

Mesolite catalyzed one pot synthesis of quinoline-3-carbonitrile derivatives

Ganesh T. Pawar, Rameshwar R. Magar, Machhindra K. Lande*

Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad (M.S.), 431004, India.

Received 29 December 2015; received in revised form 9 March 2016; accepted 29 March 2016

ABSTRACT

Natural mesolite type zeolite was collected, modified by sulfuric acid treatment and characterized by using Powder-X ray diffraction (XRD), Scanning electron microscopy (SEM), Energy dispersive spectroscopy (EDS), Fourier transform infrared spectroscopy (FT-IR). Temperature programmed ammonia desorption (NH₃-TPD), Brunauer-Emmer-Teller (BET) surface area analysis. Modified dealuminated mesolite shows an efficient catalytic activity for the one-pot synthesis of quinoline-3-carbonitrile derivatives, via three-component cyclocondensation of benzaldehyde, malononitrile and aniline. The present method offers several advantages over the reported methods like simple and inexpensive modification of the catalyst, mild reaction conditions and easy separation of the catalyst, simple work-up procedures, non-chromatographic separation and purification of desired product, excellent yield and reusability of the catalyst.

Keywords: Modification of natural zeolite, Mesolite, Quinoline-3-carbonitrile, Aniline, Malononitrile, Benzaldehyde.

1. Introduction

One-pot synthesis methods have played a significant role in organic synthesis because of several advantages, such as minimum reaction time, high selectivity and atom economy. Additionally, it delivers fewer by-products as compared to the classical synthesis with lower cost, time and energy [1]. Quinoline derivatives are building blocks of a number of nitrogen containing alkaloids [2]. In recent years, quinoline derivatives especially quinoline-3-carbonitrile derivatives, have received a strong research interest because of their potent biological and pharmacological properties such as antimicrobial, anticancer, anti-malarial, cytotoxic, anti-proliferative, DNA binding properties, and inhibitors for phosphodiesterase type 4B enzyme [3-8]. Besides, this 8-hydroxy quinoline and its derivatives form stable electroluminescent complexes with Al and Zn [9]. Furthermore, tetrahydrobenzo [*h*] quinoline derivatives are well-known dyes [10]. Considering these versatile applications of quinoline scaffold, several methods were developed using various homogenous and heterogeneous catalysts for the synthesis of quinoline derivatives, such as L-Proline, 3-methyl-1-sulfonic acid imidazolium hydrogen sulfate, SBA-15,

Chloroamine-T, ionic liquid [(BmIm)Cl], NH₄OH/I₂ and AgOTf [11-17]. However, some of these methods have one or another kind of drawbacks such as long reaction time, use of volatile organic solvents, low yield expensive catalysts and harsh reaction conditions. Therefore, it is necessary to develop a simple and greener route for the synthesis of quinoline-3-carbonitrile derivatives.

Zeolites are microporous, hydrated aluminosilicates minerals found naturally in the earth crust, containing polymeric three dimensional networks of [AlO₄]³⁻ and [SiO₄]⁴⁻ tetrahedron as primary building units. These units are linked to one another by sharing oxygen atoms; they also possess channels and pores ranging in diameter 3-8 Å [18]. Zeolites are obtained either from natural deposits or synthesized. Over 150 types of frameworks of synthetic zeolites have been reported and six different natural minerals of zeolite have been found in nature with a substantial quantity and purity [19]. Natural zeolites are used as water softener, cation exchanger, adsorbent for heavy metal cations and dye molecules [20]. Natural zeolites are the good sensors for ammonia and carbon dioxide molecules [21]. Industrially natural zeolites are used as heterogeneous catalysts for alkylation, acylation, isomerization and petrochemical refining [22-25].

Mesolite is a microporous fibrous natrolite type natural zeolite. The general molecular formula of mesolite is

*Corresponding author email: mkl_chem@yahoo.com
Tel.: +91 240 240 3311; Fax: +91 240 240 3335

[Si₇₂Al₄₈O₂₄₀] having NAT framework topology [26]. There are several modification methods to improve the acidity of zeolites, such as the hydrothermal treatment, acid/base leaching, H₂O₂ and microwave irradiation [27]. Dealumination of zeolite is useful to generate strong Lewis acidic sites in zeolite framework and also to improve the thermal stability and pore structure. Previously, we have reported the scolecite type natural zeolite as a potent solid acid catalyst for several organic transformations [28-30]. In the present work, the natural mesolite type zeolite sample was collected from Aurangabad district of Marathwada region, Maharashtra state, India. It was modified by the mineral acid treatment and characterized by X-ray diffraction, FT-IR, NH₃-TPD, FT-IR, SEM-EDS, BET and used as a heterogeneous solid acid catalyst for the synthesis of quinoline-3-carbonitrile derivatives (Scheme 1).

