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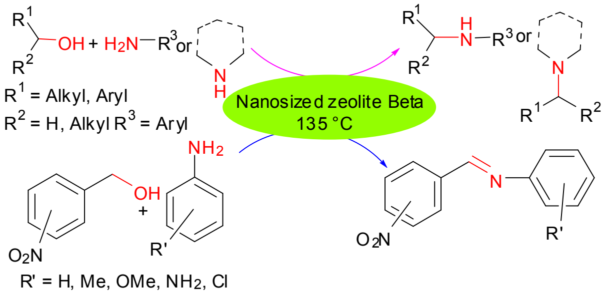
N-Alkylation of amines with alcohols over nanosized zeolite Beta

Marri Mahender Reddy, Macharla Arun Kumar, Peraka Swamy, Mameda Naresh, Kodumuri Srujana, Lanka Satyanarayana, Akula Venugopal and Nama Narender*

Nanosized zeolite Beta is highly active and selective catalyst for the synthesis of higher amines from amines and alcohols is reported.



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ARTICLE TYPE

N-Alkylation of amines with alcohols over nanosized zeolite Beta

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Direct N-alkylation of amines with alcohols was successfully performed by using nanosized zeolite Beta, which showed the highest catalytic activity among other conventional zeolites. This method has several advantages such as, eco-friendly, moderate to high yields, simple work-up procedure, catalyst was successfully recovered and reused without significant loss of activity and only water is produced as co-product. In addition, imines also efficiently prepared from the tandem reactions of amines with 2, 3 and 4-nitrobenzyl alcohols using nanosized zeolite Beta.

Introduction

Carbon-nitrogen bond-forming reaction is one of the most important transformation in organic chemistry and which plays a vital role in the elaboration and composition of biological and chemical systems.[1] N-Alkylation of amines is of fundamental importance in organic synthesis because resulting higher amines have widely been used as synthetic intermediates for pharmaceuticals, agrochemicals, fine chemicals, dyes, surfactants and functionalized materials.[2]

The most frequently used method for the preparation of N-alkyl amines is the coupling of amines with alkyl halides[3] in the presence of stoichiometric amounts of inorganic bases, but this method is often associated with environmental problems. Toxic nature of alkyl halides and related alkylating agents, the selectivity to the desired secondary amines is generally low. In addition, this reaction produces large amounts of (in)organic salts. Reductive amination of carbonyl compounds with amines[4] is the another known route to higher-order amines, which requires the use of strong reducing agents or hydrogen gas.

An alternative environmentally-benign approach to these methods is the N-alkylation with alcohols as alkylating agents. The advantage of the use of alcohols instead of alkyl halides/carbonyl compounds are, that it produces only water as by-product, high atom efficiency, avoiding the use of toxic reagents and stoichiometric reducing agents. Until now, many homogeneous transition metal complexes and salts such as, ruthenium,[5] rhodium,[6] iridium,[7] palladium,[8] gold,[9] nickel,[10] copper[11] and iron[12] catalysts, have been reported for the N-alkylation of amines with alcohols. However, these homogeneous catalytical systems have disadvantages of the recovery and reuse of expensive catalysts and / or the indispensable use of co-catalysts such as bases and stabilizing agents. Transition metal-free protocols have also been reported, although they normally require harsh reaction conditions (high temperatures and pressures) to achieve reasonable yields of products.[13]

However, in these environmentally conscious and economically pressured days, homogeneous catalysts are no longer acceptable because of inherent problems, such as corrosion, toxicity, difficulty in catalyst handling, separation from the reaction system, high cost and the creation of (in)organic waste. Consequently, it has long been appreciated that the use of alternative solid (heterogeneous) catalysts to replace homogeneous catalysts is the ultimate goal in catalysis science and engineering. Heterogeneous catalysts have many advantages over homogeneous ones, such as low cost, tolerance to a wide range of temperatures and pressures, easy and inexpensive removal from the reaction mixture by simple filtration or centrifugation, easy and safe disposal, safe storage, long lifetime, eco-friendly nature, regenerability and reuse.

Although there are several reports on the N-alkylation using heterogeneous catalysts,[14] most of them suffer from harsh reaction conditions, low turnover numbers (TONs) and frequencies (TOFs), limited substrate scope and catalysts having poor recyclabilities. Therefore, the development of more active and selective heterogeneous catalysts for the N-alkylation of amines with alcohols is still challenging.

