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Silica-Supported Yttrium Nitrate Hexahydrate as a Heterogeneous Catalyst for the Synthesis of 2-Amino-4*H*-Chromenes in Water

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ABSTRACT

Silica-supported yttrium nitrate hexahydrate ($Y(NO_3)_3.6H_2O/SiO_2$) has been found to be an efficient and reusable catalyst for the synthesis of 2-amino-4*H*-chromenes *via* a one-pot aqueous three-component reaction between arylaldehydes, malononitrile and β-naphthol in high yields. This method has many appealing attributes such as excellent yields, short reactions time, reusability of the catalyst and simple work-up procedure.

KEYWORDS

Silica-supported yttrium nitrate hexahydrate, 2-amino-4*H*-chromene, malononitrile, arylaldehyde, β-naphthol.

Introduction

Heterogeneous supported catalysts have been used in various organic transformations since they possess a number of advantages.[1–5] Immobilization of catalysts on a solid support improves their available active site, stability, product separation and recovery, which are all factors important in industry.[6] Therefore, use of supported and reusable catalysts in organic transformations has economical and environmental benefits. Although supported catalysts are available on different supports including charcoal, alumina, silica and polymer, silica has many other advantages such as no swelling, good mechanical and thermal stability and ease of scalability.[7] Silica-supported yttrium nitrate hexahydrate is a reusable silica-supported catalyst that is a stable solid with elevated Lewis acid characteristics.[8] This inexpensive and reusable catalyst can be easily handled and separated from the reaction mixture, which contributes to make reactions cleaner, faster and higher yielding.

Chromene derivatives are very important heterocyclic compounds due to the fact that many are key core elements of various natural and biologically active molecules including anticancer, antibacterial and antiviral agents.[9,10] Many chromenes are also photoactive and can be used in various photo-induced reactions, affording diverse heterocyclic compounds.[11] The development of new and convenient synthetic approaches to these scaffolds is therefore of great interest to the medicinal chemistry community.[12–15]

Organic reactions in aqueous media have attracted much attention in synthetic organic chemistry, not only because water is one of the most abundant, cheap and environmentally friendly solvents, but also because water exhibits unique reactivity and selectivity, properties that are different from those of conventional organic solvents. Therefore, organic reactions in water has become highly desirable in recent years to meet environmental considerations.[16,17]

In continuation of our recent works on application of solid acid in the synthesis of heterocyclic compounds,[18–21] we wish to report a new methodology for the synthesis of 2-amino-4*H*-chromenes (**4**) *via* the reaction between aromatic aldehydes (**1**), malononitrile (**2**), and *β*-naphthol (**3**) using $Y(NO_3)_3.6H_2O/SiO_2$ as an efficient heterogeneous catalyst (Scheme 1).

2. Results and Discussion

In our preliminary experiments to optimize the reaction conditions, a model reaction between benzaldeyde (1 mmol), malononitrile (1 mmol) and *β*-naphthol (1 mmol) was carried out in the presence of various amounts of $Y(NO_3)_3.6H_2O$ under different conditions. In all cases the reaction proceeded sluggishly with a very small amount of the catalyst being recovered with difficultly. Increasing the amount of catalyst and reaction time did not have a marked influence on the product yield or reaction rate. These results prompted us to focus our attention on the model reaction using heterogeneously supported $Y(NO_3)_3.6H_2O$ on silicagel. In order to optimize the reaction conditions, a model reaction was carried out in the presence of various amounts of $Y(NO_3)_3.6H_2O/SiO_2$ and a wide range of temperatures (Table 1). The reaction was found to be efficiently carried out by adding 0.24 g (6.5 mol %) of the $Y(NO_3)_3.6H_2O/SiO_2$ under aqueous reflux. In view of our eco-friendly procedure, the recovery and reuse of the catalyst is of paramount importance. The recovered