2. Experimental

2.1 Chemicals and instruments

All solvents and chemicals were analytical grade and purchased from Merck, Avra and Spectrochem chemicals and used as such. Melting points were taken in an open capillary and are uncorrected. FT-IR spectrum was recorded on Bruker advance. Thin layer chromatography was performed on Merck pre-coated silica gel 60-F-254 plates. ¹H NMR spectra were recorded on a 400 MHz FT-NMR spectrometer in CDCl₃ as solvent and chemical shifts values were recorded δ (ppm) relative to tetramethylsilane (Me₄Si) as an internal standard. The X-ray diffraction (XRD) patterns were recorded on Bruker 8-D advance X-ray diffractometer using monochromatic Cu-Kα radiation (λ = 1.5405 Å). Scanning of the electron microscope image with energy dispersive X-ray spectroscopy (SEM-EDS) was obtained on JSM - 6390LV6330 LA operated at 30.0 kV. The surface area was calculated by N₂ adsorptions. Desorption isotherm was performed on the Quantachrome CHEMBET 3000 instrument. NH₃-TPD was recorded on micromeritics instrument from room temperature to 700°C with heating rate 10°C/min.

2.2. Modification of natural mesolite type zeolite

Natural mesolite powder was washed and refluxed with distilled water for 3 hours and dried in the oven at

150°C for 4 h. 5 g of dried sample was mixed with 20 ml of 0.1 N H₂SO₄. The resulting mixture was stirred continuously for 3 h and filtered by sintered glass crucible. The products so obtained were washed with distilled water and dried in the oven at 110 °C for overnight. Finally, the resulting material was calcined in the muffle furnace (SONAR) at 500 °C for 5 h under air atmosphere. The sample was naturally cooled and further named as dealuminated mesolite.

2.3. Typical reaction procedure for the synthesis of quinoline-3-carbonitrile derivatives

A mixture of aromatic aldehyde (1 mmol), aniline (1 mmol), malononitrile (1 mmol), and catalytic amount dealuminated mesolite (0.1g) was refluxed in ethanol (15 ml) for the time shown in Table. 3. The progress of the reaction was monitored by TLC (petroleum ether: ethyl acetate =7:3 as eluent). After completion of the reaction, the reaction mass was filtered, the filtrate was concentrated under reduced pressure, and the crude product obtained was recrystallized from ethanol to afford pure product.

Selected spectral data

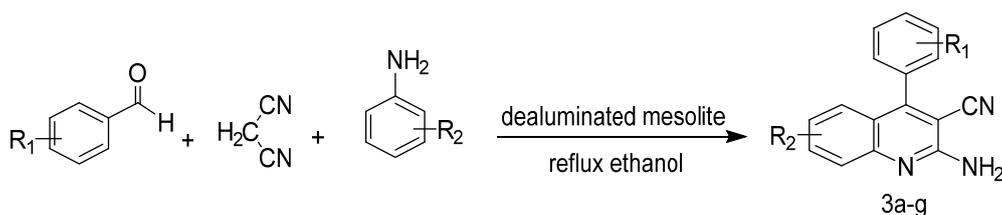
2-Amino-6-Nitro-4-(4-methoxyphenyl)-quinoline-3-carbonitrile (3a):

Yellow solid. IR (KBr): $\bar{\nu}$ = 3471, 2911, 2209, 1561 cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ = 4.3 (s, 2H, NH₂), 3.9 (s, 3H, OCH₃) 6.61-6.63 (d, 2H), 7.00 -7.02 (d, 2H), 7.6 (s, 1H), 7.8-7.9 (d, 1H), 8.05-8.08(d, 1H) ppm. ¹³C NMR (CDCl₃, 100 MHz) δ = 55.18, 95.60, 113.38, 115.15, 124.04, 126.35, 130.15, 133.46, 152.50, 158.89, 164.86 ppm.

3. Results and Discussion

3.1. XRD

XRD patterns of parent and dealuminated mesolite are given in Fig. 1 that shows intense peaks at 2θ = 13.57, 19.35, 20.39, 24.599, 25.45, 27.81, 31.14, 34.87, 39.84 with corresponding planes (0 1 1), (4 1 0), (3 3 1), (5 3 0), (1 16 0), (5 1 1), (1 9 2), (3 21 0), (2 17 2) respectively, which are characteristic peaks of mesolite type natural zeolite [31]. The diffraction planes of dealuminated mesolite shows low intensity due to loss of crystallinity and leaching of aluminum from the framework, but both samples are in orthorhombic phase [32].



Scheme 1. Synthesis of quinoline-3-carbonitrile derivatives.

