

Application of a mesoporous nanomaterial based on basic ionic liquid anchored to silica as a highly effective catalyst for the production of 2-amino-4H-chromenes

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ABSTRACT

This research describes application of a mesoporous nanostructured material based on basic ionic liquid anchored to silica, i.e. nano-2-(dimethylamino)-*N*-(silica-*n*-propyl)-*N,N*-dimethylethanaminium chloride {nano-[DMSPDE][Cl]}, as a highly effective and heterogeneous nanocatalyst for the production of 2-amino-4H-chromenes. The one-pot multi-component reaction of aromatic aldehydes with malononitrile and 1-naphthol in the presence of nano-[DMSPDE][Cl] under solvent-free conditions affords the title compounds with high yields in short times.

Keywords: 2-Amino-4H-chromene, Nanocatalyst, Basic ionic liquid anchored to silica, Nano-2-(dimethylamino)-*N*-(silica-*n*-propyl)-*N,N*-dimethylethanaminium chloride {nano-[DMSPDE][Cl]}, Multi-component reaction, Solvent-free conditions.

1. Introduction

Currently, nanocatalysts have attracted much attention in organic synthesis [1-9], because of possessing various particular properties, including eco-friendly nature, low density, enhanced activity and efficiency (due to having large surface-to-volume ratio in comparison to bulk materials), recyclability and capacity to functionalize for different catalytic applications [8]. There are several types of nanocatalysts; a significant example of them is solid-supported ones [2-9]. Among the solid-supported nanocatalysts, silica-based ones are usually preferred, because they have a variety of unique properties, consisting of safety, non-corrosiveness, high surface area, high thermal and chemical stability, easy separation from the reaction media, simple preparation and functionalization, cheapness and tunability of nano-size [6-9].

In recent years, anchoring ionic liquids (ILs) to solid supports (and consequently heterogenizing them) has been increasingly considered in catalysis researches; since they have simultaneously the advantages of ILs and heterogeneous catalysts [8-11].

The particular properties of ILs include low vapor pressure, non-flammability, easy production and functionalization, suitable thermal, chemical and electrochemical stability, environmentally benign nature, recyclability, applicability to catalyze various organic transformations and high catalytic efficacy [12-14]; and the benefits of heterogeneous catalysts are reasonable stability (chemical and thermal), simple isolation from reaction mixture, facile usage and recyclability, green nature and aptitude to promote miscellaneous kinds of organic reactions [15-17].

In multi-component reactions (MCRs), at least three components are reacted in one step (one-pot) to provide the target molecule in high selectivity; this technique is of importance in modern organic synthesis and medicinal chemistry. MCRs have many advantages compared to conventional multi-steps reactions, such as high atom economy, saving energy and time, minimizing usage of volatile organic solvents for workup and purification of products, and preventing or reducing synthesis of wastes and side-products [18-23]. Alternatively, application of volatile and toxic organic solvents, especially chlorinated hydrocarbons, causes pollution of environment; thus, it is highly desirable to achieve environmentally benign processes (e.g. MCRs) in solvent-free conditions [21-23]. The benefits of

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solvent-free technique include formation of target product in higher yield and selectivity in shorter reaction time, preventing or decreasing production of waste/by-products, easier work-up and purification of product, and saving energy [21-23].

The compounds containing 4*H*-chromene scaffold are of considerable interest as they have various pharmacological activities, such as antimicrobial [24], antiviral [25], antitumor [26], mutagenic [27], pheromonal [28], antiproliferative [29], and antiallergenic [30] properties. These oxygen-containing heterocycles have been also utilized in fluorescence markers [31], laser dyes [32], and optical brighteners [33]. The one-pot multi-component condensation of aldehydes with malononitrile and 1-naphthol is a practical synthetic route toward 2-amino-4*H*-chromenes (as an important class of 4*H*-chromene-bearing compounds); some catalysts have been reported to achieve this synthesis [34-43].

Considering the profits of nanocatalysts, heterogenized ILs, MCRs and solvent-free conditions, it is highly desirable and attractive to collect them in a research work for synthesis of useful organic compounds, e.g. 2-amino-4*H*-chromenes. Herein, we have achieved that, and introduced a mesoporous nanomaterial based on ionic liquid anchored to silica, namely nano-2-(dimethylamino)-*N*-(silica-*n*-propyl)-*N,N*-dimethyl ethanaminium chloride {nano-[DMSPDE][Cl]}, as a highly effectual catalyst for the solvent-free synthesis of 2-amino-4*H*-chromenes *via* the one-pot multi-component reaction of arylaldehydes with malononitrile and 1-naphthol.

