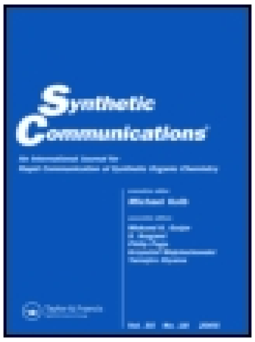

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Simple but Efficient Synthesis of Novel Substituted Benzimidazoles Over ZrO_2-Al_2O_3

N. Thimmaraju [1,2], S. Z. Mohamed Shamshuddin[1,2], S. R. Pratap [1,2], K. Raja [3], M. Shyamsundar [1,2], T. E. Mohankumar [1,2]

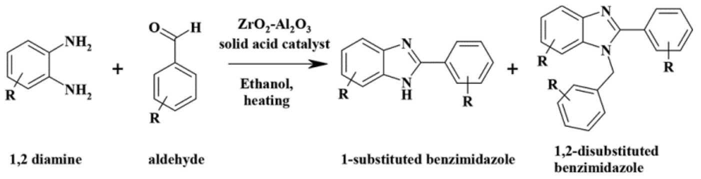
[1]Chemistry Research Laboratory, HMS Institute of Technology, Tumkur, Karnataka, India.
[2]Research and Development Center, Bharathiar University, Coimbatore, India.
[3]Department of Chemistry, Bangalore University, Bangalore, India

Corresponding to author: Mohamed Shamshuddin, E-mail: em_es@rediffmail.com

Abstract

Solid acid catalytic materials such as ZrO_2-Al_2O_3 containing 80 mole% of ZrO_2 was prepared by solution combustion method (SCM) using different fuels like urea, hexamethylene tetramine, glycine and sucrose. All the prepared solid acid catalytic materials were characterized by PXRD, NH_3-TPD, FTIR, TEM, SEM and EDAX techniques. These materials were evaluated for their catalytic activity in the synthesis of a series of novel substituted benzimidazoles. The reaction conditions were optimized by varying the solvents, reaction temperature, weight of solid acid catalyst, molar ratio of the reactants and reaction time. The ZrO_2-Al_2O_3 solid acid catalytic material prepared by urea as a fuel was found to be highly active, recyclable and reusable in the synthesis of benzimidazoles. A possible reaction mechanism for the synthesis of benzimidazoles is also proposed.

Graphical Abstract



where, R= alkyl, methoxy, F, Cl and CF_3 groups at different position of aromatic system.

KEYWORDS: ZrO_2-Al_2O_3; Solid acid catalytic materials; Solution combustion; Novel benzimidazoles.

1. INTRODUCTION

Heterogeneous solid acid catalysts such as zeolites, resins, clays, metal oxides, mixed metal oxides, doped metal oxides, heteropolyacids etc., have been used as alternatives to conventional homogeneous acid catalysts such as H_3PO_4, BF_3, H_2SO_4, HNO_3, HCl, *p*-toluenesulphonic acid, etc., because homogeneous catalysts have several drawbacks such as highly corrosive nature, difficult to separate from the reaction mixture and reuse and possibility of existence of side reaction.[1–5]

Metal oxide such as ZrO_2 has been widely used as a catalyst or a catalytic support in many organic transformations such as oxidation, esterification, transesterification, alkylation, acylation, hydrocarbon isomerization, etc.[6–9] Zirconia possesses complex physicochemical properties like simultaneous existence of reducing, oxidizing, acid and basic properties, low thermal conductivity, high toughness, very good resistance against crack propagation, good thermal resistance, etc.[8–11] Alumina has also been widely used as a catalyst or a catalytic support because of its surface area, pore size and pore volume which will have a large impact on its catalytic activity. However, alumina has relatively low thermal stability over time, which limits its usefulness at high temperatures. ZrO_2 is commonly used as a stabilizing agent to improve thermal stability of alumina (Al_2O_3). Mixed-metal oxide systems could offer interesting properties, especially when the properties of each component differ remarkably from each other. For instance, the presence of ZrO_2 may affect the thermal and structural stability of alumina support.[12–13]

Therefore, ZrO_2-Al_2O_3 has been used in many catalytic processes involving liquid, vapor and gas phase reactions.[12–14]

There are different methods of preparing ZrO_2-Al_2O_3 solid acid catalytic materials such as milling or wet milling, sol-gel, liquid precursor, co-precipitation, etc. However, these methods are time consuming and high temperature processes.[14–18] Solution combustion method (SCM) is one of the promising route for the synthesis of solid acid catalytic material because it is a simple, one step and speedy process which needs simple experimental set-up.[19–20] This method requires aqueous solution of different oxidizers (e.g. metal nitrates) and fuels (e.g. urea, glycine, hexamethylene tetra amine and glucose).

Benzimidazoles are an interesting class of heterocyclic compounds with important pharmacophore in medicinal chemistry which exhibit a wide range of biological properties. Benzimidazoles have found medicinal applications in therapeutic areas such as antihistamines, antiulcer, antitumor, antiviral, antifungal, antihypertensive, etc.[21–26] In the last decade several methods have been developed for the synthesis of substituted benzimidazoles using various catalysts.[27–34] However, only a few efficient and simple methods for the preparation of benzimidazoles exist.[35–37] Many of these methods have one or more drawbacks such as laborious, low yields, tedious separation processes, several side reactions, expensive reagents or catalysts, complex work-up and purification.

The research work reported in the present article involves the synthesis of ZrO_2-Al_2O_3 solid acid catalytic materials by solution combustion method using different fuels such as urea or hexamethylene tetramine or glycine or sucrose. These catalytic materials were characterized for their physico-chemical properties such as crystalinity, surface acidity, functionality and morphology. The major objective of this study is to investigate the catalytic ability of the prepared solid acid catalytic materials in the synthesis of novel benzimidazoles. Reaction conditions (effect of solvents, reaction temperature, weight of solid acid catalyst, molar ratio of reactants and reaction time) were optimized and reusability of these solid acid catalytic materials was also investigated.

ZrO_2-Al_2O_3 prepared by using urea as a fuel was abbreviated as ZA-U, hexamethylene tetramine (HMTA) as ZA-H, glycine as ZA-G and sucrose as ZA-S.

2. RESULTS AND DISCUSSION

2.1. Characterization Of Solid Acid Catalytic Materials

All the prepared ZrO_2-Al_2O_3 solid acid catalytic materials were characterized for their physico-chemical properties such as PXRD, NH_3-TPD, FTIR, TEM, SEM and EDAX techniques.

2.1.1. Crystalinity By Powder XRD (PXRD) Studies

PXRD technique was used to characterize the crystalline phases of zirconia-alumina solid acid catalysts. The PXRD patterns of all the prepared ZrO_2-Al_2O_3 solid acid catalytic materials are shown in Fig. 1. Interestingly no peaks corresponding to the monoclinic ZrO_2 are observed in the PXRD patterns of all solid acid catalytic samples. However, pure tetragonal phase of ZrO_2 is formed in case of ZA-U due to phase transition of stable monoclinic to tetragonal phase. Very low intense diffraction peaks corresponding to rhombohedral Al_2O_3 are also observed. In the other three solid acid catalysts Viz., ZA-H, ZA-G and ZA-S a small lump was observed at around 2θ = 30° which corresponds to moderate plateau of tetrahedral ZrO_2, which indicates the presence of an incipient crystalline structure in ZrO_2-Al_2O_3 mixed oxide.[38–39] Major peaks corresponding to Al_2O_3 were not observed in all the four solid acid catalytic materials which confirm a clear co-ordination between zirconia and alumina. More interestingly, it was observed from the PXRD pattern that full crystallization of ZrO_2-Al_2O_3 could be achieved by SCM using urea as a fuel and in case of all other fuel materials, the solid acid catalyst were amorphous in nature.

In case of urea as a fuel, ZrO_2-Al_2O_3 oxides possessed both tetragonal zirconia and low intense rhombohedral alumina crystalinity, this is due to the formation of stable polymeric intermediates which prevent the dissipation of heat and thereby sintering the oxides during combustion.[40a] In case of glycine as a fuel, metal oxide with smaller particle size was formed (amorphous ZrO_2-Al_2O_3), because of the formation of a stable product during combustion without much sintering.[40b] On the other hand ZA-H prepared by using HMTA fuel was found to have amorphous ZrO_2-Al_2O_3. This might be due to more cross-linked structure caused by the higher cross-linking ability of HMPA and resulting in the formation of smaller particles.[40c] In case of ZA prepared by using sucrose as a fuel also found to have amorphous ZrO_2-Al_2O_3 may be due to forming stable complex with sucrose solution.

2.1.2. Total Surface Acidity (TSA) By NH_3-TPD Method

The TSA values of all the prepared ZrO_2-Al_2O_3 solid acid catalytic materials obtained by NH_3-TPD are listed in Table 1 and the NH_3-TPD profiles of all the solid acid catalysts are shown in Fig. 2. The TSA values of solid acid catalysts are in the following order:

ZA-U > ZA-G > ZA-S > ZA-H.

In general the surface acidity of ZrO_2-Al_2O_3 mixed oxide is because of the coordination number of the inserted cation maintained in the host oxide lattice. i.e., when Zr^{4+} is inserted into the Al^{3+} lattice, positive charge imbalance occurs. As a result, Lewis acid sites are generated. Surface acidity can also result due to the charge imbalance formed on the surface of a metal oxide. To keep the electric neutrality, Brønsted acidity is expected to appear when the charge imbalance is negative, while Lewis acid sites will be formed when the charge imbalance is positive.[41] The ZA solid acid catalyst prepared by urea as a fuel comparatively bear higher total surface acidity than all the other ZA solid acid catalysts. This may be due to tetragonal crystalinity. ZA-H has comparatively lower surface acidity and ZA-G & ZA-S have almost same surface acidity values. This may be due to their amorphous nature. Further, desorption peaks in Fig. 2 shows that all the prepared ZrO_2-Al_2O_3 solid acid catalysts have weak, medium, strong as well as very strong acid sites.

