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An efficient and one-pot synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles catalyzed via solid acid nano-catalyst

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ABSTRACT

A simple highly versatile and efficient synthesis of 2,4,5-trisubstituted imidazoles is achieved by three component cyclocondensation of 1,2-dicarbonyl compounds, aldehydes and NH4OAc, as ammonia source using clays, zeolite, nano-crystalline sulfated zirconia (SZ) as catalyst in ethanol at moderate temperature. Moreover, the utility of this protocol was further explored conveniently for the one-pot, four component synthesis of 1,2,4,5-tetrasubstituted imidazoles in high yields, short reaction times and milder conditions, easy work-up and purification of products by non-chromatographic methods. The catalysts can be recovered for the subsequent reactions and reused without any appreciable loss of their efficiency.

1. Introduction

Imidazoles are a class of heterocyclic compounds that contain nitrogen and are currently under intensive focus due to their wide range of applications, because they have many pharmacological properties and play important roles in biochemical processes [1,2]. The potential and wide range of application of the imidazole pharmacophore may be attributed to its hydrogen bond donor–acceptor ability as well as its high affinity for metals. Many of the substituted imidazoles are known as inhibitors of p38 MAP kinase, fungicides, herbicides, plant growth regulators, antibacterial, antitumour, pesticides and therapeutic agents [3–9]. In recent years, alkylated imidazoliums are substantially used in ionic liquids [10] that have been given a new approach to 'Green Chemistry'. The imidazole compounds were also used in photography as photosensitive compound [11]. They also serve as useful building blocks for the synthesis of other classes of compounds. Owing to the wide range of pharmacological and biological activities, the synthesis of imidazoles has become an important target in current years. Among them, tri- and tetrasubstituted imidazoles have received much attention recently, and new preparative methods have appeared [12].

There are several methods reported in literature for the synthesis of imidazoles. 2,4,5-Trisubstituted imidazoles are generally synthesized by three component cyclocondensation of a 1,2-diketone, α-hydroxyketone or α-ketomonoxime with an aldehyde and ammonium acetate, which comprise the use of ionic liquids, [13] refluxing in acetic acid, [14] silica sulfuric acid, [15] $InCl_3{\cdot}3H_2O$, [16]. On the other hand, the synthesis of 1,2,4,5-tetrasubstituted imidazoles have been carried out by four-component condensation of a 1,2-diketone, α-hydroxyketone or α-ketomonoxime with an aldehyde, primary amine and ammonium acetate using microwaves, [17a] heteropolyacid, [17b] $BF_3{\cdot}SiO_2$, [12l] silica gel/$NaHSO_4$ [17c] or $HClO_4$–SiO_2 [17d]. In addition, they can also be accessed by the cycloaddition reaction of mesoionic 1,3-oxazolium-5-olates with N-(arylmethylene)-benzenesulfonamides, [18a] hetero-Cope rearrangement, [18b] condensation of a 1,2-diketone with an aryl nitrile and primary amine under microwave irradiation [18c] and by N-alkylation of trisubstituted imidazoles [18d]. Recently PEG-400 is found to be an interesting solvent system. It is inexpensive, thermally stable, non-volatile, non-toxic and easily degradable, has emerged as reaction medium in organic synthesis [19]. Many of the synthetic methods for imidazoles suffer from one or more disadvantages such as low yields, harsh reaction conditions, prolonged time period and application of hazardous and expensive catalysts. Therefore the development of greener,

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clean, and environmentally friendly approaches is still desirable and much in demand [20]. Nowadays, more and more heterogeneous Bronsted acids, e.g., zeolites and montmorilonite clay are preferred from an economical perspective as well as from an ecological viewpoint. Due to its high protonic acidity and unique shape-selective behavior, HZSM-5, have been shown to be a highly active and stable catalyst for many reactions [21,22]. In addition zirconia is attracting considerable interest on account of its potential use as a catalyst support. Recent investigations reveal that promoted zirconia is an exceptionally good solid acid catalyst for various organic synthesis and transformation reactions having enormous industrial applications [23]. Reusable heterogeneous catalysts have attracted a great deal of interest in recent years. Since most of the catalysts are expensive and contaminate the environment, the development of efficient methods for recovery and reuse of the catalysts is a very important aspect in this chemistry. In continuation of our ongoing research for the development of simple and efficient methods for the synthesis of various heterocyclic compounds [24] herein we wish to report a simple, economic, and efficient one-pot method for the synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles from benzil, ammonium acetate, aromatic aldehydes and using solid acid catalysts.

2. Experimental

2.1. Instruments and characterization

All reagents were purchased from Merck and Aldrich and used without further purification. Montmorilonite K10 was purchased from Aldrich. Products were characterized by spectroscopy data (Mass, FTIR, ^{1}H NMR and ^{13}C NMR spectra), elemental analysis (CHN) and melting points. A JASCO FT/IR-680 PLUS spectrometer was used to record IR spectra using KBr pellets. NMR spectra were recorded on a Bruker 400 Ultrasheild NMR and DMSO-d6 was used as solvent. Melting points reported were determined by open capillary method using a Galen Kamp melting point apparatus and are uncorrected. Mass Spectra were recorded on a Shimadzu Gas Chromatograph Mass Spectrometer GCMS-QP5050A/Q P5000 apparatus.

2.2. Catalyst preparation

2.2.1. Activation of montmorilonite K10 clay catalyst

This catalyst activated with 2 M HCl in the solid to liquid ratio 1:4 (400 mL, 2 M HCl for 100 g clay) for a period of 45 min and filtered. It was then washed thoroughly with distilled water for removing chloride ions and dried in an air oven at 110 °C for 2 h. Then acid activated clay was again calcined at 430 °C for a period of 2 h and used for the reaction.

2.2.2. Synthesis of ZSM-5 and HZSM-5

For synthesis of ZSM-5, hydrated aluminum sulfate and sodium silicate solution were the sources of aluminum and silicon, respectively. The tetrapropylammonium bromide was used as the structure-directing template [25]. ZSM-5 zeolite was synthesized according to the procedure described earlier. The solid phase obtained was filtered, washed with distilled water several times, dried at 120 °C for 12 h and then calcined at 550 °C for 6 h and followed by ion exchange with NH_4NO_3 solution (three times), The acid hydrogen form of the compound is prepared by transferring the oven-dried compound to a tube furnace. Heat the ammonium zeolite for 3 hours to ensure the thermal decomposition of NH_4^+ ions. Over the course of this process, zeolite should turn from a white to brown/black color [25].