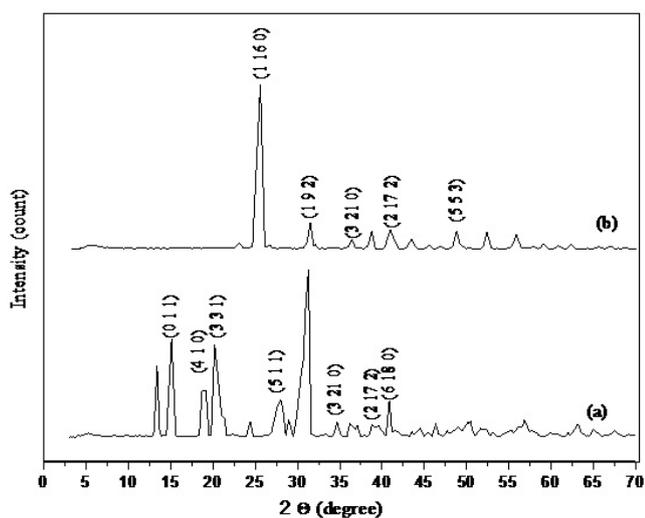


Fig. 1. Powder XRD pattern of (a) parent natural mesolite (b) dealuminated mesolite.

3.2. SEM-EDS

SEM-EDS have been extensively used to study surface morphology and elemental composition of the catalytic material. The SEM image of parent and dealuminated mesolite is presented in Fig. 2 (a) and (b) shows rod shaped crystals. The SEM image of sample (b) shows small but less bulky crystals, this may be due to generation of mesoporsity because of acid leaching. The elemental composition of mesolite is shown in Fig. 3, which shows the presence of O, Al, Si, Ca, elements with (atom %) 38.47, 20.36, 28.19, 12.2, respectively. From EDS spectrum, the empirical formula for the parent mesolite have been calculated, which is $Si_3Al_2Ca_1O_4$. Fig. 3 (b) presents EDS profile of dealuminated mesolite having elemental distribution in (atom %) O, Al, Si. 38.47, 2.34, 59.19 % respectively, with the corresponding empirical formula $Si_{30}AlO_{19}$. It has been found that Si:Al ratio increases on acid treatment.

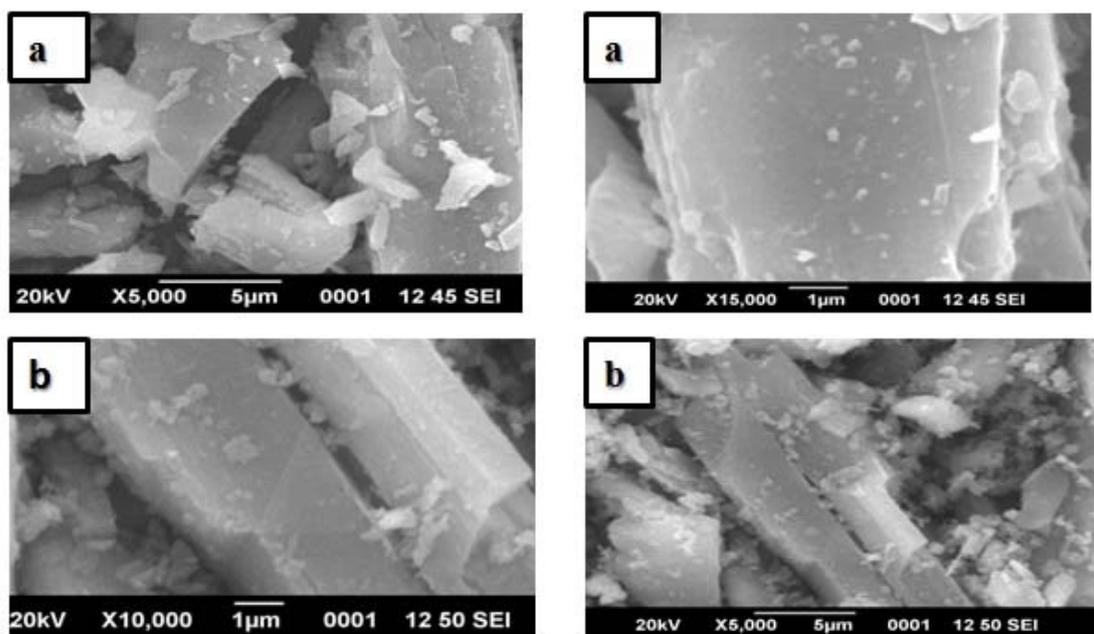


Fig. 2. SEM-images of (a) parent natural mesolite (b) dealuminated mesolite.