2.1.3. FT-IR Studies

The FT-IR spectra of all the prepared ZA solid acid catalysts are represented in Fig. 3. The broad band at ~1600 cm^{-1} is attributed to the vibrations of acidic –OH bending mode and broad band at ~3450 cm^{-1} stretching mode with hydrogen bonding that are present in all the solid acid catalysts.[42] The bands at 1050 cm^{-1}, 770 cm^{-1} and 690 cm^{-1} correspond to the O-Al vibrations.[43]

2.1.4. TEM, SEM And EDAX Studies

The TEM images of all the prepared solid acid catalytic materials are given in Fig. 4a. As seen from the figure, ZA prepared by urea as a fuel shows a uniform and compact distribution of particles and spherical geometry with particle size of 34-43 nm. In all the other samples (ZA-H, ZA-g and ZA-S), the boundary between the particles was not detectable from TEM images which may be due to interactions between the neighboring particles. This amorphous nature of ZA-H, ZA-G and ZA-S is in good agreement with the PXRD patterns because, smaller sized particles bring strong adsorption force wherein most of the particles are aggregated with each other.[44] SEM images and EDAX spectrums of all the prepared samples are presented in Figures 4b, 4c, 4d, 4e and 4f. The SEM images confirm that the catalytic particles are non-uniformly sized and are porous in nature. The EDAX spectrum of all the four solid acid solid acid catalysts showed that the atomic composition of aluminium, oxygen and zirconia are almost same. This confirms that all the prepared samples have similar atomic composition.

2.2. Catalytic Activity Studies Of Solid Acid Catalytic Materials In The Synthesis Of Benzimidazoles

In ordered to optimize the reaction conditions for the synthesis of substituted benzimidazoles, 4,5-dimethyl-benzene-1,2-diamine and 4-isopropyl-benzaldehyde were used as model substrates. To obtain highest possible yield of the benzimidazole, the reactions were carried out by varying the solid acid catalysts, solvent system, reaction temperature, weight of the ZrO_2-Al_2O_3 solid acid catalyst, molar-ratio of the reactants (4,5-dimethyl-benzene-1,2-diamine: 4-isopropyl-benzaldehyde) and reaction time. All the prepared solid acid catalysts were found to be active in the synthesis of substituted benzimidazoles and in the absence of any catalytic material negligible amount of the reaction product were observed. This indicates that the synthesis of substituted benzimidazole is a catalyzed reaction.

3.2.1. Effect Of Catalytic Materials On The Yield Of Benzimidazole Derivatives

In order to obtain better yield of benzimidazole derivatives, reaction was carried out between 4,5-dimethyl-benzene-1,2-diamine (1a in Scheme 2) and 4-isopropyl-benzaldehyde (2a in Scheme 2) in presence of 0.03 g of ZA-U, ZA-H, ZA-G and ZA-S. The reactions were conducted at 80 ^{o}C for 30 min in ethanol (solvent) and the results are presented in the Fig. 5a. According to the LCMS data conducted as a part of qualitative analysis, only two products i.e., 2-(4-isopropylphenyl)-5,6-dimethyl-1H-benzo[*d*]imidazole (3a in Scheme 2) and 1-(4-isopropylbenzyl)-2-(4-isopropylphenyl)-5,6-dimethyl-1H-benzo[*d*]imidazole (4a in Scheme 2) were formed during the reaction. The yield (%) of 3a and 4a (Scheme 2) was found to be significantly influenced by the total surface acidity of ZrO_2-Al_2O_3 solid acid catalyst and the yield of 3a and 4a (Scheme 2) were in the following order: ZA-U > ZA-G ≈ ZA-S > ZA-H. Hence, ZA-U was chosen for further optimization studies.

In order to compare the catalytic activity of ZA-U with similar catalytic materials in the synthesis of benzimidazole derivatives, the reactions were carried out in presence of Al_2O_3, ZrO_2, 10 mole% ZrO_2- Al_2O_3 (10ZA), 20 mole% ZrO_2- Al_2O_3 (20ZA), 40 mole% ZrO_2- Al_2O_3 (40ZA) and 80 mole% ZrO_2- Al_2O_3 (80ZA) at 80 °C for 30 min in ethanol as a solvent and the results are shown in Fig. 5b. When the catalytic activity of these catalytic materials was compared, ZA-U showed better yield of benzimidazole derivatives than other catalytic materials used for the present study. The better catalytic activity of ZA-U can be due to its higher surface acidity when compared to other similar metal oxides.[8]

3.2.2 Effect Of Solvents On The Yield Of Benzimidazole Derivatives

In order to find a suitable solvent for the synthesis of benzimidazoles, reactions were carried out using different solvent systems and the results are presented in Table 2. The reactions were conducted between 1a and 2a (Scheme 2) in presence of 0.03 g of ZA-U at 80 ˚C for 30 min.

The yield of 3a and 4a (Scheme 2) were moderate when the reaction was performed in the absence of any solvent. Low yields of 3a and 4a were observed when the reactions were carried out in presence of an aqueous solvent. Almost same yields of 3a and 4a were observed over ethanol, methanol, DMF and DMSO solvents. But ethanol was chosen as a solvent for further optimization of reaction conditions, because DMSO and DMF are high boiling solvents and methanol is neither safe nor green.

3.2.3. Effect Of Reaction Temperature On The Yield Of Benzimidazole Derivatives

The results of the conducted experiments at different reaction temperatures (60-100 °C) over 0.03 g of ZA-U are shown in Fig. 6. The yield of 3a and 4a increases with an increase in the temperature from 60 to 80 °C. But beyond 80 °C, the yield of both 3a and 4a remained almost constant. Therefore, the reaction temperature of 80 °C was chosen for further optimization of reaction conditions.

3.2.4 Effect Of Weight Of Solid Acid Catalyst On The Yield Of Benzimidazole Derivatives

The effect of weight of solid acid catalysts (ZA-U) on the yield of benzimidazole derivatives was studied at 80 ^{o}C for 30 min by using 0.3 g of 1a and 0.33 mL of 2a in 10 mL of ethanol as a solvent and the results are shown in Fig. 7. The yield of both 3a and 4a increases when the weight of the solid acid catalyst was increased from 0.01 g to 0.03 g and good yield of 3a and 4a were achieved over 0.03 g of ZA-U solid acid catalyst. Further, upon increase in the weight of ZA-U beyond 0.03 g, the yields of 3a and 4a were found to stabilize.

3.2.5. Effect Of Molar Ratio Of The Reactants On The Yield Of Benzimidazole Derivatives

In order to study the effect of molar ratio of the reactants i.e., 1a and 2a, reactions were carried out at different molar ratios such as 1:1, 1:1.3, 1:1.6, 1:2, 1:2.5 and 1:3 over 0.03 g of ZA-U at 80 °C for 30 min in ethanol and the results are shown in Table 3. The yield of 3a decreased drastically, when the molar ratio of 2a was increased from 1:1 to 1:2 and a negligible amount of 3a was formed when the aldehyde was used beyond 2 equivalents. Therefore, a molar ratio of 1:1 [1a:2a] was found to be the optimum molar ratio for synthesizing 2-substituted benzimidazoles and this ratio was used for the synthesis of other benzimidazole derivatives.

3.2.6 Effect Of Reaction Time On The Yield Of Benzimidazole Derivatives

The reactions were carried out at different reaction times such as 10, 20, 30 40 and 50 min over ZA-U at 80 ^{o}C by using 0.3 g of 1a and 0.33 mL of 2a in 10 mL of ethanol as a solvent and the results are shown in Fig. 8. The yield of benzimidazoles increases till 30 min and upon further increase in the reaction time, the yield as well as the selectivity of individual benzimidazoles (3a or 4a) were found to get stabilized.

3.2.7 Synthesis Of Benzimidazole Derivatives Under Optimized Reaction Conditions

The catalytic activity of ZA-U was further investigated for the synthesis of various benzimidazole derivatives under optimized reaction conditions such as molar ratio of the reactants = 1:1 (1 and 2 in Scheme 1) over 0.03 g of ZA-U at 80 °C in 10 mL of ethanol solvent and the progress of the reactions was monitored by thin layer chromatography (TLC). After completion of the reaction, the reaction mixture was cooled, filtered, residue was washed with 10 mL of ethanol to recover the solid acid catalytic material and the filtrate was evaporated to afford crude reaction product. Thus obtained crude product was purified by silica column chromatography by using a suitable mobile phase to obtain desired product and the yields (%) of the derivatives are listed in Table 4. The reaction products were characterized by melting point, LCMS, ^{1}H NMR, ^{13}C NMR and HPLC methods and the details are given the Appendix-S1 and their ^{1}H NMR, ^{13}C NMR spectra and HPLC chromatographs are presented in Appendix-S2. It is important to note that, in the compounds bearing entries 8-19 and entries 21-23 (in Table 4) two tautomers were observed. The formation of tautomers was confirmed by ^{1}H NMR which showed 0.5 protons and ^{13}C NMR multiple peaks at aromatic region. In case of compounds bearing entries 1-7 and entry 20 (in Table 4) only one tautomer was observed. The tautomeric ratios were probably dependent on the electronic effect of substituents on the diamine moiety (Compound 1 in Scheme 1).[45–46]

[**Reaction conditions:** Reaction temperature = 80 °C; molar ratio of diamine : aldehyde (1:1), weight of the solid acid catalyst=0.03 g, weight of diamine= 0.3 g and ethanol = 10 mL].

