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An efficient protocol for the synthesis of 4H-pyrano[3,2-*c*]coumarin derivatives at room temperature using nano modified SBA-15

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Abstract: A novel and efficient route has has been developed for the synthesis of 4H-pyrano[3,2-*c*]coumarin derivatives via a condensation reaction in the presence of nano modified SBA-15 in short reaction times. The major advantages of the present method are simple experimentation, use of inexpensive and ecofriendly catalyst with good yields and short reaction times.

Keywords: 4H-pyrano[3,2-*c*]coumarins, Malononitrile, Multi-component reactions, SBA-15.

Introduction

According to green chemistry principles, multi-component (MCRs) high-yielding, economical, ecofriendly reactions are green as these save efforts, costs and time for the production of targeted end products. However, not all multi-component reactions are really green if one or more of the twelve green chemistry principles are violated, such as using heavy metal pollutants, unnecesseary energy consumption, or excess of non-recyclable chemicals (e.g, solvents, catalysts) [1-3]. MCR chemistry applied to the synthesis of heterocycles with all its variations and extensions has undergone an enormous and meaningful upturn. Seeds sown in the last century, particularly appreciated by Ugi, have grown enormously and provided a plurality of novel reactions, new smart strategies as well as forward-looking methods, and high product diversity [4-6]. Also multi-component condensation reactions in wich a high molecular weight portion of a reactant is eliminated are not considered green. IT is now more than fifty years since Elnagdi and his co-workers initiated several consecutive projects designed to develop synthetic consecutive projects designed to develop synthetic approaches for biologically relevant heterocycles utilizing readily obtainable and inexpensive starting materials [7-11]. These efforts led to the preparation of a variety of biologically active substances. Several of these have been patented not only for specific biological activities but also as components of hair dye formulations as well as dyes for creatinine that are usefull in the cosmetic industr [12-16].

As a MCR, synthesis of 4H-pyrano[3,2-*c*]coumarin derivatives attracted enormous attention due to their wide applications. Chromene and hetero-fused chromenone scaffolds are important structural features of many natural products and synthetic organic compounds. The 4H-chromene nucleus is a fertile source of biologically important molecules possessing a wide spectrum of pharmacological activities, such as antimicrobial, anticancer, cytotoxic, antiHIV, anti-inflammatory, antimalarial, antimicrobial, antihyperglycemic and antidyslipidemic, anti-neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease and Huntington's disease and many more [17-21]. In addition to such pharmacological potential, pyran annulated

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heterocycles find applications in cosmetics and pigment industries, and are also useful as photoactive materials [22,23]. Hence, the synthesis of these compounds continues to attract much interest in organic chemistry. Various preparation methods of 4H-pyrano[3,2-*c*]coumarins have been reported such as InCl3 [24], HCOONa [25], KF-montmorillonite [26], TMGT / TBAB [27], $RuBr_2(PPh_3)_4$ [28], α-Fe_2O_3 [29], γ-Fe_2O_3@HAp-Si-$(CH_2)_3$-NH_2 [30], Piperidine [31-33], TiO_2-NW [34], $Na_2WO_4{\cdot}2H_2O$ [35], and even without catalyst [36].

By virtue of their large surface areas, high porosities, ordered pore arrangements, and controllable and narrowly distributed pore size, ordered mesoporous silicas are often used as adsorbents for the separation of heavy metal ions, organics, dyes, light hydrocarbons, gases, radionuclides and proteins. Inorganic solid catalyst such as SBA-15 (SBA=Santa Barbara Amorphous) are interesting for organic synthesis since they are environmental protection. The surface functionalization of mesoporous silica by grafting or condensation is a promising approach for preparing efficient solid base catalysts. Because of the excellent and unique properties of SBA-15, studies on the synthesis and characterization of the SBA-15 were blooming there after, to give complete understanding on this material and utilize its advantage for special use, including as catalyst supports [37]. The synthesis conditions (e.g.,pH. block copolymer, and hydrothermal temperature) can be altered in a widerange, leading to various textural properties while keeping the framework unchanged [38]. SBA-15 is the most well-known representative of this class of materials with interesting textural properties. Such as large specific surface areas (above 1000 m^2/g). highly ordered hexagonal structure, uniform-sized pores (in range 4-30 nm), hydrothermal stability, small crystallite size of primary particles and complementary textural porosity and thicker walls in comparison with Mobile composition of matter number 41 (MCM-41) [39-40]. The advantage of the use of SBA-15 material as support includes also its high surface-to-volume ratio and variable framework compositions [10-41]. However, the low chemical activity of the SBA-15 surface cannot be ignored, wich could result in the reduction of sorption ability. Thereby, many researchers modify SBA-15 with organic functional groups to improve its sorption ability and selectivity [39]. Nowadays, organic-inorganic hybrids are of great interest because they combine the advantages of heterogeneous catalysts (high mechanical, thermal and structural stability) and organic molecules (flexibility and functionality).

