

Brønsted Acidic Phosphonium Based Ionic Liquid Functionalized SBA-15 [HO₃S-PhospIL@SBA-15]: Green, Recyclable, and Efficient Catalyst for the Synthesis of Pyrano[3,2-*c*]Chromenone Derivatives

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ABSTRACT: *The surface of SBA-15 was modified by diphenylphosphine; then, it was treated with butane sultone and sulfuric acid to obtain Brønsted acid HO₃S-phosphonium based ionic liquid functionalized SBA-15 with HSO₄⁻ as a counteranion. It efficiently catalyzed synthesis of pyrano[3,2-*c*]chromenone derivatives through the reaction of 4-hydroxycoumarin and chalcones at 60 °C in water/ethanol. Good yields, mild reaction conditions, and user-friendly procedure are advantages of this method. Also, the catalyst could be easily separated and reused five times without significant reduction of activity.*

KEY WORDS: *Chalcones, Functionalized SBA-15, 4-Hydroxycoumarin, Pyrano[3,2-*c*]chromenones, Supported ionic liquid.*

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INTRODUCTION

Since the first report on the use of Ionic Liquids (ILs) as a catalyst in Friedel-Crafts acylation by *Boon et al.* [1], they have attracted lots of attention due to their remarkable catalytic properties as well as other applications such as using as a reaction medium [2]. Immobilization of the ILs on the solid supports [3] particularly Mesoporous Silica Nanoparticles (MSNs) is highly desirable for their versatile properties caused by heterogeneous support. It has been revealed that using supported IL catalysts offer different benefits such as convenient separation from reaction mixture [2] and easily use in gas-phase reaction [4].

Recently, MSNs have been the center of attention owing to well-defined pores having a narrow diameter distribution, high pore volume, silanol functionalization opportunity, and specific surface area [5]. Among the various MSNs, SBA-15 material has shown important textural properties such as large specific surface areas (above 1000 m²/g), uniform-sized pores (in range 4-30 nm), small crystallite size of primary particles, thick framework walls, and complementary textural porosity [6]. These advantages have made SBA-15 a high surface-to-volume ratio, variable framework compositions and high thermal stability support [7].

Pyranocoumarins have aroused significant interest over the past decades due to a wide variety of pharmacological properties. They are ubiquitous in a large number of natural products [8, 9] as well as synthetic derivatives possessing valuable biological properties such as anti-tuberculosis [10], antiproliferative [11], anti-HIV [12], anti-inflammatory [13], and anti-cancer [14]. Among various pyranocoumarins structural space, pyrano[3,2-*c*]chromenone derivatives have occupied a position of major importance because of their widespread presence in biological active natural products [15]. At this juncture, the development of a facile, mild, inexpensive, green and high yield approaches to access these compounds is much desirable.

By the report of Moreau et al. on the synthesis of pyrano[3,2-*c*]chromenone through the reaction of 4-hydroxycoumarin derivatives and suitable electrophiles [16], various researchers have focused on the above mentioned reaction particularly the reaction of 4-hydroxycoumarin and various chlcones in different conditions using various catalyst (Scheme 1) [17-21]. Herein, we disclose

a green and high yielding synthetic protocol for the synthesis of pyrano[3,2-*c*]chromenones using [HO₃S-PhospIL@SBA-15] as a recyclable and environmentally benign catalyst.

EXPERIMENTAL SECTION

All reagents were purchased from Merck and Aldrich and used without further purification. Melting points were taken on a Kofler hot stage apparatus and are uncorrected. ¹H NMR spectra were recorded on Bruker FT-400 using TMS as an internal standard.