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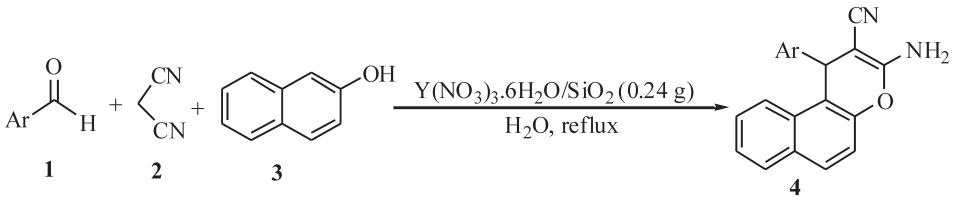


Scheme 1

$Y(NO_3)_3.6H_2O/SiO_2$-catalyzed synthesis of 2-amino-4*H*-chromenes in water.

Table 1 Optimization of reaction conditions for the one-pot preparation of **4a**.

Entry	Solvent	Catalyst loading/g	Temp./°C	Time/h	Yield/% [a]
1	None	None	80–100	24	5
2	None	0.1	90–100	4	70
3	None	0.15	90–100	4	75
4	None	0.2	90–100	4.5	80
5	None	0.24	90–100	3	80
6	None	0.3	90–100	4	65
7	EtOH	0.24	70–80	3.5	90
8	MeOH	0.24	70–80	3.5	80
9	Toluene	0.24	90–100	5.2	85
10	H_2O	0.24	100	3	90
11	CH_3CN	0.24	60–70	5	70
12	H_2O	0.30	100	3.5	85
13	H_2O	0.40	100	3.5	80

[a] Isolated yields.

Table 2 $Y(NO_3)_3.6H_2O/SiO_2$-catalyzed synthesis of 2-amino-4*H*-chromenes.

Product	Ar	Time/h	Yield/% [a]	m.p./°C Found (reported)
4a	Ph	3	90	273–274 (278–279) [22]
4b	3-MeC_6H_4	4	90	230–232 (230–232) [22]
4c	4-MeC_6H_4	4	85	260–263 (268–270) [23]
4d	4-OHC_6H_4	3	95	270–272 (272–274) [24]
4e	2-ClC_6H_4	3	94	231–233 (231–233) [25]
4f	4-ClC_6H_4	3	90	205–206 (210–215) [23]
4g	3-CNC_6H_4	1.5	90	238–240 [b]
4h	2-$NO_2C_6H_4$	2.5	85	238–240 (237–239) [25]
4i	3-$NO_2C_6H_4$	2	80	232–235 [b]
4j	4-$NO_2C_6H_4$	2.5	75	236–239 [b]
4k	2-BrC_6H_4	3.5	86	181–183 (181–183) [22]
4l	4-BrC_6H_4	2	80	220–221 (241–243) [25]
4m	3-$OMeC_6H_4$	5	75	248–250 (256–258) [25]
4n	4-$OMeC_6H_4$	4	85	185–187 (199–201) [25]
4o	3-FC_6H_4	3	70	276–278 (276–278) [22]

[a] Refers to isolated yields.
[b] Novel compound.

$Y(NO_3)_3.6H_2O/SiO_2$ from the reaction between benzaldeyde, malononitrile and β-naphthol was regenerated by washing with ethanol and drying at 100 °C for 1 h. The optimized method was used to synhesize 15 other known amino-chromenes (Table 2). Using the recycled catalyst five consecutive times in the model reaction gave the product with a gradual decreasing reaction yield (Table 3).

The probable mechanism for the formation of 2-amino-4*H*-chromenes **4** in the presence of catalytic amounts of $Y(NO_3)_3.6H_2O/SiO_2$ is outlined in Scheme 2. Activation of the carbonyl group of the aldehyde by Y(III) generates an electrophilic centre at the carbonyl carbon atom which is attacked by the malononitrile tautomer to form intermediate I. Interception of intermediate I by β-naphthol produces an open chain intermediate II which cyclizes to produce the corresponding 2-amino-4*H*-chromenes.