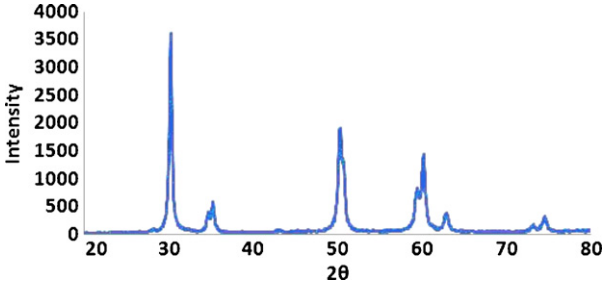


Fig. 1. XRD pattern of sulfated-zirconia catalyst.

2.2.3. Synthesis of nano-crystalline sulfated zirconia

Nano-crystalline sulfated zirconia has been prepared by one step sol–gel technique [26]. A typical synthesis involves the addition of concentrated sulfuric acid (1.02 mL) to zirconium *n*-propoxide precursor (30 wt%) followed by the hydrolysis with water. After 3 h aging at room temperature, the resulting gel was dried at 110 °C for 12 h followed by calcination at 600 °C for 2 h.

2.2.4. Characterization

X-ray diffraction pattern were recorded on diffractometer (Philips X'pert) using Cu Kα radiation ($\lambda = 1.5405$ Å), angle range was between 0 and 80° (Fig. 1), Crystallite size of the crystalline phase was determined from the peak of maximum intensity ($2\theta = 30.18$) by using Scherrer formula [27], with a shape factor (K) of 0.9, as below: Crystallite size $= K\cdot\lambda/W\cdot\cos\theta$, where, $W = W_b - W_s$ and W_b is the broadened profile width of experimental sample and W_s is the standard profile width of reference silicon sample. FTIR spectra of the catalysts were recorded by FTIR spectrophotometer in the range of 400–4000 cm^{-1} with a resolution of 4 cm^{-1} by mixing the sample with KBr (Fig. 2).

Specific surface area, pore volume and pore size distribution of sulfated zirconia samples calcined at 600 °C were determined from N_2 adsorption–desorption isotherms at 77 K (ASAP 2010 Micromeritics) (Fig. 3). Surface area was calculated by using BET equation; pore volume and pore size distribution were calculated by BJH method [28]. The samples were degassed under vacuum at 120 °C for 4 h, prior to adsorption measurement to evacuate the physisorbed moisture. The detailed imaging information about the morphology and surface texture of the catalyst was provided by SEM (Philips XL30 ESEM TMP) (Fig. 4).

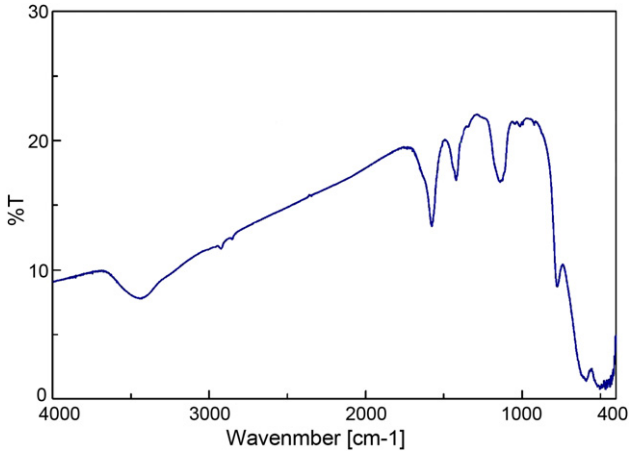


Fig. 2. FTIR spectra sulfated-zirconia catalyst.

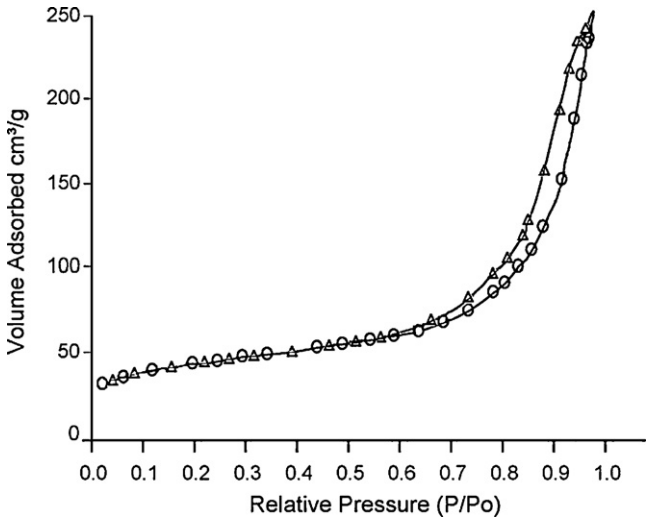


Fig. 3. N_2 adsorption–desorption isotherm of sulfated-zirconia catalyst.

2.3. General procedure for the synthesis of 2,4,5-trisubstituted imidazoles

In a 50 mL round bottom flask 1,2-diketone (1 mmol), aldehyde (1 mmol) and ammonium acetate (2 mmol) and catalyst (50 mg) stirred and refluxed in ethanol (10 mL). Then the reaction mixture was stirred for the stipulated period of time. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the filtrate was cooled to room temperature and organic layer was dried over anhydrous $MgSO_4$ and concentrated. The product was purified by chromatography through a column of silica-gel using ethyl acetate/cyclohexane ether as an eluent.

2.3.1. 2,4,5-Triphenyl-1H-imidazole (1a)

Mp 274–276 °C. FTIR (KBr, cm^{-1}): 3451, 2856, 1636, 1490; ^1H NMR (400 MHz, DMSO-d6): δ 12.69 (s, 1H), 8.09 (d, 2H), 7.56–7.22 (m, 13H); 13 C NMR (400 MHz, DMSO-d6): δ 145.6, 137.2, 135.2, 131.2, 130.4, 128.7, 128.5, 128.3, 128.2, 127.8, 127.2, 126.6, 125.3; ESI MS (*m*/*z*): 296.3 (M^+); Anal. Calcd. for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 85.18; H, 5.49; N, 9.33.

