Monatshefte für Chemie - Chemical Monthly
https://doi.org/10.1007/s00706-020-02574-w

ORIGINAL PAPER

KF/clinoptilolite nanoparticles as an efficient nanocatalyst for the Strecker synthesis of *α*-aminonitriles

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Received: 8 July 2019 / Accepted: 12 March 2020
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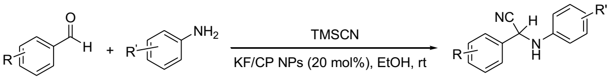
Abstract

Potassium fluoride impregnated on clinoptilolite nanoparticles (KF/CP NPs) have been explored to serve as an effective and inexpensive heterogeneous catalyst for the one-pot three-component Strecker synthesis of a variety of *α*-aminonitriles at room temperature in ethanol as a green solvent. KF/CP NPs have been synthesized using simple impregnation techniques in aqueous media from readily available inexpensive starting materials and displayed its initial catalytic activity even after five runs. The easy preparation and separation of catalyst, simple procedure, mild reaction conditions, and excellent yields of products render this method as an attractive sustainable option.

Graphic abstract



Keywords Clinoptilolite · KF/CP · Aldehydes · Strecker · *α*-Aminonitriles · Three-component

Introduction

Strecker reaction [1] is one of the most straightforward and preferred synthetic reactions in organic chemistry to afford *α*-aminonitriles from the three-component coupling of an amine, a carbonyl compound, and a cyanide source. Because of the importance of *α*-aminonitriles as valuable intermediates for preparing S- and N-containing heterocycles [2], versatile precursors of *α*-amino acids [3], and biologically active molecules [4–7], employing new catalytic approaches is currently a highly desirable goal and this reaction has been considerably extended by the employment of various catalysts, sources of amino and cyano groups, and use of different solvents. Among various cyanide ion sources, trimethylsilyl cyanide (TMSCN) is a safer and easily handled reagent [8–43]. Besides, performing the Strecker reaction under green conditions using a heterogeneous catalyst will not only improve the reaction from an ecological but also economical point of view. Accordingly, enormous efforts have been devoted to the development of efficient, recyclable, and environmentally benign catalytic methods to affect the Strecker reaction using nonpolluting reagents and solvents. In this sense, we have recently reported Strecker reaction by some heterogeneous catalysts [44, 45]. During our ongoing efforts to search for environmentally friendly and reusable nanocatalysts [44–50], we have found that KF/clinoptilolite is a heterogeneous inexpensive solid catalyst for some organic transformations [51–60]. Moreover, impregnation of potassium fluoride on clinoptilolite (CP) as a natural zeolite with a high internal surface area and high cation exchange capability particularly for K^+ is very simple without the need for any pre-activation [61, 62]. Armed with these experiences, in the current study, with the aim of developing a more convenient and simple approach towards the construction of *α*-aminonitriles, we wish to report the use of heterogeneous KF/CP NPs as recyclable catalyst in the Strecker reaction (Scheme 1).

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Published online: 28 April 2020

Scheme 1

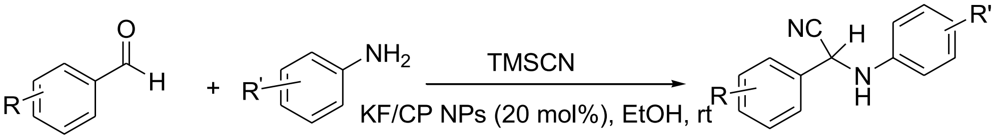


Table 1 Optimization conditions for reaction of benzaldehyde (1 mmol), aniline (1 mmol), and TMSCN (2 mmol) in the presence of different amounts of KF/CP NPs in different solvents at room temperature

Entry	Catalyst/%mol	Solvent	Time /min	Yield/%[a]
1	20	CH_2Cl_2	90	30
2	20	Toluene	90	50
3	20	$(Et)_2O$	240	45
4	20	H_2O	240	Trace
5	20	EtOH	35	92
6	10	EtOH	120	75
7	30	EtOH	50	91
8	–	EtOH	360	Trace
9	CP (20)	EtOH	360	Trace
10	KF (20)	EtOH	360	35
11	20[b]	EtOH	240	42

