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1. Introduction

modern organic chemical synthesis, In one-pot multicomponent reactions (MCRs)¹ have emerged as powerful and efficient bond-forming tools to prepare biologically active drug-like molecules with high selectivity and atom economy. MCRs are well known for successful generation of products from simple and readily available substrates without isolation of any intermediate in a single synthetic operation and thus avoiding disadvantages associated with stepwise sequential approaches such as energy consumption and hazardous waste production. These features make MCRs well-suited tools for the easy production of various valuable heterocyclic scaffolds.² Therefore, the development of new MCRs and the improvement of known MCRs are areas of substantial current interest.

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An efficient green protocol for the synthesis of tetra-substituted imidazoles catalyzed by zeolite BEA: effect of surface acidity and polarity of zeolite[†]

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In the present study, the catalytic activity of various medium (H-ZSM-5) and large pore (H-BEA, H-Y, H-MOR) zeolites were studied as solid acid catalysts. The zeolite H-BEA is found to be an efficient catalyst for the synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles through one-pot, 4-component reaction (4-CR) between benzil, NH₄OAc, substituted aromatic aldehydes and benzyl amine. The hydrophobicity, Si/Al ratio and acidic properties of zeolite BEA were well improved by controlled dealumination. The synthesized materials were characterized by various characterization techniques such as XRD, ICP-OES, BET, NH₃-TPD, FT-IR, pyridine FT-IR, ²⁷Al and ¹H MAS NMR. It has been observed that the dealumination of the parent zeolite H-BEA (**12**) results in the enhanced strength of Brønsted acidity up to a certain Si/Al ratio which is attributed to the inductive effect of Lewis acidic EFAl species, leading to the higher activity of the zeolite BEA (**15**) catalyst towards the synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles under thermal solvent-free conditions with good to excellent yields. Using the present catalytic synthetic protocol, diverse tetrasubstituted imidazoles, which are among the significant biologically active scaffolds, were synthesized in high yield within a shorter reaction time. The effect of polarity, surface acidity and extra framework Al species of the catalysts has been well demonstrated by means of pyridine FT-IR, and ²⁷Al and ¹H MAS NMR.

Heterocyclic scaffolds are one of the most important topics and receive significant attention due to their synthesis, reactions and biochemical processes. The imidazole heterocycle ring system containing a nitrogen atom is one of the most imperative motifs found in a large number of natural products and pharmacologically active compounds. The potential and broad application of the imidazole pharmacophore might be attributed to its hydrogen bond donor-acceptor capacity as well as its high affinity for metals. Amongst these, tetra-substituted imidazoles (TSIs) are important fragments which possess a wide spectrum of biological activities, covering anti-allergic, analgesic, anti-fungal, anti-bacterial, anti-tubercular, anti-inflammatory, anti-biotic, anti-mycotic, anti-ulcerative, anti-tumour, pesticidal, as a therapeutic agent, antimalarial, anti-cancer, anti-HIV and anti-viral.³ Substituted imidazoles also act as a glucagon receptor, a kinase inhibitor and an antagonist of CB1 cannabinoid.4

For the 3-component reaction (3-CR) of imidazoles, mostly variations of the method were first reported in 1882 by Radziszewski.^{5a} Later, this 3-CR approach was improved extensively by Drefahl and Herma,^{5b} showing an extra input of amine for the 4-component reaction (4-CR) of imidazoles. In the recent past, looking at the significant applications of TSIs

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Paper

in medicinal chemistry, numerous high yielding and efficient synthetic protocols have been reported on its synthesis which involve the use of a variety of catalysts. The most common method for the 4-CR of TSIs involves cyclo-condensation of a 1,2-diketone with aldehyde derivatives, ammonium acetate (NH₄OAc) and amines in the presence of various catalytic systems such as L-proline,⁶ carbon-based solid acids,⁷ SBA-15/ TFE,⁸ nano-Al-MCM-41,⁹ Cu(NO₃)₂/zeolite-HY,¹⁰ ZSM-5,^{3b} ZSM-5-SO₃H,¹¹ zeolite-HY,¹² sulfated MCM-41,¹³ H-ZSM-22,¹⁴ heteropoly acids,¹⁵ SBPPSA,¹⁶ SiO₂-Pr-SO₃H,⁴ SBA-Pr-SO₃H,¹⁷ and M/SAPO-34 nanocatalysts¹⁸ under solvent-free or classical heating conditions. This synthetic procedure also involves the use of microwave irradiation,19 ionic liquids20 and ultrasound irradiation.²¹ In addition, TSIs can also be synthesized by hetero-Cope rearrangement, cycloaddition reaction of mesoionic 1,3-oxazolium-5-olates with N-(arymethylene) benzene-sulfonamides, condensation of a 1,2 diketone with an aryl nitrile and a primary amine under microwave irradiation and by N-alkylation of tri-substituted imidazoles.²² Despite their tremendous success, several of these methods are not environmentally friendly and suffer from one or more drawbacks which include harsh reaction conditions, tedious workup and purification, strongly acidic conditions, high temperature, moderate yields, occurrence of side reactions, long reaction time, expensive or toxic catalysts and reagents, requirements of solvents and tedious separation.

Zeolite H-BEA is gaining particular interest in research due to its open framework structure with a three-dimensional system of mutually intersecting 12-membered ring channels, high thermal stability, surface area, acidity and Si/Al ratio. Zeolite H-BEA has been found to be an acidic catalyst because the acid-base properties of a zeolite are influenced greatly by the content of Si and Al in its framework. Application of zeolite H-BEA is expected to give better catalytic activity due to its higher surface area along with its moderate acidity, large pore opening and more hydrophobic nature. Zeolite H-BEA is often modified to tune its catalytic properties. Therefore, modification of zeolite H-BEA is performed via dealumination processes without destroying the microporous structure. The synthesis of TSIs via MCRs over zeolite BEA as a solid acid catalyst has not been reported so far. As a continuation of our work on zeolite catalyzed multicomponent reactions (ZCMCRs),²³ the present study deals with the green synthesis of TSIs using various acidic zeolites as heterogeneous *"E"* catalysts (eco-friendly, efficient and economical) under environmentally benign conditions (Scheme 1).

In the present endeavour, we have shown that textural properties such as topology, acidity and adsorption characteristics are influencing parameters that affect the activity of zeolite catalysts. The effects of dealumination on the textural properties and concentration of acid sites of zeolite BEA and therefore its activity toward the synthesis of TSIs have been studied by means of FT-IR and solid state NMR techniques.