3.2.8 Effect Of Re-Usability Of ZA-U On The Yield Of Benzimidazole Derivatives

In order to study the reusability of ZA-U solid acid catalyst, the reactions were carried out between 4,5-dimethyl-benzene-1,2-diamine and 4-isopropyl-benzaldehyde in presence of 0.03 g of ZA-U at 80 °C for 30 min in ethanol as a solvent. The solid acid catalyst (ZA-U) was recovered after the reaction by simple filtration, followed by washing with ethanol, dried in an oven at 120 °C for 1 h and calcined at 550 °C in a muffle furnace for 1 h. Thus thermally regenerated solid acid catalyst was re-used in the next reaction cycle. Such studies were carried out for 5 consecutive reaction cycles and the results are given in Fig. 9. It can be seen from the figure that, ZA-U solid acid catalyst could be reused at least for 5 reaction cycles without any significant loss in its catalytic activity. Further, no significant changes were observed in their TSA or PXRD phases or FTIR pattern when characterised after their reuse.

3. MECHANISM

A possible reaction mechanism (Scheme 3a) for the formation of substituted benzimidazoles over ZrO_2-Al_2O_3 solid acid catalyst which consists of both Lewis acid sites as well as Brønsted acid sites is proposed. It is supposed that the reaction proceeds via activation of an aldehyde by Lewis acid sites of ZrO_2-Al_2O_3 followed by condensation with diamine leading to the formation of an imine (d) derivative stabilized by ZrO_2-Al_2O_3. The resulting imine eventually undergoes ring closure by the intramolecular attack of second amino group on C-N double bond to give hydrobenzimidazole (e) that subsequently undergoes aromatization by aerial oxidation to afford the desired 2-substituted benzimidazole (3).

The two mechanisms for the formation of substituted benzimidazoles using Brønsted acid sites of ZrO_2-Al_2O_3 are shown in Scheme 3b. One involves the formation of di-imine (i) followed by a ring closure reaction leading to compound (j), which gives the corresponding product (4) by sequential tandem transformation. The other mechanism involves the formation of an imine (g), the resulting imine eventually undergoes ring closure by the intramolecular attack of second amino group on C-N double bond to give hydrobenzimidazole (k) that subsequently undergoes aromatization by aerial oxidation under the reaction conditions to afford the desired 2-substituted benzimidazole (3).[47]

4. EXPERIMENTAL

4.1. Chemicals

Zirconyl nitrate, aluminium nitrate nonahydrate, urea, hexamethylene tetramine, glycine and sucrose were supplied by M/S LOBA Chemie, India. Substituted *O*-phenylenediamines and substituted aromatic aldehydes were supplied by Sigma Aldrich or Alfa-Aesar and the solvents were supplied by Chemlabs, India.

4.2. Preparation Of Zro_2-Al_2O_3 (ZA) Solid Acid Catalytic Materials

ZrO_2-Al_2O_3 mixed oxide consisting of 80 mole% of ZrO_2 was prepared by solution combustion method by taking aqueous solutions containing known amounts of aluminium nitrate nonahydrate, zirconyl nitrate by using different fuels (urea, hexamethylene tetramine, glycine and sucrose).[20] In a typical method, ZrO_2-Al_2O_3 was prepared by the combustion of an aqueous mixture (20 mL) containing 10.0 g of aluminium nitrate, 12.32 g of zirconyl nitrate and 9.33 g of urea in a pyrex dish. Combustion was carried out in a preheated muffle furnace (400 ± 10 ^oC) resulting in a flaming type reaction wherein foamy solid was formed. Thus obtained foamy solid was powdered and calcined in a muffle furnace at 550 ^oC for 5 h.

ZrO_2-Al_2O_3 was prepared in the similar way by using other fuels like hexamethylene tetramine (3.64 g), glycine (7.80 g) and sucrose (6.63 g).

4.3. Characterization Of Solid Acid Catalytic Materials

The powder X-ray diffraction (PXRD) patterns of these solid acid catalytic materials were obtained from X'pert Pro Philips diffractometer equipped with a Ni filtered Cu-Kα radiation with λ=1.5418 Å using a graphite crystal monochromator in a scanning range of 10^o-70°. The total surface acidity (TSA) values of the catalytic materials were obtained from NH_3-TPD method by using Mayura TPD unit. The FT-IR spectrums were recorded with 4 cm^{-1} resolution using a Nicolet IR200 FT-IR Spectrophotometer in the range 400-4000 cm^{-1} using KBr as a standard reference. TEM images of all ZA solid acid catalytic materials were performed on PHILIPS CM200 electron microscope at an acceleration voltage of 20-200kV. SEM images and EDAX of all the prepared solid acid catalysts were obtained using a JEOL JXA-8530F microscope.

4.4. Catalytic Activity Studies Of Solid Acid Catalytic Materials In The Synthesis Of Benzimidazoles

To the stirred solution of *O*-phenylenediamines and different substituted aromatic aldehydes in a suitable solvent, ZrO_2-Al_2O_3 solid acid catalytic material was added and the resulting mixture was heated at a particular temperature and the reaction was monitored by thin layer chromatography. After the completion of the reaction, the reaction mixture was cooled, filtered and the residue was washed with ethanol to recover the solid acid catalyst. Filtrate was evaporated in vacuum to get the crude reaction product, which was then purified by silica gel column chromatography using a suitable mobile phase to separate the desired product. The reaction products were characterized by melting point, ^{1}H NMR, ^{13}C NMR spectroscopy (Bruker, 400 MHz), LC-MS (Varian) and HPLC (Waters) techniques.

4.5. Reactivation And Reusability Studies Of Solid Acid Catalytic Material

Solid acid catalytic material was filtered from the reaction mixture, washed with ethanol, dried at 120 ^{o}C for 1 h and calcined at 550 ^{o}C for 0.5 h. Thus reactivated solid acid catalyst was used in the next reaction cycle for the synthesis of benzimidazoles under similar reaction conditions.

The reactivation and reusability of the used solid acid catalyst was repeated for 5 times by following the procedure as described in the Section 2.4.

5. CONCLUSION

The authors have developed a safe, efficient and green protocol for the synthesis of benzimidazole derivatives over ZrO_2-Al_2O_3 solid acid catalyst. ZrO_2-Al_2O_3 solid acid catalytic material was prepared by solution combustion method. Experimental results reveal that ZrO_2-Al_2O_3 solid acid catalytic material prepared by using urea as a fuel was an efficient, heterogeneous, reusable, solid acid catalyst for the synthesis of benzimidazole derivatives. ZrO_2-Al_2O_3 was found to be reactivable and reusable at least up to five consecutive reaction cycles for the synthesis of benzimidazole derivatives.

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Table 1. Total surface acidity (TSA) of solid acid catalytic materials.

Sl. No.	**Solid acid catalyst**	**TSA (mmolg^{-1})**
1	ZA-U	1.33
2	ZA-H	0.94
3	ZA-G	1.18
4	ZA-S	1.13

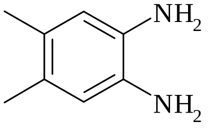
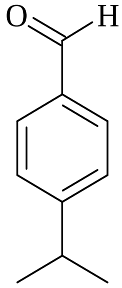
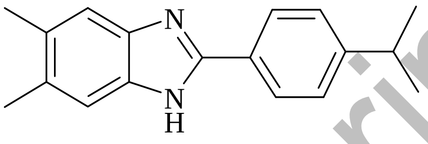
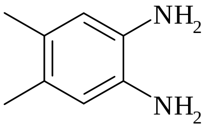
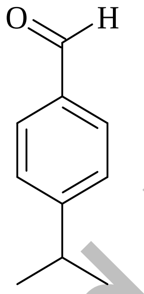
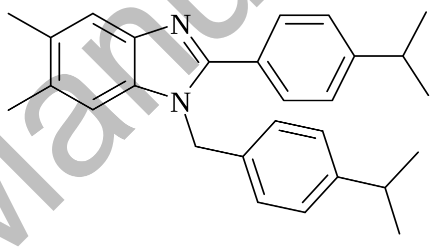
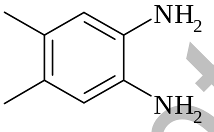
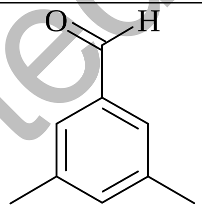
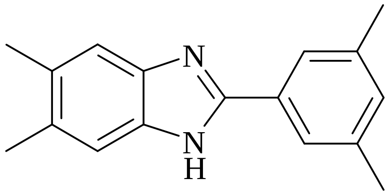
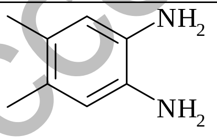
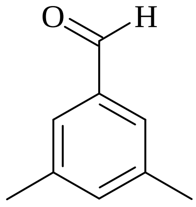
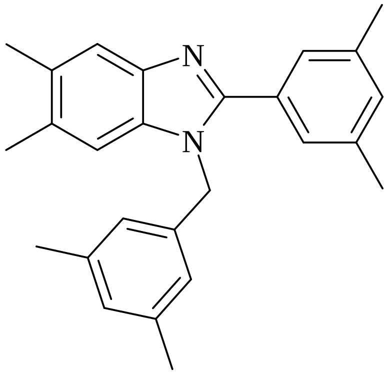
Table 2. Effect of solvents on the yield of benzimidazole derivatives with respect to the reaction of compounds 1a and 2a (Scheme 2) [Reaction conditions: 0.03 g of solid acid catalyst at 80 °C for 30 min, 1a = 0.3 g, 2a = 0.33 mL and solvent = 10 mL].