[a] Isolated yields

[b] Bulk KF/CP was used instead of KF/CP NPs

Results and discussion

Prompted by our latest results regarding different heterogeneous catalyzed Strecker reactions [44, 45], we decided to use KF/CP NPs for the promotion of the Strecker reaction. The main reason for selection of KF/CP NPs as catalyst is because of abundance, very low cost, and safety of naturally occurring zeolite CP. The analysis of structure and size distribution of the nanoparticles (NPs) was performed by scanning electron microscopy (SEM) and X-ray diffraction, with results matching the literature data. The size of prepared KF/CP NPs was reported to be 41 nm [52–55].

For initial screening, the study was designed for the synthesis of α-aminonitriles via Strecker reaction of benzaldehyde (1.0 mmol), aniline (1.0 mmol), and TMSCN (2.0 mmol) to investigate the suitability of KF/CP NPs (20 mol%) as a catalyst in different reaction conditions (Table 1). Our preliminary investigation showed that a yield of 92% of the desired product was obtained when EtOH was used as solvent at room temperature (Table 1, entry 5). Noteworthy, decreasing the amounts of KF/CP NPs (10 mol%) gave the corresponding α-aminonitrile in 80% yield even after prolonged reaction times (Table 1, entry 6), and increasing the KF/CP NPs (30 mol%) did not notably change the yield of the reaction (Table 1, entry 7). A control experiment was performed in the absence of a catalyst at room temperature and the desired product obtained in trace amounts after 360 min (Table 1, entry 8). Interestingly, the same reaction with CP and KF (Table 1, entries 9, 10) yielded trace amounts and 35% of products, respectively. Additionally, 42% of the related product obtained with using bulk KF/CP after 240 min (Table 1, entry 11). These results verify the catalytic efficiency of KF/CP NPs. Thus, the best results were obtained by the application of 20 mol% of KF/CP NPs in EtOH at ambient temperature.

At the next stage, the activity of the catalyst was tested for the synthesis of various α-aminonitriles under optimized reaction conditions to examine the universality of this catalyst's application (Table 2). The general efficiency of this reaction is evident from the variety of aryl aldehydes containing both electron-withdrawing and electron-donating groups which react in excellent yields within a short reaction time (Table 2, entries 1–15). Also, the aniline-bearing Br group in *para*-position (*p*-bromoaniline) concluded to the related products with excellent yields in short reaction times (Table 2, entries 16, 17). Noteworthy, trace amounts of product were obtained when methyl amine and ethyl amine were used as aliphatic amines (Table 2, entries 18, 19). However, the reaction proceeded efficiently at room temperature without the formation of any by-products. These conditions are extremely convenient from a practical and economic point of view since they use inexpensive recyclable KF/CP NPs and avoid wasting reagents and allow a simple work-up procedure. Summing up, a rapid, clean, and efficient method for the synthesis of α-aminonitriles at room temperature is reported and quantitative transformations achieved in short reaction time.

The proposed mechanism is described in Scheme 2. It is plausible that the reaction begins with the formation of bond between oxygen atom of carbonyl compounds and surface of catalyst to produce iminium ion intermediates. Then, the fluoride ion facilitates the formation of cyanide ion and nucleophilic attack of cyanide ion to the iminium ion intermediate leads to the formation of the corresponding α-aminonitriles.