Experimental

2.1. Materials and methods

The glassware were rinsed with distilled water followed by acetone prior to use. All the reagents used were of analytical grade. The reactants including substituted aldehydes, both amines and solvents were procured from Finar, Merck and Sigma-Aldrich chemical companies (Surat, India) in the purest form and were used without further purification. Melting points were determined using open capillary tubes and were uncorrected. All the reactions were monitored by thin layer chromatography (TLC) performed on precoated Merck silica gel 60F254. Compounds were visualized either with UV light or by placing in an iodine chamber. Product yields refer to isolated products after purification. The organic products were characterized by spectral analysis (mass, UV, FT-IR, ¹H & ¹³C NMR) and elemental analysis (C, H, N) etc. UV measurements were recorded on a Cary 50 Varian UV-vis spectrophotometer at room temperature using quartz cells with a 1.0 cm path length in the range of 200-800 nm in an ethanol medium. Mass spectra were recorded on a Waters Micromass ZQTM 400 mass spectrometer operating at an ionization potential of 10-30 eV. Fourier transform infrared (FT-IR) spectra were recorded on a DRS (8400-S-Shimadzu) FT-IR spectrophotometer using KBr pellets within the spectral range of 4000-400 cm⁻¹ and 50 scans were acquired for each spectrum. The sample for the FT-IR measurement was prepared by adding a small amount of the synthesized product into KBr (1:100 ratio) followed by drying to make the pellet. ¹H and ¹³C NMR spectra were recorded on a Bruker-400 III Avance spectrometer in a DMSO solvent at 400 MHz and 100 MHz, respectively, using TMS as an internal standard. C, H, N analysis was carried out using an Elementar Vario Micro Cube CHN analyzer.



Scheme 1 Zeolite BEA catalyzed synthesis of TSIs.

2.2. Catalyst preparation

The compositions of zeolites Na-BEA [H-BEA (12); Si/Al = 12], Na-Y [H-Y (2.43); Si/Al = 2.43], Na-mordanite [H-MOR (11); Si/ Al = 11], and Na-ZSM-5 [H-ZSM-5 (15); Si/Al = 15] were obtained from Sud-Chemie India Pvt. Ltd., India. The H-forms of the zeolites were prepared through ion-exchange of the Na-form of the zeolite samples using an aqueous solution of NH_4NO_3 (1 M), followed by overnight drying and calcining at 550 °C for 5 h.

H-BEA zeolites with different Si/Al ratios having different surface areas and acidities were prepared by dealumination of the parent zeolite [H-BEA (12)p] using HNO₃, as per a reported method.²⁴ In this process, zeolite H-BEA (12)p was dealuminated by heating at 85 °C with 55 wt% of HNO₃ (60 g acid per 1 g of zeolite) for 12 h. The dealuminated zeolite was filtered and repeatedly washed with deionised water and dried at 100 °C. After that, it was washed with dilute ammonia solution (1% solution) to remove residual acid and free of Al and dried at 100 °C for 2 h. The procedure was repeated to obtain dealuminated samples to different extents (Si/Al ratio: 15, 25, 34). All the catalysts were calcined in air at 550 °C for 5 h prior to use in the reactions.

2.3. Catalyst characterization

The crystalline phase identification and phase purity of all calcined zeolites with different Si/Al ratios were analyzed using a powder X-ray diffractometer (XRD, D8 Advance Bruker AXS, Germany) with Cu-K_{α} radiation (K_{α} = 1.5403 Å) using a nickel filter. The Si/Al ratio of the zeolite samples were measured using a Perkin Elmer Optima 3300 RL inductively coupled plasma-optical emission spectrometer (ICP-OES). The specific surface area of the zeolite samples were measured by the BET method using a Micromeritics Gemini instrument at -196 °C using N2 adsorption isotherms. Temperature programmed desorption (TPD) of ammonia was used to determine the acidity of the zeolites using a Micromeritics Chemisorb 2720 acidity analyzer. NH3 was chemisorbed at 120 °C and then desorption was carried out up to 700 °C at a heating rate of 10 °C min⁻¹. The FT-IR spectra of the zeolite BEA samples were recorded on a Shimadzu FTIR-8400-S spectrometer. The Lewis and Brønsted acidity of the zeolite samples were measured by pyridine FT-IR spectroscopy in the region 1400–1600 cm⁻¹ after pyridine adsorption on zeolite samples at 110 °C and the spectra were recorded on the same FT-IR instrument. Solid state magic angle spinning (MAS) NMR measurements were performed using a Bruker Avance AMX 400 spectrometer operating at 9.4 T static fields. ¹H MAS NMR measurements were performed at a resonance frequency of 400 MHz. Spectra were recorded using a 4 mm probe head at a spinning rate of 10 kHz, a pulse length of 2.8 ps ($\pi/4$) and a delay time of 10 s. All samples had been previously dehydrated under vacuum at 350 °C for 6 h. ²⁷A1 MAS NMR spectra were recorded at a resonance frequency of 104 MHz and at a spinning rate of 12 kHz, using a 4 mm

probe head. The pulse length was 0.58 ps, which corresponds to $\pi/12$, for non-selective excitation. The delay time was 1 s.

2.4. General procedure for the synthesis of TSIs

All the zeolites were activated by heating at 550 $^{\circ}$ C for 2–3 h before placing them into a round bottom flask (RBF).

All the reactions were carried out in a 50 ml RBF attached to a condenser and equipped with a magnetic stirrer under heating in an oil bath. In a typical reaction, a mixture of benzil (1 mmol), ammonium acetate (4 mmol), substituted aldehydes (1 mmol), both amines (1 mmol) and zeolite H-BEA (15) (2 wt%) were heated at 100 °C with continuous stirring for 15 min. The completion of reaction was monitored by TLC (n-hexane: ethyl acetate). Upon completion of reaction, the reaction mass was allowed to cool at room temperature, followed by addition of ethanol. The spent catalyst was collected from the residual reaction mixture by filtration under reduced pressure and then washed with ethanol. The crude imidazole solid product was recovered by evaporating the solvent and was further purified via recrystallization with hot ethanol to obtain the pure 1-benzyl-2,4,5-triphenyl-1Himidazole and 1,2,4,5-tetraphenyl-1H-imidazole having melting points of 160-162 °C and 214-216 °C (reported: 160-165 °C and 215–217 °C) in 99% and 86% yield with benzyl amine and aniline, respectively.

The desired product, 1-benzyl-2,4,5-triphenyl-1*H*-imidazole (5a), was confirmed by comparison of their physical and spectral data with those of authentic samples.^{6,19,22c,25} The spectral data of the novel product synthesized using 4-chloro-3-nitro benzaldehyde as a new aldehyde functionality (Table 4, entry 5h) are given below:

2.4.1. 1-Benzyl-2,4,5-triphenyl-1*H*-imidazole (5a, n = 1). Off-white solid; m.p.: 160-162 °C; anal. calcd. for C₂₈H₂₂N₂: C, 87.01, H, 5.74, N, 7.25%. Found: C, 87.13, H, 5.70, N, 7.19%; UV (λ_{max} , ethanol) = 280 nm; FT-IR (KBr, cm⁻¹): 3060 (C-H stretch), 3031, 1600 (C=N), 1497, 1483, 1447 (C=C), 1352 (C-N stretch), 769, 697 (C-H band); ¹H NMR (400 MHz, DMSO): 5.16 (s, 2H, CH₂), 6.74–7.67 (m, 20H, Ar–H) ppm; ¹³C NMR (100 MHz, DMSO): 47.6 (CH₂, C₈), 125.1 (CH_{arom}, C₂₈), 126.0 (CH_{arom}, C₂₆), 126.2 (CH_{arom}, C₃₀), 126.4 (CH_{arom}, C₁₁), 127.0 (CHarom, C15), 127.1 (CHarom, C16), 127.7 (CHarom, C20), 128.0 (CH_{arom}, C₂₁), 128.1 (CH_{arom}, C₂₅), 128.4 (CH_{arom}, C₁₃), 128.5 (CHarom, C18), 128.6 (CHarom, C27), 128.8 (C1), 128.8 (CH_{arom}, C₁₂), 128.9 (CH_{arom}, C₁₄), 130.1 (CH_{arom}, C₁₇), 130.3 (CH_{arom}, C₁₉), 130.5 (CH_{arom}, C₂₂), 130.7 (CH_{arom}, C₂₄), 131.0 (CHarom, C29), 134.4 (CHarom, C9), 135.1 (CHarom, C23), 136.8 (CHarom, C7), 137.0 (CHarom, C10), 137.2 (CHarom, C6), 145.4 (C₂), 147.0 (C₄) ppm; MS: $m/z = 387.5 (M + H)^+$.

2.4.2. 1,2,4,5-Tetraphenyl-1*H*-imidazole (5a, n = 0). Offwhite solid; m.p.: 214–216 °C; anal. calcd. for $C_{27}H_{20}N_2$: C, 87.07, H, 5.41, N, 7.52%. Found: C, 87.11, H, 5.39, N, 7.45%; UV (λ_{max} , ethanol) = 286 nm; FT-IR (KBr, cm⁻¹): 3061 (C–H stretch), 3030, 1601 (C=N), 1497, 1481, 1447 (C=C), 1352 (C–N stretch), 760, 697 (C–H band); ¹H NMR (400 MHz, DMSO): 7.15–8.11 (m, 20H, Ar–H) ppm; ¹³C NMR (100 MHz,

Table 1	Physicochemica	l properties of	f various zeolites used	d in the synthesis of	f 1-benzyl-2,4,5-triphenyl-1H-imida	zoles
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Entry	Catalysts	Si/Al ratio	Spet	Pore volume	Pore structure	Ammonia uptake (mmol g ⁻¹)		
		(wt%)	$(m^2 g^{-1})$	$(\mathrm{cm}^3 \mathrm{g}^{-1})$	(nm)	Weak	Strong	Total
1	H-BEA (12)p ^{<i>a</i>}	12	680	0.27	0.76×0.64 0.55×0.55	0.70	0.89	1.60
2	H-BEA (15)	15	710	0.30	_	0.57	0.70	1.27
3	H-BEA (25)	25	732	0.34	_	0.35	0.40	0.75
4	H-BEA (34)	34	750	0.36	_	0.22	0.30	0.52
5	H-Y (2.43)	2.43	480	0.34	0.74 imes 0.74	2.30	_	2.30
6	H-MOR (11)	11	412	0.22	0.65×0.70	2.02	2.39	4.41
7	H-ZSM-5 (15)	15	320	—	0.53×0.56	1.95	1.40	3.35
^{<i>a</i>} The pare	ent zeolite.							

DMSO): 125.1 (CH_{arom}, C₂₅ & C₂₉), 126.3 (CH_{arom}, C₁₀), 126.4 (CH_{arom}, C₁₄), 127.2 (CH_{arom}, C₁₅), 128.0 (CH_{arom}, C₁₉), 128.1 (CH_{arom}, C₂₀), 128.2 (CH_{arom}, C₂₄), 128.2 (CH_{arom}, C₂₇), 128.3 (CH_{arom}, C₁₂), 128.4 (CH_{arom}, C₁₇), 128.6 (CH_{arom}, C₁₁), 128.7 (CH_{arom}, C₁₃), 129.1 (CH_{arom}, C₁₆), 129.4 (CH_{arom}, C₁₈), 129.5 (CH_{arom}, C₂₁), 130.3 (CH_{arom}, C₂₂), 131.0 (CH_{arom}, C₂₆), 131.2 (CH_{arom}, C₂₈), 131.3 (CH_{arom}, C₂₂), 132.1 (C₁), 134.3 (CH_{arom}, C₇), 135.5 (CH_{arom}, C₆), 136.6 (CH_{arom}, C₈), 136.8 (C₂), 145.4 (CH_{arom}, C₉), 145.9 (C₄) ppm; MS: m/z = 373.0 (M + H)⁺.

2.4.3. 1-Benzyl-2-(3-nitrophenyl)-4,5-diphenyl-1*H*-imidazole (5b, n = 1). Pale yellow solid; m.p.: 151–153 °C; anal. calcd. for C₂₈H₂₁N₃O₂: C, 77.94, H, 4.91, N, 9.74%. Found: C, 77.88, H, 4.85, N, 9.60%; FT-IR (KBr, cm⁻¹): 3058 (C-H stretch), 2972, 1600 (C=N), 1520 (N-O stretch), 1497, 1480, 1450 (C=C), 1350 (C-N stretch), 735, 696 (C-H band); ¹H NMR (400 MHz, DMSO-d₆): 5.15 (s, 2H, CH₂), 6.8–8.5 (m, 19H, Ar-H) ppm; ¹³C NMR (100 MHz, DMSO): 48.4 (CH₂, C₈), 125.6 (CH_{arom}, C₂₃), 125.6 (CH_{arom}, C₂₅), 126.0 (CH_{arom}, C₂₈), 126.6 (CH_{arom}, C₁₁ & C₁₅), 127.1 (CH_{arom}, C₁₆ & C₂₆), 127.7 (CH_{arom}, C₂₀), 128.2 (CH_{arom}, C₂₇ & C₂₉), 128.5 (CH_{arom}, C₁₃ & C₁₈), 129.3 (CH_{arom}, C₁₂, C₁₄, C₁₇ & C₁₉), 130.4 (CH_{arom}, C₂₂), 132.1 (CH_{arom}, C₉), 134.3 (CH_{arom}, C₇ & C₂₁), 137.2 (CH_{arom}, C₆ & C₁₀), 129.6 (C₁), 144.4 (C₂), 147.8 (CH_{arom}, C₂₄), 150.9 (C₄) ppm; MS: m/z = 430.4 (M + H)⁺.