2.3.2. 2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole (1b)

Mp 260–262 °C. FTIR (KBr, cm^{-1}): 3452, 3065, 1635, 1323; ^1H NMR (400 MHz, DMSO-d6): δ 12.78 (s, 1H), 8.11 (d, 2H), 7.56–7.23 (m, 12H); ^{13}C (400 MHz, DMSO-d6): δ 146.3, 130.3, 129.9, 129.2, 128.5, 127.4, 127.0, 126.4, 125.5, 125.2, 123.3, 116.3; ESI MS (*m*/*z*): 330.1 (M^+); Anal. Calcd. for $C_{21}H_{15}ClN_2$: C, 76.24; H, 4.57; N, 8.47. Found: C, 76.20; H, 4.61; N, 8.41.

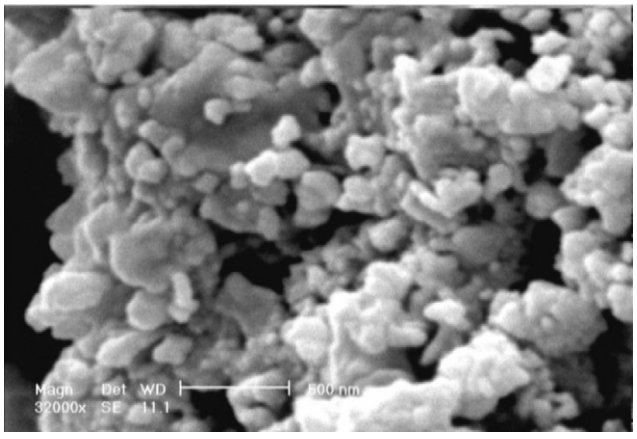


Fig. 4. SEM micrograph of sulfated-zirconia catalyst.

Table 1
Effect of catalyst type and amount of catalyst on the synthesis of imidazoles in the reaction of benzaldehyde, ammonium acetate and benzil.

Entry	Catalyst	Catalyst loading (mg)	Time (min)	Yield (%)[a]
1	K10	10	95	85
2		25	65	96
3		50	75	89
4	ZMS-5	10	110	84
5		25	80	92
6		50	95	86
7	SZ	10	100	82
8		25	75	96
9		50	90	87
10	No catalyst	–	120	–

[a] Yields after isolation of products.
Reaction condition benzaldehyde (1 mmol), ammonium acetate (2 mmol), benzil (1 mmol), in the ethanol as the solvent.

2.3.3. 2-(4-Bromophenyl)-4,5-diphenyl-1H-imidazole (1c)

Mp 254–256 °C. FTIR (KBr, cm^{-1}): 3450, 3070, 1615, 1320; ^1H NMR (400 MHz, DMSO-d6): δ 12.68 (s, 1H), 8.15 (d, 2H), 7.50–7.13 (m, 12H); ^{13}C (400 MHz, DMSO-d6): δ 146.1, 130.5, 129.6, 129.1, 128.4, 127.2, 127.0, 126.6, 125.5, 125.1, 123.0, 116.2; ESI MS (*m*/*z*): 375.2 (M^+); Anal. Calcd. for $C_{21}H_{15}BrN_2$: C, 67.21; H, 4.03; N, 7.47. Found: C, 67.06; H, 3.71; N, 7.21.

2.3.4. 2-(4-Nitrophenyl)-4,5-diphenyl-1H-imidazole (1d)

Mp 234–236 °C. FTIR (KBr, cm^{-1}): 3402, 2928,1598,1519,1346, 856; ^1H NMR (400 MHz, DMSO-d6): δ 12.81 (s, 1H), 8.01–7.42 (m, 14H); ^{13}C NMR (400 MHz, DMSO-d6): δ 148.9, 143.7, 131.6, 130.6, 129.7, 128.4, 127.8, 127.4, 126.9, 126.1, 125.4, 124.3, 122.2, 118.5; ESI MS (*m*/*z*): 341.2 (M^+); Anal. Calcd. for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.81; H, 4.44; N, 12.37.

2.3.5. 4-(4,5-Diphenyl-1H-imidazol-2-yl)-phenol (1e)

Mp 268–270 °C. FTIR (KBr, cm^{-1}): 3590, 3454, 3284, 3064, 1701, 1283; ^1H NMR (400 MHz, DMSO-d6): δ 12.40 (s, 1H), 9.70 (s, 1H), 7.90 (d, *J*¼48.4 Hz, 2H), 7.54–7.21 (m, 10H), 6.86 (d, *J*¼48.4 Hz, 2H); ^{13}C NMR (400 MHz, DMSO-d6): δ 157.7, 146.1, 136.6, 135.4, 131.3, 128.6, 128.3, 127.5, 127.3, 127.0, 126.8, 126.3, 121.6, 115.4; ESI MS (*m*/*z*): 312.2 (M^+); Anal. Calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.79; H, 5.22; N, 8.91.

2.3.6. 4,5-Diphenyl-2-p-tolyl-1H-imidazole (1f)

Mp 232–234 °C. FTIR (KBr, cm^{-1}): 3449, 3034, 1611, 1495, 1320; ^1H NMR (400 MHz, DMSO-d6): δ 12.59 (s, 1H), 7.98 (d, *J*¼47.8 Hz, 2H), 7.54–2.21 (m, 12H), 2.35 (s, 3H); ^{13}C NMR (400 MHz, DMSO-d6): δ 145.6, 137.6, 136.9, 135.2, 131.1, 129.2, 128.6, 128.3, 128.1, 127.9, 127.6, 127.0, 126.4, 125.1, 20.8; ESI MS (*m*/*z*): 310.3 (M^+); Anal. Calcd. for $C_{22}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03. Found: C, 85.23; H, 5.79; N, 8.97.