Catalysts based on various zeolites posses major importance both in petroleum and fine chemical industries.[15] This is mainly due to the zeolites have uniform channel size, unique molecular shape selectivity, as well as strong acidity and good thermal/hydrothermal stability. The BEA-type of zeolite consists of an intergrowth of two or more polymorphs comprising of a three dimensional system of 12-membered ring channels.[16] Zeolite Beta has pore diameters of 0.76×0.64 nm and 0.55×0.55 nm. The BEA framework topology attracts much attention

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because of the large available micropore volume, large-pore channel system and the presence of active sites in different concentrations that are useful in a number of acid-catalyzed reactions.[17]

However, zeolites often exhibit insufficient activity and/or fast deactivation, mainly due to poor diffusion efficiency.[18] The slow transport in the zeolite micropores leads to slow reaction rates or unwanted secondary side reactions resulting from long residence times. In order to benefit fully from the unique sorption and shape-selectivity effects in the micropores without suffering from diffusional limitations, the diffusional path length in the micropores should be very short.[19] Nanosized zeolite crystals with narrow particle size distributions and sizes less than 100 nm have received much attention because of their great potential applications in catalysis and adsorption. The reduction of particle size from the micrometer to the nanometer scale leads to substantial changes in the properties of the material. The decrease in the crystal sizes results in high external surface areas, reduced diffusion path lengths and more exposed active sites.[20]

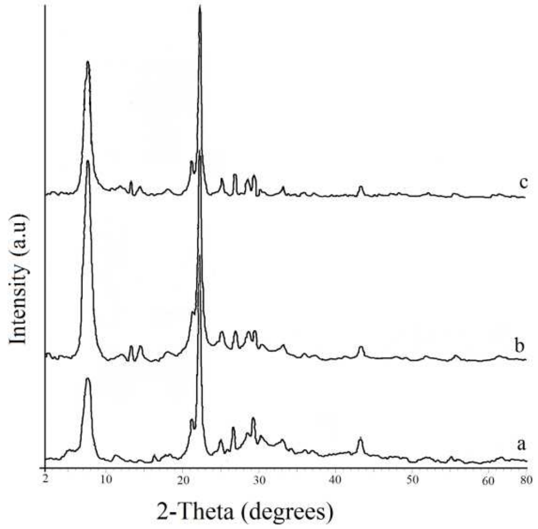

Fig. 1 XRD patterns of nanosized zeolite Beta samples: (a) uncalcined; (b) calcined; (c) reused catalyst.

As a part of our ongoing research programme to develop environmentally friendlier synthetic procedures using zeolites.[21] Herein, we report a simple and efficient catalytic method for the N-alkylation of amines with alcohols using nanosized Beta zeolite.

Experimental

Reagents and materials

Alcohols and amines were purchased from Aldrich. The following chemicals were employed for the preparation of nanosized zeolite Beta. Tetraethyl orthosilicate ($(C_2H_5O)_4Si$, 99% Lancaster), Tetraethylammonium hydroxide (TEAOH, 35% Fluka), Sodium hydroxide (NaOH, 98% Loba), Cetyltrimethylammonium bromide (CTAB, 98% Lancaster) and Aluminum sulphate ($Al_2(SO_4)_3.16H_2O$, Universal). All the chemicals used in this study were in as-received form.

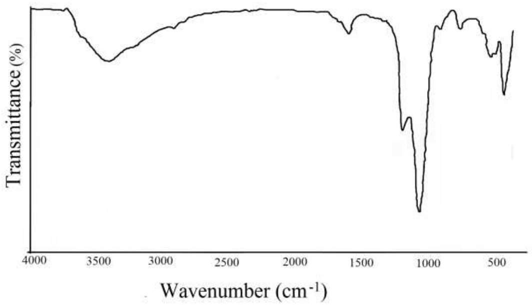

Fig. 2 FT-IR spectrum of calcined nanosized zeolite Beta.

Synthesis of nanosized zeolite Beta [22]

Tetrethylammonium hydroxide (15.5 mL (37 mmol), TEAOH 35 wt % solution in water) was slowly added to 1.2 g (30 mmol) of NaOH in 4 ml of distilled water. The resulting mixture was stirred for 10 min and added to a solution of (22.3 mL (100 mmol)) tetraethyl orthosilicate in 21 mL of distilled water at room temperature, then the mixture was allowed to stir for 30 min. 2.1 g (3.33 mmol) of aluminum sulphate ($Al_2(SO_4)_3.16H_2O$) dissolved in 10.2 mL of warm water was added to the above mixture and stirred for 1 h. Then 1.4 g (3.8 mmol) of cetyltrimethylammonium bromide (CTAB) dissolved in 40 mL of ethanol was added slowly to the above reaction mixture and the final gel was stirred for 2 h. The resulted viscous gel was heated at 90 °C with continuous stirring to complete dryness. The dry precursor lumps were coarsely crushed and transferred in to a Teflon cup placed in Teflon lined autoclave. The amount of water (ca. 0.2 mL per 1 g (dry gel)) was added into the bottom of autoclave without contacting the dry gel in the Teflon cup. The crystallization of the dry gel was carried out at 175 ºC for 24 h. After hydrothermal treatment, the solid product was filtered and washed with water until neutral and dried in air. The surfactant was removed from the as-synthesized nanosized zeolite Beta through calcination for 8 h at 550 ºC.

