

Ali Akbari*

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.

*Corresponding author: Ali Akbari, Department of Chemistry, Faculty of Science, University of Jiroft, P.O. Box 7867161167, Jiroft, Iran, e-mail: a.akbari@ujiroft.ac.ir

Introduction

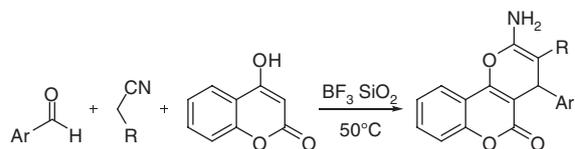
Silica-supported boron trifluoride, $\text{BF}_3 \cdot \text{SiO}_2$, is easy to prepare, shows unusually high Brønsted acidity that can be controlled by activation temperature, and exhibits considerable catalytic activity [1]. $\text{BF}_3 \cdot \text{SiO}_2$ is a solid super acid [2]. It is used as 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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References

- [1] Wilson, K.; Clark, J. H. Synthesis of a novel supported solid acid BF_3 catalyst. *Chem. Commun.* **1998**, 2135–2136.
- [2] Klapotke, T. M.; Mc Monagle, F.; Spence, R. R.; Winfield, J. M. γ -Alumina-supported boron trifluoride: catalysis, radiotracer studies and computations. *J. Fluorine Chem.* **2006**, *127*, 1446–1453.
- [3] Sadegi, B.; Mirjalili, B. F.; Hashemi, M. M. $\text{BF}_3 \cdot \text{SiO}_2$: an efficient reagent system for the one-pot synthesis of 1,2,4,5-tetrasubstituted imidazoles. *Tetrahedron Lett.* **2008**, *49*, 2575–2577.
- [4] Mirjalili, B. F.; Bamoniri, A.; Akbari, A. $\text{BF}_3 \cdot \text{SiO}_2$: an efficient alternative for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes. *Tetrahedron Lett.* **2008**, *49*, 6454–6456.
- [5] Sadegi, B.; Mirjalili, B. F.; Hashememi, M. M. $\text{BF}_3 \cdot \text{SiO}_2$: an efficient heterogeneous alternative for regio-chemo and stereoselective Claisen-Schmidt condensation. *J. Iran. Chem. Soc.* **2008**, *5*, 694–698.
- [6] Boodhoo, K. V. K.; Dunk, W. A. E.; Vicevic, M.; Jachuck, R. J.; Sage, V.; Macquarrie, D. J.; Clark, J. H. Classical cationic polymerisation of styrene in a spinning disc reactor using silica supported BF_3 catalyst. *J. Appl. Polym. Sci.* **2006**, *101*, 8–19.
- [7] Dindulkar, S. D.; Parthiban P.; Jeong, Y. T. $\text{BF}_3 \cdot \text{SiO}_2$ is a simple and efficient Lewis acid catalyst for the one-pot synthesis of polyfunctionalized piperidin-4-ones. *Monatsh Chem.* **2012**, *143*, 113–118.
- [8] Reddy, M. V.; Dindulkar, S. D.; Jeong, Y. T. $\text{BF}_3 \cdot \text{SiO}_2$ -catalyzed one-pot synthesis of α -aminophosphonates in ionic liquid and neat conditions. *Tetrahedron Lett.* **2011**, *52*, 4764–4767.
- [9] Mirjalili, B. F.; Bamoniri, A.; Akbari, A. Nano- $\text{BF}_3 \cdot \text{SiO}_2$: a reusable and eco-friendly catalyst for synthesis of quinoxalines. *Chem. Heterocycl. Comp.* **2011**, *47*, 487–491.
- [10] Mirjalili, B. F.; Bamoniri, A.; Akbari, A. One-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones (thiones) promoted by nano- $\text{BF}_3 \cdot \text{SiO}_2$. *J. Iran. Chem. Soc.* **2011**, *8*, 135–140.
- [11] Tang, Y.; Oppenheimer, J.; Song, Z.; You, L.; Zhang, X.; Hsung, R. P. Strategies and approaches for constructing 1-oxadecalins. *Tetrahedron* **2006**, *62*, 10785–10813.
- [12] McKee, T. C.; Fuller, R. W.; Covington, C. D.; Cardellina, J. H., II; Gulakowski, R. J.; Krepps, B. L.; McMahon, J. B.; Boyd, M. R. New pyranocoumarins isolated from calophyllum lanigerum and calophyllum teysmannii. *J. Nat. Prod.* **1996**, *59*, 754–758.
- [13] McKee, T. C.; Covington, C. D.; Fuller, R. W.; Bokesch, H. R.; Young, S.; Cardellina, J. H., II; Kadushin, M. R.; Soejarto, D. D.; Stevens, P. F.; Cragg, G. M.; et al. Pyranocoumarins from tropical species of the genus *Calophyllum*: a chemotaxonomic study of extracts in the national cancer institute collection. *J. Nat. Prod.* **1998**, *61*, 1252–1256.
- [14] Wu, S.-J.; Chen, I.-S. Alkaloids from *Zanthoxylum simulans*. *Phytochemistry* **1993**, *34*, 1659–1661.
- [15] Jung, E. J.; Park, B. H.; Lee, Y. R. Environmentally benign, one-pot synthesis of pyrans by domino Knoevenagel/6 π -electrocyclization in water and application to natural products. *Green Chem.* **2010**, *12*, 2003–2011.