2.3.7. 2-(4-Methoxyphenyl)-4,5-diphenyl-1H-imidazole (1g)

Mp 228–230 °C. FTIR (KBr, cm^{-1}): 3415, 3042, 1610, 1490, 1189; ^1H NMR (400 MHz, DMSO-d6): δ 12.48 (s, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.50–7.33 (m, 10H), 7.04 (d, *J* = 8.4 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (400 MHz, DMSO-d6): δ 159.5, 145.7, 128.4, 127.7, 126.7, 123.1, 114.1, 55.2; ESI MS (*m*/*z*): 326.2 (M^+); Anal. Calcd. for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.90; H, 5.51; N, 8.63.

Table 2
Effect of solvent on the reaction times and yields.

Entry	Solvent	Time (min)	Yield (%)[a]
1	H_2O	180	60
2	EtOH	80	95
3	MeOH	95	70
4	CH_3CN	110	75
5	DCM	110	65
6	Toluene	150	60

Benzaldehyde (2.0 mmol), benzil (2.0 mmol), and ammonium acetate (4 mmol) in the presence of catalyst (25 mg) under reflux condition in various solvents.

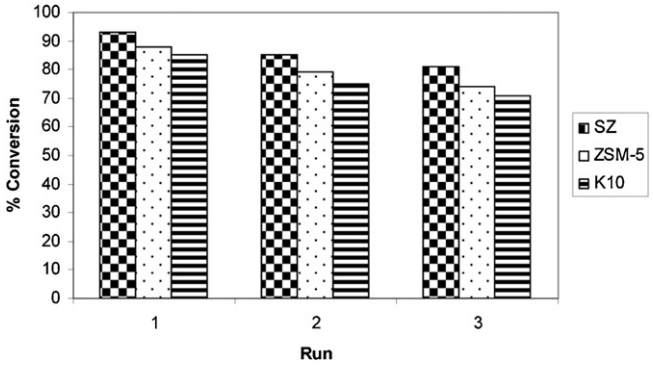


Fig. 5. The results obtained from catalyst reuse nano-crystalline sulfated zirconia (black bars), Zeolite (white bars) and montmorilonite K10 (dash bars) in the imidazole formation.

2.4. General procedure for the synthesis of 1,2,4,5-tetrasubstituted imidazoles

In a 50 mL round bottom flask 1,2-diketone (1 mmol), aromatic aldehyde (1 mmol), phenyl amine (1 mmol) and ammonium acetate (1 mmol) and catalyst (25 mg) stirred and refluxed in ethanol (10 mL). Then the reaction mixture was stirred. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the filtrate was cooled to room temperature and organic layer was dried over anhydrous $MgSO_4$ and concentrated. The product was purified by chromatography through a column of silica-gel using ethyl acetate/cyclohexane ether as an eluent.

The catalyst could be directly used with the same efficiency for four times after that a gradable decline in activity was observed. The products were characterized by IR, NMR and through comparison of their physical properties with those reported in literature.

2.4.1. 2-(4-Phenyl)-1,4,5-triphenyl-1H-imidazole (2a)

Mp 218–220 °C. FTIR (KBr, cm^{-1}): 3052, 1576, 1460; ^1H NMR (400 MHz, $CDCl_3$): δ 7.65–7.55 (m, 4H), 7.38–7.13 (m, 14H), 6.80 (d, J¼7.5 Hz, 2H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 148.1, 137.9, 137.3, 134.1, 132.7, 131.0, 130.7, 130.4, 129.1, 128.9, 128.4, 128.2, 128.6, 128.2, 127.8, 126.6, 126.2, 126.0; ESI MS (m/z): 372.1 (M^+); Anal. Calcd. for $C_{27}H_{20}N_2$: C, 87.01; H, 5.41; N, 7.52. Found: C, 86.81; H, 5.19; N, 7.20.

2.4.2. 2-(4-Chlorophenyl)-1,4,5-triphenyl-1H-imidazole (2b)

Mp 156–158 °C. FTIR (KBr, cm^{-1}): 3056, 1596, 1516, 1440; ^1H NMR (400 MHz,$CDCl_3$): δ 7.98 (d, 2H), 7.43–7.17 (m, 17H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 147.0, 144.2, 139.1, 136.5, 136.0, 133.6, 132.4, 131.0, 130.0, 129.5, 129.3, 129.2, 129.1, 128.9, 128.5, 128.4, 128.4, 128.3, 128.1, 127.2, 126.0, 125.5, 124.0, 123.2; ESI MS (m/z): 406.2 (M^+); Anal. Calcd. for $C_{27}H_{19}ClN_2$: C, 79.70; H, 4.71; N, 6.88. Found: C, 79.40; H, 4.36; N, 6.61.

2.4.3. 2-(4-Bromophenyl)-1,4,5-triphenyl-1H-imidazole (2c)

Mp 152–154 °C. FTIR (KBr, cm^{-1}): 3056, 1584, 1526, 1432; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, 2H), 7.40–7.12 (m, 17H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 147.0, 144.6, 139.7, 136.1, 136.3, 133.2, 132.6, 131.0, 130.3, 129.6, 129.4, 129.2, 129.1, 128.9, 128.6, 128.5, 128.4, 128.3, 128.1, 127.4, 126.0, 125.2, 124.4, 123.0; ESI MS (m/z): 450.1 (M^+); Anal. Calcd. for $C_{27}H_{19}BrN_2$: C, 71.85; H, 4.24; N, 6.26. Found: C, 71.32; H, 4.16; N, 6.21.

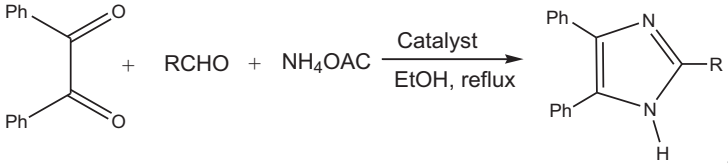
2.4.4. 2-(4-Nitrophenyl)-1,4,5-triphenyl-1H-imidazole (2d)

Mp 184–186 °C. FTIR (KBr, cm^{-1}): 3054, 1595, 1514, 1340; ^1H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J¼8.7 Hz, 2H), 7.61–7.07 (m, 17H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 147.0, 144.3, 139.3, 136.6, 136.5, 133.8, 132.4, 131.0, 129.9, 129.5, 129.4, 129.3, 129.2, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.0, 124.2, 124.0, 123.4; ESI MS (m/z): 417.2 (M^+); Anal. Calcd. for $C_{27}H_{19}N_3O_2$: C, 77.68; H, 4.59; N, 10.07. Found: C, 77.60; H, 4.56; N, 10.11.