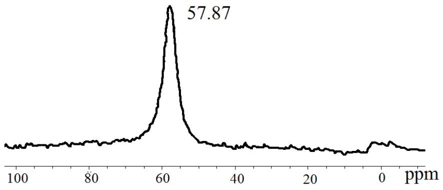

Fig. 3 ^{27}Al NMR spectrum of calcined nanosized zeolite Beta.

General procedure for the N-alkylation of amines with alcohols / tandem reactions of amines with nitrobenzyl alcohols

Reactions were performed in a magnetically stirred round bottomed flask fitted with a condenser and placed in a temperature controlled oil bath. Nanosized zeolite Beta (100 mg) was added to the well stirred solution of amine (2 mmol) in alcohol (6 mmol) and the reaction mixture was allowed to stir at 135 °C in an open (air) atmosphere. After disappearance of the amine (reaction was monitored by TLC) or after the appropriate time, the reaction mixture was cooled to room temperature. The catalyst was removed by filtration, rinsed with ethyl acetate and removal of solvent in vacuo yielded a crude residue. The crude residue was further purified by column chromatography using

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silica gel (100-200 mesh) to afford pure products. All the products were identified on the basis of NMR and mass spectral data.

Characterization and analysis

All the samples were systematically characterized by various analytical and spectroscopic techniques. The XRD patterns of the samples were obtained on a Regaku miniflux X-ray Diffractometer using Ni filtered CuK$_\alpha$ radiation at 2θ = 2–80º with a scanning rate of 2º min^{-1} and the beam voltage and currents of 30 kV and 15 mA, respectively. The FT-IR spectrum of the sample recorded on a Nicolet 740 FT-IR spectrometer at ambient conditions using KBr as the diluents. The solid state MAS-NMR analysis has been done by employing Avance-500 WB (Varian) spectrometer with a frequency of 130.31 MHz and $[Al(H_2O)_6]^{3+}$ used as a standard for ^{27}Al. Transmission electron microscopy (TEM) images of the samples were recorded using a Tecnai F 12 TEM instrument. Temperature programmed desorption (TPD) of ammonia was carried out on a laboratory-built apparatus. In a typical experiment about 0.1 g of the sample was pretreated at 300 °C for 1 h by passing helium (99.9%, 50 mL min^{-1}). After pretreatment, the sample was saturated with anhydrous ammonia (10% NH_3 balance He) at 100 °C for 1 h and subsequently flushed with He at the same temperature to remove physisorbed ammonia. Then the TPD analysis was carried out from ambient temperature to 800 °C at a heating rate of 10 °C min^{-1} and the desorbed NH_3 was measured using a gas chromatography equipped with thermal conductivity detector. The products of the coupling reaction were identified by NMR spectra using a Bruker VX NMR FT-300 or Varian Unity 500 spectrometers instrument in $CDCl_3$. Chemical shifts are reported in parts per million (ppm) downfield from TMS. ESI mass spectra were obtained by using Micromass Quattro LC mass spectrometer and High-resolution mass spectra obtained by using ESI-QTOF mass spectrometry.

Results and Discussions

Catalyst characterization

Fig. 1 displays the XRD patterns of calcined and uncalcined nanosized zeolite Beta. The Bragg peaks are corresponding to the typical reflections of BEA structure with high crystallinity.

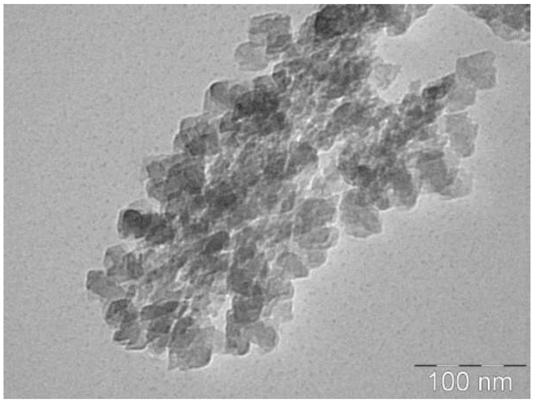
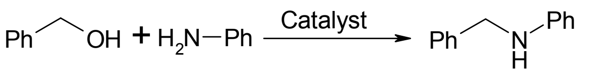


Fig. 4 TEM image of nanosized zeolite Beta.

The FT-IR spectrum of calcined nanosized zeolite Beta in the frame work vibration region is shown in Fig. 2. A band at 462 cm^{-1} characteristic to the pore opening, absorption band at 520-570 cm^{-1} which is characteristic of highly crystalline Beta zeolite.[23] The band at 900-950 cm^{-1} is due to terminal Si-O$^-$H$^+$ groups. The large and broad peak appearing in the range of 1060-1090 cm^{-1} is due to asymmetric stretching vibration ($\upsilon_{a(oTo)}$)^{24}.