2. Experimental

2.1. Chemicals and Instruments

All starting materials were purchased from Merck or Fluka Chemical Companies. For identification of known products, their spectral data and/or melting points were compared with the reported data in the literature. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The ¹H NMR (500 MHz) and ¹³C NMR (125 MHz) were run on a Bruker Avance DPX FTNMR spectrometer (δ in ppm). Melting points were recorded on a Buchi B-545 apparatus in open capillary tubes. The morphologies, particles sizes and the compositions of samples were characterized by the Field Emission Scanning Electron Microscopy (FE-SEM, MIRA3TESCAN-XMU). The size, morphology and selected area electron diffraction (SAED) patterns of nanoparticles were determined using a high resolution transmission electron microscope (FEI Titan 80-300 TEM fitted with CEOS

image corrector) at an accelerating voltage of 80-300 kV after drop coating of the colloidal CDs onto a hydrophilic carbon coated copper grid and drying in a dust protected atmosphere.

2.2. Procedure for the production of nano-[DMSPDE][Cl]

A mixture of *N,N,N',N'*-tetramethylethane-1,2-diamine (0.581 g, 5 mmol), (3-chloropropyl)trimethoxysilane (0.994 g, 5 mmol) and toluene (15 mL) in a 50 mL round-bottomed flask connected to a reflux condenser, was stirred for 12 h under reflux conditions; afterward, the solvent (toluene) was evaporated under vacuum at 95 °C to give intermediate **I**. Intermediate **I** was reacted with nano-silica gel (0.300 g, 5 mmol) in refluxed ethyl acetate (15 mL) for 8 h. The formed precipitate was separated by centrifugation and decanting, and then was washed with ethyl acetate (2 × 5 mL) and dried under vacuum at 80 °C to give nano-[DMSPDE][Cl] as a white precipitate with 98% yield [8].

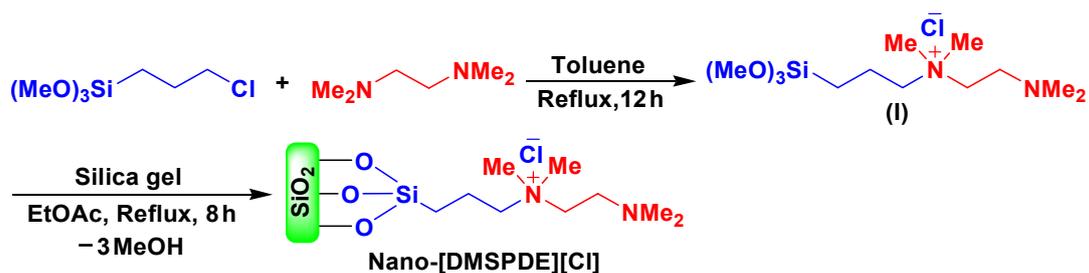
2.3. General procedure for the preparation of 2-amino-4*H*-chromenes

A mixture of aldehyde (1 mmol), malononitrile (1 mmol, 0.066 g) and 1-naphthol (1 mmol, 0.144 g) was added to nano-[DMSPDE][Cl] (0.032 g). The resulting mixture was firstly stirred magnetically at 100 °C, and after solidification of the reaction mixture, it was vigorously stirred with a small rod at the same temperature. After completion of the reaction (as monitored by TLC), the reaction mixture was cooled to room temperature, ethyl acetate (10 mL) was added, and stirred under reflux conditions for 2 min, followed by centrifugation and decanting to separate the nanocatalyst {the catalyst was washed by ethyl acetate (2×2 mL), dried and used for next run}. The solvent obtained from the decanting was evaporated, and the resulting precipitate was recrystallized from hot ethanol (95%) to give the pure product.

3. Results and Discussion

Nano-2-(dimethylamino)-*N*-(silica-*n*-propyl)-*N,N*-dimethylethanaminium chloride {nano-[DMSPDE][Cl]} was prepared according to Scheme 1. The nanocatalyst was characterized by FT-IR, energy-dispersive X-ray spectroscopy (EDS), scanning electron microscopy (SEM) and high resolution transmission electron microscopy (HRTEM) methods.

The FT-IR spectrums of intermediate **I**, nano-[DMSPDE][Cl] and the respective IR data are indicated in supplementary file. The data are in accordance with the literature [8].



Scheme 1. The synthesis of nano-[DMSPDE][Cl].

The EDS spectrum of nano-[DMSPDE][Cl] (Fig. 1) verified the presence of the expected elements in its structure, i.e. C, N, O, Si and Cl.