2.4.5. 4-(1,4,5-Triphenyl-1H-imidazol-2-yl)-phenol (2e)

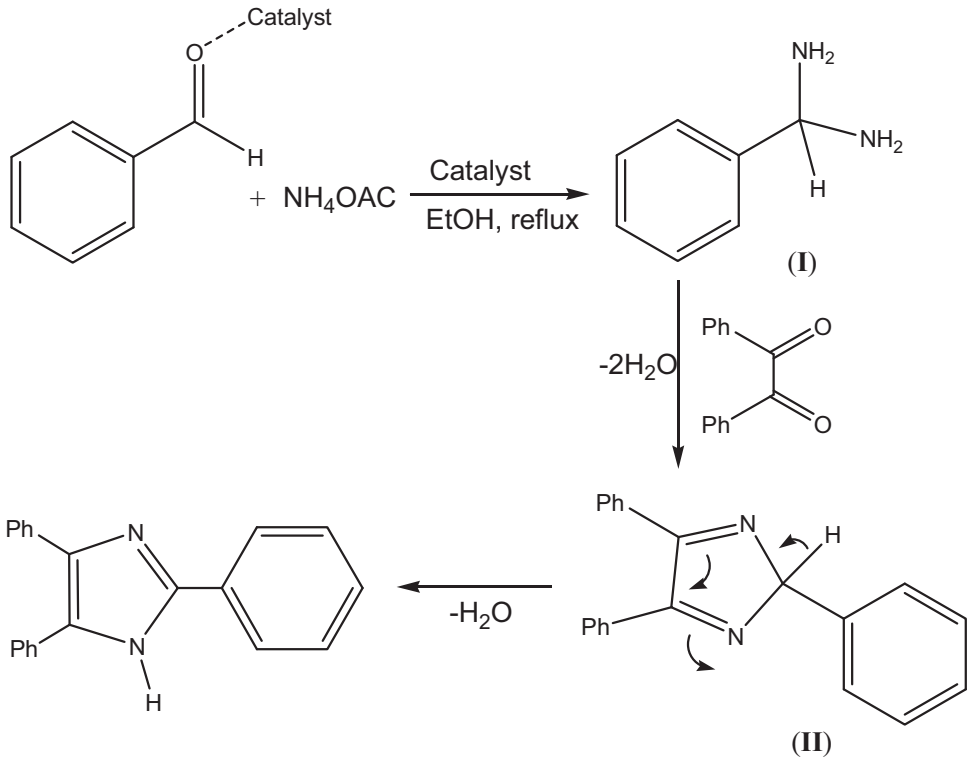
Mp 282–284 °C. FTIR (KBr, cm^{-1}): 3448, 3057, 1582; ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.76 (d, J¼8.4 Hz, 2H), 7.50–6.84

Table 3
Acid-catalyzed synthesis of 2,4,5-trisubstituted imidazoles[a]



Entry	Product	R	Time (min)/Yeild (%)[b]			MP °C (lit.) [Ref.]
			Montmorilonite K10	Zeolite	Nano-crystalline SZ	
1	1a	C_6H_5	90/70	60/80	45/87	274–276 (280–281) [12f]
2	1b	4-ClC_6H_5	95/75	75/82	60/92	260–262 (262–264) [12f]
3	1c	4-BrC_6H_5	110/75	90/75	75/81	254–256 (261.5–263.5) [12j]
4	1d	4-$NO_2C_6H_5$	90/73	80/75	70/80	234–236 (239–242) [12k]
5	1e	4-OHC_6H_5	90/75	70/80	85/82	268–270 (265–267) [12k]
6	1f	4-$CH_3C_6H_5$	100/70	90/85	90/93	232–234 (229–231) [12j]
7	1g	4-$OCH_3C_6H_5$	120/70	120/78	90/85	228–230 (226–228) [12k]

[a] The products were characterized by IR, ^1H NMR, ^{13}C NMR and mass spectroscopy.
[b] Isolated yields. The reaction conditions: aromatic aldehyde (1 mmol), 1,2-diketone (1 mmol), ammonium acetate (2 mmol) 25 mg catalysts in the ethanol as the solvent and under reflux condition.

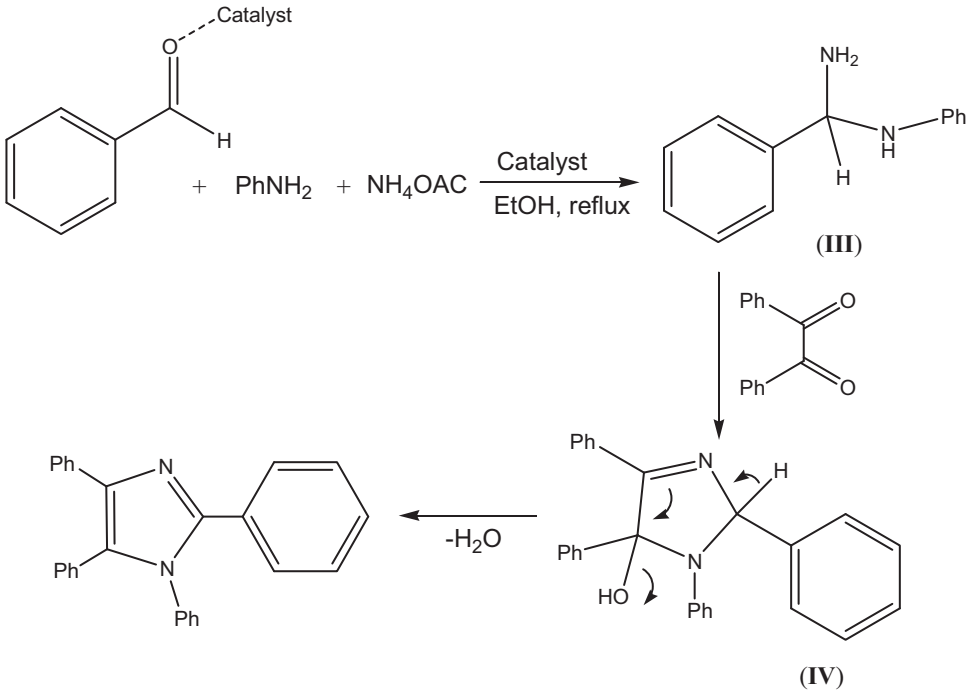


Scheme 1. A plausible mechanism for the formation of trisubstituted imidazoles.