To study the applicability of this method in larger scale synthesis, we performed selected reactions at 10 mmol scale. For this purpose, aromatic aldehydes (10 mmol) were reacted with malononitrile (10 mmol) and β-naphthol (10 mmol) in the presence of $Y(NO_3)_3.6H_2O/SiO_2$ (2.4 g) in water (50 mL) under reflux conditions; the obtained results are summarized in Table 4. As can be seen, the reactions at large scale gave the product with a gradual decreasing of reaction yield.

In conclusion, silica-supported yttrium nitrate hexahydrate can be used for the green synthesis of 2-amino-4*H*-chromenes *via* the three-component reaction between aromatic aldehydes, malononitrile, and β-naphthol in water. $Y(NO_3)_3.6H_2O/SiO_2$ is recyclable, safe and thermally stable. Use of this new method has

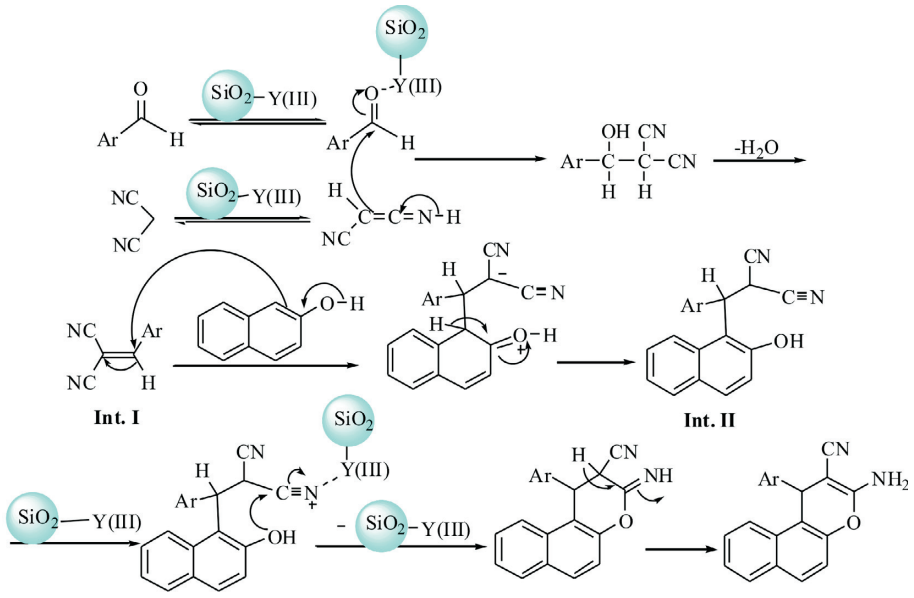
Table 3 Reusability study of $Y(NO_3)_3.6H_2O/SiO_2$ in the model reaction.

Run	1	2	3	4	5
Time/min	180	180	170	165	160
Yield/% [a]	90	85	85	85	80

[a] Refers to isolated yields.

Table 4 The large-scale synthesis of some 2-amino-4*H*-chromenes using $Y(NO_3)_3.6H_2O/SiO_2$.

Product	Ar	Time/min	Yield/%
4a	Ph	190	85
4c	4-MeC_6H_4	250	80
4d	4-OHC_6H_4	200	90
4f	4-ClC_6H_4	185	88
4g	3-CNC_6H_4	100	85
4j	4-$NO_2C_6H_4$	165	70
4l	4-BrC_6H_4	130	75
4n	4-$OMeC_6H_4$	255	80



Scheme 2
Proposed mechanism for the synthesis of **4** using $Y(NO_3)_3.6H_2O/SiO_2$.

advantages such as a simple experimental procedure, use of an eco-friendly and reusable catalyst, short reaction time and good to excellent yields, which make this method a valid contribution to existing methodologies.