- [16] Kumar, S.; Hernandez, D.; Hoa, B.; Lee, Y.; Yang, J. S.; McCurdy, A. Synthesis, photochromic properties, and light-controlled metal complexation of a naphthopyran derivative. *Org. Lett.* **2008**, *10*, 3761–3764.
- [17] Rawat, M.; Prutyranov, V.; Wulff, W. D. Chromene chromium carbene complexes in the syntheses of naphthopyran and naphthopyrandione units present in photochromic materials and biologically active natural products. *J. Am. Chem. Soc.* **2006**, *128*, 11044–11053.
- [18] Fedorova, O. A.; Maure, F.; Chebunkova, A. V.; Strokach, Y. P.; Valova, T. M.; Kuzmina, L. G.; Howard, J. A. K.; Wenzel, M.; Gloe, K.; Lokshin, V.; et al. Investigation of cation complexation behavior of azacrown ether substituted benzochromene. *J. Phys. Org. Chem.* **2007**, *20*, 469–483.
- [19] Hepworth, J. D.; Heron, B. M. Chapter 2 Synthesis and photochromic properties of naphthopyrans. *Prog. Heterocycl. Chem.* **2005**, *17*, 33–62.
- [20] Delbaer, S.; Micheau, J.-C.; Vermeersch, G. NMR kinetic investigations of the photochemical and thermal reactions of a photochromic chromene. *J. Org. Chem.* **2003**, *68*, 8968–8973.
- [21] Ren, Q.; Siau, W.-Y.; Du, Z.; Zhang, K.; Wang, J. Expedient assembly of a 2-amino-4H-chromene skeleton by using an enantioselective Mannich intramolecular ring cyclization-tautomerization cascade sequence. *Chem. Eur. J.* **2011**, *17*, 7781–7785.
- [22] Abdel-Fattah, A. H.; Hesien, A. M.; Metwally, S. A.; Elnagdi, M. H. The reaction of ethyl 6-amino-5-cyano-4-aryl-2-methyl-4H-pyran-3-carboxylate with nucleophilic reagents. *Liebigs Ann. Chem.* **1989**, 585–588.
- [23] Quintela, J. M.; Peinador, C.; Moreira, M. J. A novel synthesis of pyrano[2,3-d]pyrimidine derivatives. *Tetrahedron* **1995**, *51*, 5901–5912.
- [24] Srivastava, S.; Batra, S.; Bhaduri, A. P. A facile acid-catalyzed ring transformation of 4H-pyrans to 1,2,3,4-tetrahydropyridin-2-ones and 3,4-dihydronaphtho[1,2-b]pyran-2(H)-ones. *Indian J. Chem. Sect. B* **1996**, *35B*, 602–604.
- [25] Heravi, M. M.; Alimadadi Jani, B.; Derikvand, F.; Bamoharram, F. F.; Oskooie, H. A. Three component, one-pot synthesis of dihydropyrano[3,2-c]chromene derivatives in the presence of $H_6P_2W_{18}O_{62} \cdot 18H_2O$ as a green and recyclable catalyst. *Catal. Commun.* **2008**, *10*, 272–275.
- [26] Mehrabi, H.; Abusaidi, H. Synthesis of biscoumarin and 3,4-dihydropyrano[c]chromene derivatives catalysed by sodium dodecyl sulfate (SDS) in neat water. *J. Iran. Chem. Soc.* **2010**, *7*, 890–894.
- [27] Khurana, J. M.; Nand, B.; Saluja, P. DBU: a highly efficient catalyst for one-pot synthesis of substituted 3,4-dihydropyrano[3,2-c]chromenes, dihydropyrano[4,3-b]pyranes, 2-amino-4H-benzo[H]chromenes and 2-amino-4H-benzo[G]chromenes in aqueous medium. *Tetrahedron* **2010**, *66*, 5637–5641.