(m, 17H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 158.1, 144.4, 139.2, 136.9, 136.2, 134.0, 132.1, 131.0, 130.1, 129.6, 129.4, 129.1, 128.8, 128.5, 128.1, 127.7, 127.4, 127.3, 127.1, 124.3, 123.9, 123.2; ESI MS (*m*/*z*): 388.3 (M^+); Anal. Calcd. for $C_{27}H_{20}N_2O$: C, 83.48; H, 5.19; N, 7.21. Found: C, 83.55; H, 5.11; N, 7.29.

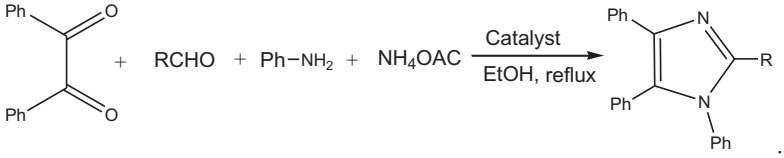
2.4.6. 1,4,5-Triphenyl-2-p-tolyl-1H-imidazole (2f)

Mp 182–184 °C. FTIR (KBr, cm^{-1}): 3044, 2923, 1665, 1593; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J¼7.2 Hz, 2H), 7.31–7.02 (m, 17H), 2.30 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 147.1, 138.1, 137.2, 134.5, 131.1, 130.7, 130.6, 128.9, 128.8, 128.4, 128.2, 128.1, 127.8,



Scheme 2. A plausible mechanism for the formation of tetrasubstituted imidazoles.

Table 4
Acid-catalyzed synthesis of 1,2,4,5-tetrasubstituted imidazoles[a]



Entry	Product	R	Time (min)/Yeild (%)[b]			MP °C (lit.) [Ref.]
			Montmorilonite K10	Zeolite	Nano-crystalline SZ	
1	2a	C_6H_5	90/75	60/80	45/87	218–220 (216–218) [12m]
2	2b	4-ClC_6H_5	100/80	80/88	60/92	156–158 (164–166) [12f]
3	2c	4-BrC_6H_5	90/73	75/83	60/85	152–154
4	2d	4-$NO_2C_6H_5$	90/70	90/72	75/76	184–186
5	2e	4-OHC_6H_5	90/75	90/80	80/85	282–284 (287–289) [12f]
6	2f	4-$CH_3C_6H_5$	100/78	90/83	85/87	182–184 (186–188) [12m]
7	2g	4-$OCH_3C_6H_5$	110/70	100/76	90/80	180–182 (185–188) [12m]

[a] The products were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopy.
[b] Isolated yields. The reaction conditions: aromatic aldehyde (1 mmol), 1,2-diketone (1 mmol), aniline (1 mmol), ammonium acetate (1 mmol) 25 mg catalysts in the ethanol as the solvent and under reflux condition.

127.6, 127.4, 126.5, 21.3; ESI MS (*m*/*z*): 386.3 (M^+); Anal. Calcd. for $C_{28}H_{22}N_2$: C, 87.01; H, 5.74; N, 7.25. Found: C, 87.03; H, 5.81; N, 7.16.

2.4.7. 1,4,5-Triphenyl-2-(4-methoxyphenyl)-1H-imidazole (2g)

Mp 180–182 °C. FTIR (KBr, cm^{-1}): 3029, 2934, 1600; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, 2H), 7.21–7.00 (m, 17H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.1, 137.2, 136.9, 134.5, 131.1, 130.9, 130.6, 129.5, 129.1, 128.4, 128.2, 128.1, 127.8, 127.6, 127.4, 126.5, 20.8; ESI MS (*m*/*z*): 402.3 (M^+); Anal. Calcd. for $C_{28}H_{22}N_2O$: C, 83.56; H, 5.51; N, 6.96. Found: C, 83.23; H, 5.21; N, 6.36.

3. Results and discussion

In a model reaction and in the reaction between benzil, ammonium acetate and benzaldehyde as an aromatic aldehyde, effect of the catalyst amount was investigated (Table 1). To minimize the formation of byproducts and to achieve good yield of the desired product, the reaction is optimized by varying the amount of catalyst (10, 25 and 50 mg). The percentage of the product formation using K10 as the catalyst was found 85, 96 and 82%, respectively (Table 1, entries 1–3). These values by using zeolite as the catalyst was obtained and 84, 92 and 86%, respectively (Table 1, entries 4–6). Product formation by application of 10, 25 and 50 mg of SZ as catalyst was found 82%, 96% and 87%, respectively (Table 1, entries 7–9). As you can see from Table 1. The same reaction when performed without catalyst for 3 h gave no product (Table 1, entry 10). When the catalyst content was increased to 50 mg, the product formation decreased to 87% (Table 1, entry 9). Therefore, it was found that the use of 25 mg of the catalyst was sufficient to promote the reaction, and greater amounts of the catalyst did not improve the yields.

We found ethanol and 25 mg of zeolite catalyst and K10 an efficient reaction medium in terms of reaction time as well as yield (Table 1, entries1–6). It is noteworthy to mention that in the absence of catalyst, no product was found even after 120 min. These results indicate that the catalyst exhibits a high catalytic activity in this transformation.

In order to optimize the reaction conditions, including solvents and temperature, the reaction of benzil, ammonium acetate and aromatic aldehydes was optimized by time of the reaction and using various solvents such as EtOH, MeOH, CH_3CN, and toluene (Table 2, entries 1–6). Reaction in toluene and dichloromethane (DCM) solvent gave low product yields even after 110 min and 150 min, respectively (Table 2, entries 5 and 6). Although the yields were moderate in case of methanol and acetonitrile under reflux condition (Table 2, entries 3 and 4).

The best results were obtained when the reaction was carried out in ethanol at reflux during 80 min in the presence of catalyst (Table 2, entry 2). Therefore, ethanol was selected as a solvent for this reaction. Although water is a desirable solvent for chemical reactions for reasons of cost, safety and environmental concerns, we found that using water in this reaction gave moderate yields of products under reflux condition after long reaction times.