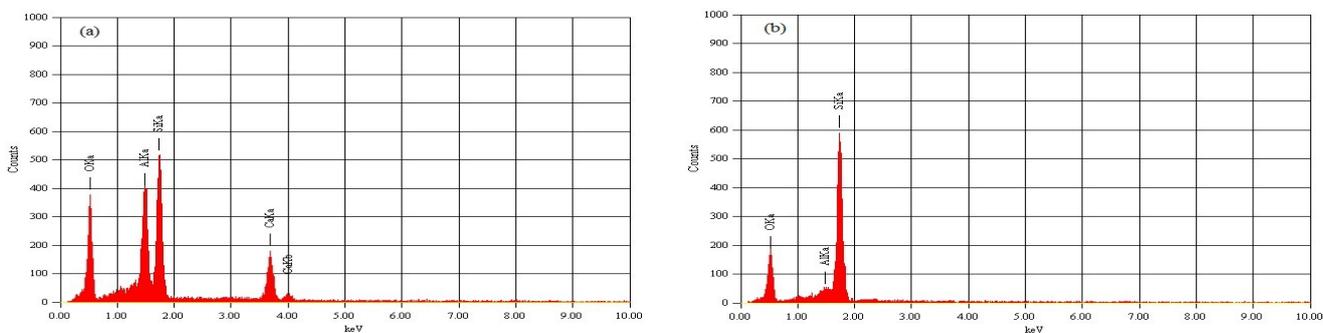


Fig. 3. EDS-Spectrum of (a) parent mesolite (b) dealuminated mesolite.

3.3. FT-IR

FT-IR Spectroscopy is used to study the framework and structural building units of zeolites. Further, this technique is also useful to identify the Bronsted and Lewis acidic sites in framework by using various probe molecules such as NH_3 , pyridine etc. [33]. Fig. 4 (a-c) shows the FT-IR spectra of the mesolite. Fig. 4 (a) shows peak at 3756 cm^{-1} is due to the Si-OH stretching vibration, 1689 cm^{-1} for the Si-OH bending mode, and 965 cm^{-1} due to the Si-O-Si or Al-O-Si stretching vibration mode [34]. Figure 4 (b) and 4 (c) show disappearance of band at 965 cm^{-1} . This may be due to breaking of Si-O-Si or Al-O-Si framework, which shows a broad band between $3479\text{-}3756 \text{ cm}^{-1}$ and confirms the presence of surface hydroxyl group i.e. Bronsted acidic center [35].

3.4. NH_3 -TPD

Fig. 5 (a) and (b) show NH_3 -TPD profile of the parent and dealuminated mesolite. Fig. 5 (a) shows two distinct peaks in the range $150\text{-}500 \text{ }^\circ\text{C}$ due to the presence of different types of acidic sites in the framework. The desorption peak observed at $196.2 \text{ }^\circ\text{C}$ is due to the presence of bridged hydroxyl group or Bronsted acidic sites while peak observed at $420.9 \text{ }^\circ\text{C}$ is due to the desorption of NH_3 from strong Lewis acidic sites. Fig. 5 (b) shows a single peak at $308.9 \text{ }^\circ\text{C}$ which is due to the desorption of ammonia from Bronsted acidic sites [36]. From (Table 1) the total acidity of parent mesolite and dealuminated mesolite is found 0.3724 and $0.5726 \text{ mmol. g}^{-1}$ respectively. Therefore, acid treated mesolite shows more acidity than the parent mesolite. This may be due to the increase in Lewis acidic sites because of dealumination. Surface area and porosity of catalysts were measured by Nitrogen adsorption desorption isotherm method (Fig. 6). The BET surface area of dealuminated mesolite was found to be $4.486 \text{ m}^2/\text{g}$, which is greater than the parent mesolite (Table 1).

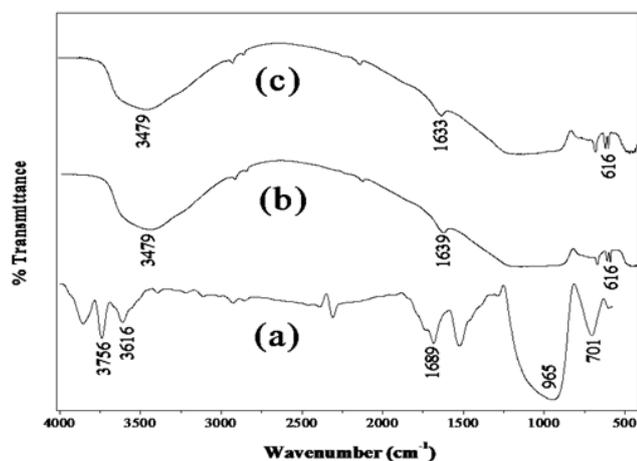


Fig. 4. FT-IR spectrum of (a) parent mesolite (b) calcined mesolite (c) dealuminated mesolite.