Table 1 Optimization for N-benzylation of aniline with benzyl alcohol[a]



Entry	Catalyst	Temperature (°C)	Time (h)	Yield[b] (%)
1	HZSM-5 (40)	135	6.3	-
2	Mordenite	135	6.3	-
3	HY	135	6.3	41
4	NaY	135	6.3	-
5	HX	135	6.3	-
6	H*β*	135	6.3	74
7	MCM-41	135	6.3	47
8	Montmorillonite K10	135	6.3	-
9	SiO_2-Al_2O_3	135	6.3	49
10	SiO_2	135	6.3	-
11	Absence of catalyst	135	6.3	-
12	Nanosized zeolite Beta	135	6.3	98
13	Nanosized zeolite Beta	145	5.3	94
14	Nanosized zeolite Beta	125	24	63
15	Nanosized zeolite Beta	100	24	21
16	Nanosized zeolite Beta	135	6.3	87[c]
17	Nanosized zeolite Beta	135	6.3	32[d]
18	Nanosized zeolite Beta	135	6.3	20[e]
19	Nanosized zeolite Beta	135	6.3	88[f]
20	Nanosized zeolite Beta	135	6.3	70[g]

[a] Reaction conditions: Benzyl alcohol (6 mmol), Aniline (2 mmol), Catalyst (100 mg), open atmosphere. [b] Products were characterized by NMR, Mass spectra and isolated yields calculated based on aniline. [c] Catalyst (50 mg), [d] Catalyst (25 mg). [e] Catalyst (10 mg). [f] Benzyl alcohol (4 mmol), Aniline (2 mmol). [g] Benzyl alcohol (2 mmol), Aniline (2 mmol).

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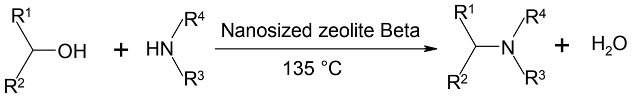
The peak appearing in 3200-3500 cm^{-1} region is characteristic of silanol groups attached through strong hydrogen bands with neighbouring silanols and hence corresponds essentially to internal Si-OH defect groups[25].

The location of the Al atoms in the sample was investigated by ^{27}Al NMR spectroscopy (Fig. 3). The ^{27}Al NMR spectrum contains only one symmetrical peak at 57.87 ppm, which is characteristic of tetrahedral Al^{+3} species in the framework. However, no octahedral aluminum was found in the zeolite. These results demonstrate that Al^{+3} species were uniformly dispersed in the nanosized zeolite Beta.

The TEM image of nanosized zeolite Beta is displayed in Fig. 4. It shows that the nanosized zeolite Beta has uniform particle size of ca. 30-40 nm.

Catalyst Screening

At the start of our studies, we investigated the reaction of aniline with benzyl alcohol (3 equiv.) as a model system to optimize the different parameters of the reaction (Table 1). In order to choose the best catalyst, first the reaction was carried out with various zeolites, montmorillonite K10, SiO_2 and SiO_2-Al_2O_3 at 135 °C. Among the catalysts examined, H*β* zeolite showed the highest catalytic activity and furnished the corresponding secondary amine in 74% yield (Table 1, entry 6). Under the same reaction conditions, HY, MCM-41, SiO_2-Al_2O_3 provided <50% yield (Table 1, entries 3, 7 and 9). Whereas, HZSM-5, mordenite, NaY, HX, montmorillonite K10 and SiO_2 delivered virtually no conversion of starting material (Table 1, entries 1,2,4,5,8 and10). Then we investigated with nanosized zeolite Beta under similar reaction conditions produced much higher yield (98%) towards corresponding product compared to other catalysts (Table 1, entry 12). The best performance of nanosized zeolite Beta is possibly due to higher acidity of nanosized zeolite Beta (412 μmol/g) than the H*β* zeolite *ca*. 269 μmol/g. Excess amount of alcohol was used not only as a reactant but also as a solvent.

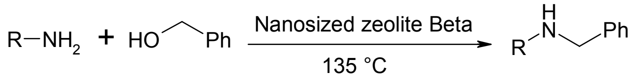


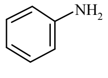
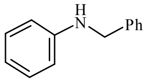
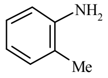
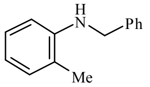
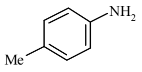
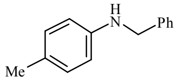
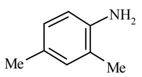
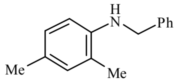
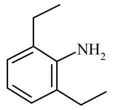
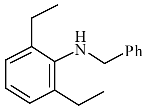
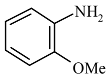
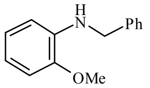
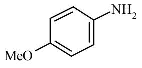
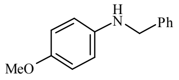
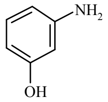
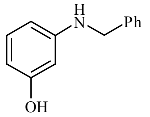
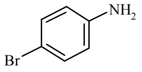
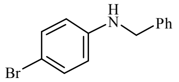
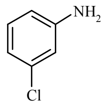
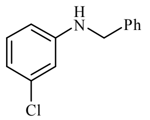
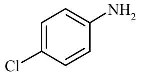
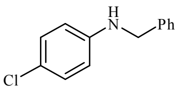
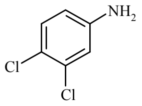
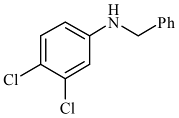
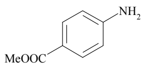
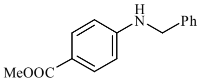
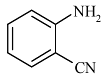
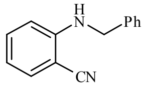
Scheme 1 Zeolite catalyzed N-alkylation of amines with alcohols.