In this work and as a part of ongoing our work towards the development of efficient green catalysts for organic synthesis [42-44], we functionalized SBA-15 by chlorodiphenylphosphine and produced a novel modification SBA-15 ionic liquid (SBA/HSO_3) heterogeneous catalyst (Scheme **1**). Catalytic activities were evaluated through the three-component condensation of 4-hydroxycoumarin, malononitrile and aldehyde.

Results and discussion

Catalyst characterization:

The FT-IR spectra of the SBA-15 and SBA-HSO_3 are presented in Figure **1**. The present integration of the organic functional groups in the structure of the prepared materials was studied over FT-IR spectroscopy. The FT-IR study illustrated variations in the spectra caused by the organo-functionalization. SBA-15 shows the typical characteristic adsorption bands of the SBA-15 silica at 452,780 and 1077 cm^{-1} for Si–O–Si bending mode. Symmetric Si–O–Si stretch and asymmetric Si–O–Si stretch, respectively. The adsorption bands at 3433 cm^{-1} and 1627 cm^{-1} are consigned to the hydrated silane group and the bending vibration of surface hydroxide, respectively.[45-47]. Moreover, the peak around 955 cm^{-1} resembles to the surface Si–OH groups of SBA-15 and they could still be seen in the FT-IR spectrum of SBA-HSO_3.[38,39]. Besides, functionalized SBA-15 shows weak characteristic bands for aliphatic C–H stretching vibrations for pendant alkyl chains and bending vibrations of around 2890 cm^{-1} and weak peaks around 1441 cm^{-1} assigned to the bending vibrations of C–H bonds in aromatic ring around 2890 cm^{-1} and 1441 cm^{-1}, respectively. The SBA-HSO_3 peak at 1503cm^{-1} could be credited to the stretching of the benzene ring from chlorodiphenylphosphine wich is absent in the FT-IR spectrum of SBA-15 [39,46,47]. The bands corresponding to the S=O stretching vibrations are typically establish in the range of 1000–1400 cm^{-1} **.** Disappointingly**,** these bands cannot be clearly observed as they are hidden by the extensive and strong band at 1077 cm^{-1} due to Si–O–Si stretching.[46,48] This results specified the successful immobilization of chlorodiphenylphosphine on the surface of SBA-15.

The XRD patterns of SBA-15 and SBA-HSO_3 are shown in Figure **2** a very strong reflection at $2\theta=0.86°$ for d_{100} and two other weaker reflections at

$2\theta=1.46°$and $2\theta=1.68°$for d_{110} and d_{200} were detected in the XRD pattern of SBA-15, respectively. Related to the quasi-regular arrangement of mesopoures with hexagonal symmetry [39,40,49]. However modification produced a notable decrease in the XRD reflection intensity for SBA-15, long range ordering and a well-formed hexagonal lattice in the structure were specified. Furthermore, the intensities of all peaks reduced and shifted towards higher angle in comparison with the SBA-15, representing the introduction of substrate inside the mesoporous channels of SBA-15 [49].

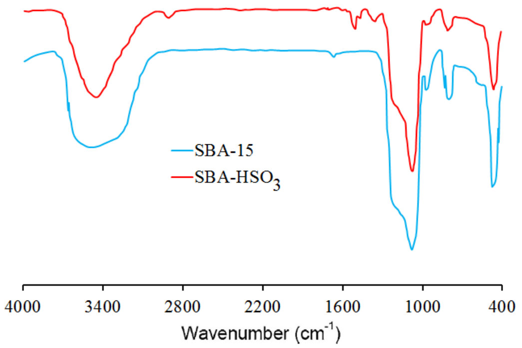


Figure 1: FT-IR spectra of the SBA-15 and SBA-HSO$_3$.

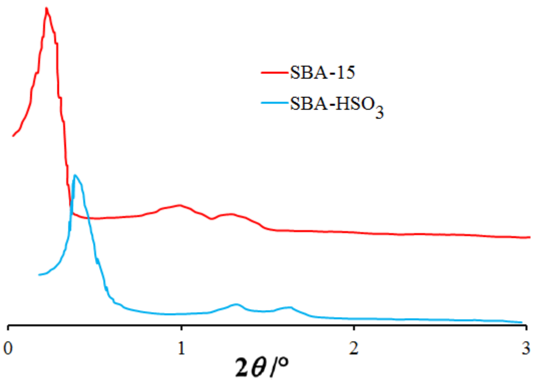


Figure 2: XRD patterns of the SBA-15 and SBA-HSO$_3$.