One of the most important advantages of heterogeneous catalysis over the homogeneous counterpart is the possibility of reusing the catalyst by simple filtration, without loss of activity. The recovery and reusability of the catalyst was investigated in the imidazole formation. After completion of the reaction, the catalyst was separated by filtration, washed 3 times with 5 mL acetone, then with doubly distilled water several times and dried at 110 °C. Then the recovered catalyst was used in the next run. The results of three consecutive runs showed that the catalyst can be reused several times without significant loss of its activity (see Fig. 5).

Several substituted aromatic aldehydes reacted with benzyl and ammonium acetate in the presence of solid acid catalysts to give the corresponding 2,4,5-trisubstituted imidazoles in good yields. The nature of the substituents on the aromatic aldehyde has not significant effect on yield of reaction. However the nature of catalyst is significant. As you can see from Table 3, the best results obtained from sulfated zirconia. The range of isolated yields that obtained was found 70–75, 75–85 and 81–93% for the K10, zeolite and SZ, respectively.

The results of synthesis of 1,2,4,5-tetrasubstituted imidazoles from benzyl, aniline, ammonium acetate and various aromatic aldehydes tabulated in Table 4. Again, it can be seen that electron donating and electron withdrawing groups does not show any difference on the reaction yields. Moreover the range of isolated yields was found 73–80, 72–88 and 76–92% for the K10, zeolite and SZ, respectively (see Table 4).

In accordance with the mechanism proposed that the solid acid facilitates the formation of diamine intermediate [I] catalyst by increasing the electrophilicity of the carbonyl group of the aldehyde. Intermediate [I], condenses with benzil to form intermediate [II], which in turn rearranges to the trisubstituted imidazole (Scheme 1).

Similarly, the plausible mechanism for the synthesis of the tetrasubstituted imidazole involves the formation of intermediate [III] by the reaction of an aldehyde, phenyl amine and ammonium acetate in the presence of catalyst. Intermediate [III] condenses with benzil to form intermediate [IV], and then the tetrasubstituted imidazole (Scheme 2).

In conclusion, a one-pot, multicomponent methodology has been developed for the synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles catalyzed by clays, zeolite and nano-crystalline SZ as catalyst in high yields. Compared to previously reported methods, Moreover, the mild reaction conditions, easy work-up, clean reaction profiles, lower catalyst loading and cost efficiency render this approach as an interesting alternative to the existing methods.