Synthesis of ordered mesoporous SBA-15 silica

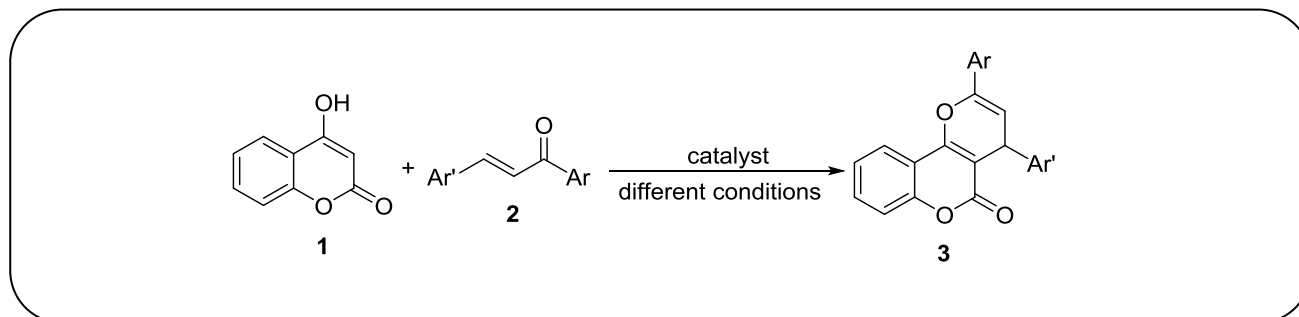
2D hexagonal SBA-15 was synthesized according to [22]. Pluronic P123 (13.9 g) was dissolved in distilled water (252 g) and concentrated HCl (7.7 g). After complete dissolution, TEOS (25.0 g) was added at once. The mixture was left under stirring at 35 °C for 24 h, followed by hydrothermal treatment at 100 °C for 48 h under static conditions. For template removal, the as-synthesized silica powders were first shortly slurried in a mixture of ethanol-HCl and subsequently calcined at 550 °C for 2 hours.

Synthesis of phosphine functionalized SBA-15

It was synthesized according to [23]. SBA-15 (1 g) and triethylamine (4 mmol) were added to a solution of chlorodiphenylphosphine (4 mmol) in dry CH₂Cl₂ (100 mL). The mixture was stirred under argon atmosphere for 24 h at room temperature, separated by filtration or centrifuge, washed with CH₂Cl₂ (3×10 ml), and dried under vacuum at 60 °C for 12 h.

Synthesis of Bronsted acidic phosphonium ionic liquid functionalized SBA-15 [HO₃S-phosphonium based IL@SBA-15]

A solution of phosphine functionalized SBA-15 (1 g) and 1,4-propane sultone (4 mmol) in toluene (50 mL) was refluxed overnight. The obtained solid was separated by filtration, washed potently with methanol and acetone to remove the unreacted 1,4-propane sultone, and dried in vacuum. Concentrated H₂SO₄ (3 mmol) was added to a solution of the later obtained solid (1 g) in dry EtOH and heated at 70°C for 24 h. The acidic phosphonium based IL supported SBA-15 was filtered, purified (by Soxhlet with toluene) to remove the unsupported residues, and



Scheme 1: Synthesis of pyrano[3,2-c]chromenone derivatives 3 [17-21].

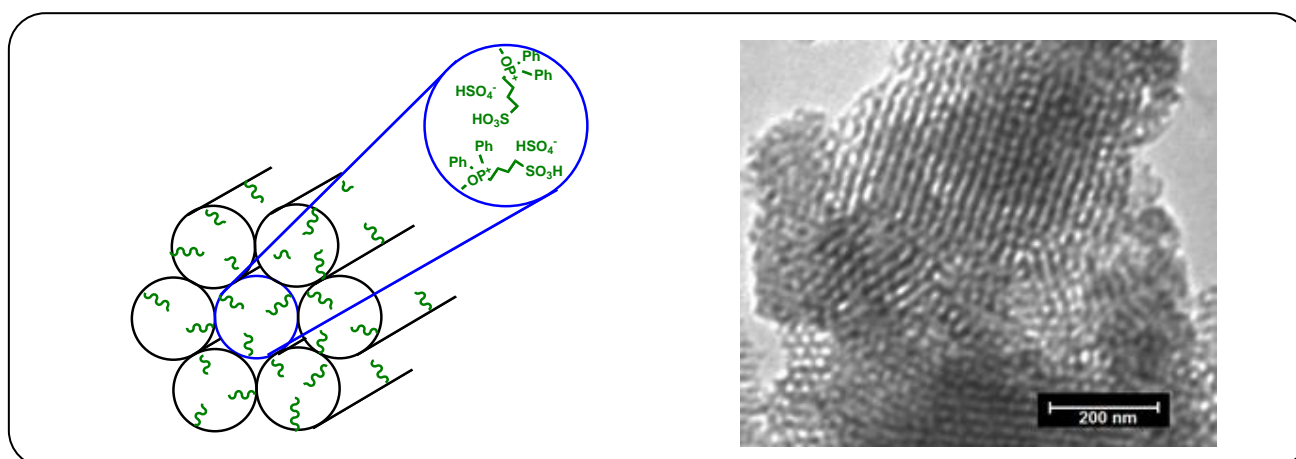


Fig. 1: Bronsted acidic phosphonium ionic liquid functionalized SBA-15 [HO₃S-phosphonium based IL@SBA-15].

dried in vacuum [24]. TEM image and the structure of the catalyst were shown in Fig. 1.

pH-analysis of [HO₃S-PhospIL@SBA-15]

The [HO₃S-PhospIL@SBA-15] (50 mg) was added to an aqueous solution of NaCl (1 M, 25 mL) with an initial pH 5.93. The mixture was stirred for 3 h when the pH was adjusted to ~1.0 indicating that 1.97 mmol SO₃H g⁻¹ has been loaded. It should be noted that this fact was confirmed by back-titration analysis of the catalyst with 0.1 M NaOH (aq) as titration agent.