2.4.4. 1-Benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole (5c, n = 1). White solid; m.p.: 161–163 °C; anal. calcd. for

 Table
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 Synthesis
 of
 1-benzyl-2,4,5-triphenyl-1H-imidazoles
 using

 various modified zeolites^a
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Entry	Catalyst	Time (min)	Yield ^b (%)
1	No catalyst	720	N. R. ^c
2	H-BEA (12)p	60	86
3	H-BEA (15)	60	95
4	H-BEA (25)	60	83
5	H-BEA (34)	60	75
6	H-Y (2.43)	165	83
7	H-MOR (11)	140	80
8	H-ZSM-5 (15)	165	70

^{*a*} Reaction conditions: benzil (1 mmol), NH₄OAc (4 mmol), benzaldehyde (1 mmol), benzyl amine (1 mmol), catalyst (2 wt%) under ethanol reflux conditions, oil bath. ^{*b*} The yield refers to the pure isolated products. ^{*c*} No reaction. C₂₈H₂₁ClN₂: C, 79.89, H, 5.03, N, 6.66%. Found: C, 79.92, H, 5.07, N, 6.61%; FT-IR (KBr, cm⁻¹): 3057 (C–H stretch), 2936, 1610, 1598 (C=N), 1477, 1448, 1414 (C=C), 1357 (C–N stretch), 757 (C–Cl stretch); ¹H NMR (400 MHz, DMSO-d₆): 5.09 (s, 2H, CH₂), 6.72–7.60 (m, 19H, Ar–H) ppm; ¹³C NMR (100 MHz, DMSO): 48.3 (CH₂, C₂₅), 125.5 (CH_{arom}, C₂₉), 126.0 (CH_{arom}, C₇), 126.2 (CH_{arom}, C₁₁), 126.4 (CH_{arom}, C₁₃), 126.5 (CH_{arom}, C₁₇), 126.6 (CH_{arom}, C₂₇), 127.3 (CH_{arom}, C₃₁), 127.9 (CH_{arom}, C₁₅), 128.5 (CH_{arom}, C₁₆), 128.7 (CH_{arom}, C₁₉), 128.8 (CH_{arom}, C₂₃), 129.2 (CH_{arom}, C₈ & C₁₀), 129.2 (CH_{arom}, C₁₄ & C₁₆), 129.5 (CH_{arom}, C₂₀), 130.4 (CH_{arom}, C₂₂), 131.1 (C₂), 134.1 (CH_{arom}, C₆), 134.3 (CH_{arom}, C₂₁), 137.4 (CH_{arom}, C₂₆), 138.8 (CH_{arom}, C₁₂),142.3 (C₄), 147.9 (C₁) ppm; MS: *m/z* = 421 (M + H)⁺.

2.4.5. 1-Benzyl-2-(4-methylphenyl)-4,5-diphenyl-1H-imidazole (5f, n = 1). Off-white solid; m.p.: 158–160 °C; anal. calcd. for C₂₉H₂₄N₂: C, 86.97, H, 6.04, N, 6.99%. Found: C, 86.88, H, 6.00, N, 6.80%; FT-IR (KBr, cm⁻¹): 3059 (C-H stretch), 3027, 1600 (C=N), 1496, 1481, 1446 (C=C), 1359 (C-N stretch), 768, 694 (C-H band); ¹H NMR (400 MHz, DMSO): 2.06 (s, 3H, CH₃), 5.0 (s, 2H, CH₂), 6.7–7.6 (m, 19H, Ar–H) ppm; ¹³C NMR (100 MHz, DMSO): 23.4 (CH₃, C₂₄), 48.4 (CH₂, C₂₄), 125.1 (CH_{arom}, C₁₉), 126.0 (CH_{arom}, C₂₃), 126.2 (CH_{arom}, C₂₉), 126.4 (CH_{arom}, C₇), 127.0 (CH_{arom}, C₁₁), 127.1 (CH_{arom}, C₁₃), 127.7 (CHarom, C17), 128.0 (CHarom, C18), 128.1 (CHarom, C27), 128.4 (CH_{arom}, C₃₁), 128.5 (CH_{arom}, C₂₈), 128.6 (CH_{arom}, C₃₀), 128.8 (CHarom, C₉), 128.8 (CHarom, C₁₅), 128.9 (CHarom, C₈), 130.1 (CH_{arom}, C₁₀), 130.3 (CH_{arom}, C₁₄), 130.5 (CH_{arom}, C₁₆), 130.7 (CHarom, C20), 131.0 (CHarom, C22), 134.4 (C2), 135.1 (CHarom, C21), 136.8 (CHarom, C6), 137.0 (CHarom, C26), 137.2 (CHarom, C_{12}), 145.4 (C_4), 147.0 (C_1) ppm; MS: $m/z = 401.0 (M + H)^+$.

2.4.6. 1-Benzyl-2-(4-chloro-3-nitrophenyl)-4,5-diphenyl-1*H*imidazole (5h, n = 1). Pale yellow solid; m.p.: 168–170 °C; anal. calcd. for C₂₈H₂₀ClN₃O₂: C, 72.18, H, 4.33, N, 9.02%. Found: C, 71.10, H, 4.51, N, 8.98%; (λ_{max} , ethanol) = 301 nm; FT-IR (KBr, cm⁻¹): 3098 (C-H stretch), 3062, 1602 (C=N), 1533 (N–O stretch), 1448 (C=C), 1352 (C–N stretch), 732 (C– H band), 699 (C–Cl stretch); ¹H NMR (400 MHz, DMSO): 5.24 (s, 2H, CH₂), 6.81–8.35 (m, 18H, Ar–H) ppm; ¹³C NMR (100 MHz, DMSO): 47.8 (CH_{arom}, C₈), 124.3 (CH_{arom}, C₂₄), 125.7 (CH_{arom}, C₃₀), 126.1 (CH_{arom}, C₁₀), 126.5 (CH_{arom}, C₁₅), 126.9

Table 3 Effect of solvent on the synthesis of 1-benzyl-2,4,5-triphenyl-1H-imidazoles^a

Entry	Solvents	Reflux temperature (°C)	Time (min)	Yield ^{b} (%)
1	Water	100	420	N. R. ^c
2	Ethanol	70	60	95
3	Methanol	65	60	86
4	Glacial acetic acid	115	60	82
5	Acetonitrile	80	150	50
6	Acetone	54	150	60
7	Toluene	105	360	94
8	Chloroform	60	360	48
9	Dichloromethane	38	360	N. R. ^{<i>c</i>}
10	Solvent-free	100	15	99

^{*a*} Reaction conditions: benzil (1 mmol), NH₄OAc (4 mmol), benzaldehyde (1 mmol), benzyl amine (1 mmol), catalyst (2 wt%) under reflux conditions, oil bath. ^{*b*} The yield refers to the pure isolated products. ^{*c*} No reaction.

