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One-pot synthesis of dihydropyrano[c]chromene derivatives by using $\text{BF}_3 \cdot \text{SiO}_2$ as catalyst

Abstract: Silica-supported boron trifluoride ($\text{BF}_3 \cdot \text{SiO}_2$) is an efficient, readily available, and reusable catalyst for the synthesis of 2-amino-5-oxo-4-aryl-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile or carboxylic acid ethyl ester derivatives by condensation of 4-hydroxycoumarin, an aldehyde, and an alkyl nitrile.

Keywords: aldehyde; alkyl nitriles; $\text{BF}_3 \cdot \text{SiO}_2$; 4-hydroxycoumarin; pyrano[3,2-*c*]chromene.

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Introduction

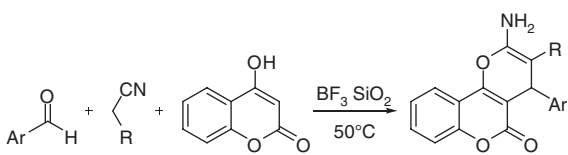
Silica-supported boron trifluoride, $\text{BF}_3 \cdot \text{SiO}_2$, is easy to prepare, shows unusually high Brønsted acidity that can be controlled by activation temperature, and exhibits considerable catalytic activity [1]. $\text{BF}_3 \cdot \text{SiO}_2$ is a solid super acid [2]. It is used as a catalyst in several organic transformations, such as Claisen-Schmidt condensations [3], synthesis of 14-substituted 14*H*-dibenzo[*a,j*]xanthenes [4] and 1,2,4,5-tetrasubstituted imidazoles [5], polymerization of styrene [6], and the preparation of polyfunctionalized piperidin-4-ones [7], α -amino phosphonates [8], quinoxalines [9], and 3,4-dihydropyrimidin-2(1*H*)-ones [10].

Pyrans constitute one of the major classes of naturally occurring compounds [11–15]. Pyran derivatives exhibit biological activities, can be photochromic [16–20], and can be used as intermediates for the synthesis of various compounds, including pyranopyridines [21], polyazanaphthalenes [22], pyrano[2]pyrimidines [23], and pyridin-2-ones [24]. Recently, several methods have been reported for the synthesis of 2-amino-5-oxo-dihydropyrano[3,2-*c*]chromene derivatives through a three-component condensation of 4-hydroxycoumarin with aldehydes and alkyl nitriles. This reaction can be catalyzed by a variety of catalysts [25–37].

Results and discussion

We report that $\text{BF}_3 \cdot \text{SiO}_2$ is an efficient and reusable catalyst for the synthesis of 2-amino-5-oxo-4-aryl-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile or carboxylic acid ethyl ester derivatives (Table 1). The reaction of 4-hydroxycoumarin (2 mmol) with 4-nitrobenzaldehyde (2.1 mmol) and malononitrile (2.1 mmol) was investigated for optimization of the reaction conditions (Table 1, entry 3). The optimized conditions are given in Experimental section. It should be noted that the best results were obtained in the absence of any solvent. The reusability of the $\text{BF}_3 \cdot \text{SiO}_2$ catalyst was also examined. After each run, the reaction mixture was cooled to room temperature, and the catalyst

Table 1 Synthesis of 2-amino-5-oxo-4-aryl-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile or carboxylic acid ethyl ester derivatives in the presence of $\text{BF}_3 \cdot \text{SiO}_2$.



Entry	Ar	R	Yield (%) / mp (°C); this work	Yield (%) / mp (°C); reported [ref.]
1	4-F-C ₆ H ₄	CN	93/260–261	96/260–262 [26]
2	2,3-Cl ₂ -C ₆ H ₃	CN	92/281–282	90/280–282 [25]
3	4-O ₂ N-C ₆ H ₄	CN	95/177–178	85/177–178 [35]
4	3-O ₂ N-C ₆ H ₄	CN	95/257–258	84/257–258 [34]
5	3-Cl-C ₆ H ₄	CN	94/247–248	86/246–248 [26]
6	4-MeO-C ₆ H ₄	CN	93/220–222	78/220–222 [34]
7	4-Cl-C ₆ H ₄	CN	92/257–259	88/256–258 [30]
8	4-Br-C ₆ H ₄	CN	93/247–248	80/247–249 [26]
9	2-Cl-C ₆ H ₄	CN	90/263–264	80/262–264 [35]
10	2-Me-C ₆ H ₄	CN	88/264–265	87/264–266 [26]
11	2,4-Cl ₂ -C ₆ H ₃	CN	90/257–258	86/255–257 [25]
12	4-Me-C ₆ H ₄	CN	89/219–220	80/219–220 [35]
13	2-Me-C ₆ H ₄	CN	88/264–265	87/264–266 [26]
14	C ₆ H ₅	CN	90/253–254	10/253–255 [34]
15	4-Cl-C ₆ H ₄	COOEt	90/192–194	89/192–194 [27]
16	3-O ₂ N-C ₆ H ₄	COOEt	91/248–250	90/247–250 [25]
17	4-O ₂ N-C ₆ H ₄	COOEt	91/240–242	91/241–243 [27]

See Experimental for conditions.

was separated from the organic product by treatment with chloroform. It was shown that the catalyst could be reused many times, although a gradual decline in activity was observed.

Conclusions

The preparation of 2-amino-5-oxo-4-aryl-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile or carboxylic acid ethyl ester derivatives by the reaction of 4-hydroxycoumarin, an aldehyde, and an alkyl nitrile is efficiently catalyzed by $\text{BF}_3 \cdot \text{SiO}_2$. In contrast to many other acidic catalysts, this reagent does not need special precautions for handling or storage.

Experimental

General

The catalyst $\text{BF}_3 \cdot \text{SiO}_2$ was prepared as previously reported [1, 2]. Products were characterized by IR and ^1H NMR spectroscopy and by

comparison of their melting points with the literature values. Melting points were determined on a Buchi melting point B-540 B.V.CHI apparatus.

General procedure for the synthesis of compounds shown in Table 1

A mixture of 4-hydroxycoumarin (2 mmol), an aldehyde (2.1 mmol), an alkyl nitrile (2.1 mmol), and $\text{BF}_3 \cdot \text{SiO}_2$ (0.6 g, 25 mol%) was heated at 50°C. The progress of the reaction was monitored by TLC. After completion of the reaction, 15–25 min, the mixture was extracted with chloroform and filtered to recover the catalyst. The chloroform extract was concentrated and the residue was crystallized from isopropanol to afford the 2-amino-5-oxo-4-aryl-4*H*,5*H*-pyrano[3,2-*c*]chromene-3-carbonitrile or carboxylic acid ethyl ester derivative.

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