Optimization of reaction conditions

Once nano Beta was found as the best catalyst for N-alkylation of aniline with benzyl alcohol, the influence of temperature was studied. By varying the reaction temperature from 100 °C to 135 °C, a gradual improvement in yield (21% to 98%) was observed and further increase of temperature did not have any accountable effect on the yield (Table 1, entries 12-15). The mole ratio of amine to alcohol also have a significant influence on the product yield. While increasing the mole ratio of amine to alcohol (1:1 to 1:3), the yield of the desired product was increased from 70% to 98% (Table 1, entries 12, 19 and 20). The present reaction was also conducted using different amounts of the catalyst and it was found that 100 mg of catalyst has shown the best results (Table 1, entries 12 and 16-18). It is observed that the reaction did not proceed in the absence of a catalyst (Table 1, entry 11), thus confirming the role of the catalyst in the reaction. The above presented results indicate that the optimized reaction conditions to get highest yield for this alkylation reaction is 1:3 mole ratio of aniline to benzyl alcohol at 135 °C over nanosized zeolite Beta (100 mg).

Table 2 N-Alkylation of amines with benzyl alcohol over nanosized zeolite Beta[a]



Entry	Amines	Time (h)	Product	Yield[b] (%)
1		6.3		98
2		19		90
3		24		69
4		24		43
5		24		-
6		24		45
7		24		14
8		24		-
9		4		53
10		24		59
11		6.3		95
12		24		67
13		24		58
14		24		65

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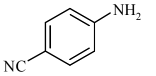
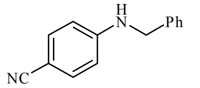
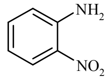
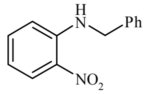
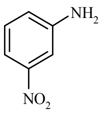
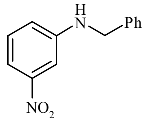
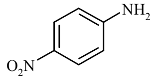
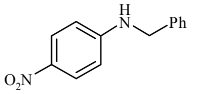
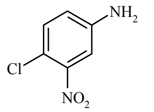
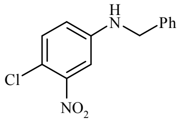
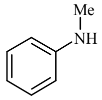
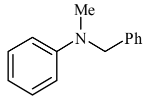
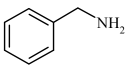
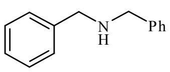
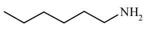
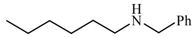
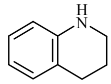
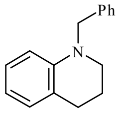
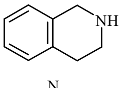
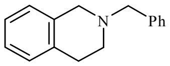
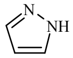
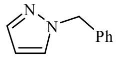
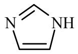
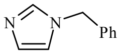
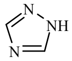
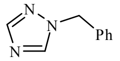
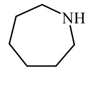
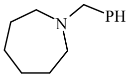
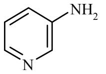
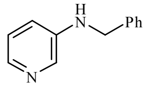
15		20		93
16		24		29
17		24		67
18		24		74
19		24		-
20		24		62
21		24		-
22		24		-
23		24		17
24		18		72
25		48		70
26		48		-
27		48		35
28		24		-
29		24		-

[a] Reaction conditions: Benzyl alcohol (6 mmol), Amine (2 mmol), Nanosized zeolite Beta (100 mg), 135 °C, open atmosphere. [b] Products were characterized by NMR, Mass spectra and isolated yields calculated based on amines.

With optimized reaction conditions in hand, we explored the scope of the nano Beta catalyzed N-alkylation with various combinations of substrates (amines and alcohols) and results are summarized in Table 2 &3 (Scheme 1).

N-Benzylation of amines

As shown in Table 2, various amines successfully reacted with benzyl alcohol in presence of nano beta afforded moderate to excellent yields of the corresponding N-benzylated products. Aniline produced the corresponding mono N-benzylated amine with 98% yield in 6.3 h (Table 2, entry 1). In order to determine the influence of substitution on aromatic ring of aniline on the reaction path with this reagent system, we studied the reaction with different substitutions. Moderately activating or deactivating groups present on aromatic ring of aniline provided moderate to excellent yields of the respective mono N-benzylated products (Table 2, entries 2-4 and 9-12) independent of the electron-donating or with-drawing character of the substituents. Highly activating groups present on aromatic ring of aniline gave less yields or no conversion was observed (Table 2, entries 6-8). Whereas, highly deactivated anilines gave moderate to excellent yields (Table 2, entries 14-18). However, the reaction with more sterically hindered 2,6-diethylaniline was unsuccessful (Table 2, entry 5).