3. Experimental

3.1. General

Chemicals were purchased from Merck and Aldrich. The reactions were monitored by TLC (silica gel 60 F_{254}, hexane/EtOAc). IR spectra were recorded on a FT-IR JASCO-680 and the NMR spectra were obtained on a Bruker-Instrument DPX-400 MHz Avance III model. The varioEl CHNS Isfahan Industrial University was used for elemental analysis.

3.2. Preparation of Catalyst

Grafted silica gel (4 g) was stirred with yttrium nitrate hexahydrate (0.766 g, 0.2 mmol) in $CHCl_3$ (10 mL) and heated under reflux for 2 h. The mixture was filtered, washed thoroughly with chloroform (3 × 10 mL) and the solid catalyst was dried.[8]

3.3. General Procedure for the Synthesis of 2-Amino-4*H*-chromene Derivatives

$Y(NO_3)_3.6H_2O/SiO_2$ (0.24 g) was added to a mixture of the aromatic aldehyde (1 mmol), malononitrile (1 mmol) and *β*-naphthol (1 mmol) in water (5 mL). The resulting mixture was heated under reflux for the appropriate time. After completion of the reaction (as indicated by TLC), boiling EtOH (10 mL) was added and the resulting mixture was stirred for 3 min. The catalyst was separated by filtration then washed with diethyl ether. Evaporation of solvent under reduced pressure gave the product. Further purification was achieved by recrystalization from $EtOH/H_2O$.

Large-scale synthesis of selected compounds: aromatic aldehydes (10 mmol) were reacted with malononitrile (10 mmol) and *β*-naphthol (10 mmol) in the presence of $Y(NO_3)_3.6H_2O/SiO_2$ (2.4 g) in water (50 mL) under reflux conditions. Workup proceeded as above. The results are summarized in Table 4.

3.4. Selected Spectral Data

*3-Amino-1-(phenyl)-1*H*-benzo[f]chromene-2-carbonitryl* (**4a**): Yield: 90 %; m.p. 273–274 °C;[22] FT-IR (KBr, cm^{-1}): 3410 and 3310 (NH_2), 3090, 2190 (CN), 1638 (C=C arom.), 1585, 1300, 720, 690; ^{1}H-NMR (400 MHz, DMSO-d_6, *δ*/ppm): 5.31 (s, 1H, aliph. CH), 7.00 (s, 2H, NH_2), 7.14–7.28 (m, 5H), 7.34–7.43 (m, 3H), 7.84–7.96 (m, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6, *δ*/ppm): 38.5 (aliph. CH), 58.4 (CN), 116.2, 117.3, 121.0, 124.1, 125.4, 127.1, 127.8, 127.5, 129.0, 129.2, 130.0, 130.7, 131.3, 146.2, 147.3, 160.2.

*3-Amino-1-(*p*-tolyl)-1*H*-benzo[f]chromene-2-carbonitryl* (**4c**): Yield: 85 %, m.p. 260–263 °C;[23] FT-IR (KBr, cm^{-1}): 3410 and 3310 (NH_2), 3050, 2190 (CN), 1640 (C=C arom), 1580, 1400, 810; ^{1}H-NMR (400 MHz, DMSO-d_6, *δ*/ppm): 2.19 (s, 3H, aliph. CH), 5.26 (s, 1H), 6.99 (s, 2H. NH_2), 7.04–7.10 (m, 4H), 7.33–7.46 (m, 3H), 7.83–7.94 (m, 3H); ^{13}C-NMR (100 MHz, DMSO-*d*6, *δ*/ppm): 21.1, 38.3, 58.5, 116.3, 117.3, 121.1, 124.0, 125.0, 127.4, 127.5, 129.0, 130.0, 129.8, 130.7, 131.3, 136.1, 143.3, 147.3, 160.0.

