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Application of unmodified microporous molecular sieves for the synthesis of poly functionalized pyridine derivatives in water

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ABSTRACT

In the present work, catalytic activity of acidic as well as basic sites present over the microporous molecular sieves has been demonstrated. These acid–base sites display the combined catalytic reactivity in tap/deionized water for the efficient synthesis of poly functionalized pyridine derivatives. During this study, testing of various solvents revealed the suitability of tap water as a reaction medium, due to its highly polar nature, presence of alkali and alkaline earth metal ions in it and hydrophobic interactions between the surface of molecular sieves and organic molecules. Most importantly, unmodified microporous molecular sieves have been used for the first time in water for organic transformation. This synthetic strategy works under essentially neutral conditions by conventional as well as ultrasound method.

1. Introduction

Organic reactions/transformations on solid supported catalysts represent a viable and convenient alternative to traditional synthetic processes realized under homogeneous conditions [1]. In the last decades, new classes of solid adsorbents/catalysts have been developed as microporous and nanoporous materials, such as silica gel, activated carbon fibers, zeolites, clays, alumina, and polymer resins. [2]. Current development in the use of these heterogeneous catalysts in combination with aqueous media is attracting a great deal of interest [3], since it offers significant environmental impact and is becoming an intense area of research in view of green chemistry.

Microporous materials with different structure and tunable pore diameters have been receiving much attention in the field of adsorption and catalysis owing to their unique textural properties [4]. In particular, zeolites, which are uniform microporous materials, have become extremely successful as clean, selective and recyclable catalysts for oil refining, petrochemistry and organic synthesis in the production of fine chemicals [5]. More significantly, it has been proved that zeolites and related crystalline molecular sieves can possess catalytically active sites, pores with uniform size/shape and voids that allow for their industrial use as shape-selective catalysts [6,7] based upon structure–property correlation.

Microporous molecular sieves i.e., zeolites are crystalline aluminosilicates with a framework consisting of SiO_4^- and AlO_4^- tetrahedral units (T-atoms) connected *via* the oxygen atoms at the corner point of tetrahedron [5]. Interestingly, it has been disclosed by the extensive research of many scientists, that these materials do possess acidic as well as basic properties [5,8,9]. It has been established that acidic nature mainly comes from the Brønsted and Lewis acid sites. Lewis acidity has been linked to tetrahedral Al atoms (Al^{3+}) and this Aluminium framework is assumed to be highly active ingredients in aluminosilicates. This aluminium site generates a negatively charged lattice and compensation of the resulting negative charge by a proton gives rise to Brønsted acid sites [10]. Moreover, basicity is related to framework oxygen (O^{2-}) present in the Al–O–Si bridging and ability of zeolites for ion exchange. Exchanging zeolites with a less electronegative charge balancing cation makes them more basic by shifting to lower O_{1s} binding energies [8,11].

This catalytic potential is clearly reflected in its high performance towards various acid/base catalyzed reactions [4,8,9b,12]. Although these materials possess such outstanding textural and catalytic properties, unfortunately, to the best our knowledge there has been few reports on their use as a catalyst, specially as an acid–base bifunctional catalyst [11] in organic transformations. Encouraged by this, we planned for the exploitation of the catalytic reactivity of microporous molecular sieves for the synthesis of pyridine derivatives.

Pyridines have been emerged as a versatile class of nitrogen containing bioactive heterocycles, because of its highly pronounced

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biological and physiological activities [13–21]. Poly functionalized pyridine derivatives especially bearing nitrile functionality have been reported to be endowed with their potential applications as potassium channel openers in the treatment of urinary incontinence [15], and their use as anti-prion [14a,16], anti-hepatitis B virus [14c] anti-bacterial [17] and anti-cancer [18] agents.

One of the most attractive routes for the synthesis of these compounds involves the cyclocondensation of aldehyde, malononitrile and thiol. Various synthetic protocols have been developed following this route with intervention of different basic [16a,21] as well as acidic catalysts [22] with their own merits and demerits. Few notable drawbacks of these routes are harsh reaction conditions, non-reusability of catalytic systems, and use of non-aqueous solvents. Even though, in this endeavor, some heterogeneous catalysts like silica nanoparticles [23a] and nanocrystalline magnesium oxide [23b] have been utilized, some limitations like commercial unavailability, longer reaction times and use of non-aqueous solvents hamper their application. Above discussed drawbacks of the reported methods prompted us to undertake the work for the development of highly efficient route for this cyclocondensation.