The SEM and HRTEM micrographs of the nanocatalyst are shown in Fig. 2 and 3. As it is clear from Fig. 2, the particles are in nano-size. Moreover, in the HRTEM micrographs (Fig. 3), agglomerates or bundles of flakes or amorphous case were observed.

To obtain most suitable reaction conditions for the production of 2-amino-4*H*-chromene derivatives using mesoporous nano-[DMSPDE][Cl], influence of the catalyst amount and temperature was studied on the one-pot multi-component condensation of 3-nitrobenzaldehyde (1 mmol) with malononitrile (1 mmol) and 1-naphthol (1 mmol) in solvent-free conditions (Scheme 2); the relevant results are summarized in Table 1.

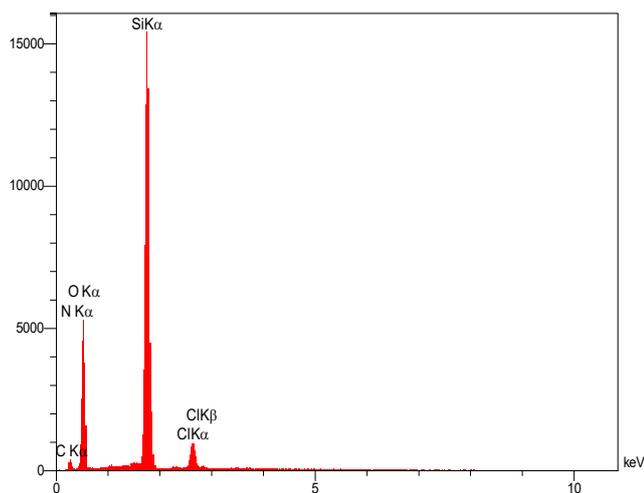


Fig. 1. The EDS spectrum of the nanocatalyst.

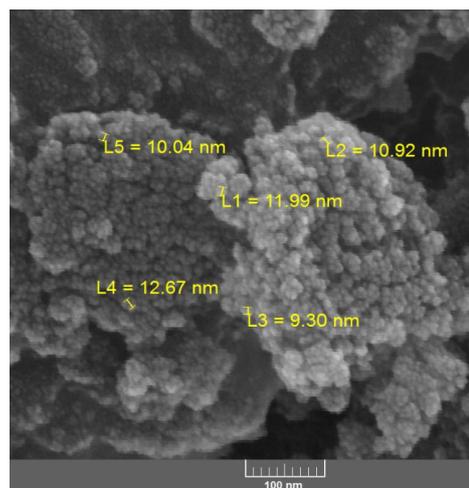


Fig. 2. The SEM image of nano-[DMSPDE][Cl].

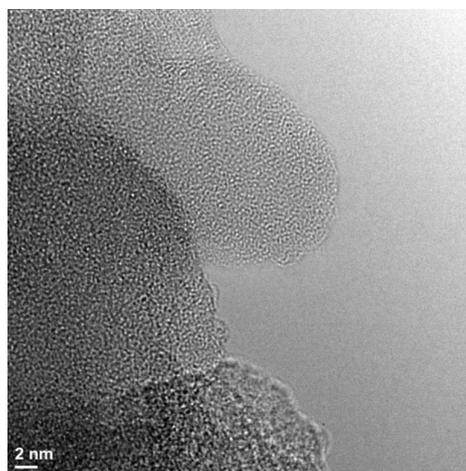
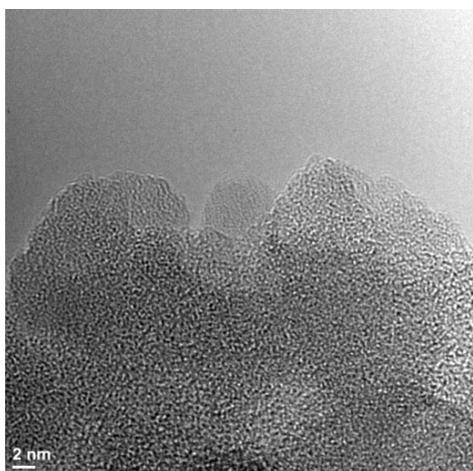
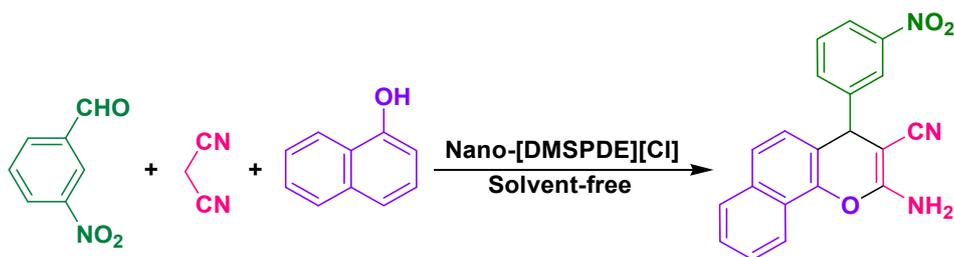


Fig. 3. The HRTEM micrographs of the nanocatalyst.