Table 4 Synthesis of TSIs using a catalytic amount of zeolite BEA (15) under solvent-free conditions^a

	-R	n	Time (min)	Vield ^c	М.Р. (°С)	
Entry ^b				(%)	Found	Reported
5a	-CHO	1	15	99	160-162	160–165 (ref. 3 <i>c</i>)
		0	30	86	216-218	217-218 (ref. 3c)
5b	3-NO ₂ -CHO	1	25	88	152-154	150-152 (ref. 25)
		0	50	81	250-252	248-250 (ref. 17)
5 c	4-Cl-CHO	1	25	94	160-162	160–162 (ref. 27)
		0	50	93	148-150	148–151 (ref. 3c)
5d	4-OH-CHO	1	20	93	133-135	131–132 (ref. 27)
		0	30	85	280-282	282–284 (ref. 3b)
5e	3-Br-CHO	1	25	90	158-160	157-160 (ref. 22c)
		0	50	89	152-154	
5f	4-CH ₃ -CHO	1	25	92	163-165	164–166 (ref. 27)
	-	0	30	83	188-190	189–190 (ref. 27)
5g	2-OCH ₃ -CHO	1	30	86	176-178	175-178 (ref. 30)
		0	60	78	150-152	149-152 (ref. 30)
5h	4-Cl-3-NO ₂ -CHO	1	15	91	168-170	Present work
	-	0	35	84	190-192	

^{*a*} Reaction conditions: benzil (1 mmol), NH₄OAc (4 mmol), aldehydes (1 mmol), benzyl amine or aniline (1 mmol) and catalyst (2 wt%) under solvent-free conditions, oil bath. ^{*b*} Products (5a–g) were characterized and compared for their physical properties with authentic samples. ^{*c*} The yield refers to the pure isolated products.

(CH_{arom}, C₁₄), 127.1 (CH_{arom}, C₁₂), 127.3 (CH_{arom}, C₃₁), 127.6 (CH_{arom}, C₂₈), 127.9 (CH_{arom}, C₂₂), 128.3 (CH_{arom}, C₃₂), 128.5 (CH_{arom}, C₂₉), 128.6 (CH_{arom}, C₁₉), 128.9 (CH_{arom}, C₁₇), 129.1 (CH_{arom}, C₁₈), 129.4 (CH_{arom}, C₁₆), 129.5 (CH_{arom}, C₁₃), 129.9 (CH_{arom}, C₁₁), 130.7 (C₁), 131.5 (CH_{arom}, C₉), 131.9 (CH_{arom}, C₂₁), 132.9 (CH_{arom}, C₇), 133.9 (CH_{arom}, C₂₀), 135.5 (CH_{arom}, C₂₇), 136.7 (CH_{arom}, C₆), 137.4 (C₂), 143.6 (CH_{arom}, C₂₃), 147.4 (C₄) ppm; MS: $m/z = 466.0 (M + H)^+$.

2.4.7. 2-(4-Chloro-3-nitrophenyl)-1,4,5-triphenyl-1*H*-imidazole (5h, n = 0). Pale yellow solid; m.p.: 189–191 °C; anal. calcd. for C₂₇H₁₈ClN₃O₂: C, 71.76, H, 4.01, N, 9.30%. Found: C, 70.96, H, 4.22, N, 9.02%; (λ_{max} , ethanol) = 299 nm; FT-IR (KBr, cm⁻¹): 3060 (C–H stretch), 1599 (C=N), 1538 (N–O stretch), 1497, 1447 (C=C), 1356 (C–N stretch), 767 (C–H band), 698 (C–Cl stretch); ¹H NMR (400 MHz, DMSO): 7.18– 8.74 (m, 18H, Ar–H) ppm; ¹³C NMR (100 MHz, DMSO): 121.6 (CH_{arom}, C₂₄), 124.1 (CH_{arom}, C₂₀), 124.6 (CH_{arom}, C₂₉), 126.3 (CH_{arom}, C₁₉), 126.7 (CH_{arom}, C₁₅), 127.2 (CH_{arom}, C₁₄), 127.6 $(CH_{arom}, C_{10}), 128.2 \ (CH_{arom}, C_{27}), 128.5 \ (CH_{arom}, C_{22}), 128.6 \\ (CH_{arom}, C_{17}), 129.3 \ (CH_{arom}, C_{12}), 129.5 \ (CH_{arom}, C_{18}), 129.7 \\ (CH_{arom}, C_{16}), 129.8 \ (CH_{arom}, C_{11}), 130.3 \ (CH_{arom}, C_{13}), 130.4 \\ (CH_{arom}, C_{21}), 131.0 \ (CH_{arom}, C_{23}), 131.7 \ (CH_{arom}, C_{9}), 132.3 \\ (CH_{arom}, C_{26}), 132.4 \ (C_{1}), 133.8 \ (CH_{arom}, C_{7}), 135.8 \ (CH_{arom}, C_{25}), 137.4 \ (CH_{arom}, C_{28}) \ ppm; MS: <math>m/z = 452.0 \ (M + H)^{+}.$

The reusability of the catalyst was investigated for each recycling by separating the spent catalyst from the reaction mixture by filtration under reduced pressure, followed by washing with ethanol, drying overnight at 100 $^{\circ}$ C and reactivating it by heating in a stream of air at 550 $^{\circ}$ C for 5 h.

Results and discussion

3.1. Catalyst characterization

3.1.1. Physicochemical characterization of zeolites. The physicochemical characterization data for various types of

zeolites, such as medium and large pore size and modified *via* dealumination, are provided in Table 1. It is observed that the surface area of zeolite H-BEA and dealuminated BEA are higher than that of the rest of the zeolites and the concentration of the acid centre for zeolite H-MOR is found to be higher than that for the rest of the zeolites. Moreover, upon controlled dealumination, the pore volume and surface area slightly increased and the total acidity decreased with the increase in Si/Al ratio.

3.1.2. XRD of the zeolite BEA. The powder XRD patterns of parent zeolite H-BEA and all dealuminated zeolite BEA synthesized via acid treatment are depicted in Fig. 1. The welldeveloped diffraction lines of the zeolite H-BEA including dealuminated zeolite BEA were discerned and they are well resolved. The crystallinity of the samples was evaluated by comparing the most intense diffraction peak at 22.3° (2 θ) to that of the parent zeolite taken as 100% crystalline. The dealuminated zeolite BEA was compared with the corresponding counterpart of H-BEA zeolite and found similar to the parent zeolite indicating that the framework structure of zeolite BEA is not affected or remains intact upon controlled dealumination of the zeolite by aqueous HNO₃. Moreover, the position of the main intense peak did not change significantly upon controlled dealumination but the relative crystallinity of the zeolite BEA showed a negligible decrease with the increase in dealumination of the BEA zeolite. All samples exhibited the typical pattern of highly crystalline zeolite BEA with broad and sharp reflection and the characteristics of an intergrowth of different polymorphs, and no other phase impurities were observed after the dealumination.

3.1.3. FT-IR and ¹H MAS NMR of the zeolite BEA. The acidic hydroxyl protons acting as catalytically active Brønsted acid sites (BAS) which can be investigated in a direct manner by FT-IR²⁶ and ¹H MAS NMR spectroscopy. The spectra of zeolite H-BEA and dealuminated BEA are shown in Fig. 2(a) and 3, respectively. Zeolite H-BEA has two main bands and these were identified in the IR spectrum at 3611

cm⁻¹ attributed to the strong acidic bridged Si(OH)Al and at 3726 cm⁻¹ assigned to weak acidic terminal Si–OH groups. Two vibrational bands of small intensities at 3661 cm⁻¹ & 3795 cm⁻¹ were assigned to hydroxyl groups associated with extra-framework aluminium species (EFAl). A band at 3250 cm⁻¹ with a very small intensity was found for the hydrogen bonded bridging –OH group. The IR spectrum of the dealuminated BEA zeolite shows that the intensities of the bands observed at 3611 cm⁻¹ attributed to the Brønsted acidic Si(OH)Al and at 3661 cm⁻¹ and 3795 cm⁻¹ attributed to the Lewis acidic sites (LAS) of EFAl (OH) considerably decreased for BEA (15) and BEA (25) as compared to the parent zeolite H-BEA (12)p, and these two bands almost disappeared for BEA (34) (Fig. 2a).

