

BF₃/nano-γ-Al₂O₃ Promoted Knoevenagel Condensation at Room Temperature

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Abstract

The Knoevenagel condensation of aromatic aldehydes with barbituric acid, dimedone and malononitrile occurred in the presence of BF₃/nano-γ-Al₂O₃ at room temperature in ethanol. This catalyst is characterized by powder X-ray diffraction (XRD), fourier transform infrared spectroscopy (FT-IR), thermal gravimetric analysis (TGA), field emission scanning electron microscopy (FESEM) and energy-dispersive X-ray spectroscopy (EDS).

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1. Introduction

Knoevenagel condensation is one of the attractive and important pathways in organic synthesis. This protocol provides an easy access for compound which plays an important role as an intermediate for the design of pharmaceuticals and organic materials [1-3]. It has been used for the preparation of wide range of substituted alkenes, synthesis of fine chemicals, intermediates such as anti-hypertensive drugs, calcium antagonists [4-7]

and coumarin derivatives which are useful in perfumes, cosmetics and bioactive compounds [8]. Although the Knoevenagel reaction has been known for a long time and various reagents for this condensation have been developed. But expand of the reaction using clean and inexpensive reagents is still attracting considerable attention and an appealing area for chemists. Therefore, various catalysts have been developed for this purpose, such as carbon nitride materials [9],

polycarbosilane supported titanium(IV) catalyst [10], graphene oxide with ethylenediamine [11], Indium (III) chloride [12], biguanide-functionalized meso-porous silica [13], zeolites [14], ionic liquids immobilized in mesoporous silica [15] and proline-functionalized polyacrylonitrile fiber [16].

Recently, a topic of current interest in the modern synthetic methods is reaction on the solid support that is one of the most employed useful in field of organic synthesis. Today, synthesis of organic compounds using solid acid catalysts is more and more attention due to the numerous advantages such as cost-effectiveness, high catalytic activity, ease of product separation, recovery of the catalyst, repeated recycling potential and good stability. In this regard, a part of our research program aimed at developing of organic synthesis via solid acid catalyst. $\text{BF}_3/\gamma\text{-Al}_2\text{O}_3$ is a solid acid catalyst that is previously synthesized, characterized and successfully used for alkylation reaction [17]. Herein we have prepared and characterized $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ and successfully used for Knoevenagel condensation.

2. Experimental procedure

2.1. General

All compounds were purchased from Merck and Fluka chemical company and used without any additional purification. FT-IR spectra were run on a Bruker, Equinox 55 spectrometer. A Bruker (DRX-400 Avance) NMR was used to record the $^1\text{H-NMR}$ spectra. Melting points were determined by a Buchi melting point B-540 B.V.CHI apparatus and were uncorrected. The thermal gravimetric analysis (TGA) was done with "NETZSCH TG 209 F1 Iris" instrument. X-ray diffraction pattern using Philips Xpert MP diffractometer. Field emission scanning electron microscopy (FESEM)

was obtained on a Mira Tescan. Energy-dispersive X-ray spectroscopy (EDS) of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ was measured by EDS instrument, Phenom pro X. The products were characterized by FT-IR, $^1\text{H-NMR}$, and a comparison of their physical properties with those reported in the literature.

2.2. General procedure for the preparation of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$

To a mixture of nano- Al_2O_3 (5 g) and CHCl_3 (10 ml), $\text{BF}_3\cdot\text{Et}_2\text{O}$ (5 ml) was added drop wise. The resulting suspension was stirred for 1 hour at room temperature, filtered, washed with chloroform, and dried at room temperature.

2.3. Preparation of 2-arylidene malononitrile from aldehyde and malononitrile

The mixture of aldehydes (1 mmol), malononitrile (1 mmol), and $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06 g) and ethanol (3 ml) was stirred at room temperature for 15 minutes. The progress of reaction was monitored by TLC. After completion of the reaction, 3 ml of ethanol was added and the heterogeneous catalyst was filtered. After evaporation of solvent, the pure solid product was achieved.