Considering the above discussed significance of microporous molecular sieves in catalysis and in continuation of our interest towards the development of ecofriendly synthetic protocols [24], herein, attempt has been made to carry out the cyclocondensation of aldehyde, malononitrile and thiol using microporous molecular sieves 4A in water for obtaining the desired pyridine derivatives. Most importantly, unmodified microporous molecular sieves have been used for the first time in water for organic transformation.

2. Experimental

2.1. General

All chemicals were purchased and used without any further purification. Melting points were recorded on a Veego apparatus and are uncorrected. Infrared spectra were recorded on a Bruker spectrophotometer in a KBr disc, and the absorption bands are expressed in cm^{-1}. ^1H NMR spectra were recorded on a Varian AS 400 MHz spectrometer in DMSO-d_6, chemical shifts (δ) are in (parts per million) ppm relative to TMS. ^{13}C NMR spectra were recorded on NMR spectrometer AC 200 in $CDCl_3$ and Varian AS 400 MHz spectrometer in DMSO-d_6. Mass spectra were recorded on a macro mass spectrometer (waters) by electro-spray (ES) method. Bandelin Sonorex (with a frequency of 35 KHz and a nominal power 200 W) ultrasonic bath was used for ultrasonic irradiation with Built-in heating, 30–80 °C thermostatically adjustable. The reaction vessel was placed inside the ultrasonic bath containing water.

2.2. Typical experimental procedure

(A) *Conventional method*: A mixture of *p*-chloro benzaldehyde **1a** (106 mg, 1 mmol), malononitrile **2** (132 mg, 2 mmol), thiophenol **3a** (110 mg, 1 mmol) and MS 4A (200 mg) in tap water (5 mL) was vigorously stirred at reflux condition. Reaction progress was monitored by TLC (ethyl acetate/*n*-hexane, 1:7). After completion of the reaction, reaction mixture was cooled to RT and extracted with ethyl acetate (5 mL × 5 mL) to remove the product from reaction mass. Then, separated organic layer was concentrated under reduced pressure to get the solid product. Thus obtained crude product (**4a**) was recrystallized from aqueous ethanol to have pure product.

(B) *Ultrasound method*: A mixture of *p*-chloro benzaldehyde **1a** (106 mg, 1 mmol), malononitrile **2** (132 mg, 2 mmol), thiophenol **3a** (110 mg, 1 mmol) and MS 4A (200 mg) in tap water (5 mL) was subjected to ultrasound irradiation at room temperature. Reaction progress was monitored by TLC (ethyl acetate/*n*-hexane, 1:7). After completion of the reaction, reaction mixture was extracted with ethyl acetate (5 mL × 5 mL) to remove the product from reaction mass. Then, separated organic layer was concentrated under reduced pressure to get the solid product. Thus obtained crude product (**4a**) was recrystallized from aqueous ethanol to have pure product.

2.3. Spectral data of representative compounds

2-Amino-4-(4-chlorophenyl)-6-phenylsulfanylpyridine-3,5-dicarbonitrile (4a): ^1H NMR (400 MHz, DMSO-d_6): δ 7.46–7.49 (m, 3H, Ar-H), 7.57 (d, 2H, J = 8.0 Hz, Ar-H), 7.59 (d, 2H, J = 8.0 Hz, Ar-H), 7.64 (d, 2H, J = 8.0 Hz, Ar-H) 7.83 (br s, 2H, $-NH_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 87.19, 93.32, 114.78, 115.19, 117.12, 125.38, 127.61, 128.92, 130.18, 130.43, 132.74, 135.29, 157.82, 159.61, 166.09; IR (KBr, cm^{-1}): ν 3489, 3342, 3221, 2216, 1628, 1544, 1487, 1259, 1091, 839, 791; ES-MS: 363.04 (M^+), 365.03 (M + 2).