The SEM and TEM images are demonstrated in Figure **3**. The SEM shows that the SBA-HSO$_3$ had some aggregation of catalyst particles in spheres, and conglomerates with uneven shapes and sizes. The TEM showed that the catalyst had long-range mesopore channels of SBA-15 highly ordered long mesochannels.[38-41].

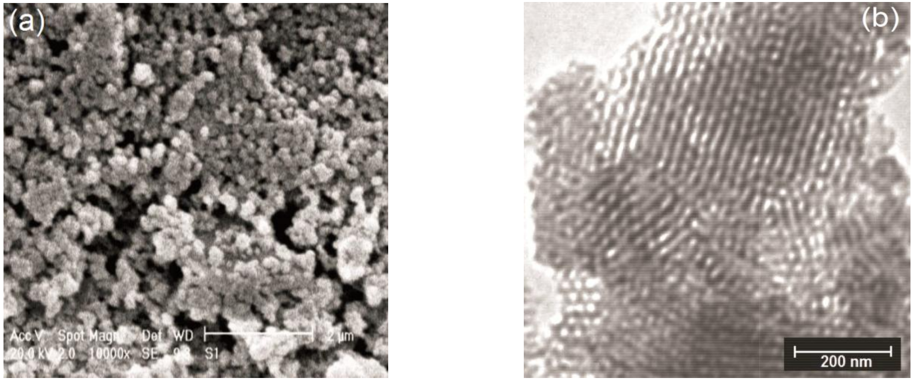


Figure 3: SEM (a) and TEM (b) of the SBA-HSO$_3$.

Catalytic activity:

Initially, the conversion of malononitrile, benzaldehyde, and 4-hydroxycoumarin to the coresponding 4H-pyrano[3,2-*c*]coumarin derivative was selected as the model substrate to determine the optimal conditions. The results are summarized in Table **1**. As can be seen from Table **1**, the best results were achieved when the reaction was performed at R.T. for 20 min (Table **1**, entry 4) with 3 mg (6 mol%) of catalyst and EtOH as solvent.

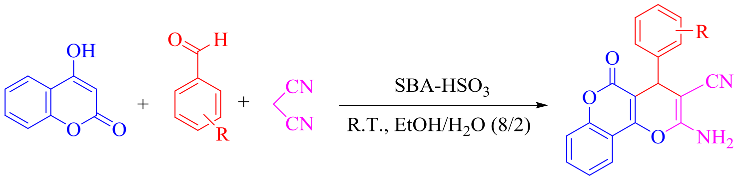
Having established the optimal conditions for the reaction, a variety of different aromatic aldehydes bearing either ED or EW substituents were subjected to react with malononitrile and 4-hydroxy-6-methylpyran-2-one to give the corresponding 4H-pyrano[3,2-*c*]coumarin derivatives in fair yields (51-86%) over short reaction time (5-80 min) as listed in Table **2**. The results clearly indicate that reactions can tolerate a wide range of differently substituted aldehydes. However, aliphatic aldehydes did not undergo pyranization even after a long reaction time and at an elevated temperature. The substituents at the aromatic ring had no obvious effect on yield or reaction time under the above optimal conditions. It is noteworthy that the methodology worked well for heterocyclic aldehydes, such as thenaldehyde (Table **2**, entry 13).

Table 1: Optimization of reaction conditions.[a]

Entry	EtOH	H_2O	Time (min)	Tield (%)[a]
1	80	20	20	85
2	60	40	60	70
3	50	50	88	68
4	40	60	100	65
5	20	80	115	60
6	-	100	130	20

[a] Isolated yield.

Table 2: Synthesis of 4H-pyrano[3,2-*c*]coumarins using SBA-HSO_3 at R.T.[a]



Entry	Aldehyde	Time (min)	Yield (%)	M.p[b]		Ref.
				Found	Reported	
1	C_6H_5CHO	20	85	237-239	236-238	[25,33-35]
2	4-Me-C_6H_4CHO	80	51	255-257	255-257	[25,33-35]
3	4-MeO-C_6H_4CHO	30	70	218-222	222-224	[25,33-35]
4	2-Cl-C_6H_4CHO	5	83	272-274	270-272	[25,33-35]
5	4-Cl-C_6H_4CHO	10	69	254-255	254-256	[25,33-35]
6	2-F-C_6H_4CHO	15	58	265-268	248-249	[25,33-35]
7	4-F-C_6H_4CHO	60	86	282-286	284-286	[25,33-35]
8	2-NO_2-C_6H_4CHO	5	78	255-257	254-256	[25,33-35]
9	3-NO_2-C_6H_4CHO	5	51	260-262	263-265	[25,33-35]
10	4-NO_2-C_6H_4CHO	5	70	272-275	263-265	[25,33-35]
11	Isonicotinaldehyde	20	70	270-272	269-270	[25,33-35]
12	Nicotinaldehyde	15	20	265-267	260-271	[25,33-35]
13	Thenaldehyde	60	70	270-272	260-262	[25,33-35]
14	1-Naphthaldehyde	4	70	247-250	262-264	[25,33-35]

[a] All products were characterized by M.p, IR and ^1H NMR spectral data and comparison with those of authentic samples or reported data.