Scheme 2. The reaction of 3-nitrobenzaldehyde, malononitrile and 1-naphthol (model reaction).

Table 1. Influence of the catalyst amount and temperatures on the model reaction.

Entry	Nano-[DMSPDE][Cl] (g)	Temp. (°C)	Time (min)	Yield (%) ^a
1	-	100	40	37
2	0.024	100	10	84
3	0.032	100	10	98
4	0.036	100	10	98
5	0.032	90	10	76
6	0.032	105	10	98

^aIsolated yield.

As the data in this Table illustrate, the most suitable conditions were obtained when 0.032 g of nano-[DMSPDE][Cl] was exploited at 100 °C (Table 1, entry 3).

Afterward, the synthesis of different derivatives of 2-amino-4*H*-chromenes was performed using various arylaldehydes, malononitrile and 1-naphthol under the optimal conditions, in order to

recognize effectiveness and generality of nano-[DMSPDE][Cl]; the corresponding results are displayed in Table 2.

As it can be observed in this Table, benzaldehyde and arylaldehydes having electron-withdrawing, halogen and electron-releasing substituents worked well in the reaction, and afforded the related products with high yields in short times.

Table 2. The production of 2-amino-4*H*-chromene derivatives using nano-[DMSPDE][Cl].

The reaction scheme for Table 2 shows an arylaldehyde (Ar-CHO) reacting with malononitrile and 1-naphthol in the presence of Nano-[DMSPDE][Cl] in a solvent-free environment at 100 °C. The product is a 2-amino-4H-chromene derivative with an Ar group at the 4-position of the benzene ring fused to the chromene system. The chromene ring has an NH₂ group at position 2 and a CN group at position 4.

Product	Ar	Time (min)	Yield (%) ^a	m.p. (°C)		Ref.
				Found	Reported	
1a	C ₆ H ₅	5	94	209-211	211-212	[34]
1b	3-O ₂ NC ₆ H ₄	10	98	213-215	212-214	[37]
1c	4-O ₂ NC ₆ H ₄	10	97	227-229	230	[38]
1d	4-FC ₆ H ₄	15	96	225-227	224-226	[42]
1e	4-BrC ₆ H ₄	15	93	242-244	240-242	[39]
1f	2-ClC ₆ H ₄	10	91	236-238	235-237	[39]
1g	4-ClC ₆ H ₄	5	97	233-235	233	[38]
1h	2,4-Cl ₂ C ₆ H ₃	5	93	210-212	212-214	[37]
1i	3-MeOC ₆ H ₄	15	94	234-236	231-233	[43]
1j	4-MeOC ₆ H ₄	15	90	179-181	182	[38]

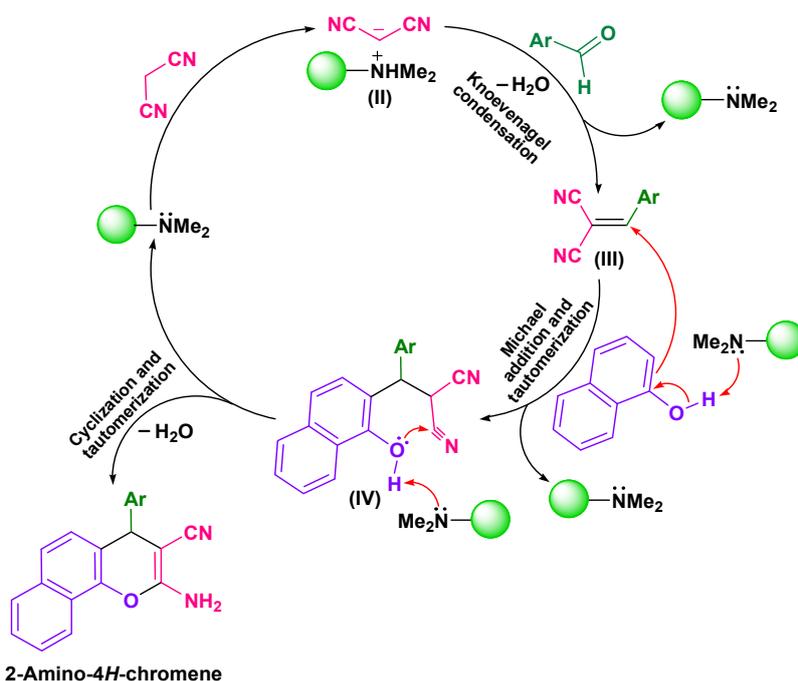
^aIsolated yield.