The position of substitution on the phenyl ring of aniline affect the reaction yield. Interestingly, moderately activating groups i.e. methyl at *ortho* position furnished higher yield compared to *para* position (Table 2, entries 2 and 3). Whilst, highly deactivating group i.e. NO_2 at *ortho* position provided lesser yield compared to *meta*/*para* position (Table 2, entries 16-18). The highly deactivated aniline i.e. 4-chloro-2-nitroaniline (Table 2, entry 19) failed to react under these reaction conditions even after prolonged reaction time (24 h). Secondary aromatic amine i,e. N-methylaniline provided the corresponding N-benzylated product (tertiary amine) in moderate yield (Table 2, entry 20). Various substituents such as methyl, methoxy, bromo, chloro, ester, cyano and nitro groups can be tolerated in the present reaction conditions.

We also examined the alkylation of aliphatic primary amines, aliphatic secondary cyclic amines and electron-poor hetero aromatic amine (3-aminopyridine) (Table 2, entries 22, 28 and 29). Unfortunately, our attempts to alkylate these amines were unsuccessful. Surprisingly, 1,2,3,4-tetrahydroquinoline gave the corresponding tertiary amine in 17% yield, whereas 1,2,3,4-tetrahydroisoquinoline yielded 72% yield of the respective tertiary amine (Table 2, entries 23 and 24). Further, the coupling reactions of benzyl alcohol with pyrazole, 1,2,4-triazole afforded the corresponding tertiary amines with 70% and 35% yield, respectively (Table 2, entries 25 and 27), while the reaction with imidazole was not quite successful (Table 2, entry 26).

N-Alkylation of aniline

Structurally diverse alcohols, including benzylic, heteroaromatic, allylic and aliphatic alcohols reacted with aniline under optimized reaction conditions and provided the corresponding mono-N-alkylated amines in moderate to excellent yield (Table 3). Benzyl alcohol with moderately activating groups reacted smoothly and furnished excellent yields of the respective mono-N-alkylated anilines (Table 3, entries 1 and 2), while substitution of moderately deactivating groups on benzene ring decreases the reactivity, yielded the corresponding mono-N-alkylated anilines in moderate yield (Table 3, entries 3-6). Benzylic secondary alcohols also reacted smoothly with aniline gave the corresponding mono-N-alkylated anilines in moderate to good yields (Table 3, entries 7-10).

In the case of hetero aryl methyl alcohols different results were observed. Furfuryl alcohol and thenyl alcohol were converted to

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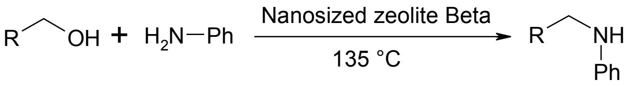
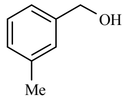
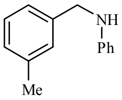
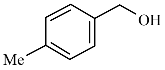
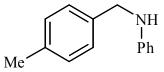
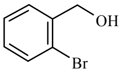
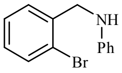
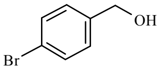
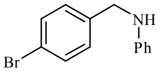
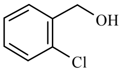
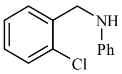
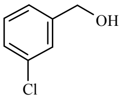
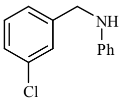
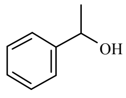
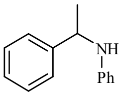
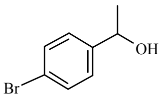
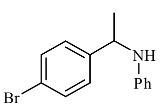
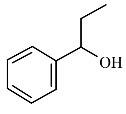
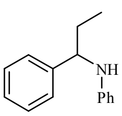
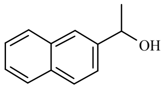
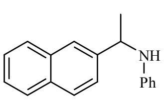
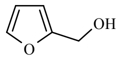
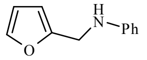
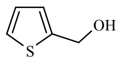
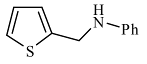
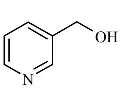
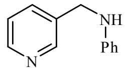
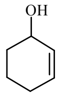
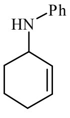
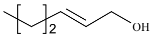
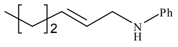
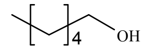
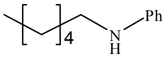
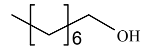
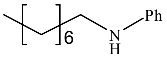
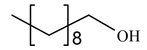
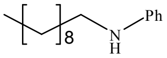
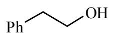
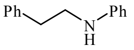
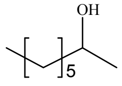
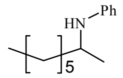
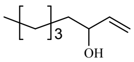
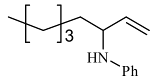
their respective secondary amines in moderate yield, whereas 3-pyridinemethanol did not react under similar reaction conditions even after prolonged reaction time (Table 3, entries 11-13). Reaction with allylic alcohols also delivered the corresponding secondary anilines in excellent yields (Table 3, entries 14 and 15). In the case of aliphatic alcohols, reactivity decreased with increasing the chain length. 1-Hexanol and 1-octanol provided the respective mono-N-alkylated products in 41% and 10% yield, respectively, whilst no reaction was observed with 1-decanol (Table 3, entries 16-18). Unfortunately, 2-phenylethyl alcohol and aliphatic secondary alcohols failed to give any product under similar conditions (Table 3, entries 19-21).