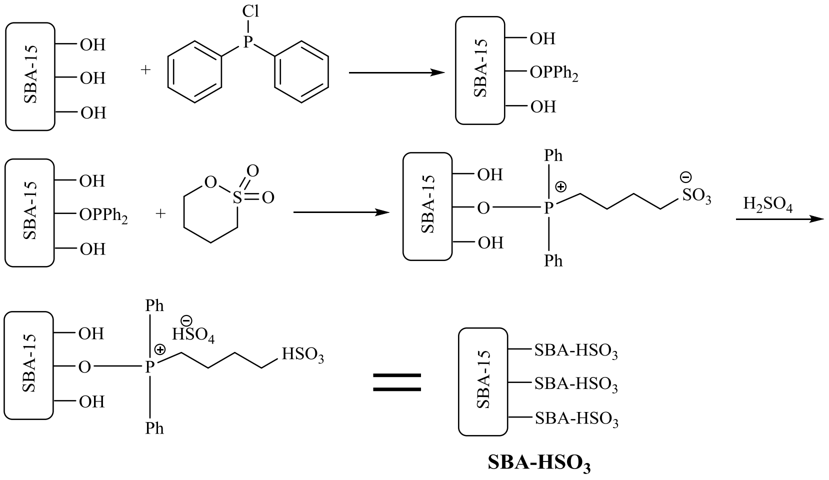
[b] Isolated yield.

Conclusion

In summary, a novel Bronsted acid was introduced and its catalytic activity was investigated for the synthesis of 4H-pyrano[3,2-*c*]coumarins by one-pot method using nano SBA-HSO_3 as a heterogeneous catalyst. The current method has the advantages of simple experimental procedure, good to high yield of products and environmentally friendly method.

Experimental

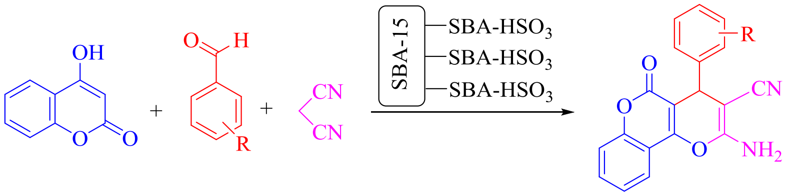
In a typical synthesis, 4 g (0.8 mmol) of $EO_{20}PO_{70}EO_{20}$ was dissolved in 150 mL of 1.6 M HCl at 35 °C. To this solution, 8.8 g (40 mmol) tetraethylorthosilicate (TEOS) was added under vigorous stirring. After stirring for several mins, the mixture was kept in static conditions at the same temperature for one day and then the white solid product was collected by filtration, washed with acetone/Et_2O (2×5 mL) and dried in an oven overnight. The resulting powders were calcined at 550 ºC for 6 h in order to obtain mesoporous silica materials. 1 g of produced SBA-15, 0.88 g (4 mmol) of chlorodiphenylphosphine and 0.54 g (4 mmol) of 1,4-butane sultone were dissolved in dry toluene (50 ml) refluxed for 36 h. The mixture was cooled down to room temperature (R.T.), the residue was washed with MeOH/acetone and then dried in an oven overnight. Finally, 1 g of resulted solid was treated with 0.5 mL of H_2SO_4 (C) and CH2Cl2 (10 mL) for 24 h. After evaporation of solvent, solid nano acid catalyst (SBA-HSO_3) was obtained.



Scheme 1: Summary of the SBA-HSO_3 preparation procedure.

General Procedure for Synthesis of 4H-pyrano[3,2-c]coumarins:

Typical experimental procedure, a mixture of 4-hydroxycoumarin (1 mmol), malononitrile (1 mmol), aldehyde (1 mmol) and catalyst (1 mol%) were stirred in EtOH (3 mL) at (R.T.) for the stipulated time. The progress of the reaction is monitored by TLC. After completion of the reaction, the reaction mixture was filtered off and the catalyst was removed. The corresponding pure solid product was obtained through recrystallized from hot EtOH affording the highly 4H-pyrano[3,2-*c*]coumarin derivatives (Scheme **2**). The physical data (M.p, IR**,** NMR) of known compounds were found to be identical with those reported in the literature.



Scheme 2: Synthesis of 4H-pyrano[3,2-*c*]coumarins.

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