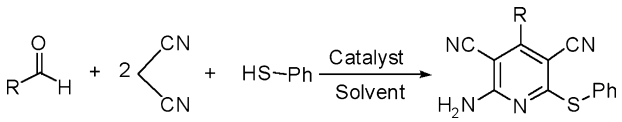
2-Amino-4-(benzo[d][1,3]dioxol-5-yl)-6-phenylsulfanylpyridine-3,5-dicarbonitrile (4h): ^1H NMR (400 MHz, DMSO-d_6): δ 6.12 (s, 2H, $-O-CH_2-O-$), 7.00–7.03 (m, 1H, Ar-H), 7.07 (d, 1H, J = 8.0 Hz, Ar-H), 7.14 (d, 1H, J = 1.2 Hz, Ar-H) 7.46–7.48 (m, 3H, Ar-H), 7.55–7.57 (m, 2H, Ar-H), 7.72 (br s, 2H, $-NH_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 92.42, 98.74, 107.08, 113.79, 114.13, 120.40, 120.65, 128.29, 132.40, 132.51, 134.67, 134.89, 140.07, 152.62, 154.25, 163.37, 164.95, 171.38; IR (KBr, cm^{-1}): ν 3458, 3338, 3229, 2907, 2217, 1636, 1558, 1492, 1251, 1037, 825; ES-MS: 373.14 (M^+).

2-Amino-4-(thiophen-2-yl)-6-phenylsulfanylpyridine-3,5-dicarbonitrile (4i): ^1H NMR (400 MHz, DMSO-d_6): δ 6.68 (t, 1H, J = 4.0 Hz, Ar-H), 7.24 (d, 1H, J = 4.0 Hz, Ar-H), 7.32–7.35 (m, 3H, Ar-H), 7.42–7.45 (m, 2H, Ar-H), 7.61 (br s, 2H, $-NH_2$), 7.94 (d, 1H, J = 4.8 Hz, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 82.46, 91.10, 112.92, 115.65, 116.13, 117.32, 127.30, 129.36, 129.96, 135.89, 143.38, 145.46, 145.91, 159.98, 169.98; IR (KBr, cm^{-1}): ν 3438, 3360, 3210, 2984, 2210, 1617, 1512, 1257, 1064, 722; ES-MS: 335.07 (M^+).

2-Amino-4-(furan-2-yl)-6-phenylsulfanylpyridine-3,5-dicarbonitrile (4j): ^1H NMR (400 MHz, DMSO-d_6): δ 7.26 (t, 1H, J = 4 Hz, Ar-H), 7.46–7.48 (m, 3H, Ar-H), 7.54–7.58 (m, 3H, Ar-H), 7.79 (br s, 2H, $-NH_2$), 7.93 (d, 1H, J = 5.2 Hz, Ar-H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 87.17, 99.01, 114.65, 115.07, 119.06, 126.99, 129.42, 129.52, 130.81, 131.52, 135.83, 137.47, 157.16, 159.27, 159.72, 169.41; IR (KBr, cm^{-1}): ν 3380, 3328, 3210, 2992, 2215, 1650, 1518, 1264, 1029, 766; ES-MS: 319.09 (M^+).

2-Amino-4-(4-hydroxy-3-methoxyphenyl)-6-(2-amino-phenylsulfa-nyl)pyridine-3,5-dicarbonitrile (4m): ^1H NMR (400 MHz, DMSO-d_6): δ 3.80 (s, 3H, $-OCH_3$), 5.37 (s, 2H, $-NH_2$(–thiophenol ring)), 6.57 (dt, 1H, J = 1.2 and 7.6 Hz, Ar-H), 6.77 (dd, 1H, J = 0.8 and 8 Hz, Ar-H), 6.91–6.98 (m, 2H, Ar-H), 7.12 (d, 1H, J = 1.6 Hz, Ar-H), 7.18 (dd, 1H, J = 1.6 and 7.6 Hz, Ar-H), 7.23 (dd, 1H, J = 1.2 and 7.6 Hz, Ar-H), 7.57 (br s, 2H, $-NH_2$(–pyridine ring)), 9.65 (s, 1H, –OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 57.43, 83.34, 96.01, 111.99, 115.61, 127.15, 127.55, 128.08, 129.38, 130.02, 130.52, 131.47, 135.85, 150.43, 159.54, 163.21, 169.71, 170.61; IR (KBr, cm^{-1}): ν 3473, 3348, 3290, 2958, 2212, 1625, 1533, 1281, 1063, 756; ES-MS: 390.02 (M^+).