2.4. Preparation of 2-arylidene-5,5-dimethylcyclohexane-1,3-dione from aldehyde and dimedone

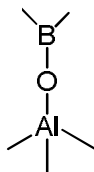
The mixture of aldehydes (1 mmol), dimedone (1 mmol) and $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06 g) and ethanol (3 ml) was stirred at room temperature for 30 minutes. The work-up of reaction was similar to 2.3.

2.5. Preparation of 5-arylidene pyrimidine-2,4,6-(1H,3H,5H)-trione from aldehyde and barbituric acid

The mixture of aldehydes (1 mmol), barbituric acid (1 mmol), $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06 g) and ethanol (3 ml) was stirred at room temperature for 30 minutes. The work-up of reaction was similar to 2.3.

3. Results and discussion

In continuation of our research on the applications of solid acids in organic synthesis, we have investigated $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ efficiency in the reaction of Knoevenagel condensation at room temperature. For identification of the structure of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$, we have studied FT-IR (ATR) spectra of $\text{nano-}\gamma\text{-Al}_2\text{O}_3$ and $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (Figure 1). In $\text{nano-}\gamma\text{-Al}_2\text{O}_3$ FT-IR spectrum, strong bands at 1742, 1370 and 1216 cm^{-1} were observed. In $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$, in addition to the above mentioned bands, three bands also appeared at 1627, 1410 and 1071 cm^{-1} . The peaks at 1410 and 1071 cm^{-1} verify the B-O and Al-O-B bonds on $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ respectively. Based on these results, we have also suggested the following structure for $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ [17] (Scheme 1).



Scheme 1. The proposed structure for $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$

The FESEM image of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ is shown in figure 2. Energy-dispersive X-ray spectroscopy (EDS) of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ was measured by EDS instrument (Figure 3). According to this data, the weight percentage of O, Al and F are 42.8, 34.9 and 22.3, respectively.

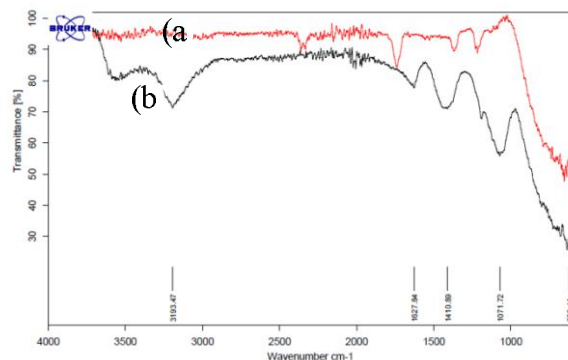


Fig. 1. FT-IR (ATR) spectrum of: (a) $\text{nano-}\gamma\text{-Al}_2\text{O}_3$, (b) $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$

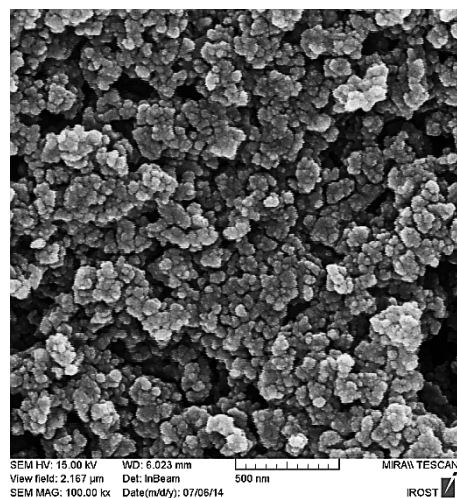


Fig. 2. The FESEM image of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$

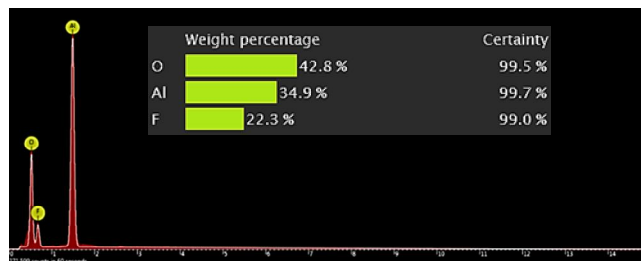
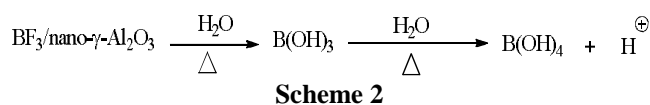