The FT-IR study of the catalysts was carried out after pyridine adsorption in order to investigate the acidic properties of the catalyst materials. The result obtained has proved the presence of LAS and BAS in the H-BEA zeolite. The spectrum of pyridine adsorbed on the samples shows characteristic bands corresponding to the C–C stretching vibrations of pyridine. All the zeolite BEA samples exhibit well resolved bands at about 1540, 1490 and 1447 cm⁻¹. The bands at 1540 and 1447 cm⁻¹ are assigned to pyridinium ions adsorbed onto BAS (protonic) and LAS (coordinatively unsaturated Al³⁺ or EFAl), respectively, while the band at 1490 cm⁻¹ is attributed to the adsorbed pyridinium ion species on both BAS and LAS (B + L).

Fig. 2(b) shows that, in the case of parent H-BEA (12)p, the band intensities of B + L and LAS are found to be higher as compared to BAS. In contrast, the band intensity of BAS is found to increase with the gradual decrease in B + L and LAS for dealuminated zeolite BEA (15). Further, upon controlled dealumination, the band intensities of LAS and B + L were found to decrease for H-BEA (25) and H-BEA (34) due to the removal of Al from the zeolite framework. It has been suggested that on dealumination of the H-BEA (12)p zeolite, some positively charged EFAl species could neutralize the



Fig. 1 XRD patterns of (a) parent zeolite H-BEA (12)p and (b-d) dealuminated BEA.



Fig. 2 (a) FT-IR and (b) pyridine FT-IR spectra of zeolite H-BEA and dealuminated BEA.

negative charge of the tetrahedra and AlO_4 consequently decreases the intensity of dealuminated zeolite acid sites. Thus, it should be concluded that removal of Al from the zeolite framework upon controlled dealumination slightly increases the BAS with a decrease in LAS and B + L. A corresponding decrease is observed in the intensity of ¹H MAS NMR signals at 4.0 and 35.1 ppm which are assigned to free bridged and hydrogen bonded bridged hydroxyls of Si(OH)Al, respectively, in the case of zeolite BEA (15) as compared to parent H-BEA (12)p. A decreased intensity is also observed in the 2.7 ppm signal which is attributed to the presence of EFAl(OH) species for BEA (15) and disappeared for BEA (25) and BEA (34) (Fig. 3).

3.2. Synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles (effect of geometry and surface acidity of zeolite)

Zeolites as solid acid catalysts with different physicochemical characteristics were used to elucidate the role of the zeolite channel system in their activity and selectivity towards the synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles (Table 1). Table 1 shows the effect of various structural features such as the Si/Al ratio, acidity, surface area and geometry (pore structure and dimension) of zeolites on the synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles.

Initially, the 4-CR of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles was carried out using benzil (1 mmol), NH₄OAc (4 mmol),



Fig. 3 ¹H MAS NMR spectra of zeolite H-BEA and dealuminated BEA.

benzaldehyde (1 mmol), and benzyl amine (1 mmol) in the absence of zeolite catalysts. It is noteworthy that no formation of products was observed in the absence of a zeolite catalyst, indicating that a catalyst is necessary for the formation of the corresponding product (Table 2, entry 1). For our investigations, subsequently, various large (H-BEA, H-Y, H-MOR) and medium (H-ZSM-5) pore size zeolites were used and we found that a micro-porous structure, strong acidity and a unidirectional channel structure do not highly favour MCRs as compared to the large pore zeolite H-BEA with a higher surface area and low to moderate acidity. As per our previous investigation on ZCMCRs,²³ it has also been found that the hydrophobic character of zeolite H-BEA due to the higher Si/Al ratio as compared to the other zeolites shows better catalytic activity towards MCRs particularly when subjected to highly polar solvents, reactants and products as well. Hence, it is concluded in the present case that low to moderate acidity, along with a higher surface area and a higher Si/Al ratio of zeolite H-BEA (Table 1), are prime factors for higher catalytic activity towards the synthesis of 1-benzyl-2,4,5-triphenyl-1H-imidazoles. Thus, the preferential order to yield 1-benzyl-2,4,5-triphenyl-1H-imidazoles was found to be: H-BEA > H-Y > H-MOR > H-ZSM-5.

3.3. Effect of surface polarity (Si/Al ratio) of zeolites

It is worth noting that the catalyst becomes more hydrophobic with increasing Si/Al framework ratio and the concentration of acid sites decreases with enhanced strength of remaining sites. According to the results and conclusions presented above, we could expect that the less polar zeolite should favour the desorption of adsorbed polar products. Hence, zeolites H-Y and H-MOR were found to be less effective towards the synthesis of 1-benzyl-2,4,5-triphenyl-1Himidazoles compared to H-BEA although they also contain large pores and exhibit higher acidity. In this context, the synthesis of 1-benzyl-2,4,5-teiphenyl-1H-imidazoles has been carried out using zeolite H-BEA with varied Si/Al ratios (12, 15, 25 and 34) in order to study the effect of the polarity of zeolite (Table 2). The results shown in Table 2 show the maximum activity for the zeolite with a Si/Al ratio of 15 which contains a much lower concentration of acid sites than the zeolite with a Si/Al ratio of 12 (Table 1). From these results, it seems that a larger number of acid sites does not guarantee a higher catalytic activity due to the adsorption inhibiting effect of reactants and products. Thus, in the present case, a less polar zeolite with a lower concentration of acid sites performs better. In fact, a yield of 95% (entry 5a) was obtained with 2 wt% of BEA (15) after 60 min.