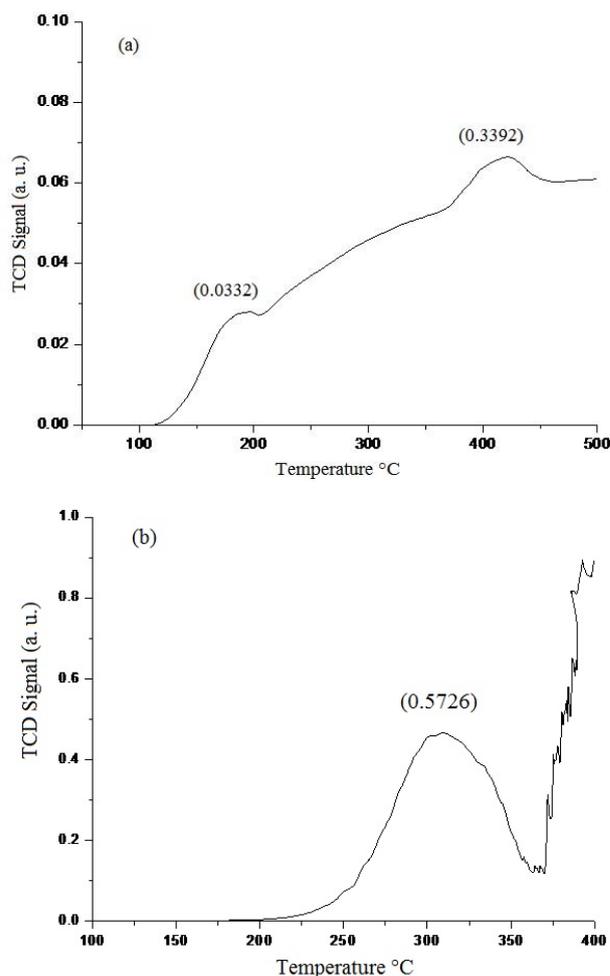


Fig. 5. (a) NH_3 -TPD of parent mesolite and (b) dealuminated mesolite.

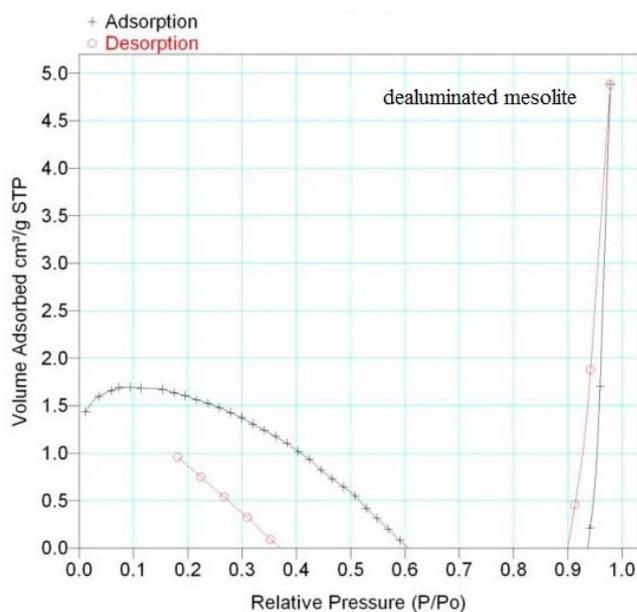


Fig. 6. Adsorption-desorption isotherm of dealuminated mesolite.

Table 1. Acid strength and BET surface area of mesolite.

Sr. No.	Catalyst	Total acidity mmol.g ⁻¹	BET surface area m ² /g.
1	Parent mesolite	0.3724	0.1485
2	Dealuminated mesolite	0.5726	4.4863

3.2 Optimization of reaction conditions

In order to investigate optimum loading of the catalyst and reaction conditions, (1mmol) 4-NO₂ aniline and (1mmol) 4-OCH₃ benzaldehyde were reacted with (1mmol) malononitrile as the model reaction with different amounts of dealuminated mesolite as the catalyst at reflux condition and results are summarized in Table 2. In the absence of the catalyst, the reaction