The possibility of the catalyst recyclability and reusability was then investigated in this system through a series of sequential synthesis of α-aminonitriles from benzaldehyde, aniline and TMSCN as model substrates (Fig. 1). After

Table 2 Synthesis of α-aminonitriles from aldehydes, amine, and TMSCN using KF/CP NPs in EtOH at room temperature

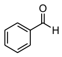
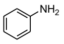
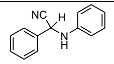
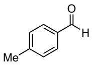
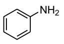
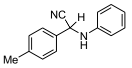
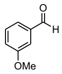
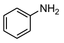
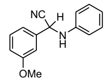
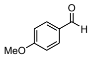
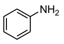
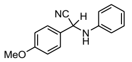
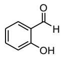
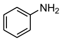
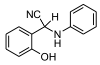
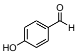
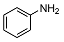
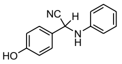
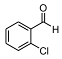
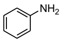
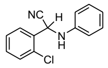
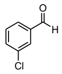
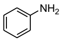
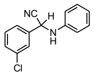
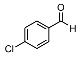
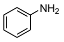
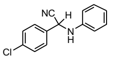
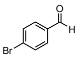
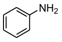
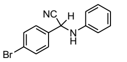
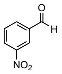
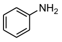
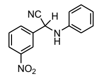
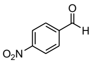
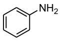
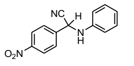
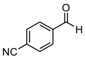
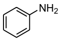
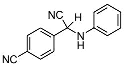
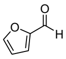
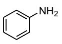
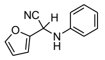
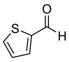
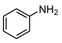
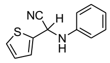
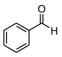
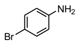
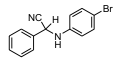
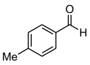
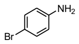
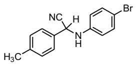
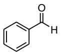
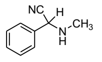
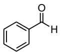
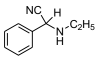
Entry	Aldehyde	Amine	Product	Time /min	Yield^a /%
1				35	92
2				30	91
3				40	90
4				25	92
5				40	81
6				40	91
7				45	92
8				30	94
9				40	89
10				40	84
11				45	92
12				55	89
13				55	80
14				40	89
15				45	90
16				25	91
17				20	88
18		CH_3NH_2		40	Trace
19		$C_2H_5NH_2$		40	Trace

Table 2 (continued)

Reaction conditions: aldehyde (1.0 mmol), amine (1.0 mmol), and TMSCN (2.0 mmol) with KF/CP NPs (20 mol%) in 5.0 cm^3 EtOH at room temperature

^{a}Isolated yields

completion of each run of reaction, hexane was added and the reaction mixture was filtered and washed with hexane. Then, the recovered catalyst was used in the successive runs. The results showed that the catalyst could be effectively used for at least five cycles. The decrease in the yield after the fifth use of the catalyst may be attributed to the leaching of KF from CP. After performing the fifth cycle of the reaction, the solid material was filtered out and then the presence of fluoride ions in the filtrate validated by SPADNS spectrophotometric method proved the leaching of KF during the recycling of catalyst.

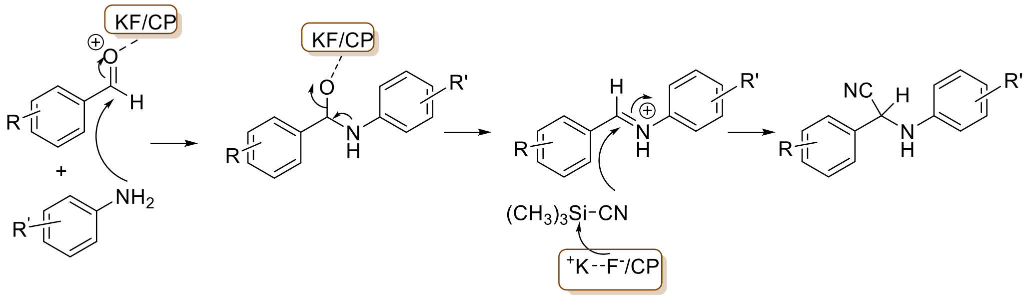
Conclusion

In summary, this study has shown that environmentally friendly heterogeneous KF/CP NPs catalyst can be used to promote highly efficient one-pot, three-component Strecker reaction of a range of aldehydes and aniline derivatives with TMSCN in EtOH at room temperature to produce α-aminonitriles. However, the reaction is limited to aromatic amines. In this process, the catalyst can be easily recovered and can be reused for the next reactions without any treatment for five consecutive runs. This method has advantages such as mild conditions, high yields, short reaction times, easy work-up, and cost effective for the synthesis of α-aminonitriles. As a result of high efficiency and activity as well as recyclability and low cost of catalyst, further applications of this catalyst to other synthetically useful transformations are currently being investigated.