Furthermore, positions of the substituents (ortho, meta and para) had no significant effect on the reaction times and yields. Considering these excellent results, nano-[DMSPDE][Cl] was a highly effective and general catalyst for the preparation of 2-amino-4*H*-chromenes.

Based on the existing reports [34,37,42], a possible mechanism for the reaction is proposed in Scheme 3. First, the basic catalyst abstracts a proton from malononitrile to afford intermediate **II**. Nucleophilic addition of **II** to aldehyde, and removing a H₂O

molecule (by assisting nano-[DMSPDE][Cl]) gives **III**. Afterward, intermediate **IV** was produced by Michael addition of 1-naphthol to **III**, and tautomerization (the nanocatalyst can also accelerate this step). Finally, intramolecular nucleophilic addition of hydroxyl group to nitrile (in **IV**), and tautomerization provide 2-amino-4*H*-chromene.

To demonstrate the supremacy of nano-[DMSPDE][Cl] with respect to the reported catalysts for the preparation of 2-amino-4*H*-chromenes, the results and the reaction conditions of these catalysts are tabulated in Table 3.



Scheme 3. The mechanism for the synthesis of 2-amino-4*H*-chromenes.

Table 3. Comparing nano-[DMSPDE][Cl] with the reported catalysts for the synthesis of 2-amino-4*H*-chromenes.

Catalyst	Conditions	Time (min)	Yield (%)	Ref.
Nano-[DMSPDE][Cl]	Solvent-free, 100 °C	5-15	90-98	This work
MNPs-SPAsp ^a	Solvent-free, 120 °C	15-45	89-97	[34]
Nanozeolite clinoptilolite	H ₂ O, reflux	15-30	85-95	[35]
[4,4'-BPyH][C(CN) ₃] ₂ ^b	Solvent-free, 80 °C	8-20	85-94	[36]
Cetyltrimethylammonium bromide	H ₂ O, r.t., ultrasound irradiation	150	83-95	[37]
MCM-41-NH ₂	H ₂ O, 70 °C	30-300	69-93	[38]
FeTiO ₃	Solvent-free, MW irradiation	9-13	85-94	[39]
SBA-15@methenamine-HPA	H ₂ O, reflux	15	89-96	[40]
Nanofibre Sepiolite	H ₂ O/EtOH, reflux	30-45	90-98	[41]
Water Extract of Lemon Fruit Shell Ash	H ₂ O, MW irradiation	2.5-4.5	73-82	[42]
[bmim][PF ₆] ^c	80 °C	120	78-81	[43]

^aSodium polyaspartate-functionalized silica-coated nano-Fe₃O₄ particles.

^b[4,4'-Bipyridine]-1,1'-diium tricyanomethanide.

^c1-Butyl-3-methylimidazolium hexafluorophosphate.

As it is obvious from the Table, our catalyst gave the better results as compared with the others in terms of one or more of these factors: the reaction times, yields and temperature. Additionally, our synthesis has been carried out in solvent-free conditions, and has the benefits of this technique. Ultrasonic and microwave methods have also not been employed in our work (ultrasonic and microwave methods need special apparatuses).

The reaction of 3-nitrobenzaldehyde, malononitrile and 1-naphthol was performed in the presence of nano-[DMSPDE][Cl], and the catalyst was recycled according to the mentioned procedure in the experimental section. It was re-used for two times without any significant loss of activity.

4. Conclusions

Briefly, we have introduced a mesoporous nanostructured catalyst, based on basic ionic liquid anchored to silica, to promote a valuable organic reaction, i.e. the synthesis of 2-amino-4*H*-chromenes. Application of nano-[DMSPDE][Cl] to catalyze this synthesis is associated with these benefits: efficacy and generality of the protocol, short reaction times, high yields, clean reaction procedure, simplicity of the nanocatalyst preparation, performing the synthesis in solvent-free conditions, purification of the products by a non-chromatographic method (recrystallization), collecting the profits of nanocatalysts, heterogenized ILs, MCRs and solvent-free conditions in our work, easy workup procedure and isolation of the catalyst, reusability of the catalyst and the good agreement with green chemistry protocols.

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