c*]chromenes using CaO@SiO$_2$@AIL as a catalyst

Table 5 Comparison of CaO@SiO$_2$@AIL with other catalysts reported in the literatures for synthesis of 2-amino-4-(4-chlorophenyl)-5-oxo-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile

Entry	Catalyst	Condition	Time (min)	Yield (%)	Ref.
1	p-TSA	H_2O/EtOH-reflux	60	35	[52]
2	Nano-Al(OH)$_3$	EtOH/reflux	120	73	[52]
3	S-proline	H_2O/EtOH-reflux	360	78	[25]
4	SDS	H_2O/60 °C	150	88	[22]
5	Nano NiO	EtOH/reflux	90	49	[53]
6	Nano Al$_2$O$_3$	EtOH/reflux	120	71	[54]
7	CaO@SiO$_2$@AIL	H_2O/r.t	20	96	Present work

Reaction conditions: 4-chlorobenzaldehyde (1 mmol), 4-hydroxycoumarin (1 mmol), malononitrile (1 mmol) and catalyst (0.01 g)

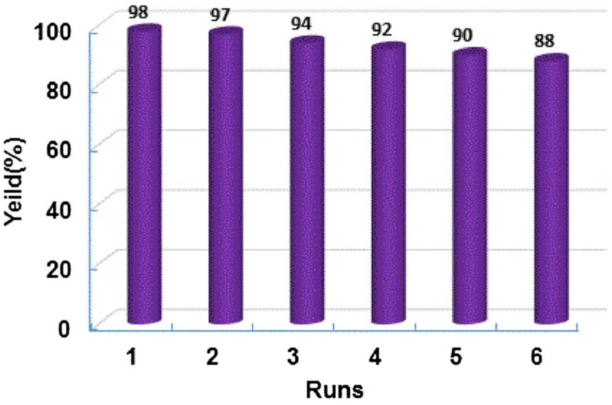


Fig. 7 Recyclability test of CaO@SiO$_2$@AIL

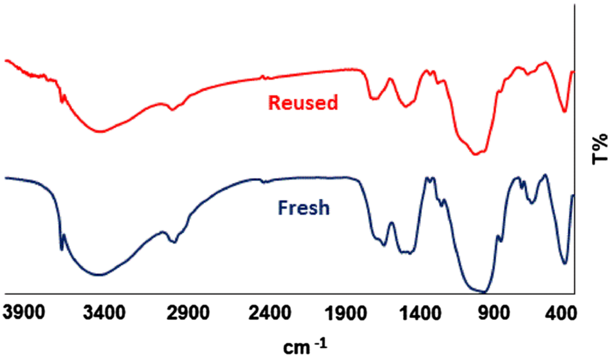


Fig. 8 FT-IR spectra of the fresh catalyst and the six-times reused catalyst

Catalyst recovery and reusability

As separation and reusability of catalyst are very important factors in viewpoints of green chemistry, the recovery and reusability of CaO@SiO$_2$@AIL was investigated in reaction of 2-hydroxybenzaldehyde (1 mmol), phenylmethanamine (1 mmol), ethyl cyanoacetate (1 mmol) and catalyst (0.01 g) under solvent-free condition. The results confirmed that the catalyst could be reused for six consecutive times without significant loss in the yield of the reaction (Fig. 7). The recovered catalyst was purified by washing with hot ethanol and drying in an oven. As shown in Fig. 8, the stability and integrity of the recovered catalyst were examined and confirmed to be as active as the originally used catalyst.

Conclusion

In this study, novel nanoparticles (CaO@SiO_2@AIL) were prepared by using a simple and inexpensive method. The size and structure of these nanomaterials were confirmed by FT-IR, EDX, SEM, WDX, XRD, TGA and elemental analyses. These CaO@SiO_2@AIL nanoparticles were used as a heterogeneous catalyst for synthesis of 2-imino-2*H*-chromenes and dihydropyrano[*c*]chromenes under mild and green conditions. A wide range of amines and aromatic aldehydes containing either electron-withdrawing or electron-donating substituent were used for synthesis of the 2-imino-2*H*-chromenes and dihydropyrano[*c*]chromenes, respectively, which gave corresponding products in high to excellent yields within short reaction times. Furthermore, the mild and green nature of reaction conditions, easy workup procedures and reusability of the catalyst are some other advantages of these methods.

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