- [28] Khurana, J. M.; Kumar, S. Tetrabutylammonium bromide (TBAB): a neutral and efficient catalyst for the synthesis of biscoumarin and 3,4-dihydropyrano[c]chromene derivatives in water and solvent-free conditions. *Tetrahedron Lett.* **2009**, *50*, 4125–4127.
- [29] Shaterian, H. R.; Oveisi, A. R. A simple green approach to the synthesis of 2-amino-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile derivatives catalyzed by 3-hydroxypropanaminium acetate (HPAA) as a new ionic liquid. *J. Iran. Chem. Soc.* **2011**, *8*, 545–552.
- [30] Mohammadi Ziarani, G.; Badiei, A.; Azizi, M.; Zarabadi, P. Synthesis of 3,4-dihydropyrano[c]chromene derivatives using sulfonic acid functionalized silica (SiO_2PrSO_3H). *Iran. J. Chem. Chem. Eng.* **2011**, *30*, 59–65.
- [31] Ghorbani-Vaghei, R.; Toghræi-Semiromi, Z.; Karimi-Nami, R. One-pot synthesis of 4H-chromene and dihydropyrano[3,2-c]chromene derivatives in hydroalcoholic media. *J. Braz. Chem. Soc.* **2011**, *5*, 905–909.
- [32] Zheng, J.; Li, Y.-Q. One-pot synthesis of tetrahydrobenzo[b]pyran and dihydropyrano[c]chromene derivatives in aqueous media by using trisodium citrate as a green catalyst. *Arch. Appl. Sci. Res.* **2011**, *3*, 381–388.
- [33] Alizadeh, A.; Khodaei, M. M.; Beygzadeh, M.; Kordestani, D.; Feyzi, M. Biguanide-functionalized Fe_3O_4/SiO_2 magnetic nanoparticles: an efficient heterogeneous organosuperbase catalyst for various organic transformations in aqueous media. *Bull. Korean Chem. Soc.* **2012**, *33*, 2547–2580.
- [34] Khoobi, M.; Ma'mani, L.; Rezazadeh, F.; Zareie, Z.; Foroumadi, A.; Ramazani, A.; Shafiee, A. One-pot synthesis of 4H-benzo[b]pyrans and dihydropyrano[c]chromenes using inorganic-organic hybrid magnetic nanocatalyst in water. *J. Mol. Catal. A: Chem.* **2012**, *359*, 74–80.
- [35] Tabatabaieian, K.; Heidari, H.; Mamaghani M.; Mahmoodi, N. O. Ru(II) complexes bearing tertiary phosphine ligands: a novel and efficient homogeneous catalyst for one-pot synthesis of dihydropyrano[3,2-c]chromene and tetrahydrobenzo[b]pyran derivatives. *Appl. Organomet. Chem.* **2012**, *26*, 56–61.
- [36] Niknam, K.; Jamali, A. Silica-bonded *n*-propylpiperazine sodium *n*-propionate as recyclable basic catalyst for synthesis of 3,4-dihydropyrano[c]chromene derivatives and biscoumarins. *Chin. J. Catal.* **2012**, *33*, 1840–1849.
- [37] Shaterian, H. R.; Arman, M.; Rigi, F. Domino Knoevenagel condensation, Michael addition, and cyclization using ionic liquid, 2-hydroxyethylammonium formate, as a recoverable catalyst. *J. Mol. Liq.* **2011**, *158*, 145–150.