Direct synthesis of imines from tandem reactions of amines with nitrobenzyl alcohols

Interestingly, when benzyl alcohol bearing a strong electron-withdrawing group i.e. NO_2 on phenyl ring reacted with aniline gave the corresponding imines in moderate to excellent yields under similar reaction condition (Table 4). 4-Nitrobenzyl alcohol furnished higher yield compared to 2 and 3-nitrobenzyl alcohols (Table 4, entries 1-3). Imines have widespread applications in laboratory and industrial synthetic processes due to their diverse reactivity.[26]

Table 3 N-Alkylation of aniline with alcohols over nanosized zeolite Beta[a]



Entry	Alcohol	Time (h)	Product	Yield[b] (%)
1		9		95
2		7		90
3		24		57
4		24		39
5		24		21
6		24		40
7		8		70
8		24		34
9		10		67
10		1.3		72
11		4		52
12		4		41
13		24		-
14		5		78
15		24		88
16		24		41
17		24		10
18		24		-
19		24		-
20		24		-
21		24		-

[a] Reaction conditions: Alcohol (6 mmol), Aniline (2 mmol), Nanosized zeolite Beta (100 mg), 135 °C, open atmosphere. [b] Products were characterized by NMR, Mass spectra and isolated yields calculated based on aniline.

Encouraged by these results, we next examined a range of different substituted anilines with 4-nitrobenzyl alcohol under similar reaction conditions and results are summarized in Table 4. Introduction of activating groups on *para* position of aniline (Table 4, entries 5, 7 and 8) provided excellent yields of the desired products (imines), whereas strongly deactivated anilines (Table 4, entries 11 and 12) did not react under these conditions even after prolonged reaction time. o*rtho*-Substituted anilines (Table 4, entries 4 and 6) gave lesser yields due to *ortho* effect (steric hindrance). In the case of 1,4-diaminobenzene excellent chemoselectivity was observed, in which only one amino group converted into imine, other amino group remains unaffected (Table 4, entry 8). When halogenated anilines treated under present reaction conditions afforded less yields or no conversion was observed (Table 4, entries 9 and 10).

The reusability of the catalyst is one of the most important property for the commercial applications and environmental proportion. The catalyst was easily separated from the reaction mixture by simple filtration and the collected catalyst was calcined at 450 °C to use in next cycle. The reusability of the

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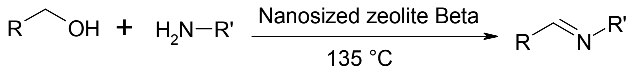
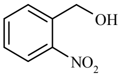
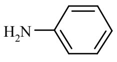
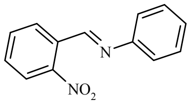
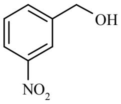
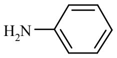
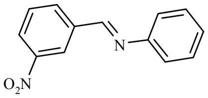
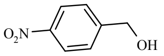
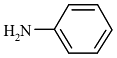
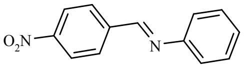
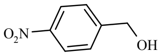
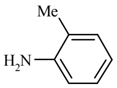
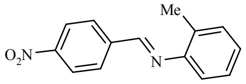
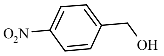
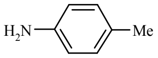
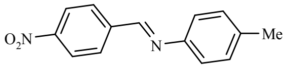
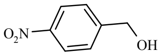
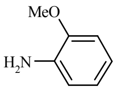
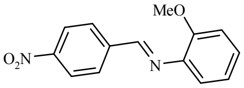
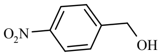
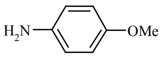
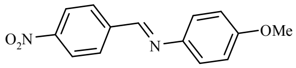
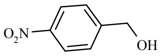
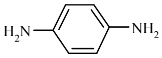
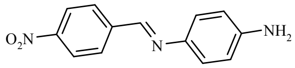
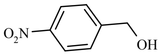
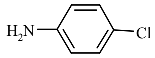
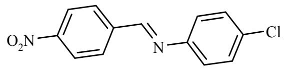
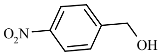
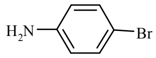
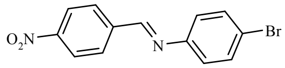
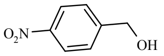
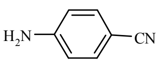
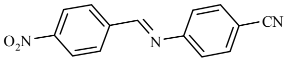
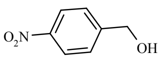
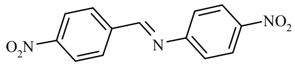
Table 4 Synthesis of imines from anilines and nitrobenzyl alcohols over nanosized zeolite Beta[a]