General procedure for the synthesis of pyrano[3,2-c]chromenone derivatives 3

A mixture of 4-hydroxycoumarin (1 mmol), chalcone derivative (1 mmol), and [HO₃S-PhospIL@SBA-15] (3 mg, 0.6 mol%) in H₂O/EtOH (1 mL, 1:1) was stirred at 60 °C. After completion of reaction (checked by TLC), the mixture was filtered off, washed with boiling EtOH,

and allowed to be recrystallized. All compounds were known and their physical data were found to be identical compared with those of reported in the literature.

2,4-Diphenyl-4H-pyrano[3,2-c]chromen-5-one (3a)

¹H NMR (400 MHz, CDCl₃): δ 8.15 (m, 1H), 7.70-7.68 (m, 2H), 7.50-7.48 (m, 1H), 7.41-7.32 (m, 9H), 7.20-7.18 (m, 1H), 5.81 (d, *J* = 4.7 Hz, 1H), 4.69 (d, *J* = 5.3 Hz, 1H).

RESULTS AND DISCUSSION

In continuation of our ongoing program on the design and synthesis of proficient catalysts [25, 26] and novel heterocycles specially chromenes [27, 28]; herein, we have developed a user-friendly, high yield, and economically and environmentally benign procedure for the synthesis of pyrano[3,2-c]chromenones using [HO₃S-PhospIL@SBA-15].

Table 1: Optimization of the reaction conditions.^a

Entry	Solvent	Temperature (°C)	Amount of catalyst (mg)	Time (h)	Yield (%) ^b
1	H ₂ O	rt	4	24	NR
2	H ₂ O	reflux	4	12	NR
3	EtOH	rt	3	12	50
4	EtOH	reflux	3	12	70
5	H ₂ O/EtOH (1:1)	rt	3	12	75
6	H ₂ O/EtOH (1:1)	60	3	8	95
7	H ₂ O/EtOH (1:1)	60	5	8	95
8	CH ₃ CN	reflux	3	8	50
9	PhMe	reflux	3	8	trace
10	CH ₂ Cl ₂	reflux	3	8	32

a) Carried out with 4-hydroxycoumarin (1 mmol) and chalcone (1 mmol) in the presence of [HO₃S-PhospIL@SBA-15].

b) Isolated yields.

Table 2: Reusability of [HO₃S-PhospIL@SBA-15 for the synthesis of 3a .a

Entry	Yield (%) ^b
1	95
2	93
3	90
4	85
5	85
6	70

a) Reaction of 4-hydroxycoumarin (1 mmol) and chalcone (1 mmol) under the optimized conditions.

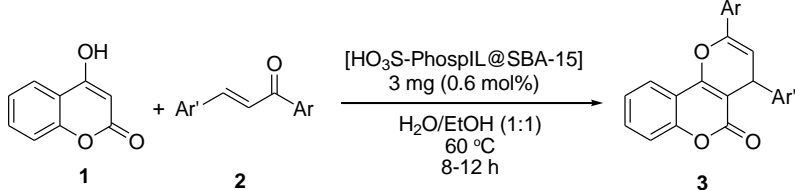
b) Isolated yields.

In this context, we prepared SBA-15 material according to [22]. Subsequently, its surface was modified through the reaction of the corresponding silica and chlorodiphenylphosphine in the presence of triethylamine in dry dichloromethane. The later compound was refluxed with a toluene solution of butane sultone leading to the formation of the heterogenized zwitterion. To obtain the desired HO₃S-Phosphonium based ionic liquid functionalized SBA-15, it was treated with concentrated H₂SO₄. Then, the acid content of catalyst was evaluated using 1 M NaCl (aq) and back-titration analysis of the catalyst with 0.1 M NaOH (aq). It was found that 1.97 mmol SO₃H g⁻¹ was loaded.