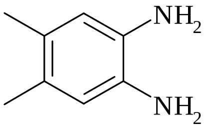
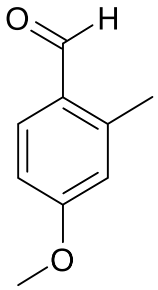
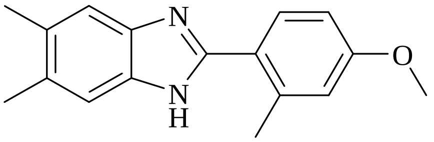
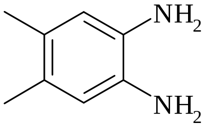
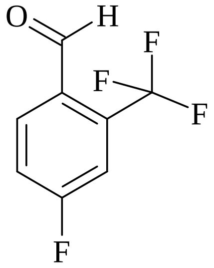
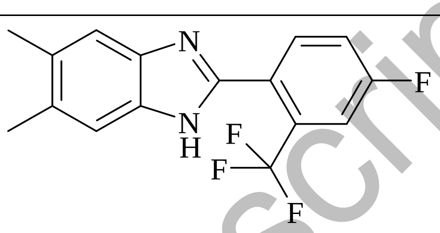
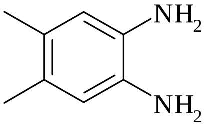
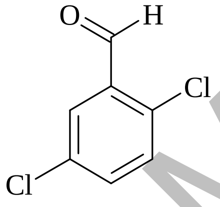
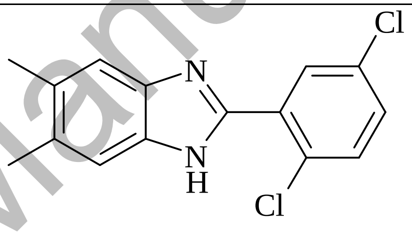
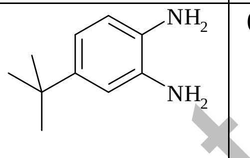
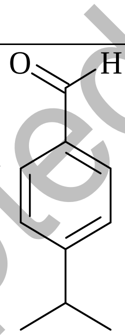
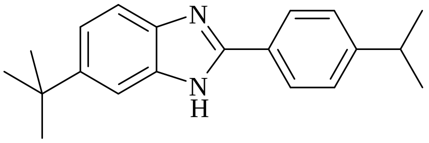
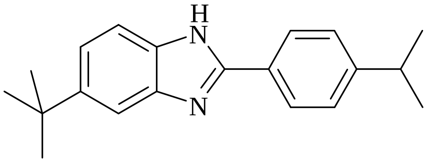
Sl. No.	**Solvent**	**Yield of 3a (%)**	**Yield of 4a (%)**
1	Without solvent	38.1	13.8
2	Water	30.7	10.2
3	Ethanol	50.5	20.6
4	Methanol	48.3	15.7
5	N,N, dimethyl formamide (DMF)	50.0	18.9
6	Dimethyl sulfoxide (DMSO)	49.3	21.1

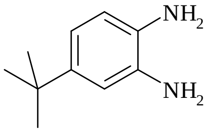
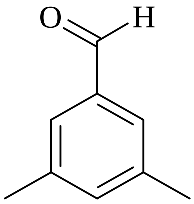
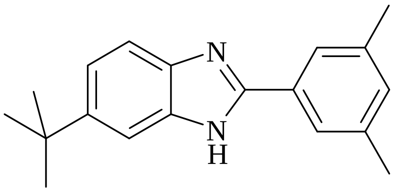
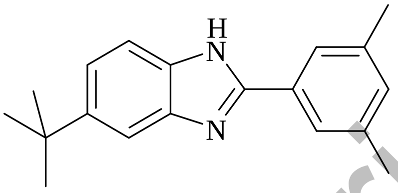
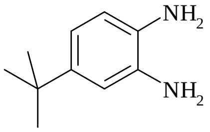
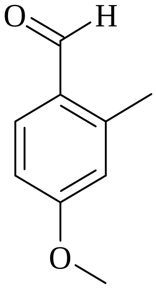
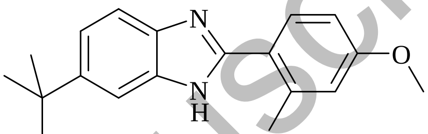
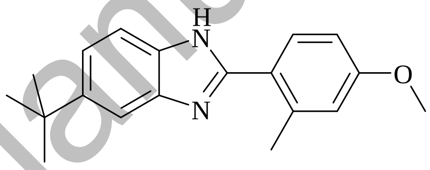
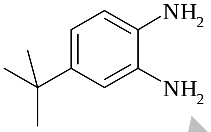
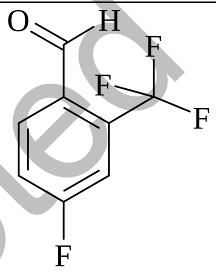
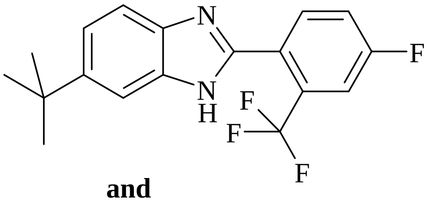
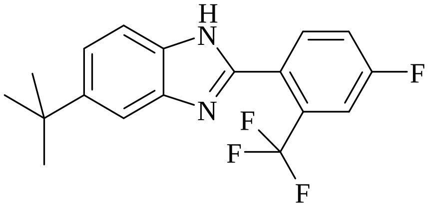
Table 3. Effect of molar ratio of 1a:2a on the yield of benzimidazole derivatives with respect to the reactants 1a and 2a (Scheme 2) [Reaction conditions: 0.03 g of ZA-U at 80 °C for 30 min, diamine (1a) = 0.3 g, and solvent = 10 mL].

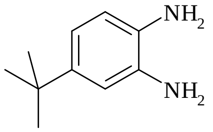
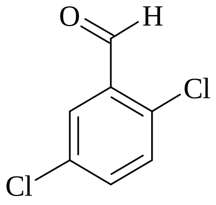
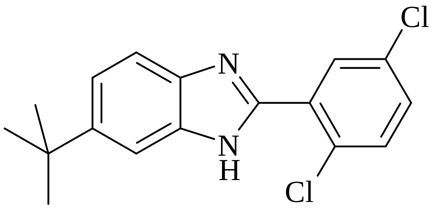
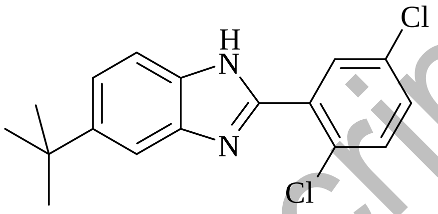
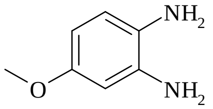
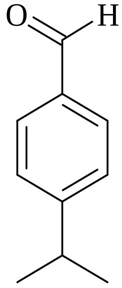
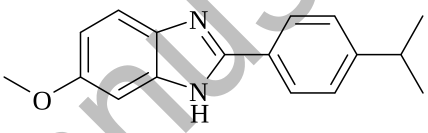
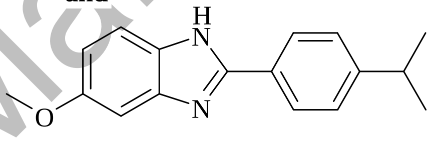
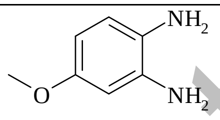
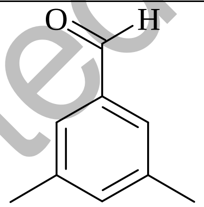
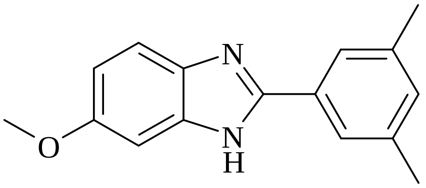
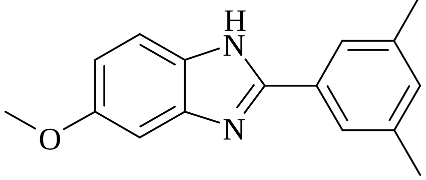
Sl. No.	Molar ratio (1a:2a)	Yield of 3a (%)	Yield of 4a (%)
1	1:1	50.5	20.6
2	1:1.3	32.1	45.7
3	1:1.6	14.9	62.4
4	1:2	5.2	90.2
5	1:2.5	1.5	93.9
6	1:3	0.0	95.7