Fig. 3. EDS analysis diagram of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$

The amount of boron in $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ was determined. For this purpose, a mixture of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.1 g) and water (50 ml) was

stirred and boiled for 20 minutes. Then, the mixture was cooled and titrated with 23 ml of standard NaOH (0.009 N) in the presence of phenolphthalein. The boron amount in catalyst was found to be 2.1 meq.g^{-1} . In this process, the attached boron in $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ was reacted with water, captured OH^- from water to produce B(OH)_4^- and H^+ . The amount of H^+ that evaluated with titration is equal boron (Scheme 2).



The X-ray diffraction (XRD) pattern of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ is shown in figure 4. According to XRD pattern of catalyst, the values of 2θ and FWHM are shown in table 1. According to XRD pattern, the two signals at 2θ equal to 14.57 and 27.96 with FWHM equal to 0.2952 and 0.1771 respectively, is similar to HBO_3 with B-O bonds. The signals at 2θ equal to 25.09, 45.91 and 66.99 are shown $\gamma\text{-Al}_2\text{O}_3$ structure. We can confirm the proposed structure for $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ in scheme 1.

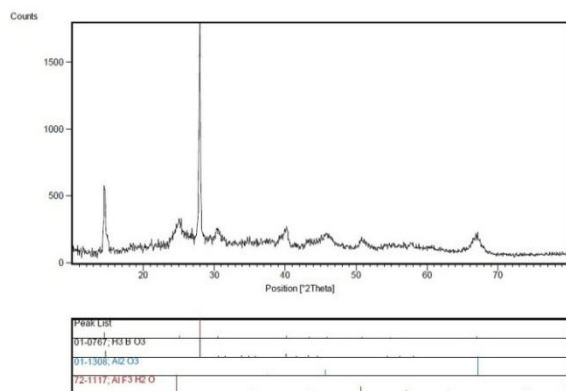


Fig. 4. X-ray diffraction (XRD) pattern of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$.

Table 1. $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ reflexes in XRD diffractogram

No.	Pos. [2 θ]	FWHM [2 θ]
1	14.5780	0.2952
2	25.0940	0.8266
3	27.9663	0.1771
4	30.4779	0.5904
5	40.2502	0.3542
6	43.4113	0.7085
7	45.9193	1.4170
8	50.7719	0.4723
9	54.8168	1.4170
10	66.9918	0.8640

Thermal gravimetric analysis (TGA) pattern of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ was detected from 50 to 800 °C (Figure 5). The catalyst is stable until 100 °C and only 10% of its weight was reduced in 115 °C. This initial reducing mass (10%) of catalyst is related to removal of catalyst moisture. By heating of catalyst between 600 °C to 660 °C, the reducing amount of its weight is 6% *via* cleavage of B-F bonds. According to TGA diagram of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$, this catalyst is stable until 100°C.

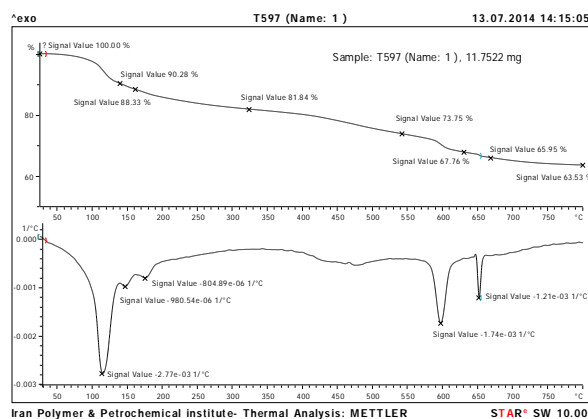


Fig. 5. Thermal gravimetric analysis (TGA-DTG) pattern of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$

In our opinion, this heterogeneous catalyst can catalyze many reactions such as Knoevenagel

condensation. In this work, we have applied $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ for synthesis of Knoevenagel products from condensation of various aldehydes with active methylene compounds such as malononitrile, dimedone and barbituric acid. To reaction of Knoevenagel condensation and find the best reaction conditions, the reaction of benzaldehyde and malononitrile under various conditions and different quantities of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ were examined (Table 2).