*3-Amino-1-(3-cyano phenyl)-1*H*-benzo[f]chromene-2-carbonitryl* (**4g**): Yield: 90 %; m.p. 238–240 °C; FT-IR (KBr, cm^{-1}): 3400 and 3300 (NH_2), 3090, 2190 (CN), 1640 (C=C arom.), 1580, 1400, 800, 740, 690; ^{1}H-NMR (400 MHz, DMSO-d_6, *δ*/ppm): 5.48 (s, 1H, aliph. CH), 7.16 (s, 2H, NH_2), 7.37 (d, J = 9.2 Hz, 1H), 7.41–7.49 (m, 4H), 7.64–7.67 (m, 1H), 7.77 (s, 1H), 7.83 (d, J = 8 Hz, 1H), 7.92–7.98 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6, *δ*/ppm): 37.9, 57.5, 111.9, 114.9, 117.4, 119.2, 120.7, 123.9, 125.6, 127.8, 129.1, 130.4, 130.7, 130.9, 131.2, 131.3, 132.5, 147.5, 147.7, 160.3.

*3-Amino-1-(3-nitro phenyl)-1*H*-benzo[f]chromene-2-carbonitryl* (**4i**): Yield: 80 %; m.p. 232–235 °C; FT-IR (KBr, cm^{-1}): 3400 and 3298 (NH_2), 3153, 2181 (CN), 1645 (C=C arom.), 1536, 1300, 806; ^{1}H-NMR (400 MHz, DMSO-d_6, *δ*/ppm): 5.82 (s, 1H, aliph. CH), 7.27 (s, 2H, NH_2), 7.36–7.48 (m, 4H), 7.81–8.12 (m, 6H); ^{13}C-NMR (100 MHz, DMSO-d_6, *δ*/ppm): 39.4, 58.2, 115.6, 117.5, 118.5, 122.9, 123.9, 124.8, 125.5, 128.9, 129.1, 129.4, 129.6, 130.4, 131.7, 132.0, 132.5, 144.0, 148.2, 166.2.

*3-Amino-1-(4-nitro phenyl)-1*H*-benzo[f]chromene-2-carbonitryl* (**4j**): Yield: 75 %; m.p. 236–239 °C; FT-IR (KBr, cm^{-1}): 3450 and 3310 (NH_2), 3153, 2200 (CN), 1645 (C=C arom.), 1580, 1530, 1355, 1218, 720; ^{1}H-NMR (400 MHz, DMSO-*d*6, *δ*/ppm): 5.82 (s, 1H, aliph. CH), 7.35–47 (m, 3H), 7.52 (d, J = 8.8 Hz, 3H), 7.81–7.85 (m, 4H), 8.05 (d, J = 8.4 Hz, 2H); ^{13}C-NMR (100 MHz, DMSO-*d*6, *δ*/ppm):

41.9, 59.2, 113.4, 116.5, 17.5, 123.6, 124.1, 125.7, 127.8, 130.0, 129.8, 130.1, 131.5, 132.0, 146.8, 148.3, 152.3, 165.1.

*3-Amino-1-(4-bromo phenyl)-1*H*-benzo[f]chromene-2-carbonitryl* (**4l**): Yield: 80 %; m.p. 220–221 °C;[22] FT-IR (KBr, cm^{-1}): 3400 and 3298 (NH_2), 3150, 2181 (CN), 1640 (C=C arom.), 1583, 1373, 1220, 837, 721, 614 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6, δ/ppm): 5.67 (s, 1H, aliph. CH), 7.23–7.47 (m, 9H), 7.77.7.92 (m, 3H); ^{13}C-NMR (100 MHz, DMSO-d_6, δ/ppm): 37.7, 59.0, 114.2, 117.4, 117.5, 120.6, 123.9, 125.6, 127.6, 128.9, 129.6, 130.7, 131.7, 131.8, 132.0, 144.2, 148.2, 164.4. After optimizing the reaction conditions, the scope of this synthetic method was examined by using a variety of different aromatic aldehydes. Both electron-rich and electron-poor aromatic aldehydes afforded the corresponding products in good to excellent yields (Table 2). Alkyl aldehydes were unreactive. The isolated products were characterized by physical and spectroscopic techniques and were compared with authentic samples.[22–25]

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