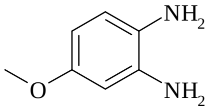
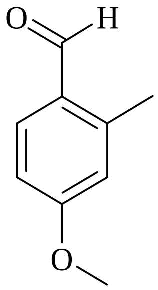
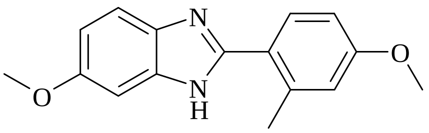
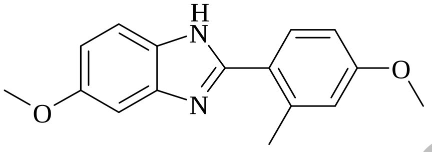
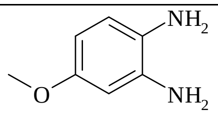
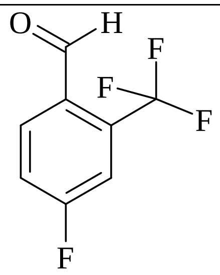
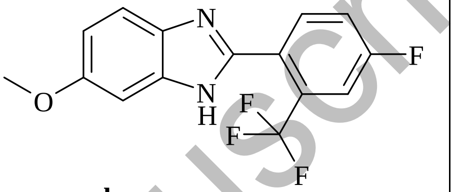
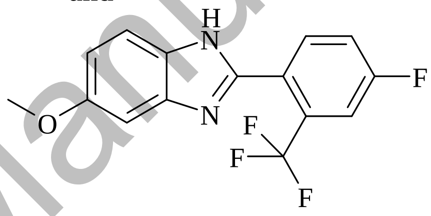
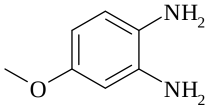
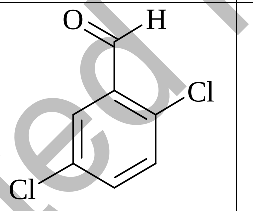
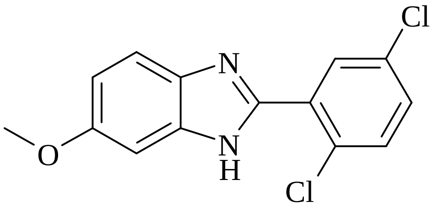
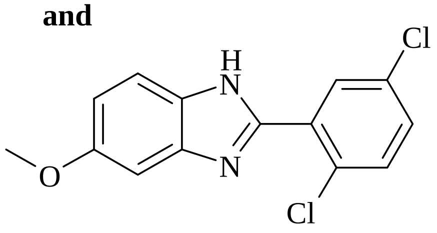
Table 4. Synthesis of various benzimidazole derivatives with different diamines and aromatic aldehydes over ZA-U solid acid catalyst.

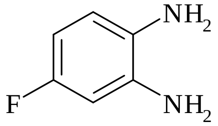
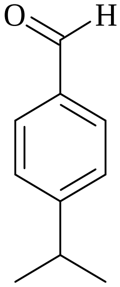
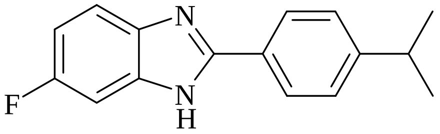
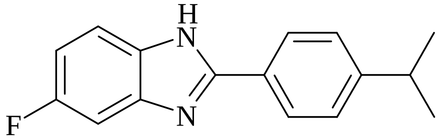
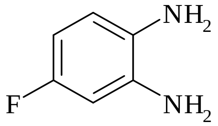
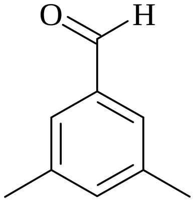
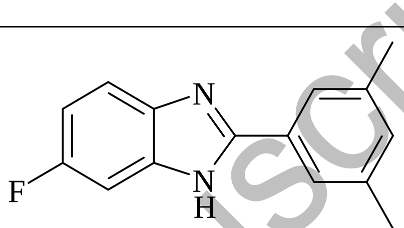
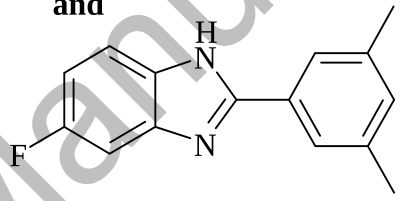
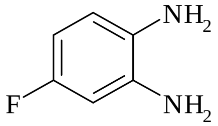
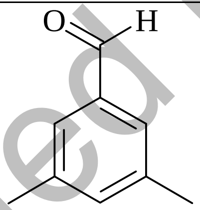
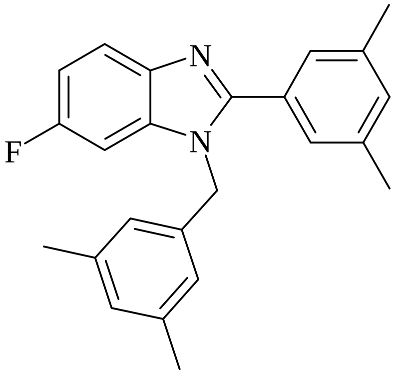
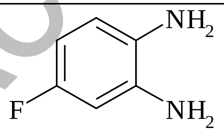
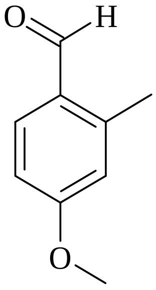
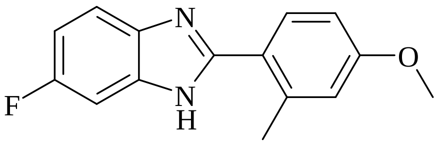
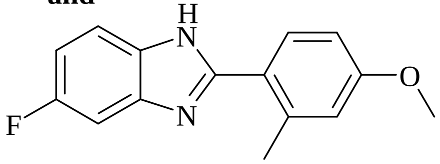
Entry	**Diamine**	**Aldehyde**	**Product**	**Time (h)**	**Yield (%)**
1				0.5	51
2				0.5	21
3				6.0	30
4				6.0	34

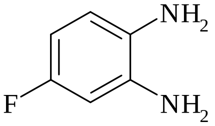
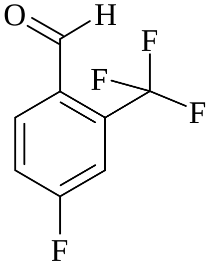
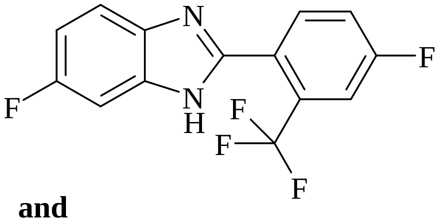
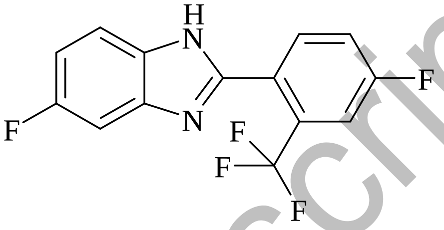
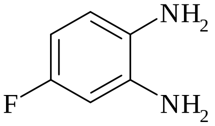
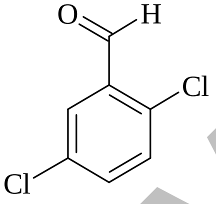
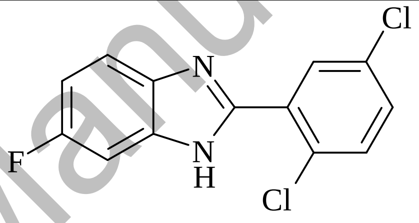
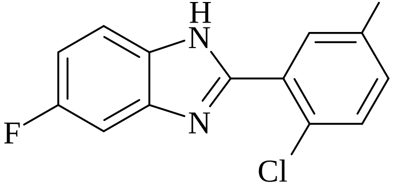
5				1.0	73
6				1.0	90
7				1.0	90
8			 **and** 	2.0	61

9			 **and** 	8.0	60
10			 **and** 	7.0	60
11			 **and** 	16.0	69

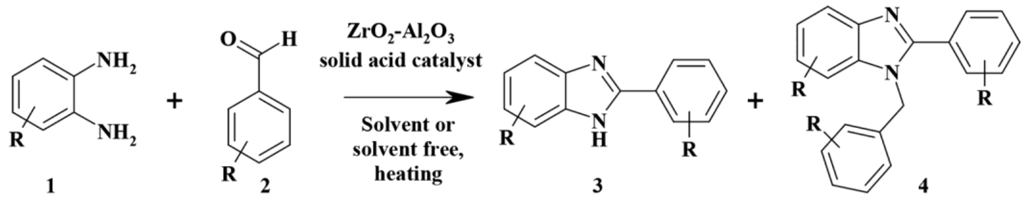
12			 **and** 	1.0	95
13			 **and** 	8.0	96
14			 **and** 	2.0	74

15			 **and** 	8.0	80
16			 **and** 	4.0	84
17			 **and** 	4.0	60

18			 **and** 	16.0	50
19			 **and** 	10.0	44
20				10.0	26
21			 **and** 	8.0	72

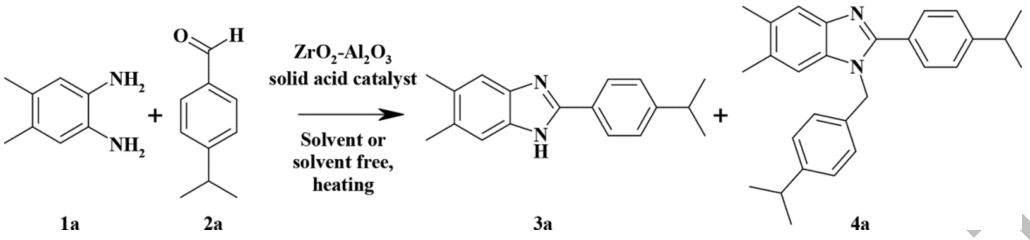
22			 **and** 	4.0	78
23			 **and** 	8.0	57

Scheme 1. Reaction of substituted aromatic 1,2-diamine with substituted aromatic aldehyde in presence of ZrO_2-Al_2O_3 solid acid catalyst.