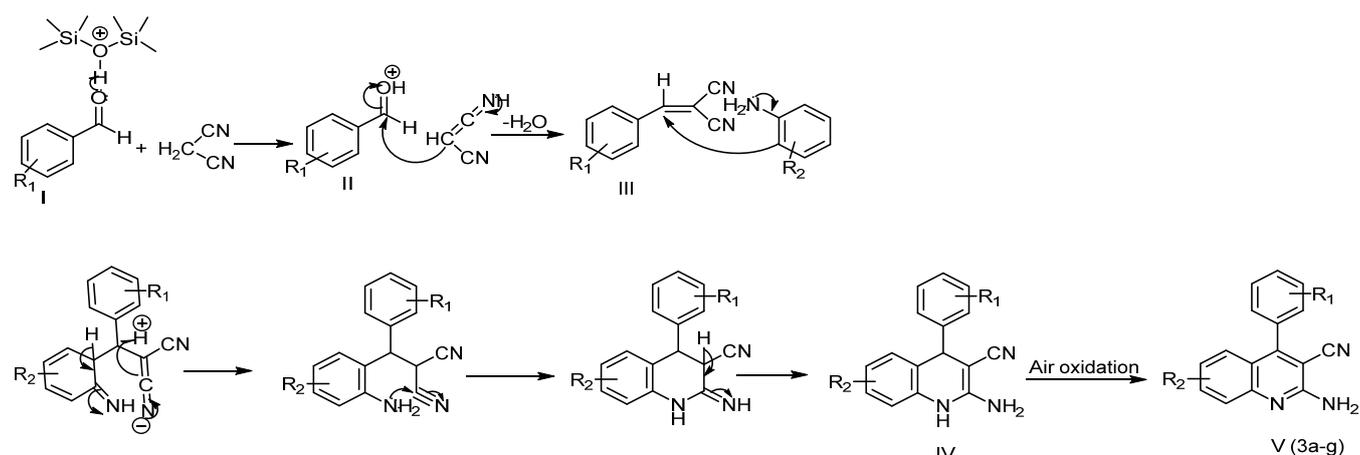
did not give the desired product (3a), which indicates a crucial role of the catalyst, 0.1 gm of dealuminated mesolite is suitable to catalyze reaction smoothly. The same reaction was carried out under different protic and aprotic solvents and it is observed that the reaction proceeds faster in protic solvents such as water and ethanol with maximum yield in reduced time as compared to non protic solvents such as tetrahydrofuran and acetonitrile which gave a lower yield (Table 2).

The plausible reaction mechanism for the mesolite catalyzed synthesis of quinoline-3-carbonitrile is depicted in Scheme 2. The reaction proceeds via Knoevengel condensation between benzaldehyde and malononitrile. The dealuminated mesolite possesses bridged hydroxyl group, which provides proton to the carbonyl oxygen thereby increasing electrophilicity of carbonyl carbon (I).

Table 2. Optimization of catalyst loading with different solvents for the synthesis of 3a.

Entry	Solvent	Catalyst amount (g)	Time (min)	Yield(%) ^a
1	Ethanol	-	120	30
2	Methanol	-	120	25
3	Acetonitrile	-	120	23
4	1,4-dioxane	-	120	27
5	Tetrahydrofuran	-	120	21
6	Water	-	120	40
7	Ethanol	0.05	30	80
8	Ethanol	0.1	30	90
9	Ethanol	0.15	30	93
10	Ethanol	0.2	30	93

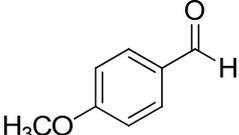
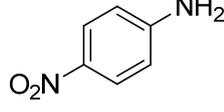
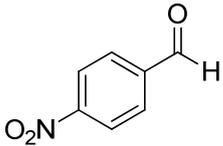
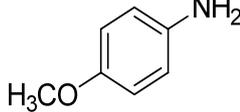
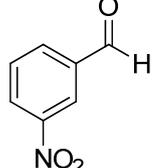
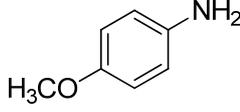
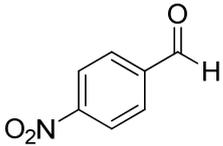
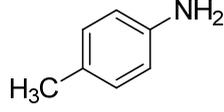
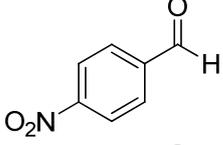
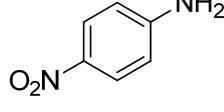
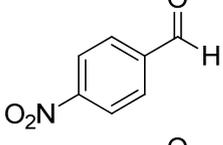
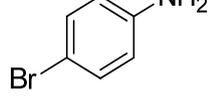
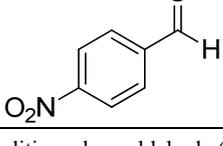
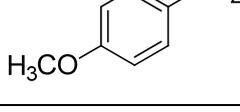
^aIsolated yield.