2-Amino-4-(4-chlorophenyl)-6-(2-amino-phenylsulfanyl)pyridine-3,5-dicarbonitrile (4o): ^1H NMR (400 MHz, DMSO-d_6): δ 5.39 (s, 2H, $-NH_2$(–thiophenol ring)), 6.56 (dt, 1H, J = 0.8 and 7.6 Hz, Ar-H), 6.78 (d, 1H, J = 8.0 s Hz, Ar-H), 7.18 (dt, 1H, J = 0.8 and 7.6 Hz, Ar-H), 7.23 (dd, 1H, J = 1.2 and 7.6 Hz, Ar-H), 7.55 (dd, 2H, J = 2.0 and 6.4 Hz, Ar-H), 7.65 (dd, 2H, J = 1.6 and 6.4 Hz, Ar-H), 7.72 (br s, 2H, $-NH_2$(–pyridine ring)); ^{13}C NMR (100 MHz, DMSO-d_6): δ 87.04, 94.20, 108.11, 115.74, 116.00, 116.18, 117.07, 129.61, 131.10, 132.42, 133.60, 135.97, 137.88, 151.90, 157.94, 160.25, 167.48; IR (KBr, cm^{-1}): ν 3465, 3354, 3281,



Scheme 1. Standard model reaction.

2219, 1632, 1527, 1269, 1020, 764; ES-MS: 378.01 (M^+), 380.12 (M + 2).

3. Results and discussion

For our initial optimization studies, one-pot three-component condensation of 4-chloro benzaldehyde (**1a**), malononitrile (**2**) and thiophenol (**3a**) was considered as a standard model reaction (Scheme 1). To effect the model reaction, evaluation of various solvents were carried out against Molecular sieves 4A (MS 4A) as a solid catalyst. Taking into account of literatures regarding excellent performance of heterogeneous catalysts in organic solvents, various non-aqueous solvents, such as, ethanol, methanol, toluene, acetonitrile, 1,4-dioxane and THF were tested at ambient temperature as well as their respective reflux conditions. Unfortunately, at ambient temperature these solvents remained unsuccessful to afford the desired product even after prolonged reaction time, whereas at reflux temperatures product was not getting in acceptable yields.

In subsequent optimization experiments, efforts were directed towards the use of water as a solvent. Increasing interest of organic chemists for the use of water as a solvent of choice and its unique properties [3] turned our attention to examine it for the present reaction. To our surprise, reaction in aqueous media was observed to proceed towards the desired product and reaction got completed after a prolonged reaction time (12 h) in 74% yield (Table 1, entry 1). Therefore, in an attempt to reduce the reaction time and increase the product yield, model reaction was tested at higher temperatures like 60 °C, 80 °C and reflux condition and enormous decrease in reaction time was observed along with increase in the reaction temperature with respective 67%, 72% and 88% yield (Table 1, entries 2–4).

Careful literature survey reveals that, first step of the reaction, i.e., knoevenagel condensation can be easily achieved in protic solvents like water at room temperature without need of any catalyst though the net result is dehydration [25], whereas the subsequent steps presumably involving Michael addition, s-Alkylation and cyclization requires intervention of catalyst, since uncatalyzed reaction does not lead to the formation of final product. Hence, although MS 4A was found to be an effective solid medium for the model reaction in water, variety of solid promoters such as Montmorillonite K10, Celite 545, Amberlyst 15, neutral alumina and silica gel were examined in order to improve the efficiency of results obtained in our initial study. When Montmorillonite K10 and Amberlyst 15 were used as catalyst, reaction afforded only knoevenagel condensation product of aldehyde and malononitrile (Table 1, entries 8 and 9). Whereas, Celite 545 resulted into 41% yield along with some side products (Table 1, entry 10). In case of neutral alumina, desired product was obtained in only 48% yield (Table 1, entry 11). In comparison, Silica gel 60 afforded the product in good yield (Table 1, entry 12). As a matter of fact, MS 4A stood out as an excellent solid promoter in aqueous medium with a dramatic influence on the reaction and revealed its suitability as a catalyst of choice for further optimization. This fact could be attributed to the effect of solvent on catalyst for the efficient catalysis. It discloses that water plays a crucial role in the activation of catalyst.

To know the exact role of water, reaction was performed under solvent-free conditions. But, it did not proceed after knoevenagel condensation of aldehyde and malononitrile at room temperature (Table 1, entry 5) as well as heating conditions up to 120 °C (Table 1, entry 6). From this, it was concluded that subsequent steps required for the formation of desired product needs some further driving forces that cannot be achieved under neat conditions.