Experimental

The raw material was an Iranian commercial CP (Afrandtooska Company) from deposits in the region of Semnan. All chemicals used in this work were purchased from Fluka or Sigma-Aldrich and were employed without further purification. The morphology of nanoparticles of KF/clinoptilolite was characterized by scanning electron microscopy (SEM) using a Holland Philips XL30 microscope. Crystalline structure of KF/CP (NPs) was characterized by X-ray diffraction (XRD) analysis at room temperature using a Holland Philips Xpert X-ray powder diffractometer, with CuKα radiation ($\lambda = 0.15406$ nm). The average crystallite size was calculated using Scherrer's formula: $D = 0.9\lambda/\beta \cos\theta$. Thin-layer chromatography (TLC) was performed using 60 mesh silica

Scheme 2



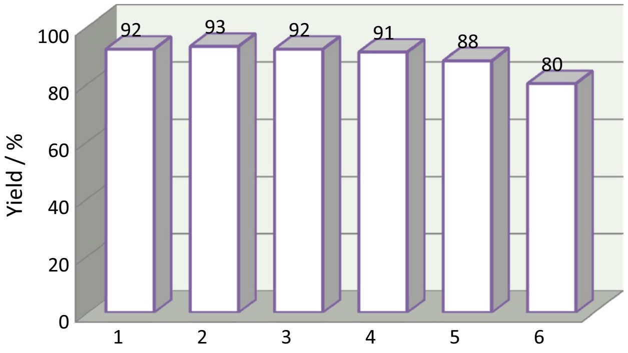


Fig. 1 Reusability of KF/CP NPS (20 mol%) for the Strecker reaction of benzaldehyde (1 mmol), aniline (1 mmol), and TMSCN (2 mmol) after 35 min at room temperature

gel Merck TLC plates. All values were analyzed using an HP GC 6890 that was equipped with a DB-5 CP column (30 m × 0.32 mm × 0.5 m).

Preparation of KF/CP NPs

Nanosized natural clinoptilolite zeolite was generated by grinding in a planetary ball mill using a zirconia vial set in dry conditions with a time period of about 20 min. KF/CP NPs was easily prepared by commercially available starting materials according to previously reported method [53] by dissolving 1.0 g KF in the mixture of 10 cm^3 distilled water containing 9.0 g nano clinoptilolite. The mixture was stirred for 1.0 h and then water was evaporated in a rotary evaporator under reduced pressure at 60–70 °C. The impregnated nano clinoptilolite was further dried at 70–80 °C in a vacuum drying oven for 30 h. The material was powdered with the help of pestle and mortar.

General procedure for the synthesis of α-aminonitriles

Strecker reaction of a mixture of aldehyde (1.0 mmol), amine (1.0 mmol), and 0.16 cm^3 TMSCN (2.0 mmol) was carried out in a 10 cm^3 round bottom flask using 0.12 g KF/CP NPs (20 mol%) in 5.0 cm^3 ethanol at room temperature. After completion of the reaction monitored by thin-layer chromatography, the reaction mixture was filtered and washed with hexane to recover the catalyst. Aqueous sodium bicarbonate (5.0 cm^3 of a 5.0% solution) was then added and the mixture extracted with hexane (3 × 5.0 cm^3). The combined organic phases were dried over anhydrous magnesium sulfate. Then, the reaction solution was concentrated under vacuum and materials were subjected to column chromatography on flash silica.

Acknowledgements The authors acknowledge the Islamic Azad University of Qaemshahr Research Councils for support of this work.

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