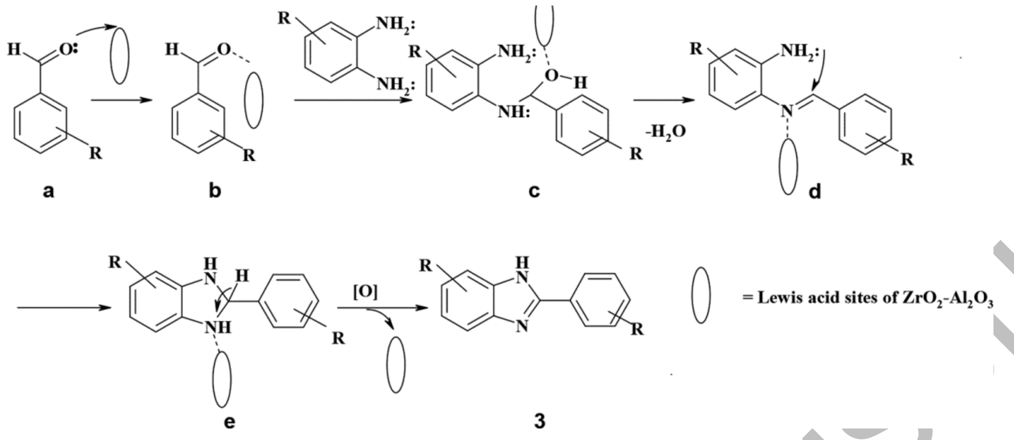


where, R = alkyl, methoxy, F, Cl and CF_3 groups at different position of aromatic system.

Scheme 2. Reaction of 4,5-dimethyl-benzene-1,2-diamine with 4-isopropyl-benzaldehyde in presence of ZrO_2-Al_2O_3 solid acid catalysts.



Scheme 3a. Possible reaction mechanism for the synthesis of substituted benzimidazoles in presence of Lewis acid sites.



Scheme 3b. Possible reaction mechanisms for the synthesis of 2-substituted benzimidazole and 2,3-disubstituted benzimidazole in presence of Brønsted acid sites.

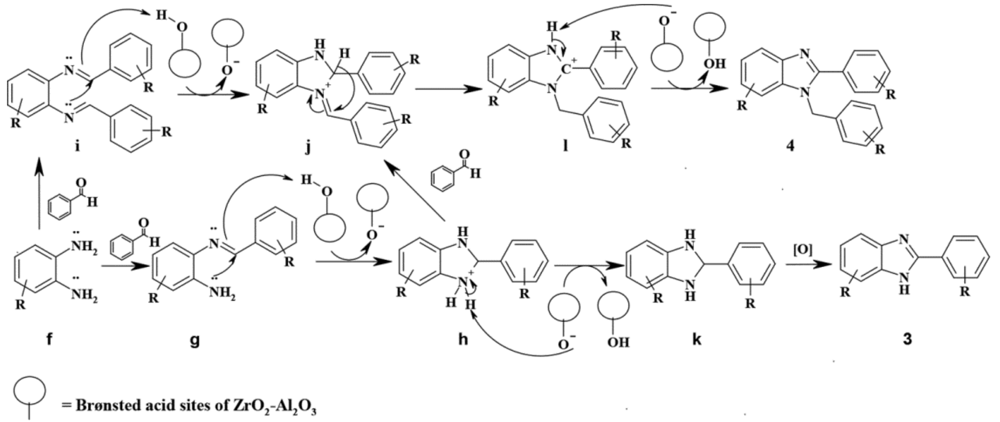


Figure 1. PXRD patterns of ZrO_2-Al_2O_3 prepared by using different fuels. *[R- rhombohedral* Al_2O_3*, T- tetragonal* ZrO_2*].*

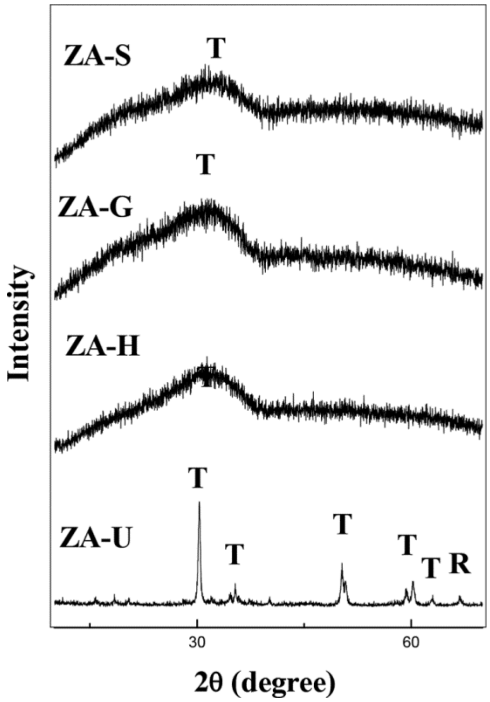


Figure 2. NH_3-TPD profiles of ZA-U, ZA-H, ZA-G and ZA-S solid acid catalysts.

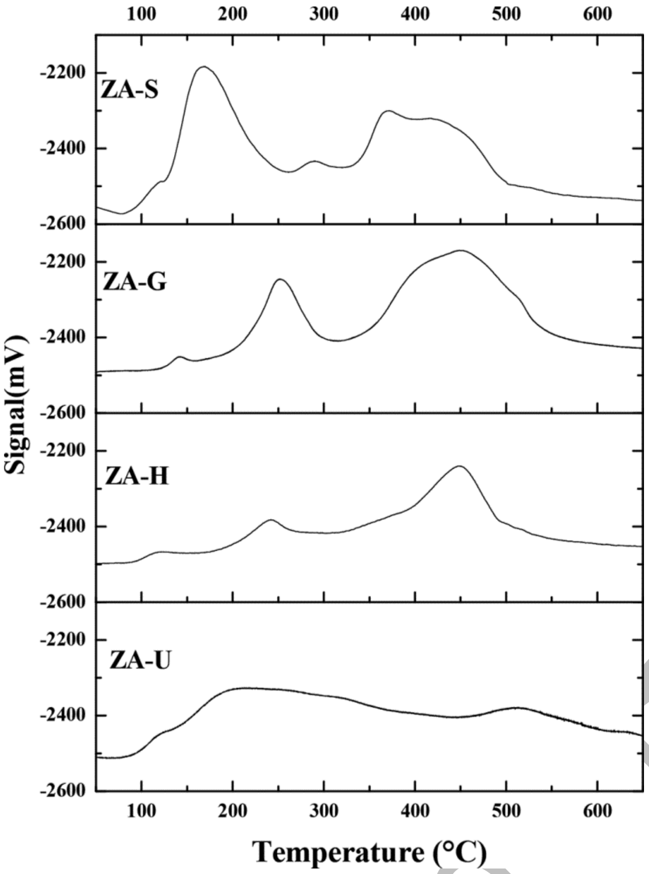


Figure 3. The FT-IR spectrum of ZA-U, ZA-H, ZA-G and ZA-S solid acid catalysts.

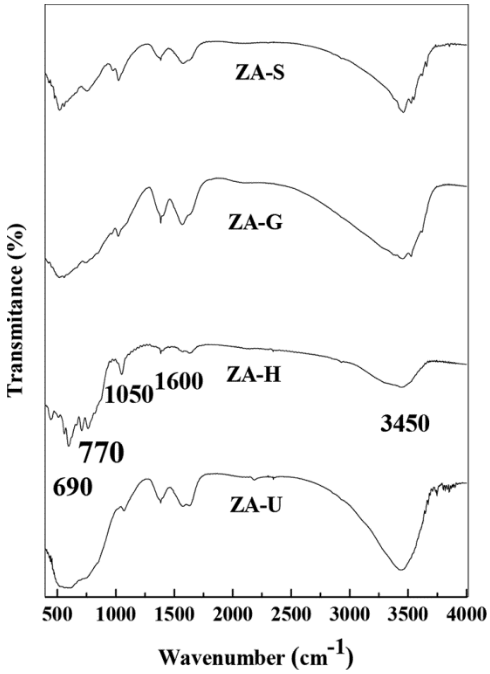


Figure 4a. TEM images of ZA-U, ZA-H, ZA-G and ZA-S solid acid catalysts.

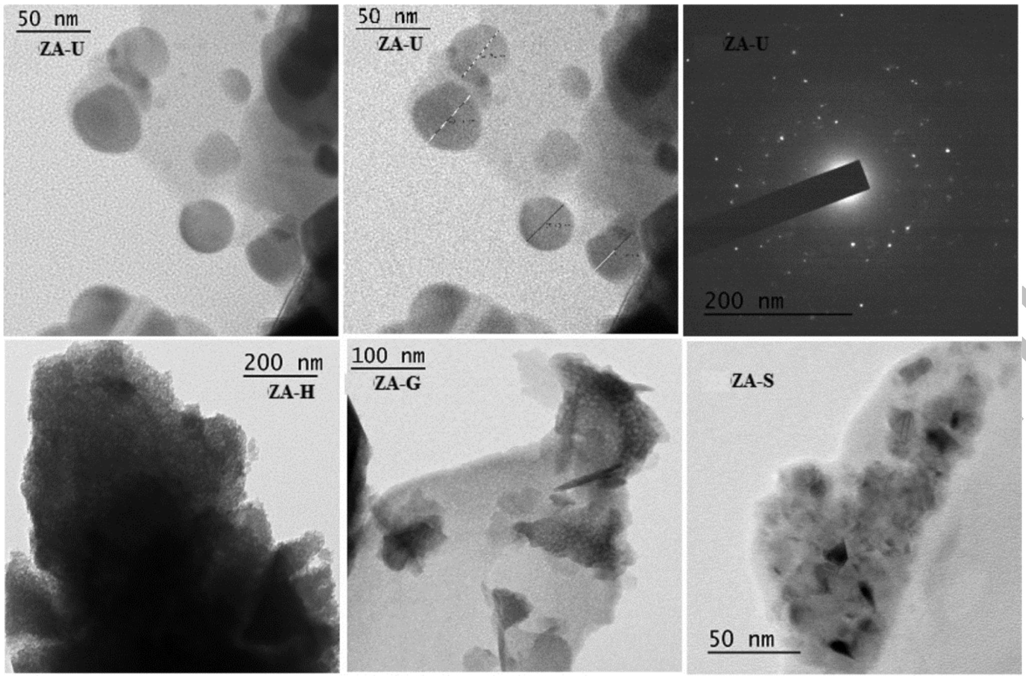


Figure 4b. SEM images of ZA-U, ZA-H, ZA-G and ZA-S solid acid catalysts.