Thereafter, with the support of ion exchange capacity of zeolites and application of ion-exchanged zeolites for base catalyzed reactions [8,11] made us to think that the water used in our earlier studies was tap water which might contains the ions that can readily exchange sodium ions from zeolite. These zeolites on ion exchange with less electronegative charge balancing cation ultimately affects the oxygen sites making them more basic by shifting to lower O_{1s} binding energies [8,11]. Additionally, it is worthy to point out that sodium ions can also be exchanged with H^+ ions if they are present in the solution giving rise to highly acidic Brønsted acid sites [5,9]. In an order to confirm the effect of ions present in tap water, reaction was carried out in deionized water instead of tap water, and it was noticed that in comparison with tap water, deionized water needed more reaction time (3 h) and delivered the product in 81% yield (Table 1, entry 7).

This experiment suggested that it would be beneficial to employ tap water as a reaction medium for further studies to obtain the best yield of pyridine derivatives in the shortest possible reaction time.

At first site, it seems reasonable that MS in water favors the reaction, because organic substrates would be expected to be firmly

Table 1
Screening of catalysts, solvents and reaction temperature.[a]

Entry	Catalyst	Solvent	Temperature (°C)	Time	Yield (%)[b]
1	MS 4A	Tap water	RT	12 h	74
2	MS 4A	Tap water	60	4 h	67
3	MS 4A	Tap water	80	4 h	72
4	MS 4A	Tap water	Reflux	60 min	88
5	MS 4A	–	RT	12 h	Nil
6	MS 4A	–	120	4 h	Nil
7	MS 4A	Deionized water	Reflux	3 h	81
8	Montmorillonite K10	Tap water	Reflux	60 min	Nil
9	Amberlyst 15	Tap water	Reflux	60 min	Nil
10	celite 545	Tap water	Reflux	60 min	41
11	Neutral alumina	Tap water	Reflux	60 min	48
12	Silica gel 60	Tap water	Reflux	60 min	79

[a] Reaction conditions: **1a** (1 mmol), **2** (2 mmol), **3a** (1 mmol), Catalyst (200 mg), in solvent (5 mL).
[b] Isolated yields.

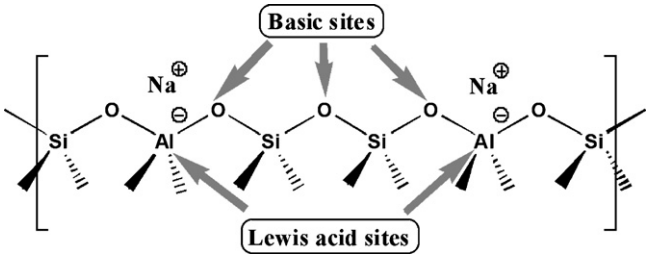


Fig. 1. Basic structure of microporous molecular sieves (zeolites); (a) Acidic nature is related to Lewis acid sites due to framework Al^{3+} and (b) Basicity is related to framework oxygen (O^{2-}).

adsorbed over MS by hydrophobic interactions between the surface of molecular sieves and organic molecules, whereas, unsuitability of non-aqueous solvents for the reaction may be attributed to homogenization of organic substrates within them, which might be causing in less firm adsorption of organic molecules on the surface of catalyst.

Particularly, success of MS 4A could be attributed to the acid and basic sites present over its surface as well as at the aperture of pores. Organic substrates get firmly adsorbed over these uniformly located active sites, thus increasing their reactivity and causing the reaction in its favor. Water being highly polar in nature with its ability of hydrogen bonding might be playing a key role in activation of acid as well as basic sites located over molecular sieves.

Presence of acidic sites in MS corresponds to the framework Al^{3+} [5,11] which act as Lewis acid sites and perform the role of acid catalyst, whereas, presence of Basic sites in MS is related to the framework oxygen (O^{2-}) located at the Al–O–Si bridging present in molecular sieves [8,11] that execute the function of basic catalyst (Fig. 1).

Water due to its ability of hydrogen bonding helps in enhancement of acidic nature of MS by partial hydrogen boding with Al^{3+} atoms, which results in the increased acidic property of these Lewis acid sites. To talk about the activation of basic sites in MS, it is important to consider that tap water contains alkali and alkaline earth metal ions which readily get exchange with the sodium ions from MS. This ion exchange with less electronegative charge balancing cation affects the oxygen sites by shifting them to lower O_{1s} binding energies [8,11] and outcome of this is the improved basicity of the basic sites (O^{2-}). In this way tap water assists in the activation of acidic and basic sites in Molecular sieves (MS).