Table 2. Condensation of benzaldehyde and malononitrile under different conditions^a

Entry	Catalyst (g), [mol%]	Conditions	Time (h) /yield ^b (%)	Ref.
1	-	ethanol/r.t.	0.25/30	-
2	nano- $\gamma\text{-Al}_2\text{O}_3$ (0.06)	ethanol/r.t.	0.25/70	-
3	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.02)	ethanol/r.t.	0.25/75	-
4	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.04)	ethanol/r.t.	0.25/85	-
5	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06)	ethanol/r.t.	0.25/96	-
6	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.08)	ethanol/r.t.	0.25/96	-
7	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06)	water/r.t.	0.25/60	-
8	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06)	water:ethanol (1:1)/r.t.	0.25/80	-
9	$\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06)	S.F./r.t.	0.25/40	-
10	boric acid (0.06)	ethanol/r.t.	0.25/50	-
11	borax (0.06)	ethanol/r.t.	0.25/85	-
12	TiO_2 [100]	$\text{CH}_2\text{Cl}_2/\text{reflux}$	48/40	[18]
13	Glycine	55°C	22/77	[19]

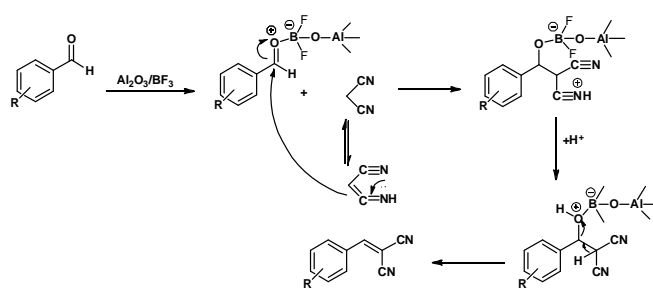
^aImmole of benzaldehyde and 1mmole of malononitrile was used.

^bIsolated yield

As shown in table 2, the most yield of reaction was acquired in ethanol at room temperature in the presence of 0.06 g $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ after 30 minutes (Table 2, Entry 6). It was noted when the reaction was performed without catalyst, desired product was obtained in low yield (Table 2, Entry 1).

The Knoevenagel condensation of a variety of active methylene compounds were reacted with malononitrile to give the desired products in excellent yields. The results are summarized in table 3.

A mechanism for the catalytic activity of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ in the reaction of Knoevenagel condensation may be postulated as shown in scheme 3.



Scheme 3

4. Conclusion

In summary, an extremely efficient and green process has been developed for Knoevenagel condensation in the presence of $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ as a heterogeneous catalyst. High yields of products, easy preparation of catalyst, easy work-up are advantages of this protocol.

Acknowledgment

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Table 3. Knoevenagel condensation of aromatic aldehydes with active methylene compounds catalyzed by $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3^{\text{a}}$

Entry	Aromatic aldehydes	Active methylene compounds	Product	Time (min)	Yield (%) ^b	C (Lit.) ^o mp.	Ref
1				15	96	83-85 (83-83.5)	[20]
2				15	97	105-107 (102-104)	[21]
3				15	90	158-160 (159-160)	[20]
4				15	85	160-162 (162-163)	[20]
5				15	80	190-193 (190-192)	[22]
6				30	65	187-190	-
7				15	93	185-187 (187-188)	[23]
8				15	95	202-204	-
9				15	81	185-187 (187-188)	[24]
10				30	80	262-263 (263-264)	[25]
11				30	95	263-265 (266-267)	[19]
12				30	84	236-237 (235)	[26]
13				60	92	205-207 (208-210)	[25]
14				60	94	227-230	-
15				90	92	266-268 (268-269)	[25]

^aReaction conditions: aldehyde (1 mmol), malononitril (1 mmol), dimedone (1 mmol), barbituric acid (1 mmol), $\text{BF}_3/\text{nano-}\gamma\text{-Al}_2\text{O}_3$ (0.06 g) in ethanol as solvent and at room temperature.

^bIsolated yield

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