Next, we focused on the reaction of 4-hydroxycoumarin **1** and various chalcones **2** (Scheme 1). For this purpose, we selected the reaction of

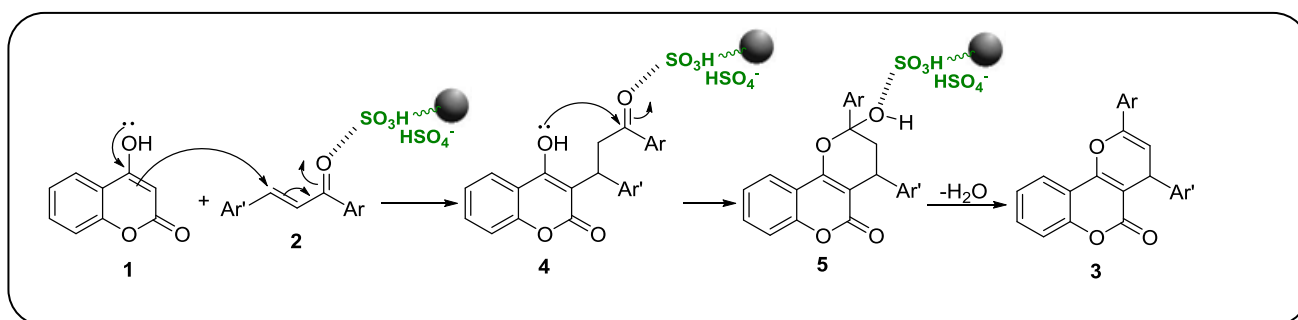
4-hydroxycoumarin **1** and chalcone **2a** as a model reaction to obtain the best reaction conditions. For the accurate screening, the model reaction was conducted in various solvents and temperature in the presence of different amount of catalyst. Some results are summarized in Table 1. As can be seen in Table 1, the best result was obtained in H₂O/EtOH (1:1) at 60 °C in the presence of 3 mg catalyst (0.6 mol%). Under the optimized conditions, the related product **3a** was obtained in 95% yield.

At the end of the reaction, the catalyst was filtered, washed with hot diethyl ether, dried at 50 °C under vacuum for 1 h, and reused in another reaction. It is worth to mention that the catalyst could be used for five times without an important change in its *activity* (Table 2). Also, the acid content of catalyst was evaluated after reaction (as described before) and no change was observed.

Table 3: Synthesis of pyrano[3,2-*c*]chromenone derivatives 3.


Entry	Ar	Ar'	Product 3	Yield (%) ^a	mp (°C)	
					Observed	Reported
1	Ph	Ph	3a	95	171-173	168-170 [19]
2	Ph	4-OMe-C ₆ H ₄	3b	92	182-184	180-181 [17]
3	4-NO ₂ -C ₆ H ₄	4-Me-C ₆ H ₄	3c	90	230-231	235-237 [19]
4	Ph	4-Cl-C ₆ H ₄	3d	89	182-183	185-186 [21]
5	4-Cl-C ₆ H ₄	4-Cl-C ₆ H ₄	3e	87	242-245	239-241 [20]
6	4-Cl-C ₆ H ₄	4-OMe-C ₆ H ₄	3f	87	219-220	220-221 [17]
7	4-Cl-C ₆ H ₄	Ph	3g	90	189-191	185-186 [21]
8	4-OMe-C ₆ H ₄	Ph	3h	90	155-157	156-157 [17]
9	4-OMe-C ₆ H ₄	4-OMe-C ₆ H ₄	3i	89	112-114	119-120 [17]
10	4-OMe-C ₆ H ₄	4-Cl-C ₆ H ₄	3j	92	160-162	156-157 [17]

a) Isolated yields

Scheme 2: Proposed mechanism for the formation of pyrano[3,2-*c*]chromenone 3.

With these results in hand, we investigated the scope of our reaction utilizing a variety of chalcones bearing different substituents on the aromatic ring (Table 3). It was found that chalcones possessing electron-donating as well as electron-withdrawing substituents afforded high yields of products 3.

A proposed mechanism is depicted in Scheme 2. Probably, the Michael addition of 4-hydroxycoumarin 1 to activated chalcone derivative 2 leads to the formation of intermediate 4 which tolerates intramolecular cyclization (formation of 5) and removal of H₂O to give the title compounds 3. It is clear that all steps including

increasing the electrophilicity of the carbonyl groups in 2 and 4 as well as removal of H₂O are catalyzed by the acidic catalyst.

CONCLUSIONS

In conclusion, various pyrano[3,2-*c*]chromenone derivatives were prepared through the reaction of 4-hydroxycoumarin and different chalcones in the presence of green, recyclable, and efficient [HO₃S-PhospIL@SBA-15] in H₂O/EtOH at 60 °C. The important advantages offered by this protocol are high yields of products, user-friendly procedure including

simple isolation and purification of the products, using environmentally friendly solvent and recyclability of catalyst. It should be noted that the catalyst could be easily separated and reused five times without significant reduction in activity.

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