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References

[1] J.G. Lambardino, E.H. Wiseman, J. Med. Chem. 17 (1974) 1182.
[2] A. Puratchikody, M. Doble, Bioorg. Med. Chem. Lett. 15 (2007) 1083.
[3] M. Antolini, A. Bozzoli, C. Ghiron, et al., Bioorg. Med. Chem. Lett. 9 (1999) 1023.
[4] L. Wang, K.W. Woods, Q. Li, et al., J. Med. Chem. 45 (2002) 1697.
[5] T. Maier, R. Schmierer, K. Bauer, et al. U.S. Patent 4820335, 1989; Chem. Abstr. 111 (1989) 19494w.
[6] J.C. Lee, J.T. Laydon, P.C. McDonnell, et al., Nature 372 (1994) 739.
[7] T. Maier, R. Schmierer, K. Bauer, et al. US Patent 4820335, 1989; Chem. Abstr. 111 (1989) 19494.
[8] R. Schmierer, H. Mildenberger, H. Buerstell, German Patent 361464, 1987; Chem. Abstr. 108 (1988) 37838.
[9] J. Heeres, L.J.J. Backx, J.H. Mostmans, et al., J. Med. Chem. 22 (1979) 1003.
[10] (a) P. Wasserscheid, W. Keim, Angew. Chem. Int. Ed. Eng. 39 (2000) 37872;
(b) D. Bourissou, O. Guerret, F.T. Ggabbai, et al., Chem. Rev. (2000) 100.
[11] I. Satoru, Japn Kokkai Tokyo Koho JP 01, 117, 867, May 10, 1989; Chem. Abstr. 111 (1989) 214482.
[12] (a) S. Samai, G.C. Nandi, P. Singh, et al., Tetrahedron 65 (2009) 10155;
(b) S.A.A. Mansour, K.U. Sadek, Chin. Chem. Lett. 20 (2009) 812;
(c) D.V. Paone, A.W. Shaw, Tetrahedron Lett. 49 (2008) 6155;
(d) A. Shaabani, A. Rahmati, E. Farhangi, et al., Catal. Commun. 8 (2007) 1149;
(e) X.C. Wang, H.P. Gong, Zh.J. Quan, et al., Chin. Chem. Lett. 20 (2009) 44;
(f) N.J. Sangshetti, N.D. Kokare, S.A. Kotharkar, et al., Chin. Chem. Lett. 19 (2008) 762;
(g) A.R. Khosropour, Ultrason. Sonochem. 15 (2008) 659;
(h) M. Ghaemy, R. Alizadeh, Eur. Pol. J. 45 (2009) 1681;
(i) M.M. Heravi, K. Bakhtiari, H.A. Oskooie, et al., J. Mol. Catal. A: Chem. 263 (2007) 279;
(j) H. Zang, Q. Su, Y. Mo, et al., Ultrason. Sonochem. 17 (2010) 749;
(k) M. Xia, Y.-d. Lu, J. Mol. Catal. A: Chem. 265 (2007) 205;
(l) B. Sadeghi, B.F. Mirjalili, M.M. Hashemi, Tetrahedron Lett. 49 (2008) 2575;
(m) M. Ghaemy, H. Behmadi, R. Alizadeh, Chin. Chem. Lett. 20 (2009) 961.
[13] (a) S.A. Siddiqui, U.C. Narkhede, S.S. Palimkar, et al., Tetrahedron 61 (2005) 3539;
(b) X. Min, Y.-d. Lu, J. Mol. Catal. A: Chem. 265 (2007) 205.
[14] (a) J. Wang, R. Mason, D.V. Derveer, et al., J. Org. Chem. 68 (2003) 5415, 68;
(b) S. Sarshar, D. Siev, A.M.M. Mjalli, Tetrahedron Lett. 37 (1996) 835;
(c) T.F. Gallagher, G.L. Seibel, S. Kassis, et al., Bioorg. Med. Chem. (1997) 49;
(d) E.A. Steck, A.R. Day, J. Am. Chem. Soc. (1943) 452.
[15] A. Shaabani, A. Rahmati, J. Mol. Catal. A: Chem. 249 (2006) 246.
[16] S.D. Sharma, P. Hazarika, D. Konwar, Tetrahedron Lett. 49 (2008) 2216.
[17] (a) S.A. Balalaie, Arabanian, Green Chem. 2 (2002) 274;
(b) M.M. Heravi, F. Derikvand, F.F. Bamoharram, J. Mol. Catal. A: Chem. 263 (2007) 112;
(c) A.R. Karimi, Z. Alimohammadi, J. Azizian, et al., Catal. Commun. 7 (2006) 728;
(d) S. Kantevari, S.V.N. Vuppalapati, D.O. Biradar, et al., J. Mol. Catal. A: Chem. 266 (2007) 109.
[18] (a) R. Consonni, P.D. Croce, R. Ferraccioli, et al., J. Chem. Res. (S) 188 (1991) 7;
(b) I. Lantos, W.-Y. Zhang, X. Shui, et al., J. Org. Chem. 58 (1993) 7092;
(c) S. Balalaie, M.M. Hashemi, M. Akhbari, Tetrahedron Lett. 44 (2003) 1709;
(d) U. Ucucu, N.G. Karaburun, I. Iskdag, Il Farmaco 56 (2001) 285.
[19] X.C. Wang, H.P. Gong, Z.J. Quan, et al., Chin. Chem. Lett. 20 (2009) 44.
[20] M. Doble, A. Kumar, Green Chemistry and Engineering, Elsevier, 2007.
[21] (a) T. Joseph, G.V. Shanbhag, D.P. Sawant, et al., J. Mol. Catal. A: Chem. 250 (2006) 210;
(b) G.V. Shanbhag, S.B. Halligudi, J. Mol. Catal. A: Chem. 222 (2004) 223;
(c) T. Joseph, G.V. Shanbhag, S.B. Halligudi, J. Mol. Catal. A: Chem. 236 (2005) 139;
(d) S. Albertazzi, I. Baraldini, G. Busca, et al., Appl. Clay Sci. 29 (2005) 224;
(e) N. Jagtap, V. Ramaswamy, Appl. Clay Sci. 33 (2006) 89;
(f) C.R. Reddy, B. Vijayakumar, P. Iyengar, et al., J. Mol. Catal. A: Chem. 223 (2004) 117;
(g) S. Lal, K.S. Anisia, M. Jhansi, et al., J. Mol. Catal. A: Chem. 265 (2006) 15;
(h) C.R. Reddy, P. Iyengar, G. Nagendrappa, et al., J. Mol. Catal. A: Chem. 229 (2005) 31;
(i) G. Sharma, R. Kumar, A.K. Chakraborti, J. Mol. Catal. A: Chem. 263 (2006) 143;
(j) N.N. Binitha, S. Sugunan, Micropor. Mesopor. Mater. 93 (2006) 82;
(k) C.R. Reddy, G. Nagendrappa, B.S. Jai Prakash, Catal. Commun. 8 (2007) 241;
(l) R.I. Kureshy, N.H. Khan, S.H.R. Abdi, et al., J. Catal. 221 (2004) 234;
(m) B. Singh, J. Patial, P. Sharma, et al., J. Mol. Catal. A: Chem. 266 (2006) 215.
[22] (a) M.F.V. Marques, S.C. Moreira, J. Mol. Catal. A: Chem. 192 (2003) 93;
(b) V. Mavrodinova, M. Popova, R.M. Mihalyi, et al., Appl. Catal. A: Gen. 248 (2003) 197;
(c) A. Corma, A.V. Orchilles, Micropor. Mesopor. Mater. 21 (2000) 35;
(d) H.H. Ingelsten, D. Zhao, A. Palmqvist, et al., J. Catal. 232 (2005) 68;
(e) D. Zhao, H.H. Ingelsten, M. Skoglundh, et al., J. Mol. Catal. A: Chem. 249 (2006) 13.
[23] (a) V. Indovina, D. Pietrogiacomi, M.C. Campa, Appl. Catal. B: Environ. 39 (2002) 115;
(b) D. Pietrogiacomi, M.C. Campa, S. Tuti, Appl. Catal. B: Environ. 41 (2003) 301;
(b) N. Li, A. Wang, J.X. Tang, Appl. Catal. B: Environ. 43 (2003) 195;
(c) B. Tsyntsarski, V. Avreyska, H. Kolev, et al., J. Mol. Catal. A: Chem. 193 (2003) 139;
(d) U.B. Demirci, F. Garin, J. Mol. Catal. A: Chem. 188 (2002) 233.
[24] (a) H.A. Dabbagh, A. Teimouri, A. Najafi Chermahini, J. Appl. Catal. B: Environ. 76 (2007) 24;
(b) A. Najafi Chermahini, A. Teimouri, F. Momenbeik, et al., J. Heterocycl. Chem. 47 (2010) 913.
[25] (a) R. J. Argauer, G.R. Landolt, US Patent No. 3 702 886, 1972;
(b) J. Dwyer, Chem. Ind. 2 (1984) 258;
(c) J.L. Guth, Non-Conventional Crystalline Microporous Solids, Zeolite Microporous Solids: Synthesis, Structure, and Reactivity, Kluwer Academic, The Netherlands, 1992, p. 49;
(d) V.R. Choudhary, D. Panjala, S. Banerjee, Appl. Catal. A: Gen. 231 (2002) 243.
[26] (a) M.K. Mishra, B. Tyagi, R.V. Jasra, J. Mol. Catal. A: Chem. 223 (2004) 6;
(b) B. Tyagi, M.K. Mishra, R.V. Jasra, Catal. Commun. 7 (2006) 52.
[27] B.D. Cullity, S.R. Stock, Elements of X-ray Diffraction, third edition, Prentice Hall, Upper Saddle River, NJ, 2001, p. 388.
[28] S.J. Gregg, K.S.W. Sing, Adsorption, Surface Area and Porosity, second edition, Academic Press, New York, 1982.