Moreover, the polarity of the solvent should also be taken into account when a zeolite catalyst is to be subjected to any organic transformations. Generally, the non-polar solvent toluene is more effective towards reactions that contain more polar reactants or produce highly polar products. In our previous study concerning ZCMCRs for the synthesis of dihydropyrimidinones (DHPMs) and diarylpyrimidinones (DAPMs), the non-polar solvent toluene was found to be more efficient along with zeolite BEA (15). Whereas, in the present case, surprisingly, the polar solvent ethanol shows better catalytic activity towards the synthesis of 1-benzyl-2,4,5-triphenyl-1Himidazoles using zeolite BEA (15) as a solid acid catalyst. In this context, in order to investigate the effect of the polarity of products with the highly polar solvent ethanol, the $\log P$ values of DHPMs, DAPMs, 2,4,5-trisubstituted imidazoles (work under study) have been compared with that 1-benzyl-2,4,5-trisubstituted imidazoles (Fig. 4). It has been seen that DHPMs and DAPMs possess lower $\log P$ values (polar) as compared to the 2,4,5-trisubstituted imidazoles and 1-benzyl-2,4,5-triphenyl-1H-imidazoles. As a consequence, the nonpolar solvent toluene is found to be more suitable for the synthesis of DHPMs and DAPMs via MCRs. Meanwhile, the polar solvent ethanol is found to be a more suitable solvent for the synthesis of 2,4,5-trisubstituted imidazoles and 1-benzyl-2,4,5triphenyl-1H-imidazoles as it has a high log P value (less polar). Further, the effects of various polar and non-polar solvents on the synthesis of 1-benzyl-2,4,5-trisubstituted imidazoles via ZCMCRs were also investigated. Many reports concerning the synthesis of 1-benzyl-2,4,5-triphenyl-1Himidazoles shows that this reaction is highly favoured in polar solvents such as ethanol and methanol.^{3a,b,11,15a,21,27,28} In the present study, the expected results were obtained and are depicted in Table 3, which shows that polar solvents are found to be more efficient as compared to the non-polar solthe synthesis of 1-benzyl-2,4,5-triphenyl-1Hvents in imidazoles.

3.4. ²⁷Al MAS NMR of zeolite BEA (effect of EFAl or LAS insights from the FT-IR and ¹H NMR studies of zeolite BEA)

In general, framework defects, tricoordinated and EFAl species contribute to LAS and are strongly affected by dealumination of zeolite H-BEA as indicated by the FT-IR and solid state NMR spectra of zeolite H-BEA and dealuminated zeolite BEA (Fig. 2 and 3). The perturbed Al(OH) hydroxyl band at 3661 cm⁻¹ and the very high frequency (VHF) hydroxyl band at 3795 cm⁻¹ generally assigned to the EFAl of transient or partially hydrolyzed coordinatively unsaturated Al species considerably decreased for the dealuminated BEA (25) and totally disappeared for BEA (34). The ²⁷Al MAS NMR spectrum of the zeolite is visualized in Fig. 5. As shown, a strong signal at 54 ppm indicates the presence of a tetrahedrally (T_d) coordinated Al framework in the zeolite BEA. There is also a weak signal at 0.6 ppm due to the residual EFAl with an octahedral $(O_{\rm h})$ coordination. Most of Al, as shown in Fig. 5, are located in the zeolite tetrahedral framework positions, giving rise to bridging OH acid centres. Moreover, the spectra of all BEA zeolites show that the intensity of the peak assigned to the extra framework octahedral Al considerably decreases in all dealuminated BEA zeolites as compared to the parent zeolite H-BEA (12)p. The results indicate that increasing the rate of dealumination of zeolite H-BEA with a mineral acid (HNO₃) causes either substantial or total



Fig. 4 Log P values of different biologically active moieties.



removal of framework and EFAl species which consequently leads to a decrease in the concentration of LAS and BAS of zeolite BEA.

Furthermore, the dealumination of zeolite resulted in the enhanced strength of the remaining Brønsted acidity up to a certain Si/Al ratio of zeolite by decreasing the total number of acid sites. The enhanced strength of this Brønsted acidity can be attributed to the partially hydrolyzed, coordinatively unsaturated Al species of LAS which inductively leads to a greater negative charge delocalization in the remaining Si–O–Al bridge, thus, creating a BAS of enhanced strength of acidity.²⁹ Thus, it can be said that the interaction between BAS and LAS may lead to the formation of BAS of enhanced strength of acidity. These observations have led to the conclusion that the decrease or removal of LAS or EFAI species not only results in lowering the concentration of Lewis acidity but also results in the decrease of the strength of the remaining Brønsted acidity. As a consequence, zeolite H-BEA (12)p and BEA (15) show higher activity towards the synthesis of 1-benzyl-2,4,5triphenyl-1*H*-imidazoles (86% and 95% yield) as compared to the highly dealuminated BEA (25) and BEA (34).

In general, the higher activity of zeolite BEA may be attributed to the higher hydrophobicity and a positive effect of the EFAL species present on H-BEA (12)p and BEA (15), which is due to an inductive effect of the LAS of EFAL species on the protonic sites. Further, dealumination increases the diffusivity of the reactants and/or products thereby enhancing accessibility of the acid sites to the reactant molecules by creating mesopores in the crystallites.

3.5. Synthesis of TSIs

In order to optimize the catalyst concentration and reaction conditions, the reaction of benzil, NH_4OAc , benzaldehyde

and benzyl amine was carried out using varied amounts of zeolite BEA (15) (1, 2 up to 5 wt%) under ethanol reflux as well as thermal solvent-free conditions. The best result was obtained by carrying out the reaction with a 1:4:1:1 molar ratio between benzil, NH₄OAc, benzaldehyde and benzyl amine and 2 wt% of zeolite BEA (15) under solvent-free conditions at 100 °C with a 99% yield within 15 min (Fig. 6).

Thus, an attempt has been made to prepare a wide range of TSIs derivatives using the optimized reaction conditions. A series of TSI derivatives were prepared in high to excellent vields in thermal solvent-free conditions. The results are summarized in Table 4. It is observed that various aromatic aldehydes having both electron-withdrawing and electrondonating substituents reacted efficiently with benzil, NH₄OAc and benzil amine in the presence of a catalytic amount of zeolite BEA (15) (2 wt%) under thermal solvent-free conditions to give the corresponding TSI derivatives in moderate to high (88-99%) yields. Various -o, m- and p- directing functional groups of aromatic aldehydes were found to be compatible under the optimized reaction conditions. The procedure worked well for all the substituted aldehyde derivatives without the formation of any side products. The novel bulkier aldehyde substituent (Table 4, entry 5 h, n = 1) also gives an excellent yield (91%) as compared to the other aldehyde substituents. All the reactions of aldehyde substituents have also been repeated with aniline instead of benzyl amine as a reactant in the synthesis of 1,2,4,5-tetraphenyl-1H-imidazoles and yielded the desired product efficiently. In this case, the reaction time was found to be nearly double and the % yield was found to be lower as compared to the benzyl amine reactant. The novel bulkier aldehyde substituent (Table 4, entry 5 h, n = 0) also gives a good yield (85%) with the aniline reactant.

A plausible mechanism for the zeolite catalyzed synthesis of TSIs *via* MCRs is outlined in Scheme 2. The zeolite catalysts have several accessible LAS and BAS to promote the reaction. As seen in Scheme 2, initially, we assumed that the acidic sites of zeolite stimulate the carbonyl group of aromatic aldehydes. Subsequently, nucleophilic attack of the nitrogen atoms of ammonia obtained from NH_4OAc and amines on the activated carbonyl group facilitates the formation of a di-imine intermediate (I) to increase the electrophilicity of the carbonyl group of the aldehydes. Now, acidic sites of the zeolite activate the carbonyl group of benzil to decrease the energy of the transition state. Then condensation of the di-imine intermediate (I) with the protonated form of benzil occurs to form intermediate (II) which in turn removes the H_2O molecule from a crude adduct and finally rearranges to give the desired TSIs product.