In conclusion, presence of Lewis acid sites (Al^{3+}) and basic sites (O^{2-}) situated over large surface area of molecular sieves, assistance of ions present in tap water causing the improvement in basic nature of O^{2-}, and hydrophobic interactions between the surface of molecular sieves and organic molecules shows the combined effect and creates the required driving forces for the completion of reaction. A probable mechanistic path leading to the formation of desired pyridine derivatives is depicted in Fig. 2.

Due to heterogeneous nature of the catalyst, some additional studies were performed to test the reusability of the catalytic system. Model reaction was carried out over four cycles using the same catalytic system, which was recovered simply by extracting the product from aqueous reaction mixture with ethyl acetate. Reused catalytic system was found to be efficient, without much loss in product yield. Practically observed fall in yield after successive runs may be due to little bit loss of catalyst during each recovery process (Table 2).

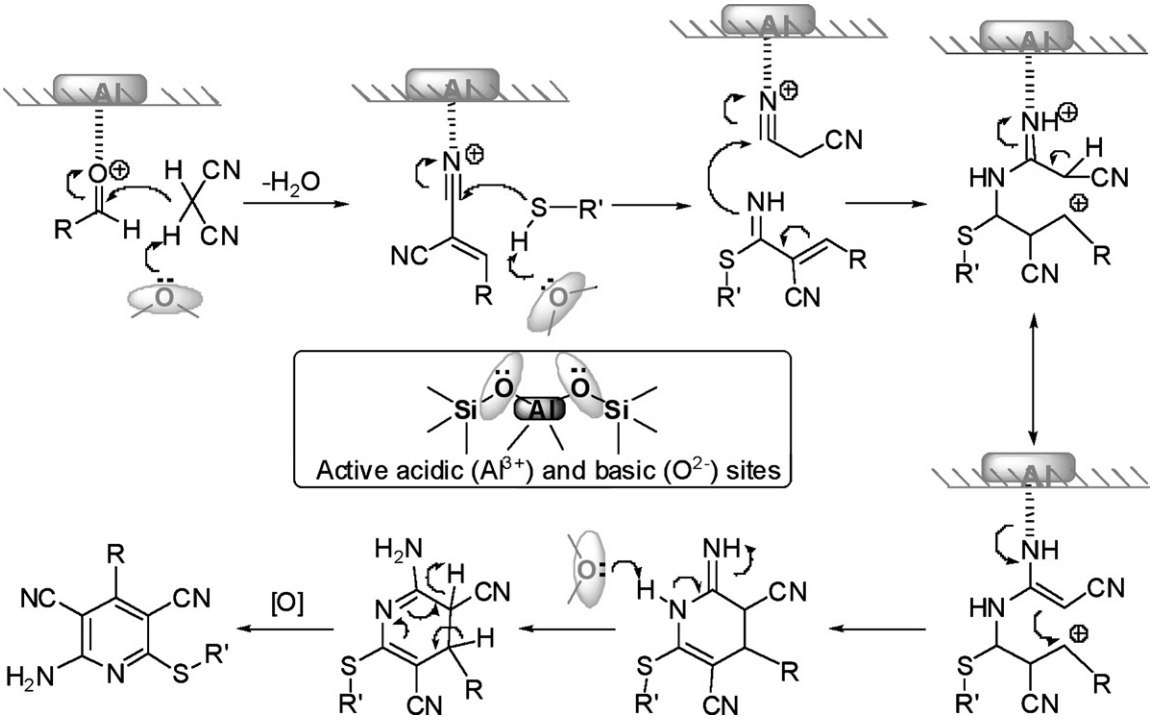


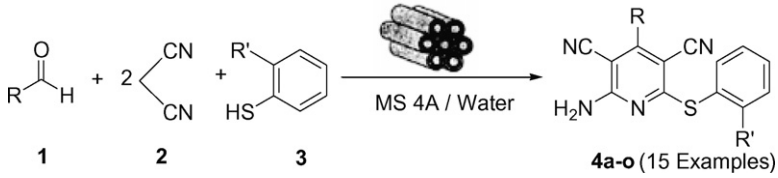
Fig. 2. Plausible mechanism for the synthesis of pyridine.