**Scheme 2.** Plausible reaction mechanism for synthesis of quinoline-3-carbonitrile catalyzed by dealuminated mesolite.

The malononitrile undergoes tautomerization, which results in generation active nucleophile (II) this facilitate formation of Knoevengel adduct intermediate (III). The Knoevengel adduct undergoes Michel addition with aniline followed by aromatization yields the desired product (3a-g). It is found that under optimized reaction conditions, oxidation of 2-amino-6-nitro-1,4-dihydro-4-methoxyphenyl quinoline-3-carbonitrile (IV) occurred insitu to produce 2-Amino-6-Nitro-4-(4-methoxyphenyl)-quinoline-3-carbonitrile (V). In order to explore the scope and importance of the present method, different aromatic aldehydes and

substituted anilines were tested under optimum reaction conditions for the synthesis of quinoline-3-carbonitrile and results are summarized in Table 3. The amines with electron donating groups at *para* position such as 4-OCH₃, 4-CH₃, reacted fast and gave the maximum yield in minimum time as compared to amines having electron withdrawing group such as 4-NO₂, 4-Cl. After optimizing reaction conditions, efforts were made towards recovery and reusability of the catalyst. The catalyst was separated by diluting reaction mixture by hot ethanol followed by filtration.

Table 3. Dealuminated mesolite catalyzed cyclocondensation of aromatic aldehyde, malononitrile and aniline.^a

Entry	Aldehyde (R ₁)	Aniline (R ₂)	Time (min)	Yield (%) ^b	m.p. (°C)	
					Observed	Literature ^d
3a			30	93(93,92), ^c	95-97	-
3b			30	94	136-138	133-137
3c			30	90	82-85	83-88
3d			30	93	95-96	97-98
3e			30	94	155-157	155-156
3f			30	92	176-180	174-176
3g			30	90	132-134	133-137

^aReaction conditions: benzaldehyde (1 mmol), aniline (1 mmol), malononitrile (1 mmol), catalyst 0.1g, and ethanol 15 ml.

^bIsolated yields.

^cYield after consecutive cycle.

^dAll from ref. [11].

The recovered catalyst was washed with acetone and dried at 100 °C for 1 h before the next catalytic run. Reusability of the catalyst was investigated for two times and it was found that the catalyst has retained almost consistent activity (Table 3, entry 3a).

4. Conclusions

In summary, we have successfully modified natural mesolite zeolite by H₂SO₄ treatments. The present modification method is simple and inexpensive. XRD and SEM-EDS analyses confirm the mesolite phase of natural zeolite. FT-IR analysis identifies bridged and surface hydroxyl groups present in a zeolite. NH₃-TPD analysis confirms the presence of both weak and strong acidic sites in a natural zeolite. It has been found that the active sites and surface area were increased by H₂SO₄ treatment as compared to the parent natural zeolite. The modified dealuminated mesolite is used as the heterogeneous catalyst for the synthesis of quinoline-3-carbonitrile derivatives by cyclo condensation of aldehyde, malononitrile and aniline. The present method offers remarkable advantages such as non-toxic, non-corrosive and an inexpensive reaction conditions. Simple recovery and reusability of the catalyst make the reaction successful under environmental benign conditions.

Acknowledgment

We are grateful to the Head of the Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad-431004 (MS), India for providing the laboratory facility. The authors are thankful to STIC Cochin and IIT Madras for providing characterization facilities.