3.6. Merits of method

In order to investigate the merits of method, a few representative examples are tabulated in Table 5, in which the efficiency of other reported methods is compared with that of zeolite BEA (15) for the synthesis of TSIs. The result shows the promising features of the zeolite BEA (15) catalyst in terms of reaction conditions and the yield of the product compared with those of various heterogeneous catalysts recently reported in the literature.

Furthermore, a comparison of the FT-IR spectra of the starting reactants and the synthesized product (Fig. 7) shows the key advantage of the multicomponent one-pot synthesis that it does not produce any side product. The IR spectra of the starting raw materials such as benzaldehyde and benzil exhibit characteristic sharp bands of C=O with strong intensities at 1696 and 1646 cm⁻¹, respectively, two bands of N-H stretching with medium intensities at 3373 and 3290 cm⁻¹ and one medium sharp band of N-H bending at 1605 cm⁻¹ for benzyl amine, a sharp band of C=O with a strong intensity at 1750 cm⁻¹ and a medium band of C=O with a small



Fig. 6 (a) Optimization of the catalyst concentration. Reaction conditions: benzil (1 mmol), NH_4OAc (4 mmol), benzaldehyde (1 mmol), benzyl amine (1 mmol) using reflux as well as solvent-free conditions (100 °C), oil bath. (b) Effect of various temperatures. Reaction conditions: benzil (1 mmol), NH_4OAc (4 mmol), benzaldehyde (1 mmol), benzyl amine (1 mmol), catalyst (2 wt%) using solvent-free conditions, oil bath. * The yield refers to the pure isolated products.



Scheme 2 Plausible mechanism for the formation of TSIs catalyzed by zeolite BEA.

 Table 5
 Comparison of various catalysts with zeolite BEA (15) for the one-pot synthesis of 1-benzyl-2,4,5-triphenyl-1H-imidazoles

Entry	Catalysts	Conditions	Time (min)	Yield (%)	References
1	L-Proline	MeOH/reflux	510-600	76-88	Samai <i>et al.</i> , 2009 (ref. 6)
2	Carbon based solid acid	SF/130 °C	60-120	86-94	Tavakoli-Hoseini et al., 2011 (ref. 7)
3	FE ₃ O ₄ (a)SiO ₂ -OSO ₃ H	SF/130 °C	15-60	87-97	Yadegarian et al., 2015 (ref. 31)
4	β-CD-Pr–SO ₃ H	SF/100 °C	15-240	68-96	Ran et al., 2015 (ref. 27)
7	SBA-15/TFE	SF/90 °C	210	92	Rostamnia et al., 2012 (ref. 8)
8	Nano-Al-MCM-41	SF/120 °C	50	92	Olyaei et al., 2016 (ref. 9)
9	$H_4[PMo_{11}VO_{40}]$	EtOH/reflux	8	88	Heravi et al., 20 007 (ref. 15a)
10	Cu(NO ₃) ₂ /zeolite-HY	MeOH/65 °C	180	56	Sivakumar <i>et al.</i> , 2010 (ref. 10)
11	ZSM-5-SO ₃ H	SF/110 °C	40	86	Vosoughi et al., 2015 (ref. 11)
12	Zeolite-HY	MW	6	85	Balalaei et al., 2000 (ref. 12)
14	Sulfated MCM-41	SF/100 °C	60	93	Vadivel et al., 2013 (ref. 13)
15	H-ZSM-22	EtOH/140 °C	30	81	Bhat <i>et al.</i> , 2016 (ref. 14)
16	TrCl or Ph ₃ CCl	SF/90 °C	32	80	Moosavi-Zare et al., 2014 (ref. 32)
17	ZSM-5	EtOH/reflux	80	92	Teimouri <i>et al.</i> , 2011 (ref. 3 <i>b</i>)
18	Zeolite BEA (15)	SF/100 °C	15	99	Present work
SF = Solve	ent-free, MW = micro-wave.				

intensity at 1070 cm⁻¹ for NH₄OAc, which completely disappeared in the IR spectrum of the synthesized final product, indicating that the synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles *via* MCRs took place without forming any side product.

3.7. Reusability of solid acid catalyst for the synthesis of 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles

In view of an environmentally friendly approach, reusability is a very significant feature for heterogeneous catalysts. The reusability study of the solid acid catalyst was carried out *via* the reaction of benzil, NH_4OAc , benzaldehyde and benzyl amine in the presence of zeolite BEA (15) under solvent-free conditions. The catalyst was separated from the crude product by addition of ethanol followed by filtration. It was washed consequently with ethanol to remove the product completely from the catalyst under reduced pressure followed by drying overnight at 100 °C and re-activating by heating in a stream of air at 550 °C for 5 h and weighed. The regenerated catalyst was found to be reusable up to six consecutive runs and is shown in Fig. 8. The yields for the six runs were found to be 99%, 98%, 98%, 96%, 95% and 95%,



Fig. 7 Comparison of the characteristic IR bands of the starting raw materials and the synthesized product.



Fig. 8 (a) Reusability of the dealuminated BEA (15) zeolite; (b) XRD patterns of fresh (black) and spent (after six runs - red) catalyst.

respectively. Furthermore, retention of the structure of the catalyst was confirmed by comparing the XRD pattern of the recovered catalysts with that of the fresh catalysts, for the model reaction. The XRD pattern of the fresh zeolite was found to be the same as that of the spent zeolite (after six runs), indicating retention of the framework structure of the zeolite throughout the course of the reaction, and hence it can be reused.

4. Conclusion

The synthesis of biologically active 1-benzyl-2,4,5-triphenyl-1*H*-imidazoles over various large pore zeolites (H-Y, H-MOR, H-BEA and dealuminated BEA) has been studied. Zeolite BEA (15) has been found to be an efficient and reusable catalyst for one-pot, 4-CR of benzil, NH₄OAc, substituted aromatic aldehydes and benzyl amine for the synthesis of

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1-benzyl-2,4,5-triphenyl-1*H*-imidazoles under solvent-free conditions.

Moreover, the FT-IR and solid state NMR spectroscopy of zeolite H-BEA and dealuminated BEA gave further insights into the effect of the nature of acid sites on the synthesis of 1-benzyl-2,4,5-triphenyl-1H-imidazoles. It has been found that the dealumination of parent zeolite BEA results in enhanced strength of Brønsted acidity up to a certain Si/Al ratio due to the inductive effect of Lewis acidic EFAl species, consequently leading to the higher activity of H-BEA (15) towards the synthesis of 1-benzyl-2,4,5-triphenyl-1H-imidazoles. This procedure provided the desired products in high vields over a short reaction time with a low catalyst loading. The solventfree protocol makes the process environmentally benign and economically viable. The present protocol will serve as a green tool and opens a new avenue in the area of environmentally benign synthesis of biologically active drug-like molecules.

Conflicts of interest

There are no conflicts to declare.

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