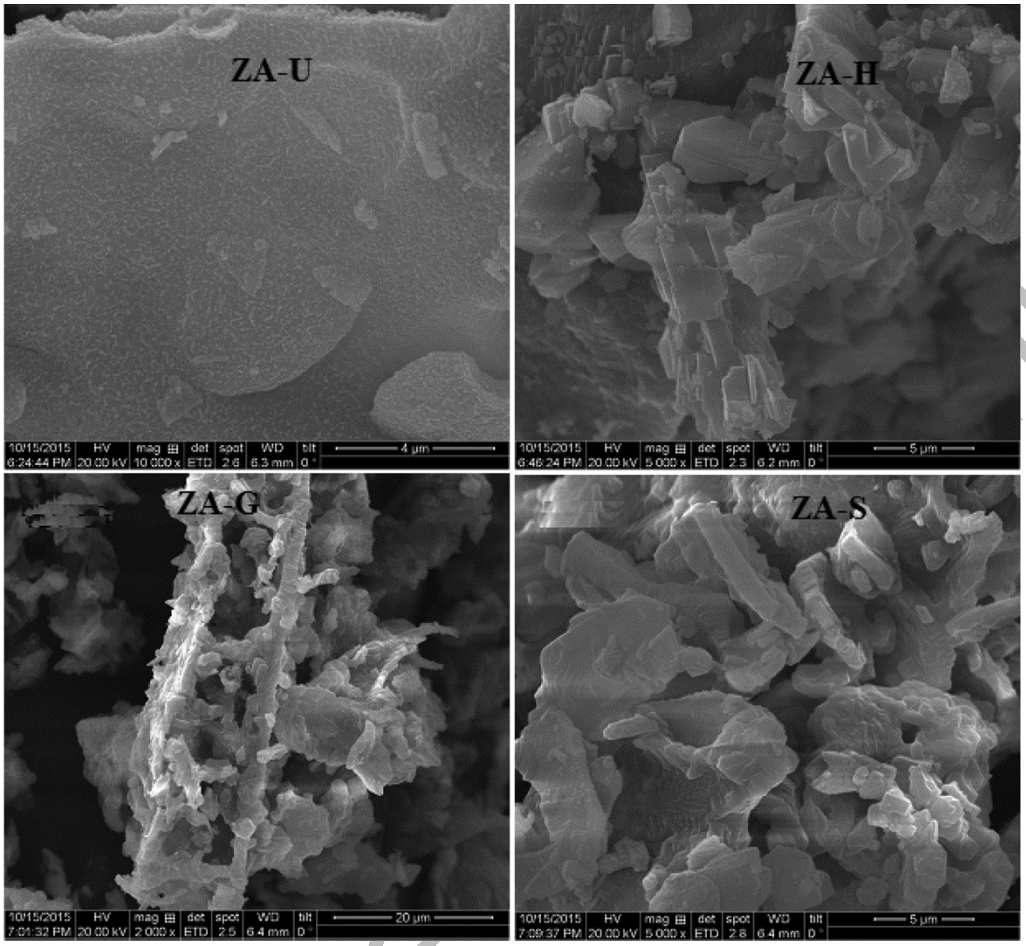


Figure 4c. EDAX spectrum of ZA-U solid acid catalyst.

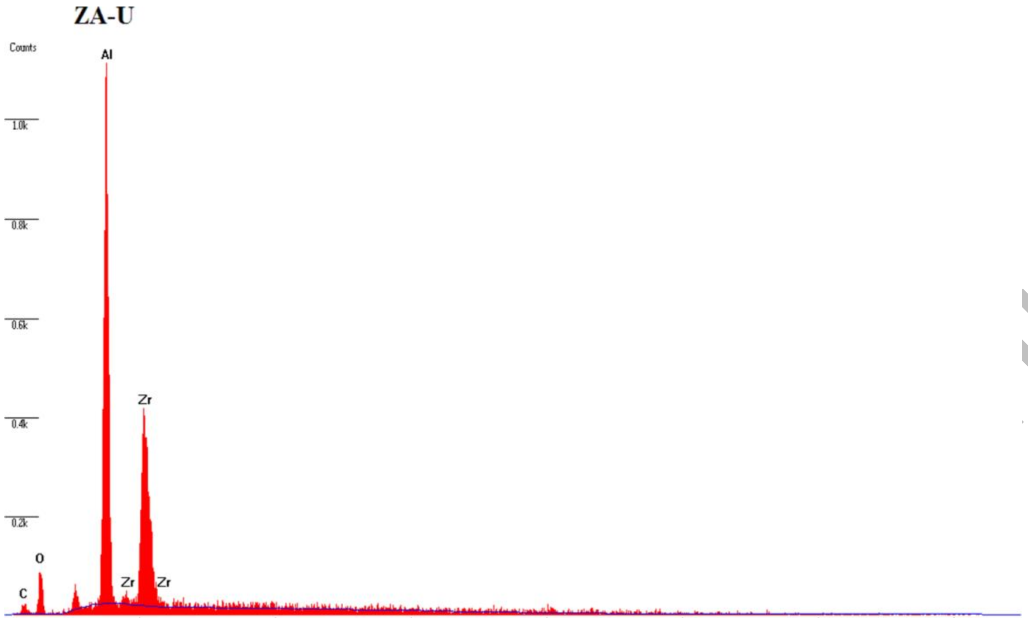


Figure 4d. EDAX spectrum of ZA-H solid acid catalyst.

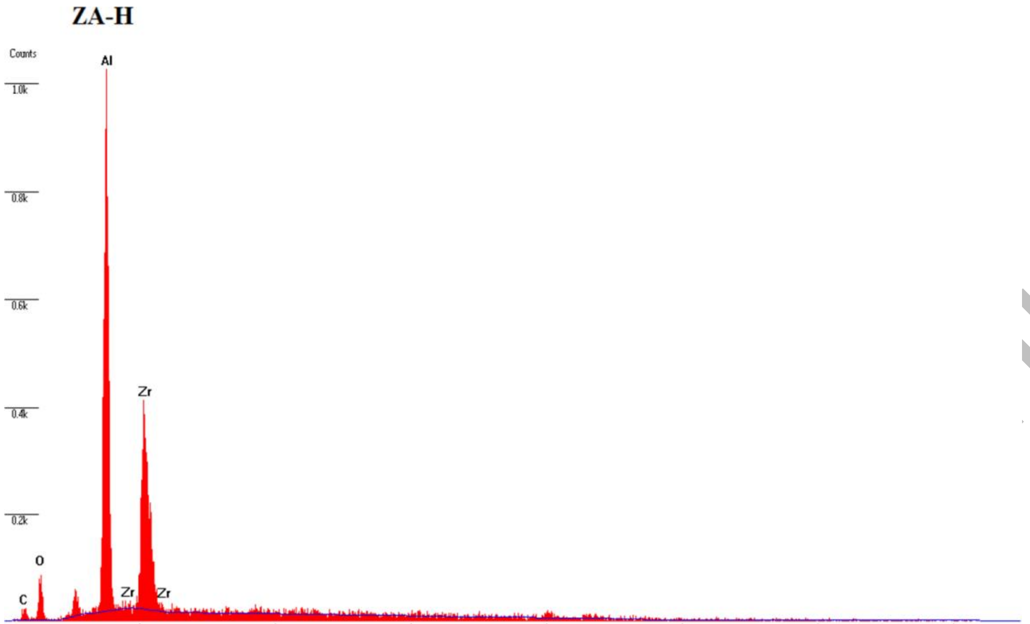


Figure 4e. EDAX spectrum of ZA-G solid acid catalyst.

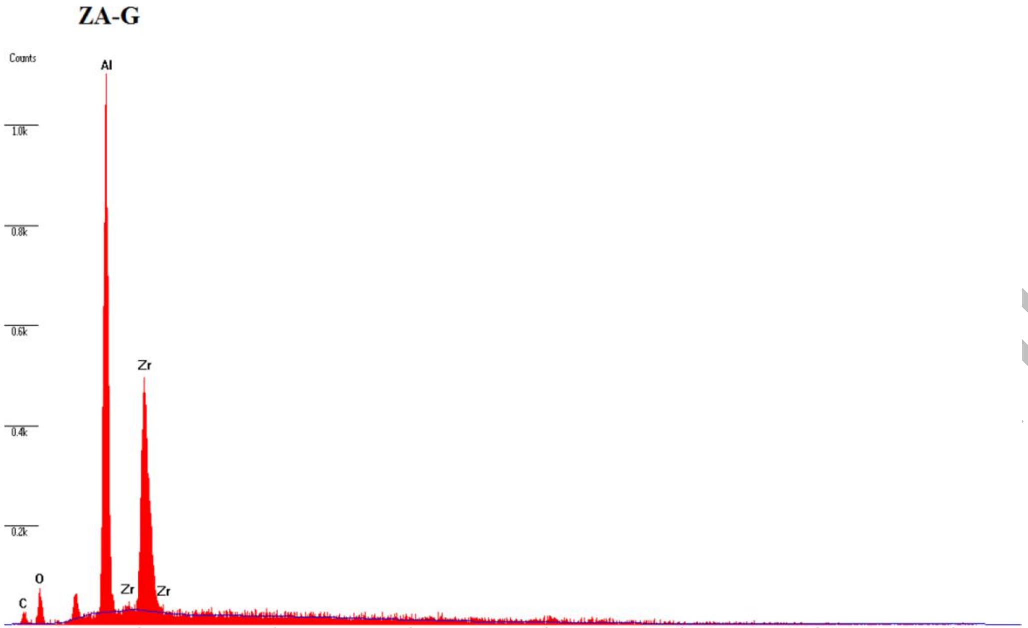


Figure 4f. EDAX spectrum of ZA-S solid acid catalyst.