References

- [1] R.C. Cioc, E. Ruijter, V.A. Romano, *Green Chem.* 16 (2014) 2958-2975.
- [2] P.M. Joseph, *Nat. Prod. Rep.* 24 (2007) 223-246.
- [3] S. Amish, Raj. Dilipsinh, *J. Saudi Chem. Soc.* 19 (2015) 73-82.
- [4] I. A. Saleh, M.A. Areej, M.A. Ahmed, N. Eman, M.G. Mostafa, *Eur. J. Med. Chem.* 45 (2010) 738-744.
- [5] A.L. Don, C.R. Elena, B. Benoit, H. Hasin-Hung, D. Latasha, J. Laure, E. Mourad, B. Katja, L.W. David, D. C. Elisabeth, *Org. Biomol. Chem.* 10 (2012) 6375.
- [6] L.Z. Shu, Z. Xin, J.Z. Shi, H. Yu. Hong, G. Ping, *Chin. Chem. Lett.* 21 (2010) 939-942.
- [7] P. Natasha, N. Raja, E. Katja, L. William, K.Z. Grace, K. Marijeta, D. Marie-Hélène, H. Marijana, *Eur. J. Med. Chem.* 80 (2014) 218-227.
- [8] K.S. Kumar, S.K. Kumar, B.Y. Shreenivas, D.R. Gorja, R. Kapavarapu, D. Rambabu, G.R. Krishna, C.M. Reddy, M.V. Basaveswara, K.V.L. Parasa, M. Pal, *Bioorg. Med. Chem.* 20 (2012) 2199-2207.
- [9] E. Debroye, G. Dehaen, V.S. Eliseeva, S, V.L. Elst, N. R. Muller, K. Binnemans, N.T. Parac-Vogt, *Dalton Trans.* 41 (2012) 10549-10556.
- [10] A.K. Salman, M.A. Abdullah, H.A. Sadd, M.F. Hassan, A.E. Sammy, *Spectrochim. Acta, Part A* 133 (2014) 141-148.
- [11] A. Khalafi-Nezhad, S. Sarikhani, E. Shaikhi Shahidzadeh, F. Panahi, *Green Chem.* 14 (2012) 2876-2884.
- [12] G.K. Nader, *Chin. J. Cat.* 35 (2014) 1858-1863.
- [13] G.M. Ziarani, N. Hosseini Nasab, M. Rahimifard, A. Abolhasani Soorki, *J. Saudi Chem. Soc.* 9 (2015) 676-681.
- [14] Y. Venkatewarlu, K.R. Kumar, P. Leelavati, *Org. Commun.* 5 (2012) 120-127.
- [15] E.A. Gilandeh, S.C. Azimia, K.R. Moghadama, A.M. Barkchaib, *Iran. J. Catal.* 3 (2013) 15-20.
- [16] A. Chandra, S. Upadhyay B. Singh, N. Sharma, M.R. Singh, *Tetrahedron Lett.* 67 (2011) 9219-9224.
- [17] J. McNulty, R. Vemula, C. Bordon, R. Yolken, J.B. Lorraine, *Org. Biomol. Chem.* 12 (2014) 255-260.
- [18] D.W. Breck, *Zeolite Molecular Sieves, Structure, Chemistry and Use.* John Wiley & Sons, New York, London, Sydney, Toronto, 1974.
- [19] S.M. Baghbanian, N. Rezaei, H. Tashakkorin, *Green Chem.* 15 (2013) 3446-3458.
- [20] E. Erdem, N. Karapinar, R. Donat, *J. Colloid Interface Sci.* 280 (2004) 309-314.
- [21] S. Wang, Z.H. Zhu, *J. Hazard. Mater.* 136 (2006) 946-952.
- [22] K. Smith, G.A. El-Hiti, *Green Chem.* 13 (2011) 1579-1608.
- [23] V.N. Sheemol, B. Tayagi, R.V. Jasara, *J. Mol. Catal. A: Chem.* 21 (2004) 201-208.
- [24] T. Pinto, P. Arquilliere. G. Niccolai, F. Lefebvre, V. Dufaud, *New J. Chem.* 39 (2015) 5300-5308.
- [25] D. Prochazkova, L. Kurfirtova, J. Pavlatova, *Catal. Today* 179 (2012) 78-84.
- [26] P. Gillet, J.M. Malezieux, J.P. Itie, *Am. Mineral.* 81 (1996) 651-657.
- [27] V. Valtchev, G. Majano, S. Mintova, J.P. Ramirez, *Chem. Soc. Rev.* 42 (2013) 263-290.
- [28] L.S. Gadekar, S.S. Katkar, S.R. Mane, B.R. Arbad, M. K. Lande, *Bull. Korean Chem. Soc.* 30 (2009) 2532-2534.
- [29] S.S. Katkar, P.H. Mohite, L.S. Gadekar, B.R. Arbad, M.K. Lande, *Green Chem. Lett. Rev.* 3 (2010) 287-292.
- [30] L.S. Gadekar, B.R. Arbad, M.K. Lande, *Bull. Korean Chem. Soc.* 30 (2009) 2532-2534.
- [31] M.M.J. Treacy, J.B. Higgins, *Collection of Simulated XRD Powder Patterns for Zeolites*, 5th ed., Amsterdam: Elsevier (2007).
- [32] S. Stefanidis, K. Kalogiannis, E.F. Iliopoulou, A.A. Lappas, J. Martínez Triguero, M.T. Navarro, A. Chicab F. Rey, *Green Chem.* 15 (2013) 1647-1658.

- [33] J.N. Kondo, R. Nishitani, E. Yoda, T. Yokoi, T. Tatsumi, K. Domen. *Phys. Chem.* 12 (2010) 11576-11586.
- [34] P.E. Poh, H. Nur, M.N.M. Muhid, H. Hamdan, *Catal. Today* 114 (2006) 257-262.
- [35] R.S. Rathod; A.B. Gambhire; B.R. Arbad, M.K. Lande, *Bull. Korean Chem. Soc.* 31 (2010) 339-343.
- [36] S. Narayan, J.J. Viaya, S. Sivasanker, M. Alam, P. Tamizhdurai, L.J. Kennedy, *Polyhedron* 89 (2015) 289-296.