Entry	Alcohols	Amines	Time (h)	Product	Yield[b] (%)
1			24		35
2			24		67
3			21		92
4			24		34
5			24		80
6			24		62
7			24		83
8			15		78
9			24		54
10			24		-
11			24		-
12			24		-

[a] Reaction conditions: Alcohol (6 mmol), Amine (2 mmol), Nanosized zeolite Beta (100 mg), 135 °C, open atmosphere.

[b] Products were characterized by NMR, Mass spectra and isolated yields calculated based on amines.

catalyst was checked by the reaction of aniline with benzyl alcohol under optimized reaction conditions. The reused catalyst showed consistent activity even after third reuse (Table 5). The catalyst was highly crystalline before and after the reaction, which was confirmed by XRD (Fig. 1). After the reaction quenching of aluminium or silicon from nanosized zeolite Beta was not observed and confirmed by elemental analysis.

To study mechanism for the formation of N-alkylated product and imine from alcohols and amines using nanosized zeolite Beta, a series of reactions were carried out at standard reaction conditions. Reaction of benzyl alcohol with aniline under air (open) or inert atmosphere gave the corresponding N-alkylated product without forming imine. Different results were obtained in case of 4-nitrobenzyl alcohol with aniline depending on reaction atmosphere. Imine was obtained under air (open), whilst corresponding N-alkylated product was formed under inert atmosphere. In order to find out the intermediate product for imine formation, the reactions (4-nitrobenzyl alcohol with aniline) were carried out at different time periods, such as, 10 h, 13 h and 16 h yielded the corresponding imine, along with small

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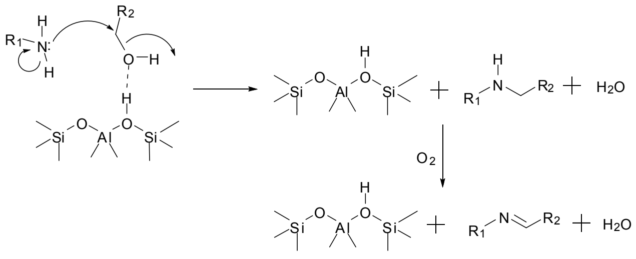
Table 5 N-benzylation of aniline with benzyl alcohol - reusability of the catalyst[a]

Entry	Cycle	Conversion of aniline (%)	*N*-Benzylaniline	
			Selectivity (%)	Yield[b] (%)
1	First	97	99	96
2	Second	95	99	94
3	Third	98	99	97

[a] Reaction conditions: Benzyl alcohol (6 mmol), Aniline (2 mmol), Nanosized zeolite Beta (100 mg), 135 °C, open atmosphere, reaction time 6.3 h. [b] Products were characterized by NMR, Mass spectra and isolated yields calculated based on aniline.

amounts of N-alkylated product. Moreover, 4-nitrobenzyl alcohol in the absence of aniline under inert or air atmosphere exclusively yielded the corresponding ether and formation of aldehyde was not observed. The same phenomenon was observed with benzyl alcohol also. Based on above experimental observations (see ESI for other experimental details) and literature reports,[27] we propose a probable mechanism for the formation of N-alkylated product and imine (Scheme 2).



Scheme 2 Plausible reaction mechanism for the formation of N-alkylated product and imine.

It is assumed that alcohol adsorbed on the Bronsted acid sites of zeolite, which subsequently reacts with amine via SN^2 pathway to give the corresponding N-alkylated product and water in one step. Whereas, in the case of nitrobenzyl alcohols further *in situ* oxidative dehydrogenation of N-alkylated product provides the corresponding imines. This may be, due to the removal of electron density from the nitro substituted aromatic ring which facilitates the oxidative dehydrogenation, while in other systems the electron density on the aromatic ring repels the oxygen moiety.

Conclusions

In summary, we have developed a highly efficient and practical procedure for producing higher amines from amines and alcohols using nanosized zeolite Beta as a catalyst. Moreover, imines were also efficiently prepared from the tandem reactions of amines with 2, 3 and 4-nitrobenzyl alcohols. Notable advantages offered by this method are broad substrate scope, high atom economy (only water is side product), reusability of catalyst, environmentally benign, higher yields of the desired products and simple work-up procedure, which make it an attractive and useful methodology for organic synthesis.

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