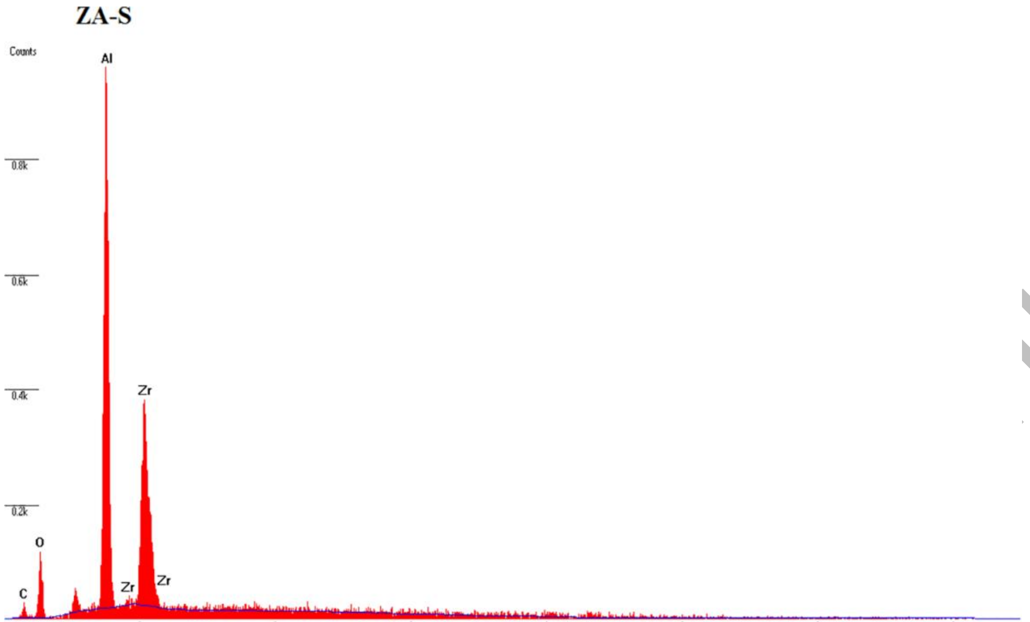


Figure 5a. Effect of catalytic materials on the yield of benzimidazole derivatives with respect to the compounds 1a and 2a (Scheme 2) [Reaction conditions: 0.03 g of solid acid catalyst at 80 °C for 30 min, diamine (1a) = 0.3 g, aldehyde (2a) = 0.33 mL, EtOH = 10 mL: ■-yield (%) of 3a and □-yield (%) of 4a].

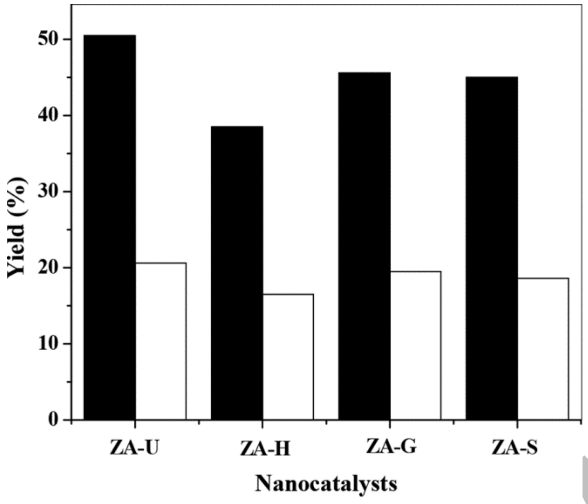


Figure 5b. Effect of different catalytic materials on the yield of benzimidazole derivatives with respect to the compounds 1a and 2a (Scheme 2) [Reaction conditions: 0.03 g of catalytic material at 80 °C for 30 min, diamine (1a) = 0.3 g, aldehyde (2a) = 0.33 mL, EtOH = 10 mL: ■-yield (%) of 3a and □-yield (%) of 4a].

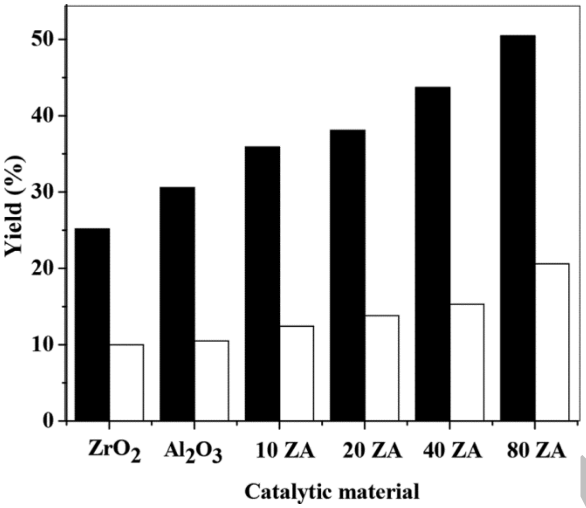


Figure 6. Effect of reaction temperature. [Reaction conditions: 0.03 g of ZA-U solid acid catalyst for 30 min, 1a = 0.3 g, 2a = 0s.33 mL, ethanol = 10 mL: ■-yield (%) of 3a and □-yield (%) of 4a].

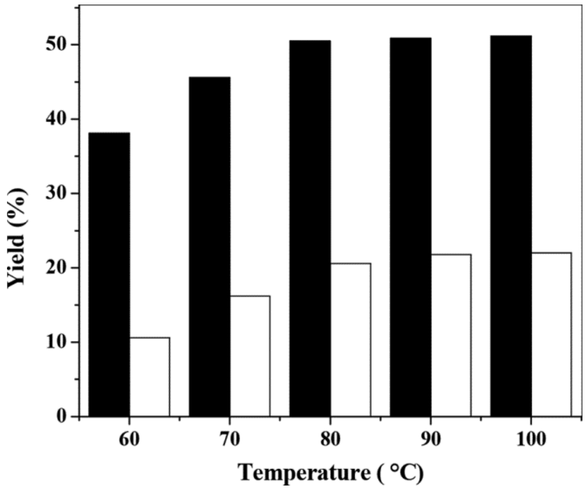


Figure 7. Effect of weight of the solid acid catalyst. [Reaction conditions: ZA-U solid acid catalyst at 80 °C for 30 min, 1a = 0.3 g, 2a = 0.33 mL, ethanol = 10 mL: ■-yield (%) of 3a and □-yield (%) of 4a].

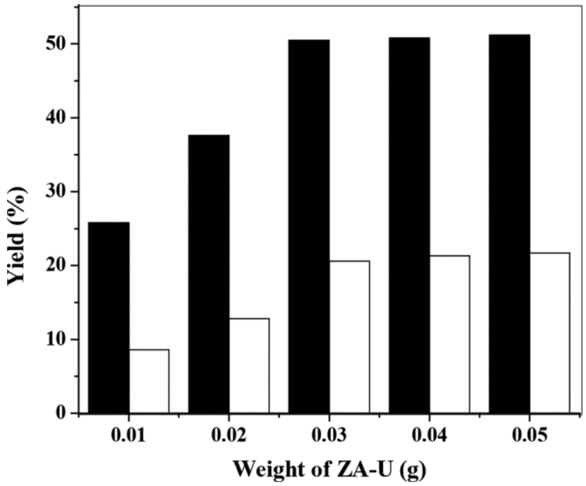


Figure 8. Effect of reaction time on the yield of benzimidazoles. [Reaction conditions: 0.03 g of ZA-U solid acid catalyst at 80 °C, 1a = 0.3 g, 2a = 0.33 mL, ethanol = 10 mL: ■-yield (%) of 3a and □-yield (%) of 4a].

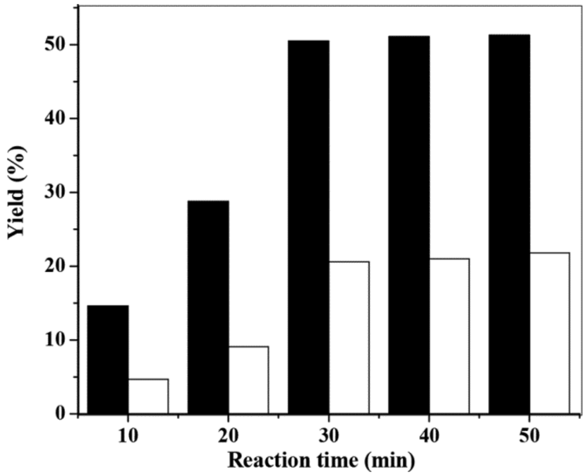


Figure 9. Effect of reusability of solid acid catalytic material (ZA-U) on the yield of benzimidazole derivative with respect to compounds 1a and 2a (Scheme 2) [<u>Reaction conditions:</u> 0.03 g of solid acid catalyst at 80 °C for 30 min, 1a = 0.3 g, 2a = 0.33 mL, EtOH = 10 mL: ■-yield (%) of 3a and □-yield (%) of 4a].