Table 2
Study of catalyst amount, its recycling and reuse.[a]

Run	Catalyst (mg)	Time (min)	Yield (%)[b]
1	50, 100, 200, 500	60	47, 65, 88, 89
2	200	60	84
3	200	90	81
4	200	120	79

[a] Reactions of **1a** (1 mmol), **2** (2 mmol), **3a** (1 mmol) and MS 4 A (200 mg) in tap water (5 mL) at reflux temperature were conducted for respective time period. Thereafter, reaction mixture was cooled to RT and extracted with ethyl acetate (5 mL × 5 mL) to remove the product from reaction mass. Thus, remaining aqueous suspension with MS 4A was reused for next run.
[b] Isolated yields.

Table 3
Synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines.[a]



	Entry compounds	R	R′	Time (min)	Yield (%)[b]	M.P. (°C)[c]
				A/B	A/B	
1	**4a**	4-Cl-Ph	H	60/40	88/89	221–222
2	**4b**	Ph	H	70/45	84/85	217–218
3	**4c**	4-F-Ph	H	50/40	87/85	225–226
4	**4d**	4-OH-Ph	H	75/50	83/86	315–317
5	**4e**	4-NO_2-Ph	H	45/30	88/90	289–290
6	**4f**	4-Me-Ph	H	60/50	83/87	206–207
7	**4g**	3,4-OMe-Ph	H	70/55	82/83	225–227
8	**4h**	Piperonyl	H	70/50	89/90	231–232
9	**4i**	2-Thienyl	H	110/60	79/81	209–210
10	**4j**	2-Furfuryl	H	120/70	78/79	178–180
11	**4k**	4-OMe-Ph	NH_2	55/45	85/84	229–231
12	**4l**	4-NO_2-Ph	NH_2	40/30	90/86	207–208
13	**4m**	4-OH-3-OMe-Ph	NH_2	45/35	91/90	233–235
14	**4n**	Ph	NH_2	65/50	83/85	226–228
15	**4o**	4-Cl-Ph	NH_2	65/40	87/87	234–236

[a] Reaction conditions: **1** (1 mmol), **2** (2 mmol), **3** (1 mmol), MS 4A (200 mg), in tap water (5 mL).
[b] Isolated yields.
[c] Melting points match with literature reports. [16,20–23] A = conventional method and B = ultrasound method.

To establish the appropriate amount of the catalyst (MS 4A), we investigated the model reaction using varied amounts of MS 4A such as 50, 100, 200 and 500 mg, and formation of product was observed in 47%, 65%, 88%, and 89% yield, respectively (Table 2, run 1). This indicated that 200 mg of MS 4A was sufficient to carry out the reaction smoothly.

Ultrasound technique has increasingly been used in organic synthesis in the recent years. Simple experimental procedure, very high yields, increased selectivities and clean reaction of many ultrasound induced organic transformations offer additional convenience in the field of synthetic organic chemistry [26]. Assistance of ultrasonic irradiation efficiently shortens the reaction times due to acoustic cavitation, which is the driving force of this phenomenon, especially, when at least one of the phases of the reaction mixture is liquid. Hence, with thiophenol as one of the liquid component of our reaction mixture we further investigated the model reaction using optimized reaction conditions under ultrasound irradiation with a view to explore whether, (i) the reaction could be expedited and (ii) the product yield could be enhanced. No significant improvement in the product yield (89%) was achieved, but the reaction time enormously reduced to 40 min at ambient temperature as compared to conventional reflux method (60 min).

Having established the optimum experimental conditions for obtaining the best yields of the poly functionalized pyridines, variety of electronically divergent aldehydes with respect to thiophenol and 2-amino thiophenol were examined under conventional and ultrasound method. Presence of electron-withdrawing and electron-releasing groups on the aromatic rings did not influence significant effect on the yields. More importantly, various heteryl aldehydes were observed to be well tolerated under optimized conditions furnishing the product in excellent yields. All the results are compiled in Table 3. Formation of the desired product was confirmed with the help of IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopic data.

In summary, an efficient catalytic activity of acidic as well as basic sites located over microporous molecular sieves and their activation in tap water at higher temperatures has been demonstrated. It is for the first time, to our knowledge, that molecular sieves has been utilized in water as a reaction medium. Present synthetic strategy works efficiently under conventional as well as ultrasound irradiation method. Various remarkable advantages, such as, non-toxic, inexpensive and easily available catalyst, aqueous reaction conditions, high isolated yields, reusability of catalytic system and reduced reaction times contributes to make this proto-

col attractive. This catalytic system could act as a key for achieving various organic transformations.

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